

**Electronic Annex 4. Summary of QT Prolongation episodes determining 35 minor adverse events in 32 patients out of the 658 treated with new and repurposed drugs in the cohort**

Setting	Gender (n.%)	Age (mean ±SD)	Max. QT value (mean (±SD)	QT prolongation episode(s) occurred (n.%)	QTcF prolongation ≥ 450 msec (n.%)	QTcF prolongation ≥500 msec (n.%)	Drugs containing-regimens (total n.%)	Drugs considered responsible of AE (total n.%)	Action taken Drug temporarily withdrawn Dose not changed Drug permanently interrupted (total n.%)	Outcome Resolved Not resolved Resolving Unknown (total n.%)
<b>Europe (n=26)</b>	Females 10/26 (38,4%)	41,0 (±13,1)	476,4 (±39,6)	1 episode 10/10 (100%)	8/10 (80%)	5/10 (50%)	FQ 16/26 (61,5%)  Cfz 9/26 (34,6%)  Bdq 26/26 (100%)  Dlm^^ 4/26 (15,3%)	FQ (Mfx) 3/26 (11,5%)  Bdq* 22/26 (84,6%)  Cfz 1/26 (3,8%)	Drug temporarily withdrawn 5/26 (19,2%)  Dose not changed 20/26 (76,9%)  Drug permanently interrupted 1/26^ (3,8%)	Resolved 17/26 (65,3%)  Not resolved 5/26 (19,2%)  Resolving 3/26 (11,5%)  Unknown 1/26 (3,8%)
	Males 16/26 (61,6%)	49,0 (±14,72)	474,0 (±41,7)	1 episode 14/16 (87,5%)  > 1 episode 2/16^^ (12,5%)	13/16 (81,2%)	4/16 (25%)				
<b>Other than Europe (n=6)</b>	Female 1/6 (16,6%)	63,0 (±0 )	466,0 (±25,6)	1 episode 1/1 (100%)	1/1 (100%)	0/1 (0%)	FQ 1/6 (16,6%)  Cfz 6/6 (100%)  Bdq 6/6 (100%)  Dlm 0/6 (0%)	Bdq 6/6 (100%)	Dose not changed 6/6 (100%)	Resolved 6/6 (100%)
	Males 5/6 ( 83,4%)	38,0 (±8)	463,2 (±14,8)	1 episode 5/5 (100%)	4/5 (80 %)	1/5 (20%)				

<b>Total (n=32)</b>	Females 11/32 (34,4 %)	43,0 (±14,1)	476,7 (± 37,6)	1 episode 11/11 (100%)	9/11 (81,8%)	5/11 (45,4%)	FQ 17/32 (53,1%)	FQ (Mfx) 3/32 (9,3%)	Drug temporarily withdrawn 5/32 (15,6%)	Resolved 23/32 (71,8%)
	Males 21/32 (65,6 %)	46,3 (±14,0)	471,4 (± 38,5)	1 episode 19/21 (90,5%)  > 1 episode 2/21 <sup>°°</sup> (9,5%)	17/21 (81%)	5/21 (23,8%)	Cfz 15/32 ( 46,8%)  Bdq (32/32,100%)  4/32 Dlm^^ (12,5%)	Bdq* 28/32 (87,5%)  Cfz 1/32 (3,1%)	Dose not changed 26/32 (81,2%)  Drug permanently interrupted 1/32^ (3%)	Not resolved 5/32 (15,6%)  Resolving 3/32 (9,3%)  Unknown 1/32 (3%)

\* in 1 case clofazimine was drug responsible in combination with bedaquiline;

\*\*in 8 cases 1 fluoroquinolone (moxifloxacin) was drug responsible in combination with bedaquiline;

°° 1 case with 2 episodes, 1 case with 3 episodes of QT prolongation

^Moxifloxacin replaced by levofloxacin after QT prolongation (QTcF 497 mc- baseline 360 msec)

^^ in 2 cases delamanid was administered in combination with bedaquiline, in other 2 cases consecutively

Legend (acronyms): QT prolongation: an electrical disturbance visible on the electrocardiogram, measuring the delayed ventricular repolarisation, when the heart muscle takes longer than normal to recharge between beats.; SD=Standard deviation; QTcF = Fridericia-corrected QT interval ; AE= adverse event; FQ= fluoroquinolones; Cfz= clofazimine; Bdq= bedaquiline; Dlm=delamanid; Mfx=moxifloxacin