Efficacy of Pozdeutinurad (AR882) in Treatment Naïve and Uncontrolled Gout or Tophaceous Gout Patients in Asia-Pacific Patients

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712

CONCLUSIONS

- Pozdeutinurad (AR882, POZD) monotherapy achieved clinically meaningful serum urate (SU) reductions below the recommended guidelines of <6mg/dL.
- High rates of complete tophus resolution were observed in patients with gout who were uncontrolled on, or naïve to, urate-lowering therapy (ULT).
- These findings support POZD as a potentially effective treatment option for Asia-Pacific patients to control symptoms of gout.

INTRODUCTION

- Patients living with gout require ULT to reduce and maintain SU levels below the target ACR guideline recommendation of <6 mg/dL.
- POZD is a selective and potent uric acid transporter-1 (URAT1) inhibitor, which blocks uric acid reabsorption in the kidney proximal tubule, resulting in normalized uric acid excretion and reduced SU levels.
- Phase 2 trials demonstrated robust serum urate (SU) lowering at both doses of POZD 50 and 75 mg QD and was generally well tolerated. [1,2]
- POZD is currently being evaluated in Phase 3 clinical trials for the treatment of gout and tophaceous gout in the United States (US) and Asia-Pacific regions.

OBJECTIVES

- This retrospective analysis explored the effectiveness of POZD in controlling SU levels and dissolution of tophi in patients who were enrolled in the Phase 2 trials at sites within the Asia-Pacific region.

METHODS

- **Trial 1:** Phase 2B trial (NCT05119686) evaluated SU lowering effect of POZD versus placebo in gout patients. 142 patients enrolled in the US, Australia, and Taiwan. Patients were randomized to POZD 50 mg, 75 mg, or placebo QD for 12 weeks. 87 patients receiving POZD treatment were evaluable for the subgroup analysis.[1]
- **Trial 2:** In the Phase 2 tophaceous gout trial (NCT05253833), conducted in the US, New Zealand, and Taiwan, 42 patients with ≥1 subcutaneous tophus were enrolled. Changes in target tophus area and complete resolution of ≥1 target tophus or >50% reduction in tophus size were assessed using digital calipers. Here we show the results for the patients enrolled in the arm receiving POZD 75 mg QD for 18 months (n=14). [2]
- In both studies, patients were eligible if they were either inadequately controlled on urate lowering therapy (ULT) with SU > 6.0 mg/dL (uncontrolled subgroup), or if they were not on ULT prior to screening with SU ≥ 7.0 mg/dL (naïve subgroup).
- Efficacy endpoints included change from baseline in SU levels.

RESULTS

SU Lowering Effect and Response Rate

- In the Asia-Pacific subgroup, both gout and tophaceous gout patients had a clinically significant and sustained SU reductions.
- Across both trials, >60% of patients achieved SU<6mg/dL by week 12 (Trial 1) or Month 3 (Trial 2) and this response was sustained through Month 18 (Table 1).
- In tophaceous gout patients, 100% patients had an SU<6 mg/dL from Month 12 and onwards (**Table 1**).

Reduction in Tophi

- In the Asia-Pacific subgroup, 50% had a complete resolution of a tophi by Month 12, and 100% of patients had a >50% reduction in the tophus areas from M6 and onwards (**Table 2**).
- The single treatment naïve patient in the Asia-Pacific subgroup had a significant baseline tophi burden but still demonstrated a 17% reduction in tophi area in only 6 months.

Table 1: Serum Urate Lowering Effect and Response Rate

Study	Dose	Group	Visit	All Patients N=101 Median SU (mg/dL) (n, change in SU, % change in SU, %resp SU<6mg/dL)	Asia-Pacific subgroup N=31 Median SU (mg/dL) (n, change in SU, % change in SU, %resp SU<6mg/dL)
Trial 1 (gout)	50 mg	Naïve	Baseline	8.2 (20)	9.1 (6)
			WK6	4.7 (18, -3.6, -40, 83)	5.2 (5, -4.4, -42, 80)
			WK12	4.7 (17, -3.7, -43, 88)	4.9 (6, -4.4, -48, 100)
		Uncontrolled	Baseline	8.8 (23)	8.6 (11)
			WK6	5.4 (19, -2.9, -32, 53)	5.2 (10, -2.9, -36, 60)
			WK12	5.5 (19, -3.3, -35, 53)	5.5 (9, -3.2, -31, 56)
	75 mg	Naïve	Baseline	8.2 (20)	8.9 (5)
			WK6	3.5 (17, -5.4, -60, 94)	3.5 (5, -5.9, -66, 80)
			WK12	3.5 (15, -5.1, -64, 87)	3.6 (4, -5.5, -63, 75)
		Uncontrolled	Baseline	8.7 (24)	8.1 (5)
			WK6	3.6 (24, -4.4, -57, 79)	3.2 (5, -4.5, -60, 80)
			WK12	3.5 (23, - 4.5, -57, 83)	3.0 (5, -5.0, -63, 80)
Trial 2 (tophaceous gout)	75 mg	Naïve	Baseline	9.1 (5)	9.6 (1)
			M3	3.5 (3, -4.4, -56, 100)	3.5 (3, -6.1, -63, 100)
			M6	3.9 (3, -4.1, -53, 100)	3.9 (1, -5.7, -60, 100)
			M12	3.8 (1, -4.0, -51, 100)	-
			M18	-	-
		Uncontrolled	Baseline	9.4 (9)	8.6 (3)
			M3	4.9 (9, -4.4, -53, 89)	3.5 (3, -4.4, -55, 100)
			M6	5.8 (9, -3.7, -44, 56)	4.0 (3, -3.7, -48, 67)
			M12	4.0 (6, -4.5, -53, 83)	3.9 (2, -4.7, -54, 100)
			M18	4.3 (6, -5.0, -54, 83)	4.3 (2, -4.4, -55, 100)

change: median absolute change from baseline in sUA**; %change:** median percent change from baseline in sUA**; resp%sUA< 6 mg/dL:** response rate (%) to achieve sUA below 6 mg/dL

Table 2: Reduction in Target Tophus Areas and Complete Resolution of at Least 1 Target Tophus or >50% of reduction (Trial 2)

Group	Dose	Visit	All Patients (14) Median sum areas (mm^2) (n, change, % change)	All Patients (14) Complete resp%, >50% reduction in sum areas	Asia-Pacific subgroup (4) Median sum areas (mm^2) (n, change, % change)	Asia-Pacific subgroup (4) Complete resp%, >50% reduction in sum areas
Naïve	75 mg	Baseline	414 (5)		742 (1)	
		Month 6	425 (3, -179, -26)	1/3 (33), 0/3 (0)	618 (1, -124, -17)	0/1 (0)
		Month 12	141 (1, 50, 55)	0/1 (0), 0/1 (0)	-	-
		Month 18	-	-	-	-
Uncontrolled	75 mg	Baseline	500 (9)	-	553 (3)	-
		Month 6	195 (9, -278, -61)	3/9 (33), 6/9 (67)	100 (3, -403,-87)	1/3 (33), 3/3 (100)
		Month 12	293 (6, -324, -70)	3/6 (50), (4/6 (67)	70 (2, -382, -86)	1/2 (50), 2/2 (100)
		Month 18	123 (6, -344, -86)	3/6 (50), (4/6, 67)	40 (2, -412, -92)	1/2 (50), 2/2 (100)

change: median absolute change from baseline in tophus area**; %change:** median percent change from baseline in tophus area**; sum areas:** sum of target tophus areas**; Complete resp%:** complete response of at least 1 target tophus**; >50% reduction in sum areas**: Percentage of greater than 50% reduction in sum of target tophus areas

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