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Baseline Pain Severity as a Predictor of Pain Improvement following Treatment with Tofacitinib in Psoriatic Arthritis

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Background/Purpose: Pain is a core domain of psoriatic arthritis (PsA), and it is recommended that all randomized controlled trials (RCTs) in patients (pts) with PsA include an assessment of pain.[1]Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. The objective of this post hoc analysis was to determine the impact of pain severity at baseline as a predictor of time to pain improvement in pts with active PsA following treatment with tofacitinib for up to 12 months.

Methods: Data from pts randomized to tofacitinib 5 mg twice daily (BID) in 2 Phase 3 RCTs were included in this analysis. Pts had active PsA and an inadequate response to ≥1 conventional synthetic DMARD (csDMARD) (OPAL Broaden; NCT01877668), or to ≥1 tumor necrosis factor inhibitor (OPAL Beyond; NCT01882439). All pts continued on a stable dose of a single csDMARD. Current arthritis pain severity was reported by pts using a 100 mm visual analog scale, where higher scores indicated greater severity of pain. Pain improvement was defined as the first post-baseline pain improvement of ≥30% (meaningful change), ≥50% (substantial change), and ≥70% relative to baseline.[2] Median time to pain improvement was assessed using a parametric model. The model was fitted to examine the relationship between baseline pain severity and time to pain improvement.

Results: Overall, 236 pts who received tofacitinib 5 mg BID were included in this analysis. The Table and Figure present an estimated relationship between baseline pain score and the median time to response. It was shown that, for pts with a baseline pain level of 90 mm, the predicted median time to achieve ≥30% pain improvement was 39.3 days, meaning that 50% of pts with baseline pain of 90 mm were estimated to achieve ≥30% pain improvement during the first 39.3 days. For a baseline pain level of 50 mm,

the predicted median time to achieve ≥30% pain improvement was 56.7 days (Table; Figure).

Conclusion: In pts with active PsA treated with tofacitinib 5 mg BID, the time to pain improvement was dependent upon baseline pain severity, with lower pain scores at baseline associated with longer time to improvement than higher pain scores. Pts with higher pain severity at baseline achieved clinically meaningful pain improvements faster than pts with lower severity of pain. It is important to consider the non-linearity of change in pain, and the decreased ability to assess change in pain among pts with lower pain scores at baseline, when interpreting these findings.

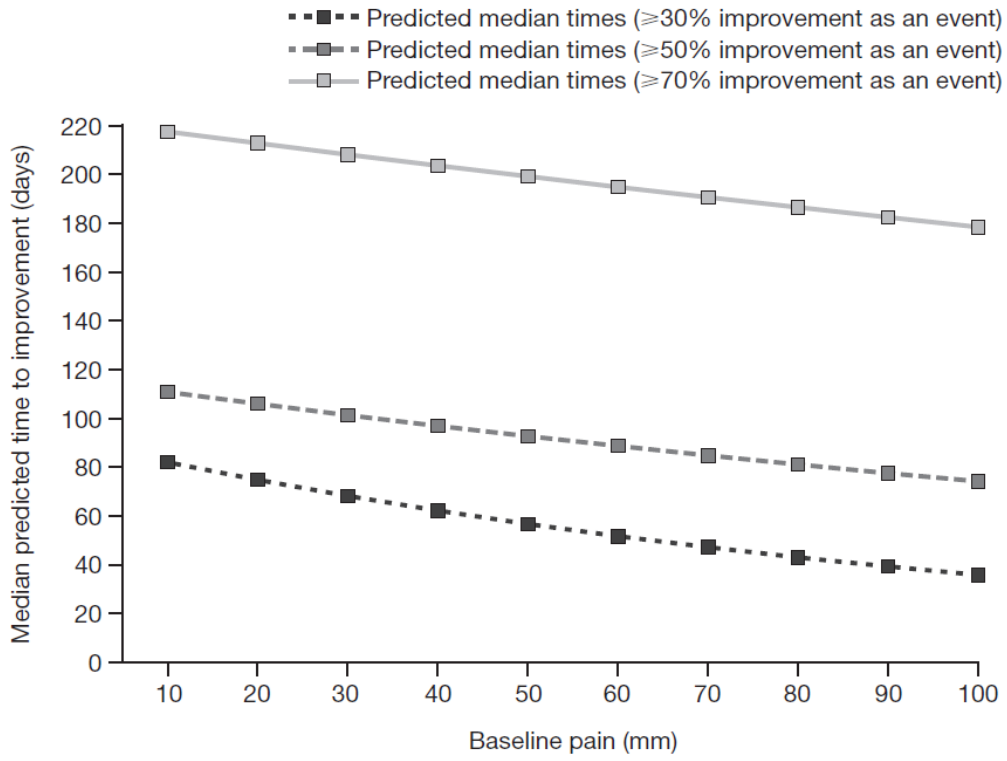
1. Orbai AM et al. Ann Rheum Dis 2017; 76: 673-80.
2. Dworkin RH et al. J Pain 2008; 9: 105-21

Table. Predicted median time (days) to pain improvement (≥30%, ≥50%, and ≥70% improvement) as a function of baseline pain severity in pts with PsA receiving tofacitinib 5 mg BID

Baseline pain, mm (VAS)	**Predicted median time to improvement, days (95% CI)**		
	≥30% improvement	**≥50% improvement**	**≥70% improvement**
10	82.0 (57.2, 117.5)	110.8 (73.9, 166.1)	217.5 (132.2, 357.9)
20	74.8 (55.4, 100.9)	106.0 (75.6, 148.5)	212.8 (140.0, 323.4)
30	68.2 (53.4, 87.1)	101.3 (76.9, 133.5)	208.1 (147.3, 294.2)
40	62.2 (51.0, 75.8)	96.9 (77.5, 121.2)	203.6 (153.0, 271.0)
50	56.7 (48.0, 67.1)	92.7 (76.7, 112.1)	199.2 (155.4, 255.2)
60	51.7 (44.0, 60.9)	88.7 (73.7, 106.6)	194.8 (152.9, 248.2)
70	47.2 (39.2, 56.8)	84.8 (68.7, 104.6)	190.6 (145.4, 249.9)
80	43.0 (34.3, 54.1)	81.1 (62.7, 104.9)	186.5 (134.7, 258.1)
90	39.3 (29.6, 52.0)	77.5 (56.5, 106.4)	182.4 (123.0, 270.5)
100	35.8 (25.5, 50.3)	74.2 (50.6, 108.7)	178.4 (111.3, 286.0)

BID, twice daily; CI, confidence interval; PsA, psoriatic arthritis; pts, patients; VAS, visual analog scale

Figure. Predicted median time (days) to pain improvement (≥30%, ≥50%, and ≥70% improvement) as a function of baseline pain severity in pts with PsA receiving tofacitinib 5 mg BID



BID, twice daily; PsA, psoriatic arthritis; pts, patients
A model (known as the Parametric Accelerated Failure Time model) was fitted to examine the relationship between baseline pain severity and the time to ≥30%, ≥50%, and ≥70% improvement