blood advances

van Rhee F, Rosenthal A, Kanhai K, et al. Siltuximab is associated with improved progression-free survival in idiopathic multicentric Castleman disease. *Blood Adv.* 2022;6(16):4773-4781.

In this study, the authors conducted a post hoc analysis of the data from the 2014 phase 2 study of siltuximab in idiopathic multicentric Castleman disease (iMCD),[1] the purpose being to better inform clinicians about the benefits of siltuximab.

After publication, it came to the authors' attention that progression-free survival (PFS) was defined differently in the Methods section of the article than in the Results section. Therefore, on page 4774 under "Clinical outcomes," the sentence "PFS was defined as the time from randomization until death resulting from any cause or clinical and/or radiologic progression assessed by a computerized tomography (CT) scan, as measured by the modified Cheson criteria" should read "PFS was defined as the time from randomization until death resulting from any cause or treatment failure due to radiologic progression assessed by a computerized tomography (CT) scan, as measured by the modified Cheson criteria."

Applying this narrower definition of disease progression (ie, defining progression based only on radiologic progression and not including clinical progression) for the post hoc analysis, the authors reported 2 deaths without disease (radiologic) progression in patients in the siltuximab arm; 2 deaths without disease progression and 2 deaths after disease progression were reported in the placebo arm. Using the broader definition of disease progression in 2014 (including clinical progression), van Rhee et al reported 2 deaths because of disease progression in the siltuximab arm, with 3 of the 4 deaths in the placebo arm as a result of disease progression and 1 of the 4 deaths resulting from bronchopneumonia and congestive heart failure.[1]

Treatment failure in the 2014 *Lancet Oncology* article and the 2022 *Blood Advances* article was defined as radiologic progression by modified Cheson criteria, initiation of therapy for MCD, sustained (≥3 weeks) increase in grade ≥2 MCD symptoms, onset of any new disease-related grade ≥3 symptom, sustained increase in an MCD symptom or onset of any new disease-related grade ≥3 symptom, or sustained (≥3 weeks) increase of more than 1 in Eastern Cooperative Oncology Group score from baseline. The 2014 publication reports patients who discontinued treatment due to treatment failure and stated, "16 (30%) of 53 patients taking siltuximab and 14 (54%) of 26 taking placebo discontinued because of treatment failure."[1] When the data set was analyzed in the *Blood Advances* study and considering the total number of treatment failure events, irrespective of discontinuation status, it was found that 20 of 53 patients (37.7%) in the siltuximab arm experienced treatment failure, compared with 16 of 26 patients (61.5%) in the placebo arm.

Finally, 2 discrepancies between the *Blood Advances* and *Lancet Oncology* papers were observed with regard to the lymph node response. There was a difference in the number of siltuximab-treated patients who were evaluated for lymph node response in the *Blood Advances* paper (N = 48) and the *Lancet Oncology* paper (N = 49). In the *Blood Advances* study, 1 patient was removed from the evaluable set because the time to lymph node response could not be calculated from the available information. The *Lancet Oncology* paper reported that 1 of the 24 patients in the placebo group achieved a lymph node response, whereas the *Blood Advances* paper (page 4776, under "Time to lymph node response") reported that 3 of 24 patients in the placebo group achieved a lymph node response. Upon further review of the primary data, the authors found that the difference arose because the new analysis stratified by the intention-to-treat population groups and followed the patients throughout the study, even after unblinding and crossover to siltuximab. Therefore, 2 of the patients in the placebo group had already been unblinded and crossed over to treatment with siltuximab by the time they achieved a lymph node response. While both approaches are acceptable, upon rereview, the authors believe that these 2 patients should have been censored from the *Blood Advances* analysis, as in the *Lancet Oncology* study.

On page 4776, in Figure 1B, "Siltuximab + BSC" under "Deaths/N" should read "2/53," not "3/53." The corrected Figure 1B is shown below.

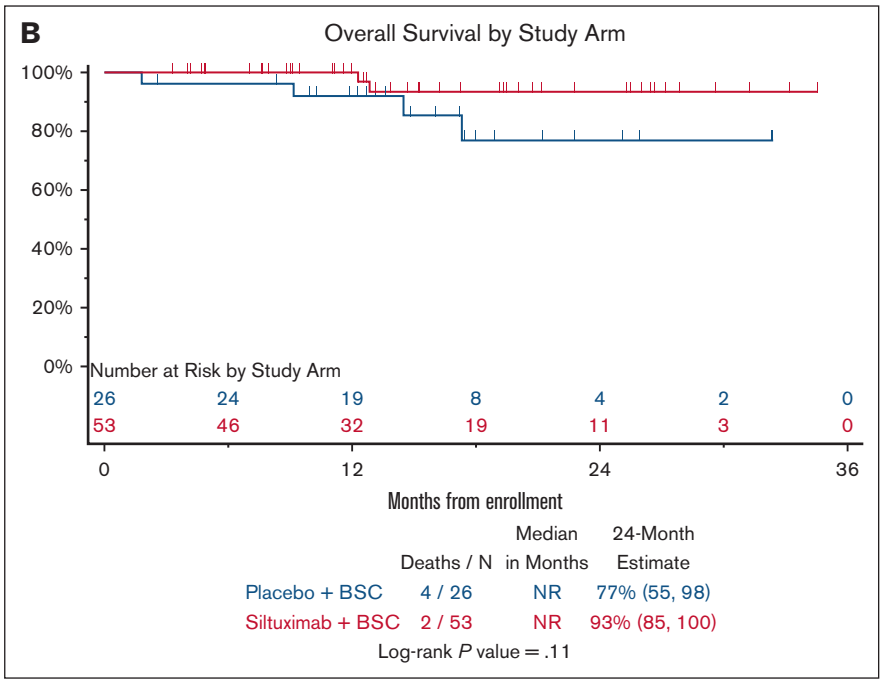

Figure 1B

Reference

1. van Rhee F, Wong RS, Munshi N, et al. Siltuximab for multicentric Castleman's disease: a randomised, double-blind, placebo-controlled trial. *Lancet Oncol.* 2014;15(9):966-974.

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