

Treating Patient, Not Disease: People-Centered Approach

7th TB Symposium – Ministry of Health of the Kyrgyz Republic
and Médecins Sans Frontières

1-2 March , 2018, BISHKEK , KYRGYZSTAN

Sputum conversion/reversion among patients on new TB drugs: endTB cohort

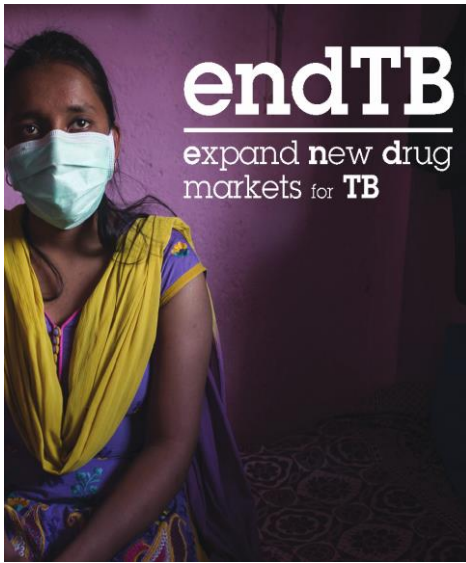
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What is endTB?

Expand New Drugs for TB



www.endTB.org

Consortium partners:

- Partners In Health (PIH)
- Médecins Sans Frontières (MSF)
- Interactive Research and Development (IRD)

Funding partner: Unitaid

Project duration: 4 years (2015-2019)

Project budget: 60.4 million USD

Goal:

- Expand access to bedaquiline & delamanid
- Produce evidence on new TB drugs: observational study





endTB project implementation

- At least 2600 patients in 17 countries



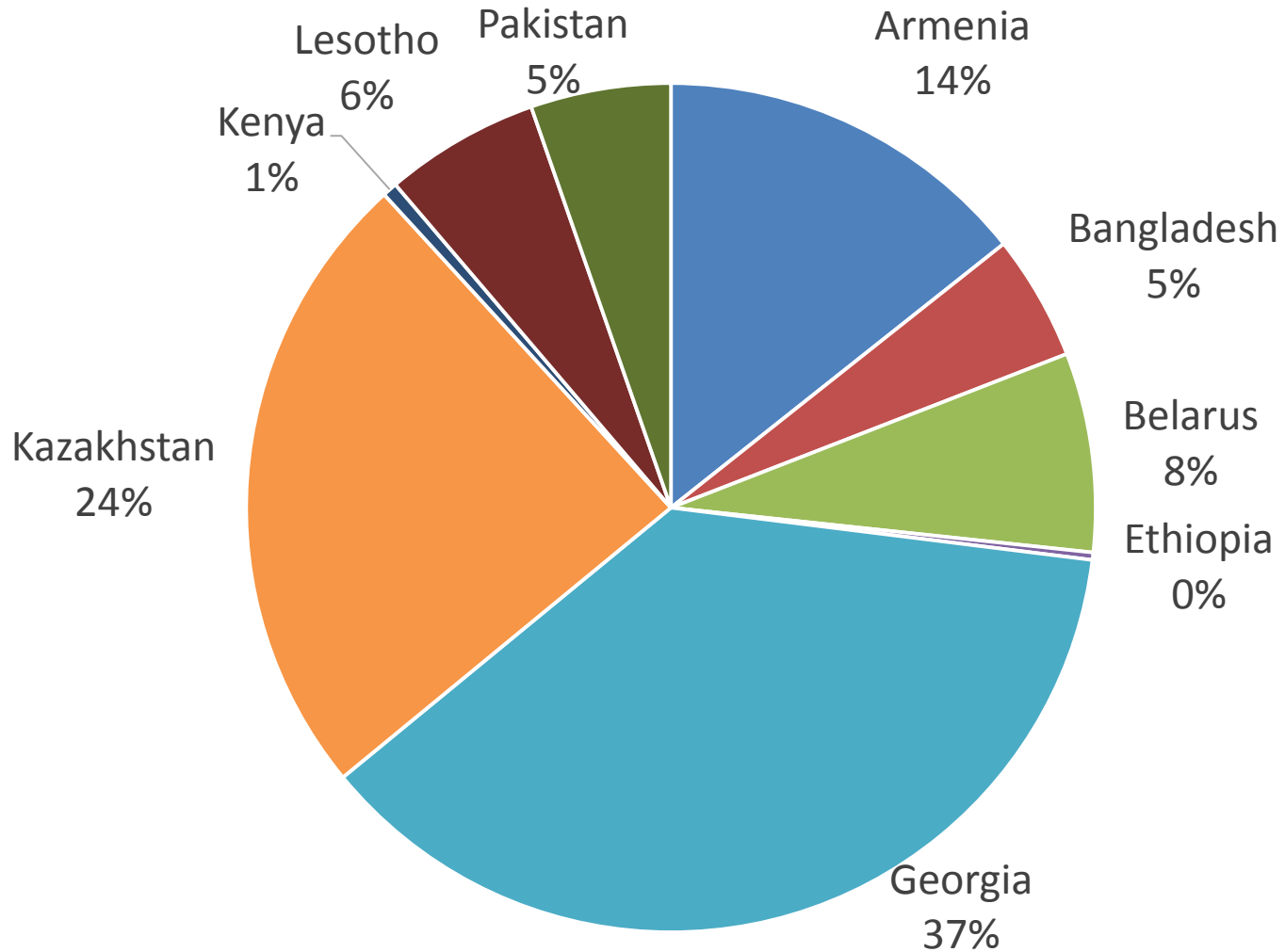
endTB observational study

- **Objectives:** Assess efficacy and safety of bedaquiline (Bdq) and delamanid (Dlm) in programmatic conditions
- **Design:** Multicentric prospective and retrospective observational cohort study
- **Population:** Patients on Bdq or Dlm who signed informed consent
- **Preliminary cohort analyses:**
 - Culture conversion by 6 months
 - Culture reversion by 12 months
 - Adverse Events of Interest and Serious Adverse Events
 - Expanded indications

Culture conversion

- We report the proportion of patients whose sputum converted to negative during the first 6 months of treatment with Bdq or Dlm
- Cohort: 1st April 2015 – 30th Sep 2016
- Population: positive sputum culture up to 90 days before Bdq or Dlm start
- Conversion date: the date of the first of two negative cultures ≥ 15 days apart

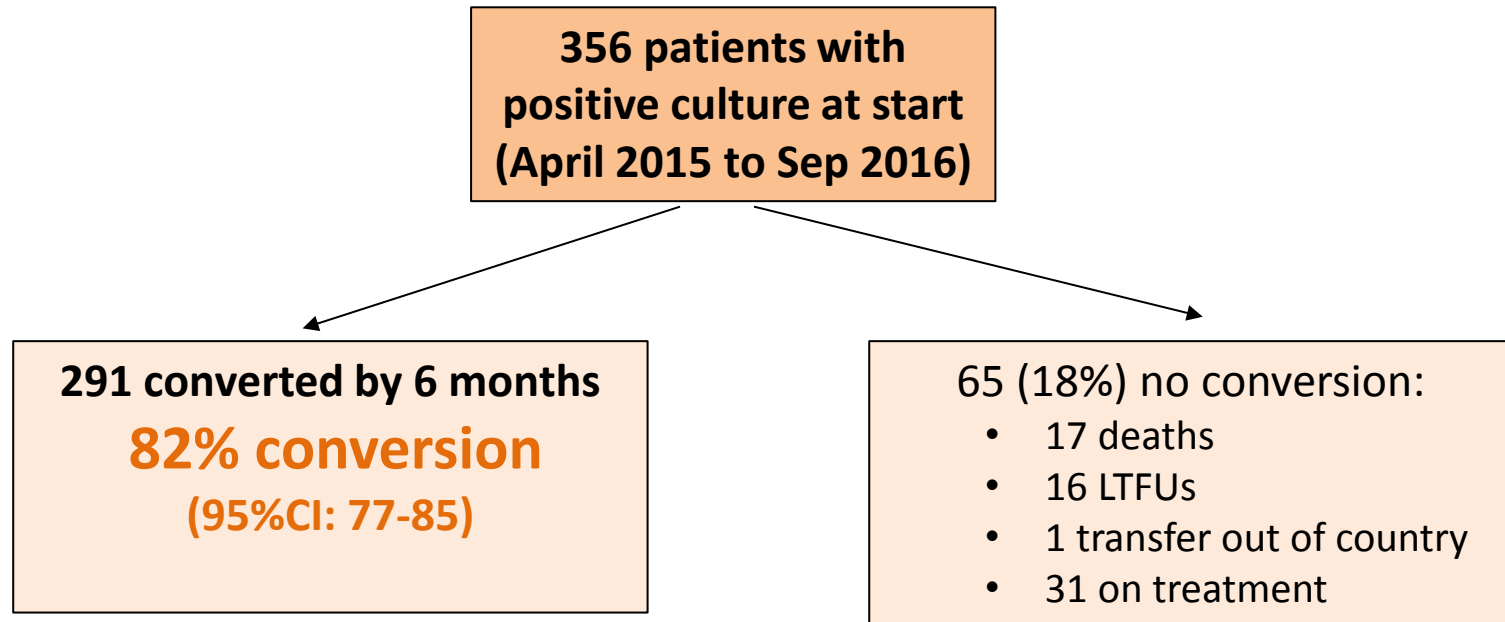
Enrollment by country (N=356)



Patient characteristics

Characteristic	n (%)
Median age [range]	38 [17-82]
Male	261 (73)
Body mass index <18.5	127 (37)
Bilateral disease	221 (68)
Resistance	
MDR or Xpert RR	51 (15)
Pre-XDR (Inj)	26 (7)
Pre-XDR (FQ)	109 (31)
XDR	161 (46)
Comorbidities	
HIV	36 (10)
Hepatitis C	65 (19)
Diabetes	42 (13)
Previously treated w/ SLDs	281 (79)

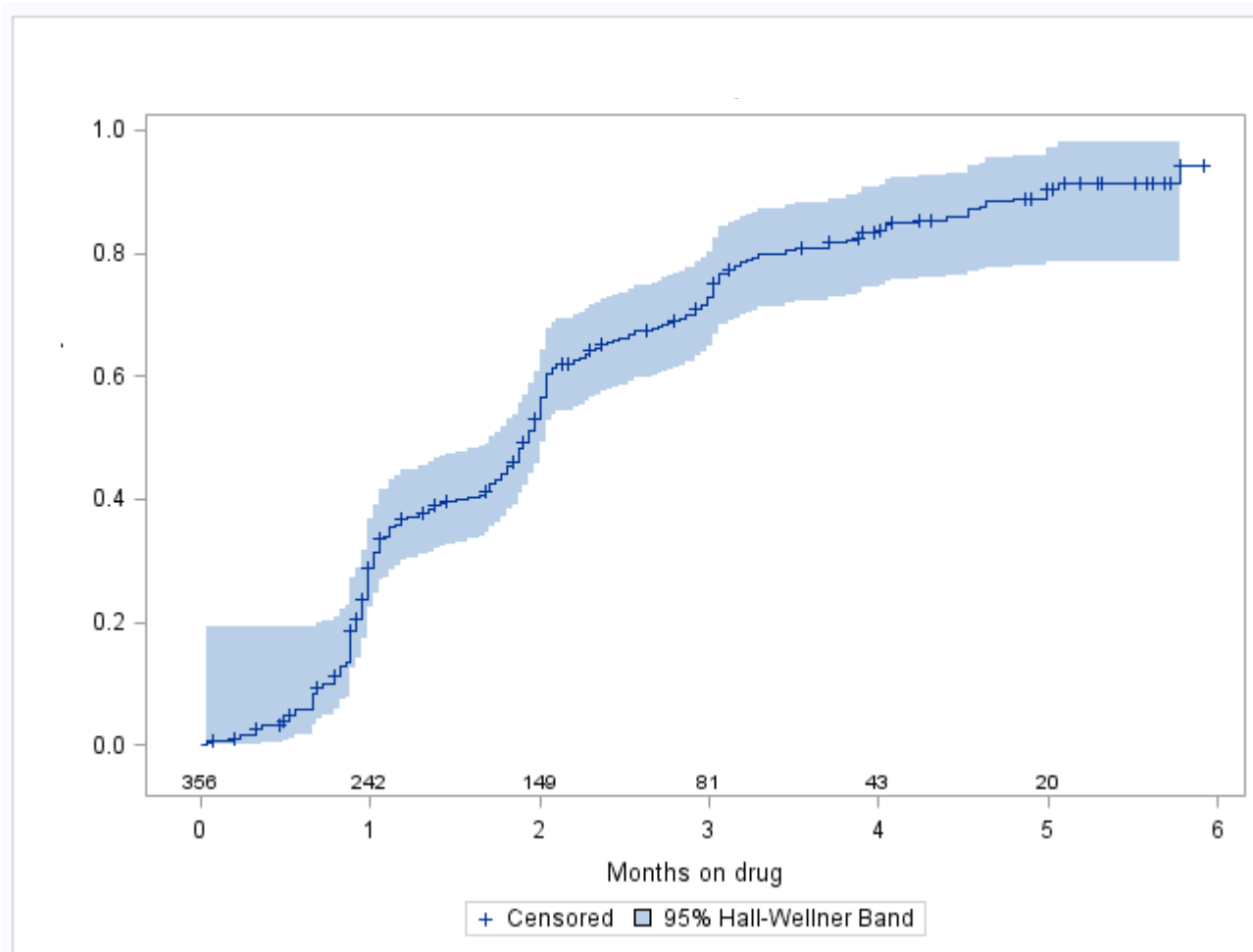
Culture conversion



Culture conversion: 2 negative cultures with sample collected at least 15 days apart

Time to culture conversion

Median conversion time among converted: 52 days [IQR: 29 – 73 days]



Conversion in subgroups

	Conversion %	p-value
HIV		
Positive (N=36)	67	0.01
Negative (N=318)	84	
Hepatitis C		
Positive (N=65)	78	0.42
Negative (N=284)	83	
Diabetes		
Yes (N=42)	86	0.55
No (n=294)	82	
XDR		
Yes (N=161)	80	0.48
No (N=189)	83	

HIV patients:

- 25% recently diagnosed
- 86% on ARVs
- 10/12 not converted died
- Time to death: 64 days
- CD4 cell count: 145

Culture reversion

- We report the proportion of patients whose sputum reverted to positive after culture conversion during the first 12 months of treatment with Bdq or Dlm
- Cohort: 1st April 2015 to 28th Feb 2016
- Reversion: two consecutive positive cultures after culture conversion
- Countries: Armenia, Belarus, Georgia, Kazakhstan, Lesotho

Patients' characteristics

- **Population: 98**
- Men: 78 (79.6%)
- Age: 39 years [IQR 31-51]
- Resistance patterns:
 - Pre-XDR Fluoroquinolones: 32 (32.6%)
 - Pre-XDR Injectables: 9 (9.2%)
 - XDR: 51 (52.0%)
- Cultures during follow-up period: 10 [IQR 7-12] /patient

Culture reversion

- **Reversion rate: 3.1%** (95%CI 0.6-8.7%)
- Time to reversion from conversion:
 - After 1, 5 and 6 months
- Time to reversion from new drug start:
 - After 2, 8 and 9 months
- Deaths during reversion period: 3



Conclusions

- Favorable conversion percentages in a cohort of treatment-experienced patients with high-grade resistance and extensive disease
- Early deaths among patients with advanced HIV drive lower conversion percentages among patients living with HIV
- Low proportion of reversion
- More data needed to identify risk factors for reversion and role of treatment duration >24 weeks and concomitant use of bedaquiline and delamanid.
- Further interim results expected in 2018

Thank you





Description of the 3 patients who reverted

	Age	Sex	Country	HIV	Hep C	Previous MDRTB failure	Resistant to FQ	Treatment regimen
Patient 1	28	M	Belarus	Neg	Neg	Yes	XDR	Lzd+Dlm+ Amx-Clv+ Cfz+Cilastatin/Imipenem
Patient 2	39	M	Georgia	Neg	Neg	No	Pre-XDR (Fq)	Bdq+Cs+Cm+ Lzd+Pto+ Lfx+Cfz
Patient 3	69	F	Kazakhstan	Neg	Neg	Yes	XDR	Bdq+Lfx+ Cm+Cs+Cfz+ Lzd