Risankizumab vs. Secukinumab in Psoriasis

Psoriatic inflammatory cascade

Phase 3 trials

Key messages

Risankizumab head-to-head trials

References and labels

Speed of onset

Sustainability

Quality of life

Safety

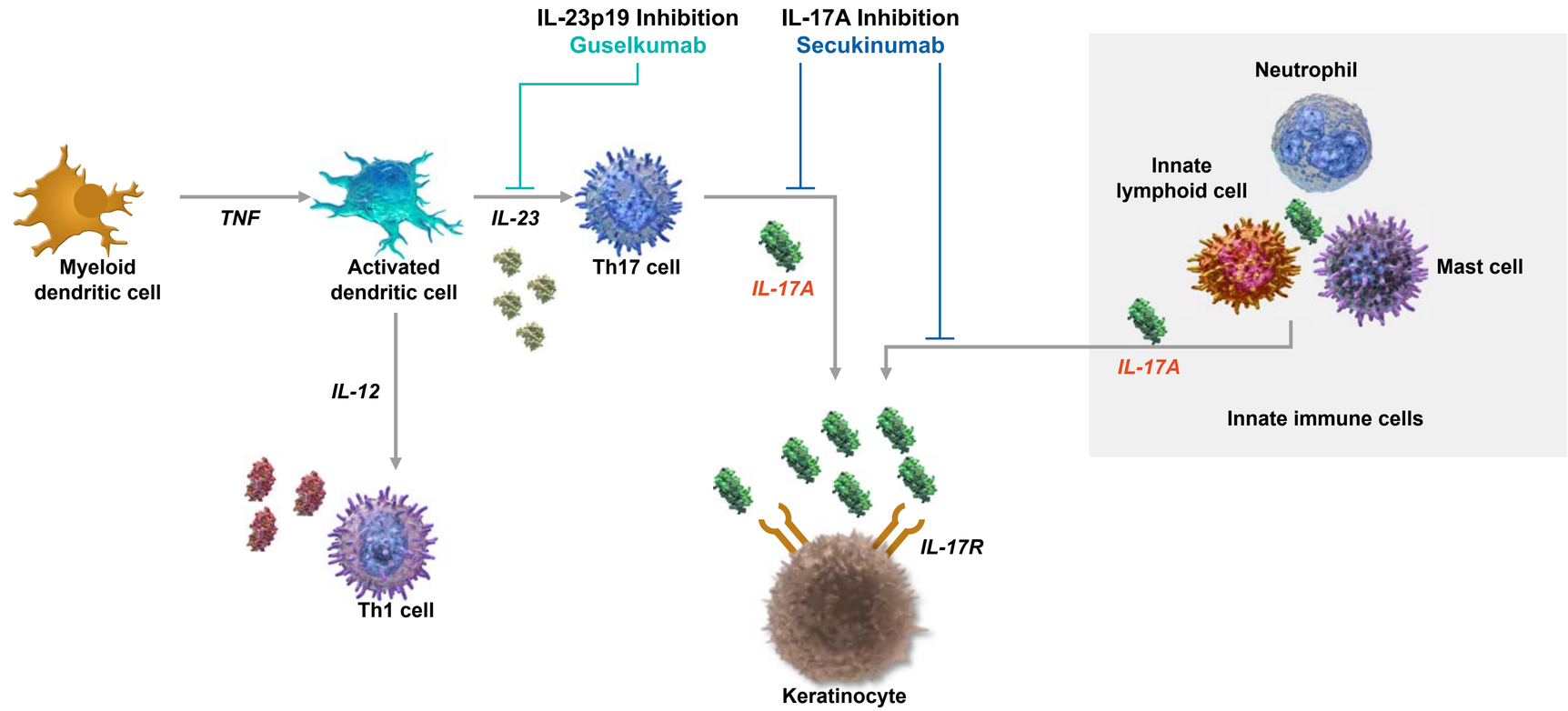
Hard-to-treat

Real-world evidence

Risankizumab Targets IL-23, an Upstream Cytokine in the Psoriatic Inflammatory Cascade

- IL-23 and IL-17A are key cytokines in psoriasis pathogenesis[1]
- IL-23, released by TNFα-activated dendritic cells, stimulates Th17 cells to produce IL-17A[2]
- But IL-17A is also produced **independently of IL-23**, by innate immune cells[2–6]
- IL-17A stimulates keratinocyte activation and release of proinflammatory mediators, thus is the main driver of psoriatic lesion formation[2,3,7,8]

Cytokines driving psoriatic inflammation[8–10]



Risankizumab

Targets the p90 subunit of IL-23, reducing IL-17A produced by Th17 cells, but not from sources produced independently of the IL-23 pathway, such as certain innate cells[11,12]

Secukinumab

Targets IL-17A directly, irrespective of its cellular source[13]

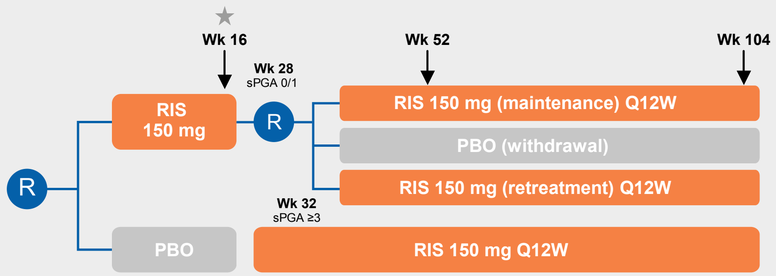
IL, interleukin; IL-17R, interleukin-17 receptor; Th, T helper cell; TNF, tumor necrosis factor

Phase 3 Clinical Trial Programs

Comparison with Placebo

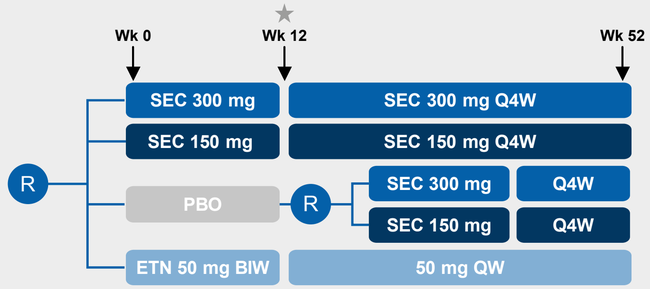
Risankizumab

IMMhance (N=507)[14,15]



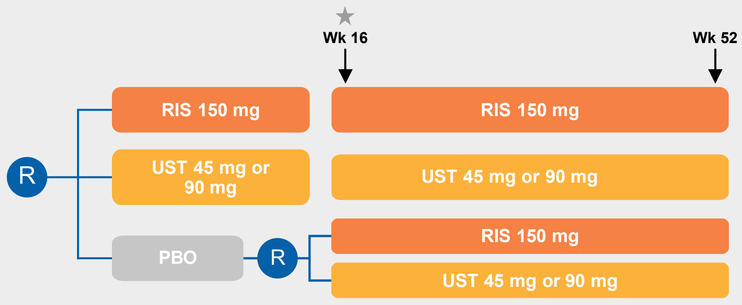
Secukinumab

FIXTURE (N=1306)[18]

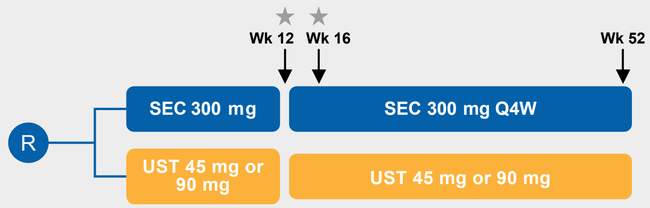


Comparison with Ustekinumab

ultIMMa-1 (N=506) and -2 (N=491)[12]

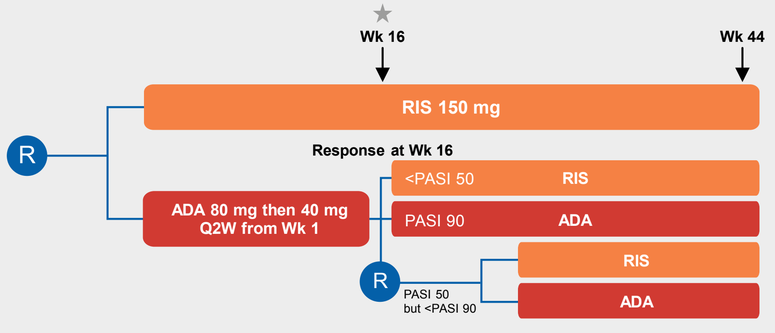


CLEAR (N=676) and CLARITY (1102)[19–21]

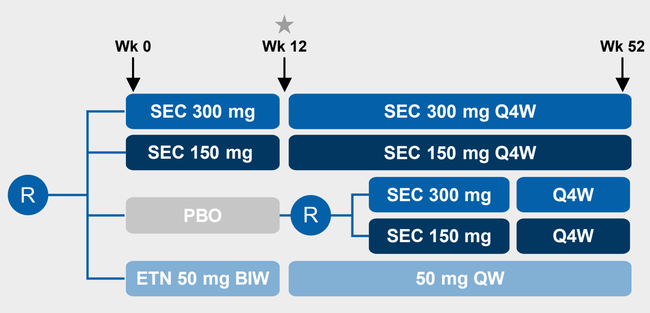


Comparison with TNF Inhibitor

IMMvent (N=605)[16,17]



FIXTURE (N=1306)[18]



★ Primary endpoint R Randomization

[a]Ustekinumab dosing: 45 mg for subjects ≤100 kg at baseline; 90 mg for subjects >100 kg at baseline

ADA, adalimumab; BIW, twice a week; ETN, etanercept; PASI, Psoriasis Area and Severity Index; PBO, placebo; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; Q12W, every 12 weeks; RIS, risankizumab; SEC, secukinumab; TNF, tumor necrosis factor; UST, ustekinumab

Phase 3 Trial Objectives and Endpoints

Risankizumab

IMMhance[14,15]

Co-primary endpoints:
PASI 90 and sPGA 0/1 at Week 16 (RIS vs. PBO)

Secondary endpoints:
PASI 100, PASI 75, sPGA 0 and DLQI 0/1 at Week 16;
PASI 75, PASI 90, PASI 100, sPGA 0/1 at Week 52

Withdrawal and retreatment:
maintenance of response and retreatment response[6]

Prior biologic exposure: 51–56%

Baseline PASI: 19.9–21.2

ultIMMa-1 and ultIMMa-2[12]

Co-primary endpoints:
PASI 90 and sPGA 0/1 at Week 16 (RIS vs. PBO, RIS vs. UST)

Secondary endpoints:
PASI 75 and sPGA 0/1 at Week 12; DLQI 0/1, PASI 100, PSS 0 and PSS change from baseline at Week 16; PASI 90, PASI 100 at Week 52

Additional secondary endpoints for ultIMMA-2:
PASI 75 at Week 16; sPGA 0/1 and PASI 75 at Week 52

Prior biologic exposure: 30–43%

Baseline PASI: 18.2–20.6

IMMvent[16,17]

Co-primary endpoints:
PASI 90 and sPGA 0/1 at Week 16 (RIS vs. ADA)

Secondary endpoints:
PASI 75 and PASI 100 at Week 16; PASI 90, sPGA 0 and sPGA 0/1 at Week 44

Prior biologic exposure: NR

Baseline PASI: NR

Secukinumab

FIXTURE[18]

Co-primary endpoints:
PASI 75 and IGA mod 2011 0/1 at Week 12 (SEC vs. PBO)

Secondary endpoints:
Superiority vs. placebo (PASI 90 at Wk 12); non-inferiority vs. ETN (PASI 75 at Wk 12); superiority vs. ETN (PASI 75 or IGA 0/1 at Wk 12); superiority vs. ETN (proportion of subjects maintaining PASI 75 or IGA 0/1 from Wk 12 to 52)

Prior biologic exposure: 11–14%

Baseline PASI: 23.2–24.1

CLEAR[19,20]

Co-primary endpoints:
Superiority of SEC vs. UST for PASI 90 at Week 16

Secondary endpoints:
Superiority of SEC vs. UST for PASI 75 at Week 4 and PASI 90 at Week 52

Prior biologic exposure: 13–14%

Baseline PASI: 21.5–21.7

CLARITY[21]

Co-primary endpoints:
Superiority of SEC vs. UST for PASI 90 and IGA 0/1 (clear/almost clear skin) at Week 12

Secondary endpoints:
Superiority of SEC vs. UST for PASI 75 at Week 12, PASI 75 at Week 4, PASI 90 at Week 16, PASI 100 at Week 16, IGA 0/1 at Week 16, PASI 100 at Week 12 and PASI 75 at Week 16

Prior biologic exposure: 20–24%

Baseline PASI: 20.8–21.3

Baseline patient characteristics

Trial baseline characteristics

ADA, adalimumab; DLQI, Dermatology Life Quality Index; ETN, etanercept; IGA, Investigator's Global Assessment; NR, not reported; PASI, Psoriasis Area and Severity Index; PBO, placebo; PSS, psoriasis symptom scale; RIS, risankizumab; SEC, secukinumab; sPGA; static Physicians Global Assessment; UST, ustekinumab

Summary of Baseline Characteristics

Risankizumab[12–15]

- Mean age: **46.2–49.6 years**
- Body weight: **87.8–92.2 kg**
- Biologic-experienced: **30–56%**
- Baseline PASI: **18.2–21.2**
- Baseline DLQI: **11.7–13.6**

Secukinumab[18,19,21]

- Mean age: **43.8–45.4 years**
- Body weight: **82–93 kg**
- Biologic-experienced: **11–24%**
- Baseline PASI: **20.8–24.1**
- Baseline DLQI: **NR**

Additional data

DLQI, Dermatology Life Quality Index; NR, not reported; PASI, Psoriasis Area and Severity Index

Skin Clearance at Week 16

Risankizumab[12,14–16]

PASI 75 — 89%

PASI 90 — 72–75%

PASI 100 — 36–51%

Secukinumab[13,20,22]

PASI 75 — 86–94%

PASI 90 — 70–79%

PASI 100 — 37–44%

TNF PBO UST

PASI, Psoriasis Area and Severity Index

Speed of Onset

Risankizumab

At Week 4

PASI **90** achieved[12,15,24]

6–7%

At Week 12

PASI **90** achieved[12,15,24]

62–68%

Secukinumab

At Week 4

PASI **90** achieved[18,20]

12–21%

At Week 12

PASI **90** achieved[18,20]

54–73%

TNF PBO UST

PASI, Psoriasis Area and Severity Index

Eliminating Disease Impact on QoL

Risankizumab

At Week 16

DLQI 0/1 achieved[12,15,24]

65–67%

At Week 52

DLQI 0/1 achieved[12,15,24]

71–75%

Secukinumab

At Week 16

DLQI 0/1 achieved[18,19]

72%

At Week 52

DLQI 0/1 achieved[18,19]

72%

PBO

UST

DLQI, Dermatology Life Quality Index; QoL, quality of life

Sustained Long-term Efficacy

Risankizumab

At Week 52

PASI **90** achieved[12]

81–82%

PASI **100** achieved[12]

56–60%

Secukinumab

At Week 52

PASI **90** achieved[13,23]

60–75%

PASI **100** achieved[13,23]

36–45%

At 5 years

PASI **90** achieved[13,23]

66%

PASI **100** achieved[13,23]

41%

Additional data

PASI, Psoriasis Area and Severity Index

Safety

Risankizumab

- 1 year safety data available[12]
- Comparable rate of AEs and SAEs across active treatment and comparator and/or placebo groups[12,14–16]
- Incidence of serious infections (0.3–3%), malignancies (0.3–1%), and MACE (0–1%) were low and similar across treatment groups[12,14–16]
- Injection-site reaction data not reported, no serious hypersensitivity events observed through 1 year[12]
- In the phase 2 study, 17 out of 124 patients developed anti-drug antibodies, with neutralizing antibodies observed in 3 patients[24]

Secukinumab

- 5 year safety data available[23]
- Favorable safety profile, used in >150,000 patients (across all approved indications)[25]
- Incidence of serious infections (0.6–1.2%), malignancies (0.3–0.6%), and MACE (0.3–0.4) were low and similar across treatment groups[18]
- <1% injection-site reactions[18]
- <1% immunogenicity, <1% neutralizing antibodies (no loss of efficacy)[26]

AE, adverse event; MACE, major adverse cardiovascular event; SAE, serious adverse event

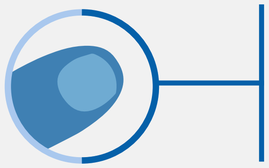
Hard-to-treat Manifestations

Risankizumab

No phase **3** data yet available regarding difficult to treat areas

Secukinumab

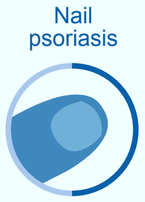
Dedicated phase **3** studies



Over **70%** improvement in NAPSI score over 2.5 years[27]

59% with PSSI 90 at Week 24[28]

59.2% improvement in ppIGA score over 2.5 years[29]



For NAPSI in TRANSFIGURE: All 10 fingernails were assessed; total score ranges from 0 to 80

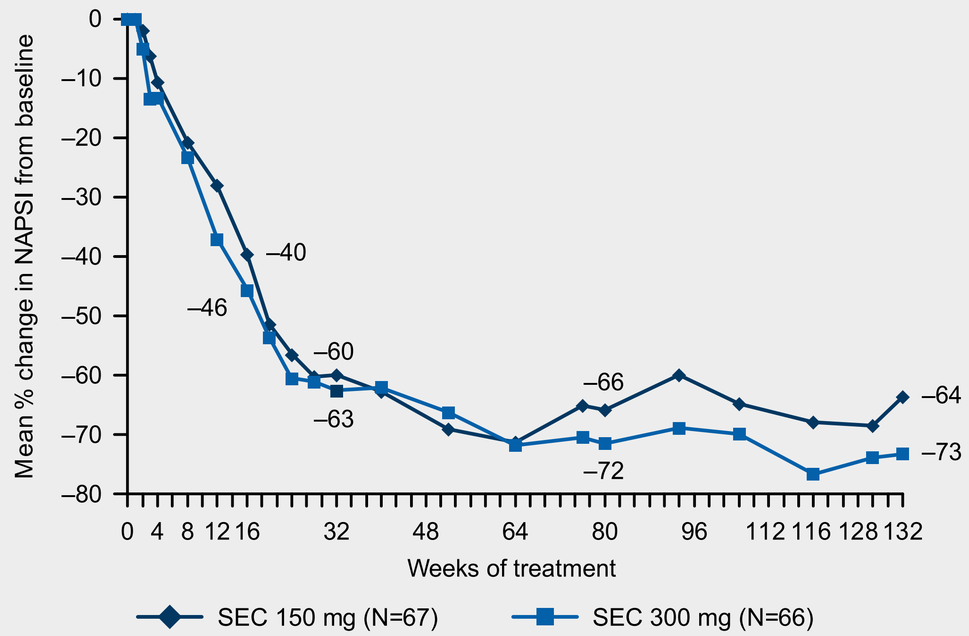
NAPSI, Nail Psoriasis Severity Index; PSSI; Psoriasis Scalp Severity Index; ppIGA, palmoplantar Investigator's Global Assessment

Secukinumab is Effective in Nail Psoriasis Through 2.5 Years Risankizumab Efficacy in Nail Psoriasis is Unknown

Risankizumab

No data currently available

Secukinumab[27]



NAPSI, Nail Psoriasis Severity Index; SEC, secukinumab

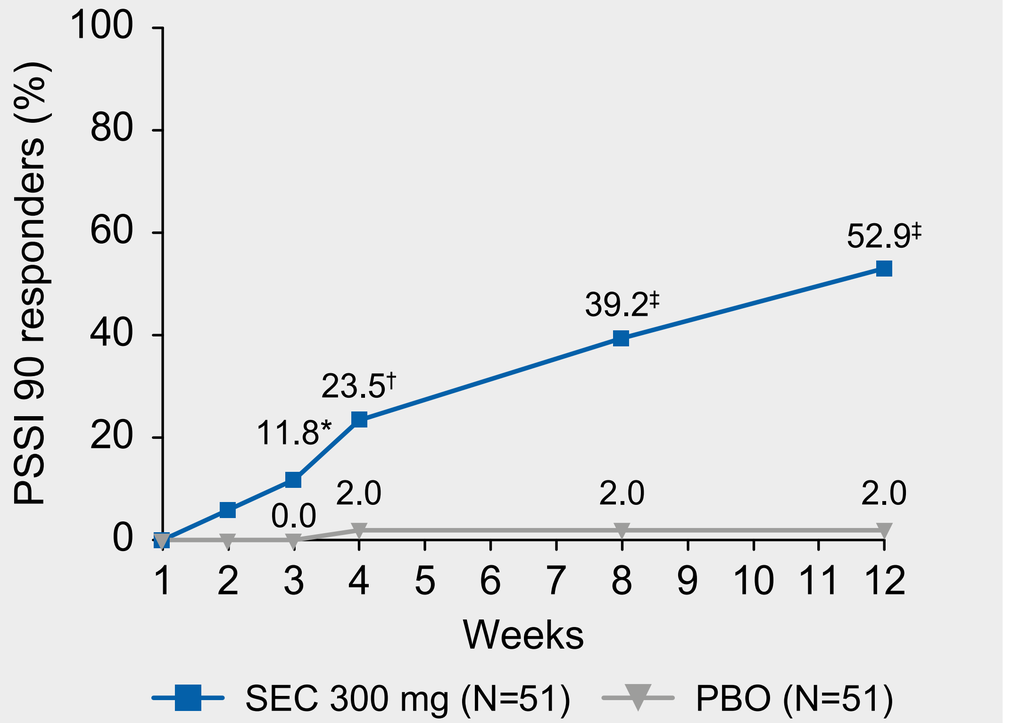
Secukinumab is Rapid and Effective in Scalp Psoriasis

Risankizumab Efficacy in Scalp Psoriasis is Unknown

Risankizumab

No data currently available

Secukinumab[28]



* $P < 0.05$, ‡ $P < 0.01$, † $P < 0.001$ SEC vs. PBO

PBO, placebo; PSSI, Psoriasis Scalp Severity Index; SEC, secukinumab

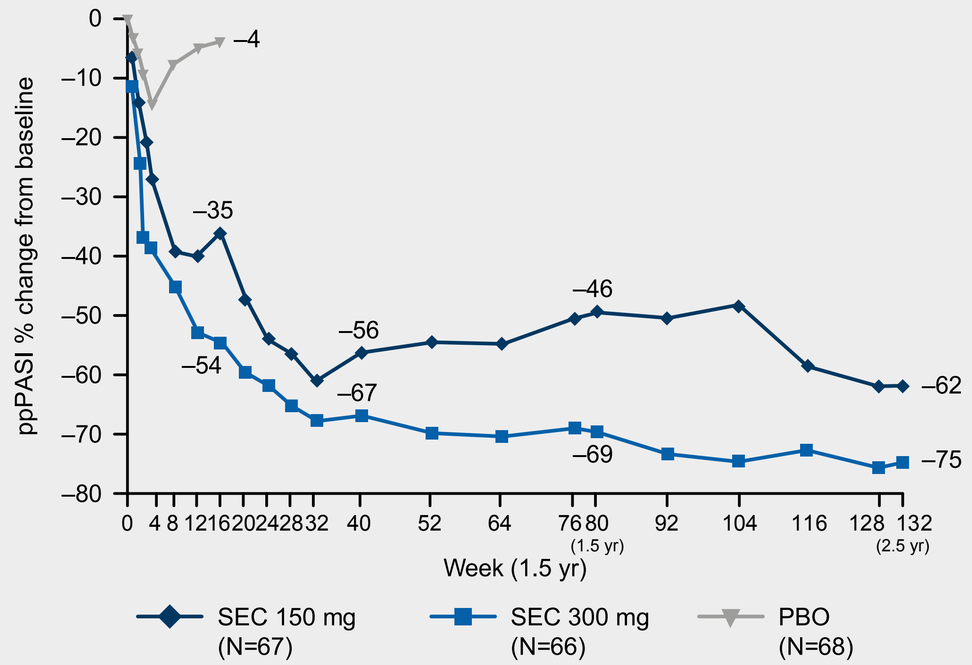
Secukinumab is Effective in Palmoplantar Psoriasis Through 2.5 Years

Risankizumab Efficacy in Palmoplantar Psoriasis is Unknown

Risankizumab

No data currently available

Secukinumab[29]



PBO, placebo; ppPASI, Palmoplantar Pustulosis Psoriasis Area and Severity Index; SEC, secukinumab

Real-World Evidence

Risankizumab

No data currently available

Secukinumab

IGA 0/1:[37]

At **6** months	At **12** months
50%	63%

PASI 90:[38,39]

At **6** months	Up to **12** months	At **18** months
49–61%	39–70%	32–89%

DLQI 0/1 or DLQI Score Reduction ≥5:[37,38]

At **6** months	Up to **12** months
55%	61–97%

Canadian PSP: a patient support program (PSP) available in Canada since February 2015 that supports all patients selected by their physicians for treatment with secukinumab for plaque psoriasis

CORRONA registry: a US independent, prospective observational cohort. Patients initiated secukinumab at enrolment and had a 6-month (window: 5 to 9 months) and/or 12-month (window: 11 to 15 months) follow-up visit as of December 31, 2017

PURE registry: a Canadian and Latin American observational study. These data are a snapshot analysis Dec 23rd 2015 to Nov 27, 2017

IGA, Investigator's Global Assessment; PASI, Psoriasis Area and Severity Index

IGA PASI DLQI

Psoriatic Arthritis

Risankizumab

PsA **phase 2** trial at Week 16[30]

ACR 20

57–65%

ACR 50

24–39%

ACR 70

7–26%

Secukinumab

PsA **phase 3** trials at Week 16[a,31,32]

ACR 20

57–60%

ACR 50

35–37%

ACR 70

15–17%

Additional data

[a]ACR 20 response at Week 24 was the primary endpoint. SEC 300 mg: 54% (P<0.0001), SEC 150 mg: 51% (P<0·0001), vs. PBO: 15%

ACR, American College of Rheumatology Criteria; PsA, psoriatic arthritis; PBO, placebo; SEC, secukinumab

Risankizumab Head-to-head Trials

Phase 3 PsO trials

Risankizumab vs. secukinumab[34]

Estimated primary completion date:

NOV 2019

Risankizumab vs. methotrexate[35]

Not yet recruiting

Risankizumab vs. Fumaderm®[36]

Estimated primary completion date:

JUN 2018

PsO, psoriasis

Key Messages

Risankizumab[12,14–16]

Effectively clears skin and improves quality of life in moderate-to-severe plaque psoriasis

No data available for longer than one year

No Phase 3 data regarding efficacy in hard-to-treat manifestations

Secukinumab[23,27–29,32]

5 year efficacy in clearing skin, safety and quality of life data

Proven efficacy in nail, scalp and palmoplantar psoriasis and psoriatic arthritis

Secukinumab targets the full spectrum of psoriatic manifestations, providing comprehensive treatment

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