Secukinumab Is Highly Efficacious and Has a Favorable Safety Profile in Pediatric Patients With Moderate to Severe Plaque Psoriasis

Nina Magnolo, MD,[1] Külli Kingo, MD, PhD,[2] Vivian Laquer, MD,[3] John Browning, MD,[4] Deborah Keefe, MD, MPH,[5] Rafal Mazur, MD,[6] Prayashi Ghelani, BSc, MSc,[7] Manmath Patekar, MD,[6] LindaAnn Wraith, MBA,[5] Adam Reich, MD, PhD[8]

[1]University Hospital Münster, Münster, Germany; [2]Tartu University Hospital and University of Tartu, Tartu, Estonia; [3]First OC Dermatology, Fountain Valley, CA; [4]University of Texas at San Antonio, San Antonio, TX; [5]Novartis Pharmaceuticals Corporation, East Hanover, NJ; [6]Novartis Pharma AG, Basel, Switzerland; [7]264957 Ontario Limited, Ontario, Canada; [8]University of Rzeszów, Rzeszów, Poland

BACKGROUND

- Psoriasis affects ≈ 1% of children and adolescents; few treatment options are available, resulting in a high unmet medical need[1,2]
- Secukinumab, a fully human monoclonal antibody that selectively binds to and neutralizes interleukin 17A, has shown long-lasting efficacy and safety in addressing the complete spectrum of manifestations of psoriatic disease, including psoriasis vulgaris[3-7]; palmoplantar, scalp, and nail psoriasis[8]; psoriatic arthritis[9]; and ankylosing spondylitis[10]
- Although secukinumab is currently being investigated in 2 phase 3 trials of pediatric patients with severe (NCT02471144) or moderate to severe psoriasis (NCT03668613), efficacy and safety have yet to be reported in these populations

OBJECTIVE

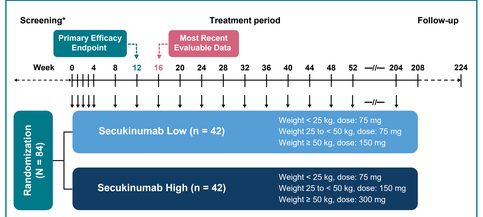
- To investigate the efficacy and safety of 2 secukinumab dosing regimens in pediatric patients with moderate to severe plaque psoriasis in an ongoing, randomized, multicenter, open-label study (NCT03668613)

METHODS

Study Design

- Patients aged 6 to < 18 years with moderate to severe plaque psoriasis were stratified by weight and disease severity and randomized 1:1 to receive subcutaneous secukinumab at a low or high dose (**Figure 1**)

Figure 1. Study Design



↓ Active dose administration, including every 4 weeks from week 52 to week 204.
* Maximum 4 weeks.

Outcomes and Data Analysis

- Efficacy was assessed through week 16 according to the proportion of randomized patients who achieved Psoriasis Area and Severity Index (PASI)75, PASI90, PASI100, and Investigator's Global Assessment modified 2011 (IGA mod 2011) 0/1 (clear/almost clear) responses (nonresponder imputation); efficacy analyses were based on the full analysis set
  - The combined primary endpoint was PASI75 response and IGA mod 2011 0/1 response at week 12
  - PASI75, PASI90, and IGA mod 2011 0/1 responses at week 12 in each arm were compared with historical placebo by predictive log-odds ratios determined by Bayesian logistic regression analysis
- Quality of life was determined through week 12 by the proportion of randomized patients who achieved Children's Dermatology Life Quality Index (CDLQI) scores of 0 or 1 (no effect on the child's life)
  - CDLQI data were recorded at baseline and at weeks 4, 8, and 12, and will be collected every 12 weeks thereafter
- The frequency of treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TE SAEs), and TEAEs leading to discontinuation was described for each treatment arm through week 16 (safety set)

RESULTS

Patient Population

- Baseline demographics and disease characteristics were broadly similar across treatment groups (**Table 1**)

Table 1. Demographics and Baseline Characteristics of Pediatric Patients With Psoriasis

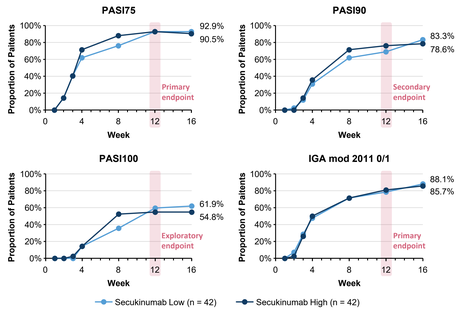
Characteristic	Secukinumab Low (n = 42)	Secukinumab High (n = 42)	Secukinumab Total (n = 84)
Age group, n (%)			
6 to < 12 years	17 (40.5)	16 (38.1)	33 (39.3)
12 to < 18 years	25 (59.5)	26 (61.9)	51 (60.7)
Age, mean (SD), years	12.5 (3.39)	12.8 (3.43)	12.6 (3.39)
Male, n (%)	22 (52.4)	17 (40.5)	39 (46.4)
White, n (%)	39 (92.9)	38 (90.5)	77 (91.7)
Weight stratum, n (%)			
< 25 kg	4 (9.5)	4 (9.5)	8 (9.5)
25 to < 50 kg	13 (31.0)	12 (28.6)	25 (29.8)
≥ 50 kg	25 (59.5)	26 (61.9)	51 (60.7)
Body mass index, mean (SD), kg/m^2	21.7 (5.17)	22.2 (4.47)	21.9 (4.81)
Baseline PASI, n (%)			
PASI ≤ 20	27 (64.3)	24 (57.1)	51 (60.7)
PASI > 20	15 (35.7)	18 (42.9)	33 (39.3)
Baseline IGA mod 2011 score, n (%)			
3 (moderate disease)	29 (69.0)	29 (69.0)	58 (69.0)
4 (severe disease)	13 (31.0)	13 (31.0)	26 (31.0)
Time since first diagnosis of plaque-type psoriasis, mean (SD), years	3.9 (3.64)	4.0 (3.78)	3.9 (3.69)

IGA mod 2011, Investigator's Global Assessment modified 2011; PASI, Psoriasis Area and Severity Index.

Efficacy of Secukinumab Through Week 16

- Patients receiving either dose of secukinumab experienced rapid clearance of psoriatic lesions based on their achievement of PASI75, PASI90, PASI100, and IGA mod 2011 0/1 responses (**Figure 2**)
- At week 16, response rates were high and similar between low and high dose groups, with > 90% and > 85% of patients achieving PASI75 and IGA mod 2011 0/1 responses, respectively; > 78% of patients achieved PASI90 and between 54.8% and 61.9% achieved a key exploratory endpoint of PASI100

Figure 2. Efficacy as Measured by PASI75, PASI90, PASI100, and IGA mod 2011 0/1 Through Week 16 Among Pediatric Patients With Psoriasis (nonresponder imputation)



IGA mod 2011, Investigator's Global Assessment modified 2011; PASI, Psoriasis Area and Severity Index.

- A Bayesian analysis was conducted to compare secukinumab efficacy responses at week 12 with historical placebo
- The efficacy response rates of both the high- and low-dose secukinumab groups were better than the historical placebo with respect to PASI75, PASI90, and IGA mod 2011 0/1 results at week 12, as supported by an estimated 100% probability that the log-odds ratio is > 0 (**Table 2**)

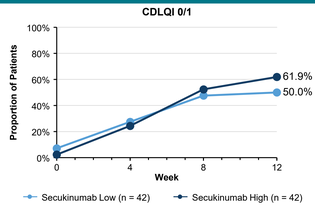
Table 2. Predictive Log-Odds Ratios (95% CrI) Between Secukinumab High or Low Doses at Week 12 Compared With Historical Placebo (nonresponder imputation)*

Criterion	Secukinumab Low (n = 42)	Secukinumab High (n = 42)
PASI75		
Predictive log-OR (95% CrI)	4.86 (3.42, 6.78)	4.84 (3.42, 6.77)
Probability of log-OR > 0	1.00	1.00
PASI90		
Predictive log-OR (95% CrI)	4.37 (2.91, 6.20)	4.71 (3.20, 6.58)
Probability of log-OR > 0	1.00	1.00
IGA mod 2011 0/1		
Predictive log-OR (95% CrI)	4.30 (2.66, 6.51)	4.43 (2.85, 6.61)
Probability of log-OR > 0	1.00	1.00

CrI, credible interval; IGA mod 2011, Investigator's Global Assessment modified 2011; OR, odds ratio; PASI, Psoriasis Area and Severity Index.
* A value of 1.00 indicates 100% probability.

- In addition to improved skin clearance, patients in both treatment arms experienced improved quality of life through week 12 (**Figure 3**)
  - 50.0% of patients in the low-dose group and 61.9% in the high-dose group achieved a CDLQI score of 0 or 1
  - Over 20% of patients achieved this response as early as week 4

Figure 3. Improvement in Quality of Life as Measured by CDLQI 0/1 Through Week 12 (last observation carried forward)*



CDLQI, Children's Dermatology Life Quality Index.
* Patients < 18 years of age at the time of assessment have been included in the summary report; CDLQI data were recorded at baseline and at weeks 4, 8, and 12 and will be collected every 12 weeks thereafter.

Safety at Week 16

- TEAEs were comparable between treatment arms and were consistent with the known safety profile of secukinumab previously reported in the adult population (**Table 3**)
- Two patients in the secukinumab high-dose arm discontinued treatment due to any adverse event (AE)
  - Of these, 1 patient discontinued due to elevated liver enzymes at randomization, which was recorded as an AE on day 2
  - The second discontinuation was due to hemorrhagic diarrhea later confirmed by a gastrointestinal specialist not to be inflammatory bowel disease
- The 1 SAE in the low-dose group was recorded as infectious mononucleosis
- Three patients receiving secukinumab low dose and 2 patients receiving secukinumab high dose experienced either neutropenia or leukopenia; 1 of the patients receiving secukinumab low dose experienced both
  - These AEs were mostly mild in severity, were transient, and were considered to be related to the study drug
  - However, none of these events led to study treatment discontinuation or interruption
- Of the 5 patients with neutropenia, 4 belonged to the same site

Table 3. TEAEs Through Week 16

Characteristic	Secukinumab Low (n = 42)	Secukinumab High (n = 42)	Secukinumab Total (n = 84)
Any TEAEs, n (%)	22 (52.4)	23 (54.8)	45 (53.6)
Any death, n (%)	0	0	0
Any nonfatal TE SAEs, n (%)	1 (2.4)	0	1 (1.2)
Discontinued study treatment due to any AE, n (%)	0	2 (4.8)*	2 (2.4)*
TEAEs of special interest, n (%)			
Infections and infestations (SOC)	15 (35.7)	17 (40.5)	32 (38.1)
Nasopharyngitis (PT)	6 (14.3)	4 (9.5)	10 (11.9)
Neutropenia (NMQ) (narrow)	3 (7.1)	2 (4.8)	5 (6.0)
Upper respiratory tract infection (PT)	0	3 (7.1)	3 (3.6)
Vulvovaginal candidiasis (PT)	0	1 (2.4)	1 (1.2)
Inflammatory bowel disease (NMQ)	0	1 (2.4)†	1 (1.2)†

NMQ; Novartis Medical Dictionary for Regulatory Activities query; PT, preferred term; SAE, serious adverse event; SOC, system organ class; TEAE, treatment-emergent adverse event.
* One discontinuation was due to an AE, and 1 discontinuation was due to lack of efficacy.
† One case of hemorrhagic diarrhea (preferred term), initially identified as inflammatory bowel disease, was later confirmed by the investigator not to be inflammatory bowel disease.

CONCLUSIONS

- Initial results from this ongoing, 4-year study indicate that secukinumab is highly efficacious through week 16 in rapidly improving skin symptoms in pediatric patients with moderate to severe plaque psoriasis
  - Predictive log-odds ratios suggest both doses of secukinumab were superior to historical placebo with respect to PASI75/90 and IGA 0/1 responses at week 12
  - Quality of life also improved through week 12 with both dose regimens, with more than half of pediatric patients being free of impact on quality of life due to psoriasis
- The observed safety profile of secukinumab in pediatric patients appears consistent with that observed in adults
- A second phase 3 trial comparing secukinumab with placebo and etanercept in pediatric patients is currently ongoing (NCT02471144)

REFERENCES

1. Silverberg NB. *Cutis*. 2015;95:147-152.
2. Burden-Teh E, et al. *Br J Dermatol*. 2016;174:1242-1257.
3. Langley RG, et al. *N Engl J Med*. 2014;371:326-338.
4. Blauvelt A, et al. *Br J Dermatol*. 2015;172:484-493.
5. Paul C, et al. *J Eur Acad Dermatol Venereol*. 2015;29:1082-1090.
6. Blauvelt A, et al. *J Am Acad Dermatol*. 2017;76:60-69.e9.
7. Bagel J, et al. *Dermatol Ther (Heidelb)*. 2018;8:571-579.
8. Armstrong AW, et al. *J Clin Aesthet Dermatol*. 2016;9(6 suppl 1):S12-S16.
9. Mease P, et al. *Ann Rheum Dis*. 2018;77:890-897.
10. Baeten D, et al. *N Engl J Med*. 2015;373:2534-2548.

DISCLOSURES

N. Magnolo has been a principal investigator in studies performed by AbbVie, Asana, Boehringer Ingelheim, Celgene, Dr. Reddy's Laboratories, Eli Lilly, Galderma, Genentech, Incyte, Janssen, Kyowa Kirin, LEO Pharma, Novartis, MSD, Pfizer, Regeneron, Sun Pharma, and UCB and is a consultant or speaker for AbbVie, LEO Pharma, and UCB. **K. Kingo** has received fees for serving as an investigator in studies sponsored by Celgene, Merck, Mitsubishi Tanabe Pharma, Novartis, Regeneron Pharmaceuticals, and Sandoz. **V. Laquer** is an investigator for AbbVie, Amgen, Biofrontera, Cara Therapeutics, Celgene, ChemoCentryx, Dermavant, Dermira, Eli Lilly, Galderma, Incyte, Kiniksa, LEO Pharma, Novartis, Pfizer, Regeneron, Sun Pharma, and UCB. **J. Browning** is an investigator for Amryt, Brickell Biotech, Celgene, ChemoCentryx, Eli Lilly, Incyte, Lenus, LEO Pharma, Mayne, Novartis, Pfizer, Regeneron, and Valeant; a consultant for Dermavant and LEO Pharma; and a speaker for Dermira, Regeneron, and Pfizer. **D. Keefe** and **L. Wraith** are employees of Novartis Pharmaceuticals Corporation. **R. Mazur** and **M. Patekar** are employees of Novartis Pharma AG. **P. Ghelani** is an employee of 264957 Ontario Limited and serves as an independent contractor for Novartis. **A. Reich** is a principal investigator or subinvestigator in clinical trials sponsored by AbbVie, Drug Delivery Solutions Ltd, Galderma, Genentech, Janssen, Kymab Ltd, LEO Pharma, Menlo Therapeutics, MetrioPharm AG, MSD, Novartis, Pfizer, and Trevi Therapeutics and a consultant or speaker for AbbVie, Bioderma, Celgene, Chema-Elektromet, Eli Lilly, Galderma, Janssen, LEO Pharma, Medac, Menlo Therapeutics, Novartis, Pierre Fabre, Sandoz, and Trevi Therapeutics.

ACKNOWLEDGMENTS

The authors thank Richard Karpowicz, PhD, of Health Interactions, Hamilton, NJ, for providing medical writing support/editorial support, which was funded by Novartis Pharma AG Basel, Switzerland, in accordance with Good Publication Practice guidelines (http://www.ismpp.org/gpp3).

This study was sponsored by Novartis Pharma AG, Basel, Switzerland.

Your document will be available for download at the following URL:
http://novartis.medicalcongressposters.com/Default.aspx?doc=c1b8e

Text: **Qc1b8e**

To: 8NOVA (86682) US Only

+18324604729 North, Central and South Americas; Caribbean; China

+447860024038 UK, Europe & Russia

+46737494608 Sweden, Europe

Note: downloading data may incur costs which can vary depending on your service provider and may be high if you are using your smartphone abroad. Please check your phone tariff or contact your service provider for more details.

Originally presented as an oral presentation at the 2020 American Academy of Dermatology virtual meeting held June 12-14, 2020.

Presented at Maui Derm Connect 2020; September 23-26, 2020.

Scan QR code to download this poster.