Breaking Resistance

Nix-TB Regimen: Overview of Non-clinical Evidence
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Background

• The challenges in contemporary treatment we aimed to address when we started the Nix-TB trial
  – Complicated treatments: 5-7 drugs
  – Long and arduous: 18+ months, 6 months injections
  – Very low cure rates: c.20% pre-bedaquiline
  – High toxicities
  – High cost

• Once we had clinical data that addressed the above, we wanted to evaluate whether the regimen
  – Will be accepted in the field?
  – Implemented?
  – Cost-effective?
  – Create savings for health systems?
Access Research Partners & Countries

- Acceptability
- Likelihood of implementation
- Cost-effectiveness
- Potential savings to health systems

6 diverse economies
4 regions
Varied TB burden and TB/HIV co-infection

NG, KG, ID, ZA, GE, PH
Acceptability of BPaL Regimen in Nix-TB Population

- Measure acceptability of the regimen as compared with the current individualized treatment regimen (ITR)
- 3 countries/regions: Nigeria, Kyrgyzstan, Indonesia
- 188 diverse stakeholders responsible for TB care: 3 categories and 9 sub-groups
- 7 parameters
- In-country focus groups and interviews to ascertain acceptability and likelihood of implementation

Focus groups, individual interviews

- Patient Friendliness
- Programmatic Aspects
- Human Resources
- Patient Support
- PSCM
- Baseline Assmt & Tx Efficacy Monitoring
- Treatment Safety Monitoring

Caregivers

Programmatic Stakeholders

Laboratory Stakeholders
Regimen Acceptability Interim Results

Overall acceptability of BPaL (Nix regimen) versus current individualized treatment regimen

- BPaL acceptability vs. ITR: up to 1.9X (range: 1.1-1.9X)
- Most notable: Patient friendliness and implementation related parameters such as programmatic aspects, HR, patient support
  - Likely drivers: shorter duration, lack of injectables, low pill burden, lesser financial burden and patient preference
- Similar score on treatment safety monitoring: benefit of shorter duration offset by uncertainty about label/guidance and potential increased monitoring requirements involving new drugs
- Overall likelihood of implementation: 88%
Cost Effectiveness of BPaL in Nix-TB Population (Interim Results)

- Population: XDR-TB, MDR-NR/TI
- Versus local SOC in 3 diverse epidemiologic & geographic settings
- Costs: pretomanid - $364; others: GHCC/VALUE-TB
- Monitoring: SOC – per country protocol; BPaL – per FDA label
- BPaL likely cost-saving in study settings
- Cost-eff. threshold for pretomanid: $2500-4300/Tx
- High HIV-TB setting: incremental cost of ART due to increased survival with BPaL considered
- Future ART costs reduce savings in HIV-TB settings
- DALYs averted: ~50% of DALYs with SOC

<table>
<thead>
<tr>
<th>Epidemiologic settings</th>
<th>BPaL component costs</th>
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<tbody>
<tr>
<td>High MDR / High HIV-TB (ZA)</td>
<td>Pretomanid $364</td>
</tr>
<tr>
<td>High MDR / Low HIV-TB (PH)</td>
<td>Bedaquiline $400*</td>
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<tr>
<td>Low MDR / Low HIV-TB (GE)</td>
<td>Linezolid $495-989</td>
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Outcomes
- Cost-effective in all three settings
- Pretomanid cut-off $2500-4300K/Tx
- DALYs averted 46-56% of SOC
Budget Impact of BPaL Use in Nix-TB Population (Interim Results)

- Objective: ascertain incremental cost of using BPaL
- Scope: diagnostic, treatment, treatment monitoring costs
- No direct/indirect patient costs
- 3 countries/regions: Nigeria, Kyrgyzstan, Indonesia
- High MDR-TB burden
- Savings potential BPaL vs. SOCs: ~$6500-11000/patient
- Notable reduction in monitoring & treatment costs

The Global Picture (estimates by McKinsey)
- Potential health systems savings until 2023: USD 0.7-1.1 bn*
- Total economic benefit could be 4.6-7.1 bn USD, including future GDP savings
- Cost per successful treatment reduced by 65-80%
- Every treated patient, frees up resources for 1-2 others
- Resources freed up for an additional ~220,000 patients

*Nix-TB & ZeNix regimens
Breakdown of Drug Costs in BPaL and Current Regimens

- Reduction in cost of drugs – BPaL vs. current SOCs: ~$4000-9000
- Current XDR-TB regimens $5-10,000
- BPaL can be as low as ~$1000
- Drivers for savings: elimination or reduction in quantity of expensive drugs

Savings on account of linezolid in all settings

Others: Cf, DLM, Imi-cila, PAS

Drug cost per patient (USD)

- Current: US$4,143
- BPaL: US$9,468
- Current: US$4,014

Drug costs USD:
- Bedaquiline
- Linezolid
- Pretomanid
- Clofazimine
- Imipenem-Cilastatin
- Delamanid
- PAS-(Na)-4-(S)
- Other drugs
Global Enablers for Access

Policy & guidelines

• Clinical and non-clinical (market research) data submitted to WHO for consideration by the Guidelines Development Group

Regulatory

• Joint regulatory prioritization with Mylan
• Mylan has commenced regulatory submissions, starting with India (July 2019)
• ~25 filings by Mylan within 1 year of FDA approval
• Mylan will seek WHO PQ for pretomanid subject to opening of EOI

Supply & Availability

• Second license (Macleods) signed: to support the aim of affordable and sustainable supplies of pretomanid
• GDF listing 2 months after FDA approval. Price of $364/Tx
For our Panelists

- Best way to support access to BPaL in light of the clinical and non-clinical evidence on the regimen?
- Roles of key stakeholders?
- Collective goals over the next 1, 2, 5 years?