Clinical trial results:
A Phase 4 Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Rimegepant in Episodic Migraine Prevention with Multiple Dosing Regimens

Summary

EudraCT number	2021-005239-22
Trial protocol	ES AT FR SE IT PL
Global end of trial date	10 December 2024

Results information

Result version number	v1 (current)
This version publication date	24 December 2025
First version publication date	24 December 2025

Trial information

Trial identification

Sponsor protocol code	C4951010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05217927
WHO universal trial number (UTN)	-
Other trial identifiers	Study ID: BHV3000-404

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	66 Hudson Boulevard East, New York, United States, NY 10001
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 June 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of every other day (EOD) and daily rimegepant dosing regimens relative to placebo as a preventive treatment for episodic migraine, as measured by the mean reduction from the Observation Phase in the number of migraine days per month over the entire Double-blind Treatment (DBT) Phase.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 March 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Canada: 31
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 52
Country: Number of subjects enrolled	Italy: 30
Country: Number of subjects enrolled	Poland: 165
Country: Number of subjects enrolled	Spain: 44
Country: Number of subjects enrolled	Sweden: 15
Country: Number of subjects enrolled	United States: 216
Country: Number of subjects enrolled	United Kingdom: 133
Worldwide total number of subjects	692
EEA total number of subjects	312

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	669
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted to evaluate the efficacy, safety, and tolerability of once every other day (EOD) and daily rimegepant dosing regimens for the prevention of episodic migraine.

Pre-assignment

Screening details:

A total of 1415 participants were enrolled in the study, of which 716 failed screening and 699 participants were randomized. Of the 699 randomized participants, 692 participantsreceived the study intervention.

Period 1

Period 1 title	DBT Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Blinding implementation details:

Double blinded study.

Arms

Are arms mutually exclusive?	Yes
Arm title	DB Rimegepant/ Placebo/ OL Rimegepant

Arm description:

Participants received rimegepant (RMG) 75 mg, orally disintegrating tablets (ODT), EOD alternating with matching placebo dosed EOD for 12 weeks in the double blind treatment (DBT) phase. Eligible participants received RMG 75 mg ODT once daily (QD) for 12 weeks in the open label extension (OLE) phase. Participants were followed up for 8 weeks after last dose of study drug.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of Rimegepant was administered PO.

Investigational medicinal product name	Rimegepant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Rimegepant 75 mg was administered orally (PO).

Arm title	DB Rimegepant/OL Rimegepant

Arm description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Eligible participants continued to receive RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Arm type	Experimental

Investigational medicinal product name	Rimegepant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Rimegepant 75 mg was administered PO.

Arm title	DB Placebo/OL Rimegepant

Arm description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Eligible participants received RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of Rimegepant was administered PO.

Investigational medicinal product name	Rimegepant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Rimegepant 75 mg was administered PO.

Number of subjects in period 1	DB Rimegepant/ Placebo/ OL Rimegepant	DB Rimegepant/OL Rimegepant	DB Placebo/OL Rimegepant
Started	232	229	231
Completed	204	209	208
Not completed	28	20	23
Adverse event, non-fatal	7	2	5
Protocol-specified withdrawal criterion met	4	6	5
Pregnancy	-	-	1
Non-compliance	1	-	-
Withdrawal of consent	8	5	7
Unspecified	7	3	4
Lost to follow-up	-	2	-
Lack of efficacy	1	-	-
Protocol deviation	-	2	1

Period 2

Period 2 title	DBT Phase to OLE phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Double blinded study.

Arms

Are arms mutually exclusive?	Yes
Arm title	DB Rimegepant/ Placebo/ OL Rimegepant

Arm description:

Participants received rimegepant (RMG) 75 mg, orally disintegrating tablets (ODT), EOD alternating with matching placebo dosed EOD for 12 weeks in the double blind treatment (DBT) phase. Eligible participants received RMG 75 mg ODT once daily (QD) for 12 weeks in the open label extension (OLE) phase. Participants were followed up for 8 weeks after last dose of study drug.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of Rimegepant was administered PO.

Investigational medicinal product name	Rimegepant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Rimegepant 75 mg was administered orally.

Arm title	DB Rimegepant/OL Rimegepant

Arm description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Eligible participants continued to receive RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Arm type	Experimental
Investigational medicinal product name	Rimegepant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Rimegepant 75 mg was administered PO.

Arm title	DB Placebo/OL Rimegepant

Arm description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Eligible participants received RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants

were followed up for 8 weeks after last dose of study drug.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of Rimegepant was administered PO.

Investigational medicinal product name	Rimegepant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Rimegepant 75 mg was administered orally.

Number of subjects in period 2	DB Rimegepant/ Placebo/ OL Rimegepant	DB Rimegepant/OL Rimegepant	DB Placebo/OL Rimegepant
Started	204	209	208
Completed	182	196	195
Not completed	22	13	13
Did not enter the OLE phase	22	13	13

Period 3

Period 3 title	OLE Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Double blinded study.

Arms

Are arms mutually exclusive?	Yes
Arm title	DB Rimegepant/ Placebo/ OL Rimegepant

Arm description:

Participants received rimegepant (RMG) 75 mg, orally disintegrating tablets (ODT), EOD alternating with matching placebo dosed EOD for 12 weeks in the double blind treatment (DBT) phase. Eligible participants received RMG 75 mg ODT once daily (QD) for 12 weeks in the open label extension (OLE) phase. Participants were followed up for 8 weeks after last dose of study drug.

Arm type	Experimental

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of Rimegepant was administered PO.

Investigational medicinal product name	Rimegepant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Rimegepant 75 mg was administered PO.

Arm title	DB Rimegepant/OL Rimegepant

Arm description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Eligible participants continued to receive RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Arm type	Experimental
Investigational medicinal product name	Rimegepant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Rimegepant 75 mg was administered PO.

Arm title	DB Placebo/OL Rimegepant

Arm description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Eligible participants received RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo of Rimegepant was administered PO.

Investigational medicinal product name	Rimegepant
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Orodispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Rimegepant 75 mg was administered PO.

Number of subjects in period 3	DB Rimegepant/ Placebo/ OL Rimegepant	DB Rimegepant/OL Rimegepant	DB Placebo/OL Rimegepant
Started	182	196	195
Completed	170	187	183
Not completed	12	9	12
Extension phase eligibility failure	1	-	-
Adverse event, non-fatal	4	1	1
Non-compliance	-	-	1
Unspecified	3	5	4
Withdrawal of consent	3	1	5
Lost to follow-up	1	2	1

Baseline characteristics

Reporting groups	
Reporting group title	DB Rimegepant/ Placebo/ OL Rimegepant
Reporting group description:	
Participants received rimegepant (RMG) 75 mg, orally disintegrating tablets (ODT), EOD alternating with matching placebo dosed EOD for 12 weeks in the double blind treatment (DBT) phase. Eligible participants received RMG 75 mg ODT once daily (QD) for 12 weeks in the open label extension (OLE) phase. Participants were followed up for 8 weeks after last dose of study drug.	
Reporting group title	DB Rimegepant/OL Rimegepant
Reporting group description:	
Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Eligible participants continued to receive RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.	
Reporting group title	DB Placebo/OL Rimegepant
Reporting group description:	
Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Eligible participants received RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.	

Reporting group values	DB Rimegepant/ Placebo/ OL Rimegepant	DB Rimegepant/OL Rimegepant	DB Placebo/OL Rimegepant
Number of subjects	232	229	231
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	42.0	43.9	42.9
standard deviation	± 11.96	± 12.05	± 12.35
Gender categorical Units: Subjects			
Male	201	192	207
Female	31	37	24

Reporting group values	Total		
Number of subjects	692		
Age Categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Male	600		
Female	92		

End points

End points reporting groups

Reporting group title	DB Rimegepant/ Placebo/ OL Rimegepant

Reporting group description:

Participants received rimegepant (RMG) 75 mg, orally disintegrating tablets (ODT), EOD alternating with matching placebo dosed EOD for 12 weeks in the double blind treatment (DBT) phase. Eligible participants received RMG 75 mg ODT once daily (QD) for 12 weeks in the open label extension (OLE) phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Rimegepant/OL Rimegepant

Reporting group description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Eligible participants continued to receive RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Placebo/OL Rimegepant

Reporting group description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Eligible participants received RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Rimegepant/ Placebo/ OL Rimegepant

Reporting group description:

Participants received rimegepant (RMG) 75 mg, orally disintegrating tablets (ODT), EOD alternating with matching placebo dosed EOD for 12 weeks in the double blind treatment (DBT) phase. Eligible participants received RMG 75 mg ODT once daily (QD) for 12 weeks in the open label extension (OLE) phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Rimegepant/OL Rimegepant

Reporting group description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Eligible participants continued to receive RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Placebo/OL Rimegepant

Reporting group description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Eligible participants received RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Rimegepant/ Placebo/ OL Rimegepant

Reporting group description:

Participants received rimegepant (RMG) 75 mg, orally disintegrating tablets (ODT), EOD alternating with matching placebo dosed EOD for 12 weeks in the double blind treatment (DBT) phase. Eligible participants received RMG 75 mg ODT once daily (QD) for 12 weeks in the open label extension (OLE) phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Rimegepant/OL Rimegepant

Reporting group description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Eligible participants continued to receive RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Placebo/OL Rimegepant

Reporting group description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Eligible participants received RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant/ Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg, ODT, once EOD alternating with matching placebo dosed EOD for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant

Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant/ Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg, ODT, once EOD alternating with matching placebo dosed EOD for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant/ Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg, ODT, once EOD alternating with matching placebo dosed EOD for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant/ Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg, ODT, once EOD alternating with matching placebo dosed EOD for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant/ Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg, ODT, once EOD alternating with matching placebo dosed EOD for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Rimegepant

Subject analysis set type	Per protocol

Subject analysis set description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB Placebo
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB RMG EOD/DB PBO EOD/ OL RMG QD
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who received RMG 75 mg, ODT alternating with matching placebo in the DBT phase received RMG 75 mg ODT QD for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB RMG QD/ OL RMG QD
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who received RMG 75 mg ODT in the DBT phase continued to receive RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Subject analysis set title	DB PBO QD/ OL RMG QD
Subject analysis set type	Per protocol

Subject analysis set description:

Participants who received placebo ODT in the DBT phase received RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Primary: Mean Change From Observation Phase (OP) in the Number of Migraine Days per Month Over Entire DBT Phase (Weeks 1 to 12)

End point title	Mean Change From Observation Phase (OP) in the Number of Migraine Days per Month Over Entire DBT Phase (Weeks 1 to 12)

End point description:

A migraine day:any calendar day in which participant experienced a qualified migraine headache.Qualified migraine headache:migraine with or without aura, lasting for >=30 minutes, and meeting either >=2 of the pain features:unilateral location;pulsating quality;moderate or severe pain intensity;aggravation by or causing avoidance of routine physical activity OR>=1 of associated symptoms:nausea and/or vomiting;photophobia and phonophobia.Number of migraine days per month were prorated to 28 days and derived for a month in on-DBT efficacy analysis period as follows:28*(total number of migraine days through Month 3 [Weeks1 to12]/(total number of e-diary efficacy data days through Month 3 [Weeks1 to12]). DB treatment efficacy (Migraine) set:participants in full analysis set who were randomized only once and took >=1 dose of DB study drug (rimegepant or placebo) and had>=14 days of eDiary efficacy data(not necessarily consecutive) in both the OP and >=1 month(4-week interval) in DBT Phase.

End point type	Primary

End point timeframe:

Observation phase (from 31 days prior to randomization), DBT phase (through Month 3 [Week 1 to 12])

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	221	220	224	
Units: Days per month				
least squares mean (confidence interval	-2.9 (-3.31 to	-4.0 (-4.44 to	-2.2 (-2.65 to	

97.5%)	-2.42)	-3.60)	-1.85)

Statistical analyses

Statistical analysis title	DB Rimegepant/ Placebo vs DB Placebo

Statistical analysis description:

Linear mixed effects model with repeated measures with the number of total migraine days per month in the OP as a covariate; treatment group, randomization stratum (use of previous prophylactic migraine medication generally considered to have efficacy), month and month-by-treatment group interaction as fixed effects.

Comparison groups	DB Rimegepant v DB Placebo
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LSM Difference
Point estimate	-1.8
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.35
upper limit	-1.19

Statistical analysis title	DB Rimegepant/ Placebo vs DB Placebo

Statistical analysis description:

Linear mixed effects model with repeated measures with the number of total migraine days per month in the OP as a covariate; treatment group, randomization stratum (use of previous prophylactic migraine medication generally considered to have efficacy), month and month-by-treatment group interaction as fixed effects.

Comparison groups	DB Rimegepant/ Placebo v DB Placebo
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022
Method	Mixed models analysis
Parameter estimate	Least square mean (LSM) Difference
Point estimate	-0.6
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.22
upper limit	-0.01

Secondary: Percentage of Participants With Greater Than Equal to (>=) 50 Percent (%) Reduction From OP in Number of Moderate to Severe Migraine Days per Month Over the Entire DBT Phase (Weeks 1 to 12)

End point title	Percentage of Participants With Greater Than Equal to (>=) 50 Percent (%) Reduction From OP in Number of Moderate to Severe Migraine Days per Month Over the Entire DBT Phase (Weeks 1 to 12)

End point description:

Percentage of participants with >= 50% reduction from OP, in number of migraine days (moderate or severe) in the overall DBT phase is reported in this outcome measure. The number of migraine days per month were prorated to 28 days and derived for a month in on-DBT efficacy analysis period as follows: 28*(total number of migraine days through Month 3 [Weeks 1 to 12]/ (total number of e-diary efficacy data days through Month 3 [Weeks 1 to 12]). Double-blind treatment efficacy (Migraine) analysis set included participants in the full analysis set who were randomized only once and took >= 1 dose of double-blind study drug (rimegepant or placebo) and had >=14 days of eDiary efficacy data (not necessarily consecutive) in both the OP and >=1 month (4-week interval) in the DBT Phase. Double-blind treatment efficacy (Migraine) analysis set was used.

End point type	Secondary

End point timeframe:

DBT phase (through Month 3 [Week 1 to 12])

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	221	220	224	
Units: Percentage of participants				
number (confidence interval 97.5%)	42.5 (35.1 to 50.0)	60.5 (53.1 to 67.8)	34.4 (27.3 to 41.5)	

Statistical analyses

Statistical analysis title	DB Rimegepant vs DB Placebo

Statistical analysis description:

Mantel-Haenszel risk estimation was used.

Comparison groups	DB Rimegepant v DB Placebo
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	26.1
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	15.8
upper limit	36.3

Statistical analysis title	DB Rimegepant/ Placebo vs DB Placebo
Statistical analysis description: Mantel-Haenszel risk estimation was used.	
Comparison groups	DB Rimegepant/ Placebo v DB Placebo
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0659
Method	Mantel-Haenszel
Parameter estimate	Difference in percentage
Point estimate	8.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.8
upper limit	18.7

Secondary: Mean Change From OP in the Number of Migraine Days per Month in the Last 4 Weeks (Weeks 9 to 12) of DBT Phase

End point title	Mean Change From OP in the Number of Migraine Days per Month in the Last 4 Weeks (Weeks 9 to 12) of DBT Phase
End point description: Migraine day:any calendar day in which participant experienced a qualified migraine headache (onset,continuation,or recurrence of migraine headache).A qualified migraine headache:a migraine with or without aura, lasting for>=30 minutes,and meeting either>=2 of pain features:unilateral location;pulsating quality;moderate or severe pain intensity;aggravation by or causing avoidance of routine physical activity OR >=1 of associated symptoms:nausea and/or vomiting;photophobia and phonophobia. Number of migraine days per month were prorated to 28 days and derived a month (i.e.,4-week interval) in on-DBT efficacy analysis period as follows: 28*(total number of migraine days in month)/(total number of e-diary efficacy data in month). Mean change in number of migraine days per month in last 4 weeks of DBT phase as compared to OP phase was calculated and reported in this endpoint. DB treatment efficacy (Migraine) analysis set.	
End point type	Secondary
End point timeframe: Observation phase (from 31 days before randomization), Week 9 to Week 12 of the DBT phase	

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	221	220	224	
Units: Days per month				
least squares mean (confidence interval 97.5%)	-3.0 (-3.59 to -2.49)	-4.2 (-4.75 to -3.75)	-2.8 (-3.33 to -2.33)	

Statistical analyses

Statistical analysis title	DB Rimegepant vs DB Placebo

Statistical analysis description:

Linear mixed effects model with repeated measures with the number of total migraine days per month in the OP as a covariate; treatment group, randomization stratum (use of previous prophylactic migraine medication generally considered to have efficacy) month and month-by-treatment group interaction as fixed effects.

Comparison groups	DB Rimegepant v DB Placebo
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.12
upper limit	-0.71

Statistical analysis title	DB Rimegepant/ Placebo vs DB Placebo

Statistical analysis description:

Linear mixed effects model with repeated measures with the number of total migraine days per month in the OP as a covariate; treatment group, randomization stratum (use of previous prophylactic migraine medication generally considered to have efficacy) month and month-by-treatment group interaction as fixed effects.

Comparison groups	DB Rimegepant/ Placebo v DB Placebo
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5314
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-0.95
upper limit	0.54

Secondary: Mean Change From OP in the Number of Migraine Days per Month in the First 4 Weeks (Weeks 1 to 4) of DBT Phase

End point title	Mean Change From OP in the Number of Migraine Days per Month in the First 4 Weeks (Weeks 1 to 4) of DBT Phase

End point description:

A migraine day:any calendar day in which participant experienced a qualified migraine headache (onset, continuation, or recurrence of the migraine headache). A qualified migraine headache: as a migraine with or without aura, lasting for >=30 minutes, and meeting either >=2 of the pain features:unilateral location;pulsating quality moderate or severe pain intensity;aggravation by or causing avoidance of routine physical activity OR >=1 of the associated symptoms:nausea and/or vomiting;photophobia and phonophobia. Number of migraine days per month were prorated to 28 days and derived a month (i.e., 4-week interval) in on-DBT efficacy analysis period as follows: 28*(total number of migraine days in the month / (total number of e-diary efficacy data in the month. Mean change in number of migraine days per month in the first 4 weeks of DBT phase as compared to OP phase was calculated and reported in this endpoint. Double-blind treatment efficacy (Migraine) analysis set was used.

End point type	Secondary

End point timeframe:

Observation phase (from 31 days before randomization), Week 1 to Week 4 of the DBT phase

End point values	DB Placebo	DB Rimegepant/ Placebo	DB Rimegepant	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	224	221	220	
Units: Days per month				
least squares mean (confidence interval 97.5%)	-1.5 (-1.97 to -1.05)	-2.7 (-3.17 to -2.16)	-3.6 (-4.10 to -3.16)	

Statistical analyses

Statistical analysis title	DB Rimegepant vs DB Placebo

Statistical analysis description:

Linear mixed effects model with repeated measures with the number of total migraine days per month in the OP as a covariate; treatment group, randomization stratum (use of previous prophylactic migraine medication generally considered to have efficacy) month and month-by-treatment group interaction as fixed effects.

Comparison groups	DB Rimegepant v DB Placebo
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-2.1
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.78
upper limit	-1.46

Statistical analysis title	DB Rimegepant/ Placebo vs DB Placebo

Statistical analysis description:

Linear mixed effects model with repeated measures with the number of total migraine days per month in the OP as a covariate; treatment group, randomization stratum (use of previous prophylactic migraine medication generally considered to have efficacy) month and month-by-treatment group interaction as fixed effects.

Comparison groups	DB Rimegepant/ Placebo v DB Placebo
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.84
upper limit	-0.47

Secondary: Mean Number of Acute Migraine-Specific Medication Days per Month Over the Entire DBT Phase (Weeks 1 to 12)

End point title	Mean Number of Acute Migraine-Specific Medication Days per Month Over the Entire DBT Phase (Weeks 1 to 12)

End point description:

An acute migraine-specific medication day was defined as any calendar day during which the participant took a migraine-specific medication (i.e., triptan or ergotamine). The number of acute migraine-specific medication days per month were prorated to 28 days and derived for on-DBT efficacy analysis period as follows: 28*(total number of acute migraine-specific medication days through Month 3/ (total number of e-Diary efficacy data days through Month 3). Double-blind treatment efficacy (Migraine) analysis set included participants in the full analysis set who were randomized only once and took >= 1 dose of double-blind study drug (rimegepant or placebo) and had >=14 days of eDiary efficacy data (not necessarily consecutive) in both the OP and >=1 month (4-week interval) in the DBT Phase.

End point type	Secondary

End point timeframe:

DBT phase (through Month 3 [Week 1 to 12])

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	221	220	224	
Units: Days per month				
least squares mean (confidence interval 97.5%)	2.3 (1.87 to 2.82)	1.5 (1.13 to 1.88)	2.8 (2.28 to 3.35)	

Statistical analyses

Statistical analysis title	DB Rimegepant vs DB Placebo
Statistical analysis description:	
Linear mixed effects model with repeated measures has treatment group, randomization stratum, month, and month-by-treatment group interaction as fixed effects.	
Comparison groups	DB Rimegepant v DB Placebo
Number of subjects included in analysis	444
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.97
upper limit	-0.65

Statistical analysis title	DB Rimegepant/ Placebo vs DB Placebo
Statistical analysis description:	
Linear mixed effects model with repeated measures has treatment group, randomization stratum, month, and month-by-treatment group interaction as fixed effects.	
Comparison groups	DB Rimegepant/ Placebo v DB Placebo
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.144
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.2
upper limit	0.25

Secondary: Mean Change From Baseline in the Migraine-Specific Quality-of-Life Questionnaire (MSQoL) Version 2.1 Restrictive Role Function Domain Score at Week 12 of the DBT Phase

End point title	Mean Change From Baseline in the Migraine-Specific Quality-of-Life Questionnaire (MSQoL) Version 2.1 Restrictive Role Function Domain Score at Week 12 of the DBT Phase

End point description:

MSQoL is a self-administered, 14-item instrument validated in 3 domains:role restriction, prevention, and emotional function. Restrictive role function domain consisted of 7 items that described how migraine limited one's daily social and work-related activities. Participants were required to respond to items using a 6-point scale ranging from 1 to 6, where 1:none of the time, 2: a little bit of time," "3: some of time,4: a good bit of time, 5: most of time, and 6: all of time. Item scores were recoded using (7 -original score). Raw dimension scores for restrictive role function domain were computed as a sum of recoded item scores and rescaled from a 0 to 100 scale such that lower score (0) indicated poor quality of life and higher scores (100) better quality of life. DB treatment efficacy analysis set included participants in the full analysis set who were randomized only once and took >= 1 dose of double-blind study drug. Here "N":number of participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 12 of the DBT phase

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	194	191	197	
Units: Units on a scale				
least squares mean (confidence interval 97.5%)	21.3 (18.37 to 24.33)	29.1 (25.79 to 32.31)	18.9 (15.91 to 21.97)	

Statistical analyses

Statistical analysis title	DB Rimegepant vs DB Placebo

Statistical analysis description:

Linear regression model with treatment group and randomization stratum as fixed effects and baseline score as covariate for participants with non-missing domain scores at both baseline and Week 12.

Comparison groups	DB Rimegepant v DB Placebo
Number of subjects included in analysis	388
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Linear
Parameter estimate	LS Mean Difference
Point estimate	10.1
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.71
upper limit	14.52

Statistical analysis title	DB Rimegepant/ Placebo vs DB Placebo

Statistical analysis description:

Linear regression model with treatment group and randomization stratum as fixed effects and baseline score as covariate for participants with non-missing domain scores at both baseline and Week 12.

Comparison groups	DB Rimegepant/ Placebo v DB Placebo
Number of subjects included in analysis	391
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2029
Method	Regression, Linear
Parameter estimate	LS Mean Difference
Point estimate	2.4
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-1.84
upper limit	6.66

Secondary: Number of Participants With Mild, Moderate and Severe Adverse Events (AEs) in DBT Phase

End point title	Number of Participants With Mild, Moderate and Severe Adverse Events (AEs) in DBT Phase

End point description:

An AE:any new untoward medical occurrence or worsening of a pre-existing medical condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. AEs were categorized as mild:usually transient and required only minimal treatment or therapeutic intervention. event did not generally interfere with usual activities of daily living. Moderate:was usually alleviated with additional specific therapeutic intervention.event interfered with usual activities of daily living,causing discomfort but posed no significant or permanent risk of harm to participant. Severe:Interrupted usual activities of daily living, significantly affected clinical status, or required intensive therapeutic intervention. AEs included non-SAEs and SAEs. DB treatment safety population included participants in the enrolled analysis set who took >=1 dose of DB study drug (rimegepant or placebo).

End point type	Secondary

End point timeframe:

DBT: From Week 1 to Week 20

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	232	229	231	
Units: Participants				
Mild	73	86	91	
Moderate	42	22	43	
Severe	4	3	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Mild, Moderate and Severe AEs OLE Phase

End point title	Number of Participants With Mild, Moderate and Severe AEs OLE Phase

End point description:

An AE: any new untoward medical occurrence or worsening of a pre-existing medical condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. AEs were categorized as mild: usually transient and required only minimal treatment or therapeutic intervention. The event did not generally interfere with usual activities of daily living. Moderate: was usually alleviated with additional specific therapeutic intervention. The event interfered with usual activities of daily living, causing discomfort but posed no significant or permanent risk of harm to the participant. Severe: Interrupted usual activities of daily living, significantly affected clinical status, or required intensive therapeutic intervention. AEs included both non-SAEs and SAEs. OL rimegepant safety population included participants in the enrolled analysis set who took >= 1 dose of OL rimegepant.

End point type	Secondary

End point timeframe:

OLE: From Week 12 to Week 32

End point values	DB RMG EOD/DB PBO EOD/ OL RMG QD	DB RMG QD/ OL RMG QD	DB PBO QD/ OL RMG QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	182	196	195	
Units: Participants				
Mild	65	57	65	
Moderate	30	22	25	
Severe	2	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Serious Adverse Events (SAEs) in DBT Phase

End point title	Number of Participants With Serious Adverse Events (SAEs) in DBT Phase

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. An SAE was any event that met any of the following criteria at any dose: death; life-threatening; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect in the offspring of the participant who received rimegepant and other important medical events. Double-blind treatment safety population included participants in the enrolled analysis set who took >= 1 dose of double-blind study drug (rimegepant or placebo).

End point type	Secondary

End point timeframe:

DBT: From Week 1 to Week 20

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	232	229	231	
Units: Participants	3	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With SAEs in OLE Phase

End point title	Number of Participants With SAEs in OLE Phase

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. An SAE was any event that met any of the following criteria at any dose: death; life-threatening; inpatient hospitalization or prolongation of existing hospitalization; persistent or significant disability/incapacity; congenital anomaly/birth defect in the offspring of the participant who received rimegepant and other important medical events. Open-label rimegepant safety population included participants in the enrolled analysis set who took >= 1 dose of open-label rimegepant.

End point type	Secondary

End point timeframe:

OLE: From Week 12 to Week 32

End point values	DB RMG EOD/DB PBO EOD/ OL RMG QD	DB RMG QD/ OL RMG QD	DB PBO QD/ OL RMG QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	182	196	195	
Units: Participants	2	2	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With AEs Leading to Study Drug Discontinuation in DBT Phase

End point title	Number of Participants With AEs Leading to Study Drug Discontinuation in DBT Phase

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical

condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. In this outcome measure, participants with adverse events leading to study drug discontinuation were reported. Double-blind treatment safety population included participants in the enrolled analysis set who took >= 1 dose of double-blind study drug (rimegepant or placebo).

End point type	Secondary

End point timeframe:

DBT: From Week 1 to Week 12

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	232	229	231	
Units: Participants	6	1	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With AEs Leading to Study Drug Discontinuation in OLE Phase

End point title	Number of Participants With AEs Leading to Study Drug Discontinuation in OLE Phase

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. In this outcome measure, participants with adverse events leading to study drug discontinuation were reported. Open-label rimegepant safety population included participants in the enrolled analysis set who took >= 1 dose of open-label rimegepant.

End point type	Secondary

End point timeframe:

OLE: From Week 12 to Week 24

End point values	DB RMG EOD/DB PBO EOD/ OL RMG QD	DB RMG QD/ OL RMG QD	DB PBO QD/ OL RMG QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	182	196	195	
Units: Participants	4	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Grade 3 to 4 Laboratory Abnormalities in DBT Phase

End point title	Number of Participants With Grade 3 to 4 Laboratory Abnormalities in DBT Phase

End point description:

Laboratory parameters were graded according to National Cancer Institute(NCI)common terminology criteria for AE(CTCAE) version 5.0 and using division of AIDS (DAIDS) toxicity grading scale version 2.1 (glucose,low density lipoprotein [LDL] cholesterol,uric acid and urinalysis) and for other parameters (eosinophils,hemoglobin,leukocytes,albumin,lymphocytes, neutrophils,platelets,alanine aminotransferase,alkaline phosphatase ,aspartate aminotransferase,bicarbonate,bilirubin,calcium, cholesterol,creatine kinase,creatinine,Lactate dehydrogenase, potassium,sodium,triglycerides)CTCAE v5.0 was used.Severity were graded as Grade1=mild AE,G2=moderate,G3=severe,G4=life-threatening consequences;urgent intervention indicated.Only laboratory abnormalities with non-zero values in any of treatment are reported.DB treatment safety population.All participants under'N'contributed data to table;however,may not have evaluable data for every row.Here"n":number of participants evaluable for specified rows.

End point type	Secondary

End point timeframe:

DBT: From Week 1 to Week 20

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	232	229	231	
Units: Participants				
Lymphocytes, low(n:225,224,224)	0	0	1	
Alanine Aminotransferase(n:225,224,225)	0	1	1	
Aspartate Aminotransferase (n:225,224,225)	0	0	1	
Creatine Kinase(n:225,224,225)	2	1	4	
Glucose, low(n:225,224,225)	0	1	0	
LDL Cholesterol(n:207,213,218)	6	4	9	
LDL Cholesterol, fasting(n:107,120,118)	4	3	3	
LDL Cholesterol, not fasting(n:102,96,102)	2	1	6	
Sodium, high(n:225,224,225)	0	0	1	
Triglycerides(n:207,213,218)	0	1	0	
Triglycerides, fasting(n:107,120,118)	0	1	0	
Urinalysis Glucose(n:204,207,213)	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Grade 3 to 4 Laboratory Abnormalities in OLE Phase

End point title	Number of Participants With Grade 3 to 4 Laboratory Abnormalities in OLE Phase

End point description:

laboratory parameters were graded according to the NCI CTCAE version 5.0 and using DAIDS toxicity grading scale version 2.1 (glucose, LDL cholesterol, uric acid and urinalysis). And for other parameters (eosinophils,hemoglobin,leukocytes,albumin, lymphocytes,neutrophils,platelets,alanine aminotransferase,alkaline phosphatase,aspartate aminotransferase,bicarbonate,bilirubin, calcium,cholesterol,creatine kinase,creatinine, lactate dehydrogenase,potassium,sodium,triglycerides) CTCAE v5.0 was used. Severity was graded as Grade 1=mild AE, G 2=moderate, G3=severe,G4=life-threatening consequences; urgent intervention indicated. Number of participants according to Grade 3 or 4 laboratory abnormalities are reported. Only laboratory abnormalities with non-zero values in any of treatment arms are reported. OL treatment safety population.All participants under'N'contributed data to table;however,may not have evaluable data for every row.Here"n":number of participants evaluable for specified rows.

End point type	Secondary

End point timeframe:

OLE: From Week 12 to Week 32

End point values	DB RMG EOD/DB PBO EOD/ OL RMG QD	DB RMG QD/ OL RMG QD	DB PBO QD/ OL RMG QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	182	196	195	
Units: Participants				
Alanine Aminotransferase(n:180,193,194)	1	1	1	
Aspartate Aminotransferase(n:180,193,194)	0	1	0	
Creatine Kinase(n:180,191,190)	3	0	5	
LDL Cholesterol(n:166,182,179)	7	8	4	
LDL Cholesterol, fasting(n:80,101,88)	4	4	0	
LDL Cholesterol, not fasting(n:89,81,92)	3	4	4	
Potassium, low(n:180,191,190)	0	1	0	
Potassium, high(n:180,191,190)	1	0	1	
Triglycerides(n:166,182,179)	0	1	0	
Triglycerides, not fasting(n:89,81,92)	0	1	0	
Urinalysis Glucose(n:162,176,175)	1	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Aspartate Aminotransferase (AST) or Alanine Aminotransferase (ALT) Elevations > 3* Upper Limit of Normal (ULN) Concurrent With (Total Bilirubin) TBL >2*ULN in DBT Phase

End point title	Number of Participants With Aspartate Aminotransferase (AST) or Alanine Aminotransferase (ALT) Elevations > 3* Upper Limit of Normal (ULN) Concurrent With (Total Bilirubin) TBL >2*ULN in DBT Phase

End point description:

Number of participants with AST or ALT >3*ULN concurrent with TBL >2*ULN in DBT phase were reported in this endpoint. Double-blind treatment safety population included participants in the enrolled analysis set who took >= 1 dose of double-blind study drug (rimegepant or placebo). Here "Overall Number of Participants Analyzed" signifies the number of participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

DBT: From Week 1 to Week 20

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	225	224	225	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With AST or ALT Elevations > 3* ULN Concurrent With TBL >2*ULN in OLE Phase

End point title	Number of Participants With AST or ALT Elevations > 3* ULN Concurrent With TBL >2*ULN in OLE Phase

End point description:

Number of participants with AST or ALT >3*ULN concurrent with TBL >2*ULN in DBT phase were reported in this endpoint. Open-label rimegepant safety population included participants in the enrolled analysis set who took >= 1 dose of open-label rimegepant. Here "Overall Number of Participants Analyzed" signifies the number of participants evaluable for this endpoint.

End point type	Secondary

End point timeframe:

OLE: From Week 12 to Week 32

End point values	DB RMG EOD/DB PBO EOD/ OL RMG QD	DB RMG QD/ OL RMG QD	DB PBO QD/ OL RMG QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	180	193	194	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Hepatic-Related AEs in the DBT Phase

End point title	Number of Participants With Hepatic-Related AEs in the DBT Phase

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. Hepatic-related AEs included: alanine aminotransferase and aspartate aminotransferase increased, liver function test abnormal, liver function test increased, bilirubin conjugated increased, blood bilirubin increased, transaminases increased and hyperbilirubinemia. Number of participants with any hepatic-related AEs in the DBT phase were reported in this endpoint measure. Double-blind treatment safety population included participants in the enrolled analysis set who took >= 1 dose of double-blind study drug (rimegepant or placebo).

End point type	Secondary

End point timeframe:

DBT: From Week 1 to Week 20

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	232	229	231	
Units: Participants	7	8	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Hepatic-Related AEs in the OLE Phase

End point title	Number of Participants With Hepatic-Related AEs in the OLE Phase

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. Hepatic AEs included: alanine aminotransferase and aspartate aminotransferase increased, liver function test abnormal, bilirubin conjugated, hepatic enzyme increased, blood bilirubin unconjugated increased, blood bilirubin and transaminases increased and hepatic function abnormal. Number of participants with any hepatic-related AEs in the OLE phase were reported in this endpoint measure. Open-label rimegepant safety population included participants in the enrolled analysis set who took >= 1 dose of open-label rimegepant.

End point type	Secondary

End point timeframe:

OLE: From Week 12 to Week 32

End point values	DB RMG EOD/DB PBO EOD/ OL RMG QD	DB RMG QD/ OL RMG QD	DB PBO QD/ OL RMG QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	182	196	195	
Units: Participants	11	4	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Hepatic-Related AEs Leading to Study Drug Discontinuation in the DBT Phase

End point title	Number of Participants With Hepatic-Related AEs Leading to Study Drug Discontinuation in the DBT Phase

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. Hepatic-related AEs included: alanine aminotransferase and aspartate aminotransferase increased, liver function test and blood bilirubin increased. Number of participants with any hepatic-related AEs leading to study drug discontinuation is reported in this endpoint measure. Double-blind treatment safety population included participants in the enrolled analysis set who took >= 1 dose of double-blind study drug (rimegepant or placebo).

End point type	Secondary

End point timeframe:

DBT: From Week 1 to Week 12

End point values	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	232	229	231	
Units: Participants	4	1	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Hepatic-Related AEs Leading to Study Drug Discontinuation in the OLE Phase

End point title	Number of Participants With Hepatic-Related AEs Leading to Study Drug Discontinuation in the OLE Phase

End point description:

An AE was defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a participant or clinical investigation participant administered an investigational (medicinal) product and that did not necessarily have a causal relationship with this treatment. Hepatic-related AEs included: aspartate aminotransferase increased and liver function test abnormal. Number of participants with any hepatic-related AEs leading to study drug discontinuation is reported in this endpoint measure. Open-label rimegepant safety population included participants in the enrolled analysis set who took >= 1 dose of open-label rimegepant.

End point type	Secondary

End point timeframe:

OLE: From Week 12 to Week 24

End point values	DB RMG EOD/DB PBO EOD/ OL RMG QD	DB RMG QD/ OL RMG QD	DB PBO QD/ OL RMG QD	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	182	196	195	
Units: Participants	1	1	1	

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 8 weeks after last dose of study drug (DBT phase: Week 1 to Week 20; OLE phase Week 12 to Week 32)

Adverse event reporting additional description:

Same event may appear as AE and SAE,but what is presented are distinct events. Event may be categorized as serious in 1 and non-SAE in another participant, or 1 participant may have experienced both.DB and OL RMG treatment safety population=participants in the enrolled analysis set who took>=1 dose of DB/OL-RMG study drug used for DBT and OL RMG.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v27.1

Reporting groups

Reporting group title	DB Rimegepant/ Placebo

Reporting group description:

Participants received RMG 75 mg, ODT, once EOD alternating with matching placebo dosed EOD for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Rimegepant

Reporting group description:

Participants received RMG 75 mg ODT, once daily for 12 weeks in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB Placebo

Reporting group description:

Participants received matching placebo for RMG 75 mg ODT once daily for 12 weeks, in the DBT phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB RMG EOD/DB PBO EOD/ OL RMG QD

Reporting group description:

Participants who received RMG 75 mg, ODT alternating with matching placebo in the DBT phase received RMG 75 mg ODT QD for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB RMG QD/ OL RMG QD

Reporting group description:

Participants who received RMG 75 mg ODT in the DBT phase continued to receive RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Reporting group title	DB PBO QD/ OL RMG QD

Reporting group description:

Participants who received placebo ODT in the DBT phase received RMG 75 mg ODT once daily for 12 weeks in the OLE phase. Participants were followed up for 8 weeks after last dose of study drug.

Serious adverse events	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 232 (1.29%)	2 / 229 (0.87%)	1 / 231 (0.43%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 232 (0.00%)	0 / 229 (0.00%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oesophageal carcinoma			
subjects affected / exposed	1 / 232 (0.43%)	0 / 229 (0.00%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 232 (0.00%)	0 / 229 (0.00%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Status migrainosus			
subjects affected / exposed	1 / 232 (0.43%)	0 / 229 (0.00%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn\'s disease			
subjects affected / exposed	1 / 232 (0.43%)	0 / 229 (0.00%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 232 (0.00%)	0 / 229 (0.00%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	0 / 232 (0.00%)	0 / 229 (0.00%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 232 (0.00%)	0 / 229 (0.00%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 232 (0.00%)	0 / 229 (0.00%)	1 / 231 (0.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected cyst			
subjects affected / exposed	0 / 232 (0.00%)	1 / 229 (0.44%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 232 (0.00%)	1 / 229 (0.44%)	0 / 231 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DB RMG EOD/DB PBO EOD/ OL RMG QD	DB RMG QD/ OL RMG QD	DB PBO QD/ OL RMG QD
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 182 (1.10%)	2 / 196 (1.02%)	2 / 195 (1.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 182 (0.00%)	1 / 196 (0.51%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oesophageal carcinoma			
subjects affected / exposed	0 / 182 (0.00%)	0 / 196 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Post procedural haemorrhage			
subjects affected / exposed	0 / 182 (0.00%)	0 / 196 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Status migrainosus			
subjects affected / exposed	1 / 182 (0.55%)	0 / 196 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Crohn\'s disease			
subjects affected / exposed	0 / 182 (0.00%)	0 / 196 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 182 (0.55%)	0 / 196 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	0 / 182 (0.00%)	1 / 196 (0.51%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 182 (0.00%)	0 / 196 (0.00%)	1 / 195 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 182 (0.00%)	0 / 196 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected cyst			

subjects affected / exposed	0 / 182 (0.00%)	0 / 196 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 182 (0.00%)	0 / 196 (0.00%)	0 / 195 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	DB Rimegepant/ Placebo	DB Rimegepant	DB Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 232 (5.60%)	13 / 229 (5.68%)	13 / 231 (5.63%)
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 232 (0.00%)	0 / 229 (0.00%)	0 / 231 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	13 / 232 (5.60%)	13 / 229 (5.68%)	13 / 231 (5.63%)
occurrences (all)	14	14	16

Non-serious adverse events	DB RMG EOD/DB PBO EOD/ OL RMG QD	DB RMG QD/ OL RMG QD	DB PBO QD/ OL RMG QD
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 182 (9.34%)	19 / 196 (9.69%)	13 / 195 (6.67%)
Infections and infestations			
COVID-19			
subjects affected / exposed	4 / 182 (2.20%)	14 / 196 (7.14%)	6 / 195 (3.08%)
occurrences (all)	4	14	6
Nasopharyngitis			
subjects affected / exposed	13 / 182 (7.14%)	5 / 196 (2.55%)	7 / 195 (3.59%)
occurrences (all)	14	6	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 January 2022	Amendment 2: The purpose of the amendment was to update the schedule of assessments, inclusion and exclusion criteria.
17 March 2022	Amendment 3: The purpose of the amendment was to update the schedule of assessments, clarified restrictions around prohibited medication use, to clarified HbA1c collection and analysis sets.
01 July 2022	Amendment 4: The purpose of the amendment was to update the exclusion criterion, clarified low dose aspirin use for cardiovascular prophylaxis and clarified the definition of the "Migraine" analysis set.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported