Secukinumab's Pooled and Long-term Safety: Analysis of 19 Psoriasis Clinical Trials up to 5 Years of Treatment

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ABSTRACT

- **Introduction:** Secukinumab, a fully human monoclonal antibody that selectively neutralizes interleukin (IL)-17A, has been shown to have significant efficacy in the treatment of moderate-to-severe plaque psoriasis and psoriatic arthritis, demonstrating a rapid onset of action and sustained responses, with a favorable safety profile. Here, we report exposure-adjusted incidence rates (IRs) for treatment-emergent adverse events per year from a pooled analysis of all secukinumab psoriasis trials to date (19 studies, 4674 patients, 10,061 patient-years exposure).
- **Methods:** Adverse event (AE) IRs (per 100 subject-years) were examined per year for subjects who received either secukinumab 300 mg or any dose of secukinumab, and for 1 year only, for subjects receiving placebo (PBO), etanercept (ETN) 50 mg, or ustekinumab (UST) 45/90 mg.
- **Results:** The duration of exposure to any dose of secukinumab/secukinumab 300 mg (patient-years) was 4093.5/1467.4 at year 1, 2631.3/859.6 at year 2, 1659.6/423.0 at year 3, 1392.2/377.5 at year 4, and 291.6/90.0 at year 5. Secukinumab pooled safety remained favorable over 5 years of treatment with no increase of AEs over time. The IRs of AEs for patients receiving any dose of secukinumab/secukinumab 300 mg were 254.1/275.6 at year 1, 169.9/168.1 at year 2, 159.8/160.2 at year 3, 104.1/111.9 at year 4, and 12.0/13.9 at year 5. The most frequent AEs with secukinumab over 5 years were nasopharyngitis, headache, and upper respiratory tract infection. The incidence of opportunistic infections, *Candida* infections, neutropenia, major adverse cardiovascular events, Crohn's disease, ulcerative colitis, and malignant or unspecified tumors (excluding nonmelanoma skin cancer) were infrequent with secukinumab. Additionally, secukinumab demonstrated a comparable pooled safety profile to that of PBO, ETN, and UST over the course of 1 year.
- **Conclusion:** This comprehensive pooled analysis supports the favorable long-term safety profile of secukinumab in patients with psoriasis.

INTRODUCTION

- Psoriasis is a chronic immune-mediated skin disease typically requiring long-term treatment, thus longitudinal data establishing the safety of approved therapies are required
- Secukinumab is a fully human monoclonal antibody that selectively neutralizes IL-17A, a key cytokine involved in the development of psoriasis. Secukinumab has shown long-lasting efficacy and safety in the complete spectrum of psoriasis manifestations, including nails, scalp, palms and soles involvement and psoriatic arthritis[1–5]
- Here we report exposure-adjusted incidence rates (IRs) for treatment-emergent adverse events per year from a pooled analysis of all secukinumab psoriasis trials to date (19 studies, 4,674 secukinumab patients, ~10,000 patient-years exposure)

METHODOLOGY

- Adverse event (AE) IRs (per 100 patient years) were examined per year for subjects who received either secukinumab 300 mg (every 4 weeks) or any dose of secukinumab (including subcutaneous 300 mg, 150 mg, 75 mg, 25 mg or intravenous infusion [1 and 3mg/kg]), and up to 1 year only for subjects receiving placebo (PBO), etanercept (ETN) or ustekinumab (UST) per label use
- AEs were classified by MedDRA System Organ Class and Preferred Term
- Data from 9 phase 2 and 10 phase 3 randomized, double-blind clinical trials were examined*
- A subject with multiple occurrences of the same AE in a one-year interval, or a prolonged occurrence of the same AE beyond a one-year interval, was counted once (i.e., in the year when the AE first occurred), while a subject with multiple occurrences of the same AE in different year intervals was counted for each year

*Phase 2 studies: A1302, A2102, A2103, A2204, A2211, A2212, A2220, A2223, A2225 (data from the A2211E1 extension study were also included); Phase 3 studies: A2302, A2303, A2304, A2308, A2309, A2317, A2312, A3301, A2313, AUS01 (data from the A2302E1 and A2304E1 extension studies were also included)

RESULTS

- Overall, baseline characteristics were comparable across treatments (**Table 1**)

Table 1. Baseline demographic and clinical characteristics in the pooled psoriasis population

Characteristic	Any Secukinumab dose (n=4674)	Secukinumab 300 mg (n=1773)	Etanercept (n=323)	Ustekinumab (n=336)	Placebo (n=1090)
Age, years	45.6 ± 13.1	45.8 ± 13.5	43.7 ± 13.0)	44.6 ± 13.6	45.6 ± 12.9
Gender-Male, n (%)	3127 (66.9)	1168 (65.9)	229 (70.9)	251 (74.7)	699 (64.1)
Race-Caucasian, n (%)	3694 (79.0)	1396 (78.7)	216 (66.9)	285 (84.8)	861 (79.0)
Body weight, kg	87.1 ± 22.7	86.2 ± 22.2	84.5 ± 20.5	87.4 ± 22.1	87.1 ± 23.5
BMI, kg/m²	29.4 ± 6.8	29.2 ± 6.6	28.7 ± 5.9	29.1 ± 6.7	29.3 ± 7.2
PASI score	20.7 ± 10.6	21.0 ± 10.4	23.3 ± 9.8	21.5 ± 8.1	19.4 ± 10.9
BSA affected, %	30.4 ± 19.1	32.0 ± 19.1	33.7 ± 18.0	32.0 ± 16.8	29.1 ± 18.3
Obesity class, n (%)					
Overweight (BMI 25–29.9)	1507 (32.2)	571 (32.2)	128 (39.6)	111 (33.0)	373 (34.2)
Obesity class I (BMI 30–39.9)	974 (20.8)	385 (21.7)	62 (19.2)	76 (22.6)	213 (19.5)
Obesity class II (BMI 35–39.9)	460 (9.8)	186 (10.5)	31 (9.6)	31 (9.2)	99 (9.1)
Obesity class III (BMI ≥40)	338 (7.2)	113 (6.4)	12 (3.7)	17 (5.1)	76 (7.0)
Psoriatic arthritis present, n (%)	833 (17.8)	324 (18.3)	45 (13.9)	52 (15.5)	182 (16.7)
CV disease risk factors, n (%)					
Hypertension	1087 (23.3)	479 (27.0)	67 (20.7)	85 (25.3)	218 (20.0)
Hyperlipidemia	666 (14.3)	302 (17.0)	43 (13.3)	49 (14.6)	141 (12.9)
Myocardial infarction	72 (1.5)	33 (1.9)	5 (1.5)	6 (1.8)	17 (1.6)
Latent TB*, n (%)	134 (2.9)	63 (3.6)	16 (5.0)	13 (3.9)	24 (2.2)
IBD, n (%)**	17 (0.4)	5 (0.3)	0 (0)	1 (0.3)	6 (0.6)
History of cancer (other than skin), n (%)	29 (0.6)	13 (0.7)	0 (0)	1 (0.3)	5 (0.5)
History of skin cancer, n (%)	3 (0.1)	1 (0.1)	0 (0)	0 (0)	0 (0)

Data are presented as mean ± SD unless otherwise stated.
*Patients diagnosed with latent TB at enrollment received prophylactic treatment. **Patients with a medical history of IBD (including Crohn's disease and ulcerative colitis)
BMI, body mass index; BSA, body surface area; CV, cardiovascular; IBD, inflammatory bowel disease; PASI, Psoriasis Area Severity Index;
SD, standard deviation; TB, tuberculosis

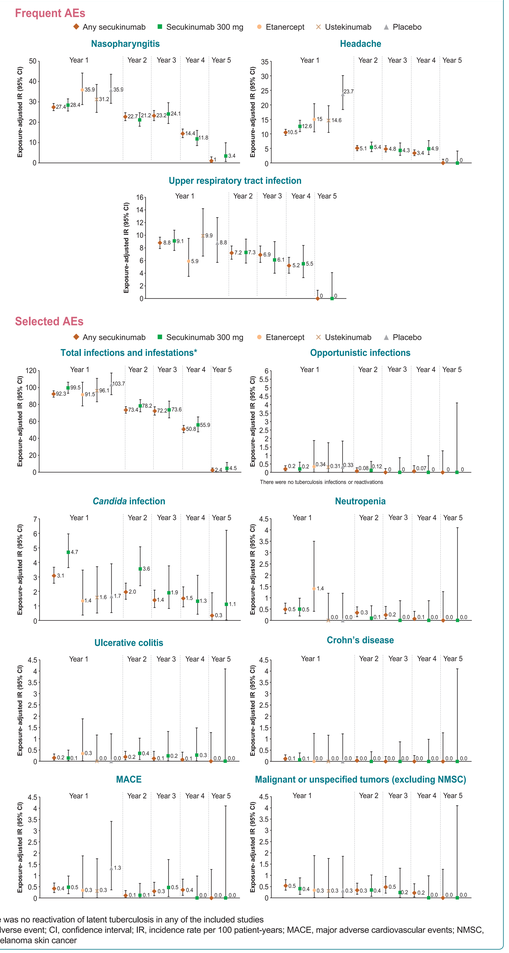
- Of the 4,674 patients who were exposed to any secukinumab dose, 3,423 patients were exposed for at least more than 1 year (**Table 2**)

Table 2. Duration of patient exposure and a summary of exposure-adjusted incidence rates for total AEs

	Year 1					Year 2		Year 3		Year 4		Year 5	
	Secukinumab		ETN 50 mg (n=323)	UST 45/90 mg (n=336)	PBO (n=1090)	Secukinumab		Secukinumab		Secukinumab		Secukinumab	
	Any dose (n=4674)	300 mg (n=1773)				Any dose (n=3423)	300 mg (n=1188)	Any dose (n=1972)	300 mg (n=572)	Any dose (n=1522)	300 mg (n=397)	Any dose (n=909)	300 mg (n=263)
Duration of exposure (patient-years)	4093.5	1467.4	296.9	318.1	301.2	2631.3	859.6	1659.6	423.0	1392.2	377.5	291.6	90.0
Total AEs	254.1	275.6	245.7	252.2	355.8	169.9	168.1	159.8	160.2	104.1	111.9	12.0	13.9
Non-fatal serious AEs	8.6	8.9	6.9	8.2	9.1	7.6	7.3	7.4	8.8	5.8	6.8	0.7	1.1

AE, adverse event; ETN, etanercept; PBO, placebo; UST, ustekinumab

Figure 1. Exposure-adjusted incidence rates for treatment-emergent AEs



*There was no reactivation of latent tuberculosis in any of the included studies
AE, adverse event; CI, confidence interval; IR, incidence rate per 100 patient-years; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer

- Secukinumab pooled safety remained favorable over 5 years of treatment with no increase of AEs over time (**Figure 1**)
- Secukinumab demonstrated a comparable pooled safety profile to that of PBO, ETN and UST over the course of 1 year (**Figure 1**)

CONCLUSIONS

- This comprehensive pooled analysis of 19 phase 2/3 trials supports the favorable long-term safety profile of secukinumab in patients with psoriasis
- No new safety signals were identified for up to 5 years of treatment and there were no increases in yearly AE rates from Year 1
- Secukinumab's safety profile was consistent with that established in previous phase 2/3 studies[6]

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DISCLOSURES

P van de Kerkhof: Clinical trials, consultant and/or speaker for AbbVie, Almirall, Amgen, Celgene, Centocor, Eli Lilly, Galderma, Janssen-Cilag, Leo Pharma, Mitsubishi, Novartis, Pfizer, Philips, and Sandoz. **K Reich:** Advisor and/or paid speaker for and/or participated in clinical trials sponsored by Abbvie, Amgen, Biogen, Boehringer-Ingelheim, Celgene, Centocor, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, Leo, Lilly, Medac, Merck Sharp & Dohme Corp., Novartis, Ocean Pharma, Pfizer, Regeneron, Takeda, UCB Pharma, Xenoport. **CL Leonardi:** Consultant for AbbVie, Amgen, Dermira, Janssen, Eli-Lilly, LEO, Sandoz, UCB and Pfizer; investigator for Actavis, AbbVie, Amgen, Celgene, Coherus, Dermira, Eli Lilly, Galderma, Janssen, Merck, Pfizer, Sandoz, Stiefel, LEO, Novartis, and Wyeth and has participated in speaker bureaus for Abbvie, Celgene, Lilly. **A Blauvelt:** Scientific consultant and clinical study investigator for AbbVie, Aclaris, Allergan, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly, Genentech/Roche, GlaxoSmithKline, Janssen, Leo, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB, Valeant, Vidac; speaker for Eli Lilly and Company, Janssen, Regeneron, Sanofi Genzyme. **NN Mehta:** full time US government employee and receives research grants to the NHLBI from AbbVie, Janssen, Novartis and Celgene. **TF Tsai:** Consultant for AbbVie, Celgene, Eli Lilly, Janssen, Leo Pharma, Galderma, Novartis, Boehringer Ingelheim, and Pfizer. **R You**, **P Papanastasiou**, **M Milutinovic:** Employees of Novartis. **CEM Griffiths:** Advisor and/or research grants from AbbVie, Almirall, BMS, GSK, Galderma, Janssen, Leo Pharma, MSD, Pfizer, Novartis, Sandoz, Eli Lilly, Sanofi-Regeneron, Roche, L'Oreal, DSM, Clarins, Walgreens Boots Alliance, UCB Pharma.

ACKNOWLEDGEMENTS

The authors thank the patients and their families and all investigators and their staff for participation in the study. Oxford PharmaGenesis, Inc., Newtown, PA, USA provided assistance with layout and printing the poster; this support was funded by Novartis Pharmaceuticals Corporation, East Hanover, NJ. The authors had full control of the contents of this poster.

This research was funded by Novartis Pharma AG, Basel, Switzerland.

Originally presented at: 8th International Psoriasis from Gene to Clinic Congress, London, UK; November 30–December 2, 2017.

Poster presented at: 13th Annual Winter Clinical Dermatology Conference, Maui, HI, USA; January 12–17, 2018.

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