REPORT ON THE SYMPOSIUM ON INNOVATION FOR ACCESS TO TREATMENT FOR NEGLECTED DISEASES

Held at the ASTMH, KASH Conference

Date: February 9th 2016
Venue: The Boma Hotel, Nairobi

DNDi AFRICA
Drugs for Neglected Diseases *initiative*

OVERVIEW

As one of its strategies towards advancing access to treatment for neglected tropical diseases (NTDs), DNDi organized a symposium titled "Innovation for Access to treatment for neglected diseases" on February 9th 2016 at the Boma Inn Hotel in Nairobi. The symposium served as a platform to bring together regional experts in neglected diseases and partners from the national government, county government, non-governmental organizations, research institutions and international organizations. This was an opportunity for them to connect, collaborate, share experiences, find solutions and pave the way for discussions on innovative ways of increasing access to treatments for neglected diseases.

There were over 100 participants in attendance from the Ministry of Health, Neglected Tropical Diseases Unit (MoH NTDU), Pharmacy and Poisons Board (PPB), MoH Marsabit County, World Health Organization (WHO) Kenya country office, Kenya Medical Research Institute (KEMRI), Science Africa, London School of Hygiene and Tropical Medicine (LSHTM), KalaCORE, KEMRI-FACES, MSF-France, CDC-FELTP, Kacheliba Hospital, MSF Belgium, KELIN, Gertrudes Hospital, University of Nairobi and DNDi.

The objectives of the symposium were:

1. To discuss innovative ways to improve access to treatments for neglected patients after successful trials are completed.
2. To develop strategies to have the most effective treatments for neglected diseases such as visceral leishmaniasis (VL) reach the patients who need them most.

Participants at the meeting

INTRODUCTION

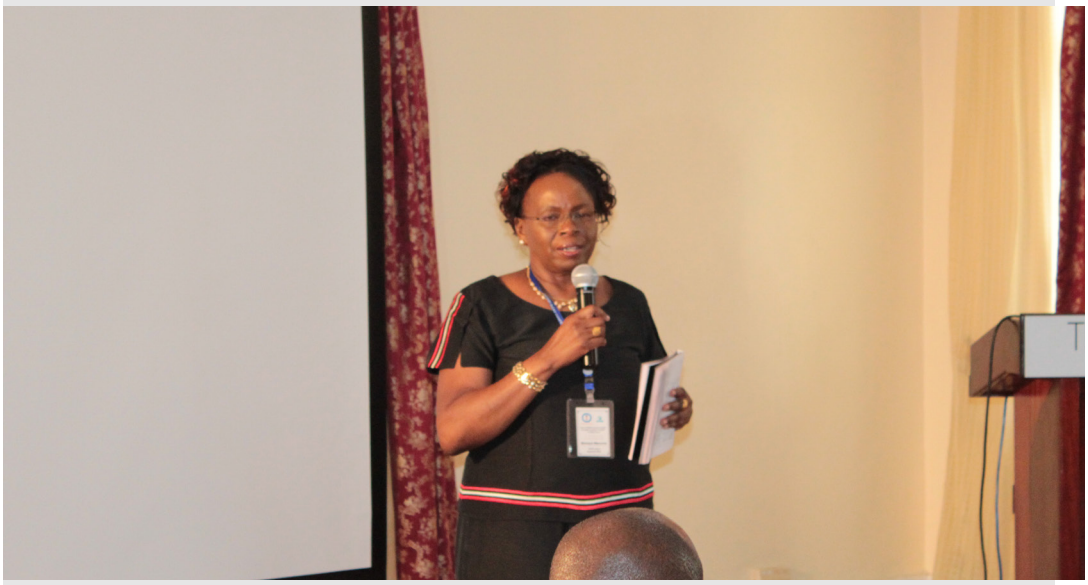
Access to essential medications especially for neglected diseases such as VL is limited in many low-to-middle income countries and those that are available are usually prohibitively expensive to the general population. For the organizations involved in research for neglected diseases, the work usually ends upon successful delivery of treatments. Experience has however shown that research does not automatically translate to access to treatments for patients. Internationally, gaps exist due to market failure thus a continuing lack of interest by pharmaceutical companies to produce and distribute drugs on sustainable basis. Regionally, slow response in ensuring that regulatory bodies adopt new treatments into their guidelines, or lack of prompt drug distribution to disease endemic areas have also contributed to low access. The end result of these challenges is that the patient suffers and sadly, some succumb to the disease. There needs to be more innovative and deliberate effort to increase access to treatments for patients especially affected by neglected diseases.

The presentations and discussions at the symposium captured access challenges from an R&D perspective, access realities on the ground, the role of stakeholders in making NTD drugs available and patient experiences in access to VL treatments.

Welcome and Introduction

By Dr. Monique Wasunna, Director , DNDi Africa Regional Office

Dr Monique Wasunna thanked the KASH organizers and indicated that the objective of the symposium was to address challenges of access to VL treatment, identify gaps and invent new ways that new therapies can be made accessible to patients. She said that DNDi has been working with neglected patients for the last 13 years. Patients suffering from neglected diseases, she said were very poor, have little or no purchasing power, they are voiceless, usually overlooked and often do not have access to life-saving treatments. Over the years, she said, DNDi and other partners have carried out research that has led to the identification of new treatments for various neglected diseases but often because of many challenges, some of these treatments have not reached the patients that need them most. She said the forum had been convened to discuss these issues and come up with innovative ways of moving forward.



Dr. Monique Wasunna gives introductory remarks at the symposium

PRESENTATIONS

Linking Innovation to access to treatments for neglected diseases

By Eric Stobbaerts, DNDi

Eric Stobbaerts speaks at the symposium

This session highlighted the fact that the fatal imbalance between R&D and access still exists and emphasized that an adapted R&D response is required. In the last 10 years, only four of the 756 New Chemical Entities (NCEs) developed were for NTDs. R&D priorities do not sufficiently originate from low and middle income countries. The R&D landscape is still nearly wholly funded and coordinated by non-endemic countries. The presentation emphasized the need for endemic regions and partners to play a much stronger role in priority setting with low and middle income countries that are disease-endemic defining the priorities. The large gaps that still exist include

1. Not linking innovation to equitable access even when there is commercial incentive to drive innovation.

2. Market incentives aligned with Intellectual Property (IP) or exclusivity do not adequately address health needs in low and middle income countries.

DNDi and Access

DNDi's new Business Plan seeks to deliver 16 to 18 treatments by 2023. DNDi has played, still has a role to play and continues to play a facilitative role in access. However, success will only be possible through innovative partnerships. Partnerships are critical to access and DNDi's concern is to keep the patient at the core of innovations to access. Capabilities do exist and reinforcing capabilities is essential. Linking innovation to access is difficult and requires many stakeholders working on collective activities. The access framework aspects should focus on:

- **Availability** i.e. in regulatory, manufacturing, forecasting, procurement, distribution and delivery.
- **Affordability** by the government, NGO and patient
- **Adoption** globally, nationally, by the care providers and the patient.

DNDi is exiting malaria after handing it over to Medicines for Malaria Venture (MMV) to help maximize their impact for the patients who need them most, but will continue with leishmaniasis, Chagas disease and Human African Trypanosomiasis (HAT). The DNDi portfolio is expanding and allowing for inclusion of new diseases such as Mycetoma, Hepatitis C, Filariasis and Paediatric HIV.

Innovation to Improve Access

After successful completion of clinical trials the lingering question remains *'how many new treatments have got into the MOH's in the affected countries?'* There is need to set up disease platforms around specific diseases e.g. LEAP, Chagas disease, Trypanosomiasis and most recently Cutaneous Leishmaniasis to strengthen existing clinical research capacity as well as to build new capacity where it is necessary. It is noted that more and more people are getting involved with the issue of access. There is need to link innovation to equitable access and although the process is complex with huge barriers, it can be achieved. Innovation should also help in disease control.

This session revealed that leadership and coordination from endemic countries is important. Partnerships are critical to access and DNDi continues to play a facilitating role. Collaborative models are needed to develop roadmaps, drug access strategies per disease and establish new organizational structures with defined roles and responsibilities, and joint key performance indicators (KPI's), for the purpose of coordinating the availability, and adoption activities.

Access at DNDi has taken many shapes and formats over the years. The concern is keeping patients at the core of innovation and the access objectives are:

1. To facilitate maximum impact via appropriate use of treatments
2. To assure effective transition of treatments to relevant access partners and implementers, including national control programmes, WHO and NGOs
3. To further demonstrate success to support the DNDi model
4. To target disease control strategies

Challenges of Access were highlighted as

- **Lack of data –** there are no accurate estimates on mortality.
- **Lack of methodology** on how to address access problem.

> ***The case of Chagas disease –*** *Chagas is endemic in 21 countries in Latin America was presented. Approximately 5.7 million people are infected and 10,000 deaths reported per year. Because of few health technologies, there are two old treatments available with only one percent of those infected receiving care while 99% remain unreached.*
>
> *DNDi and partners have been able to achieve increased medical consensus and establish a patients federation to extend the fight for the rights of individuals suffering from Chagas disease. A global coalition which aims to boost access to diagnosis, treatment and care among Chagas patients was also set up. DNDi has also stimulated innovation in new tools to fight the disease, established modalities to provide more evidence and data to highlight the impact of the disease and the challenges to access to treatment; identified two sources of production of Benzindazole and facilitated demand forecasting of drugs.*

Recommendations to facilitate access were highlighted as:

1. Collaboration with partners can increase access
2. Increasing medical consensus
3. Continuously developing and/or updating treatment guidelines – e.g. for Chagas disease there are no treatment guidelines
4. Ongoing strategies to convince manufacturers to continue production. More manufacturers will guarantee success.
5. Ensure the voice of the patient and campaigns through civil society and media.

Conclusion:

It is important to break the cycle of neglect through visibility, patient voices and awareness campaigns. Actors need to unite to bring technology to end users - the patients and to build collaborative models that are necessary for developing road maps e.g. develop drug access strategies per disease. Leadership and coordination has to come from endemic countries. New organizational structures should be established with the purpose of coordinating the availability, affordability and adoption activities, including but not limited to definition of roles and responsibilities and joint key performance indicators (KPIs). To move forward, it is important to advocate for change in the R&D landscape.

Visceral Leishmaniasis treatment access: The reality on the ground

By Margriet den Boer , KalaCORE Regional Coordinator , East Africa

Margriet den Boer presents at the meeting

Dr Margriet den Boer reviewed achievements since WHO recommended SSG&PM combination as first line treatment for VL in 2010 and years after introducing SSG&PM in national protocols and guidelines in Eastern Africa against country-wide uptake, continuous availability of drugs and diagnostics, safe use of drugs, availability of trained human resources and patient access to treatment. It is reported that the uptake of the regimen is still poor. The most important access barriers to treatment in East Africa have been established as VL is endemicity in remote and insecure areas, overdependence on NGO's and the WHO for drug supply, late stage presentation by patients, low awareness of disease among health workers and prolonged treatment duration for patients. She highlighted the background and role of KalaCORE in Eastern Africa and its plans to:

- Supply of drugs and diagnostics and supporting their immediate road transport
- Establishment of central drug buffer stocks in case of outbreaks
- Training Health care providers
- Upgrade health facilities following VL focused health facility checks
- Advocacy for food aid
- Operational research on vector control and access; and
- Analysis of disease data at hospital level including retrospective review

Standardized VL treatment facility check assessments were done with the MOH following standards defined by WHO. The findings were; drug stock-outs in more than 50% of the facilities, widespread non adherence to treatment protocols, incomplete reporting, shortage or absence of staff trained in VL, laboratories not equipped for VL testing and patient wards not meeting basic standards.

Sustainability through ensuring country registrations, continued production or availability of multiple producers, stable pricing and assured quality is crucial in creating conditions for drug access, none of which are completely in place today.

Other challenges to access were noted to include:

- Efforts by stakeholders have been scattered and partially effective
- Extremely high dependence on single sourcing (Gilead is the only manufacturer of AmBisome and only Paladin manufactures Miltefosine) with long lead times in drug supply. There are no forecasting mechanisms and no buffer stocks except those held by MSF and DNDi.

Conditions for implementing VL treatment access strategies were listed as:

- Get the basic epidemiology straight to avoid cases of poor reporting. Presently, there are discrepancies between estimated and reported cases.
- Purchase not just the drugs but the whole delivery system to ensure adequate lead times and avoid drug stock outs.
- Continue operational research to fill gaps which include mapping, access and innovative control approaches and focus on sustainable structures and financing for all aspects of implementation.
- Supply of drugs and diagnostics as well as supporting their immediate road transport, and
- Ensuring central drug buffer stocks in case of outbreaks.

To create conditions for drug access, besides the issue of registration of drugs in-countries, risk management is recommended with sustainability being key. The need to have agreements with manufacturers to create goodwill to sustain production and have better coordination and division of roles among stakeholders was suggested as the way forward in the drug access strategy. Recommendations are to ensure sustained AmBisome donation and the need for good forecasting to avoid drug stock outs.

Challenges of access to treatment for neglected diseases – Experience in Kenya

By Dr Hardley Sultani , Ministry of Health, NTD Unit

Dr. Sultani speaking at the symposium

Dr Hardley Sultani discussed the challenges of access and similarly revealed the intervention strategies that the Ministry of Health, NTD Unit is adopting to improve access to treatment of NTDs. He emphasized that the challenges of access in Kenya included poor management of drug donations, scarcity of resources for utilization of drug donations, direct procurement of drugs and resources for coordination of treatment interventions, inadequate training for health workers, weak quality assurance processes and control systems as well as stakeholders' reluctance to embrace integration mainly due to absence of platforms to provide integration as some of the barriers of access to treatment.

To mitigate these challenges, the NTD Unit has set up platforms such as the Inter-Agency Coordinating Committee (ICC) for integration and coordination purposes. Besides setting up the ICC, the unit has also adopted the following measures to mitigate the challenges: -

- Carried out review of the National Strategic plan for NTDs.
- Development of policies and guidelines
- Massive Advocacy Communication and Social Mobilization (ACSM) activities focusing on sensitization on the need for counties to take a lead on the access activities
- Improvement of programme staffing status.

The session proposed the way forward to improving access to treatment of the NTDs in Kenya as:
- Need for operational research
- Capacity building and technical support
- High level government ownership in terms of direct participation and through providing baseline funding of programme activities
- Establishing more resources, preferably local funding to support the programme
- Planning regular NTD stakeholder's forums for exchange of ideas, coordination of stakeholders; and ensuring cooperation among stakeholders.

Sodium Stibogluconate (SSG) & Paromomycin (PM): Issues of access to VL treatments

Dr. Robert Kimutai, Clinical Trial Manager, DNDi

Dr. Kimutai speaks about challenges of accessing SSG & PM at the meeting

Dr Robert Kimutai revealed that even though research has already been done, access still remains the elephant in the room. In his presentation, he highlighted the SSG&PM clinical trials, summarized the pharmacovigilance trial and highlighted the access achievements of SSG&PM. The early successes of the SSG&PM trial were highlighted as immediate incorporation and acceptance of SSG&PM to Essential Medicines List and the revision of National Guidelines following the WHO recommendation of SSG&PM as first line treatment in Eastern Africa. Continued advocacy and lobbying based on evidence through publications, policy change, community leaders engagement, stakeholders meetings, and the continued training of health workers on VL guidelines are also key achievements.

Some of the barriers to access to treatment were highlighted as slow transition from clinical trial results to patient access, low prioritization of VL needs due to lack of data and inadequate advocacy occasioned by poor funding both by national and county governments and complexities in the budgeting and procurement process.

Other challenges to access to treatment were highlighted as:
- The non-availability of PM. While SSG is accessible in most countries, PM is still not accessible in some countries.
- Challenges of adoption of VL diagnosis and treatment guidelines because recommended diagnosis, treatment and specialized care facilities are not available. There is also the pressure of diseases outbreaks and on some occasions, facilities use donated diagnostics and treatments from funders which may not necessarily be in line with the guidelines.
- High staff turnover in health facilities, inadequate follow up after health worker training, reluctance to change, late presentation by patients due to distance as well as cultural and traditional treatments are also key challenges.

The session advocated for the following as solutions to access after successful clinical trials:

- Early partnership with Ministries of the Health (MOH) and stakeholders, because this facilitates the acceptance of study results.
- Development of VL data collection and surveillance tools.
- Sharing data and advocacy for VL, in relation to budgeting and prioritization of VL in both the counties and nationally
- Training and follow up refresher trainings of health workers
- Long term strategic planning both nationally and internationally

Conclusions

The session's conclusions were:

- Early engagement and involvement of stakeholders and regulators is key to early acceptance of new treatments
- Scientifically and ethically sound research leads to registration and policy change to use new treatments. This is ongoing in Sudan, Ethiopia, Kenya and Uganda.
- There are significant challenges still to be overcome for the patients to access treatment.
- Putting patients first includes addressing access needs. SSG&PM is effective, safe, cheaper and of shorter duration. It is not ideal but the best first line in Eastern Africa.

Role of stakeholders in making NTD drugs available

Dr. Joyce Onsongo World Health Organization Kenya Country office

Dr. Joyce Onsongo from WHO

Dr Joyce Onsongo discussed the WHO NTD roadmap and preventive chemotherapy, currently recommended by WHO as one of the key public health interventions for a number of NTDs. Integrated preventive chemotherapy which is aimed at optimizing programme efficiency has proved to be relevant for multiple disease programmes and is aimed at ensuring that the global goals set for the five diseases; namely Onchocerciasis, Lymphatic filariasis, Soil-transmitted helminthiasis, Schistosomiasis and Trachoma are reached by 2020. The WHO-recommended schedule, target population groups were discussed in detail and the components of preventive chemotherapy were listed as:

- Availability of quality drugs
- High compliance
- Impact on morbidity and transmission
- Recording and reporting

The preventive chemotherapy medicines donated through WHO and the process of joint application for national programmes to WHO for the donations following the London Declaration on NTDs was outlined. The last mile of drug distribution is still a challenge and therefore the need to integrate NTD diseases beyond specific programmes was emphasized.

Access to treatment for neglected diseases – Experiences in Marsabit County

Abduba Liban, County Disease Surveillance Officer, Marsabit County

Abduba Liban revealed that the challenges of accessing treatment for visceral leishmaniasis in Marsabit County can broadly be characterized into 3 groups: community, purchase and supply as well as health worker. Some of the community level challenges include; distance to the treatment centre, lack of awareness of the disease and cultural practices resulting in seeking traditional treatments for the disease. The purchase and supply challenges are mainly related to dependency on donors from partners to access treatments, drugs are also very expensive and are usually not available in KEMSA or MEDs. The Health worker level challenges include lack of training of health workers leading to misdiagnosis and the fact that very few health workers are trained in specialized procedures such as bone marrow and splenic aspirations.

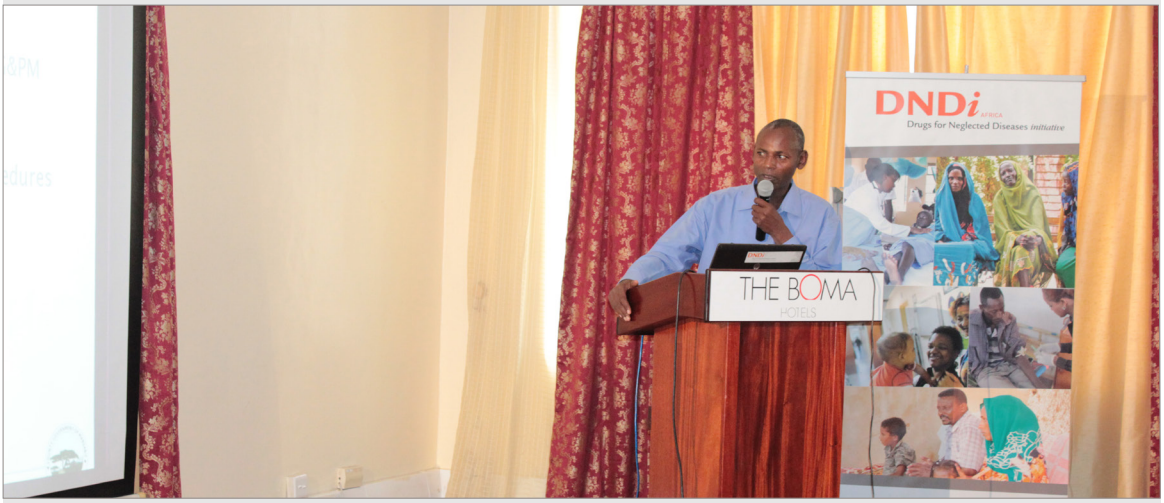
The following suggestions were made to address these challenges of access within the counties:

- Improved surveillance and reporting to different levels of the health system. This ensures a reinforced surveillance system and therefore the need to make weekly data reporting mandatory.
- Ensuring that all confirmed cases are treated using appropriate drug therapy.
- Training of hospital and health centre staff in diagnosis and treatment protocols.
- Advocacy communication and social mobilization activities such as health education to the communities, creating awareness on leishmaniasis prevention and control measures, development and distribution of brochures and banners as well as talk shows in local radio stations. There is need to prioritize VL including purchase of treatment and diagnostics.
- Undertaking of vector surveillance and control measures

Conclusions

Conclusions from this session include:

- Purchase of treatments and diagnostics.
- Improved awareness creation, advocacy and communication.
- Ensuring consistency in supplies.
- Carrying out training of health workers at facility level on VL, as well as on bone marrow and spleen aspiration procedures.
- Intensification of control measures



Abduba Liban speaks at the meeting

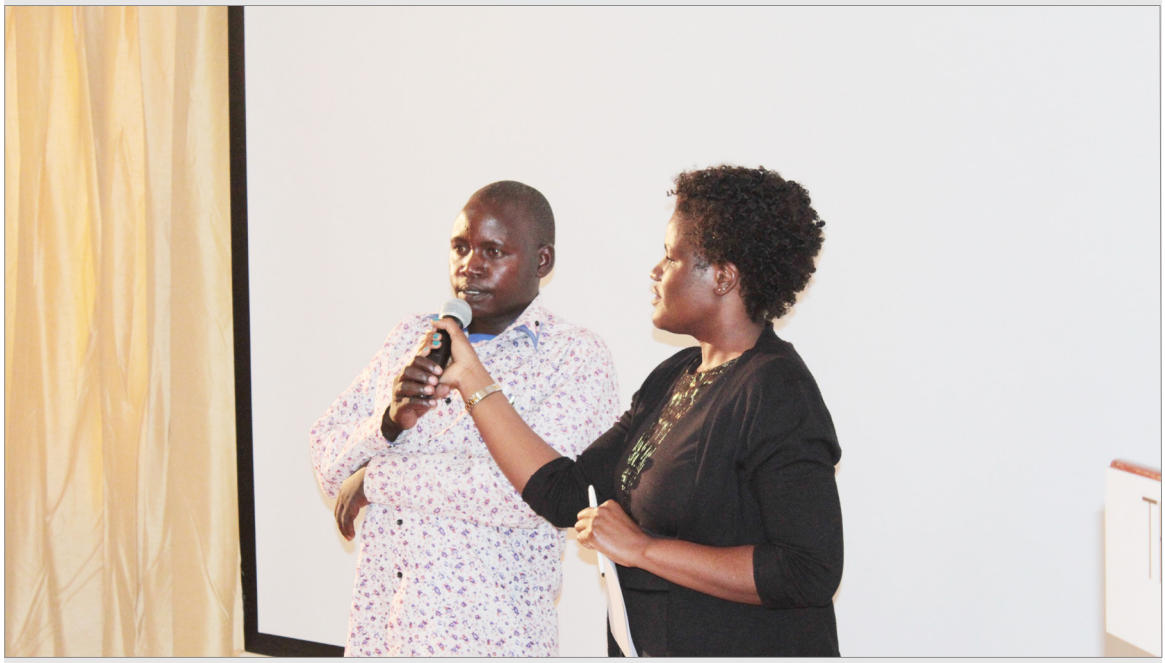
Patient experiences in access to VL treatment

Nicholas Kibet, Patient from Kimalel, Baringo County

Nicholas Kibet shared his experience of seeking treatment for kala azar. In 2014, he started experiencing malaria-like symptoms and visited a health centre near his home for treatment. There, the health workers informed him that he had malaria and gave him treatment. However, he did not get better even after Nicholas Kibet shared his experience of seeking treatment for kala azar. In 2014, he started experiencing malaria-like symptoms and visited a health centre near his home for treatment. There, the health workers informed him that he had malaria and gave him treatment. However, he did not get better even after treatment. He therefore went back to the hospital and this time was diagnosed with typhoid and treated for the same. Unfortunately the treatment did not work this time either and he was still feeling unwell when he decided to visit a traditional herbalist. Despite taking the herbs, the symptoms were persistent. One of Nicholas' neighbours then referred him to the Kimalel Health Centre, 14 kilometres away from his home, where he was diagnosed with kala azar, put on the 17 day SSG&PM treatment and thereafter discharged. He testified that since then he has not suffered the same symptoms again.

Nicholas' story was the highlight of the symposium and it was greatly appreciated by the participants especially Karen Goraleski, Executive Director at ASTMH who later tweeted:

Thank u @DNDi for bringing patient voice to VL symposium. That is why we do what we do, right? @astmh in Kenya



Nicholas Kibet, a former VL patient narrates his story in accessing treatment

QUESTIONS ASKED

Feedback Session

During the feedback session, the following are a sample of questions raised and discussed:

1. Why is Kenya not included in the composition of KalaCORE?
2. If the first line treatment recommended by WHO and included in the Kenyan treatment guidelines, why is Marsabit County providing SSG alone?
3. How can we use locally available innovative ways to facilitate access e.g. use of boda bodas to transport drugs?
4. Are there any vaccines on the pipeline for NTDs?
5. Is there Kenyan specific data on NTDs?
6. What community engagement strategies have been adopted to facilitate access to treatment in Kenya?
7. How come there are no guidelines for Chagas disease? What are the challenges?
8. Only one percent of those affected by Chagas disease have access to treatment. What is the main barrier to this?
9. With no baseline government funding, how sustainable is the access process?
10. Is VL on the WHO NTD roadmap?

RECOMMENDATIONS

The following recommendations were made

1. Access issues are complex but can be resolved through a collaborative approach
2. The development of a comprehensive framework for access is important. The access framework is shaped by social values, economic interests, political and cultural processes and is based on the 4A's: Architecture, Availability or the supply component, affordability and adoption.
3. Agreements with manufacturers are key though currently are not in place- These will be essential in creating goodwill to sustain production, providing pooled demand forecasts, supporting registrations, support achieving WHO GMP standards
4. Better coordination and division of roles among stakeholders should be encouraged as well as cooperation among stakeholders.
5. At the national level, development of policies and guidelines are crucial. Research findings should be translated into policies.
6. It is vital to interact with patients and understand their needs
7. Every relevant stakeholder has a role to play in issues of access. It is important to have better coordination and organization in order to solve the access architecture
8. Leadership from Neglected Diseases endemic countries is important in access to treatment for the neglected patients.
9. We must put patients first and give them a voice.

CONCLUSION

Access to treatment remains a significant problem for neglected patients. All the work that goes into clinical trials insignificant if the treatments cannot reach the patients who desperately need them. The symposium succeeded in coming up with a number of strategic recommendations that if implemented, would place access to treatments for neglected patients on the policy agenda of governments and stakeholders. Leadership and coordination from endemic countries in priority setting to assure an adapted R&D response to the fatal imbalance between R&D and access is crucial.

Access requires several organizations and therefore the need to harness fragmented capabilities through innovative public-private partnerships. Collaborative partnerships are essential in facilitating access to treatment for NTDs and necessary for long-term success. Integration between stakeholders in the NTD field and specific programmes within the Ministries of Health and patient participation to break the silence of neglect are key in ensuring success in increasing the availability of essential drugs.

The main challenges to overcome in facilitating access to treatment for neglected patients are those that are based on the protection of Intellectual Property (IP) rights, drug registration in endemic countries, the lack of baseline government funding and resultant effects to the programmes, and the lack of effective drug delivery systems. Improved staffing as well as development of policies and guidelines were emphasized as measures to mitigate these challenges.