

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

Expanded use of new antituberculosis drugs

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Introduction

- As access to the new TB drugs expands, clinicians are choosing to use them in ways that are not included in current WHO recommendations due to lack of evidence
- The most common such cases observed in the endTB are prescribing Bdq or Dlm:
 - For more than 24 weeks;
 - At the same time;
 - In children < 18 years of age; and
 - In pregnancy

Methods

- The following analyses are of subsets of the 687 patients who started a new TB drug (Bdq or Dlm) between 1 April 2015 and 31 October 2016

Extended use of Bdq or Dlm

- Late treatment response
 - Patient still sputum culture-positive after 3 months or more of treatment with Bdq or Dlm and not meeting the criteria for treatment failure; and
 - The bacteriological (smear and/or culture) and clinical (weight) evolution indicates positive response to the treatment
- Insufficient number of effective drugs in the treatment regimen
 - Less than 3 effective drugs in the regimen if Bdq or Dlm is stopped. If an injectable drug is present in the treatment regimen and it is planned to discontinue it, it should not be counted among these drugs
 - The paucity of effective drugs in the treatment regimen may be due to drug resistance pattern, adverse events or any other contraindications

Extended use of Bdq or Dlm

- 223 of 687 (32%) patients received more than 24 weeks of treatment:
 - 157 (70%) received Bdq extension alone
 - 38 (17%) received Dlm extension alone
 - 28 (13%) received extension of both Bdq and Dlm

Extended use: patient characteristics (N=223)

Characteristic	n (%)
Male	144 (65)
Median age [range]	36 [18 – 70]
Body mass index <18.5 (N=222)	80 (36)
Bilateral disease on x-ray (N=197)	142 (71)
Resistance (N=218)	
MDR or Xpert RR	59 (28)
Pre-XDR (FQ-R)	35 (16)
Pre-XDR (SLI-R)	11 (5)
XDR	104 (48)
Other	9 (4)
Comorbidities	
HIV (N=222)	35 (16)
Hepatitis C (N=211)	23 (11)
Diabetes (N=205)	17 (8)
Previous use of SLD (N=218)	156 (72)

Extended use of Bdq or Dlm: safety

AEI (N=91)	0 to 6 months of treatment			6 to 12 months of treatment		
	N events	% of pts	% in grade 3 or 4	N events	% of pts	% in grade 3 or 4
Increased liver enzymes (ALT increased or AST increased ($\geq 1.1 \times$ ULN))	55	24.4	5.4	32	23.0	0
Prolonged(corrected) QT interval	38	16.9	2.6	25	18.0	8.0
Peripheral neuropathy	26	11.6	15.4	9	6.5	11.1
Acute kidney injury	22	9.8	0.0	17	12.2	0

Extended use of Bdq or Dlm: safety

SAE (=91)	0 to 6 months of treatment		6 to 12 months of treatment	
	N	%	N	%
Patients with ≥ 1 SAE	14	15.4	13	14.3
Total number of SAE	17		20	
Electrocardiogram QT Corrected Interval	3	17.7	1	5.0
Increased liver enzymes	1	5.9	1	5.0
Acute kidney injury	1	5.9	0	0

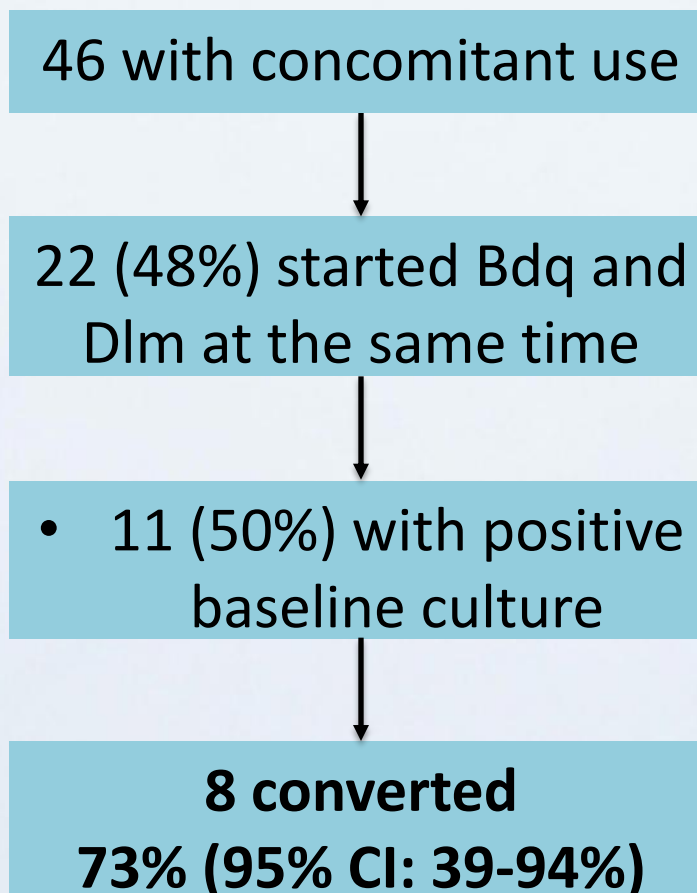
Combined Bdq / Dlm Us

- 46 patients ever received Dlm and Bdq in combination
- 22 (48%) started Dlm and Bdq combination within 7 days of each other
- 24 (52%) started Dlm and Bdq sequentially
 - Dlm added to Bdq: 18 (75%)
 - Bdq added to Dlm: 6 (25%)

Combined use: patient characteristics (N=46)

Characteristic	n (%)
Male	29 (63)
Median age [range]	37 [17-63]
Body mass index <18.5	22 (49)
Bilateral disease on x-ray (N=45)	33 (73)
Resistance (N=45)	
MDR	4 (9)
Pre-XDR (FQ-R)	8 (18)
Pre-XDR (SLI-R)	2 (4)
XDR	30 (67)
Other	1 (2)
Comorbidities	
HIV (N=45)	2 (4)
Hepatitis C (N=44)	12 (27)
Diabetes (N=45)	3 (7)

Conversion with combined use of Bdq, Dlm



Efficacy and safety of combined use with Bdq and Dlm

Includes 22 patients who started Bdq and Dlm together

AEI term (37 Aes of interest in the first 6 mos)	N	%	Number in grade 3 or 4	Median [IQR] time to AEI
Prolonged (corrected) QT interval	9	24	1	3.0 [1.5-4.6]
Increased liver enzymes (ALT increased or AST increased (\geq 1.1 x ULN))	8	22	0	2.1 [1.0-2.9]
Peripheral Neuropathy	8	22	0	3.5 [1.3-5.0]

- No SAEs were reported in the first 6 months of treatment