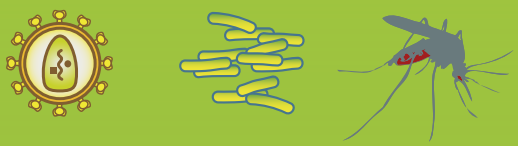
EDCTP

Seventh EDCTP Forum

The Partnership journey: New horizon for better health

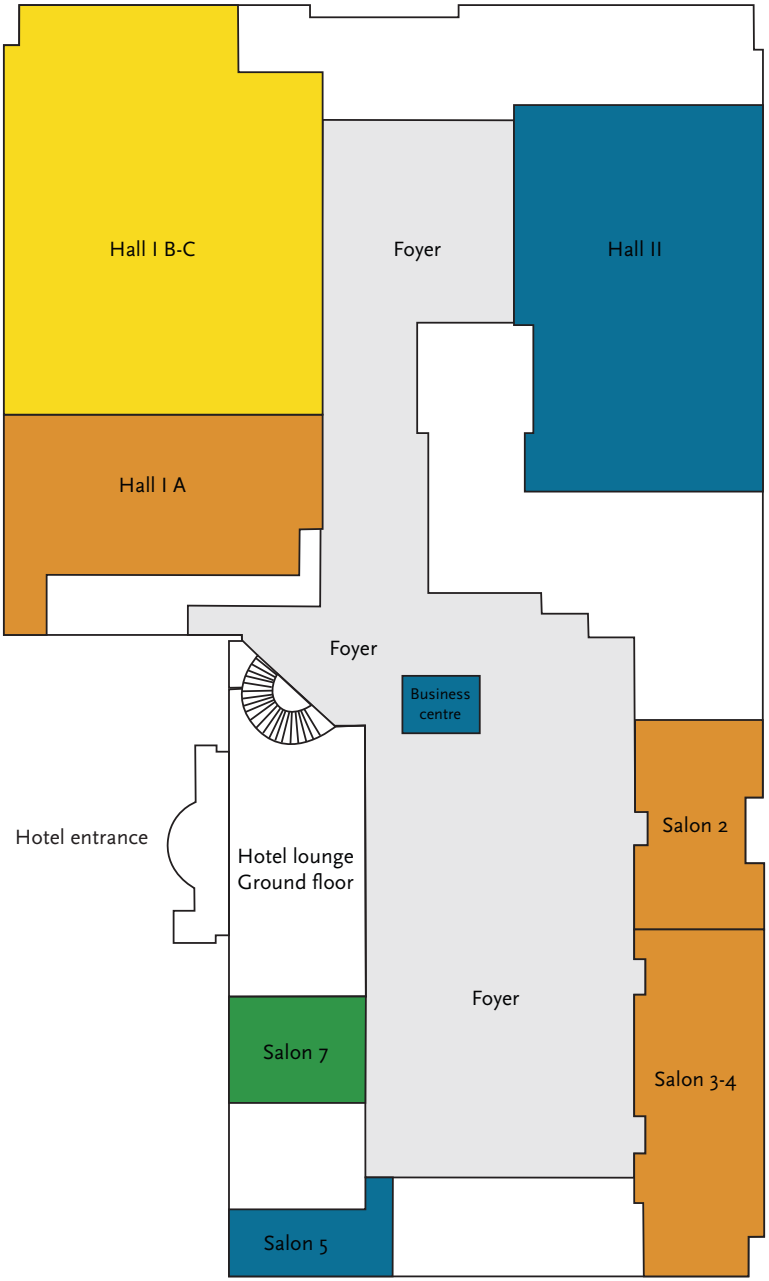
Abstract book



30 June – 2 July 2014

Berlin, Germany

Floor plan



Programme on the inside cover >>

Sunday 29 June 2014	Monday 30 June 2014
	REGISTRATION | 08:00–09:00 FOYER, CONFERENCE CENTRE
	PLENARY SESSION I | 09:00–10:30 Forum prologue | HALL I B-C
	COFFEE AND TEA BREAK HALL II | 10:30–11:00
	MARKETPLACE VIEWS HALL II | 10:30–11:00
SATELLITE MEETING | 09:00–17:00 Sustainable investment in research for health | SALON 3–4	**PLENARY SESSION II** | 11:00–12:30 Recent advances in HIV/AIDS, tuberculosis and malaria (keynote addresses) | HALL I B-C
	LUNCH HALL II | 12:30–13:30
	MARKETPLACE VIEWS HALL II | 12:30–13:30
	PLENARY SESSION III | 13:30–15:30 Recent advances in neglected infectious diseases, health services optimisation research (keynote addresses) and update on Horizon 2020 | HALL I B-C
	COFFEE AND TEA BREAK HALL II | 15:30–16:00
	MARKETPLACE VIEWS HALL II | 15:30–16:00
REGISTRATION | 16:00–18:00 FOYER, CONFERENCE CENTRE	**PARALLEL SESSIONS** | 16:00–17:00 • HIV/AIDS immunology and vaccine development | HALL I B-C • Tuberculosis therapeutic studies | SALON 2 • Malaria vaccines studies | HALL I A • Cross-cutting: policy, ethics, regulatory and trials registration activities | SALON 3–4
	MARKETPLACE VIEWS HALL II | 17:00–18:00
	SPECIAL SESSION | 17:00–18:30 EDCTP2 Fellowship Schemes | SALON 2
	SATELLITE MEETING | 17:00–18:30 Combatting neglected tropical diseases: the case of visceral leishmaniasis in Africa | SALON 7
	CONFERENCE DINNER | 19:00–20:30

Tuesday 1 July 2014

REGISTRATION | 08:00–09:00
FOYER, CONFERENCE CENTRE

SPECIAL SESSION | 08:00–08:50
EDCTP Fellowship Alumni | SALON 2

SATELLITE MEETING | 08:00–08:50
Discussion to explore ways to support clinical trials for malaria and neglected tropical diseases | SALON 3–4 *(by invitation only)*

PARALLEL SESSIONS | 09:00–11:00
- HIV/AIDS therapeutic and prevention studies | HALL I B-C
- Tuberculosis therapeutic studies | SALON 2
- Malaria therapeutic studies | HALL I A
- Cross-cutting: planning, implementation and impact evaluation of clinical trials | SALON 3–4

COFFEE AND TEA BREAK HALL II | 11:00–11:30

MARKETPLACE VIEWS HALL II | 11:00–11:30

PARALLEL SESSIONS | 11:30–13:00
- HIV/AIDS therapeutic studies | HALL I B-C
- Tuberculosis immunology and vaccine development | SALON 2
- Malaria vaccine studies | HALL I A
- Cross-cutting: interaction of neglected infectious diseases with HIV, tuberculosis and malaria | SALON 3–4

LUNCH HALL II | 13:00–14:00

MARKETPLACE VIEWS HALL II | 13:00–14:00

PARALLEL SESSIONS | 14:00–16:00
- HIV/AIDS comorbidities | HALL I B-C
- Tuberculosis studies on diagnostics | SALON 2
- Pregnancy associated malaria studies | HALL I A
- Cross-cutting: ethics and good practices | SALON 3–4

COFFEE AND TEA BREAK HALL II | 16:00–16:30

MARKETPLACE VIEWS HALL II | 16:00–16:30

PARALLEL SESSIONS | 16:30–17:10
- HIV/AIDS comorbidities | HALL I B-C
- Tuberculosis drug development and drug resistance | SALON 2
- Pregnancy associated malaria studies | HALL I A
- Cross-cutting: ethics and good practices | SALON 3–4

MARKETPLACE VIEWS HALL II | 17:10–18:00

SATELLITE MEETING | 17:30–19:00
Global TB Vaccine Partnership | SALON 3–4

SATELLITE MEETING | 17:30–20:30
ESSENCE on Health Research initiative, members' dinner meeting | SALON 2 *(by invitation only)*

Wednesday 2 July 2014

REGISTRATION | 08:00–09:00
FOYER, CONFERENCE CENTRE

PARALLEL SESSIONS | 08:00–09:30
- EDCTP and CAAST-Net Plus: Building bridges | HALL I B-C
- EDCTP Africa mapping project: current state of health research on poverty-related and neglected infectious diseases in sub-Saharan Africa | HALL I A

PARALLEL SESSIONS | 09:40–11:00
- HIV/AIDS treatment guidelines and disease progression | HALL I B-C
- Tuberculosis immunology | SALON 2
- Malaria coinfections, drug resistance and modelling | HALL I A
- Cross-cutting: training and networking activities | SALON 3–4

COFFEE AND TEA BREAK HALL II | 11:00–11:30

MARKETPLACE VIEWS HALL II | 11:00–11:30

PLENARY SESSION IV | 11:30–13:00
EDCTP Partners' session | HALL I B-C

LUNCH HALL II | 13:00–14:00

MARKETPLACE VIEWS HALL II | 13:00–14:00

PARALLEL SESSIONS | 14:00–15:30
- HIV/AIDS coinfections | HALL I B-C
- Tuberculosis | SALON 2
- Malaria immunology and diagnostics | HALL I A
- Cross-cutting | SALON 3–4

COFFEE AND TEA BREAK HALL II | 15:30–16:00

MARKETPLACE VIEWS HALL II | 15:30–16:00

PLENARY SESSION V | 16:00–17:30
Summary and closing remarks | HALL I B-C

Thursday 3 July 2014

EDCTP STAKEHOLDER MEETING ON CAPACITY DEVELOPMENT | 09:00–17:00 *(by invitation only)*
HALL I A

EDCTP

Seventh EDCTP Forum

The Partnership journey: New horizon for better health

Abstract book



30 June – 2 July 2014

Berlin, Germany

Colophon

EDCTP, June 2014
Seventh EDCTP Forum
www.edctpforum.org

Text and production: Daniela Pereira-Lengkeek, Gert Onne van de Klashorst, Wendy Morrill and Michael Makanga
Design: Sam Gobin
Print: Groen Media

European & Developing Countries Clinical Trials Partnership

Europe Office

Postal address
P.O. Box 93015
2509 AA The Hague
The Netherlands

Visiting address
Anna van Saksenlaan 51
2593 HW The Hague, The Netherlands
Phone +31 70 344 0880
Fax +31 70 344 0899

Africa Office

Postal address
P.O. Box 19070
Tygerberg 7505, Cape Town
South Africa

Visiting address
Francie van Zijl Drive, Parowvallei
Cape Town, South Africa
Phone +27 21 938 0690
Fax +27 21 938 0569

E-mail info@edctp.org
Internet www.edctp.org

Contents

Welcome

Dear EDCTP Stakeholders and Friends,

It is my honour and privilege to welcome you all to the Seventh EDCTP Forum on behalf of the Organising and Programme Committees. The theme for this Forum is: **The Partnership journey: New horizon for better health**. This theme takes into account the entire EDCTP journey from its inception to the present, connecting past peaks and valleys, as well as aspirations for a new horizon: the future of EDCTP. This Forum comes at a perfect time to share the *Partnership* story, the interface between the tail end of the first EDCTP programme (EDCTP1) and commencement of the second programme (EDCTP2).

This Forum provides information on results of projects supported by EDCTP in collaboration with all our partners. Practical experiences and lessons learnt are shared, and new strategic and scientific ideas captured, which will contribute to the future research and development agenda of the *Partnership*. In addition to showcasing EDCTP-funded work, this Forum brings together an extraordinary assembly of speakers and delegates from research institutions, universities, public–private partnerships, product development partnerships, like-minded organisations working on poverty-related diseases, governments, regional bodies and industry around the globe, especially from Africa and Europe. It therefore presents a unique networking and discussion platform for the exchange of information and stimulation of new and improved ideas to shape the future research agenda on poverty-related and neglected infectious diseases.

A highly stimulating programme comprising a wide range of topics including cutting-edge clinical research on HIV/AIDS, tuberculosis and malaria; interactions of these three major poverty-related diseases with neglected infectious diseases; cross-cutting areas on health capacity development and networking, policy, ethics and regulatory affairs, is presented. The discussions are based on real-life situations, experiences and practical examples. The format for presentations includes keynote addresses by invited speakers from North and South, oral presentations in plenary and parallel sessions, panel discussions, satellite meetings and a marketplace for research exhibitions.

We trust that this Forum is invigorating, informative and spurs us into action as we start the second leg of the *Partnership* journey with EDCTP2. We wish you a pleasant stay in Germany's historical, multi-cultural, vibrant and beautiful city of Berlin.

Michael Makanga
Director South-South Cooperation and Head of Africa Office

Forum theme

The Partnership journey: New horizon for better health

The partnership journey to better health is a long and hard journey that requires the full commitment of all the partners that have decided to undertake it. EDCTP started out a decade ago in 2003 when European and African countries resolved to join forces in combatting the three main diseases of poverty, namely HIV/AIDS, tuberculosis and malaria. Based on the then Article 169 (currently Art 185) of the Treaty on the Functioning of the European Union and armed with a mission to reduce the burden of these diseases and to generally improve the health of the people living in sub-Saharan Africa, the partnership has gone from strength to strength in pursuing its objective. This is being realised through supporting clinical trials and pertinent capacity development. As we celebrate our tenth anniversary, the programme has supported 246 projects, which include 100 clinical trials. These projects involve 259 institutions in 46 countries in Africa and Europe. The programme has supported the training of 514 health research cadres including 56 Senior and Career Development Fellows, 39 Postdoctoral scientists, 177 PhDs and 229 Master's students, among others, with a retention rate of nearly 100 per cent.

The clinical trials and capacity development that have been funded by the programme are beginning to bear tangible fruits. These include results that are informing policy at national and international levels such as the WHO guidelines on the prevention of mother-to-child transmission of HIV during pregnancy and breastfeeding; rational use of drugs in the prevention of malaria during pregnancy; and treatment of severe malaria in children. Furthermore, it is encouraging to note as we travel this journey that we see African leadership emerging and being strengthened, ushering African ownership and programme sustainability. In the programme, around 70% of the projects are led by African scientists, many of them young and up-and-coming. Furthermore, the ethical and regulatory framework continues to develop with improved ethics review, national regulatory authorities, clinical trial registration and networks of excellence in conducting clinical trials.

For the second phase of EDCTP, the stakeholders have agreed to expand the programme to include all phases of clinical trials from phase I to IV, including implementation studies on the optimisation of health services. The expansion of the programme will also include working on neglected infectious diseases. Moreover, the programme will seek closer collaboration with other partners including the private sector. It will also seek stronger African commitment and involvement in decision making. It is our sincere hope that this stronger EDCTP will lead to better health.

Charles S Mgone
EDCTP Executive Director

Sponsors

We gratefully acknowledge our sponsors for their generous support.

European Commission
http://ec.europa.eu/research

France
Agence nationale de recherche sur le sida (ANRS)
www.anrs.fr

Germany
Federal Ministry of Education and Research (BMBF)
www.bmbf.de

Ireland
Irish Aid
www. irishaid.ie

Luxembourg
Fonds National de la Recherche Luxembourg (FNR)
www.fnr.lu

Netherlands
The Netherlands-African Partnership for Capacity Development and Clinical Interventions against Poverty-related Diseases (NACCAP)
www.nwo.nl/naccap

Spain
Institute of Health Carlos III (ISCIII)
www.isciii.es

Sweden
Swedish International Development Agency (Sida)
www.sida.se

Switzerland
State Secretariat for Education, Research and Innovation (SERI)
www.sbfi.admin.ch

United Kingdom
Medical Research Council (MRC)
www.mrc.ac.uk

Aeras
www.aeras.org

Bill & Melinda Gates Foundation
www.gatesfoundation.org

BIOFABRI
www.biofabri.es

CAAST-Net Plus
www.caast-net-plus.org

Eurice
http://eurice.eu

Global Health Network
www.theglobalhealthnetwork.org

Merck Serono
www.merckserono.com

Pharmalys
http://pharmalys.com

PATH Malaria Vaccine Initiative (MVI)
www.malariavaccine.org
www.path.org

Sanofi
www.sanofi.com

TB Alliance
www.tballiance.org

Wellcome Trust
www.wellcome.ac.uk

Host

We wish to express our sincere gratitude to our host for providing invaluable support to EDCTP in organising the Seventh EDCTP Forum.

Federal Ministry of Education and Research

Bundesministerium für Bildung und Forschung

The German Federal Ministry of Education and Research (BMBF) is the German representative in EDCTP. BMBF is a part of the German federal government and supports innovative projects in various research sectors; e.g. in health research, basic sciences, sustainable development, information and communications technologies, life sciences, chemistry and materials science, transport and space research. Funding of research on poverty-related and neglected diseases in general as well as that on HIV, tuberculosis and malaria in particular is embedded in the national Health Research Programme – Health for Everyone with a budget of about 140 million € per year which is managed by a specialised project management agency (PT-DLR).
www.bmbf.de

Organisers

Chair

Michael Makanga
EDCTP Director South-South Cooperation and
Head of Africa Office

Secretariat organising committee

Hager Bassyouni (Sponsorship and satellite meetings)
Pauline Beattie (Programme and awards)
Gabrielle Breugelmans (Sponsorship and satellite meetings)
Chris Bruinings (Finance)
Ana Lúcia Cardoso (Sponsorship and satellite meetings)
Nuraan Fakier (Abstracts)
Jean Marie Vianney Habarugira (Abstracts and awards)
Suzanne Hoogervorst (Travel, venue and registration)
Gert Onne van de Klashorst (Communications and abstracts)
Mariska Louw (Registration and programme)
Wendy Morrill (Registration, abstracts, and programme)
Thomas Nyirenda (Abstracts)
Lara Pandya (Sponsorship and satellite meetings)
Daniela Pereira-Lengkeek (Communications, abstracts
and registration)

Scientific programme committee

Salim Abdulla
Eleni Aklilu
Abraham Aseffa
Manica Balasegaram
Moses Bockarie
Maryline Bonnet
Tumani Corrah
Simon Croft
Philippe Deloron
Alioune Dieye
Alison Elliott
Maria Fraga Oliveira Martins
Knut Fylkesnes
Shabbar Jaffar
Beate Kampmann
Stefan Kaufmann
Wilfred Mbacham
Clara Menéndez Santos
Mary-Louise Newell
Gita Ramjee
Philippe Sansonetti
Jean Marie Talom
Suzanne Verver
Dawit Wolday
Ali Zumla

Conference information

Badges

Badges must be worn at all times during the conference. The badge grants participants access to the opening ceremony, Forum plenary and parallel sessions, satellite meetings, special sessions and the conference dinner. Participants who have lost their badge are requested to report to the registration/information desk.

Badges have the following colour coding:

Speakers	Green
Delegates	Blue
Media	Yellow
Organisers	Red

Business Centre

The Business Centre is located on the first floor of the Maritim proArte Hotel. It provides access to international telephone and fax services, photocopying, computer workstations and Internet at set user charges.

Certificate of attendance

A certificate of attendance will be available for delegates on the last day of the Forum. Delegates who wish to receive a certificate of attendance should notify the registration desk on the first day of the Forum. The certificate will be validated for Continuous Medical Education purposes only if participants have signed the appropriate register at the registration desk every conference day.

Continuous Medical Education

The Seventh EDCTP Forum has been accredited as a General Continuous Medical Education (ABAN) event (accreditation ID 147988–249580; 18 CME points) by the Royal Dutch Medical Association (KNMG). Interested Forum participants should request a certificate of attendance with CME validation at the

registration desk on the first day of the Forum and sign the appropriate register every day. Dutch participants should also notify EDCTP of their BIG-code.

Currency

The Euro is the currency of Germany.

Evaluation

An evaluation form has been included in your Forum bag. Please complete and return the form to the registration desk. If you prefer to complete the evaluation online, please go to: https://www.regonline.co.uk/2014forumevaluation

Language

English is the official language of the Seventh EDCTP Forum.

Meals

Lunch

Monday	30 June 2014	12:30–13:30
Tuesday	1 July 2014	13:00–14:00
Wednesday	2 July 2014	13:00–14:00
Place:	Hall II	

Coffee and tea

Monday	30 June 2014	10:30–11:00 and 15:30–16:00
Tuesday	1 July 2014	11:00–11:30 and 16:00–16:30
Wednesday	2 July 2014	11:00–11:30 and 15:30–16:00
Place:	Hall II	

Medical assistance and emergency

In case of emergency please dial 112.

Registration/Information desk

Place: Foyer, Conference centre

During the Forum, staff will be available at the information desk. For registration purposes staff will be available at the following hours:

Sunday	29 June 2014	16:00–18:00
Monday	30 June 2014	08:00–09:00
Tuesday	1 July 2014	08:00–09:00
Wednesday	2 July 2014	08:00–09:00

Social event

Conference dinner

Monday	30 June 2014	19:00–20:30

Place:	Restaurant Kalkscheune
Address:	Johannisstrasse 2, 10117 Berlin
Phone:	+49 (0) 30.59 00 434–0
Website:	www.kalkscheune.de/en

The restaurant is within a walking distance from the Forum venue, Maritim proArte Hotel Berlin.

Speaker registration and check-in desk

Place: Foyer, Conference centre

Staff will be available to register presenters at the speaker registration and check-in desk at the following times:

Sunday	29 June 2014	16:00–18:00
Monday	30 June 2014	08:00–09:00
Tuesday	1 July 2014	08:00–09:00
Wednesday	2 July 2014	08:00–09:00

Presenting authors must hand in their final presentations at the speaker check-in desk during the designated days and times

noted below. PowerPoint and Keynote are the only accepted presentation formats. Presentations may be submitted on USB stick or CD. Personal laptops may not be used.

Presentation date	Presentation due at speaker check-in desk
Monday 30 June	Sunday 29 June 16:00–18:00
Tuesday 1 July	Monday 30 June 08:00–17:00
Wednesday 2 July	Tuesday 1 July 08:00–17:00

Time zone

Berlin is in the Central European Time Zone, i.e. it is always one hour later than Greenwich Mean Time.

Twitter

Follow our live tweets via the EDCTP Twitter account: http://twitter.com/EDCTP. The hashtag for all tweets about the Forum is **#edctpforum**.

Wifi

Wireless internet is available to delegates at the venue. Information on how to access the wireless connection will be provided.

Invited speakers

Pedro Alonso

Barcelona Centre for International Health Research (CRESIB), Spain

Professor Pedro Alonso is currently Director of ISGlobal, Director of the Barcelona Centre for International Health Research (CRESIB), Head of the International Health and Tropical Medicine Unit of the Hospital Clínic of Barcelona, Professor of the University of Barcelona and President of the Governing Board of the Manhiça Foundation/Manhiça Health Research Centre, CISM (Mozambique).

Prof. Alonso started his career in international health 25 years ago as a young physician working in West Africa. Since then his work has focused on the key determinants of morbidity and mortality in the two most vulnerable population groups in Africa: young children and pregnant women. He is increasingly active in building and strengthening human and institutional capacity in developing countries and Europe and in campaigning for support for other global health initiatives. Some of Prof. Alonso's most relevant work has been carried out in the field of malaria and has led to the development and testing of new tools for the prevention and treatment of *Plasmodium falciparum*. He has published more than 300 papers in international peer-reviewed journals.

Between 2005 and 2007, together with Professor Fred Binka, he led the steering committee that designed and implemented EDCTP. He has served on several national and international committees. Currently, he is a board member of the Medicines for Malaria Venture; Co-Chair of the Steering Committee of the Decade of Vaccines Collaboration an initiative promoted by the World Health Organization (WHO), UNICEF, the National Institute of Allergy and Infectious Diseases and the Bill & Melinda Gates Foundation; and Chair of the Steering Committee of the Malaria Eradication Scientific Alliance, MESA. He is also a member of the WHO Malaria Policy Advisory Committee.

Detlef Böcking

Projektträger im Deutschen Zentrum für Luft- und Raumfahrt e.V. (PT_DLR), Germany; Vice-Chair EDCTP General Assembly

Dr Detlef Böcking is Senior Scientific Officer at the DLR project management agency working for and on behalf of the German Ministry of Education and Research (BMBF), Division of Health Research. He received an undergraduate degree and a diploma degree in biology from the University of Bochum and holds a PhD degree in natural sciences of the University of Bonn. He has worked as a research assistant at the University of Bonn, Germany, the École normale supérieure, Paris and the Université Pierre et Marie Curie, Paris.

In 2001, Dr Böcking joined the DLR project management agency specialising first in national research policies in the field of infectious diseases, neurodegeneration, pain research and bioethics. Since 2009, he has been in charge of the ministry's engagement in EDCTP and deputy representative to EDCTP's General Assembly for Germany. He coordinates the DLR project management's team for global health issues and works closely with the ministry in planning and implementing the ministry's activity in research for Global Health, particularly in administering the ministry's funding concept for neglected and poverty-related diseases. Dr Böcking takes part in the German/Luxembourg constituency for the Joint Coordinating Board of WHO-TDR.

Ann Ginsberg

Aeras, United States of America

Dr Ann Ginsberg is the Chief Medical Officer of Aeras. In this role, Dr Ginsberg oversees all of Aeras' clinical programmes and projects. In addition, Dr Ginsberg is a member of Aeras' Portfolio Review Committee and manages its external Vaccine Advisory Committee.

Dr Ginsberg served as Head of Clinical Development and then Chief Medical Officer at the Global Alliance for TB Drug Development from 2004 to 2011. Prior to her work at the Global Alliance for TB Drug Development, Dr Ginsberg was Director of Project Management at Merck & Co. and served for 15 years at the U.S. National Institutes of Health in a variety of roles, including Chief of the Respiratory Diseases Branch of the National Institute of Allergy and Infectious Diseases.

Trained as a molecular biologist and Board Certified as an anatomic pathologist, Dr Ginsberg holds a BA from Harvard University, an MD from Columbia University and a PhD from Washington University. She is the author of numerous scientific publications and recipient of several prominent awards, including the Department of Health and Human Services Secretary's Award for Distinguished Service in 2000. She has served on multiple global health committees, advisory panels, and boards, and was formerly a member of the Aeras Board of Directors.

John Gyapong

University of Ghana, Ghana; Member of the EDCTP Association Board

Professor John Gyapong is the Pro-Vice Chancellor for Research Innovation and Development of the University of Ghana. He is a Public Health physician and an epidemiologist. He studied medicine in Ghana and public health (MSc) and epidemiology (PhD) at the London School of Hygiene and Tropical Medicine.

Before assuming responsibility as Pro-Vice Chancellor, he was the Vice-Dean and Professor in Epidemiology and Disease Control at the School of Public Health of the University of Ghana. Professor Gyapong is representative of Ghana in the General Assembly of the EDCTP Association. Professor Gyapong's main area of research is infectious disease epidemiology, especially lymphatic filariasis and other neglected tropical diseases. For 12 years he was Director for Research and Development of the Ghana Health Service and responsible for neglected tropical disease control in Ghana.

Shabbar Jaffar

London School of Hygiene and Tropical Medicine, United Kingdom

Professor Shabbar Jaffar is Professor of Epidemiology at the London School of Hygiene and Tropical Medicine (LSHTM) where he has been based for almost 20 years. His main research areas are HIV, HIV/TB and health services/optimisation research. He has lived and worked in The Gambia, Uganda and South Africa and is involved in a number of public health research trials in partnership with health programme managers and other colleagues in Uganda, Tanzania and Zambia. He is a joint editor of the Tropical Medicine and International Health journal. Prof. Jaffar is the former Chair of the EDCTP Partnership Board and the interim Scientific Advisory Committee.

Joachim Klein

Federal Ministry for Education and Research (BMBF), Germany; EDCTP General Assembly representative for Germany

Dr Joachim Klein has worked for the German Federal Ministry of Education and Research (BMBF) since 2008 in the division 'Strategy and Policy Issues of the Life Sciences'. Before, he was in the management team of a biotech company and responsible for business development and scientific coordination. Dr Klein has a doctorate in biology and currently works in the division 'Health Research' were he is responsible for several BMBF funding programmes, e.g. in personalised medicine and neglected and poverty-related diseases.

Renate Loskill

Federal Ministry for Education and Research (BMBF), Germany

Dr Renate Loskill received her PhD in Biology. She joined the Federal Ministry of Education and Research in 1994 as scientific officer. Since then she has worked in several Directorates General of the BMBF, i.e. DG2 'European and International Cooperation in Education and Research', DG7 'Provision for the Future – Basic and Sustainability Research' and DGZ 'Central services'. In 2013 Dr. Loskill changed to DG6 'Life Sciences-Research for Health', where she is head of the division 615 'Health Research'.

Line Matthiessen

DG Research and Innovation, European Commission

Dr Line Matthiessen leads the Unit responsible for Infectious Diseases and Public Health in the Directorate-General for Research and Innovation. The Unit promotes and supports European Union research and innovation activities in the area of global health issues with emphasis on HIV/AIDS, tuberculosis and malaria, emerging epidemics, neglected infectious diseases and antimicrobial drug resistance, as well as activities in public health and health systems research. The Unit also supports the implementation of the European & Developing Countries Clinical Trials Partnership (EDCTP).

Dr Matthiessen was Head of Unit for horizontal aspects and coordination in the Directorate for Biotechnologies, Agriculture and Food Research from July 2007 to December 2010.

Dr Matthiessen joined the European Commission in 1992. She has been responsible for strategic and policy issues in biotechnology. She held the position of Principal Scientific Officer responsible for research in Neurosciences for several years. She was also a Scientific Officer in the area of somatic gene therapy,

animal cell technology and *in vitro* testing as alternatives to animal experiments.

Dr Matthiessen was trained as an MD at the University of Odense, Denmark and received her PhD in Neurosciences from the University of Paris VI, France in 1993.

Francine Ntoumi

Fondation Congolaise pour la Recherche Médicale, Congo; Member of the EDCTP Association Board

Professor Francine Ntoumi is currently Chair and Head of Research of the Congolese Foundation for Medical Research, and Research Group Leader at the Institute for Tropical Medicine/University of Tübingen, Germany. She is also the Project Coordinator of the CANTAM (Central Africa Network on Tuberculosis, HIV/AIDS and Malaria for the conduct of clinical trials). She was the Coordinator of the Multilateral Initiative on Malaria (MIM) until August 2010. In this role, she aimed to build a pool of African malaria researchers and particularly encouraged women to enter a scientific career. Prior to 2007, she was Senior Scientific Officer at the European & Developing Countries Clinical Trials Partnership (EDCTP). In 2010 Le Metropolis magazine listed her as one of Congo's top 50 women making their mark on the country's history.

Gita Ramjee

Medical Research Council, South Africa; Member of the EDCTP Scientific Advisory Committee

Professor Gita Ramjee is Director of the HIV Prevention Research Unit at the South African Medical Research Council since 2001. She has a Bachelors degree in Chemistry and Physiology from the University of Sunderland, United Kingdom (1980) and a Master's and PhD from the University of Kwazulu Natal, South Africa (1980, 1994). Since 1994, she has been

working in the field of HIV in South Africa, where she has risen through the ranks to her current post as Unit Director. Her research expertise includes HIV epidemiology, prevention, phase I, II and III clinical trials in Africa and community-based social and behavioural interventions. She has extensive experience in management and leadership, capacity building and research governance. Recently, she received a Lifetime Achievement Award for her contribution to HIV prevention research. A former member of the EDCTP Developing Countries Coordinating Committee and the interim Scientific Advisory Committee (SAC), she will continue to provide expertise in HIV research to the EDCTP Scientific Advisory Committee.

Stefano Vella

Istituto Superiore di Sanità, Italy; Vice-Chair EDCTP General Assembly

Dr Stefano Vella is the Director of the Department of Pharmacology and Therapeutic Research of the Istituto Superiore di Sanità, Italy, since 2003. He is vice-president of the Scientific Council of the ANRS (Agence Nationale de Recherche sur le Sida et les hépatites virales), Paris, France, and coordinated the European commission-funded HIV Clinical Trials Network (NEAT), which includes 16 European countries. He served as Co-Chair of the IAS Conference on HIV Pathogenesis, Treatment and Prevention (Rome, 2011) and is currently the Co-chair of Track B (Clinical Sciences) of the 2014 International AIDS Conference (Melbourne). Dr Vella is the coordinator of the Esther-Italy programme, part of the European ESTHER Alliance, which is dedicated to fighting the HIV/AIDS epidemic and its consequences in low- and middle-income countries.

Dr Vella received his degree in Medicine from the University of Rome in 1977. He subsequently achieved specialty degrees in both Infectious Diseases (1982) and Internal Medicine (1987). After a postdoctoral experience at the University of Pennsylvania (1981–1982), he joined the medical staff at the Institute of Internal Medicine, University La Sapienza, Rome, where he developed extensive experience in the clinical management

of patients with infectious diseases and with HIV/AIDS. His research career is mainly devoted to the study of the pathogenesis and the therapy of viral infections.

Gianpietro Van de Goor

DG Research and Innovation, European Commission

Dr Gianpietro Van de Goor is Policy Officer in the European Commission for International Cooperation in Health Research where he is in charge of global health research and the European Union's participation in the European & Developing Countries Clinical Trials Partnership. He joined the Commission in 2002 and worked on industrial research and then on the NEST programme, where he shaped funding policies for research on new risks to society. From 2005 to 2010, he worked for the European Research Council. As Deputy Head of Unit 'Strategic matters and relations with the Scientific Council' he was responsible for the ERC's public relations activities. With a PhD in chemistry, Dr Van de Goor worked previously at the Swiss Federal Laboratories for Materials Testing and Research. He moved to science policy in 1998 as Advisor and then as Head of the Swiss Contact Office for Research and Higher Education in Brussels.

Special sessions

EDCTP2 Fellowship Schemes

Monday 30 June, 17:00–18:30
Salon 2

Since its inception EDCTP has funded 51 Senior Fellowships and 5 Career Development Fellowships projects. These capacity development funding schemes will continue under the second EDCTP programme (EDCTP2).

The session will include:

- An overview of the fellowships funded under the first EDCTP programme (EDCTP1), highlighting the major achievements and scientific outputs
- Presentation of the fellowship schemes proposed for EDCTP2, summarising the key features of these schemes and highlighting any differences from the EDCTP1 fellowships
- Information about the planned EDCTP2 collaborations with other stakeholders, such as WHO-TDR for a clinical research and development fellowship in collaboration with pharmaceutical companies
- Reflection on the achievements and challenges of the EDCTP fellowship programme, including presentations by two EDCTP fellows on their experiences, perspectives and feedback to EDCTP
- A question and answer session on fellowship funding in EDCTP2.

This session is open to all Forum participants.

EDCTP Fellowship Alumni

Tuesday 1 July, 08:00–08:50
Salon 2

South-South and North-South networking of institutions and scientists is a key objective of EDCTP1 that was supported through:

- Creation of four regional Networks of Excellence (NoE)
- Networking work packages in Integrated Projects
- Networking grants.

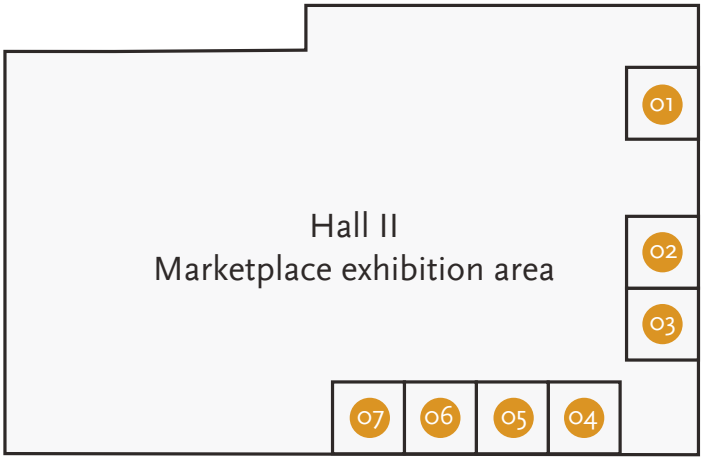
Initial consultations with EDCTP-funded fellows have indicated that establishing an Alumni group consisting of EDCTP-funded fellows would provide a useful platform to enhance South-South and North-South cooperation. This is the aim of promoting African scientific leadership and fostering scientific excellence through collaborative research. Several other funding agencies, such as WHO-TDR and Wellcome Trust have developed mechanisms for maintaining contact with and connecting their fellows.

The objectives of this session are to consider the opportunities and benefits of establishing an EDCTP Alumni Association, in particular to:

- Solicit the views of participants on the proposed EDCTP Alumni Association
- Hear first-hand accounts of fellows belonging to Alumni groups formed by other funding agencies
- Discuss the possible structure, mechanism and operations of the EDCTP Alumni Association
- Provide feedback and recommendations on next steps to the EDCTP Secretariat.

This session is open to all Forum participants. Attendance of participants with experience as fellow of international research or funding organisations is greatly encouraged.

Marketplace for exhibitors



01 EDCTP/European Commission

The European & Developing Countries Clinical Trials Partnership (EDCTP) was created in 2003 as a European response to the global health crisis caused by the three main poverty-related diseases (PRDs) of HIV/AIDS, tuberculosis and malaria. Currently EDCTP is a partnership between 16 European countries, the European Union and sub-Saharan African countries. The aim of the programme is to accelerate the development of new and improved drugs, vaccines, microbicides and diagnostics against HIV/AIDS, tuberculosis and malaria through a balanced partnership of European national research programmes on PRDs with their African counterparts in collaboration with the pharmaceutical industry and like-minded organisations.
www.edctp.org

In a changing world, the European Commission (EC) wants the European Union to become a smart, sustainable and inclusive economy. These three mutually reinforcing priorities should help the Union and its Member States deliver high levels of employment, productivity and social cohesion. The new Union programme for Research and Innovation, 'Horizon 2020' has been designed for that purpose. Running from 2014 to 2020

with a budget of nearly €80 billion, Horizon 2020 supports scientific excellence, strengthen industrial leadership in innovation and address major concerns shared by all Europeans, including global societal challenges such as health, demographic change and well-being. International cooperation is an important cross-cutting priority of Horizon 2020. In addition to Horizon 2020 being fully open to international partnerships, targeted actions with key partner countries and regions will focus on strategic priorities of common interest and mutual benefit.
http://ec.europa.eu/research

02 Merck Serono

Merck Serono is the biopharmaceutical division of Merck. With headquarters in Darmstadt, Germany, Merck Serono offers leading brands in 150 countries to help patients with cancer, multiple sclerosis, infertility, endocrine and metabolic disorders, as well as cardiovascular diseases. In the United States and Canada, EMD Serono operates as a separately incorporated subsidiary of Merck Serono. Merck Serono discovers, develops, manufactures and markets prescription medicines of both chemical and biological origin in specialist indications. Merck Serono has an enduring commitment to deliver novel therapies in our core focus areas of oncology, neurology and immunology.
www.merckserono.com

03 Global Health Network

The Global Health Network is a platform for exchanging knowledge, sharing research methods and facilitating collaboration among global health professionals to fuel faster and better evidence to improve health. The Global Health Network functions as an online science park, connecting researchers in a productive, interactive environment where they can access peers, generate research documents, acquire technical expertise, develop new protocols and generally further their research. Through its innovative digital platform, The Global Health Network provides open access to a wide range of free online seminars and courses, downloadable training kits, articles, templates and tools.
www.theglobalhealthnetwork.org

04 Pharmalys

Pharmalys is an established Contract Research Organisation (CRO) with offices in London, United Kingdom and in Dakar, Senegal. We offer a comprehensive list of services to pharmaceutical and biotech companies and provide support in conducting interventional clinical trials, epidemiological studies, data registries, observational studies and social sciences research to academic and non-academic institutions wishing to conduct clinical and non-clinical research in Africa. Pharmalys can manage entire projects or offer specific stand-alone services in a proactive and cost-conscious way. Pharmalys is also dedicated to contributing to capacity building in Africa by providing topic-led workshops and on-site training for research professionals and regulators, thereby promoting quality research in the region.
www.pharmalys.com

05 Eurice

Eurice GmbH provides comprehensive support services for the planning, initiation, and implementation of international collaborative projects. In addition to traditional project management, Eurice helps to develop and implement coherent IP strategies and supports consortia through dissemination, networking, training, and capacity building activities.
Eurice is part of the European IPR Helpdesk, an initiative of the EC Directorate General for Enterprise and Industry, offering free of charge, first-line support on IP matters, and a partner in the initiative Fit for Health 2.0 which aims to promote and enhance a sustainable participation of European industry in the health-related sector of Horizon 2020, including EDCTP.
http://eurice.eu

06 CAAST-Net Plus

CAAST-Net Plus is a network of 25 partners based in Africa and Europe. The goal is to strengthen the cooperation in research and innovation between our regions to more effectively tackle the global challenges of health, food security, and climate change. CAAST-Net Plus is supported by the Seventh Framework

Programme of the European Union, and builds on the results of the CAAST-Net project (2008–2012). Work with us today to build new bi-regional partnerships for global challenges. Find them on Twitter, Google+, YouTube, Facebook, and LinkedIn; or email enquiries@caast-net-plus.org. Together, we can.
www.caast-net-plus.org

07 PATH MVI

The PATH Malaria Vaccine Initiative (MVI) is a global programme of PATH, an international organisation that drives transformative innovation to save lives and improve health, especially among women and children. PATH accelerates innovation across five platforms – vaccines, drugs, diagnostics, devices, and system and service innovations – that harness its entrepreneurial insight, scientific and public health expertise, and passion for health equity. By mobilising partners around the world, PATH takes innovation to scale, working alongside countries primarily in Africa and Asia to tackle their greatest health needs. Together, they deliver measurable results that disrupt the cycle of poor health.
www.path.org and www.malariavaccine.org

Programme

Sunday 29 June 2014		
09:00–17:00	SATELLITE MEETING COHRED: Sustainable investment in research for health	Salon 3–4
16:00–18:00	**Registration**	Foyer

Monday 30 June 2014		
08:00–09:00	**Registration**	Foyer
09:00–10:30	PLENARY SESSION I Forum prologue CHAIRS Beate Kampmann and John Gyapong RAPPORTEUR Karin Fischer-Buder	Hall I B-C
09:00–09:10	**Dr Renate Loskill**, Federal Ministry for Education and Research, Germany *Welcome address*	
09:10–09:25	**Prof. Stefano Vella** and **Dr Detlef Böcking**, Vice-Chairs, EDCTP General Assembly *Towards EDCTP2*	
09:25–09:40	**Prof. Francine Ntoumi**, Member of the EDCTP Association Board *The evolution of EDCTP governance*	
09:40–10:00	**Dr Line Matthiessen**, DG Research and Innovation, European Commission *European Commission perspective on the EDCTP programme*	
10:00–10:30	**Prof. Charles Mgone**, EDCTP Executive Director *Introduction of the Forum theme*	
10:30–11:00	**Coffee and tea break**	Hall II
10:30–11:00	MARKETPLACE VIEWS	Hall II
11:00–12:30	PLENARY SESSION II Recent advances in HIV/AIDS, tuberculosis and malaria (keynote addresses) CHAIRS Marie-Louise Newell and Tumani Corrah RAPPORTEUR Karin Fischer-Buder	Hall I B-C
11:00–11:30	**HIV/AIDS: Gita Ramjee**, Medical Research Council, South Africa	PS.01
11:30–12:00	**Malaria: Pedro Alonso**, CRESIB, Spain	PS.02
12:00–12:30	**Tuberculosis: Ann Ginsberg**, Aeras, United States of America	PS.03
12:30–13:30	**Lunch**	Hall II
12:30–13:30	MARKETPLACE VIEWS	Hall II

Monday 30 June 2014		
13:30–15:30	PLENARY SESSION III Recent advances in neglected infectious diseases, health services optimisation research (keynote addresses) and update on Horizon 2020 CHAIRS Moses Bockarie and Knut Fylkesnes RAPPORTEUR Karin Fischer-Buder	Hall I B-C
13:30–14:00	**Neglected infectious diseases: John Gyapong**, University of Ghana	PS.04
14:00–14:30	**Health services optimisation research: Shabbar Jaffar,** London School of Hygiene and Tropical Medicine, United Kingdom	PS.05
14:30–15:30	**Horizon 2020: Line Matthiessen**, DG Research and Innovation, European Commission	
15:30–16:00	**Coffee and tea break**	Hall II
15:30–16:00	MARKETPLACE VIEWS	Hall II
16:00–17:00	PARALLEL SESSION HIV/AIDS immunology and vaccine development CHAIRS Pontiano Kaleebu and Souleymane Mboup RAPPORTEURS Photini Kiepiela and Monique Surette	Hall I B-C
16:00–16:20	**Tomáš Hanke**, University of Oxford, United Kingdom *Targeting HIV-1 by vaccines at conserved regions*	HO.01
16:20–16:40	**Keabetswe Bedi**, University of Botswana/BHP, Botswana *Evolution of neutralising antibodies in acute heterosexually acquired HIV-1 subtype C infection in Botswana*	HO.02
16:40–17:00	**Moustapha Mbow**, CHU Le Dantec, Senegal *Natural killer cells of HIV-1-exposed but uninfected subjects exhibit recall responsiveness to HIV-1 peptides*	HO.03
16:00–17:00	PARALLEL SESSION Tuberculosis therapeutic studies CHAIRS Ali Zumla and Suzanne Verver RAPPORTEURS Lyn Horn and Nesri Padayatchi	Salon 2
16:00–16:20	**Martin Boeree**, Radboud University Nijmegen, The Netherlands *What is the 'right' dose of rifampin?*	TO.01
16:20–16:40	**Amina Jindani**, St. George's, University of London, United Kingdom *High dose rifapentine with a quinolone for treatment of pulmonary tuberculosis: the RIFAQUIN trial*	TO.02
16:40–17:00	**Eleni Aklillu**, KI, Sweden *Optimisation of TB-HIV co-treatment in sub-Saharan Africa: no need to increase efavirenz dose during concomitant rifampicin-based antituberculosis therapy in HIV patients*	TO.03

Monday 30 June 2014		
16:00–17:00	PARALLEL SESSION Malaria vaccine studies CHAIRS Philippe Deloron and Francine Ntoumi RAPPORTEURS Bourema Kouriba and Jean-Marie Habarugira	Hall I A
16:00–16:20	**Michael Theisen**, SSI, Denmark and **Benjamin Mordmüller**, ITM Tübingen, Germany *Phase IIb efficacy trial of the malaria blood stage vaccine candidate GMZ2*	MO.01
16:20–16:40	**Seif Shekalaqhe**, IHI, Tanzania *Speeding up the development of malaria vaccines: the example of P27A, bridging phase Ia and Ib*	MO.02
16:40–17:00	**Bernhards Ogutu**, KEMRI-Walter Reed, Kenya *Controlled human malaria infections and irradiated whole sporozoite vaccine evaluation in Africa*	MO.03
16:00–17:00	PARALLEL SESSION Cross-cutting: policy, ethics, regulatory and clinical trials CHAIRS Maria Fraga Oliveira Martins and Abraham Aseffa RAPPORTEURS Nuraan Fakier and Elizabeth Pienaar	Salon 3–4
16:00–16:20	**Elizabeth Pienaar**, MRC, South Africa *The Pan African Clinical Trials Registry (PACTR) five years later: where are we now?*	CO.01
16:20–16:40	**Boitumelo Mokagtla-Moipolai**, COHRED, Botswana *Mapping African research ethics review and medicines regulatory capacity: the MARC project*	CO.02
16:40–17:00	**Carel IJsselmuiden**, COHRED, Switzerland *The 'Research for Health and Innovation Organiser' (RHINNO) for ethics review*	CO.03
17:00–18:00	MARKETPLACE VIEWS	Hall II
17:00–18:30	SPECIAL SESSION EDCTP2 fellowship schemes FACILITATORS Thomas Nyirenda and Gabrielle Breugelmans	Salon 2
17:00–18:30	SATELLITE MEETING DNDi: Combatting neglected tropical diseases: the case of visceral leishmaniasis in Africa	Salon 7
19:00–20:30	**Conference dinner**	

Tuesday 1 July 2014		
08:00–09:00	**Registration**	Foyer
08:00–08:50	SPECIAL SESSION EDCTP fellowship alumni FACILITATORS Thomas Nyirenda and Pauline Beattie	Salon 2
08:00–08:50	SATELLITE MEETING Discussion to explore ways to support clinical trials for malaria and neglected tropical diseases *(By invitation only)*	Salon 3–4
09:00–11:00	PARALLEL SESSION HIV/AIDS therapeutic and prevention studies CHAIRS Gita Ramjee and Marie-Louise Newell RAPPORTEURS Photini Kiepiela and Jonathan Kayondo	Hall I B-C
09:00–09:20	**Laura Ciaffi**, University of Montpellier 1 (IRD 233), France *Randomised comparison of three second line ART regimens in Africa: the 2Lady/ANRS/EDCTP study*	HO.04
09:20–09:40	**Cissy Kityo**, JCRC, Uganda *HIV drug resistance in paediatric patients initiating antiretroviral therapy in Uganda: a multicentre observational study*	HO.05
09:40–10:00	**Frank Angira**, KEMRI-CDC, Kenya *Post-antiretroviral outcomes in a cohort of women who discontinued maternal triple-antiretrovirals initially used to prevent mother-to-child transmission of HIV during pregnancy*	HO.06
10:00–10:20	**Richard Lando**, KEMRI-CDC, Kenya *Adverse foetal outcomes in HIV-1 infected women who received either NNRTI or PI-based therapy for prevention of mother-to-child transmission of HIV in western Kenya*	HO.07
10:20–10:40	**Collen Masimirembwa**, AiBST, Zimbabwe *Evaluation of genetic variants of drug metabolising enzymes and drug transporters as possible biomarkers for adverse drug reactions in an HIV/AIDS cohort*	HO.08
10:40–11:00	**Simani Gaseitsiwe**, BHP, Botswana *High K65R levels in HIV-1 subtype C-infected patients failing a tenofovir-based first-line combination antiretroviral therapy regimen in Botswana*	HO.09
09:00–11:00	PARALLEL SESSION Tuberculosis Therapeutic Studies CHAIRS Maryline Bonnet and Eleni Aklillu RAPPORTEURS Lyn Horn and Jean Nachega	Salon 2
09:00–09:20	**Michael Hoelscher**, University of Munich (LMU), Germany *Challenges of and perspectives on development and evaluations of new tuberculosis drug regimens*	TO.04
09:20–09:40	**Norbert Heinrich**, University of Munich (LMU), Germany *Results for SQ109, a new antituberculosis drug candidate, from a fourteen-day early bactericidal activity study*	TO.05

Tuesday 1 July 2014		
09:40–10:00	**Charles Mtabho**, KCRI, Tanzania *The effect of diabetes mellitus on the pharmacokinetics of tuberculosis drugs in Tanzanian patients*	TO.06
10:00–10:20	**Yolandy Lemmer**, CSIR, South Africa *Providing an address for delivery of nanoencapsulated tuberculosis drugs*	TO.07
10:20–10:30	**Prisca Rabuogi**, KEMRI/CDC, Kenya *Evaluation of tuberculosis treatment outcomes in an infant tuberculosis incidence study in western Kenya*	TO.08
10:40–11:00	**Q&A session**	
09:00–11:00	PARALLEL SESSION Malaria therapeutic studies CHAIRS Philippe Deloron and Kalifa Bojang RAPPORTEURS Charles Obonyo and Montserrat Blázquez Domingo	Hall I A
09:00–09:20	**Peter G. Kremsner**, ITM Tübingen, Germany *A simplified artesunate regimen for severe malaria in children*	MO.04
09:20–09:40	**Abdoulaye Djimdé**, MRTC, University of Bamako, Mali *Safety of artesunate-pyronaridine in the repetitive treatment of uncomplicated malaria in sub-Saharan Africa*	MO.05
09:40–10:00	**Issaka Zongo**, IRSS, Burkina Faso *Efficacy of dihydroartemisinin-piperaquine in the treatment of uncomplicated P. falciparum malaria in African patients and day 7 plasma piperaquine concentration*	MO.06
10:00–10:20	**Sidikiba Sidibe**, CNFRSR, Guinea *Therapeutic efficacy of artesunate-amodiaquine combination in the treatment of uncomplicated malaria at Mafèrinyah, Republic of Guinea*	MO.07
10:20–10:40	**Sodiomon Sirima** and **Alfred B. Tiono**, CNRFP, Burkina Faso *Impact of community screening and treatment of asymptomatic carriers of Plasmodium falciparum with artemether-lumefantrine on asymptomatic and gametocyte carriage: a 12-month, cluster-randomised study*	MO.08
10:40–11:00	**Alfred B. Tiono**, CNRFP, Burkina Faso *Treatment of asymptomatic carriers of Plasmodium falciparum with artemether–lumefantrine: impact on the prevalence of anaemia*	MO.09
09:00–11:00	PARALLEL SESSION Cross-cutting: planning, implementation and impact evaluation of clinical trials CHAIRS Knut Fylkesnes and Wilfred Mbacham RAPPORTEURS Godwin Nchinda and Lucinda Manda-Taylor	Salon 3–4

Tuesday 1 July 2014

09:00–09:20	**Maxime K. Drabo**, IRSS/Centre Muraz, Burkina Faso *Impact of clinical trials on the quality of health care services in Burkina Faso: perception of community and health staff in Nanoro and Dafra districts*	CO.04
09:20–09:40	**Elisabeth Stantley-Batchilly**, MRC, The Gambia *Factors influencing the recruitment of participants for randomised clinical trials in Africa: an observational study in The Gambia*	CO.05
09:40–10:00	**Elizabeth Ayuo**, KEMRI-CDC, Kenya *A pragmatic and innovative strategy to improve quality of clinical trials in East Africa: update from the reciprocal monitoring scheme*	CO.06
10:00–10:20	**Daniel Bauer**, University of Munich (LMU), Germany *Monitoring and evaluation of health research capacity development activities: development of tools and instruments using the example of the Fozivudine in Africa Trials Initiative*	CO.07
10:20–10:40	**Ghiorghis Belai**, Family Health International, Kenya *Implementation challenges of the WANECAM study: a monitor's perspective*	CO.08
10:40–11:00	**Q&A session**	
11:00–11:30	**Coffee and tea break**	**Hall II**
11:00–11:30	MARKETPLACE VIEWS	**Hall II**
11:30–13:00	PARALLEL SESSION HIV/AIDS therapeutic studies CHAIRS Shabbar Jaffar and Maria Fraga Oliveira Martins RAPPORTEURS Photini Kiepiela and Jonathan Kayondo	**Hall I B-C**
11:30–11:45	**Divine Avit Edi**, PAC-CI, Site ANRS, projet Monod, Côte d'Ivoire *Access to early infant diagnosis and antiretroviral therapy: barriers and challenges in Abidjan, Côte d'Ivoire in 2011–2013*	HO.10
11:45–12:00	**Nicholas Paton**, National University of Singapore, Singapore *A pragmatic randomised controlled strategy trial of three second-line treatment options for use in public health rollout programme settings: the EARNEST trial*	HO.11
12:00–12:15	**Nogbou Frédéric Ello**, CHUT, Côte d'Ivoire *The Fozivudine in Africa Trials Initiative: first results from the FATI-1 phase II trial conducted in Mbeya, Tanzania and Abidjan, Côte d'Ivoire*	HO.12
12:15–12:30	**Catherine Orrell**, University of Cape Town, South Africa *A randomised trial to explore adherence-failure relationships in a South African antiretroviral cohort: baseline data analysis*	HO.13

Tuesday 1 July 2014		
12:30–12:45	**Graeme Meintjes**, University of Cape Town, South Africa *Efficacy of third line ART in Africa: outcomes on ART salvage regimens in the Southern African private sector*	HO.14
12:45–13:00	**Kamija Phiri**, University of Malawi *Benefits and risks of iron supplementation in HIV-infected Malawian children: results of a double-blind, randomised controlled trial*	HO.15
11:30–13:00	PARALLEL SESSION Tuberculosis immunology and vaccine development CHAIRS Beate Kampmann and Martin Ota RAPPORTEURS Monique Surette and Jean-Marie Habarugira	Salon 2
11:30–11:50	**Ingrid Kromann**, SSI, Denmark *Clinical development of tuberculosis subunit vaccine H1IC*	TO.09
11:50–12:10	**Michele Tameris**, SATVI, South Africa *Phase II safety and immunogenicity study of Aeras-402 in BCG-vaccinated, HIV-uninfected infants*	TO.10
12:10–12:30	**Birahim P. Ndiaye**, Laboratoire de Bactériologie et Virologie, Senegal. *Incidence of tuberculosis among a cohort of HIV positive adults enrolled in a TB vaccine clinical trial in Senegal*	TO.11
12:30–12:50	**Novel N. Chegou**, Stellenbosch University, South Africa *Utility of Mycobacterium tuberculosis-specific host cytokine signatures in whole blood culture supernatants in the diagnosis of tuberculosis disease*	TO.12
12:50–13:00	**Q&A session**	
11:30–13:00	PARALLEL SESSION Malaria vaccine studies CHAIRS Kalifa Bojang and Francine Ntoumi RAPPORTEURS Bourema Kouriba and Eric Achidi	Hall I A
11:30–11:50	**Nicola K. Viebig**, EVI, Germany *The Malaria Vectored Vaccines Consortium (MVVC): integrating capacity building and networking in the design and conduct of clinical trials in East and West Africa*	MO.10
11:50–12:10	**Nébié Issa Ouédraogo**, CNRFP, Burkina Faso *Assessing chimpanzee adenovirus serotype ChAd63 neutralising antibodies prior to the implementation of a candidate malaria vaccine regimen based on viral vectors*	MO.11
12:10–12:30	**Alfred B. Tiono**, CNRFP, Burkina Faso *Safety and immunogenicity of heterologous prime-boost immunisation with candidate vaccines ChAd63 ME-TRAP and MVA ME-TRAP in healthy Burkinabè children aged 5–17 months*	MO.12

Tuesday 1 July 2014		
12:30–12:50	**Victorine Mensah**, University Cheikh Anta Diop, Senegal *Efficacy study of ChAd63-MVA ME-TRAP prime-boost vaccination against Plasmodium falciparum infection in healthy adults in Senegal*	MO.13
12:50–13:00	**Thomas Egwang**, Med Biotech Laboratories, Uganda *Maternal immunisation protects mice pups against malaria*	MO.14
11:30–13:00	PARALLEL SESSION Cross-cutting: Interactions of Neglected Infectious Diseases (NIDs) with HIV, tuberculosis and malaria CHAIRS Alison Elliott and Wilfred Mbacham RAPPORTEURS Ayola Akim Adegnika and Seni Kouanda	Salon 3–4
11:30–11:50	**Josephine Wanyenze**, MRC-UVRI, Uganda *HIV and schistosoma mansoni coinfections among adults in fishing communities along Lake Victoria, Uganda*	CO.09
11:50–12:10	**Marguerite Massinga Loembé**, CERMEL, Gabon *Detangling immune interactions between schistosomiasis and malaria in coinfected individuals*	CO.10
12:10–12:30	**Annemieke Geluk**, LUMC, The Netherlands *Field evaluation of an up-converting phosphor-lateral flow assay for detection of cellular and humoral immunity against mycobacteria*	CO.11
12:30–12:50	**Clovis Seumen**, University of Yaounde I, Cameroon *Effect of concurrent gastrointestinal nematode infections on anti-malarial total IgG in school-age children in Mfou*	CO.12
12:50–13:00	**Q&A session**	
13:00–14:00	**Lunch**	Hall II
13:00–14:00	MARKETPLACE VIEWS	Hall II
14:00–16:00	PARALLEL SESSION HIV/AIDS comorbidities CHAIRS Shabbar Jaffar and Knut Fylkesnes RAPPORTEURS Edwin Were and Jonathan Kayondo	Hall I B-C
14:00–14:15	**Veronica Mulenga**, University Teaching Hospital, Zambia *CHAPAS 3: A randomised trial comparing two-year toxicity and efficacy of stavudine vs zidovudine vs abacavir as NNRTI-based fixed dose combination antiretroviral drug regimens for starting or substituting from stavudine-based antiretroviral therapy in 478 HIV-infected children in Uganda and Zambia*	HO.16
14:15–14:30	**Grace Mirembe**, JCRC Kampala, Uganda *Cardiovascular structure and function in HIV-infected children in Zambia and Uganda: CHAPAS-3 trial*	HO.17

Tuesday 1 July 2014		
14:30–14:45	**Victor Musiime**, JCRC Kampala, Uganda *Anthropometric measurements and lipid profiles to detect early lipodystrophy in antiretroviral therapy experienced HIV-infected children in the CHAPAS-3 trial*	HO.18
14:45–15:00	**Chishala Chabala**, UTH, Zambia *Assessment of peripheral neuropathy among HIV-infected children on fixed-dose antiretroviral therapy in Zambia and Uganda: the CHAPAS-3 randomised clinical trial*	HO.19
15:00–15:20	**Guy Bumoko**, University of Kinshasa, Democratic Republic of Congo *Cognition abilities and daily life functioning of HIV subjects on antiretroviral therapy*	HO.20
15:20–15:40	**Seth Inzaule**, KEMRI, Kenya *Incidence and predictors of first-line antiretroviral regimen modification in western Kenya*	HO.21
15:40–16:00	**Ismail Mbowo**, Moi University, Kenya *Correlates of separation among HIV-serodiscordant couples enrolled in partners PrEP study Eldoret site clinic in Western Kenya*	HO.22
14:00–16:00	PARALLEL SESSION Tuberculosis studies on diagnostics CHAIRS Ali Zumla and Gerhard Walzl RAPPORTEURS Nesri Padayatchi and Jean Nachega	**Salon 2**
14:00–14:20	**Klaus Reither**, Swiss TPH, Switzerland *Evaluation of new and emerging diagnostics for childhood tuberculosis in high-burden countries: update from the TB CHILD project*	TO.13
14:20–14:40	**Grant Theron**, University of Cape Town, South Africa *Xpert MTB/RIF assay for the diagnosis of tuberculosis using non-sputum samples in a HIV-prevalent setting*	TO.14
14:40–15:00	**Sokoine Kivuyo**, NIMR Muhimbili, Tanzania *Diagnosing tuberculosis in advanced HIV infection in Africa: the role of the Xpert MTB/RIF assay*	TO.15
15:00–15:20	**Abigail Ayorinde**, MRC, The Gambia *Contribution of the Xpert MTB/RIF assay to the diagnosis of pulmonary tuberculosis in a West African childhood TB clinic*	TO.16
15:20–15:40	**Willy Ssengooba**, Makerere University, Uganda *Comparative effectiveness of Xpert MTB/RIF assay when used as add-on test to smear microscopy for diagnosis of pulmonary tuberculosis among HIV-infected Ugandan adults*	TO.17
15:40–16:00	**Boitumelo Fanampe**, University of Cape Town, South Africa *Development of an aptamer to a Th1 cytokine*	TO.18

Tuesday 1 July 2014

14:00–16:00	PARALLEL SESSION Pregnancy associated malaria studies CHAIRS Philippe Deloron and Eusébio Macete RAPPORTEURS Montserrat Blázquez Domingo and Pauline Byakika	Hall I A
14:00–14:20	**Raquel González**, CRESIB, Spain *Efficacy and safety of mefloquine as malaria intermittent preventive treatment in pregnancy: results from a multicentre randomised clinical trial*	MO.15
14:20–14:35	**Raquel González**, CRESIB, Spain *Efficacy and safety of mefloquine as malaria intermittent preventive treatment in pregnancy in HIV-infected women receiving daily cotrimoxazole prophylaxis*	MO.16
14:35–14:50	**Michael Ramharter**, CERMEL, Gabon *Rich and population pharmacokinetics of mefloquine intermittent preventive treatment against malaria in pregnant women in Gabon*	MO.17
14:50–15:05	**Harry Tagbor**, LSHTM, United Kingdom *A trial of intermittent screening and treatment as an alternative to intermittent preventive treatment with sulfadoxine-pyrimethamine for the control of malaria in pregnancy*	MO.18
15:05–15:20	**Kassoum Kayentao**, MRTC, University of Bamako, Mali *Intermittent preventive therapy for malaria in pregnancy using 2 versus 3 or more doses of sulfadoxine-pyrimethamine and risk of low birth weight in Africa: systematic review*	MO.19
15:20–15:40	**Feiko ter Kuile**, LSTM, United Kingdom and KEMRI, Kisumu, Kenya *Impact of sulphadoxine-pyrimethamine resistance on the effectiveness of Intermittent Preventive Therapy for malaria in pregnancy (IPTp) in Africa: A systematic review and meta-analysis*	MO.20
15:40–16:00	**Jean Louis Ndiaye**, University Cheikh Anta Diop, Senegal *Effectiveness of seasonal malaria chemoprevention combined with community case management for malaria in southern Senegal: a cluster-randomised trial*	MO.21
14:00–16:00	PARALLEL SESSION Cross-cutting: ethics and good practices CHAIRS Alioune Dieye and Wilfred Mbacham RAPPORTEURS Esther Nkandu and Elizabeth Pienaar	Salon 3–4
14:00–14:20	**Lyn Horn** and **Mariana Kruger**, Stellenbosch University, South Africa *Research Ethics in Africa: a resource for Research Ethics Committees*	CO.13

Tuesday 1 July 2014		
14:20–14:40	**Godfrey B. Tangwa**, CAMBIN, Cameroon *Small is beautiful: demystifying and simplifying SOPs: the model of the Ethics Review and Consultancy Committee of the Cameroon Bioethics Initiative*	CO.14
14:40–15:00	**Martin Matu**, ECSA-HC, Tanzania *Status of research ethics bodies in East, Central and Southern Africa Health Community region*	CO.15
15:00–15:20	**Modest Mulenga**, TDRC Ndola, Zambia *Engaging policy makers in clinical trials to accelerate policy formulation in sub-Saharan Africa*	CO.16
15:20–15:40	**Mary Kasule**, University of Botswana, Botswana *Building research capacity in Botswana: a randomised trial comparing training methodologies in the Botswana ethics training initiative*	CO.17
15:40–16:00	**Charles N. Fokunang**, University of Bamenda, Cameroon *Ethical implications in clinical genetic and genomic research for the emerging countries*	CO.18
16:00–16:30	**Coffee and tea break**	Hall II
16:00–16:30	MARKETPLACE VIEWS	Hall II
16:30–17:10	PARALLEL SESSION (CONT.) HIV/AIDS comorbidities CHAIRS Shabbar Jaffar and Maria Fraga Oliveira Martins RAPPORTEURS Photini Kiepiela and Jonathan Kayondo	Hall I B-C
16:30–16:50	**Suzanne Filteau**, LSHTM, United Kingdom *Nutritional intervention to reduce early mortality in HIV-infected African adults starting antiretroviral therapy*	HO.23
16:50–17:10	**Valériane Leroy**, University of Bordeaux Segalen, France *Twelve-month virological response in children initiated on lopinavir containing antiretroviral therapy before 2 years of age in Abidjan, Côte d'Ivoire and Ouagadougou, Burkina Faso*	HO.24
16:30–17:10	PARALLEL SESSION Tuberculsosis drug development and drug resistance CHAIRS Eleni Aklillu and Marilyn Bonnet RAPPORTEURS Michelle Nderu and Pete Murphy	Salon 2
16:30–16:50	**Patrick Kobina Arthur**, University of Ghana *Analysis of anti-mycobacterial compounds produced by marine endophytic fungi*	TO.19
16:30–16:50	**Bamidele Iwalokun**, NIMR, Nigeria *Association between leptin receptor gene (Leprgln233arg) polymorphism and tuberculosis relapse in Nigerian patients*	TO.20

Tuesday 1 July 2014		
16:30–17:10	PARALLEL SESSION (CONT.) Pregnancy associated malaria studies CHAIRS Philippe Deloron and Eusébio Macete RAPPORTEURS Charles Obonyo and Eric Achidi	**Hall I A**
16:30–16:50	**José Francisco Fernandes**, Albert Schweitzer Hospital, Lambaréné, Gabon *Fosmidomycin as an antimalarial drug: review of clinical trials*	MO.22
16:50–17:10	**Rakiswendé Serge Yerbanga**, *IRSS-DRO, Burkina Faso* *Artesunate in vivo activity on Plasmodium falciparum forms in the mosquito Anopheles coluzzii*	MO.23
16:30–17:10	PARALLEL SESSION (CONT.) Cross-cutting: ethics and good practices CHAIRS Alioune Dieye and Wilfred Mbacham RAPPORTEURS Esther Nkandu and Elizabeth Pienaar	**Salon 3–4**
16:30–16:50	**Kevin Fisher**, AVAC, United States of America *Global implementation of good participatory practice guidelines for biomedical HIV prevention and tuberculosis research: charting progress and setting milestones*	CO.19
16:50–17:10	**Dan Kajungu**, Catholic University of Leuven, Belgium/ Uganda *Paediatric pharmacovigilance: data mining algorithms for signal detection in phase IIIb clinical trials safety datasets from seven African countries*	CO.20
17:10–18:00	MARKETPLACE VIEWS	**Hall II**
17:30–19:00	SATELLITE MEETING Global TB Vaccine Partnership	**Salon 3–4**
17:30–20:30	SATELLITE MEETING ESSENCE on Health Research initiative, members' dinner meeting *By invitation only*	**Salon 2**

Wednesday 2 July 2014		
08:00–09:00	**Registration**	Foyer
08:00–09:30	PARALLEL SESSION EDCTP and CAAST-Net Plus: building bridges CHAIRS Ole Olesen and Daan du Toit RAPPORTEURS Ana Lúcia Cardoso, Lara Pandya and Katharina Kuss	Hall I B-C
08:00–09:30	PARALLEL SESSION EDCTP Africa mapping project: current state of health research on poverty-related and neglected infectious diseases in sub-Saharan Africa CHAIRS Michael Makanga and Gabrielle Breugelmans RAPPORTEURS Michelle Nderu and Hager Bassyouni	Hall I A
09:40–11:00	PARALLEL SESSION HIV/AIDS treatment guidelines and disease progression CHAIRS Gita Ramjee and Pontiano Kaleebu RAPPORTEURS Catherine Orrell and Hager Bassyouni	Hall I B-C
09:40–10:00	**Vincent Tukei**, BIPAI, Uganda *Using WHO 2010 dosing guidelines, efavirenz levels remain slightly lower and highly variable in Ugandan and Zambian children weighing 10–20 kg*	HO.25
10:00–10:20	**Gaone Retshabile**, BHP, Botswana *Sub-optimal CD4 T cell recovery in HIV-1 subtype C patients on antiretroviral therapy: a search for predictive biomarkers and baseline characteristics*	HO.26
10:20–10:40	**Deogratius Ssemwanga**, MRC-UVRI AIDS, Uganda *HIV-1 multiple infection and disease progression in a cohort of female sex workers in Uganda*	HO.27
10:40–11:00	**Thato Iketleng**, BHP, Botswana *Plasma cytokine levels in chronic asymptomatic HIV-1 subtype C infection as an indicator of disease progression in Botswana: a retrospective case control study*	HO.28
09:40–11:00	PARALLEL SESSION Tuberculosis immunology CHAIRS Beate Kampmann and Martin Ota RAPPORTEURS Michelle Ndreu and Jean Nachega	Salon 2
09:40–10:00	**Veronique Penlap Beng**, University of Yaounde 1, Cameroon *Insight of the genetic variability of Mycobacterium tuberculosis complex and drug resistance in Yaounde, Cameroon*	TO.21
10:00–10:20	**Fredrick Lutwama**, Makerere University, Uganda *Distinct T cell responses when Bacillus Calmette Guerin is delayed from birth to six weeks of age in Ugandan infants*	TO.22

Wednesday 2 July 2014		
10:20–10:40	**Niaina Rakotosamimanana**, Institut Pasteur de Madagascar *Peripheral blood TNF-α-dependent apoptotic genes expression and white blood cell count to characterise the tuberculosis clinical status of individuals in a high-burden setting*	TO.23
10:40–11:00	**Q&A session**	
09:40–11:00	PARALLEL SESSION Malaria co-infections, drug resistance and modelling CHAIRS Philippe Deloron and Maria Fraga Oliveira Martins RAPPORTEURS Bourema Kouriba and Kamija Phiri	Hall I A
09:40–10:00	**Ghyslain Mombo-Ngoma**, CERMEL, Gabon *Efficacy of mefloquine intermittent preventive treatment in pregnancy against Schistosoma haematobium infection in Gabon: a randomised controlled clinical trial*	MO.24
10:00–10:20	**Peter Kimbowa**, Save A Life Foundation, Uganda *Effect of antiretroviral therapy on malaria parasitaemia and clinical episodes among HIV-infected adults in rural Uganda, 2009: a prospective population-based cohort study*	MO.25
10:20–10:40	**Philippe Guerin**, WWARN *Investigation of sampling designs for accurate estimation of parasite clearance in the context of artemisinin resistance*	MO.26
10:40–11:00	**Issaka Sagara**, MRTC, University of Bamako, Mali *Modelling recurrent events: comparison of statistical models with continuous and discontinuous risk intervals on repeated malaria episodes data*	MO.27
09:40–11:00	PARALLEL SESSION Cross-cutting: training and networking activities CHAIRS Alioune Dieye and Dawit Wolday RAPPORTEURS Lucinda Manda-Taylor and Elizabeth Pienaar	Salon 3–4
09:40–10:00	**Photini Kiepiela**, MRC (HPRU), South Africa *Experiences in using e-learning to improve the capacity of African scientists in South Africa*	CO.21
10:00–10:20	**Peninah Menza**, DNDi, Kenya *EACCR: coordination of the malaria node activities*	CO.22
10:20–10:40	**Dembo Kanteh**, MRC, The Gambia *Towards strengthening the West African network of excellence for tuberculosis, AIDS and malaria: WANETAM Plus*	CO.23
10:40–11:00	**Hulda Swai**, CSIR, South Africa *The pan-African centre of excellence in nanomedicine research and training on poverty related diseases*	CO.24
11:00–11:30	**Coffee and tea break**	Hall II

Wednesday 2 July 2014		
11:00–11:30	MARKETPLACE VIEWS	Hall II
11:30–13:00	PLENARY SESSION IV EDCTP partners' session CHAIRS Marie-Louise Newell and Ole Olesen RAPPORTEURS Karin Fischer-Buder	Hall I B-C
13:00–14:00	**Lunch**	Hall II
13:00–14:00	MARKETPLACE VIEWS	Hall II
14:00–15:30	PARALLEL SESSION HIV/AIDS coinfections CHAIRS Souleymane Mboup and Pontiano Kaleebu RAPPORTEURS Edwin Were and Jonathan Kayondo	Hall I B-C
14:00–14:15	**Mary Mwaura**, ICHR, Kenya *The need for multipurpose prevention technologies targeting HIV and common reproductive tract infections: data from the Microbicide Safety Biomarkers study*	HO.29
14:15–14:30	**Ivete Meque**, UCM, Mozambique *Prevalence, incidence and determinants of Herpes simplex virus type 2 infection among HIV-seronegative women at high risk of HIV infection: a prospective study in Beira, Mozambique*	HO.30
14:30–14:45	**Motswedi Anderson**, BHP, Botswana *Molecular characterisation of hepatitis B virus in HIV-coinfected patients in Botswana*	HO.31
14:45–15:00	**Lerato Magosi**, BHB, Botswana *Toll-like receptor 4 polymorphisms in Botswana and impact on susceptibility to Kaposi's sarcoma in HIV-1 subtype C-infected patients*	HO.32
15:00–15:15	**Bernard Ngowi**, NIMR, Tanzania *Screening for cryptococcal meningitis in patients with advanced HIV infection: the role of serum cryptococcal antigen test*	HO.33
15:15–15:30	**Q&A session**	
14:00–15:30	PARALLEL SESSION Tuberculosis CHAIRS Tumani Corrah and Beate Kampmann RAPPORTEURS Hager Bassyouni and Pete Murphy	Salon 2
14:00–14:20	**John Hongo**, KEMRI-CDC Kenya *Real-time electronic and paper-based data capturing methods among studies conducted by the tuberculosis research branch, KEMRI-CDC programme in western Kenya*	TO.24
14:20–14:40	**Barbara Burmen**, KEMRI-CDC Kenya *Prevalence of non-tuberculous mycobacteria in HIV-infected patients, Nyanza province, Kenya*	TO.25

Wednesday 2 July 2014		
14:40–15:00	**Peter Onyango**, KEMRI-CDC Kenya *Experiences in implementing a study comparing postmortem and verbal autopsy for measuring tuberculosis mortality in Kenya*	TO.26
15:00–15:20	**Toyin Togun**, MRC, The Gambia *Assessing responses to tuberculosis treatment using a simple clinical scoring system: data from the tuberculosis case-contact cohort in The Gambia*	TO.27
15:20–15:40	**Tutty Isatou Faal-Jawara**, MRC, The Gambia *Sequencing of variable T cell epitopes of Mycobacterium tuberculosis from confirmed tuberculosis cases in The Gambia*	TO.28
14:00–15:30	PARALLEL SESSION Malaria immunology and diagnostics CHAIRS Dawit Wolday and Wilfred Mbacham RAPPORTEURS Eric Achidi and Bourema Kouriba	Hall I A
14:00–14:15	**Alphonse Ouédraogo**, CNRFP, Burkina Faso *Pyrogenic threshold for malaria disease definition in an endemic area of Burkina Faso*	MO.28
14:15–14:30	**Amidou Diarra**, CNRFP, Burkina Faso *Seasonal variation and clinical protection of antibodies against a panel of malaria antigens in children under five years of age in Burkina Faso*	MO.29
14:30–14:45	**Guillaume S. Sanou**, CNRFP, Burkina Faso *Assessing regulatory T cells in children with severe malaria in Burkina Faso*	MO.30
14:45–15:00	**Larissa Aurore Tobol Bouyoukou Hounkpatin**, CERMEL, Gabon *Reduced antibody responses against Plasmodium falciparum vaccine candidate antigens in the presence of Trichuris trichiura*	MO.31
15:00–15:15	**Maria Rebelo**, CERMEL, Gabon *Haemozoin detection assay: a novel ex vivo assay to detect antimalarial drug resistance*	MO.32
15:15–15:30	**Q&A session**	
14:00–15:30	PARALLEL SESSION Cross-cutting CHAIRS Abraham Aseffa and Alioune Deiye RAPPORTEURS Christine Wasunna and Farirai Mutenherwa	Salon 3–4
14:00–14:15	**Christine Wasunna**, KEMRI, Kenya *Establishment of a centralised clinical trials register in Kenya: a model for knowledge sharing and exchange across two institutions*	CO.25
14:15–14:30	**Joseph Gaie**, University of Botswana *Opportunities and challenges: sharing experiences of IRB/REC members in a developing country*	CO.26

Wednesday 2 July 2014		
14:30–14:45	**Kolawole Oyedeji**, NIMR, Nigeria *Capacity building and evaluation of post training operational capacities of three ethics review committees in Nigeria: best practice*	CO.27
14:45–15:00	**Galekgatlhe Bailey Balekang**, Health Research Division, Ministry of Health, Botswana *Challenges of establishing and running a community advisory board in Botswana*	CO.28
15:00–15:15	**Muhammed Afolabi**, MRC, The Gambia *Digitised audio questionnaire for assessment of informed consent comprehension in a low literacy African research population: development and psychometric evaluation*	CO.29
15:15–15:30	**Palmer Netongo**, ISHReCA, Cameroon *Towards an ISHReCA manifesto to guide researchers as they engage in health research partnerships*	CO.30
15:30–16:00	**Coffee and tea break**	Hall II
15:30–16:00	MARKETPLACE VIEWS	Hall II
16:00–17:15	PLENARY SESSION V Summary and closing remarks CHAIRS Michael Makanga and Tumani Corrah	Hall I B-C
16:00–16:30	**Karin Fischer-Buder**, Chief rapporteur *Report back from the parallel sessions focusing on summary and ideas for future strategy consideration*	
16:30–16:45	**Prof. Charles Mgone**, EDCTP Executive Director *Closing remarks from EDCTP*	
16:45–17:00	**Dr Gianpietro Van de Goor**, DG Research and Innovation, European Commission *Closing remarks from the European Commission*	
17:00–17:15	**Dr Joachim Klein**, Federal Ministry for Education and Research, Germany *Closing remarks from the German Government*	

Thursday 3 July 2014		
09:00–17:00	EDCTP STAKEHOLDER MEETING ON CAPACITY DEVELOPMENT *By invitation only*	Hall I A

Plenary speakers

PS.01

HIV/AIDS

Gita Ramjee, Medical Research Council, South Africa

The success of antiretroviral drugs (ARVs) for HIV/AIDS prevention and therapy has led to the belief that the end of AIDS may be possible even without an efficacious HIV preventative vaccine. Biomedical HIV prevention includes strategies such as barrier methods, vaccines, microbicides, and pre- and post-exposure prophylaxis (PrEP and PEP respectively). It is widely recognised that behavioural and structural challenges also play an integral part in both HIV prevention and treatment.

Advances in HIV prevention include development and testing of novel women-initiated products such as long acting vaginal ring formulations containing ARV agents to mitigate the challenges of daily adherence. New products of long acting injectables are on the horizon for prevention of HIV among women as are multiproduct technologies to prevent both HIV and pregnancies. Demonstration projects are underway for use of PrEP in gay and discordant couples after the successes observed in clinical trials.

Advances in HIV treatment have promoted the belief that HIV is now a chronic condition however it may not fully restore health due to emerging co-morbidities. Behaviour challenges of stigma, access and willingness to be tested, safe sex practices, and adherence to prevention and treatment interventions remain critical to control the epidemic. Structural challenges such as violence against women, discrimination against key populations, health systems strengthening, and effective linkage and retention in care of those at risk and infected by HIV, remain critical.

Despite the enormous strides made in the prevention and treatment of HIV, a lot remains to be done to ensure the future as an AIDS-free generation.

PS.02

Tuberculosis

Ann Ginsberg, Aeras, United States of America

In 2011, WHO reported 8.7 million new cases and 1.4 million deaths due to tuberculosis (TB). Thirteen percent (13%) of these cases were in individuals coinfected with HIV. The number of notified cases of multidrug resistant TB (MDR-TB) is increasing globally; in 2011, there were an estimated 300,000 new cases. Concerted efforts to better implement the WHO-recommended DOTS treatment programme have resulted in a 2.2% decrease in TB incidence globally from 2010–2011, far short of the 16% annual decrease in incidence needed to reach the MDG 2050 goal of elimination (one new case per million population per year).

New improved tools are urgently needed to achieve this goal. The recently introduced GeneXpert® system for TB diagnosis holds the potential for more rapid and accurate diagnosis of both drug-sensitive and drug-resistant TB if widely implemented, but rapid, point-of-care diagnostics remain elusive. One new drug for MDR-TB treatment, bedaquiline, recently received US FDA marketing approval, and progress is being made in the development of novel combination regimens to shorten and simplify treatment of both drug-sensitive and MDR-TB. Ultimately, a new safe and effective vaccine to prevent TB would be the single most effective tool in achieving TB elimination, particularly in the third of the world's population already infected with *Mycobacterium tuberculosis*. Currently, a dozen vaccine candidates are in clinical testing, and a diversity of additional approaches are being evaluated preclinically. Progress in R&D of new drugs, diagnostics, and vaccines will be reviewed, and gaps and priorities discussed.

PS.03

Malaria

Pedro Alonso, Barcelona Centre for International Health Research (CRESIB), Spain

Malaria still constitutes a major health burden globally and particularly in sub-Saharan Africa. This is the case despite significant investments during the last decade along with unprecedented efforts to control this infection, including renewed political and financial commitment and increased availability of both old and new strategies and tools.
New challenges have been added to those posed by fragile health systems in many countries: the rise of insecticide and drug resistance; the addition of vulnerable groups that require specific approaches for effective prevention and treatment of the infection, such as HIV-infected individuals, small children and pregnant women; and difficulties in increasing the coverage of key interventions.
Further research and development is crucial to achieve and sustain malaria control, which should focus not only on *Plasmodium falciparum* but also on *Plasmodium vivax*. To this end, methodologies for identifying, estimating and tracking the malaria burden, new strategies to measure transmission, increased knowledge of the mechanisms and effects of resistance to drugs and insecticides including *in vitro* and *in vivo* markers, are indispensable. The ongoing research effort to develop new antimalarial drugs, more sensitive point-of-care rapid diagnostic tests for low-density infections, and new insecticides requires substantial strengthening. The emergence of a research agenda linked to the renewed goal of malaria elimination poses an extra challenge. This objective entails new approaches, the cornerstone of which will be the radical cure of asymptomatic infections with safer and more effective drugs, of both *P. falciparum* and *P. vivax*, in the entire population, while the efforts to treat clinical episodes and prevent infections have to be maintained.

PS.04

Neglected infectious diseases

John Gyapong, University of Ghana, Ghana

Neglected infectious diseases (NIDs) are common among the world's most impoverished populations. They blight the lives of a billion people worldwide and threaten the health of millions more. Advocacy in recent times has led to significant investment by donors, governments, pharmaceutical industry and other agencies for their prevention and control. As a result, there has been significant progress against 17 NIDs identified by WHO. Progress includes the development of a new global strategy, a regular supply of quality-assured and cost-effective medicines, and strategies for mapping the distribution and burden of these infections to facilitate programme creation. Strengthening the capacity of endemic countries and streamlining supply chains to get the drugs to the people who need them, when they need them, remains a challenge. Improved diagnostics and biomarkers have been developed for many of these infections, however, more sensitive ones are needed to assess the impact of interventions and monitor resurgence. To maintain this momentum towards the goals of controlling or eliminating these NIDs, research into newer and more effective drugs, vaccines, diagnostics and delivery mechanisms is ongoing but much more is needed. What products are in the pipeline? What mechanisms are in place to facilitate product development for NIDs whose users are the poorest in the society and therefore cannot afford to pay market value of these products? This presentation will discuss recent significant advances in NID epidemiology and prevention treatment research and it will identify areas of further research urgently needed to facilitate effective control of NIDs.

PS.05

Health services optimisation research

Shabbar Jaffar, London School of Hygiene and Tropical Medicine, United Kingdom

Randomised trials are the gold standard for evaluating new interventions. However, they often do not tell us how to scale-up an intervention or how effective the intervention will be in real life settings. The translation of evidence from randomised trials into policy and practice can take decades. There are increasing calls for greater research on health services optimisation in order to support improvements in health care in resource-limited settings, but this area of research remains poorly supported. This presentation will highlight some of the key priority areas for health services optimisation research in malaria, HIV and tuberculosis. It will make the case that this research plays a critical role in translating trial results into improved patient and population outcomes.

HO.01

Targeting HIV-1 by vaccines at conserved regions

Tomáš Hanke[1,2], Nicola Borthwick[1,2], Tina Ahmed[1,2], Beatrice Ondondo[1], Peter Hayes[3], Josephine Cox[3], Stefano Colloca[4], Alfredo Nicosia[4,5], Jill Gilmour[3], Andrew J. McMichael[2], Lucy Dorrell[2]

1. University of Oxford (Jenner), United Kingdom; 2. University of Oxford (MRC/Wheatherall), United Kingdom; 3. Imperial College, London, United Kingdom; 4. Okairos Srl, Italy; 5. CEINGE, Naples, Italy

Background | Virus variability and escape from immune responses are the biggest challenges to the development of an effective vaccine against HIV-1.
Methods | We hypothesised that T cell vaccines targeting the most conserved regions of the HIV-1 proteome, which are common to most variants and bear fitness costs when mutated, will generate effectors that efficiently recognise and kill virus-infected cells early enough after transmission to impact on HIV-1 replication.
Results | Here, we demonstrate that the first-ever administration of conserved immunogen vaccines vectored using prime-boost regimens of DNA, simian adenovirus and modified virus Ankara to uninfected volunteers from the United Kingdom (HIV-CORE 002), elicited strong T cells with broad specificities. Furthermore, this artificial consensus immunogen induced CD8+ T cell effectors, which inhibited HIV-1 replication in autologous CD4+ cells by up to 5.79 log10 and virus inhibition correlated with both Gag and particularly Pol effector specificities.
Conclusion | These are very encouraging data. The same vaccine approach is currently tested in Nairobi volunteers in trial HIV-CORE 004 funded by EDCTP and the Gates Foundation to confirm vaccine immunogenicity in the South.

HO.02

Evolution of neutralising antibodies in acute heterosexually acquired HIV-1 subtype C infection in Botswana

Keabetswe Bedi[1], Sununguko Mpoloka[1], Sheron Dzoro[2], Simani Gaseitsiwe[2], Rosemary Musonda[2], Joseph Makhema[2], Vladimir Novitsky[3], and Takafira Mduluza[4]

1. University of Botswana, Botswana; 2. BHP, Botswana; 3. Harvard Public Health, United States of America; 4. University of Zimbabwe, Zimbabwe

Background | A potent and efficacious vaccine against HIV-1 infection remains elusive thirty years after the identification of the virus. Recent discovery of potent broad neutralising antibodies against HIV-1 has revived interest in their role in preventing HIV transmission. Our study investigated the role of neutralising antibodies on viral set point and prevalence of cross-reactive neutralising antibodies in HIV-1C infections in Botswana.

Methods | Plasma samples collected at different time points during follow-up of eight HIV-1C acutely infected individuals were stored at –80°C. Viral RNA was extracted from plasma collected approximately one week post enrolment and used as template for cDNA synthesis, amplification of HIV-1C gp160, cloned into pcDNA3.1D/V5-His expression vector and co-transfection of 293T cells to generate infectious pseudoviruses. A standardised TZM-bl cells-based neutralisation assay was used.

Results | Varying numbers of HIV-1C pseudoviruses (1 to 5) were generated for each of the eight acute infections. Autologous neutralising antibodies appeared between 4 weeks and 9 months post seroconversion. Generally, viruses displayed varying intra-subject and inter-subjects neutralisation sensitivities. Potency of neutralisation increased over time for all subjects except one, who had very potent autologous neutralisation that coincided with transient viral load decline. This plasma also displayed heterologous neutralisation of other viruses with significant potency.

Conclusion | HIV-1C neutralising antibodies toward transmitted virus develop around five months post seroconversion and their development lags behind. Viral set point does not appear to be affected by early appearance of neutralising antibodies. Cross-reactive neutralising antibodies were uncommon.

HO.03

Natural killer cells of HIV-1-exposed but uninfected subjects exhibit recall responsiveness to HIV-1 peptides

Moustapha Mbow[2,*], **Sabelle Jallow**[1,*], Cheikh T. Ndour[3], Martin Goodier[4], Eleanor Rilley[4], Assan Jaye[1,2]

*1. MRC, The Gambia; 2. CHU Le Dantec, Senegal; 3. Fann University Hospital, Senegal; 4. LSHTM, United Kingdom; * Equal contribution and first authorship*

Background | The function and phenotype of cells able to protect against HIV-infection or limit transmission remains unclear. Difficulties in developing effective T cell-based vaccines against this virus highlight the urgent need for the investigation of other cellular immune correlates of protective immunity in clinical trial settings and high risk cohorts. Recent appreciation of the potential of natural killer cells to contribute to antigen-specific secondary immune responses as well as to innate responses suggests that these cells deserve more attention. Here we investigated effector and recall responses of natural killer cells in HIV-infected adults and their exposed but uninfected partners.

Methods | Nine HIV-negative subjects (controls), HIV-positive individuals and their negative partners from a discordant couple cohort in Senegal were sampled. PBMCs were stimulated with overlapping peptide pools. Natural killer responses, their characteristics and the presence of recall responses were analysed by flow cytometry.

Results | Individuals who were exposed to HIV but remained uninfected, produced more degranulation, activation and functional markers compared to HIV-positive individuals and the controls, to levels that were statistically significant. A trend towards higher recall responses was observed in the exposed uninfected individuals, however this was not significant.

Conclusion | Exposure to HIV infection antigens may prime recall responses of natural killer cells, indicating that there is a great potential to use these responses as end point measurements of HIV infections.

HO.04

Randomised comparison of three second line ART regimens in Africa: the 2 Lady/ANRS/EDCTP study

Laura Ciaffi[4], A. Sawadogo[3], S.T. Ndour, N.F. Ngom, N. Manga, R. Toby, F. Kabore, H. Abessolo, S. Eymard-Duvernay[4], S. Izard, I. Diallo, S. Koulla Shiro, E. Delaporte[4]

1. 2LADY, Site ANRS, Yaounde, Cameroon; 2. CRRFP, Dakar, Senegal; 3. CHUSS, Burkina Faso; 4. University of Montpellier 1, France

Background | WHO recommends the use of a boosted Protease Inhibitor (PI/b) containing regimen in patients failing a Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)-based first line, but evidence for the choice of combination is lacking.
Methods | A 48 weeks, randomised, non-inferiority trial in Africa (Cameroon, Burkina Faso, Senegal) comparing efficacy of 3 second line regimens: Arm A: tenofovir (TDF)/emtricitabine (FTC) + lopinavir/ritonavir (LPV/r), reference arm; Arm B: abacavir (ABC) + didanosine (ddI) + LPV/r; Arm C: TDF/FTC + darunavir/ritonavir (DRV/r). Patients were eligible if they failed a first line NNRTI based ART (HIV-1 RNA ≥1,000 copies/mL) and showed adherence ≥80%. Efficacy was defined as a HIV-1 RNA <50 copies/mL at 48 weeks.
Results | From January 2010 to October 2012, 454 patients were randomised. Participants were mainly women (72%), had been on ART for a median of 49 months (IQR 33–69), had a median CD4 count of 183 cell/mm3 (IQR 87–290) and a median plasma HIV-1 RNA of 4.5 log10 (IQR 4–5.1). All but 6 had resistance to at least one first line drug. At week 48, 294 (65.2%) of the 451 analysed participants had an HIV-1 RNA<50 copies/mL, while 275 (83.2%) and 410 (90.9%) had a VL below 200 and 1000 copies/mL respectively. Primary results in ITT showed a difference of 5.6% (IC95% –5.1; 16.4) and 6.1% (IC95% –4.5; 16.7) between the arm A and arms B and C respectively, excluding non-inferiority. In multivariate analysis, VL ≤100,000 copies/ml at baseline was predictor of viral suppression. No difference among arms was observed in median CD4 gain (+127 cells/µl), mortality or adverse events.
Conclusion | Despite multiple NRTI mutations, PI/b based second line regimens showed satisfactory results. The WHO recommended regimen remains a valid option.

HO.05

HIV drug resistance in paediatric patients initiating antiretroviral therapy in Uganda: a multicentre observational study

Cissy Kityo[1], Sonia Boender[2,3], Kim Sigaloff[2,3], Elizabeth Khauda[1], Lillian Nakatudde[1], Andrew Mukuye[4], Mary Kiconco[5], Victor Musiime[1], Raph L. Hamers[2,3], Tobias F. Rinke de Wit[2,3], Peter Mugyenyi[1]

1. JCRC Kampala, Uganda; 2. AIGHD, The Netherlands; 3. University of Amsterdam, The Netherlands; 4. JCRC Mbale, Uganda; 5. JCRC Fort Portal, Uganda

Background | There is limited data on HIV drug resistance (HIVDR) in children in sub-Saharan Africa, yet they are a vulnerable population with regards to drug resistance development. This study aimed to assess prevalence of primary resistance and associated factors among children ≤12 years of age initiating first-line antiretroviral (ART) in Uganda.

Methods | Participants (319) recruited at three JCRC clinics between January 2010 and August 2011 had baseline plasma samples collected to determine viral load and genotypic drug resistance. Sequencing of the pol-gene was done on specimens with >1000 copies/ml of HIV RNA at JCRC. The 2010 IAS-USA mutation list was used to interpret drug resistance mutations. Risk factors of resistance were assessed with univariate and multivariate regression analysis.

Results | Sequencing was obtained for 95.6% of the samples with the major strain (53.8%) as subtype A. Isolates with at least one mutation for all sites was found in 30 children (10.7%); 5.7% for NRTI and 7.5% for NNRTIs; 3.2% had dual-class resistance. ART-naïve and ART-exposed children had HIVDR mutations in 7.7% and 35.7% of samples respectively. Most prevalent mutations were M184V/I (3.9%), K103N (3.9%), and Y181C (2.9%). History of PMTCT-exposure, low CD4, current breastfeeding and current maternal ART use emerged as risk factors for HIVDR at baseline.

Conclusion | HIVDR in this cohort starting ART in Uganda is classified as moderate (5%–15%) by WHO and may adversely affect response to treatment. This highlights the need for in-depth evaluation and more extensive surveys among the growing proportion of infected children initiating treatment to identify risk factors.

HO.06

Post-antiretroviral outcomes in a cohort of women who discontinued maternal triple-antiretrovirals initially used to prevent mother-to-child transmission during pregnancy

Frank Angira[1], T. Minniear[2,3], S. Girde[3], L. Mills[1,2], C. Zeh[1,2], P. Peters[2], R. Masaba[1], R. Lando[1], T. Thomas[2], A. Taylor[2]

1. KEMRI-CDC, Kenya; 2. CDC Atlanta, United States of America; 3. ICF Intl CIMS, United States of America

Background | In 2012, the World Health Organization amended its guidelines for women receiving triple-antiretrovirals (ARV) for prevention of mother-to-child transmission of HIV (PMTCT) (Option B) to include the option to continue ARV indefinitely (Option B+). Data comparing maternal and infant outcomes by maternal triple-ARV discontinuation at six months postpartum versus continuation are limited.

Methods | The Kisumu Breastfeeding Study was a prospective, non-randomised, clinical trial where 522 HIV-infected, ARV-naïve pregnant women received triple-ARVs from 34 weeks of gestation until 6 months postpartum when they were instructed to discontinue breastfeeding. Women with CD4 count less than 250 ells/mm^3 or WHO stage 3/4 continued ARV indefinitely. We used regression models to estimate the change in CD4 after discontinuing ARV and the adjusted relative risk (aRR) for factors associated with declines in maternal CD4. We compared maternal and infant outcomes following weaning by maternal ARV status between 6–24 months postpartum.

Results | At 6 months postpartum, 82 women continued while 366 discontinued ARV. Women initiating ARV with low CD4 (350–500 cells/mm^3) were more likely to decline to <350 cells/mm^3 within six months of stopping, independent of CD4 and viral load at discontinuation (aRR 9.8; p=0.002). Only, infant death (29) or HIV infection (9) was independently associated with maternal ARV discontinuation compared with continuation (10.1% *vs* 2.4%; p=0.04).

Conclusion | Evaluating CD4 count at initiation of PMTCT regimen and 6 months postpartum can identify women at risk for a steep CD4 decline that would benefit from continuing ARV for their own health.

HO.07

Adverse foetal outcomes in HIV-1-infected women who received either NNRTI or PI-based therapy for prevention of mother-to-child transmission in western Kenya

Richard Lando[1], Frank Angira[1], Rose Masaba[1], Clement Zeh[1,2], Sonali Girde[3], Craig B. Borkowf[2], Richard Ndivo[1], Isabel Nyangau[1], Kevin Achola[1], Timothy K. Thomas[1,3], Shirley Lee Lecher[2]

1. KEMRI-CDC, Kenya; 2. CDC Atlanta, United States of America; 3. ICF Intl CIMS, United States of America

Background | Although the benefit of antiretroviral therapy (ART) in pregnancy is well established, its association with adverse foetal outcomes still remains controversial. Data from clinical trials in sub-Saharan Africa where the majority of HIV-positive women live are limited.

Methods | As part of a phase IIb clinical trial to prevent mother-to-child transmission of HIV-1 in western Kenya, we enrolled 522 HIV-1-infected ARV-naïve pregnant women at 34 to 36 weeks gestation and assigned them to either combivir/nevirapine (NNRTI group) or combivir/nelfinavir (PI group). Twenty-two (22) women withdrew before delivery while 500 delivered 502 live births and 9 stillbirths. We compared rates of adverse foetal outcomes including still births, preterm deliveries (<37 weeks), low birth weight (<2500 g), and infant deaths for 394 women with baseline CD4 counts >250 to those who received either NNRTI (n=215) or PI-based regimen (n=177) using Chi-squared tests. We also computed 95% confidence intervals for the differences between rates.

Results | There were: 7 (1.8%) stillbirths; 48 (12.2%) preterm deliveries; 38 (9.6%) with low birth weight; 8 (2.0%) infant death <28 days and 14 (3.6%) infant deaths <6 months. There were no statistically significant differences in adverse foetal outcomes between the two regimens.

Conclusion | The differences in stillbirth, preterm delivery, low birth weight, or infant death rates among women with CD4 counts ≥ 250 cells/μL who received either NNRTI or PI-based therapy for prevention of mother-to-child transmission (PMTCT) were not statistically significant. These results suggest combivir/nevirapine and combivir/nelfinavir can be used for PMTCT in resource-limited settings without an increased risk of adverse foetal outcomes.

HO.08

Evaluation of genetic variants of drug metabolising enzymes and drug transporters as possible biomarkers for adverse drug reactions in an HIV/AIDS cohort

Collen Masimirembwa[1], M. Dhoro[1], B. Ngara[1], G. Kadzirange[1], C. Nhachi[1]

1. AiBST, Zimbabwe

Background | Genetic polymorphisms in genes coding for these drug metabolising enzymes and transporters are potential biomarkers for drug efficacy and safety. This study assessed occurrence of common gene variants of these genes of proteins that have potential relevance in the safe use of stavudine-, efavirenz-, nevirapine- and isoniazid-based antiretroviral treatment and/or tuberculosis (TB) treatment and possible associations with the adverse drug reactions (ADRs; lipodystrophy, skin hypersensitivity, peripheral neuropathy, and central nervous system disorders) in an HIV/AIDS cohort in Zimbabwe.

Methods | Blood samples were obtained from patients on isoniazid in their anti-TB drug regimen and those whose ART regimen included one of the following drugs: nevirapine, efavirenz and stavudine. Patients were categorised as cases and controls for each ADR: lipodystrophy, skin hypersensitivity, peripheral neuropathy, and central nervous system disorders. TaqMan genotyping assays were used to analyse for 15 SNPs, in seven genes: CYP2B6, CYP2A6, CYP3A5, TNFα, ABCB1, ABCC4, NAT 2. Chi-square and Fisher exact tests were used to determine the overall effect of genotype and allele frequency on the development of ADRs.

Results and Conclusion | Pairwise associations showed that distribution of alleles and genotypes were comparable in both case and control groups. Genetic polymorphisms in drug metabolism and transporter genes are known to contribute significantly to variation in drug response but findings from this study did not directly relate ADRs to genetic variants. The indication is that other factors ought to be considered when determining variable drug response and association with ADRs.

HO.09

High K65R levels in HIV-1 subtype C-infected patients failing a tenofovir-based first-line combination antiretroviral therapy regimen in Botswana

Simani Gaseitsiwe[1], Iain J. MacLeod[2], Thabo Diphoko[1], Victoria Maiswe[1], Hermann Bussmann[1], Chidzani Mbenge[1], Sikhulile Moyo[1], Rosemary Musonda[1], Mansour Farahani[2], Max Essex[2], Ric Marlink[2]

1. BHP, Botswana; 2. Harvard, United States of America

Background | The first-line combination antiretroviral therapy (cART) regimen of choice in Botswana is Atripla® as recommended by WHO. However, tenofovir has been implicated in the selection of the K65R mutation, which confers resistance to multiple NRTIs and thus limits future drug choices. This study aims to determine the genotypic resistance profiles of patients failing first-line therapy in Botswana.

Methods | An observational cohort study to determine the efficacy and tolerability of Truvada® based HAART among 300 HIV-1 subtype C-infected, treatment-naïve adults in Botswana. A total of 119 plasma samples were available for analysis. Viral RNA was extracted and subsequent DNA amplification of a 1.4-kb HIV-1 Protease and RT segment was carried out before Big Dye® sequencing of the amplified product.

Results | After 36 months follow up, 18/300 (6%) patients experienced virological failure and their treatment regimens had to be switched. From the 119 successfully sequenced samples, 102 were baseline and 17 were virological failures. Two out of 102 (~2%) baseline samples displayed the K103N mutation, with 2 others showing the K103R polymorphism (2%). Among virological failure samples, 17/18 were successfully sequenced and 15/17 (88%) failures displayed the K65R mutation, followed by 5/17 (29%) Y181C; 3/17 (18%) M184V and 2/17 (12%) K103N. Three virological failure patients displayed a combination of K65R, Y181C and M184V.

Conclusion | There is low prevalence of drug resistance detected at baseline in this population. Though the treatment regimen was well tolerated there was an unexpectedly high frequency of K65R in the patients who experienced virological failure in this HIV subtype C-infected population. Patients failing first-line regimen would benefit from drug resistance genotyping to guide second-line therapy.

HO.10

Access to early infant diagnosis and antiretroviral therapy: barriers and challenges in Abidjan, Côte d'Ivoire in 2011–2013

Divine Avit Edi[1], M. Folquet-Amorissani[2], C. Amani-Bossé[1], M.E. Dainguy[2], J. Eliam-Kouakou[1], V. Méa-Assandé[1,3], E.A. Aka[4], V. Kouraï-Lago[5], P. Fassinou-Ekouévi[6], R. Salamon[7], M. Timité-Konan[8], V. Leroy[7]; for the MONOD ANRS[1]2206 Study Group.

1. PAC-CI, Côte d'Ivoire; 2. CHUC, Côte d'Ivoire; 3. FSU Abobo-Avocatier, Abidjan, Côte d'Ivoire; 4. CePReF Yopougon, Côte d'Ivoire; 5. National HIV Programme, Côte d'Ivoire; 6. EGPA Foundation, Côte d'Ivoire; 7. Université Bordeaux Segalen, France; 8. CHUY, Côte d'Ivoire

Background | The national programme of Côte d'Ivoire decided to scale-up the early infant diagnosis of HIV using dried blood spot (DBS) in 2011. We describe the access to paediatric HIV early infant diagnosis and care in Abidjan, Côte d'Ivoire.

Methods | A survey was undertaken in 29 health facilities delivering paediatric HIV services in Abidjan to monitor the process of early infant diagnosis of all HIV-exposed children <12 months until the delivery of their results. Data were extracted monthly from registers: the number of DBS requested, the number returned to sites, the number of paediatric HIV infections, and the number of HIV-infected infants oriented to care.

Results | From September 2011 to January 2013, 77% of the results for the 2,396 HIV-exposed infants who had access to DBS, were returned to sites; 59% of the DBS results were communicated. Among the 183 HIV-infected infants identified, only 52% were oriented to HIV paediatric care. Several barriers were identified: the post-electoral period; the transition of strategic screening activities (transport and technical support) to local partners; the lack of a transportation system for DBS samples; the excessive delay in returning back the DBS results; the lack of motivation within the community and of health care professionals to trace HIV-exposed infants; stigma.

Conclusion | There were too many missed opportunities for access to early infant diagnosis and care in 2011–2013. Challenges still remain for improving early identification of HIV-infected infants and promoting early orientation of HIV-infected children to appropriate care. With the commitment of the National Programme, it is crucial to identify sustainable mechanisms to promote a universal and early access to infant HIV care services in Côte d'Ivoire.

HO.11

A pragmatic randomised controlled strategy trial of three second-line treatment options for use in public health rollout programme settings: the EARNEST trial

Nicholas Paton[1,2], C. Kityo[3], A. Hoppe[1], J. Hakim[4], J. van Oosterhout[5], A. Siika[6], P. Mwaba[7], A. Kambugu[8], P. Easterbrook[8], J. Boles[1], S. Walker[1], P. Mugyenyi[3]; EARNEST Trial Group

1. MRC CTU, United Kingdom; 2. National University of Singapore, Singapore; 3. JCRC Kampala, Uganda; 4. University of Zimbabwe, Zimbabwe; 5. University of Malawi, Malawi; 6. Moi University, Kenya; 7. UTH, Zambia; 8. Makerere University, Uganda

Background | Incremental benefits of new/recycled NRTIs or raltegravir (RAL) on a boosted protease inhibitor (bPI) backbone for second-line therapy in a rollout programme setting are uncertain.
Methods | Patients failing standard first-line treatment (WHO criteria, confirmed with viral load (VL) >400 copies/ml) were randomised to A) bPI +2/3 physician-selected NRTIs, B) bPI plus RAL (400 mg twice daily) or C) bPI monotherapy (+RAL induction for first 12 weeks). bPI standardised to lopinavir/ritonavir, 400 mg/100 mg b.d. Monitoring was clinical and by open CD4 count; VL and resistance testing done annually blinded, reviewed by data monitoring committee. Primary (composite) endpoint: good disease control, defined as no new WHO stage 4 events (or death) after randomisation, and CD4 count >250 cells/mm^3 and VL < 10,000 copies/ml (or >10,000 copies/ml without major/minor PI resistance mutations) at week 96.
Results | Out of a total of 1,277 patients randomised 1% had withdrawn or were lost to follow-up by week 96. Proportions for good disease control were (A) 60%, (B) 65% (absolute risk difference *vs* A: +5.7% (–0.9%, +12.3%; p=0.09)) and (C) 57% (difference *vs* A: –2.2% (–9.0%, +4.5%; p=0.52)). There was no difference in grade 3/4 adverse events between groups (P=0.39). However, 61% (C) had VL <400 copies/ml at 96 weeks *vs* 86% (A) (difference –25% (–31%, –19%; p<0.0001)) and 86% (B) (difference *vs* A –0.2% (–5%, +4%; p=0.94). Resistance data will be presented.
Conclusion | bPI +RAL is not clearly superior to bPI +2NRTI at week 96; further follow-up essential to determine whether it is advantageous over longer-term. bPI monotherapy is unsuitable for typical roll-out programme settings that lack regular/reliable VL monitoring. New/recycled NRTIs retain substantial virological activity.

HO.12

The Fozivudine in Africa Trials Initiative (FATI): first results from the FATI-1 phase II trial conducted in Mbeya, Tanzania and Abidjan, Côte d'Ivoire

Nogbou Frédéric Ello[2,3], Jimson mgaya[1], Christine Danel[2], Tessa Lennemann[1,3], Lucas Maganga[1], Serge Eholie[2,3], Raoul Moh[2,3], Zelica Diallo[3], Joseph Mwabusila[1], Roki Mugeniwalwo[1], Emmanuel Bissagnene[3], Pierre-Marie Girard[4], Tina Purnat[3], Ulrich Braun[3], Xavier Anglaret[2], Michael Hoelscher[3], Arne Kroidl[3]

1. NIMR-MMRC, Tanzania; 2. CHUT, Côte d'Ivoire; 3.University of Munich (LMU), Germany; 4. University Hospital Saint-Antoine, Paris, France

Background | Zidovudine (ZDV) is widely recommended in antiretroviral therapy, however, limited by toxicity (anaemia, neutropenia). Fozivudine (FZD) is a ZDV pro-drug with a linked lipid domain and is bio-activated intracellularly to ZVD-monophosphate by outer membrane enzymes NPP1/3 which are expressed on mononuclear but not bone marrow cells. FZD promises improved toxicity profiles and once daily dosing through drug targeting and improved pharmacokinetic characteristics.
Methods | FATI-1 is a multicentre, randomised, open label phase II trial investigating three different doses of fozivudine (800 mg OD, 600 mg BID, 1,200 mg OD) versus zidovudine (300 mg BID) with a lamivudine, Efavirenz backbone in 120 HIV-infected, ART-naïve patients from Mbeya/Tanzania and Abidjan/Côte d'Ivoire. Study endpoints are the proportion of cases with HIV-RNA <50 copies/ml and safety/toxicity outcome between arms after 24 weeks.
Results | Trial recruitment finished in January 2014 and 120 participants (66% females) were enrolled. Interim result from 45 cases showed an overall HIV-RNA suppression <50 copies/ml in 87%, with a mean HIV-RNA log reduction of 3.62 and a mean CD4 increase of 136 cells/µl after 24 weeks of treatment. Severe anaemia was reported in 3, and clinical asymptomatic severe neutropenia in 25 cases, mostly associated with cotrimoxazole co-medication.
Conclusion | The FATI-1 trial has been successfully implemented. Preliminary results of Fozivudine containing ART show promising virological and immunological responses. Neutropenia is commonly observed and the contributing impact of cotrimoxazole needs to be further evaluated.

HO.13

A randomised trial to explore adherence-failure relationships in a South African antiretroviral cohort: baseline data analysis

Catherine Orrell[1], Karen Cohen[1], David Bangsberg[1], Gary Maartens[1], Robin Wood[1]

1. University of Cape Town (DTHC), South Africa

Background | Although adult antiretroviral (ART) adherence data from resource-poor countries is reported as excellent, it may be overestimated. Recent reports describe discordance between accepted measured adherence standards and virological failure. Baseline factors impacting on adherence of ART-naïve individuals, such as disclosure of HIV status and mental health (anxiety/depression) were explored in individuals enrolling into a randomised study using a locally developed electronic adherence-monitoring device (EAMD) to examine real-time ART dosing.

Methods | Baseline data was collected from 230 ART-naïve individuals at enrolment in the randomised study. Data included demographic details (age, gender), disease status (WHO stage, CD4 count, and viral load), mental state (using the Hospital Anxiety and Depression Scale) and disclosure status. Data was summarised using mean (± standard deviation) or median (inter-quartile range) values or percentages as appropriate.

Results | Enrolment was completed by 8 April 2013 (n=230): mean age was 35.7 ± 10.0 years; 148 persons (65.2%) were female; 34.5% had WHO stage 3 or 4 HIV disease; median CD4 count was 232 cells/ml (IQR 136–290) and median viral load 4.95 log copies/ml (IQR 4.43–5.43); 97.5% had disclosed status to at least one other person; 34.2% had moderate and 7.5% had severe symptoms of depression; 30.8% experienced moderate and 11.7% severe anxiety symptoms.

Conclusion | This cohort is typical of other ART cohorts in South Africa with a low starting CD4 count and a high proportion clinically unwell. Although most people have disclosed their status, a large proportion of the population are likely to be vulnerable to poor adherence through anxiety (42.5%) or depression (41.7%).

HO.14

Efficacy of third line ART in Africa: outcomes on ART salvage regimens in the Southern African private sector

Graeme Meintjes[1,2,3], Liezl Dunn[2], Marla Coetsee[2], Leon Regensberg[2], Michael Hislop[2], Gary Maartens[1,2]

1. University of Cape Town, South Africa; 2. Aid for AIDS Management, South Africa; 3. Imperial College, London, United Kingdom

Background | In sub-Saharan African (SSA) antiretroviral therapy (ART) programmes an increasing number of patients are failing second-line ART and will require third-line. Newer ART salvage regimens have been associated with virological efficacy in clinical trials comparable to first-line. No data exists on salvage regimens in SSA. Aid for AIDS (AfA) is a private sector HIV disease management programme operating in Southern Africa.
Methods | A retrospective observational study of adults (≥18 years) on the AfA programme who started salvage ART, July 2007–December 2011. Salvage ART was defined by inclusion of darunavir or tipranavir in an ART regimen after having failed another protease inhibitor and, in most, an NNRTI regimen. For Kaplan-Meier analysis patients were followed up until event, or censored at death (for virologic outcomes), leaving the programme or October 2012.
Results | 152 patients were included. All had a genotype resistance test demonstrating requirement for salvage therapy. Salvage drugs were: darunavir/ritonavir (n=149), tipranavir/ritonavir (n=3), raltegravir (n=58) and etravirine (n=8). Median follow-up was 1.6 years (IQR=1.2–2.3). Nine patients died; 22 left programme. 121/143 achieved a VL≤400 (85%) and 98/143 achieved a VL≤50 (69%). KM estimates of cumulative proportions suppressing to a VL≤400=94% and V ≤50=89%. The KM estimate of survival was 91%.
Conclusion | Virological suppression was comparable to that demonstrated in clinical trials of salvage therapy and few deaths occurred during short-term follow-up. Third line regimens for those with multidrug resistant HIV in the region are virologically and clinically effective.

HO.15

Benefits and risks of iron supplementation in HIV-infected Malawian children: results of a double-blind, randomised, controlled trial

Kamija Phiri[1], Michael Esan[2], Michael Boele van Hensbroek[2], Ernest Nkhoma[1], Crispin Musicha[1], Sarah White[3], Feiko ter Kuile[3]

1. University of Malawi, Malawi; 2. University of Amsterdam, The Netherlands; 3. LSTM, United Kingdom

Background | It is unknown whether iron supplementation in HIV-infected children, living in regions with high infection pressure is safe or beneficial. A 2-arm double-blind randomised, controlled trial was conducted to examine the effects of iron supplementation on haemoglobin, HIV disease progression and morbidity.

Methods | HIV-infected Malawian children aged 6–59 months with moderate anaemia (Hb 7.0–9.9 g/dl) were randomised to 3 mg/kg/day of elemental iron and multi-vitamins (Vitamins A, C and D) or multi-vitamins alone for 3 months. Participants were followed for 6 months.

Results | Two-hundred and nine (209) HIV-infected children were randomised and 196 (93.8%) completed six months follow-up. Iron supplementation was associated with greater increases in haemoglobin concentrations (g/dL) at 3 and 6 months: adjusted mean difference (aMD) (95% CI) 0.62 (0.20–1.04), p=0.004 and 0.60 (0.06–1.13), p=0.03, respectively; and with a reduced risk of iron deficiency by 3 months: adjusted prevalence-ratio (95% CI) 0.28 (0.15–0.49), p<0.001. Children who received iron had a better CD4 percentage response at 3 months: aMD (95% CI) 6.00 (1.84–10.16), p=0.005, but an increased incidence of clinical malaria: 20 *vs* 9 events, adjusted incidence rate ratio (aIRR) (95% CI) 2.68 (1.08–6.63), p=0.03 and 52 *vs* 33 events, aIRR (95% CI): 1.81 (1.04–3.16), p=0.04, by 3 and 6 months, respectively.

Conclusion | Iron supplementation in HIV-infected anaemic children has beneficial effects on haemoglobin, iron deficiency and immunity, but increases the risk of malaria. Iron supplementation in similar paediatric populations living in areas with a high infection pressure, should only be provided in combination with protection from malaria.

HO.16

CHAPAS 3: A randomised trial comparing two-year toxicity and efficacy of stavudine *vs* zidovudine *vs* abacavir as NNRTI-based fixed dose combination antiretroviral drug regimens for starting or substituting from stavudine-based antiretroviral therapy in 478 HIV-infected children in Uganda and Zambia

Veronica Mulenga[1]

1. University Teaching Hospital, Zambia

Recent study findings will be presented.

HO.17

Cardiovascular structure and function in HIV-infected children in Zambia and Uganda: CHAPAS-3 trial

Grace Mirembe[1], Victor Musiime[1], Dorica Masaku[2], Dorothy Kavindele[2], Odongo Florence[1], Priscilla Wavamunno[1], Alicja Rapala[3], Veronica Mulenga[2], Cissy Kityo[1], Adrian Cook[4], Margaret Thomason[4], Diana M. Gibb[4], Nigel Klein[5], Julia Kenny[3,5]

1. JCRC Kampala, Uganda; 2. UTH, Zambia; 3. University College London, United Kingdom; 4. MRC CTU, United Kingdom; 5. University College London, United Kingdom

Background | Carotid intima-media thickness (cIMT) and pulse wave velocity (PWV) measure vascular structure and function. Caucasian HIV-infected children have abnormal cIMT values that may be related to HIV, antiretroviral therapy (ART), obesity or lifestyle factors. There are no studies from Africa where 90% of HIV-infected children live. We describe baseline results in Zambian/Ugandan children younger than 13 years of age enrolled in the CHAPAS-3 Trial.
Methods | All cooperative children had cIMT/PWV measurements at baseline. Differences between ART-naïve, ART-experienced (on d4T >2years) and HIV-uninfected children, accounting for age and ART duration, were analysed using linear regression.
Results | A total of 191 ART-naïve and ART-experienced (128:63) children had cIMT and 214 (141:73) had PWV measurements. In the ART-naive group, median age was 2.9(0.3–13.6); median CD4% 18(0–47), and CD4 count 749 (5–4639). In the ART-experienced group, median age was 6.9(5.1–12.2); median CD4% 33(10–51), and CD4 count 964(101–2794). PWV was measured in 101 HIV-uninfected children. HIV-infected children had higher PWV than HIV-uninfected; mean PWV was 5.74m/s *vs* 5.41 m/s (95% CI: 5.55, 5.72; p=0.0003). In ART-naïve *vs* ART-experienced children, mean cIMT was 0.462mm *vs* 0.467mm (95% CI: –0.01, 0.02; p=0.39) and PWV was 5.798m/s *vs* 5.627m/s (95% CI: –0.39, 0.05; p=0.12), with a non-significant increase with age cIMT (p=0.08) PWV (p=0.09). ART duration (median 3.9 years) did not influence cIMT (p=0.2) or PWV (p=0.5).
Conclusion | In this paediatric African population there is evidence of increased arterial stiffness in HIV-infection. ART exposure had no significant effect on vascular structure and function. Ongoing serial measurements, more control data, lipid levels and markers of inflammation may provide insight into mechanisms of vascular injury in HIV-infection.

HO.18

Anthropometric measurements and lipid profiles to detect early lipodystrophy in antiretroviral therapy experienced HIV-infected children in the CHAPAS-3 trial

Victor Musiime[1], A. Cook[2], J. Kayiwa[1], D. Zangata[3], C. Nansubuga[4], B. Arach[5], J. Kenny[2,6], P. Wavamunno[1], J. Komunyena[4], Desire Kabamba[3], A.R. Asiimwe[4], G. Mirembe[1], G. Abongomera[5], Veronica Mulenga[3], A. Kekitiinwa[4], C. Kityo[1], S.A. Walker[2], N. Klein[6], D.M. Gibb[2], on behalf of the CHAPAS-3 Trial team

1. JCRC Kampala, Uganda; 2. MRC CTU, United Kingdom; 3. UTH, Zambia; 4. BIPAI Uganda Mulago, Uganda; 5. JCRC Gulu, Uganda; 6. University College London, United Kingdom

Background | We compared body circumferences, skinfold thickness (SFT) and lipids in antiretroviral therapy (ART)-naïve and d4T-exposed children with HIV-uninfected controls.
Methods | HIV-infected children (ART-naïve or on d4T for ≥2years) were randomised to d4T, abacavir (ABC) or zidovudine (ZDV) with lamivudine plus NNRTI. Mid-upper arm (MUAC) and calf (CC) circumferences, SFT (biceps, triceps, sub-scapular, supra-iliac) and fasting lipids (total-cholesterol (TC), low-density-lipoprotein (LDL), high-density-lipoprotein (HDL), triglycerides (TRIG)) were measured at randomisation in all HIV-infected children, and in HIV-uninfected controls. Age/sex-adjusted z-scores of MUAC, CC, SFT and the sum-of-SFT (SSF) using Dutch references were compared across groups.
Results | Of 496 children, 49% male, n (median age (years); IQR): 299 (2.5; 1.5–4.0) were ART-naïve, 109 (6; 5.5–7.0) were ART-experienced and 88 (2.2; 1.5, 3.0) were control children. Mean (SD) weight-for-age z-scores (WAZ) and MUAC were –1.51 (1.29) *vs* –0.90 (0.88) *vs* –0.33 (1.15) and –1.56 (1.25) *vs* –1.24 (0.97) *vs* –0.65 (1.06) in naïve *vs* experienced *vs* controls respectively (all $p<0.02$). The mean (SD) of SSF were lower in the ART-experienced –0.78 (1.28) than in the ART-naïve –0.32 (1.09; $p<0.0001$) children and controls –0.29 (0.88); $p<0.002$). ART-experienced children had higher mean fasting TC, LDL and HDL but lower TRIG compared to ART-naïve ($p<0.0001$); and higher TC and HDL but lower TRIG compared to controls ($p<0.01$).
Conclusion | In ART–experienced children, lower SFT and higher TC and LDL values are likely d4T-related. During trial follow-up, we are evaluating the effect of ABC, ZDV versus d4T on lipodystrophy measurements in ART-naïve and reversibility in ART-experienced children who substituted d4T for ZDV/ABC.

HO.19

Assessment of peripheral neuropathy among HIV-infected children on fixed-dose antiretroviral therapy in Zambia and Uganda: the CHAPAS-3 randomised clinical trial

Chishala Chabala[1], Adrian Cook[2], Julia Kenny[2,3], Musaku Mwenechanya[1], Grace Mirembe[4], Victor Musiime[4], Violet Korutaro[5], Vincent Tukei[5], Alice Asiimwe[5], James Abach[6], George Abongomera[6], Veronica Mulenga[1], Addy Kekitiinwa[5], Cissy Kityo[4], Margaret Thomason[2], Diana Gibb[2], on behalf of the CHAPAS-3 Trial team.

1. UHT, Zambia; 2. MRC CTU, United Kingdom; 3. University College London, United Kingdom; 4. JCRC Kampala, Uganda; 5. BIPAI Uganda Mulago, Uganda; 6. JCRC Gulu, Uganda

Background | Peripheral neuropathy (PN) is common in HIV/AIDS and a well-recognised adverse effect of some antiretrovirals and of isoniazid prophylaxis. We developed a tool for PN assessment among children on antiretroviral therapy (ART) in the open-label Zambian/Ugandan CHAPAS-3 trial.

Methods | We recruited 478 HIV-infected children and randomised them to zidovudine/stavudine/abacavir with lamivudine and nevirapine or efavirenz as fixeddose or single, scored, dispersible solid formulations. Blinded assessment of PN was introduced at 96 and 144 weeks (earlier if starting isoniazid prophylaxis). A 6-point neuropathy symptom score (NSS) questionnaire was first piloted in Zambia, based on gait unsteadiness, pain, numbness, foot discomfort. A 10-point neuropathy disability score (NDS) used ankle reflex, temperature, vibration and pin-prick perception.

Results | In the Zambian pilot, PN assessment of each child took approximately 10–15 minutes. Among 176 children recruited by April 2013 from all centres, 116 (66%) were ART-naïve at CHAPAS-3 enrolment; median age at PN assessment was 6.2 years (IQR 4.2–7.6); 91 (52%) were males. NSS was completed in 141 (80%) children and NDS in 135 (77%); 130 (74%) children had both. NSS was based on history from the carer, child or both in 74 (43%), 57 (33%) and 42 (24%), respectively. Overall 29 assessments were incomplete, NDS most frequently missing. Age ≥5 years was significantly associated with complete PN assessment ($p<0.001$). To date, 3/141 had not any abnormal NSS score and 117/135 (87%) had a zero disability score.

Conclusion | Assessment of PN among HIV-infected children is feasible. Completed data will highlight the burden of PN and compare children never exposed to stavudine with those with current and past exposure.

HO.20

Cognition abilities and daily life functioning of HIV-infected subjects on antiretroviral therapy

Guy Bumoko[1], Robert Mussa[1], Marie-Thérese Sombo[1], Félicien Itakala[1], Gilbert Lelo[1], Gustave Bukasa[1], Tharcisse Kayembe[1], Desiré Tshala-Katumbay[1,2]

1. University of Kinshasa, Democratic Republic of Congo; 2. Oregon Health & Science University, United States of America

Background | The study aims to assess the impact of front-line HIV antiretroviral drugs on cognition and daily functioning of HIV-infected subjects.
Methods | Neuropsychological evaluation of 200 HIV-infected subjects (age 40.6 ± 10.6 years, mean nadir CD4 185.9 ± 179.9/ml, and duration of infection ranging 2 to 18 years). The evaluation was carried out with the scales for HIV dementia (HDS) and the instrumental activities of daily living (IADLs). Subjects under highly neuroactive drugs were compared to those treated with poorly neuroactive drugs as per their central nervous system penetration-effectiveness scores. Statistical analysis was performed using a logistic regression analysis at the significance level of 0.05.
Results | The level of education, occupation, nadir CD4, and the type of treatment regimen were significantly associated with the degree of cognitive impairments ($p < 0.01$). Subjects under poorly neuroactive drugs and cognition deficits were more likely to be dependent in their daily functioning, mostly with regards to adherence to treatment regimen ($p < 0.01$). The odds ratios of being under poorly neuroactive drugs or having impaired cognition were 3.4 (95% CI: 1.2–43.3) and 11.8 (95% CI: 2.47–28.08) with respect to functional dependency; or 2.8 (95% CI: 1.11–7.15) ($p < 0.01$) for poorly neuroactive drugs after adjusting for treatment regimen.
Conclusion | Poorly-neuroactive HIV antiretroviral drugs are associated with poor cognition, dependency in daily functioning of subjects, and risk of non-adherence to treatment. These findings need to be integrated with global health policies to control the HIV/AIDS pandemic.

HO.21

Incidence and predictors of first-line antiretroviral regimen modification in western Kenya

Seth Inzaule[1], Juliana Otieno[3], Joan Kalyango[2], Lillian Nafisa[1], Charles Kabugo[2], Josephine Nalusiba[2], Daniel Kwaro[4], Clement Zeh[4], Charles Karamagi[2]

1. KEMRI, Kenya; 2. Makerere University, Uganda; 3. JOOTRH, Kenya; 4. CDC, Kenya; 5. CDC, United States of America

Background | Limited antiretroviral treatment regimens in resource-constrained settings require long-term sustainability of patients on the few available options. We evaluated the incidence and predictors of combined antiretroviral treatment (cART) modifications, in an outpatient cohort of 957 patients who initiated cART between January 2009 and January 2011 in western Kenya.
Methods | Modification of cART was defined as either first-time single drug substitution or switch. Incidence and predictors of modifications were analysed by time-to-event approaches.
Results | Over a median follow-up period of 10.7 months, 179 (18.7%) participants modified regimens (incidence rate (IR): 18.8 per 100 person years 95% CI: 16.3–21.8). Incidence was higher in the first year post-cART (IR: 44.1 95% CI: 36.7–53.0) compared with second (IR: 11.4 95% CI: 8.8–14.8) and third years (IR: 3.8 95% CI: 1.8–8.0). Toxicity was the most common cited reason (65.9%). In an adjusted multivariate Cox piecewise regression model, low baseline CD4 counts ≤100 cells/mm^3 (aHR: 1.90, 95% CI: 1.10–3.27), WHO disease stage 3–4 (aHR: 1.54, 95% CI: 1.01–2.36), stavudine (d4T) and increase in age (aHR: 1.02, 95% CI: 1.0–1.04) increased risk of cART modification within first 10 months post-cART. Beyond 10 months, d4T (aHR: 3.44 95% CI: 1.58–7.49), baseline CD4 counts ≤100 cells/mm^3 (aHR: 2.16, 95% CII: 1.14–4.08), increase in age (aHR; 1.04 95% CII: 1.02–1.06) and high baseline weight >60 kg (aHR: 2.09 95% CI: 1.33–3.32) were associated with risk of modification. Zidovudine use had a reduced risk (aHR: 0.31 95% CI: 0.11–0.86).
Conclusion | Early cART initiation at higher CD4 counts and avoiding d4T use may reduce treatment modification rate and subsequently improve durability of first-line regimens.

HO.22

Correlates of separation among HIV-serodiscordant couples enrolled in partners PrEP study site clinic in Eldoret, western Kenya

Ismail Mbowo[1], N. Murgor[1], D. Oketch[1], E. Kaguiri[1], D. Jaleny[1], C. Kibet[1], L. Nambuchi[1], B. Meli[1], J. Kipyego[1], A. Komen[1], C. Apaka[1], J. Baliddawa[1], E. Were[1]

1. Moi University, Kenya

Background | HIV discordancy is a difficult experience that may result in separations. This study sought to assess factors contributing to separations among HIV-serodiscordant couples enrolled in the Partners PrEP study at the Eldoret site.

Methods | The PrEP Study was a multisite study in Kenya and Uganda. Couples in the main study were being followed for up to 36 months. This was a cross-sectional study of healthy 488 heterosexual HIV1-serodiscordant couples from western Kenya enrolled at the Partners PrEP study clinic in Eldoret between September 2008 and December 2010. During the follow-up, ongoing couple counselling was done to ascertain factors that contributed to separations. Data on age, level of education, alcohol consumption, income and duration of marriage were collected as part of screening. Descriptive analysis was done to determine the frequency of separations. Inferential analysis was used to evaluate the association between separation and social demographics.

Results | Out of 488 couples, 46 couples reported to have separated. Participants aged between 26 and 35 were more likely to separate compared to those aged under 25 years (p=0.001, OR=2.8, 95% CI: 1.2–6.5). Those married for more than 6 years were less likely to separate compared to those married for less than 2 years (p=0.001, OR=0.26, 95% CI: 0.15–0.43) while alcohol users were 2 times more likely to separate compared to the alcohol non-users (p=0.003, OR=2.22, 95% CI: 1.31–3.76). At multivariate level, only alcohol intake was associated with separation (p=0.001, OR=3.16, 95% CI: 1.67–5.9).

Conclusion | Focused counselling messages should be developed to target alcohol users, the young and the newly married couples to reduce separation among HIV-discordant couples.

HO.23

Nutritional intervention to reduce early mortality in HIV-infected African adults starting antiretroviral therapy

Suzanne Filteau[1], Joshua Siame[2], George PrayGod[3], Andrea M. Rehman[1], Susannah Woodd[1], Molly Chisenga[2], John R. Koethe[4], Douglas Heimburger[4], Henrik Friis[6], Paul Kelly[5]

1. LSHTM, United Kingdom; 2. UTH, Zambia; 3. NIMR, Mwanza, Tanzania; 4. Vanderbilt University, United States of America; 5. University of Copenhagen, Denmark, 6. QMUL, United Kingdom.

Background | The NUSTART trial investigated whether procedures similar to those for refeeding severely malnourished children can reduce the high early mortality observed among malnourished (body mass index <18.5 kg/m^2) HIV-infected African adults starting antiretroviral therapy (ART). Secondary outcomes included serious adverse events, CD4 count at 12 weeks ART, and anthropometry at 12 weeks.
Methods | HIV-infected Zambian and Tanzanian adults (n=1815) were recruited if they were ART-naive, required ART (CD4 <350/ml or stage 3 or 4 AIDS), had BMI <18.5 kg/m^2, were not pregnant, and provided informed consent. Participants were randomised to receive a lipid-based nutritional supplement (LNS) either without or with (LNS-VM) high levels of vitamins and minerals; supplements were provided in low calories from recruitment to week 2 ART and in high calories from weeks 2–6 ART.
Results | Follow-up for the primary outcome was 91%. There were 184 deaths in the VM-LNS arm, 82.5/100 person-years, and 181 deaths in the LNS arm, 83.7/100 person-years; crude rate ratio 0.99 (95% CI 0.80, 1.21; P=0.89). The increase in CD4 count from referral to 12 weeks was 152/ml (95% CI 136, 168) in the LNS-VM arm and 128/ml (95% CI 114, 141) in the control LNS arm; P=0.02. There were significant increases in waist, hip and calf circumferences in the LNS-VM compared with the LNS group.
Conclusion | The intervention did not decrease mortality but did improve CD4 and anthropometry, both secondary outcomes associated with faster recovery from malnutrition and HIV/AIDS.

HO.24

Twelve-month virological response in children initiated on lopinavir-containing antiretroviral therapy before 2 years of age in Abidjan, Côte d'Ivoire and Ouagadougou, Burkina Faso

Valériane Leroy[1], M. Coulibaly[1], C. Amani-Bossé[1], C. Devaux[4], A. Emieme[2,5], R. Ouedraogo[6], P. Van de Perre[7], N. Meda[3,8], M. Timité-Konan[2,9], S. Blanche[10]

1. Université Bordeaux Segalen, France; 2. PAC-CI, Côte d'Ivoire; 3. CRIS, Burkina Faso; 3. CRP-Santé, Luxembourg; 5. CeDReS, Côte d'Ivoire; 6. CHUCG, Burkina Faso; 7.Université Montpellier 1, France; 8. Université de Ouagadougou, Burkina Faso; 9. CePReF Yopougon, Côte d'Ivoire; 10. Université Paris Descartes, France

Background | In 2011, we launched a randomised controlled clinical trial to evaluate how to simplify ART in HIV-infected children initiated on ART before 2 years of age (ANRS 12206 MONOD trial) in Ouagadougou, Burkina Faso and Abidjan, Côte d'Ivoire.
Methods | All HIV-infected children diagnosed before 24 months of age were enrolled in an initial 12-month therapeutic cohort offering a first-line triple therapy based on LPV/r before randomisation in a simplification trial assessing a once daily triple therapy based on Efavirenz (EFV) for those virologically suppressed. Viral load (VL) was measured 3-monthly using a Biocentric RT-PCR. We measured the virological success at 12 month (2 VL <400 copies on 2 separate samples at 3-month interval), repeated at 15 months for those have 1 sample >1000 copies.
Results | In the context of low early infant diagnosis coverage, 226 HIV-infected children <2 years of age, were screened. Among them, 162 (72%) children were enrolled and initiated on ART. The baseline characteristics were as follows: median age at diagnosis and ART initiation were 8.6 months (IQR: 4.1 to 16.2) and 13.8 months (IQR: 8.3 to 18.6), respectively; 64% were from Abidjan; 54% were girls; 55% were not exposed to a prevention of mother-to-child transmission intervention; median CD4% was 20 (IQR: 14–26); median viral load was 6 log copies/ml (IQR: 6–7); 39.5% were classified WHO-stage 3, and 17.3% WHO-stage 4; 38.2% were severely malnourished. As of 31 November 2013, 71 of the 103 children who made their 12-month visit (69%; 95% confidence interval [CI]: 60.1%-77.9%) were virologically suppressed, and 7 more at 15 months 76% (95%CI: 67.8%-84.2%).
Conclusion | Challenges still remain for improving early identification of HIV-infected children in West Africa. Nevertheless, rate of virological success on LPV-ART therapy was high and comparable to those observed in South Africa or North cohorts.

HO.25

Using WHO 2010 dosing guidelines, efavirenz levels remain slightly lower and highly variable in Ugandan and Zambian children weighing 10–20 kg

Vincent Tukei[1], Quirine Fillekes[2], Sarah Walker[2], Margaret J. Thomason[2], David Burger[2], Diana Gibb[3]

1. BIPAI Uganda Mulago, Uganda; 2. Radboud University Nijmegen, The Netherlands; 3. MRC CTU, United Kingdom

Background | WHO-2010 guidelines for weight-band-based efavirenz dosing have not been evaluated in pharmacokinetic studies. Scored efavirenz tablets, that provide 200 mg, 300 mg, 400 mg divided pill doses, also await evaluation.

Methods | Thirty-one (31) HIV-infected Ugandan and Zambian children, weighing 10–20 kg and taking generic double-scored efavirenz tablets plus lamivudine/abacavir or lamivudine/zidovudine were enrolled in a pharmacokinetic study in the CHAPAS-3 trial. The once daily efavirenz doses were 200 mg and 300 mg for those weighing 10–<14 kg and 14–<20 kg, respectively. Intensive pharmacokinetic plasma sampling (t=0, 1, 2, 4, 6, 8, 12 and 24 hours after observed intake) was performed 6-weeks after ART initiation. Area under the curve (AUC_{0-24}), maximum concentration (C_{max}) and trough levels (C_{24h}) were analysed.

Results | Twenty-nine (29) children had evaluable efavirenz profiles in the 10–<14 kg (n=11)/14–<20 kg (n=18) weight-bands; 17 (57%) were boys; median (interquartile range) age was 4.6 (3.9–5.0) years. The geometric mean (95% CI) AUC_{0-24} was 46.5 (29.4–73.6) and 49.7 (30.9–79.9) h×mg/L for weight-band 10–<14 and 14–<20 kg respectively, compared to 58 h×mg/L in adults. There was no significant variation in any pharmacokinetic parameters between the weight-bands (rank-sum p>0.6). However, variability was high with CV% 133%, 104% and 156% for AUC_{0-24}, C_{max} and C_{24h}, respectively. 1/11 (9%) children (10–<14 kg) had a subtherapeutic C_{8h} and/or C_{12h} (<1.0 mg/L) and 3/11 (27%) had a supratherapeutic C_{8h} and/or C_{12h} (>4.0 mg/L). 4/18 (22%) children (14–< 20 kg) had a subtherapeutic C_{8h} and/or C_{12h} and 5/18 (28%) had a supratherapeutic C_{8h} and/or C_{12h} (exact p=0.87).

Conclusion | Efavirenz pharmacokinetic parameters in African children weighing 10–20 kg, on daily efavirenz using current 2010 WHO weight-bands and double-scored tablets, were lower and more variable than data from adults.

HO.26

Sub-optimal CD4 T cell recovery in HIV-1 subtype C patients on antiretroviral therapy: a search for predictive biomarkers and baseline characteristics

Gaone Retshabile[1], Elton Richard Kisanga[2], Simani Gaseitsiwe[1], Sikhulile Moyo[1], Hermann Bussmann[1], Joseph Makhema[1], Max Essex[3], Ric Marlink[3], Rosemary Musonda[1]

1. BHP, Botswana; 2. KCMC, Tanzania; 3. Harvard, United States of America

Background | Despite suppressive antiretroviral therapy some 15–30% of treated HIV-infected patients fail to achieve optimal CD4 T cell recovery. Sub-optimal CD4 recovery has been associated with unfavourable outcomes for patients on treatment. We assessed markers of immune activation, microbial translocation and patient baseline characteristics for associations with sub-optimal CD4 T cell recovery after treatment initiation.

Methods | This was a retrospective case control analysis based on the 'Adult Antiretroviral Treatment and Drug Resistance' study, in Botswana. Cases had CD4 ≤200 cells/µl 12 months post ART initiation and virological suppression within 6 months. Microbial translocation (sCD14) and immune activation markers (interferon-gamma) were quantified using ELISA assays on a subset of plasma samples (30 cases and 30 controls each). Analyses of associations with sub-optimal response were based on Mann-Whitney test, univariate and multivariate logistic regression.

Results | Twenty-one per cent (21%) of virologically suppressed participants (51/249) had sub-optimal CD4 recovery. Median age was 33.4 years and 69.9% were female. Baseline CD4 count below 100 cells, Zidovudine, aspartate transaminase were associated with sub-optimal recovery: adjusted OR=3.02 95% CI [1.64, 5.53], p<0.001; aOR=2.34 [1.08, 5.08], p=0.031 and aOR=1.03 [1.01, 1.06], p=0.008 respectively. The sCD14 levels were significantly different between cases and controls, p=0.011 at 12 months.

Conclusion | Baseline CD4 count, Zidovudine, aspartate transaminase and sCD14 are predictive of sub-optimal CD4 T cell recovery in this HIV-1 subtype C-infected cohort. These characteristics are potentially useful in identifying patients needing frequent monitoring to minimise unfavourable outcomes associated with poor CD4 T cell recovery.

HO.27

HIV-1 multiple infection and disease progression in a cohort of female sex workers in Uganda

Deogratius Ssemwanga[1], Andrew D. Redd[2], Sarah K. Wendel[2], Yunia Mayanja[1], Nicaise Ndembi[1], Judith Vandepitte[1], Heiner Grosskurth[1], Chris M. Parry[1], Jonathan Levin[1], Craig Martens[3], Daniel Bruno[3], Stephen F. Porcella[3], Thomas C. Quinn[2], Pontiano Kaleebu[1]

1. MRC-UVRI AIDS, Uganda; 2. NIAID NIH Baltimore, United States of America; 3. NIH NIAID Hamilton, United States of America

Background | Infection with multiple strains of HIV-1 has been documented, yet the clinical effect is unclear. We set out to compare the rate of disease progression, as measured by the rate of decline in CD4 counts, between women infected with multiple HIV strains and women infected with a single HIV-1 strain.
Methods | The rate of decline in CD4 counts over time was compared between women with multiple HIV-1 infections and those with a single infecting strain by fitting linear mixed models for repeated measurements allowing for both random intercepts and random slopes.
Results | Among 381 participants who were HIV-infected at baseline, 7 were found to be infected with multiple strains of HIV-1 and a further 7 were later infected with a different strain (i.e. were super-infected). For purposes of this analysis, these 14 participants were considered to have multiple infections and were compared to 247 participants who were infected with a single strain and who had sufficient follow-up visits (>2) before initiation of ART to allow the rate of CD4 decline to be estimated. The rate of CD4 decline was marginally significantly (P=0.089) higher on average in those participants with multiple infections (42.8 cells/µl per year) than among those with a single infecting strain (21.8 cells/µl per year).
Conclusion | The high rate of multiple infections is a reflection of continued risky behaviour in this population. The observed increase in disease progression among the multiple-infected individuals highlights the public health importance of HIV-1 prevention interventions even among infected individuals.

HO.28

Plasma cytokine levels in chronic asymptomatic HIV-1 subtype C infection as an indicator of disease progression in Botswana: a retrospective case control study

Thato Iketleng[1,3], Balthazar Nyombi[3], Sikhulile Moyo[1], Simani Gaseitsiwe[1,2], Rebecca M. Mitchell[5], Marianna K. Baum[4], Richard Marlink[2], Max Essex[2], and Rosemary Musonda[1,2]

1. BHP, Botswana; 2. Harvard, United States of America; 3. KCMC, Tanzania; 4. Florida International University, United States of America; 5. Cornell University, United States of America

Background | Understanding the influence of cytokines on HIV/AIDS disease progression may inform approaches for vaccine development and could potentially provide new tools to control disease progression through cytokine stimulation or inhibition. We characterised plasma cytokine concentration profiles in chronically HIV-1C-infected, ART-naïve participants and established their influence on disease progression.

Methods | Plasma levels of IL-1α, IL-7, IL-12p40, GMCSF and IFNγ were quantified by ELISA in 60 treatment – naïve participants stratified into progressors (P) and non-progressors (NP) based on their rates of CD4+T cell depletion during a two year longitudinal follow-up. NP and P were defined as those that had <1% and >15% CD4 T cell depletion respectively at 24 months post enrolment.

Results | Median IL-12p40 levels were significantly higher in the P than in NP at enrolment and 24 months ($p < 0.05$), but not significantly different at 12 months ($p=0.1276$). IL-12p40 displayed an inverse correlation with CD4+ T cell counts ($r=-0.45$; $p=0.0009$) and a positive correlation with viral load ($r=0.49$; $p < 0.0001$).

Conclusion | IL-12p40 was the most significant predictor of progression and its production was most likely driven by HIV replication products as evidenced by its direct correlation with viral load. In chronic HIV, CD4+ T cell counts, viral loads and plasma cytokine levels may not necessarily evolve in parallel, suggesting the involvement of other factors in determining the CD4+ T cell depletion rates and the ability to control viraemia.

HO.29

The need for multipurpose prevention technologies targeting HIV and common reproductive tract infections: data from the Microbicide Safety Biomarkers study

Mary Mwaura[1], L. Hardy[1], S. Delany-Moretlwe[1], G. Ndayisaba[1], K. Mandaliya[1], P. Cools, R. Verhelst[1], J. van de Wijgert[1], T. Crucitti, V. Jespers[1]

1. ICHR, Kenya

Background | Future microbicides and multipurpose prevention technologies could improve maternal reproductive health in developing countries. Effective products should reduce the risk of HIV infection and other reproductive tract infections (RTIs) while preserving the cervicovaginal epithelium.

Methods | The Microbicide Safety Biomarkers study is a prospective cohort study of 110 adults, 30 adolescents and 30 pregnant women both in Kenya and South-Africa, 30 women engaging in vaginal practices in South Africa and 30 high-risk and 30 HIV-positive women in Rwanda. Vaginal specimens were examined for RTIs and *Lactobacilli*. *Gardnerella vaginalis* and *Atopobium vaginae* were assessed by quantitative PCR (qPCR).

Results | Out of 376 women, 55.3% had normal Nugent scores, 7.7% intermediate and 34.6% BV scores; qPCR found a significant difference in prevalence of species in the three Nugent groups (p=<0.001). *Lactobacillus iners* and *L. vaginalis* were most frequently detected in women with normal Nugent scores. The percentage of women harbouring lactobacilli was near absent in the BV group, except for *L. iners*. A significant difference (p=0.027 to 0.001) between the study groups was present for all RTIs except for *Trichomonas vaginalis*. *Neisseria gonorrhoeae*, syphilis and HSV-2 were associated (p=<0.001) with sexual risk taking behaviour. HSV-2 was detected in 51.5% of the high risk-takers compared to 28.6% of the low risk-takers.

Conclusion | This study found a higher presence of *L. vaginalis* compared to *L. crispatus*. Furthermore, RTIs were common among African women targeted for microbicide trials. Therefore, introduction of microbicides or multipurpose prevention technologies targeting prevention of HIV and HSV-2 is warranted in these populations.

HO.30

Prevalence, incidence and determinants of *Herpes simplex* virus type 2 infection among HIV-seronegative women at high risk of HIV infection: a prospective study in Beira, Mozambique

Ivete Meque[1], Karine Dubé[2,3], Paul J. Feldblum[2], Archie C.A. Clements[4] , Arlinda Zango[1], Fidelina Cumbe[1], Pai Lien Chen[2], Josefo J. Ferro[1], Janneke van de Wijgert[5,6]

1. UCM CIDI, Mozambique; 2. FHI 360, United States of America; 3. MHRP-HJF, United States of America; 4. University of Queensland, Australia; 5. AIGHD and AMC, The Netherlands; 6. University of Liverpool, United Kingdom

Objectives | To estimate the prevalence, incidence and determinants of herpes simplex type 2 (HSV-2) infection, and associations between HSV-2 and incident HIV infection, among women at higher risk for HIV infection in Beira, Mozambique.

Methods | Between 2009 and 2012, a total of 411 women aged 18–35 years at higher risk of HIV acquisition (defined as having had two or more sexual partners in the month prior to study enrolment) were enrolled and followed up monthly for one year. At each study visit, they were counselled, interviewed, and tested for HSV-2 and HIV antibodies.

Results | The HSV-2 prevalence at baseline was 60.6% (95% CI: 55.7%–65.4%). Increasing age (aOR=2.94, 95% CI: 1.74–4.97, P <0.001 and aOR=3.39, 95% CI: 1.58–7.29, P=0.002 for age groups of 21–24 and 25–35 years old respectively), lower educational level (aOR=1.81, 95% CI: 1.09–3.02, P=0.022), working full time (aOR=8.56, 95% CI: 1.01–72.53, P=0.049) and having practiced oral sex (aOR= 3.02, 95% CI: 1.16–7.89, P=0.024) were strongly associated with prevalent HSV-2 infection. Thirty-one (31) participants seroconverted to HSV-2 (20.5%; 95% CI: 14.4%–27.9%) and 22 for HIV during the study period. The frequency of vaginal sex with a casual partner using a condom in the last 7 days was independently associated with incident HSV-2 infections (aOR=1.91, 95% CI: 1.05–3.47, P=0.034). Positive HSV-2 serology at baseline was not significantly associated with risk of subsequent HIV seroconversion.

Conclusion | Young women engaged in risky sexual behaviours in Beira had a high prevalence and incidence of HSV-2 infection. Improved primary HSV-2 control strategies are urgently needed in Beira.

HO.31

Molecular characterisation of hepatitis B virus in HIV-coinfected patients in Botswana

Motswedi Anderson[1], Simani Gaseitsiwe[1], Sikhulile Moyo[1], Terence Mohammed[1], Theresa K. Sebunya[2], Jason Blackard[3], Joseph Makhema[1], Max Essex[1,4], Rosemary Musonda[1]

1. BHP, Botswana; 2. University of Botswana, Botswana; 3. University of Cincinnati, United States of America; 4. Harvard, United States of America

Background | The hepatitis B virus (HBV) is a major coinfection in HIV-infected patients affecting 10% of the patients and it has emerged as the number one cause of death in HIV-infected patients since the start of highly active antiretroviral therapy (HAART). Ten (10) HBV genotypes have been described differing by geographic distribution, course of disease and response to treatment. Data on the prevalence of HBV genotypes in Botswana, a high HBV and HIV endemic country is non-existent. This study aims at characterising HBV in HIV-coinfected patients in Botswana.

Methods | DNA was extracted from stored plasma from 31 HbsAg-positive and HIV-positive participants recruited for various clinical studies at BHP. A 415 base pairs fragment of the polymerase gene was amplified by semi-nested PCR. The PCR product was genotyped using Big Dye® sequencing chemistry and the sequences were analysed for subtypes and drug resistance mutations. Demographic and clinical data for the participants was collected.

Results | Of the 23 samples that were successfully genotyped, genotype A was found in 12 (52.1%) participants whereas 11 (47.8%) were genotype D. No drug resistance mutations were detected in the 23 participants of whom 84% were females. The median age, CD4 count, viral load, AST and ALT at HBV diagnosis were 31, 306.5 cells/µl, 167,000 copies/ml, 32.5, 26.9, respectively.

Conclusion | Only HBV genotypes D and A were found in this cohort of HIV-coinfected patients in Botswana, consistent with findings from Southern African region. No known drug resistance mutations were found, but more representative data is needed to be able to generalise this to the population.

HO.32

Toll-like receptor 4 polymorphisms in Botswana and impact on susceptibility to Kaposi's sarcoma in HIV-1 subtype C-infected patients

Lerato Magosi[1], Simani Gaseitsiwe[1], Terence Mohammed[2], Bokang Rabasha[2], Sikhulile Moyo[1], Rosemary Musonda[1], Vlad Novitsky[2], Max Essex[2]

1. BHP, Botswana; 2. Harvard, United States of America

Background | Toll-like receptors (TLRs) are an essential part of the innate immune system. Following an invasion by pathogens, TLRs trigger a signalling cascade that culminates in the onset of host defence. Of concern, the A-896-G single nucleotide polymorphism in TLR4 influences susceptibility to AIDS defining diseases. A baseline study was carried out to determine the frequency of the A-896-G TLR4 variant in Botswana and to examine its influence on susceptibility to Kaposi's sarcoma (KS).

Methods | A total of 236 participants were selected from an on-going study in Botswana entitled 'host genetics of HIV-1C infection, progression and treatment in Africa'. Of these, 160 participants were HIV+ and 36 had KS. Real-time PCR and direct sequencing were employed to genotype TLR4.

Results | The genotypic frequency of TLR4 (A-896-G) was as follows: AA=0.928, AG=0.072 and GG=0 in line with Hardy Weinberg Equilibrium. Consistent with the haplotype distribution map, a minor allele frequency (G) of 0.036 was attained. There were no differences in minor allelic frequency between HIV+ and HIV-subjects. Moreover, no substantial links were observed between HIV status and presence of A-896-G (Odds Ratio: 0.861; 95% CI: 0.279–2.96). Although the A-896-G TLR4 variant was more apparent in the HIV+/KS– (10/104) than the HIV+/KS+ (1/36), no statistically significant relationship was observed between A-896-G and KS (Odds Ratio: 0.277; 95% CI: 0.00620–2.11).

Conclusion | Therefore, the link between the functional TLR4 (A-896-G) polymorphism and opportunistic infection may not extend to KS. Notably, this study is the first to genotype TLR4 (A-896-G) in Botswana.

HO.33

Screening for cryptococcal meningitis in patients with advanced HIV infection: the role of serum cryptococcal antigen test

Bernard Ngowi[1], Godfather Kimaro[1], Lorna Guinness[3], Victoria Simms[3], Sayoki Mfinanga[1], Shabbar Jaffar[3], Sokoine Lesikari[1], Amos Kahwa[1], Sode Matiku[4], Duncan Chanda[2], Saidi Egwaga[4]

1. NIMR, Tanzania; 2. UTH, Zambia; 3. LSHTM, United Kingdom; 4. NLTP, Tanzania

Background | Cryptococcal meningitis is a major cause of death among HIV-infected subjects. We are conducting a large trial of a complex health services intervention in Tanzania and Zambia, aimed at reducing the high mortality among people starting ART with advanced HIV/AIDS disease, which involves screening for cryptococcal meningitis.

Methods | ART-naïve patients presenting with a CD4 count lower than 200 cells/µl, were randomised to the intervention, comprising cryptococcal meningitis screening with a serum antigen test and 4–6 weeks of support by lay-workers or standard care. Here we report on the prevalence of cryptococcal meningitis among HIV/AIDS patients in the intervention arm.

Results | In total 654 subjects from the intervention arm were eligible for the cryptococcal antigen test (300 male and 354 female; mean age 36.8, IQR 30–42). A cryptococcal antigen test was done for 646 subjects and 36 subjects did not take the test due to the fact that the test kits at the time of recruitment were out of stock. Twenty-nine out of 646 (4.9%) had a positive serum cryptococcal result: prevalence was 4.7% (n=13) among patients with CD4 <50 cells/µl; 5.3% (n=13) among those with CD4 51–100 cells/µl; and 2.4% (n=3) among those with 101–200 cells/µl. Fifteen (15 or 51.7 %) of the cryptococcal-antigen-positive were in WHO clinical stage 3. Only 31% (9 of 29) agreed to have a lumbar puncture done and 4 out of these 9 were CSF-positive.

Conclusion | Rapid cryptococcal antigen test is an important screening tool in HIV-infection, but the meaning of a positive CSF antigen test needs to be defined.

TO.01

What is the 'right' dose of rifampin?

Martin Boeree[1], Andreas Diacon[2], Rod Dawson[2], Gibson Kibiki[2], Hadija Semvua[2], Klaus Reiter[2], Micheal Hoelscher[2], Norbert Heinrich[2], Stephen Gillespie[2], Patrick Phillips[2], Georgette Plemper van Balen[1], Rob Aarnoutse[1]

1. Radboud University Nijmegen, The Netherlands; 2. PanACEA consortium

Background | In 1971 the dose of 10 mg/kg rifampin (RIF) was arbitrarily chosen without a maximum tolerated dose study. Current murine and human data show that an increase in dose of rifampin may significantly shorten treatment duration.
Methods | We performed two EDCTP-funded studies. The HIGHRIF1 (Cape Town) study is a 14-day maximum tolerated dose study in 68 adult smear-positive TB patients receiving 10 and 20, 25, 30, and 35 mg/kg RIF in the first week, complemented with standard doses of isoniazid (H), pyrazinamide (Z), and ethambutol (E) in the second week. The HIGHRIF2 study (Moshi and Bagamoyo, Tanzania) is a randomised placebo-controlled double-blind study in 150 patients receiving 10, 15 and 20 mg/kg RIF for 2 months together with HZE.
Results | HIGHRIF1: All doses tested were safe and well tolerated. There was a suggestion of a dose-related effect in decline in colony forming units (CFU) and increase in time to positive. Pharmacokinetic parameters showed a clear dose related non-linear increase in exposure and C_{max}. HIGHRIF2: In general, all three doses were well tolerated and safe. There were no clear drug-related serious adverse events. Pharmacokinetic parameters showed a dose-related increase both in exposure as in C_{max} though the average was lower than in HR1. Microbiological analysis will follow.
Conclusion | The current accepted treatment dose of RIF may be too low. We will evaluate two arms with 20 mg/kg together with moxifloxacine and SQ109 and 35 mg RIF/kg administered for 12 weeks in a multiple arm, multiple stage design within the PanACEA consortium.

TO.02

High-dose rifapentine with a quinolone for treatment of pulmonary tuberculosis: the RIFAQUIN trial

Amina Jindani[1], M. Hatherill[2], H. Geldenhuys[2], S. Charalambous[3], N. Gardiner[3], S. Mungofa[4], N. Syed[4], S. Zizhou[5], L. Magweta[5], J. van Dijk[6], J. Shepherd[7], S. Nyirenda[8], P. Phillips[8], A. Nunn[8], T. Harrison[1], D. Coleman[1], D. Mitchison[1]

1. St. George's University of London, United Kingdom; 2. University of Cape Town, South Africa; 3. The Aurum Institute, South Africa; 4. Harare City Health Department, Zimbabwe; 5. Medical Directorate of Mashonaland East, Zimbabwe; 6. Macha Research Trust, Zambia; 7. CDC-BOTUSA, United States of America; 8. MRC CTU, United Kingdom

Background | RIFAQUIN is a randomised controlled trial to assess whether moxifloxacin and rifapentine given intermittently in the continuation phase is not inferior to the WHO-recommended treatment for tuberculosis (TB).
Methods | Patients with new smear-positive TB were randomly allocated to: Group A – control regimen: 2 months daily ethambutol, isoniazid, rifampicin, and pyrazinamide and 4 months daily isoniazid and rifampicin. Group B – 4-month regimen: Isoniazid replaced by moxifloxacin in the intensive phase and 2 months of twice-weekly moxifloxacin and 900 mg rifapentine. Group C – 6-month regimen: Isoniazid replaced by moxifloxacin in the intensive phase and 4 months of once-weekly moxifloxacin and 1200 mg rifapentine. HIV-infected patients not on ART were eligible provided CD4 was ≥200/mm^3. The primary efficacy outcome is unfavourable status during treatment and 18 months follow-up. The primary safety outcome is occurrence of grade 3 or 4 adverse events during treatment.
Results | 827 patients were enrolled in South Africa, Zimbabwe, Botswana and Zambia. Baseline characteristics were similar in all three arms. The difference in unfavourable outcomes between the 4-month regimen and control was 13.1% in the mITT and 13.6% in the PP analysis. The difference between the 6-month regimen and control was 0.4% in the mITT and –1.8% in the PP analysis. 46 grade 3 or 4 adverse events were reported in 39 patients; six events were hepatic.
Conclusion | The 6-month regimen with once-weekly 1200 mg rifapentine and moxifloxacin in the continuation phase was non-inferior to control. The twice-weekly 4-month regimen was significantly inferior to control. Both regimens were safe and well tolerated.

TO.03

Optimisation of TB-HIV co-treatment in sub-Saharan Africa: no need to increase efavirenz dose during concomitant rifampicin-based antituberculosis therapy in HIV patients

Eleni Aklillu[1], Eliford Ngaimisi[1,2], Abiy Habtewold[1,3], Omary Minzi[2], Eyasu Makonnen[3], Klaus-Dieter Riedel[4], Sabina Mugusi[5], Wondwossen Amogne[6], Getnet Yimer[3], Mohammed Janabi[2], Getachew Aderaye[6], Ferdinand Mugusi[2], Leif Bertilsson[1], Juergen Burhenne[4]

1. KI, Sweden; 2. MUHAS, Tanzania; 3. Addis Ababa University, Ethiopia; 4. University of Heidelberg, Germany; 5, Muhimbili National Hospital, Tanzania; 6. Addis Ababa University, Ethiopia

Background | Effect of rifampicin co-treatment on plasma efavirenz concentrations and the optimal dose of efavirenz during rifampicin co-therapy remain uncertain. We performed a parallel prospective study to evaluate the effect of rifampicin on plasma efavirenz concentrations and treatment response.
Methods | A total of 800 treatment-naive HIV patients without tuberculosis (TB) and TB-HIV-coinfected patients were enrolled prospectively and followed for up to one year in Ethiopia and Tanzania. Plasma efavirenz concentrations were determined at 4 and 16 weeks. Safety and efficacy were recorded up to 48 weeks.
Results | Plasma efavirenz concentration, frequency of CYP2B6*6 allele and extent of efavirenz auto-induction were significantly higher in Tanzanians than Ethiopians. Enzyme induction was pronounced mainly in patients with CYP2B6*1/*1 genotype. In Tanzanians, effect of rifampicin on efavirenz kinetics was apparent during early therapy but had no significant long-term effect on efavirenz plasma concentration or CD4 gain. In Ethiopians, rifampicin co-treatment paradoxically increased efavirenz plasma and intracellular concentrations, resulting in better immunological recovery without long-term eventual effect on viral response. Concomitant rifampicin based antituberculosis therapy and CYP2B6*6 increase the risk for drug induced liver injury.
Conclusion | We report a CYP2B6*6 genotype dependent and population specific effect of rifampicin on efavirenz autoinduction and pharmacokinetics. Concomitant rifampicin therapy has no significant long-term effect on efavirenz pharmacokinetics, immunological or virological response. Hence there is no need to increase efavirenz dose during rifampicin co-treatment, which supports the current WHO recommendation.

TO.04

Challenges of and perspectives on development and evaluation of new tuberculosis drug regimens

Michael Hoelscher[1], Martin Boeree[2], Norbert Heinrich[1], Rob Arnoutse[2], Tim McHugh[2], Sunita Rehal[2], Andrew Nunn[2], Patrick P.J. Phillips[2], Stephen Gillespie[2]

1. University of Munich (LMU), Germany; 2. PanACEA consortium

Background | Worldwide, tuberculosis (TB) remains one of the most important causes of death despite the availability of cheap and effective therapy. Multidrug-resistant TB is spreading globally and now poses a major threat to achievements made in global TB control. Whilst TB drug development has accelerated in recent years, the current pipeline of new drugs remains thin and is confronted with many obstacles (e.g. safety concerns, low company interest).
Methods | Using the example of the EDCTP-funded PanACEA network for TB drug development, this paper highlights recent advances and discusses concerns, shortcomings, limitations, gaps and deficiencies associated with new drug development and evaluation.
Results | An analysis of the current situation identifies that efficient evaluation of drug combinations remains an obstacle. The interest of pharmaceutical companies is to develop their compounds as rapidly as possible into a marketable product, while private public partnerships are prioritising also the compounds that they have secured IP rights for. Moreover, there is no consensus on how to select the best drug combinations prior to conducting expensive phase III studies.
Conclusion | We feel that a pluralistic approach is an important instrument for success. It is important that the drug development process is not focused on a single product, regardless how promising it might seem. A broad drug pipeline needs to be maintained and developed further. PanACEA, publicly funded, has no commercial interest and is therefore fit to be the independent broker that can evaluate drug combinations on scientific and rational grounds.

TO.05

Results for SQ109, a new antituberculosis drug candidate, from a 14-day early bactericidal activity study

Norbert Heinrich[1], Jeannine du Bois[2], Kim Narunsky[2], Amour Venter[2], Patrick Phillips[2], Carol Nacy[2], Sonja Henne[1], Rodney Dawson[2], Andreas Diacon[2], Michael Hoelscher[1]

1. University of Munich (LMU), Germany; 2. PanACEA consortium

Background | More effective antituberculosis (TB) drugs are needed to shorten treatment. SQ109 was developed by Sequella Inc. from the diamine pharmacophore of ethambutol, and inhibits MmpL3, a transporter involved in cell wall assembly. *In vitro* data suggest a synergism with rifampicin. In phase I studies, the drug was well tolerated and safe.

Methods | This study was a two-centre, prospectively randomised trial in Cape Town, South Africa. Ninety (90) patients were assigned to receive daily 75 mg SQ109, 150 mg SQ109, 300 mg SQ109, 150 mg SQ109 + 10 mg/kg RIF, 300 mg SQ109 + 10 mg/kg RIF, and 10 mg/kg RIF, daily for 14 days. Daily overnight sputum cultures were assessed for bacterial load as measured by colony forming units on solid agar, and time to positivity in liquid media.

Results | Overall, the drug was well tolerated and no SAEs emerged from treatment. Pharmacokinetic analysis showed a reduction in SQ109 exposure if given together with RIF, which was overcome by the higher SQ109 dose. All RIF-containing groups showed a linear decline in logCFU over time, with no apparent effect of SQ109 dose. There was no change from baseline in any of the SQ109 monotherapy groups.

Conclusion | SQ109 was safe and well tolerated. The drug alone or in combination with RIF did not show any effect on sputum bacterial load during the first 14 days of treatment. SQ109 might take longer than two weeks to establish its activity, and is now tested over three months as part of a multidrug regimen in the PanACEA multiple arm, multiple stage TB 01 study.

TO.06

The effect of diabetes mellitus on the pharmacokinetics of tuberculosis drugs in Tanzanian patients

Charles Mtabho[1], Hadija Semvua, Jossy Boogaard, Constantine Irongo, Martin Boeree, Angela Colbers, David Burger, Reinout Crevel, Andre Ven, Gibson Kibiki, Alma Tostmann, Rob Aarnoutse

1. KCRI, Tanzania

Background | Diabetes mellitus (DM) is a well-known risk factor for tuberculosis (TB). With the current global increase in type 2 DM, more attention is needed for optimum treatment of TB in TB-DM patients. Pharmacokinetic profiles of TB drugs in Asian and American TB-DM patients have been described, but such data are lacking in Africa. We performed a pharmacokinetic study in Tanzanian patients.

Methods | Twenty TB and 20 TB-DM patients were recruited. Plasma concentrations were determined just before and at 1, 2, 3, 4, 6, 8, 10, 24 hours after observed drug intake to estimate pharmacokinetic parameters of isoniazid, rifampicin, pyrazinamide and ethambutol using validated HPLC.

Results | The geometric mean exposure (AUC_{0-24}) of rifampicin and isoniazid (h×mg/L) were significantly lower in TB-DM (29.3 rifampicin, 5.4 isoniazid) than TB only patients (39.9 rifampicin, 10.6 isoniazid). C_{max} (mg/L) of isoniazid was also lower in TB-DM patients (1.6 versus 2.8, p=0.01); 73.7% versus 55% of patients had C_{max} of isoniazid below reference range in the TB-DM as compared to the TB only group; and for rifampicin, the proportions were 43.4% against 35%. Age and bodyweight did not affect the association between DM and pharmacokinetic parameters. All pharmacokinetic parameters for pyrazinamide and ethambutol were statistically similar between the groups.

Conclusion | Exposure to isoniazid and rifampicin is reduced in Tanzanian TB-DM patients. These effects are most likely explained by the diabetes disease. Increasing the doses of these drugs may be considered in view of accumulating evidence that exposure to TB drugs is related to response.

TO.07

Providing an address for delivery of nanoencapsulated tuberculosis drugs

Yolandy Lemmer[1], Boitumelo Semete[1], Laetitia Booysen[1,2], Lonji Kalombo[1], Lebogang Katata[1], Arwyn T. Jones[4], Chantal de Chastellier[5], Hulda. S. Swai[1], Jan A. Verschoor[3]

1. CSIR, South Africa; 2. North-West University, South Africa; 3. University of Pretoria, South Africa; 4. Cardiff University, United Kingdom; 5. INSERM, France

Background | South Africa currently has the highest incidence of tuberculosis (TB) per 100,000 people in the world. Although TB treatments exist, poor patient compliance and drug resistance pose a great challenge to TB treatment worldwide. To improve the current inadequate therapeutic management of TB, a polymeric nanodrug delivery system for anti-TB drugs, was developed that could enable entry, targeting, sustained release over a longer period, and uptake of the antibiotics in the cells. This might contribute to lower dose frequency and better patient compliance.
Methods | We aimed to prepare functionalised polymeric nanodrug delivery vehicles to target TB-infected macrophage cells.
Results | Successful nanoencapsulation of anti-TB drugs and a targeting agent (MA) was achieved. Mycolic acid (MA) may target cholesterol at the site of infection. The nanoparticles were characterised and subjected to *in vitro* analyses in order to determine their uptake, localisation and cytotoxicity in different cell lines. In another approach targeting will be achieved via attaching nucleic acid aptamers specific for the mannose receptor (MR), which is significantly over-expressed during the activation of the macrophages in the presence of *Mycobacterium tuberculosis* onto the surface of drug-carrying PLGA nanoparticles.
Conclusion | The aptamer to MR and MA to cholesterol as targeting mechanisms for nanodrug delivery systems will be discussed as well as the positive results that were obtained for the *in vitro* efficacy assays with the aptamers against the MR. Its success addresses the challenges of poor bioavailability, reduced efficacy and adverse side effects for diseases such as HIV, TB and malaria.

TO.08

Evaluation of tuberculosis treatment outcomes in an infant tuberculosis incidence study in western Kenya

Prisca Rabuogi[1], Geofrey Oduwo, Videlis Nduba, Grace Kiringa
1. KEMRI-CDC, Kenya

Background | There is limited literature on tuberculosis (TB) treatment outcomes in children under four years. Reported outcomes are frequently worse than those in adults. We investigated treatment outcomes of infants diagnosed with tuberculosis.
Methods | Infants aged 0–6 weeks were enrolled and followed for one to two years. Definite TB was microbiologically confirmed, while probable TB was based on clinical and/or radiological criteria. Cases were initiated on treatment at the district hospital and thereafter referred and followed at clinics closest to them. Final outcomes were determined from TB registers and defined as treatment completed, died, and defaulters per World Health Organization.
Results | In a total of 2,900 infants there were 49 (1.7%) cases of TB. Nine (9; 18.4%) were definite and 40 (81.6%) were probable TB cases. Additionally, 10/49 (20.4%) cases were HIV-coinfected. Treatment outcomes were as follows: completed 37/49 (75.5%); defaulters 4/49 (8.2%); transfer-out 1/49 (2.0%); deaths 7/49 (14.3%). Treatment completion was 32/39 (82%) in HIV-uninfected and 5/10 (50%) in HIV-infected; RR 1.6 (0.9, 3.1). Mortality amongst HIV-infected was 5/10 (50%) (not on antiretroviral therapy) compared with 2/39 (5.1%) in HIV-uninfected RR 4.9 (1.6, 14.9). There was no difference in treatment completion between definite and probable TB cases (p=0.86).
Conclusion | Treatment outcomes in this age group were poor and comparable to those observed in other parts of Africa. HIV coinfection increased the risk of death. There is a need to make better use of guardians as partners in TB management to improve adherence and antiretroviral therapy uptake in HIV-infected children.

– *International Journal of Tuberculosis and Lung Disease*, 2008; 12(2), pp. 186–192; 2002; 6(5), pp. 424–431.

TO.09

Clinical development of tuberculosis subunit vaccine H1IC

Ingrid Kromann[1], Søren Hoff[1] , Peter Bang[1], Markos Abebe[3], Jemal Hussein[3], Klaus Reither[5], Gavin Churchyard[4], Peter Andersen[1], Hennie Geldenhuys[2]

1. SSI, Denmark; 2. SATVI, South Africa; 3. AHRI, Ethopia; 4. Aurum Institute, South Africa; 5. Swiss TPH, Basel, Switzerland

Background | New vaccines against *Mycobacterium tuberculosis* are urgently needed. Statens Serum Institute has developed new subunit vaccine candidates which are in clinical development. Candidate H1IC combines a recombinant fusion protein with the IC31® adjuvant. The tuberculosis (TB) antigens in this candidate are two early secreted mycobacterial antigens, Ag85B and ESAT-6.
Methods | H1 is being developed to prevent active TB regardless of whether the vaccine is given before or after exposure and is aimed to be used in adolescents and young adults.
Results | H1IC was the first TB subunit vaccine tested in humans. The vaccine has been tested in several clinical studies in different populations including latently TB-infected, HIV-infected and adolescents. The clinical trials have been supported by TBVAC and EDCTP. The vaccine is shown to be safe and immunogenic and a lot of study operational lessons have been learned.
Conclusion | Data from the studies encourage further clinical development of a subunit vaccine. Thus the clinical development continues with the next generation H56 vaccine which adds an additional antigen to the H1 core. No less important, the many lessons learned throughout the operational work will be used in planning future studies.

TO.10

Phase II safety and immunogenicity study of Aeras-402 in BCG-vaccinated, HIV-uninfected infants

Michele Tameris[4], Ann Ginsberg[1], Lew Barker[1], Katie Masso[1], Gretta Blatner[1], David Hokey[1], Jasur Ishmukhamedov[1], Vicky Cárdenas[1], Macaya Douoguih[2], Maria Pau[2], Sharon Nachman[3], Hassan Mahomed[4], Videlis Nduba[5], Glenda Gray[6], Jahit Sacarlal[7]

1. Aeras, United States of America; 2. Crucell N.V., The Netherlands; 3. Stony Brook University, United States of America; 4. SATVI, South Africa; 5. KEMRI-CDC, Kenya; 6. Perinatal HIV Research Unit, South Africa; 7. CISM, Mozambique

Background | Aeras-402 is a replication-deficient human adenovirus serotype 35 vaccine that encodes 3 tuberculosis (TB) antigens and may increase T cell immunity and protection against TB.
Methods | To evaluate the safety and immunogenicity of Aeras-402, 487 BCG-vaccinated, HIV-uninfected and -unexposed healthy infants were enrolled at four centres in Kenya, Mozambique, and South Africa. In study Groups 1–4, each infant received 2 doses of Aeras-402 or placebo on study days 0 and 28, and was followed for two years for safety. A third dose was added in Group 5 and administered on study day 280 to 210 infants, who were followed for at least 6 months.
Results | Aeras-402 demonstrated an acceptable safety profile in infants in Groups 1–4, similar to Group 5 infants who received 3 doses of Aeras-402. Immunology results obtained from Groups 1–4, using ICS, demonstrated that the vaccine was capable of inducing antigen specific CD8+ T cells, although responses appeared lower than previously seen with this vaccine candidate in adults. To evaluate whether immune responses could be augmented with a delayed boost, the study was modified to include a third dose in Group 5. Blinded preliminary ICS results at study days 280 and 308 on 41 participants in Group 5 suggest that the vaccine was able to induce a Th1-mediated response driven primarily by CD8+ T cells as determined by IFNγ, IL-2, and TNF expression. Further analyses by ICS as well as ELISPOT assays are being conducted on a larger subset of Group 5 participants.
Conclusion | Aeras-402 demonstrates an acceptable safety profile after 2 and 3 doses in infants. Preliminary blinded ICS results suggest that a third dose of Aeras-402 for BCG-vaccinated, HIV-negative infants may have a modest effect on enhancement of immunological responses.

TO.11

Incidence of tuberculosis among a cohort of HIV-positive adults enrolled in a tuberculosis vaccine clinical trial in Senegal

Birahim P. Ndiaye[1], Alle B. Dieng, Siry Dièye, Ibrahim Ndiaye, Aminata Thiam, Makhtar Camara, Halimatou Diop-Ndiaye, Ndeye Fatou Ngom-Gueye, Coumba Toure-Kane, Mouhamedou Ndiaye, Papa S. Sow, Samantha Vermaak, Sharon Sutton, Souleymane Mboup, Bernard Landry, and Helen Mcshane

1. CHU Le Dantec, Senegal

Background | Tuberculosis (TB) represents a major global public health problem with 1.45 million deaths and one third of the world's population latently infected with *Mycobacterium tuberculosis*. This epidemic is exacerbated by poverty, HIV prevalence and the lack of an effective TB vaccine. This study evaluates the protective efficacy against TB disease of MVA85A/AERAS-485.

Methods | A randomised, double-blind, placebo-controlled trial was conducted in 1,400 HIV-positive adults without active TB disease. Subjects were randomised by ART status and vaccine to receive. Booster dose was administered six to nine months after initial vaccination. Participants were followed for 24 months. Subjects with TB signs/symptoms were investigated for possible pulmonary TB with chest X-Ray and sputum collection. TB cases were defined by isolation of *M. tuberculosis* from any site or identification of *M. tuberculosis* by GeneXpert® or histopathology diagnostic or choroidal tubercle or one or two acid-fast smears positive, depending on specimen collection site.

Results | A majority of 82.9% (296/357) of volunteers were stable on ART, 39.2% (140/357) had latent TB Infection with TST higher than 5mm and/or positive QuantiFERON and received five months of isoniazid chemoprophylaxis before randomisation. In addition, 6.7% (24/357) of enrolees had TB within the past three years. Data on incidence (blinded to date) will be presented.

Conclusion | Determination of incidence at potential efficacy trial sites in the populations in which vaccines will be tested is crucial for accurate planning of these trials.

TO.12

Utility of *Mycobacterium tuberculosis*-specific host cytokine signatures in whole blood culture supernatants in the diagnosis of tuberculosis disease

Novel N. Chegou[1], Jayne S. Sutherland[2], Harriet Mayanja-Kizza[3], Rawleigh Howe[4], Marieta van der Vyver[5], Desta Kassa[6], Amelia C. Crampin[7], Gerhard Walzl[1], and the AE-TBC consortium

1. Stellenbosch University, South Africa; 2. MRC, The Gambia; 3. Makerere University, Uganda; 4. AHRI, Ethiopia; 5. University of Namibia, Namibia; 6. EHNRI, Ethiopia; 7. Karonga Prevention Study, Chilumba, Malawi

Background | We previously identified host blood biomarkers following stimulation in QuantiFERON® supernatants, which showed promise as tuberculosis (TB) diagnostic candidates. The present study evaluated the utility of these host biomarkers in a large pan-African study.

Methods | Individuals suspected of having TB were recruited at seven peripheral level health care facilities in six African countries. Blood was collected into QuantiFERON® tubes. After overnight incubation, supernatants were harvested, frozen and the levels of 12 biomarkers evaluated using the Luminex® platform. On the basis of laboratory, clinical and radiological findings, participants were classified into the following groups using a pre-established diagnostic algorithm: definite TB, probable TB, possible TB, questionable disease status or non-TB.

Results | Of the 532 participants included in the study, 148 (27.8%) had definite TB; 12 (2.3%) and 19 (3.6%) were probable and possible TB cases respectively; 274 (51.5%) were non-TB cases and 61 (11.5%) had an uncertain diagnosis (questionable). When all the TB cases (definite, probable and possible) were compared to the non-cases (excluding the questionables), significant differences were observed ($p<0.05$) for the antigen-specific or unstimulated levels of IL-1ra, VEGF, IFNγ, IFNα2, sCD40L, MIP-1β, TGFα and MMP-9. A biosignature comprising of the levels of 7 markers ascertained TB with a sensitivity of 76% and specificity of 80% in the test sample set.

Conclusion | We identified good candidate markers for the diagnosis of TB disease regardless of HIV status or ethnicity. This biosignature might be useful as a screening tool for TB disease and provides the basis for the development of a rapid TB diagnostic test.

TO.13

Evaluation of new and emerging diagnostics for childhood tuberculosis in high-burden countries: update from the TB CHILD project

Klaus Reither[1,2], Martin Nsubuga[3], Francesco Aloi[3], Fred Lwilla[2], Francis Mhimbira[2], Levan Jugheli[1,2], Claudia Daubenberger[1], Hans-Peter Beck[1], Chritof Geldmacher[4], Norbert Heinrich[4], Petra Clowes[5], Elias N. Ntinginya[5], Enrico Girardi[6], Delia Goletti[6], Paolo Miotto[7], Daniela Cirillo[7], on behalf of the TB CHILD consortium

1. Swiss TPH and University of Basel, Switzerland; 2. IHI, Tanzania; 3. St.Raphael of St Francis Nsambya Hospital, AISPO, Uganda; 4. University of Munich (LMU), Germany; 5. NIMR-MMRC, Tanzania; 6. INMI, Italy; 7. San Raffaele Scientific Institute, Milan, Italy

Background | Despite recent advances, difficulties in diagnosis are still the greatest challenge to the management of paediatric tuberculosis (TB), particularly in young as well as immunocompromised children. The lack of appropriate and widely available diagnostic tests furthermore impedes a realistic assessment of the burden of childhood TB, the development of new treatment and vaccination strategies and, finally, effective disease control. Therefore, TB CHILD had the ultimate goal to evaluate a series of new diagnostics to improve TB diagnosis in children.
Methods | TB CHILD has built up new research capacity in the field of paediatric TB in three sub-Saharan trial centres (Kampala, Mbeya, and Bagamoyo) and maintains a functional North-South and South-South network. Ten different diagnostic approaches have been evaluated in two patient populations: 1) adults (TB cases n=178; healthy controls n=124), and 2) children (TB suspects n=493). The most important diagnostics tests were: Xpert MTB/RIF assay (in sputum, lymph nodes, blood), serum microRNAs as TB biomarkers, IP-10 in blood and urine, T cell activation marker-interferon gamma release assay (TAM-TB Assay), and a new lab-on-chip-based platform. TB CHILD project has supported three MSc and two PhD programmes.
Results | The final data analysis of the evaluation studies will be completed. We intend to present results from the sub-studies on the newly developed TAM-TB Assay at the EDCTP Forum.
Conclusion | The TB CHILD project has comprehensively addressed the demand for evaluation of new diagnostic tests for childhood TB and was able to support urgently needed research capacity in high-burden countries.

TO.14

Xpert MTB/RIF assay for the diagnosis of tuberculosis using non-sputum samples in an HIV-prevalent setting

Grant Theron[1], J. Peter[1], R. Meldau[1], S. Pandie[1], V. Patel[1], K. Dheda[1]
1. University of Cape Town, South Africa

Background | There is limited information about Xpert MTB/RIF performance on non-sputum specimens, especially in individuals who are infected with HIV. We have concluded several studies that assess its accuracy in 1) bronchoalveolar lavage (BAL) fluid; 2) pleural fluid; 3) cerebral spinal fluid (CSF), 4) urine, and 5) pericardial fluid.
Methods | Accuracy was calculated using liquid culture positivity for *Mycobacterium tuberculosis* as a reference standard. Patients clinically suspected of tuberculosis (TB) were considered eligible. For the BAL (n=139) and pleural studies (n=72), patients who were sputum scarce or smear-negative were eligible. The urine study (n=242) had the same criteria, but only recruited patients with advanced immunosuppression. The pericardial study (n=238) recruited patients with suspected TB pericarditis.
Results | 1. Xpert MTB/RIF assay performed on BAL fluid had a sensitivity of 91% (20/22), exceeding that of smear-microscopy 55% (12/22; p<0.01). 2. Performed on pleural fluid, Xpert MTB/RIF assay sensitivity was 25% (10/40), while smear microscopy only detected a single case. 3. When performed on CSF, Xpert MTB/RIF assay detected 47% (17/36) of TB meningitis cases, outperforming smear-microscopy considerably 14% (5/36; p<0.01). CSF concentration via centrifugation significantly improved Xpert MTB/RIF assay sensitivity to 78% (28/36; p<0.01) without any changes in specificity. 4. Xpert MTB/RIF assay performed directly on urine detected 8% (3/38) cases; however 42% (16/38) of sputum scarce cases could be detected when urine was centrifuged for testing. 5. 64% (99/154) of patients with TB pericarditis were detected, and centrifugation did not improve performance.
Conclusion | Xpert MTB/RIF assay outperforms conventional rapid diagnostics when used on non-sputum specimens. This is important in Africa, where extra-pulmonary TB is frequent.

TO.15

Diagnosing tuberculosis in advanced HIV infection in Africa: the role of the Xpert MTB/RIF assay

Sokoine Kivuyo[2], Bernard Ngowi[2], Victoria Simms[3], Duncan Chanda[1], Godfather Kimaro[2], Amos Kahwa[2], Sode Matiku[4], Lorna Guinness[3], Sayoki Mfinanga[2], Shabbar Jaffar[3], Saidi Egwaga[4]

1. IMReT-UTH, Zambia; 2. NIMR Muhimbili, Tanzania; 3. LSHTM, United Kingdom; 4. MoHSW-NTLP, Tanzania

Background | Diagnosis of tuberculosis (TB) among HIV-infected patients is challenging. The Xpert MTB/RIF assay has been evaluated extensively in research trials, but its effectiveness in real-life settings is limited.

Methods | Patients were part of a pragmatic trial integrated into six publicly funded HIV clinics in high-density urban areas of Lusaka and Dar es Salaam, with patients managed by the local health services. Study patients were adults with a CD4 count below 200 cells/ml and ART-naïve. All participants were asked to produce sputum, which was tested by Xpert MTB/RIF assay and smear microscopy. Those positive on Xpert MTB/RIF assay or positive on smear microscopy were initiated immediately on anti-TB medication.

Results | A total of 569 subjects were enrolled into the study in Tanzania. Their median CD4 count was 43 range (1–194) and 465 were at WHO stage 3 or 4. At baseline, 557 had an Xpert MTB/RIF assay, 12 were not tested because they were unable to produce sputum. Eighty-three (83) out of 556 (4.9%) were asymptomatic for TB, while the remainder had cough (42.4%), weight loss (75.5%), night sweats (20.9%) and fever (32.2%). Overall, 99/557 (17.8%. 95% CI: 14.7–21.2) were positive by the Xpert MTB/RIF assay. Of the 99 positive subjects, 10 were asymptomatic, 89 were symptomatic. Smear microscopy was done for 557 subjects and of these, 74 were smear-positive and 483 were smear-negative. Of the 483 smear-negatives, 40 (8.2%) were Xpert MTB/RIF assay-positive.

Conclusion | More TB in subjects with advanced HIV infection was diagnosed by using the Xpert MTB/RIF assay than by smear microscopy.

TO.16

Contribution of the Xpert MTB/RIF assay to the diagnosis of pulmonary tuberculosis in a West African childhood tuberculosis clinic

Abigail Ayorinde[1], Toyin Togun[1], Uzochuk wu Egere[1], Ousainou Darboe[1], Masaneh Ceesay[1], Sophie Gomez-Afolabi[1], Jacob Out[1], Martin Antonio[1], Jayne Sutherland[1], Philip Hill[2], Beate Kampmann[1,3]

1. MRC, The Gambia; 2. University of Otago, New Zealand; 3. Imperial College London, United Kingdom

Background | Clinical presentation of tuberculosis (TB) in children is non-specific and microbiological confirmation of disease is rare. Treatment in children is thus mostly commenced on the basis of clinical signs and symptoms. We assessed the utility of the Xpert MTB/RIF assay in the diagnosis of pulmonary TB and rifampicin resistance in a West African childhood TB clinic.

Methods | Induced sputum samples were obtained from all children aged <15 years with symptoms suggestive of TB seen at the childhood TB clinic of MRC Unit The Gambia from April 2012 to April 2013. Samples were tested by smear microscopy for acid fast bacilli, liquid culture by Microbacteria growth indicator tube (mgIT) and Xpert MTB/RIF.

Results | Thirty-five (35 or 8.7%) of 401 children investigated were diagnosed with active TB (9 culture-positive; 26 culture-negative). Four (4 or 44%) and 6 (67%) of the 9 culture-positive TB cases had positive smear microscopy and Xpert MTB/RIF test respectively. The Xpert MTB/RIF assay was positive in 4/4 (100%) smear-positive/culture-negative cases, 3/5 (60%) smear-negative/culture-positive cases and 1/26 (4%) smear–negative/culture-negative TB cases. Xpert MTB/RIF assay was negative in all of the samples obtained from children who did not have TB (n=366). There was no evidence of rifampicin resistance in any of the samples analysed.

Conclusion | Our results suggest that Xpert MTB/RIF assay offers a more sensitive method for detection of *M. tuberculosis* in children compared with sputum smear microscopy but cannot be recommended to replace culture methods where available. Additional methods to improve diagnosis of TB in children are needed.

TO.17

Comparative effectiveness of the Xpert MTB/RIF assay when used as add-on test to smear microscopy for diagnosis of pulmonary tuberculosis among HIV-infected Ugandan adults

Willy Ssengooba[1,4], Lydia Nakiyingi[1], Derek Armstrong[3], Frank G. Cobelens[4,5], David Alland[3,] Yukari C. Manabe[2], Susan E. Dorman[2], J. Ellner[3], Moses L. Joloba[1]

1. Makerere University, Uganda; 2. Johns Hopkins University, United States of America; 3. Boston University, United States of America; 4. AIGHD and AMC, The Netherlands; 5. KNCV Tuberculosis Foundation, The Netherlands

Background | Low income, high-tuberculosis burden countries are considering selective deployment of the Xpert MTB/RIF assay (Xpert) due to high cost per test. We compared the diagnostic gain from Xpert 'add-on strategy' with Xpert replacement strategy for pulmonary tuberculosis diagnosis among HIV-infected adults to inform its implementation.

Methods | The first diagostic sputum sample of 427 HIV-infected (67% with CD4 counts <200/mm^3) suspected for tuberculosis was tested by direct Ziehl-Neelsen (DZN) and direct fluorescent microscopy (DFM); concentrated fluorescent microscopy (CFM); Lowenstein-Jensen (LJ) and Mycobacterial Growth Indicator Tube (mgIT) culture; and Xpert. The overall diagnostic yield and senstivity was calculated using mgIT as reference comparator. The senstivity of Xpert in an add-on strategy was calculated as the number of smear negative but Xpert positive among mgIT positive patients.

Results | mgIT grew Mycobacterium tuberculosis for 123 (28.8 %) patients. The sensitivity (95% confidence interval) was 31.7% (23.6–40.7%; n=39) for DZN, 35.0% (26.5–44.0%; n=43) for DFM, 44.0% (34.9–53.1%; n=54) for CFM, 81.3% (73.2–87.7%, n=100) for LJ and 76.4% (67.9–83.6; n=94) for Xpert. Add-on strategy Xpert showed an incremental sensitivity of 44.7% (35.7–53.9%) when added to DZN, 42.3% (33.4–51.5%) when added to DFM and 35.0% (26.5–44.0%) when added to CFM. This translated to an overall sensitivity of 76.4%, 77.3% and 79.0% for add-on strategies based on DZN, DFM and CFM, respectively, compared to 76.4% for Xpert done independently.

Conclusion | In this patient population, there is little additional value of doing any type of smear examination if one does Xpert on the smear negatives.

TO.18

Development of an aptamer to a Th1 cytokine

Boitumelo Fanampe[1], Lia Rotherham[2], Makobetsa Khati[2], Grant Theron[1], Keertan Dheda[1]

1. University of Cape Town, South Africa; 2. CSIR, South Africa

Background | An emerging class of molecules known as 'aptamers' offer new, exquisitely sensitive ways of detecting molecular signatures associated with different disease states. These synthetic single-stranded nucleic acid molecules bind any target with high affinity and specificity. However, limited work has been done to apply this technology to detect cytokines relevant to TB-based research.
Methods | We used an iterative process known as Systematic Evolution of Ligands by Exponential Enrichment (SELEX) for the generation of single stranded DNA (ssDNA) aptamers for interferon gamma (IFNγ). The starting ssDNA oligonucleotide library contained 10^{14}–10^{17} different randomised sequences. The library used was flanked by constant regions, which were used as primers for the selection. Eight rounds of SELEX were performed for this study and aptamers were subsequently characterized to identify ones with the highest binding affinity.
Results | Preliminary data showed an enrichment of between 1% and 60%, where aptamers were cloned and sequenced. Secondary structure predictions were done using different bioinformatic tools. Preliminary tests indicated that the aptamers were useful in detecting IFNγ; however, further analysis is required.
Conclusion | Aptamers appear to be a promising technology for the detection of TB relevant cytokines. This may ultimately bring down the cost and improve the efficiency of detecting TB-relevant cytokines.

TO.19

Analysis of antimycobacterial compounds produced by marine endophytic fungi

Patrick Kobina Arthur[1], Clement Opoku-Temeng[1], Vincent Amarh[1], Gloria Baaba Arkaifie[1]

1. University of Ghana, Ghana

Background | Drug resistant tuberculosis (TB) is currently on the increase globally which calls for development of new and more effective TB drugs to combat the disease. Based on the fact that a great variety of marine endophytic fungi (MEF) are readily found in Ghana, a pilot project of screening these fungi found in Ghana has been ongoing for the last three years to discover the presence of bioactive new chemical entities against clinically relevant microbial pathogens.

Methods | In the initial phase, 29 marine endophytic fungi were isolated, cultured and ethyl acetate extracts of the cultures were tested for biological activity. Using the disc diffusion method, the extracts were tested against *Staphylococcus aureus*, *Escherichia Coli*, *Candida albicans*, and *Mycobacterium smegmatis*. We also have established a phenotypic array-based bioassay consisting of more than 30 conditions using *M. smegmatis* to probe the extracts further.

Results | We recorded for 22/29 MEF extract with activity against *S. aureus* (MRSA), 6/29 with activity against *E. coli* and *C. albicans*, four of which are common set of MEF extracts against the two microbes. The most frequent activity detected was antimycobacterial activity with a score of 27 out of the 29 extracts tested, which constitutes a positive hit rate of 93%. The antimycobacterial activities showed intensity of activity ranging between 9–35 mm of zones of inhibition. Using the phenotypic array-based bioassay, we have determined the pattern of activity for all the bioactive extracts in comparison with 16 standard antibiotics. We have obtained the ranking of the potency of activities for the MEF extracts, some of which compare very well with that of the standard antibiotics such as streptomycin albeit with their own distinct pattern of activities.

Conclusion | These results provide a proof of concept that marine endophytic fungi found in Ghana are a potential source of many novel antimycobacterial agents as well as some anti-MRSA and other general antimicrobial compounds. The top ranked MEFs are being scaled up in culture for product isolation and characterisation to support future clinical TB drug development.

TO.20

Association between leptin receptor gene (Leprgln233arg) polymorphism and tuberculosis relapse in Nigerian patients

Bamidele Iwalokun[1], Nkiru Nwokoye, Francisca Nwaokorie, Catherine Onibogu, Oni Idigbe

1. NIMR, Nigeria

Background | This study investigated whether changes in serum leptin level and leptin receptor (LPR Q223R, A/G) polymorphism are associated with tuberculosis (TB) relapse in Nigerian patients.
Methods | A case control study was undertaken in 69 subjects, comprising 25 TB patients (mean age=34.3 years) with relapse and 44 age-matched successfully treated TB patients (control) presenting at three private health facilities in Lagos (July–October 2012). LEPR gene 233A>G polymorphism was determined by PCR-RFLP and odd ratio/c2 of genotype and allele distribution in TB relapsed (case) versus TB recovered (control) patients was calculated for Hardy-Weinberg and association determinations with serum TNFα, leptin levels, BMI and Hb as covariates.
Results | Males outnumbered females in the study populations (66.7% *vs* 33.3%) but having TB relapse was not gender related. However, TB relapse was associated with age >40 years, persistent anaemia, incidence of fever and low body weight after adjustment for gender and residence OR, 3.4–11.8 (1.1–89.5), p<0.05. Significant (P <0.05) reductions in serum leptin (2.21 *vs* 4.05 ng/mL) and TNFα (27.2 *vs* 43.9 pg/mL) were found in TB relapsed patients compared to the control. The LEPR233A>G SNP examined was common in the study population with genetic variants in HWE. However, carriage of the GG genotype was associated 9-fold increased risk of TB relapse (p<0.05) with carrier patients further eliciting significantly (p<0.05) other indices of TB relapse in comparison to non-carrier TB patients.
Conclusion | LEPR Q223R polymorphism seems to modulate susceptibility to TB relapse through impaired body weight and persistent anaemia among Nigerian patients.

TO.21

Insight of the genetic variability of *Mycobacterium tuberculosis* complex and drug resistance in Yaounde, Cameroon

Véronique Penlap Beng[1], Larissa Ka mgue Sidze[1], Emmanuel Mouafo Tekwu[1], Jean Paul Assam Assam[1], Rob Skilton[3], Roger Pelle[3], Christopher Kuaban[4], Sara Niobe-Eyangoh[5], Stefan Niemann[6], Matthias Frank[7], Vincent Titanji[2]

1. University of Yaounde I, Cameroon; 2. University of Buea, Cameroon; 3. ILRI-BeaA-Hub, Kenya; 4. Jamot Hospital, Yaounde, Cameroon; 5. Centre Pasteur du Cameroun, Cameroon; 6. Research Centre Borstel, Germany; 7. ITM Tübingen, Germany

Background | This study investigates the genetic diversity and drug resistance spreading in *Mycobacterium tuberculosis* isolates from the central, littoral and west regions of Cameroon.
Methods | Molecular typing (spoligotyping and MIRU-VNTR) and DNA sequencing (KatG, inhA, ahpC and rpoB) were performed on a set of isolates including isoniazid and/or rifampicin resistant and susceptible strains obtained from smear-positive pulmonary tuberculosis (TB) patients.
Results | Of the isoniazid resistant isolates, about 47% harboured a KatG315 mutation. Alterations were found in the inhA (42%), and ahpC (5%) promoters. rpoB531 point mutation was the most observed amount the rifampicin resistant isolates. Spoligotyping revealed that for isolates from central region of Cameroon, the majority of strains belonged to the 'Cameroon family' (65%) followed by the Haarlem family (10%). The majority of isolates from the littoral and south west regions of Cameroon belonged to major clades of *M. tuberculosis*: Haarlem (10%), Latin American-Mediterranean (20%), and ST (47%). The predominant group of isolates (33%) was the spoligotype 53, described as 'Ghanaian strains'. MIRU-VNTR and spoligotyping showed 21 clusters of 2 to 11 strains. Comparison of our data showed that MIRU-VNTR had greater resolving power than spoligotyping and defined additional genotypes in the same cluster.
Conclusion | Genotyping confirmed the predominance of the 'Cameroon family' in the central region, and the presence of Ghanaian strains (ST53). Findings suggest that transmission and emergence of drug resistance might occur simultaneously in our setting, emphasising the importance of early diagnosis and adequate treatment.

TO.22

Distinct T cell responses when Bacillus Calmette Guerin is delayed from birth to six weeks of age in Ugandan infants

Fredrick Lutwama[1,2], B.M. Kagina[1], A. Wajja[2], F. Waiswa[2], N. Mansoor[1], S. Kirimunda[2], E.J. Hughes[1], N. Kiwanuka[2], M.L. Joloba[2], P. Musoke[2], T.J. Scriba[1], H. Mayanja-Kizza[2], C.L. Day[1,3], W.A. Hanekom[1]

1. SATVI, University of Cape Town, South Africa; 2. Makerere University, Uganda; 3. Emory University, United States of America

Background | In Uganda, the tuberculosis (TB) vaccine Bacillus Calmette Guerin (BCG) is administered on the first day of life. Infants delivered at home receive BCG at their first health care facility visit at six weeks of age. Our aim was to determine the effect of this delay in BCG administration on the induced immune response. We hypothesised that infants vaccinated at birth would show lower frequencies of BCG-specific CD4+ and CD8+ T cells compared with infants vaccinated at six weeks of age.

Methods | We assessed CD4+ and CD8+ T cell responses with a 12-hour whole blood intracellular cytokine/cytotoxic marker assay, and with a 6-day proliferation assay.

Results | We enrolled 92 infants: 50 had received BCG at birth and 42 at six weeks of age. Birth vaccination was associated with; (i) greater induction of CD4+ and CD8+ T cells expressing either IFNγ alone, or IFNγ together with perforin and, (ii) induction of proliferating cells that had greater capacity to produce IFNγ, TNFα and IL-2 together, compared with delayed vaccination.

Conclusion | Distinct patterns of T cell induction occurred when BCG was given at birth and at six weeks of age. We propose that this diversity might impact protection against TB. Further, some differences between our results and those from other studies of delayed BCG vaccination in South Africa and the Gambia were observed, suggesting population heterogeneity in BCG responsiveness.

TO.23

Peripheral blood TNFα-dependent apoptotic gene expression and white blood cell count to characterise the tuberculosis clinical status of individuals in a high-burden setting

Niaina Rakotosamimanana[1], Mark Doherty, Vincent Richard, Jean-Louis Soares, Alimudin Zumla, Voahangy Rasolofo

1. Institut Pasteur Madagascar, Madagascar

Background | Most of *Mycobacterium tuberculosis* infections remain asymptomatic. However, up to 10% of the infected hosts will progress to active tuberculosis (TB). The current tests for latent TB are yet unable to differentiate between persistent or resolved infection and active disease, increasing the need of reliable biomarkers for assessing TB disease progression risk.
Methods | To discriminate the different clinical TB spectrum, we studied the peripheral blood cell distribution and mRNA gene expression of TNFα dependent apoptotic genes (TNFR1, TNFR2, FLICE, FLIPs) in a cohort of pulmonary TB patients (n=23), their household contacts (n=80), and community controls (n=46) from Antananarivo, a TB high-burden setting during a period of up to two years. Complete blood counts and previous *M. tuberculosis* contact assessed by ELISPOT and TST was performed on inclusion and at different periods according to the clinical status.
Results | A significant elevation of FLIPs expression by infected individuals regardless of clinical status was observed, with a higher percentage of lymphocytes in the infected household contacts that remained healthy. The household contacts that subsequently developed signs of TB, had a significantly high number of monocytes. Active TB was characterised by a significant TNFR2 upregulation with a significantly higher monocytes percentage and a significantly decreased lymphocyte count.
Conclusion | TB disease may be associated with decreased T cell survival while inhibition of apoptosis in monocytes could lead to a relative increase in these cells. The current work paves the way for further investigation on biomarkers to delineate protective and weak immunity against TB.

– Rakotosamimanana et al. (2013) *PLOS ONE* 8(4): e61154

TO.24

Experiences in using real-time electronic and paper-based data capturing methods in studies conducted by the tuberculosis research branch, KEMRI-CDC programme in western Kenya

John Hongo[1], Videlis Nduba[1], Anja van 't Hoog[2], Lazarus Odeny[1]
1. KEMRI-CDC, Kenya; 2. University of Amsterdam, The Netherlands

Background | Since 2005 the KEMRI-CDC tuberculosis research branch conducted several large studies, including a vaccine trial, a drug trial, cohort studies, and a prevalence survey using various electronic and paper-based data capturing methods. We describe experiences, challenges and lessons learned in ensuring data quality, efficiency and timeliness.
Methods | For the tuberculosis (TB) prevalence survey, conducted among 20,000 participants between 2006 and 2008, PDA's, barcode scanners, and teleforms were used. Paper-based questionnaires were designed in Cardiff Teleforms® software. Completed questionnaires were scanned, verified and uploaded into Kenya Medical Research Institute (KEMRI) databases in Kisian, Kisumu. Cleaning and linking data collected on those paper forms were the greatest challenges. In 2008 to 2010 an adolescent cohort study enrolled and followed 5,000 participants using electronic case report forms (eCRF) and a mobile field server to facilitate real-time linkage. In the TB laboratory branch, lab results are currently made available by an electronic system using structured query language server databases.
Results | Printing of questionnaires, filing, tracking and manually entering data in databases is labour intensive and easily leads to data errors. The introduction of eCRF's, PDA's, barcode readers, networked laptops, and netbooks solved these challenges.

TO.25

Prevalence of non-tuberculous mycobacteria in HIV-infected patients, Nyanza province, Kenya

Barbara Burmen[1], Kimberly McCarthy[2], Surbhi Modi[2], Joseph Cavanaugh[2], Heather Alexander[2], Maxwell Adero[1], HellenMuttai[3], Kevin Cain[3]

1. KEMRI-CDC, Kenya; 2. CDC Atlanta, United States of America; 3. CDC, Kenya

Background | Limited information is available about non-tuberculous mycobacteria (NTM) in people living with HIV in resource-limited, TB/HIV high-burden countries like Kenya.
Methods | We collected two sputum specimens for acid-fast bacilli (AFB) smear microscopy and mycobacterial culture and reviewed clinical data from people living with HIV newly presenting at 10 HIV clinics in Nyanza Province, Kenya between May and December 2011. Rapid TB identification assays were performed on all AFB-positive cultures and Hain Genotype CM assay on all isolates negative for *Mycobacterium tuberculosis*. We present the results from PLHIV with NTM isolated from at least one sputum specimen.
Results | Of 562 patients reviewed, 41 (7%) had NTM isolated from at least one sputum specimen, all of which were AFB smear negative. Of these patients, 15 (39%) had unidentified mycobacterial species, 9 (23%) had *M. intracellulare*, 6 (15%) *M. fortuitum*, 5 (13%) *M. gordonae*, and 4 (10%) *M. avium*; 2 (5%) patients had NTM isolated from both specimens (1 had *M. intracellulare* in both specimens and another *M. avium* and *M. fortuitum*). Regarding thirty-three (33) patients (81%), complete clinical, radiological and laboratory data were available. Four (4 or 12%) had respiratory symptoms and abnormal chest radiography; 2 had *M. avium* isolated, 1 *M. intracellulare* and another *M. gordonae*.
Conclusion | Isolation of NTM from people living with HIV in Kenya was relatively common, but did not decrease the specificity of sputum smear microscopy for TB. Few patients had clinical and radiological findings consistent with international criteria for definitions of NTM pulmonary disease. Longitudinal data are needed to determine the clinical significance of NTM in people living with HIV in TB high-burden settings.

TO.26

Experiences in implementing a study comparing post-mortem and verbal autopsy for measuring tuberculosis mortality in Kenya

Peter Onyango[1], Gacheri Susan, Laserson Kayla, Agaya Janet, Cain Kevin, Odhiambo Frank, Sitienei Joseph

1. KEMRI-CDC, Kenya

Background | Tuberculosis (TB) kills 1.5–2 million people per year globally. Reducing mortality is the primary aim of TB control programmes, but the burden of TB-related mortality is generally not known. However, since the performance of verbal autopsy is not known, it is necessary to first validate its utility compared to a gold standard of post-mortem examination. Such studies have rarely been conducted in resource-limited settings and the feasibility of conducting such studies is not well established. We report on experiences with implementation, including recruitment, enrolment, and acceptability.

Methods | The study is a cross-sectional survey. Patients with respiratory symptoms or patients on TB treatment at the time of death who deceased in the KEMRI-CDC Health and Demographic Surveillance Systems (HDSS) area in Siaya County, were eligible for enrolment. Death notifications were issued by community health workers and reported to the study coordinator who proceeded to get informed consent from the deceased's family and transport the body to the mortuary for post-mortem examination.

Results | Between July 2012 and February 2013, we received 155 notifications of deaths and enrolled 78 cases. Post-mortem examination, including histology, TB culture and PCR-based testing were done. Seventy-seven (77) cases were missed and not enrolled, either due to refusal by next of kin to allow post-mortem or to bodies having been embalmed.

Conclusion | Autopsy-based studies were thought to be nearly impossible to conduct, but we found that they are feasible. Community acceptability is generally high. Careful attention is needed to ensure that logistics allow for the smoothest possible implementation.

TO.27

Assessing responses to tuberculosis treatment using a simple clinical scoring system: data from the tuberculosis case-contact cohort in The Gambia

Toyin Togun[1], James Jafali[1], Simon Donkor[1], Abdou K. Sillah[1], Olumuyiwa Owolabi[1], Martin Antonio[1], Jayne Sutherland[1], Ifedayo Adetifa[1], Beate Kampmann[1,2], Martin Ota[3]

1. MRC, The Gambia; 2. Imperial College London, United Kingdom; 3. WHO-AFRO, Republic of Congo

Background | Severity scoring of tuberculosis (TB) disease and the monitoring of TB treatment in patients are generally challenging, which makes classification to assess interventions difficult. We aimed to develop a TB severity scoring system and assess its response to treatment using simple clinical parameters.
Methods | Smear-positive TB cases aged ≥15 years were prospectively enrolled at the MRC Unit The Gambia. Presence of each of the 14 parameters used for the scoring including cough duration and BMI but excluding chest X-ray, was graded from 1 to 2 and 0 if absent at recruitment, two, four and six months of anti-TB treatment. Total score was generated at each time point by adding the scores for each item with a possible maximum score of 16.
Results | Overall, 247 subjects were enrolled with a mean age of 31.9 years (SD ±12.7), 74 (29.9%) were females and 16 (6.9%) were HIV-seropositive. The mean (±SD) TB score decline was progressively significant from recruitment to the sixth month of anti-TB treatment [10.3 (±2.1) *vs* 0.3 (±0.6), p<0.001] irrespective of gender, sputum smear grade at diagnosis or HIV status. Subjects with an unfavourable treatment outcome (death/lost-to-follow-up/treatment failure) had a significantly higher mean clinical score at two months of TB treatment compared to those without (cured/treatment completed) [6.0 (SD ±4.4) *vs* 1.3 (SD ±1.7), p<0.0001].
Conclusion | This simple TB score correlated with poor outcome, showed good responsiveness to treatment and could be used even at peripheral health facilities for TB prognosis and appropriate intervention.

TO.28

Sequencing of variable T cell epitopes of *Mycobacterium tuberculosis* from confirmed tuberculosis cases in The Gambia

Tutty Isatou Faal-Jawara[1], Georgetta Mbayo[1], Sebastian Gagneux[2], Beate Kampmann[1], Jayne Sutherland[1], Bouke de Jong[3], Joel Ernst[4], Richard Copin[4], Mireia Coscolla[2], Florian Gehre[1,3], Martin Antonio[1]

1. MRC, The Gambia; 2. Swiss TPH, Switzerland; 3. ITM, Belgium; 4. New York University, United States of America

Background | Tuberculosis (TB) remains a major public health concern in the world, due to the lack of adequate knowledge of the interaction of the host and the pathogen, *Mycobacterium tuberculosis* in terms of immunity. Recently, known T cell epitopes were found to be hyperconserved suggesting T cell responses are beneficial to the pathogen. Thus, it is likely that there are diverse epitopes yet to be identified.

Methods | Genome sequencing, genome-wide sequence alignment, and *in silico* prediction were used to identify putative sequence-variable T cell epitopes. Standard mycobacteriological identification and confirmation procedures such as microscopy, decontamination, culture (mgIT 960 and LJ) were performed. DNA was extracted using the CTAB method and quantified before sent for sequencing. For the whole genome sequencing, the Illumina® Mi-Seq sequencer was used and samples sequenced to identify the sequence variant at each of the putative epitope loci in each subject's infecting strain. In-house software was used to analyse the genomes.

Results | From the whole genome sequencing data, 54% of the strains were from Lineage 4 (Euro-American); 38% Lineage 6 (*M. africanum* WA 2); and 4% from both Lineage 1 (Indo-Oceanic) and Lineage 2 (East Asia, Beijing). We found considerable sequence variation at the putative epitope loci between subjects. The loci with the highest frequency of variant sequences were found in Rv0093c and Rv2714 respectively.

Conclusion | This data show that *M. tuberculosis* exhibits sequence diversity in selected human T cell epitopes. Importantly, the *in silico* predicted epitopes were found to be immunogenic in a joint study to assess host immune responses.

MO.01

Phase IIb efficacy trial of the malaria blood stage vaccine candidate GMZ2

Michael Theisen[8], S.B. Sirima[1]*, **B. Mordmüller**[2]*, P. Milligan[3], A.B. Tiono[1], A. Ouédraogo[1], T.D. Kangoye[1], D. Kargougou[1], I. Nébié[1], S. Débé[1], A. Diarra[1], E. Bougouma[1], S. Issifou[4], A.B. Hounkpatin[4], U.A. Ngoa[4], A.A. Adegnika[4], B. Lell[4], F. Joanny[4], Y.J. Honkpehedji[4], J.C. Dejon Agobe[4], M. Esen[2], A. Ajua[2], F. Atuguba[5], O. Bangre[5], V. Asoala[5], T. Anyorigiya[5], N.A. Ansah[5], F. Kironde[6], M. Kaddumukasa[6], W. Buwembo[6], E. Mworozi[6], M. Sekikubo[6], K. Bojang[7], I. Abubakar[7], B. Okech[8], D. Ejigu[8], R. Chilengi[9], R. Noor[10], P.G. Kremsner[2], S. Jepsen[8]

*1. CNRFP, Burkina Faso; 2. EKUT, Germany; 3. LSHTM, United Kingdom; 4. CERMEL, Gabon; 5. NHRC, Ghana; 6. Makerere University, Uganda; 7. MRC, The Gambia; 8. SSI, Denmark; 9. CIDRZ, Zambia; 10. HSPH, Tanzania; * Shared first authorship*

Background | A malaria vaccine that induces immunity against the blood stage of *Plasmodium falciparum* would complement and improve malaria control strategies.
Methods | Healthy children aged 12–60 months were randomised to receive three doses of either 100 µg GMZ2/ $Al(OH)_3$ or control vaccine (rabies) with 28 days interval. Participants were followed by enhanced passive surveillance for 24 months for malaria episode and adverse events. Malaria was defined as fever/history of fever with a parasite density of ≥5000/µl asexual blood stage *Plasmodium falciparum* parasites. GMZ2 and control vaccines were administered intramuscularly and participants as well as investigators were blinded. Adverse events as well as malaria episodes were collected for a total of 24 months.
Results | We will present design, challenges and successes.

MO.02

Speeding up the development of malaria vaccines: the example of P27A, bridging phase Ia and Ib

Seif Shekalaqhe[1], Salim Abdulla[1], François Spertini[2], Sophie Houard[3], Seif Sekhalake[1], Blaise Genton[2,4]

1. IHI, Tanzania; 2. CHUV, Switzerland; 3. EVI, Germany; 4. Swiss TPH, Switzerland

Background | The traditional approach of conducting one or several phase Ia studies in malaria non-endemic areas and then running phase Ib studies in endemic areas leads to slow progress in vaccine development. It was the result of previous abuse of local populations, safety issues and scientific concerns regarding immunological assessment.

Methods | We decided to conduct a combined phase Ia/b in 16 healthy malaria non-exposed European adults in Lausanne, Switzerland, and in 40 malaria exposed African adults in Bagamoyo, Tanzania, to assess the safety and immunogenicity of a blood-stage antigen (P27A) formulated in alhydrogel® or glucopyranosyl lipid A stable emulsion (GLA-SE). The first group of 8 subjects will be injected in Switzerland. If there is no safety concern after 28 days, the first group in Africa will be injected with the same antigen and adjuvant dosages. The same procedures will be performed for higher antigen and GLA-SE dosages.

Conclusion | This staggered approach should considerably speed up the process, while ensuring the safety of participating subjects. In terms of immunogenicity, we will be able to assess the potential boosting effect of the vaccine in an endemic population, and be able to choose the best Ag and adjuvant doses to proceed in younger populations. This approach not only saves time but also assesses the vaccine candidate directly in the target population for which the vaccine is intended.

MO.03

Controlled human malaria infections and irradiated whole sporozoite vaccine evaluation in Africa

Bernhards Ogutu[1,2], Stephen Hoffman[3], Seif Shekalaghe[4], Elizabeth Juma[2]

1. Strathmore University (CREATES), Kenya; 2. KEMRI, Kenya; 3. Sanaria Inc., Rockville, MD, United States of America, 4. IHI, Tanzania

Background | To facilitate phase I capacity development in Africa, controlled human malaria infection (CHMI) has been used as a dual purpose mechanism for product evaluation and capacity building.
Methods | A network of seven African research centres (Kintampo, Bagamoyo, KEMRI, Lambarene, MRTC, CNFRP, Manhiça) in partnership with one American and five European research centres (University of Maryland; Swiss TPH, University of Oxford, CRESIB, University of Tübingen, Radboud University Nijmegen) and Sanaria Inc., formed the African Controlled Human Malaria Infection studies (CHMI) platform to build capacity in African research centres and evaluate *P. falciparum* sporozoites (PfSPZ) in malaria endemic areas. This will also enhance phase I capacity in these centres and prepare the centres to evaluate the irradiated *P. falciparum* sporozoites (PfSPZ) vaccine candidate.
Results | The first two challenge studies in Africa were completed in Bagamoyo and Nairobi. Five more studies are planned on the platform in the next year. These studies will enable the characterisation of the populations at the centres and harmonisation of CHMI procedures across the centres.
Conclusion | Results of the first two studies and the proposed CHMI programme for the platform will be presented.

MO.04

A simplified artesunate regimen for severe malaria in children

Peter G. Kremsner[1], Saadou Issifou, Tsiri Agbenyega, Bernhards Ogutu, Kalifa Bojang, Terrie Taylor, Charles Newton, Marielle K. Bouyou Akotet, Benjamin Mordmüller, Stefanie Bolte, Carsten Köhler and Sanjeev Krishna

1. ITM Tübingen, Germany

Background | The goal of this project is optimisation of parenteral artesunate treatment in children with severe malaria in Africa with a simplified administration scheme. We have shown in an initial phase II dose optimisation study that a simplified once daily intravenous regimen in 3 days is equivalent to the conventional 5-day intravenous regimen. In a follow-up study within the SMAC consortium, we have now tested a simplified regimen by intramuscular route *vs* intravenous route for optimisation of artesunate usage.
Methods | In a randomised, open-label, 3-arm, follow-up trial, the standard 5-dose regimen of intramuscular artesunate was compared with simplified 3-dose intravenous and 3-dose intramuscular regimen in 1047 African children. Patients aged 6 months–10 years of age were hospitalised at seven African sites with *Plasmodium falciparum* malaria and received a total dose of 12 mg/kg artesunate. As primary endpoint, the proportion of children who cleared at least 99% of their admission parasitaemia at 24h was assessed. Safety data, secondary efficacy endpoints and pharmacokinetics were also addressed.
Results | Efficacy analysis revealed very good cure rate and excellent parasite clearance rate in all three cohorts. Study results also indicated great tolerability and similar artesunate clearance rates with all three administration schemes. We also observed delayed haemolysis in a certain number of patients which was investigated further in a sub-group of individuals.
Conclusion | Our initial phase II study showed non-inferiority of the 3-day, once daily dosing regimen for intravenous artesunate in African children hospitalised for severe malaria compared to the 5-day intravenous treatment. Data analysis of the phase III follow-up trial indicates good efficacy of intramuscular administration and supports our aim to establish a simplified treatment of severe malaria. Delayed haemolysis needs to be taken into account after artesunate treatment.

MO.05

Safety of artesunate-pyronaridine in the repetitive treatment of uncomplicated malaria in sub-Saharan Africa

Abdoulaye Djimdé[1], Issaka Sagara, Bakary Fofana, Omar Bila Traore, Jacob Dara, Isabelle Borghini, Ghiorghis Belai, Stephan Duparc, and the WANECAM Mali Team

1. WANECAM-Mali, MRTC, University of Bamako, Mali

Background | Pyramax® tablets are indicated for the treatment of acute, uncomplicated malaria infection caused by *Plasmodium falciparum* or by *Plasmodium vivax* in adults and children weighing 20 kg or more, in areas of low transmission with evidence of artemisinin resistance. Pyramax® is to be used only as a single treatment course in any given patient. The WANECAM study is entitled: 'A phase IIIb/IV comparative, randomised, multicentre, open-label, parallel 3-arm clinical study to assess the safety and efficacy of repeated administration of pyronaridine-artesunate, dihydroartemisinin-piperaquine or artemether-lumefantrine or artesunate-amodiaquine over a two-year period in children and adult patients with acute uncomplicated *Plasmodium* sp. malaria'. It is the only ongoing trial that will generate the data for the expansion of the current Pyramax® label. This presentation will focus on the safety data gathered so far from the WANECAM longitudinal trial in Mali, Burkina Faso and Guinea.
Methods | A defined subset of the WANECAM longitudinal study forms the basis of a sub-study to test non-inferiority between initial and repeat Pyramax® dosing in terms of the hepatotoxicity event rate. A qualitative review of events was also performed.
Results | To date, 219 patients received more than one Pyramax® treatment and 54 received more than two Pyramax® treatments. We observed no increase in incidence or severity of liver function test results or adverse events. The study is ongoing and updated results will be presented at the Forum.
Conclusion | Pyramax® appears, based on these preliminary data, to be well tolerated on repeat dosing.

MO.06

Efficacy of dihydroartemisinin-piperaquine in the treatment of uncomplicated *P. falciparum* malaria in African patients and day 7 plasma piperaquine concentration

Issaka Zongo[1], Fabrice A. Somé[1], Serge A.M. Somda[2], Sunil Parikh[3,4], Noel Rouamba[1], Philip J. Rosenthal[3], Joel Tarning[5,7], Niklas Lindegardh[5,7], François Nosten[5,6,7], Jean Bosco Ouédraogo[1]

1. IRSS, Burkina Faso; 2. Centre Muraz, Burkina Faso; 3. University of California, United States of America; 4. Yale University, United States of America; 5. Mahidol University, Bangkok, Thailand; 6. Shoklo Malaria Research Unit, Mae Sot, Thailand; 7. University of Oxford (Nuffield), United Kingdom

Background | We investigated the efficacy of dihydroartemisinin-piperaquine for the treatment of uncomplicated *falciparum* malaria and associations between treatment responses and day 7 plasma concentrations of piperaquine in children.

Methods | We performed a single, open-label trial in Bobo-Dioulasso, Burkina Faso. Enrolled participants received one daily dose of dihydroartemisinin-piperaquine (40 mg/320 mg) for three days and were followed up for 42 days. Day 7 plasma concentrations of piperaquine were measured in a subset of children aged 2–10 years. The primary endpoint was the risk of recurrent malaria, both unadjusted and adjusted.

Results | Of 379 enrolled participants, 96.3% completed the 42 day follow-up. Day 7 capillary sample was collected on 226 children and venous blood on 198 children. The mean daily dose of piperaquine was 18.3 mg/kg. The cumulative unadjusted treatment failure rate was 31.25% in children less than 2 years old and 16.04% in those 2–5 years of age; the risk was lower in the group 5–10 years of age 9.38% and null in children over 10 years old. After genotyping, only 3 cases were recrudescent. Piperaquine day 7 concentrations were significantly lower in patients with recurrent malaria during the 42 days of follow-up. DHA-PQ had a good safety profile and associated with rapid fever and parasite clearance within 48 hours.

Conclusion | Dihydroartemisinin-piperaquine is highly effective for uncomplicated malaria treatment. Recurrent malaria was correlated with low day 7 plasma concentration of piperaquine.

MO.07

Therapeutic efficacy of artesunate-amodiaquine combination in the treatment of uncomplicated malaria in Mafèrinyah, Republic of Guinea

Sidikiba Sidibe[1], Diallo Mamadou Saliou[1], A.H. Beavoguii, M.S. Diallo[1]; A. Togo[2], I. Sagara[2], A. Dicko[2], M.M. Sylla[1], S. Toure[2], D. Camara[1], M. Yattara[1], G. Camara[1], A. Sow[1], P. Millimono[1], M. Sylla[1], A. Cissé[1], E. Diawara[1], A. Delamou[1], M.M. Diallo[1], M. Keita[3], A. Djimdé[2], O.K. Doumbo[2]

1. CNFRSR, Guinea; 2. MRTC, University of Bamako, Mali; 3. National Malaria Control Programme of Guinea, Guinea

Background | Resistance of *Plasmodium falciparum* to antimalarial drugs requires that new ways of malaria control are identified, hence, the need for more epidemiological data. The purpose of this study was to assess prospectively the clinical and parasitological responses to artesunate+amodiaquine use in the treatment of uncomplicated *P. falciparum* malaria in the village of Mafèrinyah, Republic of Guinea.

Methods | From March 2011 to November 2012, a study of clinical efficacy of the combination of artesunate and amodiaquine was performed in a cohort of 600 subjects aged 3 months to 45 years. The WHO standard protocol of 28 days follow-up was applied to patients diagnosed with uncomplicated malaria and living in Mafèrinyah village. The subjects were treated orally for 3 consecutive days at recommended doses. Drops of blood of these subjects were collected on blotting paper at day 0 and at recommended follow-up days and were used for molecular analysis.

Results | A total of 223 subjects were included. The uncorrected adequate clinical and parasitological response (ACPR) was 94.3% (182/193). The uncorrected late treatment failure was 0.97% (2/206). As for the uncorrected late parasitological failure, it was 5.7% (11/193). After molecular correction, ACPR was 97.4%

Conclusion | These preliminary results show that the combination therapy of artesunate and amodiaquine is clinically effective in the treatment of uncomplicated malaria in Mafèrinyah. Rare side effects were dominated by low blood sugar, dizziness and physical weakness.

MO.08

Impact of community screening and treatment of asymptomatic carriers of *Plasmodium falciparum* with artemether-lumefantrine on asymptomatic and gametocyte carriage: a 12-month, cluster-randomised study

Alfred B. Tiono[1], S.B. Sirima[1], A. Ouédraogo[1], B. Ogutu[2], A. Diarra[1], S. Coulibaly[1], M. Cousin[3], C. Remy[3], A. Mukhopadhyay[4], I. Soulama[1], K. Hamed[5]

1. CNRFP, Burkina Faso; 2. KEMRI-Walter Reed, Kenya; 3. Novartis Pharma AG, Switzerland; 4. Novartis Healthcare Private Ltd, India; 5. Novartis Pharmaceuticals Corp., United States of America

Background | To reduce *Plasmodium falciparum* malaria transmission, interventions to asymptomatic carriers should also be effective against gametocytes.

Methods | A 12-month, controlled, parallel, cluster-randomised (9-intervention, 9-control) study in Burkina Faso evaluated the impact of systematic screening and artemether-lumefantrine (AL) AL/AL-dispersible treatment of asymptomatic carriers detected by rapid diagnostic test during community screening campaigns (CSCs 1–3), compared to no treatment. CSCs 1–3 occurred before the rainy season and CSC4 occurred after it, marking the end of the study. Symptomatic malaria episodes were treated with AL/alternative in both arms during study.

Results | Prevalence of asymptomatic carriers (microscopy-confirmed) in intervention and control arms was 42.8% *vs* 47.5%; 4.1% *vs* 35.7%; 2.8% *vs* 32.2% and 34.4% *vs* 37.8% at CSC1, 2, 3 and 4, respectively. Overall proportion of gametocyte carriers (GCs) in intervention and control arms was 9.5% *vs* 10.2%; 0.6% *vs* 5.5%; 0.4% *vs* 5.8%; and 4.8% *vs* 5.1% at CSC1, 2, 3 and 4, respectively. Prevalence (least square mean SE) of microscopy-confirmed GCs at CSC4 in intervention arm was 4.9 0.41 *vs* 5.1 0.41 in control arm (p=0.7208). Prevalence of GCs (1,999 randomly selected subjects across both arms) at CSC4, assessed by qRT-PCR, was 8 times greater in both arms compared to microscopy (49.7% *vs* 6.0% intervention; 47.3% *vs* 5.4% control).

Conclusion | In this community setting study, the intervention arm showed greater reductions in prevalence of asymptomatic carriers and gametocyte carriers than the control arm at CSC2 and CSC3, relative to CSC1 (p<0.0001). However, asymptomatic carriage and gametocyte carriage prevalence rose thereafter in the intervention arm to reach a level similar to the control arm at CSC4. The use of qRT-PCR can lead to higher levels of asymptomatic carrier detection and can impact disease transmission.

MO.09

Treatment of asymptomatic carriers of *Plasmodium falciparum* with artemether–lumefantrine: impact on the prevalence of anaemia

Alfred B. Tiono[1], Christine Remy[2], Alphonse Ouedraogo[1], Kamal Hamed[3]

1. CNRFP, Burkina Faso; 2. Novartis Pharma AG, Basel, Switzerland; 3. Novartis Pharmaceuticals Corp., East Hanover, NJ, United States of America

Background | Asymptomatic carriers act as parasite reservoirs and are associated with developing anaemia. This study compared the effect of systematic treatment of asymptomatic carriers of *Plasmodium falciparum* with artemether-lumefantrine (AL) on haemoglobin (Hb) levels and anaemic status with no treatment.
Methods | In a 12-month, single-centre, controlled, parallel, cluster-randomised study, inhabitants of 18 villages in Burkina Faso were randomised (1:1) to intervention and control arms. They participated in four community screening campaigns (CSC1–4). The CSC1–3 included treatment of asymptomatic carriers in the intervention arm conducted one month before the rainy season, while CSC4 was conducted after the rainy season and marked the end of the study.
Results | Mean Hb level change in all asymptomatic carriers aged >6 months from day 1 to day 28 of CSC1 was +0.53 g/dl (from 11.81 to 12.33 g/dl) in the intervention arm *vs* –0.21 g/dl (from 12.06 to 11.86 g/dl) in the control arm ($p<0.001$). During the same period, the proportion of asymptomatic carriers >6 months to <5 years of age with anaemia (mild, moderate or severe) in the intervention arm decreased by 31.1% (from 75.7% to 44.6%), compared with a decrease of 4.7% (from 76.3% to 71.6%) in the control arm. After 12 months, the proportion of asymptomatic carriers with anaemia was reduced in both arms.
Conclusion | Systematic screening and treatment of asymptomatic carriers at community level can reduce the prevalence of anaemia in children in the short term. However, the impact of the intervention was not sustained in the subsequent transmission season.

MO.10

The Malaria Vectored Vaccines Consortium (MVVC): integrating capacity building and networking in the design and conduct of clinical trials in East and West Africa

Nicola K. Viebig[1], Odile Leroy[1], Egeruan Babatunde Imoukhuede[1], Kalifa Bojang[2], Muhammed Afolabi[2], Caroline Ogwang[3], Badara Cissé[4], Philip Bejon[3], Alfredo Nicosia[5], Sodiomon Sirima[6], Adrian S. Hill[7]

1. EVI, Germany; 2. MRC, The Gambia; 3. KEMRI, Kenya; 4. Université Cheikh Anta Diop, Senegal; 5. Okairos Srl, Rome, Italy; 6. CNRFP, Burkina Faso; 7. University of Oxford, United Kingdom

Background | Malaria caused by *Plasmodium falciparum* results in the death of approximately one million people every year. The majority of deaths occur in children living in sub-Saharan Africa. A vaccine giving strong and lasting protection would provide the most cost-effective and long-term solution for the prevention of this deadly disease.

Methods | The Malaria Vectored Vaccines Consortium (MVVC) is a four and a half year project set up with the aim of integrating capacity building and networking in the design and conduct of phase I and II clinical trials of viral vectored malaria vaccine candidates in East and West African adults, children, and infants. The overall objective of the project is to develop a safe, non-reactogenic, effective and affordable malaria vaccine for use by the malaria-endemic populations of the world.

Results | Three phase Ib clinical trials were conducted in Kenya and The Gambia and three phase IIb clinical trials are ongoing in Burkina Faso, Kenya and Senegal. Substantial progress has been made in the development of clinical trial capabilities, infrastructure and human resources that would ensure the sustainability of the clinical trial sites after the end of the project. Tremendous success in developing the MVVC partners into a well-established network has been achieved.

Conclusion | An update on the results and achievements of the MVVC in the conduct of clinical trials, capacity building and networking will be presented at the Forum.

– Imoukhuede E.B., *International Innovation, Healthcare*, 2012, 15
– Ogwang C. et al., *PLOS ONE*. 2013; 8(3):e57726

MO.11

Assessing chimpanzee adenovirus serotype ChAd63 neutralising antibodies prior to the implementation of a candidate malaria vaccine regimen based on viral vectors

Nébié Issa Ouédraogo[1], Katie J. Ewer[2], Alfred B Tiono[1], Nick J. Edwards[2], Issiaka Soulama[1], Jean Baptiste Yaro[1], David Kangoye[1], Adrian V. S. Hill[2], Sodiomon B. Sirima[1]

1. CNRFP, Burkina Faso; 2. University of Oxford (Jenner), United Kingdom

Background | Adenovirus serotypes vector-based vaccines have been proven to be immunogenic and are used in clinical trials. However the adaptive immune responses to the vector may also block or reduce the induction of the desired responses against the vaccine antigen. This gave rise to concerns about the usefulness of such vaccines in target populations where pre-existing anti-vector immunity is high. The objective of this study is to assess the prevalence of neutralising antibodies to chimpanzee adenovirus serotype 63 (ChAd63) in a malaria endemic population likely to benefit from a chimpanzee adenovirus-based malaria vaccine.

Methods | The samples were collected in children from 0.5–3 years of age and in participants 10–45 years of age in a seasonal malaria transmission area in Banfora, western Burkina Faso (500 km from Ouagadougou). The ChAd63 specific neutralising antibody titres were assessed using a SEAP (secreted alkaline phosphatase) quantitation assay.

Results | The lower antibody titre was 17 and the highest dilution titre was 2,144. In children 0.5–3 years of age, the geometric mean value of neutralising antibody titres was 41.2 (95% CI: 35.6–47.8) while in adults it was 153.1 (95% CI: 120.9–193.9). The difference for geometric means between adults and children was statistically significant ($p<0.0001$). Among the study participants 77% had antibody titres below 200. This rate increases to 97.0% in children against 57% in adults volunteers.

Conclusion | The low prevalence of high titre neutralising antibodies to ChAd63 in vaccine target children is very encouraging for its potential use as a malaria vaccine vector.

MO.12

Safety and immunogenicity of heterologous prime-boost immunisation with candidate vaccines Chad63 ME-TRAP and MVA ME-TRAP in healthy Burkinabè children aged 5–17 months

Alfred B. Tiono[1], Issa Nebie[1], Jean Baptiste Yaro[1], Issiaka Soulama[1], Edith Bougouma[1], Souleymane Sanou[1], Alphonse Ouedraogo[1], Nicola Viebig[3], Katie J. Ewer[2], Alison Lawrie[2], Susanne Sheehy[2], Rachel Roberts[2], Philip Bejon[2], Nicholas Anagnostou[2], Egeruan Babatunde Imoukhuede[3], Adrian Hill[2], Bienvenu Sodiomon Sirima[1]

1. CNRFP, Burkina Faso; 2. University of Oxford (Jenner, Nuffield), United Kingdom; 3. EVI, Germany

Background | The candidate malaria vaccines ChAd63 ME-TRAP and MVA ME-TRAP consist of inactivated viral vectors (ChAd63 and MVA) containing the recombinant DNA insert ME-TRAP which has shown durable partial efficacy against *P. falciparum* infection in a United Kingdom adult phase IIa sporozoite challenge study. The vaccination with this candidate has proven to be safe and immunogenic in The Gambia and Kenya. The objective of this phase IIb trial is to assess the protective efficacy against clinical malaria in 5–17 month old infants and children living in a malaria-endemic area.
Methods | A double-blind randomised controlled trial with a lead in safety evaluation (phase Ib) followed by phase IIb efficacy of ChAd63 ME-TRAP/MVA ME-TRAP trial is planned in rural areas of the Banfora health district, Burkina Faso. The protective efficacy against clinical malaria will be assessed by the time to first episode of malaria over a period of six months follow-up after the last vaccination. Exploratory immunology will be measured on different time points of the study.
Results | Thirty (30) children were enrolled since December 2012 for the vaccine safety assessment. The enrolment of 700 children for the assessment ChAd63 ME-TRAP/MVA ME-TRAP efficacy is ongoing. Preliminary results will be analysed at the end of 2013.
Conclusion | The ChAd63 ME-TRAP/MVA ME-TRAP malaria vaccine has proven to be safe, immunogenic and partially efficacious in previous trials. Findings from this phase IIb trial malaria vaccine candidate may support its further development.

MO.13

Efficacy study of ChAd63-MVA ME-TRAP prime-boost vaccination against *Plasmodium falciparum* infection in healthy adults in Senegal

Victorine Mensah[1], Badara Cisse[1], Babacar Faye[1], Tandakha Dieye[1], Magatte Ndiaye[1], Massamba Syll[1], Aly Gueye[1], Annie Abiola[1], Amy Ndaw[1], Omar Gaye[1]; Andrian Hill[2], Suzanne Sheehy[2], Nicholas Anagnostou[2], Allison Lawrie[2], Katie Ewer[2], Rachel Roberts[2], Carly Bliss[2], Nick Edwards[2]

1. University Cheikh Anta Diop, Senegal; 2. University of Oxford (Jenner), United Kingdom

Background | Malaria transmission is in decline in some parts of Africa, which is partly due to the scaling up of control measures. Previous attempts of elimination ended with mixed success. It is currently thought that additional control measures including vaccination will be required. All previous malaria vaccine candidates showed partial protection. In recent studies, adenovirus-vectored vaccines showed good safety and immunogenic profile. Our study reports on the efficacy and immunogenicity of a prime-boost vaccine using these adenovirus vectors.

Methods | From July 2011 to February 2012 we conducted a single blinded, randomised controlled phase IIb efficacy study. A total of 120 healthy men 18–50 years of age were randomised to receive either the active vaccine (ChAd63-MVA ME-TRAP) or a control vaccination (rabies vaccine). They were vaccinated at 8 weeks interval and were followed up. The immunological status was determined by ELISPOT and ELISA to quantify the T cells response and identify the specific antibodies against *P. falciparum*. To evaluate the parasitaemia after the vaccinations, we used finger prick thick blood film and real-time PCR. All vaccinated participants received malaria treatment at the end of the vaccinations to erase all traces of parasitaemia before intensive PCR survey for time to first *P. falciparum* infection and re-infection. We assessed the reactogenicity in all adverse and serious adverse events which occurred during follow-up.

Results | Preliminary results show a good safety profile and immunogenicity of the vaccine candidate. PCR analysis is ongoing. All results on safety, immunogenicity and efficacy will be presented at the conference.

MO.14

Maternal immunisation protects mice pups against malaria

Thomas Egwang[1], Margaret Mendi[2], Toshihiro Horii[3], Hastings Ozwara[4]

1. Med Biotech Laboratories, Kampala, Uganda; 2. ICIPE, Nairobi, Kenya; 3. Osaka University, Japan; 4. Institute of Primate Research, Kenya

Background | Malaria remains a serious public health problem in infants under 5 years of age. Maternal IgG antibodies induced by natural infections and transferred to the unborn baby via the placenta and after birth via breast milk, confer passive immunity against malaria. We investigated the feasibility of protecting infants by maternal immunisation with a malaria vaccine candidate.
Methods | Female BALB/c mice were immunised intranasally three times before pregnancy with phosphate-buffered saline (PBS) or the *Plasmodium falciparum* blood stage vaccine candidate SE36, with co-administration of the chemokines RANTES and CCL28 as natural adjuvants. After delivery, mothers were boosted with SE36 alone. Pups were breast-fed daily on natural or foster mothers immunised with SE36 or PBS. Specific IgG antibodies in milk and sera of mothers and in sera of pups were measured by indirect ELISA. Pups were challenged by injection of *P. berghei*-infected mouse red blood cells and blood parasitaemia was monitored daily.
Results | The milk and sera of lactating mice immunised with SE36 contained detectable specific IgG antibodies (optical density (OD) values 0.93 ± 0.14 and 1.13 ± 0.14) while those from mice immunised with PBS had Background levels (0.19 ± 0.01 and 0.30 ± 0.05). Pups born to and breast-fed by SE36-immunised mothers (transplacental and breast milk antibodies) had 9.7 times more serum antibodies and the lowest mean parasitaemias by comparison with pups born to and breast-fed by PBS-immunised mothers which had higher mean parasitemias.
Conclusion | Maternal immunisation of female mice before pregnancy with a specific malaria vaccine candidate confers passive antimalarial immunity to mice pups.

MO.15

Efficacy and safety of mefloquine as malaria intermittent preventive treatment in pregnancy: results from a multicentre randomised clinical trial

Raquel González[1], Clara Menéndez[1], MiPPAD study group[1,2,3,4,5,6,7]

1. CRESIB, Spain; 2. IHI, Tanzania; 3. IRD, Paris, France; 4. ITM Tübingen, Germany; 5. UAC, Benin; 6. CISM, Mozambique; 7. MRC, Albert Schweitzer Hospital, Lambaréné, Gabon

Background | The current recommendation by the World Health Organization (WHO) to prevent malaria infection in pregnancy in areas of stable malaria transmission relies on: 1) the prompt and effective case management of malaria illness, 2) the use of intermittent preventive treatment (IPTp) with sulfadoxine-pyrimethamine (SP) at each scheduled antenatal clinic visit and 3) the use of insecticide-treated nets. However the spread of parasite resistance to SP has raised concerns about the medium and long-term use of SP for IPTp. The evaluation of alternative antimalarials for IPTp is thus urgently needed. Of all the current available alternative antimalarial drugs, mefloquine (MQ) is the one that offers the most comparative advantages to SP.

Methods | A randomised open-label superiority 3-arm trial was conducted in four African countries (Benin, Gabon, Tanzania and Mozambique) to compare a 2-dose MQ versus a 2-dose SP regimen for IPTp in the prevention of the adverse effects of malaria during pregnancy and to compare the tolerability of two different MQ administration regimens. The three study arms were: 1) IPTp with SP, 2) IPTp with MQ given as full dose on 1 day, 3) IPTp with MQ split dose given over 2 days. All participants received an insecticide-treated net at recruitment and were followed-up until the infants reached age one.

Results | In total 4,750 pregnant women were enrolled at the antenatal clinic from September 2009 to January 2012. The results obtained on the efficacy and safety of MQ as IPTp shall be presented.

MO.16

Efficacy and safety of mefloquine as malaria intermittent preventive treatment in pregnancy in HIV-infected women receiving daily cotrimoxazole prophylaxis

Raquel González[1], Clara Menéndez[1], MiPPAD Study Group[1,2,3,4]
1. CRESIB, Spain; 2. IHI, Tanzania; 3. CISM, Mozambique; 4. KEMRI-CDC, Kenya

Background | The current recommendation by the World Health Organization (WHO) to prevent malaria infection in pregnancy in areas of stable malaria transmission relies on: 1) the prompt and effective case management of malaria illness, 2) the use of intermittent preventive treatment (IPTp) with sulfadoxine-pyrimethamine (SP) at each scheduled antenatal clinic visit and 3) the use of insecticide-treated nets (ITNs). However, the spread of parasite resistance to SP and the significant overlap in some regions of malaria transmission and high prevalence of HIV infection have raised concerns about the medium and long-term use of SP for IPTp. The evaluation of alternative antimalarials for IPTp is thus urgently needed for HIV-infected women. Of all the current available alternative antimalarial drugs, mefloquine (MQ) is the one that offers the most comparative advantages to SP.
Methods | A randomised double-blind superiority clinical trial was conducted in three African countries (Kenya, Tanzania and Mozambique) to compare the efficacy of 3 doses of MQ as IPTp with 3-dose placebo-IPTp in HIV-infected pregnant women receiving Cotrimoxazole prophylaxis. Pregnant women were enrolled at the antenatal clinic and followed until the infants were two months old. All participants received an ITN at recruitment.
Results | In total 1,071 pregnant women were recruited from March 2011 to January 2012. The results obtained on the efficacy and safety of MQ as IPTp will be presented.

MO.17

Rich and population pharmacokinetics of mefloquine intermittent preventive treatment against malaria in pregnant women in Gabon

Michael Ramharter[4], Ghyslain Mombo-Ngoma[1], Jean-Rodolphe Mackanga[1], Rella Manego Zoleko[1], Daisy Akerey-Diop[1], Arti Basra[1], Raquel Gonzalez[5], Clara Menéndez[5], Peter Kremsner[2], Reinhold Kerb[3]

1. CERMEL, Gabon; 2. ITM Tübingen, Germany; 3. IKP, Germany; 4. Medical University of Vienna, Austria; 5. CRESIB, Spain

Background | Mefloquine is currently investigated as alternative drug for use as intermittent preventive treatment in pregnant women. To date – despite several studies on the pharmacokinetics of mefloquine treatment in pregnancy – no pharmacokinetic data are available for its use as IPTp drug. We investigated the pharmacokinetics of mefloquine IPTp in Gabon to characterise the pharmacokinetics of mefloquine when administered as a single-dose or as a split-dose regimen.
Methods | This rich and population pharmacokinetic study was performed in the course of the EDCTP-funded MIPPAD study. Mefloquine is investigated in this randomised controlled clinical trial as alternative IPTp drug compared to sulfadoxine-pyrimethamine. Mefloquine was administered at a dose of 15 mg/kg either as a single-dose or as a split-dose regimen (7.5 mg/kg on days 1 and 2, respectively).
Results | Three hundred seventeen (317) pregnant women agreed to participate in this pharmacokinetic sub-study. A rich sampling strategy was used to describe the classical pharmacokinetic parameters of single-dose and split-dose regimens. A population pharmacokinetic model was used for analysis in a larger group of patients. Mefloquine and its main inactive metabolite carboxymefloquine were analysed.
Conclusion | This study is the first to establish the pharmacokinetic characteristics of mefloquine IPTp and will provide useful evidence for informed decisions on future IPTp regimens containing mefloquine.

MO.18

A trial of intermittent screening and treatment as an alternative to intermittent preventive treatment with sulfadoxine-pyrimethamine for the control of malaria in pregnancy

Harry Tagbor[1], K. Kayentao, S.O. Coulibally, K. Mohammed, K. Bojang[1], J. Williams, F. Njie, M. Cairns, P. Milligan[1], F.O. ter Kuile[3], D. Chandramohan[2], B. Greenwood[1]

1. LSHTM, United Kingdom; 2. KNUST, Ghana; 3. LSTM, United Kingdom

Background | The incidence of malaria, including incidence in pregnant women, is declining in some African countries, and resistance to sulfadoxine-pyrimethamine (SP) is widespread. Thus, intermittent preventive treatment in pregnancy with SP (SP-IPTp) may no longer be appropriate in certain situations, and alternative strategies are needed.

Methods | A multicentre, randomised controlled non-inferiority trial was undertaken in four West African countries, including 5,000 pregnant women who slept under an insecticide-treated bed net. The standard SP-IPTp regimen (2–3 courses of SP in the second and third trimester) will be compared to intermittent screening and treatment (IST) of parasitaemia using a rapid diagnostic test at scheduled antenatal clinic visits in the second and third trimester. The primary end points of the trial are prevalence of low birth weight, mean maternal haemoglobin at 38 ±2 weeks of gestation and prevalence of placental malaria. Other outcomes affecting mothers (anaemia, parasitaemia, clinical malaria) and children (still births, perinatal mortality) will also be analysed.

Results | Recruitment and follow-up of study participants is completed. Analyses will be finalised in August 2013 and the results will be presented at the Seventh EDCTP Forum in 2014.

Conclusion | The study will provide information to national malaria control programmes in countries whether there are alternative, safe and effective methods to the WHO recommended SP-IPTp regimen for managing malaria in pregnancy. This could have particularly important implications for the control of malaria in pregnancy in areas with high levels of SP resistance.

MO.19

Intermittent preventive therapy for malaria during pregnancy using 2 *vs* 3 or more doses of sulfadoxine-pyrimethamine and risk of low birth weight in Africa: a systematic review

Kassoum Kayentao[1,2], P. Garner[1], A.M. van Eijk[1], I. Naidoo[3], C. Roper[4], A. Mulokozi[5], J.R. MacArthur[6], M. Luntamo[7], P. Ashorn[7], O.K. Doumbo[2], F.O. ter Kuile[1]

1. LSTM, United Kingdom; 2. MRTC, University of Bamako, Mali; 3. MRC, South Africa; 4. LSHTM, United Kingdom; 5. IHI, Tanzania; 6. CDC Atlanta, United States of America; 7. University of Tampere, Finland

Background | Two doses of intermittent preventive therapy (IPTp) with sulfadoxine-pyrimethamine (SP) to control malaria during pregnancy may not provide protection during the last 4 to 10 weeks of pregnancy. We performed a systematic review and meta-analysis of trials to determine whether regimens containing 3 or more doses of SP for IPTp during pregnancy are associated with a higher birth weight or lower risk of low birth weight than standard 2-dose regimens.

Methods | The following sources were searched: ISI Web of Knowledge, EMBASE, SCOPUS, PubMed, LILACS, the Malaria in Pregnancy Library, Cochrane CENTRAL, and trial registries from their inception to December 2012, without language restriction. Relative risk (RR), mean differences, and 95% CIs were calculated with random-effects models.

Results | Of 241 screened studies, 7 trials with 6,281 pregnancies were included. The median birth weight in the 2-dose group was 2,870 g (range, 2722–3239 g) and on average 56 g higher (95% CI: 29–83 g; I2=0%) in the ≥3-dose group. Three or more doses were associated with fewer low birth weight births (RR, 0.80; 95% CI: 0.69–0.94; I2=0%). The association was consistent across a wide range of SP resistance (0% to 96% dihydropteroate-synthase K540E mutations). The 3-dose group had less placental malaria (RR, 0.51; 95% CI: 0.38–0.68; I2=0%). In primi-secundigravidae, the risk of moderate to severe maternal anaemia was lower in the 3-dose group (RR, 0.60; 95% CI: 0.36–0.99; I2=20). There were no differences in rates of serious adverse events.

Conclusion | IPTp with 3 or more doses of SP was associated with a higher birth weight and lower risk of low birth weight than the standard 2-dose regimens. These data provided support for the new WHO recommendations to provide IPTp-SP at each scheduled antenatal care visit from the second trimester.

MO.20

Impact of sulphadoxine-pyrimethamine resistance on the effectiveness of intermittent preventive therapy for malaria in pregnancy (IPTp) in Africa: A systematic review and meta-analysis

Feiko ter Kuile[1]

1. LSTM, United Kingdom and KEMRI, Kisumu, Kenya

MO.21

Effectiveness of seasonal malaria chemoprevention combined with community case management for malaria in Southern Senegal: a cluster-randomised trial

Jean Louis Ndiaye[1], Youssoupha Ndiaye[2], Mamadou S. Ba[1], Badara Cisse[1], Babacar Faye[1], Maguette Ndiaye[1], Roger Tine[1], Paul Milligan[3], Oumar Gaye[1]

1. University Cheikh Anta Diop, Dakar, Senegal; 2. MSAS, Senegal; 3. LSHTM, United Kingdom

Background | Although the overall incidence of malaria has recently declined in Senegal as in some other countries, this hides the fact that the burden of malaria remains very high in the southern part of the country. Seasonal malaria chemoprevention (SMC) is known to be highly effective in preventing malaria illness but the relative advantage of making SMC available in villages with Community Medicines Distributors (CMD) for malaria has not been evaluated. SMC feasibility, tolerability and acceptability of delivery over a longer period were also assessed.

Methods | In this trial, 24 villages were randomised to deliver community case management with SMC or community case management alone. In SMC villages, CMDs gave all children under 10 years of age preventive treatment with sulfadoxine-pyrimethmine plus amodiaquine in each month from July to November 2011.

Results | The primary endpoint was the incidence of malaria (fever with a positive rapid diagnostic test). A high coverage of more than 80% has been obtained when SMC drugs were given door-to-door. This study shows an 82% protective efficacy of SMC. A positive impact on severe anaemia and parasitaemia has also been found. Only 14 reports of adverse drug reactions, (vomiting or abdominal pain) have been notified. No serious adverse events attributed to study drugs were reported.

Conclusion | SMC is now adopted as national policy in Senegal and has been implemented as pilot in 2013 in 4 districts. In 2014, it will be rolled out in the 16 eligible districts in southern Senegal, reaching a total of approximately 617,000 children under 10 years of age.

MO.22

Fosmidomycin as an antimalarial drug: review of clinical trials

José Francisco Fernandes[1], Bertrand Lell[1], Selidji Agnandji[1], Adegnika Akim [1], Peter G. Kremsner[2], Benjamin Mordmüller[2], Martin P. Grobusch[3]

1. Albert Schweitzer Hospital, Gabon; 2. ITM Tübingen, Germany; 3. University of Amsterdam, The Netherlands

Background | *Plasmodium* spp. have the capacity to develop resistance against all antimalarial agents including artemisinins. Therefore, there is an urgent need for novel alternative drugs. From the extensive work that has been carried out to identify new drugs, fosmidomycin resulted as one of the most promising candidates for the treatment of uncomplicated malaria. Fosmidomycin is a natural antibacterial agent, originally isolated from *Streptomyces lavendulae* in the late 1970s, which inhibits the 1-deoxy-D-xylulose 5-phosphate reductoisomerase, a key enzyme of the synthesis of isoprenoids which is essential for malaria parasites. During the last decade, various clinical trials have been conducted successfully but fosmidomycin is still not a registered antimalarial.

Method | In this review we will present an updated overview on the development of fosmidomycin: the current situation, controversial results and further steps that shall guide and accelerate further clinical development. Articles were retrieved from PubMed with search terms: 'fosmidomycin', 'fosmidomycin and malaria', 'fosmidomycin plus clindamycin', or 'fosmidomycin plus artesunate'. Criteria for inclusion were studies in phase I or phase II, open, controlled or uncontrolled clinical trials conducted with fosmidomycin alone or in combination therapy. Additionally, unpublished data from centres involved in its development were included in the analysis.

Results | A wealth of data on efficacy, safety and tolerability of fosmidomycin is available, although some important gaps in knowledge remain.

Conclusion | At the current stage, registration of fosmidomycin as an antimalarial drug is unlikely. Nevertheless, it remains an interesting drug candidate. Research on fosmidomycin, its derivatives and its possible role as part of an optimized combination regimen should be continued.

MO.23

Artesunate *in vivo* activity on *Plasmodium falciparum* forms in the mosquito *Anopheles coluzzii*

Rakiswendé Serge Yerbanga[1], Robert Kossivi Ouédraogo, Franck Adama Yao, Anna Cohuet, Koudraogo Bienvenue Yaméogo, Aminata Fofana, Annette Habluetzel, and Jean-Bosco Ouédraogo

1. IRSS-DRO, Burkina Faso

Background | In the fight against malaria and for effective eradication, drugs and vaccines are urgently needed to stop the transmission. Artesunate, a partner drug in ACT treatment and known for its gametocytocidal activity, was investigated for *in vivo* dose response on the sporogonic phase of *Plasmodium falciparum*. The objective of the study was to assess *in vivo* the effect of artesunate, from gametocytes fertilisation to oocyst development in the mosquito.
Methods | The assay was performed using *P. falciparum* field isolates and laboratory-adapted *Anopheles coluzzii*. Children from hyper endemic areas of Bobo-Dioulasso with *P. falciparum* mono-infection and with at least 56 gametocytes /µl of blood were selected. For each selected child, venous blood was collected into heparinised tube and a membrane feeding assay was performed with various doses of artesunate. Around 50 mosquitoes, 3–4 days old, fed on the mixed-blood through pre-warmed membrane feeders for 30 minutes. On day 7 post-feeding, mosquitoes were dissected in a drop of mercurochrome and midguts were examined for oocysts. The transmission blocking activity of the drug was evaluated by assessing oocyst prevalence and oocyst density.
Results | Results showed that at the dosages examined, 1.5 ppm to 5 ppm, oocyst prevalence ranged from 44% to 83% and densities from 1.25 to 21.91 oocysts per mosquito. While in the control group, oocyst prevalence ranged from 52 to 74 % and oocysts densities from 2.3 to 29.7 per mosquito.
Conclusion | Artesunate which is well-known for its gametocytocidal properties, did not block the sporogonic development at the tested doses.

MO.24

Efficacy of mefloquine intermittent preventive treatment in pregnancy against *Schistosoma haematobium* infection in Gabon: a randomised controlled clinical trial

Ghyslain Mombo-Ngoma[1], Arti Basra[1,2], Raquel Gonzalez[4], Clara Menéndez[4], Peter Kremsner[3], Michael Ramharter[5]

1. CERMEL, Gabon; 2. USS, Gabon; 3. ITM Tübingen, Germany; 4. CRESIB, Spain; 5. Medical University of Vienna, Austria

Background | Urogenital schistosomiasis is a major public health problem in sub-Saharan Africa, and routine programmes for screening and treatment of pregnant women are not established. Mefloquine is currently evaluated as a potential alternative to sulfadoxine-pyrimethamine as intermittent preventive treatment against malaria in pregnancy (IPTp). It is also known to exhibit activity against *Schistosoma haematobium*. In this study we evaluated the efficacy of mefloquine IPTp against *S. haematobium* infection in pregnant women.

Methods | Pregnant women with *S. haematobium* infection presenting at two antenatal health care centres in rural Gabon were invited to participate in this nested randomised controlled, assessor-blinded clinical trial comparing sulfadoxine-pyrimethamine with mefloquine IPTp. Study drugs were administered twice during pregnancy with a 1-month interval after completion of the first trimester.

Results | Sixty-five (65) pregnant women were included in this study. *Schistosoma haematobium* egg excretion rates showed a median reduction of 98% (interquartile range IQR, 70%–100%) in the mefloquine group compared to an increase of 20% (IQR, –186% to 75%) in the comparator group. More than 80% of patients showed at least 50% reduction of egg excretion and overall cure rate was 47% (IQR, 36%–70%) six weeks after the second administration of mefloquine IPTp.

Conclusion | When used as IPTp for the prevention of malaria, mefloquine shows promising activity against concomitant *S. haematobium* infection leading to an important reduction of egg excretion in pregnant women. Provided that further studies confirm these findings, the use of mefloquine may transform future IPTp programmes into a two-pronged intervention addressing two of the most virulent parasitic infections in African pregnant women.

MO.25

Effect of antiretroviral therapy on malaria parasitaemia and clinical episodes among HIV-infected adults in rural Uganda, 2009: a prospective population-based cohort study

Peter Kimbowa[1]

1. Save a Life Foundation

Background | Untreated HIV-1-induced immune-suppression is associated with an increased incidence of clinical malaria and parasitaemia. We assessed the effect of antiretroviral therapy (ART) on clinical malaria (parasitaemia with fever) and malaria parasitaemia in HIV-infected individuals.

Methods | HIV-infected and uninfected participants in a cohort were followed from 2005–2009. Blood smears were examined microscopically for malaria at quarterly visits and whenever participants had fever. CD4 cell counts were measured quarterly among individuals receiving ART, 6 monthly for those not yet on ART. From 2001, HIV-infected individuals received cotrimoxazole prophylaxis. The incidence of clinical malaria and parasitaemia was compared between HIV-uninfected and HIV-infected (not yet on ART and on ART) using rate ratios (RR).

Results | Participants were: HIV-uninfected (206), HIV-infected not yet on ART (255) and HIV-infected on ART (280). Compared to HIV-uninfected participants, clinical malaria incidence was higher among HIV-infected individuals not yet on ART (adjusted RR (aRR) 1.80 95% CI 1.30, 2.50) and individuals on ART for less than 2 years (aRR 1.83 (95% CI 1.35, 2.48), but lower among individuals on ART for 2 or more years (aRR 0.63 95% CI 0.45, 0.89). The incidence of clinical malaria decreased with increasing age (p for trend=0.002) and increasing CD4 cell counts (p for trend< 0.001). Similar observations occurred for the incidence of parasitaemia, according to HIV and ART status. *Plasmodium falciparum* (93.6%) was the commonest species identified.

Conclusion | HIV infection increases risk of both clinical malaria and parasitaemia. Over time, ART reduces both of these risks.

MO.26

Investigation of sampling designs for accurate estimation of parasite clearance in the context of artemisinin resistance

Philippe Guerin[1], Mehul Dhorda, Jennifer A. Flegg, Francois Nosten, Elizabeth A. Ashley, Arjen M. Dondorp, Rick M. Fairhurst, Duong Socheat, Steffen Borrmann, Anders Björkman, Andreas Mårtensson, Mayfong Mayxay, Paul Newton, Delia Bethell, Youry Se, Harald Noedl, Mahamadou Diakite, Abdoulaye A. Djimdé, Nicholas J. White, Kasia Stepniewska

1. WWARN, United Kingdom

Background | The pharmacodynamic measure of the artemisinin derivatives is the rate of parasite clearance in the days following treatment. Frequent assessments of the parasite density are needed to define this parasite clearance rate but it is uncertain what sampling intervals and frequency are required to ensure reliable estimates.
Methods | We selected 2,744 real-time parasitaemia patient profiles with 6-hourly counts in the first 48 hours. The WWARN Parasite Clearance Estimator (PCE) was used to estimate the parasite half-life. Nineteen (19) restricted sampling schemes were investigated; either by selecting a subset of parasite counts or through the simulation study in which parasite counts were generated from an overdispersed Poisson distribution based on the variability observed in the study data. Further, polynomial regression was used to investigate the relationship between estimated half-life and daily parasite measurements in order to derive a formula to estimate half-life.
Results | The differences between the schemes reduced as the half-life increased. Of the reduced schemes, a scheme with measurements at time windows of 00–2, 64–8, 1210–14, 2422–26, 3634–36, 4846–50, or 6, 7, 24, 25, then 24 (+1)-hourly is recommended. The formula based on daily counts gave half-life estimates within 1 hour bounds of the 'true' value in many situations which will be discussed.
Conclusion | Less frequent sampling schemes are satisfactory for characterisation of slow parasite clearance. Characterisation of short half-life requires more dense sampling schemes and should be the preferred option in locations where the level of resistance is not known.

MO.27

Modelling recurrent events: comparison of statistical models with continuous and discontinuous risk intervals on repeated malaria episodes data

Issaka Sagara[1,2], Ogobara K Doumbo[1], Abdoulaye Djimdé[1], Alassane Dicko[1], Roch Giorgi[2], Jean Gaudart[2]

1. MRTC, University of Bamako, Mali; 2. University of Aix-Marseille, France

Background | Repetitive events data analysis is quite common in biomedicine. The literature review indicates that most statistical models used for such data are often based on time to the first event or consider events within subject as independent. Also, most applied data analyses which take into account the non-independence of repeated events within subjects, are done with continuous risk interval models which may not be relevant for infectious diseases such as malaria. This study aimed to analyse repeated malaria episodes with different models in order to advise on the best models to be used on such data.

Methods | Data were collected from July 2005 to July 2007 in Bougala-Hameau, Sikasso, Mali. Patients were randomised to one of the artemisinin-based combination therapy (ACT) arms: artesunate/amodiaquine or artesunate/sulfadoxine-pyrimethamine or artemether-lumefantrine. The study's main objective was to compare malaria incidence within these three ACT-arms. The patient received the same initial treatment for each subsequent uncomplicated malaria episode during the course of the study. We used four different models to analyse the data, both with continuous and discontinuous risk interval models: the generalised estimating equation (GEE) using Poisson distribution; two extended Cox models (the Andersen-Gill counting process and the Prentice-Williams-Peterson counting process model); and the gamma frailty model.

Results | GEE Poisson distribution models provided weak to no covariates effect in respect to the comparators while the Andersen Gill counting process and the Gamma frailty model provided covariate effects.

Conclusion | The discontinuous risk interval analyses using Andersen Gill and frailty models were found to be more appropriate for such data.

MO.28

Pyrogenic threshold for malaria disease definition in an endemic area of Burkina Faso

Alphonse Ouédraogo[1], Alfred B. Tiono[1], Amidou Diarra[1], Souleymane Sanon[1], Jean Baptist Yaro[1], Esperance Ouedraogo[1], Edith C. Bougouma[1], Adama Gansané[1], Amadou T. Konate[1], Issa Nebie[1], Nora Watson[3], Megan Sanza[3], Tina J.T. Dube[3], Sodiomon Bienvenu Sirima[2]

1. CNRFP, Burkina Faso; 2. CNRFP, GRAS, Burkina Faso; 3. EMMES Corp., Rockville (MD), United States of America

Background | Development and evaluation of malaria vaccine trials demand knowledge of the regional epidemiology of malaria. In fact, malaria incidence has represented a primary endpoint of phase IIb or III of malaria vaccine trials. The parasite density cut-off defining malaria episodes are unknown and usually estimated in malaria vaccine trials. This study aims to calculate the fraction of fever attributable to malaria in a malaria vaccine trial site of Burkina Faso.
Methods | We conducted two cross-sectional surveys in children of 0 months to 5 years of age from four areas of the Saponé district. The first survey was conducted during the rainy season and the second in the dry season. Parasitological and clinical examinations were performed. A fever case was defined as objective temperature ≥37.5 °C or history of fever in the past 24 hours.
Results | The relationship between fever and *Plasmodium falciparum* parasitaemia depends on the season. The fraction of fever cases attributable to malaria was 41.9% during the rainy season and 34.5% during the dry season. The alternative parasite thresholds for the malaria case definition that achieved optimal sensitivity and specificity (70–80%) were 1,350 parasites/µl during the low season and 3,150 parasites/µl during the high season.
Conclusion | Our results confirm that malaria is a main cause of fever in the Saponé health district. The relationship between fever and parasitaemia depends on the season. Cut-off levels of parasitaemia should be used during the two seasons to define malaria cases in this area.

MO.29

Seasonal variation and clinical protection of antibodies against a panel of malaria antigens in children under five years of age in Burkina Faso

Amidou Diarra[1], Alfred Tiono[1], Cherrif Mariama[1], Issiaka Soulama[1], Alphonse Ouedraogo[1], Jean B. Yaro[1], Esperance Ouedraogo[1], Edith C. Bougouma[1], Souleymane Sanon[1], Amadou T. Konate[1], Adama Gansane[1], Giampietro Corradin[2], Daniel Dodoo[3], Sodiomon B. Sirima[1], Issa Nebie[1]

1. CNRFP, Burkina Faso; 2. University of Lausanne, Switzerland; 3. NMIMR, Ghana

Background | Seroepidemiological data have contributed to the identification of malaria vaccine candidates. The aim of this study was to establish a relationship between antibody responses against newly synthetic peptides and clinical malaria in order to identify malaria vaccine candidates.

Methods | In 2007, 529 children under five years of age were included and then actively followed up (clinically and parasitologically) for 12 months through two home visits per week to record malaria episodes. Blood samples were taken from the children enrolled in the study cohort at the beginning of the study (low malaria transmission season) and at the peak of malaria transmission season to measure antibody responses by ELISA.

Results | There was a strong seasonal variation in antibody levels, with antibody levels being higher during high malaria transmission as compared to the low transmission season for the majority of the antigens assessed except for MR198 ($P < 0.53$), 1574 ($P < 0.8$) and LR179a ($P < 0.06$). Only antibody response to LSA1 and AS155.4 were associated with protection against clinical malaria. Assessment of the type of immunological profile of these two proteins could help identifying malaria vaccine candidates.

Conclusion | The seasonal variation of antibody responses and the association with clinical malaria protection may be helpful in identifying malaria vaccine candidates.

MO.30

Assessing regulatory T cells in children with severe malaria in Burkina Faso

Guillaume S. Sanou[1], Amidou Diarra[1], Alphonse Ouédraogo[1], Jean-Baptiste Yaro[1], Esperance Ouédraogo[1], Yves Traore[2], Sodiomon B Sirima[1], Issa Nébié[1]

1. CNRFP, Burkina Faso; 2. University of Ouagadougou, Burkina Faso

Background | Resistance against malaria is led by immunity of subjects living in endemic areas. In children, the severity of malaria infections is modulated through mechanisms that require cellular activation, expansion and function. In this study, we aim to understand why some children are more susceptible to the disease (taking into account age and sex) as compared to others in a Burkina Faso context.

Methods | A cross-sectional survey was conducted in 2008 including children less than 5 years of age presenting severe symptoms of malaria and a control group with asymptomatic malaria. Venous blood was collected in heparinised tubes. Flow cytometry analysis of isolated peripheral blood mononuclear cells was performed after surface and intracellular staining.

Results | Haematological analysis has shown some differences between the severe malaria group and the healthy group. Lymphocyte count was higher in the control group with $4.32 \times 10^3/\mu l$ and $5.76 \times 10^3/\mu l$ ($p=0.0206$). When compared to asymptomatic controls, severe malaria subjects present a similar proportion of CD4+CD25+FoxP3+ regulatory T cells subset. When compared to non-parasitised controls, severe malaria subjects present a higher proportion of these cells. Regulatory cytokines production was also assessed. For IL10 producing T cells we found that the severe malaria group presented a higher proportion compared to the asymptomatic controls, 60,37% of CD4 T cells and 36,6% ($p=0.0003$), respectively.

Conclusion | Our study found that regulatory T cells might contribute to modulation of the severity of malaria infection in children. In the context of vaccine and clinical research, targeting cells responses could be an interesting tool.

MO.31

Reduced antibody responses against *Plasmodium falciparum* vaccine candidate antigens in the presence of *Trichuris trichiura*

Larissa Aurore Tobol Bouyoukou Hounkpatin[1], M. Esen, B. Mordmüller, P.M. de Salazar, A.A. Adegnika, S.T. Agnandji, F. Schaumburg, S. Brückner, M. Theisen, S. Bélard, U.A. Ngoa, S. Issifou, M. Yazdanbakhsh, P.G. Kremsner.

1. ITM Tübingen, Germany

Background | Helminth infections are highly prevalent in the tropics and may have an effect on immune responses to vaccines due to their immunomodulatory effect. The prevalence of helminth infections in young children, the target group for malaria and most other vaccines, is high. Therefore we assessed the influence of helminth infection on vaccine-induced immune responses in a phase I clinical trial of the malaria vaccine candidate GMZ2.

Methods | Twenty (20) Gabonese children of preschool age were vaccinated with GMZ2, a blood stage malaria vaccine candidate. Humoral immune response against the vaccine antigens and parasitological status were assessed. Vaccine-specific antibody concentrations and memory B cell numbers were compared in worm infected and non-infected participants.

Results | Antibody response to GMZ2 was 3.4-fold (95% CI: 1.6, 7.4) higher in *Trichuris trichiura*-negative subjects compared to positive participants, whereas immunoglobulin subclass distribution was similar. Memory B cell response was moderately increased in *T. trichiura*-negative individuals, although the difference was not significant.

Conclusion | Future malaria vaccine development programmes need to account for worm-mediated hyporesponsiveness of immune reactions.

MO.32

Haemozoin detection assay: a novel *ex vivo* assay to detect antimalarial drug resistance

Maria Rebelo[1,2], José Fernandes[1], Peter Gottfried Kremsner[1,3], Thomas Hanscheid[1,2] and Martin P. Grobusch[1,4]

1. CERMEL, Gabon; 2. IMI, Portugal; 3. ITM Tübingen, Germany; 4. AMC, Amsterdam, The Netherlands

Background | Resistance to the first-line treatment of malaria has been described, constituting a threat for malaria control. Sensitivity tests are crucial to detect and monitor resistance. Available assays have some drawbacks that limit their application. The recently developed haemozoin (Hz) detection assay may overcome some of the limitations of existing assays. In this field trial we assess the performance of the Hz detection assay using blood samples from Gabonese patients with malaria.

Methods | The remaining blood samples from patients with confirmed malaria, collected for full blood counts, were incubated with chloroquine, artesunate and artemisinin. On site, a flow cytometer (Cyflow) was easily modified to detect depolarisation caused by Hz. The percentage of Hz-containing infected erythrocytes, detected by flow cytometry, was used as maturation indicator determined at 24 and 48 hours of incubation.

Results | By assessing the percentage of Hz-containing infected erythrocytes, parasite maturation and antimalarial drug effects could be detected after 24-hours of incubation. Inhibitory concentrations of 50% (IC50) of >200 nM, 7–30 nM and 9–16 nM were obtained for chloroquine, artesunate, and artemisinin, respectively.

Conclusion | These preliminary results showed that resistance to chloroquine still exists in Gabon. However, IC50s obtained for artemisinin and artesunate were higher than the ones previously reported, which may be a consequence of the higher parasitaemias used in the Hz assay. Even though further investigation is needed, these results indicate that the novel Hz assay can determine the sensitivity/resistance pattern of parasites in clinical isolates after only one day of incubation.

CO.01

The Pan African Clinical Trials Registry five years later: where are we now?

Elizabeth Pienaar[1], Amber Abrams[1], Babalwa Zani[1], Vittoria Lutje[2], Tamara Kredo[1]

1. SACC, South Africa; 2. CIDG, United Kingdom

Background | Clinical trials registries are databases where key administrative and scientific information, sufficient to identify specific trials, is stored. The Pan African Clinical Trials Registry (www.pactr.org) is currently the only WHO Primary Register in Africa. The registry can be used by stakeholders to understand the trial landscape, locate trials, network with collaborators, minimise duplication of research, or to align funding with research needs and capacities. The objective of this presentation is to describe clinical trial activity through a review of trials registered on www.pactr.org.
Methods | We analysed www.pactr.org applications over time. We evaluated the following data items: country, disease, intervention, principal investigator, funding source. The analysis was done using Excel and descriptive statistics.
Results | In February 2014, 263 trials completed registration. Eighty-two (82) trials are multicentre trials with sites in 27 African countries, and principal investigators are from 24 countries. The funders are inter-governmental agencies; non-governmental organisations; governments; universities; investigator-sponsored and partnerships between these. The majority of registered trials are in the field of HIV/AIDS (57), followed by malaria (36), and tuberculosis (25). There are 141 trials in other, non-communicable diseases. Of the registered trials 79 include children. Registered trials focus on treatment (102), prevention (40) and diagnosis (12). There were 9, 40, 60 and 113 registrations in 2009, 2011, 2012 and 2013, respectively.
Conclusion | The WHO-endorsement of PACTR as primary registry coupled with active promotion increased trial registration rates. Registration numbers have tripled in a single year, highlighting the value of a regional registry of on-going trials for researchers.

CO.02

Mapping African research ethics review and medicines regulatory capacity: the MARC project

Boitumelo Mokgatla-Moipolai[1], Carel IJsselmuiden[1], Doug Wassenaar[2]

1. COHRED, Switzerland/Botswana; 2. UKZN, South Africa

Background | Ethical review is widely acknowledged as a cornerstone of international guidelines on research with human participants. The ever increasing clinical trial activity in Africa has resulted in a commensurate rise in the need for sound ethical review structures and functions. In recent years, many African countries have begun to pay greater attention to developing or strengthening ethics review capacities. The MARC project aimed to document this capacity in Africa, to promote the strengthening of existing capacity and contribute to capacity building initiatives.

Methods | Using a list server and online questionnaires, information was gathered from research ethics committees (RECs) and Medicines Regulatory Authorities (MRAs) across Africa. The MARC website (www.researchethicsweb.org) was created to document, map and ensure easy access to the collected data.

Results | One hundred seventy-one (171) RECs and 26 MRAs were identified in 37 and 26 African countries respectively, with great variability in skills, resources and membership. MARC found rapid uptake in Latin America with >1000 RECs mapped. Further assessments of the African research ethics landscape were conducted including hosting the first ever African conference for administrators of RECs. The MARC social network ETHICall was developed to facilitate communication between RECs and MRAs. The online discussion forums can be used to find or discuss solutions to complex ethical issues. RHInnO Ethics, an information management system, was developed to improve the capacity of RECs to better manage the ethics review process.

Conclusion | MARC and its flexible use, is a valuable tool to all key stakeholders especially at the current increase in scope, complexity and magnitude of health research in Africa.

CO.03

The 'Research for Health and Innovation Organiser Ethics'

Carel IJsselmuiden[1], Boitumelo Mokgatla-Moipolai[1]
1. COHRED, Switzerland/Botswana

Background | Institutions around the world that handle large volumes of research frequently rely on effective information management systems to facilitate their strategic and operational activities. In Africa, the majority of research ethics committees (RECs) rely on complex paper-based systems to manage their research ethics review process, from submission of protocols, to project registration, to conducting reviews and communication with researchers and reviewers. Results from the first phase of the MARC project (www.researchethicsweb.org) reveal that it takes an average of 12 months to get ethical clearance in Africa.
Methods | The Research for Health and Innovation Organiser Ethics (RHInnO Ethics) is a web-based ethics review tool. It was developed as a result of the findings of the EDCTP-funded MARC project. It is intended to help improve: the quality of ethics review, the efficiency of RECs, the communication among REC members and between REC members and researchers, thereby ultimately reducing significantly the review period in African RECs. RHInnO Ethics digitally manages the entire life cycle of the research ethics review process.
Results | The product development is complete. To address quality and implementation issues, RHInnO Ethics was piloted in several African countries. We have begun the implementation of RHInnO Ethics in some African institutions including private RECs, and we are currently exploring funding avenues for a mass roll-out of RHInnO Ethics in Africa, which will clearly be an important step towards harmonisation of ethics review processes in Africa.
Conclusion | Given the constantly increasing complexity of clinical trials and the workload of RECs, there is no doubt that the implementation of RHInnO Ethics in Africa will be one of the greatest achievements in improving the capacity of African research ethics committees.

CO.04

Impact of clinical trials on the quality of health care services in Burkina Faso: perception of community and health staff in Nanoro and Dafra districts

Maxime K. Drabo[1], Léa Paré Toé[1], James Akizili[2], Sebastian Hachizovou[3], Frank Baiden[2], Halidou Tinto[1], Shepart Kondhowe[3], Yacouba Cissao[1], Raffaella M. Ravinetto[4], Koen Peeters Grietens[4], Umberto D'Alessandro[4].

1. IRSS/Centre Muraz, Burkina Faso; 2. NHRC, Ghana; 3. TDRC Ndola, Zambia; 4. ITM Antwerp, Belgium

Background | Clinical trials allow the development of new and efficacious medicines. The trial staffs usually work with local health institutions and communities. What is the impact of clinical trials on the quality of routine care? To answer this question a survey focussing on changes as perceived by the community and local health staff involved in trials has been carried out in Burkina Faso.

Methods | Based on qualitative and quantitative approaches, a survey was conducted with the 37 local health providers and 420 community members involved in clinical trials in the Nanoro and Dafra districts in Burkina Faso.

Results | An average of 61,6% of community members declared that the clinical trials had a positive impact on the quality of care in term of better diagnostics (51%) and quicker treatment (65%), in terms of involvement of routine health care workers (68.7%), health care staff workplace relationships (54.6%), and the staff's availability for routine work (59.4%). According to the health care providers, the clinical trials induced more accountability to patients (57.8%), better financial motivation (41.2%) and an increase of the workload (43.9%). The declared impact of clinical trials on the quality of health care services is not sustainable according to 69.3% of the community members due to the high turnover of health staff and the reduction of financial support over time.

Conclusion | The clinical trials induced positive changes related to the perceived quality of care, but the sustainability of these changes was seen as not ensured. Clinical trials should include activities which contribute to greater sustainability of the induced positive changes in attitude and behaviour.

CO.05

Factors influencing the recruitment of participants for randomised clinical trials in Africa: an observational study in The Gambia

Elisabeth Stanley-Batchilly[1], Joan Vives-Tomas[1] and Martin Ota[1,2]
1. MRC, The Gambia; 2. WHO-AFRO, Republic of Congo

Background | There is a global effort to develop new vaccines for the control of infectious diseases. The majority of these vaccines are tested in the developing countries where infectious diseases are most prevalent. Most of these are randomised clinical trials involving the recruitment of study participants. Delays in recruitment may easily affect duration, costs and validity of the study.
Methods | We aimed to determine factors that further the recruitment of study participants for randomised clinical trials in a developing country through a descriptive retrospective study. A questionnaire addressing several aspects of recruitment was administered to clinicians, project managers and field workers involved in randomised clinical trials at the MRC Unit The Gambia between 2009 and 2012.
Results | A total of 28 workers on 9 different trials completed the questionnaires. Identified as factors which significantly contributed to enhancing participation were: community sensitisation through an initial presentation of the project to head and leaders of the community; regular home visits; and telephone calls to the individual study participants. More than 75% of the respondents considered these factors effective or very effective when coupled with: open days for the study; workshops; regular meetings of investigators/staff; supportive statements from opinion leaders; visits to centres by the principal investigator; employing extra staff; and training and information videos.
Conclusion | Which methods were adopted, depended on a number of factors such as environment, social organisation, available channels of communication, literacy, and socio-cultural Background. Experience of the research team conducting the trial is an important factor to be taken into consideration. A tailored recruitment strategy plan for each intervention is recommended.

CO.06

A pragmatic and innovative strategy to improve quality of clinical trials in East Africa: update from the reciprocal monitoring scheme

Elizabeth Ayuo[1], A. Nanvubya[2], G. Miiro[3], K. Laserson[1], T. Lang[4], P. Kaleebu[3,5]

1. KEMRI-CDC, Kenya; 2. UVRI-IAVI, Uganda; 3. UVRI, Uganda; 4. University of Oxford, United Kingdom; 5. MRC-UVRI, Uganda

Background | Contract research organisations (CROs) are conventionally used to monitor quality of clinical trials. They are expensive for resource-constrained settings and are associated with limited capacity strengthening. As a sustainable alternative, the EDCTP-funded East African Consortium for Clinical Research (EACCR) initiated a reciprocal monitoring scheme (RMS) with in-built monitoring. This was implemented in partnership with the University of Oxford.
Methods | Between September 2011 and April 2013, two coordinators further developed a reciprocal monitoring scheme that was designed in Kilifi Kenya. Following consultation with heads of research institutions, and principal investigators, a plan to conduct cross-site monitoring of trials in eastern Africa using existing trial staff was established. The coordinators from Kenya and Uganda facilitated operational oversight, logistical support and mentoring of the nominated monitors. Experienced monitors were paired with new or less experienced colleagues to generate an expanding pool of monitors. Assigned pairs then conducted the introductory and subsequent monitoring visits for trials in which they were not otherwise involved.
Results | We conducted three skill-sharing workshops for 28 potential clinical trial monitors from Kenya, Uganda, Tanzania, Sudan and Ethiopia. Those trained then monitored 16 clinical trials through 32 completed paired visits. Moreover, we attracted and completed two consultancy requests from two research sites within the region.
Conclusion | This is a pragmatic mechanism for monitoring the quality of clinical trials in resource-constrained settings and for training and mentoring new monitors which also has the potential to expand networking and generate additional funds.

CO.07

Monitoring and evaluation of health research capacity development activities: development of tools and instruments using the example of the Fozivudine in Africa Trials Initiative

Daniel Bauer[1], M.R. Fischer[1], J. Huber[1], I. Wessels[1], A. Kroidl[2], M. Hoelscher[2], T. Lennemann[2,3], K.A. Eberhardt[4,5], J. Kapungu[3], F.S. Sarfo[5], L. Maganga[3], Y. Schönemann[6], B. Jordan-Harder[7], C. Kiessling[1]

1. University of Munich (Klinikum), Germany; 2. University of Munich (LMU), Germany; 3. NIMR-MMRC, Tanzania; 4. ITM Hamburg, Germany; 5. KATH, Ghana; 6. PROFILE/ GIZ GmbH, Germany; 7. ESTHER/GIZ GmbH, Germany

Background | The impact of international research collaboration on individual and institutional research capacities is under-researched due to a lack of context-sensitive tools. As a subprogramme of the 'Fozivudine in Africa Trial Initiative' (FATI), this project seeks to develop indicators and instruments that enable the evaluation of health research capacity development.
Methods | The first step was to develop an evaluation framework in cooperation with the FATI study team in Germany, Tanzania, and the Deutsche Gesellschaft für Internationale Zusammenarbeit (German Society for International Cooperation). Then, the evaluation tools were either selected from the literature or self-developed. Focus of the evaluation was a needs assessment among German, Tanzanian, and Ghanaian research staff, an analysis of current structure and input parameters at the sites, and the evaluation of four capacity development activities on-site. Data analyses were quantitative and qualitative.
Results | A sample of 20 persons in Mbeya and 14 persons in Kumasi were interviewed. Depending on their tasks, additional questionnaires about job satisfaction, research skills ('research spider'), and networking were completed. Reliability statistics indicated acceptable to good reliability for the questionnaires (Cronbach's alphas between 0.653 and 0.925). The four capacity development activities were all evaluated very positively with high overall satisfaction of the participants (94–100% agreement). Further results will be presented.
Conclusion | Interviews were an adequate approach to assess the needs, motivators and barriers for conducting health research. The questionnaires that were used needed adaptation to the specific context of health research. The long-term objective is to create a comprehensive monitoring and evaluation manual that will be available to other research projects.

CO.08

Implementation challenges of the WANECAM study: a monitor's perspective

Ghiorghis Belai[1], Issaka Sagara[2], Abdoul Habib Beavogui[3], Ismaila Thera[2], Siriman Traore[2], Abdoulaye Djimdé[2]

1. Family Health International, Nairobi, Kenya; 2. WANECAM-Mali, MRTC, University of Bamako, Mali; 3. WANECAM-Guinea, CNFRSR, Guinea

Background | The WANECAM study entitled 'A phase IIIb/IV comparative, randomised, multicentre, open-label, parallel 3-arm clinical study to assess the safety and efficacy of repeated administration of pyronaridine-artesunate, dihydroartemisinin-piperaquine or artemether-lumefantrine or artesunate-amodiaquine over a two-year period in children and adult patients with acute uncomplicated *Plasmodium* sp. malaria' has succesfully complied with national and international guidelines. However, many challenges had to be overcome during its implementation. This presentation aims to highlight some of the challenges faced by the network in implementing the trial in a uniform manner across six sites in three countries.
Methods | We highlight some of the challenges experienced by the investigators and sites in implementing the WANECAM study as well as some of the solutions adopted across the trial network in order to make the study comply with the gold standards of clinical trials. The information in this presentation is an aggregation of the experiences in the trial of the investigators, funders and monitors of the study. This presentation will focus mainly on issues related to laboratory testing and data management.
Results | We present the major challenges experienced by the investigators, sponsors and monitors in implementing a large study over three countries in a uniform manner. The overall result is that the trial is progressing well despite these challenges.
Conclusion | Despite numerous challenges related to laboratory and IT infrastructure, the WANECAM network has managed to find sustainable solutions that may be useful in implementing trials in resource constrained areas.

CO.09

HIV and *Schistosoma mansoni* coinfections among adults in fishing communities along Lake Victoria, Uganda

Josephine Wanyenze[1], Andrew Abaasa, Gershim Asiki, Pietro Pala, Anatoli Kamali, Alison Elliott, Pontiano Kaleebu

1. MRC-UVRI AIDS, Uganda

Background | In sub-Saharan Africa, helminth infections constitute a major group of neglected tropical diseases and a huge potential for dual infection with HIV. During screening for an ongoing schistosomiasis intervention trial of the effect of praziquantel on HIV/AIDS disease progression, we estimated the prevalence and associated factors of *Schistosoma mansoni* infection among HIV-infected adults in fishing communities on the shores of Lake Victoria, Uganda.
Methods | We identified HIV-infected participants through community-based counselling and testing. Consenting adults (age ≥18 years) were interviewed to determine demographic factors and requested to provide stool samples on three consecutive days for Kato-Katz detection of *S. mansoni* eggs. Logistic regression models were fitted to identify factors independently associated with *S. mansoni* infection.
Results | Out of 720 (60% men) HIV-infected participants screened between August 2012 and February 2014, 397 (55%) had *S. mansoni*. The prevalence was higher among men compared to women (72% *vs* 29%) and fishermen compared to other occupations (80% *vs* 34%). These factors remained statistically significant at the multivariable analysis: male gender (adjusted odds ratio (aOR) 95%CI: (3.2) 2.0–5.0 and being a fisherman: (4.0) 2.5–6.3 or in fish processing: (2.2) 1.2–4.1.
Conclusion | We have recorded a very high rate of *S. mansoni* coinfection in HIV-infected individuals in fishing communities. Observed gender and occupational variations are attributable to degree of water-contact. Further research is urgently needed in these communities to evaluate the impact of coinfections on clinical outcomes.

CO.10

Detangling immune interactions between schistosomiasis and malaria in coinfected individuals

Marguerite Massinga Loembé[1], Honorine Mbenkep Lima, Sanne E. de Jong, Ulysse Ateba Ngoa, Hermelijn H. Smits, Peter G. Kremsner, Maria Yasdanbakhsh, Ayola Akim Adegnika

1. CERMEL, Gabon

Background | Malaria and helminths coexist epidemiologically in developing countries. In Gabon and specifically in the study area of Lambarene, *Plasmodium falciparum* and helminth infections, including *Schistosoma haematobium*, are highly prevalent. There is accumulating evidence that helminths have strong immune modulatory effects, which may affect responses to unrelated antigens. We therefore undertook to characterise regulatory T and B cell responses during coinfection with *S. haematobium* and *P. falciparum*, with the underlying hypothesis that helminth infection, by inducing regulatory T and B cells, may suppress effective immune responses to *P. falciparum*.
Methods | In a cross-sectional study conducted in the Lambarene area, children 6–14 years of age, permanently residing in the town's vicinity, were screened for *P. falciparum* and *S. haematobium* infections, and blood was drawn from 127 of them for immunological analysis. The children were classified as either: malaria-infected only (n=14), schistosomiasis-infected only (53), coinfected (9) or uninfected (51). Freshly isolated PBMC were fixed/frozen for immunophenotyping by flow cytometry. Cytokine secretion profiles were further characterised by ICS following *in vitro* stimulation with *Plasmodium* antigens (infected erythrocytes: iRBc) and controls (uninfected erythrocytes: uRBc and culture medium only).
Results | Our preliminary results indicate higher frequencies of Th2 committed cells and regulatory B cells in the schistosomiasis-infected only group. Moreover there was a trend for lower INFγ production in response to malaria antigens in *S. haematobium*-coinfected individuals.
Conclusion | Further analyses taking into account confounding factors will be required to complete interpretation of crude immunological data.

CO.11

Field evaluation of an up-converting phosphor-lateral flow assay for detection of cellular and humoral immunity against mycobacteria

Annemieke Geluk[1], Kidist Bobosha[1,3], Elisa Tjon el Fat[2], Karin Dijkman[1], Yonas Bekele[3], Jolien J. van der Ploeg-van Schip[1], John S. Spencer[4], Kees L.M.C. Franken[1], Tom H.M. Ottenhoff[1], Paul L.A.M. Corstjens[2]

1. LUMC, The Netherlands; 3. AHRI, Ethiopia; 4. Colorado State University, United States of America

Background | Diagnostic tests, applicable in non-expert settings, for detection of asymptomatic mycobacterial infection or prediction of progression of infection to clinical disease, are urgently required. Variability in clinical manifestations of leprosy parallels the immunity to *Mycobacterium leprae* as evidenced by the characteristic spectrum ranging from high Th1 immunity in paucibacillary leprosy to high IgM against *M. leprae*-specific PGL-I in multibacillary leprosy. Previously, we developed an up-converting phosphor lateral flow assay (UCP-LFA) for detection of IFNγ, IL-10 and anti-PGL-I Ab in response to *M. leprae*. Since an up-converting phosphor lateral flow assay (UCP-LFA) for IP-10, as marker for infection in tuberculosis, was developed in a dry-format in a parallel study, allowing storage and shipment at ambient temperature, we tested this for leprosy diagnostics in Ethiopia.
Methods | UCP-LFA for single detection of IP-10 or anti-PGL-I Ab (dry-format) and IL-10 and IFNγ (wet-format) were tested with 24 hour stimulated whole blood samples of leprosy patients and endemic controls using portable readers. Identical samples were tested in ELISAs. LF-strips were analysed by a reader capable to scan 20 strips simultaneously. Finally, samples were tested for IP-10 and anti-PGL-I using multiplexed UCP-LFA.
Results | Excellent correlation with ELISAs was demonstrated for all four UCP-LFA as well multiplex detection of IP-10 and anti-PGL-I Ab. Measurements of LF-strips by portable readers and microtitre-plate reader indicated good robustness.
Conclusion | The UCP-LFA is a field-friendly assay allowing simultaneous detection of cellular and humoral immunity, covering biomarker detection for the full immunological leprosy spectrum. Therefore, it is well-suited for diagnosis of clinical outcomes of several mycobacterial infections.

CO.12

Effect of concurrent gastrointestinal nematode infections on antimalarial total IgG in school-age children in Mfou

Clovis Seumen[1], Viviane Tchinda, Jude Bigoga, Philomena Fogako, Amédée Motsebo, Roger Moyou, Rose Leke

1. University of Yaounde I, Cameroon

Background | Gastrointestinal nematode infections (GINi) are common in malaria endemic areas, particularly in sub-Saharan Africa. Interaction between these parasites and malaria would be of considerable public health importance. The present study aimed at determining the effects of concomitant malaria and GINi on the antimalarial total immunoglobulin Gamma level in school-age children in Mfou, in the Centre Region of Cameroon.
Methods | Thick and thin blood smears were made from finger prick blood samples and examined for the presence of malaria parasites, parasite species and densities. Fresh stool samples were collected, processed and examined for gastrointestinal nematodes using the Kato-Katz technique. Immunoglobulin gamma levels for three asexual stage recombinant antigens were measured by ELISA.
Results | Of the 503 children enrolled, 204 (40.56%) were malaria positive, while 148 (29.42%) harboured one or two GINi. The majority of GINi were light intensity infections. A total of 69 (33.82%) malaria-positive children had single or mixed coinfection with predominance of *Plasmodium falciparum/Acaris lumbricoïdes*. The majority of samples tested by ELISA (66 or 75%) showed high titres of antimalarial IgG antibodies. Mixed coinfected children had higher total IgG than those with simple coinfection. There was no statistically significant correlation between the levels of total IgG and presence of malaria infection alone, GINi alone, or both malaria and GINi.
Conclusion | These findings show that malaria and GINi coinfection have no effect on the production of antimalarial total IgG in children. However, further study is required to determine the effect of coinfection on antimalarial IgG subclasses.

CO.13

Research ethics in Africa: a resource for research ethics committees

Lyn Horn[1], **Mariana Kruger**[1], Paul Ndebele[2]

1. University of Stellenbosch, South Africa; 2. MRC Zimbabwe, Zimbabwe

Background | The burden of disease in Africa and the globalisation of research have led to a significant increase in biomedical, social and behavioural research in Africa. This necessitates adequate local systems to provide oversight of all aspects of the research process, including the protection of human research participants. The aim of this project was to develop a research ethics resource for African research ethics committee (REC) to further assist in strengthening research ethics capacity in Africa.
Methods | Members of RECs throughout Africa and other appropriately qualified and experienced academics were invited through a competitive selection process to a workshop held at Stellenbosch University South Africa in August 2011, funded by EDCTP. Selection was based on previous research ethics experience and training, as well as current active involvement in an REC. After discussion of key issues in research ethics in Africa, a consensus was reached regarding chapters and topics and the allocation of authors to topics.
Results | The final result is the book *Research ethics in Africa: A resource for Research Ethics committees*, which will be available both in print and as a free download for researchers and REC members. There are four parts. Part I provides an overview of the historical development and current situation; part II addresses the actual functioning of RECs with suggested review guidelines; part III focusses on specific topics of interest from an African perspective; and part IV provides useful resources including educational resources.
Conclusion | This is the first guidebook aimed at REC members in Africa, written by African authors.

CO.14

Small is beautiful: Demystifying and simplifying SOPs. A model from the Ethics Review and Consultancy Committee of the Cameroon Bioethics Initiative (CAMBIN)

Godfrey B. Tangwa[1], Nchangwi Syntia Munung, Odile Ouwe-Missi-Oukem-Boyer

1. CAMBIN, Cameroon

Background | Everywhere ethics review committees have become increasingly important with the ever-expanding nature and complexity of research on humans. Standard operating procedures (SOPs) are crucially important for the work and functioning of these committees. Most committee SOPs, however, tend to be long and detailed, if not intricate and complex. This is an undesirable situation, especially in the African context, where ethics committee members generally are unpaid volunteers within a predominantly oral rather than literate culture who moreover can afford very little time to dedicate to review work.

Methods | Within an EDCTP-funded project for strengthening ethical review capacity in Central Africa, we set out to design for our ethics review committee, the CAMBIN ERCC, standard operating procedures (SOPs) that would be neither longer nor more complex than the Declaration of Helsinki. We strove for brevity, clarity and simplicity, in order to make them more user-appropriate in our specific context.

Results | Our completed SOPs are seven pages long and are written in a language that any conscientious twelfth-grader could comprehend.

Conclusion | We believe that our abridged, user-friendly SOPs leave out little that is essential for a smooth functioning of an ethics review committee or for rigorous and satisfactory protocol review. We therefore propose our SOPs as a model and template for similarly situated ethics committees.

CO.15

Status of research ethics bodies in the East, Central and Southern Africa Health Community region

Martin Matu[1], Josephine Kibaru-Mbae, Arthur Rutaroh, Egbert Moustache and Stephen Muleshe

1. ECSA-HC, Tanzania

Background | Many Institutional Review Boards (IRBs) in developing countries lack the necessary mix of expertise, accountability as well as independence. Technical, financial and human resources are often constrained, which could lead to compliance issues. A rapid needs assessment was conducted to identify gaps in the operations of IRBs in the ECSA region with the aim of establishing a regional research ethics body.

Methods | A detailed semi-structured questionnaire was sent to IRBs in ten ECSA-HC member states including 14 registered IRBs in Kenya, and one in each of the following countries: Lesotho, Malawi, Mauritius, Swaziland, Seychelles, Tanzania, Uganda, Zambia and Zimbabwe. The questionnaire evaluated compliance regarding major aspects of IRB operations with emphasis on: organisational aspects; membership and continuous education for IRB members and investigators; available resources and workload; process and modalities for protocol submission as well as the policies, guidelines and procedures governing the operations of the IRBs. The data analysis consisted of simple descriptive statistics. Fifty-nine (59) items were identified as the main elements of an IRB compliance review.

Results | Response rate was 43% (10 of the 23 IRBs). IRBs from at least four member states did not comply with more than 30% of the 59 items identified as critical elements necessary for effective and efficient operation of an IRB.

Conclusion | The assessment identified major gaps in compliance of IRB operations in the ECSA Member states. A regional research ethics committee is necessary to support capacity building of the IRBs and to coordinate review of multi-country research studies in the region.

CO.16

Engaging policy makers in clinical trials to accelerate policy formulation in sub-Saharan Africa

Modest Mulenga[1,2], Josephine Kibaru-Mbae[2], Jasper Ogwal-Okeng[3]
1. ECSA-HC, Tanzania; 2. TDRC Ndola, Zambia; 3. Makerere University, Uganda

Background | Substantial financial investment has been put into clinical trials to generate evidence for improved health care. However, processes in order to accelerate the incorporation of clinical trial results into policies remain a major challenge in many African countries. This may partly be attributed to the lack of liaison between researchers and policy makers which leads to a stifling of research efforts into futility. This discussion highlights some proposals for action by potential EDCTP researchers to accelerate the uptake of research evidence from clinical trials into health policies.
Methods | This article summarises contributions from senior African scientists who expressed their opinion on the impediments to the uptake of research evidence into policy and suggested solutions.
Results | The general agreement is that lack of effective engagement with policy makers is a major impediment to the acceptance of research results for policy formulation. Researchers should deliberately strategise to actively engage with policy makers and other stakeholders throughout the research project development process. Efforts could be aimed at setting common priorities and engaging in continued dialogue through regular meetings, communication or briefs. Media could be involved to make progress in research publicly known. Funders should assist researchers to allocate financial and other resources to support such engagements with policy makers.
Conclusion | For research to have speedy impact on policy, it is imperative that researchers proactively engage with policy makers and other stakeholders in the entire research project development processes. Research funding should be supportive to the effort of keeping the interest of policy makers alive throughout the project execution process.

CO.17

Building research capacity in Botswana: a randomised trial comparing training methodologies in the Botswana ethics training initiative

Mary Kasule[1], Francis H. Barchi, Megan Kasimatis-Singleton, Pilate Khulumani, Jon F. Merz

1. COHRED, Botswana

Background | A randomised controlled trial was conducted in Botswana in 2010 to assess the effectiveness of a case-based intervention using email to augment in-person seminars.
Methods | Seventy-one (71) participants attended two 2-day seminars and were randomly assigned to one of two on-line arms of the trial. Participants in both arms completed on-line international modules from the Collaborative Institutional Training Initiative. Between seminars, intervention-arm participants also received via email a weekly case to analyse in response to set questions. Responses and individualised faculty feedback were exchanged via email. Tests assessing ethics knowledge were administered at the start of each seminar. The post-test included an additional section in which participants were asked to identify the ethical issues highlighted in five case studies from a list of multiple-choice responses. Results were analysed using regression and analysis of variance.
Results | Of the 71 participants (36 control, 35 intervention) enrolled at the first seminar, 41 (57.7%) attended the second seminar (19 control, 22 intervention). In the intervention arm, 19 (54.3%) participants fully completed and 8 (22.9%) partially completed all six week cases. The mean score was higher on the post-test (30.3/40) than on the pre-test (28.0/40), and individual post – and pre-test scores were highly correlated ($r=0.65$, $p<0.0001$). Group assignment alone did not have an effect on test scores ($p>0.84$), but intervention-arm subjects who completed all assigned cases answered an average of 3.2 more questions correctly on the post-test than others, controlling for pre-test scores ($p=0.003$).
Conclusion | Completion of the case-based intervention improved test scores of the respondents.

CO.18

Ethical implications in clinical genetic and genomic research for the emerging countries

Charles N. Fokunang[1,3], E.A. Tembe-Fokunang[1], M. Djuidje Ngounoue[1], J. Ateudjieu[2], G. Magne[5], R. Langsi[3], P. Awah[1], J. Ngongang[1], T. Asonganyi[1], D. Sprumont[6], S.E. Hamsel[7], O.M.T. Abena[1], L.A. Kaptue[4]

1. University of Yaounde, Cameroon; 2. University of Dschang, Cameroon; 3. University of Bamenda, Cameroon; 4. NREC, Cameroon; 5. Université Des Montagnes, Bagangté, Cameroon; 6. University of Neuchâtel, Switzerland; 7. CPP Montpellier, France

Background | Rapid advances in genetic research during the past two decades have challenged scientists, health care professionals, ethicists, government regulators, legislators, and consumers to reflect on new developments. Being constantly updated on the scientific advances and their implications is important for all stakeholders involved in making informed decisions about the ways in which genetic research and information will affect the lives of current and future generations.

Methods | The potential benefit and risks associated with genetic and genomics research is different from the types of potential benefits and risks associated with other types of health research like clinical trials and biomedical research involving human subjects. Unlike most potential risks associated with biomedical research or clinical trials which are in most cases biological in nature, potential risks associated with genomic research are mostly socioeconomic in nature.

Results | The peculiarity of some of the aspects of genetic research and the complexity of the science involved are identified. The extent, to which these characteristics hinder issues of disclosure of information, is a practical challenge that tends to be exaggerated in most situations. Genetic and genomic research since the unraveling of the human genome has the potential for drug discovery and development of new drugs and biologics like vaccines for poverty-related diseases of developing nations.

Conclusion | This contribution presents the various types of genetic research and illustrates some ethical issues. It is followed by a proposal on possible ways of managing some of the major challenges in emerging countries.

CO.19

Global implementation of good participatory practice guidelines for biomedical HIV prevention and tuberculosis research: charting progress and setting milestones

Kevin Fisher[3], Deborah Baron[1], Linda Gail Bekker[2], Stacey Hannah[3], Simon Sigirenda[4], Stephanie Seidel[5]

1. WRHI, Wits University, South Africa; 2. University of Cape Town (DTHC), South Africa; 3. AVAC, United States of America; 4. IAVI, Uganda; 5. TB Alliance, United States of America and South Africa

Background | Actively engaging stakeholders in HIV prevention research is vital to ethically robust, locally appropriate clinical trials. In 2007, UNAIDS and AVAC published the *Good Participatory Practice: Guidelines for biomedical HIV prevention trials* (GPP), providing the first normative framework for effective engagement of stakeholders in the design and conduct of research. GPP Guidelines were revised in 2011 after a global consultation, and GPP is now utilised in both HIV and tuberculosis (TB) trials.

Methods | Six years after the initial publication of GPP, a systematic review was conducted of: 1) GPP application in HIV and TB trials; 2) GPP-specific training courses involving research teams and other stakeholders; and 3) national and international forums in which GPP was referenced.

Results | Support for and awareness of GPP have increased dramatically over the past seven years. GPP has been implemented in key trials, including the FACTS 001 and ASPIRE trials, within trial network organisations, and at national level, e.g. incorporation into national ethics guidelines in Uganda and the United States. There is, however, a continued need for technical support to increase utilisation of GPP principles across HIV prevention and TB research activities. Common gaps included documentation, expansion outside of HIV prevention trials, planning around contentious issues and trial results, and stakeholder input in trial protocols.

Conclusion | While stakeholder engagement has long been an accepted practice in HIV prevention research, multiple implementation processes suggest the value and power of applying a systematic framework to practices. Implementation of GPP has increased dramatically, however continued progress requires sustained commitments, resources and action on the part of community-level, national and international stakeholders.

CO.20

Paediatric pharmacovigilance: data mining algorithms for signal detection in phase IIIb clinical trial safety datasets from seven African countries

Dan K. Kajungu[1,4,12], A. Erhart[2], A. Otau Talisuna[3,4], Q. Bassat[5], C. Karema[6], C. Nabasumba[7], M. Nambozi[8], H. Tinto[9], P. Kremsner[13], M. Meremikwu[10], U. D'Alessandro[2,11], N. Speybroeck[1]

1. UCL, Belgium; 2. ITM Antwerp, Belgium; 3. KEMRI-Wellcome Trust, Kenya; 4. UMSP/IDRC, Uganda; 5. CISM, Mozambique; 6. Ministry of Health, Rwanda; 7. Epicentre, France and MUST, Uganda; 8. TDRC, Zambia; 9. IRSS, Burkina Faso; 10. University of Calabar, Nigeria; 11. MRC, The Gambia; 12. SSARI, Uganda; 13. ITM Tübingen, Germany

Background | All drugs need to be monitored for their entire market life because early detection of adverse drug reactions can lead to alerts that prevent harm in both paediatric and adult patients. The common method for discovering previously unknown safety issues during post-marketing is through spontaneous reports. This study examines the use of data mining algorithms to identify signals from adverse events reported in a phase IIIb clinical trial.
Methods | We used paediatric safety data from a multi-site, multi-country clinical study conducted in 12 sites in seven African countries (Burkina Faso, Gabon, Nigeria, Rwanda, Uganda, Zambia, and Mozambique). Each site compared three out of four ACTs, namely amodiaquine-artesunate (ASAQ), dihydroartemisinin-piperaquine (DHAPQ), artemether-lumefantrine (AL) or chlorproguanil/dapsone and artesunate (CD+A). We applied and assessed two methods of pharmacovigilance signal generation: proportional reporting ratio (PRR) and Bayesian confidence propagation neural network (BCPNN).
Results | The 4,116 children (6–59 months old) with uncomplicated *P. falciparum* malaria who were treated, reported a total of 6,238 adverse events within 28 days of follow-up, resulting into 346 drug-event combinations. Nine signals were generated both by proportional reporting ratio and Bayesian Confidence Propagation Neural Network. A review of the manufacturer package leaflets or an online Multi-Drug Symptom/Interaction Checker (DoubleCheckMD©) and further by therapeutic area experts reduced the signals to five.
Conclusion | These two methods worked well in predicting signals. Use of experts and resources like manufacturer package leaflets are essential in reviewing signals. Phase IIIb clinical trial safety data can be used to supplement reports from spontaneous reporting systems and to validate previously reported adverse drug reactions.

CO.21

Experiences in using e-learning to improve the capacity of African scientists in South Africa

Photini Kiepiela[1], Jean-Pierre Kraehenbuhl[2], Jonathan Fuchs[1,3,4], Gita Ramjee[1]

1. MRC HPRU, South Africa 2. HSeT, Switzerland; 3.University of Cape Town, South Africa; 4. SATVI, South Africa;

Background | Health Science e-Training (HSeT) has developed web-based programmes in health sciences, creating e-learning opportunities to support innovative face-to-face workshops globally (http://HDI.bio-med.ch/). Collaboration was established between HSeT, MRC HIV Prevention Research Unit (HPRU), OCTAVE, University of Cape Town and SATVI through EDCTP funding, to undertake four e-learning workshops on relevant topics in South Africa to improve the skills of African post-graduate scientists.
Methods | Prior to each workshop HSeT created a workshop-specific e-learning portal (http://enterprise.bio-med.ch/). The portal housed curricula developed by the HSeT team and workshop faculty, i.e. topic-specific Background materials, articles and interactive pre-workshop activities which trainees had to complete prior to the face-to-face workshop. The three-day face-to-face workshop combined small group exercises and focused lectures given by experts in the field. A paper-based survey was administered to scholars at the end of the workshop to assess various aspects of the pre-workshop and face-to-face workshop material.
Results | The target audience (n=20–25) were scientists of Master's to post-doctorate level, directly involved in HIV prevention and treatment; statistical research; tuberculosis; and HIV/HPV mucosal immunity. Participants found that lectures and group exercises made excellent learning tools and benefited from open communication with experienced faculty members. Certain facets of the workshop called for improvement, viz. an extended workshop time frame and lecture time allocated to review basic principles of the topics.
Conclusion | The evaluation confirmed that the workshops successfully met their objectives. This calls for future regional capacity-building efforts for post-graduate students committed to HIV and tuberculosis vaccine discovery.

CO.22

EACCR: coordination of the malaria node activities

Peninah Menza[1], Nobert Peshu[2], Martha Lemnge[3], Roma Chilengi[4]
1. DNDi, Kenya; 2. KEMRI-Wellcome Trust, Kenya; 3 NIMR, Tanzania. 4. CIDRZ, Zambia

Background | Despite substantial achievements in research and development on malaria, the disease scourge continues to be unbearable for many African countries. This necessitates development of a critical mass of indigenous African researchers who would be able to participate in finding solutions and effective interventions for malaria.
Methods | Research institutions in Eastern Africa formed a consortium, the East Africa Consortium for Clinical Research (EACCR) in response to an EDCTP call for regional centres of excellence. The consortium's objectives are: to strengthen research capacity; to network amongst partners and improve south-to-north and south-south collaborations; to facilitate EDCTP's vision of accelerating the development of new drugs and tools to control malaria; and to provide development support to junior trial sites within the East African region. The centre at Kilifi was responsible – as Malaria Node – for the coordination of the malaria activities, and specifically worked on project management, capacity building, networking and mentorship programmes.
Results | Five students were selected and supported to complete master degree training in fields relevant to malaria R&D. The node conducted 10 trial site assessments to evaluate young sites and provided small sub-grants to each of the sites. South-South mentorship was achieved through short term placement and training of staff from younger sites at senior sites. The common fields addressed for mentorship included data management, trial monitoring, laboratory, finance and project management.
Conclusion | The EACCR Malaria Node is a success at demonstrating that capacity exists within the region which if harnessed can result in addressing gaps at trial sites. This is a sustainable model of networking that will result in a strong research capacity base in the region.

CO.23

Towards strengthening the West African network of excellence for tuberculosis, HIV/AIDS and malaria: WANETAM Plus

Dembo Kanteh[1], M.R. Thorpe, J.P. N'guessan, U. D'Alessandro, H. Tinto, B. de Jong, M. Antonio, K. Bojang, S. Mboup, T. Corrah, A. Jaye

1. MRC, The Gambia

Background | The capacity for biomedical research and clinical trials is generally weak in Africa. However, WANETAM has made major capacity building in-roads. Synergising WANETAM, the WANETAM Plus project integrated research and training programmes from two member states, United Kingdom (Medical Research Council) and Belgium (Institute of Tropical Medicine). The initiative strengthened the training of scientists and scientific support staff on key pre-defined gaps in order to consolidated regional collaborative training and research.

Methods | Training of core scientists was conducted through the following courses: tailored, collaboratively designed courses in GCP/GCLP; malaria genotyping; virology; tuberculosis microscopy. Moreover, a scientific support training – a newly designed Biomedical Engineering and Equipment Maintenance (BEEM) programme – was developed, focusing on technical and management skills. Intensifying networking, WANETAM Plus integrated into WANETAM more partners from North and South, expanding the number of partners to 20. Wider website information exchange and scientific programme sharing are enabled through a network Basecamp® online communication tool.

Results | A total of 26 scientists were trained in courses including GCP/GCLP, genotyping for malaria, fluorescence microscopy and quality control and IATA shipping. Twenty-one (21) biomedical engineers from eight institutions were trained and a unique BEEM model for lab support has now been created in West Africa. Twenty-two (22) Francophone and Lusophone scientists received English language training which enabled two of them to gain entry to post-graduate modular courses in clinical trials. The WANETAM website has been enhanced to include new partners.

Conclusion | The results of WANETAM Plus contributed to extension of network collaboration and to include new research projects in tuberculosis, HIV/AIDS and malaria among partner institutions. The network provides a broad constituency for encouraging regional multisite clinical intervention trials.

CO.24

The Pan-African Centre of Excellence in Nanomedicine: research and training on poverty-related diseases

Hulda Swai[1], Lonji Kalombo, Rose Hayeshi, Yolandy Lemmer, Paula Melariri, Admire Dube, Phillip Labuschagne

1. CSIR, South Africa

Background | Sub-Saharan Africa bears the brunt of poverty related diseases (PRDs) such as tuberculosis (TB) and malaria. Current therapies against PRDs are inadequate and warrant a quantum leap in drug development approaches. Nanomedicine is a rapidly advancing area of biomedical research with great potential to revolutionise new and current treatments for PRDs, as it is doing for other diseases such as cancer.

Methods | The Pan-African Centre of Excellence in Nanomedicine is an initiative of the African Network for Drugs and Diagnostics Innovation (ANDI). We are developing nanomedicines that will improve the current inadequate therapeutic management of TB, malaria and other PRDs such as neglected infectious diseases.

Results | TB is the leading cause of death in South Africa. The Pan-African Centre of Excellence in Nanomedicine has shown in mice that, using nanomedicine, the dose frequency for current TB treatment could be reduced from daily to once-a-week, without the inherent unpleasant side effects.

Conclusion | Having made the most advances in nanomedicine-based PRD research in Africa, especially in TB, the Pan-African Centre seeks to further the application of nanomedicine in neglected infectious diseases like schistosomiasis. Given this advantage, it has an urgent responsibility to advance nanomedicine research in Africa, while simultaneously generating highly qualified human capacity. It seeks meaningful impact not only at a continental but also at a global level. Towards this goal, the Pan-African Centre of Excellence in Nanomedicine aims to deliver on nanomedicine as an alternative therapy against PRDs through sharing of resources, know-how and technologies. This approach contributes to avoiding wasteful duplication of effort and allows for the most efficient use of existing structures.

CO.25

Establishment of a centralised clinical trials register in Kenya: a model for knowledge sharing and exchange across two institutions

Christine Wasunna[1], Jayesh Pandit[2], Steve Wanyee[4], Edward Abwao[2]
1. KEMRI, Kenya; 2. Bayer HealthCare; 3. Pharmacy and Poison's Board, Kenya; 4. IntelliSOFT Ltd, Kenya

Background | In 2010, the Kenya Medical Research Institute (KEMRI), the Pharmacy and Poisons Board (PPB) and the Drug Regulatory Authority, established a common initiative to create a national clinical trials register in Kenya to promote the exchange of clinical research information across institutional boundaries. An Expert Committee on Clinical Trials (ECCT) at the PPB evaluates applications for investigational medical products and devices to be used in clinical trials and approves their import once a study has received a favourable opinion from a research ethics committee. The clinical trials registry (www.ctr.pharmacyboardkenya.org) was established with support from KEMRI in partnership with EDCTP.
Methods | The information in the national clinical trials register database was extracted from the comma-separated value (cvs) files and exported to SPSS version 17.0 for descriptive analysis.
Results | As at February 2014, the data captured in the national clinical trial register (CTR) indicates that therapeutic trials are predominant over non-therapeutic trials and a majority of the clinical trials recorded are safety and efficacy studies (11 phase I studies; 16 phase II studies, 42 phase III studies and 12 phase IV studies). A significant number of paediatric trials conducted in Kenya from 2008 to the present, are in the field of HIV/AIDS and malaria. Less than 5% of trials conducted over this period cover neglected tropical diseases. The CTR system is also integrated with the pharmacovigilance electronic reporting system where a total of 423 reports were filed electronically directly from the healthcare facilities in the country up from 291 in the year 2012. More than 70% of the reports are ARVs-related with Stavudine as the leading cause of the adverse drug reactions.
Conclusion | Currently, KEMRI and PPB benefit from open communication and complementary coordination in the review of clinical trial applications. The centralised clinical trials register also provides a platform for dissemination of clinical research information and identification of critical research gaps. This resource serves as an evidence-based platform for the regulatory bodies.

CO.26

Opportunities and challenges: sharing experiences of institutional review board and research ethics committee members in a developing country

Joseph B.R. Gaie[1]

1. University of Botswana, Botswana

Background | Institutional review boards and research ethics committees (IRB/RECs) are relatively new in most of Africa, especially in the sub-Saharan region. Recently, the number of IRB/RECs in African countries has been growing. The necessity to increase their numbers has in large part to do with the emergence of HIV/AIDS, which tremendously increased the need to conduct clinical research. IRB/RECs the world over have faced challenges such as lack of resources and institutional support, disinterestedness of academics, lack of training for IRB/REC members and many others. In the case of some African developing countries, some of the challenges take a peculiar form. This paper shares experiences of the members of an IRB. It relates some challenges and opportunities and calls for a willingness to learn from these experiences.

Methods | The paper mainly employs the extant literature on IRB/RECs in developing countries particularly in Africa. It also uses experiences of some IRB/REC members to identify challenges and opportunities in this case which other developing countries may experience as well.

Results | Qualitative answers will show the kind of problems and opportunities that the case study presents. They will suggest what probably needs to be done in order to achieve progress. Examples of unethical behaviour which may compromise the operation of an IRB or REC, will be discussed.

Conclusion | Challenges that normally trouble IRBs/RECs are common but some are peculiar to the case study. Opportunities are there but challenges need to be overcome first if there is to be progress. Unethical behaviour itself can be one of the major problems of IRB/RECs.

CO.27

Capacity building and evaluation of post-training operational capacities of three ethics review committees in Nigeria: best practice

Kolawole Oyedeji[1], Morenike Ukpong[3], Oliver Ezechi[2], Timothy Abolarinwa[2], David Johnson[2], Kehinde Oluwadiya[4], Ibraheem Katibi[5], Philip Olatunji[6]

1. University of Lagos; 2. NIMR, Nigeria; 3. NHVMAS, Lagos, Nigeria; 4. Ekiti State University, Nigeria; 5. University of Ilorin, Nigeria; 6. Olabisi Onabanjo University, Ogun State, Nigeria

Background | In Nigeria, the regulatory body for ethical conduct of health research – the National Health Research Ethic Committee (NHREC), published the National code for health research ethics in 2006. To date, most of the Ethics Review Committees (ERCs) are not conversant with this code and lack expertise to review research protocols. The aim of this project was to train ERC members in Nigeria in reviewing research protocols and provide constructive feedback in addition to provision of infrastructural support for improved performance.

Methods | A participatory workshop training style was adopted with a pre-test and a post-test. The post-training evaluation was conducted using a qualitative and quantitative approach. The respondents were ERC secretariat staff, ERC members and ERC subscribers (researchers/investigators).

Results | The evaluation of the workshop showed that participants' knowledge of ethics review improved significantly(pre-test=46.8%, post-test=73.4%, p=0.0009).Generally, the respondents assessed the training as having improved the operational capacities of the ERC post-training. The specific impacts observed include among others: provision of constructive feedback, improved turnaround time, improved organisation of protocol submission, and better communication with subscribers.

Conclusion | While the EDCTP project provided both human capacity building and infrastructural support which had a positive impact on the overall operational capacities of the ERCs, there remains a gap in research monitoring. Therefore, there is a need for continued support in this regard.

CO.28

Challenges of establishing and running a community advisory board in Botswana

Galekgatlhe Bailey Balekang[1]

1. Health Research Division, Ministry of Health, Botswana

Background | Establishing Community Advisory Boards is now seen as standard practice for Clinical Vaccine and drug trials worldwide. Growing attention is paid to the principle of establishing community advisory boards in order to advise investigators on the conduct of health research. In the past, most community advisory boards were established by activists and lobbyists to monitor HIV/AIDS vaccine and drugs trials in developed countries.

Methods | A descriptive approach was used to identify the processes and challenges of establishing and running community advisory boards. A sample of 30 respondents was included in the study.

Results | A range of issues about the potential value and challenges of running and establishing community advisory boards in Botswana were identified by the study. The challenges included lack of clear understanding of the roles of the community advisory boards members, failure of board members to attend meetings, lack of funding for the boards, and also no sitting allowance for community advisory board members.

Conclusion | In conclusion, community advisory boards are but one form of community involvement in clinical trials but the formation of such boards is seen as the best approach for research institutions to engage the community on issues pertaining to research activities in the population. For better results, the challenges faced by community advisory boards need to be addressed and the health literacy of the community needs to be improved. Standards should be considered for the purpose and parameters of community involvement. Mechanisms should be put into place for real community participation instead of just consultation and placation.

CO.29

Digitised audio questionnaire for assessment of informed consent comprehension in a low-literacy African research population: development and psychometric evaluation

Muhammed O. Afolabi[1,2], Kalifa Bojang[1], Umberto D'Alessandro[1,2], Martin O.C Ota[3], Heidi J. Larson[2], Egeruan B. Imoukhuede[4], Raffaella M. Ravinetto[5], Nuala McGrath[6], Daniel Chandramohan[2]

1. MRC, The Gambia; 2. LSHTM, United Kingdom; 3. WHO AFRO, Republic of Congo; 4. University of Oxford (Jenner), United Kingdom; 5. ITM Antwerp, Belgium; 6. University of Southampton, United Kingdom

Background | Comprehension of information provided during an informed consent process remains a major challenge in low-literacy communities of Africa. Written translations and back-translations of informed consent documents pose greater challenges in The Gambia because local languages do not have accepted methods of writing. Furthermore, no adequate methods exist to measure comprehension in this population.

Methods | We developed a 34-item informed consent comprehension questionnaire consisting of closed-ended, open-ended and multiple-choice question items to assess comprehension of key concepts like autonomy, blinding, placebo, and randomisation. The questionnaire underwent face and content validation by a panel of experienced researchers. To bypass the challenge of written translation and back-translation, we audio-recorded the questionnaire in three major Gambian languages: Mandinka, Wolof and Fula. The audio-recorded questionnaire was further developed into an Audio Computer Assisted Interview format. The digitised questionnaire was administered to 250 clinical trial participants in urban and rural Gambia, and re-administered to half of the participants one week after first administration.

Results | Item reduction by factor analysis showed that 21 of the question items have strong factor loadings. These were retained along with 5 other items which were fundamental components of informed consent. The 26-item questionnaire has high internal consistency with Cronbach's alpha of 0.73–0.79 and intra-class correlation coefficient of 0.94 (95% CI 0.923–0.954). Hypotheses testing also showed that the questionnaire has positive correlations with a similar questionnaire and discriminates between participants with and without education.

Conclusion | We have developed a reliable and valid measure of comprehension of informed consent information for a Gambian research population. This is a major step towards engendering comprehension of consent information among research participants with low literacy.

CO.30

Towards an ISHReCA manifesto to guide researchers as they engage in health research partnerships

Palmer Netongo[1], S. Kinyanjui, W. Mbacham, S. Sirima, H. Ghannem, A. Hodgson, E. Madela-Mntla, A. Aseffa, M.E. Elhassan, H. Swai, and N. Sewankambo.

1. ISHReCA, Cameroon

Background | Health research is a collaborative effort of multiple partners from different areas of competence and at various levels of capacity. Effective health research partnership requires appropriate recognition of the value of the contributions of each partner. Where there is disparity in resources, as is commonly seen in collaborations between high-income countries and African research teams, the tendency for a 'top-down' relationship exists to the disadvantage of resource-poor countries.

Methods | In this paper, ISHReCA explores the concepts of ethics in research partnership, including Background, experiences, mechanisms and practical tools for partnership assessment. Presentations from invited experts and discussion at an ISHReCA session at the 16th ICASA meeting are summarised. This presentation is intended to serve as a basis for an enlarged consultation of research stakeholders.

Results | This paper underscores some innovative strategies to strengthen health research capacity building in Africa through 'ethics of research partnership'. It stresses the need to recognise the true worth of local and indigenous knowledge, on-site resources, personnel time, skills and an enabling environment alongside the financial and technical input of the better resourced partners. Equity and justice in partnerships is highlighted as beneficial for sustained productivity in research.

Conclusion | A dashboard of recommendations is presented for an extensive consultation of stakeholders to guide health researchers as they engage in partnerships. These recommendations will be developed into an ISHReCA 'manifesto' aimed at encouraging durable North-South and South-South research partnerships.

Satellite meetings

Sustainable investment in research for health

Co-organised by	The Ministry of Public Health Senegal, the West African Health Organisation (WAHO), The New Partnership for Africa's Development (the NEPAD Agency) and the Council on Health Research for Development (COHRED)
Date and time	Sunday 29 June 2014, 9:00–17:00
Place	Salon 3–4

This meeting aims to explore practical strategies for increasing predictable resourcing towards priority research in countries and to highlight African countries' experiences in managing research for health.

Objectives

- Highlight current domestic and external investment strategies in research for health and discuss challenges and best practices
- Present platforms that facilitate monitoring of research investment and discuss wider use of these platforms
- Engage country, regional and global partners in a dialogue aimed at defining strategies to increase predictable resourcing towards priority research in countries.

Expected outcomes

- Strategies for improved domestic and external resourcing of research for health, with concrete action points for follow up by participating partners
- Report of the meeting.

The meeting will follow a participatory format, including open space and world café sessions, thus engaging participants in creative thinking and strategising for innovative approaches to research financing. Participants are invited to bring their experiences to the meeting and share these through short informal presentations.

A networking event will be organised immediately following the formal parts of the meeting.

Combatting neglected tropical diseases: The case of visceral leishmaniasis in Africa

Co-organised by	Drugs for Neglected Diseases initiative (DNDi)
Date and time	Monday 30 June 2014, 17:00–18:30
Place:	Salon 7

Objectives of the meeting

- To provide an overview of visceral leishmaniasis (VL) and the current epidemiological trends, including geographic variability, co-infection with HIV, and the post-kala-azar dermal leishmaniasis (PKDL) syndrome
- To provide an extensive overview of the holistic and coordinated strategy to address the current R&D needs to combat VL in Africa
- To show the challenges of ensuring that research results lead to appropriate policies for the effective control of leishmaniasis in the region. A concrete example of the clinical trials conducted for the combination treatment Sodium Stibogluconate (SSG) & Paromomycin (PM) will be given
- To highlight the need for strengthening national and regional clinical research capacities in order to facilitate the development, delivery, and registration of new treatments for leishmaniasis. Here, the activities of the Leishmaniasis East Africa Platform (LEAP) will be introduced.

Expected outcomes

- Overview of the strengths of a global and holistic approach to address R&D gaps for visceral leishmaniasis
- Stimulate discussion on the R&D activities to combat visceral leishmaniasis and to reach the WHO NTDs Roadmap targets.

PROGRAMME >>

PROGRAMME

CHAIR	**Daniel Argaw Dagne**, Leishmaniasis Programme, Department of Control of Neglected Tropical Diseases, WHO
17:00–17:05	**Daniel Argaw Dagne**, Leishmaniasis Programme, Department of Control of Neglected Tropical Diseases, WHO *Introduction and welcome*
17:05–17:20	**Jorge Alvar**, Head of Leishmaniasis Clinical Program, DNDi *A global approach to combat visceral leishmaniasis* The presentation introduces DNDi's global coordinated strategy to cover the current R&D gaps of treatment and control of the human transmission of visceral Leishmaniasis through innovative mechanisms
17:20–17:35	**Ahmed Musa Mudawi**, Institute of Endemic Diseases University of Khartoum, Sudan *Translation of science into policy of new control tools for the management of African visceral leishmaniasis* The presentation will introduce the prerequests and the barriers that must be overcome, in order to acquire approvals and achieve international standards when conducting clinical trials. It will provide a case-study of the combination treatment SSG&PM developed by DNDi and its partners to fight visceral leishmaniasis in East Africa
17:35–17:50	**Monique Wasunna**, Head of DNDi Africa *Capacity strengthening to deliver a new first-line treatment for Kala Azar in East Africa: the leading role of the LEAP platform* The presentation will provide an overview of the role of the LEAP Platform in building and retaining clinical trial capacities within disease-endemic countries and how such research networks can facilitate registration of and access to new treatments
17:50–18:25	**Open discussion**
18:25–18:30	**Daniel Argaw Dagne**, Leishmaniasis Programme, Department of Control of Neglected Tropical Diseases, WHO *Summary and ending conclusions*

Global TB Vaccine Partnership

Organised by	Global TB Vaccine Partnership
Date and time	Tuesday 1 July 2014, 17:30–19:00
Place	Salon 3–4

The session will present and discuss the Global TB Vaccine Partnership currently being developed by the European Commission, European Investment Bank, Bill & Melinda Gates Foundation in collaboration with Aeras, the TuBerculosis Vaccine Initiative (TBVI) and EDCTP.

PROGRAMME

CHAIRS:	**Charles Mgone**, Executive Director, EDCTP **Samia Saad**, Senior Program Officer for Global Health R&D Policy & Advocacy, Bill & Melinda Gates Foundation
Georges Thiry, Chairman of Product Development Team, TBVI *The TB vaccine landscape*	
Line Matthiessen, Head of Unit, DG Research and Innovation, European Commission *Global TB Vaccine Partnership: The way forward?*	
Ann Ginsberg, Chief Medical Officer, Aeras *How to select the best TB vaccine candidates?*	
Shiva Dustdar, Head of Research, Development and Innovation, European Investment Bank *Innovative research funding models: the case study of the Global TB Vaccine Partnership*	
Gérald Voss, Director Vaccine Development Partnerships, GSK *The industrial perspective*	
Panel discussion and questions from the audience	

ESSENCE on Health Research initiative, members' dinner meeting

Organised by	ESSENCE on Health Research initiative, Special Programme for Research and Training in Tropical Diseases (TDR), World Health Organization
Date and time	Tuesday 1 July 2014, 17:30–20:30
Place	Salon 2

By invitation only

ESSENCE on Health Research (Enhancing Support for Strengthening the Effectiveness of National Capacity Efforts) is a collaborative framework between funding agencies to scale up research capacity. It aims to improve the impact of investments in institutions and people, and provides enabling mechanisms that address needs and priorities within national strategies on research for health.

Institute acronyms

AHRI, Ethiopia	Armauer Hansen Research institute, Addis Ababa, Ethiopia
AiBST, Zimbabwe	African Institute of Biomedical Science and Technology, Harare, Zimbabwe
AIGHD, The Netherlands	Amsterdam Institute for Global Health and Development, Academic Medical Centre, University of Amsterdam, The Netherlands
AMANET, Tanzania	African Malaria Network Trust, Dar Es Salaam, Tanzania
AMC, The Netherlands	Academic Medical Center of the University of Amsterdam, Amsterdam, The Netherlands
BHP, Botswana	Botswana-Harvard School of Public Health AIDS Initiative Partnership for HIV Research and Education, Gaborone, Botswana
BIPAI Uganda Mulago, Uganda	Baylor College of Medicine, Bristol-Myers-Squibb Children's Clinical Centre of Excellence at Mulago Hospital, Uganda
CAMBIN, Cameroon	Cameroon Bioethics Initiative, Yaounde, Cameroon
CDC-BOTUSA, United States of America	US Centres for Disease Control and Prevention, Botswana-USA Partnership, Atlanta, GA, United States of America and Gaborone, Botswana
CDC, Kenya	US Centers for Disease Control & Prevention, Kenya
CDC, United States of America	Centers for Disease Control and Prevention, Atlanta, GA, United States of America
Centre Muraz, Burkina Faso	Institut de Recherche en Sciences de la Santé – Centre Muraz, Burkina Faso
CePReF Yopougon, Côte d'Ivoire	Service pédiatrie, Centre de Prise en Charge, de Recherche et de Formation, Site Aconda-vs, Yopougon, Abidjan, Côte d'Ivoire
CERMEL, Gabon	Centre de Recherches Médicales de Lambaréné, Gabon
CHUC, Côte d'Ivoire	Centre Hospitalier Universitaire Cocody, Abidjan, Côte d'Ivoire
CHUCG, Burkina Faso	Centre Hospitalier Universitaire Charles de Gaulle, Ouagadougou, Burkina Faso
CHUSS, Burkina Faso	Centre Hospitalier Universitair de Souro Sanou, Bobo-Dioulasso, Burkina Faso
CHUT (PAC-CI), Côte d'Ivoire	Centre Hospitalier Universitaire de Treichville, Programme PAC-CI, Abidjan, Côte d'Ivoire
CHUT, Côte d'Ivoire	Centre Hospitalier Universitaire de Treichville, Abidjan, Côte d'Ivoire

CHUV, Switzerland	Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
CHUY, Côte d'Ivoire	Centre Hospitalier Universitaire (CHU) de Yopougon, Abidjan, Côte d'Ivoire
CIDG, United Kingdom	Cochrane Infectious Diseases Review Group, Liverpool, United Kingdom
CIDRZ, Zambia	Centre for Infectious Disease Research in Zambia, Lusaka, Zambia
CISM, Mozambique	Centro de Investigação em Saúde da Manhiça, Manhiça, Mozambique
CNFRSR, Guinea	Centre National de Formation et de Recherche en Santé Rurale, Maferinyah, Guinea
CNRFP, Burkina Faso	Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso
COHRED, Switzerland/Kenya	Council on Health Research for Development, Geneva/Nairobi, Switzerland/Kenya
CPP Montpellier, France	Comité de Protection des Personnes, Montpellier, France
CRESIB, Spain	Barcelona Centre for International Health Research (Hospital Clinic, University of Barcelona), Barcelona, Spain
CRIS, Burkina Faso	Centre de Recherche Internationale pour la Santé
CRMN, Gabon	The Medical Research Center of the province Ngounie in Fougamou, Gabon
CRRFP Dakar, Senegal	Centre Régional de Recherche et de Formationà la prise en charge clinique, Dakar, Senegal
CSIR, Ghana	Council for Scientific and Industrial Research, Legon-Accra, Ghana
DNDi, Kenya	Drugs for Neglected Diseases initiative, Switzerland and Kenya
ECSA-HC, Tanzania	East, Central and Southern African Health Community, Arusha, Tanzania
EHNRI, Ethiopia	Ethiopian Health and Nutrition Research Institute, Addis Ababa, Ethiopia
EKUT, Germany	Eberhard Karls University, Tübingen
ESTHER/GIZ GmbH, Germany	ESTHER Germany – University & Hospital Partnerships, Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH, Germany
EVI, Germany	European Vaccine Initiative, Heidelberg, Germany
FHI 360, United States of America	FHI 360, Clinical Sciences Unit, Durham, NC, United States of America

GRAS, Burkina Faso	Groupe de Recherche Action en Santé, Ouagadougou, Burkina Faso
Harvard Public Health, United States of America	Department of Immunology and Infectious Diseases, and the Harvard School of Public Health AIDS Initiative, Harvard School of Public Health, Boston, MA, United States of America
HSeT, Switzerland	Foundation for Health Science e-Training, Lausanne Epalinges, Switzerland
ICF Intl CIMS, United States of America	ICF international, CDC Information Management Services, Atlanta, GA, United States of America
ICHR, Kenya	International Centre for Reproductive Health Kenya, Mombasa, Kenya
IHI, Tanzania	Ifakara Health Institute (Formerly, Ifakara Health Research and Development Centre), Tanzania
IKP, Germany	Dr. Margarete Fischer-Bosch Institute for Clinical Pharmacology, Stuttgart, Germany
IMI, Portugal	Instituto de Medicina Molecular, Lisboa, Portugal
IMRet-UTH, Zambia	Institute for Medical Research & Training (IMReT) – University Teaching Hospital, Lusaka, Zambia
INMI, Italy	National Institute for Infectious Diseases, Rome, Italy
INSERM, France	Institut National de la Santé et de la Recherche Médicale, France
IRD Paris, France	Institut de Recherche pour le Développement, Paris, France
IRSS, Burkina Faso	Institut de Recherche en Sciences de la Santé, Direction Régionale de l'Ouest, Bobo Dioulasso, Burkina Faso
IRSS, Burkina Faso	Institut de Recherche en Sciences de la Santé, Bobo Dioulasso, Burkina Faso
ISHReCA, Cameroon	Initiative to Strengthen Health Research Capacity in Africa, University of Yaounde I, Cameroon
ITM Antwerp, Belgium	Institute of Tropical Medicine, Antwerp, Belgium
ITM Hamburg, Germany	Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany
ITM Tübingen, Germany	Institute for Tropical Medicine, University of Tübingen, Tübingen, Germany
JCRC Fort Portal, Uganda	Joint Clinical Research Centre, Fort Portal, Uganda
JCRC Gulu, Uganda	Joint Clinical Research Centre, Gulu, Uganda

JCRC Kampala, Uganda	Joint Clinical Research Centre, Kampala, Uganda
JCRC Mbale, Uganda	Joint Clinical Research Centre, Mbale, Uganda
JOOTRH	Jaramogi Oginga Odinga Teaching and Referral Hospital, Kisumu, Kenya
KATH, Ghana	Komfo Anokye Teaching Hospital, Kumasi, Ghana
KCMC, Tanzania	Kilimanjaro Christian Medical Centre, Moshi, Tanzania
KCRI, Tanzania	Kilimanjaro Clinical Research Institute, Moshi, Tanzania
KEMRI	Kenya Medical Research Institute, Nairobi, Kenya
KEMRI-CDC, Kenya	Kenya Medical Research Institute – Centers for Disease Control & Prevention Research & Public Health Collaboration, Kenya
KEMRI-Walter Reed, Kenya	KEMRI – Walter Reed Project-Centre for Clinical Research, Nairobi, Kenya
KNUST, Ghana	Kwame NKrumah University of Science and Technology
LSHTM, United Kingdom	London School of Hygiene & Tropical Medicine, London, United Kingdom
LSTM, United Kingdom	Liverpool School of Tropical Medicine, Liverpool, United Kingdom
LUMC, The Netherlands	Leiden University Medical Center, Leiden, The Netherlands
MHRP-HJF, United States of America	United States Military HIV Research Program (MHRP), Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc. (HJF), Bethesda, MD, United States of America
MoHSW-NTLP, Tanzania	Ministry of Health and Social Welfare – National Tuberculosis and Leprosy Programme, Dar es Salaam
MRC (HPRU), South Africa	Medical Research Council, HIV Prevention Research Unit (HPRU), Durban, South Africa
MRC CTU, United Kingdom	Medical Research Council, Clinical Trials Unit, London, United Kingdom
MRC-UVRI AIDS, Uganda	Medical Research Council-Uganda Virus Research Institute, Uganda Research Unit on AIDS
MRC, South Africa	Medical Research Council, South Africa
MRC, The Gambia	Medical Research Council Unit The Gambia, Banjul, The Gambia
MRC, Zimbabwe	Medical Research Council of Zimbabwe, Harare, Zimbabwe

MRTC, University of Bamako, Mali	Malaria Research and Training Centre, University of Bamako, Bamako, Mali
MSAS, Senegal	Ministère de la Santé et de l'Action Sociale, Dakar, Senegal
MUHAS, Tanzania	Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
MUST, Uganda	Mbarara University of Science and Technology, Uganda
NHRC, Ghana	Navrongo Health Research Centre, Navrongo, Ghana
NHVMAS, Lagos, Nigeria	New HIV Vaccine and Microbicide Advocacy Society, Lagos, Nigeria
NIH NIAID Hamilton, United States	National Institutes of Health National Institute of Allergy and Infectious Diseases, Rocky Mountain Laboratory, Hamilton, MT, United States of America
NIMR Muhimbili, Tanzania	National Institute for Medical Research, Muhimbili Centre, Dar es Salaam, Tanzania;
NIMR-MMRC, Tanzania	NIMR-Mbeya Medical Research Center, Mbeya, Tanzania
NIMR, Nigeria	Nigerian Institute of Medical Research, Nigeria
NIMR, Tanzania	National Institute for Medical Research, Dar es Salaam, Tanzania
OCTAVE	*OCTAVE* Project : Online Collaborative Training for AIDS Vaccine Evaluation
PAC-CI, Côte d'Ivoire	Programme national/ANRS/coopération française-Côte d'Ivoire
PanACEA Consortium	Pan-African Consortium for Evaluation of Anti-tuberculosis Antibiotics (PanACEA) consortium
PROFILE/GIZ GmbH, Germany	Programm zur Förderung von Innovation, Lernen und Evidenz in HIV – und Gesundheits-programmen der deutschen Entwicklungspolitik (PROFILE)/Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ) GmbH, Bonn, Germany
QMUL, United Kingdom	Queen Mary University of London, United Kingdom
SACC, South Africa	South African Cochrane Centre, South Africa
SATVI, South Africa	South African Tuberculosis Vaccine Initiative, South Africa
SSARI-A, Uganda	Santé Statistical and Analytical Research Institute – Africa [research company], Kampala, Uganda

Strathmore University (CREATES), Kenya	Centre for Research in Therapeutic Sciences (CREATES), Strathmore University, Centre for Clinical Research, Kenya
Swiss TPH, Switzerland	Swiss Tropical and Public Health Institute, Basel, Switzerland
TDRC, Zambia	Tropical Disease Research Centre, Ndola, Zambia
UCL, Belgium	Université Catholique de Louvain, Belgium
UCM CIDI, Mozambique	Catholic University of Mozambique (UCM), Centro de Investigação de Doenças Infecciosas/ Center for Infectious Disease Research (CIDI), Beira, Mozambique
UKZN, South Africa	University of KwaZulu Natal (UKZN), South Africa
University of Cape Town (DTHC), South Africa	Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa
University of Oxford (Jenner), United Kingdom	The Jenner Institute Laboratories, University of Oxford, Oxford, United Kingdom
University of Oxford (MRC/Wheatherall), United Kingdom	MRC Human Immunology Unit, Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, United Kingdom
University of Oxford (Nuffield), United Kingdom	Centre for Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, United Kingdom
USS	Université des sciences de la santé, Gabon
UTH, Zambia	University Teaching Hospital, Lusaka, Zambia
UVRI-IAVI, Uganda	Uganda Virus Research Institute – IAVI HIV Vaccine Programme, Entebbe, Uganda
UVRI, Uganda	Uganda Virus Research Institute, Entebbe, Uganda
WANECAM-Guinea / CNFRSR, Guinea	West African Network for Clinical Trials of Antimalarial Drugs – Guinea / Centre National de Formation et de Recherche en Santé Rurale, Maferinyah, Guinea
WANECAM-Mali / MRTC, University of Bamako, Mali	West African Network for Clinical Trials of Antimalarial Drugs – Mali / MRTC, University of Bamako, Mali
WHO-AFRO, Republic of Congo	World Health Organization Regional Office for Africa, Brazzaville, Republic of Congo
WRHI, Wits University, South Africa	Wits Reproductive Health & HIV Institute, Johannesburg, South Africa, Wits University, Johannesburg, South Africa
WWARN	WorldWide Antimalarial Resistance Network

Presenter index

M

N

O

P

R

S

T

V

W

Y

Z

Sunday 29 June 2014	Monday 30 June 2014
	REGISTRATION | 08:00–09:00 FOYER, CONFERENCE CENTRE
	PLENARY SESSION I | 09:00–10:30 Forum prologue | HALL I B-C
	COFFEE AND TEA BREAK HALL II | 10:30–11:00
	MARKETPLACE VIEWS HALL II | 10:30–11:00
SATELLITE MEETING | 09:00–17:00 Sustainable investment in research for health | SALON 3–4	**PLENARY SESSION II** | 11:00–12:30 Recent advances in HIV/AIDS, tuberculosis and malaria (keynote addresses) | HALL I B-C
	LUNCH HALL II | 12:30–13:30
	MARKETPLACE VIEWS HALL II | 12:30–13:30
	PLENARY SESSION III | 13:30–15:30 Recent advances in neglected infectious diseases, health services optimisation research (keynote addresses) and update on Horizon 2020 | HALL I B-C
	COFFEE AND TEA BREAK HALL II | 15:30–16:00
	MARKETPLACE VIEWS HALL II | 15:30–16:00
REGISTRATION | 16:00–18:00 FOYER, CONFERENCE CENTRE	**PARALLEL SESSIONS** | 16:00–17:00 • HIV/AIDS immunology and vaccine development | HALL I B-C • Tuberculosis therapeutic studies | SALON 2 • Malaria vaccines studies | HALL I A • Cross-cutting: policy, ethics, regulatory and trials registration activities | SALON 3–4
	MARKETPLACE VIEWS HALL II | 17:00–18:00
	SPECIAL SESSION | 17:00–18:30 EDCTP2 Fellowship Schemes | SALON 2
	SATELLITE MEETING | 17:00–18:30 Combatting neglected tropical diseases: the case of visceral leishmaniasis in Africa | SALON 7
	CONFERENCE DINNER | 19:00–20:30

Tuesday 1 July 2014

REGISTRATION | 08:00–09:00
FOYER, CONFERENCE CENTRE

SPECIAL SESSION | 08:00–08:50
EDCTP Fellowship Alumni | SALON 2

SATELLITE MEETING | 08:00–08:50
Discussion to explore ways to support clinical trials for malaria and neglected tropical diseases | SALON 3–4 *(by invitation only)*

PARALLEL SESSIONS | 09:00–11:00
- HIV/AIDS therapeutic and prevention studies | HALL I B-C
- Tuberculosis therapeutic studies | SALON 2
- Malaria therapeutic studies | HALL I A
- Cross-cutting: planning, implementation and impact evaluation of clinical trials | SALON 3–4

COFFEE AND TEA BREAK HALL II | 11:00–11:30

MARKETPLACE VIEWS HALL II | 11:00–11:30

PARALLEL SESSIONS | 11:30–13:00
- HIV/AIDS therapeutic studies | HALL I B-C
- Tuberculosis immunology and vaccine development | SALON 2
- Malaria vaccine studies | HALL I A
- Cross-cutting: interaction of neglected infectious diseases with HIV, tuberculosis and malaria | SALON 3–4

LUNCH HALL II | 13:00–14:00

MARKETPLACE VIEWS HALL II | 13:00–14:00

PARALLEL SESSIONS | 14:00–16:00
- HIV/AIDS comorbidities | HALL I B-C
- Tuberculosis studies on diagnostics | SALON 2
- Pregnancy associated malaria studies | HALL I A
- Cross-cutting: ethics and good practices | SALON 3–4

COFFEE AND TEA BREAK HALL II | 16:00–16:30

MARKETPLACE VIEWS HALL II | 16:00–16:30

PARALLEL SESSIONS | 16:30–17:10
- HIV/AIDS comorbidities | HALL I B-C
- Tuberculosis drug development and drug resistance | SALON 2
- Pregnancy associated malaria studies | HALL I A
- Cross-cutting: ethics and good practices | SALON 3–4

MARKETPLACE VIEWS HALL II | 17:10–18:00

SATELLITE MEETING | 17:30–19:00
Global TB Vaccine Partnership | SALON 3–4

SATELLITE MEETING | 17:30–20:30
ESSENCE on Health Research initiative, members' dinner meeting | SALON 2 *(by invitation only)*

Wednesday 2 July 2014

REGISTRATION | 08:00–09:00
FOYER, CONFERENCE CENTRE

PARALLEL SESSIONS | 08:00–09:30
- EDCTP and CAAST-Net Plus: Building bridges | HALL I B-C
- EDCTP Africa mapping project: current state of health research on poverty-related and neglected infectious diseases in sub-Saharan Africa | HALL I A

PARALLEL SESSIONS | 09:40–11:00
- HIV/AIDS treatment guidelines and disease progression | HALL I B-C
- Tuberculosis immunology | SALON 2
- Malaria coinfections, drug resistance and modelling | HALL I A
- Cross-cutting: training and networking activities | SALON 3–4

COFFEE AND TEA BREAK HALL II | 11:00–11:30

MARKETPLACE VIEWS HALL II | 11:00–11:30

PLENARY SESSION IV | 11:30–13:00
EDCTP Partners' session | HALL I B-C

LUNCH HALL II | 13:00–14:00

MARKETPLACE VIEWS HALL II | 13:00–14:00

PARALLEL SESSIONS | 14:00–15:30
- HIV/AIDS coinfections | HALL I B-C
- Tuberculosis | SALON 2
- Malaria immunology and diagnostics | HALL I A
- Cross-cutting | SALON 3–4

COFFEE AND TEA BREAK HALL II | 15:30–16:00

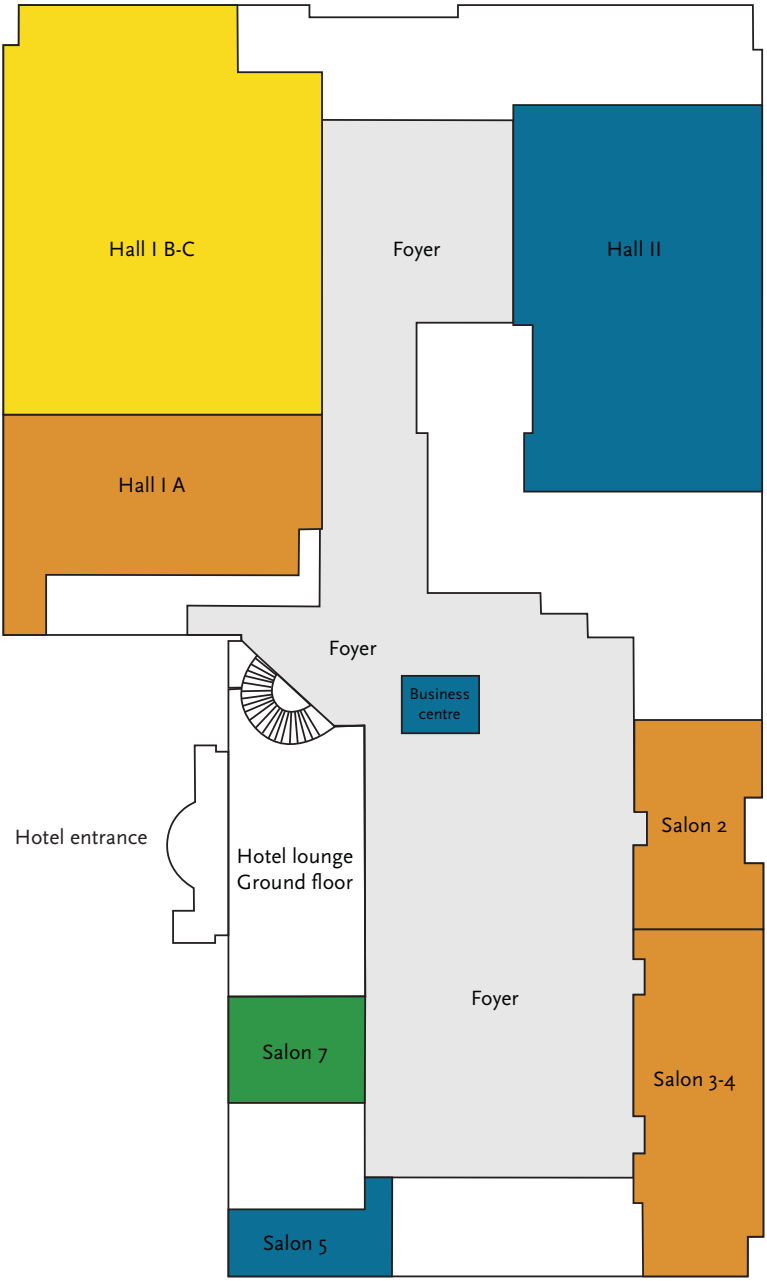
MARKETPLACE VIEWS HALL II | 15:30–16:00

PLENARY SESSION V | 16:00–17:30
Summary and closing remarks | HALL I B-C

Thursday 3 July 2014

EDCTP STAKEHOLDER MEETING ON CAPACITY DEVELOPMENT | 09:00–17:00 *(by invitation only)*
HALL I A

Floor plan



<< Programme on the inside cover