DNDi
Drugs for Neglected Diseases *initiative*

Visceral Leishmaniasis treatment access: The reality on the ground

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2015, photo by KalaCORE


2015, photo by KalaCORE


PLP
Disposable Syringe
3ml
AmBisome
AmBisome
HANDLE WITH CARE
OC 1

SSG+PM introduction in Africa: history

- **1992-1994:** First clinical studies conducted by MSF in South Sudan investigating the effectiveness of a new combination treatment under field conditions (SSG+PM).
- **2007:** Publication of retrospective analysis of the use of SSG+PM vs SSG alone in South Sudan, concluding that SSG+PM is both safer and more effective in remote field settings.
- **2012:** Publication of a DNDi multi-centre trial of the efficacy of SSG+PM combination therapy. SSG+PM and SSG alone were shown to have a similar efficacy and safety.
- **From 2012 on:** acceptance of SSG+PM in national policies
- **2014:** DNDi SSG+PM multi-country pharmacovigilance studies demonstrated excellent safety.

Taking stock

Years after introducing SSG+PM in national protocols and guidelines in East Africa and roll out, did we achieve:

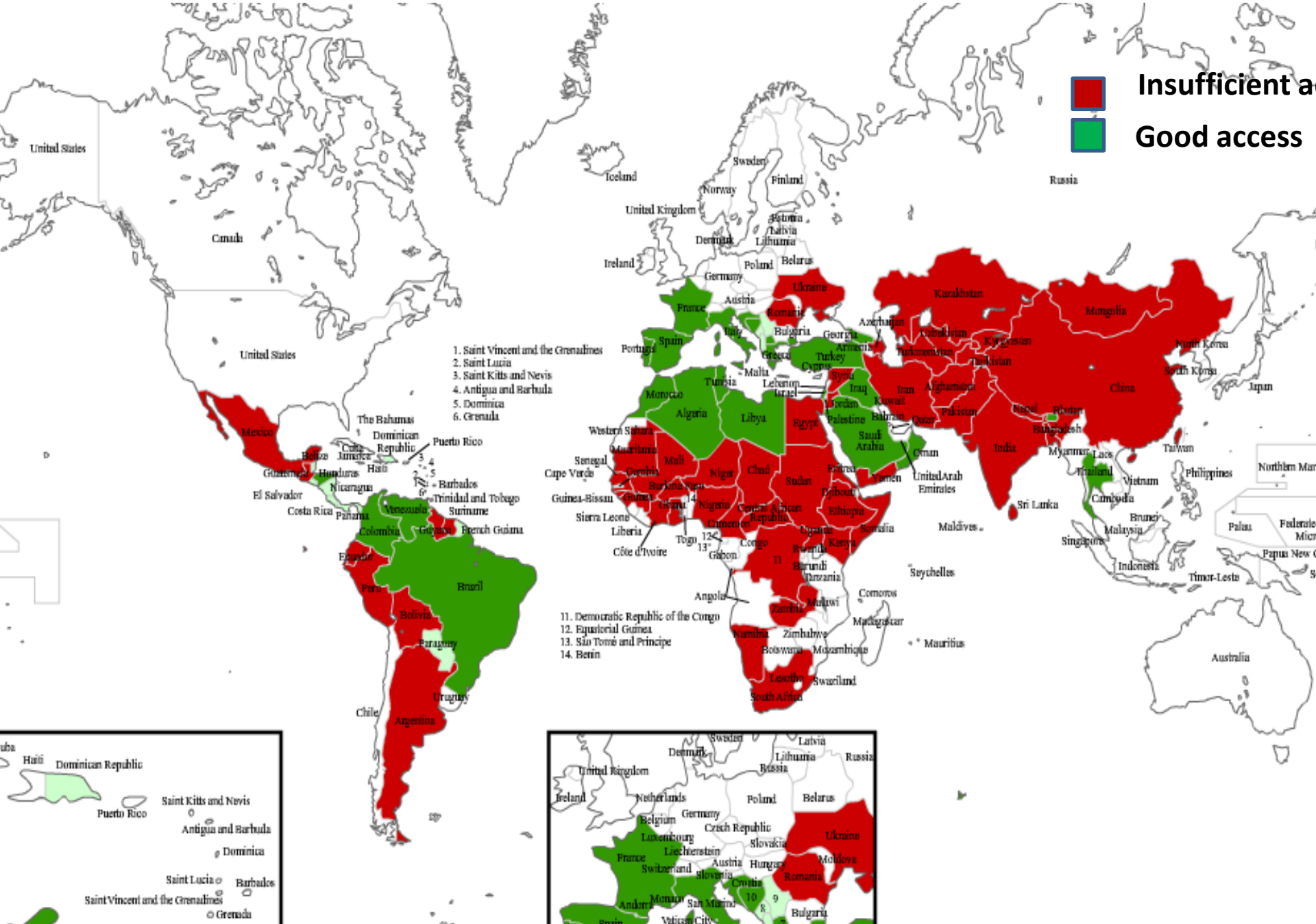
- Country-wide uptake
- Continuous availability of drugs and diagnostics
- Safe use of drugs: precautions and monitoring
- Trained human resources
- Hospital readiness
- Access to treatment for all patients
- All conditions for patients met (shelter, food, RUTF)
- Tackling HIV/VL

Most important access barriers East Africa

- Extremely remote and/or insecure areas
- Dependency on NGO's/WHO for drug supply
- Patients first seek care from traditional healers and present in very late stage of disease
- Low awareness among health workers
- Staying away from home/work causes great losses



ACCESS TO TREATMENT FOR LEISHMANIASIS as judged by countries



Conditions for implementation

- Getting the basic epidemiology straight

	Reported	Estimated
Sudan	3742	15,700-30,300
Ethiopia	1860	3,700-7,400

- Purchase not just the drugs but the whole delivery system
- Involve, educate and motivate health workers and all other stakeholders on the ground
- Focus on sustainable structures and financing for all aspects of implementation
- Continued operational research to fill gaps: mapping, access, innovative control approaches

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- UK commitment to NTD's; DFID bid for "Tackling VL in South Asia and East Africa" Project - £ 27.3 million for 5 years (until April 2019) Target countries:
- South Asia: India, Bangladesh, Nepal
- East Africa: Sudan, South Sudan, Ethiopia

KALACORE Consortium for Control and Elimination of Visceral Leishmaniasis in South Asia and East Africa (2014-18)

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Mott MacDonald

MEDECINS SANS FRONTIERES

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

KalaCORE plans

- Supply of drug and diagnostics and supporting their immediate road transport
- Central drug buffer stocks in case of outbreaks
- Human resources gap: sustainable university-based training programs and clinical mentoring
- VL-focused health facility checks and subsequent upgrade
- Advocacy for food aid
- Operational research on vector control and access
- Analysis of disease data at hospital level including retrospective review

Standardized VL treatment facility checks

Assessments together with MoH; standards defined by WHO

Findings:

- Recent stock gaps of VL drugs and diagnostics in >50% of facilities;
- Wide-spread protocol non-adherence;
- Incomplete reporting;
- Shortage or absence of staff trained in VL;
- Laboratory not equipped for VL testing;
- Patients wards not meeting basic standards;

Compound	Commercial name and manufacturer	Price information
Liposomal amphotericin B (L-Amb)	*AmBisome®, Gilead, US* **Single-source**	**DONATION or** **WHO negotiated price:** 18 USD/50 mg vial
Miltefosine (MF)	*Impavido®, Paladin, Canada* **Single-source** **Price status uncertain**	**WHO negotiated price (status?)** For adults: 45.28 - 54.92 Euro for 56 (50mg) capsules For children: 34.36 - 39.3 Euro for 56 (10mg) capsules
Paromomycin (PM)	*Paromomycin, Gland Pharma, India* **Single-source** **Price status uncertain** **Ownership dossier?**	App. price 15 USD per adult course of 21 days
WHO approved generic sodium stibogluconate (SSG)	*SSG, Albert David, India* **Single-source**	5,65 Euro/30 ml vial 100 mg/ml
Meglumine antimoniate (MA)	*Glucantime®, Sanofi* **Single-source**	**WHO negotiated price** 1.2 USD/5 ml vial 85 mg/ml

Creating conditions for drug access: Risk management

- Sustainability is key:
  - Country registrations
  - Continued production/multiple producers
  - Stable pricing
  - Assured quality

-> None of which are completely in place today

-> Efforts by stakeholders have been scattered and partially effective

-> Extremely high dependency on single source AmBisome, paromomycin

Paromomycin (PM)

- Originally marketed in the 1960's as IV antibiotic
- Further developed for VL by WHO and BMGF Foundation (iOWH) and registered in India in 2006
- Clinical multicentre study and PV by DNDi and registration facilitated by DNDi
- Produced by Gland Pharma in India. **Quality problems leading to supply gaps** have occurred in the past
- Price is low but **long term sustainability is a concern**
- No forecasting mechanism and no buffer stocks except those held by MSF and DNDi – **lead times can be very long**
- **Ownership dossier** is unclear and no agreements are in place

Miltefosine (MF)

- Originally developed for breast cancer and developed with public funds through WHO/TDR for VL
- Reduced place in therapy (WHO expert Committee 2010) – current consumption foreseen to remain low. **No binding agreements on price and sustainability of production**: dependency on goodwill Paladin despite existing MoU with WHO.
- WHO negotiated price for large quantities – **no agreement on preferential price for small orders**. Currently >250 USD per single Tx for non profit sector and >2000 USD for private market.
- No forecasting mechanism and very small buffer stock held by Paladin – **lead times can be long (3-6 months)**

Drug registrations

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	Asia (India, B'desh)	Africa
AmBisome (Gilead Sc. India)	Registered in India and Bangladesh	**Not registered in Sudan, Ethiopia, Kenya, Uganda**
Generic SSG (Albert David, India)	n.a.	Registered in Sudan, Uganda. **Not registered in Ethiopia, registration expired in Kenya**
Paromomycin (Gland Pharma, India)	Registered in India **Not registered in Bangladesh**	Registered in Uganda, Kenya. **Not registered in Sudan and Ethiopia; both in process ***
Miltefosine (Paladin, Canada)	Registered in India, Bangladesh	**Not registered in Sudan, Ethiopia, Kenya, Uganda**

* With DNDi facilitation

Way forward: drug access strategy

- Agreements with manufacturers are key; these are not in place
  - AmBisome donation must be sustained
  - Creating goodwill to sustain production: providing pooled demand forecasts, supporting registrations, support in achieving WHO GMP standards
  - Better coordination and division of roles among stakeholders
    - Governments endemic countries: forecasting, drug financing
    - DNDi: supporting drug licensing and registration
    - MSF: advocacy/exposure
    - WHO: GMP inspections, legal agreements on maintaining production and low prices, central buffer stocks

With thanks to:

Many thanks to DNDi for my travel grant