NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

secukinumab

Trial Indication

Psoriasis

Protocol Number

CAIN457A2403

Protocol Title

A 16-week randomized, open-label, multicenter study to assess the superiority of secukinumab over guselkumab in the complete treatment of ustekinumab resistant psoriatic plaques - ARROW

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase 2a

Study Start/End Dates

Study Start Date: January 2019
Primary Completion Date: January 2020
Study Completion Date: January 2020

Study Design/Methodology

This was a 16-week, randomized, open-label, parallel-group, active-control, Phase 2a study comparing secukinumab 300 mg subcutaneous (s.c.) versus guselkumab 100 mg s.c. in subjects with plaque psoriasis who had an inadequate response to ustekinumab. Inadequate responders were defined as subjects who, after treatment with ustekinumab at a dose equal or higher than that on the label for at least 24 weeks, presented a PASI of 1-10 and one or more refractory skin plaques, defined by a TCS of at least 6 and an area ≥ 10 cm2 at Baseline.

At Baseline (Day 1), subjects were randomized to treatment with secukinumab or guselkumab in a 1:1 ratio. Secukinumab was self-administered as two 150-mg s.c. injections at Baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 12 inclusive. Guselkumab was self-administered as 100-mg s.c. injections at Baseline, Week 4, and Week 12. The initiation of study treatment at Baseline was not to happen earlier than 12 weeks after the last administration of ustekinumab.

Forty subjects were to be enrolled and treated for 16 weeks. Additional unscheduled visits could be called by the Investigators according to their own judgement and personal clinical experience.

At Baseline, two 6-mm punch biopsies were taken from all the subjects, one from the identified active plaque (TCS ≥ 6) and one from never-lesional skin. At the End-of-study Visit, one biopsy was taken from the same area of the active plaque sampled at Baseline. Whenever possible, biopsies were to be taken from the trunk to avoid scars in visible body areas.

The duration of enrollment was expected to be 6 months, however, the actual duration was 8 months (from 14-Jan-2019 to 18-Sep-2019).

Centers

14 centers in 3 countries: Canada (1), Germany (9), United States (4)

Objectives:

Primary objective:

To assess the superiority of secukinumab over guselkumab in controlling clinical activity in psoriatic plaques resistant to treatment with ustekinumab

Exploratory objectives:

Exploratory objectives will be presented voluntarily in a future update of this report.

Test Products, Doses, and Modes of Administration

Secukinumab treatment arm: 20 subjects with plaque psoriasis with an inadequate response to ustekinumab self-administered 300 mg secukinumab as two 150-mg subcutaneous (s.c.) injections at Baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 12 inclusive.

Guselkumab treatment arm: 20 subjects with plaque psoriasis with an inadequate response to ustekinumab self-administered guselkumab as 100-mg s.c. injections at Baseline, Week 4, and Week 12.

The planned duration of treatment was 16 weeks

Statistical Methods

The number (%) of subjects whose target plaque achieve “clear” or “almost clear” status (TCS = 0-2) at Week 16 (i.e., responders) are provided based on the Full Analysis Set (FAS) together with the 95% confidence interval using the exact method for the treatment difference in proportions of responders in each arm.

Furthermore, a 1-sided Fisher’s exact test for the difference in the proportions of responders in the secukinumab (P1) and guselkumab (P2) arms, H0: P1-P2 = 0 versus H1: P1-P2 > 0 at a type I error rate of 0.05 were performed.

The total clinical score (TCS) was assessed at all study visits. At Baseline, it was performed before the first administration of study treatment. The TCS for the target plaque was determined (ideally by the same evaluator) as the sum of 3 scores: erythema (0-3), scaling (0-3) and infiltration (0-3) rated according to their severity. The TCS can range from 0 (all signs absent) to 9 (all signs severe).

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:

Chronic plaque-type psoriasis considered inadequately controlled after treatment with ustekinumab according to the following criteria:

- Ustekinumab administered at a dose equal or higher than that on the label for at least 24 weeks. The last administration must be at least 12 weeks before randomization
  - absolute PASI score of 1-10 at Screening
  - Presence of at least 1 refractory skin plaque, defined by a TCS of at least 6 and severity score of at least 2 or 3 (moderate) for each individual item, with an area ≥ 10 cm2 at screening.

Exclusion Criteria:

- Forms of psoriasis other than chronic plaque-type (e.g., pustular, erythrodermic and guttate psoriasis) at Screening or Baseline
- Drug-induced psoriasis (i.e., new onset or current exacerbation from beta-blockers, calcium channel inhibitors or lithium) at Baseline
- Previous treatment with more than one TNFα inhibitor or with IL-17A (including secukinumab), IL-17R or IL-23 (including guselkumab) inhibitors
- Use of other investigational drugs within 4 weeks before enrolment, or within a period of 5 half lives of enrollment/initiation of the study treatment, whichever is longer
- Ongoing use of prohibited treatments
- Known immunosuppression (e.g., AIDS) at Screening

Participant Flow Table

Overall Study

	secukinumab	guselkumab	Total
Arm/Group Description	20 subjects with plaque psoriasis with an inadequate response to ustekinumab self-administered 300 mg secukinumab as two 150-mg s.c. injections at Baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 12 inclusive	20 subjects with plaque psoriasis with an inadequate response to ustekinumab self-administered guselkumab as 100 mg s.c. injections at Baseline, Weeks 4, and 12.	
Started	20	20	40
Completed	20	19	39
Not Completed	0	1	1

Physician Decision	0	1	1

Baseline Characteristics

	secukinumab	guselkumab	Total
Arm/Group Description	20 subjects with plaque psoriasis with an inadequate response to ustekinumab self-administered 300 mg secukinumab as two 150-mg s.c. injections at Baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 12 inclusive	20 subjects with plaque psoriasis with an inadequate response to ustekinumab self-administered guselkumab as 100 mg s.c. injections at Baseline, Weeks 4, and 12.	
Number of Participants [units: participants]	20	20	40
Age Continuous (units: Mean) Mean ± Standard Deviation			
	47.6±15.10	48.5±12.30	48.1±13.60
Age Categorical (units:) Count of Participants			
<=18 years	0	0	0
Between 18 and 65 years	17	19	36
>=65 years	3	1	4
Sex: Female, Male (units:) Count of Participants			
Female	6	5	11
Male	14	15	29
Race/Ethnicity, Customized			

(units: Participants)
Count of Participants

White	17	0	17
Black or African American	2	0	2
Asian	1	0	1

Primary Outcome Result

Proportion of subjects whose plaque achieves “clear” or “almost clear” status (TCS = 0-2)

(Time Frame: 16 week)

	secukinumab	**guselkumab**
Arm/Group Description	20 subjects with plaque psoriasis with an inadequate response to ustekinumab self-administered 300 mg secukinumab as two 150-mg s.c. injections at Baseline, Weeks 1, 2, 3, 4 and then every 4 weeks until Week 12 inclusive	20 subjects with plaque psoriasis with an inadequate response to ustekinumab self-administered guselkumab as 100 mg s.c. injections at Baseline, Weeks 4, and 12.
Number of Participants Analyzed [units: participants]	20	20
Proportion of subjects whose plaque achieves “clear” or “almost clear” status (TCS = 0-2) (units: participants) Count of Participants		
	12 (60%)	8 (40%)

Statistical Analysis

Groups	secukinumab, guselkumab	Proportion of subjects whose plaque achieves “clear” or “almost clear” status (TCS = 0-2)
P Value	0.1715	

Method	Fisher Exact	The statistical model was the 1-sided Fisher's exact test for the difference in proportions.
Difference secukinumab vs guselkumab	20.0	
95% Confidence Interval 2-Sided	-13.3 to 50.3	

Exploratory Outcome Results

The analysis of biomarkers has been delayed. The vendor in charge of these analyses had to close operations following government-imposed restrictions related to the global coronavirus pandemic of 2020, thus, the biomarker-related exploratory objectives were not evaluated in the present report; but will be presented in a voluntary future update.

Safety Results

All-Cause Mortality

	Secukinumab N = 20	**Guselkumab N = 20**
Arm/Group Description	Secukinumab	Guselkumab
Total participants affected	0 (0.00%)	0 (0.00%)

Serious Adverse Events by System Organ Class

Time Frame	Adverse Events (AEs) were collected for duration of study to week 16
Additional Description	AEs are any untoward sign or symptom that occurs during the study treatment period

Source Vocabulary for Table Default	MedDRA (20.1)
Assessment Type for Table Default	Systematic Assessment

	Secukinumab N = 20	**Guselkumab N = 20**
Arm/Group Description	Secukinumab	Guselkumab
Total participants affected	2 (10.00%)	1 (5.00%)
Gastrointestinal disorders		
Gastritis	1 (5.00%)	0 (0.00%)
Hepatobiliary disorders		
Cholelithiasis	0 (0.00%)	1 (5.00%)
Infections and infestations		
Pneumonia	1 (5.00%)	0 (0.00%)

Other Adverse Events by System Organ Class

Time Frame	Adverse Events (AEs) were collected for duration of study to week 16
Additional Description	Adverse Events (AEs) are any untoward sign or symptom that occurs during the study treatment period
Source Vocabulary for Table Default	MedDRA (20.1)
Assessment Type for Table Default	Systematic Assessment
Frequent Event Reporting Threshold	2%

	Secukinumab N = 20	Guselkumab N = 20
Arm/Group Description	Secukinumab	Guselkumab
Total participants affected	11 (55.00%)	5 (25.00%)
Eye disorders		
Dacryostenosis acquired	1 (5.00%)	0 (0.00%)
Infections and infestations		
Bronchitis	0 (0.00%)	1 (5.00%)
Erysipelas	1 (5.00%)	0 (0.00%)
Herpes zoster	1 (5.00%)	0 (0.00%)
Nasopharyngitis	2 (10.00%)	1 (5.00%)
Postoperative wound infection	1 (5.00%)	0 (0.00%)
Sepsis	1 (5.00%)	0 (0.00%)
Vulvovaginal mycotic infection	1 (5.00%)	0 (0.00%)
Injury, poisoning and procedural complications		
Wound dehiscence	1 (5.00%)	0 (0.00%)
Investigations		
Blood bilirubin increased	1 (5.00%)	0 (0.00%)
Metabolism and nutrition disorders		
Gout	2 (10.00%)	0 (0.00%)
Hyperglycaemia	1 (5.00%)	0 (0.00%)

Musculoskeletal and connective tissue disorders		
Back pain	0 (0.00%)	1 (5.00%)
Renal and urinary disorders		
Acute kidney injury	1 (5.00%)	0 (0.00%)
Reproductive system and breast disorders		
Balanoposthitis	1 (5.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Asthma	1 (5.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders		
Dyshidrotic eczema	0 (0.00%)	1 (5.00%)
Eczema	0 (0.00%)	1 (5.00%)
Hyperhidrosis	0 (0.00%)	1 (5.00%)
Miliaria	1 (5.00%)	0 (0.00%)

Conclusion

- While the number of responders was higher in the secukinumab arm compared to the guselkumab arm 60% (12/20) vs 40% (8/20), respectively, no statistically significant difference was achieved (1-sided p-value = 0.1715, Fisher's exact test)
- The safety profiles of both treatments in this study were consistent with the known safety profiles, no new or unexpected safety signals were observed

Date of Clinical Trial Report

17 August 2020