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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

AIN457 (Secukinumab)

Trial Indication(s)

Lupus Nephritis

Protocol Number

CAIN457Q12301

Protocol Title

A two-year, phase III randomized, double-blind, parallel-group, placebo-controlled trial to evaluate the safety, efficacy, and tolerability of 300 mg s.c. secukinumab versus placebo, in combination with SoC therapy, in patients with active lupus nephritis

Clinical Trial Phase

Phase 3

Phase of Drug Development

Phase III

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Study Start/End Dates

Study Start Date: July 07, 2020 (Actual)
Primary Completion Date: September 13, 2023 (Actual)
Study Completion Date: September 13, 2023 (Actual)

Reason for Termination (If applicable)

Study terminated by sponsor due to futility analysis

Study Design/Methodology

This was a pivotal, randomized, double-blind, placebo-controlled trial evaluating at Week 52 the efficacy and safety of secukinumab versus placebo in patients with active Lupus Nephritis (LN) also receiving background Standard of Care (SoC) regimen.

The study consisted of the following parts:

- Screening (up to 42 days/6 weeks)
- Run-in period (optional): For subjects who received Mycophenolic acid (MPA) as SoC induction therapy as per investigator's decision and who were not already on MPA at Screening, MPA dosing was initiated during a run-in period before Randomization (for up to 4 weeks prior to the first dose of secukinumab)
- Treatment Period: Duration of 104 weeks of treatment with secukinumab/placebo in addition to SoC treatment (with last dose given at Week 100)
- Secukinumab dosing was started with initial dosing of 300 mg s.c. injections at Baseline, Weeks 1, 2, 3, and 4, followed by dosing every 4 weeks
- Follow-up period: Duration of 8 weeks (last visit performed 12 weeks after last dose of study medication) for all except for subjects entering extension study CAIN457Q12301E1

A total of 275 subjects were enrolled and were randomized to secukinumab 300 mg (n = 137) or placebo (n = 138) until study termination. Recruitment in this study was stopped on 26-May-2023.

Centers

106 centers in 34 countries: Slovakia (Slovak Republic)(1), Czech Republic(3), Spain(3), Japan(5), Switzerland(1), Russia(5), Germany(1), Thailand(3), Turkey(3), Sweden(1), Australia(1), Portugal(4), Colombia(4), Brazil(7), Korea, Republic of(2), Philippines(4), Vietnam(3), United States(8), Norway(1), Guatemala(3), Denmark(1), Taiwan(4), Greece(2), China(13), Croatia(1), India(2), Romania(5), Mexico(4), Argentina(3), France(1), Chile(4), Canada(1), Italy(1), Peru(1)

Objectives:

Primary Objective

- To demonstrate that secukinumab 300 mg was superior to placebo in Complete Renal Response (CRR) rate at Week 52 in active lupus nephritis (International Society of Nephrology/Renal Pathology Society (ISN/RPS) Class III or IV, with or without co-existing Class V features) patients on a background of SoC therapy

Secondary Objective

- To demonstrate superiority of secukinumab compared to placebo in change from baseline in 24-hour UPCR (Urine Protein-to-Creatinine Ratio) at Week 52
- To demonstrate superiority of secukinumab compared to placebo in proportion of patients achieving partial renal response (PRR) at Week 52
- To demonstrate superiority of secukinumab compared to placebo in average daily dose of oral corticosteroids administered between Week 16 and Week 52
- To demonstrate superiority of secukinumab compared to placebo in proportion of patients achieving PRR at Week 24
- To demonstrate superiority of secukinumab compared to placebo in time to achieve CRR
- To demonstrate superiority of secukinumab compared to placebo in time to achieve PRR
- To demonstrate superiority of secukinumab compared to placebo in time to achieve first morning void UPCR ≤ 0.5 mg/mg
- To demonstrate superiority of secukinumab compared to placebo in change in Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue©) score at Week 52
- To demonstrate superiority of secukinumab compared to placebo in patient's health related quality of life via Medical Outcome Short Form Health Survey (SF-36 Physical Component Summary (PCS)) score at Week 52

- To demonstrate superiority of secukinumab compared to placebo in change of LupusQoL (Physical Health) score at Week 52
- To evaluate the safety and tolerability of secukinumab s.c. as an add-on therapy to Standard of Care in lupus nephritis patients
- To estimate the proportion of patients with maintained renal response at Week 104
- To estimate the proportion of patients with improved or maintained renal response at Week 104

Test Product (s), Dose(s), and Mode(s) of Administration

- Secukinumab 150 mg for s.c. injection was supplied as 150 mg in a 1 mL prefilled syringe.
- Secukinumab placebo for s.c. injection was supplied as 0 mg/1 mL prefilled syringes, matching the appearance of secukinumab syringes.

Statistical Methods

Analysis sets

- The Randomized Set (RS) consisted of all randomized subjects. Regardless of whether they actually received study medication, subjects were analyzed according to the treatment assigned at randomization.
- The Full Analysis Set (FAS) consisted of all analyzable subjects from the randomized set to whom study treatment was assigned. According to the intent to treat principle, subjects were analyzed according to the treatment assigned during the randomization procedure, but according to actual stratum. Mis-randomized subjects (mis-randomized in Interactive Response Technology IRT) were excluded from the FAS.
- The Full Analysis Set 2 (FAS2) consisted of all analyzable subjects from the randomized set to whom study treatment was assigned and who had or would have had an opportunity to reach 52 weeks of treatment at the study termination (including subjects who discontinued study treatment). According to the intent to treat principle, subjects were analyzed according to the treatment assigned during the randomization procedure, but according to actual stratum. FAS2 was used as the primary analysis set for the main analysis of the primary estimand at the final abbreviated CSR analysis.
- The Safety Set included all subjects who received at least one dose of study treatment. Subjects were analyzed according to the study treatment received.

- PK Analysis Set included all subjects who had at least one PK/PD assessment and received at least one dose of study drug.

Efficacy analysis

Primary endpoint and estimand: The statistical hypothesis tested for the primary objective was that there is "no difference in the proportion" of subjects fulfilling the response criteria at Week 52 between the secukinumab and placebo regimens.

Let pj denote the proportion of responders at Week 52 for treatment regimens j, j=0, 1 where

- 0 corresponds to placebo regimen,
- 1 corresponds to secukinumab,

In statistical terms, H1: p1 = p0, HA1: p1 ≠ p0, i.e.,

H1: secukinumab is not different from placebo regimen with respect to CRR at Week 52

Logistic regression model adjusting for SoC, race and baseline UPCR was used for the primary analysis. Difference in marginal response proportions with p-value and respective 95% confidence interval was estimated from the logistic regression model. The default level of significance was set to 5% (two-sided, family-wise type-I-error). Two-sided p-value was provided only to the primary analysis.

- Handling of intercurrent events of primary estimand
- Major intercurrent events of primary estimand were addressed with the following strategies (considering that these events occurred before the assessments at Week 52):
  - Treatment discontinuation (for reasons other than "study terminated by sponsor") for any reason: non-responder (composite endpoint strategy)
  - Overuse of corticosteroid (> 10mg/day prednisone equivalent for ≥ 3 consecutive days or ≥ 7 days in total) between Week 44 and Week 52: non-responder (composite endpoint strategy)
- Handling of missing values not related to intercurrent events
- The main analysis of the primary estimand was performed on FAS2. Of the subjects in FAS2, those who did not have the required data to compute CRR at Week 52 were classified as non-responders.
- Supplementary analyses: A supplementary analysis of the primary endpoint summarized CRR descriptively with observed data without considering intercurrent events. This analysis was performed using FAS population.

Secondary endpoints: Due to the early termination of the study, secondary efficacy analyses were summarized with descriptive statistics only. Continuous and binary variables were summarized descriptively, and time to response variables presented with Kaplan-Meier curve for each treatment.

Safety analyses: All safety analyses (AEs, SAEs, AESIs, and laboratory data) performed on the Safety set and summarized descriptively.

Study Population: Key Inclusion/Exclusion Criteria

Key inclusion criteria:
1. Adult male and female subjects aged 18 - 75 years old at the time of Baseline.
2. Confirmed diagnosis of:
• SLE with documented history of at least 4 of the 11 criteria for SLE as defined by the American College of Rheumatology (ACR) (Tan et al 1982) revised by (Hochberg 1997). [NOTE: The 4 criteria did not have to be present at the time of Screening],
OR
• LN as the sole clinical criterion in the presence of ANA or anti-dsDNA antibodies.
3. Active lupus nephritis, as defined by meeting the 4 following criteria:
• Biopsy within 6 months prior to Screening visit indicating active glomerulonephritis WHO or ISN/RPS Class III or IV LN [excluding III (C), IV-S (C) and IV-G (C)]; patients are permitted to have co-existing Class V. If no biopsy was performed within 6 months of screening, a biopsy was to be performed during the Screening period
• UPCR ≥ 1 mg/mg at Screening.
• eGFR > 30 mL/min/1.73 m2 by Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI).
• Active urinary sediment (presence of cellular casts (RBC or WBC casts)) or hematuria (> 5 RBC per high power field or above the laboratory reference range).
4. Subjects must have currently been on MPA, or willing to initiate SoC induction therapy for LN according to the institutional practices using MPA or low-dose CYC in addition to corticosteroids. For guidance, see published guidelines such as by (Bertsias et al 2012, Hahn et al 2012).
5. Subjects must had been treated with anti-malarials (e.g. hydroxychloroquine), unless contra-indicated, and the dose had been stable for at least 10 days prior to Randomization.
6. Able to provide signed informed consent.

Key Exclusion criteria:
1. Severe renal impairment as defined by i.) Stage 4 CKD, or ii.) presence of oliguria (defined as a documented urine volume < 400 mL/24 h), or iii.) ESRD required dialysis or transplantation.
2. Known intolerance/hypersensitivity to MPA, or oral corticosteroids, or any component of the study drug(s).

3. Subjects received any other biologic immunomodulatory therapy within 6 months prior to Screening, excluding belimumab where 3 months were acceptable.
4. Previous exposure to secukinumab (AIN457) or any other biologic drug targeting IL-17 or the IL-17 receptor.
5. Subjects received any investigational drug within 1 month or five times the half-life of enrollment, whichever was longer.
6. Receipt of more than 3000 mg i.v. pulse methylprednisolone (cumulative dose) within the 12 weeks prior to Baseline.
7. Treatment with a systemic calcineurin inhibitor (e.g. cyclosporine, tacrolimus) within 12 weeks prior to Baseline
8. CYC use (i.v. or oral) within the month prior to Baseline.
9. Subjects requiring dialysis within the previous 12 months before Screening.
10. History of renal transplant.
11. Any severe progressive or uncontrolled concurrent medical condition, including recent severe thromboembolic events, that, in the opinion of the principal investigator, renders the subject unsuitable for the trial.
12. Active ongoing inflammatory diseases that might confound the evaluation of the benefit of secukinumab therapy, including inflammatory bowel disease.
13. Presence of investigator-identified significant medical problems which at the investigator's discretion would prevent the subject from participating in the study, included but not limited to the following: myocarditis, pericarditis, poorly controlled seizure disorder, acute confusional state, depression, severe manifestations of neuropsychiatric SLE (NPSLE).
14. Chest X-ray, computerized tomography (CT) scan, or MRI with evidence of ongoing infectious or malignant process, obtained within 3 months preceding the Screening visit and evaluated by a qualified physician.
15. History of chronic, recurrent systemic infections, active tuberculosis infection, or active systemic infections during the last two weeks (exception: common cold) prior to Randomization.
16. Known infection with human immunodeficiency virus (HIV), hepatitis B or hepatitis C at Screening or Randomization.
17. History of lymphoproliferative disease or any known malignancy or history of malignancy of any organ system treated or untreated within the past 5 years, regardless of whether there was evidence of local recurrence or metastases (except for skin Bowen's disease or basal cell carcinoma or actinic keratoses that had been treated with no evidence of recurrence in the past 12 weeks, carcinoma in situ of the cervix or non-invasive malignant colon polyps that had been removed).
18. Any of the following abnormal laboratory values on Screening evaluations as reported by Central Laboratory:
• Aspartate aminotransferase (AST), alanine aminotransferase (ALT), or amylase > 2.5xULN
• Hemoglobin < 8g/dL
• Neutrophils < 1.0 x 109/L
• Platelet count < 50 x 109/L
21. Pregnant or lactating women.
22. Women of childbearing potential, defined as all women physiologically capable of becoming pregnant, unless they were using highly effective methods of contraception during the entire study or longer if required by locally approved prescribing information (e.g., in European Union (EU) 20 weeks). Of note: the highly effective methods of contraception were mandated due to SoC

medications used as per protocol (MPA and CYC).
In case local regulations deviated from the contraception methods listed above, local regulations applied and were described in the informed consent form (ICF).
If stricter female or male contraception requirements were specified in the country-specific label for induction and maintenance standard of care medications, they had to be followed.
Note: Women were considered post-menopausal and not of childbearing potential if they had 12 months of natural (spontaneous) amenorrhea with an appropriate clinical profile (e.g., age appropriate, history of vasomotor symptoms) or had surgical bilateral oophorectomy (with or without hysterectomy), total hysterectomy or tubal ligation at least six weeks prior to enrollment. In the case of oophorectomy alone, only when the reproductive status of the woman had been confirmed by follow-up hormone level assessment was she considered not of childbearing potential.

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Participant Flow Table

Overall Study

	Secukinumab 300 mg	Placebo	Total
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).	
Started	137	138	275
Full Analysis Set 2	91	91	182
Pharmacokinetic Set	136	0	136
Completed	23	23	46
Not Completed	114	115	229
Adverse Event	1	3	4
Lost to Follow-up	1	1	2
Physician Decision	1	3	4
Pregnancy	0	1	1
Lack of Efficacy	2	2	4
Study terminated by sponsor	95	97	192
Subject decision	11	4	15
Death	1	1	2
Protocol deviation	1	0	1
Withdrawal of informed consent	1	3	4

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Baseline Characteristics

	Secukinumab 300 mg	Placebo	Total
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).	
Number of Participants [units: participants]	137	138	275
Baseline Analysis Population Description			
Age, Customized (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
< 30 years	55	64	119
>= 30 years	82	74	156
Age Continuous (units: Years) Analysis Population Type: Participants Mean ± Standard Deviation			
	34.1±10.84	33.2±11.28	33.6±11.05
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	116	124	240

Male	21	14	35
Race (NIH/OMB) (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
American Indian or Alaska Native	21	21	42
Asian	67	56	123
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	9	15
White	42	52	94
More than one race	1	0	1
Unknown or Not Reported	0	0	0

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Primary Outcome Result(s)

Percentage of participants achieving Complete Renal Response (CRR) at Week 52

Description	Complete Renal Response (CRR) is a composite endpoint defined as: ● Estimated Glomerular Filtration Rate (eGFR) >= 60 mL/min/1.73 m^2 or no less than 85% of core Baseline values and ● 24-hour Urine-to-Protein Creatinine Ratio (UPCR) =< 0.5mg/mg ● No treatment discontinuation before Week 52 ● The subject did not receive more than 10 mg/day prednisone or equivalent for >= 3 consecutive days or for >= 7 days in total during Week 44 through Week 52. Non-responder imputation (NRI) was used for participants who did not have the required data to compute responses at Week 52 or who had discontinued study treatment before Week 52. A logistic regression model was used for the analysis of this endpoint.
Time Frame	Baseline, Week 52
Analysis Population Description	Full Analysis Set 2.

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	91	91
Percentage of participants achieving Complete Renal Response (CRR) at Week 52 (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	25.9 (16.8 to 34.9)	38.6 (28.5 to 48.7)

Statistical Analysis

Groups	Secukinumab 300 mg, Placebo	Complete Renal Response (CRR) at Week 52

Type of Statistical Test	Superiority	
P Value	0.0662	
Method	Regression, Logistic	
Mean Difference (Final Values)	-12.7	Difference from placebo and 95% CI are from a logistic regression model with treatment group, stratification factor (SoC) and race as factors and baseline UPCR as a covariate using marginal standardization method.
95 % Confidence Interval 2-Sided	-26.3 to 0.9	

Secondary Outcome Result(s)

Change from Baseline in 24-hour Urine Protein-to Creatinine Ratio (UPCR)

Description	Urine Protein-to-Creatinine Ratio (UPCR) was determined by a central laboratory by dividing the protein concentration by the creatinine concentration as measured in the urine collected (24-hour urine collection sample).
Time Frame	Baseline, Week 52
Analysis Population Description	Full Analysis Set. Only participants with a value at both Baseline and post-baseline visit included.

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).

Number of Participants Analyzed [units: participants]	67	63
Change from Baseline in 24-hour Urine Protein-to Creatinine Ratio (UPCR) (units: mg/mg)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	-2.204 ± 3.5162	-2.741 ± 5.9448

Percentage of participants achieving Partial Renal Response (PRR) at Week 52

Description	Partial Renal Response (PRR) is a composite endpoint defined as: ● >= 50% reduction in 24-hour Urine-to-Protein Creatinine Ratio (UPCR) to sub-nephrotic levels (=< 3 mg/mg) and ● Estimated Glomerular Filtration Rate (eGFR) >= 60 mL/min/1.73 m^2 or no less than 85% of Baseline
Time Frame	Baseline, Week 52
Analysis Population Description	Full Analysis Set. Only participants with a value at both Baseline and post-baseline visit included.

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	73	72
Percentage of participants achieving Partial Renal Response (PRR) at Week 52 (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	56.2 (44.1 to 67.8)	63.9 (51.7 to 74.9)

Statistical Analysis

Groups	Secukinumab 300 mg, Placebo	Partial Renal Response (PRR) at Week 52
Type of Statistical Test	Other	
Mean Difference (Final Values)	-7.7	95% Confidence Intervals (CIs) are constructed using the exact binomial test.
95 % Confidence Interval 2-Sided	-23.7 to 8.4	

Average daily dose of oral corticosteroids

Description	Average daily dose of oral corticosteroids doses was used to assess efficacy of secukinumab compared to placebo in the averaged daily dose of oral corticosteroids administered between Week 16 and Week 52.
Time Frame	Week 16 to Week 52
Analysis Population Description	Full Analysis Set

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	137	138
Average daily dose of oral corticosteroids (units: mg/day)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	8.1243 ± 6.38329	7.4791 ± 5.61958

Percentage of participants achieving Partial Renal Response (PRR) at Week 24

Description	Partial Renal Response (PRR) is a composite endpoint defined as: ● >= 50% reduction in 24-hour Urine-to-Protein Creatinine Ratio (UPCR) to sub-nephrotic levels (=< 3 mg/mg) and ● Estimated Glomerular Filtration Rate (eGFR) >= 60 mL/min/1.73 m^2 or no less than 85% of Baseline
Time Frame	Baseline, Week 24
Analysis Population Description	Full Analysis Set. Only participants with a value at both Baseline and post-baseline visit included.

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	108	110
Percentage of participants achieving Partial Renal Response (PRR) at Week 24 (units: Percentage of participants)	**Number (95% Confidence Interval)**	**Number (95% Confidence Interval)**
	52.8 (42.9 to 62.5)	43.6 (34.2 to 53.4)

Incidence rate of participants achieving Complete Renal Response (CRR) up to Week 52

Description	Time to achieve Complete Renal Response (CRR) up to week 52 was evaluated by 4-week interval by using Kaplan-Meier estimates. Participants who did not achieve CRR were censored at the date of their last non-missing CRR result (including participants who completed week 52 without achieving CRR). * Subjects at risk = Subjects who did not achieve CRR and were not censored before or at the start of the specified interval. Participants had an event when achieving CRR. * Incidence rate (%) = (number of subjects with event/number of subjects at risk) x 100.

Time Frame	Baseline to Week 52
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure. Day 1 = Date of randomization.

	Secukinumab 300 mg	Placebo
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	131	132
Incidence rate of participants achieving Complete Renal Response (CRR) up to Week 52 (units: Percentage of participants)		
1 to 28 days	0.0	0.8
29 to 56 days	0.0	0.0
57 to 84 days	3.1	5.4
85 to 112 days	11.7	16.8
113 to 140 days	0.0	2.2
141 to 168 days	0.0	3.4
169 to 196 days	20.4	20.0
197 to 224 days	1.4	0.0
225 to 252 days	0.0	0.0
253 to 280 days	14.8	3.6
281 to 308 days	0.0	2.1
309 to 336 days	0.0	0.0

337 to 364 days	2.3	7.3

Incidence rate of participants achieving Partial Renal Response (PRR) up to Week 52

Description	Time to achieve Partial Renal Response (PRR) up to week 52 was evaluated by 4-week interval by using Kaplan-Meier estimates. Participants who did not achieve PRR were censored at the date of their last non-missing PRR result (including participants who completed week 52 without achieving PRR). Participants had event when achieving PRR. * Subjects at risk = Subjects who did not achieve PRR and were not censored before or at the start of the specified interval. * Incidence rate (%) = (number of subjects with event/ number of subjects at risk) x 100.
Time Frame	Baseline to Week 52
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure. Day 1 = Date of randomization.

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	131	132
Incidence rate of participants achieving Partial Renal Response (PRR) up to Week 52 (units: Percentage of participants)		
1 to 28 days	0.0	0.8
29 to 56 days	0.0	0.0
57 to 84 days	7.0	5.4
85 to 112 days	27.8	30.5
113 to 140 days	1.3	2.6
141 to 168 days	0.0	4.1

169 to 196 days	32.4	14.9
197 to 224 days	2.4	0.0
225 to 252 days	2.6	0.0
253 to 280 days	11.8	16.3
281 to 308 days	4.0	2.9
309 to 336 days	0.0	0.0
337 to 364 days	0.0	6.5

Time to achieve first morning void Urine Protein-to-Creatinine Ratio (UPCR) <= 0.5 mg/mg up to week 52

Description	Time to achieve first morning void Urine Protein-to-Creatinine Ratio (UPCR) <= 0.5 mg/mg up to week 52 was evaluated by 4-week interval by using Kaplan-Meier estimates. Participants who did not achieve UCPR were censored at the date of their last non-missing UCPR result (including participants who completed week 52 without achieving UCPR). Participants had event when achieving UCPR. * Subjects at risk = Subjects who did not achieve UCPR and were not censored before or at the start of the specified interval. * Incidence rate (%) = (number of subjects with event/ number of subjects at risk) x 100.
Time Frame	Baseline to Week 52
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure. Day 1 = Date of randomization.

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	135	136

Time to achieve first morning void Urine Protein-to-Creatinine Ratio (UPCR) <= 0.5 mg/mg up to week 52
(units: Percentage of participants)

1 to 28 days	19.3	21.3
29 to 56 days	2.8	5.6
57 to 84 days	8.7	7.0
85 to 112 days	11.8	9.7
113 to 140 days	7.6	7.4
141 to 168 days	9.9	6.9
169 to 196 days	9.7	3.2
197 to 224 days	7.5	11.9
225 to 252 days	4.2	6.0
253 to 280 days	4.4	0.0
281 to 308 days	12.2	4.5
309 to 336 days	0.0	5.1
337 to 364 days	3.1	2.9

Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue) mean change from Baseline up to Week 52

Description	The FACIT-Fatigue is a 13-item questionnaire that assesses self-reported fatigue and its impact upon daily activities and function over the past week. The purpose of the FACIT-Fatigue in this study was to assess the impact of fatigue on subjects with lupus nephritis (LN). The level of fatigue was measured on a 5-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much) based on their experience of fatigue during the past 2 weeks. The scale score is computed by summing the item scores, after reversing those items that are worded in the negative direction. FACIT-Fatigue scale score range from 0 to 52, where higher scores represent less fatigue.
Time Frame	Baseline, Week 12, Week 24, Week 36, Week 52
Analysis Population Description	Full Analysis Set. Only participants with a value at both Baseline and post-baseline visit included.

	Secukinumab 300 mg	**Placebo**

Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	131	131
Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue) mean change from Baseline up to Week 52 (units: Unit on a scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 12	-2.8 ± 8.47	-1.9 ± 8.46
Week 24	-1.4 ± 9.66	-2.0 ± 8.93
Week 36	-2.6 ± 9.21	-2.1 ± 9.67
Week 52	-2.0 ± 10.18	-2.0 ± 9.51

Short Form Health Survey (SF-36) Version 2 (Acute Form) mean change from Baseline in Physical Component Score (PCS) up to Week 52

Description	The SF-36 questionnaire consists of eight scales yielding two summary measures: physical and mental health. The physical health measure includes four scales of physical functioning (10 items), role-physical (4 items), bodily pain (2 items), and general health (5 items). The mental health measure is composed of vitality (4 items), social functioning (2 items), role-emotional (3 items), and mental health (5 items). In this trial, SF-36-PCS responder (improvement of >= 2.5 points) were evaluated. Responses to items allow for direct calculation of scale scores, while the physical component summary (PCS) scores are computed from weighted scale scores. For all scales and summary measures, higher scores indicate better health outcomes (PCS scores range 0 to 100).
Time Frame	Baseline, Week 12, Week 24, Week 36, Week 52
Analysis Population Description	Full Analysis Set. Only participants with a value at both Baseline and post-baseline visit included.

	Secukinumab 300 mg	**Placebo**

Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	131	131
Short Form Health Survey (SF-36) Version 2 (Acute Form) mean change from Baseline in Physical Component Score (PCS) up to Week 52 (units: Unit on a scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 12	2.306 ± 6.4306	2.210 ± 6.8760
Week 24	2.873 ± 6.4502	1.687 ± 6.5346
Week 36	2.910 ± 6.8234	3.152 ± 7.0623
Week 52	3.410 ± 7.7123	2.707 ± 6.8887

Lupus Quality of Life (LupusQoL) physical health score mean change from Baseline up to Week 52

Description	The LupusQoL is a disease-specific, 34-item, self-report questionnaire designed to measure the health-related quality of life (HRQoL) of subjects with SLE within 8 domains (i.e., physical health (8 items), emotional health (6 items), body image (5 items), pain (3 items), planning (3 items), fatigue (4 items), intimate relationships (2 items), and burden to others (3 items)). Responses are based on a 5-point Likert scale where 0 (all of the time) to 4 (never). Each domain of the LupusQoL was scored separately. Transformed scores range from 0 (worst HRQoL) to 100 (best HRQoL).
Time Frame	Baseline, Week 12, Week 24, Week 36, Week 52
Analysis Population Description	Full Analysis Set. Only participants with a value at both Baseline and post-baseline visit included.

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was

	was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	131	131
Lupus Quality of Life (LupusQoL) physical health score mean change from Baseline up to Week 52 (units: Unit on a scale)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 12	5.32 ± 16.031	6.18 ± 19.248
Week 24	4.84 ± 18.184	5.55 ± 20.485
Week 36	5.59 ± 20.684	7.89 ± 23.112
Week 52	7.62 ± 23.275	8.55 ± 20.589

Incidence of adverse events (AEs), serious adverse events (SAEs)

Description	The distribution of adverse events was done via the analysis of frequencies for treatment emergent Adverse Event (TEAEs), Serious Adverse Event (TESAEs) and Deaths due to AEs, through the monitoring of relevant clinical and laboratory safety parameters.
Time Frame	From first dose of study treatment up to approximately 2 years
Analysis Population Description	Safety Set (SAF).

	Secukinumab 300 mg	**Placebo**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Number of Participants Analyzed [units: participants]	137	138

Incidence of adverse events (AEs), serious adverse events (SAEs) (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
Deaths	1 (.73%)	1 (.72%)
Serious Adverse Event (TESAEs)	30 (21.9%)	39 (28.26%)
Treatment Emergent Adverse Event (TEAEs)	120 (87.59%)	123 (89.13%)
TESAEs leading to study medication discontinuation	8 (5.84%)	10 (7.25%)

Percentage of participants with Complete Renal Response (CRR) at Week 104 within those who had achieved CRR at Week 52 in the secukinumab group

Description	The percentage of participants with maintained renal response (CRR) at Week 104 in the secukinumab group was evaluated
Time Frame	Week 52 to Week 104
Analysis Population Description	Participants in the Full Analysis Set who received secukinumab. Subset of participants who achieved CRR at Week 52 and had an available CRR assessment at Week 104.

	Secukinumab 300 mg
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).
Number of Participants Analyzed [units: participants]	6
Percentage of participants with Complete Renal Response (CRR) at Week 104 within those who had achieved CRR at Week 52 in the secukinumab group (units: Participants)	**Count of Participants (Not Applicable)**
Response status at Week 104 : Achieve CRR	5 (83.33%)

Response status at Week 104 : Not Achieve CRR	1 (16.67%)

Percentage of participants with improved or maintained response (PRR or CRR) at Week 104 in those who had achieved at least PRR at Week 52 in the secukinumab group

Description	The percentage of participants with improved or maintained renal response (CRR) at Week 104 in the secukinumab group was evaluated
Time Frame	Week 52 to Week 104
Analysis Population Description	Participants in the Full Analysis Set who received secukinumab. Subset of participants who achieved PRR or CRR at Week 52 and had an available PRR or CRR assessment at Week 104.

	Secukinumab 300 mg
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).
Number of Participants Analyzed [units: participants]	12
Percentage of participants with improved or maintained response (PRR or CRR) at Week 104 in those who had achieved at least PRR at Week 52 in the secukinumab group (units: Participants)	**Count of Participants (Not Applicable)**
Response status at Week 104 : Achieve PRR or CRR	11 (91.67%)
Response status at Week 104 : Not achieve PRR or CRR	1 (8.33%)

Other Pre-Specified Outcome Result(s)

No data identified.

Post-Hoc Outcome Result(s)

No data identified.

Safety Results

Time Frame	On-treatment adverse events and deaths were reported from first dose of study treatment to 84 days after last dose of study medication, assessed up to approximately 2 years.
Additional Description	Any sign or symptom that occurred during the treatment and safety follow-up. The Safety Set included all subjects who received at least one dose of study treatment.
Source Vocabulary for Table Default	MedDRA (26.1)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Secukinumab 300 mg N = 137	**Placebo N = 138**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Total Number Affected	1	1
Total Number At Risk	137	138

Serious Adverse Events

Time Frame	On-treatment adverse events and deaths were reported from first dose of study treatment to 84 days after last dose of study medication, assessed up to approximately 2 years.
Additional Description	Any sign or symptom that occurred during the treatment and safety follow-up. The Safety Set included all subjects who received at least one dose of study treatment.
Source Vocabulary for Table Default	MedDRA (26.1)
Collection Approach for Table Default	Systematic Assessment

	Secukinumab 300 mg N = 137	**Placebo N = 138**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Total # Affected by any Serious Adverse Event	30	39
Total # at Risk by any Serious Adverse Event	137	138
Blood and lymphatic system disorders		
Anaemia	1 (0.73%)	0 (0.00%)
Blood loss anaemia	0 (0.00%)	1 (0.72%)
Pancytopenia	1 (0.73%)	0 (0.00%)
Cardiac disorders		
Pericardial effusion	0 (0.00%)	1 (0.72%)

Eye disorders		
Cataract	2 (1.46%)	1 (0.72%)
Gastrointestinal disorders		
Dyspepsia	1 (0.73%)	1 (0.72%)
Gastric ulcer	1 (0.73%)	0 (0.00%)
Gastritis	1 (0.73%)	0 (0.00%)
General disorders and administration site conditions		
Generalised oedema	1 (0.73%)	0 (0.00%)
Pyrexia	0 (0.00%)	1 (0.72%)
Hepatobiliary disorders		
Drug-induced liver injury	0 (0.00%)	1 (0.72%)
Immune system disorders		
Anaphylactic reaction	1 (0.73%)	0 (0.00%)
Drug hypersensitivity	0 (0.00%)	1 (0.72%)
Hypogammaglobulinaemia	0 (0.00%)	1 (0.72%)
Infections and infestations		
Cellulitis	0 (0.00%)	1 (0.72%)
Chronic sinusitis	0 (0.00%)	1 (0.72%)
COVID-19	3 (2.19%)	4 (2.90%)
Dengue fever	0 (0.00%)	1 (0.72%)
Dengue haemorrhagic fever	0 (0.00%)	1 (0.72%)
Diarrhoea infectious	1 (0.73%)	0 (0.00%)
Endometritis	0 (0.00%)	1 (0.72%)

Gastroenteritis	1 (0.73%)	1 (0.72%)
Genital herpes	0 (0.00%)	1 (0.72%)
Haematological infection	0 (0.00%)	1 (0.72%)
Herpes zoster	0 (0.00%)	1 (0.72%)
Herpes zoster disseminated	0 (0.00%)	1 (0.72%)
Influenza	1 (0.73%)	0 (0.00%)
Meningitis	1 (0.73%)	0 (0.00%)
Oesophageal candidiasis	1 (0.73%)	0 (0.00%)
Parotitis	0 (0.00%)	1 (0.72%)
Pneumonia	5 (3.65%)	3 (2.17%)
Pneumonia bacterial	0 (0.00%)	1 (0.72%)
Pyelonephritis	1 (0.73%)	0 (0.00%)
Pyelonephritis acute	2 (1.46%)	1 (0.72%)
Renal cyst infection	1 (0.73%)	0 (0.00%)
Respiratory tract infection viral	0 (0.00%)	1 (0.72%)
Septic shock	1 (0.73%)	0 (0.00%)
Soft tissue infection	0 (0.00%)	1 (0.72%)
Urinary tract infection	0 (0.00%)	2 (1.45%)
Injury, poisoning and procedural complications		
Traumatic haemorrhage	0 (0.00%)	1 (0.72%)
Metabolism and nutrition disorders		
Hypervolaemia	1 (0.73%)	0 (0.00%)
Metabolic acidosis	0 (0.00%)	1 (0.72%)
Musculoskeletal and connective tissue disorders		

Osteonecrosis	1 (0.73%)	0 (0.00%)
Systemic lupus erythematosus	1 (0.73%)	1 (0.72%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Anogenital warts	1 (0.73%)	0 (0.00%)
Nervous system disorders		
Cerebral ischaemia	0 (0.00%)	1 (0.72%)
Dyskinesia	0 (0.00%)	1 (0.72%)
Incoherent	0 (0.00%)	1 (0.72%)
Intracranial pressure increased	0 (0.00%)	1 (0.72%)
Post herpetic neuralgia	1 (0.73%)	0 (0.00%)
Transient ischaemic attack	0 (0.00%)	1 (0.72%)
Psychiatric disorders		
Bipolar disorder	0 (0.00%)	1 (0.72%)
Major depression	0 (0.00%)	1 (0.72%)
Renal and urinary disorders		
Acute kidney injury	1 (0.73%)	4 (2.90%)
Azotaemia	0 (0.00%)	1 (0.72%)
End stage renal disease	0 (0.00%)	1 (0.72%)
Lupus nephritis	4 (2.92%)	5 (3.62%)
Nephrotic syndrome	1 (0.73%)	0 (0.00%)
Renal failure	0 (0.00%)	1 (0.72%)
Reproductive system and breast disorders		
Endometriosis	0 (0.00%)	1 (0.72%)

Genital tract inflammation	0 (0.00%)	1 (0.72%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea	0 (0.00%)	1 (0.72%)
Haemoptysis	1 (0.73%)	0 (0.00%)
Pulmonary congestion	1 (0.73%)	0 (0.00%)
Pulmonary hypertension	0 (0.00%)	1 (0.72%)
Vascular disorders		
Deep vein thrombosis	0 (0.00%)	1 (0.72%)
Hypertension	1 (0.73%)	0 (0.00%)
Hypertensive urgency	0 (0.00%)	1 (0.72%)

Other (Not Including Serious) Adverse Events

Time Frame	On-treatment adverse events and deaths were reported from first dose of study treatment to 84 days after last dose of study medication, assessed up to approximately 2 years.
Additional Description	Any sign or symptom that occurred during the treatment and safety follow-up. The Safety Set included all subjects who received at least one dose of study treatment.
Source Vocabulary for Table Default	MedDRA (26.1)
Collection Approach for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 2%

	Secukinumab 300 mg N = 137	**Placebo N = 138**
Arm/Group Description	A blinded, weekly, subcutaneous (s.c.) secukinumab 300 mg loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 786 days).	A blinded, weekly, subcutaneous (s.c.) matching placebo loading regimen was administered for the first 4 weeks followed by a monthly maintenance dose in all randomized subjects thereafter (maximum treatment exposure during the core study: 794 days).
Total # Affected by any Other Adverse Event	111	116
Total # at Risk by any Other Adverse Event	137	138
Blood and lymphatic system disorders		
Anaemia	12 (8.76%)	13 (9.42%)
Iron deficiency anaemia	3 (2.19%)	4 (2.90%)
Leukopenia	6 (4.38%)	10 (7.25%)
Lymphopenia	3 (2.19%)	1 (0.72%)
Neutropenia	3 (2.19%)	3 (2.17%)
Eye disorders		
Dry eye	3 (2.19%)	2 (1.45%)
Vision blurred	3 (2.19%)	6 (4.35%)
Gastrointestinal disorders		
Abdominal pain	3 (2.19%)	6 (4.35%)
Abdominal pain upper	2 (1.46%)	4 (2.90%)
Aphthous ulcer	3 (2.19%)	2 (1.45%)

Constipation	1 (0.73%)	6 (4.35%)
Diarrhoea	23 (16.79%)	21 (15.22%)
Dyspepsia	5 (3.65%)	2 (1.45%)
Gastritis	4 (2.92%)	2 (1.45%)
Gastrooesophageal reflux disease	2 (1.46%)	5 (3.62%)
Haemorrhoids	3 (2.19%)	1 (0.72%)
Mouth ulceration	5 (3.65%)	3 (2.17%)
Nausea	11 (8.03%)	5 (3.62%)
Toothache	3 (2.19%)	2 (1.45%)
Vomiting	7 (5.11%)	4 (2.90%)
General disorders and administration site conditions		
Chest discomfort	3 (2.19%)	0 (0.00%)
Fatigue	4 (2.92%)	2 (1.45%)
Oedema	2 (1.46%)	4 (2.90%)
Oedema peripheral	3 (2.19%)	8 (5.80%)
Peripheral swelling	4 (2.92%)	2 (1.45%)
Pyrexia	8 (5.84%)	3 (2.17%)
Infections and infestations		
Bronchitis	3 (2.19%)	3 (2.17%)
Conjunctivitis	1 (0.73%)	4 (2.90%)
COVID-19	25 (18.25%)	22 (15.94%)
Gastroenteritis	6 (4.38%)	7 (5.07%)
Herpes zoster	10 (7.30%)	7 (5.07%)
Influenza	3 (2.19%)	3 (2.17%)
Nasopharyngitis	11 (8.03%)	11 (7.97%)

Oral candidiasis	8 (5.84%)	3 (2.17%)
Oral herpes	5 (3.65%)	2 (1.45%)
Pharyngitis	4 (2.92%)	11 (7.97%)
Pneumonia	6 (4.38%)	0 (0.00%)
Upper respiratory tract infection	19 (13.87%)	26 (18.84%)
Urinary tract infection	19 (13.87%)	30 (21.74%)
Viral upper respiratory tract infection	1 (0.73%)	3 (2.17%)
Injury, poisoning and procedural complications		
Contusion	2 (1.46%)	4 (2.90%)
Investigations		
Weight increased	4 (2.92%)	3 (2.17%)
White blood cell count decreased	2 (1.46%)	3 (2.17%)
Metabolism and nutrition disorders		
Dyslipidaemia	7 (5.11%)	5 (3.62%)
Hypercholesterolaemia	3 (2.19%)	1 (0.72%)
Hyperlipidaemia	4 (2.92%)	1 (0.72%)
Hyperuricaemia	7 (5.11%)	1 (0.72%)
Hypocalcaemia	2 (1.46%)	3 (2.17%)
Hypokalaemia	9 (6.57%)	11 (7.97%)
Iron deficiency	1 (0.73%)	3 (2.17%)
Vitamin D deficiency	1 (0.73%)	3 (2.17%)
Musculoskeletal and connective tissue disorders		
Arthralgia	13 (9.49%)	19 (13.77%)
Back pain	5 (3.65%)	4 (2.90%)

Muscle spasms	6 (4.38%)	2 (1.45%)
Pain in extremity	0 (0.00%)	4 (2.90%)
Systemic lupus erythematosus	1 (0.73%)	4 (2.90%)
Nervous system disorders		
Dizziness	6 (4.38%)	3 (2.17%)
Headache	21 (15.33%)	14 (10.14%)
Tremor	3 (2.19%)	2 (1.45%)
Psychiatric disorders		
Anxiety	3 (2.19%)	4 (2.90%)
Depression	3 (2.19%)	2 (1.45%)
Insomnia	8 (5.84%)	6 (4.35%)
Renal and urinary disorders		
Acute kidney injury	6 (4.38%)	2 (1.45%)
Lupus nephritis	2 (1.46%)	3 (2.17%)
Reproductive system and breast disorders		
Menstrual disorder	6 (4.38%)	1 (0.72%)
Menstruation irregular	4 (2.92%)	1 (0.72%)
Vaginal discharge	1 (0.73%)	3 (2.17%)
Respiratory, thoracic and mediastinal disorders		
Cough	8 (5.84%)	14 (10.14%)
Oropharyngeal pain	4 (2.92%)	4 (2.90%)
Rhinitis allergic	3 (2.19%)	1 (0.72%)
Rhinorrhoea	1 (0.73%)	4 (2.90%)

Skin and subcutaneous tissue disorders		
Acne	1 (0.73%)	3 (2.17%)
Alopecia	6 (4.38%)	11 (7.97%)
Dermatitis allergic	0 (0.00%)	3 (2.17%)
Dry skin	3 (2.19%)	0 (0.00%)
Erythema	1 (0.73%)	3 (2.17%)
Pruritus	4 (2.92%)	3 (2.17%)
Rash	1 (0.73%)	5 (3.62%)
Rash erythematous	0 (0.00%)	3 (2.17%)
Skin hyperpigmentation	5 (3.65%)	1 (0.72%)
Vascular disorders		
Hypertension	8 (5.84%)	8 (5.80%)
Hypotension	5 (3.65%)	4 (2.90%)

Other Relevant Findings

None

Conclusion:

- The study was terminated early by Novartis due to futile results from planned IA1, as no clinically meaningful benefit of secukinumab above the current SoC was observed in the futility analysis; the pre-specified futility threshold of a predictive power of less than 10% was met. This was confirmed based on the analysis of the primary endpoint (CRR at Week 52) performed on subjects who had a chance to reach Week 52 (FAS2)
- The overall incidence of TEAEs including infections were similar between the two groups (secukinumab + SoC immunosuppression) vs (placebo + SoC immunosuppression). As expected, the incidence of herpes zoster and fungal infections was numerically higher for secukinumab than for placebo. These are known risk for secukinumab and do not represent a new safety signal. On the other hand, numerically higher incidence of other infections was reported for placebo. Study treatment discontinuation due to infections was numerically lower for the secukinumab 300 mg than for placebo. Furthermore, no MACE was reported for secukinumab 300 mg in this population with known increased risk for cardiovascular diseases due to LN
- The safety profile of secukinumab 300 mg in this study was consistent with the known safety profile for secukinumab in adults in the approved indications for secukinumab, and showed no new or unexpected safety signals

Date of Clinical Trial Report

24-May-2024