Low Probability of Clinical Worsening Following Switching Biologic Disease-Modifying Antirheumatic Drug in Patients With Rheumatoid Arthritis and Partial Response to Adalimumab

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BACKGROUND AND OBJECTIVES

- Guidelines recommend adjusting therapy in patients with RA who fail to reach low disease activity or remission;[1,2] however, patients may decline to change treatment after a partial response for fear of clinical worsening and/or losing the response that was achieved[3,4]
- No data currently exist that address the likelihood of clinical worsening following a switch in therapy in patients who had a partial response and who did not achieve a predetermined treatment goal. While data on clinical response are available, a lack of clinical response does not equate to clinical worsening
- To assess the likelihood of clinical worsening, we performed a post hoc analysis of the MONARCH OLE to assess the effects of switching from adalimumab to sarilumab in patients who had only partially responded to adalimumab during the double-blind phase (DBP)

METHODS

- The MONARCH study (NCT02332590) evaluated the efficacy and safety of the anti–interleukin-6 (IL-6) antibody sarilumab as monotherapy (200 mg subcutaneously [SC] q2w) versus adalimumab monotherapy (40 mg SC q2w) in patients with RA who had an inadequate response or intolerance to methotrexate[5]
- In the OLE, patients who had been randomized to DBP adalimumab were switched to open-label sarilumab 200 mg q2w (switch group), and those randomized to DBP sarilumab 200 mg q2w continued open-label sarilumab 200 mg q2w (continuation group)
  - The continuation group was included as a control group to evaluate for potential bias related to receiving open-label treatment
- Only patients with a partial, inadequate response in the DBP were included in the present analysis. Partial response was defined as patients with continuing moderate-to-high disease activity (CDAI >10) at OLE baseline, despite an improvement of at least the minimal clinically important difference (MCID) in CDAI during the DBP
  - For patients with high disease activity at DBP baseline (CDAI >22), the MCID improvement threshold was 12 units
  - For those with moderate disease activity at DBP baseline (CDAI >10 to ≤22), the MCID improvement threshold was 6 units
- Following treatment switch at the end of the DBP, various thresholds for subsequent meaningful clinical worsening or improvement were assessed, relative to OLE baseline, including: CDAI, ±6 and ±12; swollen or tender joint counts (SJC or TJC), ±1; physician or patient global assessments (MDGA or PtGA), ±10 and ±20; and Disease Activity Score 28-joint count Erythrocyte Sedimentation Rate (DAS28-ESR) scores, ±0.6 and ±1.2
  - For each measure, any value between the thresholds for worsening and improvement was considered to represent no meaningful change
- Data are presented based on observed cases only, without nonresponder imputation

RESULTS

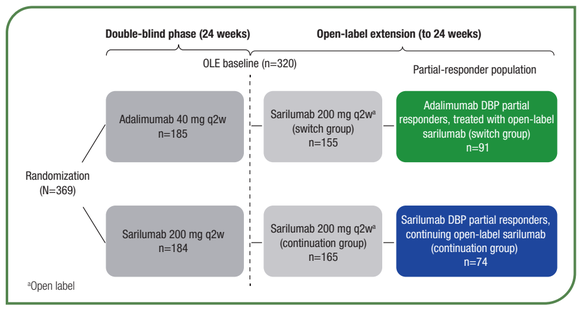
Patient characteristics

- Of 369 patients enrolled in the MONARCH DBP, 320 (87%) entered the OLE: 155 switching from adalimumab to sarilumab and 165 continuing sarilumab (**Figure 1**)
  - 52% were partial responders at OLE baseline: as expected, there were more partial responders in the switch group, n=91/155 (59%), versus the continuation group, n=74/165 (45%)
  - Partial responders in the continuation group had similar but numerically lower disease activity scores at entry into the OLE vs partial responders in the switch group, except for SJC and TJC

Efficacy

- Observations for efficacy measures were available at OLE Week 24 for 83 patients in the switch group and 70 patients in the continuation group
  - One additional patient in the switch group had an OLE Week 24 DAS28-ESR score but no other Week 24 efficacy measures

Figure 1. Schematic of the present analysis of partial responders



CONCLUSIONS

- Among partial but inadequate responders to adalimumab who, on average, had moderate-to-high disease activity (based on CDAI) at OLE baseline, only a few patients (6%) experienced clinical worsening at Week 24 after switching to sarilumab
- In contrast, more than half these patients experienced clinically meaningful improvement
- A small risk of worsening with the substantial likelihood of meaningful improvement may help alleviate patient fears of worsening when considering a switch to an alternative therapy, such as sarilumab

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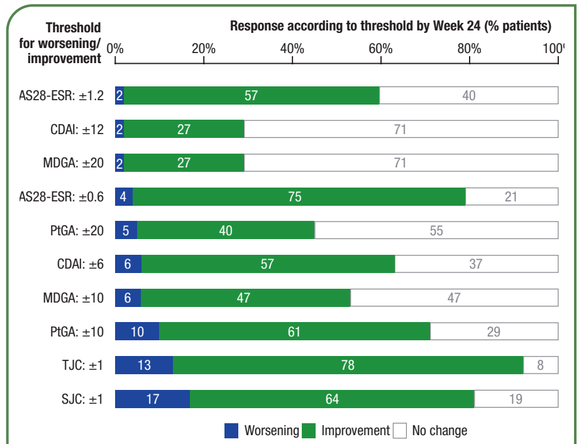
Figure 2. Summary of worsening, improvement, or no change in efficacy parameters and PROs from OLE baseline to Week 24 among partial responders in the switch group



n=83 for all measures, except DAS28-ESR (n=84). PROs, patient reported outcomes

- Among partial responders, based on a CDAI worsening threshold of 6 units, very few patients experienced worsening in disease activity in either the switch (6%; n=5/83; **Figure 2**) or continuation (4%; n=3/70) groups
- Among partial responders, based on a CDAI improvement threshold of 6 units, improvement in disease activity was observed in 57% (n=47/83) of switch and 43% (n=30/70) of continuation patients
- No change in disease activity, based on change in CDAI between –6 and +6, was evident in 37% (n=31/83) and 53% (n=37/70) of switch and continuation partial responders, respectively
- The proportion of partial responders with clinical worsening subsequent to switch was small, 2–17% depending on endpoint
- Mean changes from OLE baseline to Week 24 were numerically greater in the switch group compared with the continuation group in all efficacy parameters and PROs, with the exception of SJC28 (**Table 1)**

Safety

- The safety profile of sarilumab was consistent with that observed in Phase 3 trials and with that anticipated for an IL-6 receptor inhibitor[6–9]

Table 1. Mean (standard error) changes from OLE baseline to Week 24 in efficacy parameters and PROs in the partial-responder populations

	Adalimumab → sarilumab switch group	Sarilumab → sarilumab continuation group
OLE baseline cases	n=91	n=74
Week 24 observed cases	n=83	n=70
CDAI		
OLE baseline	19.6 (0.9)	19.0 (1.0)
Change from OLE baseline	–7.4 (1.1)	–5.5 (0.9)
SJC28		
OLE baseline	4.1 (0.3)	4.6 (0.4)
Change from OLE baseline	–1.3 (0.5)	–1.9 (0.3)
TJC28		
OLE baseline	7.5 (0.6)	7.6 (0.6)
Change from OLE baseline	–3.4 (0.6)	–2.3 (0.7)
MDGA (0–100mm)		
OLE baseline	31.9 (1.8)	26.0 (1.7)
Change from OLE baseline	–11.3 (1.8)	–5.6 (1.8)
PtGA (0–100mm)		
OLE baseline	47.6 (2.1)	41.5 (2.4)
Change from OLE baseline	–15.7 (2.3)	–7.5 (1.8)
DAS28-ESR		
OLE baseline	4.9 (0.1)	4.2 (0.1)
Change from OLE baseline	–1.6 (0.2)[a]	–0.8 (0.1)

[a]n=84

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