Secukinumab treatment demonstrated high efficacy and safety in pediatric patients with moderate to severe plaque psoriasis: 52-week results from a randomized trial

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INTRODUCTION

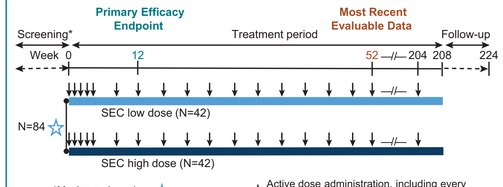
- Psoriasis is prevalent in ~1% of children and adolescents[1–3]. Plaque psoriasis is the most common variant of psoriasis in pediatric patients[4–5]
- Limited treatment options have been approved for pediatric psoriasis, resulting in a need for more and better treatment alternatives in pediatric patients[6]
- Secukinumab (SEC) is a fully human monoclonal antibody that selectively neutralizes interleukin-17A, a cornerstone cytokine involved in the development of psoriasis. It has demonstrated sustained long-term efficacy with a favorable safety profile in various psoriatic disease manifestations in adults[7,8]
- Here, we report the efficacy and safety of two SEC dosing regimens (low dose and high dose) in pediatric patients with moderate to severe plaque psoriasis up to 52 weeks

METHODS

Study Design and Patients

- This is a randomized, open-label, parallel-group, multicenter study (NCT03668613) in pediatric patients aged 6 to <18 years at randomization, with moderate to severe chronic plaque psoriasis
- Patients were randomized in a 1:1 ratio to receive low dose (75/75/150mg; N=42) or high dose (75/150/300mg; N=42) subcutaneous SEC. Randomization was stratified by weight (<25kg/25kg−<50kg/≥50kg) and disease severity (moderate/severe) (**Figure 1**)

Figure 1. Study design



N, number of randomized patients; SEC, secukinumab

Study outcomes

- The co-primary and secondary endpoints were to evaluate proportion of patients with Psoriasis Area and Severity Index [PASI] 75/ Investigator's Global Assessment modified 2011 [IGA mod 2011] 0/1 response and proportion of patients with PASI 90 response, respectively, at Week 12, compared to historical placebo (Bayesian logistic regression analysis with pure non-responder imputation)
- Clinical safety of SEC was evaluated up to Week 52
- The exploratory endpoints of the study were to evaluate the proportion of responders achieving PASI 75/90/100 and IGA mod 2011 0/1 scores over time up to Week 52 and absolute and percentage change in PASI and IGA mod 2011 responses from baseline, over time up to Week 52
- The quality of life (QoL) of patients (<18 years at the time of assessment) was evaluated by Children's Dermatology Life Quality Index (CDLQI) 0/1 responses (last observation carried forward), over time up to Week 52

RESULTS

- A total of 84/92 patients completed the screening phase and were randomized to receive SEC low dose and high dose
- The mean (standard deviation [SD]) PASI score at baseline was 18.5 (5.2) for low dose and 19.3 (6.7) for the high dose group (**Table 1**)
- At baseline, 72.6% (61) and 27.4% (23) patients had moderate and severe plaque psoriasis, respectively

Table 1. Demographics and baseline characteristics

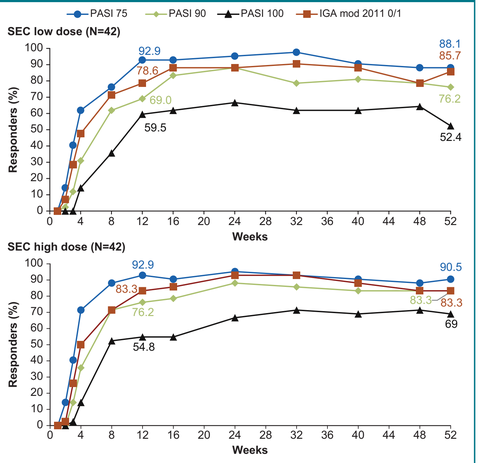
Characteristics (All subjects randomized)	SEC low dose (N=42)	SEC high dose (N=42)	SEC total (N=84)
Age group, n (%)			
6 to <12 years	17 (40.5)	16 (38.1)	33 (39.3)
12 to <18 years	25 (59.5)	26 (61.9)	51 (60.7)
Female, n (%)	20 (47.6)	25 (59.5)	45 (53.6)
Caucasian, n (%)	39 (92.9)	38 (90.5)	77 (91.7)
Weight strata, 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)
BMI (kg/m²), mean (SD)	21.7 (5.2)	22.2 (4.5)	21.9 (4.8)
Disease severity strata* (as per randomization), n (%)			
Moderate	30 (71.4)	31 (73.8)	61 (72.6)
Severe	12 (28.6)	11 (26.2)	23 (27.4)
PASI, mean (SD)	18.5 (5.2)	19.3 (6.7)	18.9 (6.0)
Baseline CDLQI total score, mean (SD)	10.6 (6.0)	13.0 (7.0)	—

*Disease severity strata: moderate = PASI score 12-<20 and IGA mod 2011 score 3/4 or PASI score ≥20 and IGA mod 2011 score 3 and severe = PASI score ≥20 and IGA mod 2011 score 4. BMI, body mass index; CDLQI, Children's Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; SD, standard deviation; SEC, secukinumab

Efficacy

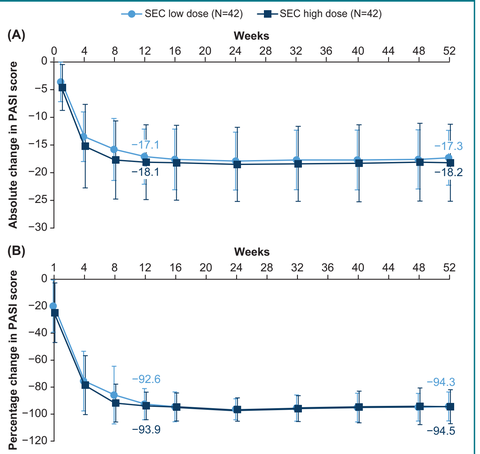
- The study achieved its primary and key secondary objectives. The co-primary (PASI 75 and IGA mod 2011 0/1) and secondary endpoint (PASI 90) demonstrated superiority of SEC over historical placebo, at Week 12[9]
- At Week 12, the PASI 75 response rate was 92.9% in both SEC low dose and high dose groups and the IGA mod 2011 0/1 response rate was 78.6% and 83.3%, respectively (**Figure 2**)
- The proportion of patients who achieved PASI 90 response at Week 12 was 69.0% (low dose) and 76.2% (high dose) (**Figure 2**)
- PASI 75/IGA mod 2011 0/1 responses increased until Week 16 (low dose: 92.9%/88.1% and high dose: 90.5%/85.7%) and Week 24 (low dose: 95.2%/88.1% and high dose: 95.2%/92.9%) and were sustained up to Week 52 (low dose: 88.1%/85.7% and high dose: 90.5%/83.3%), respectively (**Figure 2**). At Week 52, PASI 90/100 responses were 76.2%/52.4% (low dose) and 83.3%/69.0% (high dose), respectively (**Figure 2**)
- Absolute PASI change (mean [SD]) at Week 52 from baseline was -17.3 (5.0) and -18.2 (7.0), corresponding to a change of -94.3% and -94.5% for the low dose and high dose groups, respectively (**Figure 3**)

Figure 2. PASI 75/90/100* and IGA mod 2011 0/1 responses up to Week 52 (non-responder imputation; full analysis set)



*PASI 75/90/100, percentage of patients who achieved a ≥75%/≥90%/100% reduction in PASI score from baseline. IGA mod 2011 0/1, Investigator's Global Assessment modified 2011; PASI, Psoriasis Area and Severity Index; SEC, secukinumab

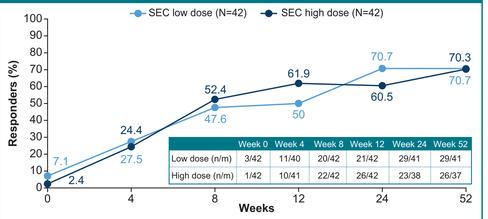
Figure 3. Absolute and percentage change in PASI score from baseline (mean ± SD) up to Week 52 (last observation carried forward; full analysis set)



PASI, Psoriasis Area and Severity Index; SEC, secukinumab

- CDLQI 0/1 response was achieved in 50.0% and 61.9% of patients at Week 12, which increased to 70.7% and 70.3% at Week 52, in the low dose and high dose groups, respectively (**Figure 4**)

Figure 4. Percentage of patients with CDLQI 0/1* response through Week 52 (last observation carried forward; full analysis set)



*0/1, no impairment in patient's quality of life. CDLQI, Children's Dermatology Life Quality Index; m, number of patients evaluable; n, number of patients with response; SEC, secukinumab

- Treatment-emergent adverse events (TEAEs) were consistent with the known safety profile from adult studies with no new safety signals observed (**Table 2**)

Table 2. TEAEs through Week 52 (Safety set)

Characteristics	SEC low dose (N=42)	SEC high dose (N=42)	SEC total (N=84)
Any TEAEs, n (%)	**28 (66.7)**	**27 (64.3)**	**55 (65.5)**
Any non-fatal SAEs, n (%)	2 (4.8)	1 (2.4)	3 (3.6)
Discontinued study treatment due to any AE, n (%)	0	2 (4.8)	2 (2.4)
Death	0	0	0
Most frequent TEAEs (by SOC)*, n (%)			
Infections and infestations	19 (45.2)	21 (50.0)	40 (47.6)
Gastrointestinal disorders	4 (9.5)	8 (19.0)	12 (14.3)
Skin and subcutaneous tissue disorders	8 (19.0)	4 (9.5)	12 (14.3)
Most frequent TEAEs (by PT), n (%)**			
Nasopharyngitis	9 (21.4)	6 (14.3)	15 (17.9)
Acne	5 (11.9)	1 (2.4)	6 (7.1)
Influenza	3 (7.1)	1 (2.4)	4 (4.8)
Leukopenia	3 (7.1)	1 (2.4)	4 (4.8)
Pyrexia	3 (7.1)	1 (2.4)	4 (4.8)
AEs of interest			
Hypersensitivity (SMQ)	3 (7.1)	1 (2.4)	4 (4.8)
Infections and infestations (SOC)	19 (45.2)	21 (50.0)	40 (47.6)
Neutropenia (NMQ)	3 (7.1)	2 (4.8)	5 (6.0)
Diarrhea hemorrhagic (PT)†	0	1 (2.4)	1 (1.2)
Suicide/self-injury (SMQ)‡	1 (2.4)	0	1 (1.2)

*≥10% in SEC total group. **≥4% in SEC total group. †The event was resolved with concomitant treatment. ‡The patient had a history of anxiety and depressed mood, which was being treated with psychological behavior therapy. Psychiatric evaluation concluded that the patient's life had not been endangered at any moment. The investigator assessment did not suspect a relationship between the intentional self-injury and study medication. AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; NMQ, Novartis MedDRA query; PT, Preferred Term; SAE, serious adverse event; SMQ, Standardised MedDRA Query; SEC, secukinumab; SOC, System Organ Class; TEAE, treatment-emergent adverse event

CONCLUSIONS

- SEC is highly efficacious in rapidly clearing skin (PASI 75/90/100 and IGA mod 2011 0/1). There is sustained efficacy through Week 52 with both doses in pediatric patients with moderate to severe plaque psoriasis
- The safety profile in pediatric patients is consistent with that of the adult population
- The proportion of patients achieving CDLQI 0/1 continued to increase up to Week 24 and reached 70.3% in the high dose and 70.7% in the low dose group, up to Week 52

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DISCLOSURE

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, Janssen, Novartis, 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, Arcutis, Brickell Biotech, Celgene, ChemoCentryx, Eli Lilly, Galderma, 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. **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, UCB 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. **J. C. Szepietowski** is an advisory board member of AbbVie, LEO Pharma, Novartis, Pierre-Fabre, Menlo Therapeutics, Sienna Biopharmaceuticals, and Trevi Therapeutics, principal investigator for AbbVie, Novartis, Menlo Therapeutics, Trevi Therapeutics, Janssen, Merck, Regeneron, Amgen, Boehringer Ingelheim, Galapagos, Galderma, InflaRX, Kymab Ltd., Pfizer, UCB, Helm and Incyte; and a speaker for AbbVie, Novartis, Janssen, Eli Lilly, Sanofi-Genzyme, Sunfarm and Berlin-Chemie Mennarini. **D. Keefe** is an employee of Novartis Pharmaceuticals Corporation, USA. **R. Mazur**, **P. Forrer** and **M. Patekar** are employees of Novartis Pharma AG, Basel.

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