

A woman with her hair in braids is crouching on a rocky bank of a stream, washing clothes. She is wearing a patterned top and a blue skirt with a butterfly pattern. A green plastic tub is in the foreground. The background shows lush greenery and water.

Filarial Disease Program

Filarial Network Meeting
Uganda 2018

Filarial Diseases: Unmet Medical Needs

- Unmet medical needs:
 - IVM is microfilaricidal (repeated application)
 - No macrofilaricidal treatment available
 - *Loa-loa* coinfections with risk of serious adverse events
- Major feasibility concerns
 - *Loa loa* coinfection (areas w/o treatment)
 - Political and economical situations
 - Recrudescence / Parasites adapt
 - Resistance
- Alternative therapy for:
 - case management / morbidity management
 - “mop-up” campaigns to contribute to elimination as public health problem
 - Test and Treat (TNT) approaches
 - Potentially safe treatment in *Loa loa* coendemic regions

Possible mode of actions: direct vs indirect

Direct acting drugs: Emodepside, Oxfendazole	Indirect-acting drugs (anti-wolbachial): TylAMac
<p>PoC: Macrofil. (Oncho-Loa coinfecting areas) Macrofil. + microfilaria. (Oncho only areas)*</p> <p>Advantage: Proven MoA in veterinary medicine Fast-killing, morbidity management* Potentially used for multiple nematodes</p> <p>Disadvantage: Risk of AE due to microfilaria. activity (Emod.)</p> <p>Possible: Combination treatments</p>	<p>PoC: Macrofil. (Oncho-Loa coinfecting areas)</p> <p>Advantage: slow-killing, MoA well known, Reduction of inflammation due to removal of <i>Wolbachia</i> No side effects in loiasis infected individuals</p> <p>Disadvantage: long time to death of the adult parasite</p> <p>Possible: Combination treatments</p>

High attrition rates: need for a variety of candidates

Pursue both approaches are valuable and build up the anti-filarial tool-kit

Clinical Trials

- Aim:
 - Determine the maximum tolerated dose (MTD) of the new treatment
 - MTD is found by escalating the treatment dose until dose-limiting toxicity (DLT) is reached
- First in Human:
 - SAD: single ascending dose
 - MAD: multiple ascending dose
 - Food Effect
 - Relative bioavailability
- Proof of concept:
 - Multicenter Trial
 - Safety: UHAS (N. Opoku)
 - Safety and Efficacy: DNDi HAT Platform

- Improving the Onchocerciasis Network to get the job done
 - Increase connectivity
 - Increase visibility of the network
 - Share resources and know-how across the countries
 - Create sustainability beyond onchocerciasis in clinical trials in Africa

**Thanks to all of you for
being our partner**

DNDi
Drugs for Neglected Diseases *initiative*

Find new tools for elimination and case management

Discovery programs =
New Clinical Entities

New indications for existing drugs
= Repurposing Strategy

Supportive Activities

Long-term projects

Medium-term projects

Short-term projects



Research



Translation



Development



Implementation

Long-term

AbbVie (anti-*Wolbachia*),
Celgene (lead optimization
macrofilaricide)
Filarial Clinical Trial and
Research Platform

Medium-term

Repurposing of veterinary:
Emodepside (**Bayer**), oxfendazole
Based on known mode of action:
TylAMac (**AbbVie**)
Fingerprint studies

Short-term

Explore pediatric IVM
Modelling of distribution/morbidity
to address the patients needs
Modelling of CT endpoints
Surrogate Biomarker