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Effect of Ranolazine on Myocardial Perfusion Assessed by Serial Quantitative Exercise SPECT Imaging

This study has been completed.

Sponsor:	Gilead Sciences
Collaborators:	
Information provided by (Responsible Party):	Gilead Sciences
ClinicalTrials.gov Identifier:	NCT01221272

Purpose

This study enrolled participants with documented exercise-induced myocardial ischemia in order to evaluate whether ranolazine, when taken prior to exercise, can improve blood flow to the heart (myocardial perfusion), as assessed by exercise-induced myocardial perfusion defect size (PDS) and total perfusion deficit (TPD), using gated single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI).

This was a 2-period crossover study. The last dose of each period must have been taken 3-4 hours prior to conduct of the exercise SPECT MPI. After the research exercise SPECT MPI was performed at the end of Period 1, participants discontinued the treatment they were randomized to for that period and began the other treatment in Period 2.

Condition	Intervention	Phase
Myocardial Perfusion Imaging Myocardial Ischemia	Drug: Ranolazine Drug: Placebo to match ranolazine Procedure/Surgery: SPECT MPI Behavioral: Exercise	Phase 4

Study Type: Interventional
Study Design: Treatment, Crossover Assignment, Double Blind (Subject, Investigator), Randomized, Safety/Efficacy Study
Official Title: A Phase 4, Randomized, Double-Blind, Placebo-Controlled, Cross-over Trial to Evaluate the Effects of Ranolazine on Myocardial Perfusion Assessed by Serial Quantitative Exercise SPECT Imaging

Further study details as provided by Gilead Sciences:

Primary Outcome Measure:

- Exercise-induced Perfusion Defect Size (PDS) Following Ranolazine and Placebo Treatment [Time Frame: Up to 33 days] [Designated as safety issue: No]
  PDS is the amount (percent) of the myocardium with decreased blood flow. A lower percentage means more of the myocardium is receiving blood flow. Measurements were obtained by gated single photon emission computed tomography (SPECT) imaging following exercise at the end of the ranolazine and placebo treatment periods.
- Exercise-induced Total Perfusion Deficit (TPD) Following Ranolazine and Placebo Treatment [Time Frame: Up to 33 days] [Designated as safety issue: No]
  TPD is a score that measures the overall impact of a region of decreased myocardial blood flow, incorporating both the amount and severity of the decreased flow. TPD is measured on a scale of 0-100, with higher scores being worse and lower scores being better. Measurements were obtained by SPECT imaging following exercise at the end of the ranolazine and placebo treatment periods.

Secondary Outcome Measures:

- Perfusion Defect Severity at Baseline, End of Period 1, and End of Period 2 [Time Frame: Up to 33 days] [Designated as safety issue: No]
  Perfusion defect severity was assessed for each participant as the percentage of the 17 myocardium segments with a relative perfusion defect score of 3 or 4 on a 0-4 scale. Segment scores are: 0 = normal perfusion; 1 = mild reduction in counts-not definitely abnormal; 2 = moderate reduction in counts-definitely abnormal; 3 = severe reduction in counts; 4 = absent uptake (lower scores correspond to less severity and higher scores correspond to increased severity). A lower percentage means fewer segments have severely reduced blood flow. Measurements were obtained by SPECT imaging following exercise at baseline and at the end of Periods 1 and 2.
- Exercise-induced Reversible Perfusion Defect Size (PDS) at Baseline, End of Period 1, and End of Period 2 [Time Frame: Up to 33 days] [Designated as safety issue: No]
  Exercise-induced reversible PDS was derived as the exercise PDS at baseline and at the end of Periods 1 and 2 minus the resting PDS at baseline. A lower percentage means more of the myocardium is receiving blood flow. Measurements were obtained by SPECT imaging at baseline both at rest and following exercise and following exercise at the end of Periods 1 and 2.
- Exercise-induced Reversible Total Perfusion Deficit (TPD) at Baseline, End of Period 1, and End of Period 2 [Time Frame: Up to 33 days] [Designated as safety issue: No]
  Exercise-induced reversible TPD was derived as the exercise TPD at baseline and at the end of Periods 1 and 2 minus the resting TPD at baseline. TPD is measured on a scale of 0-100, with higher scores being worse and lower scores being better. Measurements were obtained by SPECT imaging at baseline both at rest and following exercise and following exercise at the end of Periods 1 and 2.

Enrollment: 81
Study Start Date: September 2010
Primary Completion Date: September 2012
Study Completion Date: September 2012

Arms	Assigned Interventions
Experimental: Ranolazine/Placebo Participants received ranolazine from Day 1 through Day 15 (± 2 days) of Period 1, followed by an exercise SPECT MPI study, then received placebo to match ranolazine from Day 1 through Day 15 (± 2 days) of Period 2, followed by an exercise SPECT MPI study.	Drug: Ranolazine • One 500 mg tablet in the evening on Day 1 of the period • One 500 mg tablet, twice daily on Days 2-3 of the period • Two 500 mg tablets (1000 mg total), twice daily from Day 4 to the end of the period (Day 15 ± 2 days)

Arms	Assigned Interventions
	Other Names: Ranexa® Drug: Placebo to match ranolazine Placebo to match ranolazine administered in the same form and frequency as the active drug. Procedure/Surgery: SPECT MPI Gated single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) to confirm the presence of reversible exercise-induced left ventricular perfusion defect size (PDS) performed within 12 weeks prior to baseline or at the baseline visit, and at the end-of-period 1 and end-of-period 2 visits. Behavioral: Exercise Treadmill stress test
Experimental: Placebo/Ranolazine Participants received placebo to match ranolazine from Day 1 through Day 15 (± 2 days) of Period 1, followed by an exercise SPECT MPI study, then received ranolazine from Day 1 through Day 15 (± 2 days) of Period 2, followed by an exercise SPECT MPI study.	Drug: Ranolazine • One 500 mg tablet in the evening on Day 1 of the period • One 500 mg tablet, twice daily on Days 2-3 of the period • Two 500 mg tablets (1000 mg total), twice daily from Day 4 to the end of the period (Day 15 ± 2 days) Other Names: Ranexa® Drug: Placebo to match ranolazine Placebo to match ranolazine administered in the same form and frequency as the active drug. Procedure/Surgery: SPECT MPI Gated single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) to confirm the presence of reversible exercise-induced left ventricular perfusion defect size (PDS) performed within 12 weeks prior to baseline or at the baseline visit, and at the end-of-period 1 and end-of-period 2 visits. Behavioral: Exercise Treadmill stress test

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Key Inclusion Criteria:

- Exercise SPECT MPI study (stress and rest) showing at least 10% reversible myocardial ischemia (as confirmed by the core nuclear laboratory using Corridor4DM imaging software) performed not more than 12 weeks prior to screening, OR
- Exercise SPECT MPI study (stress and rest) conducted during screening (after consultation with the Medical Monitor and after informed consent was obtained) showing at least 10% reversible myocardial ischemia (as confirmed by the core nuclear laboratory)
- Stable antianginal medical therapy (excluding short-acting nitroglycerin)

Key Exclusion Criteria:

- Left bundle branch block
- Automated implantable defibrillator and/or pacemaker (selected subjects with permanent pacemakers who had an intact sinus mechanism may have been included following consultation with the Medical Monitor)
- Intervening coronary revascularization between the time of qualifying exercise SPECT MPI study and randomization
- Acute myocardial infarction (MI) within 60 days prior to screening or at any time after the qualifying exercise SPECT MPI study, or MI undergoing staged intervention during a subject's participation in the trial
- Unstable angina within 30 days prior to screening, or at any time after the qualifying exercise SPECT MPI study
- Coronary artery bypass graft surgery within 60 days prior to screening or at any time after the qualifying exercise SPECT MPI study, or percutaneous coronary intervention within 30 days prior to screening or at any time after the qualifying exercise SPECT MPI study
- Anticipated coronary revascularization during the trial period
- Cerebrovascular attack or transient ischemic attack within 90 days prior to screening
- History of serious arrhythmias
- Current atrial fibrillation or atrial flutter
- QTc interval > 500 milliseconds
- Diagnosed as having New York Heart Association Class III or IV heart failure
- Inability to exercise or exercise limitation due to other comorbidities that may have interfered with ability to perform required exercise SPECT MPI study
- Body mass index greater than or equal to 38 kg/m^2 (may have been up to 40 kg/m^2 after consultation with the Medical Monitor)
- Any absolute contraindications to exercise stress testing

Contacts and Locations

Locations

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United States, California

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United States, Florida
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Investigators

Study Director:	Patrick Yue, MD	Gilead Sciences, Inc.

More Information

Responsible Party:	Gilead Sciences
Study ID Numbers:	GS-US-259-0103
Health Authority:	United States: Food and Drug Administration United States: Institutional Review Board Canada: Health Canada Canada: Ethics Review Committee Czech Republic: Ethics Committee Czech Republic: State Institute for Drug Control Finland: Ethics Committee Finland: Finnish Medicines Agency Israel: Ethics Commission Israel: Israeli Health Ministry Pharmaceutical Administration Italy: Ethics Committee Italy: The Italian Medicines Agency Singapore: Domain Specific Review Boards Singapore: Health Sciences Authority United Kingdom: Medicines and Healthcare Products Regulatory Agency United Kingdom: Research Ethics Committee

Study Results

Participant Flow

Recruitment Details	Participants were enrolled in a total of 27 study sites in the United States, Canada, Czech Republic, and Israel. The first participant was screened on 29 September 2010. The last participant observation was on 27 September 2012.
Pre-Assignment Details	Number screened: 222; randomized and treated (RAT; Safety Analysis Set): 81

	Efficacy Analysis Set: 61 RAT participants with data for both end-of-period (EOP) scans, completed ≥ 7 consecutive days treatment in each period, took the morning dose before each EOP scan, and had baseline perfusion defect size ≥ 5% as measured by QPS imaging software.

Reporting Groups

	Description
Ranolazine/Placebo	Period 1: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise gated single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) study. Period 2: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.
Placebo/Ranolazine	Period 1: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Period 2: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.

Period 1

	Ranolazine/Placebo	Placebo/Ranolazine
Started	41	40
Completed	39	38
Not Completed	2	2
Adverse Event	2	0
Consent Withdrawal	0	1
Significant Dosing Noncompliance	0	1

Period 2

	Ranolazine/Placebo	Placebo/Ranolazine
Started	39	39 [1]
Completed	39	37
Not Completed	0	2
Adverse Event	0	2

[1] 1 participant did not complete Period 1, but started and completed Period 2.

Baseline Characteristics

Analysis Population Description
Safety Analysis Set

Reporting Groups

	Description
All Participants	Baseline characteristics were analyzed as a single group (Safety Analysis Set). All participants were assigned to complete the same treatment periods in the same manner. Ranolazine Treatment Period: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Placebo Treatment Period: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.

Baseline Measures

	All Participants
Number of Participants	81
Age, Continuous [units: years] Mean (Standard Deviation)	66 (9.0)
Age, Customized [units: participants]	
18 to 39 years	0
40 to 64 years	29
65 to 74 years	39
≥ 75 years	13
Gender, Male/Female [units: participants]	
Female	6
Male	75
Race/Ethnicity, Customized [units: participants]	

	All Participants
White	72
African-American	5
Other	4
Race/Ethnicity, Customized [units: participants]	
Hispanic Or Latino	9
Not Hispanic Or Latino	62
Not Reported	5
Unknown	5
Region of Enrollment [units: participants]	
United States	38
Czech Republic	2
Canada	27
Israel	14
Body mass index [units: kg/m^2] Mean (Standard Deviation)	29.6 (3.8)
Weight [units: kg] Mean (Standard Deviation)	88.6 (14.2)

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Exercise-induced Perfusion Defect Size (PDS) Following Ranolazine and Placebo Treatment
Measure Description	PDS is the amount (percent) of the myocardium with decreased blood flow. A lower percentage means more of the myocardium is receiving blood flow. Measurements were obtained by gated single photon emission computed tomography (SPECT) imaging following exercise at the end of the ranolazine and placebo treatment periods.
Time Frame	Up to 33 days
Safety Issue?	No

Analysis Population Description

Efficacy Analysis Set: 61 randomized and treated participants with data for both end-of-period (EOP) scans, completed ≥ 7 consecutive days treatment in each period, took the morning dose before each EOP scan, and had baseline perfusion defect size ≥ 5% as measured by QPS imaging software

Reporting Groups

	Description
Ranolazine	Ranolazine treatment period: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.
Placebo	Placebo treatment period: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.

Measured Values

	Ranolazine	Placebo
Number of Participants Analyzed	61	61
Exercise-induced Perfusion Defect Size (PDS) Following Ranolazine and Placebo Treatment [units: percentage of myocardium] Least Squares Mean (Standard Error)	21.54 (1.51)	20.87 (1.51)

Statistical Analysis 1 for Exercise-induced Perfusion Defect Size (PDS) Following Ranolazine and Placebo Treatment

Statistical Analysis Overview	Comparison Groups	Ranolazine, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.29
	Comments	The null hypothesis that ranolazine treatment had no effect on PDS would be rejected if the PDS and TPD p-values were less than 0.05 or the PDS p-value was less than 0.05/2 = 0.025.
	Method	Mixed Models Analysis
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Mixed Models Analysis]

	Estimated Value	0.67
	Confidence Interval	(2-Sided) 95% -0.6 to 1.9
	Estimation Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Exercise-induced Total Perfusion Deficit (TPD) Following Ranolazine and Placebo Treatment
Measure Description	TPD is a score that measures the overall impact of a region of decreased myocardial blood flow, incorporating both the amount and severity of the decreased flow. TPD is measured on a scale of 0-100, with higher scores being worse and lower scores being better. Measurements were obtained by SPECT imaging following exercise at the end of the ranolazine and placebo treatment periods.
Time Frame	Up to 33 days
Safety Issue?	No

Analysis Population Description

Efficacy Analysis Set

Reporting Groups

	Description
Ranolazine	Ranolazine treatment period: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.
Placebo	Placebo treatment period: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.

Measured Values

	Ranolazine	Placebo
Number of Participants Analyzed	61	61
Exercise-induced Total Perfusion Deficit (TPD) Following Ranolazine and Placebo Treatment [units: units on a scale] Least Squares Mean (Standard Error)	17.23 (1.26)	16.57 (1.26)

Statistical Analysis 1 for Exercise-induced Total Perfusion Deficit (TPD) Following Ranolazine and Placebo Treatment

Statistical Analysis Overview	Comparison Groups	Ranolazine, Placebo
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.22
	Comments	The null hypothesis that ranolazine treatment had no effect on TPD would be rejected if the PDS and TPD p-values were less than 0.05 or the TPD p-value was less than 0.05/2 = 0.025.
	Method	Mixed Models Analysis
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other [Mixed Models Analysis]
	Estimated Value	0.65
	Confidence Interval	(2-Sided) 95% -0.4 to 1.7
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Perfusion Defect Severity at Baseline, End of Period 1, and End of Period 2
Measure Description	Perfusion defect severity was assessed for each participant as the percentage of the 17 myocardium segments with a relative perfusion defect score of 3 or 4 on a 0-4 scale. Segment scores are: 0 = normal perfusion; 1 = mild reduction in counts-not definitely abnormal; 2 = moderate reduction in counts-definitely abnormal; 3 = severe reduction in counts; 4 = absent uptake (lower scores correspond to less severity and higher scores correspond to increased severity). A lower percentage means fewer segments have severely reduced blood flow. Measurements were obtained by SPECT imaging following exercise at baseline and at the end of Periods 1 and 2.
Time Frame	Up to 33 days
Safety Issue?	No

Analysis Population Description

Efficacy Analysis Set

Reporting Groups

	Description
Ranolazine/Placebo	Period 1: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Period 2: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.
Placebo/Ranolazine	Period 1: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Period 2: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.

Measured Values

	Ranolazine/Placebo	Placebo/Ranolazine
Number of Participants Analyzed	30	31
Perfusion Defect Severity at Baseline, End of Period 1, and End of Period 2 [units: percentage of segments] Mean (Standard Error)		
Baseline	11.4 (2.0)	8.5 (2.0)
End of Period 1	11.6 (1.9)	10.2 (2.1)
End of Period 2	10.4 (1.9)	9.5 (2.0)

4. Secondary Outcome Measure:

Measure Title	Exercise-induced Reversible Perfusion Defect Size (PDS) at Baseline, End of Period 1, and End of Period 2
Measure Description	Exercise-induced reversible PDS was derived as the exercise PDS at baseline and at the end of Periods 1 and 2 minus the resting PDS at baseline. A lower percentage means more of the myocardium is receiving blood flow. Measurements were obtained by SPECT imaging at baseline both at rest and following exercise and following exercise at the end of Periods 1 and 2.
Time Frame	Up to 33 days
Safety Issue?	No

Analysis Population Description
Efficacy Analysis Set

Reporting Groups

	Description
Ranolazine/Placebo	Period 1: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Period 2: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.
Placebo/Ranolazine	Period 1: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Period 2: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.

Measured Values

	Ranolazine/Placebo	Placebo/Ranolazine
Number of Participants Analyzed	30	31
Exercise-induced Reversible Perfusion Defect Size (PDS) at Baseline, End of Period 1, and End of Period 2 [units: percentage of myocardium] Mean (Standard Error)		
Baseline exercise minus baseline resting	12.5 (1.1)	13.5 (1.3)
End of Period 1 exercise minus baseline resting	12.7 (1.2)	14.1 (1.4)
End of Period 2 exercise minus baseline resting	12.4 (1.0)	15.2 (1.4)

5. Secondary Outcome Measure:

Measure Title	Exercise-induced Reversible Total Perfusion Deficit (TPD) at Baseline, End of Period 1, and End of Period 2
Measure Description	Exercise-induced reversible TPD was derived as the exercise TPD at baseline and at the end of Periods 1 and 2 minus the resting TPD at baseline. TPD is measured on a scale of 0-100, with higher scores being worse and lower scores being better. Measurements were obtained by SPECT imaging at baseline both at rest and following exercise and following exercise at the end of Periods 1 and 2.
Time Frame	Up to 33 days

Safety Issue?	No

Analysis Population Description
Efficacy Analysis Set

Reporting Groups

	Description
Ranolazine/Placebo	Period 1: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Period 2: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.
Placebo/Ranolazine	Period 1: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Period 2: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.

Measured Values

	Ranolazine/Placebo	Placebo/Ranolazine
Number of Participants Analyzed	30	31
Exercise-induced Reversible Total Perfusion Deficit (TPD) at Baseline, End of Period 1, and End of Period 2 [units: units on a scale] Mean (Standard Error)		
Baseline exercise minus baseline resting	10.5 (0.9)	10.5 (1.0)
End of Period 1 exercise minus baseline resting	10.5 (0.9)	10.7 (1.0)
End of Period 2 exercise minus baseline resting	10.1 (0.8)	11.6 (1.1)

Reported Adverse Events

Time Frame	Up to 33 days

Additional Description	All participants were assigned to complete the ranolazine and placebo treatment periods during the study, the only difference being which treatment period they started first.

Reporting Groups

	Description
Onset Following Ranolazine	This reporting group includes participants dosed with ranolazine and their events for which the last dosed treatment was ranolazine, ie, events with onset during the ranolazine treatment period or during post-ranolazine treatment period follow-up. Ranolazine Treatment Period: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Placebo Treatment Period: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.
Onset Following Placebo	This reporting group includes participants dosed with placebo and their events for which the last dosed treatment was placebo, ie, events with onset during the placebo treatment period or during post-placebo treatment period follow-up. Ranolazine Treatment Period: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Placebo Treatment Period: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.
Onset at Any Time Following Ranolazine	This reporting group includes participants dosed with ranolazine and their events with onset at any time following ranolazine treatment. Ranolazine Treatment Period: Participants received ranolazine 1 × 500 mg tablet administered once in the evening on Day 1, 1 × 500 mg tablet twice daily on Days 2-3, and 2 × 500 tablets twice daily from Day 4 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study. Placebo Treatment Period: Participants received placebo to match ranolazine from Day 1 to the end of the period (Day 15 ± 2 days), followed by an exercise SPECT MPI study.

Serious Adverse Events

	Onset Following Ranolazine	Onset Following Placebo	Onset at Any Time Following Ranolazine
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/80 (2.5%)	0/79 (0%)	2/80 (2.5%)
Infections and infestations			

	Onset Following Ranolazine	Onset Following Placebo	Onset at Any Time Following Ranolazine
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Bronchitis [A] †	1/80 (1.25%)	0/79 (0%)	1/80 (1.25%)
Investigations			
Electrocardiogram ST segment elevation [A] †	1/80 (1.25%)	0/79 (0%)	1/80 (1.25%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (16.0)

Other Adverse Events

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

	Onset Following Ranolazine	Onset Following Placebo	Onset at Any Time Following Ranolazine
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	25/80 (31.25%)	7/79 (8.86%)	28/80 (35%)
Cardiac disorders			
Angina pectoris [A] †	3/80 (3.75%)	1/79 (1.27%)	4/80 (5%)
Gastrointestinal disorders			
Constipation [A] †	6/80 (7.5%)	1/79 (1.27%)	6/80 (7.5%)
Nausea [A] †	5/80 (6.25%)	2/79 (2.53%)	5/80 (6.25%)
Nervous system disorders			
Dizziness [A] †	11/80 (13.75%)	0/79 (0%)	11/80 (13.75%)
Headache [A] †	3/80 (3.75%)	3/79 (3.8%)	4/80 (5%)
Respiratory, thoracic and mediastinal disorders			
Dyspnoea [A] †	7/80 (8.75%)	2/79 (2.53%)	9/80 (11.25%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (16.0)

Limitations and Caveats

[Not specified]

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

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