Some concerns from Turkey

We read the paper written by Kaneko *et al* with great interest.[1] This study demonstrates the safety and efficacy of tocilizumab in patients with adult-onset Still's disease (AOSD). This randomised placebo-controlled study could be one of the pioneer studies about the use of biological therapy in AOSD. We wanted to ask about some raising concerns.

ACR20, ACR50 and ACR70 responses were used as composite indexes to assess disease activity. In the studies which investigate the effectiveness of a biologic agent in rheumatoid arthritis, general approach is to allow non-steroidal anti-inflammatory drugs (NSAID) if the dose had been stable for a while.[2] However, we could not find any data of NSAIDs in the paper except for a patient with drug eruption related to a painkiller. Did the patients use NSAIDs on demand or a stable dose?

Second, another point that should be clarified is the results about the glucocorticoid sparing effect of tocilizumab. Baseline prednisolone doses, the percentage of decrements and daily dosage of prednisolone at 12th week of tocilizumab and placebo groups are shown in table 1 . If we calculate the decrement mentioned in the paper, there is a disparity in data written in the paper and calculated data. Actually, baseline prednisolone dose of both groups was non-homogeneously distributed. Thus, a median (IQR 25–75) would be more useful to reflect the data better. A non-parametric statistical analysis could be useful in this setting.

Third, it is unclear whether the data of patients who escaped from part 2 of the trial in both study arms integrated into analysis or not. It was shown in the article by Kaneko *et al* that one patient was withdrawn in part 2 of the trial and three patients escaped because of either unmet ACR20 response criteria at the beginning of part 2 or unmet ACR50 response criteria during the part 2 of the trial[1] . In addition to this, the proportion of patients with an ACR50 response was given as 61.5% (8 of 13) at week 12. When considering all these data, we would ask: Were the data of withdrawn patient considered for analysis or excluded? If excluded, ACR50 response rate should be calculated over 12 patients. Also, there should be five patients who did not meet ACR50 response criteria. Even supposing that the withdrawn patient was considered as non-responder, one patient who did not meet ACR50 criteria is missing. Should that patient be another escaper?

Finally, although authors concluded that the investigators must have selected patients who can tolerate placebo to the placebo group, patients in placebo group seem to have more active disease according to the number of swollen joints, ferritin levels, and so on. Considering the outcome measures, we would expect worse results in placebo group because of having more active disease. But except glucocorticoid sparing effect, no differences in outcome measures were obvious between groups in this study. As the baseline disease activity may have an effect on outcome measures, we think a more sophisticated, validated tool or scoring system is needed to determine the disease activity of patients with AOSD.

Thank you again for such great work!

Table 1 Prednisolone data at baseline and 12th week in both groups

	Tocilizumab	Placebo
Baseline prednisolone (mg/day (SD))	23.0 (16.2)	32.5 (20.4)
Decrement at end of 12th week (%)	46.2	21
Mean prednisolone dose (mg/day (SD)) at end of 12th week	9.4 (3.4)	16.3 (6.8)
Calculated mean prednisolone dose (mg/day) at end of 12th week	12.4	25.7

Emre Bilgin,[1] İrem Ozarli,[2] Levent Kılıç,[1] Ertuğrul Çağrı Bölek,[1] Gözde Kübra Yardımcı,[1] Ömer Karadağ[1]

[1]Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Hacettepe University, Ankara, Turkey
[2]Department of Internal Medicine, Faculty of Medicine, Hacettepe University, Ankara, Turkey

Correspondence to Dr Emre Bilgin, Division of Rheumatology, Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara 06100, Turkey; dr.emrebilgin@gmail.com

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Contributors All authors contributed equally.

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