Sponsor

Novartis

Generic Drug Name

Secukinumab (AIN457)

Therapeutic Area of Trial

Psoriasis

Approved Indication

Investigational

Protocol Number

CAIN457A2225

Title

An exploratory study to investigate the distribution of secukinumab (AIN457) into dermal interstitial fluid using open flow microperfusion after a single subcutaneous administration of 300 mg in healthy subjects and psoriatic patients

Study Phase

I

Study Start/End Dates

01-Feb-2012 to 28-Jan-2013

Study Design/Methodology

This was a two parts, single center, open label, exploratory study to evaluate the distribution of subcutaneous administered secukinumab 300 mg into dermal interstitial fluid (ISF) in healthy volunteers (Part I) and psoriatic patients (Part II) using open flow microperfusion (OFM).

Centers

Austria (one center)

Publication

2013 International Investigative Dermatology Meeting, Edinburgh International Conference Centre, Edinburgh, Scotland, May 8 – 11, 2013, PubMed 23607128

Absolute levels of the novel anti-IL-17A antibody, secukinumab, in skin can be quantified by dermal open flow microperfusion (dOFM), Journal of Investigative Dermatology (2013) 133, S17–S55, Abstract 308.

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

A single dose of 300 mg secukinumab was administered subcutaneously on Day 1. Sinistrin, as reference molecule was used to measure the absolute concentration of a molecule in the skin tissue fluid, and administered at Day 1, Day 8, and Day 15.

Statistical Methods

The primary variables were concentrations of secukinumab in dermal interstitial fluids after single subcutaneous administration of 300 mg secukinumab in healthy subjects and in lesional and non-lesional skin in psoriasis patients. For both Part I and Part II, descriptive statistics were used to summarize the secukinumab concentrations in dermal ISF by visit and site (e.g. lesional/non-lesional). Descriptive statistics may include mean, SD, and CV, min, max and median.

Study Population: Inclusion/Exclusion Criteria and Demographics

There were two study populations: healthy volunteers (Part I) and psoriasis patients (Part II).

The key inclusion criteria were:

For Part I: Healthy male and female subjects 18 to 65 years of age inclusive.

For Part II: Chronic plaque-type psoriasis (with or without arthritis) diagnosed for at least 6 months before enrollment including at least one plaque accessible for OFM with at least moderate severity.

Key exclusion criteria for Part I and Part II: Women of child-bearing potential unwilling to use effective contraception; History of an ongoing, chronic or recurrent infectious disease, or evidence of tuberculosis infection as defined by a positive TB-test at screening.

For Part I: Use of any prescription drugs, herbal supplements, within 4 weeks prior to initial dosing.

For Part II: Ongoing use of concomitant psoriasis treatments. Washout periods have to be adhered to.

Other protocol-defined inclusion/exclusion criteria may apply.

Participant Flow

	Part I **N=8** **n**	**Part II** **N=8** **n**
Subjects Completed	8	8

Baseline Characteristics

		Part I	Part II
Age (units:years)	Mean (SD)	26 +/- 6	39 +/-8
Gender – n	Male	6	8
	Female	2	0

Outcome measures

Primary Outcome Result(s)

Dermal ISF concentrations of secukinumab

	Part I		Part II			
Timepoint	Day 8	Day 15	Day 8	Day 8	Day 15	Day 15
Type of skin	Healthy skin	Healthy skin	Lesional	Non-lesional	Lesional	Non-lesional
Number of participants	8	8	8	8	8	8
Mean +/- SD [µg/mL]	7.8 +/- 1.3	8.0 +/- 3.2	6.8 +/- 2.7	8.3 +/- 3.4	5.7 +/- 1.8	6.4 +/- 3.4

Secondary Outcome Result(s)

Sinistrin concentrations in Part I

Adjusted Geometric means (µg/mL)

Serum	ISF
277	288

Safety Results

Incidence of AEs Part I (healthy volunteers)

Subjects with AE(s)	Secukinumab+ N=8 n (%)	Total N=8 n (%)
Any Body System	5 (62.5)	5 (62.5)
Eye disorders	1 (12.5)	1 (12.5)
- Conjunctivitis allergic	1 (12.5)	1 (12.5)
General disorders and administration site conditions	3 (37.5)	4 (50.0)
- Asthenia	1 (12.5)	1 (12.5)
- Injection site pain	1 (12.5)	1 (12.5)
- Injection site reaction	1 (12.5)	1 (12.5)
- Oedema peripheral	0 (0.0)	1 (12.5)
Infections and infestations	2 (25.0)	2 (25.0)
- Nasopharyngitis	2 (25.0)	2 (25.0)
- Rhinitis	1 (12.5)	1 (12.5)
Injury, poisoning and procedural complications	1 (12.5)	1 (12.5)
- Post procedural haematoma	1 (12.5)	1 (12.5)

Subjects with AE(s)	Secukinumab+ N=8 n (%)	Total N=8 n (%)
Nervous system disorders	1 (12.5)	1 (12.5)
- Headache	1 (12.5)	1 (12.5)
Respiratory, thoracic and mediastinal disorders	1 (12.5)	1 (12.5)
- Oropharyngeal pain	1 (12.5)	1 (12.5)
Skin and subcutaneous tissue disorders	1 (12.5)	1 (12.5)
- Erythema	1 (12.5)	1 (12.5)

A subject with multiple occurrences of an adverse event is counted only once in the AE category.
A subject with multiple adverse events within a body system is counted only once in the total row.
N = number of subjects studied n = number of subjects with at least one AE in the category

Incidence of AEs - Part II (psoriasis patients)

Subjects with AE(s)	Secukinumab N=8 n (%)	Total N=8 n (%)
Any Body System	6 (75.0)	6 (75.0)
Infections and infestations	2 (25.0)	2 (25.0)
- Nasopharyngitis	2 (25.0)	2 (25.0)
Musculoskeletal and connective tissue disorders	1 (12.5)	1 (12.5)
- Arthralgia	1 (12.5)	1 (12.5)
Nervous system disorders	2 (25.0)	2 (25.0)
- Headache	2 (25.0)	2 (25.0)
Respiratory, thoracic and mediastinal disorders	1 (12.5)	1 (12.5)
- Oropharyngeal pain	1 (12.5)	1 (12.5)
Vascular disorders	1 (12.5)	1 (12.5)
- Haematoma	1 (12.5)	1 (12.5)

A subject with multiple occurrences of an adverse event is counted only once in the AE category.
A subject with multiple adverse events within a body system is counted only once in the total row.
N = number of subjects studied n = number of subjects with at least one AE in the category

Serious Adverse Events and Deaths

None

Other Relevant Findings

None

Date of Clinical Trial Report

26-Jul-2013

Date Inclusion on Novartis Clinical Trial Results Database

7 January 2013

Date of Latest Update