Clinical trial results:
Early Access of TMC207 in Combination With Other Anti-tuberculosis (TB) Drugs in Subjects With Extensively Drug Resistant (XDR) or Pre-XDR Pulmonary TB

Summary

EudraCT number	2010-021125-12
Trial protocol	LT
Global end of trial date	01 December 2016

Results information

Result version number	v1 (current)
This version publication date	15 December 2017
First version publication date	15 December 2017

Trial information

Trial identification

Sponsor protocol code	TMC207TBC3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01464762
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Infectious Diseases BVBA
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, 2340
Public contact	Clinical Registry Group, Janssen Infectious Diseases BVBA, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Infectious Diseases BVBA, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 December 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 December 2016
Global end of trial reached?	Yes
Global end of trial date	01 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to provide early access to bedaquiline for subjects who had pulmonary infection due to strains of Mycobacterium tuberculosis (M. tuberculosis) with resistance to Isoniazid (INH), Rifampicin/Rifampin (RMP), and to a Fluoroquinolone (FQ) and/or injectable second-line Tuberculosis (TB) drug (Kanamycin [KAN], Amikacin [AMK], or Capreomycin [CAP]).

Protection of trial subjects:

The safety assessments included monitoring of adverse events (AEs), changes in clinical laboratory test values (hematology, serum chemistry and urinalysis), vital sign measurements, physical examination results, chest X-ray, microbiological status, specific toxicities and electrocardiogram (ECG) from the screening phase through study completion at defined timepoints.

Background therapy:

The selection of the background (BR) was the responsibility of the investigator and had to be constructed with at least 3 anti-TB drugs to which the subject’s TB isolate was known to be susceptible from recent drug susceptibility testing (DST) results (within the previous 6 months) or likely to be susceptible based on known treatment history.

Evidence for comparator:

Not applicable

Actual start date of recruitment	11 January 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Lithuania: 3
Country: Number of subjects enrolled	Russian Federation: 54
Worldwide total number of subjects	57
EEA total number of subjects	3

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	57
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 11 January 2012 to 1 December 2016 at 04 sites in 2 countries.

Pre-assignment

Screening details:

A total 61 subjects were screened, of whom 57 were enrolled and treated. 43 subjects completed the study and 14 subjects discontinued the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Bedaquiline/BR

Arm description:

Subjects received bedaquiline 400 milligram (mg) as (4*100 mg) oral tablet once daily for 2 weeks followed by 200 mg as (2*100 mg) oral tablet three times per week for 22 weeks, along with background regimen (BR) drugs (Investigational treatment phase). After the last intake of bedaquiline, all subjects continued to take their BR, under the supervision of their treating physician or local health center/hospital in accordance with national tuberculosis program (NTP) guidelines and local multidrug resistant tuberculosis including Pre-extensively drug resistant tuberculosis (pre-XDR) and XDR (MDR-TB) treatment practice up to weeks 96 (BR only phase).

Arm type	Experimental
Investigational medicinal product name	Bedaquiline
Investigational medicinal product code	TMC207
Other name	JNJ-16175328-AEP, R403323
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received bedaquiline 400 mg as (4*100 mg) oral tablet once daily for 2 weeks followed by 200 mg as (2*100 mg) oral tablet three times per week for 22 weeks.

Number of subjects in period 1	Bedaquiline/BR
Started	57
Completed	43
Not completed	14
Adverse event, serious fatal	3
Consent withdrawn by subject	2
Adverse event, non-fatal	2
Other	5
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Bedaquiline/BR

Reporting group description:

Subjects received bedaquiline 400 milligram (mg) as (4*100 mg) oral tablet once daily for 2 weeks followed by 200 mg as (2*100 mg) oral tablet three times per week for 22 weeks, along with background regimen (BR) drugs (Investigational treatment phase). After the last intake of bedaquiline, all subjects continued to take their BR, under the supervision of their treating physician or local health center/hospital in accordance with national tuberculosis program (NTP) guidelines and local multidrug resistant tuberculosis including Pre-extensively drug resistant tuberculosis (pre-XDR) and XDR (MDR-TB) treatment practice up to weeks 96 (BR only phase).

Reporting group values	Bedaquiline/BR	Total	
Number of subjects	57	57	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	57	57	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous Units: years			
arithmetic mean	31.2		
standard deviation	± 10.87	-	
Title for Gender Units: subjects			
Female	33	33	
Male	24	24	

End points

End points reporting groups

Reporting group title	Bedaquiline/BR

Reporting group description:

Subjects received bedaquiline 400 milligram (mg) as (4*100 mg) oral tablet once daily for 2 weeks followed by 200 mg as (2*100 mg) oral tablet three times per week for 22 weeks, along with background regimen (BR) drugs (Investigational treatment phase). After the last intake of bedaquiline, all subjects continued to take their BR, under the supervision of their treating physician or local health center/hospital in accordance with national tuberculosis program (NTP) guidelines and local multidrug resistant tuberculosis including Pre-extensively drug resistant tuberculosis (pre-XDR) and XDR (MDR-TB) treatment practice up to weeks 96 (BR only phase).

Subject analysis set title	Bedaquiline (Overall Treatment Phase)
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects received bedaquiline 400 milligram (mg) orally once daily for 2 weeks followed by 200 mg orally three times weekly for 22 weeks, along with background regimen drugs. After 22 weeks subjects were continued to take their background regimen for 96 weeks.

Primary: Number of Subjects with Adverse Event

End point title	Number of Subjects with Adverse Event[1]

End point description:

An adverse event is any untoward medical event that occurs in a subject administered an investigational product, and it does not necessarily indicate only events with clear causal relationship with the relevant investigational product. Safety data were analyzed based on the Intent- to- Treat (ITT) population, which included all subjects who had at least one intake of bedaquiline, regardless of their compliance with the protocol.

End point type	Primary

End point timeframe:

Screening up to weeks 120

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics was performed and no inferential statistical analyses was performed for this endpoint.

End point values	Bedaquiline (Overall Treatment Phase)			
Subject group type	Subject analysis set			
Number of subjects analysed	57			
Units: subjects	50			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Mycobacterial Status Over Time

End point title	Number of Subjects with Mycobacterial Status Over Time

End point description:

Mycobacterial growth culture was measured locally as per local standard of care (smear, culture, drug susceptibility testing {DST}). Subjects overall result was classified as: Positive, if at least one result was

positive from qualitative results available for both media; Negative, if both results were negative or if one result was negative and the other unknown. Intent-to-treat (ITT) population includes all subjects who had at least one intake of bedaquiline, regardless of their compliance with the protocol.

End point type	Secondary

End point timeframe:

Baseline, Weeks 24, 48, 72, 96 and 120

End point values	Bedaquiline (Overall Treatment Phase)			
Subject group type	Subject analysis set			
Number of subjects analysed	57			
Units: Subjects				
Baseline, Positive	52			
Baseline, Negative	4			
Week 24, Positive	5			
Week 24, Negative	35			
Week 48, Positive	4			
Week 48, Negative	27			
Week 72, Positive	3			
Week 72, Negative	19			
Week 96, Positive	1			
Week 96, Negative	5			
Week 120, Positive	0			
Week 120, Negative	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening up to 120 weeks

Adverse event reporting additional description:

A third subject died during the Follow up phase after the overall treatment phase.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Bedaquiline (Overall treatment phase)

Reporting group description:

Subjects received bedaquiline 400 milligram (mg) orally once daily for 2 weeks followed by 200 mg orally three times weekly for 22 weeks, along with background regimen drugs. After 22 weeks subjects were to continue to take their background regimen for 120 weeks.

Serious adverse events	Bedaquiline (Overall treatment phase)		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 57 (14.04%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix Carcinoma Stage 0			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary Haemorrhage			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Psychiatric disorders			

Psychotic Disorder			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary Tuberculosis			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Bedaquiline (Overall treatment phase)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 57 (87.72%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Hypotension			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Facial Pain			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Pain			

subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Ovarian Cyst			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Pelvic Fluid Collection			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Prostatitis			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Bronchitis Chronic			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	4 / 57 (7.02%)		
occurrences (all)	8		
Dyspnoea			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	4		
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	4		
Depression			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	4		
Depressive Symptom			

subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	3		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	15 / 57 (26.32%)		
occurrences (all)	27		
Aspartate Aminotransferase Increased			
subjects affected / exposed	28 / 57 (49.12%)		
occurrences (all)	44		
Bilirubin Conjugated Increased			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Blood Amylase Increased			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	3		
Blood Bilirubin Increased			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	3		
Blood Pressure Increased			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Blood Creatinine Increased			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	5		
Blood Thyroid Stimulating Hormone Increased			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	4		
Blood Urea Increased			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Blood Uric Acid Increased			

subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Electrocardiogram QT Prolonged			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Electrocardiogram Repolarisation Abnormality			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Glomerular Filtration Rate Decreased			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Arrhythmia Supraventricular			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Atrioventricular Block			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Atrioventricular Block First Degree			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Bundle Branch Block Left			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Cardiomyopathy			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Sinoatrial Block			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Sinus Bradycardia			

subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Ventricular Extrasystoles			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Nervous system disorders			
Complex Regional Pain Syndrome			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Encephalopathy			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	3		
Exertional Headache			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Hemianopia Heteronymous			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Neuropathy Peripheral			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Peripheral Sensory Neuropathy			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Polyneuropathy			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	13 / 57 (22.81%)		
occurrences (all)	16		
Anaemia			

subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Hearing Impaired			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	3		
Conductive Deafness			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Tinnitus			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Eye disorders			
Amblyopia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Retinopathy Hypertensive			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Vitreous Opacities			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Abdominal Pain Upper			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	3		
Disbacteriosis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Dyspepsia			

subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	4		
Gastritis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	2		
Gastritis Atrophic			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Gastroduodenitis			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	3		
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Hiatus Hernia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	8 / 57 (14.04%)		
occurrences (all)	11		
Odynophagia			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Pancreatitis Acute			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	3 / 57 (5.26%)		
occurrences (all)	5		
Hyperbilirubinaemia			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Acne			

subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Dermatitis			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	3		
Dermatitis Allergic			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Dermatitis Contact			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Dry Skin			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Hyperkeratosis			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	2		
Renal and urinary disorders			
Cystitis Noninfective			
subjects affected / exposed	1 / 57 (1.75%)		
occurrences (all)	2		
Haematuria			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	3		
Leukocyturia			
subjects affected / exposed	2 / 57 (3.51%)		
occurrences (all)	4		
Nephropathy Toxic			
subjects affected / exposed	7 / 57 (12.28%)		
occurrences (all)	16		

Proteinuria subjects affected / exposed occurrences (all)	3 / 57 (5.26%) 6		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) Primary Hypothyroidism subjects affected / exposed occurrences (all)	 4 / 57 (7.02%) 4 1 / 57 (1.75%) 1		
Musculoskeletal and connective tissue disorders Fibromyalgia subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Muscle Twitching subjects affected / exposed occurrences (all) Neck Pain subjects affected / exposed occurrences (all) Osteochondrosis subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all) Osteoporosis subjects affected / exposed occurrences (all) Tendonitis subjects affected / exposed occurrences (all)	 1 / 57 (1.75%) 1 3 / 57 (5.26%) 6 1 / 57 (1.75%) 1 1 / 57 (1.75%) 1 2 / 57 (3.51%) 2 1 / 57 (1.75%) 1 1 / 57 (1.75%) 1 1 / 57 (1.75%) 1		
Infections and infestations			

Bronchitis				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Cervicitis				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Ear Infection				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Hepatitis C				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Herpes Simplex				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Oesophageal Candidiasis				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Oral Herpes				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Papilloma Viral Infection				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Rash Pustular				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Respiratory Tract Infection				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	2			
Respiratory Tract Infection Viral				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	1 / 57 (1.75%)			
occurrences (all)	1			

Sinusitis subjects affected / exposed occurrences (all)	1 / 57 (1.75%) 1		
Tonsillitis subjects affected / exposed occurrences (all)	1 / 57 (1.75%) 1		
Vaginal Infection subjects affected / exposed occurrences (all)	1 / 57 (1.75%) 1		
Vaginitis Bacterial subjects affected / exposed occurrences (all)	2 / 57 (3.51%) 2		
Vulvovaginal Candidiasis subjects affected / exposed occurrences (all)	1 / 57 (1.75%) 1		
Metabolism and nutrition disorders Hyperkalaemia subjects affected / exposed occurrences (all)	2 / 57 (3.51%) 2		
Hypernatraemia subjects affected / exposed occurrences (all)	1 / 57 (1.75%) 1		
Hyperuricaemia subjects affected / exposed occurrences (all)	2 / 57 (3.51%) 2		
Hypokalaemia subjects affected / exposed occurrences (all)	5 / 57 (8.77%) 8		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	1 / 57 (1.75%) 1		
Hypomagnesaemia subjects affected / exposed occurrences (all)	3 / 57 (5.26%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2012	Based on new safety information regarding an effect on QT interval corrected for heart rate according to Fridericia (QTcF) during concomitant use of clofazimine and bedaquiline in study TMC207-TiDP13-C209, and based on feedback from the Food and Drug Administration (FDA) relative to the special protocol assessment for study TMC207-TiDP13-C210, the sponsor decided to add visits (Week 1, 3, 4, 6, and 8) for subjects who were taking clofazimine with bedaquiline to enable additional electrocardiogram (ECG) monitoring (on mandatory planned visits: Day 1, Week 2, 12 and 24, these subjects also require ECG monitoring). Directly observed treatment short course (DOT) verification had to take place at all additional visits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

No control arm was included in this study and only subjects with Pre-extensively drug resistant (pre-XDR) or XDR tuberculosis (TB) were allowed to participate. Enrollment was predominantly in Russia.

Notes: