Clinical trial results:
A Phase 2b Dose Ranging Study to Evaluate the Efficacy and Safety of Rozibafusp Alfa (AMG 570) in Subjects With Active Systemic Lupus Erythematosus (SLE) With Inadequate Response to Standard of Care (SOC) Therapy

Summary

EudraCT number	2019-000328-16
Trial protocol	HU FR PT GR IT
Global end of trial date	25 July 2023

Results information

Result version number	v1 (current)
This version publication date	07 August 2024
First version publication date	07 August 2024

Trial information

Trial identification

Sponsor protocol code	20170588

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04058028
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, United States,
Public contact	Amgen (EUROPE) GmbH, IHQ Medical Info-Clinical Trials, MedInfoInternational@amgen.com
Scientific contact	Amgen (EUROPE) GmbH, IHQ Medical Info-Clinical Trials, MedInfoInternational@amgen.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	25 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was Evaluate the efficacy of rozibafusp alfa at Week 52 as measured by the SLE Responder Index (SRI-4).

Protection of trial subjects:

Before participants begin participation in any study-specific activities/procedures, Amgen requires a copy of the site's written institutional review board/independent ethics committee (IRB/IEC) approval of the protocol, informed consent form, and all other participant information as applicable.
This study was conducted in accordance with the protocol and with:

- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines
- Applicable International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines
- Applicable ICH laws and regulations

The participant signed the IRB/IEC and Amgen approved informed consent form before starting study-specific procedures. Enrollment occurred when the investigator confirmed all eligibility criteria were met and documented this decision in the participant's medical record and enrollment case report form (CRF). If eligible at the baseline/day 1 visit, the participant was randomized to a treatment regimen. Participants failing to meet baseline/day 1 visit criteria after passing screening were considered screen fails and could rescreen up to 2 times. Each participant entering the screening period received a unique participant identification number via interactive response technology (IRT), used throughout the study. This number remained constant, unaffected by rescreening, and might differ from the randomization number.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 February 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: 30
Country: Number of subjects enrolled	Bulgaria: 27
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Hong Kong: 2
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Italy: 6

Country: Number of subjects enrolled	Japan: 13
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Mexico: 27
Country: Number of subjects enrolled	Poland: 52
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Russian Federation: 25
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	United States: 40
Worldwide total number of subjects	244
EEA total number of subjects	103

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)	238
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants with active SLE were recruited across 81 centers in Argentina, Bulgaria, Canada, Czech Republic, France, Germany, Greece, Hong Kong, Hungary, Italy, Japan, Mexico, Poland, Portugal, Russia, South Korea, Spain, and the United States from February 2020 to July 2023.

Pre-assignment

Screening details:

Response adaptive randomization was used to assign eligible participants to receive rozibafusp alfa subcutaneously (SC) every 2 weeks (Q2W) at 70, 280, and 420 mg or matching placebo. Randomization started with a 1:1:1:1 ratio and was subsequently adapted according to clinical efficacy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received matching placebo SC Q2W for a maximum duration of 52 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Matching dose of rozibafusp alfa, administered SC.

Arm title	Rozibafusp Alfa 70mg

Arm description:

Participants received Rozibafusp Alfa 70mg SC Q2W for a maximum duration of 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Rozibafusp alfa
Investigational medicinal product code	
Other name	AMG 570
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

70mg SC.

Arm title	Rozibafusp Alfa 280mg

Arm description:

Participants received Rozibafusp Alfa 280mg SC Q2W for a maximum duration of 52 weeks.

Arm type	Experimental

Investigational medicinal product name	Rozibafusp alfa
Investigational medicinal product code	
Other name	AMG 570
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
208mg SC.

Arm title	Rozibafusp Alfa 420mg

Arm description:
Participants received Rozibafusp Alfa 420mg SC Q2W for a maximum duration of 52 weeks.

Arm type	Experimental
Investigational medicinal product name	Rozibafusp alfa
Investigational medicinal product code	
Other name	AMG 570
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:
420mg SC.

Number of subjects in period 1	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg
Started	62	58	36
Completed	36	44	28
Not completed	26	14	8
Withdrawal of Consent from Study	12	8	6
Decision by Sponsor	13	4	1
Death	-	1	-
Lost to follow-up	1	1	1

Number of subjects in period 1	Rozibafusp Alfa 420mg
Started	88
Completed	46
Not completed	42
Withdrawal of Consent from Study	7
Decision by Sponsor	35
Death	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo SC Q2W for a maximum duration of 52 weeks.	
Reporting group title	Rozibafusp Alfa 70mg
Reporting group description:	
Participants received Rozibafusp Alfa 70mg SC Q2W for a maximum duration of 52 weeks.	
Reporting group title	Rozibafusp Alfa 280mg
Reporting group description:	
Participants received Rozibafusp Alfa 280mg SC Q2W for a maximum duration of 52 weeks.	
Reporting group title	Rozibafusp Alfa 420mg
Reporting group description:	
Participants received Rozibafusp Alfa 420mg SC Q2W for a maximum duration of 52 weeks.	

Reporting group values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg
Number of subjects	62	58	36
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	61	56	35
From 65-84 years	1	2	1
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	42.6	44.6	42.2
standard deviation	± 10.3	± 12.3	± 10.5
Gender Categorical Units: Subjects			
Female	57	56	33
Male	5	2	3
Race/Ethnicity Units: Subjects			
Hispanic or Latino	24	14	5
Not Hispanic or Latino	37	44	31
Unknown or Not Reported	1	0	0
Race/Ethnicity Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	3	6	2
Black (or African American)	4	4	4

Multiple	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Unknown	0	0	0
White	53	47	30
Other	2	0	0

Reporting group values	Rozibafusp Alfa 420mg	Total	
Number of subjects	88	244	
Age Categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	86	238	
From 65-84 years	2	6	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	44.0		
standard deviation	± 10.5	-	
Gender Categorical Units: Subjects			
Female	82	228	
Male	6	16	
Race/Ethnicity Units: Subjects			
Hispanic or Latino	25	68	
Not Hispanic or Latino	63	175	
Unknown or Not Reported	0	1	
Race/Ethnicity Units: Subjects			
American Indian or Alaska Native	2	3	
Asian	8	19	
Black (or African American)	5	17	
Multiple	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Unknown	0	0	
White	71	201	
Other	2	4	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo SC Q2W for a maximum duration of 52 weeks.	
Reporting group title	Rozibafusp Alfa 70mg
Reporting group description:	
Participants received Rozibafusp Alfa 70mg SC Q2W for a maximum duration of 52 weeks.	
Reporting group title	Rozibafusp Alfa 280mg
Reporting group description:	
Participants received Rozibafusp Alfa 280mg SC Q2W for a maximum duration of 52 weeks.	
Reporting group title	Rozibafusp Alfa 420mg
Reporting group description:	
Participants received Rozibafusp Alfa 420mg SC Q2W for a maximum duration of 52 weeks.	

Primary: Number of Participants with a SLE Responder Index (SRI-4) Response at Week 52

End point title	Number of Participants with a SLE Responder Index (SRI-4) Response at Week 52[1]

End point description:

SRI-4 response at Week 52 is defined as a ≥ 4-point decrease in the hybrid Systemic Lupus Erythematosus Disease Activity Index (hSLEDAI) score, and no new British Isles Lupus Assessment Group (BILAG) 2004 A score, no greater than 1 new BILAG B domain scores compared with baseline, and a less than 0.3-point deterioration from baseline in Physician Global Assessment (PGA) (scale 0 to 3), and no use of more than protocol allowed therapies. The Full Analysis Set (FAS) included all randomized participants. Only participants who had the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included in the analysis.

End point type	Primary

End point timeframe:

Week 52

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: No additional statistical analysis was pre-specified for this endpoint.

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	51	35	48
Units: Participants				
SRI-4 Response	26	29	21	35

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved a BILAG Based Combined Lupus Assessment (BICLA) Response at Week 24

End point title	Number of Participants who Achieved a BILAG Based Combined Lupus Assessment (BICLA) Response at Week 24

End point description:

The BICLA response is defined as:
1) An improvement in baseline BILAG domain scores across all body systems with moderate (domain B) or severe disease activity (domain A)
2) No new BILAG 2004 A domain score and no > 1 new BILAG 2004 B domain scores compared with baseline
3) No worsening of the hSLEDAI score from baseline
4) No ≥ 0.3-point deterioration from baseline in PGA
5) No use of more than protocol-allowed therapies
6) No disallowed changes in concomitant medications, mainly including increases in corticosteroids, immunosuppressants.
The FAS included all randomized participants. Only participants who had the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included in the analysis.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	58	36	66
Units: Participants				
BICLA Response	24	19	18	35

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With a SRI-4 Response at Week 24

End point title	Number of Participants With a SRI-4 Response at Week 24

End point description:

SRI-4 response at Week 24 is defined as a ≥ 4-point decrease in the hSLEDAI score, and no new BILAG 2004 A score, no greater than 1 new BILAG B domain scores compared with baseline, and a less than 0.3-point deterioration from baseline in PGA (scale 0 to 3), and no use of more than protocol allowed therapies. The FAS included all randomized participants. Only participants who had the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included in the analysis.

End point type	Secondary

End point timeframe:

Week 24

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	58	36	66
Units: Participants				
SRI-4 Response	33	30	20	46

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved a Lupus Low Disease Activity State (LLDAS) Response at Week 52

End point title	Number of Participants who Achieved a Lupus Low Disease Activity State (LLDAS) Response at Week 52

End point description:

LLDAS was defined as meeting all the following conditions: 1) hSLEDAI ≤ 4, with no activity in major organ system (renal, central nervous system [CNS], cardiopulmonary, vasculitis, fever) and hemolytic anemia or gastrointestinal activity; 2) No new lupus disease activity as compared with the previous assessment; 3) PGA ≤ 1 (on a scale of 0 to 3); 4) Current prednisone or equivalent dose of ≤ 7.5 mg/day; 5) Well-tolerated standard maintenance doses of immunosuppressive drugs and approved treatments, as allowed and specified in the protocol. The FAS included all randomized participants. Only participants who had the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included in the analysis.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	51	35	48
Units: Participants				
LLDAS Response	12	18	6	21

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Moderate and Severe Flare Rate Over 52 Weeks as Measured by Safety of Estrogens in Systemic Lupus Erythematosus National Assessment [SELENA] -Systemic Lupus Erythematosus Disease Activity Index [SLEDAI] Flare Index (SFI)

End point title	Annualized Moderate and Severe Flare Rate Over 52 Weeks as Measured by Safety of Estrogens in Systemic Lupus Erythematosus National Assessment [SELENA] -Systemic Lupus Erythematosus Disease Activity Index [SLEDAI] Flare Index (SFI)

End point description:

The SFI, serves as a composite outcome measure incorporating the SELENA-SLEDAI score, and classifications of flares into mild, moderate, and severe, along with the PGA of disease activity. The SFI details specific clinical manifestations for each organ system and categorizes flares into mild, moderate, and severe based on treatment decisions. Moderate and severe flare: • Moderate: meeting criteria like SELENA-SLEDAI score change of 3 to 12 points, SLE symptom development, prednisone dose increase, non-steroidal anti-inflammatory drugs (NSAIDs)/hydrochloroquine addition, or PGA score increase by 1 to 2.5. • Severe: meeting criteria like SELENA-SLEDAI increase over 12 points, onset or worsening of severe symptoms, significant prednisone dose escalation, introduction of potent immunosuppressants, hospitalization, or PGA score reaching 2.5 or higher. FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	58	36	88
Units: Flares/year				
number (not applicable)				
Annualized moderate and severe flare rate	0.34	0.52	0.46	0.34
Annualized severe flare rate	0.21	0.24	0.30	0.16

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved a SRI-4 Response With a Reduction of Oral Corticosteroids (OCS) to ≤ 7.5 mg/day by Week 44 and Sustained Through Week 52 In Participants with a Baseline OCS Dose ≥ 10 mg/day

End point title	Number of Participants who Achieved a SRI-4 Response With a Reduction of Oral Corticosteroids (OCS) to ≤ 7.5 mg/day by Week 44 and Sustained Through Week 52 In Participants with a Baseline OCS Dose ≥ 10 mg/day

End point description:

SRI-4 response is defined as a ≥ 4-point decrease in the hSLEDAI score, and no new BILAG 2004 A score, no greater than 1 new BILAG B domain scores compared with baseline, and a less than 0.3-point deterioration from baseline in PGA (scale 0 to 3), and no use of more than protocol allowed therapies. The FAS included all randomized participants. Only participants who had a baseline OCS dose ≥ 10 mg/day and had the opportunity to complete Week 52 visit by the date of the study termination were included in the analysis.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	16	19	25
Units: Participants	5	1	2	8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Achieved a BICLA Response at Week 52

End point title	Number of Participants who Achieved a BICLA Response at Week 52

End point description:

The BICLA response is defined as:
1) An improvement in baseline BILAG domain scores across all body systems with moderate (domain B) or severe disease activity (domain A)
2) No new BILAG 2004 A domain score and no > 1 new BILAG 2004 B domain scores compared with baseline
3) No worsening of the hSLEDAI score from baseline
4) No ≥ 0.3-point deterioration from baseline in PGA
5) No use of more than protocol-allowed therapies
6) No disallowed changes in concomitant medications, mainly including increases in corticosteroids, immunosuppressants.
The FAS included all randomized participants. Only participants who had the opportunity to complete the visit by the date of the study termination decision being communicated to sites were included in the analysis.

End point type	Secondary

End point timeframe:

Week 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	51	35	48
Units: Participants				
BICLA Response	21	20	15	29

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Severe Flare Rate Over 52 Weeks as Measured by SFI

End point title	Annualized Severe Flare Rate Over 52 Weeks as Measured by SFI

End point description:

The SFI, serves as a composite outcome measure incorporating the SELENA-SLEDAI score, and classifications of flares into mild, moderate, and severe, along with the PGA of disease activity. The SFI details specific clinical manifestations for each organ system and categorizes flares into mild, moderate,

and severe based on treatment decisions. Moderate and severe flare: • Moderate: meeting criteria like SELENA-SLEDAI score change of 3 to 12 points, SLE symptom development, prednisone dose increase, non-steroidal anti-inflammatory drugs (NSAIDs)/hydrochloroquine addition, or PGA score increase by 1 to 2.5. • Severe: meeting criteria like SELENA-SLEDAI increase over 12 points, onset or worsening of severe symptoms, significant prednisone dose escalation, introduction of potent immunosuppressants, hospitalization, or PGA score reaching 2.5 or higher. FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	58	36	88
Units: Flares/year				
number (not applicable)				
Annualized severe flare rate	2.21	0.24	0.30	0.16

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Flare Rate Over 52 Weeks as Measured by BILAG Score Designation of "Worse" or "New" Resulting in a B-Score In ≥ 2 Organs or an A-Score in ≥ 1 Organ

End point title	Annualized Flare Rate Over 52 Weeks as Measured by BILAG Score Designation of "Worse" or "New" Resulting in a B-Score In ≥ 2 Organs or an A-Score in ≥ 1 Organ

End point description:

The BILAG flare index was derived from BILAG 2004, as measured by BILAG score designation of 'worse' or 'new' resulting in a B score in >= 2 organs or an A score in >= 1 organ. The FAS included all randomized participants.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	58	36	88
Units: Flares/year				
number (not applicable)				
Annualized flare rate as measured by BILAG score	0.13	0.22	0.30	0.31

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with a Cutaneous Lupus Erythematosus Area and Severity Index (CLASI) Activity Score ≥8 at Baseline Achieving ≥50% Improvement from Baseline at Weeks 12, 24, 36, and 52

End point title	Number of Participants with a Cutaneous Lupus Erythematosus Area and Severity Index (CLASI) Activity Score ≥8 at Baseline Achieving ≥50% Improvement from Baseline at Weeks 12, 24, 36, and 52

End point description:

The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) is an assessment tool consisting of two scores: one for disease activity and one for damage.

Activity Score: Ranges from 0 to 70, and is assessed based on erythema, scale/hyperkeratosis, mucous membrane involvement, acute hair loss, and non-scarring alopecia. Higher scores indicate more severe disease activity.
Damage Score: Ranges from 0 to 56, and is evaluated through dyspigmentation and scarring, including scarring alopecia. Dyspigmentation that remains visible for more than 12 months is considered permanent, and its score is doubled. Higher scores indicate greater damage.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	10	12	16
Units: Participants				
Week 12 (N = 13, 10, 12, 4)	3	2	5	4
Week 24 (N = 10, 10, 12, 11)	3	3	6	3
Week 36 (N = 9, 10, 12, 8)	1	5	7	2
Week 52 (N = 8, 9, 12, 7)	0	4	7	3

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with ≥6 Tender and Swollen Joints in Hands and Wrists at Baseline Achieving ≥50% Improvement From Baseline at Weeks 12, 24, 36, and 52

End point title	Number of Participants with ≥6 Tender and Swollen Joints in Hands and Wrists at Baseline Achieving ≥50% Improvement From Baseline at Weeks 12, 24, 36, and 52

End point description:

The tender and swollen joint count is a physical assessment where for each swollen and tender joint a score of 1 is assigned. Scores are then summed up to provide a total score for both swollen and tender joints. Higher total score indicate a severe disease activity and a lower score indicates a lees severe disease activity. The FAS included all randomized participants. Only participants who had ≥ 6 tender and swollen joints involving hands and wrists at baseline and had opportunity to complete the visit by the date of the study termination were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	35	13	46
Units: Participants				
Week 12 (N = 34, 35, 13, 46)	20	16	8	31
Week 24 (N = 32, 35, 13, 39)	23	23	7	34
Week 36 (N = 31, 34, 12, 34)	26	22	10	29
Week 52 (N = 26, 29, 12, 30)	19	20	9	27

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient-Reported Outcome Measurement Information System Fatigue Short Form 7a Instrument (PROMIS-Fatigue SF7a) Score at Weeks 12, 24, 36, 44, and 52

End point title	Change from Baseline in Patient-Reported Outcome Measurement Information System Fatigue Short Form 7a Instrument (PROMIS-Fatigue SF7a) Score at Weeks 12, 24, 36, 44, and 52

End point description:

The PROMIS-Fatigue SF7a is a 7-item instrument that assesses the experience of fatigue as well as its impact on physical, mental and social activities. Each item is scored on a 5-point Likert scale, ranging from "1" (Never) to "5" (Always). The scores of all 7 items are summed up with a total raw score range of 7(low level of fatigue)-35(high level of fatigue). Raw scores are converted to a T-score ranging from 29.4(low level of fatigue)-83.2(high level of fatigue). The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	28	22	43
Units: T-score				
arithmetic mean (standard deviation)				
Week 12 (N = 30, 28, 22, 43)	-8.40 (± 9.61)	-6.86 (± 5.71)	-4.22 (± 8.45)	-8.01 (± 7.60)
Week 24 (N = 27, 25, 14, 31)	-6.48 (± 11.97)	-5.61 (± 8.54)	-5.86 (± 7.76)	-8.82 (± 6.02)
Week 36 (N = 22, 23, 14, 23)	-7.26 (± 8.26)	-7.12 (± 8.00)	-3.26 (± 7.64)	-8.73 (± 8.98)
Week 44 (N = 22, 24, 17, 23)	-4.44 (± 7.94)	-8.65 (± 9.75)	-4.47 (± 7.23)	-8.25 (± 10.38)

Week 52 (N = 19, 21, 15, 21)	-8.57 (± 8.36)	-10.22 (± 8.89)	-6.57 (± 7.25)	-7.88 (± 11.88)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Short Form 36 Version 2 (SF-36v2) Health Survey Physical Component Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the Short Form 36 Version 2 (SF-36v2) Health Survey Physical Component Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 67)	4.612 (± 8.241)	4.261 (± 7.609)	4.013 (± 8.456)	5.409 (± 6.207)
Week 24 (N = 45, 46, 30, 50)	6.055 (± 8.043)	5.440 (± 8.807)	4.570 (± 8.994)	5.847 (± 6.971)
Week 36 (N = 40, 39, 28, 44)	6.652 (± 7.957)	6.536 (± 9.646)	5.360 (± 8.736)	6.833 (± 9.467)
Week 44 (N = 36, 36, 28, 36)	4.881 (± 9.200)	7.298 (± 9.903)	3.508 (± 7.538)	7.522 (± 9.735)
Week 52 (N = 31, 36, 27, 35)	7.235 (± 7.097)	6.598 (± 9.452)	5.056 (± 9.429)	5.456 (± 9.151)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Lupus Quality of Life Questionnaire (LupusQoL) Score at Weeks 12, 24, 36, 44, and 52

End point title	Change from Baseline in Lupus Quality of Life Questionnaire

	(LupusQoL) Score at Weeks 12, 24, 36, 44, and 52

End point description:

The LupusQoL consists of 8 domains: physical health, pain, planning, intimate relationships (IR), burden to others, emotional health, body image, and fatigue. Each domain is scored on a 0-5 scale and scores are summed up for a total score range of 0 to 100. Higher scores represent better quality of life or functioning within the specific domain being measured, and lower scores signify poorer quality of life or functioning within the domain. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	46	32	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Planning: Week 12 (N = 51, 46, 32, 67)	10.294 (± 23.368)	11.594 (± 24.551)	5.469 (± 23.817)	12.438 (± 22.631)
Planning: Week 24 (N = 45, 45, 30, 50)	10.185 (± 23.763)	6.667 (± 29.226)	9.722 (± 24.279)	9.500 (± 23.988)
Planning: Week 36 (N = 41, 40, 27, 44)	11.179 (± 21.214)	9.583 (± 23.232)	13.272 (± 21.836)	14.773 (± 29.414)
Planning: Week 44 (N = 36, 36, 28, 36)	9.491 (± 26.959)	13.426 (± 20.919)	9.821 (± 19.779)	12.037 (± 27.418)
Planning: Week 52 (N = 31, 36, 27, 35)	16.129 (± 19.357)	8.565 (± 23.257)	9.568 (± 24.428)	12.381 (± 22.810)
Physical Health: Week 12 (N = 51, 46, 32, 67)	9.498 (± 22.989)	12.160 (± 15.607)	8.398 (± 20.992)	9.748 (± 16.541)
Physical Health: Week 24 (N = 45, 45, 30, 50)	12.986 (± 24.461)	14.097 (± 21.972)	11.667 (± 18.856)	11.063 (± 16.551)
Physical Health: Week 36 (N = 41, 40, 27, 44)	12.729 (± 21.678)	14.375 (± 22.610)	13.542 (± 17.313)	13.991 (± 21.264)
Physical Health: Week 44 (N = 36, 36, 28, 36)	11.892 (± 25.253)	16.753 (± 22.124)	11.049 (± 15.625)	12.760 (± 17.008)
Physical Health: Week 52 (N = 31, 36, 27, 35)	18.448 (± 22.827)	13.976 (± 19.799)	8.449 (± 20.156)	14.107 (± 18.847)
Pain: Week 12 (N = 51, 46, 32, 67)	14.869 (± 27.199)	14.493 (± 22.800)	12.240 (± 26.939)	14.552 (± 22.349)
Pain: Week 24 (N = 45, 45, 30, 50)	16.296 (± 29.460)	13.148 (± 22.647)	15.556 (± 23.947)	17.667 (± 20.800)
Pain: Week 36 (N = 41, 40, 27, 44)	14.837 (± 26.972)	13.125 (± 19.327)	15.123 (± 23.912)	18.939 (± 27.159)
Pain: Week 44 (N = 36, 36, 28, 36)	14.815 (± 31.755)	16.667 (± 23.905)	11.905 (± 21.328)	17.824 (± 24.893)
Pain: Week 52 (N = 31, 36, 27, 35)	25.538 (± 23.367)	14.352 (± 24.929)	14.815 (± 28.898)	19.524 (± 23.565)
IR: Week 12 (N = 37, 32, 21, 50)	6.76 (± 26.94)	3.52 (± 24.64)	0.60 (± 30.99)	4.75 (± 20.81)
IR: Week 24 (N = 29, 32, 18, 34)	2.59 (± 24.86)	5.47 (± 28.74)	0.69 (± 20.77)	6.25 (± 23.08)
IR: Week 36 (N = 27, 27, 19, 29)	4.63 (± 26.66)	9.26 (± 27.21)	-2.63 (± 20.66)	5.17 (± 23.27)
IR: Week 44 (N = 25, 25, 19, 26)	5.00 (± 31.46)	8.00 (± 23.90)	-3.95 (± 21.67)	9.13 (± 31.54)
IR: Week 52 (N = 21, 23, 17, 27)	11.90 (± 27.80)	3.26 (± 23.30)	-1.47 (± 18.69)	4.17 (± 19.61)

Burden to Others: Week 12 (N = 51, 46, 32, 67)	12.092 (± 22.068)	5.072 (± 20.373)	13.281 (± 30.590)	9.577 (± 27.762)
Burden to Others: Week 24 (N = 45, 45, 30, 50)	10.556 (± 30.896)	9.444 (± 27.328)	15.000 (± 25.931)	11.500 (± 27.914)
Burden to Others: Week 36 (N = 41, 40, 27, 44)	16.260 (± 27.320)	11.042 (± 22.754)	18.827 (± 28.457)	13.447 (± 29.268)
Burden to Others: Week 44 (N = 36, 36, 28, 36)	14.120 (± 28.159)	14.352 (± 23.955)	15.476 (± 26.324)	13.194 (± 26.902)
Burden to Others: Week 52 (N = 31, 36, 27, 35)	13.710 (± 27.348)	8.333 (± 25.973)	15.741 (± 30.865)	17.143 (± 29.632)
Emotional Health: Week 12 (N = 51, 46, 32, 67)	7.435 (± 23.940)	4.529 (± 15.611)	6.250 (± 21.997)	9.142 (± 19.493)
Emotional Health: Week 24 (N = 45, 45, 30, 50)	8.056 (± 22.322)	7.963 (± 19.337)	7.778 (± 16.109)	13.083 (± 22.096)
Emotional Health: Week 36 (N = 41, 40, 27, 44)	5.589 (± 19.557)	3.958 (± 16.150)	6.173 (± 20.359)	13.920 (± 25.903)
Emotional Health: Week 44 (N = 36, 36, 28, 36)	6.134 (± 23.369)	9.722 (± 15.685)	7.292 (± 15.533)	13.194 (± 23.853)
Emotional Health: Week 52 (N = 31, 36, 27, 35)	7.258 (± 23.545)	6.134 (± 19.606)	8.951 (± 20.888)	14.167 (± 21.561)
Body Image: Week 12 (N = 51, 46, 32, 67)	9.2 (± 24.4)	3.7 (± 23.9)	13.1 (± 31.7)	10.1 (± 23.9)
Body Image: Week 24 (N = 45, 45, 30, 50)	5.9 (± 26.2)	-0.1 (± 24.9)	0.2 (± 29.7)	14.9 (± 26.4)
Body Image: Week 36 (N = 41, 40, 27, 44)	4.4 (± 25.0)	3.8 (± 24.3)	4.8 (± 27.7)	11.1 (± 29.2)
Body Image: Week 44 (N = 36, 36, 28, 36)	11.3 (± 27.3)	4.6 (± 26.4)	12.7 (± 32.0)	10.4 (± 20.2)
Body Image: Week 52 (N = 31, 36, 27, 35)	8.9 (± 20.2)	-5.0 (± 26.7)	7.0 (± 31.3)	9.6 (± 24.0)
Fatigue: Week 12 (N = 51, 46, 32, 67)	10.049 (± 21.253)	8.424 (± 19.509)	6.250 (± 20.880)	10.541 (± 22.488)
Fatigue: Week 24 (N = 45, 45, 30, 50)	9.861 (± 23.175)	10.972 (± 20.127)	6.458 (± 17.790)	10.625 (± 23.257)
Fatigue: Week 36 (N = 41, 40, 27, 44)	9.909 (± 19.664)	9.219 (± 20.363)	7.407 (± 17.076)	15.057 (± 28.220)
Fatigue: Week 44 (N = 36, 36, 28, 36)	10.764 (± 17.205)	12.153 (± 18.717)	9.821 (± 16.876)	12.500 (± 22.952)
Fatigue: Week 52 (N = 31, 36, 27, 35)	12.500 (± 22.765)	9.722 (± 20.291)	9.954 (± 18.036)	9.464 (± 21.404)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Patient Global Assessment Score (PtGA) at Weeks 12, 24, 36, 44, and 52

End point title	Change from Baseline in Patient Global Assessment Score (PtGA) at Weeks 12, 24, 36, 44, and 52

End point description:

The PtGA assesses disease activity on a 10 cm numeric rating scale (NRS; 0 to 10 cm). The scale for the assessment ranges from "very well" (0) to "very poor" (10). The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	44	31	65
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 44, 31, 65)	-0.9 (± 2.8)	-1.1 (± 1.9)	-1.8 (± 3.0)	-1.7 (± 2.2)
Week 24 (N = 45, 44, 30, 49)	-1.9 (± 2.6)	-1.2 (± 2.7)	-1.7 (± 2.7)	-2.2 (± 2.1)
Week 36 (N = 40, 37, 28, 44)	-2.0 (± 2.6)	-1.7 (± 2.5)	-1.6 (± 2.3)	-2.6 (± 2.6)
Week 44 (N = 36, 35, 28, 36)	-2.1 (± 3.0)	-2.1 (± 2.8)	-2.0 (± 2.8)	-2.6 (± 2.3)
Week 52 (N = 30, 33, 27, 35)	-2.3 (± 2.7)	-1.8 (± 2.5)	-2.6 (± 2.5)	-2.1 (± 2.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Participants who Experienced Treatment-emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any negative medical occurrence linked to an intervention in humans, regardless of its relation to the intervention. TEAEs occurred after the first intervention dose. Serious adverse events (SAEs) included outcomes such as death, life-threatening situations, hospitalization or an extended hospital stay, significant incapacity, congenital defects, or other crucial medical events. AE severity followed the CTCAE Version 5.0 scale: grade 1 (mild), grade 2 (moderate), grade 3 (severe), grade 4 (life-threatening), and grade 5 (death). Clinically significant lab results or other assessments (e.g., ECGs, scans, vital signs) that worsened from baseline and were deemed important by the investigator, independent of disease progression, were also considered. The Safety Analysis Set (SAS) included all randomized participants who received at least one dose of IP. Participants in this set were analyzed according to the actual treatment received.

End point type	Secondary

End point timeframe:

Up to approximately 68 weeks

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	58	36	87
Units: Number or participants				
All TEAEs	42	47	23	71
Fatal AEs	0	0	0	0
SAEs	6	7	5	3

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Rozibafusp Alfa

End point title	Serum Concentration of Rozibafusp Alfa[2]

End point description:

The pharmacokinetic (PK) concentration analysis set contained all participants who received at least one dose of IP and had at least one quantifiable PK sample collected. PK concentration data was analyzed according to the actual treatment received.

End point type	Secondary

End point timeframe:

Week 1, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 36, Week 44, Week 52, Week 56, Week 60, Week 64, and Week 68

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: No additional statistical analysis was pre-specified for this endpoint.

End point values	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	36	84	
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 1 (N = 57, 36, 84)	0.0 (± 0.0)	0.0 (± 0.0)	0.0 (± 0.0)	
Week 4 (N = 49, 31, 68)	1.29 (± 1.34)	20.7 (± 10.8)	26.2 (± 17.1)	
Week 8 (N = 46, 29, 61)	1.70 (± 1.93)	26.6 (± 15.7)	40.7 (± 21.8)	
Week 12 (N = 42, 23, 66)	2.05 (± 2.03)	31.3 (± 16.5)	46.8 (± 24.6)	
Week 16 (N = 40, 24, 62)	2.58 (± 2.67)	29.8 (± 18.9)	47.0 (± 28.4)	
Week 20 (N = 40, 26, 55)	3.42 (± 3.15)	35.4 (± 19.8)	48.9 (± 30.0)	
Week 24 (N = 41, 27, 53)	3.69 (± 3.37)	35.8 (± 19.1)	55.5 (± 30.6)	
Week 36 (N = 36, 25, 43)	3.62 (± 3.73)	40.5 (± 20.7)	54.7 (± 35.9)	
Week 44 (N = 38, 24, 38)	2.98 (± 3.78)	39.0 (± 18.6)	54.1 (± 38.3)	
Week 52 (N = 35, 23, 32)	4.15 (± 4.50)	43.8 (± 25.3)	51.6 (± 30.8)	
Week 56 (N = 33, 18, 34)	0.230 (± 0.495)	11.3 (± 8.03)	13.3 (± 12.4)	
Week 60 (N = 29, 20, 34)	0.00346 (± 0.0120)	3.45 (± 4.31)	3.08 (± 4.45)	
Week 64 (N = 35, 23, 36)	0.0 (± 0.0)	0.609 (± 1.07)	0.718 (± 1.41)	
Week 68 (N = 39, 22, 36)	0.0 (± 0.0)	0.0484 (± 0.125)	0.102 (± 0.271)	

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Half-life of Rozibafusp Alfa

End point title	Terminal Half-life of Rozibafusp Alfa

End point description:

Per the SAP, data for this outcome measure was not to be analyzed unless it could be adequately estimated.

End point type	Secondary
End point timeframe: Up to Week 68	

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[3]	0[4]	0[5]	0[6]
Units: days				
arithmetic mean (standard deviation)	()	()	()	()

Notes:

[3] - Data for this outcome measure was not collected.

[4] - Data for this outcome measure was not collected.

[5] - Data for this outcome measure was not collected.

[6] - Data for this outcome measure was not collected.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the SF-36v2 Health Survey Mental Component Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the SF-36v2 Health Survey Mental Component Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary
End point timeframe: Week 12, 24, 36, 44, and 52	

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 67)	5.433 (± 10.477)	1.941 (± 8.689)	2.235 (± 11.754)	4.965 (± 9.413)
Week 24 (N = 45, 46, 30, 50)	4.889 (± 10.772)	1.123 (± 7.767)	5.008 (± 8.063)	5.786 (± 9.278)
Week 36 (N = 40, 39, 28, 44)	5.002 (± 9.405)	1.407 (± 10.943)	2.111 (± 11.263)	6.531 (± 10.543)
Week 44 (N = 36, 36, 28, 36)	6.556 (± 12.984)	3.208 (± 9.125)	1.914 (± 9.247)	5.903 (± 10.847)

Week 52 (N = 31, 36, 27, 35)	6.675 (± 12.074)	3.778 (± 9.910)	2.613 (± 10.841)	7.186 (± 9.185)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the SF-36v2 Health Survey Physical Functioning Domain Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the SF-36v2 Health Survey Physical Functioning Domain Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	68
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 68)	14.019 (± 25.397)	11.383 (± 21.076)	10.000 (± 22.966)	12.595 (± 18.765)
Week 24 (N = 45, 46, 30, 51)	15.777 (± 23.930)	13.043 (± 22.961)	13.000 (± 24.657)	14.048 (± 21.031)
Week 36 (N = 40, 39, 28, 45)	17.752 (± 22.417)	15.640 (± 21.031)	11.608 (± 23.533)	16.142 (± 21.924)
Week 44 (N = 36, 36, 28, 37)	15.001 (± 24.582)	17.222 (± 24.007)	8.036 (± 19.924)	17.200 (± 20.702)
Week 52 (N = 31, 36, 27, 36)	20.807 (± 21.138)	15.416 (± 23.002)	12.778 (± 22.632)	16.568 (± 18.357)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the SF-36v2 Health Survey Physical Role Domain Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the SF-36v2 Health Survey Physical Role Domain Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 67)	15.074 (± 25.378)	7.979 (± 24.090)	9.961 (± 21.701)	13.713 (± 22.957)
Week 24 (N = 45, 46, 30, 50)	20.278 (± 28.240)	10.190 (± 28.788)	11.667 (± 19.609)	16.625 (± 27.217)
Week 36 (N = 40, 39, 28, 44)	19.219 (± 24.160)	12.660 (± 29.991)	13.839 (± 23.653)	19.886 (± 30.863)
Week 44 (N = 36, 36, 28, 36)	16.319 (± 28.554)	18.924 (± 28.169)	10.714 (± 22.876)	20.313 (± 32.915)
Week 52 (N = 31, 36, 27, 35)	23.387 (± 22.475)	17.708 (± 27.730)	9.028 (± 23.852)	14.464 (± 31.933)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the SF-36v2 Health Survey Bodily Pain Domain Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the SF-36v2 Health Survey Bodily Pain Domain Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 67)	15.5 (± 25.7)	12.0 (± 23.1)	10.9 (± 21.5)	18.4 (± 19.5)
Week 24 (N = 45, 46, 30, 50)	17.5 (± 26.7)	14.4 (± 27.6)	13.5 (± 24.6)	18.3 (± 19.4)
Week 36 (N = 40, 39, 28, 44)	18.7 (± 23.2)	15.9 (± 27.9)	14.1 (± 24.0)	22.1 (± 26.3)
Week 44 (N = 36, 36, 28, 36)	18.9 (± 23.9)	19.2 (± 31.9)	10.7 (± 20.5)	26.0 (± 29.4)
Week 52 (N = 31, 36, 27, 35)	19.8 (± 22.5)	16.7 (± 28.4)	16.6 (± 23.0)	21.8 (± 25.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the SF-36v2 Health Survey General Health Domain Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the SF-36v2 Health Survey General Health Domain Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	68
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 67)	5.90 (± 14.71)	5.85 (± 16.06)	4.69 (± 14.87)	9.97 (± 14.15)
Week 24 (N = 45, 46, 30, 51)	7.44 (± 15.97)	6.98 (± 16.11)	9.13 (± 14.83)	11.75 (± 14.11)
Week 36 (N = 40, 39, 28, 45)	10.35 (± 16.43)	10.15 (± 16.97)	5.96 (± 16.28)	11.40 (± 17.81)
Week 44 (N = 36, 36, 28, 37)	7.61 (± 19.32)	11.81 (± 18.99)	3.11 (± 16.92)	11.76 (± 16.74)
Week 52 (N = 31, 36, 27, 36)	9.55 (± 21.62)	12.54 (± 18.23)	5.81 (± 19.60)	9.58 (± 18.22)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the SF-36v2 Health Survey Vitality Domain Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the SF-36v2 Health Survey Vitality Domain Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 67)	10.662 (± 22.441)	8.112 (± 18.054)	8.594 (± 21.402)	11.287 (± 20.361)
Week 24 (N = 45, 46, 30, 50)	10.556 (± 24.419)	7.880 (± 15.780)	12.083 (± 18.346)	13.125 (± 18.482)
Week 36 (N = 40, 39, 28, 44)	11.094 (± 20.090)	10.256 (± 19.102)	8.036 (± 18.854)	15.199 (± 22.083)
Week 44 (N = 36, 36, 28, 36)	7.465 (± 24.313)	11.632 (± 19.489)	5.804 (± 19.089)	15.104 (± 21.670)
Week 52 (N = 31, 36, 27, 35)	12.903 (± 23.659)	11.806 (± 20.199)	8.796 (± 21.249)	11.250 (± 21.693)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the SF-36v2 Health Survey Social Role Functioning Domain Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the SF-36v2 Health Survey Social Role Functioning Domain Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 67)	14.46 (± 22.83)	8.24 (± 20.40)	9.77 (± 24.54)	15.11 (± 23.89)
Week 24 (N = 45, 46, 30, 50)	15.28 (± 26.23)	7.88 (± 25.05)	14.58 (± 19.72)	15.25 (± 21.32)
Week 36 (N = 40, 39, 28, 44)	15.63 (± 25.28)	7.05 (± 25.78)	14.29 (± 23.00)	19.60 (± 23.72)
Week 44 (N = 36, 36, 28, 36)	17.71 (± 27.61)	8.68 (± 27.52)	7.14 (± 22.16)	14.24 (± 23.75)
Week 52 (N = 31, 36, 27, 35)	23.79 (± 25.07)	10.42 (± 26.98)	13.89 (± 23.34)	17.50 (± 21.90)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the SF-36v2 Health Survey Emotional Role Domain Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the SF-36v2 Health Survey Emotional Role Domain Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 67)	13.888 (± 26.961)	5.141 (± 26.384)	2.083 (± 27.189)	12.935 (± 27.382)

Week 24 (N = 45, 46, 30, 50)	13.888 (± 27.352)	5.072 (± 23.339)	11.111 (± 20.800)	15.334 (± 28.540)
Week 36 (N = 40, 39, 28, 44)	15.208 (± 24.306)	4.058 (± 21.364)	6.250 (± 29.886)	14.773 (± 29.742)
Week 44 (N = 36, 36, 28, 36)	20.139 (± 32.512)	8.564 (± 21.314)	7.441 (± 25.493)	16.899 (± 30.045)
Week 52 (N = 31, 36, 27, 35)	18.011 (± 30.814)	10.647 (± 25.008)	6.481 (± 28.620)	19.762 (± 23.491)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the SF-36v2 Health Survey Mental Health Domain Score at Weeks 12, 24, 36, 44 and 52

End point title	Change from Baseline in the SF-36v2 Health Survey Mental Health Domain Score at Weeks 12, 24, 36, 44 and 52

End point description:

The SF-36v2 (acute version) Health Survey consists of 36 items and serves as a patient-reported measure of health status. It assesses 8 domains of health-related quality of life: physical limitations, social limitations, role limitations due to physical health, bodily pain, mental health, role limitations due to emotional health, vitality, and general health perceptions. Each domain of the SF-36v2 produces a score ranging from 0 to 100, with higher scores indicating better health-related quality of life. The FAS included all randomized participants. Only participants with observed data were included in the analysis.

End point type	Secondary

End point timeframe:

Week 12, 24, 36, 44, and 52

End point values	Placebo	Rozibafusp Alfa 70mg	Rozibafusp Alfa 280mg	Rozibafusp Alfa 420mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	32	67
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 12 (N = 51, 47, 32, 67)	10.7 (± 21.5)	4.3 (± 16.2)	6.4 (± 21.0)	8.9 (± 17.1)
Week 24 (N = 45, 46, 30, 50)	10.1 (± 22.7)	2.7 (± 15.3)	9.2 (± 15.1)	10.6 (± 18.0)
Week 36 (N = 40, 39, 28, 44)	10.0 (± 18.7)	5.5 (± 21.8)	3.0 (± 20.2)	13.1 (± 19.3)
Week 44 (N = 36, 36, 28, 36)	11.8 (± 24.3)	10.3 (± 16.0)	3.0 (± 16.1)	12.5 (± 20.1)
Week 52 (N = 31, 36, 27, 35)	12.3 (± 21.4)	9.0 (± 19.0)	4.6 (± 17.4)	13.9 (± 18.3)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to approximately 68 weeks	
Adverse event reporting additional description:	
The SAS included all randomized participants who received at least 1 dose of IP. All-cause mortality is reported for all participants enrolled/randomized in the study. Treatment-emergent serious adverse events and other adverse events are reported for all participants who received at least one dose of study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo SC Q2W for a maximum duration of 52 weeks	
Reporting group title	Rozibafusp alfa 70 mg Q2W
Reporting group description:	
Participants received Rozibafusp Alfa 70mg SC Q2W for a maximum duration of 52 weeks.	
Reporting group title	Rozibafusp alfa 280 mg Q2W
Reporting group description:	
Participants received Rozibafusp Alfa 280mg SC Q2W for a maximum duration of 52 weeks.	
Reporting group title	Rozibafusp alfa 420 mg Q2W
Reporting group description:	
Participants received Rozibafusp Alfa 420mg SC Q2W for a maximum duration of 52 weeks.	

Serious adverse events	Placebo	Rozibafusp alfa 70 mg Q2W	Rozibafusp alfa 280 mg Q2W
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 62 (9.68%)	7 / 58 (12.07%)	5 / 36 (13.89%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign pancreatic neoplasm			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	0 / 36 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	0 / 36 (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

Gastric cancer			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	0 / 36 (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
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	0 / 36 (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
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	0 / 36 (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 / 62 (0.00%)	1 / 58 (1.72%)	0 / 36 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 62 (1.61%)	1 / 58 (1.72%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	0 / 36 (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
Cholecystitis			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	0 / 36 (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
Respiratory, thoracic and mediastinal disorders			

Bronchial hyperreactivity			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	0 / 36 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord thickening			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	0 / 36 (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
Haemoptysis			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	0 / 36 (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
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	0 / 36 (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
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	0 / 36 (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

Nephrotic syndrome			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	0 / 36 (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 / 62 (0.00%)	1 / 58 (1.72%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SLE arthritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 62 (0.00%)	1 / 58 (1.72%)	0 / 36 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Rozibafusp alfa 420 mg Q2W		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 87 (3.45%)		

number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign pancreatic neoplasm			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric cancer			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Upper limb fracture			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Serositis			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vocal cord thickening			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrotic syndrome			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Systemic lupus erythematosus			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SLE arthritis			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			

subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Rozibafusp alfa 70 mg Q2W	Rozibafusp alfa 280 mg Q2W
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 62 (46.77%)	34 / 58 (58.62%)	20 / 36 (55.56%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 62 (1.61%)	3 / 58 (5.17%)	1 / 36 (2.78%)
occurrences (all)	1	3	1
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 62 (4.84%)	5 / 58 (8.62%)	3 / 36 (8.33%)
occurrences (all)	6	5	4
Dizziness			
subjects affected / exposed	1 / 62 (1.61%)	0 / 58 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	1 / 62 (1.61%)	3 / 58 (5.17%)	0 / 36 (0.00%)
occurrences (all)	1	3	0
Injection site reaction			
subjects affected / exposed	1 / 62 (1.61%)	1 / 58 (1.72%)	1 / 36 (2.78%)
occurrences (all)	3	1	3

Injection site erythema			
subjects affected / exposed	2 / 62 (3.23%)	0 / 58 (0.00%)	3 / 36 (8.33%)
occurrences (all)	9	0	6
Pyrexia			
subjects affected / exposed	1 / 62 (1.61%)	3 / 58 (5.17%)	1 / 36 (2.78%)
occurrences (all)	1	3	2
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 62 (0.00%)	2 / 58 (3.45%)	2 / 36 (5.56%)
occurrences (all)	0	2	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 62 (3.23%)	3 / 58 (5.17%)	1 / 36 (2.78%)
occurrences (all)	2	3	1
Abdominal pain			
subjects affected / exposed	0 / 62 (0.00%)	4 / 58 (6.90%)	2 / 36 (5.56%)
occurrences (all)	0	4	2
Reproductive system and breast disorders			
Cervical dysplasia			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	0 / 62 (0.00%)	0 / 58 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	4 / 62 (6.45%)	0 / 58 (0.00%)	1 / 36 (2.78%)
occurrences (all)	5	0	1
Rash			
subjects affected / exposed	2 / 62 (3.23%)	1 / 58 (1.72%)	2 / 36 (5.56%)
occurrences (all)	2	2	3
Skin ulcer			
subjects affected / exposed	1 / 62 (1.61%)	1 / 58 (1.72%)	2 / 36 (5.56%)
occurrences (all)	1	1	2
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 62 (1.61%)	1 / 58 (1.72%)	2 / 36 (5.56%)
occurrences (all)	1	1	2
Arthralgia			
subjects affected / exposed	1 / 62 (1.61%)	3 / 58 (5.17%)	2 / 36 (5.56%)
occurrences (all)	1	3	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 62 (4.84%)	2 / 58 (3.45%)	2 / 36 (5.56%)
occurrences (all)	5	2	2
Urinary tract infection			
subjects affected / exposed	6 / 62 (9.68%)	9 / 58 (15.52%)	4 / 36 (11.11%)
occurrences (all)	12	12	7
Nasopharyngitis			
subjects affected / exposed	0 / 62 (0.00%)	3 / 58 (5.17%)	1 / 36 (2.78%)
occurrences (all)	0	3	1
Influenza			
subjects affected / exposed	1 / 62 (1.61%)	3 / 58 (5.17%)	0 / 36 (0.00%)
occurrences (all)	1	3	0
COVID-19			
subjects affected / exposed	5 / 62 (8.06%)	13 / 58 (22.41%)	3 / 36 (8.33%)
occurrences (all)	6	14	3
Upper respiratory tract infection			
subjects affected / exposed	8 / 62 (12.90%)	6 / 58 (10.34%)	6 / 36 (16.67%)
occurrences (all)	8	7	8

Non-serious adverse events	Rozibafusp alfa 420 mg Q2W		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 87 (58.62%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 87 (3.45%)		
occurrences (all)	3		
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 87 (9.20%)		
occurrences (all)	9		

Dizziness subjects affected / exposed occurrences (all)	5 / 87 (5.75%) 6		
General disorders and administration site conditions Oedema peripheral subjects affected / exposed occurrences (all) Injection site reaction subjects affected / exposed occurrences (all) Injection site erythema subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 0 / 87 (0.00%) 0 5 / 87 (5.75%) 10 1 / 87 (1.15%) 2 4 / 87 (4.60%) 4		
Blood and lymphatic system disorders Iron deficiency anaemia subjects affected / exposed occurrences (all)	 1 / 87 (1.15%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	 4 / 87 (4.60%) 4 1 / 87 (1.15%) 1		
Reproductive system and breast disorders Cervical dysplasia subjects affected / exposed occurrences (all)	 0 / 87 (0.00%) 0		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Pruritus	 0 / 87 (0.00%) 0 		

subjects affected / exposed	6 / 87 (6.90%)		
occurrences (all)	9		
Rash			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences (all)	1		
Skin ulcer			
subjects affected / exposed	0 / 87 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 87 (5.75%)		
occurrences (all)	7		
Arthralgia			
subjects affected / exposed	4 / 87 (4.60%)		
occurrences (all)	6		
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 87 (4.60%)		
occurrences (all)	4		
Urinary tract infection			
subjects affected / exposed	13 / 87 (14.94%)		
occurrences (all)	16		
Nasopharyngitis			
subjects affected / exposed	8 / 87 (9.20%)		
occurrences (all)	10		
Influenza			
subjects affected / exposed	1 / 87 (1.15%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	19 / 87 (21.84%)		
occurrences (all)	19		
Upper respiratory tract infection			
subjects affected / exposed	8 / 87 (9.20%)		
occurrences (all)	9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 February 2020	- Remove detectable SLE SOC drug levels from the inclusion criteria list. - Substitute SLEDAI 2K by hybrid SLEDAI as part of the efficacy assessment. - Simplify and reduce screening period. - Introduce home health care visits. - Add LLDAS to key secondary endpoints. - Reduce period required for OCS stable dose prior to screening visit. - Changes to OCS dose permitted between 0 to 4 weeks - from up to 20 mg/day increase in prednisone dose (or equivalent) over baseline to up to 5 mg/day increase (10 mg/day of prednisone or equivalent allowed if OCS being temporarily initiated between 0 to 4 weeks). In both cases, return to baseline dose within 2 weeks is required. - Remove body surface requirements for rash sore in SLEDAI at screening visit-rash is being evaluated through (CLASI) instrument and there is no need to impose restrictions relatively to the extension of rash (which are difficult to achieve in SLE participants). - Add language relative to management of NSAIDs and analgesic therapies throughout the study. - Substitute FACIT-Fatigue by Patient-Reported Outcome Measurement Information System (PROMIS)-Fatigue scale as part of Participant Reported outcomes (PROs) – PROMIS able to assess impact of fatigue. - Add optional sub-study for the development of a new Lupus Symptoms Questionnaire. - Revise washout period for prior biologic drugs. - Add additional lab parameters – added CRP, ESR, GGT as part of regular chemistry assessments, add lipid profile (Baseline and Week 52 only), add antiphospholipid antibodies (Baseline, Week 24 and 52), add aPTT as part of regular coagulation assessments.

13 October 2020	- Incorporate changes to the study design to enable the study to support registration, if the results are positive; these changes include: Update study from phase 2 to phase 2b, revise primary endpoint to SRI-4 response rate at Week 52 and make SRI-4 response rate at Week 24 a secondary endpoint, change all key secondary endpoints to secondary endpoints and add secondary disease flare endpoints, revise the exploratory endpoints (eg, include PGA-VAS, refine exploratory disease flares endpoints, and remove baseline SLE SOC serum drug levels since it is included as a covariate in Section 10.2.2), and revise statistical methods, including sample size estimate, planned analyses, and efficacy analyses methods for primary and secondary endpoints. - Clarify options for a participant to proceed in the study if the participant discontinues investigational product prior to Week 52. - Clarify contraceptive guidance and pregnancy and lactation information: Adjust the duration for contraceptive requirements and collection of pregnancy and lactation information to at least 10 additional weeks after the last dose of IP for female subjects of childbearing potential, specify that pregnancy testing should be performed monthly during both the treatment period and at the first 2 safety follow-up visits, and clarify the definition of females of childbearing potential. - Specify home health care visits will be centrally provided by the sponsor starting at Week 22 and will be optional for participant who have not experienced adverse effects from IP administration. - Modify the optional PRO sub-study: Revise data collection time points to every other week, and add the Patient Global Impression of Change (PGIC) and Patient Global Impression of Severity (PGIS) to the optional PRO sub-study. - Clarify initiation or increase in oral corticosteroid dosing. - Add IDMC description. - Administrative, typographical, and formatting changes were made throughout the protocol.
24 May 2022	- Remove requirement for a separate blinded joint assessor - Clarify that the same investigator must perform all efficacy assessments at every time point for a given subject. In order to ensure consistency, it is clarified that the same investigator/assessor should perform the assessments throughout the study for a given participant - Clarify data collection process - Improve clarity of the definition of SRI-4 response in section 9.2.2.11 and BILAG-based BICLA response in section 9.2.2.12. - Clarify events that classify joints as non-evaluable - Clarify that SRI-4 response cannot be achieved regardless of protocol deviations, since the Important Protocol Deviation list is now used to define 'more than protocol-allowed therapies' - Remove language defining SRI-4 response from the Objectives/Endpoints table, as it is described in detail in other sections of the protocol - Endpoint for secondary objective aiming to evaluate efficacy of AMG 570 on joint count was updated to clarify that the combined tenderness and swelling of joint count will be conducted for joints in hands and wrists - Clarify that the endpoint for secondary objective aiming to describe efficacy of AMG 570 using patient-reported outcomes includes the 2 component measures of physical and mental health to be assessed by the Medical Outcomes Short Form 36 version 2 Questionnaire - Clarify that one of exploratory objectives aim is to evaluate the pharmacodynamic effects of AMG 570 - Addition of a new exploratory objective endpoint to evaluate the efficacy of AMG 570 on joint count, assessing tenderness and swelling in all 28 joints evaluable

24 May 2022	- Timing of sample collection for PK and anti-AMG 570 antibody assessments during safety follow-up was described for clarity purposes - Additionally, for simplification and improved clarity, information pertaining to safety follow-up was removed from protocol synopsis, overall design description, and treatment period - Clarification of when an individual participants is considered to have completed the study - Clarification of when an individual participants is considered to have completed the study - Clarify within the table for Analyses Schedule that after the 7th interim analysis, additional interim analyses are planned after every 32 subjects are randomized and have had the opportunity to complete the week 24 assessment until full enrollment - Interim analysis language was updated to remove details related to the hypothetical Phase 3 study as they do not impact the conduct of this study and will be pre-specified in the study data monitoring committee charter, statistical analysis plan, and simulation report, as appropriate - Clarify that the adjudication reviews occur at study entry to determine eligibility and throughout the study period on blinded endpoint data from enrollment to week 52 for all randomized participants and for all visits - Clarify that participants taking more that protocol-allowed therapies are considered treatment failures for the primary efficacy endpoint analyses but will be allowed to continue investigational product and/or the study at the investigator’s discretion except those initiating specific treatments with immunosuppressant/immunomodulators - Title of section 9.2.6.1 was changed to Biomarker Assessment During the Study given that not all biomarkers listed in that section have established pharmacodynamic activity.
24 May 2022	- Specify that all participants who at the end of study visit have clinical sequelae considered potentially related to an anti-AMG 570 antibody response will be asked to return for additional testing. Additionally, it was clarified that follow-up results will be communicated to sites after database is locked to prevent potential risk of unblinding the sites for treatment assignment - Clarify what is included in baseline covariates - Clarify inclusion criterion 105 by re-organizing SLE treatments that participants must be taking to meet protocol-specific rules applied during screening. One treatment was included to this criterion, leflunomide - For consistency, criterion 208 was updated to align with the updates made to Schedule of Activities regarding monitoring of viral load frequency to evaluate hepatitis B and C - Add thalidomide treatment within 4 weeks prior to screening to the treatment listed in exclusion criterion 212. For consistency, thalidomide was also added as an excluded treatment during study period - Decreased washout period for Janus kinase (JAK) inhibitor from 3 to 1 month prior to screening based on information available for the PK/pharmacodynamic (PD) profile of these drugs (criterion 213). - Clarify criterion 215 by adding immunosuppressive or immunomodulatory activity to treatment with a biologic agent, reduce washout period for abatacept to 3 months prior to screening based on its PK/PD profile, and clarify that PD activity of other biologics at screening should be considered when evaluating washout periods - Clarify the timeframe within which a subject must not plan to receive a live vaccine

24 May 2022	- Revise washout period for treatment with an investigational product or device to consider the PK and PD profile of those products at screening - Include Gilbert's Syndrome as an exception for presence of laboratory abnormalities during screening in serum total bilirubin since these patients present non clinically relevant elevated bilirubin levels (criterion 221) - Clarify that serum pregnancy test is required at screening and urine pregnancy test is required at day 1 visit (criterion 225) - Clarify that this table applies for the subset of participants that completed the planned 52-week treatment period and emphasize that participants are required to attend as many visits as necessary to ensure a minimum of 16 weeks of safety follow-up after last dose of the investigational product - Clarify that safety follow-up visits should be scheduled in relation to last administration of the investigational product and not visit week 52 - Add frequency for monitoring viral load to evaluate hepatitis B and C o Remove urine pregnancy tests from the last two safety follow-up visits - Minor updates were included in the footnotes of the Schedule of Activities Treatment Period to clarify information regarding starting time of home health care visits, the option of conducting a QuantiFERON-TB test locally, assessment frequency of serum viral DNA and RNA for hepatitis B and C, and lymphocyte subset analysis. Additionally, for clarity purposes details no longer relevant to the assessments were removed - Accountability instructions for AMG 570 was updated to remove requirement to record the amount used in AMG 570 preparation on the electronic case report form for each participant - Simplify language around disease flares as a possible reason to discontinue protocol-required investigational product or procedural assessments (section 8.1) - The description of AMG 570 was updated (section 3.2.2)
24 May 2022	- For rescreening, it was clarified that tuberculosis tests and serologies for hepatitis B virus, hepatitis C virus, and human immunodeficiency virus (HIV) are not required to be repeated when rescreening occurs within 12 months of screening visit, provided that those test results were negative and there is no patient's medical/epidemiological history suggestive of infection or recent exposure to cases of infection (section 9.1.1) - Clarify the types of corticosteroid treatments that are allowed in the study and specify that participants requiring such treatments can continue the investigational product at the investigator's discretion (section 7.1.4.2). - Simplify Treatment Period section by removing information outside the scope of this section (section 9.1.2) - Include the option for local laboratory to conduct the QuantiFERON-TB test for eligibility using a local kit procured by the site (section 9.2.4.3.2) - Clarify the rating scale used for patient global assessment of disease activity (section 9.2.10.4) - Information collected for screen failure was updated to remove medical history and prior therapies as these are not considered required forms for screen failure per electronic case report form standard instructions (section 6.5) - Remove the efficacy analysis set (section 10.2.1.2) - Include a footnote in Analyte Listing table to instruct that local lab testing may be conducted if central lab testing is unavailable and add that QuantiFERON-TB test can also be conducted locally. For clarity purposes, details no longer relevant to the analyte listing were removed - Add a clarification note that clinical assessments to evaluate hepatoxicity in participants for whom investigational product is withheld due to potential drug-induced liver injury can be performed locally as required per investigator discretion (section 12.7)

24 May 2022	- Updates have been implemented to align collection and reporting of safety events with current procedures - Clarify that tapering of oral corticosteroids is allowed before week 24 at the investigator's discretion (sections 1.1 and 7.1.4.2) - Anti-drug Antibody Testing Procedures section was updated to remove sentence describing that follow-up testing will not be required where it is established that the participant did not receive AMG 570 (section 9.2.8). - The definition of the alphabetical score used to evaluate disease activity in 9 separate organ system was updated only for D by replacing stable with no activity (section 9.2.2.2) - Administrative, typographical, abbreviations, and formatting changes were made throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported