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Elimination of Neglected Tropical Diseases: progress and future challenges in sleeping sickness

New oral treatments for sleeping sickness in adults and children
Sleeping sickness: from unacceptable to better, towards tools for elimination

10 years ago:
Eflornithine
Melarsoprol

Since 2009:
NECT combination therapy

2016
Oral treatment & simplified diagnosis
Currently available treatments for sleeping sickness

**Stage 1 HAT**

*Tb rhodesiense*

**Suramin** (1920s) 1 IV injection/week during 6 weeks

*Tb gambiense*

**Pentamidine** (1940) 1 IM injection/day, 7 days

**Stage 2 HAT**

*Tb rhodesiense*

**Melarsoprol** (1949) 9-10 IV once daily injections (10-26 days) painful & toxic (~5% mortality)

*Tb gambiense*

**Eflornithine** (1981) 4 IV infusions/day during 14 days

NECT: **Nifurtimox - eflornithine combination therapy** (2009)

eflornithine 2 IV infusions/day, 7 days + oral nifurtimox 3 doses/day, 10 days

Developed by MSF, DNDi and partners

WHO Essential Medicines List (2009)

WHO EML for children (2013)
NECT combination therapy: improved but not ideal

In relation to eflornithine monotherapy

- Reduced number of infusions (14 instead of 56)
- Shorter treatment period (10 days instead of 14)

All drugs and materials for 4 NECT treatments = 36 kg box
Target Product Profile (TPP):

- Oral formulation, short course
- Effective against both parasites (*Tb gambiense* & *Tb rhodesiense*), stage 1 and 2 HAT
- >95% efficacy
- Safe during pregnancy and breastfeeding
- Adult and paediatric formulations
- Heat stability >3 years
DNDi’s current HAT pipeline

Two new oral compounds:
- **Fexinidazole**: oral once a day for 10 days, after food
- **SCYX-7158**: single oral dose
Fexinidazole
DNDi clinical trials in endemic countries

- Three trials **ongoing** for *Tb gambiense*
  - 004 Pivotal, patients over 15 years of age, stage 2 comparative with NECT
  - 005 Cohort, adults, stage 1 and early stage 2
  - 006 Cohort, children over 6 years and over 20 kg weight, both stages

- One **in preparation** for *Tb rhodesiense*
  - 007 Cohort, both stages, adults and children over 6 years and over 20 kg
Rehabilitation of sites

Before…
Rehabilitation of sites

After…
Rehabilitation of sites
Good Clinical Practice (GCP) & informed consent

Visual informed consent form

Based on the recommendation of the pre-review meeting, DNDi rewrote & shortened the consent form and created a toolkit of drawings illustrating key information & interventions to be used to improve understanding by illiterate patients.

DNDi
Drugs for Neglected Diseases Initiative
Oxaborole SCYX-7158
From lead optimization to clinical candidate

- First candidate issued from DNDi Lead Opt Programme
- Clinical Phase I study completing Q2 2015
- Start Phase II/III Q4 2015 (DRC)

Potential to be oral, effective against both stages of Sleeping Sickness

Key partners:
Scynexis, Anacor, Pace University, Sandler Center UCSF, Swiss TPH
DNDi support for elimination

**Aim:** under WHO coordination, integration of new tools into national and global policies

- **2015** fexinidazole submission for EMA positive opinion (Art.58)
  - Registration in endemic countries (2016)

- **2016** Extension of fexinidazole use:
  - Field study IIIb/IV in all studied age groups of both stages
    - Extended to pregnant & breastfeeding women
    - Pharmacovigilance study
    - 20 sites

- **By 2018:**
  - Progressive extension of fexinidazole use
  - Submission of SCYX-7158 for registration
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