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Zasocitinib (TAK-279), an Oral, Selective Tyrosine Kinase 2 Inhibitor: Achievement of Remission and Additional Improvements in Disease Activity in Patients with Psoriatic Arthritis Enrolled in a Phase 2b Trial

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SESSION INFORMATION

Date: Monday, November 18, 2024

Session Type: Abstract Session

Title: Abstracts: SpA Including PsA – Treatment II

Session Time: 1:00PM-2:30PM

Background/Purpose: Zasocitinib (TAK-279) is an oral, selective TYK2 inhibitor under investigation for the treatment of immune-mediated inflammatory diseases including psoriatic arthritis (PsA). In a phase 2b trial in patients with active PsA (NCT05153148), 12-week ACR20 response rates were significantly greater among patients receiving zasocitinib 15 or 30 mg once daily (QD) than those receiving placebo (PBO, primary endpoint; p=0.002).[1] PsA treat-to-target recommendations state that the treatment target should be remission or low disease activity (LDA);[2] here, additional disease activity data are presented.

Methods: This was a phase 2b, randomized, multicenter, double-blind, placebo-controlled, multiple-dose study. Patients (18–70 years) with active PsA were randomized 1:1:1:1 to receive oral zasocitinib 5, 15 or 30 mg QD or PBO for 12 weeks.[1] Secondary endpoints included change from baseline (BL) to Week 12 in Disease Activity Index for PsA (DAPSA). Exploratory endpoints included changes from BL to Week 12 in PsA Disease Activity Score (PASDAS) and Disease Activity Score 28 with high-sensitivity C-reactive protein (DAS28-hsCRP), and the proportion of patients achieving improvements in PsA Response Criteria (PsARC) at Week 12. Differences were assessed using a Mantel–Haenszel test (binary endpoints) and a mixed model for repeated measures (continuous endpoints). All p values are nominal.

Results: In total, 290 patients were randomized and treated. BL disease characteristics were generally comparable across groups; mean (standard deviation; SD) PsA disease duration was 6.9 (7.1) years and mean hsCRP level was 7.0 (12.2) mg/L. Mean (SD) tender joint count and DAPSA at BL

were lower in the zasocitinib 30 mg arm (14.0 [9.4] and 33.4 [15.8], respectively) than in the PBO (18.5 [14.7] and 38.3 [20.7], respectively), zasocitinib 5 mg (18.4 [15.2] and 39.0 [21.6], respectively) and zasocitinib 15 mg (18.0 [12.8] and 40.1 [18.0], respectively) arms. Greater numbers of patients receiving zasocitinib 15 or 30 mg than those receiving PBO or zasocitinib 5 mg were considered in remission or achieved LDA at Week 12, as measured using DAPSA, PASDAS and DAS28-hsCRP (**Table 1**). Least-squares mean changes from BL to Week 12 in DAPSA, PASDAS and DAS28-hsCRP were generally greater in patients receiving zasocitinib than in those receiving PBO, at all doses tested (**Figure 1**). Compared with PBO, patients receiving zasocitinib 15 or 30 mg had greater reductions in DAPSA (–17.99 [p=0.018] and –16.79 [p=0.056], respectively), PASDAS (–1.91 [p< 0.001] and –1.75 [p=0.001], respectively) and DAS28-hsCRP (–1.20 [p=0.002] and –1.15 [p=0.006], respectively) at Week 12. At Week 12, a numerically higher proportion of patients receiving zasocitinib 15 mg or 30 mg achieved a PsARC response versus those receiving PBO (p=0.024 and p=0.140, respectively).

Conclusion: Treatment with zasocitinib 15 and 30 mg resulted in higher rates of remission or LDA after 12 weeks in patients with PsA compared with placebo. Zasocitinib shows promise as a novel oral therapy in PsA and warrants further investigation in phase 3 trials.

References:

1. Kivitz A *et al*. *Arthritis Rheumatol* 2023;75 (Suppl 9).

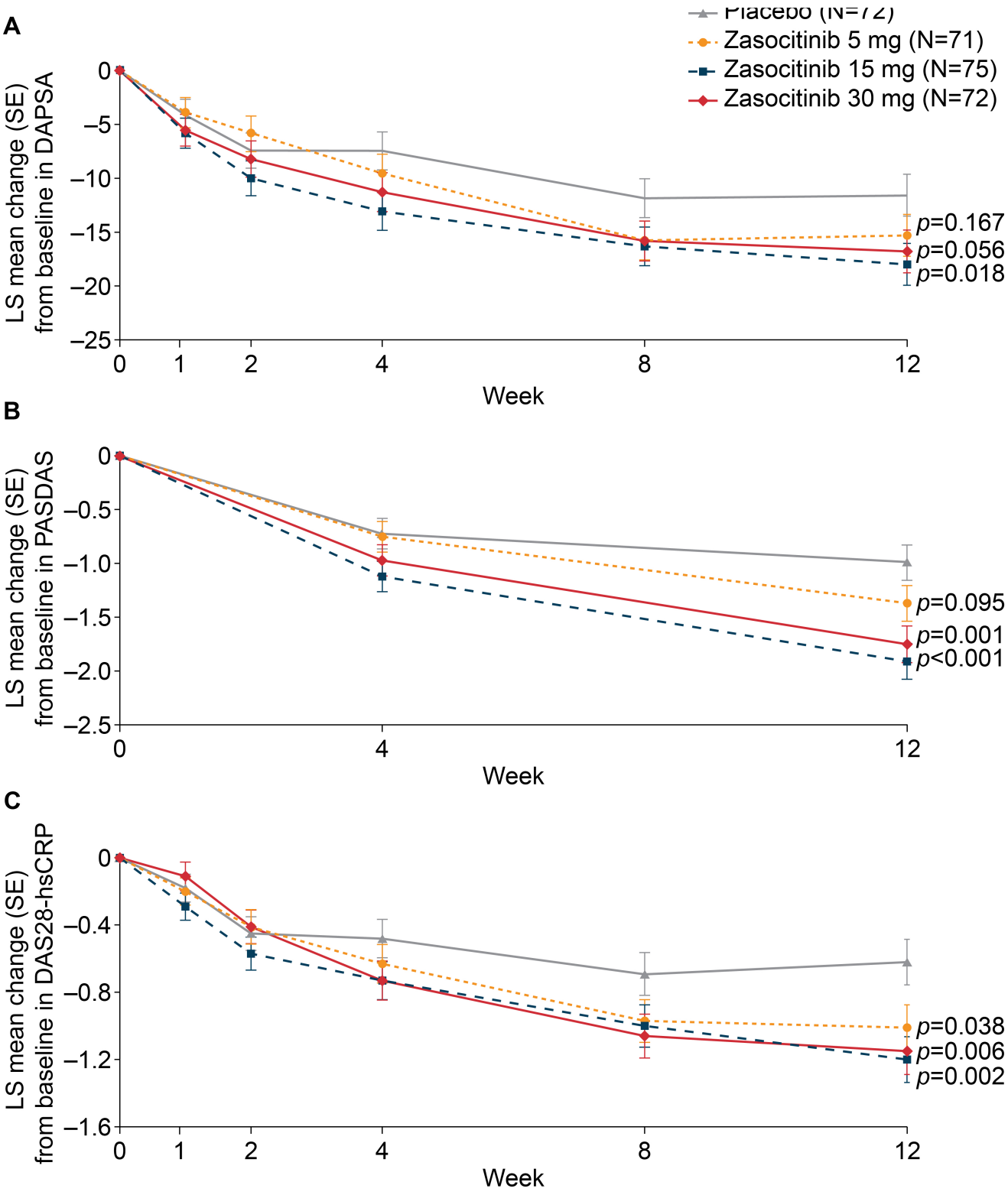
2. Gossec L *et al*. *Ann Rheum Dis* 2024;83:706–19.

Table 1. Proportion of patients achieving REM, LDA and MDA at Week 12 according to DAPSA, PASDAS and DAS28-hsCRP.

n/N (%)	Placebo (N=72)	Zasocitinib 5 mg (N=71)	Zasocitinib 15 mg (N=75)	Zasocitinib 30 mg (N=72)
DAPSA†				
REM	3/66 (4.5)	7/64 (10.9)	11/64 (17.2)	10/62 (16.1)
LDA	16/66 (24.2)	17/64 (26.6)	23/64 (35.9)	22/62 (35.5)
MDA	24/66 (36.4)	23/64 (35.9)	20/64 (31.3)	20/62 (32.3)
PASDAS¶				
REM	3/64 (4.7)	3/64 (4.7)	9/63 (14.3)	7/60 (11.7)
LDA	9/64 (14.1)	13/64 (20.3)	16/63 (25.4)	21/60 (35.0)
MDA	37/64 (57.8)	36/64 (56.3)	27/63 (42.9)	23/ 60 (38.3)
DAS28-hsCRP‡				
REM	9/66 (13.6)	19/64 (29.7)	20/64 (31.3)	24/62 (38.7)
LDA	10/66 (15.2)	9/64 (14.1)	13/64 (20.3)	13/62 (21.0)
MDA	36/66 (54.5)	33/64 (51.6)	27/64 (42.2)	20/62 (32.3)

'n' represents the number of patients who met the criteria at the visit. 'N' represents the number of patients with a non-missing measurement at the visit. Percentages are calculated based on 'N'.
†REM: ≤4; LDA: 4 to ≤14; MDA: 14 to ≤28.
¶REM: ≤1.9; LDA 1.9 to <3.2; MDA: 3.2 to ≤5.4.
‡REM <2.6; LDA: 2.6 to <3.2; MDA: 3.2 to ≤5.1.
DAPSA, Disease Activity Index for Psoriatic Arthritis; hsCRP, high-sensitivity C-reactive protein; LDA, low disease activity; MDA, medium disease activity; REM, remission; PASDAS, Psoriatic Arthritis Disease Activity Score.

Figure 1. LS mean changes from baseline to Week 12 in DAPSA, PASDAS and DAS28-hsCRP.



LS mean and nominal *p* values were obtained from a mixed model for repeated measures. The model included treatment group, visit, treatment-by-visit interaction, previous treatment with biologics or nontraditional disease-modifying anti-rheumatic drugs, and region as fixed effects, and baseline score as a covariate.
DAPSA, Disease Activity Index for Psoriatic Arthritis; DAS28, Disease Activity Score 28; hsCRP, high-sensitivity C-reactive protein; LS, least-squares; PASDAS, Psoriatic Arthritis Disease Activity Score; SE, standard error.

Disclosures: P. Mease: AbbVie, 2, 5, Aclaris Therapeutics, 2, 5, Aclyrin, 2, 5, Amgen, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Myers Squibb, 2, 5, CorEvitas, 2, 5, Galápagos, 2, 5, Gilead, 2, 5, Inmagene, 2, 5,

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