Experiences from participation in the clinical study for arpraziquantel and the expected impact of the potential new pediatric treatment on patients
Outline

1. Schistosomiasis situation in Kenya and KEMRI’s role in disease control
2. Experience through the clinical study
3. How Ped PZQ will bring positive impact?
4. Next steps for access of ped PZQ – ADOPT study
Consortium founded in 2012

International non-profit R&D Consortium with a focus on extended partnership into endemic countries

In kind and/or in cash contribution by partners

Continually seeking funding and advice from external experts and partners

International Expert Panel (World Health Organization) as observer

Grants:
- Bill & Melinda Gates Foundation
- GHIT Fund (3x)
- EDCTP

Exit Oct 2017
Kenya Medical Research Institute (KEMRI)

State Corporation responsible for carrying out research for human health in Kenya

www.kemri.org

Centre for Biotechnology Research & Development (CBRD)
Centre for Clinical Research (CCR)
Centre for Public Health Research (CPHR)
Centre for Microbiology Research (CMR)
Centre for Respiratory Diseases Research (CRDR)
Centre for Traditional Medicine & Drug Research (CTMDR)
Centre for Virus Research (CVR)
Eastern and Southern Africa Centre of International Parasite Control (ESACIPAC)
KEMRI Graduate School of Health Sciences (KGSHS)

Centre for Infectious & Parasitic Diseases Control Research (CIPDCR)
Centre for Global Health Research (CGHR)
Centre for Geographic Medicine Research, Coast (CGMRC)
Distribution of schistosomiasis in Kenya and the study site in western Kenya

Distribution of schistosomiasis in Kenya, latest data available

GAHI, 2010

Sang et al. 2014
Risk factors for Schistosomiasis transmission around Lake Victoria

Stothard et al, 2013. Trends in Parasitology
Consequences of excluding PSACs in routine deworming for schisto....

Control of schistosomiasis in Kenya

Strategy:
Preventive Chemotherapy (PC) targeted to high risk groups is the control strategy.

Main goal of PC is to avoid the severe consequences of chronic infections.

PC is implemented through the National School-based Deworming (NSBDP) program.

Using the school system and teachers to deliver deworming tablets is a very cost-effective approach.

Institution/structure or National entities in charge of Schistosomiasis control in Kenya:
- Ministry of Health (MoH)
- Ministry of Education, Science & Technology
- Technical assistance from Deworm the World Initiative (DtWI) at Evidence Action

Consequences of excluding PSACs in routine deworming for schistosomiasis.

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### Challenges in conducting clinical trials in an endemic country

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Remarks</th>
<th>Affected ped PZQ study? (Mitigation measures)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unanticipated events</strong></td>
<td>e.g. current COVID-19 pandemic, unpredictable political climate, weather etc</td>
<td><strong>Yes – COVID-19.</strong> (Temporal suspension for 6 months)</td>
</tr>
<tr>
<td><strong>Weak or Inadequate local clinical trial human resource capacities and clinical trial infrastructure in SSA</strong></td>
<td>Required to host and manage clinical trials in accordance with ICH-E6 GCP compliant trials. Even when these are improved, there is often the secondary challenge of <strong>sustaining the established competent trial sites</strong> due to huge disparities and/or fluctuations in research funding which is largely from external sources (less from domestic) - hampers sustainability for future research</td>
<td><strong>Somewhat</strong> (Hiring staff with prior clinical trial experience, Regular trainings, Refurbishments of spaces, Equipment purchase)</td>
</tr>
<tr>
<td><strong>Weak or Inadequate regulatory capacity for Ethical and regulatory oversight</strong></td>
<td>Strong regulatory and ethical infrastructure are critical in ensuring both the safety of research subjects and the scientific integrity of clinical data</td>
<td><strong>No</strong> (N/A)</td>
</tr>
<tr>
<td><strong>Challenges that can be enhanced by cultural and geographical differences – specific culturally-sensitive ethical issues</strong></td>
<td>e.g. obtaining valid/adequate informed consent from trial participants, trial reimbursement as compensation for trial participation as well as trial insurance, collection of blood samples, issues around standard of care and reasonable availability of future interventions, differences in ages for legal consent, use of LAR vs guardian</td>
<td><strong>Yes</strong> (Revision of text in ICFs, proper Community sensitization &amp; quick response to rumors/misinformation)</td>
</tr>
</tbody>
</table>
# Challenges in conducting clinical trials in an endemic country

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<tr>
<td>Institutional bureaucracies</td>
<td>Slow turnaround in procurement processes, full execution of contractual agreements</td>
<td>Yes (Submission of requests early enough, Working closely with relevant departments)</td>
</tr>
<tr>
<td>Delays in supply chain issues/Customs clearances</td>
<td>esp. International purchases (POC-CCA kits, urine filtration kits)</td>
<td>Yes (Submission of requests early enough, Working closely with relevant departments &amp; RA)</td>
</tr>
<tr>
<td>Poor road infrastructure</td>
<td>Affects access to participants and participants access to clinical sites</td>
<td>Yes (Use of 4x4 cars, extra field team, community support when cars got stuck)</td>
</tr>
<tr>
<td>Mixed <em>S. mansoni</em> &amp; <em>S. haematobium</em> infections</td>
<td>This was an exclusion criteria for ped PZQ study</td>
<td>Yes (Leverage local knowledge on disease epidem by DVBNTD &amp; Health facilities, extra field team)</td>
</tr>
<tr>
<td>Managing different partner/stakeholder expectations</td>
<td>Partners (both International &amp; local will have different expectations – some might be misplaced/unrealistic</td>
<td>Yes (Providing accurate information, Regular meetings/dialogue, transparency)</td>
</tr>
</tbody>
</table>
Village setting & Field work

Community members giving a helping hand
Challenges during Fieldwork........

Field team navigating the community
Study clinical site - Homabay County Teaching & Referral Hospital
Study participant ward

Before study
Study Pharmacy room
Outline

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Current Challenges/needs for schistosomiasis control in pre-school age children (PSAC)

- Treatment issues with current PZQ (600mg) for drug dosing and administration:
  - Table size (dose splitting) and risk of choking
  - Palatability (bitter taste) and taste-masking (crushing and mixing)

- Access to treatment:
  - Operational challenges for large-scale treatment in view of the current PZQ (main targets = SAC using school platforms)
  - Lack of recommendations for inclusion of children <4 years in current WHO guidelines

- Regulatory: mostly off-label use and non-licensure of PZQ for use in PSAC
New formulation represents an unprecedented opportunity to improve the health and wellbeing of children and communities as a whole while advancing Kenya’s progress towards UHC and the SDGs.

Smooth downstream processes in relation to registration, procurement and delivery of medicines including local manufacturing – knowledge & tech transfer to a local CMO - Universal. Tech transfer & training will lead to self-sufficiency in terms of product manufacturing, potentially allowing Kenya and other regional endemic countries to meet the needs of their communities timely without external support.

Development of Clinical trial Infrastructure/capacity building – Setting up/improvement of existing trial site ensures sustainable clinical trial infrastructure for future research - strong local scientific capabilities, ethical and regulatory oversight.

Fostered local credibility and trust, which will enhance uptake of medicines as the focus now shifts to access. Harnessing/Leveraging on the expertise on local disease epidemiology & experience - allowed study to be conducted according to GCP & local guidelines. Benchmarking for future trials – not-for-profit PP partnership & also - country-level input in design to reflect public health needs and priorities of the country.

How will the ped PZQ bring positive impact?
Global & National Targets

Fig. 12. Critical actions for each disease and disease group to reach the 2030 targets

<table>
<thead>
<tr>
<th>Critical action 1</th>
<th>Critical action 2</th>
<th>Critical action 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>TARGETED FOR ELIMINATION AS A PUBLIC HEALTH PROBLEM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>Define indicator for measuring morbidity.</td>
<td>Implement effective interventions, including extending preventive chemotherapy to all populations in need and ensuring access to the necessary medicines; implement targeted snail control with updated guidelines; continue micro-mapping and targeting.</td>
</tr>
<tr>
<td>Develop diagnostic tests, including standardized point-of-care diagnostic, and develop new interventions, including alternatives to praziquantel and methods of snail control.</td>
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<td></td>
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</tbody>
</table>

WHO, 2020

https://big4.delivery.go.ke/
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ADOPT program – KEMRI’s participation

- Implementation research program bringing together relevant stakeholders from pharma, science and implementing countries

- Phases and activities relating to:
  - Pre-licensure (preparatory): social science, strategy development, planning (2 years)
  - Post-licensure (implementation): delivery, monitoring and (re-) evaluation (3 years)

- Staged approach based on findings of WPs: 1st identify → 2nd pilot & evaluate → 3rd upscale & evaluate

- Duration: 5 years, start NOW

- Dimension: 3 countries
ADOPT program – outcome

Final outcome of the ADOPT program

An implementation plan backed by policy and donors and supported by a practical toolkit to guide endemic countries through the preparatory steps leading up to the introduction of Levo-Praziquantel for paediatric schistosomiasis control through routine practice in community settings.

<table>
<thead>
<tr>
<th>GHIT5</th>
<th>EDCTP2</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 2 years, start Q4 2020</td>
<td>• 5 years, start Q1 2021</td>
</tr>
<tr>
<td>• Supporting activities pre-licensure</td>
<td>• Activities pre- and post-licensure</td>
</tr>
<tr>
<td>• Uganda</td>
<td>• Kenya and Côte d’Ivoire</td>
</tr>
</tbody>
</table>
Thank You

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