Three clinical research platforms in Africa and Latin America to build sustainable research capacities

Author: Dr Augustin KADIMA EBEJA (HAT Platform) **Coauthors:** Monique Wasunna (LEAP Platform), Isabela Ribeiro and Mariana Abdalla (Chagas Clinical Research Platform)

INTRODUCTION

The Drugs for Neglected Diseases *initiative* (DND*i*), as an integral part of its business model and with a view to developing field adapted treatments for neglected diseases, has supported the set-up of three regional disease-specific platforms in Africa and Latin America for the three kinetoplastid diseases (human African trypanosomyasis or sleeping sickness, visceral leismaniasis and Chagas disease). These platforms serve to define patients needs, strengthen local capacities, conduct clinical trials, and facilitate registration and uptake of new treatments.

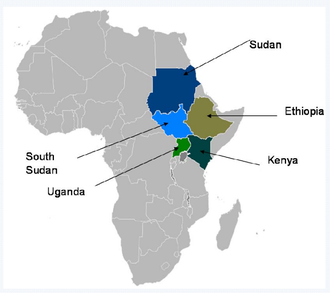
DNDi
Drugs for Neglected Diseases *initiative*

Leishmaniasis East Africa Platform

Why focus on Visceral Leishmaniasis (VL) in East Africa?

- Almost all clinically symptomatic patients die within months if untreated
- Field-relevant treatments are scarce and far from optimal
- VL in Africa primarily affects children (over 60%)
- East Africa is one of the most important foci for VL in the world. Population displacements have exacerbated its spread.

About the Platform



Launched in 2003 with the support of DND*i*, LEAP brings together scientists and institutions like regulators and ministries of health in East Africa to develop clinical trial capacity in order to bring new treatment options to neglected VL patients in the region. LEAP is coordinated by the DND*i* Africa office based in Nairobi, Kenya, at the Kenya Medical Research Institute (KEMRI).

Objectives

The overall aim of the platform is to strengthen clinical research capacity, which is lacking in part due to the remoteness and geographic spread of the patients, most of whom live in the most impoverished regions of Africa. This platform also serves as a base for ongoing educational cooperation between the countries in the East African region and standardization of procedures and practices within the region, as far as possible within the confines of local regulations. LEAP evaluates, validates, and facilitates registration of improved treatment options that address needs for VL in East Africa (Ethiopia, Kenya, Sudan, and Uganda).

Achievements

The LEAP Platform has provided support to seven treatment centres/clinical trial sites in the VL endemic areas - Kenya (2), Uganda (1), Sudan (2), and Ethiopia (2) by building and/or renovating infrastructure as well as providing staff training, drugs, medical equipment, and material.

Significant capacity building was provided to local partners particularly in strengthening institutions like Institute of Endemic Diseases (Sudan), Kenya Medical Research Institute (Kenya), Addis Ababa University (Ethiopia), University of Makarere (Uganda).

In 2010, the LEAP completed a multi-centre, multi-country clinical trial (LEAP 0104) sponsored by DND*i* in Kenya, Ethiopia, Sudan, and Uganda. The study involved over 1'100 VL patients and showed that a short-course combination of Sodium Stibogluconate and Paramomycin (SSG&PM) had a similar safety and efficacy as the standard SSG monotherapy treatment for 30 days. The platform is now working to facilitate egistration of paramomycin and the implementation of SSG&PM in East Africa. DND*i* and the LEAP Platform will also provide training and facilitate implementation of pharmacovigilance and observational studies to meet each country's requirements.

SSG&PM
Sodium Stibogluconate & Paromomycin Combination Therapy

Since its inception, LEAP has become an important regional network of *leishmania* research and control, trusted by the international scientific community.


Uganda, South-South capacity building: Sudanese doctor and inverstigator train Ugandan colleagues on VL diagnosis and treatment, 2008

Partners

- Center for Clinical Research, Kenya
- Medical Research Institute, Kenya
- Ministry of Health, Kenya
- Institute of Endemic Diseases, University of Khartoum, Sudan
- Federal Ministry of Health, Sudan
- Addis Ababa University, Ethiopia
- Gondar University, Ethiopia
- Federal Bureau of Health, Ethiopia
- Makerere University, Uganda
- Ministry of Health, Uganda
- Médecins Sans Frontières
- i+ Solutions
- Institute for OneWorld Health (iOWH)
- AMC/KIT/University of Slotervaart, Amsterdam, The Netherlands
- London School of Hygiene and Tropical Medicine (LSHTM), UK.

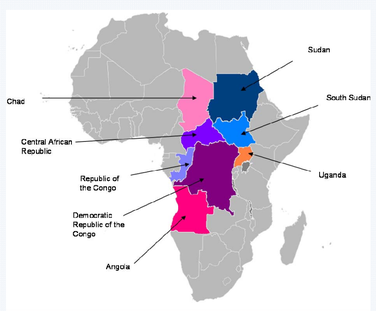
HAT Platform (Human African Trypanosomiasis)


New Laboratory after rehabilitation in Katanda Hospital, Kasai, RDC

Why focus on Human African Trypanosomiasis, or sleeping sickness in Africa?

- Human African Trypanosomiasis (HAT), also known as sleeping sickness, is one of the neglected diseases in Sub-Saharan Africa with severe social and economic consequences.
- Transmitted by the tsetse fly, it is fatal if left untreated
- 36 countries at risk
- The estimated number of actual cases is currently approximately 30,000
- Available treatments are few, old, highly toxic for some of them, and stage-specific.

About the Platform



Launched in Kinshasa (DRC) in 2005 and coordinated by DND*i*, the HAT Platform is a clinical research network that brings together regional actors involved in the control of HAT in endemic countries, notably Ministries of Health and National Control Programmes, regulatory agencies, academia, clinicians, and civil society groups from Angola, Chad, Central African Republic, Democratic Republic of Congo, Republic of Congo, Sudan, and Uganda.

Objectives

The HAT platform's mission is to build and strengthen treatment methodologies and clinical trial capacity in HAT-endemic countries, so that new treatments for this fatal disease can be rapidly and effectively evaluated, registered, and made available to patients. After the success of the Nifurtimox-Eflornithine Combination Therapy (NECT), included in the WHO List of Essential Medicines for the treatment of stage 2 HAT, the primary goals of the HAT Platform are to develop appropriate clinical trial methodologies for HAT, overcome system challenges related to administrative and regulatory requirements, strengthen clinical trial capacity (human resources, infrastructure, equipment), and share information and strengthen ties among endemic countries.

Achievements

The HAT Platform facilitates the implementation and access of nifurtimox-eflornithine combination therapy (NECT) for stage 2 HAT in 10 endemic countries, by working closely with national authorities and control programmes. Thanks to its work, more than half (62%) of stage 2 HAT patients were treated with NECT in African endemic countries in 2010. NECT is included in the Essential Medicines List (EML) since 2009.

NECT
Nifurtimox-Eflornithine Combination Therapy

The Platform participates in the ongoing clinical trial NECT-Field, assessing the clinical response of NECT co-administration under field conditions. It will also participate into the coming clinical trial on Fexinidazole, the promising oral drug candidate for second stage HAT.

Every year, the HAT Platform organizes 2-3 trainings on Good Clinical Practices (GCP) for researchers, on Ethics, and on HAT patient examination for clinical monitors and general practitioners. Since its inception, the HAT Platform has trained investigators and clinical monitors to run six clinical trial sites.

Partners

- National Control Programmes of the most affected endemic countries (Angola, Central African Republic, Chad, Democratic Republic of the Congo, Republic of the Congo, South Sudan, and Uganda)
- Institut National de Recherche Biomédicale (INRB), DRC
- Centre Interdisciplinaire de bioéthique pour l'Afrique francophone (CIBAF), DRC
- Tropical Medicine Research Institute (TMRI), Sudan
- Kenya Agricultural Research Institute – Trypanosomiasis Research Centre (KARI-TRC), Kenya
- Institut Pasteur (Bangui), Central African Republic
- Regional networks such as Eastern Africa Network for Trypanosomosis (EANETT)
- Swiss Tropical and Public Health Institute (Swiss TPH), Switzerland
- Institute of Tropical Medicine (ITM), Antwerp, Belgium
- Médecins Sans Frontières (MSF) International
- Epicentre, France
- Foundation for Innovative New Diagnostics (FIND), Switzerland
- World Health Organization (WHO), Department of Control of Neglected Tropical Diseases, observer

Chagas Clinical Research Platform

Why focus on Chagas disease in Latin America?

- 21 countries in Latin America are endemic
- 100 million people are at risk of contracting Chagas disease
- Approximately 8 million people live with Chagas disease
- Chagas disease kills more people in the region each year than any other parasite-born disease, including malaria
- Chagas is the leading cause of infectious heart disease (cardiomyopathy) worldwide
- Existing drugs (benznidazole and nifurtimox) were discovered 40 years ago, have limited efficacy in the chronic phase, poor tolerability profile in adults, long treatment period and no paediatric formulation

About the Platform

The Chagas Clinical Research Platform was launched in 2009 and brings together partners, experts, and stakeholders in a network, which provides support to the evaluation and development of new treatments for Chagas disease. The Chagas Disease Research Platform is coordinated by DND*i* Latin America office based in Rio de Janeiro, Brazil.


Meeting of the Chagas Clinical Research Platform, Brazil, 2010

Objectives

The overall aim of the Chagas Platform is to strengthen capacities in Latin America to conduct clinical trials, review and facilitate registration and recommendation of new therapies for Chagas disease. The platform also provides a forum for technical discussions and facilitates the implementation of new treatments such as paediatric benznidazole.

Achievements

The expert meeting which led to the creation of Chagas platform defined a new drug target product profile (TPP) for Chagas disease that has been updated every year since.

Paediatric Benznidazole: A new adapted treatment for children affected by Chagas disease

DND*i* and the Pharmaceutical Laboratory of Pernambuco (LAFEPE) joined in 2008 to develop the first paediatric formulation of Benznidazole. Scheduled for release in late 2011, the new paediatric formulation will soon be fissionable, which will facilitate the treatment of children and babies. The product is designed for patients up to 2 years of age and up to 20 kg, and will be sold at cost to countries that show the need.

In 2009, the platform was instrumental in launching a global advocacy campaign to raise awareness on R&D and treatment needs for Chagas disease on the occasion of the 100th anniversary of the discovery of the disease.

WAKE UP! RESEARCH ON NEGLECTED DISEASES TIME TO TREAT CHAGAS DISEASE!

A New Scenario

The year of 2011 reflects a new scenario for the development of new drugs for Chagas disease due to the initiation of several clinical studies in Latin America and Spain, pointing out potential paths for a new perspective of hope in the future for thousands of people living with Chagas:

- E1224 – DND*i* & Eisai
- PCR – DND*i* & MSF
- Posaconazole (CHAGASAZOL & STOP Chagas) – ICS Spain & Merck
- BENEFIT – Canadian Institutes of Health Research; Dante Pazzanese Cardiology Institute; Population Health Research Institute; Hospital das Clínicas of Ribeirão Preto/ USP; WHO/TDR
- TRAENA – National Parasitology Institute Dr. Mario Fatala Chabén, Argentina

DND*i* also organized trainings in Good Clinical Practices (GCP) and in pharmacovigilance as well as standardized methodology courses to evaluate the effectiveness of drugs used for treating the Chagas infection.

CONCLUSIONS

1. The three regional platforms have the specificity of **bringing together regional actors**, notably Ministries of Health and National Control Programmes, regulatory agencies, academia, clinicians, NGOs, and pharmaceutical companies with a common goal.
2. They **define patient needs** in the local and national contexts where the diseases are endemic.
3. They utilize, capitalize upon, and **reinforce research and clinical capacities** in endemic regions, particularly by creating clinical trial methodologies in compliance with Good Clinical Practices (GCP) standards as well as by providing on-site training in clinical research in sometimes very remote settings. They also address **infrastructural requirements** where necessary.
4. They are crucial to increasing the chances of registration, uptake, and **sustainable patient access** to new treatments.

The work of the platforms was vital to making available **2 new treatments** against neglected diseases: NECT against sleeping sickness, and SSG&PM against visceral leishmaniasis.