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Sustained and Increasing Skin Clearance with Continuous Envudeucitinib in Moderate-to-Severe Plaque Psoriasis: Results from the ONWARD3 Long-Term Extension Study

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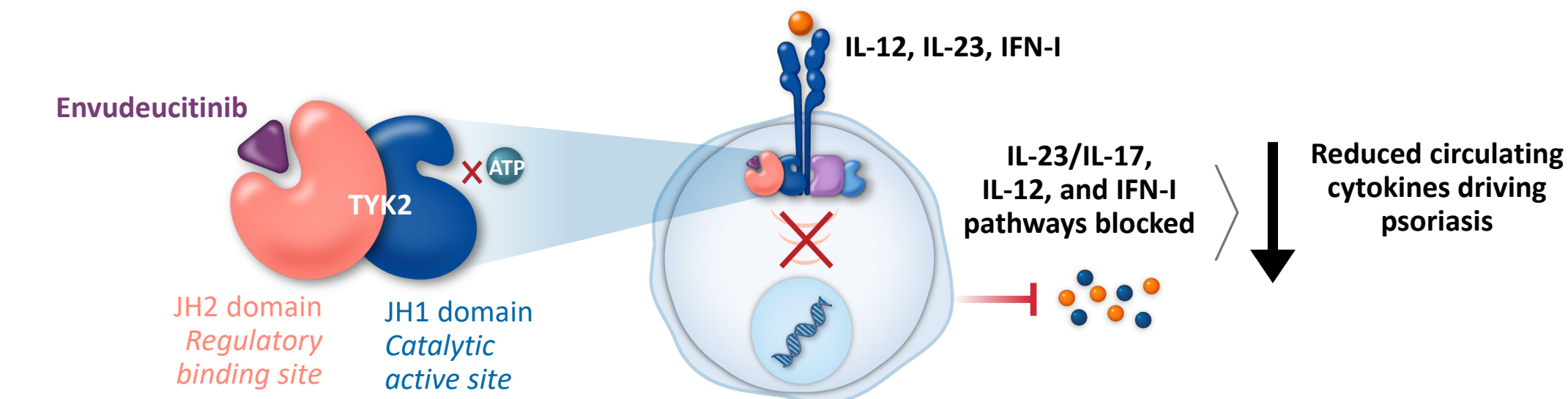
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Synopsis

- **Envudeucitinib** (ESK-001)*, a **next-generation**, oral, **allosteric** TYK2i, provides **maximal inhibition** over a 24-hour period in patients with psoriasis¹⁻³
- **Envudeucitinib** demonstrated **efficacy** across all **coprimary** and **key secondary endpoints**, with **favorable tolerability**, in the replicate Phase 3 **ONWARD1** and **ONWARD2** trials in moderate-to-severe psoriasis⁴
- **Objective:** Report maintenance of efficacy and safety through 48 weeks of total treatment in patients who completed ONWARD1 or 2 and enrolled in the ONWARD3 long-term extension

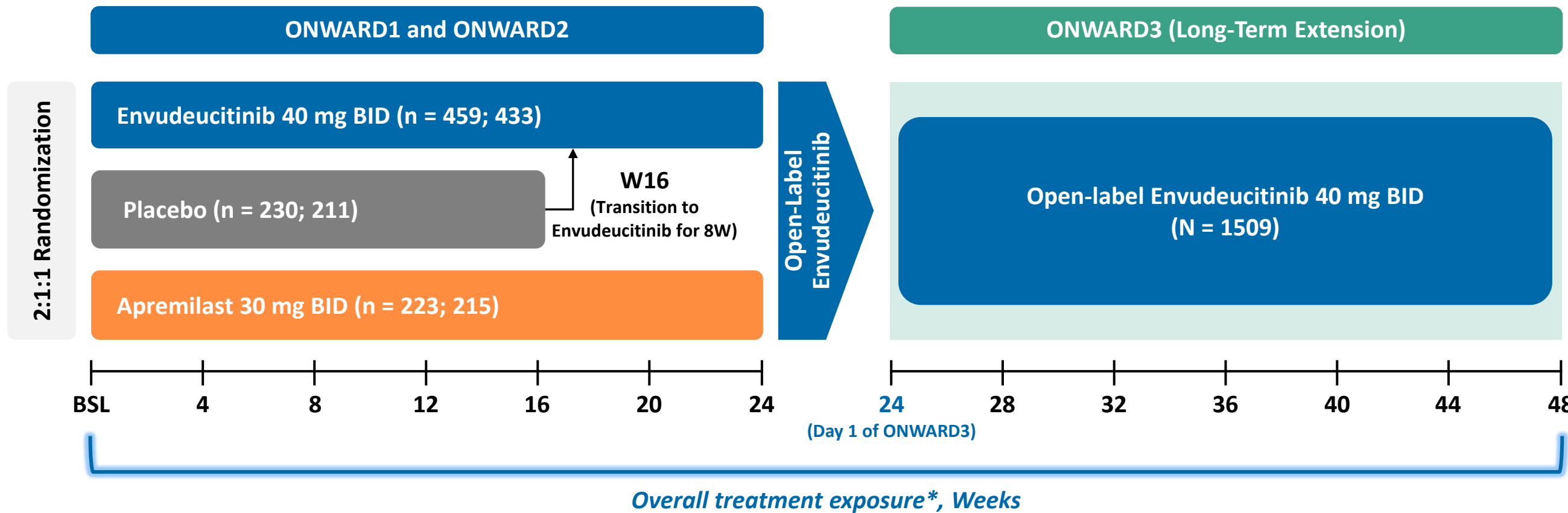
Figure 1. Envudeucitinib mechanism of action



IFN- γ , interferon type γ ; IL-12/17/23, interleukin 12/17/23; JH1/2, Janus kinase homology 1/2; TYK2i, tyrosine kinase 2 inhibitor.
*Envudeucitinib is an investigational therapy not reviewed or approved by any regulatory agency.

Methods

Figure 2. ONWARD3 study design



Reflects actual enrollment in ONWARD1 (NCT06586112); ONWARD2 (NCT06588738); ONWARD3 (NCT06846541). *Total envudeucitinib exposure differs by parent-study arm (Table 1).
BID, bis in die (twice daily); BSL, baseline; CI, confidence interval; DLQI 0/1, Dermatology Life Quality Index score of 0 or 1 (no effect); LTE, long-term extension; NRS, numeric rating scale; PASI 90, 90% or 100% improvement in Psoriasis Area and Severity Index; sPGA-Q/sPGA-Q/1, Static Physician's Global Assessment score of 0 (clear)/score of 1 (almost clear); ss, scalp-specific; W, week.

- Patients who completed Week 24 of ONWARD1 or 2, and consented were enrolled in ONWARD3
- All patients received open-label envudeucitinib for 24 weeks regardless of original treatment
 - Randomized treatment withdrawal period began after 24 weeks in ONWARD3 for first 200 patients; data not reported
- Maintenance of response assessed among patients that achieved a response at entry in ONWARD3 and maintained it after 48 weeks of continuous envudeucitinib for each respective endpoint
- Baseline response rates for ONWARD3 encompass 24 weeks treatment duration in ONWARD1 and 2 (Figure 2); PASI 90, 100, and NRS endpoints defined as long-term improvement, and analyses of ss-PGA, NRS, and DLQI are restricted to patients with parent baseline ss-PGA ≥ 3 , NRS ≥ 4 , and DLQI ≥ 2
- Exposure to envudeucitinib varied based on parent-study assignment (i.e., 48, 32, and 24 weeks for the parent-envudeucitinib, -placebo, and -apremilast, respectively)
- Nonresponse imputation applied; analyses are descriptive
- The 95% CIs for each arm's proportion are obtained using Clopper-Pearson methods

Conclusion

- **Continuous envudeucitinib treatment over 48 weeks was associated with sustained or improved efficacy responses and a generally favorable benefit/risk profile**
 - 75% and 54% had PASI 90 and PASI 100 responses
 - Over 80% achieved and maintained **clear or almost clear scalp**
 - Nearly 80% of patients reported clinically-meaningful improvements in **itch** and >70% demonstrated sustained **quality of life** improvements
- Patients transitioning to **envudeucitinib** showed rapid improvement, with responses approaching those of continuously treated patients
- Safety findings were **consistent** with ONWARD1 and 2 and the Phase 2 program, with no new safety signals or patterns observed

Results

Baseline demographics were balanced across groups

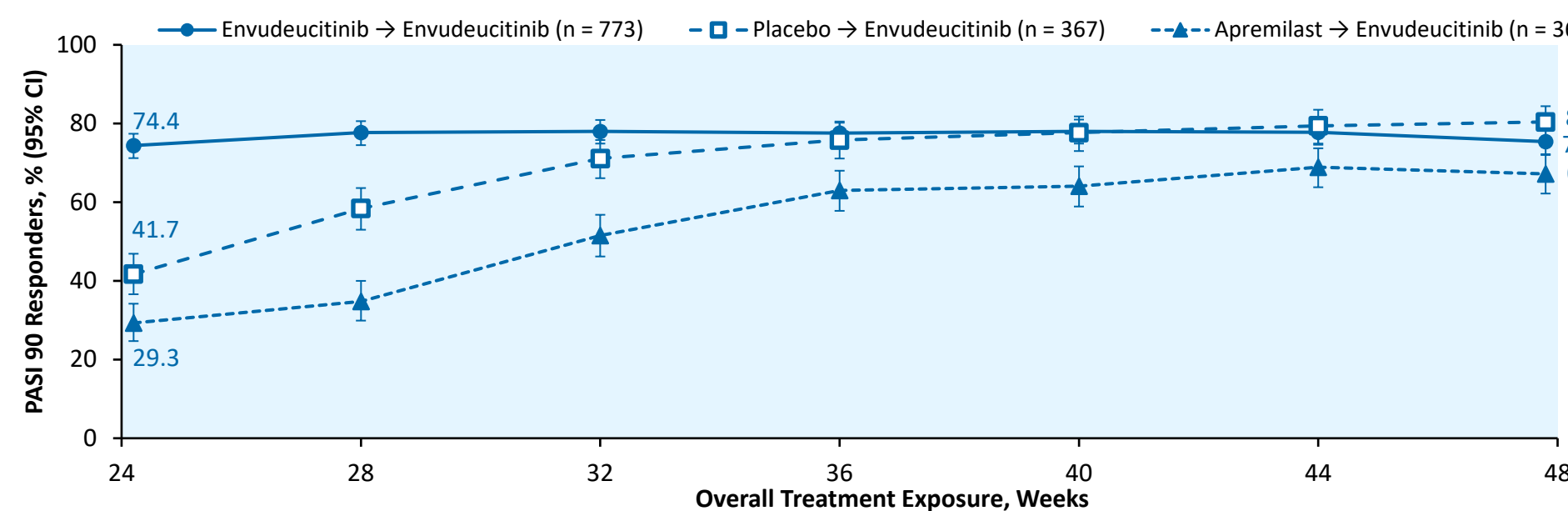
Table 1. Baseline characteristics at start of ONWARD3

	Envudeucitinib 40 mg BID → Envudeucitinib 40 mg BID (n = 773)	Placebo → Envudeucitinib 40 mg BID (n = 367)	Apremilast 30 mg BID → Envudeucitinib 40 mg BID (n = 369)
Envudeucitinib exposure at start of ONWARD3, weeks	24	8	0
Age, years, mean (SD)	49.6 (13.2)	50.6 (13.3)	49.1 (12.4)
Duration of disease, years, mean (SD)	20.2 (13.5)	20.1 (13.8)	19.0 (13.0)
Prior systemic psoriasis treatment, n (%) ^a	395 (51.1)	185 (50.4)	186 (50.4)
PASI, mean (SD)	1.9 (3.6)	4.5 (5.5)	6.7 (7.0)
ss-PGA ≥ 3 , n (%)	18 (2.3)	21 (5.7)	58 (15.7)
BSA % affected, mean (SD)	3.8 (7.7)	9.4 (12.3)	10.7 (13.2)
Worst pruritus NRS score, mean (SD)	1.3 (1.9)	2.0 (2.3)	3.1 (2.8)
DLQI, mean (SD)	1.8 (3.1)	2.9 (3.8)	4.0 (4.9)

^aAny prior exposure to systemic therapies for psoriasis (excluded phototherapy); all patients were required to meet protocol-defined exclusion and washout criteria prior to Study Day 1.

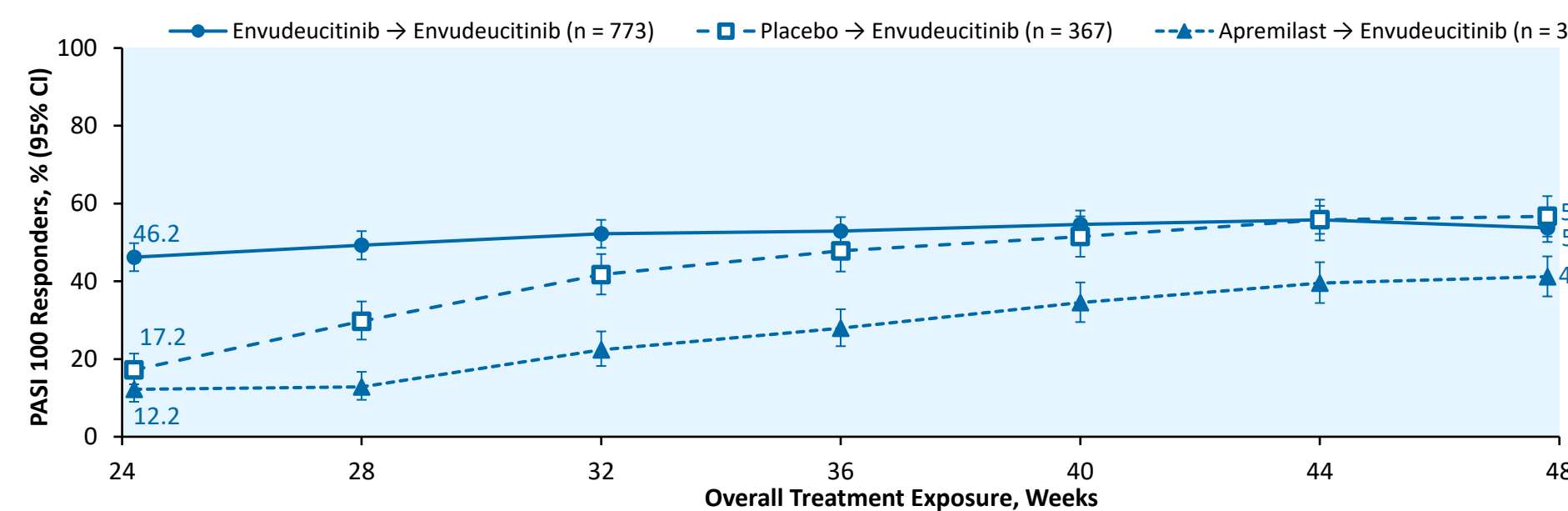
Skin clearance was sustained or increased through Week 48, with over half of continuously treated patients achieving PASI 100

Figure 3. PASI 90 responses through Week 48^a



^a1–24 weeks reflect parent-study treatment; 24–48 weeks reflect open-label envudeucitinib; total envudeucitinib exposure differs by group (Table 1).

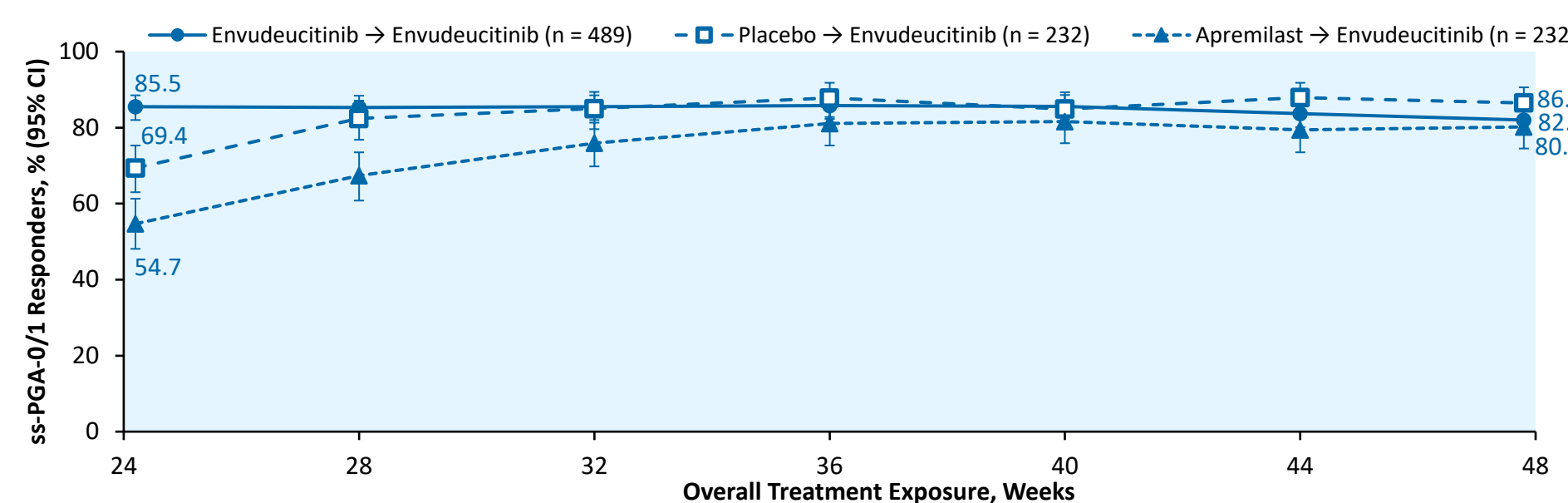
Figure 4. PASI 100 responses through Week 48^a



^a1–24 weeks reflect parent-study treatment; 24–48 weeks reflect open-label envudeucitinib; total envudeucitinib exposure differs by group (Table 1).

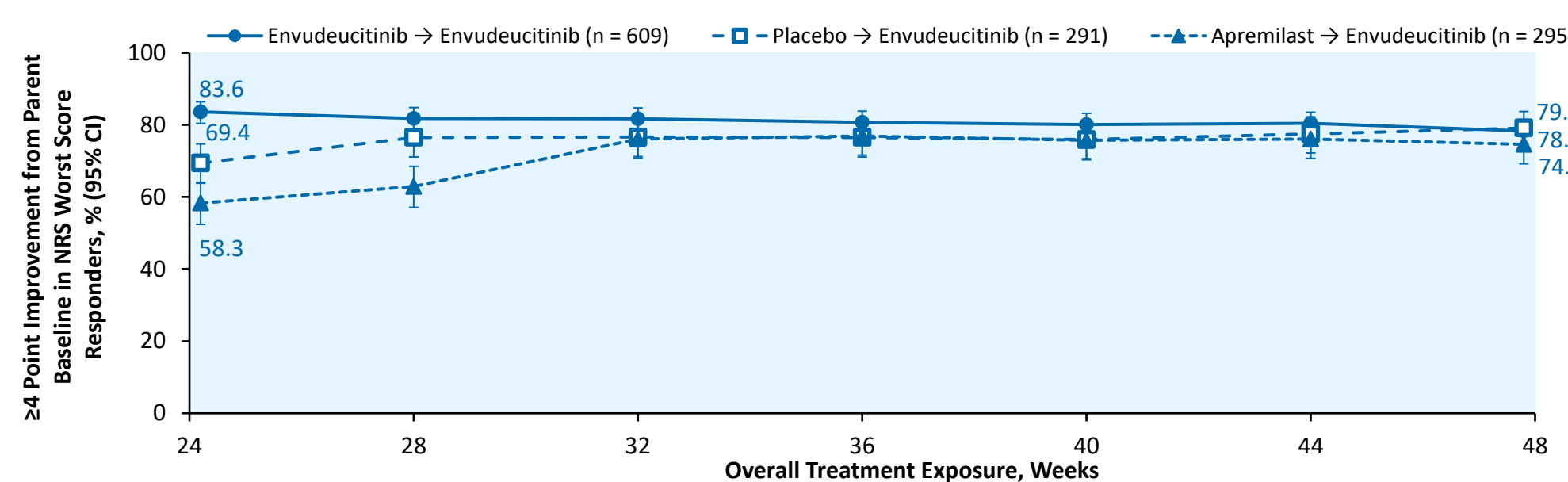
After switching, scalp, itch, and quality of life rapidly improved to match continuous treatment by Week 48

Figure 5. Patients achieving ss-PGA-0/1 through Week 48^a



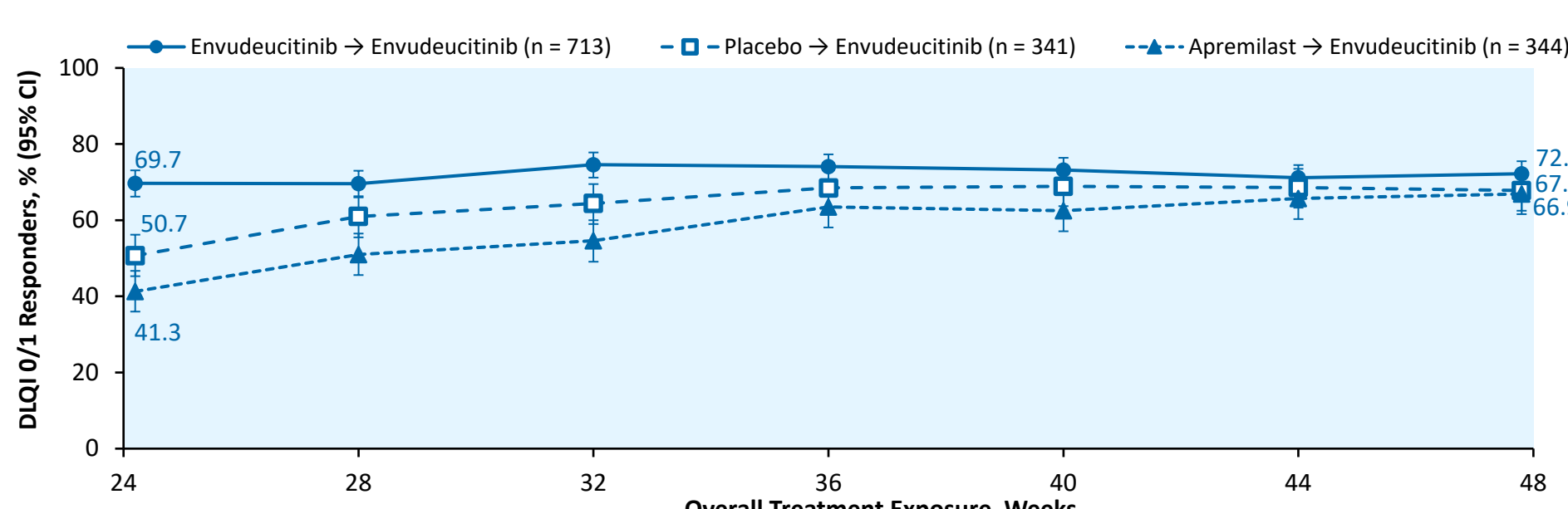
^aAmong patients with parent-study baseline ss-PGA ≥ 3 . 1–24 weeks reflect parent-study treatment; 24–48 weeks reflect open-label envudeucitinib; total envudeucitinib exposure differs by group (Table 1).

Figure 6. Patients achieving a clinically meaningful ≥ 4 -point reduction in worst pruritus NRS^a



^aAmong patients with parent-study baseline worst pruritus NRS ≥ 4 . 1–24 weeks reflect parent-study treatment; 24–48 weeks reflect open-label envudeucitinib; total envudeucitinib exposure differs by group (Table 1).

Figure 7. DLQI 0/1 responses through Week 48^a



^aAmong patients with parent-study baseline DLQI ≥ 2 . 1–24 weeks reflect parent-study treatment; 24–48 weeks reflect open-label envudeucitinib; total envudeucitinib exposure differs by group (Table 1).

Robust maintenance of response across all assessed endpoints

Table 2. Maintenance of response at 48 weeks among ONWARD1 and 2 responders

	Achieved response at the end of ONWARD1 and 2	Maintained response after 24 weeks in ONWARD3 (48 weeks of total exposure) % (95% CI)
PASI 75	678	89.8 (87.3, 92.0)
PASI 90	575	89.4 (86.6, 91.8)
sPGA-0/1	584	87.5 (84.5, 90.1)
PASI 100	357	80.1 (75.6, 84.1)
sPGA-0	365	79.5 (74.9, 83.5)
ss-PGA-0/1 ^a	418	89.5 (86.1, 92.2)
≥ 4 -Point Improvement from parent baseline in NRS worst pruritus ^b	509	86.2 (82.9, 89.1)
DLQI-0/1 ^c	497	86.3 (83.0, 89.2)

Maintenance of response assessed among patients that achieved a response at the entry in ONWARD3 and maintained it after 48 weeks of continuous envudeucitinib treatment.

^aAmong patients with parent baseline ss-PGA ≥ 3 .^bAmong patients with parent baseline NRS worst score ≥ 4 .^cAmong patients with parent baseline DLQI ≥ 2 .

Safety

Table 3. ONWARD3 safety summary

	Envudeucitinib 40 mg BID → Envudeucitinib 40 mg BID (n = 773)	Placebo → Envudeucitinib 40 mg BID (n = 367)	Apremilast 30 mg BID → Envudeucitinib 40 mg BID (n = 369)
	n (%)	EAIR ^a	n (%) EAIR ^a
Total patient years, years	532.6	259.7	249.6
≥ 1 TEAE	521 (67.4)	177.9	185.4
≥ 1 SAE	25 (3.2)	4.7	6.3
TEAEs grade ≥ 3	45 (5.8)	8.6	12.5
TEAEs leading to discontinuation	23 (3.0)	4.3	11 (3.0)
Related TEAEs	104 (13.5)	21	52 (14.2)
Most-frequent TEAEs			
Nasopharyngitis	109 (14.1)	22.2	67 (18.3)
Upper respiratory tract infection	92 (11.9)	18.4	44 (12.0)
Influenza	34 (4.4)	6.5	19 (5.2)
Urinary tract infection	37 (4.8)	7.1	9 (2.5)
Acne	14 (1.8)	2.6	9 (2.5)

^aEAIR is based on exposure in ONWARD 3 only. ^bThree positive tuberculosis tests were reported with no clinical signs or symptoms; none discontinued study treatment.

EAIR, exposure adjusted incidence rate per 100 patient years; MACE, major adverse cardiovascular event; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

- Approximately 80-90% of ONWARD1 and 2 responders maintained their response through Week 48 on envudeucitinib
- 80% of patients maintained complete clearance

- Safety was consistent with ONWARD1 and 2, and the Phase 2 program

- Majority of TEAEs were non-serious, grade 1 and 2, resolved and did not lead to study discontinuation

- There were no deaths, no MACE events, no clinically significant lab abnormalities, no lymphomas, and no tuberculosis reactivation^b

- Malignancies and serious infections occurred at rates consistent with expected background rates in a psoriasis population

References

1. Ucpinar S, et al. *Clin Transl Sci*. 2024;17(12):e70094. 2. Blauvelt A, et al. *J Am Acad Dermatol*. 2026;94(1):57-65. 3. Armstrong AW, et al. *Dermatol Ther (Heidelb)*. 2026;16(6):2661-73. 4. Blauvelt A, et al. Presented at American Academy of Dermatology; March 27-31, 2026.

Disclosures

Funding support was provided by Alumis Inc. The study protocols were approved by institutional review boards or respective ethics committees; all patients provided written informed consent.

*Received honoraria as a scientific speaker and/or advisor from multiple pharmaceutical companies. *Received research grants and/or funding from multiple pharmaceutical companies. *Author is an employee and shareholder of Alumis Inc.