New Frontiers: Innovation and Access

Modifications to the short regimens and operational research conditions

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Overview

• Why a short regimen?
• Current recommendations
• Review of data
• Ongoing studies
• Opportunities
Why a short regimen?

- In 2014:
  - Include >1 new drug
  - Active against MDR/XDR
  - Include 3-5 drugs
  - All oral treatment & simple dosing schedule
  - Minimal interaction with ART
  - Maximum 6 months
Why a short regimen?

• Potential benefits:
  – Improved adherence and treatment completion
  – Back to work quicker
  – Resources available to treat more people
  – Cheaper
  – Potential for non-DOT models of care
Current recommendations

- In MDR/RR-TB patients who have **not been previously treated for more than one month** with second-line medicines used in the shorter MDR regimen or in whom **resistance to fluoroquinolones and second-line injectable agents has been excluded**, a shorter MDR-TB regimen of 9–12 months may be used instead of the longer regimens.
Available data

- STREAM study
  - Multi-country RCT comparing the standardised short regimen with longer recommended treatment
  - 424 patients randomised between 2012-2015
  - 79% success for those receiving short regimen
  - 80% success for those receiving longer regimen
  - Severe AEs similar, more QTcF prolongation, severe hearing loss in both groups (6%), more hepatoxicity
Available data

• STREAM study
  – Health system costs and patient-related costs were lower with the short regimen
  – Patients receiving the short regimen returned to work faster than those receiving the longer regimen
Available data

• By the end of 2017, approximately 10 000 people had started the short regimen in that year alone
• Data from 2625 people from 15 countries was include in the meta-analysis for the guideline update
• Patients with confirmed resistance to Pza or Eto/Pto had worse outcomes than those susceptible
• Higher treatment interruption in those receiving longer regimens
• Comparisons made against long regimens without newer drugs
Ongoing studies

- RR/MDR/XDR-TB
  - MDR-END
    - 9-12m – Dlm – Lzd backbone
  - STREAM 2
    - 6-9m – Bdq – Cfz backbone
  - endTB (-Q)
    - 9m – Bdq – Dlm – Lzd backbone
  - TB-PRACTECAL
    - 6m – Pa – Bdq – Lzd backbone
  - SimpliciTB (NC-008)
    - 6m – Pa – Bdq backbone
  - BEAT-TB
    - 6m – Bdq – Dlm – Lzd backbone
  - NiX-TB & ZeNiX
    - 6m – Pa – Bdq – Lzd backbone
  - Observational cohorts
    - South Africa, Belarus, DestroyTB

New Frontiers: Innovation And Access
8th TB Symposium – Ministry of Health of the Republic of Uzbekistan and Médecins Sans Frontières
Modifications

STREAM B
Lzd (2)  Bdq (6)
Km  H  Pto  Mfx  Cfz  E  Z

STREAM C
Bdq
H  Pto  Mfx/Lfx  Cfz  E  Z

STREAM D
Bdq
Km  H  Lfx  Cfz  Z

South Africa

* Slide courtesy of Askar Yedilbayev
Opportunities

• “Regimens that vary substantially from the recommended composition and duration (e.g. a standardized 9-12 month shorter MDR-TB regimen in which the injectable is replaced by bedaquiline) can be explored under operational research conditions”

WHO treatment guidelines for multidrug- and rifampicin-resistant tuberculosis
2018 update
Opportunities

• Availability of generic protocol for supporting operational research
• Choices regarding drug composition
• Multiple partners offering support
• Note: clinical trials investigating treatment shortening using Bdq, Dlm, Pa, Lzd backbone
Regimen selection

• Adjustments to recommended short regimen
  – E.g. replace injectable with Bdq, include Lzd
  – Cheaper
  – Expecting programmatic data from South Africa soon

• Investigate clinical trial regimens in “real world”
  – WHO recommended combinations, but shorter duration
  – Likely more effective given reliance on newer drugs
  – DST not yet universally available
Summary

- Shorter treatment regimens are required to improve adherence, access and costs.
- Including newer drugs in shorter regimens are likely to improve effectiveness and reduce toxicity.
- Sharing experience from the region to support future guideline updates is important.
- Using regimens under operational research conditions is possible with partners willing to support.