Clinical trial results:
A randomized, double-blind, placebo-controlled, multi-center, dose-ranging Phase 2 study of rilzabrutinib followed by an open-label extension phase in patients with moderate-to-severe chronic spontaneous urticaria (CSU) who remain symptomatic despite the use of H1 antihistamine treatment

Summary

EudraCT number	2021-002609-93
Trial protocol	ES DE IT PL GR NL
Global end of trial date	23 April 2024

Results information

Result version number	v1 (current)
This version publication date	08 May 2025
First version publication date	08 May 2025

Trial information

Trial identification

Sponsor protocol code	DRI17224

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05107115
WHO universal trial number (UTN)	U1111-1263-4226

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	82 avenue Raspail, Gentilly, France, 94250
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	05 July 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of rilzabrutinib in study participants with CSU who remained symptomatic despite the use of H1-antihistamine (H1-AH).

Protection of trial subjects:

Participants were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the participant and considering the local culture. During the course of the trial, participants were provided with individual participant cards indicating the nature of the trial the participant is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 November 2021
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	Argentina: 32
Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	Chile: 16
Country: Number of subjects enrolled	Germany: 10
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Poland: 15
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Taiwan: 13
Worldwide total number of subjects	160
EEA total number of subjects	57

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	151
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 59 active centers in 13 countries. A total of 240 participants were screened between 24 November 2021 and 28 February 2023, of which 80 were screen failures. Screen failures were mainly due to not meeting the eligibility criteria.

Pre-assignment

Screening details:

A total of 160 participants were enrolled in the study. Randomization was stratified by region and prior use of omalizumab. Here reasons for not completed indicates reasons for treatment discontinuation.

Period 1

Period 1 title	Double-Blind Period (Up to 12 Weeks)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	DB Period: Placebo TID

Arm description:

Participants received 1 tablet of matching placebo orally three times a day (TID) from Day 1 to Week 12 during the double-blind (DB) period.

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

Dosage and administration details:

Placebo matched to rilzabrutinib was available as tablets (modified-capsule shaped tablets/caplets) and 1 tablet were administered orally TID from Day 1 to Week 12.

Arm title	DB Period: Rilzabrutinib 400 mg QPM + Placebo

Arm description:

Participants received 1 tablet of rilzabrutinib 400 milligrams (mg) orally once every evening (QPM) and 2 tablets of matching placebo daily from Day 1 to Week 12 during the DB period.

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

Dosage and administration details:

Placebo matched to rilzabrutinib was available as tablets (modified-capsule shaped tablets/caplets) and 2 tablets were administered orally twice daily from Day 1 to Week 12.

Investigational medicinal product name	Rilzabrutinib
Investigational medicinal product code	
Other name	SAR444671, PRN1008
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rilzabrutinib was available as 400 mg tablets (modified-capsule shaped tablets/caplets) and 1 tablet was administered orally QPM from Day 1 to Week 12.

Arm title	DB Period: Rilzabrutinib 400 mg BID + Placebo

Arm description:

Participants received 1 tablet of rilzabrutinib 400 mg orally twice a day (BID) and 1 tablet of matching placebo daily from Day 1 to Week 12 during the DB period.

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

Dosage and administration details:

Placebo matched to rilzabrutinib was available as tablets (modified-capsule shaped tablets/caplets) and 1 tablet was administered orally once daily from Day 1 to Week 12.

Investigational medicinal product name	Rilzabrutinib
Investigational medicinal product code	
Other name	SAR444671, PRN1008
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rilzabrutinib was available as 400 mg tablets (modified-capsule shaped tablets/caplets) and 1 tablet was administered orally BID from Day 1 to Week 12.

Arm title	DB Period: Rilzabrutinib 400 mg TID

Arm description:

Participants received 1 tablet of rilzabrutinib 400 mg orally TID from Day 1 to Week 12 during the DB period.

Arm type	Experimental
Investigational medicinal product name	Rilzabrutinib
Investigational medicinal product code	
Other name	SAR444671, PRN1008
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rilzabrutinib was available as 400 mg tablets (modified-capsule shaped tablets/caplets) and 1 tablet was administered orally TID from Day 1 to Week 12.

Number of subjects in period 1	DB Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	DB Period: Rilzabrutinib 400 mg BID + Placebo
Started	40	38	41
Completed	37	34	35
Not completed	3	4	6
Consent withdrawn by subject	3	2	4
Adverse event, non-fatal	-	-	1
Unspecified	-	1	-

Poor compliance to protocol	-	1	1

Number of subjects in period 1	DB Period: Rilzabrutinib 400 mg TID
Started	41
Completed	36
Not completed	5
Consent withdrawn by subject	4
Adverse event, non-fatal	1
Unspecified	-
Poor compliance to protocol	-

Period 2

Period 2 title	OLE Period (Weeks 13 to 52: 40 Weeks)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OLE Period: Rilzabrutinib 400 mg BID

Arm description:

Participants who completed DB period entered the open-label extension (OLE) period received 1 tablet of rilzabrutinib 400 mg orally BID from Week 13 to Week 52.

Arm type	Experimental
Investigational medicinal product name	Rilzabrutinib
Investigational medicinal product code	
Other name	SAR444671, PRN1008
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rilzabrutinib was available as 400 mg tablets (modified-capsule shaped tablets/caplets) and 1 tablet was administered orally BID from Week 13 to Week 52.

Arm title	OLE Period: Rilzabrutinib 400 mg TID

Arm description:

Participants who completed DB period entered the OLE period received 1 tablet of rilzabrutinib 400 mg orally TID from Week 13 to Week 52.

Arm type	Experimental
Investigational medicinal product name	Rilzabrutinib
Investigational medicinal product code	
Other name	SAR444671, PRN1008
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rilzabrutinib was available as 400 mg tablets (modified-capsule shaped tablets/caplets) and 1 tablet was administered orally TID from Week 13 to Week 52.

Number of subjects in period 2[1]	OLE Period: Rilzabrutinib 400 mg BID	OLE Period: Rilzabrutinib 400 mg TID
Started	9	128
Completed	6	98
Not completed	3	30
Consent withdrawn by subject	3	17
Adverse event, non-fatal	-	7
Unspecified	-	3
Poor compliance to protocol	-	1
Lack of efficacy	-	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Post completion of double-blinded period, only eligible participants entered open-label extension period.

Baseline characteristics

Reporting groups	
Reporting group title	DB Period: Placebo TID
Reporting group description:	
Participants received 1 tablet of matching placebo orally three times a day (TID) from Day 1 to Week 12 during the double-blind (DB) period.	
Reporting group title	DB Period: Rilzabrutinib 400 mg QPM + Placebo
Reporting group description:	
Participants received 1 tablet of rilzabrutinib 400 milligrams (mg) orally once every evening (QPM) and 2 tablets of matching placebo daily from Day 1 to Week 12 during the DB period.	
Reporting group title	DB Period: Rilzabrutinib 400 mg BID + Placebo
Reporting group description:	
Participants received 1 tablet of rilzabrutinib 400 mg orally twice a day (BID) and 1 tablet of matching placebo daily from Day 1 to Week 12 during the DB period.	
Reporting group title	DB Period: Rilzabrutinib 400 mg TID
Reporting group description:	
Participants received 1 tablet of rilzabrutinib 400 mg orally TID from Day 1 to Week 12 during the DB period.	

Reporting group values	DB Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	DB Period: Rilzabrutinib 400 mg BID + Placebo
Number of subjects	40	38	41
Age categorical Units: Participants			
Age Continuous Units: years			
arithmetic mean	40.2	42.1	45.5
standard deviation	± 14.0	± 12.7	± 13.4
Sex: Female, Male Units: Participants			
Female	26	28	25
Male	14	10	16
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	9	11	8
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	31	27	33
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Weekly Urticaria Activity Score (UAS7)			
The UAS7 score is a composite score containing both the hive severity score (HSS, ranging from 0 = None to 3 = more than 50 hives) and the itch severity score (ISS, ranging from 0 = None to 3 = intense). The daily UAS scores ranged from 0 to 6 points per day. Daily UAS scores were summed over a 7-day period to create the UAS7, ranging from 0 to 42, and are composed of the HSS7 and ISS7 components. A higher score indicates worse disease.			
Units: score on a scale			

arithmetic mean	30.0	31.4	30.2
standard deviation	± 8.6	± 7.3	± 7.2
Weekly Itch Severity Score (ISS7)			
The ISS represents the itch severity on a scale and was recorded by the participant in their electronic (e)-diary ranging from 0 (None) to 3 (intense). The ISS7 is the sum of ISS for the previous 7 days. The ISS7 represents itch severity on a scale ranging from 0 (minimum) to 21 (maximum). Higher scores indicate greater intensity of itch.			
Units: score on a scale			
arithmetic mean	15.6	16.5	15.8
standard deviation	± 4.2	± 3.5	± 3.7

Reporting group values	DB Period: Rilzabrutinib 400 mg TID	Total	
Number of subjects	41	160	
Age categorical			
Units: Participants			
Age Continuous			
Units: years			
arithmetic mean	48.5		
standard deviation	± 12.2	-	
Sex: Female, Male			
Units: Participants			
Female	33	112	
Male	8	48	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	10	38	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	30	121	
More than one race	0	0	
Unknown or Not Reported	0	0	
Weekly Urticaria Activity Score (UAS7)			
The UAS7 score is a composite score containing both the hive severity score (HSS, ranging from 0 = None to 3 = more than 50 hives) and the itch severity score (ISS, ranging from 0 = None to 3 = intense). The daily UAS scores ranged from 0 to 6 points per day. Daily UAS scores were summed over a 7-day period to create the UAS7, ranging from 0 to 42, and are composed of the HSS7 and ISS7 components. A higher score indicates worse disease.			
Units: score on a scale			
arithmetic mean	29.9		
standard deviation	± 8.6	-	
Weekly Itch Severity Score (ISS7)			
The ISS represents the itch severity on a scale and was recorded by the participant in their electronic (e)-diary ranging from 0 (None) to 3 (intense). The ISS7 is the sum of ISS for the previous 7 days. The ISS7 represents itch severity on a scale ranging from 0 (minimum) to 21 (maximum). Higher scores indicate greater intensity of itch.			
Units: score on a scale			
arithmetic mean	15.9		
standard deviation	± 4.4	-	

End points

End points reporting groups

Reporting group title	DB Period: Placebo TID
Reporting group description:	
Participants received 1 tablet of matching placebo orally three times a day (TID) from Day 1 to Week 12 during the double-blind (DB) period.	
Reporting group title	DB Period: Rilzabrutinib 400 mg QPM + Placebo
Reporting group description:	
Participants received 1 tablet of rilzabrutinib 400 milligrams (mg) orally once every evening (QPM) and 2 tablets of matching placebo daily from Day 1 to Week 12 during the DB period.	
Reporting group title	DB Period: Rilzabrutinib 400 mg BID + Placebo
Reporting group description:	
Participants received 1 tablet of rilzabrutinib 400 mg orally twice a day (BID) and 1 tablet of matching placebo daily from Day 1 to Week 12 during the DB period.	
Reporting group title	DB Period: Rilzabrutinib 400 mg TID
Reporting group description:	
Participants received 1 tablet of rilzabrutinib 400 mg orally TID from Day 1 to Week 12 during the DB period.	
Reporting group title	OLE Period: Rilzabrutinib 400 mg BID
Reporting group description:	
Participants who completed DB period entered the open-label extension (OLE) period received 1 tablet of rilzabrutinib 400 mg orally BID from Week 13 to Week 52.	
Reporting group title	OLE Period: Rilzabrutinib 400 mg TID
Reporting group description:	
Participants who completed DB period entered the OLE period received 1 tablet of rilzabrutinib 400 mg orally TID from Week 13 to Week 52.	
Subject analysis set title	DB Period: Rilzabrutinib 400 mg QPM
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received 1 tablet of rilzabrutinib 400 mg orally QPM from Day 1 to Week 12 during DB period.	
Subject analysis set title	DB Period: Rilzabrutinib 400 mg BID
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants received 1 tablet of rilzabrutinib 400 mg orally BID from Day 1 to Week 12 during DB period.	

Primary: Change From Baseline in Weekly Urticaria Activity Score (UAS7) at Week 12

End point title	Change From Baseline in Weekly Urticaria Activity Score (UAS7) at Week 12
End point description:	
The UAS7 score is a composite score containing both the hive severity score (HSS, ranging from 0 = None to 3 = more than 50 hives) and the itch severity score (ISS, ranging from 0 = None to 3 = intense). The daily UAS scores ranged from 0 to 6 points per day. Daily UAS scores were summed over a 7-day period to create the UAS7, ranging from 0 to 42, and are composed of the HSS7 and ISS7 components. A higher score indicates worse disease. Baseline is defined as the sum of the 7 days measurements obtained on and prior to the target visit day. Omalizumab-naïve population consisted of all randomized omalizumab-naïve participants. Participants were analyzed according to the study treatment allocated by the randomization. Only participants with data collected at Baseline and Week 12 are reported.	
End point type	Primary
End point timeframe:	
Baseline and Week 12	

End point values	DB Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	DB Period: Rilzabrutinib 400 mg BID + Placebo	DB Period: Rilzabrutinib 400 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	30	26	28
Units: score on a scale				
least squares mean (standard deviation)	-10.14 (± 2.05)	-9.74 (± 2.00)	-14.24 (± 2.06)	-16.89 (± 2.04)

Statistical analyses

Statistical analysis title	placebo, rilzabrutinib
Comparison groups	DB Period: Placebo TID v DB Period: Rilzabrutinib 400 mg QPM + Placebo
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8856
Method	ANCOVA
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.08
upper limit	5.89

Statistical analysis title	placebo, rilzabrutinib
Comparison groups	DB Period: Placebo TID v DB Period: Rilzabrutinib 400 mg BID + Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1441
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-4.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.59
upper limit	1.4

Statistical analysis title	placebo, rilzabrutinib
Comparison groups	DB Period: Placebo TID v DB Period: Rilzabrutinib 400 mg TID
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0159
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-6.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.23
upper limit	-1.26

Primary: Change From Baseline in Weekly Itch Severity Score (ISS7) at Week 12

End point title	Change From Baseline in Weekly Itch Severity Score (ISS7) at Week 12

End point description:

The ISS represents the itch severity on a scale and was recorded by the participant in their e-diary ranging from 0 (None) to 3 (intense). The ISS7 is the sum of ISS for the previous 7 days. The ISS7 represents itch severity on a scale ranging from 0 (minimum) to 21 (maximum). Higher scores indicate greater intensity of itch. Baseline is defined as the sum of the 7 days measurements obtained on and prior to the target visit day. Omalizumab-naïve population consisted of all randomized omalizumab-naïve participants. Participants were analyzed according to the study treatment allocated by the randomization. Only participants with data collected at Baseline and Week 12 are reported.

End point type	Primary

End point timeframe:

Baseline and Week 12

End point values	DB Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	DB Period: Rilzabrutinib 400 mg BID + Placebo	DB Period: Rilzabrutinib 400 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	30	26	28
Units: score on a scale				
least squares mean (standard deviation)	-5.77 (± 1.05)	-5.19 (± 1.02)	-7.73 (± 1.06)	-9.21 (± 1.05)

Statistical analyses

Statistical analysis title	placebo, rilzabrutinib
Comparison groups	DB Period: Placebo TID v DB Period: Rilzabrutinib 400 mg QPM

	+ Placebo
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6869
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.24
upper limit	3.4

Statistical analysis title	placebo, rilzabrutinib
Comparison groups	DB Period: Placebo TID v DB Period: Rilzabrutinib 400 mg TID
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0168
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-3.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.25
upper limit	-0.62

Statistical analysis title	placebo, rilzabrutinib
Comparison groups	DB Period: Placebo TID v DB Period: Rilzabrutinib 400 mg BID + Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1728
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	-1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.77
upper limit	0.86

Secondary: Change From Baseline in Weekly Urticaria Activity Score at Week 4

End point title	Change From Baseline in Weekly Urticaria Activity Score at Week 4

End point description:

The UAS7 score is a composite score containing both the hive severity score (HSS, ranging from 0 = None to 3 = more than 50 hives) and the itch severity score (ISS, ranging from 0 = None to 3 = intense). The daily UAS scores ranged from 0 to 6 points per day. Daily UAS scores were summed over a 7-day period to create the UAS7, ranging from 0 to 42, and are composed of the HSS7 and ISS7 components. A higher score indicates worse disease. Baseline is defined as the sum of the 7 measurements obtained within the 7 days prior to randomization. Omalizumab-naïve population consisted of all randomized omalizumab-naïve participants. Participants were analyzed according to the study treatment allocated by the randomization. Only participants with data collected at Baseline and Week 4 are reported.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	DB Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	DB Period: Rilzabrutinib 400 mg BID + Placebo	DB Period: Rilzabrutinib 400 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	37	33	32
Units: score on a scale				
least squares mean (standard error)	-7.06 (± 1.72)	-9.14 (± 1.66)	-12.89 (± 1.73)	-13.66 (± 1.72)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Weekly Urticaria Activity Score Less Than or Equal to (≤)6 at Week 12

End point title	Percentage of Participants With Weekly Urticaria Activity Score Less Than or Equal to (≤)6 at Week 12

End point description:

The UAS7 score is a composite score containing both the hive severity score (HSS, ranging from 0 = None to 3 = more than 50 hives) and the itch severity score (ISS, ranging from 0 = None to 3 = intense). The daily UAS scores ranged from 0 to 6 points per day. Daily UAS scores were summed over a 7-day period to create the UAS7, ranging from 0 to 42, and are composed of the HSS7 and ISS7 components. A higher score indicates worse disease. Here, a score ≤6 indicates well-controlled disease. Omalizumab-naïve population consisted of all randomized omalizumab-naïve participants. Participants were analyzed according to the study treatment allocated by the randomization.

End point type	Secondary

End point timeframe:

At Week 12

End point values	DB Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	DB Period: Rilzabrutinib 400 mg BID + Placebo	DB Period: Rilzabrutinib 400 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	35	35
Units: percentage of participants				
number (not applicable)	11.1	5.4	20.0	34.3

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Hives Severity Score (HSS7) at Week 12

End point title	Change From Baseline in Weekly Hives Severity Score (HSS7) at Week 12

End point description:

The HSS7 represents hive severity score on a scale recorded on e-diary ranging from 0 (None) to 3 (more than 50 hives). A weekly score (HSS7) was sum of the average daily scores of the previous 7 days. The possible range of the weekly score was 0-21 (highest hives activity). Baseline is defined as the sum of the 7 days measurements obtained on and prior to the target visit day. Omalizumab-naïve population consisted of all randomized omalizumab-naïve participants. Participants were analyzed according to the study treatment allocated by the randomization. Only participants with data collected at Baseline and Week 12 are reported.

End point type	Secondary

End point timeframe:

Baseline and Week 12

End point values	DB Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	DB Period: Rilzabrutinib 400 mg BID + Placebo	DB Period: Rilzabrutinib 400 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	32	30	26	28
Units: score on a scale				
least squares mean (standard error)	-4.40 (± 1.06)	-4.49 (± 1.04)	-6.52 (± 1.07)	-7.64 (± 1.06)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Weekly Urticaria Activity Score Equal to 0 at Week 12

End point title	Percentage of Participants With Weekly Urticaria Activity Score Equal to 0 at Week 12

End point description:

The UAS7 score is a composite score containing both the hive severity score (HSS, ranging from 0 = None to 3 = more than 50 hives) and the itch severity score (ISS, ranging from 0 = None to 3 = intense). The daily UAS scores ranged from 0 to 6 points per day. Daily UAS scores were summed over a 7-day period to create the UAS7, ranging from 0 to 42, and are composed of the HSS7 and ISS7 components. A higher score indicates worse disease. Here, score 0 indicates an absence of both itches and hives and a complete resolution of CSU symptoms. Omalizumab-naïve population consisted of all randomized omalizumab-naïve participants. Participants were analyzed according to the study treatment allocated by the randomization.

End point type	Secondary

End point timeframe:

At Week 12

End point values	DB Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	DB Period: Rilzabrutinib 400 mg BID + Placebo	DB Period: Rilzabrutinib 400 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	36	37	35	35
Units: percentage of participants				
number (not applicable)	11.1	2.7	14.3	20.0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (TESAEs), Treatment-Emergent Adverse Events of Special Interest (AESIs), and Withdrawals due to Treatment-Emergent Adverse Events

End point title	Number of Participants With Treatment-Emergent Adverse Events (TEAEs), Treatment-Emergent Serious Adverse Events (TESAEs), Treatment-Emergent Adverse Events of Special Interest (AESIs), and Withdrawals due to Treatment-Emergent Adverse Events

End point description:

Adverse event (AE): any untoward medical occurrence in participant or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. TEAEs: AEs that developed or worsened or became serious during TE period, defined as time from first administration of study treatment (on Day 1) to last administration of study treatment + 7 days. SAE: any AE, at any dose: resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or was a medically important event. An AESI was an TEAE (serious or nonserious) of scientific and medical concern specific to Sponsor’s product or program. Safety population consisted of all randomized participants who took at least 1 dose of study treatment. Participants were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

From first dose of study treatment (Day 1) up to last dose of study treatment + 7 days, approximately 13 weeks for DB period) and approximately 41 weeks for OLE period

End point values	DB Period: Placebo TID	OLE Period: Rilzabrutinib 400 mg BID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	OLE Period: Rilzabrutinib 400 mg TID
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	9	38	128
Units: participants				
TEAEs	23	7	23	89
TESAEs	1	1	0	4
Treatment-Emergent AESIs	2	4	4	5
Withdrawals due to TEAEs	0	0	0	6

End point values	DB Period: Rilzabrutinib 400 mg BID + Placebo	DB Period: Rilzabrutinib 400 mg TID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: participants				
TEAEs	30	31		
TESAEs	0	2		
Treatment-Emergent AESIs	4	3		
Withdrawals due to TEAEs	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Rilzabrutinib

End point title	Plasma Concentration of Rilzabrutinib[1]

End point description:

Plasma samples were collected at specified timepoints for evaluation of rilzabrutinib pharmacokinetic (PK) concentrations. PK population consisted of safety population without important deviation related to study treatment administration, and with at least 1 post-baseline PK sample with adequate documentation of dosing and sampling dates and times. Participants having received only placebo were not part of the PK population. Participants were analyzed according to the study treatment they actually received. Only participants who received study treatment with data collected at specified timepoints are reported and denoted by 'n' in categories. Here, '9999' indicates data was not calculated as 0 participants were analyzed.

End point type	Secondary

End point timeframe:

Pre-dose and 2 hours post-dose at Day 1 and Week 4; pre-dose at Week 12 (DB period); pre-dose and 2 hours post-dose at Week 16; pre-dose at Weeks 20, 24 and 52 (OLE period)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only participants who received rilzabrutinib were analyzed for this endpoint.

End point values	OLE Period: Rilzabrutinib 400 mg BID	OLE Period: Rilzabrutinib 400 mg TID	DB Period: Rilzabrutinib 400 mg TID	DB Period: Rilzabrutinib 400 mg QPM
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	6	106	39	36
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1: pre-dose (n= 38,0,0,36,40)	9999 (± 9999)	9999 (± 9999)	0.00 (± 0.00)	0.00 (± 0.00)
Day 1: 2 hours post-dose (n= 38,0,0,35,40)	9999 (± 9999)	9999 (± 9999)	181.16 (± 139.41)	1.43 (± 8.49)
Week 4: pre-dose (n= 39,0,0,33,38)	9999 (± 9999)	9999 (± 9999)	27.73 (± 67.72)	13.83 (± 26.40)
Week 4: 2 hours post-dose (n= 38,0,0,34,35)	9999 (± 9999)	9999 (± 9999)	266.13 (± 232.15)	5.63 (± 9.60)
Week 12: pre-dose (n= 31,0,0,32,28)	9999 (± 9999)	9999 (± 9999)	25.18 (± 76.01)	5.68 (± 7.79)
Week 16: pre-dose (n= 0,6,106,0,0)	2.49 (± 1.66)	24.90 (± 44.17)	9999 (± 9999)	9999 (± 9999)
Week 16: 2 hours post-dose (n= 0,6,101,0,0)	153.22 (± 145.99)	236.47 (± 204.47)	9999 (± 9999)	9999 (± 9999)
Week 20: pre-dose (n= 0,6,95,0,0)	1.97 (± 0.82)	34.85 (± 83.79)	9999 (± 9999)	9999 (± 9999)
Week 24: pre-dose (n= 0,6,100,0,0)	3.31 (± 1.40)	16.01 (± 29.32)	9999 (± 9999)	9999 (± 9999)
Week 52: pre-dose (n= 0,4,70,0,0)	3.51 (± 1.96)	20.77 (± 39.33)	9999 (± 9999)	9999 (± 9999)

End point values	DB Period: Rilzabrutinib 400 mg BID			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1: pre-dose (n= 38,0,0,36,40)	0.00 (± 0.00)			
Day 1: 2 hours post-dose (n= 38,0,0,35,40)	133.77 (± 113.67)			
Week 4: pre-dose (n= 39,0,0,33,38)	26.46 (± 62.95)			
Week 4: 2 hours post-dose (n= 38,0,0,34,35)	186.40 (± 122.19)			
Week 12: pre-dose (n= 31,0,0,32,28)	11.83 (± 18.80)			
Week 16: pre-dose (n= 0,6,106,0,0)	9999 (± 9999)			
Week 16: 2 hours post-dose (n= 0,6,101,0,0)	9999 (± 9999)			
Week 20: pre-dose (n= 0,6,95,0,0)	9999 (± 9999)			
Week 24: pre-dose (n= 0,6,100,0,0)	9999 (± 9999)			
Week 52: pre-dose (n= 0,4,70,0,0)	9999 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study treatment (Day 1) up to last dose+7 days (approximately 13 weeks: DB period) and (approximately 41 weeks: OLE period). Death was assessed from signing of informed consent form up to approximately 125 weeks.

Adverse event reporting additional description:

Analysis was performed on safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	DB Period: Placebo TID

Reporting group description:

Participants received 1 tablet of matching placebo orally TID from Day 1 to Week 12 during the DB period.

Reporting group title	DB Period: Rilzabrutinib 400 mg QPM + Placebo

Reporting group description:

Participants received 1 tablet of rilzabrutinib 400 mg orally QPM and 2 tablets of matching placebo daily from Day 1 to Week 12 during the DB period.

Reporting group title	OLE Period: Rilzabrutinib 400 mg TID

Reporting group description:

Participants who completed DB period entered the OLE period received 1 tablet of rilzabrutinib 400 mg orally TID from Week 13 to Week 52.

Reporting group title	DB Period: Rilzabrutinib 400 mg TID

Reporting group description:

Participants received 1 tablet of rilzabrutinib 400 mg orally TID from Day 1 to Week 12 during the DB period.

Reporting group title	OLE Period: Rilzabrutinib 400 mg BID

Reporting group description:

Participants who completed DB period entered the OLE period received 1 tablet of rilzabrutinib 400 mg orally BID from Week 13 to Week 52.

Reporting group title	DB Period: Rilzabrutinib 400 mg BID + Placebo

Reporting group description:

Participants received 1 tablet of rilzabrutinib 400 mg orally BID and 1 tablet of matching placebo daily from Day 1 to Week 12 during the DB period.

Serious adverse events	DB Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	OLE Period: Rilzabrutinib 400 mg TID
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	0 / 38 (0.00%)	4 / 128 (3.13%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Iatrogenic Injury			

subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (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
Ligament Rupture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (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
Joint Dislocation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (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
Immune system disorders			
Anaphylactic Shock			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Vogt-Koyanagi-Harada Disease			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar Abscess			

subjects affected / exposed	1 / 40 (2.50%)	0 / 38 (0.00%)	0 / 128 (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

Serious adverse events	DB Period: Rilzabrutinib 400 mg TID	OLE Period: Rilzabrutinib 400 mg BID	DB Period: Rilzabrutinib 400 mg BID + Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 41 (4.88%)	1 / 9 (11.11%)	0 / 41 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Iatrogenic Injury			
subjects affected / exposed	1 / 41 (2.44%)	0 / 9 (0.00%)	0 / 41 (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
Ligament Rupture			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (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
Joint Dislocation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (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
Immune system disorders			
Anaphylactic Shock			
subjects affected / exposed	0 / 41 (0.00%)	0 / 9 (0.00%)	0 / 41 (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
Eye disorders			
Vogt-Koyanagi-Harada Disease			
subjects affected / exposed	0 / 41 (0.00%)	0 / 9 (0.00%)	0 / 41 (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
Skin and subcutaneous tissue disorders			
Urticaria			

subjects affected / exposed	1 / 41 (2.44%)	0 / 9 (0.00%)	0 / 41 (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
Infections and infestations			
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 41 (0.00%)	0 / 9 (0.00%)	0 / 41 (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
Peritonsillar Abscess			
subjects affected / exposed	0 / 41 (0.00%)	0 / 9 (0.00%)	0 / 41 (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 Period: Placebo TID	DB Period: Rilzabrutinib 400 mg QPM + Placebo	OLE Period: Rilzabrutinib 400 mg TID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 40 (35.00%)	20 / 38 (52.63%)	59 / 128 (46.09%)
General disorders and administration site conditions			
Peripheral Swelling			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 40 (2.50%)	1 / 38 (2.63%)	1 / 128 (0.78%)
occurrences (all)	1	1	1
Reproductive system and breast disorders			
Abnormal Uterine Bleeding			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 40 (0.00%)	2 / 38 (5.26%)	0 / 128 (0.00%)
occurrences (all)	0	2	0

Epistaxis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Sleep Disorder			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 40 (0.00%)	2 / 38 (5.26%)	1 / 128 (0.78%)
occurrences (all)	0	2	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 40 (0.00%)	2 / 38 (5.26%)	7 / 128 (5.47%)
occurrences (all)	0	2	8
Hypoaesthesia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	1 / 40 (2.50%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences (all)	1	0	1
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Presbyopia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal Pain			
subjects affected / exposed	2 / 40 (5.00%)	1 / 38 (2.63%)	5 / 128 (3.91%)
occurrences (all)	2	4	5
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 40 (0.00%)	1 / 38 (2.63%)	2 / 128 (1.56%)
occurrences (all)	0	1	2
Dyspepsia			
subjects affected / exposed	1 / 40 (2.50%)	2 / 38 (5.26%)	1 / 128 (0.78%)
occurrences (all)	1	2	1
Diarrhoea			
subjects affected / exposed	6 / 40 (15.00%)	3 / 38 (7.89%)	19 / 128 (14.84%)
occurrences (all)	6	3	24
Abdominal Pain Upper			
subjects affected / exposed	0 / 40 (0.00%)	1 / 38 (2.63%)	2 / 128 (1.56%)
occurrences (all)	0	1	2
Nausea			
subjects affected / exposed	2 / 40 (5.00%)	5 / 38 (13.16%)	17 / 128 (13.28%)
occurrences (all)	2	5	19
Gastritis Erosive			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic Steatosis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Chronic Spontaneous Urticaria			
subjects affected / exposed	0 / 40 (0.00%)	3 / 38 (7.89%)	1 / 128 (0.78%)
occurrences (all)	0	4	1
Urticaria			
subjects affected / exposed	3 / 40 (7.50%)	3 / 38 (7.89%)	7 / 128 (5.47%)
occurrences (all)	3	3	8
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Nocturia			

subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	5 / 128 (3.91%)
occurrences (all)	0	0	7
Muscle Spasms			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Covid-19			
subjects affected / exposed	2 / 40 (5.00%)	2 / 38 (5.26%)	2 / 128 (1.56%)
occurrences (all)	2	2	2
Nasopharyngitis			
subjects affected / exposed	2 / 40 (5.00%)	1 / 38 (2.63%)	9 / 128 (7.03%)
occurrences (all)	2	1	10
Sinusitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences (all)	0	0	1
Vulvovaginal Candidiasis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	1 / 128 (0.78%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 40 (0.00%)	0 / 38 (0.00%)	0 / 128 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	DB Period: Rilzabrutinib 400 mg TID	OLE Period: Rilzabrutinib 400 mg BID	DB Period: Rilzabrutinib 400 mg BID + Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 41 (60.98%)	7 / 9 (77.78%)	26 / 41 (63.41%)
General disorders and administration site conditions			
Peripheral Swelling			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Fatigue			

subjects affected / exposed	2 / 41 (4.88%)	1 / 9 (11.11%)	1 / 41 (2.44%)
occurrences (all)	2	1	1
Reproductive system and breast disorders			
Abnormal Uterine Bleeding			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	5	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 41 (0.00%)	0 / 9 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Sleep Disorder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	2	0
Agitation			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	3 / 41 (7.32%)	0 / 9 (0.00%)	1 / 41 (2.44%)
occurrences (all)	3	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	2 / 41 (4.88%)
occurrences (all)	0	1	3
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 41 (9.76%)	0 / 9 (0.00%)	6 / 41 (14.63%)
occurrences (all)	5	0	7
Hypoaesthesia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Sciatica			

subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Presbyopia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	5 / 41 (12.20%)
occurrences (all)	0	4	5
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 41 (2.44%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	1	1	0
Dyspepsia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 9 (11.11%)	1 / 41 (2.44%)
occurrences (all)	1	1	1
Diarrhoea			
subjects affected / exposed	12 / 41 (29.27%)	1 / 9 (11.11%)	12 / 41 (29.27%)
occurrences (all)	14	5	14
Abdominal Pain Upper			
subjects affected / exposed	1 / 41 (2.44%)	1 / 9 (11.11%)	1 / 41 (2.44%)
occurrences (all)	1	1	1
Nausea			
subjects affected / exposed	8 / 41 (19.51%)	1 / 9 (11.11%)	7 / 41 (17.07%)
occurrences (all)	8	1	7
Gastritis Erosive			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hepatic Steatosis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			

Chronic Spontaneous Urticaria			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	1 / 41 (2.44%)	0 / 9 (0.00%)	3 / 41 (7.32%)
occurrences (all)	1	0	4
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Nocturia			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 9 (11.11%)	3 / 41 (7.32%)
occurrences (all)	1	1	3
Muscle Spasms			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			
Covid-19			
subjects affected / exposed	2 / 41 (4.88%)	3 / 9 (33.33%)	4 / 41 (9.76%)
occurrences (all)	2	3	4
Nasopharyngitis			
subjects affected / exposed	2 / 41 (4.88%)	3 / 9 (33.33%)	1 / 41 (2.44%)
occurrences (all)	2	4	1
Sinusitis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	1 / 41 (2.44%)
occurrences (all)	0	1	1
Vulvovaginal Candidiasis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 9 (11.11%)	0 / 41 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased Appetite			

subjects affected / exposed occurrences (all)	1 / 41 (2.44%) 1	1 / 9 (11.11%) 1	0 / 41 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 February 2022	The main purpose of this amendment was to incorporate feedback from health authorities, expand the population to include omalizumab-incomplete responders, as well as other clarifications and corrections deemed necessary by the Sponsor. In addition, other minor editorial changes (e.g, grammatical and minor typographical error corrections) were implemented throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported