Time to First Clinically Meaningful Efficacy Responses in Musculoskeletal and Patient-Reported Outcomes in Patients With Active Psoriatic Arthritis Treated With Risankizumab: A Post Hoc Analysis of the Phase 3 KEEPsAKE 1 and KEEPsAKE 2 Trials

1467

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OBJECTIVE

- To evaluate the median time to first achievement of clinically meaningful musculoskeletal (MSK) efficacy responses and patient-reported outcomes (PROs) in patients with active PsA who are treated with risankizumab (RZB)

INTRODUCTION

- PsA is a heterogenous disease with key MSK manifestations in peripheral joints, the spine, as well as skin, which negatively affects quality of life (QoL)[1,2]
- The phase 3 KEEPsAKE 1 (NCT03675308) and KEEPsAKE 2 (NCT03671148) randomized double-blind clinical trials demonstrate that RZB provides a high level of durable improvement in MSK as well as dermatological manifestations[3,4]
- Long-term results from the KEEPsAKE trials have also demonstrated a favorable safety profile in psoriatic disease, as published in previous reports[3,4]
- This post hoc analysis evaluates the median time to first achievement of clinically meaningful MSK efficacy responses and PROs in patients with active PsA who are treated with RZB

METHODS

STUDY DESIGN

- The ongoing KEEPsAKE 1 and KEEPsAKE 2 phase 3 trials enrolled patients ≥ 18 years with active PsA who responded inadequately or were intolerant to ≥ 1 conventional synthetic DMARD (csDMARD), and patients with previous inadequate response or intolerance to 1 or 2 biological therapies (Bio-IR) and/or ≥ 1 csDMARD, respectively

METHODS (CONTINUED)

- Patients were randomized at baseline to receive either RZB 150 mg or placebo (PBO) at weeks 0 and 4, and every 12 weeks thereafter until week 24 (period 1)
- Following period 1, all patients received RZB 150 mg at 12-week intervals

PATIENT POPULATION

- This post hoc study included:
  - Bio-naïve patients pooled from the KEEPsAKE 1 and 2 trials who received continuous RZB 150 mg starting at baseline
  - Bio-IR patients from the KEEPsAKE 2 trial who received continuous RZB 150 mg starting at baseline

ANALYSES

- 15 outcomes related to MSK efficacy responses and PROs were evaluated for the bio-naïve and bio-IR population as indicated in **Table 1**, **Table 2**, and **Figure 1**, respectively
- The median and 25th percentiles of time to first achievement of efficacy outcomes were calculated using Kaplan-Meier estimates by week 52; patients who did not achieve the outcomes by week 52 were censored at their last visit by the cutoff date
- For the bio-naïve population only, the cumulative days of response for ≥ 50% improvement in TJC, ≥ 50% improvement in SJC, minimum clinically important difference (MCID) in pain, and MCID in BASDAI were calculated by the average number of days with each response up to week 52, and estimated by the percentage of the maximum area under the curve (AUC) over study duration of 52 weeks (365 days)[5,6]

RESULTS

BIO-NAÏVE PATIENTS

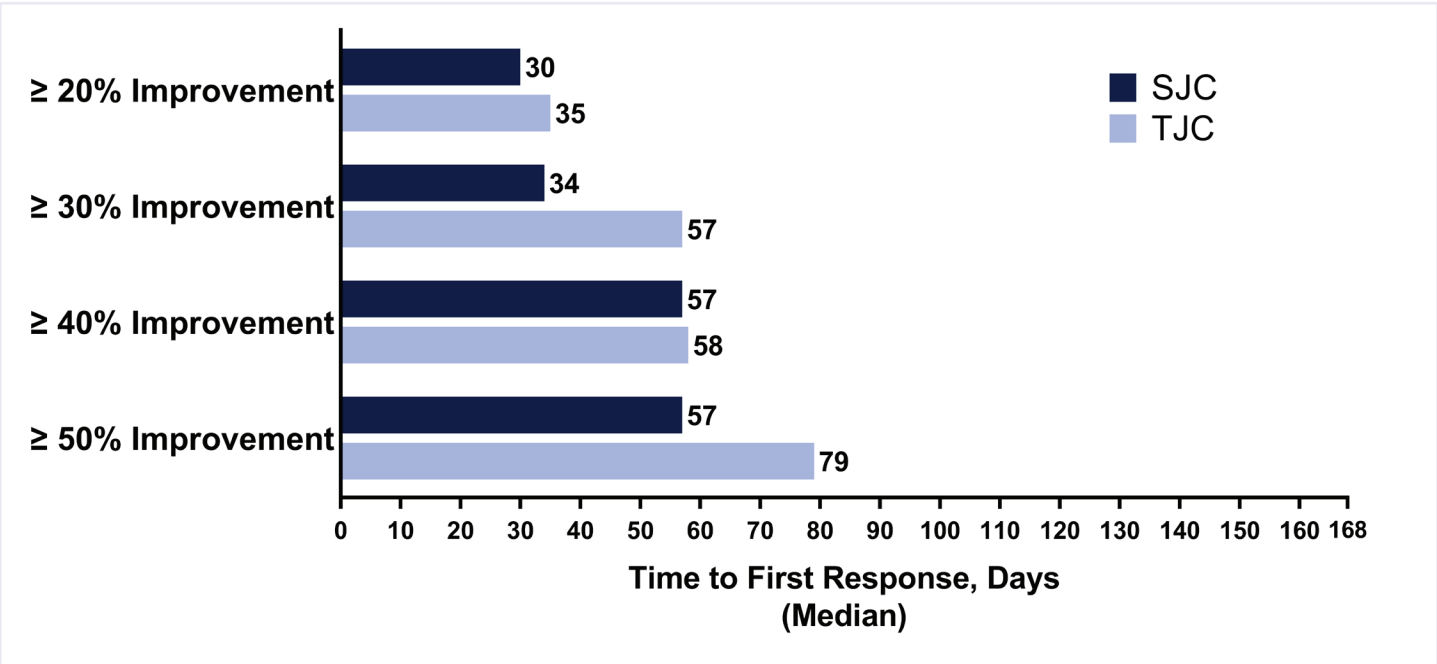
- A total of 598 bio-naïve patients from the KEEPsAKE 1 and 2 trials were included in the pooled analysis, with a high number of responders across the assessed outcomes **(Table 1)**
- Median time to first achieve ≥ 20% improvement in TJC, ≥ 30% improvement in TJC, ≥ 40% improvement in TJC, and ≥ 50% improvement in TJC was 35, 57, 58, and 79 days, respectively **(Table 1** and **Figure 1)**
- Median time to first achieve ≥ 20% improvement in SJC, ≥ 30% improvement in SJC, ≥ 40% improvement in SJC, and ≥ 50% improvement in SJC was 30, 34, 57, and 57 days, respectively **(Table 1** and **Figure 1)**
- Median time to first achieve achieve MCID in pain and MCID in BASDAI was 55 and 92 days, respectively **(Table 1)**
- Median time to first achieve MCID in PtGA, HAQ-DI, SF-36 PCS, SF-36 MCS, and FACIT-F was 53, 64, 88, 93, and 93 days, respectively **(Table 1)**

Table 1. Time to First Response for MSK Outcomes and PROs in Bio-Naïve Patients on Continuous RZB 150 mg

Efficacy Outcome	No. of First Responders, n/N	Time to First Response, Days	
		25th Percentile	Median
Musculoskeletal Outcomes			
≥ 20% improvement in TJC	584/598	29	35
≥ 20% improvement in SJC	589/598	29	30
≥ 50% improvement in TJC	560/598	50	79
≥ 50% improvement in SJC	582/598	29	57
MCID in Pain	521/582	29	55
MCID in BASDAI	93/116	85	92
Patient-Reported Outcomes			
MCID in PtGA	534/583	29	53
MCID in HAQ-DI	394/513	30	64
MCID in SF-36 PCS	510/598	85	88
MCID in SF-36 MCS	442/598	85	93
MCID in FACIT-F	464/598	85	93

FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue Questionnaire; MCID, minimum clinically important difference; PtGA, Patient Global Assessment of Disease Activity; SF-36 MCS, 36-Item Short Form Health Survey Mental Component Summary; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary.
MCID in pain (≥ 10 point decrease on the 0-100 visual analogue scale), for patients with baseline score ≥ 10 mm.
MCID in BASDAI (≥ 1.1 point decrease), for patients with spondylitis at baseline.
MCID in PtGA (≥ 10 point decrease), for patients with baseline score ≥ 10.
MCID in HAQ-DI (≥ .35 point decrease), for patients with baseline score ≥ 0.35.
MCID in SF-36 PCS (≥ 2.5 point increase).
MCID in SF-36 MCS (≥ 2.5 point increase).
MCID in FACIT-F (≥ 4 point increase).

Figure 1. Median Time to First Improvement in SJC and TJC in Bio-Naïve Patients on Continuous RZB 150 mg



Data are presented as median days to first response.
X axis represents 24 weeks (168 days) of the randomized placebo-controlled trials (period 1).

RESULTS (CONTINUED)

BIO-IR PATIENTS

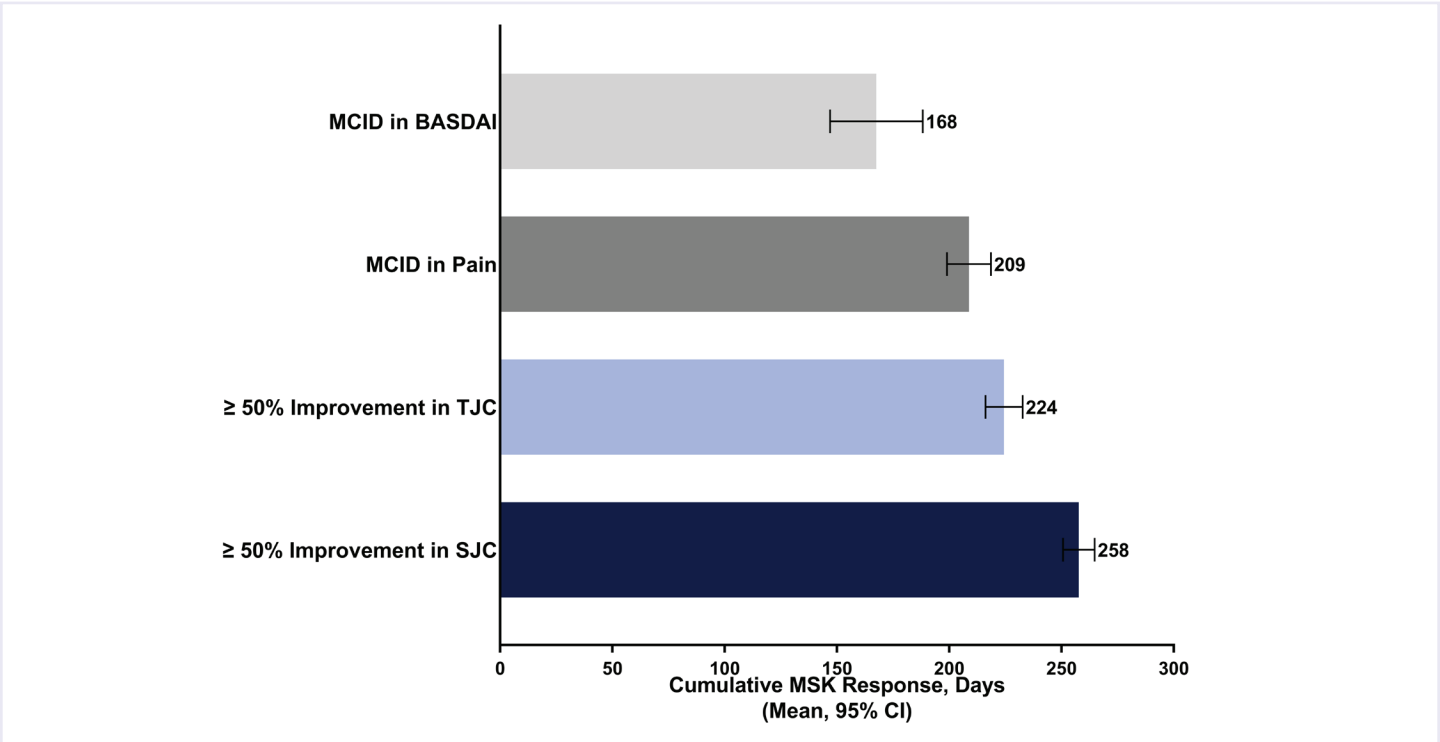
- A total of 106 bio-IR patients from the KEEPsAKE 2 trial were included in the analysis **(Table 2)**
- Median time to first achieve ≥ 20% improvement in TJC and ≥ 50% improvement in TJC was 55 and 85 days, respectively **(Table 2)**
- Median time to first achieve ≥ 20% improvement in SJC and ≥ 50% improvement in SJC was 31 and 57 days, respectively **(Table 2)**
- Median time to first achieve achieve MCID in pain and MCID in BASDAI was 58 and 169 days, respectively **(Table 2)**; median time to first achieve MCID in PtGA, HAQ-DI, SF-36 PCS, SF-36 MCS, and FACIT-F was 57, 169, 92, 171, and 166 days, respectively **(Table 2)**
- In the bio-naïve patient population, patients treated with continuous RZB 150 mg over 52 weeks (365 days) experienced ≥ 50% improvement in TJC, ≥ 50% improvement in SJC, MCID in pain, and MCID in BASDAI (among patents with spondylitis at baseline) for approximately 224 days, 258 days, 209 days, and 168 days, respectively **(Figure 2)**

Table 2. Time to First Response for MSK Outcomes and PROs in Bio-IR Patients on Continuous RZB 150 mg

Efficacy Outcome	No. of First Responders, n/N	Time to First Response, Days	
		25th Percentile	Median
Musculoskeletal Outcomes			
≥ 20% improvement in TJC	101/106	29	55
≥ 20% improvement in SJC	105/106	29	31
≥ 50% improvement in TJC	97/106	56	85
≥ 50% improvement in SJC	100/106	30	57
MCID in Pain	85/103	30	58
MCID in BASDAI	21/25	85	169
Patient-Reported Outcomes			
MCID in PtGA	95/103	29	57
MCID in HAQ-DI	68/97	56	169
MCID in SF-36 PCS	87/106	85	92
MCID in SF-36 MCS	73/106	86	171
MCID in FACIT-F	81/106	85	166

FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue Questionnaire; MCID, minimum clinically important difference; PtGA, Patient Global Assessment of Disease Activity; SF-36 MCS, 36-Item Short Form Health Survey Mental Component Summary; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary.
MCID in pain (≥ 10 point decrease on the 0-100 visual analogue scale), for patients with baseline score ≥ 10 mm.
MCID in BASDAI (≥ 1.1 point decrease), for patients with spondylitis at baseline.
MCID in PtGA (≥ 10 point decrease), for patients with baseline score ≥ 10.
MCID in HAQ-DI (≥ .35 point decrease), for patients with baseline score ≥ 0.35.
MCID in SF-36 PCS (≥ 2.5 point increase).
MCID in SF-36 MCS (≥ 2.5 point increase).
MCID in FACIT-F (≥ 4 point increase).

Figure 2. Cumulative Days of Improvement in Key MSK Outcomes and PROs in Bio-Naïve Patients on Continuous RZB 150 mg



The analyses are based on AO with imputation data. 95% CIs are calculated based on t-statistics.
MCID in pain (≥ 10 point decrease on the 0-100 visual analogue scale), for patients with baseline score ≥ 10 mm.
MCID in BASDAI (≥ 1.1 point decrease), for patients with spondylitis at baseline.
MCID, minimum clinically important difference; MSK, muscoskeletal; PRO, patient-reported outcomes.

CONCLUSION

- Bio-naïve patients treated with RZB achieved early median times to clinically meaningful MSK outcomes and PROs
- Similar trends in median time to first response in key muscoloskeletal outcomes were observed between bio-naïve and bio-IR patients treated with RZB
- This study provides an estimate for the cumulative days of response (range, 168 to 258) to RZB treatment in outcomes such as peripheral arthritis, overall pain, and in patients with axial involvement

REFERENCES

1. Gladman DD, et al. *Ann Rheum Dis.* 2005;64(Suppl 2):ii14–ii17.
2. Kavanaugh A, et al. *Rheumatol and Therapy.* 2016;3:91–102.
3. Kristensen, et al. *Ann Rheum Dis*. 2022;81(2):225–31.
4. Östör A, et al. *Ann Rheum Dis*. 2022;81:351–8.
5. Blauvelt A, et al. *Dermatol Ther (Heidelb)*. 2022;12:727–40.
6. Armstrong AW, et al. *Dermatol Ther (Heidelb)*. 2024;14,1891–99.

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