MOXIDECTIN FOR ONCHOCERCIASIS ELIMINATION

Studies completed

Studies in preparation

• Michel Mandro, Tony Ukety (investigators studies in DRC),
• Nicholas Opoku (investigator study in Ghana)
• C. Chesnais, J. Kamgno, M. Boussinesq (investigator study in Cameroon)

• Mark Sullivan (Founder and Managing Director, Medicines Development for Global Health),
• Annette C. Kuesel (TDR)
On the road from Monrovia to Lofa County, Liberia (J. Kealy)
6 Phase 1 pharmacokinetic and safety studies in healthy volunteers

- First in Human dose ranging study with liquid formulation
- Relative bioavailability of liquid and tablet formulation developed for onchocontrol programme use
- Milk-excretion study
- Drug interaction study
- Food effect study
- Cardiovascular safety study

2 comparative SINGLE DOSE safety and efficacy studies in *O. volvulus* infected volunteers

- Phase 2 study (Ghana, dose ranging)
- Phase 3 study (Ghana, DRC, Liberia, 8 mg)
PHASE 3 EFFICACY DATA FOR US FDA APPROVED DOSE OF 8MG

A. 1 month, n=492
B. 6 months, n=491
C. 12 months, n=480
D. 18 months, n=386

E. 1 month, n=973
F. 6 months, n=962
G. 12 months, n=947
H. 18 months, n=764
PHASE 3 SAFETY DATA
STUDIES FOR ONCHOCERCIASIS IN PREPARATION

Multi-dose comparative efficacy study (DRC)
Single dose comparative safety study (DRC)
Pharmacokinetic and safety study in < 12 year olds (Ghana)
Single dose comparative safety and efficacy study in *Loa loa* infected individuals (Cameroon)
MULTI-DOSE COMPARATIVE EFFICACY STUDY (ITURI)

- Adults and adolescents ≥ 12 years
- *O. volvulus* infected (mf +ve by 2 skin snips)
- N=1000

**Efficacy**

- Moxidectin 8mg Annual (n=375)
- Ivermectin 150µg/kg Annual (n=125)
- Moxidectin 8mg Biannual (n=375)
- Ivermectin 150µg/kg Biannual (n=125)

**Adverse events**

- Active (in-village assessments) to 6 days after Treatment, thereafter
- Passive

**Follow up**

- 6 months
- 12 months
- 18 months
- 24 months
- 30 months
- 36 months
**SINGLE DOSE COMPARATIVE SAFETY STUDY**

- **Moxidectin 8 mg (n=8,000)**
- **Ivermectin 150 µg/kg (n=2,000)**

- Adults and adolescents > 12 years
- Reside in *O. volvulus* endemic area
- N=10,000

Adverse events

- Passive - mf
- Active (in-village assessments) to 6 days after Treatment, thereafter
Adolescents and Children with/at risk of *O. Volvulus* (from meso- or hyperendemic Volta region of Ghana)

Exposure will be assessed but not required for study eligibility

N=9/per cohort

**Pharmacokinetic sampling:** Hour 0, 1, 2, 4, 8, 24; day 3, 7, 14 and 28; Week 12

**Safety:** Adverse Events, physical examination, changes in vital signs, laboratory values

**Dose Selection for Cohort 3:** safety profile, pharmacokinetic data, pharmacokinetic modelling
ASCENDING INTENSITY OF INFECTION EFFICACY-SAFETY STUDY IN LOA LOA INFECTED INDIVIDUALS

**Cohort I**
Loa loa mf/ml 1-99  
n=160

- Moxi 2 mg
- IVM 150 µg/kg

**Cohort II**
Loa loa mf/ml 100-499  
n=160

- Moxi 2 mg
- IVM 150 µg/kg

**Cohort III**
Loa loa mf/ml 500-1000  
n=160

- Moxi 2 mg
- IVM 150 µg/kg

**Efficacy:** TBS preTx, D1, D7, D15, D90, D180, D365  
**Safety:** Active FU in village D1-D7, adverse events, laboratory values (CBC, proteinurea, leukocyturia, liver function)