Increased Moxifloxacin Dosing among MDR-TB Patients with Low-Level Resistance to Moxifloxacin did not Improve Treatment Outcomes in a Tertiary Care Center in Mumbai, India

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Disclosures

➢ Nothing to Disclose
**Background**

- Tuberculosis is the #1 infectious disease killer worldwide
  - 26.8% of global cases in India\(^1\)
  - Rates of MDR-TB are increasing in India\(^2\)
  - Mumbai disproportionately affected
- Outcomes relate directly to drug resistance:
  - Susceptible TB: 88% good outcome
  - MDR-TB: 46% good outcome
  - XDR-TB: 12% good outcome\(^3\)

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\(^1\)WHO Global Tuberculosis Report 2017
\(^2\)Revised National TB Control Program Annual Reports 2011–2017
\(^3\)Pietersen E, et al. Lancet 2014
Prospective Observational Cohort of MDR-TB

- **Study Site**: P. D. Hinduja National Hospital and Medical Research Centre in Mumbai, India
  - Extensive clinical experience with complex resistance, bedaquiline, and delamanid
  - CAP & NABL accredited BSL 2+ lab (>32,000 samples/yr)
  - Diagnostic test and pharmacokinetic assessments

- **Participants**: MDR-TB patients treated at the study site

- **Outcome**: Improved rates of “good” (cure/completion) vs. “bad” (death, default, relapse, loss to follow-up) outcome associated with moxifloxacin 600mg

- **Data Analyzed**:
  - Participant visit data from October 2015-October 2019
  - 573 total cohort participants
  - 344 (60%) moxifloxacin R at 0.5ug/mL
  - 283 (82.2%) prescribed 600mg daily
  - 1650 patient visits

**Diagram**:
- All Participants with MDR-TB (N=573)
  - Moxifloxacin Resistance Not Tested, N=103 (18.0%)
  - MDR-TB Patients with Moxifloxacin Resistance Results, N=470
    - Moxifloxacin Susceptible at 0.5 µg/mL, N=126 (26.8%)
    - MDR-TB Patients Resistant to Moxifloxacin at 0.5 µg/mL, N=344
      - MDR-TB Patients Not Treated with Moxifloxacin, N=61
        - Good Outcomes: N=30 (49.2%)
        - Bad Outcomes: N=19 (31.1%)
        - Ongoing Treatment: N= 3 (4.9%)
        - Transferred: N= 9 (14.8%)
      - MDR-TB Patients Treated with 600mg Moxifloxacin, N=283
        - Good Outcomes: N=146 (51.6%)
        - Bad Outcomes: N= 74 (26.1%)
        - Ongoing Treatment: N= 39 (13.8%)
        - Transferred: N= 24 (8.5%)
No significant difference in demographics, treatment, or outcomes

- More frequent self-reported joint pain with moxifloxacin
Underweight and # of effective drugs were associated with good outcome
Moxifloxacin 600mg daily was not significantly associated with outcomes
Conclusions

- In a large single site prospective observational cohort with complex drug resistance and individualized treatment:
  - Moxifloxacin resistance at 0.5ug/mL is common
  - Moxifloxacin 600mg daily did not improve treatment outcomes compared no moxifloxacin
    - This was true independent of specific drugs and additional resistance data
    - Also not associated with culture conversion at 2M, culture conversion at 6M, or time to culture conversion
    - It was associated with joint pain (OR 3.3 (1.2-11.4)
  - # of effective drugs associated with improved outcomes in adjusted and unadjusted analysis
  - Results for moxifloxacin 600mg daily may not be generalizable to moxifloxacin 800mg daily
Acknowledgements

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Underweight and number of effective drugs were the strongest predictors of treatment outcomes.

Moxifloxacin 600mg daily was not significantly associated with outcomes.
Role of Additional Treatment

Hazard of Bad Treatment Outcome Associated with Concomitant Treatment, by Drug

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<th>Drug</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
<th>p-value</th>
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<tr>
<td>Linezolid</td>
<td>0.56 (0.35-0.90)</td>
<td>0.018</td>
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<tr>
<td>Bedaquiline</td>
<td>0.45 (0.18-1.10)</td>
<td>0.091</td>
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<tr>
<td>Clofazimine</td>
<td>0.66 (0.44-1.00)</td>
<td>0.056</td>
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<tr>
<td>Cycloserine</td>
<td>0.44 (0.29-0.67)</td>
<td>&lt;0.001</td>
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<tr>
<td>Ethambutol</td>
<td>0.90 (0.33-2.50)</td>
<td>0.850</td>
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<tr>
<td>Pyrazinamide</td>
<td>0.52 (0.19-1.40)</td>
<td>0.200</td>
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<tr>
<td>Ethionamide</td>
<td>1.60 (0.97-2.70)</td>
<td>0.068</td>
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<tr>
<td>Injectable (Amikacin, Kanamycin, or Capreomycin)</td>
<td>0.56 (0.37-0.86)</td>
<td>0.008</td>
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<td>PAS During Study</td>
<td>0.65 (0.43-1.00)</td>
<td>0.048</td>
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<td>Delamanid During Study</td>
<td>0.36 (0.09-1.50)</td>
<td>0.160</td>
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Summarized by Number of Concurrent Drugs

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<td>Number of Effective Drugs Prescribed</td>
<td>0.81 (0.72-0.92)</td>
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<td>Took At Least 4 Effective Drugs</td>
<td>0.49 (0.32-0.76)</td>
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- Confirmed benefit of additional treatments, across WHO drug groups
- Linezolid, cycloserine, injectable, drugs, and PAS demonstrated protection (P<0.05)
- These were summarized as number of effective drugs prescribed