Clinical trials for anti-trypanosomonal drug development: impact on efforts towards disease elimination

4th Scientific meeting
HAT Platform-EANETT
Conakry Sept 20-22, 2016

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Fexinidazole

3 clinical trials ongoing

<table>
<thead>
<tr>
<th>Trial</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEX-04</td>
<td>Pivotal phase II/III Stage 2 HAT in adults (n=394)</td>
</tr>
<tr>
<td>FEX-05</td>
<td>Adult patients stage 1 and early stage 2 HAT (n=230)</td>
</tr>
<tr>
<td>FEX-06</td>
<td>Children 6-14 years old, all stages (n=125)</td>
</tr>
</tbody>
</table>

2 clinical trials starting

<table>
<thead>
<tr>
<th>Trial</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>OXA-02</td>
<td>Pivotal phase II/III Stage 2 HAT + stage 1 in adults (n=350)</td>
</tr>
<tr>
<td>FEX-09</td>
<td>Adult + Children in &amp; outpatients, all stages (n=174)</td>
</tr>
</tbody>
</table>
Plan of the presentation

• SITE SELECTION
• SITE PREPARATION
• CASE DETECTION
SITE SELECTION
Site selection process

• Epidemiology: Check the highest case report rate
  ➢ through available documents,
  ➢ refined in the field, to estimate feasible inclusion rate.

• Needs assessment for:
  ➢ infrastructure,
  ➢ equipment,
  ➢ human resources

• Accessibility: Air, river, road.

• Telecommunications: Internet, telephone.
HAT foci in DRC: Geographic distribution


Optimized for printing in A3 format

HAT cases
(T. b. gambiense)

Active screening
(T. b. gambiense)

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the WHO or FAO concerning the legal status of any country, territory, city or area or its authorities, or concerning the delimitation of its frontiers or boundaries. Dates shown do not represent availability of data for that year, but rather the year in which results were first made available.

Citation: Lembembe et al. (2016). Human African trypanosomiasis in the Democratic Republic of the Congo: these data are not the official of any country or territory. In: Human Geog., 1(2), 422. doi: 10.1360/020142-2.5.4217
HAT Clinical trial sites in DRC
SITE PREPARATION
Achieving the required international standards for clinical trials

IMPACT IN:

• General environment of care in health structures
• Build capacity in staff concerned by clinical trials
• Passive and active screening activities
Hospitalisation

MUSHIE

Gestion des déchets
Laboratory rehabilitation

Masi Manimba (after)

Bagata (before)
Training for clinical trials

- Good Clinical Practice for researchers, monitors, and practitioners.
- Trial protocol and procedures for all involved staff at Investigator’s meeting and site initiation visits.
- Laboratory HAT diagnosis and specific trial procedures
- HAT patient examination techniques, including those specific to the trials
- Standard Precautions and waste management
- Pharmacovigilance both during trials and after registration
- Continuous quality assurance
CASE DETECTION
Increase case detection and surveillance

• DNDi supports an increasing number of PNLTHA mobile teams in active case-finding (10 teams from July 2016)
• This will be complemented in 2017 by support to strengthen passive surveillance: upgrading and monitoring the current network of passive screening set up by NSSCP in areas of ongoing clinical trials.
• That is expected not only to contribute to identifying more candidates for inclusion in clinical trials, but also to establish a passive surveillance system for sustainable elimination.
Total Screened Population and HAT cases in DRC

Cases

Year


Year


TSP

0 1000000 2000000 3000000 4000000 5000000 6000000 7000000 8000000 9000000


FEXI trials started Oct 2012

NECT introduced


FEXI trials started Oct 2012

NECT introduced
Screening efforts in 2014

<table>
<thead>
<tr>
<th>N</th>
<th>Screened Total DRC</th>
<th>Cases detected (Total DRC)</th>
<th>Screened in FEX CTs area</th>
<th>Cases detected in FEX CTs area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>1585539</td>
<td>1781</td>
<td>409730</td>
<td>385</td>
</tr>
<tr>
<td>%</td>
<td>0.11% (of screened)</td>
<td>25.8% (of DRC)</td>
<td>0.09% (of screened in FEX area)</td>
<td></td>
</tr>
<tr>
<td>Passive</td>
<td>271435</td>
<td>1425</td>
<td>62047</td>
<td>301</td>
</tr>
<tr>
<td>%</td>
<td>0.52% (of screened)</td>
<td>22.9% (of DRC)</td>
<td>0.49% (of screened in FEX area)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1856974</td>
<td>3216</td>
<td>471777</td>
<td>686</td>
</tr>
<tr>
<td>%</td>
<td>0.17% (of screened)</td>
<td>25.4% (of DRC)</td>
<td>0.15% (of screened in FEX area)</td>
<td></td>
</tr>
</tbody>
</table>

- 25.4% of the total examined population in DRC was screened in FEX CTs areas
- 8.4% of all worldwide declared cases (319/3796) were included in one of the three FEX clinical trials (52% of all cases detected by the direct screening efforts)
- DNDi-FEX-HAT-04: 153; DNDi-FEX-HAT-05: 110; DNDi-FEX-HAT-06: 56
Conclusions

• Due to the low prevalence of HAT, **epidemiology is the main factor** to select a clinical trial site

• **Sites** do not need to be ready for clinical trials beforehand, but they **need to be prepared up to international standards** regarding infrastructure, equipment and human resources

• Highest prevalence areas still need **enhanced case detection activities** to achieve expected sample sizes for clinical trials
Thanks to our partners and our donors

- PNLTHA (RDC)
- INRB (RDC)
- Swiss TPH (CH)
- HAT Platform
- IRD (France)
- IMT (Belgium)
- MSF Logistique (France)
- Dr. Victor Kande
- Equipe de Coordination et Supervision
- Investigateurs et staff du terrain

- BMGF (USA)
- MSF (Int)
- DFID (UK)
- Norad (Norway)
- BMBF (Germany)
- Canton de Genève (CH)
- AFD (France)
- SDC (CH)
- Other individual donors and foundations
THANK YOU

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