PLATEFORME REGIONALE DE RECHERCHE CLINIQUE THA
TRYPANOSOMIASE HUMAINE AFRICAINE
HUMAN AFRICAN TRYPANOSOMIASIS
HAT REGIONAL PLATFORM FOR CLINICAL RESEARCH

HAT Platform

REGIONAL PLATFORM FOR CLINICAL RESEARCH

NEWSLETTER N°21

February 2021

Cascade training of health workers on the use of fexinidazole, Bangui, CAR, 16-23 November 2020

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EDITORIAL COMMITTEE

Contents

EDITORIAL

Dear Readers,

The 21st HAT Platform Newsletter is dedicated to the preparations for access to fexinidazole, the first all-oral treatment for human African trypanosomiasis, following its inclusion in the WHO's Essential Medicines List. The HAT Platform and WHO are together planning a programme to extend the use of this new medicine to the remotest locations, thus bringing diagnosed patients closer to treatment centres.

In this issue, we will also discuss the HAT Platform steering committee meeting and the Platform's participation in the 35th Conference of the International Scientific Council for Trypanosomiasis Research and Control, held on 23-27 September 2019. In all our issues, we continue to point out that an integrated approach to control of neglected tropical diseases (NTDs) is supported by the WHO, and that research is moving in this direction. Therefore, we will also address the launch of impact assessment surveys supported by DND*i* on onchocerciasis in the DRC to prepare the upcoming clinical studies on the development of a new drug against onchocerciasis.

We also invite you to read the articles published in a 2020 special edition of *Tropical Medicine and Infectious Disease journal* entitled *Human African Trypanosomiasis (Sleeping Sickness): The Road to Elimination Revisited—Achievements and Remaining Challenges*. Finally, we pay tribute to the three co-founding members of the HAT Platform who passed away this year: Prof. Marleen Boelaert from Belgium, and Prof. Josenando Théophile and Dr. Miguel Kiassekoka from Angola. These eminent scientists not only gave impetus to the HAT Platform activities in its early days, but also contributed to the training of young researchers.

Happy reading to all.

Dr. Florent Mbo Kuikumbi

Participation of the HAT Platform in the 35th Conference of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC), held in Abuja, Nigeria, on 22-27 September 2019

The HAT Platform supported the participation of its members and other scientists whose abstracts were accepted for this conference.

The participating members of the HAT Platform came from the DRC (15), Guinea (3), Chad (3), Republic of Congo (2), and 1 participant each from Sudan, Uganda, Mali, Malawi and Switzerland.

For the HAT Platform, the highlight of this conference was the participation of its members and guests in the HAT session on 24-25 September 2019. The session was chaired by the Chad HAT focal point and its rapporteur was the HAT Platform Coordinator.

The session dedicated to human African trypanosomiasis included 19 oral presentations, divided into three sessions on diagnosis & treatment, epidemiology and control, with a thematic presentation by the WHO entitled Advances in HAT Elimination. Towards a Lasting Elimination of gambiense HAT in 2030: Challenges and Opportunities.

One of the oral presentations given during the trypanosomiasis session is summarised below:

Strategy for the active detection of suspected CATT-positive cases not confirmed with parasitology tests, implemented by a team from Bagata health zone in the Democratic Republic of the Congo

Background: The World Health Organization aims to eliminate human African trypanosomiasis (HAT) as a public health issue in 2020, with full elimination (no cases) by 2030. One of strategies used to achieve this is the active follow-up of all serological suspects detected during passive screening and not confirmed with parasitology tests. This active follow-up is important because such cases can maintain HAT transmission and cause a re-emergence of the disease.

Methods: To improve case finding at low cost in the target population, a notice was sent to aparasitaemic serological suspects on the availability of diagnosis confirmation at the general referral hospital. Transport was facilitated for re-testing. The initial examinations were carried out in health centres from Bagata Health Zone (HZ) in the DRC between January 2017 and April 2019. This strategy of using a HZ team has not been previously documented.

Results: From a total sample of 74 serological suspects listed by the health centres, 36 cases were re-examined at the general reference hospital: 19% (7/36) self-presented and 81% (29/36) were actively followed up by HZ personnel.

Of those re-examined at the general reference hospital, the parasitology tests confirmed the diagnosis in 39% (14/36). Of the 14 people

diagnosed with HAT, 14% (2/14) had self-presented and the remaining 86% (12/14) were diagnosed through active follow-up of suspected cases. This new strategy active follow up of suspects by facilitating transport from the villages, has an added value contributing to the detection of 12 HAT cases, compared to only 2 new HAT cases with the passive approach based on self-presentation. The cost was 70 USD per detected case in the group of 7 suspects who self-presented for testing at the hospital, versus 346 USD per detected case in the group of 29 patients actively followed-up by health zone staff.

Conclusion: Targeted active follow-up of aparasitaemic serological suspects by HZ teams is a cost-effective and promising approach to identifying additional HAT cases in areas of very low prevalence, which would contribute to the HAT elimination goal set by the World Health Organization.

Matthieu Nkieri, Florent Mbo, Papy Kavunga, Pathou Nganzobo, Titus Mafolo, Chalet Selego and Eric Mwamba Miaka. *Trop. Med. Inf. Dis.* 2020, 5, 53; doi: 10.3390 / tropicalmed5020053

The following highlights or points for attention were recorded during the session on trypanosomiasis:

- The decline of HAT cases to less than 1,000 in 2018 follows sustained screening, diagnosis and treatment efforts by the mobile units, managed by the national programmes and supported by partners with WHO coordination and guidance.
- Current interventions are effective in terms of HAT control, but they must be adapted to this new epidemiological situation with a reduced number of cases, focusing on:
- Integration of HAT control and surveillance into the healthcare system
- Ownership by and commitment from the political authorities in endemic countries through advocacy
- Tailoring of surveillance and control tools to this low prevalence situation
- Development of a long-term financing plan
- Conflict zones or epidemics (Ebola) in HAT endemic countries may slow down efforts towards elimination or even trigger a resurgence of HAT due to the interruption of activities.
- The cost of active detection for each HAT case is rising in this low prevalence context. Strategies, such as the integration of activities in primary healthcare, must be adapted. Enhanced passive screening combined with reactive case detection (RCD) would be more efficient and may also improve case detection. The involvement of communities, including traditional practitioners, in the detection and referral of clinical HAT suspects may also help improve the detection of HAT cases.
- The HAT Atlas is an important tool that can help in the planning, evaluation and monitoring of the activities of national HAT control programmes.
- Given its high specificity and sensitivity, the immune trypanolysis test could be used as a tool of choice to follow-up unconfirmed seropositive cases with negative parasitology tests.
- Quality control is necessary in a low prevalence context. A microscope fitted with a camera (images and photos) or connected

to a smartphone can help confirm cases and improve quality control.

- In endemic areas, CATT tests or HAT RDTs can be used as safety markers prior to a blood transfusion, to avoid this poorly documented mode of HAT transmission.
- The arrival of the new treatment fexinidazole is a major step. Efforts must be maintained to improve patient access.
- With decreasing HAT prevalence and loss of expertise on the disease (death or retirement of experienced personnel), practical training of health personnel becomes even more necessary. The use of live trypanosomes, e.g. from infected mice, is a great help to learning in a situation close to field conditions.

The following needs and gaps were identified:

- The epidemiological roles of animal reservoirs, as well as skin infection and latent infection in humans, which may maintain HAT transmission and resurgence
- Understanding the disease's epidemiological status in certain regions with little or no surveillance, as well as the impact of climate and environmental changes
- Simplified diagnostic and screening tests suited to field conditions
- Tools to assess absence of the disease
- Ensure availability of and access to screening and diagnostic tests with the help of the manufacturers
- The on-going clinical studies with the single-dose oral treatment (acoziborole) are promising and may help integrate the treatment into the primary healthcare system
- Loss of HAT expertise due to the disease's low prevalence and ageing of specialised personnel

Recommendations to the participants following the HAT session

Given that advances in HAT control and the disease's falling prevalence in most endemic countries may result in demobilisation of health personnel and health authorities and slow down efforts, the following measures were recommended:

1. HAT endemic countries must commit to elimination of the disease and take ownership of HAT control activities, including participating in their financing, supported by the partners and coordinated by the WHO.
2. The countries must gradually adapt their strategies as well as their HAT control and surveillance tools to the new low prevalence situation to ensure efficient control.
3. With the help of partners, endemic countries must focus on the training of healthcare personnel to compensate for the loss of expertise on HAT and facilitating integration of the activities into the healthcare system.

INTERNATIONAL SCIENTIFIC COUNCIL FOR TRYPANOSOMIASIS RESEARCH AND CONTROL (ISCTRC) ABUJA DECLARATION

Final communiqué, 19 Septembre 2019

ON RENEWED COMMITMENT FOR ACCELERATED PROGRESS TOWARDS RESEARCH, CONTROL AND ERADICATION OF TSETSE AND TRYPANOSOMIASIS CONSTRAINTS IN THE AFRICAN CONTINENT

The 35th Meeting of the ISCTRC and the 18th PATTEC National Coordinators' meeting held in Abuja, Nigeria, from 23 to 27 September 2019 acknowledged that the tsetse and trypanosomiasis (T&T) problem continues to constrain the socio-economic development of the African continent. While recognizing achievements made for the control and eradication of T&T as declared by heads of state or government at the AU Summit in Lomé Togo in July 2000 (Decision AGH/Dec.156-XXXVI), such as the reduction in human African trypanosomiasis (HAT) cases, the meeting noted with concern the slow progress towards achieving the objectives of T&T control and eradication.

A sense of urgency was therefore expressed about tackling the problem to safeguard the gains made on the road to the elimination and eventual eradication of the T&T constraint.

The meeting urged a renewed commitment at all levels towards control and elimination/ eradication of the T&T constraint.

The meeting emphasized that the T&T problem should be tackled within the broader context of One Health, sustainable rural development and poverty reduction, urging countries to develop appropriate agriculture transformation strategies in the face of changing climate conditions. Furthermore, it was emphasized that new innovative strategies, policies, advocacy and awareness, partnerships and effective coordination are of paramount importance to accelerate progress with clear and achievable milestones agreed upon at country, regional and continental levels.

Report of the regional HAT Platform steering committee meeting, Abuja, Nigeria, 22 September 2019

The meeting was co-chaired by a DRC representative assisted by the representative of the Republic of the Congo, with the help of the HAT Platform Coordinator. Before presenting the participants, the HAT Platform Coordinator asked for a minute's silence in memory of Prof. Henri Joseph Parra, one of the focal points of the HAT Platform in the Republic of Congo and one of the founders of the HAT Platform, who died on 29 May 2019 in Brazzaville.

Then the floor was given to the participants and especially those attending the steering committee meeting for the first time, so they could introduce themselves and give their impressions.

The member countries participating in this meeting included Angola, Republic of Congo, Guinea, Uganda, CAR, DRC, Sudan, South Sudan and Chad. Malawi and Mali were present as observers. Before presenting the activities conducted in 2018 and during the first semester of 2019, the Coordinator of the HAT Platform reviewed the implementation of the recommendations given after the last meeting held in Kampala, Uganda

The HAT Platform activities from 2018 to September 2019, and the outlook for 2020, are summarised below:

Activities performed in 2018 and 2019

- Advocacy on the use of fexinidazole following the favourable opinion issued by the European Medicines Agency, approval in the DRC and training of trainers organised by the WHO
- HAT Platform steering committee meeting and member participation in the 35th general conference of the International Scientific Council for Trypanosomiasis Research and Control, Abuja, 23-27 September 2019
- Participation in the training of trainers on the use of fexinidazole organised by the WHO in Kinshasa
- Support for the revision of national HAT treatment guidelines, including fexinidazole (DRC)
- Support for the workshop preparing training tools and modules for the providers (NSSCP DRC)
- Support for partners' activities (evaluation of the FIND project in the Republic of Congo)
- Participation in scientific conferences (9th EDCTP forum, 67th ASTMH)
- Production of Newsletter N°20
- Participation in the Congo HAT Platform meeting

Activities planned for the fourth quarter 2019 and for 2020

Continue member country advocacy towards fexinidazole approval in 2020

Supporting program strategic reviews

Supporting ethics committees to develop their own guidelines (Guinea, Republic of Congo)

Presentation of the WHO and HAT Platform member countries

World Health Organization (WHO)

The WHO representative reviewed the fexinidazole access procedure in endemic countries, and the algorithm for its use. A second training of trainers was announced for French-speaking countries (+ Angola and Equatorial Guinea) on new treatment algorithms, including the fexinidazole treatment algorithm and pharmacovigilance, to ensure treatment compliance, which was held in Brazzaville in October 2019. Cascade training will then be given to the providers in these countries, once fexinidazole has been approved by the health ministries and included in their national treatment protocols.

Country presentations

Each country presented its report on activities carried out. Difficulties or challenges hindering HAT research, coordination or control were outlined.

Angola

- Lack of financial and material resources to carry out the platform's activities in the countries
- Lack of qualified personnel to conduct entomological surveys
- Need regular support from the HAT platform

Central African Republic

- Unavailability of mAECT kits and HAT RDTs for HAT diagnosis
- Obsolescence of the biomedical equipment used for HAT control

Chad

- Population mobility
- Retention issues with personnel trained by NSSCP
- Administrative complexity of the resource mobilisation and allocation procedure
- Lack of financing of the NSSCP Operational Action Plan by partners
- Unavailability of HAT RDTs

South Sudan

- No new HAT control activities were conducted due to socio-political unrest

Guinea

- Low community involvement in certain foci due to the impact of the Ebola epidemic
- Difficulties in implementing control activities for neglected tropical diseases in spite of the creation of a single coordinating group

Democratic Republic of the Congo

- The achievements of political advocacy on HAT control by the NSSCP with the government and INRB activities were described to the participants.

After the presentation of the country reviews, the Advocacy programme, with the help of PATH, described its achievements with the NSSCP in the DRC:

- National HAT control day granted by ministerial decree
- Organisation of a national HAT forum
- Vote on an edict creating a fund to promote HAT control

The last presentation, given by DND*i*, sponsor of the HAT Platform, reviewed the changes in HAT treatment from melarsoprol to fexinidazole, as well as the on-going clinical studies on acoziborole. The DND*i* representative initiated a discussion on the target product profile of a new drug designed to eliminate the disease and to be used in clinical studies. The participants were also asked to consider this and submit proposals through the HAT Platform coordinating committee.

The new participants or members of the HAT Platform were invited to give their opinions and impressions, and the meeting was then closed at 5.30pm.

The following recommendations were made:

1. The countries must strive to mobilise internal resources for HAT control, in spite of its low prevalence, to support its elimination (e.g. Angola). PATH can provide help at the countries' request.

2. The programme coordinators must raise awareness among their authorities to include fexinidazole in their national policies in 2020.

3. Experience sharing between endemic countries about entomological surveys and technician training must be encouraged, with the help of the HAT Platform.

International meetings in 2020 (virtual)

- 16-18 November 2020: 8th Geneva Health Forum. Improving access to Health: Learning from the Field
- 20-24 November 2020: 68th Annual meeting of ASTMH (American Society of Tropical Medicine and Hygiene),Toronto, Canada.

Overview of the fexinidazole access project supported by DND*i* with its partners and implemented by the HAT Platform

- The project includes a set of actions focusing on fexinidazole access as well as on HAT diagnosis in affected populations or communities that are aware of the issue, to support the HAT elimination objective set by the WHO through multi-donor funding [Agence Française pour le Développement (AFD), European & Developing Countries Clinical Trials Partnership (EDCTP), Takeda Pharmaceutical Company Limited, ELMA Foundation, and the World Bank].

These actions include:

- Capacity building (diagnosis, treatment, detection of serological suspects, supervision, rehabilitation, equipment, communication)
- Access to the new fexinidazole treatment
- Support for the healthcare system [including screening and fexinidazole treatment in primary healthcare facilities, supporting healthcare systems through the NSSCP, and strengthening the pharmacovigilance system of the five countries (DRC, Guinea, CAR, Angola and South Sudan)]. Only the training aspects will be covered for the other endemic countries.
- Community outreach (behavioural research, information, education and communication)

Once implemented, all these activities will aim to improve or increase knowledge on the safety and efficacy of the new drug fexinidazole, improve the treatment practices of healthcare providers, and promote early case detection and management to eliminate HAT, using suitable new evidence-based communication tools. The lessons learned from these actions could be shared during international scientific meetings. The objective is that 80% of the affected populations in the target endemic areas are aware of the disease and have access to diagnosis and treatment with fexinidazole.

Fexinidazole: clinical trial for the treatment of rhodesiense HAT

DND*i*'s long-term goal for sleeping sickness is to develop and register two new drugs that are effective against both stage 1 and stage 2 of the disease, also known as human African trypanosomiasis (HAT), and both subspecies of the parasite, *Trypanosoma brucei gambiense* and *Trypanosoma brucei rhodesiense.*

Fexinidazole, the first all-oral drug for sleeping sickness developed in clinical trials led by DND*i* and added to the World Health Organization's List of Essential Medicines in July 2019, is currently indicated only for the treatment of *gambiense* sleeping sickness, the most common form of the disease. The 10-day once-a-day treatment can be taken at home.

Better treatments for *rhodesiense* sleeping sickness are urgently needed: the only treatment available for stage 2 *rhodesiense* sleeping sickness is melarsoprol, a toxic arsenic drug dating from 1949 that kills up to 5% of patients it is meant to cure. While the treatment option for stage 1, suramin, is less toxic, it is difficult to administer, requiring five intravenous injections given every seven days for a month. Without prompt diagnosis and treatment, sleeping sickness is usually fatal. *Rhodesiense* sleeping sickness progresses more rapidly than *gambiense* sleeping sickness, causing death within months.

HAT-r-ACC Consortium

To collect data evaluating the safety and efficacy of fexinidazole on both stages of *rhodesiense* sleeping sickness (r-HAT), we created the HAT-r-ACC consortium with funding from the European & Developing Countries Clinical Trials Partnership (EDCTP). The consortium is working on a five-year project in Uganda and in Malawi, two countries which together account for 83% of r-HAT cases worldwide in 2019.

The project, with its clinical study, aims to support the WHO's control and elimination efforts in East Africa, by providing evidence on the potential of a new oral drug that is less toxic and easier to administer.

The consortium also aims to support the national HAT control programmes in Malawi and Uganda in raising awareness in communities affected by r-HAT and increasing early case detection.

The HAT-r-ACC consortium brings together a wide range of partners with expertise in sleeping sickness and in capacity building in remote health areas. This experience in research, training and community outreach is essential to carrying out the clinical study in remote settings with very small target populations.

The consortium partners include:

- Drugs for Neglected Diseases *initiative* (DND*i*), Switzerland
- Association Epicentre, France

- Research Institute for Development (IRD), France

Makerere University, Uganda

Ministry of Health and Population, Malawi

Swiss Tropical and Public health Institute (Swiss TPH), Switzerland

Uganda National Health Research Organization (UNHRO), Uganda

Universidade Nova de Lisboa, Instituto de Higiene e Medicina Tropical (IHMT), Portugal

Project update

To assess fexinidazole for the treatment of *rhodesiense* HAT, a Phase II/III study aiming to enrol 34 stage 2 patients, was initiated in Rumphi, Malawi, in October 2019. A total of 28 patients (20 stage 2 patients) were recruited in October 2020. All patients survived the treatment and 23 have already completed the 6-month follow-up visits, without any efficacy or safety issues. The study was approved in Uganda in early 2020 but the preparation activities were suspended due to the COVID-19 pandemic. Once the risk management plan was finalised, the Lwala team resumed the final preparations and the study will start as soon as a patient is detected and referred to the hospital.

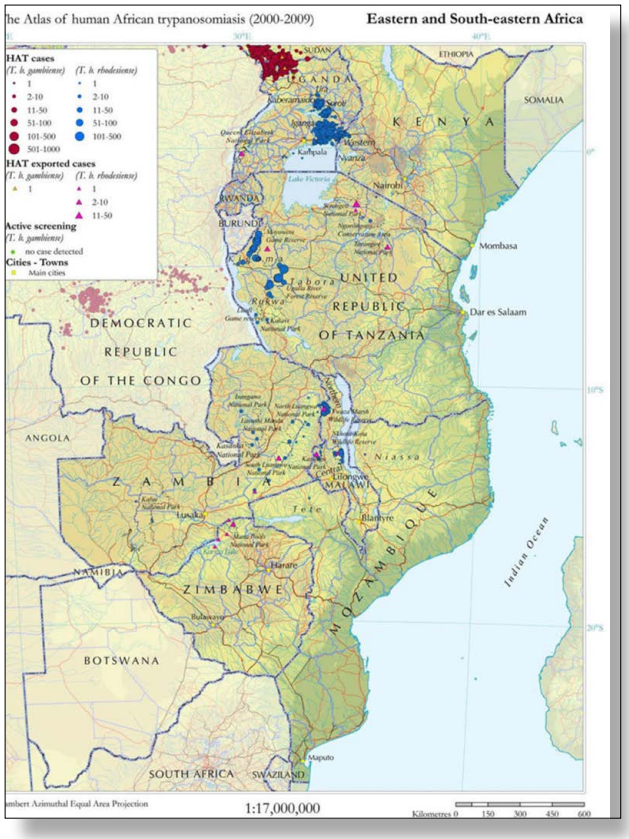
An ethnographic evaluation was carried out in the Kaberamaido and Dokolo districts in Uganda, and the final report will help design a communication campaign at community level. Plans are in progress to conduct a similar study in Malawi before the end of 2020.

Funding

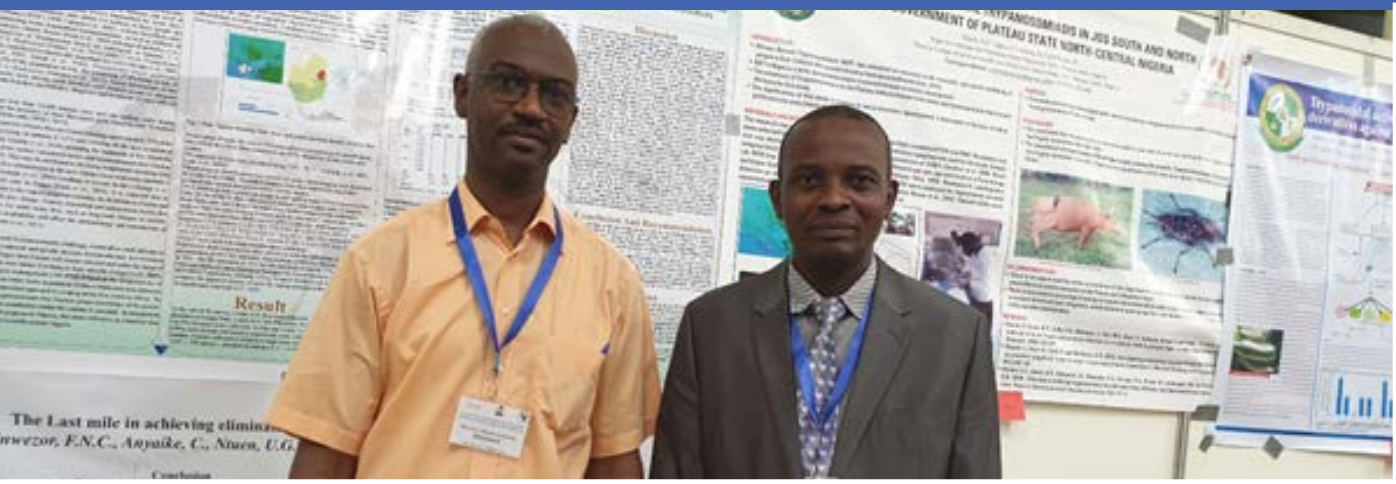
- Europe & Developing Countries Clinical Trials Partnership (EDCTP)

- Fundação para a Ciência e a Tecnologia (FCT), Portugal

This project is part of the EDCTP2 programme, which is supported by the European Union.



35TH CONFERENCE OF THE INTERNATIONAL SCIENTIFIC COUNC
HELD IN ABUJA, NIGERIA,



IL FOR TRYPANOSOMIASIS RESEARCH AND CONTROL (ISCTRC), ON 22-27 SEPTEMBER 2019

An Award to promote the implementation of fexinidazole

In December 2020, the Else Kröner Fresenius Award for Development Cooperation in Medicine acknowledged Dr Florent Mbo for this commitment in combatting human African trypanosomiasis. This Award is specifically honouring the fexinidazole project, led by DND*i* and supported notably by the HAT Platform, which will contribute to the sustainable elimination of HAT in DRC and other African endemic countries.

Xavier Vahed-DND*i*

"Now the challenge is to ensure wide access to this new treatment, to contribute to the sustainable elimination of sleeping sickness. DND*i* through the HAT Platform plans to facilitate the delivery and the uptake of fexinidazole in DRC and other African endemic countries".

Dr. Florent Mbo, HAT Platform Coordinator* & *Access Senior Project Manager,* DND*i

Summary of two articles published as part of the IRD project

A. The challenge of detecting the last patients for HAT elimination

With the nationwide decline of HAT prevalence, passive surveillance has become the primary strategy to eliminate the disease as a public health concern in Côte d'Ivoire. In August 2017, following a study conducted by the DiTECT-HAT programme (https://www.ditect-hat.eu/), passive surveillance was implemented in 10 healthcare facilities in the Bonon and Sinfra districts, the only Côte d'Ivoire districts still endemic for HAT. The strategy was integrated into the national health system and additional tests were performed in clinical suspects.

The article entitled *The complex health seeking pathway of a human African trypanosomiasis patient in Côte d'Ivoire underlines the need of setting up passive surveillance systems*, recently published in the open-access journal *Plos Neglected Tropical Diseases* (https://doi.org/10.1371/journal.pntd.0008588), describes the difficulties faced by a young patient and her family to obtain the correct HAT diagnosis. Although she was taken to dozens of public and private health centres and consulted over one hundred heath workers who prescribed inappropriate treatments, she received the correct HAT diagnosis only after 3 years. Following the onset of symptoms in October 2014, she dropped out of school and was stigmatised and accused of being possessed by a "demon" because of the neurological disorders caused by HAT (for a detailed clinical description, see Bony KE, Akani AF, Kaba D, Gnazegbo A, Diakite I, Karidioula HA, et al. Mouvements anormaux du sujet jeune et human African trypanosomiasis: un couple presque oublié. *Prat Neurol-FMC*. 2019; 10: 162–166. https://doi.org/10.1016/j.praneu.2019.01.012). She was finally diagnosed when in a coma in September 2017 and treated.

The young girl, currently in great shape, is now back at school, but she still suffers from neurological sequelae preventing her from living her teenage life to the full. The diagnostic delay imposed a heavy social and financial burden on the patient and her family. This situation is largely due to the current HAT status in Côte d'Ivoire, where it has become a rare and gradually forgotten disease by healthcare professionals and is no longer perceived as a threat by the population.

This individual story highlights the difficulty of eliminating sleeping sickness in Côte d'Ivoire. It illustrates clearly the "collateral damage" to be expected in countries that have managed to reduce HAT transmission considerably, and where such cases will become more frequent. Therefore, in such situations, it is important to maintain research, control and surveillance efforts to detect the last remaining patients and succeed in eradicating the disease in the near future, and to use passive surveillance as a cost-effective and promising strategy to support HAT elimination on the continent.

Minayegninrin Koné

B. Analytical sensitivity of loopamp and quantitative real-time PCR on dried blood spots and their potential role in monitoring human African trypanosomiasis elimination

Thanks to the achievements of HAT control efforts over the last two decades (case detection and treatment and vector control), the total number of reported cases fell gradually to less than 1,000 in 2018. The objective set by the WHO to eliminate human African trypanosomiasis (HAT) as a public health issue by 2020 has been reached.

Each country wishing to officially declare the nationwide elimination of HAT as a public health issue must submit a dossier to the WHO for approval. However, these countries should also use appropriate strategies and tools to maintain this status, i.e. avoid re-emergence, to reach the next objective which is to interrupt HAT transmission by 2030.

The International Centre for Research and Development on Livestock in the Subhumid Zone (CIRDES, Bobo-Dioulasso, Burkina Faso, www.cirdes.org) carried out a study to compare the analytical sensitivity of Loopamp, M18S quantitative real-time PCR (M18S qPCR) and TgsGP qPCR as molecular diagnostic tests for the presence of *Trypanosoma brucei gambiense* in DBS.

This study was carried out as part of a clinical diagnosis study evaluating the performance and feasibility of different diagnostic methods and algorithms for post-elimination HAT follow-up (DiTECT-HAT, www.ditect-hat.eu). Two reference strains of *Trypanosoma brucei gambiense* were amplified in mice, and their blood was used to prepare successive dilutions with concentrations ranging from 1 million to 1 trypanosome per ml of blood. Using these dilutions, blood spots were prepared on filter paper, whatman 4 and whatman 1001 following SDS lysis (Figure 1) to perform the following tests: LAMP and M18S qPCR, which detect the Trypanozoon group, and TgsGP which specifically detects *Trypanosoma brucei gambiense* (Figure 2 and Figure 3). Our results show that for both strains, the lower detection limits in both dilution series were 1,000 and 10,000 trypanosomes/ml for M18S qPCR and TgsGP qPCR, respectively. The lower detection limit for the LAMP test was 100 trypanosomes/ml for both strains.

Our results show that the challenge and need to develop an appropriate molecular tool to monitor HAT elimination remain. Neither method, particularly qPCR, is able to effectively detect trypanosomes in the blood of HAT patients, in whom trypanosome blood levels are often below the detection limit.

Additionally, the analysis of dried blood spots on filter paper is too time-consuming to be suitable for high throughput tests. The development of a molecular tool based on dried blood spots on filter paper and suitable for monitoring HAT elimination is a challenge, relying on a balance between sensitivity/specificity and the need for high throughput testing.

The three methods chosen for this study do not present these requirements. A combination of antibody detection tests followed by nucleic acid detection tests, to confirm or rule out an active infection, offers a solution that takes into account the limits of both methods. Therefore, we recommend examining the diagnostic performance and feasibility of various algorithms, combining serological and molecular tests to monitor HAT elimination.

Detailed results of this study were published recently (Compaoré CFA, Ilboudo H, Kaboré

J, Kaboré JW, Camara O, Bamba M, Sakande H, Koné M, Camara M, Kaba M, Belem AMG, Deborggraeve S, Büscher P, Bucheton B, Lejon V, Jamonneau V. Analytical sensitivity of loopamp and quantitative real-time PCR on dried blood spots and their potential role in monitoring human African trypanosomiasis elimination. Experimental Parasitology 219, Dec 2020. https://doi.org/10.1016/j.exppara.2020.108014). The results can also be provided by the authors (Charlie COMPAORE: compaore77charlie@gmail.com).

Compaore Charlie Franck Alfred

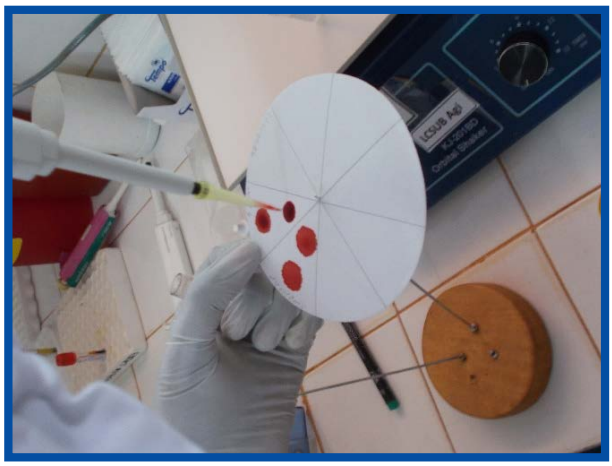


Figure 1 - Blood spots on filter paper

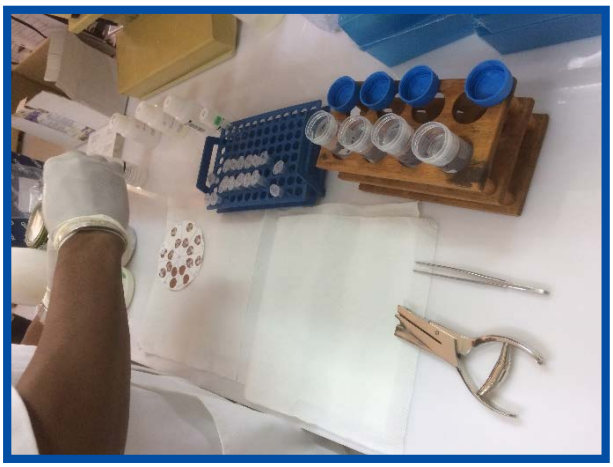


Figure 2 - Extraction of DNA from dried blood spots on filter paper prior to molecular analysis

Figure 3 - qPCR blood analysis on filter paper

Visits and meetings

Participation in the National Human African Trypanosomiasis Day in the DRC, Kinshasa, DRC, 30 January 2019

Participation in the HAT forum organised by PATH, Kinshasa, DRC, 17-18 April 2019

Contact meeting with the 5 countries involved (DRC, Angola, RCA, Guinea and South Sudan) regarding the study on fexinidazole pharmacovigilance, Kinshasa, DRC, 19-20 April 2019

Joint HAT Platform and FIND mission to assess the cross-border project for HAT elimination in the Republic of Congo, 10-13 July 2019

Participation in the meeting on the cross-border project for HAT elimination in the DRC, Angola and Republic of Congo, 22-23 July 2019, Kinshasa, DRC

Participation in the training of trainers on the use of fexinidazole, Kinshasa, DRC, 8-11 July 2019

Participation in the 2nd joint meeting on neglected tropical diseases using preventive chemotherapy and case management, organised by the WHO, Addis Ababa, Ethiopia,16-18 July 2019

Participation in the National Human African Trypanosomiasis Day in the DRC, Kinshasa, DRC, 30 January 2020

Participation in revision workshop on treatment algorithms of PNLTHA Guinea, Conakry, 6-8 February 2020

Launch of the project “programmatic support for the implementation of activities in the human African trypanosomiasis control program”, Kinshasa, 29 September 2020

Participation in the health workers' cascade training on the use of fexinidazole, Libreville, Gabon, 26-28 October 2020

Participation in the health workers' cascade training on the use of fexinidazole, Bangui, CAR, 26-28 October 2020

Scientific Publications in 2019-2020

1. Christian Burri. Sleeping Sickness at the Crossroads. *Trop. Med. Infect. Dis.* 2020, 5, 57, doi:10.3390/tropicalmed5020057

2. Emma Michelle Taylor and James Smith. Product Development Partnerships: Delivering Innovation for the Elimination of African Trypanosomiasis? *Trop. Med. Infect. Dis.* 2020, 5, 11, doi:10.3390/tropicalmed5010011

3. Philippe Neau, Heinz Hänel, Valérie Lameyre, Nathalie Strub-Wourgaft and Luc Kuykens. Innovative Partnerships for the Elimination of Human African Trypanosomiasis and the Development of Fexinidazole Reprinted from: *Trop. Med. Infect. Dis.* 2020, 5, 17, doi:10.3390/tropicalmed5010017.

4. Florent Mbo, Wilfried Mutombo, Digas Ngolo, Patrice Kabangu, Olaf Valverde Mordt, Nathalie Strub-Wourgaft and Erick Mwamba. How Clinical Research Can Contribute to Strengthening Healthcare systems in Low Resource Countries. *Trop. Med. Infect. Dis.* 2020, 5, 48, doi:10.3390/tropicalmed5020048

5. Shona J Lee, Renah J Apio and Jennifer J Palmer. Centering Patient Expectations of a Novel Home-Based Oral Drug Treatment among *T. b. rhodesiense* Human African Trypanosomiasis Patients in Uganda. *Trop. Med. Infect. Dis.* 2020, 5, 16, doi:10.3390/tropicalmed5010016

6. Jean-Benoît Falisse, Erick Mwamba-Miaka and Alain Mpanya Whose Elimination? Frontline Workers' Perspectives on the Elimination of the Human African Trypanosomiasis and Its Anticipated Consequences. *Trop. Med. Infect. Dis.* 2020, 5, 6, doi:10.3390/tropicalmed5010005

7. Jennifer J. Palmer, Caroline Jones, Elizeous I Surur and Ann H Kelly. Understanding the Role of the Diagnostic 'Reflex' in the Elimination of Human African Trypanosomiasis. *Trop. Med. Infect. Dis.* 2020,5,52,doi:10.3390/tropicalmed5020052

8. Matthieu Nkieri, Florent Mbo, Papy Kavunga, Pathou Nganzobo, Titus Mafolo, Chalet Selego and Eric Mwamba Miaka. An Active Follow-up Strategy for Serological Suspects of Human African Trypanosomiasis with Negative Parasitology Set up by a Health Zone Team in the Democratic Republic of Congo. *Trop. Med. Infect. Dis.* 2020, 5, 53, doi:10.3390/tropicalmed5020053

9. Enock Matovu, Claire Mack Mugasa, Peter Waiswa, Annah Kitibwa, Alex Boobo and Joseph Mathu Ndung'u. Haemoparasitic Infections in Cattle from a Trypanosoma brucei Rhodesiense Sleeping Sickness Endemic District of Eastern Uganda. *Trop. Med. Infect. Dis.* 2020, 5, 24, doi:10.3390/tropicalmed5010024

10. Jorge Seixas, Jorge Atouguia, Teofilo Josenando, Gedeao Vatunga, Constantin Miaka Mia Bilenge, Pascal Lutumba and Christian Burri. Clinical Study on the Melarsoprol-Related Encephalopathic Syndrome: Risk Factors and HLA Association. *Trop. Med. Infect. Dis.* 2020, 5, 5, doi:10.3390/tropicalmed5010005

11. Capewell P, Atkins K, Weir W, Jamonneau V, Camara M, Clucas C, et al. Resolving the apparent transmission paradox of African sleeping sickness. *PLoS Biol.* 2019;17(1):e3000105.

12. Frean J, Sieling W, Pahad H, Shoul E, Blumberg L. Clinical management of East African trypanosomiasis in South Africa: Lessons learned. *Int J Infect Dis.* 2018;

DND*i* Geneva Filariasis Programme activities in 2019 and 2020

The DND*i* Geneva filariasis programme carried out the following activities with the involvement of the DND*i* Kinshasa office:

*DND*i *and National Programme for Neglected Tropical Diseases Control using Preventive Chemotherapy (PCT- NTD programme) consultation meeting on the onchocerciasis clinical trial project, Kinshasa, DRC, 2 July 2019*

1. Feasibility and evaluation visits in Masimanimba and Kimpese sites

The DND*i* Geneva Filariasis team carried out a second visit to the clinical sites at Kimpese, Hôpital Roi Baudouin and Masimanimba to assess the capacity of these sites to conduct clinical trials and to manage or refer patients with adverse effects.

They also met the Director of the National Programme for Neglected Tropical Diseases Control using Preventive Chemotherapy (PNMTN-CTP), and they carried out a field visit at the Masimanimba clinical trial site in Kwilu province.

It should be pointed out that the sites to be used for the Phase IIa clinical trials of the drug Tylamac are undergoing rehabilitation in Masimanimba and Kimpese.

2. Intensive care training for the personnel in the potential onchocerciasis sites at Masimanimba, Kimpese and Roi Baudouin

To ensure the proper management of mild or serious adverse events, the personnel of the

potential sites at Kimpese, Masimanimba and Roi Baudouin received training on the basic concepts of intensive care. This training was provided by intensive care specialist physicians.

3. Training on the geolocation of onchocerciasis endemic villages

To improve the quality of georeferenced data collection in villages endemic for onchocerciasis or other filariasis in these provinces, training for PNMTN-CTP DRC personnel was organised on data collection tools (e.g. OziExplorer software) and the geolocation of endemic villages on maps, in which patients could be recruited for the clinical trials on onchocerciasis planned in the provinces of Kwilu and Kongo Central.

This training was organised jointly with the NSSCP with the help of their statistician, Shampa. A total of 12 people from PNMTN-CTP and the DND*i* office have been trained. This training will help PNMTN-CTP personnel correctly geolocate the endemic villages for epidemiological surveys.

4. Epidemiological surveys on onchocerciasis in endemic villages after 10 years of treatment

The PNLMN-CTP, in partnership with DND*i*, initiated this epidemiological survey to determine trends in the prevalence of *Onchocerca volvulus* infection after at least 10 years of treatment, and to identify the clinical trial sites to be used for the development of a macrofilaricide for onchocerciasis control.

The epidemiological survey was conducted from 18 October to 16 November in 38 villages in the province of Kongo Central, 31 villages in the province of Kwilu and 7 villages in the province of Kwango that met the following criteria:

- Being located in an area defined as hyper-endemic by REMO (Rapid Epidemiological Mapping of Onchocerciasis).
- Being on the front line, i.e. there must be no village between the selected village and the river (breeding sites for the vector *Simulium* flies).
- Having a stable population, with only few people entering and leaving the village.

The PNMTN-CTP investigators made the following observations:

Kongo Central Province

The standardised prevalence in 15 of the 38 villages surveyed exceeded the accepted threshold of 5%, ranging from 5.3% in the village of Lalu in the Masa health zone to 23.4% in the village of village Mbanza Di in the Sonabata health zone. The gross nodule prevalence exceeded the accepted threshold of 20% in 12 villages, the highest prevalence being 36.8% in the village of Kimpevolo in the Nsonampangu health zone. The microfilarial burden ranged from 0 to 1.47% in Mbanza Idi in the Sonabata health zone.

Migration surveys showed that most positive subjects had never left their health zone. They also showed massive treatment compliance with mectizan by the communities in most surveyed villages. Treatments were completed and the populations asked for more mectizan, in spite of adverse reactions, which explains the reduced prevalence in some of the villages when surveyed a second time compared to the survey 7 years ago.

Palpation-based detection of nodules identified 442 cases out of 3183 examined, i.e. 13.9%. This examination also revealed skin lesions (depigmentation, filarial scabies) and visual disorders (particularly loss of visual acuity) in many people.

Kwilu and Kwango Provinces

The standardised prevalence in 19 of the 38 villages surveyed exceeded the accepted threshold of 5%, ranging from 5.3% in the village of Kangala gala in the Pay Kongila health zone to 69.6% in the village of Kinzimbu in the Masimanimba health zone. The gross nodule prevalence exceeded the accepted threshold of 20% in 8 of the 38 villages, the highest prevalence being 44.1% in the village of Kindinga in the Moanza health zone. The microfilarial burden ranged from 0 to 14.7% in the village of Kinzimbu in the Masimanimba health zone.

These epidemiological surveys also showed that in certain villages in the Kenge and Kimbao health zones, the inhabitants admitted that some of them did not take ivermectin; according to the community distributors, this was due to drug shortages. This population is asking for ivermectin.

It should be noted that in the Pay Kongila and Masimanimba health zones where nodule prevalence is high, the treatment had not yet started.

Rehabilitation of the clinical trial sites for TylAMac, a macrofilaricide drug

The rehabilitation of sites in DRC to host onchocerciasis clinical trials using TylAMac is being finalised.

Birth announcements

Elif Margarita-Barata Mulamba
Born on December, 10th, 2020
Daughter of Dr Edmond Mulamba,
Monitor DND*i* DRC

Dimercia Ngolo Shirley
Born on September, 12th, 2020
Daughter of Dr Digas Ngolo, Access
Project Manager

Marius masengu Tshimanga
Born on August, 18th; 2020
Son of Dieudonné Tshimanga, laboratory
Assistant DND*i* DRC

Obituary

Tribute to Dr Jean-Baptiste Rayaisse, researcher at the International Centre for Research and Development on Livestock in the Subhumid Zone (CIRDES) in Bobo-Dioulasso

by IRD

The French Institute for Research and Development IRD was saddened to learn of the death in Burkina Faso on 23 March 2020

of an internationally recognised researcher and long-standing partner of IRD, Dr Jean-Baptiste Rayaisse.

This news deeply moved IRD and CIRAD researchers who had the privilege of working alongside him, as well as the members of the department of Mobilisation of Research and Innovation for Development who worked closely with him. Engineer by training and working as an entomologist at the International Centre for Research and Development on Livestock in the Subhumid Zone (CIRDES) in Bobo-Dioulasso, as well as Senior Research Fellow at CAMES, Jean-Baptiste Rayaisse was one of the world's leading experts on tsetse flies, the vector of animal and human trypanosomiases in Sub-Saharan Africa.

As leader of JEAI IRD ECOVECTRYP (2011-2014), he was fully invested in training activities, particularly regarding scientific writing, driven by his conviction of the crucial importance of mastering networks and international scientific standards.

IRD shares the pain of his CIRDES colleagues and his scientific community, and expresses its deepest sympathies to his family and loved ones.

Tribute to Prof Marleen Boelaert of the Institute of Tropical Medicine Antwerp

by Prof. Philippe Buscher

Although not unexpected, the death of Prof Marleen Boelaert on 12 June 2020 was another piece of sad news which marks a disastrous year, 2020. I met

Prof Marleen Boelaert more than a quarter of a century ago at the Institute of Tropical Medicine Antwerp, although it took several years before we started working together. I shall always remain extremely grateful for all the things she taught me and her unwavering support. For me, she was an example of vision and dynamism in the fight against neglected tropical diseases,

particularly leishmaniasis and human African trypanosomiasis. Without her continued commitment, even during her long illness, the number of sleeping sickness patients in the DRC would not be as low as it is today. Let Prof Boelaert be an example to all scientists who aim for better health for everyone, everywhere in the world.

Tribute to Prof Théophile Josenando

by Dr Augustin Ebeja

I was extremely saddened to learn early on 5 October 2020 of the death of Prof Théophile Josénando. I would like to pay a personal tribute to my friend Théophile who was a fighter against HAT, and who was one of the first in his country to earn a PhD in this field and become a professor. Everyone will remember him as a proud man and a staunch defender of Africa's sovereignty, and especially that of his country Angola and of its institution ICCT (Instituto de Combate e Controlo das Tripanossomiases). He was among co-founders of the HAT Platform with late Constantin Miaka and Miguel Kiassekoka.

I certify that Josénando had a remarkable presence and his contributions always enriched the debate. He was also keen to bring young people to scientific meetings so they could learn about scientific advances and further their training.

He was also a close friend of Miguel Kiassekoka, with whom he shared many laughs. He also often talked of his family and his children, to whom he wished to give everything so they could lead a successful and fruitful life.

Now that Josénando is no longer with us, it falls to each one of us to continue his work towards HAT elimination and especially towards a better world. Farewell Theo.

Tribute to Dr Miguel Kiassekoka

by Florent MBO

Dr Miguel Kiassekoka was the Coordinator of the HAT Platform Angola and together with Prof Josenando, Director of ICCT Angola, they formed a strong Angolan delegation at HAT Platform scientific meetings. In spite of his move to Portugal for health reasons, he still participated in HAT Platform meetings and continued to fight to secure the support of partners for the HAT control programme in Angola (ICCT Angola).

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