

Table 1 Overall summary of treatment-emergent AEs through week 16, week 24 and week 52

	Placebo-controlled (through week 16)		Active comparator-controlled (through week 24)		Through week 52		
	Placebo (N = 237)	Icotrekinra (N = 632)	Icotrekinra (N = 632)	Deucravacitinib (N = 634)	Placebo → icotrekinra (N = 215) ^b	Icotrekinra (N = 632)	Deucravacitinib → icotrekinra (N = 584) ^c
Combined ADVANCE 1 and ADVANCE 2 ^a							
Mean weeks per total PYs of follow-up	15.5/70.4	15.9/192.6	23.6/285.3	23.3/283.0	35.5/146.3	49.5/599.1	27.8/311.3
Any AE	137 (58)	308 (49)	368 (58)	417 (66)	148 (69)	466 (74)	317 (54)
Incidence per 100 PYs (95% CI)	316 (257–364)	230 (205–256)	207 (186–229)	269 (243–295)	186 (168–239)	167 (152–182)	165 (146–183)
Serious AE	4 (2)	14 (2)	18 (3)	20 (3)	8 (4)	31 (5)	17 (3)
Incidence per 100 PYs (95% CI)	6 (< 1–9)	7 (3–11)	6 (3–9)	7 (4–10)	6 (1–9)	5 (3–7)	6 (3–8)
AE leading to discontinuation	12 (5)	14 (2)	17 (3)	19 (3)	2 (1)	24 (4)	6 (1)
Incidence per 100 PYs (95% CI)	17 (7–25)	7 (3–11)	6 (3–9)	7 (4–10)	1 (0–3)	4 (2–6)	2 (< 1–3)
Infection	74 (31)	146 (23)	193 (31)	254 (40)	101 (47)	310 (49)	199 (34)
Incidence per 100 PYs (95% CI)	130 (96–154)	87 (72–100)	82 (70–93)	119 (104–134)	94 (80–121)	75 (66–83)	82 (70–92)
Serious infection	1 (< 1)	1 (< 1)	3 (< 1)	5 (1)	0	6 (1)	4 (1)
Incidence per 100 PYs (95% CI)	1 (0–9)	1 (0–3)	1 (< 1–3)	2 (< 1–4)	0 (0–4)	1 (< 1–2)	1 (< 1–4)
Gastrointestinal AE	14 (6)	45 (7)	55 (9)	82 (13)	15 (7)	83 (13)	37 (6)
Incidence per 100 PYs (95% CI)	21 (11–36)	24 (17–32)	20 (15–26)	31 (25–38)	11 (5–15)	15 (12–18)	12 (8–16)
Malignancy	1 (< 1)	3 (< 1)	3 (< 1)	2 (< 1)	0	4 (1)	2 (< 1)
Incidence per 100 PYs (95% CI)	1 (0–9)	2 (< 1–5)	1 (< 1–3)	1 (< 1–3)	0 (0–4)	1 (< 1–2)	1 (< 1–2)

AE, adverse event; CI, confidence interval; PYs, participant-years. Data are provided as *n* (%) unless otherwise noted. Incidence per 100 PYs: number of participants with AEs/total PYs at risk × 100. CI based on study-size adjusted Wald statistics, except malignancy, which was based on the Wald statistic with continuity correction. ^aSafety analysis set included all randomized and treated participants [ADVANCE 1 and 2: placebo, 155 and 82 (placebo → icotrekinra, 141 and 74); icotrekinra, 310 and 322; deucravacitinib, 307 and 327 (deucravacitinib → icotrekinra, 283 and 301)]. ^bIncludes data after week 16 for participants randomized to placebo who transitioned to receive icotrekinra. ^cIncludes data after week 24 for participants randomized to deucravacitinib who transitioned to receive icotrekinra.

(indicating very large effect on daily life). By week 24, 61–63% of participants randomized to icotrekinra achieved CMI in itch, 22–29% reported complete psoriasis symptom resolution, and 59–66% indicated no impact of psoriasis on their HRQoL; these improvements continued to increase to 73–75%, 39–45% and 64–70% by week 52, respectively. These findings demonstrate that long-term icotrekinra treatment not only provides durable skin clearance, but also delivers meaningful, sustained benefits in symptoms and HRQoL.

Previously reported ADVANCE 1 and 2 findings through week 24, in which icotrekinra met all coprimary and key secondary endpoints vs. placebo and deucravacitinib,¹⁵ are supported by novel findings through week 52 from participants who transitioned from placebo or deucravacitinib to icotrekinra at weeks 16 or 24, respectively. Participants who transitioned from placebo or deucravacitinib achieved clear or almost clear skin (71–80%), completely clear skin (42–57%), CMI in itch (76–84%), psoriasis symptom resolution (33–46%) and no impact of psoriasis on daily life (66–75%), comparable to those treated continuously with

icotrekinra through week 52. This evidence highlights that icotrekinra may provide benefits to patients previously treated with another oral psoriasis therapy.

Safety findings of icotrekinra through week 52 aligned with previously reported phase II/III data, showing a similar AE profile vs. placebo and numerically lower AE and infection rates vs. deucravacitinib.^{11,13–15,30,31} Exposure-adjusted AE rates with icotrekinra remained stable over time, and no new safety signals were observed through week 52. Taken together, these results support icotrekinra as a durable and efficacious systemic therapy option with a favourable safety profile for patients with moderate-to-severe plaque psoriasis.

Strengths of these studies include the large sample size, global enrolment, and evaluation of deucravacitinib transition, allowing assessment of both clinician-reported and patient-reported outcomes for icotrekinra following transition from deucravacitinib. One limitation was that only adults were included in these studies; however, results from adolescents enrolled in ICONIC-LEAD and ICONIC-TOTAL provide supportive evidence for this population.^{13,14,24,31}