



ART SEQUENCING WORKSHOP

Resetting the agenda according to the needs: Antiretroviral sequencing or the best use of existing and promising pipeline HIV drugs.

Thursday 22 – Friday 23 September 2011

Centre de Conférences de Varembe (CCV), Geneva, Switzerland

An Independent meeting organised by Médecins Sans Frontières (MSF) with participation from Ensemble pour une Solidarité Thérapeutique Hospitalière en Réseau (Esther) and Solidarité Thérapeutique & Initiatives contre le SIDA (Solthis).

Objectives and expected outcomes:

- To develop a set of recommendations for sequencing of existing and pipeline ARV molecules for resource-limited settings in the medium and long-term for adults and children.
- To define the specifications of the regimen and formulations we will need for the future in order to treat HIV in the community.
- To develop recommendations and principles to guide treatment strategies, diagnostic strategies (including viral load), and an operational research agenda.

Agenda:

Day One: Thursday 22 September

- 8.30am - 8.40am** **Welcome and introduction.** Dr. Nathan Ford, MSF, 10mins
8.40am - 8.55am **In the middle of contradictions: the political context.** Craig Mc Lure, WHO, 15mins

8.55am - 10.30am: Plenary session: Contexts and specifications: what do we need to manage HIV patients at community level?

Moderators: Craig Mc Lure, WHO, and Dr. Nathan Ford, MSF

Note taker: Janice Lee

- 8.55am- 9.25am** **Challenges of scaling up long-term treatment and decentralisation at community level: what is the point of view of the PLWHA?**
Otwoma Nelson, National Empowerment Network of People Living with HIV/AIDS in Kenya: NEPHAK, 30 mins

- *Describe the perceptions, challenges and solutions from the patient and community point of view regarding: massive scaling up, perspectives of treatment as prevention, detection and management of HIV patients at community level.*

- 9.25am -10.00am** **Scaling up and decentralisation of care at the community level: field experience from the south African region. What do we need to treat HIV in the community? Drug specifications, strategies, delivery systems.**

Dr. Eric Goemaere, MSF South Africa, 35 mins

- *Describe the KZN treatment as a prevention project focusing on its community component, exploring the challenges met and solutions identified.*
- *Describe different community-based systems MSF is implementing in order to decentralise and scale-up community-based HIV care.*
- *Describe difficulties of sequencing in the decentralisation process.*
- *Challenge the specifications of drugs, formulations, monitoring tools and delivery systems we will need in the near future to manage HIV and TB-HIV at community level.*

- 10.00am -10.30am** **Discussion and initial recommendations** of specifications of regimen and formulations, 30 mins

- *What are the specifications of drugs, formulations, monitoring tools and delivery systems we will need in the near future to manage HIV and TB-HIV at community level?*

- 10.30 am -11.00am** **Tea Break**

11.00am -12.30pm Plenary paediatric session.

Moderators: Polly Clayden, i-base, and Janice Lee, MSF

Note taker: Polly Clayden

11:00am -11:15am Integration of paediatric care at community level: a field perspective. Where we are and how do we get there?

Dr. Siobhan Crowley, UNICEF South Africa, 15 mins

- *Overview of paediatric and adult HIV treatment integration in the field.*
- *What are the major challenges?*
- *How to provide integrated care at community level? Or what needs to happen?*

11:15am -11:30am Should paediatric regimens be aligned with adults and what needs to happen?

Dr. Shaffiq Essajee, WHO, 15 mins

- *Pros and cons of paediatric and adult regimen alignment.*
- *Challenges of regimen alignment, describe gap of R&D.*
- *Is there a middle way?*

11:30am -11:50am Are the current paediatric HIV regimens for developing world optimized?

Dr. Marc Lallemand, DNDi, 20 mins

- *What are the general challenges to sequence for paediatric HIV?*
- *List of pipeline drugs and expected trial completion.*
- *New treatment strategies: induction & maintenance.*
- *List of priority drugs.*

11:50am -12:30pm Q&A (discussion of initial recommendations of regimens and formulations to be further developed in the closed expert workshop, see below), 40 mins

12.30pm - 1.30pm: Lunch

1.30pm - 3.30pm Plenary session: First line adults treatment strategies.

Moderators: Prof. Elli Katabira, IAS Uganda, and Prof. Bernard Hirschel, Hôpitaux Universitaires de Genève (HUG)

Note taker: Yazdanpanah Yazdan

1.30pm - 1.50pm WHO update on treatment 2.0, optimization work CADO strategies.

Dr. Marco Vitoria, WHO, 20 mins

1.50pm - 2.10pm A perspective of promising pipeline HIV drugs and its potential use in resource poor settings.

Prof. Pedro Cahn, Fundación Huesped Argentina, 20 mins

- *What is the place of new HIV drugs and new classes in the current guidelines for resource poor settings?*
- *This includes marketed drugs such as RAL, DVR, ETV, RPV and those in clinical trials: elvitegravir, dolutegravir, GSK 1265744, entry inhibitors, maturation inhibitors, new NNRTIs (rilpivirine, BILR 355, lersivirine, dapivirine, RDEA 806) , NRTI (Amdoxovir, apricitabine, elvucitabine, festinavir, fozivudine, GSK 7340, racivir) and PIs(PP-100, TMC-310911, CPT-518)...*
- *How can we foresee their potential future role?*

2.10pm - 2.40pm Considerations for a needs-based first –line regimen.

Dr. Alexandra Calmy, HUG, 30 mins

- *Which is /are the best initial regimen(s) today for maximal simplification, decentralization, scaling-up, community care for Test and Treat strategies? Define the specifications of improved first lines and select the drugs, define which delivery systems could help.*
- *Describe alternative treatment strategies: using existing and new drugs, what can be the added value of blocs, monotherapies, and induction - maintenance regimen strategies according to cd4 threshold at initiation?*
- *What are the remaining obstacles of improved first line regimens to be initiated or delivered for stable patients at community level?*
- *What are the main unanswered questions and what are the operational research priorities?*

2.40pm - 3.30pm Discussion & recommendations, 50 mins

Questions:

- *What is the best first line now, what will it be in 5-10 years time?*
- *Which treatment strategies will we use in 5 years?*
- *What are the remaining obstacles for first line regimens to be delivered at community level?*
- *What are the main unanswered questions and what are the operational research priorities?*

1.30pm - 3:30pm: Closed expert workshop on paediatric sequencing.

[To run in parallel with plenary session on adult treatment strategies]

Moderators: Dr. Marianne Gale, MSF, and Prof. Di Gibb, MRC

Participants requested: P. Clayden, S. Crowley, S. Essajee, M. Lallemand, J. Lee, N. Sugandhi, plus others (maximum 15 participants).

Note taker: Polly Clayden

(2 hours)

Objectives of discussion:

- *To come up with a strategy for sequencing ARV in paediatrics. While pipeline ARVs will first be tested and available for the adults, the studies in children usually lag behind and are thus not meaningful to sequence according to adult's study completion timeline. Extra effort may be needed to ensure priority ARV or research be conducted in a timely manner. Are there other treatment strategies e.g. induction or maintenance which should be researched?*
- *Based on the sequencing strategy, list the research gaps with a 5 year time frame*
- *Prioritise the research list*
- *Discuss the next steps to achieve these objectives*

Topics for discussion:

- *Defining a strategy for sequencing ARV in paediatrics*
- *Defining a list of research gaps in paediatric HIV*
- *Prioritising the list of research gaps in paediatric HIV*

3.30pm - 4.00 pm Tea Break

4.00pm - 5.30 pm: Plenary Laboratory Monitoring session: How can we combine technologies to create access to viral loads for the community level?

Moderators: Prof. Paula Munderi, MRC Uganda, and Dr. Teri Roberts, MSF

Note taker: Teri Roberts

- *Objectives of the session: early infant diagnosis, simple viral loads testing, genotyping, point of care viral loads, high throughput VL platforms...How can we combine strategies to create access to viral loads for the community level?*

4.00pm - 4.15pm Implementation of VL strategy at field level - field experience: Challenges and perspectives: SAMBA HIV-a point-of-care viral load test for resource limited settings.

Prof. Helen Lee, Cambridge University, 15 mins

- *Describe the results of clinical trials at MSF sites*
- *What are the plans for the future? Further steps of development, commercialisation, registration, manufacturing, scaling-up.*
- *Price of test and instrumentation.*

4.15pm - 4.30pm Decentralisation of simple viral loads strategies: the Alere viral load point of care.

Dr. Eugen Remantraut, Clondiag, 15 mins

- *The new viral load test (size, performance, time to result, diagnostic target, preliminary results, sample preparation etc)*
- *Alere's experience with implementing the PIMA POC test with respect to in-country requirements (registration etc), ease of decentralisation, quality control, training etc (i.e. barriers and lessons learnt)*

4.30pm - 4.45pm Opening the viral load world to competition.

Prof. Benjamin Coriat, ANRS, 15 mins

- *Current viral load oligopoly*
- *Solutions to opening up the market*
- *Open lab-based systems*
- *Point-of-care tests*

4.45pm - 5.00pm High throughput open lab-based systems:

Prof. Christine Rouzioux, ANRS, 15 mins

- *Open lab-based systems*
- *Usefulness of polyvalency (i.e. testing more than one pathogen on the same instrument)*
- *How well do current, commercially available viral load tests cover HIV diversity?*
- *Lab-based tests best suited to remote and low resource settings (e.g. space, complexity, affordability, reliability)*
- *Best tests for HIV-2 (serological RDTs and viral load)*

5.00pm - 5.30pm Discussion and recommendations, 30 mins

Questions:

- *How can we combine strategies to create access to early infant diagnostics and viral loads for the decentralization process, in a 5-10 year's perspective?*
- *What is the added value of high throughput platforms versus POCs?*

4.00pm - 5.30pm: Closed expert workshop: First-line adult sequencing.

[To run in parallel with plenary session on Laboratory Monitoring]

Moderators: Prof. Yazdanpanah Yazdan, ANRS, S.Collins.

Participants requested: A. Calmy, C. Katlama, S. Collins, M. Vitoria, B. Hirschel, E. Katabira, Di Gibb, P. Cahn, A. Hill, A. Owen, plus others (maximum 15 participants).

(1.5 hours)

Note taker: Simon Collins

Objectives of the session:

- *To propose independent recommendations about the best drugs to develop and combine to make efficient, robust, well tolerated, TB friendly, child bearing women friendly first line regimens, from a "now-5-10 years perspective".*
- *To highlight the research and operational research needs related to adult sequencing.*

5.30pm - 6.30pm: Summary of plenary sessions and closed expert workshops/ preparation of recommendations for Friday afternoon wrap up: preliminary feedback.

Moderators: Prof. Yazdanpanah Yazdan, ANRS and Polly Clayden, i-base

(1 hour)

- *Summary of context session: note taker Janice Lee*
- *Summary paediatric sessions: Polly Clayden*
- *Summary of adult first line sessions: Yazdan Yazdanpanah*

8pm Dinner

Day Two: Friday 23 September

8.30am - 10.30am: Plenary session: How to manage treatment experienced patients in resource limited settings? Which regimen can we sequence for long-term survival in remote settings?

Moderators: Dr. A. Calmy, HUG, and Dr. Stephen Becker, Bill & Melinda Gates Foundation

Note taker: Gilles Raguin

8.30am - 8.45am Trends in failure.

Prof. Olivia Keiser, University of Bern, 15 mins

- *Presentation of the broader epidemiological overview in resource limited settings, including rates/ risk factors for treatment failure.*
- *Presentation of the outcomes of ART in programmes with and without access to routine viral load monitoring in Southern Africa.*

8.45am -9.05am The virologist point of view.

Prof. Vincent Calvez, ANRS, 20 mins

- *Description of the dynamic of resistances, primary transmitted and secondary resistances, and their consequences for drug sequencing for HIV-1 and HIV-2.*
- *Description of resistance accumulation according to time of exposure to a failing regimen.*
- *Will antiretrovirals used as Prep play a role in resistance induction?*
- *New antiretroviral drugs, new classes: what is the potential added value of these new components from a virological point of view?*
- *Comment the VL thresholds for adherence monitoring and treatment switches.*
- *Place of genotyping in RLS.*

9.05am - 9.20am The pharmacologist point of view: how can we solve the problem of second –line HIV and TB drug interactions?

Prof. Andrew Owen, Liverpool HIV Pharmacology Unit, 15 mins

- *Description of the interactions between HIV protease inhibitors (LPV/r, ATV/r, DRV/r) and rifampicine: Can we lower the dose of ritonavir? Can we replace ritonavir? Are there are alternatives to rifampicine? Do we need broad access to rifabutine? Can other anti-HIV drugs be used to build a TB-friendly second line regimen? What are the steps forward?*

9.20am - 9.40am Clinical Presentation: management treatment experienced patients.

Prof. Christine Katlama, ANRS, 20 mins

- *Define the best treatment strategies for RLS for HIV-1 and HIV-2 treatment experienced patients.*
- *Do we need to improve sequencing of PI? What about the use of PIs and rifampicine interaction?*

- *Do we still need NRTIs for treatment experienced patients? What is the added value of new classes?*
- *Do we need new co-formulations?*
- *What kind of innovative strategies we could propose to treatment experienced patients? Induction-maintenance, monotherapies...*
- *Debate access to third line versus improved second line.*

9.40am - 10.30am **Discussion & recommendations, 50 mins**

Questions:

- *Second line sequencing: what do we need to improve in L2 regimen? Specifications, drugs, OR agenda*
- *Desirable co-formulations from an immediate mid to long term perspective.*
- *Management of resistances in RLS. Is it a key issue?*

8.30am - 10.30am Closed expert workshop: laboratory monitoring.

[To run in parallel with plenary session on treatment experience]

Moderators: Prof. Paula Munderi, MRC Uganda, and Dr. Teri Roberts, MSF

Participants requested: C. Rouzioux, B. Coriat, E. Remantraut, H. Lee, S. Yerly, plus others (maximum 15 participants).

Note taker: Paula Munderi

(2 hours)

Objectives of the session:

- *To define the recommendations of the expert meeting regarding access to EID and VL for resource limited settings.*
- *To discuss the practical complementarities to be expected between high throughput and POC VL machines.*
- *To define the priority operational research agenda.*

10.30am -11.00am Tea Break

11:00am – 12.30pm: New Delivery System in HIV.

Moderators: Dr. Isabelle Andrieux-Meyer, MSF and Simon Collins, i-base

Note taker: Simon Collins

11:00am - 11:30am Drug Delivery System: A focus on nanotechnology and its implications in treatment of HIV.

Prof. Steve Rannard, University of Liverpool, 30 mins

- *A general overview of the various drug delivery systems and introduction to nanotechnology.*
- *Why is there no investment on drug delivery system by pharmaceutical companies on ARVs?*
- *Advantages and disadvantages of nanotechnology application in ARV formulation.*
- *What is the future for nanotechnology application in ARV formulation?*

11:30am - 12:00pm Long-acting formulation for HIV treatment: A fantasy or a reality?

Dr. Andrew Levin, Clinton Health Access Initiative, 30 minutes

- *Why do we need long acting formulation?*
- *Overview of potential molecules suitable for long-acting formulation*
- *Potential combinations for treatment*
- *Why pharmaceutical companies are not making long-acting HAART?*
- *What needs to happen?*
- *Potential new long acting formulations?*

12:00pm - 12.30pm Q&A and discussion, 30 mins

Questions:

- *Long acting formulations: is it the magic bullet?*
- *Which delivery systems would improve / facilitate adherence, once a week or once an X regimen? Apart from the pills, what will we be able to use?*

11.00am - 12.30pm Closed expert workshop: After the first failure.

[To run in parallel with plenary session on New Delivery System in HIV]

Moderators: Dr. Marco Vitoria, WHO, Dr. Suna Balkan, MSF

Participants requested: C. Katlama, V. Calvez, B. Hirschel, M. Pujades, D. Descamps, E. Katabira, P. Cahn, O. Keiser, plus others (maximum 15 participants).

Note taker: Suna Balkan

(1.5 hours)

Objectives of the session:

- *To propose independent recommendations about the best drugs to develop and combine to make efficient, robust, well tolerated, TB friendly, child bearing women friendly second line regimens, from a “now-5-10 years perspective”.*
- *To propose recommendations about the best strategies of treatment of treatment experienced patients.*
- *To highlight the research and operational research needs related to adult sequencing.*

12.30pm - 13.30 pm Lunch

1.30pm - 4.30pm: Plenary session: Unresolved issues: Operational & clinical research vision and agenda.

Moderators: Dr. Nathan Ford, MSF and Dr. Gilles Raguin, Esther

Note taker: Polly Clayden

1.30pm – 3.00pm: **Unresolved issues: operational and clinical research needed to solve: vision for adults and children:** wrap up and 10 years perspective, 1.5 hours

- Wrap-up from morning discussions. G. Raguin, S. Collins, P.Munderi
- Group discussion.

3.00pm - 3.15pm Tea Break

3.15pm – 4.30pm **Conclusions and recommendations:** 1.15 hours

4.30pm End