exchanges through our platform.

NECT: 1000 TREATMENTS NOW AVAILABLE IN THE DEMOCRATIC REPUBLIC OF CONGO

During the 5th International Congress on Infectious and Parasitic Diseases (CIPIP5) in Kinshasa, Dr. Pere Simarro announced on 6th November 2009, that the first batch of NECT treatment kits, sent by the WHO via MSF-Logistique, had arrived at the Matadi port in DRC. And this was not the end of the good news. He also announced officially that the DRC Minister of Public Health had signed that morning the document authorising the use of NECT in his country. Over 70% of patients with human African trypanosomiasis are from DRC.
All this was made possible thanks to the involvement and dedication of numerous partners, which we wish to thank.

The sequence of events is detailed below:

Clinical trial Time
Protocols - Ethics committees 1 year (08/2002 to 08/2003)
Inclusion - Result 5 years (08/2003 to 08/2008
Inclusion on the WHO's Essential Medicines List (EML) 9 months (08/2008 to 05/2009
TOTAL 6 years and 9 months
Implementation
NECT kit 1 month (05/2009 to 06/ 2009)
Bayer agreement 4 months (05/2009 to 09/2009)
Training in 8 countries 2 months (09/2009 to 11/2009)
Distribution 2 months (09/2009 to 11/2009
TOTAL 6 months

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Table inspired from the presentation given by Dr. Pere Simarro during the 5th International Congress on Infectious and Parasitic Diseases.

In the drug combination NECT, nifurtimox is administered orally and eflornithine by injection. With this combination, the number of eflornithine intravenous injections is reduced from 56 to 14, and the hospital stay is reduced from 14 to 10 days, which lightens the treatment considerably. As the administration of NECT requires only two intravenous injections per day during daytime, it is also easier on the nursing staff and better suited to local living conditions, where medical centres have limited resources and are situated in isolated or remote places where patients with sleeping sickness live.

© Photo W Mutombo

Participants and two Facilitators of NECT trainning at ROI BAUDOUIN hospital Kinshasa, DRC, November 2009

We hope to be able to include very soon other African countries affected by Human African trypanosomiasis where the use of NECT will become widespread, as it is done in DRC. This way, we hope to reduce to a minimum the number of people still treated with melarsoprol, a highly toxic drug associated with numerous unpleasant side effects.

THE WHO ORGANISES JOINTLY WITH DRC'S PNLTHA A TRAINING COURSE FOR FRENCH-SPEAKING NURSES ON THE USE OF THE NIFURTIMOX +EFLORNITHINE COMBINATION.

In its memo to medias dated 15 to 22 November 2009, the WHO representative office in DRC announced that « with the support of the WHO, DRC was organising an international technical training course on the combined treatment of human African trypanosomiasis (HAT) starting on Monday 23 November 2009 ».
The drug combination is nifurtimox-eflornithine (NECT), which we did speak about at great length in this Newsletter.
This training course forms an important stage of the process the WHO is putting into place to support Member States who decide to include this drug combination in their national policy on HAT treatment.
The course was aimed at nurses and doctors in charge of the management of trypanosomiasis patients in their respective countries. The countries who sent representatives were the Republic of Congo with two participants, Gabon with one participant, Chad with two participants, Central African Republic with one participant, Cameroon with one participant and Ivory Coast with one participant, thus bringing the total to seven nurse and one doctor. The participants are now expected to train the personnel involved with the management of trypanosomiasis patients in their country.
The training program organised by the WHO was well structured, based on experienced facilitators from the DRC, one nurse and one doctor who had participated in the NECT study.
Dr. Kande, head of PNLTHA, declared "It's a pilot experiment on the control of sleeping sickness, which has never been tried before". The Democratic republic of Congo is very proud to share this experience with colleagues from other African countries, and thus contribute to improving training in the treatment of sleeping sickness.
Dr José Ramon Franco in charge of this training declared that the hard work put behind this project shows the commitment of the WHO in supporting the countries in their efforts to control human African trypanosomiasis.

Dr Augustin K. Ebeja
HAT Platform Coordinator

Welcome to DNDi's new HAT team!!!

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As coordinator of the HAT platform, I wish to say goodbye to Els Torreele, former HAT project manager at DNDi, who after five years in this capacity, is moving on to new scientific challenges. We shall all remember her dedication, her presence in the field and her very important contribution in setting up our platform.
It is true to say that people come and go, and that institutions remain. To carry on onto the road of success, DNDi hired new people for its trypanosomiasis control project. We have the pleasure to present Olaf Valverde and Séverine Blesson, whom I welcome warmly to the

HAT platform.

Olaf Valverde, Project Manager

Dr. Olaf Valverde Mordt joined DNDi as Clinical Project Manager on 22 June 2009. Dr. Valverde was local coordinator for Médecins du Monde in Indonesia, and has accumulated over twenty years of experience in developing countries, including four years as a field agent for Médecins sans Frontières, working on their access to drugs campaign in Guatemala and Indonesia. He participated in the initial stages of the implementation of the access to AIDS treatment in Central America.

From 1987 to 2006, Olaf Valverde held various positions at Médecins sans Frontières in Latin America, Africa, and Asia, where he supervised numerous efficacy studies for ACT, and epidemiological studies, particularly on malaria. He was then appointed Director General of the Spanish section of Médecins sans Frontières from 1996 to 1997. Olaf gained experience on Human African trypanosomiasis in Uganda in 1989, in Angola in 1995 and in DRC in 2003. In the latter two countries, he explored and prepared two intervention proposals on the regions with trypanosomiasis epidemics.
He obtained his medical degree from the University Complutense in Madrid in 1984, then a diploma in Tropical Medicine from the University of Barcelona in 1988. He then completed a master's degree in Public Health Sciences in developing countries at the London School of Hygiene and Tropical Medicine in 1994.

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Séverine Blesson, Clinical Project Coordinator

Dr. Séverine Blesson joined DNDi in July 2009 as coordinator of the HAT projects. Her mission was to coordinate the clinical trials on the treatment of human African trypanosomiasis (sleeping sickness) in Europe and in Africa.

Before that, she was project manager at ANRS, the national French agency for research on AIDS and viral hepatitis, and was specifically in charge of the management of clinical and epidemiological trials in Africa and in South-East Asia.

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Dr. Séverine Blesson obtained her degree in veterinary medicine from the Ecole Nationale Vétérinaire d'Alfort in France. She then completed a master's degree in Immunology at the University René Descartes in Paris, and obtained a degree in statistics applied to medicine.

6) Upcoming events

- Clinical Trials in Emerging Markets, 1-2 March 2010, Prague, Czech Republic
- 14th International Congress on Infectious Diseases (ICID), 9-12 March 2010, MIAMI, FLORIDA, USA
- Geneva Health Forum, 19 – 21 April 2010, Geneva
- Epicentre Scientific Day, June 2010, Paris
- EANETT meeting September 2010 Mombassa/Kenya
- HATcap platform meeting September 2010 Mombassa /Kenya
- 2nd HAT Conference in RoC, November 2010, Brazzaville, RoC
- ICOPA (XIIth International Congress of Parasitology), 15-20th August 2010, Melbourne, Australia

7) Recent publications on HAT

1. Bacchi, C. J. (2009). «Chemotherapy of human African trypanosomiasis.» Interdiscip Perspect Infect Dis 2009: 195040.
2. Brun, R., J. Blum, et al. (2009). «Human African trypanosomiasis.» Lancet. Online publication 13.10.2009.
3. d'Alessandro, E. (2009). «[Medecins Sans Frontieres (MSF) and sleeping sickness control. From bush to international health space].» Bull Soc Pathol Exot 102(1): 41-8.
4. Hotez, P. J. and A. Kamath (2009). «Neglected tropical diseases in sub-Saharan Africa: review of their prevalence, distribution, and disease burden.» PLoS Negl Trop Dis 3(8): e412.
5. Kuepfer, I. and C. Burri (2009). «Reflections on clinical research in sub-Saharan Africa.» Int J Parasitol.
6. Louis, F. J., N. A. Djimadoum, et al. (2009). «[The Mandoul human African trypanosomiasis focus in Chad: from evaluation to control].» Med Trop (Mars) 69(1): 7-12.
7. Opigo, J. and C. Woodrow (2009). «NECT trial: more than a small victory over sleeping sickness.» Lancet 374(9683): 7-9.
8. Priotto, G., S. Kasparian, et al. (2009). «Nifurtimox-eflornithine combination therapy for second-stage African Trypanosoma brucei gambiense trypanosomiasis: a multicentre, randomised, phase III, non-inferiority trial.» Lancet 374(9683): 56-64.
9. Rosenblatt, J. E. (2009). «Laboratory diagnosis of infections due to blood and tissue parasites.» Clin Infect Dis 49(7): 1103-8.
10. Voelker, R. (2009). «Attention sought for neglected diseases.» Jama 301(17): 1755-6.
11. Buscher, P., D. Mumba Ngoyi, et al. (2009). «Improved Models of Mini Anion Exchange Centrifugation Technique (mAECT) and Modified Single Centrifugation (MSC) for sleeping sickness diagnosis and staging.» PLoS Negl Trop Dis 3(11): e471.

HAT Platform

DECEMBER 2009, NEWSLETTER N°6

EDITORIAL

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Dr Augustin Kadima Ebeja
HAT Platform Coordinator

This is already the sixth issue of our Newsletter. We are feeling very upbeat, boosted by the positive feedback we received on the previous issues. This one is packed with useful information aimed at scientists, political decision makers, people involved in HAT control, patients, and any interested reader.
We are proud to announce the integration of two new countries in our HAT platform, the Central African Republic (CAR) and Chad.
In this issue, we present some of the progress achieved by INRB Kinshasa relevant to the HAT platform. Several studies are being conducted in the various countries of the platform, two of which are highlighted here because they have reached significant and promising milestones.
We encourage our members to attend the various scientific meetings organised by the platform, and to look up recent publications (see our non-exhaustive list at the end of the Newsletter).

As we are approaching the end of 2009, we take this opportunity to thank all our partners and members of the HAT platform for their commitment during the past year.
We extend our best wishes to all for 2010, which we hope will carry us further down the road of success.

Sommaire

2) The HAT platform is expanding

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HAT Platform team in Ndjemena CHAD, August 2009

The human African trypanosomiasis (HAT) platform, created by DNDi in 2005 in Kinshasa, DRC, is a network of specialists working to strengthen clinical research on the disease in endemic countries. The platform includes researchers, clinicians and experts in these regions, as well as international specialists. Our platform is open to any partner wishing to share experience and capacities, learn new ones, or exchange knowledge with a view to meet the platform's objectives, i.e. strengthening clinical trials on HAT in endemic countries.

The Central African Republic and Chad can be rightly viewed as endemic countries, as the WHO has listed these two nations in the category reporting 100 to 1000 cases per year. The directors of their national program of human African trypanosomiasis control contacted the coordination of our platform. Our representatives then travelled to the countries to finalise the partnership with these countries. In close collaboration with the medical authorities and local partners involved in HAT control and research, the platform representatives examined the practical aspects of the implementation of activities in these regions.
The integration of the two new countries into the platform was formally adopted by all the members of the platform's steering committee during the two meetings held in June in Nairobi, Kenya, and in September in Kampala, Uganda. « We are very happy to welcome these two new countries in our organisation, dedicated to bringing together all the expertise necessary to control the disease », declared Augustin Kadima Ebeja, Coordinator of the Regional HAT Platform in Kampala. « It is by combining efforts with the main endemic countries that we will make decisive progress in HAT research and control. »

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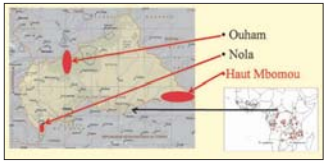
HAT Platform team in Bangui CAR, July 2009

Now that they are part of our network, a basic training will be given to the members of the ethics committees of these two countries, early 2010. In addition, the support and coordination given by our platform to these countries to optimise the HAT control have already helped them initiate changes in their treatment policy, and adopt the nifurtimox-eflornithine combination.
« We are very proud to have added two more countries to our platform, thus increasing the number of member countries from five to seven », said Augustin Kadima Ebeja. « We hope to expand our platform further into the endemic regions, for the benefit of those affected by this disease. »

Central African Republic (CAR)



The Central African Republic is a landlocked country, with common borders with five countries: Cameroun, Chad, Sudan, Democratic Republic of Congo, and the Republic of Congo.
It has a surface area of 622,984 km2, with an estimated population of 4,500,000 inhabitants and a density of 6.01 inhabitants per km2.

In terms of HAT epidemiology, it is important to note that over 180,000 inhabitants in the Central African Republic are estimated to be exposed to the disease. The prevalence varies between 0.1% and 3% depending on the foci and village locations. The hyperendemic foci – marked in red on the map - include Batangafo and Maitikoulou (>3%) and the regions bordering southern Chad. The endemic focus Tambura situated in the Haut-Mbomou (prevalence =1%) shares a border with Sudan.
The endemic foci in Nola and Lobaye, neighbouring the Equatorial focus in the Democratic Republic of Congo, have a low prevalence (0%). (source: National HAT Program C.A.R)

Chad

The Republic of Chad has a surface area of 1,284,000 km2. It shares borders with six other countries: Libya, Sudan, Niger, Nigeria, Cameroon and the Central African Republic. In 2006, its population was estimated at 9.2 million inhabitants. The population density is variable, greater in the south where it ranges from 54 to 108 inhabitant/km2. The country is divided into three climate zones, each with its sown specific vegetation.

In terms of the epidemiology of T. b gambiense, there are four foci in the southern part of the country: Moïssala, Bodo, Goré and Tapol.
The Mandoul focus which includes Moïssala and Bodo is the most active, with 110 cases recorded in 2007 and 194 cases in 2008.
The prevalence varies between 1% and 14% depending on the villages (source: report National HAT program Chad) .

Dr K.Ebeja Augustin.
HAT Platform Coordinator

3) INRB Kinshasa makes progress in the control of human African trypanosomiasis

INRB (Institut National de Recherche Biomédicale) is a national reference laboratory for public health in Kinshasa, the capital of the Democratic Republic of Congo. The institute houses the national reference laboratory for Human African Trypanosomiasis LNRTHA.

The laboratory has made notable progress and has provided major contributions to the control of sleeping sickness. Its deputy director, Dr Karhemere, plays an important role on the HAT platform. Some recent contributions of this laboratory to our fight against the disease are presented below.

© Photo INRB

INRB, Kinshasa RDC

3.1. The clinical study THARSAT (prospective observational study on shortening of post treatment follow-up in gambiense human African trypanosomiasis)

The clinical study THARSAT launched in May 2005 on shortening of post treatment follow-up in patients with trypanosomiasis was completed and closed in May 2008 by the team of Professor Philippe Büscher of the Institute of Tropical Medicine in Antwerp and Dr Mumba's team at INRB. The study results are to be published in the Journal of Infectious Diseases. The article will highlight the authors' proposal to reduce post-treatment follow-up in HAT control programmes from the currently recommended 24 months to 12 months.

3.2 Mini Anion Exchange Centrifugation Technique (mAECT) production site

The production site of mAECT kits at INRB in Kinshasa, DRC, is continuing its research on human African trypanosomiasis screening. The site produces 3000 kits per month. A modified tube model for simple centrifugation is also available to users. This device comes with an internal and external quality control system run jointly with the Institute of Tropical Medicine in Antwerp. (See also publication Buescher et al 2009)

Dr Dieudonné Mumba
LNRTHA INRB

4) Research update

A) NECT-FIELD: a field study to evaluate the clinical tolerability, feasibility, and effectiveness of NECT in "real-life" conditions for late stage HAT

Map of DRC indicating the HAT treatment centers participating in NECT FIELD

The NECT-FIELD study documents the clinical tolerability, feasibility and effectiveness of the combination in real-life settings, under National HAT Control Programme conditions (and / or NGO treatment centers). The inclusion criteria mimic as closely as possible the criteria to assign patients to treatment for stage 2 HAT normally used in the field by the implementing and treating bodies. As children form a substantial proportion of the population it was also convened that they will be included.

Partners for this study so far include DNDi, PNLTHA DRC, STI, MSF-CH, whereas DNDi is the sponsor of the study and STI as the assigned coordinating partner the responsible for the overall implementation in all sites plus the training of the study staff, monitoring of the trial and associated logistics. In DRC, the National HAT Control Programme PNLTHA is the executing partner.

NECT-FIELD was approved by the respective ethics committees (Basel /Switzerland, Kinshasa DRC) and started to enroll the first patients in the DRC: Dipumba and Katanda (East Kasai) by mid-April 2009, followed by Ngandajika (East Kasai), Bandundu and Kwamouth (Bandundu Province) by early June 2009 and finally in Yasa Bonga (Bandundu province) in November 2009 (see map).

By the end of November 2009, half of the anticipated number of patients has already received their treatment (310 patients) and the first patients were already examined for their 6 months follow up. So far, between 8 – 20% of all patients seen at the diverse centres were children <12 years and included in the study (average 15%). The safety of NECT remains in the expected nature and frequency of adverse events as was anticipated from the results of the first clinical trial by Epicentre / MSF /DNDi.

Cécile Schmid, STI

B) DEVELOPMENT UPDATE ON FEXINIDAZOLE

DNDi established a target product profile to facilitate access to treatment and contribute to the disease elimination. The goal is an oral drug, stable, effective in the two stages of the disease, with low toxicity.

Fexinidazole is a new promising drug candidate, rediscovered among more than 500 compounds of the Nitroimidazole family. In animal models and in vitro studies, it has been shown safe and effective against Trypanosomiasis. After careful toxicity studies, it started Phase I clinical trial in human healthy volunteers on September 22, 2009. The first part of the human study involves a gradual increase of a single dose of Fexinidazole, while carefully measuring blood levels and assessing possible toxicity, in order to find the adequate dose to continue the drug development. Up to the end of November, a good plasmatic profile and no toxic effects have been found, leaving the door open to continue with the next phases of the clinical research. DNDi plans to get ready to start research on efficacy in patients by the end of 2010.

Olaf Valverde, HAT Manager Project DNDi

5) Focus on science: recent events and News

HAT platform at the 5th International Congress of Infectious and parasitic Diseases (CIPIP) in Kinshasa, DRC

Our platform also participated in the 5th International Congress on Infectious and Parasitic Diseases (CIPIP5) held from November 4-6 2009 in Kinshasa, DRC, which provided an opportunity for our platform to increase its awareness and contribute to scientific exchanges. For the first two days, the congress covered infectious and parasitic diseases in general. During the third day spent exclusively on HAT, five of the seven member countries of our platform were present: the Central African Republic, the Republic of Congo, Uganda, Sudan and the Democratic Republic of Congo. Our main international partners were also present, including the WHO, DNDi, Swiss Tropical Institute (STI), FIND and MSF (Médecins sans Frontières).
During the congress, we presented the achievements of our platform over the past four years and organised a round table on NECT.
The NECT FIELD investigators presented to the scientific community the convincing results, their experience, and the successful collaboration between various partners which characterises the NECT study. NECT constitutes a major step forward in the treatment of patients with stage 2 sleeping sickness. However, scientists and participants at the round table emphasised the need for supporting information on the use and impact of this drug combination under field conditions. This is why the platform embraced a second study, called NECT-Field in April 2009.
DNDi's HAT project manager, Dr Olaf Valverde, presented another very promising molecule called fexinidazole, currently undergoing a phase I clinical trial (see "Research Update" section in this Newsletter).

Synergies are also being created behind the scene. The representative of the Central African Republic (Mariette Dethoua), researcher at Institut Louis Pasteur in Bangui, used the occasion to visit the premises of INRB in Kinshasa. This visit lead to very fruitful exchanges, interesting for the future. We are very proud to be able to contribute to such

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HAT Platform Members at 5th CIPIP in Kinshasa DRC, November 2009