Supplementary material

This material has been provided by the authors to give readers additional information about their work.

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Supplementary material

Safety of prolonged treatment with bedaquiline in programmatic conditions

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Supplementary Table 1. Bacteriological, clinical and laboratory assessment schedule of the patients.

Measure to be monitored	**Time point(s)**
Vital signs	At baseline, monthly during treatment and semi-annually during follow-up period
Weight	At baseline, monthly during treatment and semi-annually during follow-up period
Brief peripheral neuropathy screen	At baseline and monthly during treatment
Visual acuity and colorblindness screen	At baseline and monthly during treatment
Smear and culture	At baseline, monthly during treatment and semi-annually during follow-up period
LPA (Hain GenoType MTBDRsl)	At baseline and if susceptibility sustained, then in case of smear- or culture-positivity after 3rd month of treatment
Culture-based second-line DST	At baseline and if smear- or culture-positive after 3rd month of treatment
Full blood count (hemoglobin, white blood cells and platelets)	At baseline and monthly during treatment
Liver function tests (AST, ALT, ALP, bilirubin)	At baseline and monthly during treatment
Serum creatinine	At baseline and monthly during treatment
Serum potassium, calcium, magnesium	At baseline and monthly during treatment
Glucose	At baseline and monthly during treatment
Hepatitis Bs antigen	At baseline
Hepatitis C antibody	At baseline
HIV testing	At baseline
ECG	At baseline, 2nd week and monthly thereafter during treatment. QT interval correction was calculated according to Fridericia formula (QTcF)
Chest X-Ray	At baseline, quarterly during treatment and semi-annually during follow-up period

ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; DST: drug susceptibility test; ECG: electrocardiogram; HIV: human immunodeficiency virus; LPA: line probe assay.

Supplementary Table 2. List of registered serious events within 5 months of Bedaquiline stop.

Patient ID	Age	Sex	Event	Time of event from treatment start (days)	Time event ended if resolved) from treatment start (days)	Received Standard or Prolonged Bedaquiline	Event possibly bedaquiline-related?	Grade of the event	Patient hospitalized?	Event outcome
1	27	F	Pancreatitis	49	84	Standard	Yes	3	No	Resolved
2	40	M	Hyperuricaemia	21	55	Standard	Yes	3	No	Resolved
2	40	M	Liver enzyme elevation [AST]	147	231	Standard	Yes	3	No	Resolved
3	34	F	QTc prolongation	182	271	Prolonged	No	3	No	Resolved
3	34	F	QTc prolongation	308	U	Prolonged	No	3	No	Resolved
4	18	F	Hypokalaemia	63	151	Standard	No	3	No	Resolved
5	31	M	Liver enzyme elevation [GGT]	126	N/A	Standard	No	3	No	Not resolved
5	31	M	Liver enzyme elevation [ALT]	126	323	Standard	No	3	No	Resolved
5	31	M	Liver enzyme elevation [ALT]	140	152	Standard	No	4	Yes	Resolved
5	31	M	Liver enzyme elevation [AST]	154	323	Standard	No	3	No	Resolved
6	16	M	Hypomagnesaemia	98	227	Standard	No	3	No	Resolved
7	50	F	Neoplasm	28	N/A	Standard	No	4	No	Not resolved
8	25	F	Hypokalaemia	98	N/A	Prolonged	No	4	No	Not resolved
9	30	M	Seizure	35	U	Standard	No	4	No	Resolved
9	30	M	Liver enzyme elevation [AST]	217	359	Standard	No	3	No	Resolved
10	53	M	Eosinophilia	119	210	Standard	No	3	No	Resolved
11	23	F	Psychomotor agitation	14	U	Prolonged	No	3	Yes	Unknown
12	33	F	QTcF prolongation	210	327	Standard	Yes	3	No	Resolved
12	33	F	Hypokalaemia	217	237	Standard	No	4	No	Resolved
13	52	M	QTcF prolongation	112	161	Prolonged	Yes	3	No	Resolved
14	27	F	Eosinophilia	35	272	Standard	No	3	No	Resolved
15	31	M	Hypokalaemia	35	181	Standard	No	3	No	Resolved
15	31	M	Eosinophilia	35	212	Standard	No	3	No	Resolved
16	42	M	Liver enzyme elevation [AST]	182	270	Standard	No	3	No	Resolved
17	34	F	Blood enzyme elevation	35	97	Standard	No	3	No	Resolved
17	34	F	Liver enzyme elevation [GGT]	35	97	Standard	No	3	No	Resolved
17	34	F	Liver enzyme elevation [AST]	35	65	Standard	No	3	No	Resolved
18	44	M	Hypocalcaemia	308	N/A	Prolonged	No	4	No	Not resolved
19	58	M	Liver enzyme elevation [GGT]	63	306	Standard	No	3	No	Resolved
20	39	M	Liver enzyme elevation [GGT]	252	N/A	Prolonged	No	3	No	Not resolved
21	18	M	Liver enzyme elevation [GGT]	91	114	Standard	No	3	No	Resolved
21	18	M	Eosinophilia	91	176	Standard	No	3	No	Resolved
22	27	M	Eosinophilia	168	252	Standard	No	3	No	Resolved
23	40	M	Liver enzyme elevation [GGT]	28	N/A	Standard	No	3	No	Not resolved
24	56	M	Liver enzyme elevation [GGT]	119	U	Standard	No	3	No	Resolved
25	31	F	QTcF prolongation	343	N/A	Prolonged	No	4	No	Died
25	31	F	Thrombosis	350	N/A	Prolonged	No	5	No	Died
26	55	M	Liver enzyme elevation [GGT]	224	U	Standard	No	3	No	Resolved
27	34	M	Hypomagnesaemia	140	U	Standard	No	3	No	Resolved
28	28	F	Eosinophilia	182	299	Standard	No	4	No	Resolved
29	44	M	Hypokalaemia	175	203	Standard	No	3	No	Resolved
30	50	M	Hypocalcaemia	322	471	Prolonged	No	3	No	Resolved
30	50	M	Hypokalaemia	322	623	Prolonged	No	3	No	Resolved
31	49	M	Eosinophilia	91	246	Standard	No	3	No	Resolved
31	49	M	Liver enzyme elevation [AST]	126	N/A	Standard	No	3	No	Not resolved
31	49	M	Liver enzyme elevation [ALT]	154	246	Standard	No	3	No	Resolved
31	49	M	Hypomagnesaemia	154	N/A	Standard	No	3	No	Not resolved
31	49	M	Liver enzyme elevation [GGT]	154	N/A	Standard	No	3	No	Not resolved
32	29	M	Hypokalaemia	210	240	Standard	No	3	No	Resolved
33	19	F	QTcF prolongation	35	U	Standard	Yes	4	No	Resolved
33	19	F	Hypomagnesaemia	35	273	Standard	No	3	Yes	Resolved
33	19	F	Hypokalaemia	35	U	Standard	No	4	No	Resolved
34	51	M	Liver enzyme elevation [AST]	63	91	Prolonged	No	3	No	Resolved
35	20	F	Eosinophilia	91	217	Standard	No	3	No	Resolved
36	29	F	Liver enzyme elevation [GGT]	42	101	Standard	No	3	No	Resolved
37	53	M	QTcF prolongation	364	371	Prolonged	No	3	Yes	Resolved

38	30	F	Eosinophilia	28	383	Prolonged	No	3	No	Resolved
38	30	F	Hypokalaemia	112	175	Prolonged	No	3	No	Resolved
39	40	F	Hyperglycaemia	42	N/A	Prolonged	No	3	No	Not resolved
40	31	M	Hypomagnesaemia	35	339	Prolonged	No	3	No	Resolved
40	31	M	Hypokalaemia	35	339	Prolonged	No	3	No	Resolved
41	41	M	Cardiac Failure	42	N/A	Standard	Yes	5	Yes	Died
41	41	M	Respiratory Failure	42	N/A	Standard	No	5	Yes	Died

F: female; M: male; QTcF: QT interval corrected using Fredericia formula; U: unknown; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; GGT: Gamma-glutamyl transferase

Supplementary Table 3. Comparison of serious adverse events that occurred within five-months of cessation of bedaquiline between patients of standard and prolonged bedaquiline group.

Variable	Events / person-months	Univariate IRR (95% CI)	Univariate p-value	Multivariate IRR (95% CI)
Bedaquiline duration[1]				
Less than 6 months	38 / 767	1.0 (Reference)		1.0 (Reference)
More than 6 months	18 / 405	0.90 (0.48 to 1.72)	0.75	0.82 (0.42 to 1.61)
Sex				
Female	21 / 316	1.0 (Reference)		1.0 (Reference)
Male	35 / 857	0.62 (0.33 to 1.16)	0.14	0.73 (0.35 to 1.53)
Age				
Per 10-year increase		0.78 (0.58 to 1.06)	0.11	0.88 (0.64 to 1.20)
Concomitant anti-TB medicines				
Per additional concomitant anti-TB medicine		0.96 (0.76 to 1.21)	0.74	--
Injectable received				
No	24 / 772	1.0 (Reference)		1.0 (Reference)
Yes	32 / 401	2.55 (1.31 to 4.96)	0.01	2.42 (1.14 to 5.13)
BMI				
BMI ≥ 18.5 kg/m^2	43 / 929	1.0 (Reference)		
BMI < 18.5 kg/m^2	13 / 243	1.16 (0.59 to 2.25)	0.67	--
Baseline ECG[2]				
Per 10 ms increase		0.95 (0.88 to 1.04)	0.26	--
Alcohol				
No alcohol abuse	49 / 995	1.0 (Reference)		
Alcohol abuse	7 / 177	0.80 (0.34 to 1.89)	0.61	--
Diabetes				
No diabetes	52 / 1098	1.0 (Reference)		
Has diabetes	4 / 74	1.14 (0.28 to 4.60)	0.86	--
HIV				
No HIV	55 / 1140	1.0 (Reference)		
Has HIV	1 / 32	0.65 (0.12 to 3.45)	0.61	--
Surgery				
No MDR surgery	49 / 992	1.0 (Reference)		
Had MDR surgery	7 / 181	0.78 (0.36 to 1.71)	0.54	--
Baseline Sputum smear[3]				
Smear negative	44 / 950	1.0 (Reference)		
Smear positive	10 / 212	1.02 (0.49 to 2.15)	0.95	--
Chest X-Ray findings				
No cavitation	19 / 404	1.0 (Reference)		
Cavitation	37 / 768	1.03 (0.53 to 1.97)	0.94	--

BMI: body mass index; ECG: electrocardiography; HIV: human immunodeficiency virus; IRR: incidence rate ratio; MDR: multidrug-resistant tuberculosis; TB: tuberculosis.

Estimates generated using generalized estimating equations with a Poisson distribution and log-link to estimate incidence rate ratios and their 95% confidence intervals (using robust standard errors).

[1]: Person-months reflective of follow-up time, not the duration of bedaquiline receipt. [2]: only 100 patients. [3]: only 104 patients. Note: no difference in findings if all predictors included in multivariate model.

Supplementary Table 4. Comparison of serious adverse events up to the first 190 days of treatment with bedaquiline between patients of standard and prolonged bedaquiline group (N=105).

Variable	Events / person-months	Univariate IRR (95% CI)	Univariate p-value	Multivariate IRR (95% CI)
Bedaquiline duration				
Less than 6 months	33 / 410	1.0 (Reference)		1.0 (Reference)
More than 6 months	10 / 187	0.67 (0.30 to 1.50)	0.33	0.73 (0.33 to 1.61)
Sex				
Female	17 / 163	1.0 (Reference)		1.0 (Reference)
Male	26 / 434	0.57 (0.26 to 1.25)	0.16	0.80 (0.35 to 1.83)
Age				
Per 10-year increase		0.69 (0.46 to 1.03)	0.07	0.76 (0.52 to 1.11)
Concomitant anti-TB Medicines				
Per additional concomitant anti-TB medicine		0.76 (0.56 to 1.02)	0.07	0.97 (0.68 to 1.40)
Injectable received				
No	13 / 344	1.0 (Reference)		1.0 (Reference)
Yes	30 / 253	3.14 (1.42 to 6.97)	<0.01	2.81 (1.23 to 6.43)
BMI				
BMI ≥ 18.5 kg/m^2	35 / 477	1.0 (Reference)		
BMI < 18.5 kg/m^2	8 / 120	0.91 (0.38 to 2.16)	0.83	--
Baseline ECG[1]				
Per 10ms increase		0.96 (0.87 to 1.06)	0.41	--
Alcohol				
No alcohol abuse	39 / 507	1.0 (Reference)		
Alcohol abuse	4 / 90	0.58 (0.18 to 1.86)	0.36	--
Diabetes				
No diabetes	39 / 557	1.0 (Reference)		
Has diabetes	4 / 39	1.45 (0.35 to 6.02)	0.61	--
HIV				
No HIV	42 / 579	1.0 (Reference)		
Has HIV	1 / 18	0.79 (0.14 to 4.42)	0.79	--
Surgery				
No MDR surgery	41 / 504	1.0 (Reference)		1.0 (Reference)
Had MDR surgery	2 / 93	0.27 (0.07 to 1.04)	0.06	0.26 (0.08 to 0.88)
Baseline Sputum Smear[2]				
Smear negative	36 / 491	1.0 (Reference)		
Smear positive	5 / 101	0.68 (0.21 to 2.16)	0.51	--
Chest X-Ray findings				
No cavitation	15 / 208	1.0 (Reference)		
Cavitation	28 / 389	1.00 (0.45 to 2.19)	0.99	--

BMI: body mass index; ECG: electrocardiography; HIV: human immunodeficiency virus; IRR: incidence rate ratio; MDR: multidrug-resistant tuberculosis; TB: tuberculosis.

Estimates generated using generalized estimating equations with a Poisson distribution and log-link to estimate incidence rate ratios and their 95% confidence intervals (using robust standard errors).

[1]: only 100 patients. [2]: only 104 patients. Note: no difference in findings if all predictors included in multivariate model.

Supplementary Table 5. Comparison of serious adverse events that occurred in the first 189 days vs. beyond 189 days up to 5 months after bedaquiline stop in the prolonged bedaquiline group (N=30).

Variable	Events / person-months	Univariate IRR (95% CI)	Univariate p-value	Multivariate IRR (95% CI)
Time period of bedaquiline receipt[1]				
First 189 days of treatment	10 / 187	1.0 (Reference)		1.0 (Reference)
From Day 190 to up to 5 months after stop	8 / 212	0.71 (0.26 to 1.99)	0.52	0.75 (0.30 to 1.88)
Sex				
Female	9 / 113	1.0 (Reference)		1.0 (Reference)
Male	9 / 285	0.40 (0.15 to 1.06)	0.07	0.13 (0.03 to 0.64)
Age				
Per 10-year increase		0.89 (0.57 to 1.38)	0.59	1.63 (0.82 to 3.39)
Concomitant anti-TB medicines				
Per additional concomitant anti-TB medicine		0.84 (0.55 to 1.29)	0.42	--
Injectable received				
No	10 / 229	1.0 (Reference)		
Yes	8 / 169	1.08 (0.39 to 3.02)	0.88	--
BMI				
BMI $\geq$ 18.5 kg/m^2	8 / 265	1.0 (Reference)		1.0 (Reference)
BMI < 18.5 kg/m^2	10 / 133	2.50 (0.95 to 6.59)	0.06	3.04 (0.97 to 9.50)
Baseline ECG[2]				
Per 10 ms increase		1.05 (0.91 to 1.22)	0.48	--
Alcohol				
No alcohol abuse	13 / 321	1.0 (Reference)		
Alcohol abuse	5 / 77	1.59 (0.62 to 4.07)	0.34	--
Diabetes				
No diabetes	17 / 386	1.0 (Reference)		
Has diabetes	1 / 12	1.92 (0.47 to 7.88)	0.36	--
HIV				
No HIV	18 / 398	1.0 (Reference)		
Has HIV	0 / 0	--	--	--
Surgery				
No MDR surgery	14 / 322	1.0 (Reference)		
Had MDR surgery	4 / 76	1.22 (0.36 to 4.19)	0.75	--
Baseline sputum smear				
Smear negative	10 / 272	1.0 (Reference)		
Smear positive	8 / 126	1.72 (0.61 to 4.83)	0.31	--
Chest X-Ray findings				
No cavitation	8 / 107	1.0 (Reference)		1.0 (Reference)
Cavitation	10 / 291	0.46 (0.17 to 1.25)	0.13	0.31 (0.13 to 0.76)

BMI: body mass index; ECG: electrocardiography; HIV: human immunodeficiency virus; IRR: incidence rate ratio; MDR: multidrug-resistant tuberculosis; TB: tuberculosis.

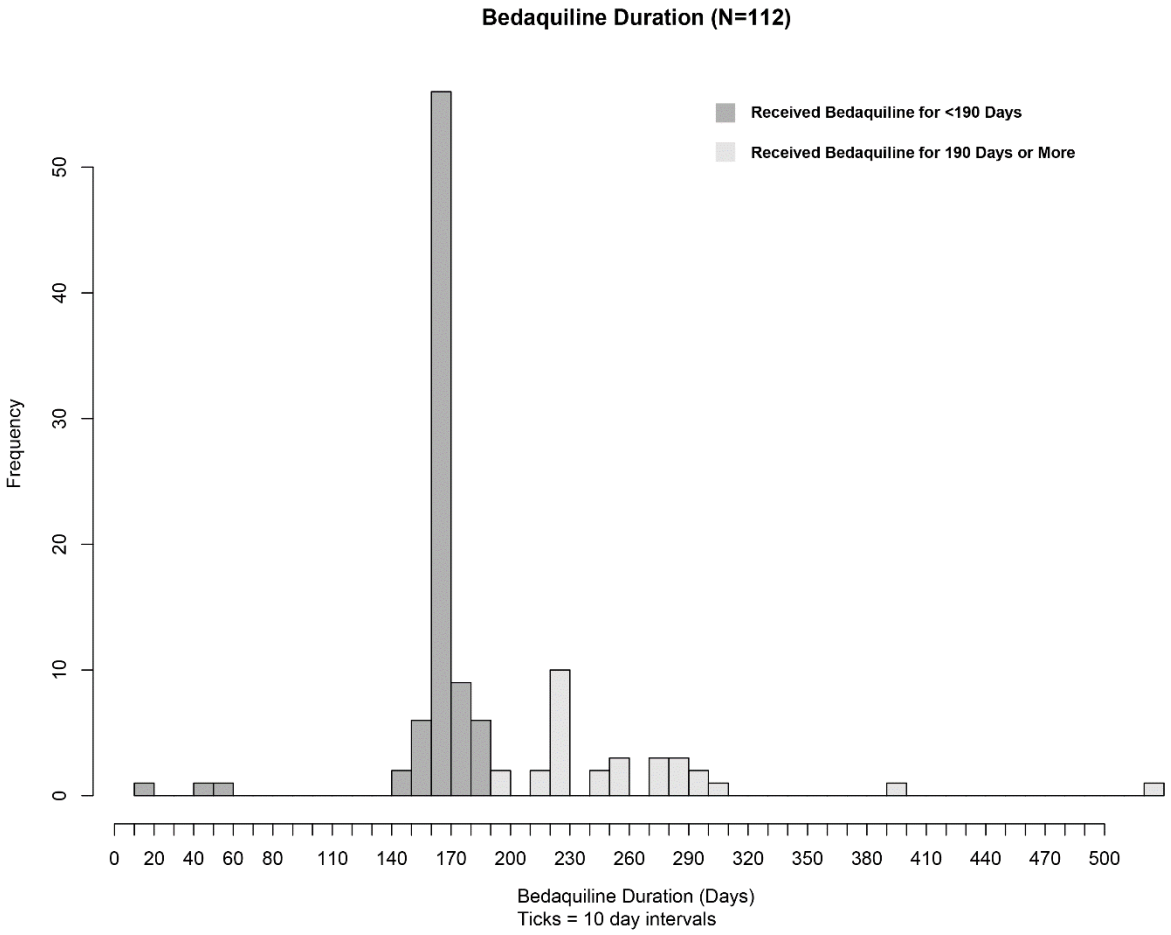
Estimates generated using generalized estimating equations with a Poisson distribution and log-link to estimate incidence rate ratios and their 95% confidence intervals (using robust standard errors).

[1]Person-months reflective of follow-up time, not the duration of bedaquiline receipt. [2]: only 27 patients. Note: no difference in findings if all predictors included in multivariate model.

Supplementary Appendix 1. Bacteriological tests used during the study.

All cultures were done using BACTEC broth media using a fluorometric BACTEC MGIT960 system (Becton Dickinson, Sparks, MD, USA). The full drug susceptibility testing (DST) was performed as an indirect test by the proportion method rifampicin (1.0 µg/mL), isoniazid (0.1 µg/mL), streptomycin (1.0 µg/mL), ethambutol (5.0 µg/mL), pyrazinamide (100.0 µg/mL), levofloxacin (1,5 µg/mL), moxifloxacin (0,5 µg/mL), kanamycin (30.0 µg/mL), capreomycin (40.0 µg/mL), amikacin (1.0 µg/mL) and prothionamine (40.0 µg/mL). DST to linezolid, clofazimine and bedaquiline was not available at the time of the study. Genotypic DST was obtained with commercially available assays: Xpert MTB/RIF (Cepheid, Sunnyvale, CA, USA), GenoType MTBDRplus and GenoType MTBDRsl (Hain Lifescience, Nehren, Germany). If resistance was identified to rifampicin, the respective isolate was tested against the rest of the first- and second-line anti-TB drugs.

Supplementary Appendix 2.



Histogram of the duration of bedaquiline use by the patients. Based on a histogram of the duration of bedaquiline use, we grouped the patients to those, who received bedaquiline for <190 days (referred to as receiving standard treatment with bedaquiline) and to patients, who received bedaquiline for ≥190 days (referred to as receiving prolonged treatment with bedaquiline).

Supplement Appendix 3.
List of registered events classified as per system organ class.

System.Organ.Class	Total events
Investigations	879
Metabolism and nurtrition disorders	417
Blood and lymphatic system disorders	201
Cardiac Disorders	188
Hepatobiliary disorders	69
Gastrointestinal Disorders	59
Ear and labirynth disorders	39
Nervous system disorders	31
Skin and subcutaneous system disorders	30
Infections and Infestations	29
Psychiatric disorders	23
Musculoskeletal and connective tissue disorders	19
General disorders and administration site conditions	14
Renal and urinary disorders	9
Respiratory, thoracic and mediastinal disorders	9
Eye disorders	7
Endocrine disorders	4
Vascular disorders	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1

List of registered events classified as per category.

Category	Total events
Hepatobiliary investigations	353
Cardiac and vascular investigations	203
Renal and urinary tract investigations and urinalyses	192
Glucose metabolism disorders	142
Cardiac arrhythmias	139
White blood cell disorders	120
Bone, calcium, magnesium and phosphorus metabolism disorders	111
Enzyme investigations	107
Purine and pyrimidine metabolism disorders	93
Hepatic and hepatobiliary disorders	69
Electrolyte and fluid balance conditions	65
Anaemias (non-haemolytic) and marrow depression	44
Gastrointestinal signs and symptoms	41
Platelet disorders	36
Epidermal and dermal conditions	28
Gastrointestinal investigations	27
Hearing disorders	22
Cardiac disorder signs and symptoms	19
Fungal infectious disorders	14
Coronary artery disorders	13
Myocardial disorders	13

Rash	11
Joint disorders	11
Anxiety disorders and symptoms	9
Sleep disorders and disturbances	9
General system disorders	8
Inner ear and cranial nerve disorders	8
Gastrointestinal motility and defaecation conditions	7
Muscle disorders	7
Neurological disorders	7
Body temperature conditions	6
Middle ear infections and inflammations	6
Protein and amino acid metabolism disorders	6
Seizures	6
Peripheral neuropathies	5
Respiratory disorders	5
Vertigo	5
Gastrointestinal inflammatory conditions	4
Sleep disorders	4
Viral infectious disorders	4
Aural disorders	3
Nephropathies	3
Upper respiratory tract disorders	3
Urinary tract signs and symptoms	3
Vision disorders	3
Depressed mood disorders and disturbances	2
Diabetic complications	2
Eye disorders	2
Headaches	2
Mood disorders and disturbances	2
Movement disorders	2
Ocular infections, irritations and inflammations	2
Thyroid gland disorders	2
Tongue conditions	2
Adjustment disorders	1
Angioedema and urticaria	1
Bronchial disorders	1
Embolism and thrombosis	1
Exocrine pancreas condition	1
Gastrointestinal atonic and hypomotility disorders	1
Gastrointestinal conditions	1
Gastrointestinal ulceration and perforation	1
Haematopoietic neoplasm	1
Musculoskeletal and connective tissue disorders	1
Oral soft tissue conditions	1
Pericardial disorders	1
Renal and urinary tract neoplasm benign	1
Renal disorders	1
Skin and subcutaneous tissue disorders	1

Urinary Tract Neoplasms	1
Urolithiases	1
Vascular haemorrhagic disorders	1

List of registered events.

Event	Total Events
Aspartate aminotransferase increased	165
Eosinophilia	115
Alanine aminotransferase increased	113
Electrocardiogram abnormal	99
Hyperuricaemia	93
Electrocardiogram QT prolonged	89
Hyperglycaemia	85
Gamma-glutamyl transferase increased	75
Blood alkaline phosphatase increased	67
Blood creatinine increased	67
Hyperbilirubinaemia	66
Blood urea increased	65
Glomerular filtration rate decreased	60
Hypomagnesaemia	60
Hypoglycaemia	57
Hypocalcaemia	46
Anaemia	44
Hypokalaemia	41
Blood Lactate Dehydrogenase Increased	37
Sinus tachycardia	28
Amylase increased	26
Thrombocytopenia	26
Bradycardia	25
Hyperkalaemia	24
Tachycardia	22
Nausea	18
Sinus bradycardia	16
Haemoptysis	13
Pruritus	12
Rash	12
Arrhythmia supraventricular	11
Arthralgia	11
Supraventricular extrasystoles	11
Chest pain	10
Thrombocytosis	10
Vomiting	10
Upper respiratory tract infection	9
Abdominal pain	8
Atrial hypertrophy	8
Insomnia	8
Oral candidiasis	8

Tinnitus	8
Arrhythmia	7
Cochlear nerve deafness	7
Diarrhoea	7
Fatigue	7
Hearing decreased	7
Ventricular hypertrophy	7
Fever	6
Hypoalbuminaemia	6
Anxiety	5
Dyspepsia	5
Dyspnoea	5
Leukopenia	5
Seizure	5
Ventricular extrasystoles	5
Vertigo	5
Bundle branch block right	4
Cochlear nerve damage	4
Hypercalcemia	4
Muscle pain	4
Palpitation	4
Sleep disorders	4
Vaginal candidiasis	4
Blood pressure increased	3
Cramps legs	3
Ear pain	3
Gastritis	3
Hearing impaired	3
Hepatitis toxic	3
Hypoaesthesia	3
Influenza	3
Nephropathy toxic	3
Otitis media	3
Panic reaction	3
Right ventricular hypertrophy	3
Bundle branch block left	2
Eczema	2
Electrocardiogram QT interval abnormal	2
Epistaxis	2
Eustachitis	2
Headache	2
Myocardial infarction	2
Myopia	2
Neuritis	2
Polyneuropathy	2
Retinal disorder	2
Sinoatrial block	2
Syncope	2

Tachyarrhythmia	2
Taste bitter	2
Abnormal dreams	1
Accommodation disorder	1
Adjustment disorders	1
Albuminuria	1
Aspergillosis	1
Atrial conduction time prolongation	1
Atrioventricular block	1
Back pain	1
Bad mood	1
Blood creatine phosphokinase increased	1
Blood pressure decreased	1
Candidiasis	1
Cardiac hypertrophy	1
Cardiomyopathy	1
Chest discomfort	1
Chills	1
Chronic obstructive airways disease exacerbated	1
Conjunctivitis	1
Depression	1
Dermatitis Allergic	1
Diabetic neuropathy	1
Diabetic retinopathy	1
Dizziness	1
Duodenal ulcer	1
Duodenitis	1
Electrocardiogram QRS complex prolonged	1
Eyelid oedema	1
Fear	1
Gastroesophageal reflux	1
FALSE	1
Haematoma	1
Haematuria	1
Herpes zoster	1
Hyperaemia eye	1
Hypermagnesaemia	1
Hypothyroidism	1
Kidney stone	1
Lactate Blood Increase	1
LDH Increased Serum	1
Lipase increased	1
Loss of consciousness	1
Lymphatic system neoplasm	1
Mood disorder	1
Myocardial ischaemia	1
Nasal septum ulceration	1

Negative thoughts	1
Neuralgia	1
Neuropathy peripheral	1
Nodal arrhythmia	1
Oesophageal disorder	1
Otitis media chronic	1
Pancreatitis chronic	1
Papular rash	1
Partial Loss of Consciousness	1
Pericardial disease	1
Pneumonia	1
Psychomotor agitation	1
Renal cyst	1
Renal failure chronic	1
Renal pain	1
Skin ulceration	1
Stomatitis	1
Sudden hearing loss	1
Thrombosis	1
Thyroid Stimulating Hormone Increased	1
Tremor	1
Urinary Bladder Sarcoma	1
Urticaria	1
Ventricular tachycardia	1

Average QTcF measurement resultss by month of patients grouped by the length of bedaquiline treatment

Month	Standard (ms)	Prolonged (ms)
Baseline	384	388
Month 1	400	410
Month 2	411	431
Month 3	415	420
Month 4	419	427
Month 5	420	432
Month 6	420	435
Month 7	--	418
Month 8	--	411
Month 9	--	434
Month 10	--	442