endTB

Updates from the observational study

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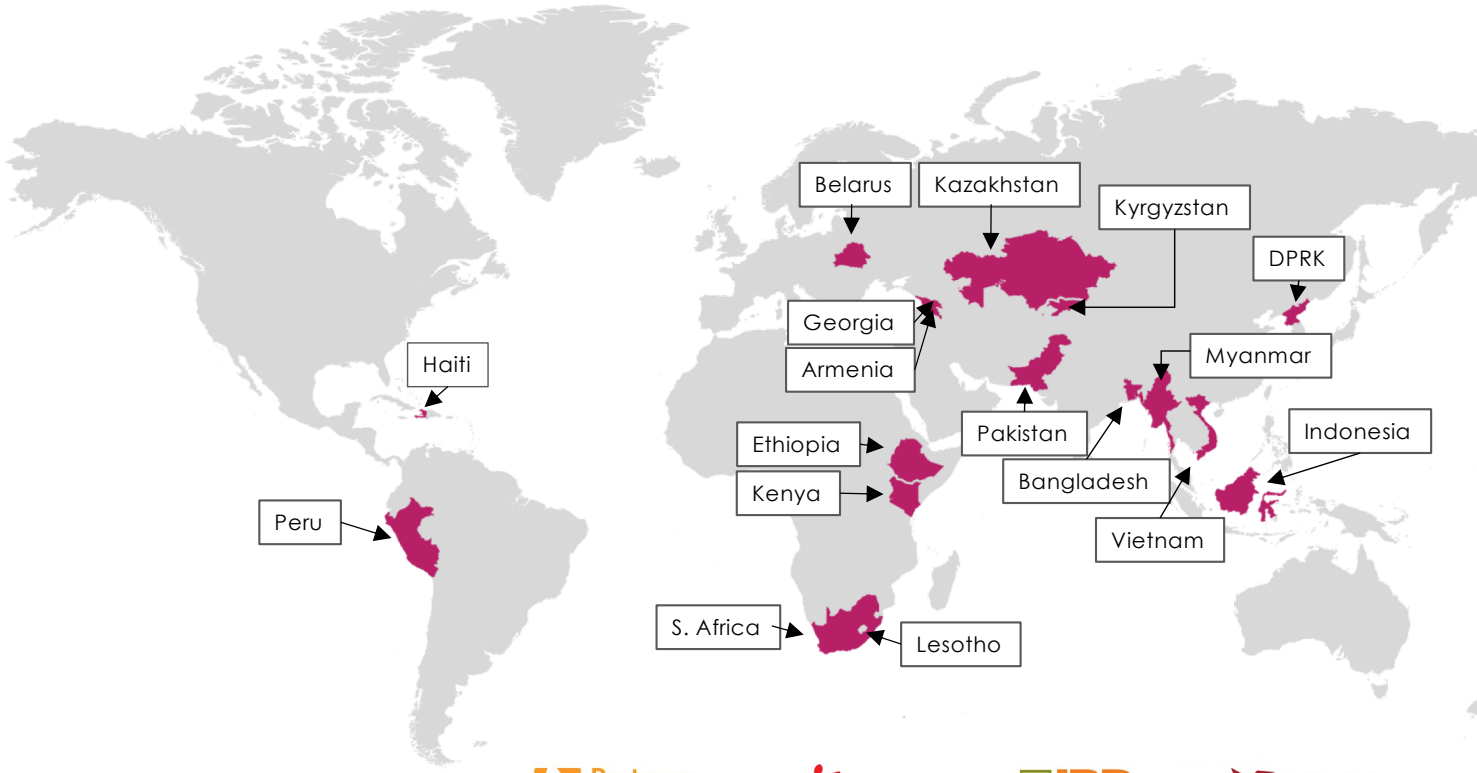
[On behalf of the endTB consortium]
15 Nov 2018

endTB Observational Study

Largest multi-centric observational study on regimens containing bedaquiline and/or delamanid

17 Countries

> 2600 Patients



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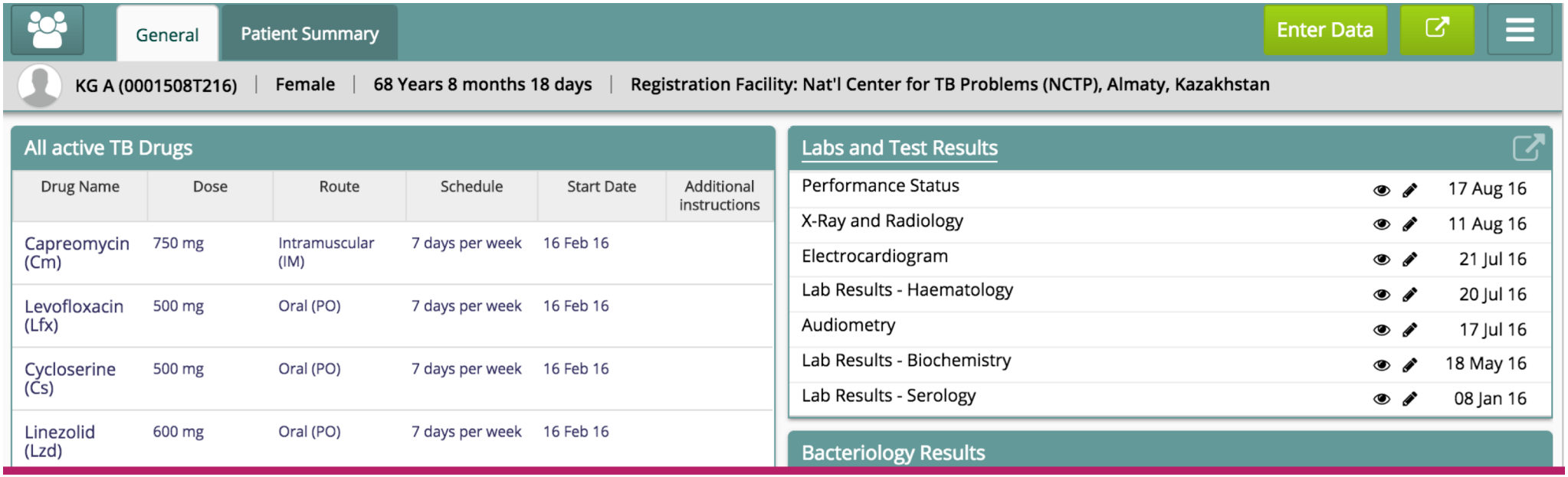


Methods

Cohort analysis of research-consented patients

- Receiving MDR-TB treatment regimen including bedaquiline and/or delamanid per WHO recommendations

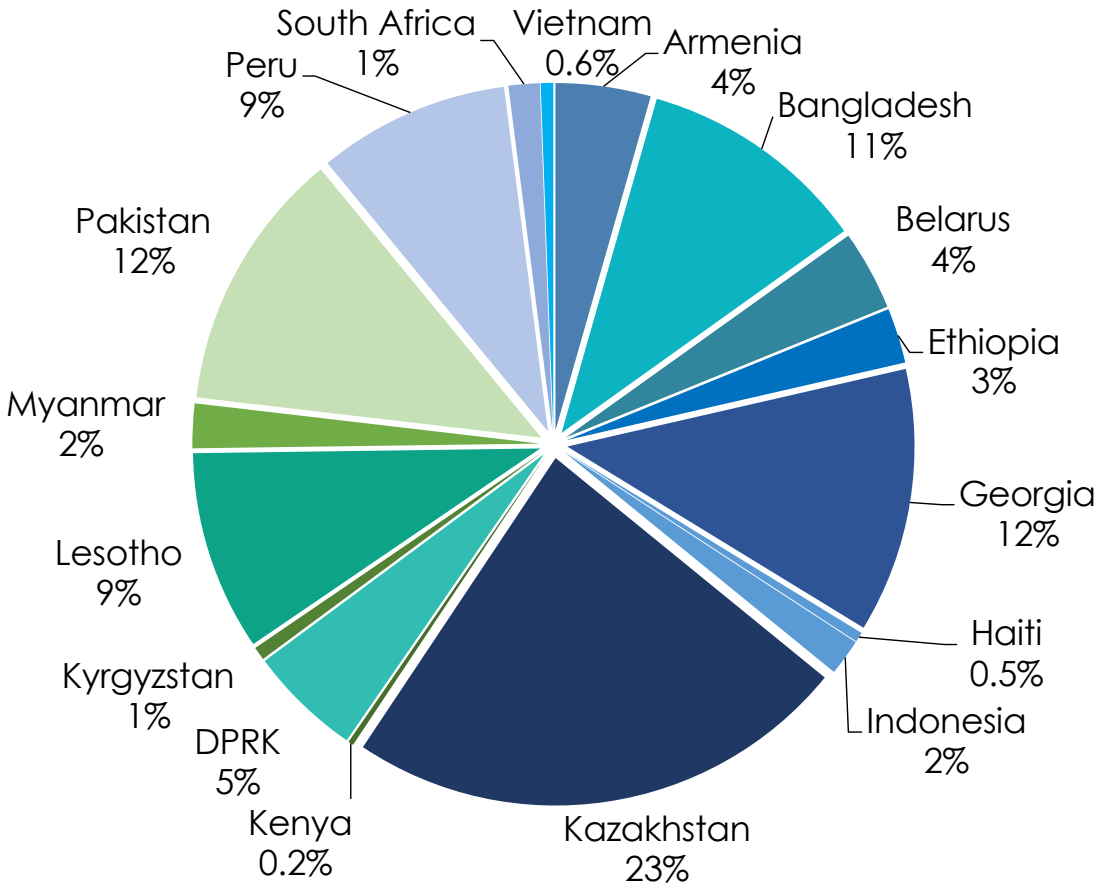
Data capture

- Standardized data collection at project sites
- Electronic medical record (OpenMRS, Bahmni), pharmacovigilance database
- Standardized endpoints

Cohort Description

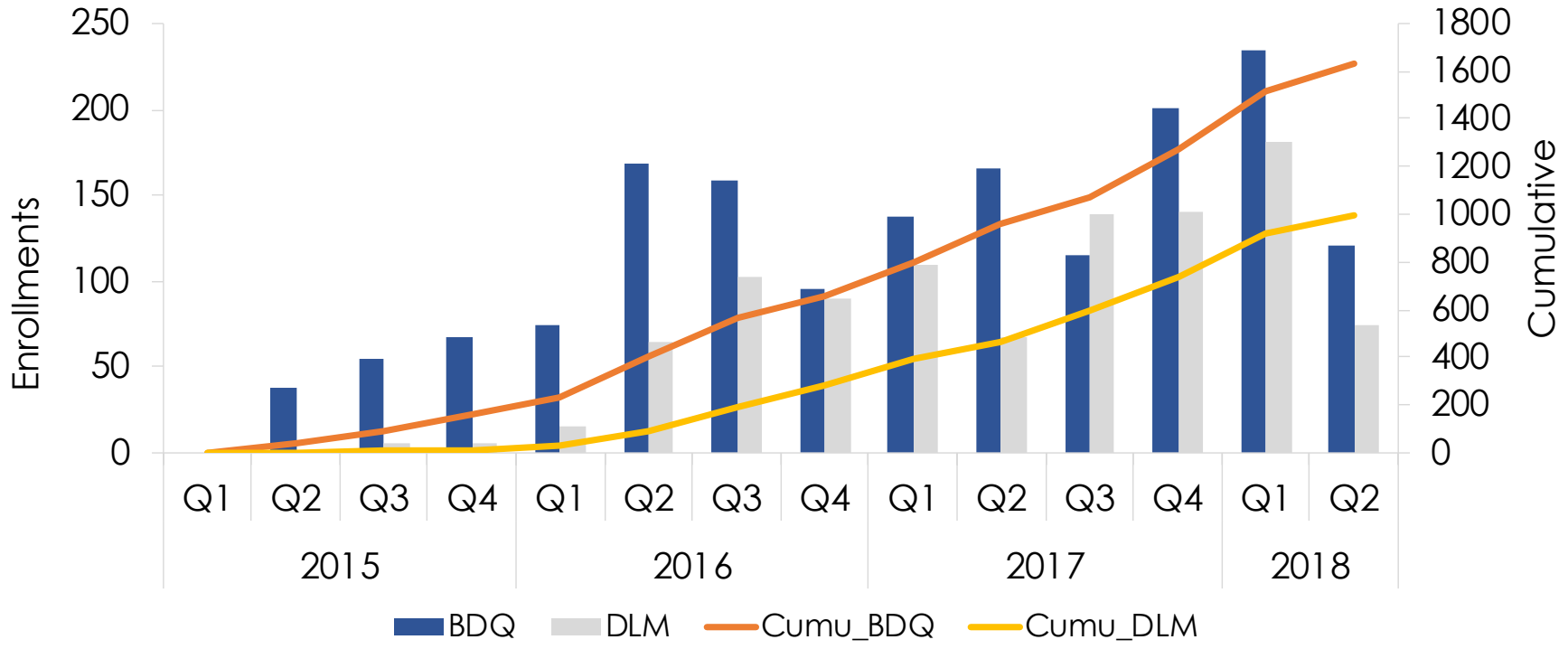
April 1, 2015 to May 31, 2018

2241 patients
starting Bdq or Dlm



Use of Bedaquiline Predated Use of Delamanid

Enrolled until May 31 2018

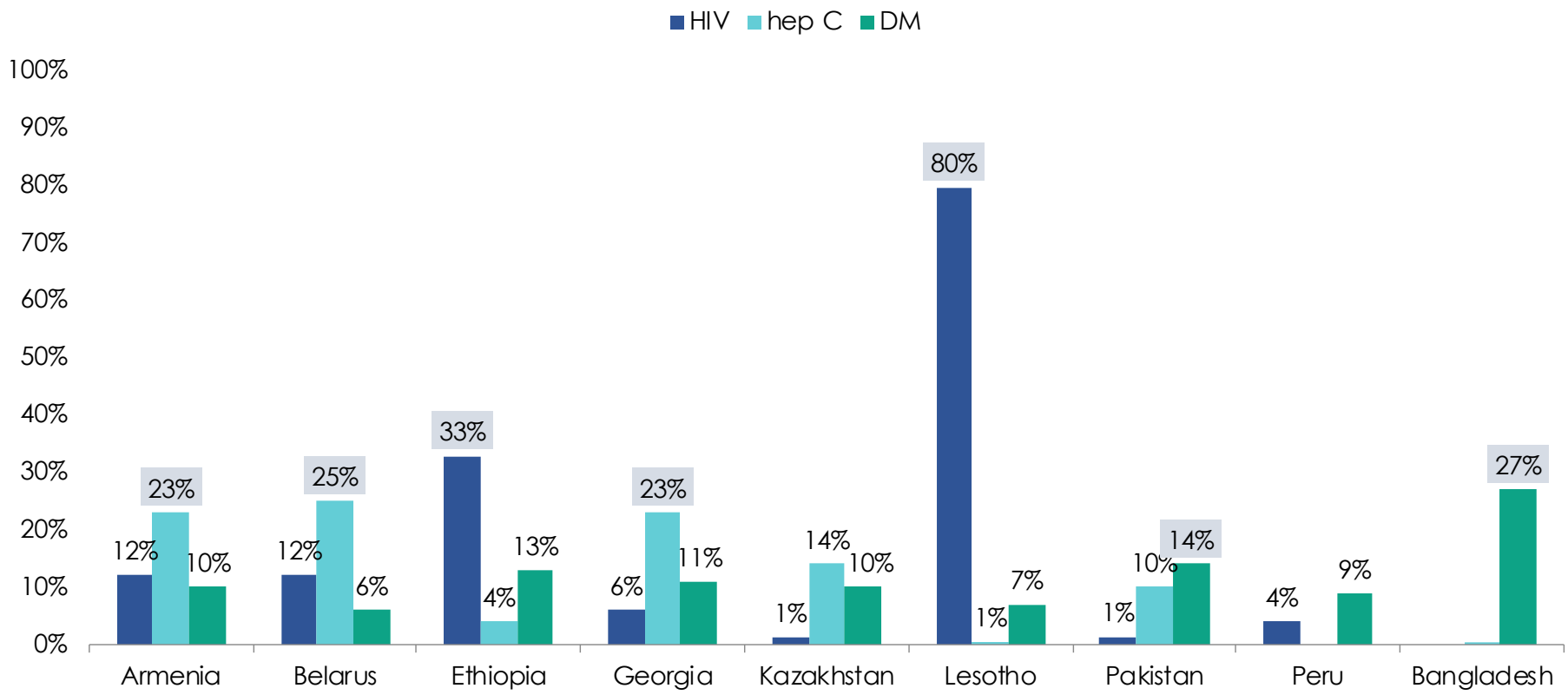


Patient Characteristics

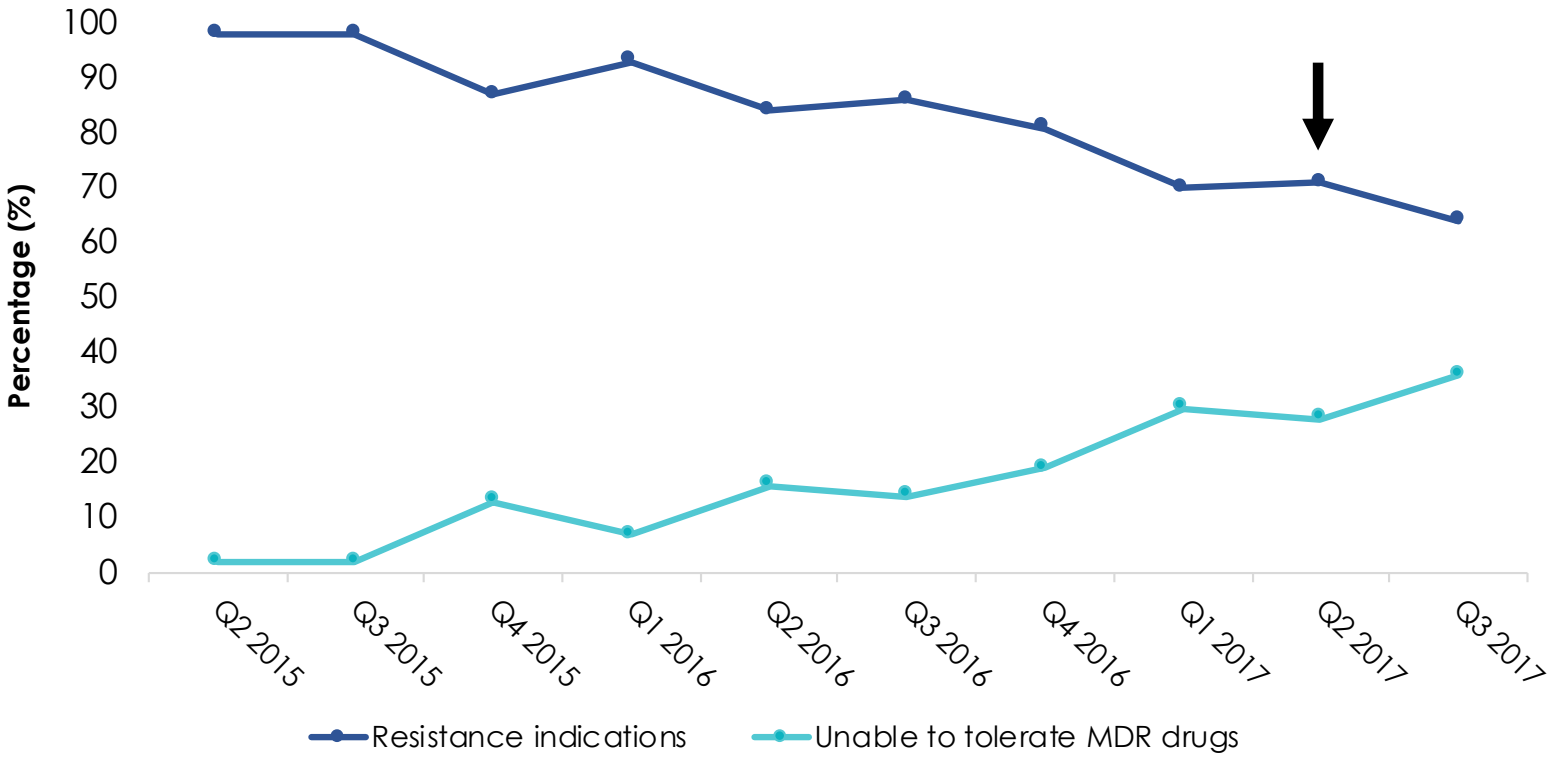
April 1, 2015 – 31 May 2018

Characteristic	Total N (%) N=2241
Median age [range]	37 [9 – 88]
Female	794 (35)
Body mass index <18.5 (n=2207)	928 (42)
Resistance (n=2137)	
RR/MDR-TB	697 (31)
Pre-XDR (FQ)	519 (23)
Pre-XDR (Inj)	270 (12)
XDR	651 (29)
Comorbidities	
HIV (N=2217)	297 (13)
Hepatitis C (N=2194)	236 (11)
Diabetes (N=2107)	266 (13)
Previously treated w/ SLDs (N=2240)	1638 (73)

Proportion of Patients with HIV, hep C and DM



Patients Enrolled Early were Chronic & Sicker



endTB Patients

Indonesia

2014

DS-TB Rx at a private clinic, outcome unknown

Started treatment at another private clinic. Doctor suggests patient should seek treatment in Malaysia

2015

Patient traveled to Malaysia and stayed there for 2 months without improvement

Returned to Jakarta. Got hospitalized at a private hospital. After discharge, did not return to the hospital

2016

Patient started treatment again at a private hospital, after a few months patient was asked to go to RS Islam Cempaka Putih

2017

– now – Received MDR TB treatment at RS Islam Cempaka Putih (enrolled on endTB in October 2017)

endTB Interim Analysis

1. What is the evidence for or against the use of delamanid in multidrug regimens for RR/MDR-TB?

2. What is the evidence for or against the use of injectable-sparing regimens for RR/MDR-TB when BDQ &/or DLM are available?

3. What is the range of adverse event (AE) profiles observed in multidrug regimens that include bedaquiline and/or delamanid?

Overall

Interim Analysis
Delamanid Efficacy & Toxicity

- ≥ Grade 3 QTc interval prolongation infrequent
- Culture conversion occurs in **~ 80%**, including among XDR and patients with comorbidities
  - Conversion in HIV coinfected lower
- Balance of efficacy and safety supports delamanid use

Overall

Interim Analysis

Injectable Efficacy & Toxicity

- Important! toxicity common among patients receiving SL injectable
  - 20% of patients had hearing loss
  - 36% had injectable-related AE (hearing loss, acute renal failure, electrolyte imbalance)
- Balance of evidence does not support universal use of SL injectable (also supported by the IPD analysis – WHO recommendations)
  - Consider treatment options, patient preference
  - effective monitoring

BDQ- and DLM-containing multidrug-regimens achieve excellent interim treatment response without safety concerns

endTB Interim Analysis

http://www.endtb.org/resources/endtb-interim-analysis-july2018