REVERSIBLE DECREASES IN ABSOLUTE NEUTROPHIL COUNT (ANC) IN RHEUMATOID ARTHRITIS (RA) PATIENTS (PTS) ON SARILUMAB: COMPARISON OF DOSE DELAY AND DOSE DECREASE VS CONTINUED TREATMENT

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Background: In randomized studies (RCTs: MOBILITY, TARGET and MONARCH), and open-label (OLE) EXTEND, for those patients who experienced decreases in ANC this typically occurred early after initiating sarilumab. For sarilumab patients with decreased ANC in the RCTs and the OLE, we assessed the outcomes associated with either continuing treatment, decreasing the sarilumab dose or delaying the dose.

Objectives: The effects of a dose decrease (200 to 150 mg), dose delay (>17 days), or no change in treatment were evaluated in RA patients who experienced decreased ANC while on sarilumab 150 or 200 mg q2w. Outcomes data from patients in MONARCH, MOBILITY and TARGET, and MOBILITY and TARGET patients entering EXTEND were analyzed to compare the three strategies. In MONARCH, patients received sarilumab 200 mg q2w. In MOBILITY and TARGET, patients received sarilumab 150 or 200 mg q2w. In EXTEND, patients were switched to, or initiated on, 200 mg q2w.

Methods: In RCTs, patients were required to have baseline neutrophil levels >2000/mm³. In RCTs and EXTEND, patients who experienced ANC <500/mm³ (grade 4 [G4] neutropenia) or <500 to <1000/mm³ (grade 3 [G3] neutropenia) and signs of infection were required to permanently discontinue treatment. Patients with G3 neutropenia (no signs of infection) temporarily discontinued treatment (or permanently discontinued at the investigators discretion); patients were retested 48 hrs after identifying decreased ANC and before the next scheduled dose, and could resume if ANC >1000/mm³. In RCTs, patients restarted sarilumab at their randomized dose. In OLE, patients restarted sarilumab at 150 mg q2w, as per the protocol, or otherwise were able to restart at 200 mg q2w at the investigators discretion. In OLE, patients who required a dose decrease to 150 mg q2w sarilumab received the reduced dose for the remainder of the treatment period. ANC normalization was defined as a return to the patient’s baseline or within normal ranges.

Results: Of the 6–11% of patients who experienced ANC <1000/mm³ at any time, 81/105 (RCTs) and 132/147 (OLE) were able to continue or reintiate sarilumab; the majority of patients who experienced ANC <1000/mm³ one or more times displayed normalized ANC levels and continued treatment when ANC >1000/mm³ (25/38 in RCTs; 29/31 in OLE). The majority of patients who dose delayed (27/43 in RCTs; 68/82 in OLE) or dose decreased (5/62, OLE) before ANC normalized resumed treatment.

Conclusions: More than three-quarters of patients who discontinued treatment until ANC normalized were able to reintiate at their randomized dose (RCT), or at the open-label study dose (200 mg q2w; OLE) or were able to resume at the lower dose (150 mg q2w; OLE).

Disclosure of Interest: None declared


Table 1 Outcomes following dose delay, dose decrease, or continued treatment with sarilumab among pts who experienced ANC <1000/mm³ at any time

<table>
<thead>
<tr>
<th>ANC &lt;1000/mm³ at any time</th>
<th>G3</th>
<th>G4</th>
<th>No dose change</th>
<th>Dose delay</th>
<th>Dose decrease</th>
<th>Normalized on treatment after 3 episodes of ANC &lt;1000/mm³</th>
<th>Reinitiate/Restart sarilumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>In RCTs</td>
<td>25</td>
<td>27</td>
<td>30</td>
<td>20</td>
<td>22</td>
<td>(5)</td>
<td>13</td>
</tr>
<tr>
<td>In OLE</td>
<td>9</td>
<td>15</td>
<td>17</td>
<td>12</td>
<td>10</td>
<td>12</td>
<td>16</td>
</tr>
</tbody>
</table>

Table 2 Outcomes among pts who experienced ANC <1000/mm³ at any time

<table>
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<th>ANC &lt;1000/mm³ at any time</th>
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LONG-TERM EFFICACY WITH 5-YEAR-RADIOPHASIC RESULTS AND SAFETY OF SARILUMAB IN COMBINATION WITH CSMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Long-term data are being collected on sarilumab in combination with csDMARDs in patients with RA originally enrolled in six trials (TARGET, NCT01709578; MOBILITY, NCT01061736; NCT01764997; NCT01768572; NCT02057250; NCT01217814) including those who continued into extension trials.

Objectives: To assess efficacy and safety of long-term treatment with sarilumab plus csDMARDs in patients with RA.

Methods: Long-term efficacy and safety data were available in patients enrolled in placebo-controlled trials of sarilumab 150 or 200 mg sc q2w who continued into the open-label EXTEND trial of sarilumab 200 or 150 mg sc q2w (NCT01146652). Safety data were evaluated in 2887 patients who received ≥1 dose of sarilumab sc in combination with csDMARDs.

Results: Clinical and radiographic efficacy of sarilumab plus csDMARDs was maintained over 5 years’ follow-up (table 1; figure 1). Initial treatment with either dose of sarilumab was associated with significantly better radiographic outcome than placebo. Initial treatment with sarilumab 200 mg portended better radiographic outcome than sarilumab 150 mg or placebo. Mean duration of sarilumab treatment in the safety population was 2.6 years (max. 6.8), representing 7412 cumulative patient-years of exposure. Incidence rate of adverse events of special interest (AESIs; table 2) was generally stable over >5 years’ treatment, with no signal for increased rate of any AESI (including serious AEs and serious infection) over time. Incidences of infection site reaction, ANC <1 Giga/L, & elevated ALT declined over time.

Disclosure of Interest: None declared

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