ORIGINAL ARTICLE

Safety and efficacy of envudeucitinib, a highly selective, oral allosteric TYK2 inhibitor, in patients with moderate-to-severe plaque psoriasis: Results from the 52-week open-label extension period of the phase 2 STRIDE study

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Background: Envudeucitinib (ESK-001), a highly selective, oral tyrosine kinase 2 inhibitor, was well-tolerated and effective in patients with plaque psoriasis in the STRIDE study.

Objective: To assess long-term safety and efficacy of envudeucitinib throughout 52 weeks in the ongoing phase 2 open-label extension in patients who completed STRIDE.

Methods: Patients completing STRIDE were eligible to enroll in the long-term open-label extension study (NCT05739435) and received envudeucitinib 40-mg once or twice daily.

Results: In the open-label extension which enrolled 165 patients, envudeucitinib was generally well-tolerated, with an overall 3.7% study drug discontinuation rate due to adverse events, as well as no clinically concerning laboratory or electrocardiogram findings. After 52 weeks of treatment with envudeucitinib 40-mg twice daily, 78% of patients achieved Psoriasis Area and Severity Index (PASI)-75, 61% achieved PASI-90, 39% achieved PASI-100, and 39% achieved sPGA-0. Moreover, 62% showed continued improvement in PASI response over time versus STRIDE week 12. In addition, approximately 80% reported pruritus Numerical Rating Scale <4 and 61% achieved Dermatology Life Quality Index 0/1.

Limitations: This was an open-label study with limited sample size and no control.

Conclusion: Envudeucitinib 40-mg twice daily in adults with moderate-to-severe plaque psoriasis demonstrated increasing and durable improvements in skin clearance and pruritus and was well-tolerated throughout 52 weeks of treatment. (J Am Acad Dermatol https://doi.org/10.1016/j.jaad.2025.10.005.)

Key words: durability; efficacy; envudeucitinib; ESK-001; long-term extension; phase 2; plaque psoriasis; safety; STRIDE; TYK2.

INTRODUCTION

Envudeucitinib (formerly known as ESK-001) is an oral, highly selective tyrosine kinase 2 (TYK2) inhibitor under development for moderate-to-severe plaque psoriasis. Envudeucitinib inhibits TYK2 in a dose-dependent manner, with maximal target

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inhibition over 24 hours at the highest dose of 40-mg twice daily (BID).[1] Inhibition of TYK2, by reducing the signaling and production of key pathogenic cytokines, including interleukin (IL)-12, IL-23, IL-17, and type I interferons (IFNs), is an established approach for treatment of moderate-to-severe plaque psoriasis.[2-8]

The clear dose-response and efficacy of envudeucitinib was demonstrated in the phase 2 STRIDE study, with 40-mg BID at week 12 showing the most promising benefit/risk profile.[3]

Patients completing STRIDE were eligible to enter an open-label extension (OLE) study to assess long-term safety and efficacy of envudeucitinib. Eligible patients were allocated to continue treatment with envudeucitinib 40-mg QD or 40-mg BID. Here, safety and efficacy data from patients who completed 52 weeks of envudeucitinib treatment are reported.

CAPSULE SUMMARY

- Envudeucitinib, a novel, highly selective, oral TYK2 inhibitor, demonstrated efficacy with a clear dose response and well-tolerated safety profile over 12 weeks (NCT05600036).
- Long-term treatment with envudeucitinib 40-mg twice daily for 52 weeks achieved increasing and durable improvements in skin clearance and pruritus, while maintaining a well-tolerated safety profile.

METHODS

Study design

The OLE is an ongoing phase 2 study (NCT05739435) to assess the safety and efficacy of envudeucitinib in adults with moderate-to-severe plaque psoriasis who completed STRIDE.[3] Patients were eligible for the OLE regardless of treatment response in STRIDE and were enrolled at the time of or within 28 days following the STRIDE end-of-study visit. This study was conducted at North American sites only. At the time of enrollment, patients were assigned to 40-mg QD or 40-mg BID (Supplementary Fig 1, available via Mendeley at https://doi.org/10.17632/vwzkp28fwb.1). Patients receiving 10-mg QD or 20-mg QD in STRIDE entered the 40-mg QD OLE arm, while those on 20-mg or 40-mg BID in STRIDE entered the 40-mg BID OLE arm; STRIDE patients on placebo and 40-mg QD were allocated to either OLE dose arm (more details provided in the Supplementary Material, available via Mendeley at https://doi.org/10.17632/vwzkp28fwb.1). During the study, data from STRIDE[3] and interim OLE data indicated that the 40-mg BID dose offered the most robust benefit/risk profile compared to the QD regimen. The findings prompted a protocol amendment on 2 January 2024 to transition all patients in the study to the 40-mg BID dose (between weeks 40 and 64). Of note, the first patient entered OLE on 17 January 2023.

Patients were assessed for safety and efficacy at study visit day 1, weeks 2, 4, 8, 12, 16, and every 12 weeks thereafter. Pharmacokinetic (PK) samples were collected throughout the 52 weeks on day 1, weeks 4, 16, and every 6 months thereafter.

This OLE study was conducted in accordance with the Declaration of Helsinki, the International Council for Harmonisation guidelines for Good Clinical Practice, and all applicable local regulations. Key eligibility criteria are provided in the Supplementary Material, available via Mendeley at https://doi.org/10.17632/vwzkp28fwb.1.

Endpoints and assessments

The primary endpoint was the incidence of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs). The secondary endpoints were as follows: change from baseline in Psoriasis Area and Severity Index (PASI), static Physician's Global Assessment (sPGA), body surface area (% BSA), and pruritus Numerical Rating Scale (NRS) to assess long-term efficacy; change from baseline in Dermatology Life Quality Index (DLQI) to assess the change in quality of life (QoL); and envudeucitinib plasma concentrations and PK parameters. Safety assessments also included vital signs, clinical laboratory assessments, and electrocardiograms (ECGs).

Statistical analysis

Descriptive summaries of continuous and discrete variables were performed. Formal power calculations were not performed to determine the sample size. The number of patients included in this study was based on the number of patients who completed STRIDE, qualified for, and chose to enroll in this study. All efficacy analyses were based on the modified intent-to-treat (mITT) analysis population, which included all patients who received at least 1 dose of study drug according to the assigned treatment. For efficacy analyses, baseline was defined as the patients' values obtained on Day 1 of STRIDE. A modified non-responder imputation (mNRI) was applied for responder-type analyses where patients who discontinued the study due to adverse events (AEs) or inadequate response were treated as non-responders and patients who

Abbreviations used:

AE:	adverse event
BID:	twice daily
BMI:	body mass index
BSA:	body surface area
COVID-19:	coronavirus 2019
C_{trough}:	concentration reached by a drug immediately before the next dose is administered
DLQI:	Dermatology Life Quality Index
ECG:	electrocardiogram
IFN:	interferon
IL:	interleukin
IRB:	Institutional Review Board
JAKi:	Janus kinase inhibitor
mITT:	modified intent-to-treat
mNRI:	modified non-responder imputation
NRS:	Numerical Rating Scale
OLE:	open-label extension
PASI:	Psoriasis Area and Severity Index
PK:	pharmacokinetic
pSTAT:	phosphorylated signal transducer and activator of transcription
QD:	once daily
QoL:	quality of life
SAE:	serious adverse event
SD:	standard deviation
sPGA:	static Physician's Global Assessment
TEAE:	treatment-emergent adverse event
TYK2:	tyrosine kinase 2

discontinued for all other reasons had their last observation carried forward. The safety analysis population included all patients who received at least 1 dose of study drug analyzed according to the actual treatment received. The PK analysis population included patients who received at least 1 dose of envudeucitinib and had at least one PK concentration measurement.

RESULTS

Participants

A total of 165 patients were enrolled in this OLE study. One enrolled patient was diagnosed with coronary artery occlusion at week 16 of STRIDE[3] (at day 1 of the OLE) prior to dosing in OLE and, therefore, came off study. In the mITT population, 82 patients were assigned to the 40-mg QD and 40-mg BID arms, respectively (Supplementary Table I and Fig 2, available via Mendeley at https://doi.org/10.17632/vwzkp28fwb.1).

Patient demographics and baseline characteristics were comparable to a general moderate-to-severe psoriasis population (ITT), with the majority of patients being male (70.9%) and white (80.6%); 47.9% were previously treated with biologics and 2.4% with Janus kinase inhibitors (JAKi). The mean age was 49.2 years and the average disease duration was 19.8 years (Table I).

Treatment was ongoing for 126 patients (76.4%) of the 165 patients enrolled in the OLE at the cut-off date for the 52-week data analyses (Supplementary Table I and Fig 2, available via Mendeley at https://doi.org/10.17632/vwzkp28fwb.1). Overall, most study discontinuations were due to withdrawal by patient (7.9%) or lost to follow-up (6.1%) (Supplementary Table I, available via Mendeley at https://doi.org/10.17632/vwzkp28fwb.1). One patient discontinued from study due to pregnancy and 1 due to partner's pregnancy. Six patients (3.7%) discontinued envudeucitinib due to an AE (Table II). Out of these patients, 1 discontinued envudeucitinib due to an AE of osteomyelitis, but had not discontinued the study at the time of the cut-off date.

Safety

Treatment with envudeucitinib over 52 weeks in the OLE was generally safe and well-tolerated with no deaths and a low rate of study drug discontinuation due to AEs (3.7%) (Table II). The overall number of patients with at least 1 TEAE was 65.9%, with the majority of TEAEs being mild or moderate in severity (23.8% and 37.2%, respectively). The most common AEs (occurring in 5% or more patients in any treatment group) were nasopharyngitis (8.5%), upper respiratory tract infections (9.8%), headache (6.1%), and COVID-19 infections (6.7%). Rates of acne and folliculitis were low at 3.0% and 2.4%, respectively, all being mild or moderate in severity and self-limited.

Comparison of the 40-mg QD arm and the 40-mg BID arm showed no dose-dependent effects on the overall frequency of AEs, nor on the numbers of most frequent TEAEs. Overall, 61.0% and 49.7% of patients experienced at least 1 TEAE in the 40-mg QD and BID arms, with exposure-adjusted incidence rates of 122.76 and 102.33 per 100 patient years, respectively. TEAEs considered related to the study drug occurred in 14.6% of patients in the 40-mg QD arm compared to 10.2% in the 40-mg BID arm, while SAEs related to the study drug occurred in 2 patients in each group (2.4% and 1.4%, respectively).

The overall frequency of patients with at least 1 SAE was 3.7% (n = 6) (Table II). Four SAEs reported in 4 patients were considered related to study drug by the investigator: peritonsillar abscess (40-mg BID), non-small cell lung cancer in a patient with a strong family history (3 first-degree relatives) and genetic subtype consistent with familial lung cancer (40-mg QD), clear-cell type renal cell carcinoma incidentally identified during the course of

Table I. Demographic and baseline characteristics for all patients who entered the OLE study in the ITT population

	Original envudeucitinib 40-mg QD (*N* = 82)	Original envudeucitinib 40-mg BID* (*N* = 83†)	Overall (*N* = 165†)
Age (y), mean (SD)	47.5 (12.7)	50.8 (12.1)	49.2 (12.4)
Sex, *n* (%)			
Male	56 (68.3)	61 (73.5)	117 (70.9)
Female	26 (31.7)	22 (26.5)	48 (29.1)
Race, *n* (%)			
American Indian or Alaska Native	0 (0)	0 (0)	0 (0)
Asian	7 (8.5)	4 (4.8)	11 (6.7)
Black or African American	5 (6.1)	1 (1.2)	6 (3.6)
Native Hawaiian or Other Pacific Islander	1 (1.2)	2 (2.4)	3 (1.8)
White	63 (76.8)	70 (84.3)	133 (80.6)
Other	6 (7.3)	5 (6.0)	11 (6.7)
Not reported	0 (0)	1 (1.2)	1 (0.6)
Ethnicity, *n* (%)			
Hispanic or Latino	26 (31.7)	25 (30.1)	51 (30.9)
Not Hispanic or Latino	56 (68.3)	58 (69.9)	114 (69.1)
Not reported	0 (0)	0 (0)	0 (0)
Weight (kg), mean (SD)	98.1 (28.5)	94.0 (23.2)	96.0 (26.0)
BMI (kg/m^2), mean (SD)	33.1 (8.8)	31.7 (7.4)	32.4 (8.1)
Duration of psoriasis (y), mean (SD)	17.2 (10.9)	22.3 (14.3)	19.8 (13.0)
Prior treatment with biologics, *n* (%)	37 (45.1)	42 (50.6)	79 (47.9)
Prior treatment with JAKi, *n* (%)	1 (1.2)	3 (3.6)	4 (2.4)
PASI, mean (SD)	10.2 (7.2)	6.8 (7.0)	8.5 (7.2)
sPGA score, *n* (%)			
0	1 (1.2)	5 (6.0)	6 (3.6)
1	10 (12.2)	26 (31.3)	36 (21.8)
2	19 (23.2)	19 (22.9)	38 (23.0)
3	39 (47.6)	23 (27.7)	62 (37.6)
4	12 (14.6)	7 (8.4)	19 (11.5)
5	0 (0)	0 (0)	0 (0)
BSA involvement (%), mean (SD)	12.9 (13.4)	8.7 (11.1)	10.8 (12.5)
DLQI, mean (SD)	5.8 (5.8)	4.5 (4.8)	5.2 (5.3)
Average pruritus NRS score, mean (SD)	4.6 (3.0)	4.0 (3.1)	4.3 (3.1)

BID, Twice daily; *BMI*, body mass index (calculated as weight in kilograms divided by height meters squared); *BSA*, body surface area; *DLQI*, Dermatology Life Quality Index; *ITT*, intent-to-treat; *JAKi*, Janus kinase inhibitor; *mITT*, modified intent-to-treat; *n*, number of patients in specific category; *N*, total number of patients; *NRS*, numerical rating scale; *OLE*, open-label extension; *PASI*, Psoriasis Area and Severity Index; *QD*, once daily; *SD*, standard deviation; *sPGA*, static Physician's Global Assessment score.

*Based on original dose assignment at start of OLE.

†One participant was randomized, but not dosed in the OLE study, and therefore was not included in the mITT population, safety analysis set, and PK analysis set.

evaluation for urolithiasis (40-mg BID), and arthritis in a patient with history of prior inflammatory arthritic event (40-mg QD). Separately, 1 patient with multiple co-morbidities, including diabetes, long-standing foot ulcer, and recurrent episodes of lower limb cellulitis, had SAEs of sepsis, septic shock, and cellulitis (40-mg BID), and 1 patient with positive medical history had a SAE of asthma exacerbation, all considered unrelated to study drug (after switch from 40-mg QD to 40-mg BID).

Laboratory assessments did not show any clinically significant abnormalities, including no episodes of acute liver or renal dysfunction, nor identified any liver, renal, or hematological trends of concern. Throughout 52 weeks of envudeucitinib treatment, mean lab values remained stable and within normal limits across both dose arms (Supplementary Figs 3 to 5, available via Mendeley at https://doi.org/10.17632/vwzkp28fwb.1). Consistent with the co-morbidities associated with psoriasis and high BMI

Table II. Summary of adverse events through week 52 in the safety analysis population

	Original envudeucitinib 40-mg QD (*N* = 82)	Overall envudeucitinib 40-mg BID (*N* = 147)	Overall (*N* = 164)
Patients with ≥1 TEAE, *n* (%) [EAIR]	50 (61.0) [122.76]	73 (49.7) [102.33]	108 (65.9) [108.18]
Patients with TEAE leading to study drug discontinuation, *n* (%) [EAIR]*	1 (1.2) [1.55]	5 (3.4) [4.19]	6 (3.7) [3.26]
Patients with TEAE ≥ Grade 3, *n* (%) [EAIR]	3 (3.7) [4.66]	6 (4.1) [5.12]	8 (4.9) [4.42]
Most frequent TEAE, *n* (%) [EAIR]†,‡			
Upper respiratory tract infection	3 (3.7) [4.71]	13 (8.8) [11.66]	16 (9.8) [9.20]
Nasopharyngitis	10 (12.2) [16.88]	6 (4.1) [5.15]	14 (8.5) [8.09]
COVID-19	3 (3.7) [4.74]	8 (5.4) [6.88]	11 (6.7) [6.17]
Headache	5 (6.1) [8.28]	5 (3.4) [4.28]	10 (6.1) [5.71]
Patients with ≥1 TE SAE, *n* (%) [EAIR]	2 (2.4) [3.10]	4 (2.7) [3.39]	6 (3.7) [3.29]
Patients with SAEs related to study drug, *n* (%) [EAIR]	2 (2.4) [3.10]	2 (1.4) [1.67]	4 (2.4) [2.17]
Patients with TEAE leading to death, *n* (%) [EAIR]	0 (0) [-]	0 (0) [-]	0 (0) [-]

Envudeucitinib 40-mg QD data presented is for all patients who were dosed with 40-mg QD up to the time of discontinuation from envudeucitinib treatment or switch to 40-mg BID. Envudeucitinib 40-mg BID data presented is for all patients reaching week 52, including patients who were randomized to envudeucitinib 40-mg BID from the start of OLE and who switched from 40-mg QD to 40-mg BID.
-, Not applicable; *BID*, twice daily; *COVID-19*, coronavirus disease 2019; *EAIR*, exposure-adjusted incidence rate per 100 patient years, *N*, total number of patients; *n*, number of patients in specific category; *OLE*, open-label extension; *QD*, once daily; *SAE*, serious adverse event; *TE(AE)*, treatment-emergent (adverse event).
*TEAEs leading to drug discontinuation in 6 patients included dyspepsia, hypersensitivity, osteomyelitis, pruritus, renal cell carcinoma (envudeucitinib 40-mg BID), and non-small cell lung cancer (envudeucitinib 40-mg QD).
†TEAEs reported by 5% or more patients in any treatment group.
‡All events of upper respiratory tract infection, nasopharyngitis, COVID-19, and headache were grade 1 (mild) or grade 2 (moderate) in severity.

of the study population, the day 1 lipid panel values were at the upper limit of normal and remained stable throughout the 52 weeks (Supplementary Fig 4, available via Mendeley at https://doi.org/10.17632/vwzkp28fwb.1). There were no AEs of cytopenia or rhabdomyolysis, and no cases of tuberculosis. There were 2 cases of herpes zoster, neither of which resulted in envudeucitinib treatment interruption or study discontinuation, and both cases completely resolved (1 with and 1 without antiviral treatment). There were neither significant changes in ECG findings during 52 weeks of envudeucitinib treatment, nor were thromboembolic events reported.

Efficacy

Similar to STRIDE,[3] dose-dependent effects were observed across all efficacy measures, with the envudeucitinib 40-mg BID dose demonstrating greater efficacy compared to the 40-mg QD dose (Fig 1, *A* and *B*). After 52 weeks of envudeucitinib treatment, 78%, 61%, and 39% of patients (mITT) on 40-mg BID achieved PASI-75, PASI-90, and PASI-100, respectively, indicating sustained improvements over time (Fig 1, *A*, Table III). An increased sPGA response was also observed with 40-mg BID, with 61% of patients reaching sPGA-0/1 at week 52 and 39% reaching sPGA-0 (Fig 1, *B*, Table III). The majority of patients achieved PASI-75 and PASI-90, comparing OLE week 52 to STRIDE week 12, with a continued increasing trend for the proportion of patients achieving PASI-100 (Fig 1, *A*).

Efficacy response rates achieved with envudeucitinib were maintained with continued treatment over time. Of the PASI-75 responders at week 12 in STRIDE who entered the OLE, 80% of patients in the OLE 40-mg BID arm maintained their PASI-75 response at week 52.[9] Moreover, of the patients who did not achieve PASI-100 at week 12 in STRIDE, 62% in the OLE 40-mg BID arm showed continued

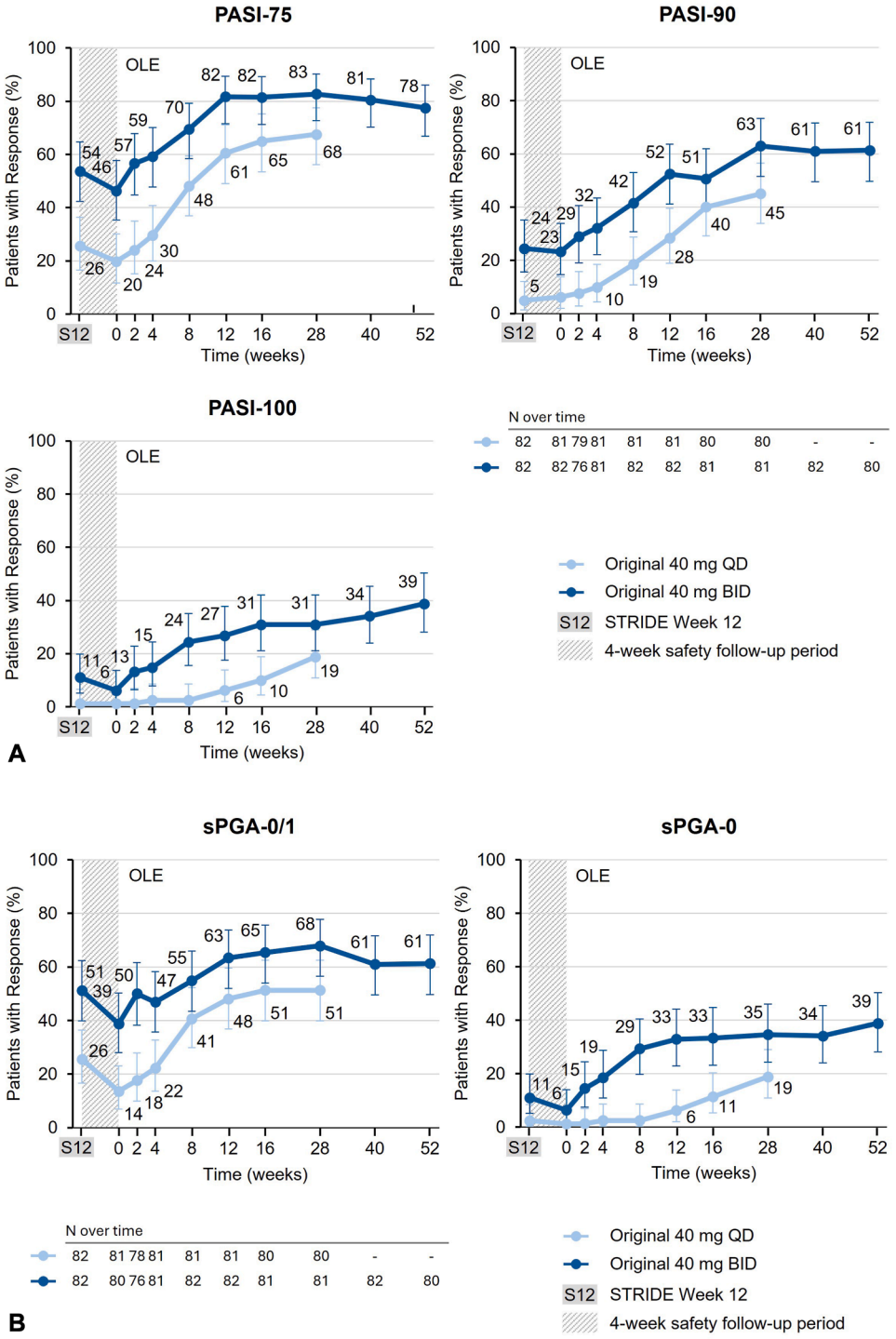

Fig 1. PASI **(A)** and sPGA **(B)** response rates based on n mNRI imputation for patients with moderate-to-severe plaque psoriasis following 40-mg QD and 40-mg BID envudeucitinib in the OLE study. Response rates at week 12 of STRIDE are the mean response of all the patients from the parent STRIDE dose arms (placebo or envudeucitinib 10-mg QD, 20-mg QD, or 40-mg QD) who were allocated to the 40-mg QD OLE arm or of all the patients from the parent STRIDE dose arms (placebo or envudeucitinib 20-mg BID, 40-mg QD, or 40-mg BID) who were allocated to the 40-mg BID OLE arm.[3] Error bars represent 95% confidence intervals. *BID*, Twice daily; *mNRI*, modified non-responder imputation; *N*, total number of patients; *OLE*, open-label extension; *PASI*, Psoriasis Area and Severity Index; *QD*, once daily; *sPGA*, static Physician's Global Assessment score.

improvement in PASI response at OLE week 52 (Supplementary Table II, available via Mendeley at https://doi.org/10.17632/vwzkp28fwb.1).

Improvements in signs and symptoms were accompanied by dose-dependent improvements in QoL, as measured by DLQI and pruritus NRS (Table III). In the 40-mg BID arm at week 52, 61% of patients achieved DLQI-0/1 and approximately 80% of patients achieved itch symptom control at week 52 (NRS <4). Post-hoc analysis showed that 62% of patients in the 40-mg BID overall group achieved ≥4 point improvement from baseline in worst pruritus NRS score at week 52, with onset of improvement shown as early as week 4.

Pharmacokinetics

On day 1 post-dose, mean plasma concentrations reached approximately 200 ng/mL around 2 hours after drug administration. At week 16, mean steady-state C_{trough} levels were approximately 54 ng/mL for the 40-mg QD dose and 170 ng/mL for the 40-mg BID dose. The 40-mg BID regimen achieved continuous IC90 coverage at trough over 24 hours, surpassing the in vitro human whole blood pSTAT-IFNα IC90 (144 ng/mL) and ensuring sustained TYK2 inhibition for optimal target engagement.[1] Higher envudeucitinib exposures were associated with improved PASI outcomes, with patients achieving PASI-90 and PASI-100 showing greater mean exposures compared to those achieving PASI-75. PK analyses showed no clinically significant food effect on envudeucitinib.[1]

DISCUSSION

Selective TYK2 inhibition was demonstrated to treat psoriasis effectively in STRIDE.[3] In this OLE study, 52 weeks of envudeucitinib treatment was generally safe and well-tolerated in patients with a long-standing history of plaque psoriasis, multiple co-morbidities, and nearly half of patients previously treated with biologics or JAKi. PASI response rates increased over time consistently throughout week 52, with efficacy across all outcomes approaching that observed with IL-17 biologics for PASI-75/90/100, sPGA-0/1, itch, and DLQI.[10,11] Moreover, 80% of patients who achieved PASI-75 at week 12 in STRIDE[3] maintained the same level of improvement after 52 weeks of 40-mg BID dosing in the OLE.

Envudeucitinib achieved maximal and continuous TYK2 inhibition, as demonstrated by continuous IC90 coverage at trough levels for 24 hours with 40-mg BID. Envudeucitinib inhibits key proinflammatory drivers of psoriasis, including IL-23, IL-17, and type 1 IFN, shown in both blood and skin samples,[12] while avoiding potential off-target adverse effects, such as lab abnormalities and opportunistic infections.[1] Further, no clinically significant food effect was observed.

As per literature, long-term data reported up to 4 years with TYK2 inhibition continues to demonstrate a positive benefit/risk profile.[6] The majority of AEs with envudeucitinib were mild or moderate, unrelated to study drug, resolved with conventional therapies, and led to a low AE-related discontinuation rate (3.7%). Additionally, the SAEs observed were confounded by concomitant or preexisting conditions. No laboratory abnormalities, ECG findings, nor safety signals associated with JAK inhibition (cytopenia, anemia) were observed.[13,14] The rate of muco-cutaneous AEs was also low, and not associated with dose.

Maximal IC90 TYK2 inhibition over an extended duration resulted in clinically meaningful and sustained improvements in clinical outcomes, substantiating the findings from available histological and proteomic assessments. However, important limitations of this open-label study should be acknowledged, including the lack of placebo or active comparator and the relatively small sample size.

Envudeucitinib 40-mg BID demonstrated a favorable benefit/risk profile over 52 weeks, supporting its potential for long-term use in patients with plaque psoriasis, including those with co-morbidities. Ongoing phase 3 studies will further validate these findings.

CONCLUSIONS

Maximal and continuous allosteric inhibition of TYK2 with envudeucitinib over 52 weeks demonstrated a robust benefit/risk profile, with increasing and sustained improvements in skin and patient-reported outcomes. These findings support the potential of envudeucitinib as a next-generation oral treatment option for patients with moderate-to-severe plaque psoriasis.

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Conflicts of interest

Dr Papp has received research grants from AbbVie, Acelyrin, Alumis, Amgen, Arcutis, Bausch Health/Valeant, Bristol Myers Squibb, Can-Fite BioPharma, Celltrion, Concert Pharmaceuticals, CorEvitas, Dermavant, Dermira, Dice Pharmaceuticals, Dice Therapeutics, Eli Lilly, Evelo Biosciences, Galderma, Horizon Therapeutics, Incyte, Janssen, Kymab, Leo Pharma, Meiji Seika Pharma, Nimbus Therapeutics, Novartis, Pfizer, Sanofi-Aventis/Genzyme, Sun Pharma, Takeda, Tarsus Pharmaceuticals, Inc, UCB Pharma, and Zai Lab Co, Ltd; is a consultant for

Table III. Summary of efficacy outcomes in the mITT analysis population

	Wk 28	Wk 52	
	Original envudeucitinib 40-mg QD (*N* = 80)	Original envudeucitinib 40-mg BID (*N* = 80)	Overall envudeucitinib 40-mg BID (*N* = 144)
Clinical endpoints			
PASI-75, *n* (%)	54 (67.5)	62 (77.5)	112 (77.8)
95% CI	56.1, 77.6	66.8, 86.1	70.1, 84.3
PASI-90, *n* (%)	36 (45.0)	49 (61.3)	90 (62.5)
95% CI	33.8, 56.5	49.7, 71.9	54.1, 70.4
PASI-100, *n* (%)	15 (18.8)	31 (38.8)	47 (32.6)
95% CI	10.9, 29.0	28.1, 50.3	25.1, 40.9
sPGA-0/1, *n* (%)	41 (51.3)	49 (61.3)	86 (59.7)
95% CI	39.8, 62.6	49.7, 71.9	51.2, 67.8
sPGA-0, *n* (%)	15 (18.8)	31 (38.8)	47 (32.6)
95% CI	10.9, 29.0	28.1, 50.3	25.1, 40.9
PRO endpoints			
DLQI 0/1, *n* (%)	41 (51.3)	49 (61.3)	87 (60.4)
95% CI	39.8, 62.6	49.7, 71.9	51.9, 68.5
DLQI 4-point decrease, *n* (%)	49 (61.3)	55 (68.8)	103 (71.5)
95% CI	49.7, 71.9	57.4, 78.7	63.4, 78.7
Pruritus NRS score <4			
Average NRS, *n* (%)	54 (67.5)	65 (81.3)	115 (79.9)
95% CI	56.1, 77.6	71.0, 89.1	72.4, 86.1
Worst NRS, *n* (%)	51 (63.8)	63 (78.8)	112 (77.8)
95% CI	52.2, 74.2	68.2, 87.1	70.1, 84.3
Improvement in pruritus NRS score ≥4*			
Worst NRS, *n* (%)	44 (55.0)	47 (58.8)	89 (61.8)
95% CI	43.5, 66.2	47.2, 69.6	53.3, 69.8

All data are based on an mNRI imputation methodology. Non-response was imputed for patients who discontinued due to inadequate response or adverse events, and LOCF if discontinued for all other reasons.

The week 28 data is presented for original envudeucitinib 40-mg QD. These patients then switched to 40-mg BID after week 28. The week 52 data is presented for the original and overall envudeucitinib 40-mg BID cohorts. Overall envudeucitinib 40-mg BID includes those who switched from 40-mg QD to 40-mg BID, and patients who were originally assigned to envudeucitinib 40-mg BID.

BID, Twice daily; *CI*, confidence interval; *DLQI*, Dermatology Life Quality Index; *LOCF*, last observation carried forward; *mITT*, modified intention to treat; *mNRI*, modified non-responder imputation; *N*, total number of patients; *n*, number of patients in specific category; *NRS*, numerical rating scale; *PASI*, Psoriasis Area and Severity Index; *PASI-75*, ≥75% reduction from baseline in PASI; *PASI-90*, ≥90% reduction from baseline in PASI; *PASI-100*, 100% reduction from baseline in PASI; *PRO*, patient-reported outcome; *QD*, once daily; *sPGA-0/1*, static Physician's Global Assessment score of 0 or 1; *sPGA-0*, static Physician's Global Assessment score of 0.

*Based on post-hoc analysis.

AbbVie, Acelyrin, Akros, Amgen, Arcutis, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite Biopharma, Celltrion, Dermavant, Dermira, Dice Pharmaceuticals, Eli Lilly, Evelo Biosciences, Forbion, Galderma, Incyte, Janssen, Kyowa Hakko Kirin, Leo Pharma, Meiji Seika Pharma, Mitsubishi Pharma, Novartis, Pfizer, Reistone, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, and Takeda, UCB Pharma; is a speaker for AbbVie, Amgen, Bausch Health/Valeant, Eli Lilly, Galderma, Incyte, Janssen, Kyowa Hakko Kirin, Novartis, and Sanofi-Aventis/Genzyme; has an honoraria from Dice Pharmaceuticals; is a scientific officer for Akros, Arcutis, Can-Fite Biopharma, Dice Pharmaceuticals, and Kyowa Hakko Kirin; and serves on the steering committee or advisory board for AbbVie, Amgen, Bausch Health/Valeant, Boehringer Ingelheim, Bristol Myers Squibb, Can-Fite Biopharma, Dermavant, Eli Lilly, Galderma, Incyte, Janssen, Novartis, Pfizer, Reistone, Sanofi-Aventis/Genzyme, Sandoz, Sun Pharma, and UCB Pharma. Dr Sofen has received research grants and funding from Abbvie; Acelyrin, Alumis, Amgen, BMS, Dermavant, Lilly, Meiji, Sanofi, UCB. Dr Bukhalo has served as a research investigator to Eli Lilly, Alumis, Takeda, Janssen, Galderma, Medicus, Novum, Abbvie, Incyte, Opsidio, 10xBio LLC, and Veradermics. Dr Blauvelt has served as a speaker (received honoraria) for Eli Lilly and Company, UCB, and Almirall; has served as a scientific adviser (received honoraria) for AbbVie, Almirall, Alumis, Amgen, Anaptysbio, Apogee, Arcutis, Astria, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Corvus, Dermavant, Eli Lilly and Company, Galderma, GlaxoSmithKline, Immunovant, Incyte, IQVIA, Janssen, Leo, Lipidio, Merck, Novartis, Oruka, Paragon, Pfizer, Regeneron, Sanofi, Spherix Global Insights, Sun Pharma,

Syncona, Takeda, UCB, Union, and Zai Lab; has acted as a clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Almirall, Alumis, Amgen, Arcutis, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Incyte, Janssen, Leo, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, Takeda, and UCB; and owns stock in Lipidio and Oruka.

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