



Reply: Letter to the Editor Regarding “Autologous Stem Cell Transplantation for Systemic Sclerosis: A Systematic Review and Meta-Analysis”



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To the Editor:

Systemic sclerosis (SSc) is a heterogeneous disease with a pervasive impact on quality of life and high rates of associated morbidity and mortality. Three randomized controlled trials (RCTs) and a retrospective study have suggested that autologous stem cell transplantation (ASCT) is an effective treatment modality for this devastating disease [1–4]. We have previously performed a meta-analysis to provide a pooled estimate of trials comparing ASCT and standard treatment in patients with severe SSc [5]. Our analysis demonstrates that ASCT is a disease-modifying antirheumatic treatment for severe SSc. It decreases all-cause mortality and can reverse skin and lung damage, thereby changing the disease course.

Nikapour et al question the methodology of the systematic review and meta-analysis, raising several points:

1. A meta-analysis is impossible because of different primary outcomes between the 3 RCTs and the retrospective study included in the meta-analysis. Indeed, outcome definition varied between studies included. However, overall mortality and treatment-related mortality were reported by all studies included [1–4], and thus can be pooled and analyzed together.

2. Outcomes in the studies included in the meta-analysis were measured at different time points, ranging from 12 months to 60 months [1–4], and thus cannot be pooled. The variability in the timing of endpoint measurements could give rise to heterogeneity in results. However, the Cochrane guidelines for performing meta-analysis implicitly advise selecting the longest follow-up from each study, when the timing is not uniform [6]. Thus, the analyzing outcomes at last follow-up, as done in our meta-analysis, is a valid choice.

3. The authors suggest that the outcome progression/event-free survival should have been discussed in the meta-analysis. This is a clinically valid endpoint. Nevertheless, it was only reported by 1 trial (SCOT) and thus cannot be analyzed. Furthermore, it involves a subjective assessment. When subjecting a patient to stem cell transplantation for a potentially fatal disease, the choice of survival as the primary outcome is more than reasonable. Therefore, overall mortality may be the optimal outcome for the meta-analysis.

In conclusion, Nikapour et al’s comments provoke some points for consideration. However, the results we have previously published are based on a standardized methodological approach, allowing scientific appraisal of trials evaluating the role of ASCT in SSc. Interestingly, in line with our results, an independent meta-analysis recently presented by Patel et al [7] reached a similar conclusion, demonstrating a survival advantage with ASCT, further supporting the significance of overall survival as a main outcome of the treatment for this disease.

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