## Title

Secukinumab in Pediatric Patients with Plaque Psoriasis: Pooled Safety Analysis from Two Phase 3 Randomized Clinical Trials

**Running heading:** Pooled Safety of Secukinumab in Pediatric Patients with Plaque Psoriasis

## Author information

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## Electronic Supplementary Material

**Table S1. Demographic and baseline disease characteristics in the adult pool**

| Characteristics | SEC 150 mg | SEC 300 mg | Any SEC | PBO | ETN |
|---|---|---|---|---|---|
| | N=692 | N=691 | N=1383 | N=694 | N=326 |
| **Age, years, mean±SD** | 45.1±13.37 | 44.9±13.31 | 45.0±13.34 | 44.7±12.78 | 43.7±12.95 |
| **Female, n (%)** | 207 (29.9) | 214 (31.0) | 421 (30.4) | 208 (30.0) | 94 (28.8) |
| **Body weight, kg, mean±SD** | 86.6±23.15 | 86.6±23.21 | 86.6±23.17 | 86.0±22.58 | 84.6±20.51 |
| **Caucasian, n (%)** | 499 (72.1) | 505 (73.1) | 1004 (72.6) | 510 (73.5) | 219 (67.2) |
| **Baseline PASI score, mean±SD** | 22.8±9.99 | 22.7±9.37 | 22.7±9.68 | 22.5±9.64 | 23.2±9.81 |
| PASI score ≤20, n (%) | 368 (53.2) | 354 (51.2) | 722 (52.2) | 365 (52.6) | 163 (50.0) |
| PASI score >20, n (%) | 324 (46.8) | 337 (48.8) | 661 (47.8) | 327 (47.1) | 163 (50.0) |
| **Baseline total BSA, mean±SD** | 33.3±18.90 | 33.0±18.76 | 33.2±18.82 | 32.2±17.77 | 33.6±17.97 |
| **Baseline IGA mod 2011 score, n (%)** | | | | | |
| 3 (moderate disease) | 439 (63.4) | 436 (63.1) | 875 (63.3) | 424 (61.1) | 195 (59.8) |
| 4 (severe disease) | 253 (36.6) | 255 (36.9) | 508 (36.7) | 268 (38.6) | 131 (40.2) |
| **Severity of psoriasis[a], n (%)** | | | | | |
| Moderate | 499 (72.1) | 493 (71.3) | 992 (71.7) | 490 (70.6) | 226 (69.3) |
| Severe | 193 (27.9) | 197 (28.5) | 390 (28.2) | 201 (29.0) | 100 (30.7) |
| **Time since first diagnosis of plaque-type psoriasis, years, mean±SD** | 18.0±12.46 | 17.0±12.01 | 17.5±12.25 | 17.5±12.21 | 16.4±12.01 |
| **Previous biologic psoriasis therapy, n (%)** | 161 (23.3) | 147 (21.3) | 308 (22.3) | 148 (21.3) | 45 (13.8) |
| **Previous systemic psoriasis therapy, n (%)** | 449 (64.9) | 441 (63.8) | 890 (64.4) | 422 (60.8) | 215 (66.0) |

[a]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 BSA involvement of ≥10 %, and severe=PASI score ≥20 and IGA mod 2011 score 4 and BSA involvement of ≥10 %.
BSA, body surface area; ETN, etanercept; HD, high dose; IGA mod 2011, Investigator's Global Assessment modified 2011; LD, low dose; N, total number of patients; n, number of patients; PASI, Psoriasis Area and Severity Index; PBO, placebo; SEC, secukinumab

**Table S2. Duration of exposure to study treatment by population (pediatric and adult): Up to Week 12 (Safety set)**

| Duration of exposure | Pediatric pool | | | | | Adult pool | | | |
|---|---|---|---|---|---|---|---|---|---|
| | SEC LD N=82 | SEC HD N=82 | Any SEC N=164 | PBO N=41 | ETN N=41 | SEC 150 mg N=692 | SEC 300 mg N=690 | Any SEC N=1382 | ETN N=323 |
| **Any, n (%)** | 82 (100.0) | 82 (100.0) | 164 (100.0) | 41 (100.0) | 41 (100.0) | 692 (100.0) | 690 (100.0) | 1382 (100.0) | 323 (100.0) |
| **Exposure categories weeks, n (%)** | | | | | | | | | |
| ≥12 weeks | 73 (89.0) | 69 (84.1) | 142 (86.6) | 35 (85.4) | 35 (85.4) | 528 (76.3) | 538 (78.0) | 1066 (77.1) | 253 (78.3) |
| **Days** | | | | | | | | | |
| Mean±SD | 84.4±9.45 | 83.9±9.25 | 84.1±9.33 | 84.6±15.97 | 86.3±8.78 | 82.8±9.82 | 83.3±8.46 | 83.1±9.16 | 82.6±9.45 |
| Median | 84.0 | 84.0 | 84.0 | 84.0 | 84.0 | 84.0 | 84.0 | 84.0 | 84.0 |
| Min–Max | 9–105 | 15–126 | 9–126 | 24–136 | 77–133 | 8–141 | 1–141 | 1–141 | 9–96 |
| Patient-time | 19.0 | 18.8 | 37.8 | 9.5 | 9.7 | 156.9 | 157.5 | 314.4 | 73.0 |

Patient-time in patient years is calculated as the sum of individual patient durations in days divided by 365.25
ETN, etanercept; LD, low dose; HD, high dose; N, total number of patients; n, number of patients; PBO, placebo; SD, standard deviation; SEC, secukinumab

**Table S3. Duration of exposure to study treatment by population (pediatric and adult): Up to Week 52 (Safety set)**

| Duration of exposure | Pediatric pool | | | | Adult pool | | | |
|---|---|---|---|---|---|---|---|---|
| | Any SEC LD N=98 | Any SEC HD N=100 | Any SEC N=198 | ETN N=41 | Any SEC 150 mg N=999 | Any SEC 300 mg N=990 | Any SEC N=1989 | ETN N=323 |
| Any exposure, n (%) | 98 (100.0) | 100 (100.0) | 198 (100.0) | 41 (100.0) | 999 (100.0) | 990 (100.0) | 1989 (100.0) | 323 (100.0) |
| **Exposure categories weeks, n (%)** | | | | | | | | |
| ≥52 weeks | 73 (74.5) | 58 (58.0) | 131 (66.2) | 30 (73.2) | 471 (47.1) | 477 (48.2) | 948 (47.7) | 223 (69.0) |
| **Days** | | | | | | | | |
| Mean±SD | 345.0±53.86 | 336.1±69.05 | 340.5±62.00 | 338.2±72.64 | 319.4±70.42 | 323.1±69.26 | 321.3±69.85 | 335.3±83.29 |
| Median | 364.0 | 364.0 | 364.0 | 364.0 | 363.0 | 363.0 | 363.0 | 364.0 |
| Min–Max | 9–393 | 15–421 | 9–421 | 109–393 | 8–421 | 1–407 | 1–421 | 9–449 |
| Patient time | 92.6 | 92.0 | 184.6 | 38.0 | 873.7 | 875.8 | 1749.5 | 296.5 |

Patient-time in patient years is calculated as the sum of individual patient durations in days divided by 365.25
ETN, etanercept; LD, low dose; HD, high dose; N, total number of patients; n, number of patients; SD, standard deviation; SEC, secukinumab

## 1. Safety

### 1.1.1 Up to Week 12

The incidence of adverse events (AEs) in pediatric patients treated with secukinumab was generally comparable with the placebo group and with adult patients treated with secukinumab, and lower than in the etanercept group in the pediatric pool (**Table S4**). In the pediatric pool, the most affected system organ class (SOC) was "Infections and Infestations," with similar incidences in the secukinumab treatment groups (low dose (LD): 31.7%; high dose (HD): 35.4%), which was lower than that in the placebo group (39.0%) and slightly higher than that in the etanercept group (26.8%). Similarly, in the adult pool, the most affected SOC was "Infections and Infestations" with a comparable incidence between the "Any secukinumab" group in adults (29.1%) and pediatric (33.5 %) patients (**Table S4**).

The most commonly reported preferred terms (PTs) were nasopharyngitis, pharyngitis, abdominal pain, Upper respiratory tract infection (URTI), and headache in the pediatric pool, and nasopharyngitis, diarrhea, oropharyngeal pain, URTI, and headache in adult pool. Nasopharyngitis was reported in 14.0% and 11.8% in the "Any secukinumab" groups, 9.8% and 11.5% in the etanercept groups, and 2.4% in the placebo group in the pediatric and adult pools, respectively (**Table S4**). In addition, URTIs were also analyzed by Customized MedDRA Query (CMQ). In the pediatric and adult populations, URTI (CMQ) was reported in 22.6% and 18.8% in the "Any secukinumab" groups, 19.5% and 15.8% in the etanercept groups, and 26.8% in the placebo group. AEs leading to discontinuation of study treatment in the "Any secukinumab" groups were similar in the pediatric (1.2%) and adult (1.3%) pools. In the etanercept groups, 2.4% in the pediatric pool and 1.9% in the adult pool had AEs leading to discontinuation of study treatment; it was 2.4% in the placebo group **(Table S4).** Overall, serious AEs (SAEs) were observed in 2 pediatric patients (1.2%) and 30 adult patients (2.2%) who received secukinumab, 4 pediatric patients (9.8%) and 3 adult patients (0.9%) receiving etanercept, and no patients in the placebo group **(Table S4).** SAEs are further described in **Table S5.**

**Table S4. Absolute and relative frequencies for TEAEs in pediatric and adult population: Up to Week 12 (Safety set)**

| n (%) 95% CI | Pediatric population | | | | | Adult population | | | |
|---|---|---|---|---|---|---|---|---|---|
| | SEC LD N=82 | SEC HD N=82 | Any SEC N=164 | PBO N=41 | ETN N=41 | SEC 150 mg N=692 | SEC 300 mg N=690 | Any SEC N=1382 | ETN N=323 |
| **Total AEs** | 42 (51.2) (40.0, 62.3) | 44 (53.7) (42.4, 64.6) | 86 (52.4) (44.5, 60.2) | 22 (53.7) (37.6, 69.0) | 25 (61.0) (44.5, 75.4) | 415 (60.0) (56.2, 63.6) | 390 (56.5) (52.7, 60.2) | 805 (58.2) (55.6, 60.9) | 187 (57.9) (52.3, 63.3) |
| **SAEs** | 1 (1.2) (0.1, 7.5) | 1 (1.2) (0.1, 7.5) | 2 (1.2) (0.2, 4.8) | 0 (0.0) (0.0, 10.7) | 4 (9.8) (3.2, 24.1) | 15 (2.2) (1.3, 3.6) | 15 (2.2) (1.3, 3.6) | 30 (2.2) (1.5, 3.1) | 3 (0.9) (0.2, 2.9) |
| **Treatment discontinuation due to AEs** | 0 (0.0) (0.0, 5.6) | 2 (2.4) (0.4, 9.4) | 2 (1.2) (0.2, 4.8) | 1 (2.4) (0.1, 14.4) | 1 (2.4) (0.1, 14.4) | 9 (1.3) (0.6, 2.5) | 9 (1.3) (0.6, 2.6) | 18 (1.3) (0.8, 2.1) | 6 (1.9) (0.8, 4.2) |
| **Most frequent AEs (by SOC)[a]** | | | | | | | | | |
| Infections and infestations | 26 (31.7) (22.1, 43.0) | 29 (35.4) (25.3, 46.8) | 55 (33.5) (26.5, 41.4) | 16 (39.0) (24.6, 55.5) | 11 (26.8) (14.8, 43.2) | 205 (29.6) (26.3, 33.2) | 197 (28.6) (25.2, 32.1) | 402 (29.1) (26.7, 31.6) | 80 (24.8) (20.2, 29.9) |
| Gastrointestinal disorders | 7 (8.5) (3.8, 17.3) | 12 (14.6) (8.1, 24.6) | 19 (11.6) (7.3, 17.7) | 7 (17.1) (7.7, 32.6) | 10 (24.4) (12.9, 40.6) | 77 (11.1) (8.9, 13.8) | 88 (12.8) (10.4, 15.5) | 165 (11.9) (10.3, 13.8) | 32 (9.9) (7.0, 13.8) |
| Skin and subcutaneous tissue disorders | 8 (9.8) (4.6, 18.8) | 7 (8.5) (3.8, 17.3) | 15 (9.1) (5.4, 14.9) | 3 (7.3) (1.9, 21.0) | 1 (2.4) (0.1, 14.4) | 76 (11.0) (8.8, 13.6) | 80 (11.6) (9.3, 14.3) | 156 (11.3) (9.7, 13.1) | 35 (10.8) (7.8, 14.9) |
| General disorders and administration site conditions | 6 (7.3) (3.0, 15.8) | 7 (8.5) (3.8, 17.3) | 13 (7.9) (4.5, 13.5) | 3 (7.3) (1.9, 21.0) | 5 (12.2) (4.6, 27.0) | 48 (6.9) (5.2, 9.2) | 43 (6.2) (4.6, 8.4) | 91 (6.6) (5.4, 8.1) | 58 (18.0) (14.0, 22.7) |
| Respiratory, thoracic, and mediastinal disorders | 3 (3.7) (0.9, 11.1) | 6 (7.3) (3.0, 15.8) | 9 (5.5) (2.7, 10.5) | 3 (7.3) (1.9, 21.0) | 1 (2.4) (0.1, 14.4) | 45 (6.5) (4.8, 8.7) | 54 (7.8) (6.0, 10.2) | 99 (7.2) (5.9, 8.7) | 16 (5.0) (3.0, 8.1) |
| **Most frequent AEs (by PT)[a]** | | | | | | | | | |
| Nasopharyngitis | 13 (15.9) (9.0, 26.0) | 10 (12.2) (6.3, 21.7) | 23 (14.0) (9.3, 20.5) | 1 (2.4) (0.1, 14.4) | 4 (9.8) (3.2, 24.1) | 84 (12.1) (9.8, 14.9) | 79 (11.4) (9.2, 14.1) | 163 (11.8) (10.2,13.6) | 37 (11.5) (8.3, 15.6) |
| Pharyngitis | 3 (3.7) (0.9, 11.1) | 3 (3.7) (0.9, 11.1) | 6 (3.7) (1.5, 8.2) | 4 (9.8) (3.2, 24.1) | 0 (0.0) (0.0, 10.7) | 7 (1.0) (0.4, 2.2) | 8 (1.2) (0.5, 2.4) | 15 (1.1) (0.6, 1.8) | 0 (0.0) (0.0, 1.5) |
| Abdominal pain | 3 (3.7) (0.9, 11.1) | 2 (2.4) (0.4, 9.4) | 5 (3.0) (1.1, 7.3) | 0 (0.0) (0.0, 10.7) | 3 (7.3) (1.9, 21.0) | 4 (0.6) (0.2, 1.6) | 3 (0.4) (0.1, 1.4) | 7 (0.5) (0.2, 1.1) | 3 (0.9) (0.2, 2.9) |
| URTI | 2 (2.4) (0.4, 9.4) | 3 (3.7) (0.9, 11.1) | 5 (3.0) (1.1, 7.3) | 3 (7.3) (1.9, 21.0) | 1 (2.4) (0.1, 14.4) | 22 (3.2) (2.1, 4.9) | 17 (2.5) (1.5, 4.0) | 39 (2.8) (2.0, 3.9) | 7 (2.2) (1.0, 4.6) |
| Headache | 2 (2.4) (0.4, 9.4) | 3 (3.7) (0.9, 11.1) | 5 (3.0) (1.1, 7.3) | 4 (9.8) (3.2, 24.1) | 1 (2.4) (0.1, 14.4) | 38 (5.5) (4.0, 7.5) | 45 (6.5) (4.8, 8.7) | 83 (6.0) (4.8, 7.4) | 23 (7.1) (4.7, 10.6) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **AEs of special interest** | | | | | | | | | |
| Hypersensitivity (SMQ) (narrow) | 3 (3.7) (0.9, 11.1) | 2 (2.4) (0.4, 9.4) | 5 (3.0) (1.1, 7.3) | 1 (2.4) (0.1, 14.4) | 2 (4.9) (0.8, 17.8) | 31 (4.5) (3.1, 6.4) | 32 (4.6) (3.2, 6.6) | 63 (4.6) (3.5, 5.8) | 17 (5.3) (3.2, 8.5) |
| Neutropenia (NMQ) (narrow) | 3 (3.7) (0.9, 11.1) | 2 (2.4) (0.4, 9.4) | 5 (3.0) (1.1, 7.3) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 2 (0.3) (0.1, 1.2) | 4 (0.6) (0.2, 1.6) | 6 (0.4) (0.2, 1.0) | 2 (0.6) (0.1, 2.5) |
| Neutropenia (PT) | 2 (2.4) (0.4, 9.4) | 1 (1.2) (0.1, 7.5) | 3 (1.8) (0.5, 5.7) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 1 (0.1) (0.0, 0.9) | 2 (0.3) (0.1, 1.2) | 3 (0.2) (0.1, 0.7) | 2 (0.6) (0.1, 2.5) |
| IBD[b] (NMQ) (narrow) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 2.9) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 1 (0.1) (0.0, 0.9) | 1 (0.1) (0.0, 0.9) | 2 (0.1) (0.0, 0.6) | 1 (0.3) (0.0, 2.0) |
| MACE (MI, Stroke, CV death) (NMQ) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 2.9) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 1 (0.1) (0.0, 0.9) | 2 (0.3) (0.1, 1.2) | 3 (0.2) (0.1, 0.7) | 0 (0.0) (0.0, 1.5) |
| Malignant or unspecified tumors (SMQ) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 2.9) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 4 (0.6) (0.2, 1.6) | 1 (0.1) (0.0, 0.9) | 5 (0.4) (0.1, 0.9) | 0 (0.0) (0.0, 1.5) |
| *Candida* infections (HLT) | 0 (0.0) (0.0, 5.6) | 2 (2.4) (0.4, 9.4) | 2 (1.2) (0.2, 4.8) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 4 (0.6) (0.2, 1.6) | 8 (1.2) (0.5, 2.4) | 12 (0.9) (0.5, 1.6) | 1 (0.3) (0.0, 2.0) |
| Nail *candida* (PT) | 0 (0.0) (0.0, 5.6) | 1 (1.2) (0.1, 7.5) | 1 (0.6) (0.0, 3.9) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 0.7) | 0 (0.0) (0.0, 0.7) | 0 (0.0) (0.0, 0.3) | 0 (0.0) (0.0, 1.5) |
| Vulvovaginal *candidiasis(PT)* | 0 (0.0) (0.0, 5.6) | 1 (1.2) (0.1, 7.5) | 1 (0.6) (0.0, 3.9) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 2 (0.3) (0.1, 1.2) | 1 (0.1) (0.0, 0.9) | 3 (0.2) (0.1, 0.7) | 0 (0.0) (0.0, 1.5) |
| Suicide/self-injury (SMQ) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 2.9) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 1 (0.1) (0.0, 0.9) | 0 (0.0) (0.0, 0.7) | 1 (0.1) (0.0, 0.5) | 0 (0.0) (0.0, 1.5) |
| Suicide attempt (PT) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 5.6) | 0 (0.0) (0.0, 2.9) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 1 (0.1) (0.0, 0.9) | 0 (0.0) (0.0, 0.7) | 1 (0.1) (0.0, 0.5) | 0 (0.0) (0.0, 1.5) |
| ISRs[c] | 3 (3.7) (0.9, 11.1) | 1 (1.2) (0.1, 7.5) | 4 (2.4) (0.8, 6.5) | 2 (4.9) (0.8, 17.8) | 3 (7.3) (1.9, 21.0) | 4 (0.6) (0.2, 1.6) | 6 (0.9) (0.4, 2.0) | 10 (0.7) (0.4, 1.4) | 33 (10.2) (7.2, 14.2) |

"Any SEC" for both the treatment groups (LD and HD) includes all patients treated with SEC from the start of the study

[a]AEs ordered according to the incidence in Any secukinumab group in pediatric population; [b]One patient reported a mild AE of hemorrhagic diarrhea which was resolved and confirmed not to be an IBD; [c]ISRs corresponding to event coded with HLT 'Injection-site reaction' and some with HLT 'Administration-site reaction' or 'Application- and instillation-site reactions'

AE, adverse event; CI, confidence interval; CV, cardiovascular; ETN, etanercept; HD, high dose; HLT, high level term; IBD, inflammatory bowel disease; ISR, injection-site reaction; LD, low dose; LLN, lower limit of normal; MACE, major adverse cardiovascular event; MedDRA version 23.0, Medical Dictionary for Regulatory Activities; MI, myocardial infarction; N, total number of patients; NMQ, Novartis customized MedDRA Query; PBO, placebo; PT, preferred term; SAE; serious AE; SMQ, Standardized MedDRA Query; SEC, secukinumab; SOC, system organ class; TEAE, treatment-emergent AE; URTI, upper respiratory tract infection

**Table S5. Absolute and relative frequencies for treatment-emergent SAEs by PT and population (pediatric and adult): Up to Week 12 (Safety set)**

| PT, n (%) 95% CI | Pediatric pool | | | | | Adult pool | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Any SEC LD N=82 | Any SEC HD N=82 | Any SEC N=164 | PBO N=41 | ETN N=41 | Any SEC 150 mg N=692 | Any SEC 300 mg N=690 | Any SEC N=1382 | ETN N=323 |
| Any PT, Total | 1 (1.2) (0.1, 7.5) | 1 (1.2) (0.1, 7.5) | 2 (1.2) (0.2, 4.8) | 0 (0.0) (0.0, 10.7) | 4 (9.8) (3.2, 24.1) | 15 (2.2) (1.3, 3.6) | 15 (2.2) (1.3, 3.6) | 30 (2.2) (1.5, 3.1) | 3 (0.9) (0.2, 2.9) |
| Alanine aminotransferase increased | 1 (1.2) (0.1, 7.5) | 0 (0.0) (0.0, 5.6) | 1 (0.6) (0.0, 3.9) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 0.7) | 0 (0.0) (0.0, 0.7) | 0 (0.0) (0.0, 0.3) | 0 (0.0) (0.0, 1.5) |
| Toxic shock syndrome | 0 (0.0) (0.0, 5.6) | 1 (1.2) (0.1, 7.5) | 1 (0.6) (0.0, 3.9) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 10.7) | 0 (0.0) (0.0, 0.7) | 0 (0.0) (0.0, 0.7) | 0 (0.0) (0.0, 0.3) | 0 (0.0) (0.0, 1.5) |

PTs are sorted in descending order of frequency in the "Any SEC" column for the pediatric pool
Only SAEs which occurred in the secukinumab-treated pediatric population, and the corresponding SAEs in other treatment groups and adults are presented
CI, confidence interval; ETN, etanercept; HD, high dose; LD, low dose; N, total number of patients; n, number of patients; PBO, placebo; PT, preferred term; SAE, serious adverse event; SEC, secukinumab

**Table S6. EAIRs for treatment-emergent SAEs by preferred term and population (pediatric and adult): Up to Week 52 (Safety set)**

| PT, EAIR/100 patient-years (95% CI) | Pediatric pool | | | | Adult pool | | | |
|---|---|---|---|---|---|---|---|---|
| | Any SEC LD N=98 | Any SEC HD N=100 | Any SEC N=198 | ETN N=41 | Any SEC 150 mg N=999 | Any SEC 300 mg N=990 | Any SEC N=1989 | ETN N=323 |
| Any PT, Total | 7.8 (3.1, 16.1) | 6.7 (2.5, 14.6) | 7.3 (3.9, 12.4) | 14.5 (4.7, 33.9) | 7.5 (5.8, 9.6) | 7.5 (5.8, 9.6) | 7.5 (6.3, 9.0) | 6.9 (4.2, 10.7) |
| Alanine aminotransferase increased | 1.1 (0.0, 6.1) | 0.0 (0.0, 4.0) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Appendicitis | 0.0 (0.0, 4.0) | 1.1 (0.0, 6.1) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.1 (0.0, 0.6) | 0.1 (0.0, 0.3) | 0.0 (0.0, 1.2) |
| Arthritis reactive | 1.1 (0.0, 6.0) | 0.0 (0.0, 4.0) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Bronchitis | 1.1 (0.0, 6.1) | 0.0 (0.0, 4.0) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Clavicle fracture | 0.0 (0.0, 4.0) | 1.1 (0.0, 6.1) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.1 (0.0, 0.6) | 0.1 (0.0, 0.3) | 0.3 (0.0, 1.9) |
| Enterocolitis bacterial | 0.0 (0.0, 4.0) | 1.1 (0.0, 6.1) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Infectious mononucleosis | 1.1 (0.0, 6.1) | 0.0 (0.0, 4.0) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Infectious pleural effusion | 0.0 (0.0, 4.0) | 1.1 (0.0, 6.1) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Intentional self-injury | 1.1 (0.0, 6.0) | 0.0 (0.0, 4.0) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Lung abscess | 0.0 (0.0, 4.0) | 1.1 (0.0, 6.1) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Lymphadenopathy | 0.0 (0.0, 4.0) | 1.1 (0.0, 6.1) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.1 (0.0, 0.6) | 0.0 (0.0, 0.4) | 0.1 (0.0, 0.3) | 0.0 (0.0, 1.2) |
| Major depression | 1.1 (0.0, 6.0) | 0.0 (0.0, 4.0) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Pneumonia | 0.0 (0.0, 4.0) | 1.1 (0.0, 6.1) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.2 (0.0, 0.8) | 0.2 (0.0, 0.8) | 0.2 (0.1, 0.6) | 0.0 (0.0, 1.2) |
| Suicidal ideation | 1.1 (0.0, 6.0) | 0.0 (0.0, 4.0) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |
| Testicular torsion | 1.1 (0.0, 6.0) | 0.0 (0.0, 4.0) | 0.5 (0.0, 3.0) | 0.0 (0.0, 9.7) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.4) | 0.0 (0.0, 0.2) | 0.0 (0.0, 1.2) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Thrombophlebitis | 0.0<br>(0.0, 4.0) | 1.1<br>(0.0, 6.1) | 0.5<br>(0.0, 3.0) | 0.0<br>(0.0, 9.7) | 0.0<br>(0.0, 0.4) | 0.0<br>(0.0, 0.4) | 0.0<br>(0.0, 0.2) | 0.0<br>(0.0, 1.2) |
| Toxic shock syndrome | 0.0<br>(0.0, 4.0) | 1.1<br>(0.0, 6.1) | 0.5<br>(0.0, 3.0) | 0.0<br>(0.0, 9.7) | 0.0<br>(0.0, 0.4) | 0.0<br>(0.0, 0.4) | 0.0<br>(0.0, 0.2) | 0.0<br>(0.0, 1.2) |
| Venous thrombosis limb | 0.0<br>(0.0, 4.0) | 1.1<br>(0.0, 6.1) | 0.5<br>(0.0, 3.0) | 0.0<br>(0.0, 9.7) | 0.0<br>(0.0, 0.4) | 0.0<br>(0.0, 0.4) | 0.0<br>(0.0, 0.2) | 0.0<br>(0.0, 1.2) |

PTs are sorted in descending order of IR in the "Any SEC" column for the pediatric pool. Only SAEs which occurred in the secukinumab-treated pediatric population and the corresponding SAEs in other treatment groups and adults are presented

CI, confidence interval; EAIR, exposure-adjusted IR per 100 patient-years; ETN, etanercept; HD, high dose; IR, incidence rate; LD, low dose; N, total number of patients; n, number of patients; PT, preferred term; SAE, serious adverse event; SEC, secukinumab

# 1 Subgroup analysis

## 1.1. Up to Week 12

### 1.1.1. By Age

In the <12-year subgroup, the incidence of AEs (44%) was lower with "Any secukinumab" than with etanercept (70%) and was similar to the placebo group (40%). The incidence of AEs with "Any secukinumab" was higher in the ≥12-years-subgroup (56.1%). The most frequently affected SOCs were gastrointestinal disorders, blood and lymphatic system disorders, general disorders, and administration-site conditions and injury, poisoning, and procedural complications in the <12-year group compared with gastrointestinal disorders, skin and subcutaneous tissue disorders, general disorders and administration-site conditions, and respiratory, thoracic, and mediastinal disorders in the ≥12-year group (**Table S7[i]** & **[ii]**). Nasopharyngitis, the most commonly reported AE (by PT), was less frequent in patients aged <12 years compared with those aged ≥12 years (6.0% vs 17.5%) in patients treated with "Any secukinumab" dose. The incidence of nasopharyngitis in both subgroups on etanercept was 10.0% and 9.7%, respectively. In the placebo group, 10.0% of patients experienced nasopharyngitis in the <12-year subgroup compared with none in the ≥12-year subgroup (**Table S7 [i]** & **[ii]**). Abdominal pain (8%) and nasopharyngitis (17.5%) were the most commonly reported AE (by PT) in the <12-year and ≥12-year group, respectively, and were 8% and 17.5% for patients with "Any secukinumab" (**Table S7 [i]** & **[ii]**). Neutropenia (Novartis customized MedDRA Query [NMQ]) was observed in 4.0% of patients in the <12-year age group and 2.6% in the ≥12-year groups of the pediatric population who received "Any secukinumab" (**Table S7 [i]** & **[ii]**).

**Table S7. Absolute and relative frequencies for treatment-emergent AEs in pediatric population by age strata**: **Up to Week 12 (Safety set)**

**(i) Age group: <12 years**

| **Age group: <12 years** | | | | | |
|---|---|---|---|---|---|
| **n (%) 95% CI** | **SEC LD N=25** | **SEC HD N=25** | **Any SEC N=50** | **PBO N=10** | **ETN N=10** |
| **Total AEs** | 10 (40.0) (21.8, 61.1) | 12 (48.0) (28.3, 68.2) | 22 (44.0) (30.3, 58.7) | 4 (40.0) (13.7, 72.6) | 7 (70.0) (35.4, 91.9) |
| **SAEs** | 0 (0.0) (0.0, 16.6) | 1 (4.0) (0.2, 22.3) | 1 (2.0) (0.1, 12.0) | 0 (0.0) (0.0, 34.5) | 1 (10.0) (0.5, 45.9) |
| **Treatment discontinuation due to AEs** | 0 (0.0) (0.0, 16.6) | 2 (8.0) (1.4, 27.5) | 2 (4.0) (0.7, 14.9) | 0 (0.0) (0.0, 34.5) | 0 (0.0) (0.0, 34.5) |
| **Top five most frequent AEs (by SOC)[a]** | | | | | |
| Infections and infestations | 6 (24.0) (10.2, 45.5) | 9 (36.0) (18.7, 57.4) | 15 (30.0) (18.3, 44.8) | 2 (20.0) (3.5, 55.8) | 3 (30.0) (8.1, 64.6) |
| Gastrointestinal disorders | 3 (12.0) (3.2, 32.3) | 4 (16.0) (5.3, 36.9) | 7 (14.0) (6.3, 27.4) | 0 (0.0) (0.0, 34.5) | 2 (20.0) (3.5, 55.8) |
| Blood and lymphatic system disorders | 1 (4.0) (0.2, 22.3) | 2 (8.0) (1.4, 27.5) | 3 (6.0) (1.6, 17.5) | 1 (10.0) (0.5, 45.9) | 0 (0.0) (0.0, 34.5) |
| General disorders and administration-site conditions | 3 (12.0) (3.2, 32.3) | 0 (0.0) (0.0, 16.6) | 3 (6.0) (1.6, 17.5) | 0 (0.0) (0.0, 34.5) | 2 (20.0) (3.5, 55.8) |
| Injury, poisoning, and procedural complications | 2 (8.0) (1.4, 27.5) | 1 (4.0) (0.2, 22.3) | 3 (6.0) (1.6, 17.5) | 0 (0.0) (0.0, 34.5) | 0 (0.0) (0.0, 34.5) |
| **Top five most frequent AEs (by PT)[a]** | | | | | |
| Abdominal pain | 2 (8.0) (1.4, 27.5) | 2 (8.0) (1.4, 27.5) | 4 (8.0) (2.6, 20.1) | 0 (0.0) (0.0, 34.5) | 1 (10.0) (0.5, 45.9) |
| Nasopharyngitis | 2 (8.0) (1.4, 27.5) | 1 (4.0) (0.2, 22.3) | 3 (6.0) (1.6, 17.5) | 1 (10.0) (0.5, 45.9) | 1 (10.0) (0.5, 45.9) |
| Arthropod bite | 1 (4.0) (0.2, 22.3) | 1 (4.0) (0.2, 22.3) | 2 (4.0) (0.7, 14.9) | 0 (0.0) (0.0, 34.5) | 0 (0.0) (0.0, 34.5) |
| Diarrhea | 1 (4.0) (0.2, 22.3) | 1 (4.0) (0.2, 22.3) | 2 (4.0) (0.7, 14.9) | 0 (0.0) (0.0, 34.5) | 0 (0.0) (0.0, 34.5) |
| Leukopenia | 1 (4.0) (0.2, 22.3) | 1 (4.0) (0.2, 22.3) | 2 (4.0) (0.7, 14.9) | 0 (0.0) (0.0, 34.5) | 0 (0.0) (0.0, 34.5) |
| **AEs of special interest** | | | | | |
| Infections and infestations (SOC) | 6 (24.0) (10.2, 45.5) | 9 (36.0) (18.7, 57.4) | 15 (30.0) (18.3, 44.8) | 2 (20.0) (3.5, 55.8) | 3 (30.0) (8.1, 64.6) |
| Neutropenia (NMQ) (narrow) | 1 (4.0) (0.2, 22.3) | 1 (4.0) (0.2, 22.3) | 2 (4.0) (0.7, 14.9) | 0 (0.0) (0.0, 34.5) | 0 (0.0) (0.0, 34.5) |
| Hypersensitivity (SMQ) (narrow) | 0 (0.0) (0.0, 16.6) | 0 (0.0) (0.0, 16.6) | 0 (0.0) (0.0, 8.9) | 1 (10.0) (0.5, 45.9) | 2 (20.0) (3.5, 55.8) |
| ISRs | 1 (4.0) (0.2, 22.3) | 0 (0.0) (0.0, 16.6) | 1 (2.0) (0.1, 12.0) | 0 (0.0) (0.0, 34.5) | 1 (10.0) (0.5, 45.9) |

"Any SEC" for both the treatment groups (LD and HD) includes all patients treated with SEC from the start of the study and those who switched from PBO to SEC at Week 12

[a]AEs ordered according to pediatric population

AE, adverse event; ETN, etanercept; HD, high dose; ISR, injection-site reaction; LD, low dose; N, total number of patients; n, number of patients; NMQ, Novartis customized MedDRA Query; PBO, placebo; PT, preferred term; SAE, serious AE; SEC, secukinumab; SMQ, standardized MedDRA Query; SOC, system organ class

**(ii) Age group: ≥12 years**

| Age group: ≥12 years | | | | | |
|---|---|---|---|---|---|
| **n (%) 95% CI** | **SEC LD N=57** | **SEC HD N=57** | **Any SEC N=114** | **PBO N=31** | **ETN N=31** |
| **Total AEs** | 32 (56.1) (42.4, 69.0) | 32 (56.1) (42.4, 69.0) | 64 (56.1) (46.5, 65.3) | 18 (58.1) (39.3, 74.9) | 18 (58.1) (39.3, 74.9) |
| **SAEs** | 1 (1.8) (0.1, 10.6) | 0 (0.0) (0.0, 7.9) | 1 (0.9) (0.0, 5.5) | 0 (0.0) (0.0, 13.7) | 3 (9.7) (2.5, 26.9) |
| **Treatment discontinuation due to AEs** | 0 (0.0) (0.0, 7.9) | 0 (0.0) (0.0, 7.9) | 0 (0.0) (0.0, 4.1) | 1 (3.2) (0.2, 18.5) | 1 (3.2) (0.2, 18.5) |
| **Top five most frequent AEs (by SOC)[a]** | | | | | |
| Infections and infestations | 20 (35.1) (23.2, 48.9) | 20 (35.1) (23.2, 48.9) | 40 (35.1) (26.5, 44.7) | 14 (45.2) (27.8, 63.7) | 8 (25.8) (12.5, 44.9) |
| Gastrointestinal disorders | 4 (7.0) (2.3, 17.8) | 8 (14.0) (6.7, 26.3) | 12 (10.5) (5.8, 18.0) | 7 (22.6) (10.3, 41.5) | 8 (25.8) (12.5, 44.9) |
| Skin and subcutaneous tissue disorders | 6 (10.5) (4.4, 22.2) | 6 (10.5) (4.4, 22.2) | 12 (10.5) (5.8, 18.0) | 3 (9.7) (2.5, 26.9) | 1 (3.2) (0.2, 18.5) |
| General disorders and administration-site conditions | 3 (5.3) (1.4, 15.5) | 7 (12.3) (5.5, 24.3) | 10 (8.8) (4.5, 15.9) | 3 (9.7) (2.5, 26.9) | 3 (9.7) (2.5, 26.9) |
| Respiratory, thoracic, and mediastinal disorders | 3 (5.3) (1.4, 15.5) | 4 (7.0) (2.3, 17.8) | 7 (6.1) (2.7, 12.7) | 2 (6.5) (1.1, 22.8) | 1 (3.2) (0.2, 18.5) |
| **Top five most frequent AEs (by PT)[a]** | | | | | |
| Nasopharyngitis | 11 (19.3) (10.5, 32.3) | 9 (15.8) (7.9, 28.4) | 20 (17.5) (11.3, 26.0) | 0 (0.0) (0.0, 13.7) | 3 (9.7) (2.5, 26.9) |
| Headache | 2 (3.5) (0.6, 13.2) | 3 (5.3) (1.4, 15.5) | 5 (4.4) (1.6, 10.4) | 4 (12.9) (4.2, 30.8) | 1 (3.2) (0.2, 18.5) |
| Dysmenorrhea | 2 (3.5) (0.6, 13.2) | 2 (3.5) (0.6, 13.2) | 4 (3.5) (1.1, 9.3) | 0 (0.0) (0.0, 13.7) | 1 (3.2) (0.2, 18.5) |
| Pharyngitis | 2 (3.5) (0.6, 13.2) | 2 (3.5) (0.6, 13.2) | 4 (3.5) (1.1, 9.3) | 4 (12.9) (4.2, 30.8) | 0 (0.0) (0.0, 13.7) |
| Abdominal pain upper | 0 (0.0) (0.0, 7.9) | 3 (5.3) (1.4, 15.5) | 3 (2.6) (0.7, 8.1) | 2 (6.5) (1.1, 22.8) | 2 (6.5) (1.1, 22.8) |
| **AEs of special interest** | | | | | |
| Infections and infestations (SOC) | 20 (35.1) (23.2, 48.9) | 20 (35.1) (23.2, 48.9) | 40 (35.1) (26.5, 44.7) | 14 (45.2) (27.8, 63.7) | 8 (25.8) (12.5, 44.9) |
| Hypersensitivity (SMQ) (narrow) | 3 (5.3) (1.4, 15.5) | 2 (3.5) (0.6, 13.2) | 5 (4.4) (1.6, 10.4) | 0 (0.0) (0.0, 13.7) | 0 (0.0) (0.0, 13.7) |
| Neutropenia (NMQ) (narrow) | 2 (3.5) (0.6, 13.2) | 1 (1.8) (0.1, 10.6) | 3 (2.6) (0.7, 8.1) | 0 (0.0) (0.0, 13.7) | 0 (0.0) (0.0, 13.7) |
| ISRs | 2 (3.5) (0.6, 13.2) | 1 (1.8) (0.1, 10.6) | 3 (2.6) (0.7, 8.1) | 2 (6.5) (1.1, 22.8) | 2 (6.5) (1.1, 22.8) |

'Any SEC' for both the treatment groups (LD and HD) includes all patients treated with secukinumab from the start of the study and those who switched from placebo to secukinumab at Week 12

[a]AEs ordered according to pediatric population

AE, adverse event; CI, confidence interval; ETN, etanercept; HD, high dose; ISR, injection-site reaction; LD, low dose; N, total number of patients; n, number of patients; NMQ, Novartis customized MedDRA Query; PBO, placebo; PT, preferred term; SAE, serious AE; SEC, secukinumab; SMQ, standardized MedDRA Query; SOC, system organ class

**1.1.2. By Bodyweight**

The overall incidence of treatment-emergent AEs in patients treated with "Any secukinumab" dose was lower in the <25-kg subgroup (46.2%) compared with the 25- to <50- (49.1%) and the ≥50-kg (55.3%) bodyweight

subgroups (**Table S8 [i], [ii]** & **[iii]**). Neutropenia (NMQ, narrow) was observed in 15.4% and 3.2% in the <25- and ≥50-kg subgroups of the pediatric population who received "Any secukinumab," respectively (**Table S8 [i], [ii]** & **[iii]**).

**Table S8. Absolute and relative frequencies for treatment-emergent AEs in the pediatric population by bodyweight strata: Up to Week 12 (Safety set)**

**(i) Bodyweight group: <25 kg**

| **Bodyweight group: <25 kg** | | | | | |
|---|---|---|---|---|---|
| **n (%) 95% CI** | **SEC LD N=6** | **SEC HD N=7** | **Any SEC N=13** | **PBO N=3** | **ETN N=4** |
| **Total AEs** | 2 (33.3) (6.0, 75.9) | 4 (57.1) (20.2, 88.2) | 6 (46.2) (20.4, 73.9) | 2 (66.7) (12.5, 98.2) | 2 (50.0) (9.2, 90.8) |
| **SAEs** | None | None | None | None | None |
| **Treatment discontinuation due to AEs** | None | None | None | None | None |
| **Top five most frequent AEs (by SOC)[a]** | | | | | |
| Infections and infestations | 1 (16.7) (0.9, 63.5) | 3 (42.9) (11.8, 79.8) | 4 (30.8) (10.4, 61.1) | 1 (33.3) (1.8, 87.5) | 0 (0.0) (0.0, 60.4) |
| Blood and lymphatic system disorders | 1 (16.7) (0.9, 63.5) | 2 (28.6) (5.1, 69.7) | 3 (23.1) (6.2, 54.0) | 1 (33.3) (1.8, 87.5) | 0 (0.0) (0.0, 60.4) |
| Eye disorders | 0 (0.0) (0.0, 48.3) | 1 (14.3) (0.8, 58.0) | 1 (7.7) (0.4, 37.9) | 0 (0.0) (0.0, 69.0) | 0 (0.0) (0.0, 60.4) |
| Gastrointestinal disorders | 0 (0.0) (0.0, 48.3) | 1 (14.3) (0.8, 58.0) | 1 (7.7) (0.4, 37.9) | 0 (0.0) (0.0, 69.0) | 0 (0.0) (0.0, 60.4) |
| Investigations | 0 (0.0) (0.0, 48.3) | 1 (14.3) (0.8, 58.0) | 1 (7.7) (0.4, 37.9) | 0 (0.0) (0.0, 69.0) | 1 (25.0) (1.3, 78.1) |
| **Top five most frequent AEs (by PT)[a]** | | | | | |
| Leukopenia | 1 (16.7) (0.9, 63.5) | 1 (14.3) (0.8, 58.0) | 2 (15.4) (2.7, 46.3) | 0 (0.0) (0.0, 69.0) | 0 (0.0) (0.0, 60.4) |
| Nasopharyngitis | 1 (16.7) (0.9, 63.5) | 1 (14.3) (0.8, 58.0) | 2 (15.4) (2.7, 46.3) | 0 (0.0) (0.0, 69.0) | 0 (0.0) (0.0, 60.4) |
| Abdominal pain upper | 0 (0.0) (0.0, 48.3) | 1 (14.3) (0.8, 58.0) | 1 (7.7) (0.4, 37.9) | 0 (0.0) (0.0, 69.0) | 0 (0.0) (0.0, 60.4) |
| Asthma | 0 (0.0) (0.0, 48.3) | 1 (14.3) (0.8, 58.0) | 1 (7.7) (0.4, 37.9) | 0 (0.0) (0.0, 69.0) | 0 (0.0) (0.0, 60.4) |
| Chalazion | 0 (0.0) (0.0, 48.3) | 1 (14.3) (0.8, 58.0) | 1 (7.7) (0.4, 37.9) | 0 (0.0) (0.0, 69.0) | 0 (0.0) (0.0, 60.4) |
| **AEs of special interest** | | | | | |
| Infections and infestations (SOC) | 1 (16.7) (0.9, 63.5) | 3 (42.9) (11.8, 79.8) | 4 (30.8) (10.4, 61.1) | 1 (33.3) (1.8, 87.5) | 0 (0.0) (0.0, 60.4) |
| Neutropenia (NMQ) (narrow) | 1 (16.7) (0.9, 63.5) | 1 (14.3) (0.8, 58.0) | 2 (15.4) (2.7, 46.3) | 0 (0.0) (0.0, 69.0) | 0 (0.0) (0.0, 60.4) |
| ISRs | 0 (0.0) (0.0, 48.3) | 0 (0.0) (0.0, 43.9) | 0 (0.0) (0.0, 28.3) | 0 (0.0) (0.0, 69.0) | 1 (25.0) (1.3, 78.1) |

"Any SEC" for both the treatment groups (LD and HD) includes all patients treated with SEC from the start of the study and those who switched from PBO to SEC at Week 12

[a]AEs ordered according to pediatric population

AE, adverse event; CI, confidence interval; ETN, etanercept; HD, high dose; ISR, injection-site reaction; LD, low dose; N, total number of

patients; n, number of patients; NMQ, Novartis customized MedDRA Query; PBO, placebo; PT, preferred term; SAE, serious AE; SEC, secukinumab; SMQ, Standardized MedDRA Query; SOC, system organ class

**(ii) Bodyweight group: ≥25 to <50 kg**

| **Bodyweight group: ≥25 kg and <50 kg** | | | | | |
|---|---|---|---|---|---|
| **n (%) 95% CI** | **SEC LD N=30** | **SEC HD N=27** | **Any SEC N=57** | **PBO N=17** | **ETN N=16** |
| **Total AEs** | 14 (46.7) (28.8, 65.4) | 14 (51.9) (32.4, 70.8) | 28 (49.1) (35.8, 62.6) | 5 (29.4) (11.4, 56.0) | 10 (62.5) (35.9, 83.7) |
| **SAEs** | 0 (0.0) (0.0, 14.1) | 1 (3.7) (0.2, 20.9) | 1 (1.8) (0.1, 10.6) | 0 (0.0) (0.0, 22.9) | 2 (12.5) (2.2, 39.6) |
| **Treatment discontinuation due to AEs** | 0 (0.0) (0.0, 14.1) | 2 (7.4) (1.3, 25.8) | 2 (3.5) (0.6, 13.2) | 0 (0.0) (0.0, 22.9) | 0 (0.0) (0.0, 24.1) |
| **Top five most frequent AEs (by SOC)[a]** | | | | | |
| Infections and infestations | 7 (23.3) (10.6, 42.7) | 8 (29.6) (14.5, 50.3) | 15 (26.3) (15.9, 39.9) | 3 (17.6) (4.7, 44.2) | 6 (37.5) (16.3, 64.1) |
| Gastrointestinal disorders | 5 (16.7) (6.3, 35.5) | 5 (18.5) (7.0, 38.7) | 10 (17.5) (9.2, 30.4) | 2 (11.8) (2.1, 37.7) | 4 (25.0) (8.3, 52.6) |
| General disorders and administration-site conditions | 5 (16.7) (6.3, 35.5) | 1 (3.7) (0.2, 20.9) | 6 (10.5) (4.4, 22.2) | 1 (5.9) (0.3, 30.8) | 2 (12.5) (2.2, 39.6) |
| Skin and subcutaneous tissue disorders | 4 (13.3) (4.4, 31.6) | 1 (3.7) (0.2, 20.9) | 5 (8.8) (3.3, 20.0) | 1 (5.9) (0.3, 30.8) | 0 (0.0) (0.0, 24.1) |
| Injury, poisoning, and procedural complications | 3 (10.0) (2.6, 27.7) | 1 (3.7) (0.2, 20.9) | 4 (7.0) (2.3, 17.8) | 1 (5.9) (0.3, 30.8) | 0 (0.0) (0.0, 24.1) |
| **Top five most frequent AEs (by PT)[a]** | | | | | |
| Abdominal pain | 2 (6.7) (1.2, 23.5) | 2 (7.4) (1.3, 25.8) | 4 (7.0) (2.3, 17.8) | 0 (0.0) (0.0, 22.9) | 2 (12.5) (2.2, 39.6) |
| Nasopharyngitis | 3 (10.0) (2.6, 27.7) | 1 (3.7) (0.2, 20.9) | 4 (7.0) (2.3, 17.8) | 1 (5.9) (0.3, 30.8) | 1 (6.3) (0.3, 32.3) |
| Arthropod bite | 1 (3.3) (0.2, 19.1) | 1 (3.7) (0.2, 20.9) | 2 (3.5) (0.6, 13.2) | 0 (0.0) (0.0, 22.9) | 0 (0.0) (0.0, 24.1) |
| Asthenia | 1 (3.3) (0.2, 19.1) | 1 (3.7) (0.2, 20.9) | 2 (3.5) (0.6, 13.2) | 0 (0.0) (0.0, 22.9) | 0 (0.0) (0.0, 24.1) |
| Conjunctivitis | 1 (3.3) (0.2, 19.1) | 1 (3.7) (0.2, 20.9) | 2 (3.5) (0.6, 13.2) | 0 (0.0) (0.0, 22.9) | 0 (0.0) (0.0, 24.1) |
| **AEs of special interest** | | | | | |
| Infections and infestations (SOC) | 7 (23.3) (10.6, 42.7) | 8 (29.6) (14.5, 50.3) | 15 (26.3) (15.9, 39.9) | 3 (17.6) (4.7, 44.2) | 6 (37.5) (16.3, 64.1) |
| Hypersensitivity (SMQ) (narrow) | 1 (3.3) (0.2, 19.1) | 1 (3.7) (0.2, 20.9) | 2 (3.5) (0.6, 13.2) | 1 (5.9) (0.3, 30.8) | 2 (12.5) (2.2, 39.6) |
| ISRs | 2 (6.7) (1.2, 23.5) | 0 (0.0) (0.0, 15.5) | 2 (3.5) (0.6, 13.2) | 1 (5.9) (0.3, 30.8) | 1 (6.3) (0.3, 32.3) |

"Any SEC" for both treatment groups (LD and HD) includes all patients treated with SEC from the start of the study and those who switched from PBO to SEC at Week 12

[a]AEs ordered according to pediatric population

AE, adverse event; CI, confidence interval; ETN, etanercept; HD, high dose; ISR, injection-site reaction; LD, low dose; N, total number of patients; n, number of patients; NMQ, Novartis customized MedDRA Query; PBO, placebo; PT, preferred term; SAE, serious AE; SEC, secukinumab; SMQ, standardized MedDRA Query; SOC, system organ class

**(iii) Bodyweight group: ≥50 kg**

| **Bodyweight group: ≥50 kg** | | | | | |
|---|---|---|---|---|---|
| **n (%) 95% CI** | **SEC LD N=46** | **SEC HD N=48** | **Any SEC N=94** | **PBO N=21** | **ETN N=21** |
| **Total AEs** | 26 (56.5) (41.2, 70.8) | 26 (54.2) (39.3, 68.4) | 52 (55.3) (44.7, 65.5) | 15 (71.4) (47.7, 87.8) | 13 (61.9) (38.7, 81.0) |
| **SAEs** | 1 (2.2) (0.1, 13.0) | 0 (0.0) (0.0, 9.2) | 1 (1.1) (0.1, 6.6) | 0 (0.0) (0.0, 19.2) | 2 (9.5) (1.7, 31.8) |
| **Treatment discontinuation due to AEs** | 0 (0.0) (0.0, 9.6) | 0 (0.0) (0.0, 9.2) | 0 (0.0) (0.0, 4.9) | 1 (4.8) (0.2, 25.9) | 1 (4.8) (0.2, 25.9) |
| **Top five most frequent AEs (by SOC)[a]** | | | | | |
| Infections and infestations | 18 (39.1) (25.5, 54.6) | 18 (37.5) (24.3, 52.7) | 36 (38.3) (28.6, 48.9) | 12 (57.1) (34.4, 77.4) | 5 (23.8) (9.1, 47.5) |
| Skin and subcutaneous tissue disorders | 4 (8.7) (2.8, 21.7) | 6 (12.5) (5.2, 25.9) | 10 (10.6) (5.5, 19.1) | 2 (9.5) (1.7, 31.8) | 1 (4.8) (0.2, 25.9) |
| Gastrointestinal disorders | 2 (4.3) (0.8, 16.0) | 6 (12.5) (5.2, 25.9) | 8 (8.5) (4.0, 16.6) | 5 (23.8) (9.1, 47.5) | 6 (28.6) (12.2, 52.3) |
| General disorders and administration-site conditions | 1 (2.2) (0.1, 13.0) | 6 (12.5) (5.2, 25.9) | 7 (7.4) (3.3, 15.2) | 2 (9.5) (1.7, 31.8) | 2 (9.5) (1.7, 31.8) |
| Respiratory, thoracic, and mediastinal disorders | 3 (6.5) (1.7, 18.9) | 3 (6.3) (1.6, 18.2) | 6 (6.4) (2.6, 13.9) | 1 (4.8) (0.2, 25.9) | 0 (0.0) (0.0, 19.2) |
| **Top five most frequent AEs (by PT)[a]** | | | | | |
| Nasopharyngitis | 9 (19.6) (9.9, 34.4) | 8 (16.7) (8.0, 30.8) | 17 (18.1) (11.2, 27.7) | 0 (0.0) (0.0, 19.2) | 3 (14.3) (3.8, 37.4) |
| Pharyngitis | 3 (6.5) (1.7, 18.9) | 2 (4.2) (0.7, 15.4) | 5 (5.3) (2.0, 12.5) | 3 (14.3) (3.8, 37.4) | 0 (0.0) (0.0, 19.2) |
| Dysmenorrhea | 2 (4.3) (0.8, 16.0) | 2 (4.2) (0.7, 15.4) | 4 (4.3) (1.4, 11.2) | 0 (0.0) (0.0, 19.2) | 0 (0.0) (0.0, 19.2) |
| Headache | 2 (4.3) (0.8, 16.0) | 2 (4.2) (0.7, 15.4) | 4 (4.3) (1.4, 11.2) | 2 (9.5) (1.7, 31.8) | 0 (0.0) (0.0, 19.2) |
| Neutropenia | 2 (4.3) (0.8, 16.0) | 1 (2.1) (0.1, 12.5) | 3 (3.2) (0.8, 9.7) | 0 (0.0) (0.0, 19.2) | 0 (0.0) (0.0, 19.2) |
| **AEs of special interest** | | | | | |
| Infections and infestations (SOC) | 18 (39.1) (25.5, 54.6) | 18 (37.5) (24.3, 52.7) | 36 (38.3) (28.6, 48.9) | 12 (57.1) (34.4, 77.4) | 5 (23.8) (9.1, 47.5) |
| Hypersensitivity (SMQ) (narrow) | 2 (4.3) (0.8, 16.0) | 1 (2.1) (0.1, 12.5) | 3 (3.2) (0.8, 9.7) | 0 (0.0) (0.0, 19.2) | 0 (0.0) (0.0, 19.2) |
| Neutropenia (NMQ) (narrow) | 2 (4.3) (0.8, 16.0) | 1 (2.1) (0.1, 12.5) | 3 (3.2) (0.8, 9.7) | 0 (0.0) (0.0, 19.2) | 0 (0.0) (0.0, 19.2) |
| ISRs | 1 (2.2) (0.1, 13.0) | 1 (2.1) (0.1, 12.5) | 2 (2.1) (0.4, 8.2) | 1 (4.8) (0.2, 25.9) | 1 (4.8) (0.2, 25.9) |

"Any SEC" for both the treatment groups (LD and HD) includes all patients treated with SEC from the start of the study and those who switched from placebo to SEC at Week 12

[a]AEs ordered according to pediatric population

AE, adverse event; ETN, etanercept; HD, high dose; ISR, injection-site reaction; LD, low dose; N, total number of patients; n, number of patients; NMQ, Novartis customized MedDRA Query; PBO, placebo; PT, preferred term; SAE, serious AE; SEC, secukinumab; SMQ, standardized MedDRA Query; SOC, system organ class

**Table S9: Absolute neutrophils: number (%) of patients with newly occurring or worsening CTCAE grades after baseline by treatment and bodyweight (pediatric pool) – Up to Week 52 (Safety set)**

| | Any SEC dose | | | | | |
|---|---|---|---|---|---|---|
| | <25 kg, N=8 | | ≥25 to <50 kg, N=71 | | ≥50 kg, N=111 | |
| **Criterion** | **n/m** | **% (95% CI)** | **n/m** | **% (95% CI)** | **n/m** | **% (95% CI)** |
| Grade 1 (<LLN–1.5×$10^9$/L) | 0/15 | 0.0 (0.0, 25.3) | 3/66 | 4.5 (1.2, 13.6) | 13/107 | 12.1 (6.9, 20.2) |
| Grade 2 (<1.5–1.0×$10^9$/L) | 4/15 | 26.7 (8.9, 55.2) | 9/67 | 13.4 (6.7, 24.5) | 9/110 | 8.2 (4.0, 15.4) |
| Grade 3 (<1.0–0.5×$10^9$/L) | 0/15 | 0.0 (0.0, 25.3) | 1/68 | 1.5 (0.1, 9.0) | 0/110 | 0.0 (0.0, 4.2) |
| Grade 4 (<0.5×$10^9$/L) | 0/15 | 0.0 (0.0, 25.3) | 0/69 | 0.0 (0.0, 6.6) | 0/110 | 0.0 (0.0, 4.2) |

A patient with multiple variable measurements is counted only once under the worst condition.
CTCAE, Common Terminology Criteria for Adverse Events; LLN, lower limit of normal; m, Number of patients with evaluable criterion who were better than the criterion at baseline; n, number of patients with most extreme value meeting the criterion post-baseline and that is newly occurring, or worsening compared to baseline; SEC, secukinumab.