FRONTIER-2: A phase 2b, long-term extension, dose-ranging study of oral JNJ-77242113 for the treatment of moderate-to-severe plaque psoriasis

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Background: More patients with moderate-to-severe plaque psoriasis achieved responses with JNJ-77242113, a targeted oral peptide inhibiting interleukin-23 receptor signaling, versus placebo (PBO) at week (W)16 of the phase 2 FRONTIER-1 study.

Objective: FRONTIER-2, a long-term extension of FRONTIER-1, evaluated JNJ-77242113 through 1 year.

Methods: FRONTIER-1 participants received JNJ-77242113 at doses from 25 mg daily to 100 mg twice daily or PBO through W16. Patients completing FRONTIER-1 could enroll in FRONTIER-2 and continue JNJ-77242113 at the same dose through W52. Those on PBO crossed over to JNJ-77242113 100 mg daily for W16−52. Safety follow-up continued through W56.

Results: Most (89%) FRONTIER-1 patients continued to FRONTIER-2. Across outcomes, response rates were maintained from W16−52. The highest response rates generally occurred with JNJ-77242113 100 mg twice daily. At W52, 76% of patients achieved up to 75% improvement in Psoriasis Area and Severity Index (PASI75) with 100 mg twice daily; rates of clear or almost clear skin were 64% (PASI90), 74% (Investigator's Global Assessment 0/1), 40% (PASI100), and 43% (Investigator's Global Assessment 0). From W16−56, 59% of JNJ-77242113−treated patients had ≥1 adverse events. Serious adverse events, considered unrelated to treatment by investigators, occurred in 4% of patients.

Limitations: The study was limited by the small number of patients in each treatment group and the descriptive nature of the longer-term data.

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Conclusion: Rates of skin clearance with JNJ-77242113 were durable to 1 year and no safety signals were identified. (J Am Acad Dermatol 2025;92:495-502.)

Key words: IL-23; JNJ-77242113; long-term extension; oral; phase 2; plaque psoriasis.

INTRODUCTION

Treatment options for plaque psoriasis (PsO) have expanded with the approval of monoclonal antibodies that target inflammatory cytokines or their receptors.[1] A number of these treatments, including ustekinumab, guselkumab, tildrakizumab, and risankizumab,[1] target interleukin (IL)-23, which plays a critical role in pathogenic T-cell activation.[2] While these biologics have demonstrated efficacy and acceptable long-term safety profiles,[3-6] they are administered via subcutaneous injection,[1,7] which may not be the preferred mode of administration for all patients.[8,9] The oral therapies apremilast (targeting phosphodiesterase 4) and deucravacitinib (targeting tyrosine kinase 2) are approved to treat PsO, but they have demonstrated only moderate efficacy and long-term safety data for tyrosine kinase 2-targeted therapies, like deucravacitinib, are limited.[10-12] Thus, there is a need for safe and effective oral PsO therapies.

JNJ-77242113 is a targeted oral peptide that binds the IL-23 receptor to block IL-23 signaling. Studies in preclinical models and in healthy human participants have demonstrated that orally administered JNJ-77242113 results in selective, systemic inhibition of the IL-23 pathway.[13] In a phase 2b study evaluating the efficacy and safety of JNJ-77242113 in patients with moderate-to-severe PsO (FRONTIER-1; NCT05223868), JNJ-77242113 showed a significant dose-response effect at week 16.[14] Higher response rates were observed among patients receiving higher doses of JNJ-77242113, with 79% of those in the highest dose group (100 mg twice daily) achieving ≥75% improvement in Psoriasis Area and Severity Index (PASI 75) and 64% reaching an Investigator's Global Assessment (IGA) score of 0/1 at week 16. The safety profiles for JNJ-77242113 and placebo (PBO) were similar through week 16.

To further assess the efficacy and safety of orally administered JNJ-77242113, a long-term extension (LTE) of FRONTIER-1 (FRONTIER-2; NCT05364554) evaluated JNJ-77242113–treated patients with moderate-to-severe plaque PsO through 1 year of treatment.

CAPSULE SUMMARY

- Inhibition of the interleukin-23 pathway with monoclonal antibodies has demonstrated efficacy and safety in treating moderate-to-severe plaque psoriasis
- Results from the FRONTIER-2 study indicate that JNJ-77242113, a targeted oral peptide blocking the interleukin-23 receptor, provides durable skin clearance and a stable safety profile with 52 weeks of oral administration

METHODS

Patients

Eligibility criteria for FRONTIER-1 have been detailed elsewhere.[14] Briefly, patients were adults (≥18 years of age) diagnosed with moderate-to-severe plaque PsO (PASI ≥12, IGA score ≥3, and a body surface area involvement ≥10%) for ≥6 months prior to first study treatment and were candidates for phototherapy or systemic PsO therapy. Those who had previously received a biologic targeting IL-23 were excluded. Patients who completed FRONTIER-1 could elect to participate in the LTE, FRONTIER-2.

Trial design

In FRONTIER-1, a randomized, double-blind, PBO-controlled, dose-ranging, phase 2b study, patients were randomized 1:1:1:1:1:1 to oral JNJ-77242113 at 25 mg daily, 25 mg twice daily, 50 mg daily, 100 mg daily, 100 mg twice daily, or PBO from week 0–16.[14] In FRONTIER-2, patients randomized to JNJ-77242113 continued to receive the dose assigned in FRONTIER-1, in a blinded manner, through week 52. Patients randomized to PBO in FRONTIER-1 crossed over to receive JNJ-77242113 100 mg daily (PBO → 100 mg daily) from week 16-52 of FRONTIER-2. A 4-week safety follow-up period followed the last study treatment at week 52.

End points

Efficacy end points were assessed for patients randomized to JNJ-77242113 and those PBO-randomized patients who enrolled in the LTE (PBO → 100 mg daily group). For end points that measured change from baseline, week 0 of FRONTIER-1 was considered baseline. The primary end point was the proportion of patients who

Abbreviations used:

AE:	adverse event
COVID-19:	coronavirus disease 19
GI:	gastrointestinal
IGA:	Investigator's Global Assessment
IL:	interleukin
LSM:	least squares mean
LTE:	long-term extension
MedDRA:	Medical Dictionary for Regulatory Activities
MMRM:	mixed models for repeated measures
PASI:	Psoriasis Area and Severity Index
PBO:	placebo
PsO:	psoriasis
PSSD:	Psoriasis Symptoms and Signs Diary
SD:	standard deviation
ss-IGA:	scalp-specific IGA

achieved PASI 75 at week 52. Secondary end points, also at week 52, included the proportion of patients achieving PASI 90, PASI 100, IGA 0/1 (minimal involvement/almost clear skin) or IGA 0 (clear skin) on a scale of 0-4,[15] Dermatology Life Quality Index 0/1,[16] or Psoriasis Symptoms and Signs Diary (PSSD)[17] sign scores or PSSD symptom scores of 0 (among patients with baseline PSSD scores ≥1), and change from baseline in PASI, PSSD sign, or PSSD symptom scores. A reduction of ≥4 points in PSSD itch or pain scores was considered a clinically meaningful improvement.[18] Among patients with a scalp-specific IGA (ss-IGA) score ≥2 at baseline (week 0 of FRONTIER-1), the proportion of patients achieving an ss-IGA of 0/1 with a ≥2-grade improvement from baseline was an exploratory end point; ss-IGA measures redness, thickness, and scaliness of scalp lesions (0: no disease; 4: severe disease).[19] Frequency and type of adverse events (AEs) (coded using the Medical Dictionary for Regulatory Activities V25.1) and serious AEs were assessed through week 56 in patients in the LTE who received ≥1 dose of JNJ-77242113. Laboratory data were summarized by type of test (eg, hematology), and laboratory parameters were summarized by Common Terminology Criteria for AEs.

Statistical analysis

No formal hypothesis testing occurred in the LTE; data were summarized through descriptive statistics. Analyses of efficacy end points used nonresponder imputation and mixed models for repeated measures (MMRM).

For binary efficacy end points, patients who discontinued due to lack of efficacy or worsening of PsO, or who initiated a prohibited PsO treatment, were considered nonresponders after the occurrence; patients with missing data were also considered nonresponders. For continuous end points (eg, change from baseline in PASI or PSSD symptom/sign score), zero change was assigned to patients who discontinued due to lack of efficacy or worsening of PsO or who initiated a prohibited PsO treatment. Missing data were handled by MMRM under missing-at-random assumptions. Least squares mean (LSM) values were based on the MMRM model with treatment group, visit, treatment group-by-visit interaction, baseline weight category (≤90 kg, >90 kg), baseline weight category-by-visit interaction, baseline score, and baseline score-by-visit interaction as covariates.

RESULTS

Patients

Of the 255 patients who were randomized and received ≥1 dose of study treatment in FRONTIER-1 (first patient screened February 2022), 227 (89%) continued treatment in FRONTIER-2 (first patient dosed June 2023), including 35 patients in the PBO→100 mg daily group (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1). The most common reason for discontinuation of treatment in FRONTIER-2 was lack of efficacy, which was more notable in the lower versus higher dose groups (only 2 patients receiving 100 mg daily and 1 receiving 100 mg twice daily discontinued treatment due to lack of efficacy).

Demographics and baseline clinical characteristics at the start of FRONTIER-1 were previously described.[14] Across randomized treatment groups, the mean ± standard deviation (SD) age was 44 ± 13 years; 69% of patients were men and 75% were White. Patients had a mean duration of PsO of 18 ± 13 years. At baseline, the mean PASI score was 19.0 ± 5.8, with an IGA score of 3 in 79% of patients and an IGA score of 4 in 21%. Patients reported mean PSSD symptom and sign scores of 51.8 ± 23.8 and 64.6 ± 18.2, respectively. Most patients (87%) had an ss-IGA score ≥2 at baseline. Twenty-two percent of patients had received prior treatment with biologics.

PASI 75 response at week 52 (primary end point)

PASI 75 response rates at week 16 in FRONTIER-1[14] were maintained through week 52 of FRONTIER-2 (Fig 1, *A*) and greater PASI 75 response rates generally continued to be seen with higher JNJ-77242113 doses. At week 52, the respective proportions of patients achieving PASI 75 were 49%, 58%, 70%, 65%, and 76% with 25 mg daily, 25 mg twice daily, 50 mg daily, 100 mg daily, and 100 mg twice daily. In the PBO→100 mg daily group, PASI 75 response rates rapidly converged with those of

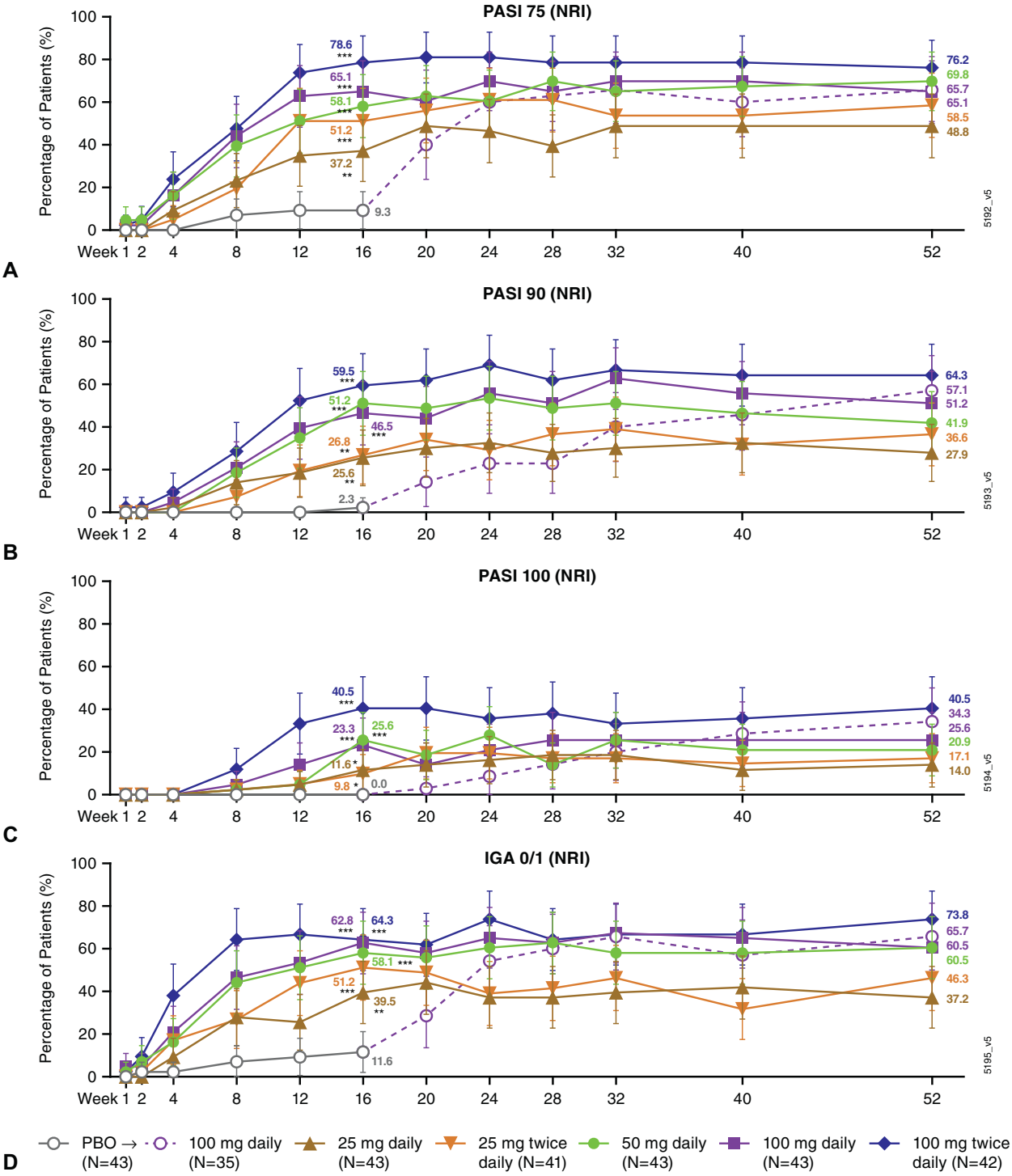

Fig 1. Proportions of patients (%) achieving PASI 75 (**A**), PASI 90 (**B**), PASI 100 (**C**), and IGA 0/1 (**D**) responses through week 52. Patients who discontinued study agent due to lack of efficacy/worsening of PsO, or who initiated a prohibited PsO treatment were considered nonresponders after the occurrence. Patient with missing data were considered nonresponders. *Nominal $P < .05$ versus PBO. **Nominal $P < .01$ versus PBO. ***Nominal $P < .001$ versus PBO. Error bars denote 95% CI. *CI*, Confidence interval; *IGA*, Investigator's Global Assessment of psoriasis; *NRI*, nonresponder imputation; *PASI*, Psoriasis Area and Severity Index; *PBO*, placebo; *PsO*, psoriasis.

the JNJ-77242113—randomized patients, reaching 66% at week 52 (Fig 1, *A*; Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1).

Secondary efficacy end points

The proportions of patients attaining PASI 90 and PASI 100 response at week 16 (eg, 60% and 40%, respectively, in the 100 mg twice daily group) were generally maintained through week 52 (eg, 64% and 40%, respectively, in the 100 mg twice daily group; Fig 1, *B* and *C*; Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1). PASI 90 and PASI 100 response rates in the PBO→100 mg daily group approached those seen in the other JNJ-77242113 100 mg treatment groups. LSM changes in PASI from baseline to week 52 were −12.9, −13.6, −14.3, −15.5, and −17.4 in the 25 mg daily, 25 mg twice daily, 50 mg daily, 100 mg daily, and 100 mg twice daily groups, respectively, and −14.0 in the PBO→100 mg daily group; corresponding values for LSM percent change in PASI from baseline to week 52 were −65.9%, −69.3%, −76.8%, −80.4%, −90.2%, and −72.9%, respectively (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1).

Similar to the pattern observed in PASI responses, proportions of patients reaching IGA 0/1 and IGA 0 at week 16 (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1) were maintained through week 52 and were greater with higher doses of JNJ-77242113 (Fig 1, *D*; Supplementary Fig 2, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1; Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1). Among patients randomized to JNJ-77242113 with baseline ss-IGA scores ≥2, ss-IGA 0/1 response rates were consistent between week 16 and week 52 (eg, both 75% with 100 mg twice daily), as were rates of ss-IGA 0 response (eg, 69% and 67% with 100 mg twice daily; Supplementary Fig 3, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1). In the PBO→100 mg daily group, ss-IGA 0/1 and ss-IGA 0 response rates increased substantially between week 16 and week 52.

Patient-reported outcomes

Improvements in patient-reported outcome measures at week 16 were also generally maintained through week 52. The LSM changes in PSSD sign score and PSSD symptom score (Supplementary Fig 4, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1), as well as proportions of patients reporting PSSD sign score of 0, PSSD symptom score of 0, or Dermatology Life Quality Index score of 0/1 (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1), were consistent between week 16 and week 52. Of note, the proportions of patients reporting clinically meaningful improvements (≥4-point reduction) in PSSD itch and pain scores at week 52 were greater with higher JNJ-77242113 doses, reaching 75% and 76%, respectively, in the 100 mg twice daily group at week 52 (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/23tcsdt2hc/1).

Safety

From week 16 through week 56, 59% of patients had ≥1 AE (Table I). No dose-dependent increase in the occurrence of AEs was observed. The most common AEs were nasopharyngitis, upper respiratory tract infection, and COVID-19 (18%, 10%, and 5%, respectively, across treatment groups). Rates of gastrointestinal (GI)-related AEs through week 16 were 12% in PBO-treated patients and 11% across JNJ-77242113—treated patients[14]; across JNJ-77242113 treatment groups, rates of GI AEs did not increase from week 16 through week 56 (6%; Table I).

Serious AEs occurred in 4% of patients from week 16 through week 56 (Table I). All serious AEs were considered unrelated to study treatment by investigators, with no evidence of a dose-related increase in serious AEs. From week 16 through week 56, serious AEs included 1 occurrence each of coronary artery disease and noncardiac chest pain (same patient in the 50 mg daily group), ventricular dysfunction (25 mg twice daily), foot deformity (50 mg daily), intervertebral disc protrusion (100 mg daily), diverticulitis (100 mg daily), ligament injury (25 mg twice daily), uterine leiomyoma (100 mg twice daily), cerebrovascular accident (PBO→100 mg daily), and tonsillar hypertrophy (25 mg twice daily). No safety signals or trends toward a dose-related effect were observed among liver enzymes or hematologic laboratory results (data not shown), and no deaths occurred during the study.

DISCUSSION

In FRONTIER-2, the high response rates and improved patient-reported outcomes seen with JNJ-77242113 in FRONTIER-1[14] were sustained through 1 year of treatment. Response rates increased rapidly among patients in the PBO→100 mg daily group and approached those seen in the highest dose group (100 mg twice daily) by week 52 or earlier. Consistent with observations from FRONTIER-1,[14]

Table I. Patients with ≥1 treatment-emergent AEs with frequency of ≥5% of preferred terms in any treatment group from week 16 through week 56

		JNJ-77242113					
	PBO→100 mg daily* (*N* = 35)	25 mg daily (*N* = 35)	25 mg twice daily (*N* = 40)	50 mg daily (*N* = 39)	100 mg daily (*N* = 40)	100 mg twice daily (*N* = 38)	Combined† (*N* = 227)
Mean weeks of follow-up	37.8	36.6	35.0	38.4	35.9	38.6	37.0
Adverse events, *n* (%)	23 (65.7)	18 (51.4)	27 (67.5)	19 (48.7)	27 (67.5)	19 (50.0)	133 (58.6)
Infections and infestations	16 (45.7)	12 (34.3)	17 (42.5)	16 (41.0)	20 (50.0)	14 (36.8)	95 (41.9)
Nasopharyngitis	9 (25.7)	3 (8.6)	6 (15.0)	7 (17.9)	11 (27.5)	5 (13.2)	41 (18.1)
Upper respiratory tract infection	4 (11.4)	6 (17.1)	3 (7.5)	3 (7.7)	2 (5.0)	4 (10.5)	22 (9.7)
COVID-19	2 (5.7)	1 (2.9)	1 (2.5)	3 (7.7)	2 (5.0)	3 (7.9)	12 (5.3)
Influenza	1 (2.9)	0	3 (7.5)	1 (2.6)	1 (2.5)	1 (2.6)	7 (3.1)
Urinary tract infection	2 (5.7)	1 (2.9)	1 (2.5)	1 (2.6)	0	2 (5.3)	7 (3.1)
Bronchitis	1 (2.9)	1 (2.9)	1 (2.5)	3 (7.7)	0	0	6 (2.6)
Sinusitis	0	0	2 (5.0)	1 (2.6)	0	0	3 (1.3)
Investigations	4 (11.4)	1 (2.9)	3 (7.5)	3 (7.7)	2 (5.0)	4 (10.5)	17 (7.5)
Alanine aminotransferase increased	2 (5.7)	1 (2.9)	0	1 (2.6)	0	2 (5.3)	6 (2.6)
Aspartate aminotransferase increased	1 (2.9)	1 (2.9)	0	1 (2.6)	0	2 (5.3)	5 (2.2)
Musculoskeletal and connective tissue disorders	2 (5.7)	0	1 (2.5)	4 (10.3)	8 (20.0)	1 (2.6)	16 (7.0)
Arthralgia	1 (2.9)	0	0	1 (2.6)	2 (5.0)	0	4 (1.8)
Gastrointestinal disorders	1 (2.9)	1 (2.9)	3 (7.5)	3 (7.7)	5 (12.5)	0	13 (5.7)
Vomiting	0	0	0	0	2 (5.0)	0	2 (0.9)
Nervous system disorders	1 (2.9)	3 (8.6)	4 (10.0)	0	4 (10.0)	1 (2.6)	13 (5.7)
Headache	0	2 (5.7)	3 (7.5)	0	3 (7.5)	0	8 (3.5)
Injury, poisoning, and procedural complications	3 (8.6)	2 (5.7)	3 (7.5)	1 (2.6)	2 (5.0)	1 (2.6)	12 (5.3)
Meniscus injury	0	1 (2.9)	2 (5.0)	0	0	0	3 (1.3)
Vascular disorders	1 (2.9)	0	2 (5.0)	1 (2.6)	1 (2.5)	1 (2.6)	6 (2.6)
Hypertension	1 (2.9)	0	2 (5.0)	1 (2.6)	1 (2.5)	1 (2.6)	6 (2.6)
Serious adverse events‡, *n* (%)	1 (2.9)	0	3 (7.5)	2 (5.1)	2 (5.0)	1 (2.6)	9 (4.0)

Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. AEs are coded using MedDRA, version 25.1.

AE, Adverse event; *COVID-19*, coronavirus disease 19; *MedDRA*, Medical Dictionary for Regulatory Activities; *PBO*, placebo.

*PBO crossover patients were included in the PBO→100 mg daily column only after crossover to JNJ-77242113 treatment.

†Includes all JNJ-77242113 treatment columns.

‡Serious AEs were defined as an AE that required hospitalization, resulted in significant disability, or was life-threatening. Serious AEs included one occurrence each of coronary artery disease, ventricular dysfunction, foot deformity, intervertebral disc protrusion, noncardiac chest pain, diverticulitis, ligament injury, uterine leiomyoma, cerebrovascular accident, tonsillar hypertrophy.

more robust effects were observed in groups treated with higher doses of JNJ-77242113 in FRONTIER-2. In the highest dose groups, the proportions of patients achieving clear or almost clear skin with oral JNJ-77242113 appear comparable to those observed with some injectable IL-23 antibodies[10,12,20] and may exceed the response rates reported with currently approved oral therapies.[21,22] Larger trials are needed to confirm the impact of JNJ-77242113 on PsO signs and symptoms.

Scalp PsO can be recalcitrant to treatment. Substantial and durable clearance of scalp PsO was observed in FRONTIER-2, with 75% of patients receiving JNJ-77242113 100 mg twice daily achieving ss-IGA 0/1 at week 52. Although differences in study design, patient characteristics (including severity of disease), and efficacy measures limit any direct comparisons, rates of scalp clearance (measured by ss-Physician's Global Assessment of 0/1) reported for the oral therapies deucravacitinib and apremilast were 64% and 44%, respectively, at week 52.[23,24] Larger studies examining the impact of JNJ-77242113 on PsO in other special areas that may have a considerable impact on patient quality of life (eg, hands, feet, genitals, or nails) are ongoing. As pain and itch may be particularly disruptive to quality of life,[25,26] the meaningful improvements in patient-reported pain and itch reported by

JNJ-77242113—treated patients in FRONTIER-2 are noteworthy.

Data from long-term clinical trials and real-world studies of multiple monoclonal antibodies to IL-23 have demonstrated favorable safety profiles,[3-6] supporting the tolerability of targeting the IL-23 signaling pathway. Importantly, AE rates (including GI AEs), which were comparable to PBO in FRONTIER-1,[14] did not appear to increase through 1 year of treatment with JNJ-77242113.

While efficacy is considered the most critical attribute of treatment in patients with moderate-to-severe PsO, mode of administration is also of high importance and patients report a preference for oral rather than injectable treatments.[9] Thus, an oral therapy that provides high and durable rates of skin clearance and a favorable safety profile has the potential to be a compelling option for patients with PsO.

FRONTIER-2 assessed a variety of validated clinical end points, including both physician- and patient-reported measures, to thoroughly assess the effect of treatment. Data analyses employed nonresponder imputation, a stringent method intended to conservatively estimate the efficacy of JNJ-77242113 over time. The study was limited by the small number of patients in each treatment group and the descriptive nature of the longer-term data. Larger, phase 3 studies of JNJ-77242113, some of which include active-comparator arms, are ongoing (NCT06095102; NCT06095115; NCT06143878; NCT06220604) and will provide a more complete understanding of the efficacy and safety of JNJ-77242113 in treating broad populations of patients with moderate-to-severe plaque PsO.

CONCLUSIONS

The improvements in clinical and patient-reported efficacy seen with JNJ-77242113 at week 16 were durable and no safety signals were identified through up to 1 year of treatment. This study demonstrates that patients with moderate-to-severe PsO can attain sustained, advanced efficacy and safety using an oral, targeted IL-23—receptor inhibitor.

Conflicts of interest

Dr Ferris served as an investigator for AbbVie, Acelyrin, Amgen, Apogee, Arcutis, Aristea, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, DermTech, Eli Lilly, Galderma, GRAIL, Incyte, Janssen, Leo Pharma, Moberg, Mobius, Novartis, Regeneron, SkinAnalytics, Takeda, and UCB; consultant for AbbVie, Amgen, Apogee, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Dermavant, DermTech, Janssen, Leo Pharma, Novartis, Pfizer, Regeneron, and Takeda; speaker for AbbVie, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, and Regeneron. Dr Bagel has research funds payable to Psoriasis Treatment Center from AbbVie, Amgen, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Corrona, Dermavant, Dermira/UCB, Eli Lilly, Glenmark, Janssen, Kadmon, Leo Pharma, Lycera, Menlo, Novartis, Pfizer, Regeneron, Sun, Taro, and Valeant; consultant/speaking fees from AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Leo Pharma, Novartis, Sun, and Valeant; and fees for speaking from AbbVie, Celgene, Eli Lilly, Janssen, and Novartis. Dr Huang has conducted clinical trials for or received honoraria as a consultant for AbbVie, Bristol Myers Squibb, Celgene, Eli Lilly, Johnson & Johnson Innovative Medicine, Novartis, and Pfizer Pharmaceuticals. Dr Pink served as an investigator, advisor, speaker, or received educational support from AbbVie, Almirall, Amgen, BI, BMS, Galderma, Janssen, Johnson & Johnson, Leo, Lilly, Novartis, Pfizer, Sanofi, and UCB. Dr Tyring has received grants, consultant/speaker honoraria (paid to institution) from AbbVie, Agenus, AiCuris GmbH, Almirall, Amgen, Bayer, BMS, Demira, Dr Reddy's Laboratory, Eli Lilly, Foamix Pharma, Galderma, Genocea Biosciences, GlaxoSmithKline Immunology, Glenmark Pharma, IQVIA, Janssen Research & Development, Kiniksa Pharma, LEO Laboratories, Menlo Therapeutics, Merck, Novartis, Nycomed Amersham, Parexel, Quintiles Pharma, Regeneron Pharma, Sanofi, Trevi Therapeutics, UCB, and Vical. Dr Kokolakis is or has acted as a speaker and/or advisory board member for honoraria from AbbVie, Abbott, Actelion Pharmaceuticals, Amgen, Basilea Pharmaceutica, Bayer, Biogen IDEC, Boehringer, Bristol Myers Squibb, Celgene, Hexal, Janssen-Cilag, LEO Pharma, Lilly, MSD, Mylan, Novartis, Parexel, Pfizer, Sanofi-Aventis, Takeda, and UCB. Drs DeLozier, Li, Shen, Iaconangelo, and Ota are employees of Janssen Research & Development, LLC; employees may own stock/stock options in Johnson & Johnson. Dr Bissonnette is an advisory board member, consultant, speaker, and/or investigator for and received honoraria and/or grants from AbbVie, Alumis, Amgen, Arcutis, Bausch Health, BMS/Celgene, Boston Pharma, Dermavant, Eli Lilly, Janssen, LEO Pharma, Nimbus, Novartis, Pfizer, Regeneron, UCB, VentyxBio, and Xencor; also, an employee and shareholder of Innovaderm Research.

REFERENCES

1. Yang K, Oak ASW, Elewski BE. Use of IL-23 inhibitors for the treatment of plaque psoriasis and psoriatic arthritis: a comprehensive review. *Am J Clin Dermatol*. 2021;22:173-192. https://doi.org/10.1007/s40257-020-00578-0
2. Elloso MM, Gomez-Angelats M, Fourie AM. Targeting the Th17 pathway in psoriasis. *J Leukoc Biol*. 2012;92:1187-1197. https://doi.org/10.1189/jlb.0212101
3. Papp KA, Langley RG, Lebwohl M, et al. Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2). *Lancet*. 2008;371:1675-1684. https://doi.org/10.1016/S0140-6736(08)60726-6

4. Reich K, Armstrong AW, Foley P, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: results from the phase III, double-blind, placebo- and active comparator-controlled VOYAGE 2 trial. *J Am Acad Dermatol*. 2017;76:418-431. https://doi.org/10.1016/j.jaad.2016.11.042
5. Reich K, Gooderham M, Thaci D, et al. Risankizumab compared with adalimumab in patients with moderate-to-severe plaque psoriasis (IMMvent): a randomised, double-blind, active-comparator-controlled phase 3 trial. *Lancet*. 2019;394:576-586. https://doi.org/10.1016/S0140-6736(19)30952-3
6. Reich K, Papp KA, Blauvelt A, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. *Lancet*. 2017;390:276-288. https://doi.org/10.1016/S0140-6736(17)31279-5
7. Fragoulis GE, Siebert S. The role of IL-23 and the use of IL-23 inhibitors in psoriatic arthritis. *Muscoskel Care*. 2022;20:S12-S21. https://doi.org/10.1002/msc.1694
8. Feldman SR, Holmen Moeller A, Erntoft Idemyr ST, Gonzalez JM. Relative importance of mode of administration in treatment preferences among plaque psoriasis patients in the United States. *J Health Econ Outcomes Res*. 2017;4:141-157. https://doi.org/10.36469/9817
9. Komine M, Kim H, Yi J, et al. A discrete choice experiment on oral and injection treatment preferences among moderate-to-severe psoriasis patients in Japan. *J Dermatol*. 2023;50:766-777. https://doi.org/10.1111/1346-8138.16746
10. Armstrong AW, Puig L, Joshi A, et al. Comparison of biologics and oral treatments for plaque psoriasis: a meta-analysis. *JAMA Dermatol*. 2020;156:258-269. https://doi.org/10.1001/jamadermatol.2019.4029
11. Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker J. Psoriasis. *Lancet*. 2021;397:1301-1315. https://doi.org/10.1016/S0140-6736(20)32549-6
12. Sbidian E, Chaimani A, Guelimi R, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. *Cochrane Database Syst Rev*. 2023;7:CD011535. https://doi.org/10.1002/14651858.CD011535.pub6
13. Fourie A, Cheng X, Chang L. First-in-class oral peptide systemically targeting IL-23 pathway. *J Invest Dermatol*. 2023;143:S190.
14. Bissonnette R, Pinter A, Ferris LK, et al. An oral interleukin-23-receptor antagonist peptide for plaque psoriasis. *N Engl J Med*. 2024;390:510-521. https://doi.org/10.1056/NEJMoa2308713
15. Langley RG, Feldman SR, Nyirady J, van de Kerkhof P, Papavassilis C. The 5-point Investigator's Global Assessment (IGA) Scale: a modified tool for evaluating plaque psoriasis severity in clinical trials. *J Dermatolog Treat*. 2015;26:23-31. https://doi.org/10.3109/09546634.2013.865009
16. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994;19:210-216. https://doi.org/10.1111/j.1365-2230.1994.tb01167.x
17. Mathias SD, Feldman SR, Crosby RD, Colwell HH, McQuarrie K, Han C. Measurement properties of a patient-reported outcome measure assessing psoriasis severity: the psoriasis symptoms and signs diary. *J Dermatolog Treat*. 2016;27:322-327. https://doi.org/10.3109/09546634.2015.1114567
18. Basra MK, Fenech R, Gatt RM, Salek MS, Finlay AY. The Dermatology Life Quality Index 1994-2007: a comprehensive review of validation data and clinical results. *Br J Dermatol*. 2008;159:997-1035. https://doi.org/10.1111/j.1365-2133.2008.08832.x
19. Foley P, Gordon K, Griffiths CEM, et al. Efficacy of guselkumab compared with adalimumab and placebo for psoriasis in specific body regions: a secondary analysis of 2 randomized clinical trials. *JAMA Dermatol*. 2018;154:676-683. https://doi.org/10.1001/jamadermatol.2018.0793
20. Fahrbach K, Sarri G, Phillippo DM, et al. Short-term efficacy of biologic therapies in moderate-to-severe plaque psoriasis: a systematic literature review and an enhanced multinomial network meta-analysis. *Dermatol Ther*. 2021;11:1965-1998. https://doi.org/10.1007/s13555-021-00602-z
21. Armstrong AW, Gooderham M, Warren RB, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. *J Am Acad Dermatol*. 2023;88:29-39. https://doi.org/10.1016/j.jaad.2022.07.002
22. Strober B, Thaci D, Sofen H, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, phase 3 program for evaluation of TYK2 inhibitor psoriasis second trial. *J Am Acad Dermatol*. 2023;88:40-51. https://doi.org/10.1016/j.jaad.2022.08.061
23. Blauvelt A, Rich P, Sofen H, et al. Deucravacitinib, a selective, allosteric tyrosine kinase 2 inhibitor, in scalp psoriasis: a subset analysis of two phase 3 randomized trials in plaque psoriasis. *J Am Acad Dermatol*. 2024;90:775-782. https://doi.org/10.1016/j.jaad.2023.11.060
24. Stein Gold L, Papp K, Pariser D, et al. Efficacy and safety of apremilast in patients with mild-to-moderate plaque psoriasis: results of a phase 3, multicenter, randomized, double-blind, placebo-controlled trial. *J Am Acad Dermatol*. 2022;86:77-85. https://doi.org/10.1016/j.jaad.2021.07.040
25. Hawro M, Sahin E, Stec M, et al. A comprehensive, tri-national, cross-sectional analysis of characteristics and impact of pruritus in psoriasis. *J Eur Acad Dermatol Venereol*. 2022;36:2064-2075. https://doi.org/10.1111/jdv.18330
26. Sahin E, Hawro M, Weller K, et al. Prevalence and factors associated with sleep disturbance in adult patients with psoriasis. *J Eur Acad Dermatol Venereol*. 2022;36:688-697. https://doi.org/10.1111/jdv.17917