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Word from the Director, DNDi Africa Regional Office

DR MONIQUE WASUNNA, DIRECTOR, DND*i* AFRICA REGIONAL OFFICE

Dear LEAP members,

As you all aware, the Leishmaniasis

East Africa Platform (LEAP) was founded in 2003 in Khartoum, Sudan, by the Drugs for Neglected Diseases initiative (DNDi), bringing together stakeholders from Kenya, Ethiopia and Sudan, and was joined by those from Uganda in 2006. LEAP's main objective is to facilitate clinical testing and improved access to better treatments for leishmaniasis in the region. At that time, and even to date, new, improved, treatment options were needed to address the specific needs of the eastern African region patients, such as drug combinations, less toxic and more affordable shorter course treatments and, ideally, an effective, safe, oral treatment. Existing therapies had serious drawbacks, and there were concerns about resistance and cardiotoxicity, some were expensive and teratogenic and need to be administered intravenously.

I am extremely excited that as we celebrate fifteen years of our existence, we have made a lot of strides. LEAP has grown and is currently composed of 60 individual members representing over 20 institutions, covering the spectrum of clinical research, working with Ministries of Health and disease control organizations in leishmaniasis-endemic countries in Sudan, Uganda, Kenya and Ethiopia. The secretariat is coordinated by DNDi's Africa Regional Office in Nairobi.

We have achieved a lot together because all stakeholders are involved from the beginning in the LEAP platform activities, including priority-setting, clinical trials, capacity strengthening and dissemination of results. Including investigators and clinicians

in decision-making has ensured a strong ownership of the platform and empowered them to initiate additional collaborations. Throughout the process, DNDi and LEAP have worked with regulatory authorities and Ministries of Health. This has helped their understanding of the issues and patient needs, ensuring LEAP efforts are aligned with programmatic needs and, if successful, resulting in an easier uptake of results into policy. Our first clinical trial of SSG&PM combination yielded excellent results and has been incorporated into the revised guidelines of some of the LEAP countries.

Over the years, we continue to have some challenges. Patient access treatment challenges persist and the platform must continue to work with Ministries of Health and affected communities to ensure SSG&PM is purchased for all VL patients. In order to avoid the lengthy regulatory approvals processes seen in some countries, further capacity building is important for ethics and drug regulatory authorities and regulatory harmonization within the LEAP countries to become possible. By joining efforts and engaging the scientific community and regulatory authorities regionally, LEAP has overcome political and cultural differences to define a regional strategy for alleviating the burden of visceral leishmaniasis (VL) in eastern Africa. The platform has enabled efficient translation of research into policy by giving ownership to its members and promoting communication and exchanges of information and skills across borders

Looking to the future, LEAP has recently undergone restructuring dubbed LEAP 2.0. This means that LEAP has an Advisory Committee and can now work in other forms of leishmaniasis- Post Kala Azar Leishmaniasis (PKDL) and cutaneous leishmaniasis. Other new areas include basic science research. vaccines, epidemiology, vector and disease control, diagnostics, access to treatments, sharing of expertise. will continue to provide a solid clinical research environment, fostering ongoing collaborations and encouraging and mentoring young scientists. In addition, we would like to offer improved infrastructure to ensure capacity at a regional level, such as for Phase I studies, pharmacovigilance studies and data collection and analysis. We envisage to have other countries like Eritrea, Somalia and South Sudan join the platform.

I take this opportunity to thank all of you, stakeholders, our governments and the newly created LEAP Advisory Committee.

HAPPY BIRTHDAY LEAP!!

Thank you DNDi and donors who have stood by us and supported us for so long. Together we shall continue the search for improved treatments for the neglected leishmaniasis patients.

Word from the LEAP Chairperson

A wake-up call!- Rekindling commitment for R&D targeting cutaneous leishmaniasis





PROF. ASRAT HAILU ADDIS ABABA UNIVERSITY

As we release the sixth issue of the Leishmaniasis Eastern Africa Platform (LEAP) Newsletter, I would like to draw your attention specifically towards cutaneous leishmaniasis (CL), a form of leishmaniasis that continues to be neglected especially in eastern Africa. With the launch of LEAP 2.0 last year, we are beginning to pay more attention to CL in the region.

Overall, the eastern Africa region bears a high burden of leishmaniases. The diseases are transmitted by infected female sand-flies. Both CL and visceral leishmaniasis (VL) are widely prevalent, albeit at varying magnitudes. VL is found in Eritrea, Ethiopia, Kenya, Somalia,

South Sudan, Sudan and Uganda. Countries endemic for CL are Eritrea, Ethiopia, Kenya, and Sudan. Presently, eastern Africa reports the highest number of VL cases in the world, with nearly 40,000 patients estimated yearly.

CL remains a huge health problem specifically in the highlands of Ethiopia, Kenya and Sudan with an incidence of over 20,000 patients each year. This disease causes mutilating skin lesions, with clinical variants that are untreatable by existing anti-leishmanial drugs. The lesions are stigmatizing and psycho-socially demeaning.

Research and development (R&D) efforts by DNDi and translational researches carried out by LEAP have brought paradigm shifts in how VL patients are treated even though they are still far from ideal. Sadly, when it comes to CL, there isn't a single effective treatment and there are no promises that one will be available soon. Due to the multitude of species that cause CL, more than one treatment is needed. People's livelihoods and how they interact with nature are important determinants of disease transmission and are thus part of the problem causing control tools to be limited.

The task of control or eradication of CL is huge and will need multisectoral engagement. Public health responsiveness is a collective responsibility of scientists, health workers, funders, policy makers and multi-lateral organizations.

The Ministries of Health in Ethiopia, Kenya, Sudan and Uganda have set up control programs. This is remarkable progress in itself; however, the lack of an effective treatment for CL has rendered the programs ineffective. R&D efforts should be enhanced to facilitate the process of vaccine and drug discovery. Let us join forces to sketch an R&D agenda so that the neglect can be halted.

Prof. Asrat Hailu

Addis Ababa University

11th DNDi Partners' Meeting celebrates African leadership in innovation for R&D and access to medicines

PUBLISHED IN DND/ E-NEWS ON 17 OCTOBER 2018



The Prime Minister of Uganda, the Right Honourable Dr Ruhakana Rugunda, who called the meeting a "true testament of collaboration and partnership for neglected patients"

On 4 October 2018, DNDi held its 11th Partners' Meeting in Kampala, Uganda. The meeting gathered together more than 400 partners and stakeholders from over 150 institutions and more than 40 countries, primarily African.

The event celebrated African leadership in innovation for R&D and access to medicines and was the first of several events planned to mark the occasion of DNDi's 15th anniversary. Panel discussions highlighted the importance of partnerships and the continuing need to break new ground in Africanled R&D, harmonized regulation, and health access strategies for neglected patients that would ultimately provide a template for universal health coverage.

The meeting was opened by the Prime Minister of Uganda, the Right Honourable Dr Ruhakana Rugunda, who called the meeting a "true testament of collaboration and partnership for neglected patients" and reiterated his own government's commitment to supporting the search for improved treatments for neglected diseases and patients.

The Prime Minister's remarks were prefaced by the Honourable Sarah Opendi, Minister of State for Health, Uganda.

A powerful keynote was delivered by Dr Kelly Chibale, Director of the H3D Centre, the drug discovery institute at the University of Cape Town University, who was recently named by Fortune magazine as one of the top 50 global leaders for 2018. In conversation with Dr Nick White, Chair, DNDi Scientific Advisory Committee, Dr Chibale set the tone for the day with his call for innovation in Africa, by Africa, for Africa and for the world.

A ministerial panel comprising Dr Henry Mwebesa, Director-General Health Services, Ministry of Health, Uganda, Dr Rashid Abdi Aman, the Chief Administrative Secretary, Ministry of Health, Kenya, and the Honourable Abdelhakim Hassan Nugud Salih, the Minister of Health, Gedaref State, Sudan spoke about the urgent need for improved treatments for neglected tropical diseases and for children living with HIV, and their work to increase treatment access and reach elimination goals in their respective countries.

The Partners' Meeting was the culmination of several days of disease-specific meetings in Kampala and benefited from summary presentations on the progress, challenges and current priorities of several, including: the 25th Leishmaniasis East Africa Platform (LEAP) Meeting; the 5th Joint human African trypanosomiasis Platform-East Africa Network for Trypanosomiasis Scientific Meeting; a meeting of the Onchocerciasis Network; and the first meeting of the Paediatric HIV Network.

Other panels included perspectives from three Eastern African countries on enhancing medical research capacities and a lively conversation among eight speakers, moderated by DNDi Board Chair Dr Marie-Paule Kieny and Executive Director Dr Bernard Pécoul, on building an enabling environment to enhance Africa's R&D and regulatory capacities.

For more information go to: https://www.dndi.org/2018/media-centre/news-views-stories/news/dndi-11th-partnersmeeting/





The Meeting AT A GLANCE



417 stakeholders and partners attended



159 institutions from all over the world represented



42 countries represented



Over 10 different meetings held through the



Over 25 key speakers in 6 key sessions









- 1. Over 400 participants drawn from partner organizations attended the meetings.
- 2. Representatives of the health ministries of Uganda, Kenya and Sudan, and the DNDi leadership team greet the Prime Minister of Uganda, the Right Honourable Dr Ruhakana Rugunda.
- 3. Dr Bernard Pécoul, DND*i* Executive Director gives his welcome remarks.
- 4. Prof. Kelly Chibale of University of Cape town, South Africa (left) and Prof Nick White, Chair of DNDi Scientific Advisory Committee discuss innovations in health Research and Development for Africa.
- 5. Dr Nilima Kshirsagar National Chair Clinical Pharmacology, Indian Council of Medical Research, New Delhi gives her feedback at the event.
- 6. Participants during the 25th LEAP Platform Meeting.



Pharmacokinetics made simple

BY THOMAS P.C. DORLO, PHD

Pharmacokinetics (PK) is generally regarded as a pivotal component of drug development. Unfortunately, its concepts and its underlying mathematics are often regarded as 'difficult' by the uninitiated and it is therefore often neglected or ignored. This is a pity because these concepts are the basis for how we should dose and treat patients.

The term pharmacokinetics originates from the Ancient Greek words pharmakon "medicine" and kineticos "moving". In simple terminology, pharmacokinetics is a study of the movement of a drug through the body. Typically, we characterize with pharmacokinetics the whole journey from ingestion of the drug until reaching the site where the drug molecule exerts its action.

Medicines are like chocolate cake

Let's compare the lifetime of a drug in the body to eating a chocolate cake. After a bite of a delicious chocolate cake, the cake ends up in your stomach and eventually in your intestines. From there, your body starts absorbing the important nutrients in the cake, mainly sugar and fat. After absorption, the body distributes these nutrients to different tissues such as muscles, brain, etc. Within these tissues the nutrients are being converted by the body into energy, adipose tissue, among others. Leftover nutrients are eventually eliminated from the body.

The fate of a drug is not any different: after you swallow a pill, it is transferred to your stomach where it will fall apart. The drug dissolves slowly within the gastrointestinal tract and your body starts absorbing it. Once absorbed, the drug is distributed to different tissues in the body. Take leishmaniasis for example, we want the drug to be distributed to liver, bone marrow and spleen where the parasites are located. The body usually recognizes, however, that the drug molecules are foreign and tries to get rid of them: particularly in the liver. Drug molecules are therefore converted into other molecules, called metabolites, that are easier to be eliminated from the body. These metabolites are then transported to the kidneys to be excreted.

Math and pharmacokinetics

Pharmacokinetic scientists use mathematical equations to describe all the separate processes in the body described above. Drug concentrations in the body are often measured in blood, since that is relatively easy to sample from patients. These drug concentrations in the blood depend mainly on 4 things: how much drug the pill that a patient has taken contains, the time since that pill was swallowed, the rate with which it is being absorbed from the gut, and the rate with which the drug is being eliminated from the body. These rates define how the drug moves through the body and the mathematical formulas make sure that they can be estimated and characterized for each patient.

We can practically use pharmacokinetics data to design the regimen for a treatment or adapt the dosing for some specific patient population. One example is the miltefosine study that DNDi and LEAP partners have implemented in Kenya and Uganda, that helped us understand how to better treat children affected by VL. This research can be found at

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ ciy747/5090844.







Creating a culture of quality within clinical trials:

BY GODFREY NYAKAYA

Clinical Trial: Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), with the object of ascertaining its safety and/or efficacy.

Quality: The absence of errors that matter to decision making—that is, errors which have a meaningful impact on the safety of trial participants or credibility of the results.

linical trials are designed to Cinvestigate and provide solutions to health problems affecting our communities thus reduce disease burden and improve the quality of life. With colossal investment in time and cost, and with high risk involved, quality remains paramount in clinical trials, at all stages - design, conduct, recording and reporting stages. Good clinical Practices (GCP) is an international quality standard that has been set to ensure that clinical trials are conducted with undeniable quality, human subjects are protected, and reliability of trial results are made the main focus.

DNDi conducts clinical trials in remote settings and it is therefore important to identify and promote practices that will increase and sustain the quality of the conduct of clinical trials among all stakeholders involved. There are a number of quality aspects that can be adopted to create a culture of quality within clinical trials:

- Involving investigators in protocol development and discussions around quality. This is aimed at integrating quality procedures into the design of the trial and avoiding possible errors at the protocol design phase.
- creating an environment that that goes beyond sole dependence on set tools and checklists. This is done by enhancing critical thinking and dialogue on quality issues. Proactive dialogue and development of methods that ensure quality should be encouraged while overreliance on checklists and inflexible "one size fits all" approach discouraged.
- The focus on activities essential to the credibility of the study outcomes is vital. This is best with a risk-based approach that emphasizes on most critical areas and those that require attention first. These activities would include training, personnel roles and responsibilities, policies and procedures standardization, trial monitoring, auditing, periodic quality meetings, conferences and seminars on specific areas

of interest, record retention, corrective and prevention actions and trial oversight both at sponsor level and Principal Investigator level.

To achieve these, it is important to define standard procedures. In practice, this can be in the form of standard operating procedures, controlled work instructions, or policies. Both the investigator and the sponsor should embrace these procedures to enhance the quality of the trial. Additionally, the role of Ethics Committees cannot be overemphasized. Approvals of the protocol, informed consent documents, advertisements or other information given to subjects must be sought and reports generated by the investigator as appropriate in their jurisdictions.

The launch of AfriKADIA: partnerships towards better treatments for visceral leishmaniasis

By Christina Sander



In April 2018, a group of institutions gathered in Addis Ababa Ethiopia to launch the AfriKADIA consortium whose main objective is to find improved treatments and diagnostic tools for visceral leishmaniasis (VL) in eastern Africa.

This large-scale Phase III clinical trial aims to deliver a new, efficacious treatment regimen for VL – replacing the sodium stibogluconate toxic component of the current SSG-PM 17 days with oral miltefosine and paromomycin.

LEAP Platform members – the Kenya Medical Research Institute in Kenya, Institute of Endemic Diseases, University of Khartoum in Sudan, University of Gondar in Ethiopia; Makerere University in Uganda; London School of Hygiene & Tropical Medicine in the United Kingdom, Foundation for Innovative New Diagnostics in Switzerland, Drugs for Neglected Diseases initiative (DNDi), Academic Medical Center at the University of Amsterdam, Instituto de Salud Carlos III in Spain and the Netherlands Cancer Institute (NKI), are members of this new consortium.

In January 2018, the AfriKADIA consortium, begun a clinical trial to find a safer, efficacious and more patient-friendly treatment for people with visceral leishmaniasis (VL). The clinical trial and diagnostic study is taking place in Ethiopia, Kenya, Sudan, and Uganda.

This large-scale Phase III clinical trial aims to deliver a new, efficacious treatment regimen for VL – replacing the sodium stibogluconate toxic component of the current SSG-PM 17 days with oral miltefosine and paromomycin. The study will be

implemented over three years and enrol 576 patients.

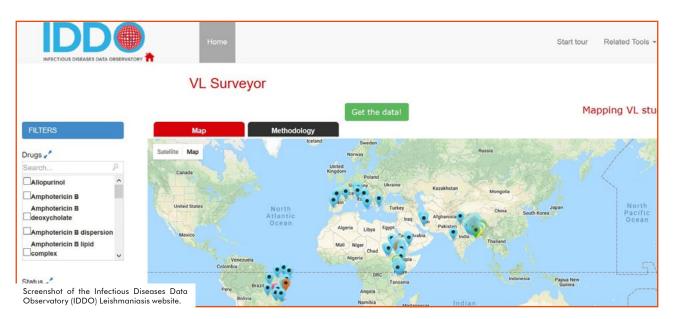
The clinical trial and diagnostic study is taking place in Ethiopia, Kenya, Sudan, and Uganda.

The study will run hand-in-hand with an assessment of innovative non-invasive diagnostic tools in managing VL cases within routine patient care. Both the clinical trial and the diagnostic studies aim to fill gaps that will directly impact VL diagnosis and treatment in eastern Africa. Strengthening clinical trial capacity is also an integral part of AfriKADIA's mission.

This project is part of the European & Developing Countries Clinical Trials Partnership (EDCTP)2 programme supported by the European Union under Horizon 2020, its Framework Programme for Research and Innovation.

Embracing the VL online data sharing platform to strengthen NTD research

By Michael Otieno



The integration of patient data from visceral leishmaniasis (VL) clinical trials, into a newly established online platform will enable scientists and clinicians to pool data from different clinical trials in order to enhance the statistical power, address knowledge gaps and save patient lives with better treatment.

A systematic review of published literature, published in *PLOS Neglected Tropical Diseases*, identified 145 VL clinical trials conducted over the last three decades. The trials enrolled nearly 27,000 patients, the majority in the last 15 years.

Building on the findings of the review, and with funding from the Wellcome Trust (a global charitable foundation, supporting scientists and researchers, take on big problems globally), the Infectious Diseases Data Observatory (IDDO) has been working with Drugs for Neglected Diseases initiative has and the Leishmaniasis East Africa Platform to establish a dedicated VL data platform.

The platform was officially launched at the 6th World Congress on Leishmaniasis, held in Spain in 2017. It

A systematic review of published literature, published in *PLOS Neglected Tropical Diseases*, identified 145 VL clinical trials conducted over the last three decades. The trials enrolled nearly 27,000 patients, the majority in the last 15 years.

enables researchers to securely share collated data, so they can be curated and provided for analysis, ultimately enhancing their potential to fill key knowledge gaps that have been an obstacle in understanding the diagnosis and treatment of the disease.

The vision of the data sharing platform goes beyond sharing data from past trials to supporting researchers with tools that enable them to effectively utilise the available data. This includes interactions with the community through workshops, training and symposia.

It is for this reason that in January 2018, the partners organised a workshop for early career researchers facilitated by a team of data management and statistics experts from the DNDi Data Center, IDDO, the University of Cape Town and Strathmore University to share data management skills and expertise.

Members of the research community have been invited to contribute data to the VL platform using the secure online submission portal on the IDDO website. Once data have been curated, contributors may be invited to form or join collaborative study groups which take advantage of the common data formats to perform pooled analyses. The setting up of the VL platform is informed by the lessons from World Wide Antimalarial Resistance Network, a data platform developed for malaria that is now part of IDDO.

Find out more at iddo.org/vl or email info@iddo.org



LEAP platform strengthens capacities of healthcare workers to fight kala-azar in eastern Africa.

By Danyell Odhiambo

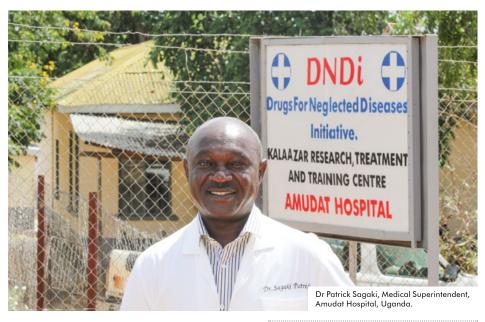
The road to finding better medication for the grossly neglected disease kalazar, is marred by a myriad of challenges that health workers working in the region know too well.

Driving across the two kalaazar clinical trials sites in Amudat (Uganda) and Kacheliba (Kenya), you will encounter three distinctive features. First, you will be greeted by towering anthills peeping beneath the thick acacia canopies. Second, are the manoeuvring of gaping potholes along the dilapidated road network, that is proof of the neglect in this region and third is the visible absence of healthcare centres in the vicinity.

For these prevailing situations to be tackled and clinical trials conducted, it is imperative to strengthen the capacity of select remote facilities and health workers in the region. This is part of the mandate of the Leishmaniasis East Africa Platform (LEAP) for the past fifteen years. LEAP has been on the frontline striving to build robust and sustainable clinical research capacity and delivery of new treatments for patients suffering from kala-azar.

Dr. Patrick Sagaki, who is in charge of the Amudat District hospital in northern Uganda has benefitted from the capacity building process and this has enabled him to not only participate in high level global clinical trials but also effectively manage the hospital. His journey begun in 2007.

"At that time, we were facing a crisis that was brought about by capacity gaps to effectively handle



kala-azar cases. Luckily, LEAP came to our rescue by facilitating our maiden training on diagnostics, treatment and management of kala-azar complications," he re-counts.

Having interacted with kala-azar patients for the past 14 years at the Amudat hospital, Sagaki admits that the paradigm shift witnessed in the effective service delivery is majorly attributed to the staff trainings.

"By investing in staff skills, DNDi and LEAP has helped patients access comprehensive quality healthcare services in the region," he says.

Dr. Sagaki has also been able to pursue a fully-funded graduate programme abroad through LEAP support. "I felt so motivated when I was accorded the rare opportunity to study tropical medicine in Thailand. As part of the study experience I broadened my understanding of tropical diseases particularly kalaazar," he states.

The training enhanced his ability to make more informed decisions while supporting diagnosis, treatment

W By investing in staff skills, DNDi and LEAP has helped patients access comprehensive quality healthcare services in the region," says Dr. Sagaki.

and management of kala-azar complications and also bolstered his capacity to participate in the kala-azar clinical trials.

"By strengthening Kala-azar interventions, we weaken its impact on the affected populations through finding treatments and diagnostic tools that are safer, affordable and easily accessible," he concludes. To date, LEAP supported over 800 short-term and 20 long-term trainings across the region.



HIV-VL patient remains hopeful despite difficulties of treatments

By Linet Otieno



Nigatu Abebe's story describes the state of a person caught between a rock and a hard place. He is a middle-aged man fighting two battles; Leishmaniasis and HIV infection. These two diseases have ravished him for the past 11 years. In the process he has had four relapses, lost his source of income and has experienced stigmatization from friends and colleagues.

His desperate search for treatment recently took him to the Leishmaniasis Research and Treatment Centre (LRTC) at the Gondar University Hospital. The LRTC was constructed by DNDi to strengthen the capacity of Gondar University Hospital in conducting clinical trials but now also supports treatment of patients in the region.

#I had to travel to Gondar all the way from Sudan to receive treatment. This was very costly for me"

"I had to travel to Gondar all the way from Sudan to receive treatment. This was very costly for me," he says.

Nigatu contracted VL for the first time in 2007 while working as a Farm Labourer in Abdurafi in the North-Western part of Ethiopia. Ignoring his symptoms, he only went to hospital four months later when he was already very frail and weak. He sought his first treatment at the Abdurafi Hospital where he was diagnosed with both diseases.

// I cannot stop seeking treatment despite the difficulties. I have to do this for me and my family"

He was later treated with sodium stibogluconate for VL and then provided with ARVs for HIV treatment. Two years later, he relapsed and went back to hospital. This time, he was given a treatment combination of Miltefosine and Ambisome.

His health greatly improved and for over six years he lived normally, even travelling as far as Sudan to work. His economic situation also significantly improved. However, after his most recent relapse a few weeks back, he has almost spent all his savings.

In Gondar, he has been receiving treatment combination of miltefosine and Ambisome; which is currently the preferred treatment for HIV-VL co-infection. Following a research conducted by DNDi, it was found that the efficacy of the combination increased with extended treatment. HIV-VL remains difficult to treat but patients like Nigatu are hopeful that they can live for many more years with this treatment.

A determined Nigatu poses his last remarks as he walks into the health facility for his routine checkup.

"I cannot stop seeking treatment despite the difficulties. I have to do this for me and my family."



Down but not out: Loteroi sees a bright future for kala-azar patients despite his state of visual impairment

By Danyell Odhiambo

Forty-five-year-old, visually impaired father, Lwalatta Loteroi, throws random blank stares upon hearing footsteps approaching the hospital bed where he is seated. He has been blind since birth. It

is two weeks since his youngest son, two **//**I am grateful to the and a half-year-old Lorus Tuliamúk, was admitted at the kalaazar ward of Kacheliba care and treatment offered sub-district hospital to my son. My only worry in West Pokot County, Kenya.

the continuous pain associated Oblivious of looming danger, it is a with the daily treatment common occurrence to see children like injections" Tuliamuk playing giant around the

anthills or leaning against the hollow tree trunks that harbor female sandflies. It is in such places that they get exposed to kala-azar after experiencing bites from infected sand flies.

The sight of Tuliamuk's abnormally swollen stomach indicates an enlarged spleen. A condition brought about by the leishmania parasites infecting the internal body organs, particularly the spleen.

"My distress began the moment

my son started showing symptoms of high fever, coughing, loss of appetite and loss of weight. Coincidentally, this happened during a tough time when my pregnant wife also due for delivery," he briefly pauses and rubs the back of his

health workers for the

now is how to control the

whimpering

"We rushed Tuliamuk to a local health clinic where he was treated for malaria and typhoid but his condition kept worsening. It is a good Samaritan, previously treated for

kala-azar here, who referred us to this hospital," he says.

Fortunately, Tuliamuk is already out of danger after undergoing treatment.

"I am grateful to the health workers for the care and treatment offered to my son. My only worry now is how to control the continuous pain associated with the daily treatment injections,

States Loteroi as he firmly grips a long stick he uses as his guiding cane.

Despite his condition, Loteroi remains high-spirited and optimistic that kalaazar patients will one day have an oral treatment. This may be closer than he is aware since in 2018, DNDi and partners begun a clinical trial to assess the efficacy and safety of a combination of oral miltefosine (MF) and injectable paromomycin (PM) in treating kala-azar. If found to be efficacious, introducing this novel combination will significantly reduce the difficulty in treatment administration and lengthy hospital stays for patients like Tuliamuk. This significant study is taking place in four eastern Africa countries; Ethiopia, Kenya, Sudan and Uganda.

There is even more good news for patients with new oral chemical entities moving into the clinical phase of development. If this phase succeeds, studies to evaluate their efficacy could be conducted in eastern Africa in the next few years.



Amudat Governor advocated for the start of kala-azar treatment in the region

BY JOY MALONGO



Kiyonga Francis Adamson is a governor at the amudat local government and the district chairperson. He was also a member of parliament from 1996-2001 and 2006-2010. He was crucial in bringing attention to neglected kala-azar patients in his region and ensuring they received treatment.

What would you say about kala-azar treatment in the Amudat region?

I cannot emphasize the gratitude that this community has for the kala-azar project supported by DNDi. Medecins Sans Frontieres (MSF) started working on kala-azar here in 1997, people were dying, and the government did not even know that this disease existed. In my family, we lost three girls between 1992 to 1995. Now, this has improved. I have not heard of cases of death from kala-azar reported recently, and for this, I appreciate DNDi, who took over from MSF, and its partners.

What are the current challenges faced by kala-azar patients here?

While there has been great improvement in kala-azar treatment, there are two things that remain as challenges. First, there is insufficient interest for kalaazar patients. I look forward to a time where a budget would be provided at the national level to support treatment of kala-azar. Second, structures and facilities dedicated towards kala-azar are lacking. The renovated and new

structures that have been put up here in Amudat Hospital around outpatient department and the kala-azar ward by MSF and DNDi have been pivotal to patient care but more is required.

How did kala-azar treatment begin in this region?

In 1997 I traveled to Bunia, a town in the Democratic Republic of Congo (DRC). I was heading to Sudan to study how the resettlement of refugees was taking place since we were planning to resettle refugees who were in Kenya back into Uganda. While in DRC, I met an MSF team treating kala-azar. I interacted with them and told them that the disease was affecting patients in Amudat but treatments were not available. Patients had to travel across the border in Kenya, many kilometres away to get treatment. To do this, they had to sell three to six cows. Many people were therefore dying because they could not afford the treatment.

After my trip, I took time to persuade the Church of Uganda which owns Amudat Hospital that we needed the facility to focus on treatment of kalaazar. Thereafter we negotiated with the government and to change the

policy and accept NGO support for hospitals. Finally, MSF came to Amudat and discovered that the disease covered the whole region including neighbouring Kenyan town of Kacheliba and Baringo further on.

Do you think research is crucial for kala-azar patients?

Research is very crucial for kalaazar patients and we as a community are always open to paticipate in and support research activities. We know that research conducted here in Amudat by DNDi and others has put Uganda on the global map. We want to offer the sponsors and the scientists an enabling environment to conduct research in this institution. The local leadership will give this support to benefit the community here.



Towards winning the VL war in South Sudan against emerging challenges

BY LINET OTIENO AND DANYELL ODHIAMBO



Lexson Mabrouk Manibe is the Director for Case Management for Neglected Tropical Diseases (CM-NTDs) programme at the Ministry of Health, South Sudan. His office focuses on two Neglected Tropical Diseases: sleeping sickness and visceral leishmaniasis (VL). On 3rd May 2018, Mr. Mabrouk visited DNDi Africa Regional Office (ARO) in Nairobi to discuss potential LEAP collaboration with partners from South Sudan.

What are some of the key highlights of VL in South Sudan?

Four states in the eastern region of South Sudan are regarded as VL endemic areas. These states are Eastern Equatorial, Jonglei, Upper Nile and Unity. The health facilities in these states are in very remote and inaccessible locations. Some villages are literally cut off by the dilapidated road network. During the rainy season, the few earth roads are normally flooded and rendered impassable. Due to the unpredictable security situation in the country, we are sometimes forced to relocate or abandon established health There was a major outbreak in the number of VL infections between 2008 and 2009. As a result of this crisis, we brought together partners and relevant actors in government and established the CM-NTDs unit.

How would you describe the current burden of the disease?

Going by the data available, in 2017, 2,722 cases including 56 deaths were reported from 23 treatment centres in the country. Majority of these patients were children between the ages of five and 14 years old. This year, 273 cases including 6 deaths have been reported from 14 treatment centres between January to April 2018. Out of the 273 cases reported, 222 were new cases and seven were PKDL cases.

What are your key milestones in the management of VL in South Sudan?

I have two major things that I am proud of. We have enhanced capacity building through training health workers in the remote facilities on prompt diagnosis and effective treatment. I am also glad to mention we have introduced Direct Agglutination Test (DAT) testing in National Public Health Laboratory (NPHL) for diagnosis of VL.

On the flipside, what are the major challenges in the management of VL in the country?

Although we have made significant progress, our greatest challenge remains lack of adequate capacity to diagnose, treat and manage VL related complications. Unfortunately, our efforts to build capacity have further been paralyzed by high staff turnover. Another major hindrance is the recurrent insecurity situation being experienced in the country. This has affected the delivery of urgent medical supplies and retention of skilled manpower. We also lack reliable data to support some of the critical research and development interventions.

In conclusion, what would be your way forward or recommendation about existing treatments and diagnosis?

We would like the support of DNDi and LEAP to do a comprehensive situational analysis. This is to help identify the needs and the state of existing health facilities, skills and equipment in the field sites to effectively perform recommended diagnostics and treatment.



LEAP portal offers a platform for consistent interaction among members

By Joy Malongo

Over the past 15 years, LEAP has supported capacity building initiatives and clinical trials for new kala-azar treatments across the eastern Africa region. To do this, LEAP has conducted a number of meetings, events and trainings. There is need to document and evaluate these efforts more effectively. As part of the movement towards LEAP 2.0, DNDi has invested in building a community portal that will support the automated management of events and controlled access to internally stored resources.



Those who have access to the portal will be able to register for upcoming events posted online and also discuss/exchange views and opinion. The goal of the community portal is to connect/establish a strong link between DND*i* and its partners and make them grow together.

VL clinical trial results disseminated to communities and stakeholders in Ethiopia and Kenya

By Joy Malongo

Community and stakeholder engagement is an important element of the successful translation of research.

Towards achieving this, DNDi, organized community meetings in May 2017 in Amudat, Uganda and Kacheliba, Kenya to share the findings of the LEAP 0714 clinical trial which was conducted to determine the appropriate dosage for miltefosine for children under twelve years.

In the same year (June 2017), another meeting was held in Addis Ababa, Ethiopia, where findings from the LEAP 0511, a clinical trial testing treatment for patients with VL and HIV co-infection, were disseminated to government officials from Ethiopia,



Kenya and Sudan, World Health Organization representatives, Ethics Committee representatives, researchers, and regulatory officials.



Renewed hope for PKDL patients in Sudan as DNDi and its partners embark on a clinical trial to find shorter course treatment

By Linet Otieno



In May 2018, DNDi and the Institute of Endemic Diseases (IEND) begun a clinical trial to find a better treatment for severe cases of Post Kala-azar Dermal Leishmaniasis (PKDL), in Sudan. The objective of this clinical trial is to deliver a treatment which is safer to use and easy to administer. PKDL is a non-lethal form of visceral leishmaniasis (VL) which usually develops after VL treatment.

The current treatment for PKDL in eastern Africa is sodium stibogluconate (SSG), an expensive and fairly toxic drug administered through injections for 40-60 days. SSG is also impractical, as it is an injectable drug that needs to be administered under close supervision in a hospital setting, due to its side effects.

The trial, which targets to enrol 110 participants, will assess the safety and efficacy of two treatment combinations. The first is Paromomycin, an injectable treatment used in combination with SSG to treat VL in eastern Africa with Miltefosine, the first oral treatment for leishmaniasis currently used in Asia for PKDL treatment. The second treatment arm is of Ambisome, second-line treatment for VL in eastern Africa combined with Miltefosine.

LEAP Member, Prof Khalil recognized as Immunologist of the Month

Prof. Eltahir Khalil, a member of LEAP, was recognized by Immunopaedia, as the December 2017 Immunologist of the Month. Immunopaedia is a non-profit educational website which aims to promote cutting-edge knowledge and research in basic and clinical immunology worldwide. The Immunologist of the Month is awarded to a person at the cutting-edge of research and education. Prof Khalil was celebrated for his immense positive contribution in research on vaccines for VL, Latent Tuberculosis (TB) infections and Hepatitis B immunotherapy that have impacted the field of immunology.



CONGRATULATIONS TO PROF. KHALIL ON THIS ACHIEVEMENT.



PROF. ELTAHIR KHALIL
IMMUNOLOGIST OF THE MONTH





Kenyan Ministry of Health launches new leishmaniasis guidelines

By Joy Malongo

On February 28th, 2018, the Ministry of Health launched the revised Kenya National Guidelines on Prevention, Diagnosis, and Treatment of Leishmaniasis in Kenya at the Silver Springs Hotel in Nairobi.

In a speech read by Dr Anne Wamai, Head of Quality Assurance, Standards and Regulation on behalf of Dr Jackson Kioko, the Director of Medical Services he reiterated the government's collaborative commitment in combating the kala-azar through finding better treatments.

Dr. Monique Wasunna, the Director, DNDi Africa Regional Office commended the participatory process, which involved stakeholders, adopted in reviewing the guidelines. "The process of coming up with the guidelines was an illustration of the results that can be realized through partnerships and collaborations by many individuals, institutions, organizations, and partners".

DHIS2 training to help shape new health record management systems in Kenya

By Danyell Odhiambo

In June 2018, DND*i* joined officials from Kenyan Ministry of Health and the World Health Organization (WHO) in Machakos County, eastern Kenya, for a five-day training on the District Health Information System (DHIS2). DHIS2 is a free and open source data platform used to manage health information.

This training was geared towards identifying key gaps and emerging opportunities in the implementation of the data management tool that was piloted in 2017 for VL data management. By embracing the web-based system in the management of government health records, researchers will have easy access to reliable and accurate data which has been a major impediment in the VL interventions. The training brought together about 20 government health information officers drawn from six leishmaniasis endemic counties in Kenya which was the first country in Sub-Saharan Africa to deploy an online health information system (HIS) powered by DHIS2, which was completed in September 2011.



DNDi office in Nairobi trains staff and partners on financial management

By Winfred Wangara

Embracing Good Financial Practice (GFP) is the key to unlocking effective management of funds and successful realization of the project objectives. In July 2018, the DND*i* Regional Office in Nairobi trained its staff and partners from Ethiopia, Kenya, Sudan, and Uganda on GEP to better understand the importance

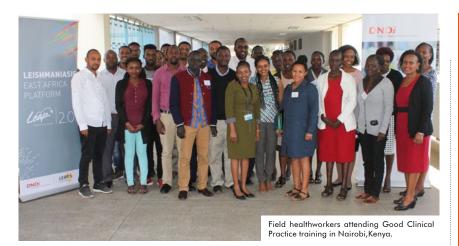
of optimal financial management in clinical research procedures.

The training, which was facilitated by facilitated by Simon Bolo the Regional Operations Leader, DNDi Africa Regional Office, enabled them to put into practice the approved standard operating procedures in the different financial processes. This includes budgeting, accounting, financial reporting and other related functions. This training was provoked by the need to strengthen DNDi's research and development infrastructure through streamlining service delivery in clinical research.



Prof. Asrat Hailu receives certificate from Dr Monique Wasunna after completing the training.





Embracing Good Clinical Practice: The global hallmark in conducting clinical trial procedures.

By Danyell Odhiambo

A functional group of five gathers at one corner of a meeting room at the Kenya AIDS Vaccine Initiative Institute of Clinical Research (KAVI-ICR) in Kenya. The task assigned is to discuss and compile a list of documentation required in a successful clinical trial. The group represents a section of the 26 participants drawn from Kenya, Uganda, Sudan and Ethiopia attending a two-day training on Good Clinical Practices (GCP) from May 28, 2018. Drugs for Neglected Diseases initiative (DNDi) through the LEAP platform sponsored the training which was facilitated by clinical trial experts from the KAVI-ICR institute.

Dr. Eleni Ayele, from Leishmaniasis Research and Treatment Centre at the Gondar university hospital in Ethiopia, participated in this exercise for the first time. "I'm optimistic that the GCP training will present me with a chance to not only expand my knowledge and skills but also handle study participants appropriately."

DNDi participates in the 8th KEMRI Annual Scientific and Health

Conference

By Linet Otieno

DND*i* participated in the 8th KEMRI Annual Scientific and Health [KASH] Conference held on 14th – 16th February 2018. KASH is an annual meeting that brings together scientists to disseminate, share outputs from scientific research and highlight planned activities. This year's conference was themed **'Health Research and Sustainable Development'**. DND*i* hosted a symposium titled **DND***i* Fifteen Years Later – What We have achieved, challenges and lessons learnt. This symposium highlighted crucial milestones by DND*i* since its inception. The symposium also included a panel discussion to discuss the way forward under the theme **'What is critical in the fight of neglected diseases in the next 15 years?'** The session attracted about 100 participants drawn from the Ministry of Health, partner institutions and the media.



Officials from WHO and MOH Uganda visit Amudat Hospital

By Joy Malongo

On June 13, 2018, a team from the World Health Organisation (WHO), Uganda's Ministry of Health (MOH) and DND*i* visited Amudat Hospital, in north west Uganda.

The visit whose objective was to discuss collaboration for VL activities was led by Dr. José Postigo the Head of Leishmaniasis programme, WHO, Geneva. Others in attendance were Dr. Beshah Abate Mulugeta, WHO AFRO, Dr. Kaggwa, WHO Uganda and Dr. Alfred Mubangizi, MOH Uganda VL Programme Manager.

The visiting team was received by representatives from the Amudat local government including Mr Kiyonga Francis Adamson, the Governor, Mr Seraphine Alia, Chief Administrative Officer (CAO), Dr Patrick Sagaki, the Amudat Hospital Medical Superintendent/Officer in Charge, and Dr Gina Ouattara, DNDi Clinical Trials Manager.





'Best Partner Organization of the Year': DNDi scoops top award at University of Gondar graduation

DNDi's commitment to forge successful partnerships was recognized recently after the University of Gondar (UoG) presented the organization with the "Best Partner Organization of the Year" award during a student graduation ceremony held on 7th July 2018. The award comes against the backdrop of a longstanding relationship between UoG and DNDi since 2004 when it became part of the LEAP platform. Together, DNDi and UoG established and inaugurated the Leishmaniasis Research and Treatment Centre (LRTC) in May 2008.



THE AWARD WAS PRESENTED AT A CEREMONY ATTENDED BY SENIOR GOVERNMENT OFFICIALS, UNIVERSITY TOP MANAGEMENT, ACADEMIC STAFF AND OVER 7,000 GRADUATING STUDENTS.





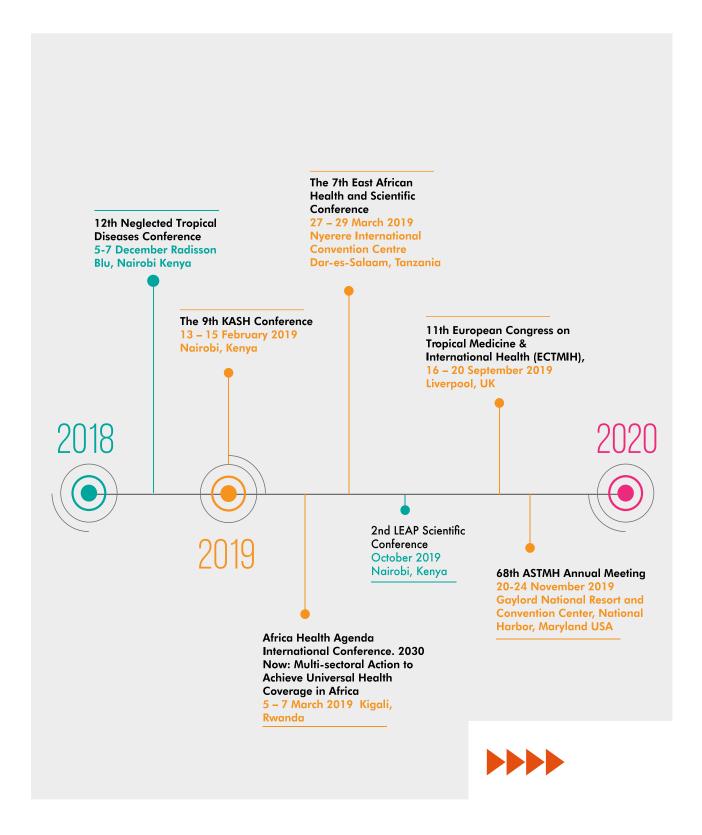


- 1. Panel discussion on access during the 25th LEAP Meeting.
- 2. Participants follow discussions at the meeting.

LEAP marks 15 years of delivering treatments to Leishmaniasis patients

A total of 73 participants, drawn from six leishmaniasis endemic countries in Africa and other countries around the world from which LEAP draws its members and collaborators gathered in Kampala, Uganda on 3rd and 4th October to attend the 25th LEAP platform meeting. With the theme; Improving access to treatments for leishmaniasis patients through partnerships, the meeting presented a forum to review the collaborative approaches that LEAP and its partners have adopted within the region and to consider future strategies towards the management of leishmaniasis. This year marked 15 years since the inception of the LEAP Platform. The leishmaniasis endemic countries represented at the meeting included Ethiopia, Uganda, Somalia, South Sudan, Sudan and Kenya which together, carry the highest burden for the disease in the world. The meeting also attracted representatives from key research organizations, academic institutions and Ministries of Health.

UPCOMING EVENTS





In the Media:



BUSINESS DAILY

Business Daily, Kenya, 6th November 2018. Neglected tropical disease, Kala-azar, takes a heavy toll

The East African

The East African, 1st November 2018. New treatments offer hope for tropical diseases in Africa

DAILY NATION

The Daily Nation, Kenya, 9th October 2018. Clinical trial seeks better treatment for kala-azar



New Business, Ethiopia, 3rd October 2018. New clinical trials for neglected diseases in Eastern Africa in progress

THE HUFFINGTON POST

Huffington Post, 20th September 2017. In Rural Kenya, Escaping A Deadly Disease Sometimes Takes A Little Luck: There are 400,000 new kala-azar cases each year, but treatment is scarce.

BUSINESS DAILY

Business Daily, Kenya, 17th July 2017. Neglected diseases that wreak havoc on northern Kenya

THE HUFFINGTON POST

Huffington Post, 22nd June 2017. Neglected "tropical" diseases: a symptom of profound global inequality



The Guardian, 18th May 2017. Hope in battle against 'deadliest disease you've never heard of': Second only to malaria as a deadly parasite, visceral leishmaniasis is a major killer – but also a key cause of poverty



VL Publications

- 1. Alves, F., Bilbe, G., Blesson, S., Goyal, V., Monnerat, S., Mowbray, C., Muthoni Ouattara, G., Pécoul, B., Rijal, S., Rode, J., Solomos, A., Strub-Wourgaft, N., Wasunna, M., Wells, S., Zijlstra, E., Arana, B. and Alvar, J. (2018). Recent Development of Visceral Leishmaniasis Treatments: Successes, Pitfalls, and Perspectives. Clinical Microbiology Reviews, 31(4). doi:10.1128/cmr.00048-18
- 2. Kip, A. E., Wasunna, M., Alves, F., Schellens, J. H. M., Beijnen, J. H., Musa, A. M., Khalil, E. A. G. And Dorlo, T. P. C. (2018). Macrophage Activation Marker Neopterin: A Candidate Biomarker for Treatment Response and Relapse in Visceral Leishmaniasis. Frontiers In Cellular And Infection Microbiology, 8. doi: 10.3389/fcimb.2018.00181
- 3. Mbui, J., Olobo, J., Omollo, R., Solomos, A., Kip, A. E., Kirigi, G., Sagaki, P., Kimutai, R., Were, L., Omollo, T., Egondi, T. W., Wasunna, M., Alvar, J., Dorlo, T. P. C. And Alves, F. (2018). Pharmacokinetics, safety and efficacy of an allometric miltefosine regimen for the treatment of visceral leishmaniasis in Eastern African children: an open-label, phase-II clinical trial. Clinical Infectious Diseases. doi: 10.1093/cid/ciy747
- 4. Alves, F., Gillon, J., Arana, B., & Dorlo, T. P. (n.d.). Chapter 3. From Bench to Bedside: Development and Optimization of Clinical Therapies for Visceral Leishmaniasis. Drug Discovery Drug Discovery for Leishmaniasis, 37-54. doi:10.1039/9781788010177-00037
- 5. Fontoura, I. G., Barbosa, D. S., Paes, A. M., Santos, F. S., Neto, M. S., Fontoura, V. M., Costa J., Silva, A. L. (2018). Epidemiological, clinical and laboratory aspects of human visceral leishmaniasis (HVL) associated with human immunodeficiency virus (HIV) coinfection: A systematic review. Parasitology,145(14), 1801-1818. doi:10.1017/s003118201800080x
- 6. Bi, K., Chen, Y., Zhao, S., Kuang, Y., & John Wu, C. (2018). Current Visceral Leishmaniasis Research: A Research Review to Inspire Future Study. Biomed Research International, 2018, 1-13. doi: 10.1155/2018/9872095
- 7. Molina, R., Ghosh, D., Carrillo, E., Monnerat, S., Bern, C., Mondal, D., & Alvar, J. (2017). Infectivity of Post-Kala-azar Dermal Leishmaniasis Patients to Sand Flies: Revisiting a Proof of Concept in the Context of the Kala-azar Elimination Program in the Indian Subcontinent. Clinical Infectious Diseases, 65(1), 150-153. doi: 10.1093/cid/cix245
- 8. Dorlo, T. P., Kip, A. E., Younis, B. M., Ellis, S. J., Alves, F., Beijnen, J. H., Njenga S, Kirigi G, Hailu A, Olobo J, Musa AM, Balasegaram M, Wasunna M, Karlsson MO, Khalil EAG. (2017). Visceral leishmaniasis relapse hazard is linked to reduced miltefosine exposure in patients from Eastern Africa: A population pharmacokinetic/pharmacodynamic study. Journal of Antimicrobial Chemotherapy,72(11), 3131-3140. doi:10.1093/jac/dkx283
- 9. Hirve, S., Kroeger, A., Matlashewski, G., Mondal, D., Banjara, M., & Das, P. Be, A. N., Arana, B., Olliaro, P., (2017). Towards elimination of visceral leishmaniasis in the Indian subcontinent—Translating research to practice to public health. PLOS Neglected Tropical Diseases, 11(10), e0005889. doi: 10.1371/journal.pntd.0005889
- 10. Rahman, R., Goyal, V., Haque, R., Jamil, K., Faiz, A., Samad, R., Ellis, S., Balasegaram, M., Boer, M. D., Rijal, S., Strub-Wourgaft, N., Alves, F., Alvar, J. & Sharma, B. (2017). Safety and efficacy of short course combination regimens with AmBisome, miltefosine and paromomycin for the treatment of visceral leishmaniasis (VL) in Bangladesh. PLOS Neglected Tropical Diseases, 11(5), e0005635. doi: 10.1371/journal.pntd.0005635



Amudat Hospital: A partner in LEAP since 2006

Amudat Hospital is a 120-bed private not for profit hospital started in 1957 by the British missionaries. It was handed over to the Church of Uganda in 1972. The hospital operates as a rural mission health facility under the Church of Uganda and serves as a field site for clinical trial studies implemented by DNDi. This is the only kala-azar diagnostic, treatment, training, and research centre in Uganda. The hospital serves a population of over 200,000 people from both Kenya and Uganda since it is along the borderline.





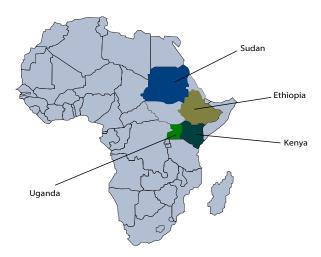


- Prof. Eltahir Khalil engages Dr Monique Wasunna and Joy Malongo in a discussion during a recent courtesy call in Nairobi, Kenya.
- Health-workers drawn from VL endemic counties in north western Kenya attending a training workshop on treatment and diagnostics in Lodwar, Turkana County, Kenya.
- DNDi supports Kacheliba District
 Hospital in West Pokot County, Kenya
 in acquiring a new vehicle to improve
 access to VL treatment.



Makerere University Facts:

- One of the oldest and most prestigious universities in Africa.
- It was established in 1922 as a technical school and became an independent national university in 1970.
- The College of Health Sciences (MakCHS) was established in 1924 as Makerere University Medical School.
- Joined the LEAP Platform in 2006 represented by Prof. Joseph Olobo.





Leishmaniasis East Africa Platform (LEAP)

LEAP - is a clinical research network that brings together experts from leishmaniasis endemic eastern African countries to facilitate clinical testing and improved access to better treatments for leishmaniasis in the region

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