Zasocitinib (TAK-279), a Selective, Oral TYK2 Inhibitor, Reduces Body Surface Area Involvement in a Phase 2b Trial in Moderate-to-Severe Plaque Psoriasis

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Synopsis

- Zasocitinib (TAK-279) is an oral, allosteric, potent and selective TYK2 inhibitor in late-stage clinical development (**Figure 2**).[1]
- In a phase 2b trial in patients with moderate-to-severe plaque psoriasis (NCT04999839), zasocitinib demonstrated efficacy and acceptable safety, and was generally well tolerated at all doses tested.[2]
  - A significantly higher proportion of patients receiving zasocitinib at doses ≥ 5 mg QD achieved the primary endpoint of a ≥ 75% reduction in PASI score (PASI 75) at Week 12 than patients receiving placebo.[2]
  - Overall, 33% and 15% of patients receiving the highest doses of zasocitinib (30 mg and 15 mg, respectively) achieved a PASI 100 response (complete skin clearance) at Week 12 (**Figure 1**).[2]

Objective

- To further evaluate the efficacy of zasocitinib in the phase 2b study using the measure of BSA in patients with moderate-to-severe plaque psoriasis.

Methods

- In the phase 2b, randomized, multicenter, double-blind, placebo-controlled trial (NCT04999839), patients were randomized 1:1:1:1:1 to receive oral zasocitinib (2 mg, 5 mg, 15 mg or 30 mg) or placebo QD for 12 weeks (**Figure S1**; access via QR code).
- Here, data for the two highest doses of zasocitinib used in the study (15 mg and 30 mg) are reported and compared with the placebo arm.

Scan the QR code to see the **supplementary material** for further details of the study design, efficacy endpoints and statistical analyses included in this poster.

Results

Figure 1. Representative images showing a patient who achieved a PASI 100 response at Week 12 after treatment with zasocitinib 15 mg QD.

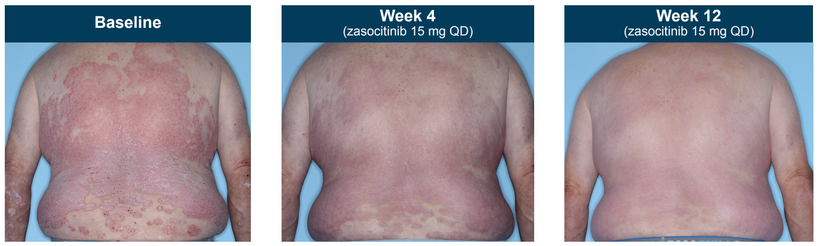


Figure 2. Zasocitinib binds with high specificity to the JH2 domain of TYK2 but not to JAK family members, blocking downstream proinflammatory signaling.[1,3]

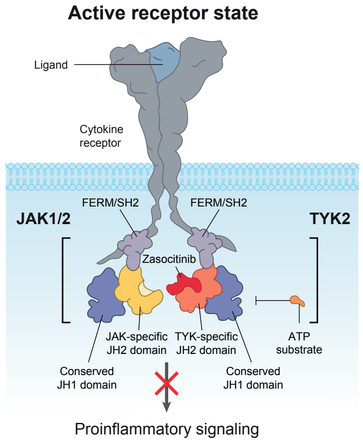
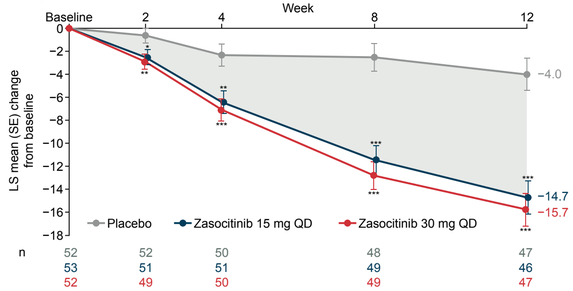


Table 1. Demographic and baseline clinical characteristics were generally similar between treatment groups.

	Placebo (n = 52)	Zasocitinib 15 mg QD (n = 53)	Zasocitinib 30 mg QD (n = 52)
Age at consent, years, mean (SD)	48.8 (12.7)	46.2 (13.0)	48.5 (11.4)
Male, n (%)	31 (59.6)	34 (64.2)	33 (63.5)
Race, n (%)			
White	44 (84.6)	46 (86.8)	42 (80.8)
Asian	5 (9.6)	2 (3.8)	3 (5.8)
Black/African American	2 (3.8)	3 (5.7)	4 (7.7)
Other[a]	1 (1.9)	2 (3.8)	3 (5.8)
Weight, kg, mean (SD)	88.4 (15.8)	92.7 (16.8)	90.0 (18.3)
Body mass index, kg/m^2, mean (SD)	31.3 (5.1)	32.0 (4.9)	30.4 (5.4)
Plaque psoriasis duration, years, mean (SD)	12.7 (10.5)	17.6 (14.6)	17.3 (11.1)
PASI score, mean (SD)	18.3 (8.1)	15.5 (4.5)	17.6 (6.2)
PGA score, mean (SD)	3.2 (0.4)	3.2 (0.4)	3.2 (0.4)
3 (moderate), n (%)	41 (78.8)	40 (75.5)	42 (80.8)
4 (severe), n (%)	11 (21.2)	13 (24.5)	10 (19.2)
BSA, %, mean (SD)	21.3 (13.6)	18.3 (10.3)	22.2 (14.3)
DLQI score, mean (SD)	12.4 (7.0)	11.9 (7.1)	12.5 (6.9)
Bio-experienced, n (%)	8 (15.4)	9 (17.0)	8 (15.4)

[a]Other includes American Indian or Alaska natives, native Hawaiian or other Pacific Islanders and those of multiple races/ethnic origins.

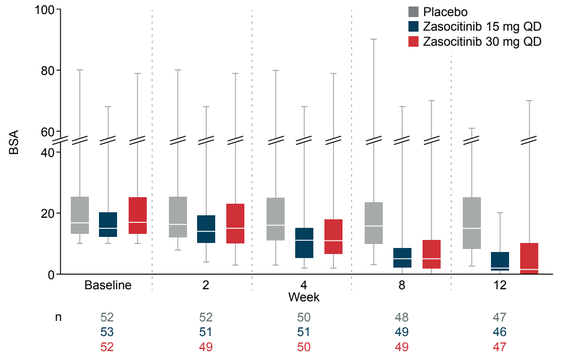
Figure 3. Significantly greater reductions from baseline in BSA were observed in the zasocitinib 15 mg and 30 mg groups versus placebo as early as Week 2, and through to Week 12.



*p < 0.05, **p < 0.01, ***p < 0.001, versus placebo.
Data are from the mITT analysis set, which included patients who received ≥ 1 dose of study treatment.

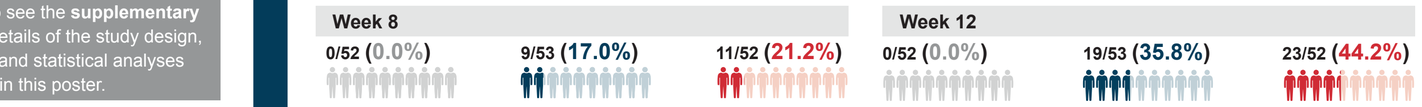
Scan the QR code to see the data values in **Figure S2**.

Figure 4. Over 12 weeks, absolute median BSA scores were increasingly lower in the zasocitinib 15 mg and 30 mg groups versus placebo.



Data are from the mITT analysis set, which included patients who received ≥ 1 dose of study treatment.
Solid horizontal lines represent medians; upper and lower boundaries of boxes represent interquartile ranges; whiskers represent the ranges.

Figure 5. Greater proportions of patients achieved a threshold of BSA ≤ 1% in the zasocitinib 15 mg and 30 mg groups versus placebo, which was observed from Week 8.



Data are from the mITT analysis set, which included patients who received ≥ 1 dose of study treatment.
Data for Weeks 2 and 4 are not shown because they were all 0.

Conclusions

Patients with moderate-to-severe plaque psoriasis who received zasocitinib 15 mg or 30 mg achieved significantly greater reductions in BSA versus placebo over 12 weeks, and the reductions were observed as early as Week 2.

- A numerically higher proportion achieved BSA ≤ 1% with zasocitinib 30 mg than with 15 mg at Week 12.

Ongoing phase 3 trials (NCT06088043 and NCT06108544) are investigating the efficacy and safety of zasocitinib in patients with moderate-to-severe plaque psoriasis across multiple endpoints, over a longer duration and in a larger patient population than in this phase 2b study.

Abbreviations: ATP, adenosine triphosphate; BSA, body surface area; DLQI, Dermatology Life Quality Index; FERM, band-4.1, erzin, radixin, moesin; JAK, Janus kinase; JH, Janus homology; LS, least-squares; mITT, modified intent-to-treat; PASI, Psoriasis Area and Severity Index; PGA, Physician's Global Assessment; QD, once daily; SD, standard deviation; SE, standard error; SH, Src homology; TYK2, tyrosine kinase 2.

Disclosures: VL: research for AbbVie, Acelyrin, Acrotech, Amgen, Arcutis, Argenx, Aslan, Biofrontera, Bristol Myers Squibb, Cara Therapeutics, Dermavant, Eli Lilly, Galderma, Horizon Therapeutics, Incyte, Janssen, LEO Pharma, Novartis, Padagis, Pfizer, Q3Bio, Rapt, Sun Pharma, UCB and Ventyx Biosciences. **LHK:** speaker, investigator, consultant and/or advisory board member for Abbott Laboratories, AbbVie, Allergan, Almirall, Amgen, Arcutis, Biogen Idec, Boehringer Ingelheim, Breckinridge Pharma, Bristol Myers Squibb, Celgene, Cellceutix, Centocor, Cipher, Combinatrix, Connetics, Coria, Dermavant, Dermira, Dow Pharmaceutical Sciences, Dr. Reddy's Laboratories, Eli Lilly, Galderma, Genentech, GSK, Idera, Johnson & Johnson, LEO Pharma, Maruho, Medicis, Merck, Nimbus,* Novartis, Pfizer, Pharmaderm, Promius, Stiefel Laboratories, Sun Pharma, Taro, UCB, Valeant, Ventyx and XenoPort. **NS:** consultant, investigator, speaker/faculty education, advisory board member, board of directors member, stockholder, independent contractor and/or other for AbbVie, Aclaris Therapeutics, Acorn Biolabs, Advalight, Allergan, Alma Lasers, American Academy of Dermatology, American Hair Research Society, American Society of Dermatologic Surgery, Amgen, ASDS, ASLAN, Aurigene Discovery Technologies, Bausch Health, Bellus Health, Biorasi LLC, Biosion, Bristol Myers Squibb, Canfield Scientific, Cara Therapeutics, Castle Biosciences, Celgene, Cell Research Corp, Concert Pharmaceuticals, Cutera, Derm Advance, Dermira, DermTech International, Distinct Dermatology, Dr. Reddy's Laboratory, Eirion Therapeutics, Eli Lilly, EndyMed Medical, Foundation for Research & Education of Dermatology, Galderma USA, Gerson Lehrman Group, Highlightll Pharmaceutical, Incyte Corporation, Informa, Janssen, Kadmon Corporation LLC, Kimera Labs, LCN Consulting, LEO Pharma, Lumenis Be, Lumisque, Merz Aesthetics, NFlection Therapeutics Inc., Nimbus Therapeutics,* NUMAB Therapeutics AG, Nutrafol, Pfizer, Philips Healthcare, PPD Inc., RegenLab, Rho Inc., Scientus Pharma Inc., Suzhou Connect Biopharmaceuticals, Taylor & Francis, Union Therapeutics, Vanda Pharmaceuticals Inc., Venus Concept, Viora and Vydence Medical. **JW:** research grants from AbbVie, Alumis, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Dermira, Eli Lilly, Galderma, Merck, Pfizer, Regeneron, Sanofi and Takeda. **JB**, **WZ**, **JU** and **WW:** employees and equity holders in Takeda. **MG:** investigator, speaker and/or advisor for AbbVie, Akros, Amgen, AnaptysBio, Apogee, Arcutis Biotherapeutics, Aristea, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly, Galderma, GSK, Incyte, Inmagene, JAMP, Janssen, Kyowa Kirin, LEO Pharma, MedImmune, Meiji, MoonLake Immunotherapeutics, Nimbus,* Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, Takeda, Tarsus Pharmaceuticals, UCB, Union Therapeutics, Ventyx Biosciences and Vyne Therapeutics.

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*Nimbus refers to the group of entities including Nimbus Therapeutics LLC, Nimbus Discovery, Inc., and Nimbus Lakshmi, Inc. (NB: Nimbus Lakshmi, Inc., was acquired by Takeda Pharmaceuticals in February 2023).

This poster is intended for healthcare professionals

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