

LEAP

LEISHMANIASIS
EAST AFRICA PLATFORM

News LETTER

ISSUE 4

OCTOBER 2015



LEAP meeting in 2014

Twelve Years of LEAP: Achievements and Future Perspectives

By Prof. Yalemtehay Mekonnen

The birth of LEAP

As one of the long-serving academic staff members in Biological Sciences at the Addis Ababa University, it was not surprising that I received an official invitation to attend a conference for the establishment of Drugs for Neglected Diseases initiative (DNDi) – Africa office in Nairobi in May 2003. I accepted the invitation with great pleasure recognizing the huge problems we face in addressing neglected diseases in Africa. At that conference, there were over 70 partic-

ipants from different institutions within Africa and around the world.

During the sessions, the importance of addressing neglected diseases in Africa was emphasised by Dr Bernard Pécoul, the DNDi Executive Director and other neglected diseases experts. Participants were divided into groups to discuss the formation of a team that will address these diseases. I still remember vividly how I found myself in the *leishmania* discussion group with my good friend Dr Monique Wasunna (now the Director DNDi-Africa Office). Some of the members of the same group were,

Dr Ahmed Musa, from the Institute of Endemic Diseases Sudan and Dr Rashid Juma from Kenya Medical Research Institute. The discussions we had were very motivating and I felt honoured to be part of this group of highly dedicated professionals.

After the conference, we went back to our home institutions. A few weeks later, I received an email from Dr Wasunna asking me to map out *leishmania*-related scientific work in Ethiopia. I gladly compiled this information and in August 2003, the first *leishmania* group meeting was held in Khartoum,



Some of the LEAP Principal Investigators meet with the DNDi team in a past event

Sudan. Participants were drawn from Ethiopia, Kenya, Sudan, Médecins Sans Frontières, and DNDi Geneva. At this historical event, the Leishmaniasis East Africa Platform (LEAP) was born. In the following years, more members joined the platform including i+ Solutions; OneWorldHealth, AMC/KIT/University of Slotervaart, and London School of Hygiene and Tropical Medicine.

Project Development & Clinical Trials

At the first LEAP meeting, there were discussions on how to address and reach the many people in endemic areas affected by leishmaniasis. There were also questions about how a regional platform would operate. A Chairperson for the platform was selected and members agreed to meet biannually on a rotational basis in the member countries. Finally, LEAP was ready to launch its first clinical trial which had tremendous results. The trial showed the success of using the combination therapy of Sodium Stibogluconate (SSG) and Paromomycin (PM) in treating VL. Using this therapy reduced the treatment period from 30 to 17 days. Other clinical trials soon followed.

The Hurdles

As is characteristic with many groups, there were many hurdles to overcome at the beginning of LEAP. Members were from different countries with varying cultural backgrounds and professional exposures and this posed some difficulties. It took careful discussions, understanding and collaboration to make decisions. The consensus building process eventually became easier.

The other major challenge was the process of creating partnerships with the member countries' regulatory bodies, ethical boards and institutions' administrative bodies. It is through the concerted effort of LEAP clinical trials' Primary Investigators with the support of Project Leaders that such challenges were resolved.

Capacity Strengthening of Sites in the LEAP Platform

The financial and logistical support by DNDi has significantly contributed to building the human and infrastructural capacity. Young professionals have benefited from high-level trainings such as MSc and PhD as well as shorter trainings such as Good Clinical Practices and Good Laboratory Practices. The experience gathered by clinical monitors, members of the Data and Safety Monitoring Board, medical doctors and other scientists is extremely important for the region. The physical infrastructure constructed and purchased during clinical trials has transformed hospitals and benefited many patients. The other benefit of the platform is the development of cultural links that have strengthened important relationships among like-minded scientists.

The Future Perspective

It is now twelve years since LEAP was born by dedicated Eastern Africa professionals with the unreserved support of DNDi. It is a remarkable achievement to sustain the objectives of the platform to this date. In the first LEAP Scientific conference held in Bahir Dar, Ethiopia in September 2014, Dr John H. Amuasi from the Kumasi Centre for Collaborative Research in Tropical Medicine, Ghana said in his keynote speech: 'LEAP has walked, run, and leaped...' This is indeed a good metaphor for the path LEAP has followed. So at this stage in the journey, what should be the way forward? Could we ponder a different organizational structure or level of growth, horizontal and vertical? Should it go on leaping or sustain its rhythm? These questions can be a good start to critically and objectively think of the future direction of the platform. Whichever way we want LEAP to go, we can be certain that as a regional platform, it has proven to be an exemplary one. It can be a model for similar regional platforms and collaborations in Africa or in other parts of the world.

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Expensive Disease Affecting Poor Patients: The Economic Impact of Visceral Leishmaniasis



Most of the people affected by visceral leishmaniasis are either pastoralists or subsistence farmers

By Simon Bolo

Visceral Leishmaniasis (VL) is endemic in arid and semi-arid regions of East Africa. It affects poor people in the most remote areas whose main income generating activities include pastoralism and subsistence farming. Treatment for VL can be expensive and sadly, very few health facilities have the expertise to diagnose and treat the disease. This makes the disease a major economic burden for these poor communities.

According to a study carried out in Baringo County, Kenya, in 2012 to determine the economic impact of VL on households (HHs), 70% of patients could not afford VL treatment (which at that time was Sodium Stibogluconate alone for 30 days). Moreover, time spent in treatment had an extensive negative impact on households.

The unpublished data from the study, titled **'The Economic impact of VL in Baringo, Kenya'** used different financial models to determine the monthly income of 30 former VL patients who were treated at Kimalel Health Centre and Marigat Sub-district Hospital.

The average income of the former patients interviewed was Kshs 3000 (USD 30) per month. In comparison, the cost – direct and indirect- of treating one VL episode is about Kshs 31,200 (USD 312). This is triple the average monthly household income or 1.6 times their annual per capita income. Direct costs are both medical (consultation, diagnosis, drugs) and non-medical (transport to seek treatment, food, informal payments). Indirect costs are the opportunity costs of time lost because the patient is unable to carry out his/her normal productive activities due to ill-health associated with VL treatment.

Most patients affected by VL are children and youth, who on many occasions require parental care at the hospital during the VL treatment duration. For the communities in Baringo County, whose main income generating activities are subsistence farming and pastoralism, this has a great impact because households lose their most energetic worker and are at times forced to hire casuals to fill in the gaps. Younger children have to miss school or are accompanied to the hospital by an adult, who is also pulled away from economic activities.

Despite this, treatment for VL is imper-

ative and without it, the result is fatalities. Communities therefore have to find coping mechanisms for treatment. According to the study, households have to seek loans and sell produce and livestock meant for food to take care of the cost of treatment. The huge financial burden of treating VL and the subsequent coping mechanisms contributes to a cycle of poverty and further illness, which undermines development in endemic communities

To mitigate some of these issues, the study recommends the adoption of innovative mechanisms that will enable VL patients to speedily reach competent diagnostic facilities and receive medical attention without compromising livelihoods. The national insurance provider should also enhance customer enrolment among the communities affected by VL. An integrated approach that involves prevention; research and development of field adapted diagnostic tools and affordable medications; control programmes and eradication plans were also suggested. This will however require increased collaboration and partnerships as well as increased action from the government.

Drug Discovery Booster Experiment to Accelerate and Expand Discovery of New Drugs for Leishmaniasis and Chagas disease

By Linet Otieno

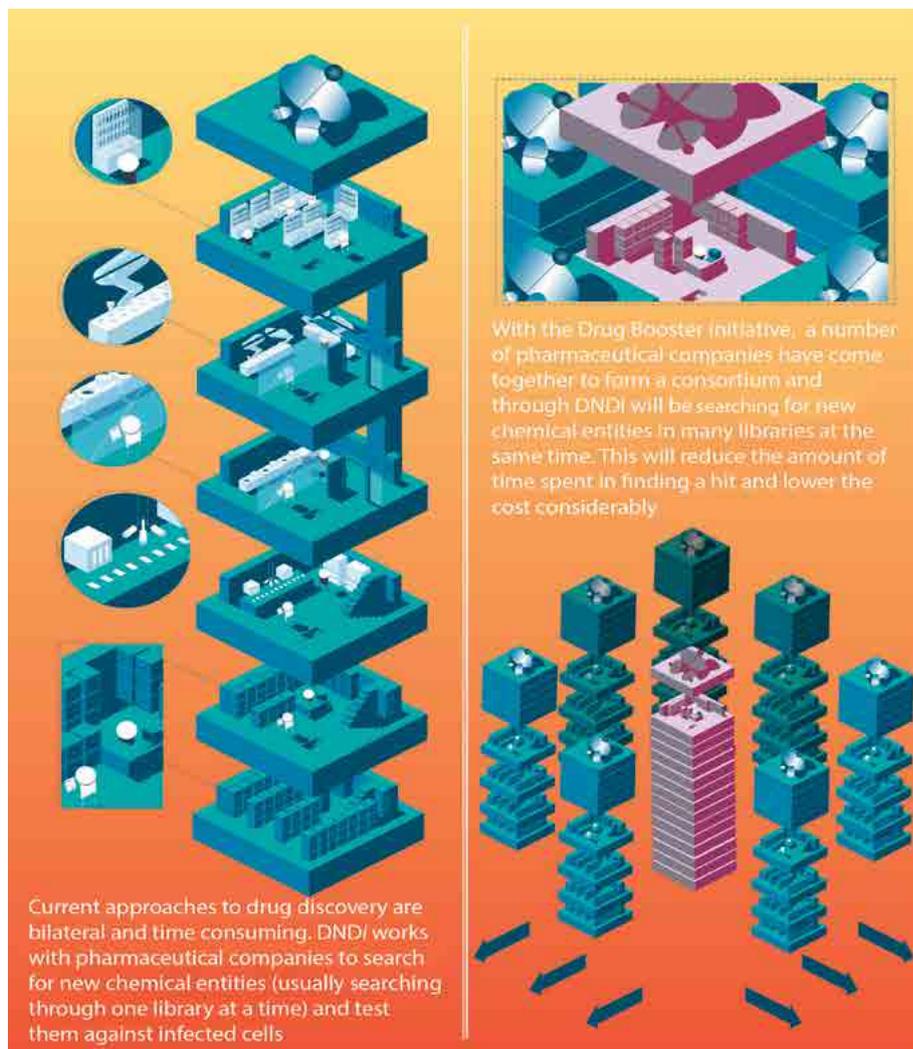
Radical improvement of therapies for leishmaniasis and Chagas disease requires identification, evaluation, and development of new drugs that are better than current therapies. Ordinarily, early stage drug discovery process to find new treatments is expensive and time-consuming. However, a partnership between DNDi and four pharmaceutical firms, Eisai Co Ltd, Shionogi & Co Ltd, Takeda Pharmaceutical Ltd, and AstraZeneca plc could change this by greatly reducing the time and cost of drug discovery.

The partnership, which was announced in May 2015, marked the start of an initiative to accelerate and cut the cost of early stage drug discovery for leishmaniasis and Chagas disease which 450 million people are at risk of contracting worldwide. Traditionally, it takes between 12-24 months to screen and produce a lead. With the booster this can be reduced to 6-9 months with further reduction from 24 to 12 months from hit series to lead optimization.

The 'Neglected Tropical Diseases Drug Discovery Booster' consortium, launched earlier this year, will circumvent early stage commercial barriers between the four pharmaceutical participants, allowing DNDi, for the first time, to search millions of unique compounds simultaneously, in the hunt for new treatment leads for the two diseases.

By using a multilateral, simultaneous search process across the four global pharmaceutical companies, DNDi will access millions of unique compounds, generated over many decades of research, to screen for potential treatments or cures for these diseases. The innovation of the Drug Discovery Booster not only lies in the multilateral approach, but also in the iterative nature of the search, meaning companies will continually examine their libraries for better matches as the search is refined.

The new process starts with DNDi providing all four companies with a common chemical starting point, the 'seed' compound. This compound will have shown promising results against Leish-



mania or *Trypanosoma cruzi*, the parasites that cause leishmaniasis and Chagas disease, but may not yet be optimal for use as a future treatment. The four companies will then search their own full collections of high-quality chemical compounds for similar and potentially better molecules, and will select and send the most promising to DNDi, which will then have them screened for potential effectiveness against the two deadly parasitic diseases.

DNDi will then select the best 'hits' for further testing. This process will be repeated up to three times, with each new iteration – or round – starting from an improved seed compound identified from within one of the four partner's collections and shared with all. The initial

project explores the consortium's compound libraries for at least four promising seed compounds for each disease. It is expected that at least two of the resulting novel series of compounds will move to the next stage of development towards a new medicine. As of September 2015, three compounds had been sent to Institute Pasteur Korea and one compound to pharmaceutical partners.

Any progress or successful new treatment for leishmaniasis or Chagas disease resulting from the Drug Discovery Booster will be attributed to the collective effort of all partners, which have also agreed that no intellectual property barriers will be imposed to a new treatment if successful.

VIEWPOINT

Moving Closer to an Oral Treatment for Kala Azar

By Linet Otieno and Lilian Were

On a warm day in West Pokot County, North Western Kenya, a group of young men are seated under a tree at Kacheliba Hospital speaking in hushed tones. Most of them are here to seek treatment for kala azar which is rampant in the area. One of the men in the group is 20-year-old Ngoriatodo Natukei who comes from Amoler village about 170km from the hospital. Two weeks earlier, he came to Kacheliba to begin his treatment. It took him two hours on a motorcycle and another hour on foot to get to the hospital.

'When I saw my abdomen swelling, I knew I had kala azar and I had to urgently come here for treatment', he says.

Since he started his treatment, his health has greatly improved. Each day, for past 16 days, he has been receiving two injections: a combination of sodium stibogluconate and paromomycin (SSG & PM), which is the current first-line treatment for kala azar in Kenya and most of the other East African countries.

The WHO recommended treatment for kala azar in Eastern Africa was revised in 2010 from SSG alone for 30 days to the combination of SSG & PM for 17 days following a landmark study conducted in the region by the Leishmaniasis East Africa Platform (LEAP). Even though this treatment is a great improvement from the previous one, patients still have to endure painful injections and 17 days of hospitalization. In addition, there are life-threatening toxicities associated with the use of SSG. Daily injections are very painful and patients like Ngoriatodo sometimes adopt a slight limp as a result.

DNDi and the LEAP are continuing the search for better treatments for kala azar that are safe, effective, affordable, and short course. A study is currently going on in Kacheliba and Amudat in Uganda to determine if a new oral drug miltefosine is safe and effective in treating the disease. This study is targeting children between 4- 12 years who are below 30



Health workers attend to a patient at Kacheliba Hospital



Ngoriatodo Natukei

kg. It is a follow-up of another study which revealed that a dose of miltefosine linearly based on weight (mg/kg), does not provide similar drug exposure in children as compared to adults. The study is therefore using the allometric technique to determine the best dosage for the children.

The idea of an oral drug delights Ngoriatodo. 'After spending most of my days lying on my stomach because my buttocks were too swollen and I couldn't sit properly, the idea of taking an oral drug will be a much more welcome alternative!', he declares.

'I long to see the day when kala azar treatment is oral', says seasoned community mobilizer

By Linet Otieno and Lilian Were

Tall, dark, medium-built, soft-spoken and passionate are the adjectives that describe Andrew Ochieng, a Community Mobilizer from Amudat in Eastern Uganda. The father of three has over 17 years' experience working with both Kenyan and Ugandan communities to create awareness about kala azar. Whenever he speaks about his work, his enthusiasm is unmistakable.

This passion can be traced back to a time he was eight years old. He got infected with kala azar and his mother took him to a traditional healer for treatment. Thankfully, although it took long time, he improved and was soon strong enough to get back to his normal life. His neighbour was not so lucky though. He also fell sick but died in the hands of a traditional healer due to excessive bleeding. Andrew therefore refers to his healing as a miracle.

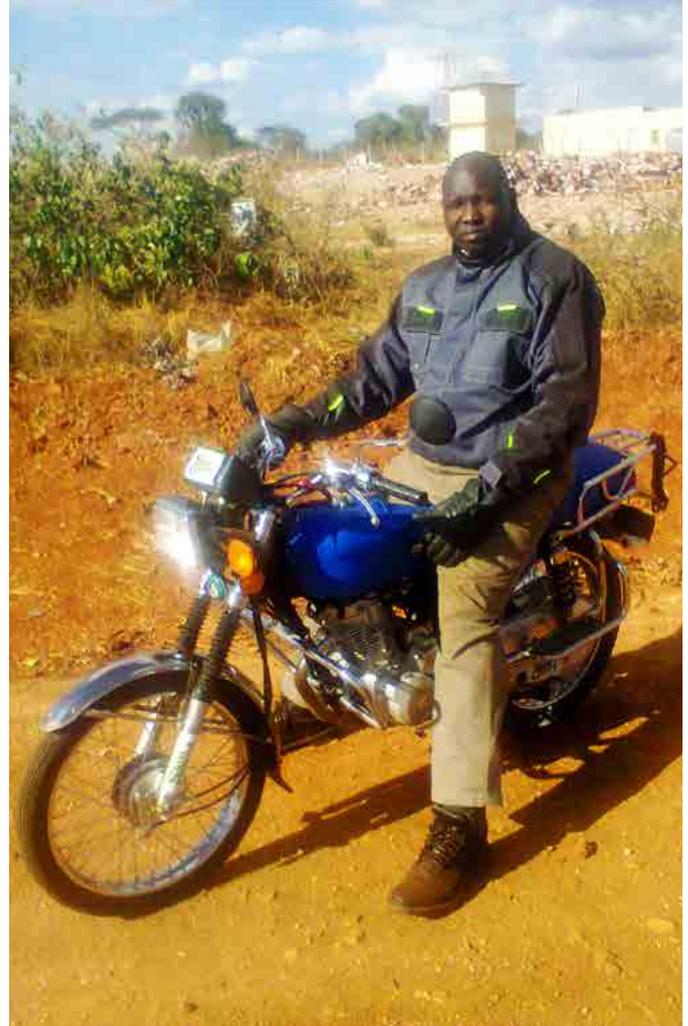
After he completed his high school education, Andrew heard about Médecins Sans Frontières' (MSF) work in kala azar at Amudat Hospital. He developed an interest in the organization's activities and when MSF announced a job vacancy seeking a Community Mobilizer, he applied, seeing it as an opportunity to create awareness for the disease that had ailed his community for many years.

Several people were interested in the position but since Andrew speaks six languages, he became the preferred choice. Since then, Andrew has worked hard to spread the kala azar message in his community. He has slept in tents in the middle of the forest, contended with bandits, and gone for many days without seeing his family to create awareness about the disease.

He has been involved in most of the kala azar studies carried out by LEAP in Kenya and Uganda. 'Kala azar is my passion, I can do this every day without remuneration', he says excitedly, 'In the 17 years I have worked as a community mobilizer, I have seen some die, but I have also seen many get treatment.'

During a landmark trial by LEAP, which succeeded to show that using the Sodium Stibogluconate (SSG) and Paromomycin (PM) combination therapy for 17 days is just as effective as the original treatment of SSG alone for 30 days, he was engaged as a Community Mobilizer. Recently, he has also been engaged in an ongoing study to determine whether an oral drug known as miltefosine could be an effective treatment for kala azar. In his position, he is expected to ensure that the required number of participants are recruited in the Amudat site and also that study patients go for their follow up visits at the hospital.

Andrew admits that working with the community is an arduous task. 'I work with nomadic communities, and following them up is not easy.' On many occasions, he has gone to a village only to find that the patients have moved away with their livestock. He has learned to keep good records to ensure that he can track them despite their whereabouts.



Andrew on his motorcycle

Andrew's life working with the community is also one of sacrifice. 'I spend a lot of time away from my family so that I can build relationships with the community.' From time to time, he has had to singlehandedly take a child to the hospital so that they can access treatment because the parents or guardians are either too busy or could not afford the transport costs. This shows that he has developed a close relationship with the community.

In his time, Andrew has seen the transition of treatments, from SSG alone to SSG and PM. He is, however, most excited about the prospect of an oral drug. 'Those injections are painful and sometimes children run away because they fear the treatment. This study is therefore an important first step towards an ideal oral treatment for kala azar', he says.

Improved treatment for kala azar has always been Andrew's life desire. 'I would like to offer my support LEAP's work in looking for improved treatment until we find the best oral drug for this disease', he concludes.

My Story

Samuel Chepkok Chirchir, Field Supervisor

By Joy Malongo

Sixty-year-old Samuel Chepkok Chirchir is a father of 12 and a Field Supervisor in Baringo County, Kenya. He was born and raised in Loruk, Kiplelchony village (238km North of Nairobi, Kenya's capital city) where he lives to date. Chirchir's interest in nursing began over 30 years ago when missionaries running a Mobile Clinic near his village sought to train locals to assist in running the clinic. 'I joined the Kapedo Mission Medical Training College in 1979 to train as an Enrolled Nurse and after graduating, in 1981, I started my own mobile clinic, under a tree', says Chirchir.

Later, Chirchir was employed by the Kenya Medical Research Institute (KEMRI) as a Field Worker. During this time DNDi began kala azar activities in the



Samuel Chepkok Chirchir

region and Chirchir supported the team as a Field Supervisor based in Loruk. 'I love what I do - working in the field is an incredibly rewarding job', he reveals. However, he faces transport and logistical challenges due to the remote environment he works in. On a typical day, he travels as far as 20km away from home to help patients get to the Kimalel Health Centre.

'My passion is to serve God's people. Having passion for what I do gives me the energy to keep going in tough times. After a long challenging and exhausting day a "thank you *daktari*" [doctor in Swahili] from a patient cured of kala azar keeps me motivated to do more', Chirchir says.

Early this year, Chirchir retired from his position at KEMRI but he continues to support DNDi's kala azar activities as Field Supervisor. He also works with his community serving at a different capacity. He was recently elected the Chairman Livestock Drought and Survival (LIDDROSUR), a community-based peace initiative that champions peaceful co-existence among the Pokot and Tugen in the rustling prone areas of North and East Baringo counties.

Study to Contribute Towards New Diagnostics for Kala azar

By Gabriel Omwalo

Forsyth University, Cambridge USA, DNDi, and KEMRI under the auspices of the LEAP platform are collaborating to conduct a study geared towards collecting specimen for developing new tests that can use urine to diagnose kala azar. Current diagnostic tests for kala azar are invasive and risky hence it is important to continue the search for new tests that are more accurate and easy to administer.

In this study, urine specimen will be collected from 35 patients who have tested positive of kala azar and 20 patients who are kala azar negative to act as controls. Through these samples, proteins that are unique to patients with kala azar will be identified, which could then be used to develop a new test.

The study will be conducted in the Kimalel Health Centre, Baringo County and the Kacheliba District hospital, West Pokot County. It is hoped that the study will lead to a development of an antigen detection assay that will accurately diagnose and monitor treatment of kala azar. Such a test has the potential for future development into a point of care test in the form of a dipstick.



Current rapid diagnosis tests



A health worker conducts a splenic aspirate. The procedure is very invasive

Community Leaders offer their Support to Fight Kala azar



Laban Selemoi, A County Official, gives a speech during the event

By Linet Otieno

Over 25 elders, religious leaders, political leaders, and other community leaders attended a stakeholders' meeting organized by Kacheliba Hospital with the support of DNDi on 6 August 2015. The event marked renewed collaboration between the community and the hospital where LEAP is currently undertaking a study to determine the effectiveness of oral drug miltefosine in treating visceral leishmaniasis (VL) among children.

The event began at 9:00 am with a visit to the hospital's Kala Azar Ward where the leaders had an opportunity to interact with patients. Many were saddened to see the impact of the disease on, especially, young children. However, it was not surprising to them because kala azar is a common disease in the region and some of the leaders had also been affected. Updates about the miltefosine study provided much needed optimism, which lingered with them throughout the day. Their excitement grew when they were informed how the study had contributed immensely to building the capacity of the hospital.

The leaders cheered and clapped when they saw the new generator set up because of the study but which has been beneficial to the entire hospital. The new equipment in the laboratory purchased because of the study were also received with enthusiastic cheers. 'We are happy about the capacity building done in this hospital', declared Laban Selemoi, a County Official. 'You have done what the County is yet to do.'

During the meeting, the leaders were informed about kala



Leaders at the hospital's laboratory



Community leaders walk towards the hospital

azar, strides made in the search for new, improved treatments and more importantly their role in reducing the impact of the disease within their community. Nearly all the leaders made a commitment to partner with the hospital to ensure that patients within their communities would go for treatment. 'I will tell everyone in my baraza [meeting] about this disease', said the area Chief.

With this new partnership, it is hoped that more patients will seek treatment for kala azar.

VIEWPOINT

VL Guideline Training in Marsabit



Group photo after the training

By Linet Otieno and Robert Kimutai

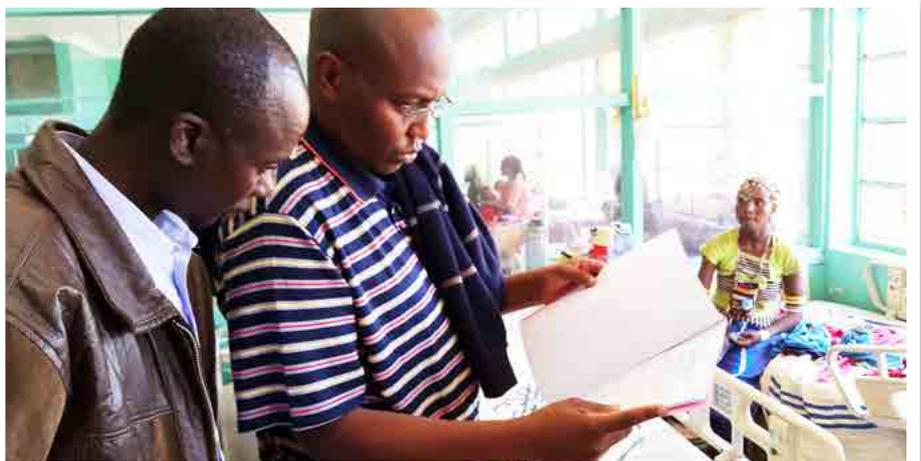
On 21 September 2015, DNDi and the Kenyan Ministry of Health (MoH) organized a training to update health workers in Marsabit County on the national visceral leishmaniasis (VL) guidelines. The national guidelines outline standards for diagnostic techniques, treatment regimens, and disease management for VL. Although they were launched in 2012, many health workers still lack the knowledge and expertise to diagnose and treat the disease in line with the guidelines.

'We don't have the knowledge and tools to manage this disease', said Stephen Labarakwe, the County Executive for Health in Marsabit County during his opening speech made at the training.

A visit to the County Hospital suspected VL cases but which had not been confirmed due to lack of accurate diagnostics. Furthermore, although the approved first-line treatment for VL is a combination of Sodium Stibogluconate (SSG) and Paramomycin (PM) for 17 days, health workers are reverting to SSG for 30 days because they believe that PM is too toxic.

The training was lauded by the County health officials as well as the participants. 'The specialists have told us how to manage this disease, we must not to be silent about this', said Stephen.

Twenty-two health workers from the



Dr. Robert Kimutai from DNDi and Mark Riongoita from Kacheliba Hospital who were facilitators at the training, review kala azar patient documents at Marsabit Hospital



Stephen Labarakwe, the County Executive for Health in Marsabit County in his office

county and sub-county hospitals attended the training. Dr Robert Kimutai from DNDi, Dr David Wachira from Neglected Tropical Disease Programme, MoH and Mark Riongoita from Kacheliba Hospital, where DNDi is carrying out studies in VL, conducted the training.

VIEWPOINT

DNDi Unveils New Business Plan



Dr Alwyn Mwinga, Patient Representative in the DNDi Board, gives a speech during the launch of the Business Plan

On 7 September 2015, DNDi unveiled an updated business plan (2015-2023) that features a more flexible, dynamic portfolio approach, integrating various operating models to better respond to the patient needs. The plan also paves the way for new diseases to be taken up in DNDi's portfolio.

As part of this new plan, DNDi remains committed to developing treatments for African sleeping sickness, leishmaniasis, and Chagas disease as well as filarial diseases and paediatric HIV. DNDi will also soon be launching new research and development (R&D) projects for hepatitis C and mycetoma, two very different diseases that share, with other important global health issues such as anti-microbial resistance, one key challenge: the existing system of biomedical innovation has failed to deliver safe, effective, quality products that are affordable to poor populations.

Below is a summary of key highlights from the new business plan:

1. A patients' needs-driven approach –



Copies of the Business Plan summary

- This will entail a more dynamic portfolio approach to address patient needs. Most of the current neglected diseases will remain at the core, with new diseases taken on progressively.
2. A steadfast commitment to promote open sharing of research knowledge and data while ensuring an access-oriented approach to intellec-

tual property (IP) management and licensing.

3. By 2023, DNDi aims to deliver 16 to 18 new treatments.
4. Fostering of innovative, collaborative partnerships will remain vital.
5. Diversification of funding sources to ensure scientific independence will be maintained.

Flashback: First LEAP Conference



By Joy Malongo

'Bridging the Gap: Progress on the Current Research Innovation & Access to Visceral Leishmaniasis Treatment in Africa' – this was the theme of the First Leishmaniasis East Africa Platform (LEAP) Conference held at Bahir Dar in Ethiopia on 29 and 30 September 2014. A total of 133 participants from 14 countries attended the event, the main objective was to promote networking for researchers in the region by creating a platform to discuss critical issues affecting research, innovation, and access to visceral leishmaniasis (VL) treatment in Africa. The conference also sought to offer a platform for stakeholders to assess evidence and deliberate on progress and challenges of treatment for VL and other neglected tropical diseases (NTDs).

It was an appropriate moment to celebrate the positive developments and progress made in research and development (R&D), diagnosis, treatment, and leishmaniasis patient access to treatments in the East African region. It was also an opportunity to recommend actions to tackle issues affecting research and innovation. The forum sought a declaration of commitment from key stakeholders towards enhancing use of and patient



access to Sodium Stibogluconate (SSG) and Paramomycin (PM) combination therapy.

The conference was a progression of bi-annual meetings that LEAP has held since its formation. At the end of the conference, participants expressed strengthened resolve and commitment to regulatory and ethics harmonization efforts in Eastern Africa. An SSG&PM Pharmacovigilance (PV) Steering Committee and PV Stakeholders meetings were held to disseminate results of the SSG&PM pharmacovigilance study to stakeholders from Ethiopia and Sudan.



PICTORIAL: First LEAP Conference



2015 Leishmaniasis Publications

Use of Pentamidine As Secondary Prophylaxis to Prevent Visceral Leishmaniasis Relapse in HIV Infected Patients, the First Twelve Months of a Prospective Cohort Study by Diro E, Ritmeijer K, Boelaert M, Alves F, Mohammed R, Abongomera C, Ravinetto R, De Crop M, Fikre H, Adera C, Colebunders R, van Loen H, Menten J, Lynen L, Hailu A, van Griensven J. *PLoS Neglected Tropical Diseases*. 2015 Oct 2;9(10):e0004087. doi: 10.1371/journal.pntd.0004087. eCollection 2015

Development and Validation of a Novel *Leishmania donovani* Screening Cascade for High-Throughput Screening Using a Novel Axenic Assay with High Predictivity of Leishmanicidal Intracellular Activity by Nühs A, De Rycker M, Manthri S, Comer E, Scherer CA, Schreiber SL, Ioset JR, Gray D. W., *PLoS Neglected Tropical Diseases*, 9(9): e0004094. doi:10.1371/journal.pntd.0004094, 2015

Aminothiazoles: Hit to Lead Development to Identify Antileishmanial Agents by Bhuniya D, Mukkavilli R, Shivahare R, Launay D, Ravindra T, Dere, Deshpande A, Verma A, Vishwakarma P, Moger M, Pradhan A, Pati H, Gopinath VS, Suman Gupta*, Puri SK, and Martin D., *European Journal of Medicinal Chemistry*, 2015, doi:10.1016/j.ejmech.2015.08.01

Polymorphisms in the TOLLIP Gene Influence Susceptibility to Cutaneous Leishmaniasis Caused by *Leishmania guyanensis* in the Amazonas State of Brazil by Felipe Jules de Araujo, Luan Diego Oliveira da Silva, Tirza Gabrielle Mesquita, Suzana Kanawati Pinheiro, Wonei de Seixas Vital, Anette Chrusciak-Talhari, Jorge Augusto de Oliveira Guerra, Sinésio Talhari, Rajendranath Ramasawmy PLOS Published: June 24, 2015 doi: 10.1371/journal.pntd.0003875

A Cross-Sectional Survey of Knowledge, Attitude and Practices Related to Cutaneous Leishmaniasis and Sand Flies in Punjab, Pakistan by Ayesha Akram, Hafiz Azhar Ali Khan, Abdul Qadir, Arshad Makhdoom Sabir, PLOS Published: June 19, 2015 DOI: 10.1371/journal.pone.0130929

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A Comprehensive Review of Cutaneous Leishmaniasis in Kerman Province, Southeastern Iran - Narrative Review Article by Sharifi I, Aflatoonian MR, Fekri AR, Hakimi Parizi M, Aghaei Afshar A, Khosravi A, Sharifi F, Aflatoonian B, Khamesipour A, Dowlati Y, Modabber F, Nadim A. *Iran J Public Health*, Vol. 44, No.3, Mar 2015, pp.299-307

Structural basis for selective targeting of leishmanial ribosomes: aminoglycoside derivatives as promising therapeutics by Moran Shalev; Haim Rozenberg; Boris Smolkin; Abedelmajeed Nasereddin; Dmitry Kopyansky; Valery Belakhov; Thomas S ..., *Nucleic Acids Research*, 2015
Transcriptomic profiling of gene expression and RNA processing during *Leishmania* major differentiation by Laura A. L. Dillon; Kwame Okrah; V. Keith Hughitt; Rahul Suresh; Yuan Li; Maria Cecilia Fernandes; A. Trey Belew; He ..., *Nucleic Acids Research*, 2015

Innate immunity against leishmania infections by Prajwal Gurung, Thirumala Devi Kanneganti, *Cellular Microbiology*, 2015

DDT-based indoor residual spraying suboptimal for visceral leishmaniasis elimination in India [Applied Biological Sciences] by Michael Coleman; Geraldine M. Foster; Rinki Deb; Rudra Pratap Singh; Hanafy M. Ismail; Pushkar Shivam; Ayan Kumar Gh ..., *Proceedings of the National Academy of Sciences* current issue, 2015

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(-)-Bisabolol, a Promising Oral Compound for the Treatment of Visceral Leishmaniasis by Victoriano Corpas-López; Francisco Morillas-Márquez; M. Concepción Navarro-Moll; Gemma Merino-Espinosa; Victoriano D ..., *Journal of Natural Products*, 2015

[Perspective] Overcoming neglect of kinetoplastid diseases 29-May-2015 | Graeme Bilbe, *Science*, 2015

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THE LEISHMANIASIS EAST AFRICA PLATFORM (LEAP)

About LEAP

The Leishmaniasis East African Platform was launched in 2003 with the support of DNDi. It brings together scientists and institutions from East Africa and around the world to develop clinical trial capacity and seek new and accessible treatment options for visceral leishmaniasis (VL) patients in the region. The platform is also a base for ongoing educational cooperation among the countries in East Africa and standardization of procedures and practices within the region, as far as is possible within the confines of local regulations.

Objectives of LEAP

- Evaluate, validate, and register improved options that address regional needs for leishmaniasis
- Facilitate clinical testing and registration of new treatments for VL in the region
- Provide capacity strengthening for drug evaluation and clinical studies in the region

Why Focus on VL in Africa?

- If left untreated, VL is generally fatal
- Treatments are scarce and far from optimal
- 60% of patients infected by VL in Africa are children
- VL affects mostly poor people living in remote areas
- East Africa is one of the most important foci for VL in the world

Achievements of LEAP

Delivery of New Treatment

LEAP has delivered SSG&PM combination treatment for VL. SSG &PM is a 17-day treatment recommended by the World Health Organization (WHO) as first-line treatment for VL in East-

ern Africa. SSG&PM has been included in the national guidelines of Sudan, South Sudan, Ethiopia, and Kenya. PM is registered in Uganda (2011) and Kenya (2013), and is in the process of registration in Sudan and Ethiopia.

Supporting Treatment Access

- Continuous advocacy efforts to promote the use of SSG&PM as first-line treatment in East Africa has led to its inclusion in countries' national guidelines
- Support to Ministries of Health of member countries to facilitate patient access to treatments and diagnostics

Capacity Building

1. Training

- Good Clinical Practice (GCP)/Good Laboratory Practice (GLP) training for investigators, nursing staff, and laboratory technologists
- Development of regional data management capacity
- In Kenya, training of health workers on the VL national guidelines has been undertaken
- Sponsorship of investigators and other clinical trial staff to attend key national and global conferences

2. Infrastructure

- Support the setting up of generators and purchase of laboratory equipment at study sites (for example in Amudat, Uganda and Kacheliba, Kenya)
- Building of two research and treatment centres in Ethiopia: Arba Minch and Gondar
- Significant upgrading and opening of Professor El Hassan Centre for Tropical Medicine, Doka, Sudan



Laboratory equipment at Kacheliba Hospital, purchased at the beginning of the Miltefosine Study

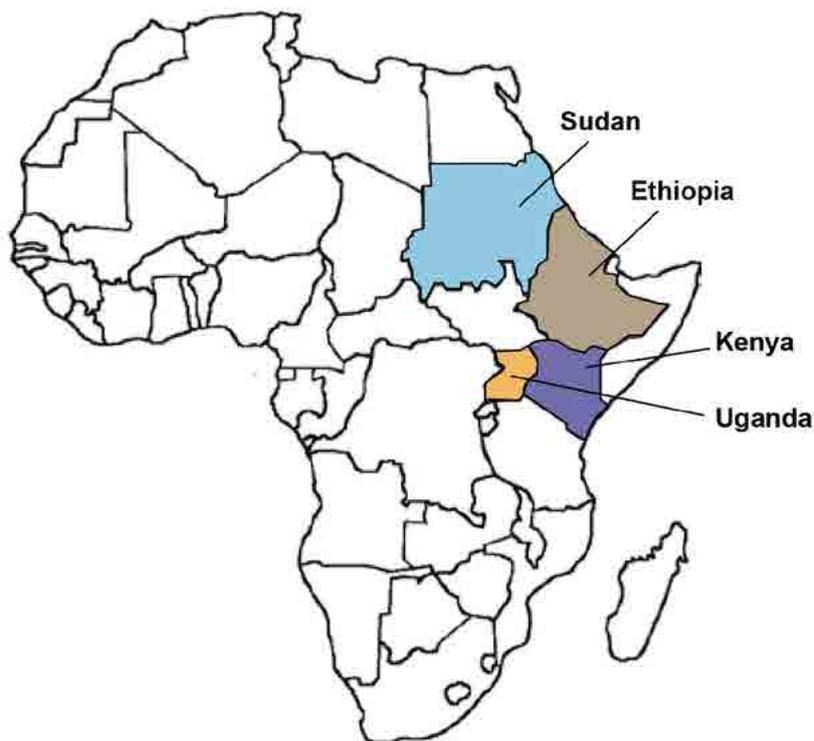
Ongoing Studies in LEAP Sites

NAME OF STUDY	VL/HIV Co-infection Study
ACRONYM OF STUDY	0511 HIV VL
GEOGRAPHICAL LOCATION	Gondar and Arab Minch, Ethiopia
YEAR STUDY BEGAN	2014
SUMMARY PROFILE OR OBJECTIVE OF THE STUDY	This study is evaluating the efficacy of a combination regimen of Ambisome with Miltefosine, and of Ambisome (at a higher dose) monotherapy in Ethiopian VL patients co-infected with HIV. A secondary objective is to assess relapse-free survival one year after initial cure.
NO OF STUDY PARTICIPANTS TO BE ENROLLED	Up to 132 patients
PROGRESS	60 patients have been recruited into the study. In August 2015 recruitment for the study was stopped.

NAME OF STUDY	Miltefosine Pharmacokinetics (PK) Study
ACRONYM OF STUDY	LEAP 0714
GEOGRAPHICAL LOCATION	Kacheliba, Kenya and Amudat, Uganda
YEAR STUDY BEGAN	May 2015
SUMMARY PROFILE OR OBJECTIVE OF THE STUDY	<p>This trial is a follow up to the LEAP 0208 study that assessed the safety and efficacy, of the combinations Ambisome + SSG, Ambisome + Miltefosine and Miltefosine monotherapy in treating VL. Data from this study indicated that children were underexposed when they received conventional linear dosage of 2.5mg per kilogram body weight per day.</p> <p>The proposed study aims to assess whether drug exposure in children can be safely increased to equivalent adult drug exposure by using the miltefosine allometric dose given twice daily for 28 days in paediatric VL patients aged 4-12 years and whether this dose is tolerable.</p>
NO OF STUDY PARTICIPANTS	Up to 30
PROGRESS	The study has completed recruitment and is now at follow up stage

UPCOMING EVENTS - 2015

NO	EVENT	VENUE	DATE
1.	LEAP Meeting	Khartoum, Sudan	28 - 30 October
2.	SSG & PM Pharmacovigilance Stakeholders meeting, Kenya	Nairobi, Kenya	16 -17 November
3.	SSG & PM pharmacovigilance Stakeholders meeting, Uganda	Kampala, Uganda	19 - 20 November
4.	Kenya Science Journalists Congress 2015	Nairobi, Kenya	25 - 27 November
5.	Good Financial Practices Training for partners	Nairobi, Kenya	23 - 24 November
6.	5th African Network for Drugs and Diagnostics Innovation Stakeholder Meeting, 2015	Nairobi Kenya	23 - 25 November
7.	World AIDs Day, 2015	Worldwide	1 December
8.	International Conference on AIDS and STIs In Africa (ICASA)	Harare, Zimbabwe	29 November - 4 December



LEAP SITES

Sudan: 2 sites
(Dooka, and Um El Kher)

Ethiopia: 2 sites
(Gondar and Arba Minch)

Kenya: 2 sites
(Kacheliba and Kimalel)

Uganda: 1 site
(Amudat)

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