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Trial record **1 of 1** for: CR012352

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To Evaluate the Safety, Tolerability, and Efficacy of TMC207 as Part of an Individualized Multi-drug Resistant Tuberculosis (MDR-TB) Treatment Regimen in Participants With Sputum Smear-positive Pulmonary MDR-TB.

This study has been completed.

Sponsor:
Janssen Infectious Diseases BVBA

Information provided by (Responsible Party):
Janssen Infectious Diseases BVBA

ClinicalTrials.gov Identifier:
NCT00910871

First received: May 28, 2009
Last updated: April 8, 2015
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History of Changes

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Results First Received: January 30, 2013

Study Type:	Interventional
Study Design:	Endpoint Classification: Safety/Efficacy Study; Intervention Model: Single Group Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Tuberculosis
Interventions:	Drug: TMC207 Drug: Background Regimen (BR) for MDR-TB

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
A Phase II open label trial with TMC207 as part of multi-drug resistant mycobacterium tuberculosis (MDR-TB) treatment regimen in participants with sputum smear-positive pulmonary infection with MDR-TB.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
A total of 241 participants were enrolled in the study; 8 participants were withdrawn from the study before study drug administration and 233 started treatment with study drug.

Reporting Groups

	Description
TMC207	Participants will receive 400 milligram (mg) TMC207 tablets orally 2 times a day along with background regimen from Day 1 to Week 2 followed by 200 mg TMC207 tablets orally 3 times a day from Week 3 to Week 24 along with background regimen, then background therapy from Week 25 to end of study (Week 120).

Participant Flow: Overall Study

	TMC207

STARTED	**233**
COMPLETED	**179**
NOT COMPLETED	**54**
Adverse Event	**5**
Death	**12**
Lost to Follow-up	**8**
Protocol Violation	**11**
Withdrawal by Subject	**12**
Subject didn't meet eligibility criteria	**5**
Undefined	**1**

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat (ITT) population included all participants who had at least 1 dose of TMC207, regardless of their compliance with the protocol.

Reporting Groups

	Description
TMC207	Participants will receive 400 milligram (mg) TMC207 tablets orally 2 times a day along with background regimen from Day 1 to Week 2 followed by 200 mg TMC207 tablets orally 3 times a day from Week 3 to Week 24 along with background regimen, then background therapy from Week 25 to end of study (Week 120).

Baseline Measures

	TMC207
Number of Participants [units: participants]	**233**
Age [units: years] Mean (Standard Deviation)	**34.6 (12.1)**
Gender [units: participants]	
Female	**83**
Male	**150**

Outcome Measures

Hide All Outcome Measures

1. Primary: The Median Time to Sputum Culture Conversion [Time Frame: Up to Week 24]

Measure Type	Primary
Measure Title	The Median Time to Sputum Culture Conversion
Measure Description	The table below shows the median time in days to culture conversion for the modified intent-to-treat (mITT) population up to Week 24. Sputum culture conversion is defined as 2 consecutive sputum cultures negative for multi-drug

	resistant tuberculosis (MDR-TB) taken at least 25 days apart. Participants who discontinued during the 24-week period were considered non-responders (based on Mycobacteria Growth Indicator Tube [MGIT]).
Time Frame	Up to Week 24
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The modified intent-to-treat (mITT) population used for all efficacy analyses included all randomized participants who received at least 1 dose of TMC207 excluding participants with drug-susceptible tuberculosis (DS-TB) or participants that were not evaluable for efficacy.

Reporting Groups

	Description
TMC207	Participants will receive 400 milligram (mg) TMC207 tablets orally 2 times a day along with background regimen from Day 1 to Week 2 followed by 200 mg TMC207 tablets orally 3 times a day from Week 3 to Week 24 along with background regimen, then background therapy from Week 25 to end of study (Week 120).

Measured Values

	TMC207
Number of Participants Analyzed [units: participants]	**205**
The Median Time to Sputum Culture Conversion [units: Days] Median (95% Confidence Interval)	**57 (56.00 to 83.00)**

No statistical analysis provided for The Median Time to Sputum Culture Conversion

2. Secondary: The Percentage of Participants With Sputum Culture Conversion [Time Frame: Week 120]

Measure Type	Secondary
Measure Title	The Percentage of Participants With Sputum Culture Conversion
Measure Description	The table below shows the percentage of participants who were responders to treatment. Sputum culture conversion is defined as 2 consecutive sputum cultures negative for multi-drug resistant tuberculosis (MDR-TB) taken at least 25 days apart. Participants who discontinued or died during the trial were considered non-responders.
Time Frame	Week 120
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The modified intent-to-treat (mITT) population used for all efficacy analyses included all randomized participants who received at least 1 dose of TMC207 excluding participants with drug-susceptible tuberculosis (DS-TB) or participants that were not evaluable for efficacy.

Reporting Groups

	Description
TMC207	Participants will receive 400 milligram (mg) TMC207 tablets orally 2 times a day along with background regimen from Day 1 to Week 2 followed by 200 mg TMC207 tablets orally 3 times a day from Week 3 to Week 24 along with background regimen, then background therapy from Week 25 to end of study (Week 120).

Measured Values

	TMC207
Number of Participants Analyzed [units: participants]	**205**
The Percentage of Participants With Sputum Culture Conversion [units: Percentage of Participants]	**72.2**

No statistical analysis provided for The Percentage of Participants With Sputum Culture Conversion

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Baseline up to Week 120
Additional Description	Only participants who had at least one of the treatment emergent adverse events (TEAEs) listed in the other (non-serious) adverse events table are included in the total number of participants with non-serious adverse events.

Reporting Groups

	Description
TMC207	Participants will receive 400 milligram (mg) TMC207 tablets orally 2 times a day along with background regimen from Day 1 to Week 2 followed by 200 mg TMC207 tablets orally 3 times a day from Week 3 to Week 24 along with background regimen, then background therapy from Week 25 to end of study (Week 120).

Serious Adverse Events

	TMC207
Total, serious adverse events	
# participants affected / at risk	**47/233 (20.17%)**
Blood and lymphatic system disorders	
Anaemia * 1	
# participants affected / at risk	**2/233 (0.86%)**
Cardiac disorders	
Cardiac failure * 1	
# participants affected / at risk	**1/233 (0.43%)**
Cardiac failure congestive * 1	
# participants affected / at risk	**2/233 (0.86%)**
Cor pulmonale * 1	
# participants affected / at risk	**1/233 (0.43%)**
Ear and labyrinth disorders	
Deafness * 1	
# participants affected / at risk	**1/233 (0.43%)**
Gastrointestinal disorders	
Ileus paralytic * 1	
# participants affected / at risk	**1/233 (0.43%)**
Vomiting * 1	
# participants affected / at risk	**1/233 (0.43%)**
Alcoholic pancreatitis * 1	
# participants affected / at risk	**1/233 (0.43%)**

Gastritis [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Inguinal hernia [*1]	
# participants affected / at risk	**1/233 (0.43%)**
General disorders	
Treatment failure [*1]	
# participants affected / at risk	**2/233 (0.86%)**
Hepatobiliary disorders	
Cholelithiasis [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Liver disorder [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Hepatitis [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Infections and infestations	
Gastroenteritis [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Lung infection [*1]	
# participants affected / at risk	**2/233 (0.86%)**
Pneumonia [*1]	
# participants affected / at risk	**3/233 (1.29%)**
Tuberculosis [*1]	
# participants affected / at risk	**6/233 (2.58%)**
Hepatitis a [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Lung abscess [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Lymph node tuberculosis [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Pyopneumothorax [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Injury, poisoning and procedural complications	
Concussion [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Contusion [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Investigations	
Blood glucose fluctuation [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Electrocardiogram qt prolonged [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Metabolism and nutrition disorders	
Decreased appetite [*1]	
# participants affected / at risk	**1/233 (0.43%)**

Dehydration [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Diabetes mellitus inadequate control [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Hyponatraemia [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Musculoskeletal and connective tissue disorders	
Pain in extremity [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Fistula [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Basal cell carcinoma [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Nervous system disorders	
Cerebral haemorrhage [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Ischaemic cerebral infarction [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Neurotoxicity [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Psychiatric disorders	
Emotional disorder [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Hallucination [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Psychiatric symptom [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Renal and urinary disorders	
Renal impairment [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Ureteric stenosis [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Respiratory, thoracic and mediastinal disorders	
Chronic obstructive pulmonary disease [*1]	
# participants affected / at risk	**1/233 (0.43%)**
Dyspnoea [*1]	
# participants affected / at risk	**2/233 (0.86%)**
Hydropneumothorax [*1]	
# participants affected / at risk	**2/233 (0.86%)**
Pneumothorax [*1]	
# participants affected / at risk	**5/233 (2.15%)**
Cough [*1]	

# participants affected / at risk	1/233 (0.43%)
Haemoptysis * 1	
# participants affected / at risk	4/233 (1.72%)
Pulmonary bulla * 1	
# participants affected / at risk	1/233 (0.43%)
Pulmonary haemorrhage * 1	
# participants affected / at risk	1/233 (0.43%)
Respiratory failure * 1	
# participants affected / at risk	1/233 (0.43%)
Surgical and medical procedures	
Surgery * 1	
# participants affected / at risk	1/233 (0.43%)
Lung operation * 1	
# participants affected / at risk	1/233 (0.43%)
Vascular disorders	
Hypertension * 1	
# participants affected / at risk	1/233 (0.43%)
Hypovolaemic shock * 1	
# participants affected / at risk	1/233 (0.43%)

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 12.1

Other Adverse Events

Hide Other Adverse Events

Time Frame	Baseline up to Week 120
Additional Description	Only participants who had at least one of the treatment emergent adverse events (TEAEs) listed in the other (non-serious) adverse events table are included in the total number of participants with non-serious adverse events.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
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Other Adverse Events

	TMC207
Total, other (not including serious) adverse events	
# participants affected / at risk	179/233 (76.82%)
Blood and lymphatic system disorders	
Anaemia * 1	
# participants affected / at risk	13/233 (5.58%)

Ear and labyrinth disorders	
Tinnitus [*1]	
# participants affected / at risk	**18/233 (7.73%)**
Gastrointestinal disorders	
Diarrhoea [*1]	
# participants affected / at risk	**27/233 (11.59%)**
Nausea [*1]	
# participants affected / at risk	**35/233 (15.02%)**
Vomiting [*1]	
# participants affected / at risk	**26/233 (11.16%)**
Abdominal pain [*1]	
# participants affected / at risk	**14/233 (6.01%)**
Dyspepsia [*1]	
# participants affected / at risk	**14/233 (6.01%)**
General disorders	
Injection site pain [*1]	
# participants affected / at risk	**15/233 (6.44%)**
Chest pain [*1]	
# participants affected / at risk	**17/233 (7.30%)**
Infections and infestations	
Nasopharyngitis [*1]	
# participants affected / at risk	**17/233 (7.30%)**
Upper respiratory tract infection [*1]	
# participants affected / at risk	**13/233 (5.58%)**
Investigations	
Blood uric acid increased [*1]	
# participants affected / at risk	**20/233 (8.58%)**
Alanine aminotransferase increased [*1]	
# participants affected / at risk	**12/233 (5.15%)**
Aspartate aminotransferase increased [*1]	
# participants affected / at risk	**14/233 (6.01%)**
Hepatic enzyme increased [*1]	
# participants affected / at risk	**12/233 (5.15%)**
Metabolism and nutrition disorders	
Hyperuricaemia [*1]	
# participants affected / at risk	**36/233 (15.45%)**
Hypokalaemia [*1]	
# participants affected / at risk	**19/233 (8.15%)**
Decreased appetite [*1]	
# participants affected / at risk	**12/233 (5.15%)**
Musculoskeletal and connective tissue disorders	
Arthralgia [*1]	
# participants affected / at risk	**35/233 (15.02%)**

Pain in extremity * 1	
# participants affected / at risk	**16/233 (6.87%)**
Nervous system disorders	
Dizziness * 1	
# participants affected / at risk	**13/233 (5.58%)**
Headache * 1	
# participants affected / at risk	**31/233 (13.30%)**
Psychiatric disorders	
Insomnia * 1	
# participants affected / at risk	**18/233 (7.73%)**
Respiratory, thoracic and mediastinal disorders	
Haemoptysis * 1	
# participants affected / at risk	**17/233 (7.30%)**
Skin and subcutaneous tissue disorders	
Pruritus * 1	
# participants affected / at risk	**18/233 (7.73%)**
Rash * 1	
# participants affected / at risk	**13/233 (5.58%)**

* Events were collected by non-systematic assessment
1 Term from vocabulary, MedDRA 12.1

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
In Participant Flow, the 12 deaths shown are restricted to those that occurred during the trial and do not include 4 deaths reported after discontinuation in long-term survival follow-up.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.
The agreement is: ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. ☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo. Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed. ☑ **Restriction Description:** It is the policy of the sponsor not to allow the investigators to publish their results or findings prior to the sponsor's publication of the overall trial results.The investigator agrees that before he/she publishes any results of this trial, he/she shall provide the sponsor with at least 45 days for full review of the prepublication manuscript prior to submission of the manuscript to

the publisher.

Results Point of Contact:

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Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Pym AS, Diacon AH, Tang SJ, Conradie F, Danilovits M, Chuchottaworn C, Vasilyeva I, Andries K, Bakare N, De Marez T, Haxaire-Theeuwes M, Lounis N, Meyvisch P, Van Baelen B, van Heeswijk RP, Dannemann B; TMC207-C209 Study Group. Bedaquiline in the treatment of multidrug- and extensively drug-resistant tuberculosis. Eur Respir J. 2016 Feb;47(2):564-74. doi: 10.1183/13993003.00724-2015. Epub 2015 Dec 2.

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