Reply to: Use of upadacitinib in giant cell arteritis

Sirs,

The comments by Drs Ogun and Ozguler on the recent phase 3 study evaluating upadacitinib for giant cell arteritis (GCA; SELECT-GCA, NCT03725202) (1) provide an opportunity to reinforce some findings of the trial.

In the SELECT-GCA trial, ischaemia-related vision loss was observed in 56 out of 428 patients (13.1%) at baseline across the three treatment groups. A prespecified subgroup analysis (Supplementary Fig. S4) showed that rates of sustained remission at week 52 were consistent between patients with ischaemia-related vision loss and the broader trial population, with outcomes favouring upadacitinib 15 mg combined with a 26-week glucocorticoid taper *versus* placebo with a 52-week glucocorticoid taper. Similar results were observed for the secondary endpoint of sustained complete remission from week 12 through week 52 (2). While we recognise the interest in further analysing outcomes among specific subsets of patients with vision loss, the limited sample sizes preclude conducting meaningful additional stratifications. Such *post-hoc* analyses risk overinterpretation and should be approached with caution.

Regarding differences in outcomes between patients with new-onset and relapsing GCA, findings of a prespecified analysis indicate similar efficacy in both groups, consistent with the overall population trend for sustained remission (Supplementary Fig. S4) (1) and sustained complete remission (2).

Glucocorticoids have long been the mainstay of treatment for GCA due to their efficacy and low cost, despite their associated toxicities and frequent relapse occurrences (3). Recent guidelines for the treatment of GCA from the European Alliance of Associations for Rheumatology, British Society of Rheumatology, and American College of Rheumatology all recommend therapy with high-dose glucocorticoids (40–60 mg/day prednisone-equivalent) for induction of remission, followed by tapering of glucocorticoids (4-6). These guidelines differ regarding when adjunctive therapies, such as methotrexate or tocilizumab, may be introduced. The SELECT-GCA study was not designed to evaluate multiple treatment strategies, such as including a tocilizumab arm, nor was it structured to assess the efficacy of upadacitinib in patients for whom interleukin-6 inhibitors were ineffective.

Upadacitinib is now approved for the treatment of adults with GCA in many countries including the United States and the European Union (7-9). As the first oral targeted treatment available for GCA, upadacitinib provides patients with a new option to achieve sustained remission, including patients with complications such as vision loss.

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W. Zhao and A.R. Setty are employees of AbbVie and may hold stock or options.
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