



Safety of Icotrokinra Through 1 Year for the Treatment of Moderate-to-Severe Plaque Psoriasis and Psoriasis Affecting High-Impact Sites: Pooled Results Across the ICONIC-LEAD, ICONIC-TOTAL, and ICONIC-ADVANCE 1 and 2 Phase 3 Trials

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ABSTRACT

Introduction: Icotrokinra, a first-in-class targeted oral peptide, precisely blocks the interleukin (IL)-23 receptor and inhibits IL-23 pathway

signaling. In phase 3 studies (ICONIC-LEAD, ICONIC-TOTAL, ICONIC-ADVANCE 1 and 2), icotrokinra provided superior skin clearance versus placebo and deucravacitinib in adults and adolescents with moderate-to-severe psoriasis and psoriasis affecting high-impact sites. This

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analysis evaluates icotrokinra safety through 1 year using pooled data from these four studies.

Methods: Icotrokinra-randomized participants received 200-mg pills once daily, and placebo-randomized participants crossed over to icotrokinra at week 16; participants randomized to deucravacitinib 6 mg (ICONIC-ADVANCE 1 and 2 only) switched to icotrokinra at week 24. Pooled safety data are summarized for the placebo-controlled period (week 0–16, all studies), active-controlled period (week 0–24, ICONIC-ADVANCE 1 and 2), and through week 52 (all studies).

Results: During the placebo-controlled period across all studies, 568 participants received placebo and 1296 received icotrokinra. From week 0 to 24 in the ICONIC-ADVANCE studies, 632 participants received icotrokinra and 634 received deucravacitinib. Through week 52, 2400 icotrokinra-treated participants contributed 1840 participant-years [PY] of follow-up. Through week 16, in the icotrokinra and placebo groups, respectively, exposure-adjusted

incidence rates/100 PY of adverse events (AEs; 232 and 269), serious AEs (5.2 and 6.6), infections (91 and 104), and AEs leading to discontinuation (6.6 and 10.0) were comparable between groups. Through week 24, in the ICONIC-ADVANCE studies, rates/100 PY with icotrokinra versus deucravacitinib were as follows: AEs, 204 vs 265; serious AEs, 6.4 vs 7.2; infections, 81 vs 119; AEs leading to discontinuation, 5.7 vs 6.8. Through week 52, event rates/100 PY in icotrokinra-treated participants were as follows: AEs, 167; serious AEs, 4.6; infections, 76; AEs leading to discontinuation, 3.0.

Conclusion: In this analysis of 2400 icotrokinra-treated participants with psoriasis followed through 1 year, icotrokinra demonstrated favorable safety; event rates through week 16 were similar to placebo and remained consistent through week 52.

Infographic available for this article.

ClinicalTrials.gov: NCT06095115, NCT06095102, NCT06143878, NCT06220604.

Infographic

Safety of Icotrokinra Through 1 Year for the Treatment of Moderate-to-Severe Plaque Psoriasis and Psoriasis Affecting High-Impact Sites

Pooled Results Across the ICONIC-LEAD, -TOTAL, and -ADVANCE 1 and 2 Phase 3 Trials

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A NOVEL ORAL THERAPY

Icotrokinra is a first-in-class targeted oral peptide that precisely blocks the IL-23 receptor and inhibits the IL-23 pathway.



RECENTLY FDA APPROVED

Approved to treat moderate-to-severe plaque psoriasis in adults and adolescents.

COMPREHENSIVE POOLED SAFETY ANALYSIS

This manuscript presents a comprehensive pooled safety analysis of data from four Phase 3 studies in patients with moderate-to-severe plaque psoriasis and psoriasis affecting high-impact sites

ICONIC TRIALS

LEAD: Adults & adolescents with moderate-to-severe psoriasis, icotrokinra vs placebo

TOTAL: Adults & adolescents with high-impact site psoriasis, icotrokinra vs placebo

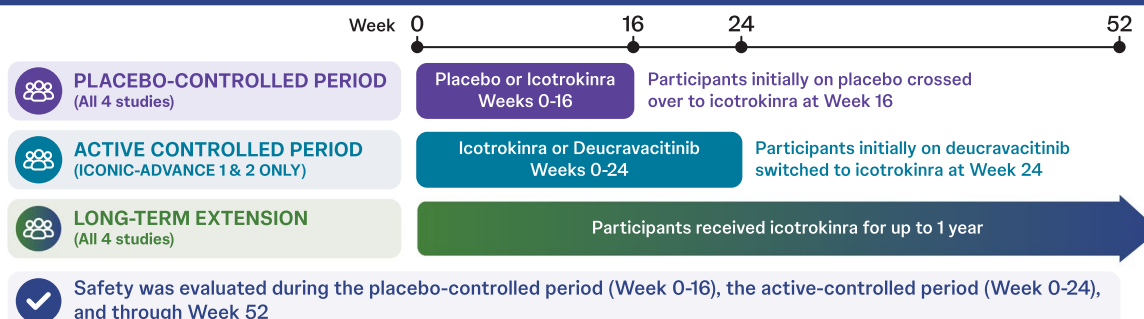
ADVANCE 1 & 2: Adults with moderate-to-severe psoriasis, icotrokinra vs placebo and deucravacitinib

2,400
Adults and adolescents received icotrokinra

1,840
Participant-years of exposure

Up to 1 YEAR
of treatment

STUDY DESIGN: COMPARISON WITH PLACEBO AND ACTIVE COMPARATOR



KEY SAFETY RESULTS: EXPOSURE-ADJUSTED INCIDENCE RATES (PER 100 PARTICIPANT-YEARS)

SAFETY OUTCOME	WEEK 0-16 (Placebo-Controlled)		WEEK 0-24 (Active Comparator: Deucravacitinib)*		THROUGH WEEK 52
	Placebo (N=568)	Icotrokinra (N=1296)	Icotrokinra (N=632)	Deucravacitinib (N=634)	All Icotrokinra (N=2400)
Adverse Events (AEs)	269	232	204	265	167
Serious Adverse Events (SAEs)	6.6	5.2	6.4	7.2	4.6
AEs Leading to Discontinuation	10.0	6.6	5.7	6.8	3.0
Infections	104	91	81	119	76
Serious Infections	1.1	0.5	1.1	1.8	0.7
Active or Latent Tuberculosis Events	0	0	0	0	0
Major Adverse Cardiovascular Events (MACE)	0	0.8	0.7	1.1	0.2
Malignancy (excluding NMSC)	0.5	1.3	0.7	0.7	0.4
Gastrointestinal AEs	21.4	22.7	20.3	31.0	13.0

*ICONIC-ADVANCE 1 and 2 studies only for Week 0-24 comparison.

NMSC, non-melanoma skin cancer.



Rates remained stable with up to 1 year of icotrokinra treatment.

CONCLUSION: Icotrokinra had a favorable safety profile.

- Safety event rates were **similar with icotrokinra and placebo** through Week 16.
- The safety profile of icotrokinra **remained consistent** through 1 year of treatment.
- The favorable icotrokinra safety profile supports its use as a new oral treatment option for adults and adolescents with moderate-to-severe plaque psoriasis and psoriasis affecting high-impact sites.



The infographic represents the opinions of the authors. For a full list of declarations, including funding and author disclosure statements, and copyright information, please see the full text online.

PEER-REVIEWED
FEATURE

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Keywords: Icotrokinra;
Deucravacitinib; Oral; Psoriasis

Safety;

Key Summary Points

Why carry out this study?

Icotrokinra is a first-in-class targeted oral peptide that precisely blocks the interleukin-23 receptor and inhibits interleukin-23 pathway signaling; in the ICONIC phase 3 psoriasis clinical trial program, icotrokinra demonstrated significant efficacy compared with placebo and deucravacitinib.

Data across the four ICONIC phase 3 studies were pooled to evaluate safety in 2400 participants who were treated with icotrokinra for up to 1 year (1840 participant-years of exposure).

What was learned from the study?

Pooled safety event rates in icotrokinra-treated participants were similar to those observed with placebo (week 0–16) and were stable through 1 year of treatment.

Results of this analysis support a favorable safety profile of icotrokinra, a new oral therapy for adults and adolescents with moderate-to-severe psoriasis and psoriasis affecting high-impact sites.

cases, individuals with moderate-to-severe psoriasis or psoriasis affecting high-impact sites (e.g., scalp, genitals, hands, and feet) require continuous long-term treatment with systemic therapy to achieve sustained skin clearance [2–4]. Biologic therapies targeting interleukin (IL)-23 are highly effective and have safety profiles that are generally considered to be more favorable than those of several other systemic therapies [5–9]. However, biologics are only available by injection or infusion, which can be undesirable and inconvenient for many patients [10, 11]. Studies show that up to 50% of children and adolescents and up to 30% of adults have a fear of needles, and this fear has resulted in many patients and providers reporting a willingness to make psoriasis treatment decisions that may compromise efficacy in favor of oral administration [11–13]. In some regions (e.g., USA, China), surveys show that roughly 90% of patients and providers would prefer oral over injectable treatments, especially if other treatment characteristics (e.g., efficacy, safety, and cost) were similar [10, 14–16].

The conventional oral psoriasis therapies of cyclosporine, methotrexate, and acitretin have limited efficacy and/or are associated with serious side effects and major monitoring requirements [17–19]. Newer advanced oral therapies, including the phosphodiesterase 4 inhibitor apremilast and the tyrosine kinase 2 (TYK2) inhibitor deucravacitinib, provide modest efficacy relative to biologics [4, 20] and have limitations related to safety, including observed gastrointestinal intolerance with apremilast and risk of infections and acne with TYK2 inhibitors [21–23].

Icotrokinra (JNJ-77242113) is a first-in-class targeted oral peptide that precisely blocks the IL-23 receptor and inhibits IL-23 pathway signaling. Icotrokinra was recently approved by the US Food and Drug Administration to treat moderate-to-severe plaque psoriasis in adults and adolescents (≥ 12 years of age who weigh ≥ 40 kg) who are candidates for systemic therapy or phototherapy [24].

In the phase 3 ICONIC-LEAD [25], ICONIC-TOTAL [26], and ICONIC-ADVANCE 1 and 2 studies [27], icotrokinra provided significantly higher rates of clear or almost clear skin

DIGITAL FEATURES

This article is published with digital features, including an infographic to facilitate understanding of the article. To view digital features for this article go to <https://doi.org/10.6084/m9.figshare.33111116>.

INTRODUCTION

Psoriasis is a chronic, multisystem, immune-mediated disease that affects approximately 125 million people worldwide [1]. In many

Table 1 Overview of psoriasis phase 3 randomized controlled trials in the 52-week integrated icotrokinra safety analysis

	ICONIC-LEAD NCT06095115	ICONIC-TOTAL NCT06095102	ICONIC-ADVANCE 1 NCT06143878	ICONIC-ADVANCE 2 NCT06220604
Key inclusion criteria	Age $\geq$ 12 years IGA $\geq$ 3 PASI $\geq$ 12 BSA $\geq$ 10% Candidate for phototherapy or systemic treatment	Age $\geq$ 12 years IGA $\geq$ 2 BSA $\geq$ 1% At least 1 high-impact site with at least moderate psoriasis (ss-IGA $\geq$ 3, sPGA-G $\geq$ 3, or hf-PGA $\geq$ 3) Failed $\geq$ 1 topical therapy Candidate for phototherapy or systemic treatment	Age $\geq$ 18 years IGA $\geq$ 3 PASI $\geq$ 12 BSA $\geq$ 10% Candidate for phototherapy or systemic treatment	Age $\geq$ 18 years IGA $\geq$ 3 PASI $\geq$ 12 BSA $\geq$ 10% Candidate for phototherapy or systemic treatment
Treatment groups (randomization through week 52)	Icotrokinra ($N = 456$) 200 mg QD week 0–24 Week 24–52: randomized withdrawal and re-treatment based on PASI 75 and IGA 0/1 response (adults only; all adolescents continued icotrokinra) Placebo ($N = 228$) Placebo QD week 0–16 Icotrokinra 200 mg QD week 16–52	Icotrokinra ($N = 208$) 200 mg QD week 0–52 Placebo ($N = 103$) Placebo QD week 0–16 Icotrokinra 200 mg QD week 16–52	Icotrokinra ($N = 311$) 200 mg QD week 0–52 Placebo ($N = 156$) Placebo QD week 0–16 Icotrokinra 200 mg QD week 16–52 Deucravacitinib ($N = 307$) Deucravacitinib 6 mg QD week 0–24 Icotrokinra 200 mg QD week 24–52	Icotrokinra ($N = 322$) 200 mg QD week 0–52 Placebo ($N = 82$) Placebo QD week 0–16 Icotrokinra 200 mg QD week 16–52 Deucravacitinib ($N = 327$) Deucravacitinib 6 mg QD week 0–24 Icotrokinra 200 mg QD week 24–52

BSA body surface area, hf-PGA Physician's Global Assessment of hands and feet, IGA Investigator's Global Assessment, PASI Psoriasis Area and Severity Index, QD once daily, sPGA-G Static Physician's Global Assessment of Genitalia, ss-IGA scalp-specific Investigator's Global Assessment

compared with placebo at week 16 in adults and adolescents with moderate-to-severe plaque psoriasis and psoriasis affecting high-impact sites. Icotrokinra also demonstrated superior skin clearance versus deucravacitinib at week 16 and 24 in adults with moderate-to-severe psoriasis [27], and provided significant improvements in participant-reported psoriasis symptoms, including itch, across all studies [25–27].

This analysis evaluated the safety profile of icotrokinra through 1 year using pooled data from the ICONIC-LEAD, ICONIC-TOTAL, and ICONIC-ADVANCE 1 and 2 studies, which included 2400 participants exposed to icotrokinra for 1840 participant-years (PY).

METHODS

Studies and Participants

Safety data were pooled from the four randomized, double-blind, phase 3 studies of icotrokinra described in Table 1 [25–27]. These four studies were conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with Good Clinical Practice. All study protocols were approved by an institutional review board or ethics committee. All participants provided written informed consent.

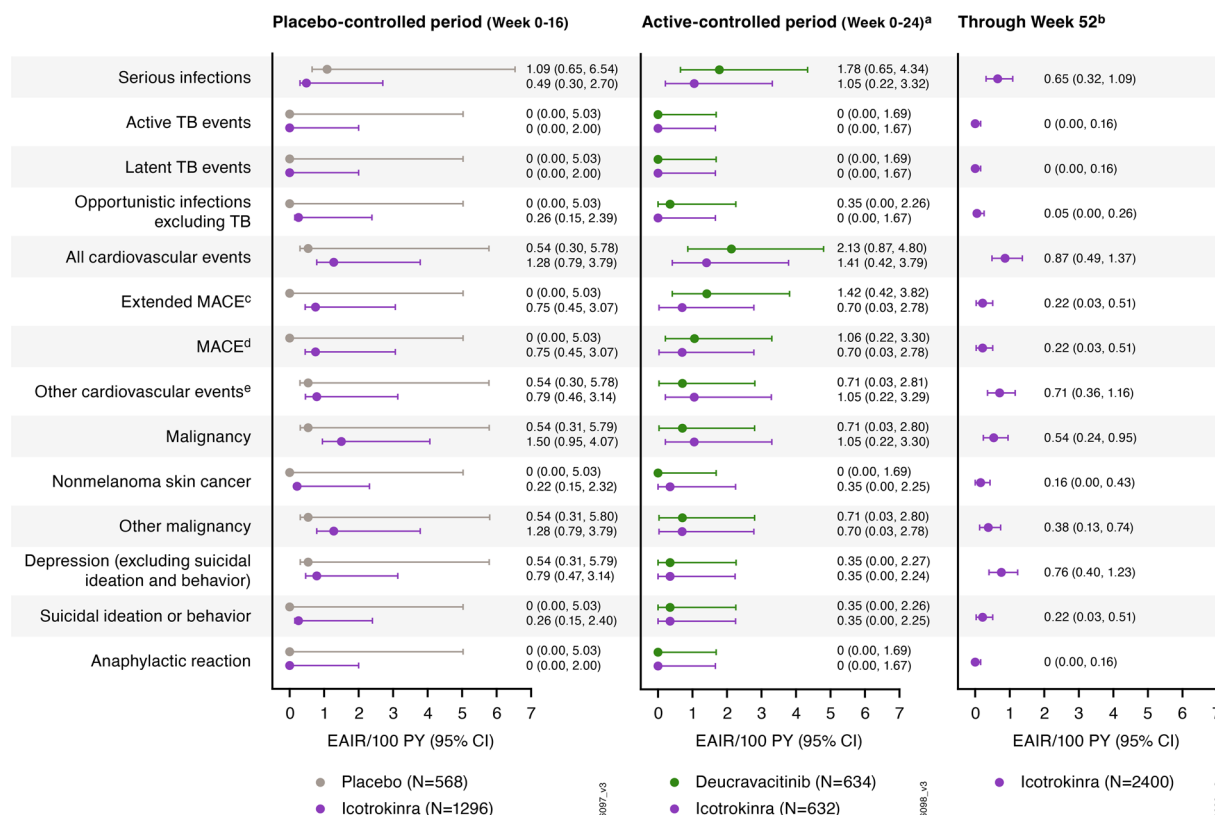


Fig. 1 Exposure-adjusted rates of participants with events per 100 PY of follow-up (95% CI) for specific adverse events during the placebo- and active-controlled periods and through 1 year. CI, confidence interval; EAIR, exposure-adjusted incidence rate; MACE, major adverse cardiovascular event; PY, participant-years; TB, tuberculosis. To account for the different placebo-to-icotrokinra randomization ratio in ICONIC-ADVANCE 2 versus the other studies, week 0–16 rates were adjusted by the total follow-up from the combined placebo and icotrokinra treatment groups in a study. ^aICONIC-ADVANCE 1 and 2 studies only. ^bIncludes data for participants randomized to icotrokinra, data after week 16 for participants randomized to placebo who crossed over to icotrokinra, and data after week 24 for participants randomized to deucra-

vacitinib who switched to icotrokinra. For the ICONIC-LEAD study, events that occurred during the withdrawal period (on or after week 28 and before re-treatment) were excluded for participants who were re-randomized to placebo at week 24. ^cIncludes all MACE events, hospitalization for unstable angina, and coronary revascularization (without myocardial infarction, unstable angina, or heart failure). ^dIncludes cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke. ^eIncludes transient ischemic attack, venous and peripheral arterial vascular thrombotic events, congestive heart failure, cardiac arrhythmia (no evidence of ischemia), and other serious non-MACE cardiovascular events such as syncope of a cardiovascular origin and severe/accelerated hypertension leading to hospitalization

All studies included a 16-week placebo-controlled period, and ICONIC-ADVANCE 1 and 2 also included a 24-week active-controlled period with deucravacitinib [27]. ICONIC-LEAD included a randomized-withdrawal and re-treatment period during which adults who achieved $\geq 75\%$ improvement in Psoriasis Area and Severity Index (PASI 75) or Investigator's

Global Assessment 0 or 1 (cleared skin or minimal disease) with ≥ 2 -grade improvement from baseline at week 24 were re-randomized 1:1 to continue icotrokinra or switch to placebo. Those who switched to placebo were re-treated with icotrokinra 200 mg once daily upon loss of $\geq 50\%$ of their week 24 PASI improvement.

Full eligibility criteria for all studies have been reported previously [25–27]. ICONIC-LEAD and ICONIC-TOTAL enrolled adults and adolescents (≥ 12 years of age); ICONIC-ADVANCE 1 and 2 enrolled adults (≥ 18 years of age). Relevant to safety analyses, individuals with stable concomitant medical conditions considered not to interfere with evaluation of psoriasis or compromise participant well-being were generally eligible for enrollment if all other inclusion and exclusion criteria were satisfied. Individuals were not eligible to participate if they had a current diagnosis or signs or symptoms of severe, progressive, or uncontrolled renal, hepatic, cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, psychiatric, or metabolic disturbances. Adults were excluded if they had a history of suicidal ideation or behavior in the 26 weeks prior to screening and were considered at risk by the investigator. Adolescents were excluded if they had suicidal ideation or non-suicidal self-injurious behavior in the 26 weeks prior to screening or a history of any suicidal behavior in their lifetime. Individuals were also excluded if they tested positive at screening for hepatitis B infection, hepatitis C infection, or HIV; had a history of chronic or recurrent infectious disease; had a history of known or suspected immunodeficiency; had a serious infection within 8 weeks of screening; tested positive for or had been exposed to COVID-19 within 4 weeks of the first dose of study agent; had a current malignancy or history of malignancy within 5 years of screening (except adequately treated, nonrecurrent nonmelanoma skin cancer [NMSC] or cervical cancer in situ); or had a history of signs or symptoms of active tuberculosis (TB) at screening. Individuals with latent TB infection (LTBI) identified during screening were eligible if active TB was ruled out. In the ICONIC-LEAD and ICONIC-TOTAL studies, preventive treatment of LTBI was at the discretion of the investigator. LTBI treatment was required in the ICONIC-ADVANCE 1 and 2 studies because this is a label requirement for deucravacitinib [28].

Individuals who received prior treatment with icotrokinra or who had primary efficacy failure with ≥ 1 agent directly targeting IL-23

were excluded from all studies. Those with previous exposure to deucravacitinib or primary efficacy failure with any TYK2 inhibitor were excluded from the ICONIC-ADVANCE studies. Use of B cell-depleting agents was prohibited within 26 weeks of the first dose of study agent. Use of biologic therapy was prohibited within 12 weeks or 5 half-lives (whichever is longer) of the first dose of study agent. Other systemic immunomodulators and phototherapy were prohibited within 4 weeks, and topical medications that could affect psoriasis evaluations were prohibited within 2 weeks of the first dose of study agent. Live virus or bacterial vaccination and BCG vaccination were prohibited within 4 weeks and 1 year, respectively, prior to the first dose of study agent.

Safety Assessments

The safety analysis population included all randomized participants who received at least one dose of study drug. Safety was evaluated using pooled data across the four pivotal ICONIC phase 3 studies, including participants randomized and treated with placebo or icotrokinra through week 16 in all studies and participants randomized and treated with deucravacitinib or icotrokinra through week 24 in the ICONIC-ADVANCE studies. Icotrokinra pooled safety results through week 52 include data for participants randomized to icotrokinra, data after week 16 for participants randomized to placebo who crossed over to icotrokinra, and data after week 24 for participants randomized to deucravacitinib who switched to icotrokinra. ICONIC-LEAD data collected during the withdrawal period (on or after week 28 and before re-treatment) were excluded for participants who were re-randomized to placebo at week 24.

Adverse events (AEs) were classified using the Medical Dictionary for Regulatory Activities (MedDRA) version 27.0. Protocol-defined AEs of special interest included malignancies, active TB, and possible Hy's law (defined as alanine aminotransferase [ALT] or aspartate aminotransferase [AST] ≥ 3 times the upper limit of normal (ULN) together with total bilirubin ≥ 2 times

ULN or international normalized ratio (INR) > 1.5, if measured). Cardiovascular and opportunistic infection adjudicated events were identified using Standardized MedDRA Query (SMQ) and/or high-level term. Positively adjudicated cardiovascular events were defined as (1) major adverse cardiovascular events (MACE; cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke), (2) extended MACE (includes MACE, hospitalization for unstable angina, and coronary revascularization), or (3) other cardiovascular events (defined in Fig. 1 footnote e). Positively adjudicated opportunistic infection events were categorized as (1) opportunistic or (2) TB (active or latent). Other AEs analyzed included treatment-emergent serious infections (i.e., infections reported as serious AEs [SAEs]), gastrointestinal AEs, hepatic AEs (including hepatic events leading to discontinuation and serious hepatic events [MedDRA SMQ of drug-related hepatic disorders—comprehensive search (narrow scope)]), hypersensitivity reactions, anaphylactic reactions, suicidal ideation and behavior, and depression (excluding suicidal ideation and behavior).

Statistical Analyses

Treatment-emergent AEs were defined as new or worsening AEs occurring at or after initiation of study intervention and within 4 weeks after the last dose or treatment discontinuation. Rates of AEs, AEs leading to study drug discontinuation, SAEs, infections, and other AEs of interest were adjusted for duration of follow-up and reported per 100 PY. Study-size adjusted Wald statistics were used to calculate 95% confidence intervals (CIs) for these types of AEs. In addition, study-size adjusted Wald statistics with continuity corrections were used to create 95% CIs for AEs of serious infections, active TB, treatment-emergent LTBI, opportunistic infections, cardiovascular events, malignancies, depression, suicidal ideation and behavior, hypersensitivity reactions, and anaphylactic reactions.

To contextualize the frequency of malignancy, the National Institutes of Health Surveillance, Epidemiology, and End Results (SEER) database (2000–2021) was used to estimate the expected number of individuals with malignancies in the

general US population, adjusting for age, sex, and race. Standardized incidence ratios (SIRs) were calculated as the number of malignancies other than NMSC and cervical cancer in situ reported in icotrokinra-treated participants divided by the expected number of malignancies in the general US population [29].

RESULTS

Participants

Across the four ICONIC phase 3 studies, there were 2498 participants included in the pooled safety analysis population. Baseline demographic and disease characteristics were generally similar across studies. Participants were predominantly male (66.8%) and White (76.4%), with a mean (standard deviation [SD]) age of 45.2 (14.5) years and mean (SD) body mass index of 29.5 (6.9) kg/m². Consistent with differences in study design, participants in ICONIC-TOTAL had lower mean PASI scores and lower mean percent body surface area affected by psoriasis at baseline than in the other studies. Baseline medical history shows that roughly half of participants in ICONIC-TOTAL and ICONIC-ADVANCE 1 and 2 reported current or former use of nicotine products, compared with 40% in ICONIC-LEAD; differences may be due to inclusion of 66 adolescents in ICONIC-LEAD. Common comorbidities (affecting > 10% of participants) included hypertension, hyperlipidemia, psoriatic arthritis, and diabetes mellitus (Table 2). Roughly half of all participants in each study had previously used conventional systemic therapies, and between one-quarter and one-third of participants had previously used ≥ 1 biologic therapy (Table 3).

Across all four studies, during the 16-week placebo-controlled period, 568 participants received placebo (170 PY) and 1296 received icotrokinra (395 PY). During the 24-week active-controlled period in ICONIC-ADVANCE 1 and 2, 632 participants received icotrokinra (285 PY) and 634 received deucravacitinib (283 PY). Through week 52 in all studies, 2400 participants received icotrokinra (1840 PY). In the ICONIC-LEAD

Table 2 Baseline demographics, psoriasis disease characteristics, and medical history by study (safety analysis population)

	ICONIC-LEAD	ICONIC-TOTAL	ICONIC-ADVANCE 1	ICONIC-ADVANCE 2	Total
Participants, <i>n</i>	684	311	772	731	2498
Demographic characteristics					
Age, years	42.6 (16.4)	44.7 (14.3)	46.7 (13.4)	46.1 (13.6)	45.2 (14.5)
Sex, <i>n</i> (%)					
Male	447 (65.4)	200 (64.3)	526 (68.1)	496 (67.9)	1669 (66.8)
Female	237 (34.6)	111 (35.7)	246 (31.9)	235 (32.1)	829 (33.2)
Race, <i>n</i> (%)					
White	494 (72.2)	243 (78.1)	568 (73.6)	604 (82.6)	1909 (76.4)
Asian	167 (24.4)	61 (19.6)	180 (23.3)	89 (12.2)	497 (19.9)
Black or African American	8 (1.2)	2 (0.6)	11 (1.4)	22 (3.0)	43 (1.7)
American Indian or Alaska Native	1 (0.1)	0	3 (0.4)	2 (0.3)	6 (0.2)
Native Hawaiian or other Pacific Islander	2 (0.3)	0	2 (0.3)	5 (0.7)	9 (0.4)
Multiple	1 (0.1)	1 (0.3)	0	3 (0.4)	5 (0.2)
Unknown or not reported	11 (1.6)	4 (1.3)	8 (1.0)	6 (0.8)	29 (1.2)
Weight, ^a kg	86.2 (22.2)	85.7 (22.1)	87.4 (22.7)	89.0 (20.6)	87.3 (21.9)
Body mass index, ^b kg/m ²	29.3 (7.0) ^a	29.2 (7.1)	29.5 (7.1)	29.8 (6.5)	29.5 (6.9)
Psoriasis characteristics					
Age at psoriasis diagnosis, years	25.7 (14.9)	28.6 (15.1)	29.4 (15.3)	28.6 (15.3)	28.0 (15.2)
Duration of psoriasis, years	17.1 (13.5)	16.3 (12.4)	17.4 (12.2)	17.6 (13.1)	17.2 (12.8)
PASI (range, 0–72)	19.9 (7.5)	14.4 (7.4)	20.1 (7.3)	19.8 (6.9)	19.2 (7.5)
Percent BSA affected	25.5 (15.0)	16.0 (12.9)	26.2 (15.6)	25.8 (14.2)	24.6 (15.1)
IGA, <i>n</i> (%)					
2 (mild)	0	17 (5.5)	0	0	17 (0.7)
3 (moderate)	514 (75.1)	226 (72.7)	614 (79.5)	586 (80.2)	1940 (77.7)
4 (severe)	170 (24.9)	68 (21.9)	158 (20.5)	145 (19.8)	541 (21.7)
Medical history, <i>n</i> (%)					
Psoriatic arthritis	91 (13.3)	50 (16.1)	121 (15.7)	93 (12.7)	355 (14.2)
Coronary artery disease	13 (1.9)	7 (2.3)	20 (2.6)	14 (1.9)	54 (2.2)
Myocardial infarction	5 (0.7)	1 (0.3)	13 (1.7)	10 (1.4)	29 (1.2)
Angina pectoris	0	2 (0.6)	2 (0.3)	3 (0.4)	7 (0.3)
Coronary artery bypass graft	1 (0.1)	2 (0.6)	4 (0.5)	2 (0.3)	9 (0.4)

Table 2 continued

	ICONIC-LEAD	ICONIC-TOTAL	ICONIC-ADVANCE 1	ICONIC-ADVANCE 2	Total
Percutaneous coronary intervention	3 (0.4)	2 (0.6)	9 (1.2)	5 (0.7)	19 (0.8)
Peripheral vascular disease	5 (0.7)	6 (1.9)	17 (2.2)	7 (1.0)	35 (1.4)
Transient ischemic attack	2 (0.3)	1 (0.3)	2 (0.3)	0	5 (0.2)
Stroke	3 (0.4)	0	7 (0.9)	3 (0.4)	13 (0.5)
Diabetes mellitus	77 (11.3)	36 (11.6)	91 (11.8)	76 (10.4)	280 (11.2)
Hyperlipidemia	102 (14.9)	62 (19.9)	153 (19.8)	131 (17.9)	448 (17.9)
Hypertension	172 (25.1)	79 (25.4)	240 (31.1)	220 (30.1)	711 (28.5)
Asthma	35 (5.1)	15 (4.8)	41 (5.3)	47 (6.4)	138 (5.5)
Depression	37 (5.4)	30 (9.6)	47 (6.1)	57 (7.8)	171 (6.8)
Chronic liver disease ^c	19 (2.8)	12 (3.9)	29 (3.8)	18 (2.5)	78 (3.1)
Skin squamous cell carcinoma	2 (0.3)	1 (0.3)	3 (0.4)	3 (0.4)	9 (0.4)
Skin basal cell carcinoma	3 (0.4)	1 (0.3)	5 (0.6)	5 (0.7)	14 (0.6)
Ulcerative colitis	2 (0.3)	1 (0.3)	4 (0.5)	3 (0.4)	10 (0.4)
Crohn's disease	1 (0.1)	1 (0.3)	1 (0.1)	1 (0.1)	4 (0.2)
Anxiety	43 (6.3)	29 (9.3)	48 (6.2)	50 (6.8)	170 (6.8)
Current or former nicotine use ^d	273 (39.9)	142 (45.7)	396 (51.3)	358 (49.0)	1169 (46.8)
Current or former alcohol use ^e	338 (49.4)	195 (62.7)	487 (63.1)	441 (60.3)	1461 (58.5)
Family history or early coronary artery disease ^f	43 (6.3)	21 (6.8)	48 (6.2)	49 (6.7)	161 (6.4)
Family history of cancer in 1st degree relative ^g	117 (17.1)	62 (19.9)	168 (21.8)	149 (20.4)	496 (19.9)
Family history of psoriasis	249 (36.4)	112 (36.0)	264 (34.2)	273 (37.3)	898 (35.9)
Family history of myocardial infarction	68 (9.9)	36 (11.6)	101 (13.1)	82 (11.2)	287 (11.5)
Family history of stroke	53 (7.7)	38 (12.2)	85 (11.0)	61 (8.3)	237 (9.5)

Data are presented as mean (standard deviation) unless otherwise specified

BSA body surface area, *IGA* Investigator's Global Assessment, *PASI* Psoriasis Area and Severity Index

^aICONIC-TOTAL, *n* = 305; ICONIC-ADVANCE 2, *n* = 730; total, *n* = 2491

^bICONIC-LEAD, *n* = 682; ICONIC-TOTAL, *n* = 304; ICONIC-ADVANCE 2, *n* = 729, total, *n* = 2487

^cE.g., fatty liver disease, alcohol-induced, cirrhosis

^dIncludes cigarettes, cigars, pipes, smokeless tobacco, patches/gum, and e-cigarettes or equivalent

^eIncludes beer, wine, and distilled spirits

^fDiagnosed at age < 55 years

^gExcluding skin squamous cell and basal cell carcinomas

and ICONIC-TOTAL studies, 72 adolescent participants were exposed to icotrokinra (98.6% [71/72] were exposed for at least 6 months, and 62.5% [45/72] were exposed for 1 year).

Adverse Events

During the 16-week placebo-controlled period, exposure-adjusted incidence rates (EAIRs; defined as the number of participants with events per 100 PY) of AEs were 232/100 PY and 269/100 PY in the icotrokinra and placebo groups, respectively. In the ICONIC-ADVANCE studies through week 24, EAIRs of AEs were 204/100 PY and 265/100 PY in the icotrokinra and deucravacitinib groups, respectively. The EAIR of AEs in the icotrokinra group did not increase over time and was 167/100 PY through week 52 (Table 4). The EAIRs of SAEs were 5.20/100 PY and 6.55/100 PY in the icotrokinra and placebo groups, respectively, through week 16, 6.40/100 PY and 7.18/100 PY in the icotrokinra and deucravacitinib groups, respectively, through week 24,

and 4.58/100 PY with icotrokinra through week 52. EAIRs of severe AEs were 5.32/100 PY and 9.45/100 PY with icotrokinra and placebo through week 16, 4.96/100 PY and 6.46/100 PY with icotrokinra and deucravacitinib through week 24, and 3.86/100 PY with icotrokinra through week 52 (Table 4). The EAIR of AEs leading to discontinuation was 6.60/100 PY in the icotrokinra group and 10.0/100 PY in the placebo group through week 16; EAIRs through week 24 were 5.66/100 PY and 6.77/100 PY, respectively, in the icotrokinra and deucravacitinib groups. The EAIR of AEs leading to discontinuation remained stable for all icotrokinra-treated participants through week 52 (2.95/100 PY) (Table 4).

Through week 52, three deaths (hematemesis, myocardial infarction, and toxicity to various agents) with confounding factors were reported in icotrokinra-treated participants. These deaths are described in previous reports of pooled data from the ICONIC-ADVANCE 1 and 2 studies [27, 30].

Table 3 Previous psoriasis medications by study (safety analysis population)

	ICONIC-LEAD	ICONIC-TOTAL	ICONIC-ADVANCE 1	ICONIC-ADVANCE 2	Total
Participants, <i>n</i>	684	311	772	731	2498
Topical agents, <i>n</i> (%) ^a	589 (86.1)	309 (99.4)	668 (86.5)	648 (88.6)	2214 (88.6)
Conventional nonbiologic therapy, <i>n</i> (%) ^b	326 (47.7)	158 (50.8)	401 (51.9)	367 (50.2)	1252 (50.1)
Biologic therapy, <i>n</i> (%) ^c	233 (34.1)	103 (33.1)	206 (26.7)	181 (24.8)	723 (28.9)
Phototherapy, <i>n</i> (%) ^d	203 (29.7)	124 (39.9)	265 (34.3)	238 (32.6)	830 (33.2)
Oral nonbiologic systemic therapy, <i>n</i> (%) ^e	54 (7.9)	22 (7.1)	71 (9.2)	31 (4.2)	178 (7.1)

JAK Janus kinase, *PDE4* phosphodiesterase 4, *PUVA* psoralen + ultraviolet B, *UVB* ultraviolet B

^aIncludes topical anthralin, calcineurin inhibitors, calcipotriene and other vitamin D analogues, corticosteroids, JAK inhibitors, PDE4 inhibitors, and tazarotene

^bIncludes PUVA, methotrexate, cyclosporin, acitretin, azathioprine, and fumarate

^cIncludes etanercept, infliximab, adalimumab, ustekinumab, briakinumab, secukinumab, ixekizumab, brodalumab, guselkumab, risankizumab, tildrakizumab, alefacept, efalizumab, natalizumab, and certolizumab pegol

^dIncludes PUVA or UVB

^eIncludes apremilast, deucravacitinib (ICONIC-LEAD and ICONIC-TOTAL only), and tofacitinib

Table 4 Key safety results during the placebo- and active-controlled periods and through 1 year

	Placebo-controlled period (week 0–16) ^a		Active-controlled period (week 0–24) ^b		Through week 52 ^c
	Placebo	Icetrokinra	Icetrokinra	Deucravacitinib	Icetrokinra
Treated participants, <i>n</i>	568	1296	632	634	2400
Total PY of follow-up	170	395	285	283	1840
Median PY of follow-up	0.3	0.3	0.5	0.5	0.7
Average duration of follow-up, weeks	15.6	15.9	23.5	23.3	40.0
EAIRs of events per 100 PY of follow-up (95% CI) ^d					
≥ 1 AE	269 (237, 300)	232 (214, 250)	204 (183, 225)	265 (240, 291)	167 (158, 175)
AEs leading to discontinuation	10.0 (5.17, 14.9)	6.60 (4.05, 9.14)	5.66 (2.89, 8.44)	6.77 (3.73, 9.83)	2.95 (2.17, 3.74)
≥ 1 SAE	6.55 (2.84, 10.2)	5.20 (2.97, 7.42)	6.40 (3.46, 9.40)	7.18 (4.03, 10.3)	4.58 (3.60, 5.57)
≥ 1 AE of severe intensity	9.45 (4.73, 14.2)	5.32 (3.04, 7.60)	4.96 (2.37, 7.57)	6.46 (3.48, 9.44)	3.86 (2.96, 4.76)

AE adverse event, CI confidence interval, EAIR exposure-adjusted incidence rate, PY participant-years, SAE serious AE

^aTo account for the different placebo-to-icetrokinra randomization ratio in ICONIC-ADVANCE 2 versus the other studies, rates were adjusted by the total follow-up from the combined placebo and icetrokinra treatment groups in a study

^bICONIC-ADVANCE 1 and 2 studies only

^cIncludes data for participants randomized to icetrokinra, data after week 16 for participants randomized to placebo who crossed over to icetrokinra, and data after week 24 for participants randomized to deucravacitinib who switched to icetrokinra. For the ICONIC-LEAD study, events that occurred during the withdrawal period (on or after week 28 and before re-treatment) were excluded for participants who were re-randomized to placebo at week 24

^dDefined as the number of participants with events per 100 PY

Infections

EAIRs of infections were 91.0/100 PY and 104/100 PY in the icetrokinra and placebo groups, respectively, through week 16, 81.3/100 PY and 119/100 PY in the icetrokinra and deucravacitinib groups through week 24, and 75.8/100 PY in icetrokinra-treated participants through week 52. Nasopharyngitis and upper respiratory tract infection were the most common infections in all treatment groups and treatment periods. Nasopharyngitis EAIRs were 24.7/100 PY and 24.1/100 PY in the icetrokinra and placebo groups, respectively, through week 16; 20.5/100 PY and 29.2/100 PY in the icetrokinra and deucravacitinib groups, respectively, through week 24; and 21.4/100 PY in icetrokinra-treated

participants through week 52. Upper respiratory tract infection EAIRs were 16.1/100 PY and 17.6/100 PY with icetrokinra and placebo, respectively (week 0–16), 12.2/100 PY and 18.0/100 PY with icetrokinra and deucravacitinib, respectively (week 0–24), and 13.9/100 PY among all icetrokinra-treated participants through week 52. Notable other infection AEs that were more common with deucravacitinib than with icetrokinra through week 24 in ICONIC-ADVANCE 1 and 2 included oral herpes (4.29/100 PY vs 1.41/100 PY) and folliculitis (3.20/100 PY vs 1.41/100 PY).

EAIRs of serious infections were low through week 16 in the icetrokinra (0.49/100 PY) and placebo (1.09/100 PY) groups and through week 24 in the icetrokinra (1.05/100 PY) and

deucravacitinib (1.78/100 PY) groups (Fig. 1). Serious infections in participants who received icotrokinra through week 16 included one event each of bacterial gastroenteritis and infective exacerbation of chronic obstructive airways disease. Serious infections in the placebo group included one event each of bacterial arthritis and COVID-19 pneumonia with sepsis. Through week 24 and after week 16, two additional serious infections were reported in the ICONIC-ADVANCE icotrokinra group, infective exacerbation of chronic obstructive airways disease and pneumonia. Serious infections reported through week 24 with deucravacitinib were one event each of wound infection, viral infection, campylobacter colitis, viral upper respiratory tract infection, and lower respiratory tract infection. The serious infection EAIR remained low through week 52 in the icotrokinra group (0.65/100 PY).

Through week 52, there was one icotrokinra-treated participant (EAIR, 0.05/100 PY) with two positively adjudicated opportunistic infection events of fungal laryngitis with confounding factors (smoker, inhaled salbutamol, and oral prednisone). There was also one deucravacitinib-treated participant with an opportunistic infection of lower respiratory tract infection that tested positive for *Legionella* bacteria.

There were no AEs of active TB or LTBI through week 52 in any treatment group. Of note, 173 participants had LTBI at or prior to screening; 17.9% (31/173) received no LTBI treatment before or during the study, including 30 participants who were exposed to icotrokinra.

Malignancies

From week 0–16 across all four studies, there was 1 (0.54/100 PY) malignancy in the placebo group (invasive ductal breast cancer) and 6 (1.50/100 PY) malignancies in the icotrokinra group (Fig. 1). The malignancies in the icotrokinra group included one participant with two events of squamous cell carcinoma (SCC; keratoacanthoma type, days 35 and 66) who had

prior history of keratoacanthoma, and one event each of malignant melanoma in situ (day 110) in a participant with prior history of malignant melanoma, prostate cancer (day 57) in a participant with elevated prostate-specific antigen level before baseline, colon adenocarcinoma (day 15) in a participant with pre-existing symptoms, pancreatic cancer with liver metastasis (day 60), and breast cancer (day 14). From week 0–24 in the ICONIC-ADVANCE studies, there were 2 (0.71/100 PY) malignancies (oral cavity SCC and malignant melanoma in situ) in the deucravacitinib group and no additional malignancies in the icotrokinra group (1.05/100 PY) other than those reported through week 16. Two additional NMSC events (both SCC; total NMSC EAIR = 0.16/100 PY) and two additional other malignancies (prostate cancer and chronic lymphocytic leukemia; total EAIR = 0.38/100 PY) were reported in icotrokinra-treated participants through week 52.

The number of malignancies other than NMSC and cervical cancer in situ among icotrokinra-treated participants through week 52 ($n = 7$) was similar to the number (adjusted for age, sex, and race) expected in the general US population ($n = 8.79$). The SIR (95% CI) for the icotrokinra-treated group versus SEER was 0.80 (0.32–1.64).

Positively Adjudicated Cardiovascular Events

From week 0–16, there were no MACE or extended MACE in the placebo group and three MACE (0.75/100 PY) in the icotrokinra group in participants with underlying risk factors: one cardiovascular death, one nonfatal myocardial infarction, and one nonfatal stroke. MACE EAIRs through week 24 in the ICONIC-ADVANCE studies were 0.70/100 PY with icotrokinra and 1.06/100 PY with deucravacitinib (extended MACE were 0.70/100 PY and 1.42/100 PY, respectively) (Fig. 1). Through week 52, there was one additional MACE (cardiovascular death reported as cocaine toxicity-induced hypertensive cardiovascular death), for a total of four MACE among the 2400 icotrokinra-treated participants (0.22/100 PY). The EAIR of other

cardiovascular events through week 52 was 0.71/100 PY. Across all time periods, there were no extended MACE (hospitalization for unstable angina or coronary revascularization without myocardial infarction, unstable angina, or heart failure) in any icotrokinra-treated participants, other than the MACE reported above.

Gastrointestinal Events

Through week 16, EAIRs of gastrointestinal AEs were 21.4/100 PY in the placebo group and 22.7/100 PY in the icotrokinra group; the most frequently reported AEs were diarrhea (placebo, 6.54/100 PY; icotrokinra, 6.92/100 PY) and nausea (placebo, 1.77/100 PY; icotrokinra, 3.83/100 PY). In the ICONIC-ADVANCE studies through week 24, EAIRs of gastrointestinal AEs were 20.3/100 PY in the icotrokinra group and 31.0/100 PY in the deucravacitinib group (diarrhea, 6.43/100 PY and 5.74/100 PY, respectively; nausea, 1.76/100 PY and 2.50/100 PY, respectively). Through week 52, the gastrointestinal disorders EAIR was 13.0/100 PY among icotrokinra-treated participants (diarrhea, 2.87/100 PY; nausea, 1.26/100 PY); gastrointestinal disorder SAEs were uncommon (0.33/100 PY).

Inflammatory bowel disease was defined as MedDRA preferred terms of Crohn's disease and ulcerative colitis. Through week 52, there was 1 (0.05/100 PY) AE of ulcerative colitis reported for a participant who switched from deucravacitinib to icotrokinra in ICONIC-ADVANCE 2. There were no AEs of Crohn's disease in any treatment group.

Hepatic Events

Through week 16, there were no hepatic SAEs in the placebo group and 2 (0.51/100 PY) hepatic SAEs in the icotrokinra group; there was also one hepatic AE leading to discontinuation in both the placebo (0.59/100 PY) and icotrokinra (0.25/100 PY) group. Through week 24 in ICONIC-ADVANCE 1 and 2, there was 1 (0.35/100 PY) hepatic SAE in the icotrokinra group and zero in the deucravacitinib group; there were no hepatic AEs

leading to discontinuation with icotrokinra and 1 (0.35/100 PY) with deucravacitinib. Through week 52, there was one additional hepatic SAE and no additional discontinuations due to hepatic AEs with icotrokinra. Across all studies through week 52, there were no cases of Hy's law.

Hypersensitivity

There were no serious hypersensitivity reactions in any treatment group, and no treatment-emergent anaphylactic reactions were reported through week 52 (Fig. 1).

Suicidal Ideation and Behavior and Depression

EAIRs for suicidal ideation or behavior reported during all assessment time periods are shown in Fig. 1. A total of four icotrokinra-treated participants reported suicidal ideation through week 52; all events were scored as 1 (least severe ideation) on the Columbia-Suicide Severity Rating Scale [31]. One deucravacitinib-treated participant reported suicidal ideation during the active-controlled period in ICONIC-ADVANCE 2. No participants in any study reported suicidal behavior.

AEs of depression excluding suicidal ideation and behavior were infrequent. Depression AEs were reported for 1 (0.54/100 PY) participant in the placebo group and 3 (0.79/100 PY) participants in the icotrokinra group through week 16, and for 1 (0.35/100 PY) participant each in the icotrokinra and deucravacitinib groups from week 0–24. Through week 52, a total of 14 (0.76/100 PY) icotrokinra-treated participants had AEs of depression (Fig. 1).

Safety in Adolescents

The safety profile of icotrokinra in the 72 adolescent participants in ICONIC-LEAD and ICONIC-TOTAL was consistent with that of the overall pooled safety population. No serious infections, malignancies, MACE, suicidal ideation or behavior, or deaths were reported in adolescent participants through week 52.

DISCUSSION

This analysis of pooled data through 1 year across the ICONIC phase 3 program (2400 participants; 1840 PY of follow-up) shows that icotrokinra had a favorable safety profile that was consistent over time. No safety signals were identified. Safety results through week 16 were similar for icotrokinra and placebo. EAIRs of AEs, AEs leading to discontinuation, SAEs, severe AEs, and infections were numerically lower with icotrokinra than with placebo.

The icotrokinra safety profile also compared favorably versus deucravacitinib. Through week 24 in ICONIC-ADVANCE 1 and 2, the overall EAIR for AEs was lower with icotrokinra based on non-overlapping 95% CIs (icotrokinra, 204/100 PY [183–225]; deucravacitinib, 265/100 PY [240–291]). This difference is due, in part, to higher incidence of AEs known to be associated with deucravacitinib, including infections (icotrokinra, 81.3/100 PY; deucravacitinib, 119/100 PY) and skin disorders (icotrokinra, 20.6/100 PY; deucravacitinib, 30.9/100 PY). Specific AEs reported as most common in deucravacitinib studies [21–23, 32] that were less common with icotrokinra versus deucravacitinib in the ICONIC program included nasopharyngitis (20.5 vs 29.2/100 PY), upper respiratory tract infection (12.2 vs 18.0/100 PY), acne (1.1 vs 8.4/100 PY), oral herpes (1.4 vs 4.3/100 PY), folliculitis (1.4 vs 3.2/100 PY), aphthous ulcer (0.0 vs 3.2/100 PY), and mouth ulceration (0.0 vs 2.1/100 PY).

In this analysis, the safety profile of the IL-23 receptor blocker icotrokinra was consistent with pooled safety results reported for biologic IL-23 inhibitors [5, 33]. No icotrokinra safety concerns have been identified based on observed AEs, SAEs, AEs leading to discontinuation, or specific AEs of interest (infections, malignancy, MACE, gastrointestinal AEs, hepatic AEs, hypersensitivity, depression, and suicidal ideation or behavior).

The safety profile of icotrokinra was consistent in adults and adolescents through 1 year. Most of the adolescents who participated in

the ICONIC studies (66 of 72) were enrolled in the ICONIC-LEAD study. ICONIC-LEAD adolescent safety results through week 52 show that EAIRs/100 PY of key safety outcomes were similar to results for the overall pooled population reported in this analysis (AEs, 164 vs 167; SAEs, 7.1 vs 4.6; infections, 77.7 vs 75.8; gastrointestinal AEs, 8.9 vs 13.0) [34].

Certain systemic treatments for psoriatic disease, including tumor necrosis factor- α inhibitors and Janus kinase inhibitors, increase TB risk [35]. Therefore, historical psoriasis treatment guidelines have recommended screening patients for TB before initiating treatment with deucravacitinib or biologic therapies and prescribing preventive treatment for individuals with LTBI [36–38]. However, on the basis of a comprehensive review of available clinical and real-world evidence, the National Psoriasis Foundation and International Psoriasis Council published updated guidance in November 2025 that LTBI screening is not required prior to or during treatment of psoriasis with IL-23 inhibitors [39]. Consistent with the data supporting these guidelines, there were no active TB or LTBI events in any icotrokinra-treated study participants in the ICONIC phase 3 program, which included 30 icotrokinra-treated participants with untreated LTBI.

To date, all available icotrokinra safety data are from randomized clinical trials, which required participants to meet inclusion criteria related to previous medical and treatment history. To fully characterize the icotrokinra safety profile, data are needed from prospective real-world studies. Post-marketing surveillance will provide safety data across broad populations of patients exposed to icotrokinra in real-world settings. Additionally, longer-term safety analyses will be important to more fully characterize risks for events with potentially long latency periods, such as cardiovascular events and malignancies.

CONCLUSION

In this pooled safety analysis of 2400 participants who were treated for up to 1 year in the ICONIC studies, icotrokinra was well tolerated. Safety event rates were similar in the icotrokinra and placebo groups through week 16. The safety profile of icotrokinra remained consistent through 1 year of treatment. The favorable safety profile observed for icotrokinra supports its use as a new oral treatment option for adults and adolescents with moderate-to-severe plaque psoriasis and psoriasis affecting high-impact sites.

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Declarations

Conflict of Interest. Mark G. Lebwohl is an employee of Mount Sinai and receives research funds from AbbVie, Arcutis, Avotres, Boehringer Ingelheim, Bristol Myers Squibb, Cara, Clexio, Dermavant, Eli Lilly, Incyte, Inozyme, Johnson & Johnson, Oruka, Pfizer, Sanofi-Regeneron, and UCB; and is a consultant for AbbVie, Added Health, Aikium, Almirall, AltruBio, Alumis, Amgen, Apogee, Arcutis, AstraZeneca, Atomwise,

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Ethical Approval. All studies were conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with Good Clinical Practice. All study protocols were approved by an institutional review board or ethics committee. All participants provided written informed consent.

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REFERENCES

1. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis: a review. *JAMA*. 2020;323(19):1945–60. <https://doi.org/10.1001/jama.2020.4006>.
2. Strober B, Ryan C, van de Kerkhof P, et al. Recategorization of psoriasis severity: Delphi consensus from the International Psoriasis Council. *J Am Acad Dermatol*. 2020;82(1):117–22. <https://doi.org/10.1016/j.jaad.2019.08.026>.
3. Strober B, Zhong Y, Sima A, et al. Criteria for identifying candidates for systemic psoriasis treatment in the real world: application of the International Psoriasis Council Guidelines in patients in North America. *J Psoriasis Psoriatic Arthritis*. 2024;10(1):22–7. <https://doi.org/10.1177/24755303241302070>.
4. Sbidian E, Chaimani A, Guelimi R, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. *Cochrane Database Syst Rev*. 2025;8(8):CD011535. <https://doi.org/10.1002/14651858.CD011535.pub7>.
5. Lebwohl MG, Merola JF, Rowland K, et al. Safety of guselkumab treatment for up to 5 years in patients with moderate-to-severe psoriasis: pooled analyses across seven clinical trials with more than 8600 patient-years of exposure. *Br J Dermatol*. 2023;189(1):42–52. <https://doi.org/10.1093/bjd/ljad115>.
6. Strober B, Coates LC, Lebwohl MG, et al. Long-term safety of guselkumab in patients with psoriatic disease: an integrated analysis of eleven phase II/III clinical studies in psoriasis and psoriatic arthritis. *Drug Saf*. 2024;47(1):39–57. <https://doi.org/10.1007/s40264-023-01361-w>.
7. Reich K, Gordon KB, Strober BE, et al. Five-year maintenance of clinical response and health-related quality of life improvements in patients with moderate-to-severe psoriasis treated with guselkumab: results from VOYAGE 1 and VOYAGE 2. *Br J Dermatol*. 2021;185(6):1146–59. <https://doi.org/10.1111/bjd.20568>.
8. Papp KA, Blauvelt A, Puig L, et al. Long-term safety and efficacy of risankizumab for the treatment of moderate-to-severe plaque psoriasis: interim analysis of the LIMMitless open-label extension trial up to 5 years of follow-up. *J Am Acad Dermatol*. 2023;89(6):1149–58. <https://doi.org/10.1016/j.jaad.2023.07.1024>.
9. Jairath V, Acosta Felquer ML, Cho RJ. IL-23 inhibition for chronic inflammatory disease. *Lancet*. 2024;404(10463):1679–92. [https://doi.org/10.1016/S0140-6736\(24\)01750-1](https://doi.org/10.1016/S0140-6736(24)01750-1).
10. Myers JT, Dam JV, Imran M, Hashim M, Dhalla AK. Preference for a novel oral alternative to parenterally administered medications. *Patient Prefer Adherence*. 2024;18:1547–62. <https://doi.org/10.2147/PPA.S463354>.
11. McLenon J, Rogers MAM. The fear of needles: a systematic review and meta-analysis. *J Adv Nurs*. 2019;75(1):30–42. <https://doi.org/10.1111/jan.13818>.
12. Smith SD, Fifer S, Edwards M, et al. Tradeoffs and decision-making in moderate to severe psoriasis for oral versus injectable treatments: data from patients and dermatologists in Australia. *J Dermatolog Treat*. 2024;35(1):2339440. <https://doi.org/10.1080/09546634.2024.2339440>.
13. Feldman SR, Holmen Moeller A, Erntoft Idemyr ST, González JM. Relative importance of mode of administration in treatment preferences among plaque psoriasis patients in the United States. *J Health Econ Outcomes Res*. 2016;4(2):141–57. <https://doi.org/10.36469/9817>.
14. Aletaha D, Husni ME, Merola JF, et al. Treatment mode preferences in psoriatic arthritis: a qualitative multi-country study. *Patient Prefer Adherence*. 2020;14:949–61. <https://doi.org/10.2147/PPA.S242336>.
15. Kuang Y, Li Y, Lv C, et al. Unmet needs and treatment preference of systemic treatments for moderate-to-severe psoriasis from the perspectives of patients and dermatologists in China. *Dermatol Ther (Heidelb)*. 2024;14(5):1245–57. <https://doi.org/10.1007/s13555-024-01159-3>.

16. Stein Gold L, Soung J, Trenkler N, et al. Unmet needs and disease burden: perspectives from adults with psoriasis and clinicians treating psoriasis in the US. *J of Skin* 2025;9(6):s644. <https://doi.org/10.25251/nkn06k92>.
17. Kalb RE, Strober B, Weinstein G, Lebwohl M. Methotrexate and psoriasis: 2009 National Psoriasis Foundation Consensus Conference. *J Am Acad Dermatol*. 2009;60(5):824–37. <https://doi.org/10.1016/j.jaad.2008.11.906>.
18. Rosmarin DM, Lebwohl M, Elewski BE, Gottlieb AB. Cyclosporine and psoriasis: 2008 National Psoriasis Foundation Consensus Conference. *J Am Acad Dermatol*. 2010;62(5):838–53. <https://doi.org/10.1016/j.jaad.2009.05.017>.
19. Menter A, Gelfand JM, Connor C, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol*. 2020;82(6):1445–86. <https://doi.org/10.1016/j.jaad.2020.02.044>.
20. Armstrong AW, Puig L, Joshi A, et al. Comparison of biologics and oral treatments for plaque psoriasis: a meta-analysis. *JAMA Dermatol*. 2020;156(3):258–69. <https://doi.org/10.1001/jamadermatol.2019.4029>.
21. Tan H, Chen X, Ou X, Chen Y. Safety evaluation of deucravacitinib: a real-world analysis based on the FDA adverse event reporting system database. *Int J Clin Pharm*. 2025;47(6):1821–9. <https://doi.org/10.1007/s11096-025-01980-6>.
22. Merola JF, Ferris LK, Sobell JM, et al. Deucravacitinib: adverse events of interest across phase 3 plaque psoriasis trials. *Dermatol Ther*. 2025;15(2):453–62. <https://doi.org/10.1007/s13555-025-01337-x>.
23. Xu Y, Liu X, Guo L, Jiang X. Adverse events associated with apremilast and deucravacitinib for psoriasis: a pharmacovigilance study based on the FAERS database. *Clin Cosmet Investig Dermatol*. 2025;18:1121–35. <https://doi.org/10.2147/CCID.S439643>.
24. ICOTYDE™ (icotrokinra). Package insert. Janssen Biotech, Inc., Horsham, PA, USA; 2026.
25. Bissonnette R, Soung J, Hebert AA, et al. Oral icotrokinra for plaque psoriasis in adults and adolescents. *N Engl J Med*. 2025;393(18):1784–95. <https://doi.org/10.1056/NEJMoa2504187>.
26. Gooderham M, Lain E, Bissonnette R, et al. Targeted oral peptide icotrokinra for psoriasis involving high-impact sites. *NEJM Evid* 2025;4(12):EVIDoa2500155. <https://doi.org/10.1056/EVIDoa2500155>.
27. Stein Gold L, Armstrong AW, Bissonnette R, et al. 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. *Lancet*. 2025;406(10510):1363–74. [https://doi.org/10.1016/S0140-6736\(25\)01576-4](https://doi.org/10.1016/S0140-6736(25)01576-4).
28. SOTYKTU™ (deucravacitinib). Package insert. Bristol Myers Squibb, Princeton, NJ, USA; 2026.
29. National Cancer Institute. Surveillance, Epidemiology and End Results Program. Overview of the SEER program. Available at: <http://SEER.cancer.gov/about/overview.html>. Accessed June 4, 2026.
30. Stein Gold L, Armstrong AW, Soung J, et al. Durability of response to icotrokinra in adults with moderate-to-severe plaque psoriasis: one-year results from the phase 3, placebo- and active comparator-controlled ICONIC-ADVANCE 1 & ICONIC-ADVANCE 2. *Br J Dermatol*. 2026. <https://doi.org/10.1093/bjd/ljag264>.
31. Posner K, Brown GK, Stanley B, et al. The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. *Am J Psychiatry*. 2011;168(12):1266–77. <https://doi.org/10.1176/appi.ajp.2011.10111704>.
32. Mansilla-Polo M, Morgado-Carrasco D. Biologics versus JAK inhibitors. Part II: risk of infections. a narrative review. *Dermatol Ther (Heidelb)*. 2024;14(8):1983–2038. <https://doi.org/10.1007/s13555-024-01203-2>.
33. Huang YW, Tsai TF. A drug safety evaluation of risankizumab for psoriasis. *Expert Opin Drug Saf*. 2020;19(4):395–402. <https://doi.org/10.1080/14740338.2020.1736034>.
34. Soung J, Lebwohl MG, Hebert A, et al. Improvements in clinical and patient-reported outcomes and durability of response with the targeted oral peptide icotrokinra in adolescents with moderate-to-severe plaque psoriasis: one-year results from the ICONIC-LEAD randomized controlled trial. *J Am Acad Dermatol*. 2026;S0190-9622(26)02677-0. <https://doi.org/10.1016/j.jaad.2026.05.035>.
35. Jha DK, Kakadiya R, Sharma A, Naidu S, De D, Sharma V. Assessment and management for latent tuberculosis before advanced therapies for immune-mediated inflammatory diseases: a comprehensive review. *Autoimmun Rev*. 2025;24(3):103758. <https://doi.org/10.1016/j.autrev.2025.103758>.

36. Torres T, Chiricozzi A, Puig L, et al. Treatment of psoriasis patients with latent tuberculosis using IL-17 and IL-23 inhibitors: a retrospective, multinational, multicentre study. *Am J Clin Dermatol*. 2024;25(2):333–42. <https://doi.org/10.1007/s40257-024-00845-4>.
37. Nogueira M, Warren RB, Torres T. Risk of tuberculosis reactivation with interleukin (IL)-17 and IL-23 inhibitors in psoriasis - time for a paradigm change. *J Eur Acad Dermatol Venereol*. 2021;35(4):824–34. <https://doi.org/10.1111/jdv.16866>.
38. Nast A, Altenburg A, Augustin M, et al. S3 guideline for the treatment of psoriasis vulgaris, adapted from EuroGuiDerm - part 1: treatment recommendations and monitoring. *JDDG J Dtsch Dermatol Ges*. 2026;24(1):122–37. <https://doi.org/10.1111/ddg.16002>.
39. Blauvelt A, Strober BE, Eakin GS, et al. Joint position statement from the National Psoriasis Foundation Medical Board and the International Psoriasis Council on routine testing for latent tuberculosis infection prior to and during treatment of psoriasis patients with interleukin 17 or interleukin 23 inhibitors. *J Am Acad Dermatol*. 2026;94(3):802–9. <https://doi.org/10.1016/j.jaad.2025.11.033>.

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