

SEIN SEIN THI<sup>1</sup>, SYLVIE JONCKHEERE<sup>1</sup>, CHINMAY LAXMESHWAR<sup>1</sup>, GUSTAVO CORREA<sup>1</sup>, SARTHAK A RASTOGI<sup>1</sup>, PARVATI NAIR<sup>1</sup>, SUYOG S SHETYE<sup>1</sup>, DINESH P SAWANT<sup>1</sup>, MRINALINI DAS<sup>1</sup>, HOMA MANSOOR<sup>1</sup>, PETROS ISAAKIDIS<sup>1,2</sup>

<sup>1</sup>MÉDECINS SANS FRONTIÈRES, MUMBAI, INDIA

<sup>2</sup>MÉDECINS SANS FRONTIÈRES, OPERATIONAL RESEARCH UNIT, LUXEMBOURG CITY, LUXEMBOURG

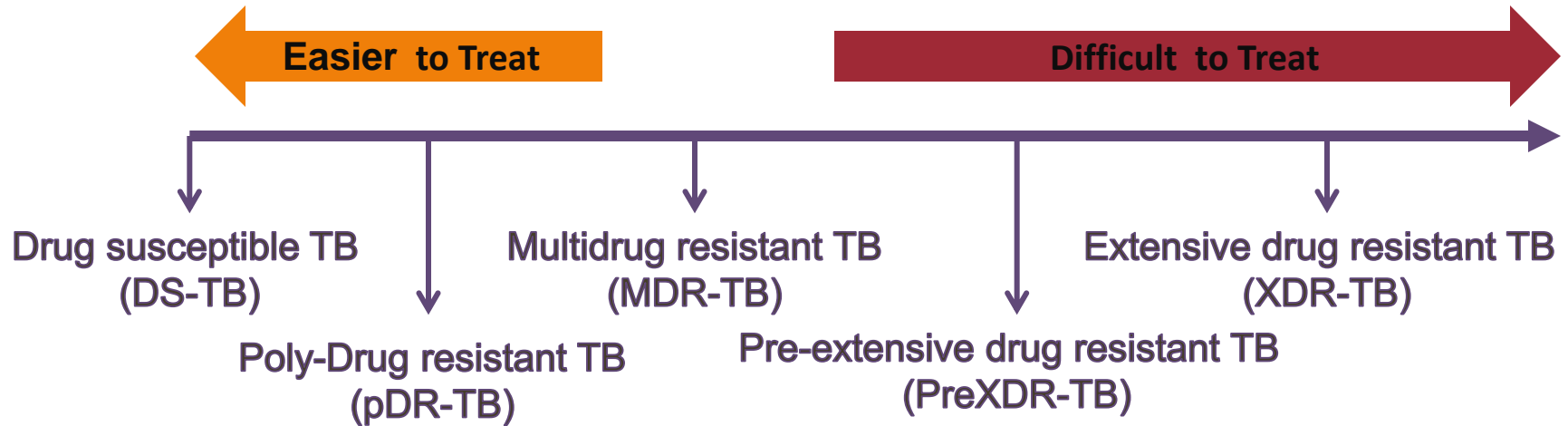


# Too little, too late; new anti-TB drugs for patients with complex drug-resistant tuberculosis in Mumbai

Sylvie Jonckheere  
MSF OCB, Mumbai, India



# Setting the DR-TB stage



➤ For all types of TB, treatment should contain > 4 effective drugs

# Treating DR-TB

- Current recommended regimen for DR-TB:
  - Lack of clinical trial evidence
  - Toxic
  - Very long (up to 2 years)
- Outcome of DR TB treatment
  - Treatment success in MDR TB 48%
  - HIV/DR TB co-infected 38%



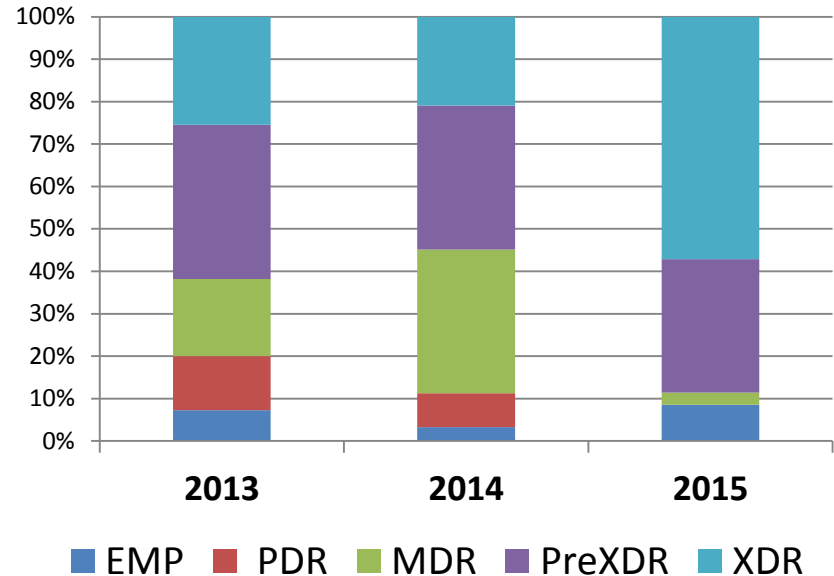
## DR-TB 2 New Drugs

- since Rifampicin > 50 years ago
- Bedaquilline (Bdq) & Delamanid (Dlm )
  - validated by WHO with “monitoring of pharmacovigilance”
  - The price of new drugs is still high – Bdq: 900 USD/course, Dlm: 1700 USD /course
- New drugs are available to only 2% of patients who need them (AC)
  - Compassionate Use programs and restrictive protocols for Dlm
  - Bdq Conditional Access Programs that is about to start in India

# Setting –MSF Clinic in Mumbai

- Provides ambulatory free DR TB and HIV treatment services since 2006
- 1101 HIV and 253 TB/DR TB beneficiaries
- Increasing proportion of complex DR TB cases (PreXDR and XDR)
- Access to Bdq through CU in 2013 – Aug 2015, Dlm since June 2015
- Counseling and consent

Enrolled DR TB patients (2013-2015)



# Method of study

- Retrospective cohort analysis of
  - 12 patients registered for Bdq
  - 14 patients for Dlm,
  - from Feb 2013 to Feb 2015
- MSF ERB approval



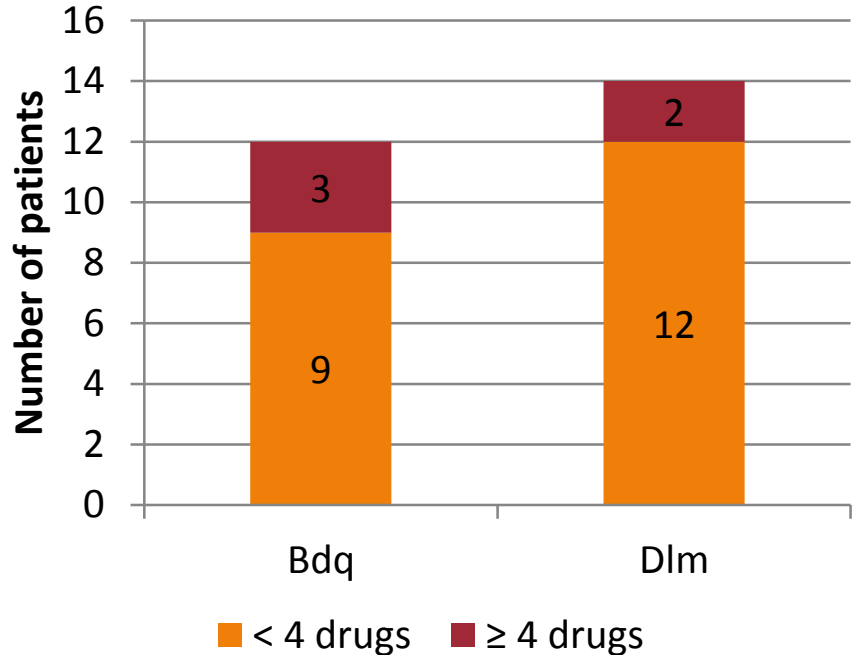
# Characteristic of patients

	Bedaquiline Group (n=12)	Delamanid Group (n=14)
Age (years)	18-37	17-47
Gender (M:F)	4 : 8	4 : 10
HIV co-infected	2	0
Type of DR TB (based on 13 drugs Drug Susceptibility Testing)		
Pre XDR	3	2
XDR	9	12
Prior exposure to 2 <sup>nd</sup> line anti-TB drugs	12	12

# Results

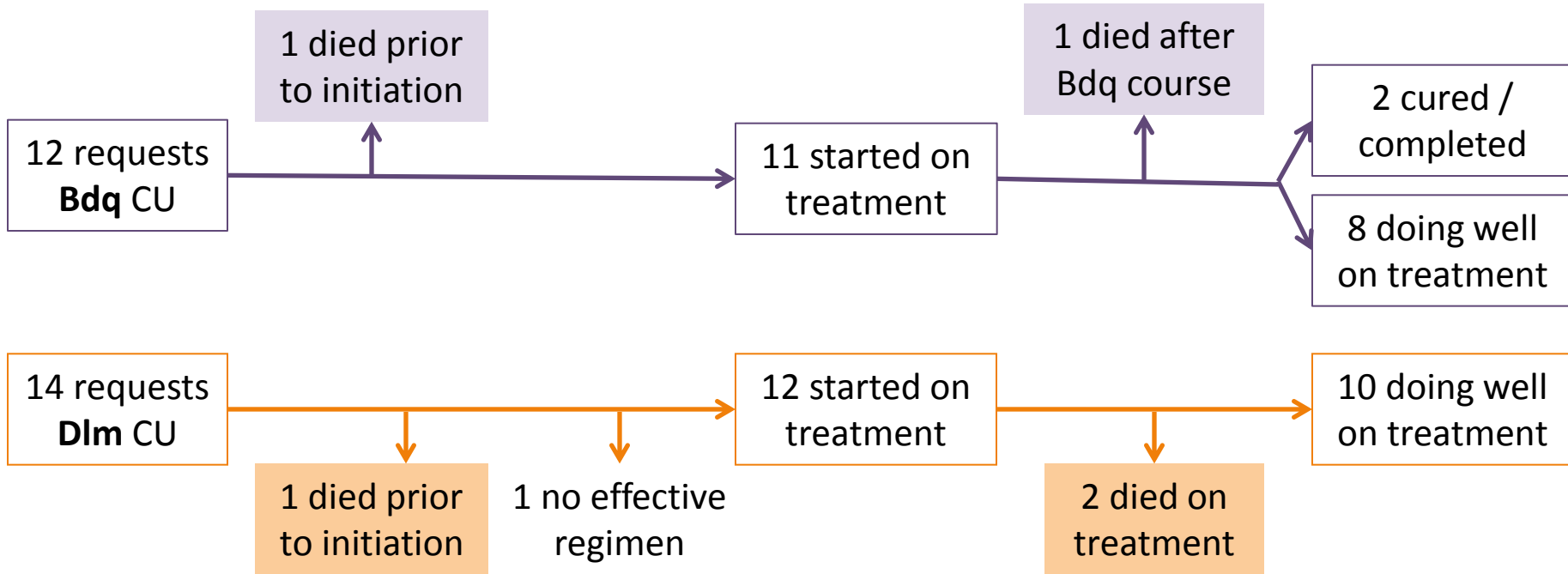
No of patients by  
 $\geq 4$  and  $< 4$  likely working drugs\*  
including 1 new drug

\*likely working drugs arbitrarily defined as  
➤ drugs sensitive in DST-results  
➤ and/ or  $< 3$  month-of-exposure





# Outcome



# Results – Major SAE

	Death during treatment	Severe Cardio-toxicity (QTc > 500ms)	Other severe Adverse Events
Bdq (n=11)	1	2	0
Dlm (n=12)	2	2*	2*

- 3 deaths = probably not attributable to new drugs
- Dlm - cardio-toxicity triggered by electrolytes imbalance (vomiting) \*
- No need for permanent discontinuation

# Discussion

- We can offer ambulatory treatment with adequate monitoring (clinical, lab & ECG)
- Promising outcomes: sustained culture conversion – 16/20 cases
- Limitation: Small cohort (10% of global DIm cohort at time of analysis)



- 21 patients with < 4 likely working drugs,
  - Diagnosed too late
  - Too few drugs  $\approx$  sub-standard regimens
- Started on treatment too late: patients are likely to die before accessing new drugs (2/26) - Complex / restricted access
- 2 patients with no drug exposure  $\approx$  on-going transmission in the community

# Conclusions & Programmatic Implications

- Implementation of new treatment implies capacity-building in
  - Pharmacovigilance
  - Intensified treatment monitoring.
- Treat DR-TB promptly and aggressively
  - Urgent need for broader access to combination treatment with Bdq + Dlm
- Need to tackle community transmission of DR TB

# Acknowledgements

MSF team in  
Mumbai/Delhi

&

***Our Patients*** on  
their difficult life-  
journey with  
DR TB



**Thank You!**