



TRYLEIDIAG PRESS REVIEW

March 2009

Content

Events Highlights and Grants

- *The 2009 British Society for Parasitology Spring Meeting*
- *International Scientific Council for Trypanosomiasis Research and Control*
- *Programme Committee meeting of the Programme against African Trypanosomiasis*

Research news

- *Genetic identification of Chagas*
- *Increased CXCL-13 levels in human African trypanosomiasis meningo-encephalitis*
- *Towards the Atlas of human African trypanosomiasis.*
- *Novel S-adenosylmethionine Decarboxylase Inhibitors for the Treatment of Human African Trypanosomiasis.*
- *WITHDRAWN: A potential peptide vaccine against trypanosomiasis: 3 cattle field trials.*
- *Human African trypanosomiasis, chemotherapy and CNS disease.*
- *Disseminated central nervous system disease caused by Trypanosoma evansi in a horse.*
- *Trypanosoma cruzi: adaptation to its vectors and its hosts.*
- *Comparison of operational criteria for treatment outcome in gambiense human African trypanosomiasis.*
- *Host-parasite interactions in trypanosomiasis: on the way to an antidisease strategy.*
- *Current treatment for cutaneous leishmaniasis: a review.*
- *Comparison of PCR methods for diagnosis of canine visceral leishmaniasis in conjunctival swab samples.*
- *Designing therapies against experimental visceral leishmaniasis by modulating the membrane fluidity of antigen presenting cells.*

Political and regulatory

- *EPISOUTH: A Network for Communicable Diseases in the Mediterranean Region and the Balkans.*
- *FIND and University of Geneva renew their efforts towards a new test for sleeping sickness*

Nifurtimox-Eflornithine Combination Therapy:
An Improved Treatment for Sleeping Sickness



EVENTS HIGHLIGHTS

The 2009 British Society for Parasitology Spring Meeting

April 6th - 8th, 2009

Edinburgh University, Edinburgh, UK

For more information, please visit the website <http://www.bsp.uk.net/events.php?id=2>

International Scientific Council for Trypanosomiasis Research and Control

September 21st – 25th, 2009

Entebbe, Kampala, Uganda

For more information, please visit the website <http://au-ibar.org/isctrc.html>

Programme Committee meeting of the Programme against African Trypanosomiasis

May 07th - 08th, 2009

Smolenice, Slovak Republic

For more information, please visit the website <http://au-ibar.org/isctrc.html>



RESEARCH NEWS

Genetic identification of Chagas

SciDev.Net, 4 March 2009

Concurrent Detection of *Trypanosoma cruzi* Lineages I and II in Domestic *Triatoma dimidiata* from Guatemala. Pennington et al. *Am J Trop Med Hyg.* 2009; 80: 239-241

Article in Spanish

Increased CXCL-13 levels in human African trypanosomiasis meningo-encephalitis

Trop Med Int Health. 2009 Mar 2.

Courtioux B, Pervieux L, Vatunga G, Marin B, Josenando T, Jauberteau-Marchan MO, Bouteille B, Bisser S.

Institut de Neurologie Tropicale, Université de Limoges, Limoges, France.

Summary Objectives To determine the role of the B-cell attracting chemokine CXCL-13, which may initiate B-cell trafficking and IgM production in diagnosing HAT meningo-encephalitis. **Methods** We determined CXCL-13 levels by ELISA on paired sera and CSF of 26 patients from Angola and of 16 controls (six endemic and ten non-endemic). Results were compared to standard stage determination markers and IgM intrathecal synthesis. **Results** CXCL-13 levels in patients' sera had a median value of 386.6 pg/ml and increased levels were associated with presence of trypanosomes in the CSF but not with other stage markers. CXCL-13 levels in patients' CSF had a median value of 80.9 pg/ml and increased levels were associated with all standard stage determination markers and IgM intrathecal synthesis. **Conclusion** CXCL-13 levels in CSF increased significantly during the course of HAT. Hence the value of CXCL-13 for diagnosis, follow-up or as a marker of disease severity should be tested in a well-defined cohort study.

Towards the Atlas of human African trypanosomiasis.

Int J Health Geogr. 2009 Mar 18;8(1):15.

Cecchi G, Paone M, Franco JR, Fevre EM, Diarra A, Ruiz JA, Mattioli RC, Simarro PP.

ABSTRACT: BACKGROUND: Updated, accurate and comprehensive information on the distribution of human African trypanosomiasis (HAT), also known as sleeping sickness, is critically important to plan and monitor control activities. We describe input data, methodology, preliminary results and future prospects of the HAT Atlas initiative, which will allow major improvements in the understanding of the spatial distribution of the disease. **METHODS:** Up-to-date as well as historical data collected by national sleeping sickness control programmes, non-governmental organizations and research institutes have been collated over many years by the HAT Control and Surveillance Programme of the World Health Organization. This body of information, unpublished for the most part, is now being screened, harmonized, and analysed by means of database management systems and geographical



information systems (GIS). The number of new HAT cases and the number of people screened within a defined geographical entity were chosen as the key variables to map disease distribution in sub-Saharan Africa. RESULTS: At the time of writing, over 600 epidemiological reports and files from seventeen countries were collated and included in the data repository. The reports contain information on approximately 20,000 HAT cases, associated to over 7,000 different geographical entities. The oldest epidemiological records considered so far date back to 1985, the most recent having been gathered in 2008. Data from Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea and Gabon from the year 2000 onwards were fully processed and the preliminary regional map of HAT distribution is presented. CONCLUSIONS: The use of GIS tools and geo-referenced, village-level epidemiological data allow the production of maps that substantially improve on the spatial quality of previous cartographic products of similar scope. The significant differences between our preliminary outputs and earlier maps of HAT transmission areas demonstrate the strong need for this systematic approach to mapping sleeping sickness and point to the inaccuracy of any calculation of population at risk based on previous maps of HAT transmission areas. The Atlas of HAT will lay the basis for novel, evidence-based methodologies to estimate the population at risk and the burden of disease, ultimately leading to more efficient targeting of interventions. Also, the Atlas will help streamline future field data collection in those parts of Africa that still require it.

Novel S-adenosylmethionine Decarboxylase Inhibitors for the Treatment of Human African Trypanosomiasis.

Antimicrob Agents Chemother. 2009 Mar 16.

Barker RH Jr, Liu H, Hirth B, Celatka CA, Fitzpatrick R, Xiang Y, Willert EK, Phillips MA, Kaiser M, Bacchi CJ, Rodriguez A, Yarlett N, Klinger JD, Sybertz E.

Genzyme Corporation, 153 Second Avenue, Waltham MA USA 02451; University of Texas Southwestern Medical Center, Department of Pharmacology, 6001 Forest Park Road, Dallas, TX 75390-9041, USA; Swiss Tropical Institute, Parasite Chemotherapy, Socinstrasse 57 P.O. Box CH-4002, Basel, Switzerland; Pace University, Haskins Laboratory, Dept of Biological and Health Sciences, Dept of Chemistry and Physical Sciences, 41 Park Row, New York, NY 10038.

Trypanosomiasis remains a significant disease across the sub-Saharan African continent, with a prevalence of 50-70,000. Utility of current therapies is limited by issues of toxicity and the need to administer compounds intravenously. We have begun a program to pursue lead optimization around MDL 73811, an irreversible inhibitor of S-adenosylmethionine decarboxylase (AdoMetDC). This compound is potent, but in previous studies cleared rapidly from the blood of rats (Byers et al, 1991 Biochem J 274:527-533). One of the analogs synthesized (Genz-644131) was shown to be highly active against *Trypanosoma brucei rhodesiense*, in vitro (IC₅₀ = 400 pg/ml). Enzyme kinetic studies showed Genz-644131 to be approximately 5-fold more potent than MDL 73811 against the T. b. brucei AdoMetDC-prozyme complex. This compound was stable in vitro in rat and human liver microsomal and hepatocyte assays, was stable in rat whole blood assays, did not significantly inhibit human cytochrome P450 (CYP) enzymes, had no measurable efflux in CaCo-2 cells and was only 41% bound by serum proteins. Pharmacokinetic studies in mice following intraperitoneal dosing showed that the half-life of Genz-644131 was 3-fold greater than that of MDL 73811 (7.4 hr vs. 2.5 hr). Furthermore, brain penetration of Genz-644131 was 4.3-fold higher than that of MDL 73811. Finally, in vivo efficacy studies in T. b. brucei strain STIB 795-infected mice showed that Genz-644131 significantly extended survival (from 6.75 days for controls to >30 days for treated animals) and cured animals infected with T. b. brucei strain LAB 110 EATRO. Taken together, the data strengthen validation of AdoMetDC as an important parasite target and these studies have shown that analogs of MDL 73811 can be synthesized with improved potency and brain penetration.



WITHDRAWN: A potential peptide vaccine against trypanosomiasis: 3 cattle field trials.

Vaccine. 2009 Mar 12.

Powell CN, Odhiambo TR.

The Skirball Institute of Biomolecular Medicine, The New York University Medical Center, 540 First Avenue, New York, NY 10016, USA.

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Human African trypanosomiasis, chemotherapy and CNS disease.

J Neuroimmunol. 2009 Mar 6.

Rodgers J.

Institute of Comparative Medicine, Faculty of Veterinary Medicine, University of Glasgow, Bearsden Road, Glasgow, G61 1QH, United Kingdom.

Trypanosomes have been recognised as human pathogens for over a century. Human African trypanosomiasis is endemic in an area sustaining 60 million people and is fatal without chemotherapeutic intervention. Available trypanocidal drugs require parenteral administration and are associated with adverse reactions including the development of a severe post-treatment reactive encephalopathy (PTRE). Following infection the parasites proliferate in the systemic compartment before invading the CNS where a cascade of events results in neuroinflammation. This review summarises the clinical manifestations of the infection and chemotherapeutic regimens as well as the current research findings and hypotheses regarding the neuropathogenesis of the disease.

Disseminated central nervous system disease caused by *Trypanosoma evansi* in a horse.

Vet Parasitol. 2009 Feb 6.

Berlin D, Loeb E, Baneth G.

School of Veterinary Medicine, The Hebrew University, P.O. Box 12, Rehovot 76100, Israel.

Trypanosomiasis caused by *Trypanosoma evansi* ("Surra") is mainly a wasting disease affecting equids, camels and cattle as well as other domestic and wild animal species. In horses, infection may cause severe neurological abnormalities; however, the clinical progression, pathogenesis and molecular ante-mortem detection of this form of the disease have not been described in detail. A mare with progressive ataxia, head tilt, nystagmus and cranial nerve deficits submitted to treatment was diagnosed with central nervous system trypanosomiasis following the detection of a *Trypanosoma* tryposmastigote in cerebrospinal fluid cytology. Histopathology following necropsy showed that the brain, spinal cord and kidneys were the main affected tissues with disseminated multifocal non-



suppurative meningoencephalitis of the central nervous system and membranoproliferative glomerulonephritis. Serology for *T. evansi* was positive and PCR indicated the presence of parasite DNA in the cerebellum, brain stem, spinal cord and bone marrow but not in other organs and confirmed the identity of causative agent as *T. evansi*. This is the first report of ante-mortem detection of *T. evansi* in the cerebrospinal fluid of a horse and the first description of post-mortem PCR identification of the parasite DNA in the nervous system.

Trypanosoma cruzi: adaptation to its vectors and its hosts.

Vet Res. 2009 Mar 3;40(2):26.

Noireau F, Diosque P, Jansen AM.

American trypanosomiasis is a parasitic zoonosis that occurs throughout Latin America. The etiological agent, *Trypanosoma cruzi*, is able to infect almost all tissues of its mammalian hosts and spreads in the environment in multifarious transmission cycles that may or not be connected. This biological plasticity, which is probably the result of the considerable heterogeneity of the taxon, exemplifies a successful adaptation of a parasite resulting in distinct outcomes of infection and a complex epidemiological pattern. In the 1990's, most endemic countries strengthened national control programs to interrupt the transmission of this parasite to humans. However, many obstacles remain to the effective control of the disease. Current knowledge of the different components involved in elaborate system that is American trypanosomiasis (the protozoan parasite *T. cruzi*, vectors Triatominae and the many reservoirs of infection), as well as the interactions existing within the system, is still incomplete. The Triatominae probably evolve from predatory reduvids in response to the availability of vertebrate food source. However, the basic mechanisms of adaptation of some of them to artificial ecotopes remain poorly understood. Nevertheless, these adaptations seem to be associated with a behavioral plasticity, a reduction in the genetic repertoire and increasing developmental instability.

Comparison of operational criteria for treatment outcome in gambiense human African trypanosomiasis.

Trop Med Int Health. 2009 Feb 17.

Mumba Ngoyi D, Lejon V, N'siesi FX, Boelaert M, Büscher P.

Institut National de Recherche Biomédicale, Avenue de la Démocratie, Kinshasa, Democratic Republic of the Congo.

Summary Objective To develop a simple and standard operational decision tool for the diagnosis of relapse after treatment for human African trypanosomiasis (HAT), by evaluating the performance of several criteria currently used by HAT control programs and research projects. **Methods** We identified 10 different criteria for relapse, based on trypanosome presence and/or white blood cell count in cerebrospinal fluid, and compared their specificity, sensitivity and time to diagnosis on a data set containing 63 relapsed and 247 cured T.b. gambiense patients. **Results** At any time point, the criterion 'Trypanosomes present and/or a cerebrospinal white blood cell count $\geq 50/\mu\text{l}$ ' allowed accurate and timely detection of HAT relapse, irrespective of disease stage. This criterion was 13-25% more sensitive ($P \leq 0.013$) than trypanosome detection alone and was $>97\%$ specific. Lumbar punctures at the end of treatment and at 3-month post-treatment provided limited clinical information. **Conclusions** Adequate detection of relapse was possible with a simple criterion but these findings should be validated in a prospective study before adoption in clinical practice.



Host-parasite interactions in trypanosomiasis: on the way to an antidisease strategy.

Infect Immun. 2009 Apr;77(4):1276-84. Epub 2009 Jan 21.

Antoine-Moussiaux N, Büscher P, Desmecht D.

Tropical Veterinary Institute, Veterinary College, University of Liege, 20 Boulevard de Colonster, 4000 Liege, Belgium. nantoine@ulg.ac.be

Current treatment for cutaneous leishmaniasis: a review.

Palumbo E.

Am J Ther. 2009 Mar-Apr;16(2):178-82.

Department of Pediatric, Hospital of Sondrio, Foggia, Italy. emipalu2003@yahoo.it

Cutaneous leishmaniasis is the most common form of leishmaniasis. It is a skin infection caused by a single-celled parasite that is transmitted by sand fly bites. There are about 20 species of *Leishmania* that may cause cutaneous leishmaniasis. Some *Leishmania* species are closely linked to humans and are therefore found in cities (*Leishmania tropica*), whereas some are more traditionally associated with animal species and are therefore considered zoonoses (*Leishmania major*). The evidence for optimal treatment of cutaneous leishmaniasis is patchy. Although the cutaneous form of the disease is often self-limiting, it does result in significant scarring and can spread to more invasive, mucocutaneous disease. Therefore, treatment may be considered to prevent these complications. Drugs for systemic and topical treatment are presented and discussed with regard to their application, use, and adverse effects.

Comparison of PCR methods for diagnosis of canine visceral leishmaniasis in conjunctival swab samples.

Res Vet Sci. 2009 Mar 17.

Pilatti MM, Ferreira SD, Melo MN, Andrade AS.

Centro de Desenvolvimento da Tecnologia Nuclear (CDTN), Rua Professor Mário Werneck S/N, Cidade Universitária-Campus da UFMG, 31120-970 Belo Horizonte, MG, CEP, Brazil.

Four PCR assays for detection of *Leishmania* DNA in conjunctival swab samples were compared. All methods had two steps: a first amplification followed by hybridization or by a new amplification (nested or seminested). Two methods (kDNA PCR-hybridization and kDNA snPCR) used primers targeted to the minicircles of kinetoplast DNA (kDNA) and the other two methods to the coding (LnPCR) and intergenic noncoding regions (ITS-1 nPCR) of ribosomal rRNA genes. kDNA PCR-hybridization was positive for 22/23 dogs (95.6%) and for 40/46 samples (86.9%), considering the right and the left conjunctivas. kDNA snPCR was positive for 21/23 dogs (91.3%) and for 40/46 samples (86.9%). The ITS-1 nPCR and LnPCR were both able to detect the parasites in 17/23 dogs (73.9%) and 29/46 (63%) and 30/46 (65.2%) samples, respectively. The positivities of the kDNA based methods were



significantly higher; however the choice of the best method will depend on the kind of information required with the diagnosis.

Designing therapies against experimental visceral leishmaniasis by modulating the membrane fluidity of antigen presenting cells.

Infect Immun. 2009 Mar 16.

Banerjee S, Ghosh J, Sen S, Guha R, Dhar R, Ghosh M, Datta S, Raychaudhury B, Naskar K, Haldar AK, Lal CS, Pandey K, Das VN, Das P, Roy S.

Indian Institute of Chemical Biology, Council of Scientific & Industrial Research, 4, Raja S.C. Mullick Road, Kolkata - 700032, India; Rajendra Memorial Research Institute of Medical Sciences, Indian Council of Medical Research, Patna- 800007, India.

The membrane fluidity of APCs has a significant bearing on the T-cell stimulating ability and is dependent on the cholesterol content of the membrane. The relationship, if any, between the membrane fluidity and the defective cell mediated immunity (CMI) in visceral leishmaniasis has been investigated. Systemic administration of cholesterol by liposome delivery (Cholesterol-liposome) in *Leishmania donovani* (LD) infected hamsters was found to cure the infection. Splenic macrophages as a prototype of APCs of infected hamsters showed decreased membrane cholesterol and inability to drive T-cells, which was corrected by cholesterol-liposome treatment. The effect was cholesterol specific because liposomes made up of analogue 4-cholesten-3-one showed hardly any protection. Infection led to increase in IL-10, TGF-beta and IL-4 with concomitant decrease in IFN-gamma, TNF-alpha and iNOS signals, which was reverted upon cholesterol-liposome treatment. The antileishmanial T-cell repertoire, whose expansion appeared to be associated with protection, was presumably of Th1 type as evident from enhanced IFN-gamma signals and predominance of IgG2 isotype. The protected group produced significantly higher ROS and NO compared to the infected groups, culminating in the killing of LD parasites. Therefore cholesterol-liposome treatment promises to be yet another simple strategy to enhance CMI response in LD infection. To our knowledge this is the first report on the therapeutic role of cholesterol-liposome in any form of the diseases.



Political and regulatory

FIND and University of Geneva renew their efforts towards a new test for sleeping sickness

Geneva, Switzerland

FindDiagnostics Press Release
16 February 2009

FIND today extended its support to the University of Geneva by signing a three year funding agreement. The research team, headed by Dr Jean-Charles Sanchez, is undertaking research that is expected to pave the way for the development of a new, safe, accurate and low-cost test that will help doctors to better treat – and cure – sleeping sickness. The funding is for 462,000 CHF in the first year, with budgets for subsequent years to be negotiated.

Human African trypanosomiasis (HAT), more commonly known as sleeping sickness, is a parasitic disease that is transmitted to humans through the bite of a tsetse fly.

“More than 60 million people are at risk of this disease which, if untreated, invariably leads to death,” said Dr Giorgio Roscigno, Executive Director of FIND. “At the moment, treatment is severely hampered by difficulties in determining whether a patient is at stage 1 or stage 2 of the disease. Stage 2 patients need appropriate treatment, but the drugs in use are highly toxic and kill around 8% of patients. Prescription of these drugs should be guided by accurate determination of the stage of the disease.”

The University of Geneva researchers, working with partners at Makerere University in Uganda, and the Institute of Tropical Medicine in Belgium, have already made progress in identifying biomarkers in patients' cerebrospinal fluid (CSF) that indicate the stage of the disease. The extended funding will allow further studies to determine whether this knowledge can be applied to the development of a simple test, similar to a home pregnancy test, which can be readily used in countries throughout Africa, even in clinics and hospitals with the most basic resources.

The development of a simple staging test would represent a huge advance on the present situation. Currently, HAT patients have to undergo a lumbar puncture – a painful procedure that requires a skilled health worker, carries with it the risk of infection, and does not always yield accurate results.

“Making breakthroughs in the lab, which can later save lives, is the dream of any researcher,” said Dr Sanchez. “There is a real urgency to our current work, and our collaboration with FIND and colleagues in Uganda and Belgium ensures that the progress we make here in Geneva will have an impact on one of the most neglected poverty-related diseases of our time.”

For more information, please visit
<http://www.finddiagnostics.org/export/sites/default/media/press/090216.html>

EPISOUTH: A Network for Communicable Diseases in the Mediterranean Region and the Balkans.



Eurosurveillance, Vol14, Issue 5, 5 February 2009

M G Dente, M Fabiani¹, R Gnesotto, G Putoto, C Montagna, F Simon-Soria, C Martin de Pando, P Barboza, F Ait-Belghiti, M Kojouharova, N Vladimirova, R Vorou, K Mellou, G Thinus, S Declich, for the EpiSouth Network

The countries around the Mediterranean Sea share epidemiological characteristics and public health problems. In 2006 the EpiSouth Project was started as a framework for collaboration for communicable diseases surveillance and training in the Mediterranean Basin. As of December 2008, 26 countries from southern Europe, the Balkans, North Africa and the Middle-East are members of EpiSouth and several international organisations and institutions collaborate: the European Commission (EC), the European Centre for Disease Prevention and Control (ECDC), the Italian Ministry of Work, Health and Social Policies and the World Health Organization (WHO). The project is coordinated by the Italian national public health institute and three work packages (WPs) *Cross-border epidemic intelligence*, *vaccine preventable diseases and migrants* and *Cross-border emerging zoonoses* are operated by the national institutes of France, Bulgaria and Greece. These WPs constitute technical pillars on which the project develops. *Networking* and *Training* are WPs dedicated to capacity building and are run by the Padua Teaching Hospital (Italy) and the Spanish national public health institute. A steering committee guides EpiSouth's activities while all countries collaborate through WP steering teams and focal points. A number of outcomes have been accomplished and documents with results are available from the EpiSouth website which hosts a public website and a restricted area for direct sharing of information among the participants. Five electronic bulletins were published, two trainings for 63 participants performed, national epidemic intelligence systems were evaluated, a preliminary survey on vaccine-preventable diseases and migrants performed, and a list of priorities for emerging zoonoses in the Mediterranean area was selected. Overall the network succeeded in creating cohesion, mutual trust and concrete collaboration on cross-border public health issues in a geographical area that is not addressed as a whole by any other initiative or organisation.



Nifurtimox-Eflornithine Combination Therapy: An Improved Treatment for Sleeping Sickness

By Gerardo Priotto, Principal Investigator, Epicentre and Ann-Marie Sevcsik, DND's Scientific Communications Manager

The NECT Phase III pivotal study conclusively demonstrates that the coadministration of oral nifurtimox and intravenous eflornithine (NECT) is a safe, effective treatment for stage 2 HAT patients, and more practical than eflornithine monotherapy.

Background: the need for combination therapies for stage 2 HAT

The rationale for the NECT (nifurtimoxeflornithine combination therapy) study lies in the fact that, for stage 2 HAT, there were few available drugs, each with serious limitations, and not even one new drug in clinical development. With the third major HAT epidemic of the twentieth century devastating rural communities in sub-Saharan Africa – particularly in Angola, the Democratic Republic of the Congo (DRC), southern Sudan, and northwestern Uganda – from the late 1980s through the late 1990s, many health practitioners felt an urgency to do something to improve patient care. The toxic side effects of melarsoprol, its declining efficacy, and the lack of realistic alternatives prompted the search for a viable better alternative which could drastically reduce the use of this very toxic drug becoming ineffective.

NECT emerges as most promising of combination therapies for stage 2 HAT

The Institute of Tropical Medicine (ITMA) in the DRC, in addition to Médecins Sans Frontières (MSF) and Epicentre in Uganda, carried out much of the early work examining combinations. In two clinical studies in Uganda looking at combinations of melarsoprol, eflornithine, and/or nifurtimox, the combination of nifurtimox and eflornithine was shown to be the most promising option **(1) (2)**, but more research was needed to identify a suitable dose regimen and to confirm its safety and efficacy.

Epicentre and MSF undertake the NECT study in Congo-Brazzaville

Encouraged by these early results, in 2003 a team from Epicentre and MSF began a randomised, controlled trial (RCT) **(3)** in Nkayi, the Republic of the Congo. A simplified schedule of 7-days eflornithine in combination with 10-days nifurtimox (NECT) was compared with the standard, 14-day eflornithine schedule. With the aim to enrol a minimum of 140 patients for each treatment option to statistically determine noninferiority, the primary objectives were to evaluate the efficacy and safety of NECT in comparison with eflornithine monotherapy. Unfortunately, enrolment could not be completed at the Nkayi site due to the drastic reduction of HAT incidence related to the intensive screening and treatment activities of MSF in the region. By the end of 2004, a total of 103 patients (of the 280 needed) had been enrolled in the study.

DNDi joins in support of NECT

In April 2004, a group of experts including representatives from Epicentre, Médecins Sans Frontières (MSF), Swiss Tropical Institute (STI), TDR (the UNICEF/UNDP/World Bank, and WHO Special Programme for Research and Training in Tropical Diseases), World Health Organization (WHO), and DNDi met to review the available clinical evidence on the use of nifurtimox for HAT. The group was informed of the ongoing NECT study and its promising initial results. Considering the expected benefit to patients if this simplified combination regime worked, and the huge effort already made to enrol over 100 patients, it was decided that the best way forward would be to work together to strengthen and expand the trial and ensure sufficient enrolment for statistically relevant results. At the meeting, DNDi committed to sponsor three sites in the Democratic Republic of the Congo (DRC). In addition to Epicentre and MSF who implemented and managed the study in Isangi, new implementation partners



included the national HAT control programme of DRC and the STI. Epicentre continued to ensure the medical coordination, data management, and analysis for the full study. Epicentre also worked with all partners to prepare a protocol amendment to extend the study into a multicentre, multicountry setting.

Implementing three new study sites in DRC

Together with the national HAT control programme (PNLTHA) in DRC, DND*i* and Epicentre made several trips to assess and identify possible study sites in Isangi, Dipumba, and Katanda. These visits included an assessment of what was needed to conduct the trial to international Good Clinical Practice (GCP) research standards and to strengthen overall clinical research capacities. The Isangi site was first chosen in the Oriental province of DRC, where MSF had started a HAT screening and treatment activity at the local hospital. After refurbishment of the clinical and laboratory facilities and study-specific training of the staff, MSF and Epicentre started implementing the study in July 2005. In eleven months, 64 patients were enrolled at this site. Meanwhile, two additional study sites were selected, the Dipumba hospital in Mbuji Mayi and the HAT treatment centre of Katanda, about 70 kilometres away. After a similar round of rehabilitation, equipment and training, the first patients were enrolled in April and May of 2006, respectively. At these sites, the Swiss Tropical Institute (STI) worked in close association with the PNLTHA teams to implement the study, with Epicentre as the medical coordinator. The three DND*i*-sponsored sites were regularly monitored by STI.

NECT is shown to be safe and efficacious in a randomised, controlled, GCP-compliant trial with excellent follow-up

By November 2006, the targeted enrolment of 280 patients had been reached, with the three DND*i*-supported sites in DRC enrolling 184 patients to complement the 103 enrolled by MSF/Epicentre in Nkayi. Taking into account the 18 month follow-up period for the primary efficacy measure, final data analysis was completed in September 2008. The final results demonstrate the noninferiority of NECT for efficacy, and a favourable safety profile. With an excellent patient follow-up at 18 months after treatment of 93%, cure rate was shown to be comparable between the two treatment arms, and NECT showed a significant advantage in a number of secondary indicators. In terms of safety, both treatments were well tolerated and had low fatality rates. These data confirm that NECT represents an improved alternative over current first-line treatment options for stage 2 HAT - a less toxic, more efficacious cure than melarsoprol, and easier to use than eflornithine monotherapy. A submission for inclusion of nifurtimox, to be used in combination with eflornithine in the WHO Essential Medicines List 2009 is being prepared. Final study results are being presented at a number of international meetings (including the 17th International Congress on Tropical Medicine and Malaria (ICTM17), held early October 2008 in Jeju, South Korea, the HAT Platform meeting, mid November 2008 in Brazzaville, Republic of the Congo, and the 57th Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH) which will be held in New Orleans, USA, 7-11 December 2008) and will be submitted for publication early 2009.

1 Priotto G, Fogg C, Balasegaram M, et al. Three drug combinations for late-stage *Trypanosoma brucei* gambiense sleeping sickness: a randomized clinical trial in Uganda. *PLoS Clin Trials*. 2006;1(8):e39.

2 Checchi F, Piola P, Ayikoru H, Thomas F, Legros D, Priotto G. Nifurtimox plus Eflornithine for Late-Stage Sleeping Sickness in Uganda: A Case Series. *PLoS Negl Trop Dis*. 2007;1(2):e64.

3 Priotto G, Kasparian S, Ngouama D, et al. Nifurtimoxeflornithine combination therapy for second-stage *Trypanosoma brucei* gambiense sleeping sickness: a randomized clinical trial in Congo. *Clin Infect Dis*. Dec 1 2007;45(11):1435-1442