



Clinical trial results:

A Phase 2, Long-Term Extension (LTE) Study With Elsubrutinib and Upadacitinib Given Alone or in Combination (ABBV-599) in Subjects With Moderately to Severely Active Systemic Lupus Erythematosus Who Have Completed the M19-130 Phase 2 Randomized Controlled Trial (RCT)

Summary

EudraCT number	2020-001690-72
Trial protocol	NL HU DE BG IT
Global end of trial date	03 January 2024

Results information

Result version number	v1 (current)
This version publication date	04 January 2025
First version publication date	04 January 2025

Trial information

Trial identification

Sponsor protocol code	M20-186
-----------------------	---------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04451772
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co. KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.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	03 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 January 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Systemic Lupus Erythematosus (SLE) is an immune-mediated disease associated with inflammation of multiple organ systems. This study will evaluate how well elsubrutinib and upadacitinib given alone or as the ABBV-599 combination (elsubrutinib/upadacitinib) works within the body, in participants who completed study M19-130. This study will assess the change in disease symptoms.

ABBV-599 is an investigational drug being developed for the treatment of Systemic Lupus Erythematosus (SLE). Adult participants with a diagnosis of SLE will be enrolled and will receive oral elsubrutinib capsules and/or oral upadacitinib tablets once daily for up to 56 weeks. Participants who were receiving elsubrutinib and/or upadacitinib in M19-130 will continue to receive the same treatment in this study. Participants who were receiving placebo in M19-130 will be re-randomized to one of the 2 combination treatment arms in this study.

Protection of trial subjects:

Subjects or their legally authorized representative (if required per local regulations) must have understood and personally, voluntarily signed and dated an informed consent, approved by an independent ethics committee (IEC)/institutional review board (IRB), prior to the initiation of any screening or study-specific procedures. In Japan, subjects under 20 years of age must have voluntarily signed and dated an informed consent, in addition to their parent or legal guardian. Legally authorized representation did not apply in the case of Germany and France, and protected persons such as minors, adults under guardianship, pregnant women, persons deprived of their liberty and persons incapable or unable to express their consent were not included in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 July 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 19
Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	China: 6
Country: Number of subjects enrolled	Colombia: 15
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Italy: 1

Country: Number of subjects enrolled	Japan: 13
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Mexico: 15
Country: Number of subjects enrolled	New Zealand: 3
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Puerto Rico: 10
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Taiwan: 16
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 46
Worldwide total number of subjects	185
EEA total number of subjects	34

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)	180
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects who completed Study M19-130 were eligible to enroll in this study. Only those subjects who met all of the specified eligibility criteria had the option to enter this long-term extension (LTE) study to receive continued therapy, provided the subject was willing and the investigator believed that continuing therapy was appropriate.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	ABBV-599 High Dose -> ABBV-599 High Dose

Arm description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsule; Oral

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Film-coated tablet; Oral

Arm title	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg
------------------	--

Arm description:

Participants received placebo capsules for elsubrutinib once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

Arm type	Experimental
----------	--------------

Investigational medicinal product name	Placebo for Elsubrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsule; Oral

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Film-coated tablet; Oral

Arm title	Els Pbo/Upa Pbo -> ABBV-599 High Dose
------------------	---------------------------------------

Arm description:

Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day in the current study (M20-186) for up to 56 weeks.

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsule; Oral

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Film-coated tablet; Oral

Arm title	ABBV-599 Low -> ABBV-599 Low
------------------	------------------------------

Arm description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsule; Oral

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Film-coated tablet; Oral

Arm title	Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo
------------------	--

Arm description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsule; Oral

Investigational medicinal product name	Placebo for Upadacitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Film-coated tablet; Oral

Arm title	Els + Upa Pbo -> ABBV-599 Low
------------------	-------------------------------

Arm description:

Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in the current study (M20-186) for up to 56 weeks.

Arm type	Experimental
Investigational medicinal product name	Elsubrutinib
Investigational medicinal product code	
Other name	ABBV-105
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsule; Oral

Investigational medicinal product name	Upadacitinib
Investigational medicinal product code	
Other name	ABT-494, RINVOQ
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Film-coated tablet; Oral

Number of subjects in period 1	ABBV-599 High Dose -> ABBV-599 High Dose	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg	Els Pbo/Upa Pbo -> ABBV-599 High Dose
Started	45	47	35
Completed	41	38	31
Not completed	4	9	4
Sponsor decision based on interim analysis data	-	-	-
Adverse event, non-fatal	1	-	1
Other, not specified	1	2	1
Withdrawal by subject	2	7	2

Number of subjects in period 1	ABBV-599 Low -> ABBV-599 Low	Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo	Els + Upa Pbo -> ABBV-599 Low
Started	19	25	14
Completed	6	1	1
Not completed	13	24	13
Sponsor decision based on interim analysis data	11	23	9
Adverse event, non-fatal	1	-	3
Other, not specified	-	-	1
Withdrawal by subject	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	ABBV-599 High Dose -> ABBV-599 High Dose
Reporting group description:	
Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.	
Reporting group title	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg
Reporting group description:	
Participants received placebo capsules for elsubrutinib once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.	
Reporting group title	Els Pbo/Upa Pbo -> ABBV-599 High Dose
Reporting group description:	
Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day in the current study (M20-186) for up to 56 weeks.	
Reporting group title	ABBV-599 Low -> ABBV-599 Low
Reporting group description:	
Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.	
Reporting group title	Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo
Reporting group description:	
Participants received elsubrutinib 60 mg capsules once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.	
Reporting group title	Els + Upa Pbo -> ABBV-599 Low
Reporting group description:	
Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in the current study (M20-186) for up to 56 weeks.	

Reporting group values	ABBV-599 High Dose -> ABBV-599 High Dose	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg	Els Pbo/Upa Pbo -> ABBV-599 High Dose
Number of subjects	45	47	35
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	42.8 ± 11.39	42.5 ± 12.00	40.6 ± 11.75
Gender categorical Units: Subjects			
Female	42	42	35
Male	3	5	0

Race			
Units: Subjects			
American Indian or Alaska Native	3	0	2
Asian	6	10	12
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	6	0
White	32	26	20
More than one race	2	5	1
Unknown or Not Reported	0	0	0

Reporting group values	ABBV-599 Low -> ABBV-599 Low	Els 60 mg/Upa Pbo - > Els 60 mg/Upa Pbo	Els + Upa Pbo -> ABBV-599 Low
Number of subjects	19	25	14
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	38.3	41.2	42.5
standard deviation	± 10.52	± 11.60	± 11.57
Gender categorical			
Units: Subjects			
Female	18	24	14
Male	1	1	0
Race			
Units: Subjects			
American Indian or Alaska Native	1	2	0
Asian	6	3	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	1
White	10	16	10
More than one race	1	3	1
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	185		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	175		
Male	10		

Race			
Units: Subjects			
American Indian or Alaska Native	8		
Asian	39		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	11		
White	114		
More than one race	13		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	ABBV-599 High Dose -> ABBV-599 High Dose
Reporting group description: Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.	
Reporting group title	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg
Reporting group description: Participants received placebo capsules for elsubrutinib once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.	
Reporting group title	Els Pbo/Upa Pbo -> ABBV-599 High Dose
Reporting group description: Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day in the current study (M20-186) for up to 56 weeks.	
Reporting group title	ABBV-599 Low -> ABBV-599 Low
Reporting group description: Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.	
Reporting group title	Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo
Reporting group description: Participants received elsubrutinib 60 mg capsules once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.	
Reporting group title	Els + Upa Pbo -> ABBV-599 Low
Reporting group description: Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in the current study (M20-186) for up to 56 weeks.	

Primary: Number of Participants With Treatment-Emergent Adverse Events

End point title	Number of Participants With Treatment-Emergent Adverse Events ^[1]
End point description: Adverse event (AE): any untoward medical occurrence in a patient/clinical investigation subject administered a pharmaceutical product and which doesn't necessarily have a causal relationship with this Tx. Serious adverse event (SAE): an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs) are defined as an adverse event with an onset date that is on or after the first dose of study drug from Study M20-186, and no more than 30 days after the last dose of study drug from Study M20-186. For more details on adverse events please see the Adverse Event section.	
Analysis population: subjects rcvd ≥ 1 dose of study drug in Study M20-186, grouped by Tx rcvd	
End point type	Primary

End point timeframe:

From the first dose of study drug in Study M20-186 up to 30 days after the last dose of study drug, up to 442 days

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive data are summarized for this end point per protocol.

End point values	ABBV-599 High Dose -> ABBV-599 High Dose	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg	Els Pbo/Upa Pbo -> ABBV-599 High Dose	ABBV-599 Low -> ABBV-599 Low
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	47	35	19
Units: participants				
Any TEAE	34	31	30	11
TESAE	5	5	1	2

End point values	Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo	Els + Upa Pbo -> ABBV-599 Low		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	14		
Units: participants				
Any TEAE	11	7		
TESAE	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving Systemic Lupus Erythematosus (SLE) Responder Index (SRI)-4

End point title	Percentage of Participants Achieving Systemic Lupus Erythematosus (SLE) Responder Index (SRI)-4 ^[2]
-----------------	--

End point description:

SLE Responder Index (SRI)-4 is defined as follows with all criteria compared to Baseline in Study M19-130:

- ≥4-point reduction in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score
- No worsening of the overall condition (< 0.3 point increase in Physician's Global Assessment [PhGA])
- No new British Isles Lupus Assessment Group (BILAG) A or more than 1 new BILAG B disease activity scores (i.e., no organ system changes from baseline B/C/D/E to A and no more than 1 organ system changes from baseline C/D/E to B). A letter score is assigned to each organ system with following indications: A = severe, B = moderate, C = mild, D = inactive with prior history, and E = inactive with no history.

Analysis population: Full Analysis Set: all randomized subjects who received at least 1 dose of study drug in Study M20-186; as observed (AO) analysis.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline of Study M19-130 (Week 0), Weeks 56, 64, 72, 80, 88, 96, 104

Notes:

[2] - 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: When 50% of planned participants in Study M19-130 had completed Week 24 or withdrawn from the study, the ABBV-599 Low Dose and elsubrutinib 60 mg treatment groups were terminated as these groups did not meet projected efficacy. Per protocol, terminated groups were removed from the efficacy analyses.

End point values	ABBV-599 High Dose -> ABBV-599 High Dose	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg	Els Pbo/Upa Pbo -> ABBV-599 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	46	35	
Units: percentage of participants				
number (confidence interval 95%)				
Week 56 (n=45, 46, 35)	71.1 (57.9 to 84.4)	76.1 (63.8 to 88.4)	54.3 (37.8 to 70.8)	
Week 64 (n=44, 45, 34)	70.5 (57.0 to 83.9)	75.6 (63.0 to 88.1)	58.8 (42.3 to 75.4)	
Week 72 (n=41, 45, 34)	80.5 (68.4 to 92.6)	88.9 (79.7 to 98.1)	64.7 (48.6 to 80.8)	
Week 80 (n=40, 45, 33)	75.0 (61.6 to 88.4)	82.2 (71.1 to 93.4)	57.6 (40.7 to 74.4)	
Week 88 (n=40, 42, 33)	82.5 (70.7 to 94.3)	85.7 (75.1 to 96.3)	48.5 (31.4 to 65.5)	
Week 96 (n=41, 39, 32)	82.9 (71.4 to 94.4)	76.9 (63.7 to 90.1)	62.5 (45.7 to 79.3)	
Week 104 (n=41, 39, 31)	85.4 (74.5 to 96.2)	82.1 (70.0 to 94.1)	61.3 (44.1 to 78.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Achieving British Isles Lupus Assessment Group (BILAG)-Based Combined Lupus Assessment (BICLA) Response

End point title	Percentage of Participants Achieving British Isles Lupus Assessment Group (BILAG)-Based Combined Lupus Assessment (BICLA) Response ^[3]
-----------------	---

End point description:

BICLA is a composite responder index. Achievement of BICLA response is defined as improvement in all initial A and B BILAG scores, with no more than one new BILAG B score without worsening of the overall condition (no worsening in Physician's Global Assessment [PhGA], < 0.3 point increase) and no worsening of the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score.

Analysis population: Full Analysis Set: all randomized participants who received at least 1 dose of study drug in Study M20-186; as observed (AO) analysis.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline of Study M19-130 (Week 0), Weeks 56, 64, 72, 80, 88, 96, 104

Notes:

[3] - 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: When 50% of planned participants in Study M19-130 had completed Week 24 or withdrawn from the study, the ABBV-599 Low Dose and elsubrutinib 60 mg treatment groups were terminated as these groups did not meet projected efficacy. Per protocol, terminated groups were removed from the efficacy analyses.

End point values	ABBV-599 High Dose -> ABBV-599 High Dose	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg	Els Pbo/Upa Pbo -> ABBV-599 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	46	35	
Units: percentage of participants				
number (confidence interval 95%)				
Week 56 (n=45, 46, 35)	73.3 (60.4 to 86.3)	67.4 (53.8 to 80.9)	60.0 (43.8 to 76.2)	
Week 64 (n=44, 45, 34)	75.0 (62.2 to 87.8)	84.4 (73.9 to 95.0)	55.9 (39.2 to 72.6)	
Week 72 (n=41, 45, 34)	73.2 (59.6 to 86.7)	88.9 (79.7 to 98.1)	61.8 (45.4 to 78.1)	
Week 80 (n=40, 45, 33)	70.0 (55.8 to 84.2)	77.8 (65.6 to 89.9)	57.6 (40.7 to 74.4)	
Week 88 (n=40, 42, 33)	80.0 (67.6 to 92.4)	85.7 (75.1 to 96.3)	57.6 (40.7 to 74.4)	
Week 96 (n=41, 39, 32)	78.0 (65.4 to 90.7)	76.9 (63.7 to 90.1)	59.4 (42.4 to 76.4)	
Week 104 (n=41, 39, 31)	78.0 (65.4 to 90.7)	69.2 (54.7 to 83.7)	54.8 (37.3 to 72.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Daily Prednisone Dose Over Time

End point title	Change From Baseline in Daily Prednisone Dose Over Time ^[4]
-----------------	--

End point description:

Participants' current use of steroid therapy was assessed at each study visit, and the amount of daily prednisone was documented.

Analysis population: Full Analysis Set: all randomized participants who received at least 1 dose of study drug in Study M20-186; as observed (AO) analysis.

End point type	Secondary
----------------	-----------

End point timeframe:

Baseline of M19-130 (Week 0), Weeks 56, 64, 72, 80, 88, 96, 104

Notes:

[4] - 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: When 50% of planned participants in Study M19-130 had completed Week 24 or withdrawn from the study, the ABBV-599 Low Dose and elsubrutinib 60 mg treatment groups were terminated as these groups did not meet projected efficacy. Per protocol, terminated groups were removed from the efficacy analyses.

End point values	ABBV-599 High Dose -> ABBV-599 High Dose	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg	Els Pbo/Upa Pbo -> ABBV-599 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	35	
Units: mg				
arithmetic mean (standard deviation)				
Week 56 (n=45, 47, 35)	-3.9 (± 5.96)	-3.5 (± 5.99)	-4.9 (± 6.99)	
Week 64 (n=45, 46, 35)	-4.2 (± 5.51)	-3.7 (± 5.97)	-5.0 (± 6.87)	
Week 72 (n=42, 46, 34)	-4.0 (± 6.59)	-4.9 (± 7.23)	-5.2 (± 6.88)	
Week 80 (n=41, 45, 34)	-5.1 (± 5.96)	-4.4 (± 8.05)	-5.2 (± 6.88)	
Week 88 (n=41, 42, 33)	-5.5 (± 5.83)	-5.2 (± 6.02)	-6.2 (± 7.04)	
Week 96 (n=41, 40, 32)	-5.5 (± 5.88)	-5.7 (± 5.78)	-7.3 (± 6.54)	
Week 104 (n=41, 39, 31)	-5.8 (± 6.02)	-5.5 (± 5.65)	-7.7 (± 6.64)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Flares Per Patient-year by Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) SLE Disease Activity Index (SLEDAI) Flare Index Through Week 104

End point title	Number of Flares Per Patient-year by Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA) SLE Disease Activity Index (SLEDAI) Flare Index Through Week 104 ^[5]
-----------------	--

End point description:

The SELENA SLEDAI flare index defines mild/moderate or severe SLE flares using the SLEDAI score, definitions of worsening signs and symptoms, treatment changes, and Physician's Global Assessment of Disease Activity.

Analysis population: Full Analysis Set: all randomized participants who received at least 1 dose of study drug in Study M20-186; as observed (AO) analysis.

End point type	Secondary
----------------	-----------

End point timeframe:

From Week 56 through Week 104

Notes:

[5] - 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: When 50% of planned participants in Study M19-130 had completed Week 24 or withdrawn from the study, the ABBV-599 Low Dose and elsubrutinib 60 mg treatment groups were terminated as these groups did not meet projected efficacy. Per protocol, terminated groups were removed from the efficacy analyses.

End point values	ABBV-599 High Dose -> ABBV-599 High Dose	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg	Els Pbo/Upa Pbo -> ABBV-599 High Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	47	35	
Units: Events per patient-year				
number (confidence interval 95%)				
Mild/Moderate	0.62 (0.39 to 0.84)	1.41 (1.06 to 1.75)	1.39 (0.99 to 1.78)	

Severe	0.00 (0.00 to 0.00)	0.04 (-0.02 to 0.10)	0.17 (0.03 to 0.31)	
Overall	0.62 (0.39 to 0.84)	1.45 (1.10 to 1.80)	1.56 (1.14 to 1.97)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and adverse events were collected from the time informed consent was signed through the end of the study.

Adverse event reporting additional description:

Median time on follow-up was for 422 days for the ABBV-599 High -> ABBV-599 High group; 423 days for the Upa -> Upa and Pbo -> ABBV-599 High groups; 245 days for the ABBV-599 Low -> ABBV-599 Low group; 163 days for the Els -> Els group; and 142.5 days for the Pbo -> ABBV-599 Low group.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	26.0
--------------------	------

Reporting groups

Reporting group title	ABBV-599 High Dose -> ABBV-599 High Dose
-----------------------	--

Reporting group description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg filmcoated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

Reporting group title	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg
-----------------------	--

Reporting group description:

Participants received placebo capsules for elsubrutinib once a day by mouth and upadacitinib 30 mg film-coated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

Reporting group title	Els Pbo/Upa Pbo -> ABBV-599 High Dose
-----------------------	---------------------------------------

Reporting group description:

Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 30 mg film-coated tablets once a day in the current study (M20-186) for up to 56 weeks.

Reporting group title	ABBV-599 Low -> ABBV-599 Low
-----------------------	------------------------------

Reporting group description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg filmcoated tablets once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

Reporting group title	Els 60 mg/Upa Pbo -> Els 60 mg/Upa Pbo
-----------------------	--

Reporting group description:

Participants received elsubrutinib 60 mg capsules once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants continued on this regimen in the current study (M20-186) for up to 56 weeks.

Reporting group title	Els + Upa Pbo -> ABBV-599 Low
-----------------------	-------------------------------

Reporting group description:

Participants received placebo capsules for elsubrutinib once a day by mouth and placebo film-coated tablets for upadacitinib once a day by mouth for 48 weeks in Study M19-130. Participants received elsubrutinib 60 mg capsules once a day by mouth and upadacitinib 15 mg film-coated tablets once a day by mouth for 48 weeks in the current study (M20-186) for up to 56 weeks.

Serious adverse events	ABBV-599 High Dose -> ABBV-599 High Dose	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg	Els Pbo/Upa Pbo -> ABBV-599 High Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 45 (11.11%)	5 / 47 (10.64%)	1 / 35 (2.86%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (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			
FRACTURED SACRUM			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 35 (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
JOINT DISLOCATION			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 35 (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
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 35 (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
PELVIC FRACTURE			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 35 (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
SUBDURAL HAEMATOMA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (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
SKULL FRACTURED BASE			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (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
TRAUMATIC INTRACRANIAL HAEMORRHAGE			

subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (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
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 35 (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
Nervous system disorders			
CEREBRAL HAEMATOMA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (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 DISORDER			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (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
LUMBAR RADICULOPATHY			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MIGRAINE			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 35 (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
General disorders and administration site conditions			
SEROSITIS			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 35 (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
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 35 (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
Reproductive system and breast disorders			
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
SYSTEMIC LUPUS ERYTHEMATOSUS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (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			
ABSCESS LIMB			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA SEPSIS			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 35 (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
GASTROENTERITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (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
TONSILLITIS			

subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 35 (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
Metabolism and nutrition disorders			
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (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

Serious adverse events	ABBV-599 Low -> ABBV-599 Low	Els 60 mg/Upa Pbo - > Els 60 mg/Upa Pbo	Els + Upa Pbo -> ABBV-599 Low
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 19 (10.53%)	1 / 25 (4.00%)	2 / 14 (14.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
UTERINE LEIOMYOMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
FRACTURED SACRUM			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
PELVIC FRACTURE			

subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
SUBDURAL HAEMATOMA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (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
SKULL FRACTURED BASE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (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
TRAUMATIC INTRACRANIAL HAEMORRHAGE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (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
Surgical and medical procedures			
ABORTION INDUCED			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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			
CEREBRAL HAEMATOMA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (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
NERVOUS SYSTEM DISORDER			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (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
LUMBAR RADICULOPATHY			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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

MIGRAINE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
General disorders and administration site conditions			
SEROSITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
Gastrointestinal disorders			
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
Reproductive system and breast disorders			
CERVICAL DYSPLASIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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			
SYSTEMIC LUPUS ERYTHEMATOSUS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABSCESS LIMB			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
COVID-19			

subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
ESCHERICHIA SEPSIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
GASTROENTERITIS			
subjects affected / exposed	0 / 19 (0.00%)	1 / 25 (4.00%)	0 / 14 (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
TONSILLITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (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
Metabolism and nutrition disorders			
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (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

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

Non-serious adverse events	ABBV-599 High Dose -> ABBV-599 High Dose	Els Pbo/Upa 30 mg -> Els Pbo/Upa 30 mg	Els Pbo/Upa Pbo -> ABBV-599 High Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 45 (53.33%)	18 / 47 (38.30%)	30 / 35 (85.71%)
Vascular disorders			
HAEMATOMA			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 35 (0.00%)
occurrences (all)	0	4	0
HYPERTENSION			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
HYPOTENSION			

subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
GRANULOMA			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
OEDEMA			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
PYREXIA			
subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 2	1 / 47 (2.13%) 1	1 / 35 (2.86%) 1
OEDEMA PERIPHERAL			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
Reproductive system and breast disorders			
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
DYSпноEA			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	1 / 47 (2.13%) 1	2 / 35 (5.71%) 2
NASAL CONGESTION			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
HYPERSENSITIVITY PNEUMONITIS			
subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0

SINUS PAIN subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
Psychiatric disorders INSOMNIA subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	1 / 35 (2.86%) 1
Investigations NEUTROPHIL COUNT DECREASED subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 2	0 / 47 (0.00%) 0	1 / 35 (2.86%) 1
Injury, poisoning and procedural complications ANIMAL BITE subjects affected / exposed occurrences (all) FALL subjects affected / exposed occurrences (all) IMMUNISATION REACTION subjects affected / exposed occurrences (all) LOWER LIMB FRACTURE subjects affected / exposed occurrences (all) SKIN LACERATION subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0 0 / 45 (0.00%) 0 0 / 45 (0.00%) 0 0 / 45 (0.00%) 0 0 / 45 (0.00%) 0	0 / 47 (0.00%) 0 0 / 47 (0.00%) 0 0 / 47 (0.00%) 0 0 / 47 (0.00%) 1 / 47 (2.13%) 2	2 / 35 (5.71%) 2 0 / 35 (0.00%) 0 0 / 35 (0.00%) 0 0 / 35 (0.00%) 0 0 / 35 (0.00%) 0
Congenital, familial and genetic disorders TYPE V HYPERLIPIDAEMIA subjects affected / exposed occurrences (all) PYLORIC STENOSIS subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0 0 / 45 (0.00%) 0	0 / 47 (0.00%) 0 0 / 47 (0.00%) 0	0 / 35 (0.00%) 0 0 / 35 (0.00%) 0
Cardiac disorders			

MITRAL VALVE INCOMPETENCE subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
Nervous system disorders			
MIGRAINE subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	3 / 35 (8.57%) 3
HEADACHE subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 3	1 / 47 (2.13%) 1	2 / 35 (5.71%) 2
DIZZINESS subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
BRAIN OEDEMA subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
POST HERPETIC NEURALGIA subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	1 / 35 (2.86%) 1
SYNCOPE subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
Blood and lymphatic system disorders			
LEUKOCYTOSIS subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
ANAEMIA subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
IRON DEFICIENCY ANAEMIA subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
THROMBOCYTOSIS subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 47 (0.00%) 0	0 / 35 (0.00%) 0
Eye disorders			

CATARACT			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
DRY EYE			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
DUODENAL ULCER			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
GASTRITIS			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
IMPAIRED GASTRIC EMPTYING			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
LARGE INTESTINAL ULCER			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	0 / 35 (0.00%)
occurrences (all)	2	1	0
Skin and subcutaneous tissue disorders			

RASH			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	2 / 35 (5.71%)
occurrences (all)	1	0	2
PRURITUS			
subjects affected / exposed	4 / 45 (8.89%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	5	0	0
CUTANEOUS VASCULITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
ACNE			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	2 / 35 (5.71%)
occurrences (all)	1	0	2
SKIN ULCER			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
LUPUS NEPHRITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
PROTEINURIA			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
ARTHRALGIA			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	2 / 35 (5.71%)
occurrences (all)	1	0	2
CONNECTIVE TISSUE DISORDER			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

CELLULITIS			
subjects affected / exposed	0 / 45 (0.00%)	3 / 47 (6.38%)	0 / 35 (0.00%)
occurrences (all)	0	6	0
COVID-19			
subjects affected / exposed	8 / 45 (17.78%)	11 / 47 (23.40%)	7 / 35 (20.00%)
occurrences (all)	8	11	7
DIVERTICULITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
EAR INFECTION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	2 / 35 (5.71%)
occurrences (all)	1	0	2
EPSTEIN-BARR VIRUS INFECTION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
HERPES ZOSTER			
subjects affected / exposed	2 / 45 (4.44%)	1 / 47 (2.13%)	1 / 35 (2.86%)
occurrences (all)	2	1	1
ORAL HERPES			
subjects affected / exposed	2 / 45 (4.44%)	2 / 47 (4.26%)	2 / 35 (5.71%)
occurrences (all)	2	2	2
NASOPHARYNGITIS			
subjects affected / exposed	3 / 45 (6.67%)	2 / 47 (4.26%)	2 / 35 (5.71%)
occurrences (all)	4	2	2
MYCOPLASMA INFECTION			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
OTITIS MEDIA			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
TINEA PEDIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	3

TINEA VERSICOLOUR			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
TONSILLITIS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 45 (8.89%)	3 / 47 (6.38%)	6 / 35 (17.14%)
occurrences (all)	5	4	7
URINARY TRACT INFECTION			
subjects affected / exposed	7 / 45 (15.56%)	3 / 47 (6.38%)	6 / 35 (17.14%)
occurrences (all)	9	7	8
VAGINAL INFECTION			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
HYPOCALCAEMIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 45 (0.00%)	0 / 47 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	ABBV-599 Low -> ABBV-599 Low	Els 60 mg/Upa Pbo - > Els 60 mg/Upa	Els + Upa Pbo -> ABBV-599 Low
-----------------------------------	---------------------------------	--	----------------------------------

		Pbo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 19 (57.89%)	4 / 25 (16.00%)	6 / 14 (42.86%)
Vascular disorders			
HAEMATOMA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
HYPERTENSION			
subjects affected / exposed	2 / 19 (10.53%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	1
HYPOTENSION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
GRANULOMA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
OEDEMA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
PYREXIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 19 (5.26%)	1 / 25 (4.00%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Reproductive system and breast disorders			
HEAVY MENSTRUAL BLEEDING			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1

Respiratory, thoracic and mediastinal disorders			
DYSпноEA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
HYPERSENSITIVITY PNEUMONITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
SINUS PAIN			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Investigations			
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
ANIMAL BITE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
IMMUNISATION REACTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
LOWER LIMB FRACTURE			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
SKIN LACERATION			

subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 2	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
Congenital, familial and genetic disorders TYPE V HYPERLIPIDAEMIA subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
PYLORIC STENOSIS subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
Cardiac disorders MITRAL VALVE INCOMPETENCE subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
Nervous system disorders MIGRAINE subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
HEADACHE subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
DIZZINESS subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
BRAIN OEDEMA subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
POST HERPETIC NEURALGIA subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 25 (0.00%) 0	1 / 14 (7.14%) 1
SYNCOPE subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
Blood and lymphatic system disorders LEUKOCYTOSIS subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0

ANAEMIA			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
THROMBOCYTOSIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
CATARACT			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
DRY EYE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
CONSTIPATION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
DUODENAL ULCER			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
GASTRITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
IMPAIRED GASTRIC EMPTYING			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
LARGE INTESTINAL ULCER			

subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 25 (0.00%) 0	1 / 14 (7.14%) 1
VOMITING subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
NAUSEA subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	1 / 14 (7.14%) 1
Skin and subcutaneous tissue disorders RASH subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
PRURITUS subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
CUTANEOUS VASCULITIS subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
ACNE subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
SKIN ULCER subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
Renal and urinary disorders LUPUS NEPHRITIS subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
PROTEINURIA subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	0 / 14 (0.00%) 0
Musculoskeletal and connective tissue disorders BACK PAIN subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1	0 / 25 (0.00%) 0	1 / 14 (7.14%) 1
ARTHRALGIA			

subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
CONNECTIVE TISSUE DISORDER			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
MUSCLE SPASMS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
CELLULITIS			
subjects affected / exposed	0 / 19 (0.00%)	1 / 25 (4.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 19 (0.00%)	1 / 25 (4.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
DIVERTICULITIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
EAR INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	1 / 25 (4.00%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
GASTROENTERITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
EPSTEIN-BARR VIRUS INFECTION			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
HERPES ZOSTER			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
ORAL HERPES			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0

MYCOPLASMA INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
OTITIS MEDIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
TINEA PEDIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
TINEA VERSICOLOUR			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
SINUSITIS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
TONSILLITIS			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	1 / 25 (4.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
URINARY TRACT INFECTION			
subjects affected / exposed	3 / 19 (15.79%)	1 / 25 (4.00%)	1 / 14 (7.14%)
occurrences (all)	4	1	1
VAGINAL INFECTION			
subjects affected / exposed	0 / 19 (0.00%)	0 / 25 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
HYPOCALCAEMIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
TYPE 2 DIABETES MELLITUS			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
HYPONATRAEMIA			

subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
HYPOMAGNESAEMIA			
subjects affected / exposed	1 / 19 (5.26%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
HYPOKALAEMIA			
subjects affected / exposed	2 / 19 (10.53%)	0 / 25 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2020	<p>Version 2.0/Amendment 1</p> <ul style="list-style-type: none">• Revised the objectives to assess longer term safety, tolerability, and efficacy data• Added a reassessment of treatment assignments based on Study M19-130 interim analysis• Clarified eligibility criteria referring to active, chronic, or recurrent viral or bacterial infections• Added leflunomide, cyclosporine and tacrolimus to list of permitted concomitant medications• Added discontinuation criteria for subjects with serious infections and/or TB
28 October 2020	<p>Version 3.0/Amendment 2</p> <ul style="list-style-type: none">• Incorporated necessary protocol modifications to account for COVID-19 infections• Added 2 additional efficacy endpoints: change in PhGA from M19-130 Baseline and change in PtGA from M19-130 Baseline• Added the following as areas of safety interest: active TB; adjudicated GI perforations; and adjudicated embolic and thrombotic events (non- cardiac, non-CNS) including venous thromboembolic events defined as pulmonary embolism and deep vein thrombosis• Removed the following from the list of areas of safety interest: increased serum creatinine and CPK elevation• Added further clarification that Study M20-186 is primarily a study of longer-term safety and that efficacy outcomes are considered secondary
26 October 2021	<p>Version 4.0/Amendment 3</p> <ul style="list-style-type: none">• Treatment groups were clarified based on the completed Study M19-130 Interim Analysis• Clarified that subjects will need to successfully complete 48 weeks of Study M19-130 on placebo or a group that is currently active after the planned Study M19-130 Interim Analysis and meet all eligibility criteria to be considered eligible to enroll into LTE Study M20-186• Added the statement, "At the Sponsor's discretion, doses of study drug(s) selected for continuation in LTE Study M20-186 may be reassigned or discontinued at any time based on the outcome assessment of the Study M19-130 Interim Analysis."• Added the statement, "If the study is partially terminated, a subject in a terminated group will be asked to return for a PD visit and to perform a 30-day follow-up phone call after the last dose of study drug."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported