Sponsor
Novartis Pharmaceuticals

Generic Drug Name
Secukinumab

Trial Indication(s)
Plaque Psoriasis

Protocol Number
CAIN457ATR02

Protocol Title
A retrospective multicenter study for the assessment of effectiveness of secukinumab as assessed by Psoriasis Area and Severity Index with subcutaneous administration in adult patients with moderate to severe plaque psoriasis in Turkish population

Clinical Trial Phase
NA

Phase of Drug Development
NA

Study Start/End Dates
Study start date: 09/07/2020

Study Completion date: 31/08/2021

Reason for Termination

NA

Study Design/Methodology

The study was a retrospective, multicenter, cohort study which was based on data collection at week 4,16 and 52 of secukinumab treatment for treatment of moderate to severe plaque psoriasis.

The observational design of the study allowed data collection about secukinumab treatment patterns and clinical and demographic characteristics of plaque psoriasis patients treated with secukinumab for 52 weeks in Turkey. The adults included in the study were treated with secukinumab for 52 weeks. The adults with no available data of PASI scores at specific time points (4, 16 and 52 weeks) and no definite description of treatment cessation were excluded. The study population consisted of adults treated with secukinumab for 52 weeks and adults dropped out before 52 weeks with available data of PASI scores at 4, 16 and 52 weeks and definite description of treatment cessation.

Retrospective data collection from secondary sources (hospital medical records) allowed time and cost saving since description of patients' characteristics, analyses of outcomes of interest and their determinants could be made in a short period of time.

The study consisted of the following periods:

- The index date was the date of initiation of secukinumab
- The study (index) period is between 18 May 2018 to 31 May 2020
- The follow-up (post-index) period is 4,16 and 52 weeks post-index

Centers

Novartis Investigative Site

Objectives:

Primary objective(s)

- Assessment of the effectiveness of secukinumab in subjects with moderate to severe plaque psoriasis based on the percentage of patients have absolute PASI ≤3 at week 52 in Turkey

Secondary objective(s)

Assessment of:
• the speed of PASI response at week 4 and percentage of PASI 75 responders at week 16.
• the sustainability of PASI 90 scores between week 16 and 52
• the PASI 100 response rate at week 52.
• PASI 90 response rates for biologic naïve vs.non- naïve patients at week 52.
• the comparative effectiveness of secukinumab via PASI in smokers vs. non-smokers at week 52.
• the effectiveness of secukinumab in patients with very severe (PASI>20) psoriasis at week 52.
• the effectiveness of secukinumab in psoriatic manifestations such as nail, palmoplantar, scalp and arthritic involvements at week 52.
• describe secukinumab treatment utilization patterns

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

NA

Statistical Methods

Mean, standard deviation (SD), min-max, median, interquartile range (IQR), number of non-missing data (n) are used to summarize the quantitative variables.

The qualitative variables are summarized using number of non-missing data (n), counts and percentages

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria

- A diagnosis of psoriasis
- Age ≥ 18 years at registry baseline
- Patients with a firm diagnosis of chronic plaque psoriasis for at least 6 months before enrollment
- Secukinumab treatment should be initiated 52 weeks before data collection date
- Moderate to severe plaque psoriasis with PASI score of ≥10 before initiating secukinumab.

Exclusion criteria

- Patients diagnosed with others types of psoriasis (pustular psoriasis, erythrodermic psoriasis etc) are excluded.
- Previous exposure to secukinumab or any other biologic drug directly targeting IL-17A or IL-17RA

Participant Flow

A total of 277 patients from 14 study sites were included in the study. In line with the study design, all data about the study outcomes available in the hospital records were collected.

Baseline Characteristics

Of 277 patients included in the study, 160 (57.8%) were male and the mean age of the group was 47.2. The mean age at diagnosis was around 30. Smokers constituted 39.4% of the study population. More than half of the participants were actively working (54.9%).

Hypertension was the most common comorbidty (23.5%) followed by hyperlipidemia (17.3%) and diabetes mellitus (16.2%). Scalp (64.3%) and nail psoriasis (52.7%) were the most common additional involvement sites.

Overall, 167 patients had been previously treated with biologics. Adalimumab was the most commonly used previous biologic medication (70%).

		n (%)	Mean± SD (Min.-Max.) (Median; 25%-75%)
Sex	Men	160 (57.8)	
	Women	117 (42.2)	
Age			47.2 ±12.3 (21-81) (46; 39-56)
Height (cm) (n:269)			169.2 ±9.2 (143-196) (170; 162-176)
Weight (kg) (n:227)			81.2 ±14.8 (48-139) (80; 72-89)
BMI (n:224)			28.5 ±4.9 (1..2-57.9) (27.7; 25.6-31.2)
Educational level (n:273)	University	84 (30.8)	
	High-school	90 (33)	
	Middle school	28 (10.3)	
	Ilkokul	66 (24.2)	
	Literate	2 (07)	
	Illiterate	3 (1.1)	
	Missing	4 (1.4)	
Working status (n:266)	Yes	152 (54.9)	
	No	117 (42.1)	
	Missing	8 (2.2)	
Occupation (n:204)	Student	4 (2)	
	Officer	30 (14.7)	
	Employee (White-collar)	36 (17.6)	
	Employee (Blue-collar)	27 (13.2)	
	Artisan	15 (7.4)	
	Farmer	7 (3.4)	
	Self-employed	41 (20.1)	
	Retired (working)	3 (1.5)	
	Retired (not working)	37 (18.1)	
	Other (Housewife)	4 (2)	
	Missing	73 (26.4)	
Smoking status (n:236)	Never smoked	143 (60.6)	
	Active smoker	93 (39.4)	
Smoker	How many (per day)? (n:79)		13.9 ±7.3 (1-40) (10.5; 10-20)
	How long? (n:78)		19.3 ±11.4 (3-50) (20; 10-25)
	Pack-years? (n:78)		14.1 ±11.4 (0.5-45) (10; 5-20.5)
Comorbidities	Hyperlipidemia	48 (17.3)	
	Hypertension	65 (23.5)	
	Depression	19 (6.9)	
	Obesity	38 (13.7)	
	Diabetes mellitus	45 (16.2)	
	Others	68 (24.5)	
Age at diagnosis (years)			30.2 ±13.9 (1-72) (29; 20-40)
Psoriatic involvement	Plaque type psoriasis	277 (100)	
	Palmoplantar psoriasis	52 (18.8)	
	Nail psoriasis	146 (52.7)	
	Scalp psoriasis	178 (64.3)	
	Inverse psoriasis	39 (14.1)	
	Psoriatic arthritis	88 (31.8)	

Primary Outcome Result(s)

Absolute PASI scores were available for 257 patients at week 52. Of these patients, 223 (86.8%) had absolute PASI score ≤3. The table below summarizes the PASI scores at the pre-determined observation time-points following initiation of secukinumab. A sharp decrease was observed at week 4.

PASI scores at observation time-points following initiation of secukinumab

	n (%)	Mean.± SD (Min.-Max.) (Median; 25%-75%)
Day 0 PASI score	277	17.73 ±7.84 (10-51) (15.4; 12-20.2)
Week 4 PASI score	273	4.97 ±5.21 (0-33.3) (3.4; 1.2-7.1)
Week 16 PASI score	274	0.62±2.96 (0-19) (1; 0-2.5)
Week 52 PASI score	257	0.62±3.06 (0-24.3) (0,8; 0-2)

Secondary Outcome Result(s)

Speed of response to secukinumab according to previous biologic use

	Previous biologic use				
	Yes		No		
	n (%)	Mean± SD (Min.-Max.) (Median; 25%-75%)	n (%)	Mean± SD (Min.-Max.) (Median; 25%-75%)	p
Day 0 PASI score	167	17.61 ±7.62 (10.2-45.9) (15.9; 12.3-20)	110	17.9 ±8.19 (10-51) (15; 12-21.3)	0.754
Week 4 PASI score	165	5.26 ±5.82 (0-33.3) (3.3; 1.2-7)	108	4.51 ±4.1 (0-20.2) (3.8; 1.2-7.75)	0.751
Week 16 PASI score	165	0.62 ±3.3 (0-19) (1.2; 0-2.65)	109	0.62 ±2.29 (0-14.4) (0.8; 0-2.15)	0.071

PASI 75 response to secukinumab according to previous biologic use

		Previous biologic use				
		Yes		No		
		n (%)	Mean.± SD (Min.-Max.) (Median; 25%-75%)	n (%)	Mean.± SD (Min.-Max.) (Median; 25%-75%)	p
Week 4 PASI 75	Yes	91 (61.1)	4.35 ±1.99 (2.6-11.5) (3.82; 3-5)	58 (38.9)	4.51 ±2.01 (2.5-10.6) (3.72; 2.98-5.7)	0.760
	No	74 (59.7)	4.49 ±1.81 (2.6-11.5) (4.02; 3.27-5.06)	50 (40.3)	4.25 ±1.76 (2.5-10.2) (3.8; 3-4.67)	0.218
	p		0.222		0.682	
Week 16 PASI 75	Yes	140 (59.8)	4.26 ±1.76 (2.6-11.5) (3.77; 3-4.7)	94 (40.2)	4.59 ±2.12 (2.5-12.7) (3.8; 3-5.5)	0.510
	No	25 (62.5)	5.01 ±2.27 (2.6-11.5) (4.55; 3.21-6.1)	15 (37.5)	3.66 ±1.37 (2.5-7.87) (3.25; 2.67-4)	0.016
	p		0.060		0.071	

Achievement of PASI 75/90/100 with secukinumab at week 4, 16 and 52 and their sustainability between weeks 4-16 and 16-52

	PASI 75	PASI 90	PASI 100
Week 4 (n:273)	149 (54.6%)	83 (30.4%)	36 (13.2%)
Week 4-Week 16 Sustainability	*146 (98%)*	*77 (92.8%)*	*29 (80.6%)*
Week 16 (n:274)	234 (85.4%)	174 (63.5%)	92 (33.6%)
Week 16-Week 52 Sustainability	*213 (91%)*	*145 (83.3%)*	*63 (68.5%)*
Week 52 (n:257)	235 (91.4%)	185 (72%)	89 (34.6%)

PASI 75/90/100 response rates for biologic naïve vs. non- naïve patients at week 52

		Previous biologic use		
		Yes	No	p
Week 4 (n:273)	PASI75	91 (55.2%)	58 (53.7%)	0.814
	PASI90	49 (29.7%)	34 (31.5%)	0.754
	PASI100	19 (11.5%)	17 (15.7%)	0.313
Week 16 (n:274)	PASI75	140 (84.8%)	94 (86.2%)	0.750
	PASI90	98 (59.4%)	76 (69.7%)	0.082
	PASI100	48 (29.1%)	44 (40.4%)	0.053
Week 52 (n:257)	PASI75	138 (89%)	97 (95.1%)	0.089
	PASI90	110 (71%)	75 (73.5%)	0.655
	PASI100	50 (32.3%)	39 (38.2%)	0.324

Impact of smoking habit on PASI scores in patients treated with secukinumab

	Cigarette smoking				
	Never smoked		Smoker		
	n (%)	Mean.± SD (Min.-Max.) (Median; 25%-75%)	n (%)	Mean± SD (Min.-Max.) (Median; 25%-75%)	p
Day 0 PASI score (n:276)	143 (51.8)	17.73 ±7.76 (10-45.9) (15.9; 12-21)	93 (33.7)	18.13 ±8.48 (10-51) (15.4; 12.7-19.25)	0.745
Week 4 PASI score (n:272)	142 (52.2)	5.42 ±5.78 (0-31.5) (3; 1.2-8.05)	90(33.1)	4.23 ±4.57 (0-33.3) (3.25; 1.2-5.62)	0.421
Week 16 PASI score (n:273)	142 (51.8)	2.24 ±3.34 (0-19) (1.15; 0-2.72)	91 (33.3)	1.69 ±2.66 (0-14.4) (0.8; 0-2.10)	0.153
Week 52 PASI score (n:256)	135 (52)	1.55 ±2.5 (0-14.2) (0.8; 0-2)	82 (32)	2.04 ±4.11 (0-24.3) (0.75. 0-2)	0.916

Impact of severity of psoriatic lesions on PASI 75/90/100 achievement with secukinumab

		Baseline (pre-secukinumab) PASI scores		p
		>20 n(%)	≤20 n(%)	
Week 4 (n:273)	PASI75	38 (56.7)	111 (53.9)	0.686
	PASI90	20 (29.9)	63 (30.6)	0.910
	PASI100	5 (7.5)	31 (15)	0.111
Week 16 (n:274)	PASI75	56 (83.6)	178 (86)	0.628
	PASI90	45 (67.2)	129 (62.3)	0.474
	PASI100	22 (32.8)	70 (33.8)	0.883
Week 52 (n:257)	PASI75	56 (90.3)	179 (91.8)	0.718
	PASI90	44 (71)	141 (72.3)	0.838
	PASI100	21 (33.9)	68 (34.9)	0.885

Impact of secukinumab treatment on PASI scores in patients with additional psoriatic manifestations at study time-points

	Palmoplantar		Nail		Scalp		Inverse		Arthritis	
PASI	n (%)	Mean.± SD (Min.-Max.) (Median;25-75%)	n (%)	Mean.± SD (Min.-Max.) (Median;25-75%)	n (%)	Mean.± SD (Min.-Max.) (Median;25-75%)	n (%)	Mean.± SD (Min.-Max.) (Median;25-75%)	n (%)	Mean.± SD (Min.-Max.) (Median;25-75%
Day 0 (n:277)	52 (18.8)	20.62 ±11.82 (10-51) (15.65; 12-24.9)	146 (52.7)	18.53 ±8.59 (10-45.9) (16; 12-22.1)	178 (64.3)	18.95 ±8.51 (10-51) (16.2; 12.4-22.98)	39 (14.1)	16.74 ±7.15 (10-44.1) (15; 11.7-19)	88 (31.8)	18.78 ±8.89 (10-45.9) (16.2; 12-22)
Week 4 (n:273)	50 (18.3)	6.44 ±6.86 (0-33.3) (4.7; 1.75-8.28)	144 (52.7)	5.43 ±5.73 (0-33.3) (4; 1.6-7.45)	175 (64.1)	5.32 ±5.52 (0-33.3) (3.9; 1.6-7.6)	39 (14.3)	3.92 ±3.66 (0-15.9) (2.6; 1.2-6)	87 (31.9)	5.08 ±5.50 (0-25) (3; 0.9-7)
Week 16 (n:274)	51 (18.6)	2.57 ±3.34 (0-14.4) (1.8; 0-3)	143 (52.2)	2.29 ±3.26 (0-18.2) (1.2; 0-3)	176 (64.2)	2.11 ±3.33 (0-19) (1; 0-2.58)	39 (14.2)	1.79 ±2.65 (0-14.4) (1.2; 0-2.1)	87 (31.8)	2.12 ±3.03 (0-14.4) (0.9; 0-3)
Week 52 (n:257)	47 (18.3)	2.8 ±5.13 (0-24.3) (1; 0-2.6)	131 (50.9)	2.07 ±3.71 (0-24.3) (0.8; 0-2.3)	165 (64.2)	1.86 ±3.52 (0-24.3) (0.8; 0-2)	37 (14.4)	0.85 ±1.15 (0-5.4) (0.3; 0-1.2)	84 (32.7)	2.31 ±4.43 (0-24.3) (0.6; 0-2)

Secukinumab treatment utilization patterns

Out of 277 patients in whom secukinumab was initiated on Day 0, 257 (92.8%) were on this treatment at week 52. Four of the remaining 20 patients were lost to follow up. The reason for stopping secukinumab was insufficient effectiveness in 11 patients. Interruption of

secukinumab was reported in 4 patients. The reason for interruption was reported to be surgical operations in 2 cases. One of these patients reinitiated treatment following surgical operation during the observation period

Safety Results
NA

Other Relevant Findings
None

Conclusion
This study confirmed the effectiveness profile of secukinumab in patients with moderate-to-severe psoriasis that were treated for 52 weeks irrespectve of BMI, smoking status, sex and prior biologic use.

Date of Clinical Study Report
23 December, 2021