Clinical trial results:
A 28-week, randomized, double-blind, active-controlled, multicenter study to evaluate the efficacy of subcutaneously administered secukinumab compared to ustekinumab in adult patients with psoriatic arthritis and failure of TNF-inhibitor treatment (AgAIN)

Summary

EudraCT number	2019-004246-15
Trial protocol	DE
Global end of trial date	22 October 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	CAIN457FDE04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04632927
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@Novartis.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	22 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate that secukinumab 300 mg subcutaneously (s.c.) is superior to ustekinumab 45/90 mg s.c. at Week 28 with regard to the proportion of patients achieving an improvement in score of ≥0.35 score points vs. Baseline (referred to as HAQ-DI response).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 December 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	Germany: 119
Worldwide total number of subjects	119
EEA total number of subjects	119

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)	101
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were randomized in 28 study sites across Germany

Pre-assignment

Screening details:

A total of 144 patients overall were screened and 25 patients failed screening, while 119 patients completed the screening period successfully and underwent randomization

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, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Secukinumab

Arm description:

Participants received 300 mg of secukinumab, administered as two 150 mg subcutaneous (s.c.) injections. Treatment was administered in a double-blind manner at Baseline and at Weeks 1, 2, 3, 4, 8, 12, 16, 20, and 24.

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	AIN457
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab for subcutaneous injection was provided in a pre-filled syringe (PFS) containing 150 mg. Each 300 mg dose was administered as two separate subcutaneous injections of 150 mg each

Arm title	Ustekinumab

Arm description:

Participants received ustekinumab via s.c. injection containing 45 mg (for participants weighing ≤100 kg) or 90 mg (for participants >100 kg). One active injection was administered at Baseline, Week 4, and 16. To maintain the blind, secukinumab-matching placebo injections were administered at all treatment time points (Baseline and at Weeks 1, 2, 3, 4, 8, 12, 16, 20, and 24). Depending on whether an ustekinumab injection was scheduled, participants received either one or two placebo injections per time point.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was provided in a matching PFS.

Investigational medicinal product name	Ustekinumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe

Routes of administration	Subcutaneous use

Dosage and administration details:

Ustekinumab was provided in a PFS containing either 45 mg or 90 mg for subcutaneous injection. According to the label, patients weighing ≤ 100 kg at baseline received a 45 mg dose, while those weighing > 100 kg received 90 mg.

Number of subjects in period 1	Secukinumab	Ustekinumab
Started	56	63
Completed	56	53
Not completed	0	10
Physician decision	-	1
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	1
Subject decision	-	1
Loss of efficacy	-	1
Non-compliance with study drug	-	1
Lack of efficacy	-	4

Baseline characteristics

Reporting groups	
Reporting group title	Secukinumab
Reporting group description:	
Participants received 300 mg of secukinumab, administered as two 150 mg subcutaneous (s.c.) injections. Treatment was administered in a double-blind manner at Baseline and at Weeks 1, 2, 3, 4, 8, 12, 16, 20, and 24.	
Reporting group title	Ustekinumab
Reporting group description:	
Participants received ustekinumab via s.c. injection containing 45 mg (for participants weighing ≤100 kg) or 90 mg (for participants >100 kg). One active injection was administered at Baseline, Week 4, and 16. To maintain the blind, secukinumab-matching placebo injections were administered at all treatment time points (Baseline and at Weeks 1, 2, 3, 4, 8, 12, 16, 20, and 24). Depending on whether an ustekinumab injection was scheduled, participants received either one or two placebo injections per time point.	

Reporting group values	Secukinumab	Ustekinumab	Total
Number of subjects	56	63	119
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)	49	52	101
From 65-84 years	7	11	18
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	54.4	52.7	
standard deviation	± 8.8	± 12.7	-
Sex: Female, Male Units: Participants			
Female	39	41	80
Male	17	22	39
Race/Ethnicity, Customized Units: Subjects			
Caucasian	55	62	117
Black	1	0	1
Other	0	1	1

End points

End points reporting groups

Reporting group title	Secukinumab
Reporting group description:	
Participants received 300 mg of secukinumab, administered as two 150 mg subcutaneous (s.c.) injections. Treatment was administered in a double-blind manner at Baseline and at Weeks 1, 2, 3, 4, 8, 12, 16, 20, and 24.	
Reporting group title	Ustekinumab
Reporting group description:	
Participants received ustekinumab via s.c. injection containing 45 mg (for participants weighing ≤100 kg) or 90 mg (for participants >100 kg). One active injection was administered at Baseline, Week 4, and 16. To maintain the blind, secukinumab-matching placebo injections were administered at all treatment time points (Baseline and at Weeks 1, 2, 3, 4, 8, 12, 16, 20, and 24). Depending on whether an ustekinumab injection was scheduled, participants received either one or two placebo injections per time point.	

Primary: Proportion of patients with Health assessment questionnaire – disability index (HAQ-DI) response at Week 28

End point title	Proportion of patients with Health assessment questionnaire – disability index (HAQ-DI) response at Week 28
End point description:	
The disability assessment component of the HAQ evaluated a subject's level of functional ability through 20 questions grouped into 8 categories: dressing, rising, eating, walking, hygiene, reach, grip, and usual activities. Each item began with the prompt "Over the past week, are you able to…" and is scored on a 4-point scale: 0 (no difficulty), 1 (some difficulty), 2 (much difficulty), and 3 (unable to do). The overall score was calculated by averaging the scores across all answered domains, resulting in a total score ranging from 0 (no disability) to 3 (severe disability). A HAQ-DI response was defined as an improvement of ≥0.35 points from baseline at Week 28. Missing values were imputed as non-responders	
End point type	Primary
End point timeframe:	
Baseline, Week 28	

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	63		
Units: Participants	32	17		

Statistical analyses

Statistical analysis title	Secukinumab vs Ustekinumab
Comparison groups	Secukinumab v Ustekinumab

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.647
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.601
upper limit	8.311

Secondary: Number of participants achieving Psoriasis area and severity index (PASI) 90 response at Week 28

End point title	Number of participants achieving Psoriasis area and severity index (PASI) 90 response at Week 28

End point description:

The Psoriasis Area and Severity Index (PASI) was a composite measure that evaluates the average severity of erythema, induration, and desquamation of psoriatic lesions—each graded on a scale from 0 (none) to 4 (severe)—across four body regions: head, upper limbs, trunk (including groin), and lower limbs (to the top of the buttocks). These scores were weighted by the area of skin involvement in each region to generate a total PASI score ranging from 0 to 72, with higher scores indicating more severe disease activity.

The number of participants who achieved at least a 90% reduction in PASI score from baseline at Week 28 was assessed. Missing values were imputed as non-responders.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	63		
Units: Participants	27	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Patient’s assessment of pain on VAS at Week 28

End point title	Change from baseline in Patient’s assessment of pain on VAS at Week 28

End point description:

The patient's level of pain was evaluated using a horizontal Visual Analogue Scale (VAS), on which individuals marked their pain intensity with a vertical tick. The scale ranged from 0 mm (indicating "no

pain") to 100 mm (indicating "unbearable pain").

The change in the patient's pain assessment on the VAS from baseline to Week 28 was analyzed. A negative change from baseline indicated improvement.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	58		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-27.1 (± 25.8)	-16.4 (± 24.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients achieving PASI 100 at Week 28

End point title	Number of patients achieving PASI 100 at Week 28

End point description:

The PASI was a composite measure that evaluates the average severity of erythema, induration, and desquamation of psoriatic lesions—each graded on a scale from 0 (none) to 4 (severe)—across four body regions: head, upper limbs, trunk (including groin), and lower limbs (to the top of the buttocks). These scores were weighted by the area of skin involvement in each region to generate a total PASI score ranging from 0 to 72, with higher scores indicating more severe disease activity.

The number of participants who achieved 100% reduction in PASI score from baseline at Week 28 was assessed. Missing values were imputed as non-responders.

End point type	Secondary

End point timeframe:

Bseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	63		
Units: Participants	21	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients achieving PASI 75 at Week 28

End point title	Number of patients achieving PASI 75 at Week 28

End point description:

The Psoriasis Area and Severity Index (PASI) was a composite measure that evaluates the average severity of erythema, induration, and desquamation of psoriatic lesions—each graded on a scale from 0 (none) to 4 (severe)—across four body regions: head, upper limbs, trunk (including groin), and lower limbs (to the top of the buttocks). These scores were weighted by the area of skin involvement in each region to generate a total PASI score ranging from 0 to 72, with higher scores indicating more severe disease activity.

The number of participants who achieved at least a 75% reduction in PASI score from baseline at Week 28 was assessed. Missing values were imputed as non-responders.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	63		
Units: Participants	34	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Tender Joint Count (TJC) 68 at Week 28

End point title	Change from baseline in Tender Joint Count (TJC) 68 at Week 28

End point description:

Tender joint count (TJC) 68 was a method of assessing joint inflammation. Number of tender joints was determined by examining 68 joints and identifying the joints that were painful under pressure or to passive motion. The 68 joints assessed for tenderness included the 2 temporomandibular, 2 sternoclavicular, 2 acromioclavicular joints, 2 shoulders, 2 elbows, 2 wrists, 10 metacarpophalangeal, 10 proximal interphalangeal, 8 distal interphalangeal joints of the hands, 2 hips, 2 knees, 2 talo¬tibial, 2 mid-tarsal, 10 metatarsophalangeal, and 10 proximal interphalangeal joints of the feet.

The change from baseline in TJC68 at Week 28 was assessed. A negative change from baseline indicated improvement.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-9.6 (± 11.9)	-7.6 (± 10.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Swollen Joint Count (SJC) 66 at Week 28

End point title	Change from baseline in Swollen Joint Count (SJC) 66 at Week 28

End point description:

Swollen Joint Count (SJC) 66 was a method of assessing joint inflammation. The number of swollen joints was determined by examining 66 joints and identifying those with visible or palpable swelling suggestive of synovitis. The 66 joints assessed for swelling included the 2 sternoclavicular, 2 acromioclavicular joints, 2 shoulders, 2 elbows, 2 wrists, 10 metacarpophalangeal, 10 proximal interphalangeal, 8 distal interphalangeal joints of the hands, 2 knees, 2 talotibial, 2 mid-tarsal, 10 metatarsophalangeal, and 10 proximal interphalangeal joints of the feet.

The change from baseline in SJC66 at Week 28 was assessed. A negative change from baseline indicated improvement.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-6.8 (± 6.3)	-5.3 (± 5.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Patient’s Global Assessment of Disease Activity on VAS

End point title	Change from baseline in Patient’s Global Assessment of Disease Activity on VAS

End point description:

The patient’s global assessment of disease activity was performed using a 100 mm (VAS) ranging from 0 (=‘very good’) to 100 (=‘very poor’) after the question ‘Considering all the ways Psoriatic Arthritis affects you, please indicate with a vertical mark through the horizontal line how well you are today’.

The change in the patient’s global assessment on the VAS from baseline to Week 28 was analyzed. A negative change from baseline indicated improvement.

End point type	Secondary

End point timeframe:
Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	57		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-26.0 (± 21.8)	-15.5 (± 23.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in the Leeds Enthesitis Index (LEI)

End point title	Change from baseline in the Leeds Enthesitis Index (LEI)

End point description:

The LEI was a validated enthesitis index that used six sites to evaluate enthesitis: the left and right lateral epicondyles of the humerus, the left and right proximal Achilles tendon insertions, and the left and right medial femoral condyles.Each site was scored as 0 (non-tender) or 1 (tender), resulting in a total score ranging from 0 to 6. A higher score reflected a greater burden of enthesitis.

The change in the LEI score from baseline to Week 28 was analyzed. A negative change from baseline indicated an improvement in enthesitis severity

End point type	Secondary

End point timeframe:
Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-0.9 (± 1.8)	-0.5 (± 1.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Patient’s Global Assessment of Psoriasis and Arthritis Disease Activity on VAS

End point title	Change from baseline in Patient’s Global Assessment of Psoriasis and Arthritis Disease Activity on VAS

End point description:

The patient’s assessment of psoriasis and arthritis was performed using a 100 mm VAS ranging from 0 (=’Excellent’) to 100 (=’Poor’) after the question ’Considering all the ways PSORIASIS and ARTHRITIS affects you, please indicate with a vertical mark through the horizontal line how well you are doing over the past week’

The change in the patient’s global assessment of psoriasis and arthritis disease activity on the VAS from baseline to Week 28 was analyzed. A negative change from baseline indicated improvement.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	58		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-28.1 (± 23.6)	-16.2 (± 24.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients achieving Minimal Disease Activity (MDA) at Week 28

End point title	Number of patients achieving Minimal Disease Activity (MDA) at Week 28

End point description:

MDA was a composite endpoint used to assess low disease activity in patients with psoriatic arthritis and psoriasis. A patient was considered to have achieved MDA if they met at least 5 of the following 7 criteria:
- TJC68 ≤ 1
- SJC66 ≤ 1
- PASI ≤1 [the total score ranged from 0 (no disease) to 72 (maximal disease)] or body surface area≤3%
- Patient’s pain VAS ≤ 15 mm on a 100 mm scale, where 0 ="no pain" and 100= "pain as severe as can be imagined"
- Patient’s global assessment of disease activity (PtGA) ≤ 20 mm on a 100 mm scale, where 0 represented the lowest level of disease activity and 100 the highest
- HAQ-DI ≤ 0.5, where 0 represented no difficulty and 3 represented inability to perform activities
- Enthesitis count ≤ 1, based on the Leeds Enthesitis Index, where 0 indicated no tenderness and 6 indicated tenderness at all assessed tendon insertions

The number of participants achieving MDA at Week 28 was assessed. Missing values were imputed as non-responders.

End point type	Secondary

End point timeframe:

Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	63		
Units: Participants	20	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in the Leeds Dactylitis Index (LDI)

End point title	Change from baseline in the Leeds Dactylitis Index (LDI)

End point description:

The LDI was used to quantitatively assess dactylitis by measuring the circumference of affected digits and their corresponding control digits, along with the tenderness of each affected digit. Digits were classified as dactylitic if there was a ≥10% difference in circumference compared to the contralateral digit. When both digits were affected or a contralateral control was unavailable, a standardized reference range was applied.
For each dactylitic digit, the ratio of the affected to control circumference was multiplied by a binary tenderness score (1 = tender, 0 = non-tender). The resulting values were summed across all affected digits to calculate the total LDI score. A higher LDI score indicated more severe or widespread dactylitis.

The change in the LDI score from baseline to Week 28 was analyzed. A negative change from baseline indicated an improvement in dactylitis severity.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	59		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-9.7 (± 27.2)	-7.2 (± 25.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) response at Week 28

End point title	Percentage of participants achieving a Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) response at Week 28

End point description:

The FACIT-Fatigue Scale was used to assess fatigue and its impact on daily functioning over the previous 7 days. The instrument consisted of 13 self-administered items, each scored on a 5-point Likert scale ranging from 0 (“Not at all”) to 4 (“Very much”). The total score ranged from 0 to 52, with higher scores indicating less fatigue and better functioning.
Response was achieved if the score had improved by at least 4 points from baseline. Missing values

were imputed as non-responders

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	63		
Units: Participants	40	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Psoriatic Arthritis Quality of Life (PsAQoL)

End point title	Change from baseline in Psoriatic Arthritis Quality of Life (PsAQoL)

End point description:

The PsAQoL questionnaire was used to assess the impact of psoriatic arthritis on patients' quality of life. The PsAQoL is a validated, disease-specific, self-administered instrument consisting of 20 items with binary response options ("true" or "not true"). Items covered physical, emotional, and social domains, including fatigue, independence, and interpersonal relationships. The total score ranged from 0 to 20, with higher scores indicating greater impairment in quality of life.

The change in the PsAQoL score from baseline to Week 28 was analyzed. A negative change from baseline indicated an improvement in health-related quality of life.

End point type	Secondary

End point timeframe:

Baseline, Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	51		
Units: Score on a Scale				
arithmetic mean (standard deviation)	-2.5 (± 5.1)	-2.0 (± 5.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving a Dermatology Life Quality Index (DLQI) response at Week 28

End point title	Percentage of participants achieving a Dermatology Life Quality

	Index (DLQI) response at Week 28

End point description:

The DLQI was used to evaluate the impact of dermatological conditions on patients' quality of life over the previous 7 days. It consisted of 10 self-administered items covering symptoms, daily activities, leisure, work/school, personal relationships, and treatment burden. Each item was scored from 0 ("Not at all") to 3 ("Very much"), with a total score ranging from 0 to 30. Higher scores indicated greater impairment.

Response was achieved if the absolute score was either 0 or 1. Missing values were imputed as non-responders.

End point type	Secondary

End point timeframe:

Week 28

End point values	Secukinumab	Ustekinumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	63		
Units: Participants	30	32		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of treatment to end of study, assessed up to approximately 36 weeks	
Adverse event reporting additional description:	
The safety analysis were done on the safety population, which included all randomized subjects who received at least one dose of study medication.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups	
Reporting group title	On-Treatment SEC 300 mg s.c.
Reporting group description:	
On-Treatment SEC 300 mg s.c.	
Reporting group title	On-Treatment UST 45/90 mg
Reporting group description:	
On-Treatment UST 45/90 mg	
Reporting group title	Entire study SEC 300 mg s.c.
Reporting group description:	
Entire study SEC 300 mg s.c.	
Reporting group title	Entire study UST 45/90 mg
Reporting group description:	
Entire study UST 45/90 mg	

Serious adverse events	On-Treatment SEC 300 mg s.c.	On-Treatment UST 45/90 mg	Entire study SEC 300 mg s.c.
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 56 (5.36%)	1 / 63 (1.59%)	4 / 56 (7.14%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	1 / 56 (1.79%)	0 / 63 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Vertebrobasilar stroke			
subjects affected / exposed	0 / 56 (0.00%)	0 / 63 (0.00%)	0 / 56 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 56 (0.00%)	1 / 63 (1.59%)	0 / 56 (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			
Oesophageal candidiasis			
subjects affected / exposed	0 / 56 (0.00%)	0 / 63 (0.00%)	1 / 56 (1.79%)
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			
subjects affected / exposed	1 / 56 (1.79%)	0 / 63 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 56 (1.79%)	0 / 63 (0.00%)	1 / 56 (1.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Entire study UST 45/90 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 63 (3.17%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	0 / 63 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Vertebrobasilar stroke			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			

Psoriasis			
subjects affected / exposed	1 / 63 (1.59%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Oesophageal candidiasis			
subjects affected / exposed	0 / 63 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 63 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 63 (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	On-Treatment SEC 300 mg s.c.	On-Treatment UST 45/90 mg	Entire study SEC 300 mg s.c.
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 56 (48.21%)	31 / 63 (49.21%)	31 / 56 (55.36%)
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 56 (5.36%)	2 / 63 (3.17%)	3 / 56 (5.36%)
occurrences (all)	5	2	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 56 (8.93%)	4 / 63 (6.35%)	5 / 56 (8.93%)
occurrences (all)	6	4	6
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	3 / 56 (5.36%)	1 / 63 (1.59%)	5 / 56 (8.93%)
occurrences (all)	5	1	7
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	5 / 56 (8.93%)	5 / 63 (7.94%)	5 / 56 (8.93%)
occurrences (all)	6	5	7
Back pain			
subjects affected / exposed	3 / 56 (5.36%)	3 / 63 (4.76%)	3 / 56 (5.36%)
occurrences (all)	3	4	3
Psoriatic arthropathy			
subjects affected / exposed	2 / 56 (3.57%)	4 / 63 (6.35%)	3 / 56 (5.36%)
occurrences (all)	2	4	3
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 56 (10.71%)	7 / 63 (11.11%)	6 / 56 (10.71%)
occurrences (all)	6	7	6
Nasopharyngitis			
subjects affected / exposed	5 / 56 (8.93%)	9 / 63 (14.29%)	7 / 56 (12.50%)
occurrences (all)	10	10	12
Respiratory tract infection			
subjects affected / exposed	3 / 56 (5.36%)	1 / 63 (1.59%)	3 / 56 (5.36%)
occurrences (all)	3	1	3
Urinary tract infection			
subjects affected / exposed	4 / 56 (7.14%)	5 / 63 (7.94%)	5 / 56 (8.93%)
occurrences (all)	6	5	7
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	0 / 56 (0.00%)	4 / 63 (6.35%)	0 / 56 (0.00%)
occurrences (all)	0	4	0

Non-serious adverse events	Entire study UST 45/90 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 63 (50.79%)		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 63 (3.17%)		
occurrences (all)	2		
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	4 / 63 (6.35%) 4		
Skin and subcutaneous tissue disorders Psoriasis subjects affected / exposed occurrences (all)	1 / 63 (1.59%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Psoriatic arthropathy subjects affected / exposed occurrences (all)	 5 / 63 (7.94%) 5 3 / 63 (4.76%) 4 6 / 63 (9.52%) 6		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 8 / 63 (12.70%) 8 9 / 63 (14.29%) 10 1 / 63 (1.59%) 1 6 / 63 (9.52%) 9		
Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all)	 4 / 63 (6.35%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 September 2024	Changes due to early termination of recruitment: • Update/removal of some exploratory endpoints • Specification that analyses will only be descriptive Changes to accommodate current requirements regarding patient safety: • Update of AE safety follow-up to align with SAE safety follow-up • SAE reporting: Inclusion of Hy's law language • Update of reporting requirements for study treatment errors including misuse/abuse

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported