Protocol Registration Receipt
10/30/2014

Grantor: CDRH IND/IDE Number: 43,735 Serial Number: 0419

Type 2 Diabetes Evaluation of Ranolazine in Subjects With Chronic Stable Angina (TERISA)

This study has been completed.

Sponsor:	Gilead Sciences
Collaborators:	
Information provided by (Responsible Party):	Gilead Sciences
ClinicalTrials.gov Identifier:	NCT01425359

Purpose

This study will evaluate the effect of ranolazine compared to placebo on the average weekly angina frequency in subjects with chronic stable angina and coronary artery disease (CAD) who have a history of type 2 diabetes mellitus (T2DM), and whether ranolazine can reduce the frequency of angina (chest pain) attacks, compared to a placebo. Subjects will be asked to record their daily angina episodes in a diary at the end of each study day. Ranolazine is approved for the treatment of chronic angina, and is not approved for the treatment of T2DM.

Condition	Intervention	Phase
Angina Pectoris Coronary Artery Disease Type 2 Diabetes Mellitus	Drug: Ranolazine Drug: Ranolazine placebo	Phase 4

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor), Randomized, Efficacy Study
Official Title: A Phase 4, Randomized, Double-Blind, Placebo-Controlled, Parallel Study of Ranolazine in Subjects With Chronic Stable Angina and Coronary Artery Disease With a History of Type 2 Diabetes Mellitus

Further study details as provided by Gilead Sciences:

Primary Outcome Measure:

- Average Weekly Angina Frequency Over the Last 6 Weeks of Treatment [Time Frame: 6 weeks] [Designated as safety issue: No]
  Average weekly angina frequency was defined as the total number of angina episodes reported during the last 6 weeks of treatment divided by 6 weeks. For subjects who terminated with less than 6 weeks of treatment, frequency was calculated as the total number of angina episodes reported during the treatment period divided by the subject's actual duration of treatment.

Secondary Outcome Measures:

- Average Weekly Frequency of Sublingual Nitroglycerin Use Over the Last 6 Weeks of Treatment [Time Frame: 6 weeks] [Designated as safety issue: No]
  Average weekly frequency of sublingual nitroglycerin use was defined as the total number reported during the last 6 weeks of treatment divided by the duration corresponding to the last 6 weeks of treatment.
- Percentage of Weeks Participants Achieved at Least a 50% Reduction in Angina Frequency [Time Frame: 6 weeks] [Designated as safety issue: No]
  For each participant, the percentage of the last 6 weeks on treatment during which the angina frequency was less than or equal to 50% of the baseline average weekly angina frequency was determined.
- Percentage of the Last 6 Weeks on Treatment During Which the Angina Frequency Was ≤ 50% of the Baseline Average Weekly Angina Frequency [Time Frame: 6 weeks] [Designated as safety issue: No]
- Change From Baseline in the Short-Form 36® (SF-36) Mental and Physical Component Scores [Time Frame: Up to 8 weeks] [Designated as safety issue: No]
  The range of each health domain score is 0-100, with 0 indicating a poorer health state and 100 indicating a better health state. An increase in score indicates an improvement in health state. Participants were asked to complete the survey at randomization (prior to receiving treatment), and at end of treatment visit (Week 8) or early study drug discontinuation or early termination visit. The survey asked participants for responses specific to the preceding 4 weeks prior to completing the survey.
- Patient's Global Impression of Change (PGIC) Scale Score [Time Frame: 8 weeks] [Designated as safety issue: No]
  The PGIC was completed at the end of treatment/last visit.The PGIC scale measures the change in the participant's overall status since the beginning of

the study on a scale ranging from 1 (no change or worse) to 7 (very much improved).

Enrollment: 949
Study Start Date: September 2011
Study Completion Date: October 2012
Primary Completion Date: October 2012

Arms	Assigned Interventions
Placebo Comparator: Placebo Qualifying phase: Participants will enter a 2-week washout period if needing to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period will be randomized to the treatment period. Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.	Drug: Ranolazine placebo
Experimental: Ranolazine Qualifying phase: Participants will enter a 2-week washout period if needing to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period.	Drug: Ranolazine Other Names: Ranexa® Drug: Ranolazine placebo

Arms	Assigned Interventions
Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period will be randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.	

Participants who meet the eligibility criteria at screening will enter a 4-to 6-week Qualifying Period. The allowed concomitant antianginal medication(s) must be maintained at a stable dose throughout the study. Participants will document the number of angina episodes, number of sublingual nitroglycerin doses taken, and a dyspnea score (on a scale from 1 to 5) on a daily basis in a diary. Participants eligible to stay in the study after the Qualifying Period will enter the 8-week double-blind dosing phase. Participants will have study visits at the end of Weeks 2 and 8. Participants will continue to document the number of angina episodes and number of sublingual nitroglycerin doses taken as well as a dyspnea score on a daily basis by the end of each day in their diary. In addition, participants will be called during Week 2 and at the end of Week 5 to encourage compliance. A safety follow-up phone call will be made 14 days after the last study visit or early discontinuation.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both

Inclusion Criteria:

- Written informed consent
- Males and females aged at least 18 years
- At least a 3-month history of chronic stable angina triggered by physical effort and relieved by rest and/or sublingual nitroglycerin
- CAD documented by one or more of the following:

    a. Angiographic evidence of ≥ 50% stenosis of one or more major coronary arteries

b. History of myocardial infarction (MI) documented by positive myocardial muscle creatine kinase (CK-MB) enzymes, troponins, or electrocardiogram (ECG) changes
c. Cardiac imaging study or exercise test diagnostic for CAD

- Treatment with up to 2 antianginal therapies at a stable dose for at least 2 weeks prior to the Qualifying Period.
- Documented history of T2DM
- Willing to maintain stable tobacco usage habits throughout the study
- Willing to maintain stable activity levels throughout the study
- Females of childbearing potential must agree to utilize highly effective contraception methods from Screening throughout the duration of study treatment and for 14 days following the last dose of study drug.

Exclusion Criteria:

- New York Heart Association (NYHA) Class III and IV
- Acute coronary syndrome in the prior 2 months or planned coronary revascularization during the study period
- Stroke or transient ischemic attack within 6 months prior to Screening
- QTc > 500 milliseconds
- Uncontrolled hypertension (seated systolic blood pressure > 180 mmHg or diastolic blood pressure > 110 mmHg)
- Systolic blood pressure < 100 mmHg
- Clinically significant hepatic impairment
- Prior treatment with ranolazine, or known hypersensitivity or intolerance to ranolazine
- Females who are breastfeeding
- Positive serum pregnancy test
- Participation in another investigational drug or device study within 1 month prior to Screening
- Current treatment with trimetazidine, ivabradine, or nicorandil. Subjects will need to discontinue these medications 2 weeks prior to the Qualifying Period.
- Current treatment with potent inhibitors of cytochrome (CYP)3A (eg, ketoconazole, itraconazole, clarithromycin, nefazodone, nelfinavir, ritonavir, indinavir, and saquinavir)
- Current treatment with CYP3A and P glycoprotein (Pgp) inducers (eg, rifampicin/rifampin, carbamazepine, and St. John's wort [Hypericum perforatum])
- Current treatment with CYP3A4 substrates with a narrow therapeutic range (eg, cyclosporine, tacrolimus, and sirolimus)
- Subjects taking simvastatin who cannot reduce the dose to 20 mg once daily or who cannot switch to another statin
- Current treatment with Class I or III antiarrhythmic medications
- History of illicit drug use or alcohol abuse within 1 year of Screening
- Any other conditions that, in the opinion of the investigator, are likely to prevent compliance with the study protocol or pose a safety concern if the subject participates in the study

Contacts and Locations

Locations

United States, Arkansas

Cardiology and Medicine Clinic
Little Rock, Arkansas, United States, 72204

United States, California

Merced Heart Associates
Merced, California, United States, 95340

Spectrum Clinical Research Institute, Inc
Moreno Valley, California, United States, 92553

Sacramento Heart and Vascular Research Center
Sacramento, California, United States, 95825

United States, Florida

South Florida Research Solutions, LLC
Hollywood, Florida, United States, 33021

Baptist Heart Specialist
Jacksonville, Florida, United States, 32207

Clinical Research of Central Florida
Winter Haven, Florida, United States, 33880

United States, Georgia

Masters of Clinical Research, Inc.
Augusta, Georgia, United States, 30909

Columbus Cardiology Associates
Columbus, Georgia, United States, 31909

United States, Kentucky

Central Cardiology Associates
Elizabethtown, Kentucky, United States, 42701

Research Integrity, LLC
Owensboro, Kentucky, United States, 42303

United States, Louisiana

Alexandria Cardiology Clinic

Alexandria, Louisiana, United States, 71301

Alexandria Cardiology Clinic

Alexandria, Louisiana, United States, 71301

Clinical Trials Management, LLC

Mandeville, Louisiana, United States, 70471

United States, Michigan

Endeavor Medical Research, PLC

Alpena, Michigan, United States, 49707

United States, Minnesota

Minneapolis Heart Institute Foundation

Minneapolis, Minnesota, United States, 55407

United States, New Jersey

Cross Country Cardiology

Edgewater, New Jersey, United States, 07020

United States, Tennessee

Kore CV Research

Jackson, Tennessee, United States, 38305

Wellmont Cardiovascular Associates Heart Institute

Johnson City, Tennessee, United States, 37604

United States, Texas

Med-Tech Research

Houston, Texas, United States, 77024

Humble Cardiology Associates

Humble, Texas, United States, 77338

Belarus

State Institution "Gomel regional clinical hospital"

Gomel, Belarus, 246029

State Inst Rep Scientific and Practical center

Minsk, Belarus, 220036

Bulgaria

Military Medical Academy, Clinic of Cardiology and Intesive Care

Sofia, Bulgaria, 1606

MHAT "Tsar Boris III"

Sofia, Bulgaria, 1233

MHAT "Vita", Cardiology Department

Sofia, Bulgaria, 1505

National Cardiology Center, Cardiology Clinic - III

Sofia, Bulgaria, 1309

UMHAT "Tsaritsa Yoanna" - ISUL, Cardiology Clinic

Sofia, Bulgaria, 1527

Diagnostic Consultative Center, Ascendent Cardiological Out-Patient Office

Sofia, Bulgaria, 1202

Canada

High Desert Medical Group

Lancaster, Canada, 93534

Montreal Heart Institute

Montreal, Canada, H1T 1C8

London Road Diagnostic Clinic and Medical Centre

Ontario, Canada, N7T 4X3

Topsail Road Medical Clinic

Saint John's, Canada, A1E 2E2

Canada, Ontario

SKDS Research Inc

New Market, Ontario, Canada, L3Y 5G8

Dr. Roger Labonté Professional Medicine Corp.

Sudbury, Ontario, Canada, P3E 3B8

Aniol Gupta MD

Toronto, Ontario, Canada, M9V 4B4

Canada, Quebec

Montréal General Hospital

Montreal, Quebec, Canada, H3G 1A4

Czech Republic

Vojenska Nemocnice Brno

Brno, Czech Republic, 636 00

Cardiocentrum Kladno s.r.o.

Kladno, Czech Republic, 27280

Poliklinika Modrany - Kardiologie

Praha 4, Czech Republic, 14300

Corintez s.r.o.

Praha 5, Czech Republic, 158 00

Fakultní Nemocnice v Motole

Praha 5, Czech Republic, 150 06

Centrum klinického výzkumu, s.r.o.

Príbram, Czech Republic, 26101

Nemocnice Slaný

Slaný, Czech Republic, 27401

Georgia

Emergency Cardiology Center by Academician G. Chapidze LTD

Tbilisi, Georgia, 0159

Emergency Cardiology Center by Academician G. Chapidze LTD

Tbilisi, Georgia, 0159

Cardio-Reanimation Clinic LTD

Tbilisi, Georgia, 0159

Amtel Hospital First Clinical LLC

Tbilisi, Georgia, 0144

Clinic "Guli"

Tbilisi, Georgia, 0144

Multiprofile Clinical Hospital of Tbilisi #2 LTD

Tbilisi, Georgia, 0164

Tbilisi Heart and Vascular Clinic LTD

Tbilisi, Georgia, 0159

Tbilisi State Medical University Alexandre Aladashvili University Clinic

Tbilisi, Georgia, 0102

Germany

Charité Campus Virchow Klinikum

Berlin, Germany, 13353

Städtische Kliniken Bielefeld

Bielefeld, Germany, 33604

Sankt Johannes-Hospital Dortmund

Dortmund, Germany, 44137

Universitätsklinikum Göttingen

Göttingen, Germany, 37099

Gemeinschaftspraxis fur Kardiologie

Heidelberg, Germany, 69115

Praxis Fur Innere Medizin Kardiologie, Pneumologic und Allergologie

Mannheim, Germany, 68165

Universitätsmedizin Mannheim

Mannheim, Germany, 68169

Israel

Barzilai Medical Center, Cardiology Dept.

Ashkelon, Israel, 78287

Assaf Harofeh Medical Centre

Be'er Ya`aqov, Israel, 70300

Shaare Zedek Medical Center

Jerusalem, Israel, 91004

Kaplan Medical Center

Rehovot, Israel, 76100

Ziv Medical Center

Safed, Israel, 13100

Tel Aviv Souraski Medical Center

Tel Aviv, Israel, 64239

Poland

Pomorskie Centra Kardiologiczne S.A.

Gdansk, Poland, 80126

S.P. Specjalistyczny Szpital Zachodni im.JP II

Grodzisk, Mazowiecki, Poland, 05-825

Krakowski Szpital Specjalistyczny im.JPII

Krakow, Poland, 31-202

Centrum Badawcze Współczenej Terapii

Warszawa, Poland, 02-679

Synexus SCM Sp. z o.o. Oddział w Warszawie

Warszawa, Poland, 01-192

Slaskie Centrum Chorób Serca w Zabrzu

Zabrze, Poland, 41-800

MULTI-MED PLUS Sp. z o.o.

Lódz, Lodzkie, Poland, 90-553

Niepubliczny Zakład Opieki Zdrowotnej Przychodnia Zdrowia "Zadębie"

Skierniewice, Lodzkie, Poland, 96-100

KO-MED Marek Konieczny

Puławy, Lubelskie, Poland, 24-100

Specjalistyczna Praktyka Lekarska Leszek Bryniarski

Kraków, Malopolskie, Poland, 30-082

NZOZ Revita Poradnia Kardiologiczna

Kraków, Malopolskie, Poland, 31-949

Instytut Kardiologii

Warszawa, Mazowieckie, Poland, 02-637

Instytut Kardiologii

Warszawa, Mazowieckie, Poland, 04-628

NZOZ Sródmiescie Sp z o.o.

Gdynia, Pomorskie, Poland, 81-394

Russian Federation

Altay Regional Cardiologycal Dispensary

Barnaul, Russian Federation, 656055

"Chita State Medical Academy" Curative-Diagnostic Clinic department

Chita, Russian Federation, 672039

Sverdlovsky Regional Clinical Hospital of Wars Veterans

Ekaterinburg, Russian Federation, 620905

Non-state Institution of healthcare "Department hospital on station Kemerovo of OAO "Russian Railway"

Kemerovo, Russian Federation, 650056

Municipal Institution of Healthcare "Kemerovo Cardiology Dispensary"

Kemerovo, Russian Federation, 650002

Medical centre "Delis", LLC

Kirovsk, Russian Federation, 187342

First Moscow State Medical University I.M. Sechenov

Moscow, Russian Federation, 119991

State Healthcare institution of Moscow"Cardiology Dispensary #2"

Moscow, Russian Federation, 117556

State healthcare institution of Moscow "City Clinical hospital#15 named after O.M.Filatov"

Moscow, Russian Federation, 111539

Moscow State University of Medicine and Dentistry based on Moscow City Clinical Hospital #71

Moscow, Russian Federation, 121374

Federal State Institution "Outpatient department #3" of President Management department of Russian Federation

Moscow, Russian Federation, 129090

City Clinical Hospital named after S.P.Botkin
Moscow, Russian Federation, 125284
Federal State Institution "National Research Center for Preventive Medicine"
Moscow, Russian Federation, 101990
Moscow City Clinical Hospital #51
Moscow, Russian Federation, 121309
Moscow State Institution of Health "City Clinical Hospital #81"
Moscow, Russian Federation, 127644
State Institution of Moscow Healthcare "City Clinical Hospital named after S.P. Botkin"
Moscow, Russian Federation, 125284
City Clinical Hospital named after S.P.Botkin
Moscow, Russian Federation, 125284
FGU Central Clinical Hospital with Polyclinic of President Administrative Department of RF
Moscow, Russian Federation, 121359
State Budget Educational Institution of High Professional Education First Moscow State Medical University... #1, Cardiology Clinic, Hospital Therapy Department
Moscow, Russian Federation, 119991
State Budget Educational Institution of High Professional Education First Moscow State Medical University... #1, Cardiology Clinic, Hospital Therapy Department
Moscow, Russian Federation, 119992
State Novosibirsk Regional Clinical Hospital
Novosibirsk, Russian Federation, 630087
Regional Clinical Hospital named after N.N.Burdenko
Penza, Russian Federation, 440026
State Institution of Healthcare Perm Regional Hospital for War Veterans
Perm, Russian Federation, 614097
State Healthcare Institution "Ryazan regional clinical cardiological dispensary"
Ryazan, Russian Federation, 390026
"Clinical hospital named after S.R.Mirotvortsev"
Saratov, Russian Federation, 410054
Educational Institution of Higher Vocational Education "Smolensk State Medical Academy" on the base of Municipal Medicoprophylactic Institution "Hospital of Emergency Medical Care",
Smolensk, Russian Federation, 214000
State Healthcare institution "Municipal Out-patient Clinic #109"
St. Petersburg, Russian Federation, 192288

State Institution of Healthcare "City Hospital #40 of Kurortniy administrative district
St. Petersburg, Russian Federation, 197705
International Medical Center "SOGAZ", LLC
St. Petersburg, Russian Federation, 191186
Institution and Address: "Medical Research Institute", LLC
St. Petersburg, Russian Federation, 196084
Federal Heart, Blood and Endocrinology Centre n.a. Almazov
St. Petersburg, Russian Federation, 194156
Federal Heart, Blood and Endocrinology Centre n.a. Almazov
St. Petersburg, Russian Federation, 197341
FGU Central Clinical Hospital with Polyclinic of President Administrative Department of RF
St. Petersburg, Russian Federation, 121359
Federal State Educational Institution of High Professional Education "Military Medical Academy n.a. S.M. Kirov" of the Ministry of Defence of Russia
St. Petersburg, Russian Federation, 191124
Saint-Petersburg State Healthcare Institution
St. Petersburg, Russian Federation, 193144
Autonomous healthcare institution of Voronezh region "Voronezh regional clinic consultative and diagnostic centre"
Voronezh, Russian Federation, 394018
Municipal Institution of Healthcare "Clinical Hospital #8 of Yaroslavl"
Yaroslavl, Russian Federation, 150030
City Hospital #38 named after Semashko N.A
Pushkin, St. Petersburg, Russian Federation, 196601

Serbia

Cardiology Clinic, Clinical Center Serbia
Belgrade, Serbia, 11000
Institute of Cardiovascular Diseases
Sremska Kamenica, Serbia, 21204

Slovakia

ALIAN, s.r.o.
Bardejov, Slovakia, 085 01
Cardioconsult, s.r.o.
Bratislava, Slovakia, 811 04
Kardiovaskulárne centrum, s.r.o.
Bratislava, Slovakia, 831 01
CARDIO D&R, s.r.o.

Košice, Slovakia, 040 22

KARDIOMED, s.r.o.

Lučenec, Slovakia, 984 01

Kardiocentrum Nitra, s.r.o.

Nitra, Slovakia, 949 01

Slovenia

University Clinic of Respiratory and Allergic Diseases Golnik

Golnik, Slovenia, 4204

University Klinicni Center Ljubljana

Ljubljana, Slovenia, 1000

General Hospital Murska Sobota

Murska Sobota, Slovenia, 9001

Ukraine

Donetsk National Medical University, Department of Internal Medicine #1 based on Department of Emergency Cardiology and Rehabilitation of Institute of Urgent and Recovery Surgery named after V. K. Gusak

Donetsk, Ukraine, 83045

Central Clinical Hospital of Ukrzaliznitsia, Cardiology department

Kharkiv, Ukraine, 61103

Kharkiv Medical Academy of Postgraduate Education, Department of cardiology and functional diagnostics based on City Clinical Hospital #8, Department of Cardiology #2

Kharkiv, Ukraine, 61176

SI "Institute of Gerontology of AMS of Ukraine"

Kyiv, Ukraine, 04114

Department of Diabetology of National Medical Academy of Postgraduate Education named after P.L.Shupyk based on Day Time Hospital of Administration of Medical Service and Rehabilitation of "ARTEM" SHC

Kyiv, Ukraine, 04050

Kyiv city clinical hospital #5

Kyiv, Ukraine, 03115

Kyiv City Clinical Hospital #1, Department of Emergency Cardiology

Kyiv, Ukraine, 02091

Central polyclinic of Pechersk district, Department of cardiology

Kyiv, Ukraine, 01103

Lviv National Medical University named after Danylo Halytsky, Department of Propaedeutics of Internal Medicine #1 based on Polyclinic Department of Municipal City Clinical Hospital #5

Lviv, Ukraine, 79044

SI Odessa Regional Cardiological Dispensary
Odessa, Ukraine, 65025

Investigators

Study Director:	Patrick Yue, MD	Gilead Sciences

More Information

Responsible Party:	Gilead Sciences
Study ID Numbers:	GS-US-259-0133
Health Authority:	United States: Food and Drug Administration
	United States: Institutional Review Board
	Canada: Health Canada
	Canada: Ethics Review Committee
	Belarus: Ministry of Health
	Czech Republic: Ethics Committee
	Czech Republic: State Institute for Drug Control
	Georgia: Ministry of Health
	Germany: Federal Institute for Drugs and Medical Devices
	Germany: Ethics Commission
	Israel: Ethics Commission
	Israel: Ministry of Health
	Poland: Ethics Committee
	Poland: The Central Register of Clinical Trials
	Russia: Ethics Committee
	Russia: Ministry of Health of the Russian Federation
	Serbia and Montenegro: Agency for Drugs and Medicinal Devices
	Serbia: Ethics Committee
	Ukraine: Ethics Committee
	Ukraine: Ministry of Health
	Romania: Ethics Committee
	Romania: National Medicines Agency
	Slovak Republic: Ethics Committee
	Slovakia: State Institute for Drug Control
	Slovenia: Agency for Medicinal Products - Ministry of Health

Slovenia: Ethics Committee
Bulgaria: Bulgarian Drug Agency
Bulgaria: Ethics committee

Study Results

Participant Flow

Recruitment Details

Participants were enrolled at a total of 116 study sites in North America, Europe, and Asia. The first participant was screened on 05 October 2011. The last participant observation occurred on 25 October 2012.

Pre-Assignment Details

1142 participants entered the qualifying period.

Reporting Groups

	Description
Placebo	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.
Ranolazine	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to

	Description
	documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.

Overall Study

	Placebo	Ranolazine
Started	476	473
Completed	457	451
Not Completed	19	22
Randomized but Not Treated	2	3
Adverse Event	9	8
Revascularization	0	1
Death	0	1
Unsatisfactory Response	1	0
Protocol Violation	1	2
Subject Withdrew Consent	1	2
Investigator's Discretion	2	0
Did Not Meet Qualifying Criteria	3	5

Baseline Characteristics

Analysis Population Description

Safety Analysis Set: randomized participants who received at least one dose of study treatment.

Reporting Groups

	Description
Placebo	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.
Ranolazine	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.

Baseline Measures

	Placebo	Ranolazine	Total
Number of Participants	474	470	944
Age, Continuous [units: years] Mean (Standard Deviation)	64 (8.5)	63 (8.6)	64 (8.5)
Age, Customized [units: participants]			
< 65 years	249	264	513
65 - 74 years	170	160	330
≥ 75 years	55	46	101
Gender, Male/Female [units: participants]			
Female	182	180	362
Male	292	290	582
Race/Ethnicity, Customized [units: participants]			
Asian	1	1	2
Black or African American	2	5	7
White	471	464	935
Race/Ethnicity, Customized [units: participants]			
Hispanic or Latino	5	4	9
Not Hispanic or Latino	464	462	926
Not Reported	3	3	6
Unknown	2	1	3

	Placebo	Ranolazine	Total
Region of Enrollment [1] [units: participants]			
United States	12	15	27
Belarus	1	0	1
Serbia	3	2	5
Slovenia	0	1	1
Slovakia	12	9	21
Ukraine	53	69	122
Israel	10	14	24
Russian Federation	281	263	544
Czech Republic	3	6	9
Canada	2	1	3
Poland	53	40	93
Bulgaria	9	11	20
Georgia	36	40	76
Germany	1	2	3
Study-Specific Measure [units: kg/m^2] Mean (Standard Deviation)	31.1 (4.90)	31.3 (5.01)	31.2 (4.96)
Study-Specific Measure [units: percent HbA1c in blood] Mean (Standard Deviation)	7.3 (1.53)	7.3 (1.50)	7.3 (1.52)

[1] All randomized participants were analyzed for region of enrollment (placebo, n = 476; ranolazine, n = 473).

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Average Weekly Angina Frequency Over the Last 6 Weeks of Treatment
Measure Description	Average weekly angina frequency was defined as the total number of angina episodes reported during the last 6 weeks of treatment divided by 6 weeks. For subjects who terminated with less than 6 weeks of treatment, frequency was calculated as the total number of angina episodes reported during the treatment period divided by the subject's actual duration of treatment.
Time Frame	6 weeks
Safety Issue?	No

Analysis Population Description

Full Analysis Set (FAS): randomized participants who received at least 1 dose of randomized study drug with at least 1 postbaseline primary efficacy measurement and did not have any major eligibility violations. Participants were included in the FAS if they did not discontinue study drug prior to Day 14.

Reporting Groups

	Description
Placebo	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period.

	Description
	Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.
Ranolazine	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.

Measured Values

	Placebo	Ranolazine
Number of Participants Analyzed	465	462
Average Weekly Angina Frequency Over the Last 6 Weeks of Treatment [units: angina attacks per week] Mean (Standard Deviation)	5.2 (4.73)	4.5 (4.32)

Statistical Analysis 1 for Average Weekly Angina Frequency Over the Last 6 Weeks of Treatment

Groups	Placebo, Ranolazine
Method	Other [Generalized linear model]
P-Value	0.008

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

Angina frequency was compared by fitting a generalized linear model with log link and negative binomial distribution response.

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

2. Secondary Outcome Measure:

Measure Title	Average Weekly Frequency of Sublingual Nitroglycerin Use Over the Last 6 Weeks of Treatment
Measure Description	Average weekly frequency of sublingual nitroglycerin use was defined as the total number reported during the last 6 weeks of treatment divided by the duration corresponding to the last 6 weeks of treatment.
Time Frame	6 weeks
Safety Issue?	No

Analysis Population Description

Full Analysis Set

Reporting Groups

	Description
Placebo	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period.

	Description
	Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.
Ranolazine	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.

Measured Values

	Placebo	Ranolazine
Number of Participants Analyzed	465	462
Average Weekly Frequency of Sublingual Nitroglycerin Use Over the Last 6 Weeks of Treatment [units: nitroglycerin uses per week] Mean (Standard Deviation)	3.6 (5.35)	2.9 (4.34)

Statistical Analysis 1 for Average Weekly Frequency of Sublingual Nitroglycerin Use Over the Last 6 Weeks of Treatment

Groups	Placebo, Ranolazine
Method	Other [Generalized linear model]
P-Value	0.003

Additional details about the analysis, such as null hypothesis and power calculation:

[Not specified.]

Additional information, such as whether or not the p-value is adjusted for multiple comparisons and the a priori threshold for statistical significance:

Sublingual nitroglycerin use frequency was compared by fitting a generalized linear model with log link and negative binomial distribution response.

Other relevant information, such as adjustments or degrees of freedom:

[Not specified.]

3. Secondary Outcome Measure:

Measure Title	Percentage of Weeks Participants Achieved at Least a 50% Reduction in Angina Frequency
Measure Description	For each participant, the percentage of the last 6 weeks on treatment during which the angina frequency was less than or equal to 50% of the baseline average weekly angina frequency was determined.
Time Frame	6 weeks
Safety Issue?	No

Analysis Population Description

Participants in the Full Analysis Set with available data were analyzed.

Reporting Groups

	Description
Placebo	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period

	Description
	were randomized to the treatment period. Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.
Ranolazine	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.

Measured Values

	Placebo	Ranolazine
Number of Participants Analyzed	462	460
Percentage of Weeks Participants Achieved at Least a 50% Reduction in Angina Frequency [units: percentage of weeks] Mean (Standard Deviation)	41 (36)	46 (35)

4. Secondary Outcome Measure:

Measure Title	Percentage of the Last 6 Weeks on Treatment During Which the Angina Frequency Was ≤ 50% of the Baseline

	Average Weekly Angina Frequency
Measure Description	
Time Frame	6 weeks
Safety Issue?	No

Analysis Population Description

Full Analysis Set

Reporting Groups

	Description
Placebo	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.
Ranolazine	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.

Measured Values

	Placebo	Ranolazine
Number of Participants Analyzed	465	462
Percentage of the Last 6 Weeks on Treatment During Which the Angina Frequency Was ≤ 50% of the Baseline Average Weekly Angina Frequency [units: percentage of weeks] Mean (Standard Error)	50 (1.4)	54 (1.3)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in the Short-Form 36® (SF-36) Mental and Physical Component Scores
Measure Description	The range of each health domain score is 0-100, with 0 indicating a poorer health state and 100 indicating a better health state. An increase in score indicates an improvement in health state. Participants were asked to complete the survey at randomization (prior to receiving treatment), and at end of treatment visit (Week 8) or early study drug discontinuation or early termination visit. The survey asked participants for responses specific to the preceding 4 weeks prior to completing the survey.
Time Frame	Up to 8 weeks
Safety Issue?	No

Analysis Population Description

Participants in the Full Analysis Set with available data were analyzed.

Reporting Groups

	Description
Placebo	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.
Qualifying Phase: Participants Entered a 2-week Washout Period	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.

Measured Values

	Placebo	Qualifying Phase: Participants Entered a 2-week Washout Period
Number of Participants Analyzed	460	456

	Placebo	Qualifying Phase: Participants Entered a 2-week Washout Period
Change From Baseline in the Short-Form 36® (SF-36) Mental and Physical Component Scores [units: units on a scale] Mean (Standard Error)		
Mental Component Score	1.2 (0.37)	1.0 (0.39)
Physical Component Score	1.9 (0.25)	2.8 (0.26)

6. Secondary Outcome Measure:

Measure Title	Patient's Global Impression of Change (PGIC) Scale Score
Measure Description	The PGIC was completed at the end of treatment/last visit.The PGIC scale measures the change in the participant's overall status since the beginning of the study on a scale ranging from 1 (no change or worse) to 7 (very much improved).
Time Frame	8 weeks
Safety Issue?	No

Analysis Population Description

Participants in the Full Analysis Set with available data were analyzed.

Reporting Groups

	Description
Placebo	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.
Ranolazine	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.

Measured Values

	Placebo	Ranolazine
Number of Participants Analyzed	461	457
Patient's Global Impression of Change (PGIC) Scale Score [units: units on a scale] Mean (Standard Error)	3.9 (0.07)	4.0 (0.07)

Reported Adverse Events

Reporting Groups

	Description
Placebo	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment Period: Placebo to match ranolazine (Day 1: 1 tablet in the evening; Days 2-7: 1 tablet twice daily; 2 tablets twice daily thereafter) for up to 8 weeks.
Ranolazine	Qualifying phase: Participants entered a 2-week washout period if needed to discontinue antianginal drugs (except beta-blockers) followed by placebo to match ranolazine (1 tablet twice daily) during a 4-week run-in period. Participants with at least 85% adherence to documentation requirements (angina frequency and sublingual nitroglycerin use) over the last 21 days of the placebo run-in period were randomized to the treatment period. Treatment period: Ranolazine tablets (Day 1: 1 × 500 tablet in the evening; Days 2-7: 1 × 500 mg twice daily; 2 × 500 mg twice daily thereafter) for up to 8 weeks.

Time Frame

Baseline to Day 56 plus 30 days

Additional Description

Safety Analysis Set: randomized participants who received at least one dose of study treatment.

Serious Adverse Events

	Placebo	Ranolazine
Total # participants affected/at risk	20/474 (4.22%)	16/470 (3.4%)
Blood and lymphatic system disorders		
Anaemia †[A]		
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)
# events		
Cardiac disorders		
Acute coronary syndrome †[A]		
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)
# events		
Acute myocardial infarction †[A]		
# participants affected/at risk	3/474 (0.63%)	2/470 (0.43%)
# events		
Angina pectoris †[A]		
# participants affected/at risk	1/474 (0.21%)	1/470 (0.21%)
# events		

	Placebo	Ranolazine
Angina unstable † [A]		
# participants affected/at risk	1/474 (0.21%)	3/470 (0.64%)
# events		
Atrial fibrillation † [A]		
# participants affected/at risk	3/474 (0.63%)	0/470 (0%)
# events		
Cardiac failure acute † [A]		
# participants affected/at risk	2/474 (0.42%)	0/470 (0%)
# events		
Cardiac failure chronic † [A]		
# participants affected/at risk	0/474 (0%)	1/470 (0.21%)
# events		
Cardiogenic shock † [A]		
# participants affected/at risk	0/474 (0%)	1/470 (0.21%)
# events		
Coronary artery disease † [A]		
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)
# events		

	Placebo	Ranolazine
Ventricular tachycardia † [A]		
# participants affected/at risk	0/474 (0%)	1/470 (0.21%)
# events		
General disorders		
Chest pain † [A]		
# participants affected/at risk	1/474 (0.21%)	2/470 (0.43%)
# events		
Sudden cardiac death † [A]		
# participants affected/at risk	0/474 (0%)	1/470 (0.21%)
# events		
Thrombosis in device † [A]		
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)
# events		
Injury, poisoning and procedural complications		
Hip fracture † [A]		
# participants affected/at risk	0/474 (0%)	1/470 (0.21%)
# events		

	Placebo	Ranolazine
Metabolism and nutrition disorders		
Hyperglycaemia † [A]		
# participants affected/at risk	0/474 (0%)	1/470 (0.21%)
# events		
Nervous system disorders		
Cervical myelopathy † [A]		
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)
# events		
Ischaemic stroke † [A]		
# participants affected/at risk	3/474 (0.63%)	1/470 (0.21%)
# events		
Syncope † [A]		
# participants affected/at risk	0/474 (0%)	1/470 (0.21%)
# events		
Transient ischaemic attack † [A]		
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)

	Placebo	Ranolazine
# events		
Renal and urinary disorders		
Calculus ureteric † [A]		
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)
# events		
Calculus urinary † [A]		
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)
# events		
Respiratory, thoracic and mediastinal disorders		
Pulmonary embolism † [A]		
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)
# events		
Vascular disorders		
Circulatory collapse † [A]		
# participants affected/at risk	0/474 (0%)	1/470 (0.21%)
# events		
Hypertension † [A]		

	Placebo	Ranolazine
# participants affected/at risk	1/474 (0.21%)	0/470 (0%)
# events		

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA (15.1)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Placebo	Ranolazine
Total # participants affected/at risk	0/474 (0%)	0/470 (0%)

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

After conclusion of the study and without prior written approval from Gilead, investigators in this study may communicate, orally present, or publish in scientific journals or other media only after the following conditions have been met:

- The results of the study in their entirety have been publicly disclosed by or with the consent of Gilead in an abstract, manuscript, or presentation form; or
- The study has been completed at all study sites for at least 2 years

Limitations and Caveats:

Results Point of Contact:

Name/Official Title: Clinical Trial Disclosures
Organization: Gilead Sciences, Inc.
Phone:
Email: ClinicalTrialDisclosures@gilead.com