Clinical trial results:
A Phase 2/3, Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Baricitinib in Adult and Pediatric Japanese Patients with NNS/CANDLE, SAVI, and AGS

Summary

EudraCT number	2025-000001-16
Trial protocol	Outside EU/EEA
Global end of trial date	28 November 2024

Results information

Result version number	v1 (current)
This version publication date	12 June 2025
First version publication date	12 June 2025

Trial information

Trial identification

Sponsor protocol code	I4V-JE-JAJE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04517253
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 17571

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877-285-455,

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	28 November 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 April 2023
Global end of trial reached?	Yes
Global end of trial date	28 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the efficacy and safety of baricitinib in adult and pediatric Japanese participants with Nakajo-Nishimura Syndrome/chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (NNS/CANDLE), STING-associated vasculopathy with onset during infancy (SAVI), and Aicardi-Goutières Syndrome (AGS).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 10
Worldwide total number of subjects	10
EEA total number of subjects	0

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)	4
Adolescents (12-17 years)	1
Adults (18-64 years)	5
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Per analysis plan,only for participants with chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE),a pretreatment period lasted for 12 weeks, during which natural history data were collected. This data serves as baseline to assess changes during baricitinib treatment for evaluating some key secondary outcomes

Pre-assignment

Screening details:

Participants who met all eligibility criteria underwent an 8-week dose adjustment period,received optimized dosage of baricitinib during primary treatment period (12 weeks for CANDLE,24 weeks for SAVI or AGS participants),followed by maintenance period of up to 191.1 weeks for CANDLE, 202.9 weeks for SAVI, and up to 206.1 weeks for AGS participants

Period 1

Period 1 title	Primary Treatment Period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	CANDLE

Arm description:

Participants with chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) were administered an optimized final dosage of baricitinib, ranging from 8 mg to 12 mg daily (initially 8 mg, with gradual escalation to 10 mg and 12 mg), either as tablets or oral suspension, for 12 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and estimated glomerular filtration rate (eGFR). Participants then continued receiving baricitinib at their optimized dosage for 191.1 weeks.

Arm type	Experimental
Investigational medicinal product name	LY3009104
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants with CANDLE were administered an optimized final dosage of baricitinib, ranging from 8 mg to 12 mg daily (initially 8 mg, with gradual escalation to 10 mg and 12 mg), either as tablets or oral suspension, for 12 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 191.1 weeks.

Arm title	SAVI

Arm description:

Participants with stimulator of interferon genes (STING)-associated vasculopathy with onset during infancy (SAVI) were administered an optimized final dosage of baricitinib, ranging from 6 mg to 12 mg daily (initially 6 mg, with gradual escalation to 8 mg, 10 mg, and 12 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 202.9 weeks.

Arm type	Experimental

Investigational medicinal product name	LY3009104
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants with SAVI were administered an optimized final dosage of baricitinib, ranging from 6 mg to 12 mg daily (initially 6 mg, with gradual escalation to 8 mg, 10 mg, and 12 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 202.9 weeks.

Arm title	Aicardi-Goutières Syndrome (AGS)

Arm description:

Participants with Aicardi-Goutières Syndrome (AGS) were administered an optimized final dosage of baricitinib, ranging from 6 mg to 8 mg daily (initially 6 mg, with gradual escalation to 8 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 206.1 weeks.

Arm type	Experimental
Investigational medicinal product name	LY3009104
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants with AGS were administered an optimized final dosage of baricitinib, ranging from 6 mg to 8 mg daily (initially 6 mg, with gradual escalation to 8 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 206.1 weeks

Number of subjects in period 1	CANDLE	SAVI	Aicardi-Goutières Syndrome (AGS)
Started	5	3	2
Received at least one dose of study drug	5	3	2
Completed	4	2	2
Not completed	1	1	0
Adverse event, non-fatal	1	-	-
Death	-	1	-

Period 2

Period 2 title	Maintenance Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	CANDLE

Arm description:

Participants with CANDLE were administered an optimized final dosage of baricitinib, ranging from 8 mg to 12 mg daily (initially 8 mg, with gradual escalation to 10 mg and 12 mg), either as tablets or oral suspension, for 12 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 191.1 weeks.

Arm type	Experimental
Investigational medicinal product name	LY3009104
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants with CANDLE were administered an optimized final dosage of baricitinib, ranging from 8 mg to 12 mg daily (initially 8 mg, with gradual escalation to 10 mg and 12 mg), either as tablets or oral suspension, for 12 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 191.1 weeks

Arm title	SAVI

Arm description:

Participants with SAVI were administered an optimized final dosage of baricitinib, ranging from 6 mg to 12 mg daily (initially 6 mg, with gradual escalation to 8 mg, 10 mg, and 12 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 202.9 weeks.

Arm type	Experimental
Investigational medicinal product name	LY3009104
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants with SAVI were administered an optimized final dosage of baricitinib, ranging from 6 mg to 12 mg daily (initially 6 mg, with gradual escalation to 8 mg, 10 mg, and 12 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 202.9 weeks.

Arm title	Aicardi-Goutières Syndrome (AGS)

Arm description:

Participants with AGS were administered an optimized final dosage of baricitinib, ranging from 6 mg to 8 mg daily (initially 6 mg, with gradual escalation to 8 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 206.1 weeks.

Arm type	Experimental
Investigational medicinal product name	LY3009104
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants with AGS were administered an optimized final dosage of baricitinib, ranging from 6 mg to 8 mg daily (initially 6 mg, with gradual escalation to 8 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each

participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 206.1 weeks.

Number of subjects in period 2	CANDLE	SAVI	Aicardi-Goutières Syndrome (AGS)
Started	4	2	2
Completed	0	0	0
Not completed	4	2	2
Consent withdrawn by subject	1	-	-
Study Terminated by Sponsor	3	2	2

Baseline characteristics

Reporting groups	
Reporting group title	CANDLE
Reporting group description:	
Participants with chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) were administered an optimized final dosage of baricitinib, ranging from 8 mg to 12 mg daily (initially 8 mg, with gradual escalation to 10 mg and 12 mg), either as tablets or oral suspension, for 12 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and estimated glomerular filtration rate (eGFR). Participants then continued receiving baricitinib at their optimized dosage for 191.1 weeks.	
Reporting group title	SAVI
Reporting group description:	
Participants with stimulator of interferon genes (STING)-associated vasculopathy with onset during infancy (SAVI) were administered an optimized final dosage of baricitinib, ranging from 6 mg to 12 mg daily (initially 6 mg, with gradual escalation to 8 mg, 10 mg, and 12 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 202.9 weeks.	
Reporting group title	Aicardi-Goutières Syndrome (AGS)
Reporting group description:	
Participants with Aicardi-Goutières Syndrome (AGS) were administered an optimized final dosage of baricitinib, ranging from 6 mg to 8 mg daily (initially 6 mg, with gradual escalation to 8 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 206.1 weeks.	

Reporting group values	CANDLE	SAVI	Aicardi-Goutières Syndrome (AGS)
Number of subjects	5	3	2
Age categorical Units: Subjects			
Age continuous			
All enrolled participants who received at least one dose of study drug.			
Units: years			
arithmetic mean	39.20	9.70	7.50
standard deviation	± 13.79	± 9.81	± 2.12
Gender categorical			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
Female	1	3	1
Male	4	0	1
Ethnicity (NIH/OMB)			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	5	3	2
Unknown or Not Reported	0	0	0
Race (NIH/OMB)			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
American Indian or Alaska Native	0	0	0

Asian	5	3	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	0	0	0
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Region of Enrollment			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
Japan	5	3	2
Weight			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
>=10 -<20	0	2	2
>=40 -<50	4	1	0
>=50 -<60	1	0	0
Pre- Treatment Period:Baseline (Average) Mean Daily Diary Score			
For NNS/CANDLE, participant or caregiver was instructed to rate each symptom (fever, rash, musculoskeletal pain, headache and fatigue in the diary on a scale from 0 to 4 (where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms]. The mean daily score range was 0-4 with the higher score indicating a more severe symptom. 9999= Data Not available: SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected			
Units: score on a scale			
arithmetic mean	0.642	9999	9999
standard deviation	± 0.322	± 9999	± 9999
Pre-Treatment Period:Baseline (Average) Physician’s Global Assessment of Disease Activity Scores			
The Physician's Global Assessment of Disease Activity is used to assess the patient's current disease activity, as it relates to their signs and symptoms. The instrument uses a 21-circle Visual Analog Scale (VAS) ranging from 0 to 10 (using 0.5 increments) where 0 = "no activity" and 10 = "maximum activity" (Filocamo et al. 2010). Higher scores indicate greater disease severity. 9999= Data Not available: SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.			
Units: score on a scale			
arithmetic mean	5.45	9999	9999
standard deviation	± 1.33	± 9999	± 9999
Pre-Treatment Period: Baseline (Average) % of days where participants' daily diary score was < 0.5			
Baseline (Average) Percentage of Days Meeting the Criteria of Participant's Mean Daily Diary Score <0.5 was reported. 9999= Data Not available: SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.			
Units: percentage (%)			
arithmetic mean	35.6	9999	9999
standard deviation	± 24.4	± 9999	± 9999
Mean Daily Diary Score			
Diaries were specific to conditions (NNS/CANDLE, SAVI, AGS). For NNS/CANDLE, participants rated symptoms (fever, rash, pain, headache, fatigue), and for SAVI, participants rated symptoms (fever, rash, pain, fatigue, respiratory issues, ulcers) on a scale from 0 (no symptoms) to 4 (severe). The mean daily score range was 0-4, with higher scores indicating more severe symptoms. For AGS, symptoms (neurologic disability, crying, sleep, seizures, fever, irritability, skin findings) were rated similarly. The mean daily score range was 0-4.25. Total score was not utilized.			
Units: score on a scale			

arithmetic mean	0.92	0.786	0.705
standard deviation	± 0.345	± 0.275	± 0.77
Baseline estimated glomerular filtration rate (eGFR)			
All enrolled participants who received at least one dose of study drug.			
Units: mL/min/1.73m^2			
arithmetic mean	124.69	109.37	99.80
standard deviation	± 19.32	± 22.50	± 9.77

Reporting group values	Total		
Number of subjects	10		
Age categorical			
Units: Subjects			

Age continuous			
All enrolled participants who received at least one dose of study drug.			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
Female	5		
Male	5		
Ethnicity (NIH/OMB)			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	10		
Unknown or Not Reported	0		
Race (NIH/OMB)			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
American Indian or Alaska Native	0		
Asian	10		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	0		
More than one race	0		
Unknown or Not Reported	0		
Region of Enrollment			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
Japan	10		
Weight			
All enrolled participants who received at least one dose of study drug.			
Units: Subjects			
>=10 -<20	4		
>=40 -<50	5		
>=50 -<60	1		

Pre- Treatment Period:Baseline (Average) Mean Daily Diary Score			
For NNS/CANDLE, participant or caregiver was instructed to rate each symptom (fever, rash, musculoskeletal pain, headache and fatigue in the diary on a scale from 0 to 4 (where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms]. The mean daily score range was 0-4 with the higher score indicating a more severe symptom. 9999= Data Not available: SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected			
Units: score on a scale arithmetic mean standard deviation	- 		
Pre-Treatment Period:Baseline (Average) Physician’s Global Assessment of Disease Activity Scores			
The Physician's Global Assessment of Disease Activity is used to assess the patient's current disease activity, as it relates to their signs and symptoms. The instrument uses a 21-circle Visual Analog Scale (VAS) ranging from 0 to 10 (using 0.5 increments) where 0 = "no activity" and 10 = "maximum activity" (Filocamo et al. 2010). Higher scores indicate greater disease severity. 9999= Data Not available: SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.			
Units: score on a scale arithmetic mean standard deviation	- 		
Pre-Treatment Period: Baseline (Average) % of days where participants' daily diary score was < 0.5			
Baseline (Average) Percentage of Days Meeting the Criteria of Participant's Mean Daily Diary Score <0.5 was reported. 9999= Data Not available: SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.			
Units: percentage (%) arithmetic mean standard deviation	- 		
Mean Daily Diary Score			
Diaries were specific to conditions (NNS/CANDLE, SAVI, AGS). For NNS/CANDLE, participants rated symptoms (fever, rash, pain, headache, fatigue), and for SAVI, participants rated symptoms (fever, rash, pain, fatigue, respiratory issues, ulcers) on a scale from 0 (no symptoms) to 4 (severe). The mean daily score range was 0-4, with higher scores indicating more severe symptoms. For AGS, symptoms (neurologic disability, crying, sleep, seizures, fever, irritability, skin findings) were rated similarly. The mean daily score range was 0-4.25. Total score was not utilized.			
Units: score on a scale arithmetic mean standard deviation	- 		
Baseline estimated glomerular filtration rate (eGFR)			
All enrolled participants who received at least one dose of study drug.			
Units: mL/min/1.73m^2 arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	CANDLE

Reporting group description:

Participants with chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) were administered an optimized final dosage of baricitinib, ranging from 8 mg to 12 mg daily (initially 8 mg, with gradual escalation to 10 mg and 12 mg), either as tablets or oral suspension, for 12 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and estimated glomerular filtration rate (eGFR). Participants then continued receiving baricitinib at their optimized dosage for 191.1 weeks.

Reporting group title	SAVI

Reporting group description:

Participants with stimulator of interferon genes (STING)-associated vasculopathy with onset during infancy (SAVI) were administered an optimized final dosage of baricitinib, ranging from 6 mg to 12 mg daily (initially 6 mg, with gradual escalation to 8 mg, 10 mg, and 12 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 202.9 weeks.

Reporting group title	Aicardi-Goutières Syndrome (AGS)

Reporting group description:

Participants with Aicardi-Goutières Syndrome (AGS) were administered an optimized final dosage of baricitinib, ranging from 6 mg to 8 mg daily (initially 6 mg, with gradual escalation to 8 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 206.1 weeks.

Reporting group title	CANDLE

Reporting group description:

Participants with CANDLE were administered an optimized final dosage of baricitinib, ranging from 8 mg to 12 mg daily (initially 8 mg, with gradual escalation to 10 mg and 12 mg), either as tablets or oral suspension, for 12 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 191.1 weeks.

Reporting group title	SAVI

Reporting group description:

Participants with SAVI were administered an optimized final dosage of baricitinib, ranging from 6 mg to 12 mg daily (initially 6 mg, with gradual escalation to 8 mg, 10 mg, and 12 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 202.9 weeks.

Reporting group title	Aicardi-Goutières Syndrome (AGS)

Reporting group description:

Participants with AGS were administered an optimized final dosage of baricitinib, ranging from 6 mg to 8 mg daily (initially 6 mg, with gradual escalation to 8 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 206.1 weeks.

Primary: Change From Baseline in Mean Daily Diary Scores in Participants With CANDLE (Primary Treatment Period)

End point title	Change From Baseline in Mean Daily Diary Scores in Participants With CANDLE (Primary Treatment Period)[1][2]

End point description:

Diaries were specific to individual indications or conditions (ie, NNS/CANDLE,SAVI, or AGS). For NNS/CANDLE, participant or caregiver was instructed to rate each symptom (fever, rash, musculoskeletal pain, headache and fatigue in the diary on a scale from 0 to 4 (where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe

symptoms [equivalent to "worst" symptoms]. The mean daily score range was 0-4 with the higher score indicating a more severe symptom. Total score was not utilized.

Analysis Population Description (APD): CANDLE: All enrolled participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline, 20 weeks

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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

[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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)	-0.217 (± 0.586)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Mean Daily Diary Scores in Participants With SAVI (Primary Treatment Period)

End point title	Change From Baseline in Mean Daily Diary Scores in Participants With SAVI (Primary Treatment Period)[3][4]

End point description:

Diaries were specific to individual indications or conditions (i.e. NNS/CANDLE, SAVI, or AGS). For SAVI, participant or caregiver was instructed to rate each symptom (fever, rash, musculoskeletal pain, fatigue, respiratory/breathing problems, and ulcers/ischemic lesions in the diary on a scale from 0 to 4 (where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms,3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms].The mean daily score range was 0-4 with the higher score indicating a more severe symptom. Total score was not utilized.

APD: SAVI: All enrolled participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline, 32 weeks

Notes:

[3] - 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: The endpoint was planned only for SAVI reporting arm in the baseline period.

[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: The endpoint was planned only for SAVI reporting arm in the baseline period.

End point values	SAVI			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: score on a scale				
arithmetic mean (standard deviation)	-0.23 (± 0.238)			

Statistical analyses

No statistical analyses for this end point

Primary: Change From Baseline in Mean Daily Diary Scores in Participants With AGS (Primary Treatment Period)

End point title	Change From Baseline in Mean Daily Diary Scores in Participants With AGS (Primary Treatment Period)[5][6]

End point description:

Diaries were specific to individual indications or conditions (i.e. NNS/CANDLE, SAVI, or AGS). For AGS, participant or caregiver was instructed to rate each symptom (rating) (neurologic disability (0, 5, 7,10) crying (0, 1, 2, 3), length of uninterrupted sleep (0, 1, 2, 3), generalized seizure (0, 8), fever (0,1), excessive irritability (0, 1, 2, 3), skin findings(body) (0, 1, 2, 3), and skin findings (hands, feet, and ears) (0, 1, 2, 3) with a higher score for each symptom indicating a more severe symptom. The mean daily diary score was the average of all symptom scores and the range was 0 - 4.25 with the higher score indicating a more severe symptom. Total score was not utilized.
APD: AGS: All enrolled participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline, 32 weeks

Notes:

[5] - 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: The endpoint was planned only for AGS reporting arm in the baseline period.

[6] - 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: The endpoint was planned only for AGS reporting arm in the baseline period.

End point values	Aicardi-Goutières Syndrome (AGS)			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: score on a scale				
arithmetic mean (standard deviation)	-0.045 (± 0.164)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Daily Diary Scores in Participants With CANDLE (Primary Treatment and Maintenance Period)

End point title	Change From Baseline in Mean Daily Diary Scores in Participants With CANDLE (Primary Treatment and Maintenance Period)[7]

End point description:

Diaries were specific to individual indications or conditions (ie, NNS/CANDLE,SAVI, or AGS). For NNS/CANDLE, participant or caregiver was instructed to rate each symptom (fever, rash, musculoskeletal pain, headache and fatigue in the diary on a scale from 0 to 4 (where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms]. The mean daily score range was 0-4 with the higher score indicating a more severe symptom. Total score was not utilized.

APD : CANDLE: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 191.1 weeks

Notes:

[7] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)	-0.24 (± 0.613)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Daily Diary Scores in Participants With SAVI (Primary Treatment and Maintenance Period)

End point title	Change From Baseline in Mean Daily Diary Scores in Participants With SAVI (Primary Treatment and Maintenance Period)[8]

End point description:

Diaries were specific to individual indications or conditions (i.e. NNS/CANDLE, SAVI, or AGS). For SAVI, participant or caregiver was instructed to rate each symptom (fever, rash, musculoskeletal pain, fatigue, respiratory/breathing problems, and ulcers/ischemic lesions in the diary on a scale from 0 to 4 (where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms,3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms].The mean daily score range was 0-4 with the higher score indicating a more severe symptom. Total score was not utilized.

APD: SAVI: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 202.9 weeks

Notes:

[8] - 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: The endpoint was planned only for SAVI reporting arm in the baseline period.

End point values	SAVI			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: score on a scale				
arithmetic mean (standard deviation)	-0.286 (± 0.333)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Mean Daily Diary Scores in Participants With AGS (Primary Treatment and Maintenance Period)

End point title	Change From Baseline in Mean Daily Diary Scores in Participants With AGS (Primary Treatment and Maintenance Period)[9]

End point description:

Diaries were specific to individual indications or conditions (i.e. NNS/CANDLE, SAVI, or AGS). For AGS, participant or caregiver was instructed to rate each symptom (rating) (neurologic disability (0, 5, 7,10) crying (0, 1, 2, 3), length of uninterrupted sleep (0, 1, 2, 3), generalized seizure (0, 8), fever (0,1), excessive irritability (0, 1, 2, 3), skin findings(body) (0, 1, 2, 3), and skin findings (hands, feet, and ears) (0, 1, 2, 3) with a higher score for each symptom indicating a more severe symptom. The mean daily diary score was the average of all symptom scores and the range was 0 - 4.25 with the higher score indicating a more severe symptom. Total score was not utilized.

APD : AGS: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 206.1 weeks

Notes:

[9] - 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: The endpoint was planned only for AGS reporting arm in the baseline period.

End point values	Aicardi-Goutières Syndrome (AGS)			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: score on a scale				
arithmetic mean (standard deviation)	-0.08 (± 0.114)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Decrease in Daily Dose of Corticosteroids in Participants With CANDLE, SAVI and AGS (Primary Treatment Period)

End point title	Number of Participants With Decrease in Daily Dose of Corticosteroids in Participants With CANDLE, SAVI and AGS

	(Primary Treatment Period)

End point description:

Decrease was defined as total steroid dose at the visit <0.15 mg/kg/day (prednisone-equivalent) or >=50% decrease from baseline.

APD : CANDLE, SAVI and AGS: All enrolled participants who received at least one dose of study drug and took corticosteroids at baseline.

End point type	Secondary

End point timeframe:

CANDLE: Week 20, SAVI and AGS: Week 32

End point values	CANDLE	SAVI	Aicardi-Goutières Syndrome (AGS)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	1	1	
Units: participants				
number (not applicable)	4	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Decrease in Daily Dose of Corticosteroids in Participants With CANDLE, SAVI and AGS (Primary Treatment and Maintenance Period)

End point title	Number of Participants With Decrease in Daily Dose of Corticosteroids in Participants With CANDLE, SAVI and AGS (Primary Treatment and Maintenance Period)

End point description:

Decrease was defined as total steroid dose <0.15 mg/kg/day (prednisone-equivalent) or >=50% decrease from baseline.

End point type	Secondary

End point timeframe:

CANDLE: Week 191.1; SAVI: 202.9 and AGS: Week 206.1

End point values	CANDLE	SAVI	Aicardi-Goutières Syndrome (AGS)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	1	1	
Units: participants				
number (not applicable)	3	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With CANDLE (Primary Treatment Period)

End point title	Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With CANDLE (Primary Treatment Period)[10]

End point description:

Diaries were specific to individual indications or conditions (i.e, NNS/CANDLE,SAVI, or AGS). For NNS/CANDLE, participant or caregiver was instructed to rate each symptom (fatigue, fever, headache, musculoskeletal pain and rash in the diary on a scale from 0 to 4, where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms]). The mean daily score range was 0-4 with the higher score indicating a more severe symptom.
APD : CANDLE: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 20 weeks

Notes:

[10] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)				
Fatigue	-0.029 (± 0.997)			
Fever	0 (± 0)			
Headache	0.057 (± 0.128)			
Musculo-skeletal Pain	-0.514 (± 1.128)			
Rash	-0.6 (± 0.894)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With SAVI (Primary Treatment Period)

End point title	Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With SAVI (Primary Treatment Period)[11]

End point description:

Diaries were specific to individual indications or conditions (i.e. NNS/CANDLE, SAVI, or AGS). For SAVI, participant or caregiver was instructed to rate each symptom (fatigue, fever, musculoskeletal pain, rash, respiratory/breathing problems, and ulcers/ischemic lesions in the diary on a scale from 0 to 4, where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms]). The mean daily score range was 0-4 with the higher score indicating a more severe symptom.

APD : SAVI: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 32 weeks

Notes:

[11] - 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: The endpoint was planned only for SAVI reporting arm in the baseline period.

End point values	SAVI			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: score on a scale				
arithmetic mean (standard deviation)				
Fatigue	-0.381 (± 0.541)			
Fever	-0.095 (± 0.165)			
Musculo-skeletal Pain	-0.238 (± 0.412)			
Rash	0.333 (± 0.577)			
Respiratory / Breathing Symptoms	0.333 (± 0.577)			
Ulcers / Ischemic Lesions	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With AGS (Primary Treatment Period)

End point title	Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With AGS (Primary Treatment Period)[12]

End point description:

Diaries were specific to individual indications or conditions (i.e. NNS/CANDLE, SAVI, or AGS). For AGS, participant or caregiver was instructed to rate each symptom (rating) (crying (0, 1, 2, 3), excessive irritability (0, 1, 2, 3), fever (0,1), generalized seizure (0, 8), length of uninterrupted sleep (0, 1, 2, 3), neurologic disability (0, 5, 7,10), skin findings(body) (0, 1, 2, 3), and skin findings (hands, feet, and ears) (0, 1, 2, 3) with a higher score for each symptom indicating a more severe symptom.

APD : AGS: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 32 weeks

Notes:

[12] - 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: The endpoint was planned only for AGS reporting arm in the baseline period.

End point values	Aicardi-Goutières Syndrome (AGS)			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: score on a scale				
arithmetic mean (standard deviation)				
Crying	0 (± 0)			
Excessive Irritability	0 (± 0)			
Fever	-0.071 (± 0.101)			
Generalized Seizure	0 (± 0)			
Length of Uninterrupted Sleep	0.286 (± 0.404)			
Neurologic Disability	0 (± 0)			
Skin Findings (Body)	-0.5 (± 0.707)			
Skin Findings (Hands, Feet, Ears)	-0.707 (± 0.101)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With CANDLE (Primary Treatment and Maintenance Period)

End point title	Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With CANDLE (Primary Treatment and Maintenance Period)[13]

End point description:

Diaries were specific to individual indications or conditions (i.e, NNS/CANDLE,SAVI, or AGS). For NNS/CANDLE, participant or caregiver was instructed to rate each symptom (fatigue, fever, headache, musculoskeletal pain and rash in the diary on a scale from 0 to 4, where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms]). The mean daily score range was 0-4 with the higher score indicating a more severe symptom.

APD : CANDLE: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 191.1 weeks

Notes:

[13] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)				
Fatigue	-0.057 (± 1.172)			
Fever	0 (± 0)			
Headache	0.057 (± 0.128)			
Musculo-skeletal Pain	-0.514 (± 1.128)			
Rash	-0.686 (± 0.842)			

Statistical analyses

No statistical analyses for this end point

Secondary: change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With SAVI (Primary Treatment and Maintenance Period)

End point title	change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With SAVI (Primary Treatment and Maintenance Period)[14]

End point description:

Diaries were specific to individual indications or conditions (i.e. NNS/CANDLE, SAVI, or AGS). For SAVI, participant or caregiver was instructed to rate each symptom (fatigue, fever, musculoskeletal pain, rash, respiratory/breathing problems, and ulcers/ischemic lesions in the diary on a scale from 0 to 4, where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms]). The mean daily score range was 0-4 with the higher score indicating a more severe symptom.

APD : SAVI: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 202.9 weeks

Notes:

[14] - 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: The endpoint was planned only for SAVI reporting arm in the baseline period.

End point values	SAVI			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: score on a scale				
arithmetic mean (standard deviation)				
Fatigue	-0.381 (± 0.541)			
Fever	-0.095 (± 0.165)			
Musculo-skeletal Pain	-0.238 (± 0.412)			

Rash	-0.333 (± 0.577)			
Respiratory / Breathing Symptoms	-0.667 (± 1.155)			
Ulcers / Ischemic Lesions	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With AGS (Primary Treatment and Maintenance Period)

End point title	Change From Baseline in Patient's Symptom Specific Daily Diary Scores For Participants With AGS (Primary Treatment and Maintenance Period)[15]

End point description:

Diaries were specific to individual indications or conditions (i.e. NNS/CANDLE, SAVI, or AGS). For AGS, participant or caregiver was instructed to rate each symptom (rating) (crying (0, 1, 2, 3), excessive irritability (0, 1, 2, 3), fever (0,1), generalized seizure (0, 8), length of uninterrupted sleep (0, 1, 2, 3), neurologic disability (0, 5, 7,10), skin findings(body) (0, 1, 2, 3), and skin findings (hands, feet, and ears) (0, 1, 2, 3) with a higher score for each symptom indicating a more severe symptom.

APD : AGS: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 206.1 weeks

Notes:

[15] - 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: The endpoint was planned only for AGS reporting arm in the baseline period.

End point values	Aicardi-Goutières Syndrome (AGS)			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: score on a scale				
arithmetic mean (standard deviation)				
Crying	0 (± 0)			
Excessive Irritability	-0.071 (± 0.101)			
Fever	0 (± 0)			
Generalized Seizure	0 (± 0)			
Length of Uninterrupted Sleep	0 (± 0)			
Neurologic Disability	0 (± 0)			
Skin Findings (Body)	-0.5 (± 0.707)			
Skin Findings on (Hands, Feet, Ears)	-0.071 (± 0.101)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Physician’s Global Assessment of Disease Activity Scores in Participants With CANDLE (Primary Treatment Period)

End point title	Change From Baseline in the Physician’s Global Assessment of Disease Activity Scores in Participants With CANDLE (Primary Treatment Period)[16]

End point description:

The Physician's Global Assessment of Disease Activity is used to assess the patient's current disease activity, as it relates to their signs and symptoms. The instrument uses a 21-circle Visual Analog Scale (VAS) ranging from 0 to 10 (using 0.5 increments) where 0 = "no activity" and 10 = "maximum activity". Higher scores indicate greater disease severity.

APD : CANDLE: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 20 weeks

Notes:

[16] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)	-2.1 (± 0.82)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Physician’s Global Assessment of Disease Activity Scores in Participants With SAVI and AGS (Primary Treatment Period)

End point title	Change From Baseline in the Physician’s Global Assessment of Disease Activity Scores in Participants With SAVI and AGS (Primary Treatment Period)[17]

End point description:

The Physician's Global Assessment of Disease Activity is used to assess the patient's current disease activity, as it relates to their signs and symptoms. The instrument uses a 21-circle VAS ranging from 0 to 10 (using 0.5 increments) where 0 = "no activity" and 10 = "maximum activity". Higher scores indicate greater disease severity.

APD : SAVI and AGS: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 32 weeks

Notes:

[17] - 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: The endpoint was planned only for SAVI and AGS reporting arm in the baseline period.

End point values	SAVI	Aicardi-Goutières Syndrome (AGS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: score on a scale				
arithmetic mean (standard deviation)	-1.33 (± 1.76)	-3 (± 3.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Physician’s Global Assessment of Disease Activity Scores in Participants With CANDLE (Primary Treatment and Maintenance Period)

End point title	Change From Baseline in the Physician’s Global Assessment of Disease Activity Scores in Participants With CANDLE (Primary Treatment and Maintenance Period)[18]

End point description:

The Physician's Global Assessment of Disease Activity is used to assess the patient's current disease activity, as it relates to their signs and symptoms. The instrument uses a 21-circle Visual Analog Scale (VAS) ranging from 0 to 10 (using 0.5 increments) where 0 = "no activity" and 10 = "maximum activity". Higher scores indicate greater disease severity.

APD : CANDLE: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline, 191.1 weeks

Notes:

[18] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)	-2.6 (± 2.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Physician’s Global Assessment of Disease Activity Scores in Participants With SAVI and AGS (Primary Treatment and Maintenance Period)

End point title	Change From Baseline in the Physician’s Global Assessment of Disease Activity Scores in Participants With SAVI and AGS (Primary Treatment and Maintenance Period)[19]

End point description:

The Physician's Global Assessment of Disease Activity is used to assess the patient's current disease activity, as it relates to their signs and symptoms. The instrument uses a 21-circle VAS ranging from 0 to 10 (using 0.5 increments) where 0 = "no activity" and 10 = "maximum activity". Higher scores indicate greater disease severity.

APD : SAVI and AGS: All enrolled participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

SAVI: Baseline, 202.9 weeks; AGS: Baseline, 206.1 weeks

Notes:

[19] - 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: The endpoint was planned only for SAVI and AGS reporting arm in the baseline period.

End point values	SAVI	Aicardi-Goutières Syndrome (AGS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	2		
Units: score on a scale				
arithmetic mean (standard deviation)	-1.5 (± 1.73)	-3.75 (± 3.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Percentage of Days Meeting the Criteria of Participant's Mean Daily Diary Score <0.5 Compared to That in Pre-treatment Period in Participants With CANDLE (Primary Treatment Period)

End point title	Change of Percentage of Days Meeting the Criteria of Participant's Mean Daily Diary Score <0.5 Compared to That in Pre-treatment Period in Participants With CANDLE (Primary Treatment Period)[20]

End point description:

Change of Percentage of Days Meeting the Criteria of Participant's Mean Daily Diary Score <0.5 Compared to that in Pre-treatment period in Participants with CANDLE was evaluated

APD : CANDLE: All enrolled participants who received at least one dose of study drug. SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.

End point type	Secondary

End point timeframe:

Pre-treatment period (average of 12-week pre-treatment data), up to 20 weeks

Notes:

[20] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Percentage Change				
arithmetic mean (standard deviation)	4.4 (± 48.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Percentage of Days Meeting the Criteria of Participant's Mean Daily Diary Score <0.5 Compared to That in Pre-treatment Period in Participants With CANDLE (Primary Treatment and Maintenance Period)

End point title	Change of Percentage of Days Meeting the Criteria of Participant's Mean Daily Diary Score <0.5 Compared to That in Pre-treatment Period in Participants With CANDLE (Primary Treatment and Maintenance Period)[21]

End point description:

Change of Percentage of Days Meeting the Criteria of Participant's Mean Daily Diary Score <0.5 Compared to That in Pre-treatment Period in Participants With CANDLE was evaluated.

APD : CANDLE: All enrolled participants who received at least one dose of study drug. SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.

End point type	Secondary

End point timeframe:

Pre-treatment period (average of 12-week pre-treatment data), up to 191.1 weeks

Notes:

[21] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Percentage Change				
arithmetic mean (standard deviation)	2.0 (± 47.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Growth Velocity (Height and Weight Z Score) (Primary Treatment and Maintenance Period)

End point title	Change From Baseline in Growth Velocity (Height and Weight Z Score) (Primary Treatment and Maintenance Period)

End point description:

The change from baseline in normalized scores for body weight or height is measured using Z-scores. A Z-score indicates how many standard deviations a person's height or body weight is above or below the average for their age and gender. Z-score which was calculated by (value - [mean of the population]) /

[SD of the population] at a given age/sex.
Interpretation:
Z-score of 0: The measurement is equal to the population mean. Z-score less than 0: The measurement is below the population mean. Z-score greater than 0: The measurement is above the population mean. An increase in the Z-score for weight or height means that the weight or height of the participants has increased more than the standard population during the study. For study participants with Z-scores less than 0 at baseline, an increase in Z-score is considered a positive outcome. A Z-score within the range of -2 to +2 indicates that the height or weight is within the normal range

End point type	Secondary

End point timeframe:

CANDLE: Baseline, 191.1 weeks; SAVI: Baseline, 202.9 weeks and AGS: Baseline, 206.1 weeks
APD: CANDLE, SAVI and AGS: All enrolled participants who received at least one dose of study drug and had evaluable data for this outcome.

End point values	CANDLE	SAVI	Aicardi-Goutières Syndrome (AGS)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1[22]	2	2	
Units: Z-score				
arithmetic mean (standard deviation)				
Height	3.03 (± 99999)	0.75 (± 0.88)	0.13 (± 1.17)	
Weight	0.92 (± 99999)	1.17 (± 0.03)	0.46 (± 1.16)	

Notes:

[22] - 99999; standard deviation is not calculable as n=1

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Pre-treatment Period in Mean Daily Diary Scores For Participants With CANDLE (Primary Treatment Period)

End point title	Change From Pre-treatment Period in Mean Daily Diary Scores For Participants With CANDLE (Primary Treatment Period)[23]

End point description:

Diaries were specific to individual indications or conditions (ie, NNS/CANDLE,SAVI, or AGS). For NNS/CANDLE, participant or caregiver was instructed to rate each symptom (fever, rash, musculoskeletal pain, headache and fatigue in the diary on a scale from 0 to 4 (where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms]. The mean daily score range was 0-4 with the higher score indicating a more severe symptom.

APD : CANDLE: All participants who received at least one dose of study drug. SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.

End point type	Secondary

End point timeframe:

Pre-treatment period (average of 12-week pre-treatment data), up to 20 weeks

Notes:

[23] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)	0.061 (± 0.432)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Pre-treatment Period in Mean Daily Diary Scores For Participants With CANDLE (Primary Treatment and Maintenance Period)

End point title	Change From Pre-treatment Period in Mean Daily Diary Scores For Participants With CANDLE (Primary Treatment and Maintenance Period)[24]

End point description:

Diaries were specific to individual indications or conditions (ie, NNS/CANDLE,SAVI, or AGS). For NNS/CANDLE, participant or caregiver was instructed to rate each symptom (fever, rash, musculoskeletal pain, headache and fatigue in the diary on a scale from 0 to 4 (where a score of 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = more severe symptoms, and 4 = severe symptoms [equivalent to "worst" symptoms]. The mean daily score range was 0-4 with the higher score indicating a more severe symptom.

APD : CANDLE: All participants who received at least one dose of study drug. SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected

End point type	Secondary

End point timeframe:

Pre-treatment period (average of 12-week pre-treatment data), up to 191.1 weeks

Notes:

[24] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)	0.038 (± 0.464)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Pre-treatment Period in the Physician’s Global Assessment of Disease Activity Scores For Participants With CANDLE (Primary Treatment Period)

End point title	Change From Pre-treatment Period in the Physician’s Global Assessment of Disease Activity Scores For Participants With CANDLE (Primary Treatment Period)[25]

End point description:

The Physician's Global Assessment of Disease Activity is used to assess the patient's current disease activity, as it relates to their signs and symptoms. The instrument uses a 21-circle Visual Analog Scale (VAS) ranging from 0 to 10 (using 0.5 increments) where 0 = "no activity" and 10 = "maximum activity" (Filocamo et al. 2010). Higher scores indicate greater disease severity.

APD : CANDLE: All participants who received at least one dose of study drug. SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.
APD : CANDLE: All participants who received at least one dose of study drug. SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.

End point type	Secondary

End point timeframe:

Pre-treatment period (average of 12-week pre-treatment data), up to 20 weeks

Notes:

[25] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)	-1.75 (± 0.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Pre-treatment Period in the Physician’s Global Assessment of Disease Activity Scores For Participants With CANDLE (Primary Treatment and Maintenance Period)

End point title	Change From Pre-treatment Period in the Physician’s Global Assessment of Disease Activity Scores For Participants With CANDLE (Primary Treatment and Maintenance Period)[26]

End point description:

The Physician's Global Assessment of Disease Activity is used to assess the patient's current disease activity, as it relates to their signs and symptoms. The instrument uses a 21-circle Visual Analog Scale (VAS) ranging from 0 to 10 (using 0.5 increments) where 0 = "no activity" and 10 = "maximum activity" (Filocamo et al. 2010). Higher scores indicate greater disease severity.

APD : CANDLE: All participants who received at least one dose of study drug. SAVI and AGS did not have Pre-treatment period data therefore only CANDLE cohort data were collected.

End point type	Secondary

End point timeframe:

Pre-treatment period (average of 12-week pre-treatment data), up to 191.1 weeks

Notes:

[26] - 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: The endpoint was planned only for CANDLE reporting arm in the baseline period.

End point values	CANDLE			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: score on a scale				
arithmetic mean (standard deviation)	-2.25 (± 1.79)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

CANDLE: Baseline Up to 191.1 Weeks; SAVI: Baseline Up to 202.9 Weeks and AGS: Baseline Up to 206.1 Weeks

Adverse event reporting additional description:

All enrolled participants who received at least one dose of study drug. Based on the planned safety analysis, adverse events were collected per the treatment regimen, irrespective of dose. Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	CANDLE

Reporting group description:

Participants with CANDLE were administered an optimized final dosage of baricitinib, ranging from 8 mg to 12 mg daily (initially 8 mg, with gradual escalation to 10 mg and 12 mg), either as tablets or oral suspension, for 12 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 191.1 weeks.

Reporting group title	Aicardi-Goutières Syndrome (AGS)

Reporting group description:

Participants with AGS were administered an optimized final dosage of baricitinib, ranging from 6 mg to 8 mg daily (initially 6 mg, with gradual escalation to 8 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 206.1 weeks.

Reporting group title	SAVI

Reporting group description:

Participants with SAVI were administered an optimized final dosage of baricitinib, ranging from 6 mg to 12 mg daily (initially 6 mg, with gradual escalation to 8 mg, 10 mg, and 12 mg), either as tablets or oral suspension, for 24 weeks. This dosage was determined during a prior 8-week dose-adjustment period, tailored to each participant's weight and eGFR. Participants then continued receiving baricitinib at their optimized dosage for 202.9 weeks.

Serious adverse events	CANDLE	Aicardi-Goutières Syndrome (AGS)	SAVI
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events			
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (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			
haemorrhage intracranial			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
hypoaesthesia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (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
Blood and lymphatic system disorders			
pancytopenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (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			
nausea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (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
Infections and infestations			
atypical mycobacterial infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bronchopulmonary aspergillosis			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (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

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	CANDLE	Aicardi-Goutières Syndrome (AGS)	SAVI
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	2 / 2 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
skin papilloma			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
continuous haemodiafiltration			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
haematoma evacuation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
lung assist device therapy			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
mechanical ventilation			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
pneumonectomy			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
tracheostomy			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
oedema peripheral			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
pyrexia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
xerosis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
menstruation irregular			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed[1]	1 / 1 (100.00%)	0 / 1 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
nasal inflammation			

alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
rhinorrhoea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
upper respiratory tract inflammation			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
rhinitis allergic			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Psychiatric disorders			
head banging			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Investigations			
bk polyomavirus test positive			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	3 / 5 (60.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	3	1	0
blood creatine phosphokinase increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences (all)	1	1	2
lymphocyte count decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
lymphocyte count increased			
alternative dictionary used:			

MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
weight increased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
weight decreased			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
spinal compression fracture			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
tooth fracture			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
headache			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
neuropathy peripheral			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
restless legs syndrome			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
post herpetic neuralgia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
iron deficiency anaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
pancytopenia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
thrombocytosis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Eye disorders			
blepharitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
conjunctivitis allergic			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
dental caries			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	2 / 3 (66.67%)
occurrences (all)	0	1	3
enterocolitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
diarrhoea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2
gastritis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
mouth ulceration			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
nausea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
stomatitis			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
hepatic function abnormal			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
hepatic steatosis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
acne			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
dermatitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
eczema			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 5 (40.00%)	2 / 2 (100.00%)	1 / 3 (33.33%)
occurrences (all)	4	2	1
pruritus			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
rosacea			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
seborrhoeic dermatitis			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
urticaria			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infections and infestations			
bk virus infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
covid-19			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
adenoviral conjunctivitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
cytomegalovirus chorioretinitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
conjunctivitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
diarrhoea infectious			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
folliculitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
gastroenteritis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
influenza			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
hordeolum			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
herpes zoster			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
localised infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
metapneumovirus infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
nasopharyngitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 5 (40.00%)	2 / 2 (100.00%)	0 / 3 (0.00%)
occurrences (all)	2	23	0

otitis media			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
parotitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
periodontitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
pharyngitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
pneumocystis jirovecii pneumonia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
pneumonia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
pneumonia cytomegaloviral			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
respiratory syncytial virus infection			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
upper respiratory tract infection			
alternative dictionary used: MedDRA 27.1			

subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	17
tinea capitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
tracheitis			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Metabolism and nutrition disorders			
hyperuricaemia			
alternative dictionary used: MedDRA 27.1			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Gender specific events occurring only in male or female participants have had the number of participants at risk adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2020	- Modified endpoints for secondary objective on participant's daily diary scores - Schedule of activities were modified - Modified sentences and added information for Overall Design - inclusion and exclusion criteria were modified - Modified sentences on Adverse Events of Special Interest for virus infection and thrombocytosis (add the definition of thrombocytosis)
28 July 2020	- CANDLE was changed to NNS or NNS/CANDLE - Hepatic Monitoring Tests for Treatment-Emergent Abnormality Table was replaced with the latest version of the required template - Inequality symbols were corrected to appropriately describe patient weight class above and below40 kilogram (kg)
09 December 2020	- Schedule of Activities, Benefit/Risk Assessment, Inclusion and Exclusion criteria were modified - Added a note in Hepatic Safety Data Collection To follow latest lilly guidance for hepatic monitoring - Added new procedure during exceptional circumstances (To maintain this study during COVID-19 restrictions)
07 April 2022	- Added wording to explain that the study will be considered a postmarketing clinical trial after marketing authorization under summary of design - Updated visit and week numbers for maintenance treatment period from Visit 24 (Week 100) to Visit 30 (Week 172) - Schedule of Activities were modified - Added "The investigator will be responsible for reporting significant issues related to participant safety, participant rights, or data integrity." to align with protocol requirement update - Revised Final Report Signature to "The clinical study report (CSR) coordinating investigator will sign the final CSR for this study, indicating agreement that, to the best of his or her knowledge, the report accurately describes the conduct and results of the study."
04 September 2023	- Update visit and week numbers for maintenance treatment period from visit 30 (Week 172) to Visit 36 (Week 244) - Schedule of Activities were updated - Added relevant visits to Hepatitis B Virus DNA Monitoring To reflect changes made to the schedule of activities

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated due to efficacy/effectiveness reasons.

Notes: