Drugs for Neglected Diseases initiative

# Mycetoma, a neglected tropical disease and need for clinical trials.

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# Introduction

- Mycetoma chronic, granulomatous, progressively morbid, inflammatory disease
- Caused by true fungi or higher bacteria
- Painless subcutaneous mass, multiple sinuses, and a discharge containing grains
- Prevails in the Mycetoma belt
- Treatment is unsatisfactory.
- Newer azole-drugs promising e.g. ravuconazole has a remarkably long half-life and has a good safety profile.







LEAP meeting



### Presentation, bacterial and fungal Mycetoma

- Initial inoculation of the fungi or bacteria via thorn prick as most individuals walk bare foot and or handle especially Acacia trees etc.
- Fungal Mycetoma is more indolent resulting in late presentation.
- Bacterial cases there is a more symptomatic clinical course and responsive to antibiotics.
- Most cases are non fatal depending on the lesion location.
- There has been no reported case of spontaneous resolution.





### Mycetoma complications









# **Diagnostic Tools**

Current diagnostic tools are invasive and hospital based.

#### There are no field-adapted tools thus:

- Patients present late because of misdiagnosis. This affects cure rate
- Increases the chances of relapses and amputations



PCR and culture Histopathology

#### Ultrasonic imaging

Magnetic Resonance Imaging (MRI)







X-Ray Examination



Photography 2D & 3D



# Mycetoma in Kenya

- During the 69th WHA resolution, Mycetoma was added to the WHO list of neglected tropical diseases (NTDs).
- Most countries do not have strategies for the disease treatment and control.
- In Kenya, there was a publication in 1973 in the East African Medical journal.
- There have been case reports of Mycetoma especially amongst male, nomadic communities
- Most cases are among economically impoverished populations and because of the nature of the disease there is late presentation.



# Why is Mycetoma an Old Disease but still Highly Neglected?







### Almost No Research for mycetoma...

A literature search was done For planned, ongoing, completed trials and epidemiological studies on:

- Clinicaltrials.gov
- Pan African Clinical Trials Registry (PACTR)
- Medline/PubMed published papers on Mycetoma
- Other local journals for case reports on fungal Mycetoma in Africa.





# Global number of clinical trials Jan 2017



Colors indicate the number of studies with locations in that region

Least

Most

Labels give the exact number of studies

# Only one Clinical Trial on Mycetoma...

- There is one clinical trial registered for Mycetoma on clinical trials.gov.
- At the time of the search, a total of
- 235,391 were registered globally (1/235,391)
- 5,665 in Africa (1/5665)
- 351 trials were registered in Kenya. (0/351).



# Need for Clinical trials.

- There are no trials, and few epidemiological studies.
- Current treatment modalities for eumycetoma are disappointing.
- Response is characterized by low cure rates, high amputation rates, and subjects who drop out of follow-up with resultant high recurrence rates.
- Despite prolonged medical treatment, the causative organisms are commonly found viable within the well-encapsulated lesions during surgery, after 12 months of treatment.





#### Mycetoma recent development.





#### **Until today**

Ketoconazole and itraconazole to treat fungal form:

- Duration of 12 months
- Serious side effects
- Only 25-35% effective
- Not affordable

May 2016 - WHA Finally added to WHO NTD list!

More visibility for funding and research programmes

#### By 2023

To deliver:

A more effective, affordable, shorterterm treatment appropriate for rural settings



#### A clinical trial to address patients' needs

- Fosravuconazole (E1224)
  - Under development for Chagas, may be effective and affordable for eumycetoma (fungal form)
  - To demonstrate superiority of fosravuconazole over itraconazole
  - Phase II study to start in 2016 in Khartoum, Sudan, at the Mycetoma Research Centre
  - Partnership with





#### Challenges conducting Mycetoma Clinical Trials

- Validated endpoint measurement combination of clinical and use of MRI. Expensive.
- High prevalence have high research naïve teams, fortunately are team highly skilled in the disease management and motivated.
- Healthcare worker awareness on diagnostic criteria remains low. Epidemiological work needs to be done for disease mapping and clinical trials to develop more effective treatment options
- Logistical challenges.



#### Conclusions.

Research on mycetoma is scarce & incidence unclear. However, prevalence of 14.5 per 1,000 reported in endemic areas

Diagnostic tools are inadequate and invasive and more research is needed to find better tools Current treatments for especially eumycetoma (fungal type) have a cure rate of only 25-35%. Need for clinical trials to find effective drugs.



**DNDi's target -** To find more effective treatments for treating fungal Mycetoma (eumycetoma).

### THANK YOU

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#### Back up slides



