Once-daily oral icotrokinra versus placebo and once-daily oral deucravacitinib in participants with moderate-to-severe plaque psoriasis (ICONIC-ADVANCE 1 & 2): two phase 3, randomised, placebo-controlled and active-comparator-controlled trials

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Summary

Background Monoclonal antibodies targeting interleukin-23 and interleukin-12 are efficacious in treating plaque psoriasis but must be delivered via intravenous or subcutaneous injection. Here, we aimed to evaluate the efficacy and safety of icotrokinra (JNJ-77242113), a targeted oral peptide that selectively binds the interleukin-23 receptor, compared with both placebo and deucravacitinib in adults with moderate-to-severe plaque psoriasis.

Methods The phase 3, randomised, double-blind, placebo-controlled and active-comparator-controlled ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 trials, which are being done at 149 sites across 13 countries and 114 sites across 11 countries, respectively, randomly assigned (2:1:2 and 4:1:4, respectively) adults with moderate-to-severe plaque psoriasis diagnosed for at least 26 weeks (body-surface-area involvement ≥10%, Psoriasis Area and Severity Index [PASI] ≥12, and Investigator's Global Assessment [IGA] ≥3) to once-daily oral icotrokinra 200 mg, placebo, or deucravacitinib 6 mg; participants randomly assigned to placebo or deucravacitinib transitioned to icotrokinra at week 16 or week 24, respectively. Coprimary endpoints were proportions of participants achieving IGA 0 or 1 (clear or almost clear skin) with at least a two-grade improvement and at least 90% improvement in PASI (PASI 90) at week 16 with icotrokinra versus placebo. These studies are registered with ClinicalTrials.gov, NCT06143878 (ADVANCE 1) and NCT06220604 (ADVANCE 2), and are ongoing.

Findings ICONIC-ADVANCE 1 enrolled participants from Jan 17, 2024, to May 24, 2024, and ICONIC-ADVANCE 2 enrolled participants from March 9, 2024, to June 13, 2024. Participants (ADVANCE 1: 774 of 988 patients screened; ADVANCE 2: 731 of 917 patients screened) were randomly assigned to icotrokinra (n=311 and 322), placebo (n=156 and 82), or deucravacitinib (n=307 and 327). All coprimary endpoints were met in both trials. Higher proportions of icotrokinra-treated versus placebo-treated participants achieved IGA 0 or 1 (ADVANCE 1: 213 [68%] of 311 *vs* 17 [11%] of 156, treatment difference 95% CI 58% [50–64]; ADVANCE 2: 227 [70%] of 322 *vs* seven [9%] of 82, 62% [53–69]; both p<0·0001) and PASI 90 (ADVANCE 1: 171 [55%] of 311 *vs* six [4%] of 156, treatment difference 95% CI 51% [44–57]; ADVANCE 2: 184 [57%] of 322 *vs* one [1%] of 82, 56% [48–62]; both p<0·0001) at week 16. Across studies, adverse event rates to week 16 were 303 (48%) of 632 and 136 (57%) of 237 with icotrokinra and placebo, respectively; the most common adverse events were nasopharyngitis (37 [6%] of 632 and 13 [5%] of 237) and upper respiratory tract infection (23 [4%] of 632 and eight [3%] of 237). To week 24, adverse event rates were lower than with icotrokinra (359 [57%] of 632) than deucravacitinib (411 [65%] of 634).

Interpretation Icotrokinra showed superior clinical response rates versus placebo and deucravacitinib in phase 3 moderate-to-severe plaque psoriasis trials, with similar adverse event rates to placebo. These findings suggest the potential of once-daily oral icotrokinra to provide robust efficacy and a favourable safety profile.

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Introduction

Psoriasis is a chronic, relapsing, immune-mediated inflammatory disease that primarily affects the skin. Patients with psoriasis are often affected by other chronic conditions, including psoriatic arthritis, metabolic syndrome, cardiovascular disease, and inflammatory bowel

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Research in context

Evidence before this study

We searched PubMed for articles published before March 24, 2025, using the terms "psoriasis" and "oral" and "interleukin-23 or IL-23" in their title or abstract with clinical trials as the article type. The search identified 28 articles, of which three described randomised, controlled, phase 3 clinical trials in patients with plaque psoriasis; these studies used an oral therapy (fumaric acid esters or methotrexate) as an active comparator for an injectable IL-23 inhibitor, and all concluded that the injectable IL-23 inhibitor had greater efficacy than the oral comparator. Monoclonal antibodies targeting IL-23 or IL-12/23 (eg, guselkumab, tildrakizumab, risankizumab, and ustekinumab), which are delivered via subcutaneous injection, generally have shown efficacy in treating psoriasis and exhibit safety profiles that are considered favourable compared with conventional systemic therapies. A PubMed search for articles published before March 24, 2025, which used "icotrokinra" or "JNJ-77242113" and "psoriasis" in their title or abstract with clinical trials as the article type, identified two articles, both of which report data from phase 2 studies of icotrokinra (an IL-23 receptor-targeting oral peptide) in patients with moderate-to-severe plaque psoriasis. These studies reported rates of clear or almost clear skin that were higher in patients treated with icotrokinra compared with placebo and were within the range of response rates seen with biological, injectable inhibitors of the IL-23 p19 subunit currently approved to treat psoriasis, with a safety profile similar to placebo. A PubMed search for articles published before March 24, 2025, which used "deucravacitinib" and "apremilast" in their title or abstract with clinical trials as the article type, identified nine articles, all of which report data from phase 3 studies of deucravacitinib (an oral tyrosine kinase 2 [TYK2] inhibitor) versus apremilast (an oral phosphodiesterase 4 inhibitor) in patients with moderate-to-severe plaque psoriasis. Deucravacitinib has shown superior efficacy in treating psoriasis compared with apremilast and is generally well tolerated in adults with moderate-to-severe plaque psoriasis. Therefore, deucravacitinib was selected as the active comparator as it was the most efficacious approved advanced oral medication for the treatment of moderate-to-severe plaque psoriasis.

Added value of this study

ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 evaluated the efficacy and safety of icotrokinra compared with placebo and deucravacitinib in patients with moderate-to-severe plaque psoriasis. As such, they are the first head-to-head studies comparing an IL-23 receptor-targeting oral peptide with an active comparator, deucravacitinib, an oral TYK2 inhibitor. Across both studies, icotrokinra showed superior skin clearance versus placebo and deucravacitinib for all coprimary and key secondary endpoints. The safety profile of icotrokinra was similar to placebo across both studies.

Implications of all the available evidence

Data from the placebo-controlled phases of ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 are consistent with the findings from recently presented phase 3, randomised, controlled studies in which icotrokinra showed superior skin clearance across multiple clinical outcomes, compared with placebo, and a favourable safety profile in adults and adolescents with moderate-to-severe plaque psoriasis (ICONIC-LEAD) and in those with plaque psoriasis involving high-impact sites (ICONIC-TOTAL). Selective blockade of the IL-23 receptor with the targeted oral peptide icotrokinra showed superior skin clearance to placebo and deucravacitinib in two phase 3 trials for moderate-to-severe plaque psoriasis. Up to 16 weeks of treatment, the safety profile of icotrokinra was similar to placebo. These data suggest that once-daily oral icotrokinra can provide robust efficacy and a favourable safety profile for patients with plaque psoriasis.

disease.[1] Interleukin (IL)-23 is a key regulator of the pathogenic T-cell activation underlying psoriasis.[2] Monoclonal antibodies targeting IL-23 and IL-12/23 have shown efficacy in treating psoriasis while maintaining safety profiles that are considered preferable to conventional non-biological systemic therapies.[2–6] However, delivery of these biological therapies requires intravenous or subcutaneous injection, which might not be the preferred method of administration for all patients.[7,8] In particular, those with fear of needles[9,10] or a lifestyle that is not amenable to storage or transportation of therapeutics that require refrigeration would benefit from an oral option. Deucravacitinib (a tyrosine kinase 2 [TYK2] inhibitor)[11] and apremilast (a phosphodiesterase 4 inhibitor),[12] both small-molecule oral therapies approved for the treatment of plaque psoriasis, have modest efficacy relative to injectable biologics and have been associated with some undesirable side-effects, such as gastrointestinal intolerability, acne, and herpes zoster infections.[13–15]

Icotrokinra (JNJ-77242113) is a first-in-class targeted oral peptide that selectively binds the IL-23 receptor, blocking IL-23 cytokine binding, and thereby inhibiting IL-23 receptor-mediated signalling and downstream effector functions.[16] In a phase 2 study in adults with moderate-to-severe plaque psoriasis, participants treated for 16 weeks with icotrokinra had higher rates of skin clearance and a safety profile similar to placebo.[17] In the phase 2 long-term extension, clinical response rates were durable and the safety profile remained consistent up to 1 year of icotrokinra treatment.[18] In two recent phase 3 studies, icotrokinra showed significantly higher skin response rates compared with placebo while showing a safety profile similar to placebo in adults and adolescents with moderate-to-severe plaque psoriasis (ICONIC-LEAD; NCT06095115)[19] and

in those with plaque psoriasis involving high-impact sites (ICONIC-TOTAL; NCT06095102).[20]

The two pivotal phase 3 studies, ICONIC-ADVANCE 1 (NCT06143878; ADVANCE 1) and ICONIC-ADVANCE 2 (NCT06220604; ADVANCE 2), aimed to evaluate the efficacy and safety of icotrokinra, compared with both placebo and deucravacitinib, in adults with moderate-to-severe plaque psoriasis. Here, we report findings to week 24 of these ongoing 3-year studies.

Methods

Study design and participants

The phase 3, randomised, double-blind, placebo-controlled and active-comparator-controlled ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 trials are being done at 149 sites (dermatology offices, hospitals, and clinical research facilities) across 13 countries and 114 sites across 11 countries, respectively, to ensure broad representation of race (American Indian or Alaska Native, Asian, Black, Native Hawaiian or other Pacific Islander, or White) and ethnicity (Hispanic–Latinx, not Hispanic–Latinx). In both trials, a placebo-controlled period (weeks 0–16) occurred concurrently with the active-comparator-controlled period (weeks 0–24). Treatment compliance was assessed at each visit during the treatment period. No concomitant topical therapies, phototherapies, or systemic medications that could affect psoriasis evaluations were allowed throughout the treatment period. The studies include a 4-week safety monitoring following discontinuation of study treatment or the end of the 3-year treatment period.

These studies employed identical enrolment criteria. Adults (aged ≥18 years) with moderate-to-severe plaque psoriasis diagnosed for at least 26 weeks at screening (total body surface area [BSA] of psoriasis involvement ≥10%; Psoriasis Area and Severity Index [PASI] score ≥12; and Investigator's Global Assessment [IGA] score ≥3) and who were candidates for phototherapy or systemic treatment were eligible. Exclusion criteria included a non-plaque form of psoriasis; drug-induced psoriasis; history of chronic or recurrent infectious disease, immunodeficiency, or serious infection within 8 weeks of screening; or history of untreated latent tuberculosis or positive interferon-γ release assay (within 8 weeks of first study dose). Individuals with treated latent tuberculosis were eligible, and it was required that treatment be initiated before the first dose of study treatment and that treatment not be prematurely discontinued during the study. Exclusion criteria also included non-achievement of primary efficacy or clinically significant adverse events related to agents targeting IL-23 (previous IL-12/23 biological non-success allowed) or TYK2 inhibitors. Full eligibility criteria are described in the protocol in the appendix.

ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 are being done according to the Good Clinical Practice guidelines of the International Council for Harmonisation and the principles of the Declaration of Helsinki. All investigators received approval from an ethics committee (appendix pp 12–16), and all participants provided written informed consent.

Randomisation and masking

Participants were randomly assigned (2:1:2 in ADVANCE 1 and 4:1:4 in ADVANCE 2) to once-daily oral icotrokinra (200 mg tablet), placebo, or deucravacitinib (6 mg capsule); randomisation was stratified by weight (≤90 kg; >90 kg) and geographical region (Europe; North and South America; Asia Pacific). Participants randomly assigned to placebo or deucravacitinib transitioned to icotrokinra 200 mg daily to week 156, beginning at week 16 or week 24, respectively. Within each study, central randomisation assigned participants to one of three treatment groups by use of an interactive web response system. The permuted block randomisation was stratified by bodyweight and geographical region. Schedules for administering study treatment were the same across treatment groups and labels on study treatments were identical to maintain the mask for both participants and clinicians.

Procedures

Participants were instructed to take the study treatment with water, on waking, at approximately the same time every day, on an empty stomach, and advised not to eat for at least 30 min after. To ensure manageability, patients were involved in the study design, including the dosing regimen and schedule of assessments. Study investigators scored psoriasis disease activity using the PASI, the IGA, and the scalp-specific IGA (ss-IGA). The PASI is a composite outcome measure that includes the percentage of affected BSA and severity of erythema, scaling, and induration in four body regions;[21] scores range from 0 to 72, with higher scores indicating greater severity of disease. The IGA instrument evaluates psoriasis severity, on the basis of erythema, scaling, and induration, on a scale of 0 (clear skin) to 4 (severe psoriasis).[22] Similarly, the ss-IGA grades redness, thickness, and scaliness of scalp lesions on a scale of 0 (no disease) to 4 (severe disease).[23] Participants reported the severity of psoriasis symptoms (itch, skin tightness, burning, stinging, and pain) and signs (dryness, cracking, scaling, shedding/flaking, redness, and bleeding) using the Psoriasis Symptoms and Signs Diary (PSSD) questionnaire. Each item was graded from 0 to 10 (absent to worst imaginable; PSSD Symptom/Sign score range 0–100), with a higher score indicating a greater effect of symptoms and signs of psoriasis and a score of 0 indicating resolution of symptoms and signs of psoriasis.[24,25] A reduction in the PSSD Itch score of at least four points is considered a clinically meaningful improvement (CMI).[26]

Outcomes

See Online for appendix

Coprimary endpoints in both studies were the proportion of participants achieving an IGA score of 0 or 1 with at least a two-grade improvement from baseline (IGA 0 or 1; clear or almost clear skin) and achieving at least 90% improvement from baseline in PASI (PASI 90) at

week 16 in the icotrokinra group versus the placebo group. Key secondary endpoints in both studies compared the proportion of participants in the icotrokinra and placebo groups achieving the following: IGA 0 (week 16), PASI 75 (weeks 4 and 16), PASI 90 (week 8), PASI 100 (week 16), ss-IGA score of 0 or 1 with at least a two-grade improvement from baseline among participants with ss-IGA score of at least 2 at baseline (ss-IGA 0 or 1; week 16), PSSD Symptom score of 0 among participants with a PSSD Symptom score greater than 0 at baseline (PSSD Symptom score 0; weeks 8 and 16), and CMI (≥4 points) from baseline in PSSD Itch score among participants with a PSSD Itch score of at least 4 at baseline (PSSD Itch CMI; weeks 4 and 16). Comparisons between the icotrokinra and deucravacitinib groups evaluated proportions of participants achieving the following at weeks 16 and 24: IGA 0 or 1, IGA 0, PASI 75, PASI 90, PASI 100, and PSSD Symptom score 0 at week 16 (among participants with a PSSD Symptom score >0 at baseline).

Other secondary efficacy endpoints included change from baseline in BSA and PASI, PSSD Symptom, PSSD Sign, Dermatology Life Quality Index (DLQI), and Patient-Reported Outcomes Measurement Information System—29 scores (week 16); percentage improvement in PASI (week 16); percentage change from baseline in modified Nail Psoriasis Severity Index score (week 16); achieving a score of 0 or 1 for Physician's Global Assessment (PGA) of Hands and Feet, static PGA of Genitalia, Fingernail PGA, and Genital Psoriasis Sexual Frequency Questionnaire Item 2 (week 16), DLQI (weeks 16 and 24), and IGA (after week 24); achieving score 0 for PSSD Sign (week 16) and PSSD Symptom (week 24); and achieving PASI 75 and PASI 90 (after week 24).

Safety assessments included documentation of adverse events, serious adverse events, and clinical laboratory assessments. Adverse event data from the two studies were combined to provide a larger sample size for evaluating potentially uncommon adverse events. Full protocols are available in the appendix.

Statistical analysis

ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 sample sizes of 750 (icotrokinra n=300; placebo n=150; deucravacitinib n=300) and 675 (icotrokinra n=300; placebo n=75; deucravacitinib n=300), respectively, were estimated to provide greater than 99% power to detect significant differences for both coprimary endpoints between the icotrokinra and placebo groups at week 16; greater than 99% power to detect a 20% difference in the proportions of participants achieving PASI 75 response between the icotrokinra and deucravacitinib groups at week 16; and approximately 90% power to detect a 13% difference in the proportion of participants achieving IGA 0 or 1 between the icotrokinra and deucravacitinib groups at weeks 16 or 24, all at a two-sided significance level of 0·05.

Efficacy analyses employed the full analysis set, which included all randomly assigned participants. For the coprimary endpoints, a composite strategy (non-responder imputation) was applied to address intercurrent event (ICE) 1 (discontinuation owing to lack of efficacy or an adverse event of worsening psoriasis) or ICE 2 (initiation of a protocol-prohibited medication or therapy that could improve psoriasis). A treatment policy strategy (observed data) was applied to ICE 3 (discontinuation for other reasons). A per-protocol analysis was applied to ICEs 1–2 and observed data were used for ICE 3. Participants with missing data after application of the ICE strategies were considered non-responders.

For most binary endpoints, including coprimary endpoints, treatment comparisons were done by use of Cochran–Mantel–Haenszel tests stratified by baseline weight (≤90 kg; >90 kg) and geographical region (Europe; North and South America; Asia Pacific); achievement of PSSD Symptom score 0 at week 8 was evaluated by use of Fisher's exact test because of the low numbers in some of the cells. Each study was to be considered positive if the icotrokinra group was significantly different from the placebo group for both coprimary endpoints at a two-sided α level of 0·05.

A graphic approach was used for multiplicity control at the overall type 1 error rate of α=0·05 (two-sided) for the coprimary and key secondary analyses. Key secondary endpoint analyses were grouped into tiers. Within each tier, the Bonferroni–Holm's multiple comparison procedure[27] was used to test the endpoints in that tier at the assigned significance level; each tier was tested in a prespecified order (appendix). For all key secondary endpoint analyses, significance was claimed if the adjusted p value was less than or equal to 0·05. Key secondary endpoints comparing icotrokinra and deucravacitinib (PASI 75 and IGA 0 or 1 responses, at weeks 16 and 24) were initially tested for non-inferiority before superiority. To evaluate the robustness of the coprimary endpoint analyses, sensitivity analyses assessed the effect of missing data assumptions, without adjustment for multiplicity of comparisons (appendix p 1). Analyses of other secondary efficacy endpoints (change from baseline in BSA, PASI, PSSD Symptom, PSSD Sign, DLQI, and Patient-Reported Outcomes Measurement Information System—29 scores; percentage improvement in PASI; percentage change from baseline in modified Nail Psoriasis Severity Index score; achieving a score of 0 or 1 for PGA of Hands and Feet, static PGA of Genitalia, Fingernail PGA, and Genital Psoriasis Sexual Frequency Questionnaire Item 2, DLQI, and IGA; achieving score 0 for PSSD Sign and PSSD Symptom; and achieving PASI 75 and PASI 90) at weeks 16 and 24 will be reported in separate publications.

An independent data monitoring committee consisting of two dermatologists, a cardiologist, an infectious disease specialist, and a statistician periodically reviewed safety data and made recommendations on the continuation of studies to ensure the safety of participants.

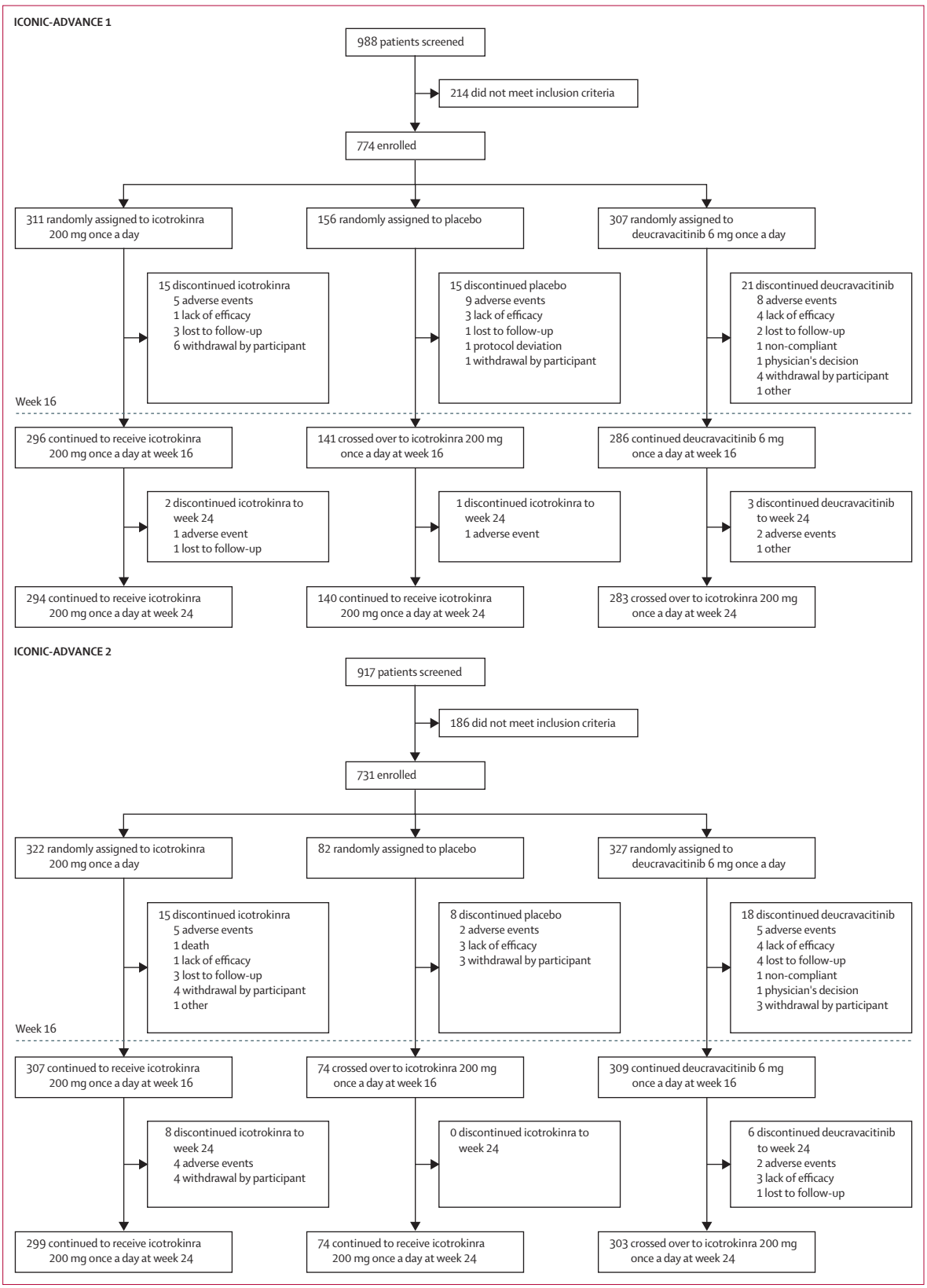

Figure 1: **Trial profile**

	ICONIC-ADVANCE 1			ICONIC-ADVANCE 2		
	Icotrokinra (n=311)	Placebo (n=156)	Deucravacitinib (n=307)	Icotrokinra (n=322)	Placebo (n=82)	Deucravacitinib (n=327)
Demographics						
Age, years	47·1 (13·19)	46·9 (12·78)	46·3 (13·87)	45·9 (13·78)	48·4 (13·90)	45·6 (13·22)
Sex						
Female	88 (28%)	51 (33%)	107 (35%)	104 (32%)	27 (33%)	104 (32%)
Male	223 (72%)	105 (67%)	200 (65%)	218 (68%)	55 (67%)	223 (68%)
Race or ethnic group						
American Indian or Alaska Native	1 (<1%)	1 (<1%)	1 (<1%)	1 (<1%)	0	1 (<1%)
Asian	69 (22%)	34 (22%)	77 (25%)	34 (11%)	15 (18%)	40 (12%)
Black	4 (1%)	3 (2%)	4 (1%)	9 (3%)	2 (2%)	11 (3%)
Native Hawaiian or other Pacific Islander	2 (1%)	0	0	2 (1%)	0	3 (1%)
White	231 (74%)	118 (76%)	221 (72%)	274 (85%)	65 (79%)	265 (81%)
Unknown or not reported	4 (1%)	0	4 (1%)	1 (<1%)	0	5 (2%)
Ethnicity						
Hispanic or Latinx	58 (19%)	25 (16%)	49 (16%)	42 (13%)	12 (15%)	48 (15%)
Not Hispanic or Latinx	250 (80%)	129 (83%)	257 (84%)	279 (87%)	70 (85%)	279 (85%)
Unknown or not reported	3 (1%)	2 (1%)	1 (<1)	1 (<1%)	0	0
Weight, kg	86·9 (21·08)	88·2 (25·08)	87·7 (23·04)	88·8 (20·12)	86·4 (18·84)	89·8 (21·43)
BMI,* kg/m²	29·2 (6·31)	29·6 (8·08)	29·9 (7·28)	29·9 (6·36)	29·5 (5·78)	29·9 (6·86)
Disease characteristics						
Age at psoriasis diagnosis, years	29·7 (14·81)	29·1 (16·13)	29·6 (15·21)	28·6 (15·69)	27·3 (16·23)	28·9 (14·63)
Duration of psoriasis, years	17·52 (11·10)	17·88 (12·75)	16·81 (12·81)	17·43 (13·38)	21·21 (15·17)	16·82 (12·03)
Psoriasis Area and Severity Index total score (0–72)	18·60 (15·50–22·70)	17·15 (14·40–21·65)	18·00 (15·00–23·40)	18·00 (15·10–22·20)	17·95 (14·30– 23·60)	17·60 (15·20–21·40)
Percentage of BSA*	20·00% (16·00–32·00)	20·00% (14·00–30·75)	21·00% (14·00–34·00)	21·00% (15·00–32·00)	22·00% (15·00–33·00)	20·00% (15·50–32·00)
Investigator's Global Assessment score						
3 (moderate)	251 (81%)	123 (79%)	242 (79%)	252 (78%)	67 (82%)	267 (82%)
4 (severe)	60 (19%)	33 (21%)	65 (21%)	70 (22%)	15 (18%)	60 (18%)
Scalp-specific Investigator's Global Assessment score†						
2 (mild)	45 (14%)	30 (19%)	55 (18%)	62 (19%)	17 (21%)	62 (19%)
3 (moderate)	177 (57%)	85 (54%)	166 (54%)	169 (52%)	48 (59%)	176 (54%)
4 (severe)	39 (13%)	19 (12%)	47 (15%)	39 (12%)	6 (7%)	40 (12%)
PSSD Symptom score‡ (1–100)	50·0 (28·0–70·0)	44·0 (24·0–68·0)	52·0 (30·0–70·0)	54·0 (30·0–76·0)	52·0 (32·0–74·0)	57·0 (32·0–76·0)
PSSD Sign score‡ (1–100)	57·0 (42·0–73·0)	51·0 (33·0–68·0)	57·0 (38·0–73·0)	60·0 (38·0–77·0)	55·0 (42·0–77·0)	63·0 (45·0–77·0)
PSSD Itch score‡	7·0 (5·0–8·0)	6·0 (4·0–8·0)	7·0 (5·0–8·0)	7·0 (5·0–8·0)	7·0 (4·0–8·0)	7·0 (5·0–8·0)
Previous psoriasis therapy						
Systemic therapy§	236 (76%)	110 (71%)	225 (73%)	225 (70%)	58 (71%)	230 (70%)
Phototherapy¶	112 (36%)	53 (34%)	97 (32%)	98 (30%)	31 (38%)	109 (33%)
Conventional non-biological systemic therapy‖	171 (55%)	79 (51%)	152 (50%)	165 (51%)	39 (48%)	163 (50%)
Novel non-biological systemic therapy**	22 (7%)	12 (8%)	38 (12%)	16 (5%)	3 (4%)	12 (4%)
Biological therapy††	86 (28%)	42 (27%)	80 (26%)	78 (24%)	26 (32%)	77 (24%)

Data are n (%), mean (SD), or median (IQR) unless otherwise noted. Percentages may not total 100 because of rounding. BSA=body surface area. PSSD=Psoriasis Symptoms and Signs Diary. PUVA=psoralen and long-wave ultraviolet light. UVB=short wave ultraviolet light. *Among 322 participants in the icotrokinra group, 82 in the placebo group, and 325 in the deucravacitinib group in ICONIC-ADVANCE 2. †Among 308 participants in the icotrokinra group, 156 in the placebo group, and 306 in the deucravacitinib group in ICONIC-ADVANCE 1 and 321, 82, and 324 participants, respectively, in ICONIC-ADVANCE 2. ‡Among 287 participants in the icotrokinra group, 142 in the placebo group, and 277 in the deucravacitinib group in ICONIC-ADVANCE 1 and 299, 71, and 290 participants, respectively, in ICONIC-ADVANCE 2. §Includes conventional non-biological systemics, novel non-biological systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. ¶Includes PUVA and UVB. ||Includes PUVA, methotrexate, cyclosporine, acitretin, azathioprine, and fumarate. **Includes apremilast and tofacitinib. ††Includes etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, and certolizumab pegol.

Table 1: **Demographics and baseline clinical characteristics**

These studies are registered with ClinicalTrials.gov, NCT06143878 (ADVANCE 1) and NCT06220604 (ADVANCE 2).

Role of the funding source

The funder of the study had a role in study design, data collection, data analysis, data interpretation, and writing of the report.

Results

ICONIC-ADVANCE 1 enrolled participants from Jan 17, 2024, to May 24, 2024, and ICONIC-ADVANCE 2 enrolled participants from March 9, 2024, to June 13, 2024. Participants (ADVANCE 1: 774 of 988 participants assessed [icotrokinra n=311; placebo n=156; deucravacitinib n=307]; ADVANCE 2: 731 of 917 participants assessed [icotrokinra n=322; placebo n=82; deucravacitinib n=327]) were randomly assigned to study treatment. In ICONIC-ADVANCE 1, 296 (95%) of 311 participants in the icotrokinra group, 141 (90%) of 156 in the placebo group, and 286 (93%) of 307 participants in the deucravacitinib group continued to receive study treatment up to week 16 (figure 1); 294 (95%) of 311 and 283 (92%) of 307 participants in the icotrokinra and deucravacitinib groups, respectively continued study treatment up to week 24. Participant retention rates in ICONIC-ADVANCE 2 were 307 (95%) of 322 in the icotrokinra group, 74 (90%) of 82 in the placebo group, and 309 (94%) of 327 in the deucravacitinib group to week 16 and 93% in both the icotrokinra (299 of 322) and deucravacitinib (303 of 327) groups to week 24. Among participants randomly assigned to placebo who transitioned to icotrokinra at week 16, only one participant (ADVANCE 1) had discontinued by week 24. One placebo-treated participant (ADVANCE 1) had a protocol deviation due to previous deucravacitinib exposure, never received study treatment, and immediately discontinued the study.

Baseline demographics, disease characteristics, and systemic therapy exposure were generally well balanced across treatment groups and consistent across studies (table 1). In both ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2, most participants were White (570 [74%] of 774; 604 [83%] of 731, respectively), not Hispanic–Latinx (636 [82%] of 774; 628 [85%] of 731, respectively), and male (528 [68%] of 774; 496 [68%] of 731, respectively). At baseline, the mean (SD) age in ICONIC-ADVANCE 1 was 46·7 (13·4) years and in ICONIC-ADVANCE 2 was 46·1 (13·6) years, and the mean (SD) weight was 87·5 kg (22·7) and 89·0 kg (20·7), respectively. At baseline, the mean (SD) psoriasis disease duration in ICONIC-ADVANCE 1 was 17·3 (12·1) and in ICONIC-ADVANCE 2 was 17·6 (13·1) years; mean (SD) PASI scores were 20·1 (7·3) and 19·8 (6·9), respectively; and the mean (SD) BSA involvement was 26·1% (15·6) and 25·8% (14·2), respectively. Across studies, 20% of participants (ADVANCE 1: 158 [20%] of 774 participants; ADVANCE 2: 145 [20%] of 731 participants) had severe disease at baseline, more than two-thirds had previously received systemic therapy, and approximately one-quarter had previous experience with a biological therapy.

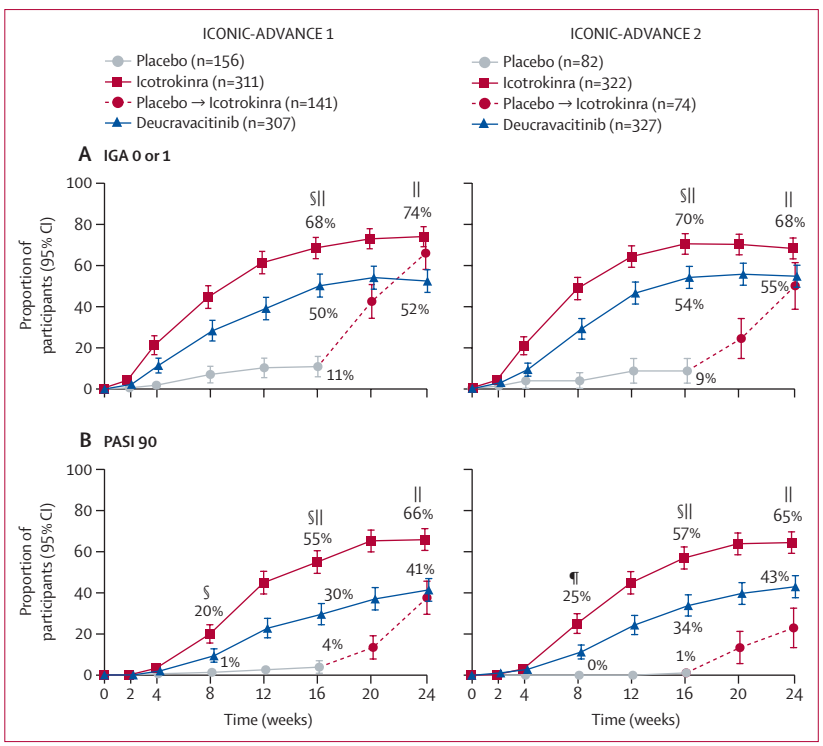

Figure 2: **Proportions of participants achieving the coprimary endpoints of IGA 0 or 1* and PASI 90 by treatment group over time†‡**

IGA=Investigator's Global Assessment. PASI=Psoriasis Area and Severity Index. *With a ≥2-grade improvement from baseline. †In ICONIC-ADVANCE 1, the rates of participants with missing IGA or PASI data at week 16 were five (3%) of 156, 14 (4%) of 311, and 15 (5%) of 307 for the placebo, icotrokinra, and deucravacitinib groups, respectively. ‡In ICONIC-ADVANCE 2, the rates of participants with missing IGA or PASI data at week 16 were four (5%) of 82, 11 (3%) of 322, and 11 (3%) of 327 for the placebo, icotrokinra, and deucravacitinib groups, respectively. §Multiplicity-adjusted p<0·001, icotrokinra versus placebo. ¶Multiplicity-adjusted p<0·01, icotrokinra versus placebo. ||Multiplicity-adjusted p<0·001, icotrokinra versus deucravacitinib. Error bars represent 95% CI.

The coprimary endpoints were met in both ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2. Significantly higher proportions of participants receiving icotrokinra than placebo achieved IGA 0 or 1 (ADVANCE 1: 213 [68%] of 311 *vs* 17 [11%] of 156, treatment difference 95% CI 58% [50–64]; ADVANCE 2: 227 [70%] of 322 *vs* seven [9%] of 82, 62% [53–69]; both p<0·0001) and PASI 90 (ADVANCE 1: 171 [55%] of 311 *vs* six [4%] of 156, treatment difference 95% CI 51% [44–57]; ADVANCE 2: 184 [57%] of 322 *vs* one [1%] of 82, 56% [48–62]; both p<0·0001) responses at week 16 (figure 2). Early separation between the icotrokinra and placebo groups in the proportion of participants achieving PASI 90 was apparent at week 8 in both studies (ADVANCE 1: 62 [20%] of 311 *vs* two [1%] of 156, treatment difference 95% CI 19% [14–24], p<0·0001; ADVANCE 2: 81 [25%] of 322 *vs* 0 of 82, 25% [20–30]; p=0·0039; appendix pp 3–4). Across studies, results from

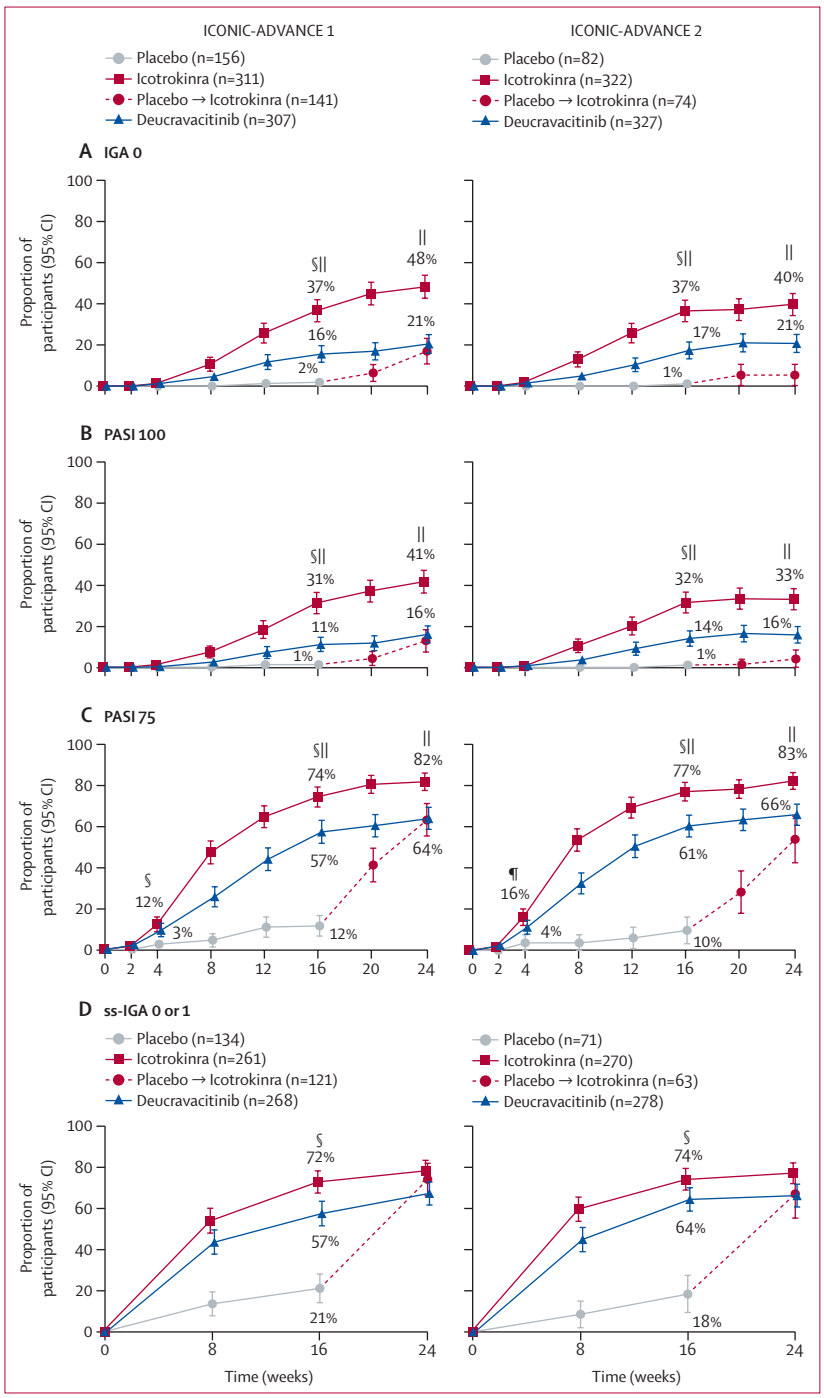

***Figure 3*: Proportions of participants achieving IGA 0, PASI 100, PASI 75, and ss-IGA 0 or 1* by treatment group over time†‡**

IGA=Investigator's Global Assessment. PASI=Psoriasis Area and Severity Index. ss-IGA=scalp-specific Investigator's Global Assessment. *With a ≥2-grade improvement from baseline. †In ICONIC-ADVANCE 1, the rates of participants with missing IGA or PASI data at week 16 were 3% (5 of 156), 4% (14 of 311), and 5% (15 of 307) for the placebo, icotrokinra, and deucravacitinib groups, respectively. ‡In ICONIC-ADVANCE 2, the rates of participants with missing IGA or PASI data at week 16 were 5% (four of 82), 3% (11 of 322), and 3% (11 of 327) for the placebo, icotrokinra, and deucravacitinib groups, respectively. §Multiplicity-adjusted p<0·001, icotrokinra versus placebo. ¶Multiplicity-adjusted p<0·01, icotrokinra versus placebo. ||Multiplicity-adjusted p<0·001, icotrokinra versus deucravacitinib. Error bars represent 95% CI.

sensitivity, treatment policy estimand, and per-protocol analyses for coprimary endpoints were consistent with primary analysis results; coprimary endpoints remained significant across the range of imputed missing values, with no tipping point identified (appendix pp 5, 9).

In ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2, icotrokinra met all multiplicity-adjusted key secondary endpoints versus placebo at weeks 4, 8, and 16. Specifically, significantly higher proportions of icotrokinra-treated versus placebo-treated participants achieved complete skin clearance at week 16 (ADVANCE 1: IGA 0: 114 [37%] of 311 *vs* three [2%] of 156, treatment difference 95% CI 35% [29–41]; PASI 100: 97 [31%] of 311 *vs* two [1%] of 156, 30% [24–36]; both p<0·0001 and ADVANCE 2: IGA 0: 118 [37%] of 322 *vs* one [1%] of 82, 36% [28–42]; PASI 100: 102 [32%] of 322 *vs* one [1%] of 82, 30% [24–36]; both p<0·0001; figure 3A and B; appendix pp 3–4). In addition, a clear separation between icotrokinra and placebo in the proportion of participants achieving PASI 75 was observed as early as week 4 (ADVANCE 1: 38 [12%] of 311 *vs* four [3%] of 156, treatment difference 95% CI 10% [5–14], p=0·0006; ADVANCE 2: 52 [16%] of 322 *vs* three [4%] of 82, 12% [5–18], p=0·0039), and the separation continued to increase to week 16 (ADVANCE 1: 231 [74%] of 311 *vs* 18 [12%] of 156, treatment difference 95% CI 63% [55–69]; ADVANCE 2: 249 [77%] of 322 *vs* eight [10%] of 82, 68% [58–74]; both p<0·0001; figure 3C). Significantly higher proportions of participants receiving icotrokinra versus placebo achieved ss-IGA 0 or 1 at week 16 (ADVANCE 1: 189 [72%] of 261 *vs* 28 [21%] of 134, treatment difference 95% CI 51% [42–59]; ADVANCE 2: 199 [74%] of 270 *vs* 13 [18%] of 71, 56% [44–65]; both p<0·0001; figure 3D).

Significantly higher proportions of icotrokinra-treated versus placebo-treated participants reported resolution of psoriasis symptoms (PSSD Symptom score 0) at week 8 (ADVANCE 1: 24 [8%] of 286 *vs* three [2%] of 142, treatment difference 95% CI 6% [1–11], p=0·011; ADVANCE 2: 27 [9%] of 298 *vs* one [1%] of 71, 8% [–1 to 12], p=0·025) and week 16 (ADVANCE 1: 68 [24%] of 286 *vs* four [3%] of 142, treatment difference 95% CI 21% [15–27]; ADVANCE 2: 64 [21%] of 298 *vs* 0 of 71, 22% [15–27]; both p<0·0001; appendix p 11). Among those with a baseline PSSD Itch score of at least 4, significantly higher proportions of icotrokinra-treated than placebo-treated participants reported early improvements in itch, as measured by CMI (≥4 points) in PSSD Itch score at week 4 (ADVANCE 1: 56 [22%] of 251 *vs* eight [7%] of 115, treatment difference 95% CI 15% [8–22], p=0·0003; ADVANCE 2: 54 [21%] of 258 *vs* three [5%] of 61, 16% [2–24], p=0·0078) and week 16 (ADVANCE 1: 155 [62%] of 251 *vs* 19 [17%] of 115, treatment difference 95% CI 45% [35–54]; ADVANCE 2: 155 [60%] of 258 *vs* nine [15%] of 61, 46% [34–56]; both p<0·0001; appendix p 11).

Compared with deucravacitinib, icotrokinra met all multiplicity-controlled key secondary endpoints at week 16 and week 24 in each study, showing superiority (appendix pp 3–4). In ICONIC-ADVANCE 1, higher proportions of participants receiving icotrokinra versus deucravacitinib achieved PASI 75 (231 [74%] of 311 *vs* 176 [57%] of 307, treatment difference 95% CI 17% [10–24]), PASI 90 (171 [55%] of 311 *vs* 91 [30%] of 307, 25% [18–33]), and IGA 0 or 1 (213 [68%] of 311 *vs* 154 [50%] of 307, 18% [11–26]) at week 16 (all p<0·0001); corresponding response rates at week 24 were 254 (82%) of 311 versus 196 (64%) of 307, 18% (11–25); 205 (66%) of 311 versus 127 (41%) of 307, 24% (17–32); and 230 (74%) of 311 versus 161 (52%) of 307, 22% (14–29), respectively (all p<0·0001; appendix pp 3–4). Findings were consistent in ICONIC-ADVANCE 2, showing higher response rates with icotrokinra versus deucravacitinib at week 16 (PASI 75: 249 [77%] of 322 *vs* 198 [61%] of 327, treatment difference 95% CI 17% [10–24]; PASI 90: 184 (57%) of 322 *vs* 111 [34%] of 327, 23% [16–30]; IGA 0 or 1: 227 [70%] of 322 *vs* 177 [54%] of 327, 16% [9–24]; all p<0·0001) and at week 24 (PASI 75: 266 [83%] of 322 *vs* 216 [66%] of 327, 17% [10–23], p<0·0001; PASI 90: 208 [65%] of 322 *vs* 141 [43%] of 327, 22% [14–29], p<0·0001; IGA 0 or 1: 220 [68%] of 322 *vs* 179 [55%] of 327, 14% [6–21], p=0·0002).

The proportions of participants achieving completely clear skin at week 16 were at least two-fold greater among those who received icotrokinra versus deucravacitinib (ADVANCE 1: PASI 100: 97 [31%] of 311 *vs* 34 [11%] of 307, treatment difference 95% CI 20% [14–26] and IGA 0: 114 [37%] of 311 *vs* 48 [16%] of 307, 21% [14–28]; ADVANCE 2: PASI 100: 102 [32%] of 322 *vs* 46 [14%] of 327, 18% [11–24] and IGA 0: 118 [37%] of 322 *vs* 57 [17%] of 327, 19% [13–26]; all p<0·0001), and the icotrokinra response rates generally increased up to week 24 (ADVANCE 1: PASI 100: 129 [41%] of 311 *vs* 49 [16%] of 307, treatment difference 95% CI 26% [19–32] and IGA 0: 150 [48%] of 311 *vs* 63 [21%] of 307, 28% [20–35]; ADVANCE 2: PASI 100: 107 [33%] of 322 *vs* 52 [16%] of 327, 17% [11–24] and IGA 0: 128 [40%] of 322 *vs* 68 [21%] of 327, 19% [12–26]; all p<0·0001; appendix pp 3–4). A clear separation between the icotrokinra and deucravacitinib ss-IGA 0 or 1 response rates was observed as early as week 8 (ADVANCE 1: 140 [54%] of 261 *vs* 116 [43%] of 268 and ADVANCE 2: 160 [59%] of 270 *vs* 124 [45%] of 278); rates of scalp clearance with icotrokinra continued to increase to week 16 (189 [72%] of 261 *vs* 153 [57%] of 268 and 199 [74%] of 270 *vs* 178 [64%] of 278) and to week 24 (203 [78%] of 261 *vs* 179 [67%] of 268 and 207 [77%] of 270 *vs* 183 [66%] of 278; figure 3D).

Patient-reported outcomes were consistent with the clinically derived findings. Significantly higher proportions of participants in the icotrokinra groups than in the deucravacitinib groups reported PSSD Symptom score 0 at week 16 (ADVANCE 1: 68 [24%] of 286 *vs* 25 [9%] of 272, treatment difference 95% CI 14% [8–21], p<0·0001; ADVANCE 2: 64 [21%] of 298 *vs* 36 [13%] of 287, 9% [3–15], p=0·0039; appendix p 11), and numerically higher proportions of icotrokinra-treated than deucravacitinib-treated participants reported a CMI in PSSD Itch score at week 16 (appendix p 11). Response rates in the icotrokinra group increased to week 24 across these patient-reported outcomes, maintaining a clear separation versus deucravacitinib.

Among participants randomly assigned to placebo who transitioned to icotrokinra at week 16, the proportions of

	Placebo-controlled (weeks 0–16)			Active-comparator controlled (weeks 0–24)		Crossover (weeks 16–24)
	Icotrokinra	Placebo	Deucravacitinib	Icotrokinra	Deucravacitinib	Placebo→icotrokinra
Number of participants	632	237	634	632	634	215
Mean weeks of follow-up (SD)	15·9 (1·88)	15·5 (2·69)	15·8 (2·25)	23·5 (3·26)	23·3 (3·94)	8·1 (0·58)
≥1 adverse event	303 (48%)	136 (57%)	360 (57%)	359 (57%)	411 (65%)	60 (28%)
Adverse events occurring in ≥5% of participants†						
Headache	26 (4%)	11 (5%)	19 (3%)	28 (4%)	20 (3%)	3 (1%)
Nasopharyngitis	37 (6%)	13 (5%)	58 (9%)	56 (9%)	77 (12%)	8 (4%)
Upper respiratory tract infection	23 (4%)	8 (3%)	33 (5%)	32 (5%)	49 (8%)	7 (3%)
Serious adverse event	14 (2%)	4 (2%)	14 (2%)	18 (3%)	20 (3%)	3 (1%)
Serious infection‡	1 (<1%)	1 (<1%)	4 (1%)	3 (<1%)	4 (1%)	0
Adverse event resulting in discontinuation	13 (2%)	12 (5%)	14 (2%)	15 (2%)	17 (3%)	0
Gastrointestinal adverse event	45 (7%)	15 (6%)	63 (10%)	55 (9%)	80 (13%)	5 (2%)
Malignancy§	3 (<1%)	1 (<1%)	1 (<1%)	3 (<1%)	2 (<1%)	0
Active tuberculosis	0	0	0	0	0	0

Values are n (%) unless otherwise noted. *The safety analysis set included all randomly assigned and treated participants. †In any treatment group. ‡Serious infections included bacterial arthritis (placebo group), campylobacter colitis (deucravacitinib group), viral infection (deucravacitinib group), infection exacerbated by chronic obstructive airways disease (icotrokinra group), lower respiratory tract infection (deucravacitinib group), viral upper respiratory tract infection (deucravacitinib group), and pneumonia (icotrokinra group). §Details on malignancies reported through week 24 of both studies are provided in the appendix (pp 2–3).

Table 2: **Combined adverse events from the ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 safety analysis sets***

participants achieving IGA 0 or 1 and PASI 90 markedly increased from week 16 to week 24 (figure 2). Other endpoints showed similar response patterns, including increased proportions of participants achieving IGA 0, PASI 100, PASI 75, and ss-IGA 0 or 1 (figure 3). Consistent with clinical outcomes, patient-reported symptoms of psoriasis improved after transition from placebo to icotrokinra (appendix p 11).

Safety findings were consistent across both trials, and adverse event rates from each study are summarised separately in the appendix (pp 6–7). Safety data from the two studies were combined to provide a larger sample size to identify any potentially uncommon adverse events, yielding 632, 237, and 634 participants in the icotrokinra, placebo, and deucravacitinib groups, respectively. Up to week 16, 303 (48%) of 632, 136 (57%) of 237, and 360 (57%) of 634 participants in the icotrokinra, placebo, and deucravacitinib groups, respectively, had at least one adverse event. The most common adverse events were nasopharyngitis and upper respiratory tract infections (table 2). Gastrointestinal adverse events occurred in 45 (7%) of 632, 15 (6%) of 237, and 63 (10%) of 634 participants in each of the combined icotrokinra, placebo, and deucravacitinib groups, respectively. Rates of serious adverse events were low, occurring in 2% (14 of 632, four of 237, and 14 of 634, respectively) of participants in each treatment group, and serious infections were rare (≤1% of participants in each group; one of 632, one of 237, and four of 634, respectively). Five instances of malignancy were reported across both studies to week 16: three in the icotrokinra group (pancreatic carcinoma, breast cancer, and keratoacanthoma [verbatim term squamous cell carcinoma (SCC) keratoacanthoma type]), one in the placebo group (invasive ductal breast carcinoma), and one in the deucravacitinib group (right buccal SCC); all events were considered unrelated to study treatments by investigators (appendix pp 1–2). To week 16, the proportions of participants with clinical laboratory abnormalities were low and similar between groups. Two participants in the icotrokinra group with substantial underlying risk factors died (appendix p 2).

To week 24, fewer participants in the combined icotrokinra versus deucravacitinib groups had at least one adverse event (359 [57%] of 632 and 411 [65%] of 634, respectively). The most common adverse events remained nasopharyngitis and upper respiratory tract infection. To week 24, gastrointestinal adverse event rates were lower in icotrokinra-treated participants (55 [9%] of 632) than in deucravacitinib-treated participants (80 [13%] of 634). Rates of oral herpes and acne were less than 1% each (four of 632 and three of 632, respectively) with icotrokinra and 12 (2%) of 634 and 23 (4%) of 634, respectively, with deucravacitinib. To week 24, serious adverse events occurred in 18 (3%) of 632 participants in the icotrokinra group and 20 (3%) of 634 in the deucravacitinib group; serious infections were rare, with no more than 1% in either group (three of 632 and four of 634, respectively). Across studies, one additional malignancy (malignant melanoma in situ) was reported in a participant in the deucravacitinib group of ICONIC-ADVANCE 2 between weeks 16 and 24.

Among participants who transitioned to icotrokinra from placebo at week 16, the icotrokinra safety profile from weeks 16 to 24 was consistent with that observed during the placebo-controlled period. Between weeks 16 and 24, 60 (28%) of 215 participants who transitioned to icotrokinra reported an adverse event. As during the placebo-controlled period, upper respiratory tract infection and nasopharyngitis were the most common adverse events; few participants (three [1%] of 215) who transitioned from placebo to icotrokinra at week 16 reported serious adverse events.

Discussion

Both coprimary endpoints and all key secondary endpoints were met in each of ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2. After 16 weeks of treatment, participants receiving icotrokinra had significantly higher IGA 0 or 1 and PASI 90 response rates versus placebo. In both studies, approximately one-third of icotrokinra-treated participants achieved completely clear skin (PASI 100 or IGA 0) at week 16 and 33–48% did so by week 24. Icotrokinra showed superiority to placebo across multiple outcome measures, including scalp clearance and patient-reported disease symptoms. Across both studies, the response rates seen in the icotrokinra groups were consistent with those seen in previous phase 2 and 3 clinical trials of icotrokinra[17,18] and were similar to rates of skin clearance (eg, PASI 90 response rates ranging from approximately 60–70% at week 16) reported for several of the injectable biologics approved to treat moderate-to-severe plaque psoriasis.[14] As early as week 4, clear and significant differences in PASI 75 response and a CMI in PSSD Itch score were observed between the icotrokinra and placebo groups. Consistent early and substantial improvements in clinical and patient-reported outcomes were observed following transition from placebo to icotrokinra.

Icotrokinra also showed superiority to deucravacitinib across clinician-reported and patient-reported outcomes in both studies. The proportions of participants achieving complete skin clearance (IGA 0 and PASI 100) were more than two-fold greater with icotrokinra than with deucravacitinib at week 16, with icotrokinra response rates maintaining or increasing to week 24. Of note, deucravacitinib response rates in the current studies were within the range of those previously reported in phase 3 studies of deucravacitinib (eg, 27–36% of participants achieved PASI 90 response at week 16).[15,28]

The safety profile of icotrokinra in these studies was similar to that of placebo to week 16 and was consistent with previous studies of icotrokinra.[17,18] Modest increases in adverse event rates were observed in both the icotrokinra and deucravacitinib groups at week 24

versus week 16, probably owing to the additional 8 weeks of follow-up. However, no safety signals were observed with icotrokinra to week 24, even when safety data from both studies were combined to afford a larger data set. Adverse event rates to week 24 were lower with icotrokinra than with deucravacitinib. Adverse events reported in the deucravacitinib group were similar to the safety profile seen in previous clinical studies of deucravacitinib.[15,28] Higher rates of oral herpes (2%) and acne (4%) were observed with deucravacitinib than with icotrokinra (both <1%) to week 24.

Surveys indicate that patients with moderate-to-severe plaque psoriasis consider mode of administration an important factor in choosing a treatment and show a preference for oral versus injectable delivery as well as an interest in oral treatment options with high-level efficacy and favourable safety.[8,29] In contrast to injectable biologics for plaque psoriasis, icotrokinra is a once-daily oral pill, allowing patients to self-administer without the need for injections. Further, compared with injections, oral delivery simplifies storage and transportation, potentially facilitating adherence and diminishing the effect of treatment administration on lifestyle.

The strengths of these studies include the large number of participants across various geographical regions, which might be representative of patients with moderate-to-severe plaque psoriasis in clinical practice. The icotrokinra groups were evaluated against both placebo and active-comparator controls, and the studies included several validated clinician-reported and patient-reported outcomes of disease, providing a comprehensive evaluation of treatment responses. The results shown here are limited by the duration of the reporting period (up to week 24); longer-term data from these 3-year studies will provide a more complete understanding of the magnitude and durability of responses and long-term safety.

Icotrokinra, a targeted oral peptide that selectively blocks the IL-23 receptor, consistently showed superior efficacy to placebo and deucravacitinib across two large, multicentre, phase 3 studies. Icotrokinra has the potential to provide high rates of skin clearance with a safety profile similar to placebo in a once-daily pill.

Contributors

LSG, AWA, RB, NM, RBV, MSe, MLG, AT, MA, PW, MSi, JR-M, SG, JW, AG-C, BS, YT, MC, BE, LKi, LKe, OR-S, BEE, JHC, CMCD, FN, and KAP provided input on the study design and contributed to the collection, analysis, and interpretation of the data. Y-KS, KC, and SL provided statistical analyses. All authors had access to the data and attest to its accuracy, provided critical review of the manuscript, and agreed to the decision to submit the manuscript for publication.

Declaration of interests

LSG is an investigator–advisor or speaker for AbbVie, Amgen, Arctis, Bristol Myers Squibb, Dermavant, Eli Lilly, Johnson & Johnson, Novartis, Pfizer, and UCB. AWA has served as a research investigator, scientific advisor, or speaker to AbbVie, Amgen, Arcutis, BMS, Boehringer Ingelheim, Dermavant Sciences, Eli Lilly, Galderma, Incyte, Johnson & Johnson, Leo Pharma, Novartis, Parexel, Pfizer, Regeneron, Sanofi, Takeda, and UCB. RB is an advisory board member, consultant, speaker, investigator for, or received honoraria or grants from AbbVie, Alumis, Amgen, AnaptysBio, Arcutis, BMS/Celgene, Eli Lilly, Johnson & Johnson, LEO Pharma, Organon, Nimbus, Takeda, UCB, VentyxBio, Vyne, Xencor, and Zurabio and is also an employee and shareholder of Innovaderm Research. NM has received honoraria for participation on advisory boards, as a speaker or for consultancy for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Dr. Wolff, Eli Lilly, Johnson & Johnson, La Roche-Posay, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB. RBV has received grants or research support, or speakers bureau–honoraria from AbbVie, Alumis, Amgen, Arcutis, Bausch, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Dermavant, Dermira, DICE, Galderma, Incyte, JAMP, Johnson & Johnson, Leo, Lilly, Meiji, Nimbus, Novartis, Organon, Orka, Pfizer, Sanofi, Sandoz, Sun, Takeda, UCB, and Zai. MS has received consulting fees or payment–honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from AbbVie, Almirall, Amgen, BMS, Leo Pharma, Sanofi, Galderma, UCB, Incyte, Johnson & Johnson, Lilly, Novartis, and Pfizer; has received payment for expert testimony from Apogee; and has received support for attending meetings or travel from AbbVie and Johnson & Johnson. MLG has served as an investigator for Amgen, BI, GSK, Johnson & Johnson, Lilly, Novartis, and Pfizer. AT has served as an investigator and received honoraria as advisor and speaker for Johnson & Johnson. MA has been a consultant or has received honoraria from AbbVie, Boehringer Ingelheim, Glenmark, Johnson & Johnson, Leo Pharma, Lilly, Novartis, Pfizer, and UCB Biopharma; has participated as an investigator in clinical studies; and has no other potential conflict of interest to declare. PW and MSi report no competing interests. JR-M has acted as consultant or speaker, or has received research funding from or participated in clinical trials for AbbVie, Almirall, Amgen, Boheringer Ingelheim, Bristol Myers Squibb, Johnson & Johnson, Leo Pharma, Lilly, Novartis, and UCB. SG served as an advisor, received speaker's honoraria or grants, or participated in clinical trials for AbbVie, Aceleryin, Adimune, Affibody, Akari Therapeutics, Almirall-Hermal, Alumis, Amgen, Apogee Therapeutics, Argenx, Aristea Therapeutics, AstraZeneca, Biogen Idec, Bioskin, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Galderma, Hexal, Incyte, Johnson & Johnson, Klinge Pharma, Kymab, LEO Pharma, Medac, MoonLake Immunotherapeutics, MSD, Neubourg Skin Care GmbH, Novartis, Pfizer, Pierre Fabre, Principia Biopharma, Regeneron Pharmaceuticals, Sandoz Biopharmaceuticals, Sanofi-Aventis, and UCB Pharma. 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Data sharing

The individual participant data collected for the study will not be made available. The data sharing policy of Johnson & Johnson is available at https://www.jnj.com/about-jnj/policies-and-positions/our-position-on-clinical-trial-data-transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access Project site at https://yoda.yale.edu.

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