Response to the Comment by Cirasino L and Semeraro S: "Need to direct immune thrombocytopenia therapy towards shared goals" Direct and indirect comparisons to determine the first choice for newly diagnosed primary immune thrombocytopenia in adults

In our previous study published in Haematologica,[1] we attempted to establish a clinically meaningful hierarchy of efficacy and safety of treatments for newly diagnosed primary immune thrombocytopenia (ITP) in adults, including all the randomized controlled studies (RCTs) available and evaluating them using the technique of network meta-analysis. The results indicated the superiority of recombinant human thrombopoietin (rhTPO)- and rituximab (RTX)-containing regimens, although they were dependent on the statistically calculated "indirect" comparisons, but not on the "direct" comparisons (head-to-head RCTs did not always exist). Considering the limited number of included RCTs and thus a relatively unstable network model, we concluded that greater numbers of "direct" comparison studies (i.e., RCTs between rhTPO and RTX) were necessary to validate our data.

Regarding our conclusion, Cirasino and Semeraro commented that (i) such "intensive" medical therapy is not acceptable as first-line treatment, and that (ii) new RCTs will need to come to a preliminary agreement as for the goal of first-line therapy.[2]

Regarding the first comment, regimens containing rhTPO and RTX were usually accompanied by corticosteroids in our analysis, and total corticosteroid dosages were smaller in these regimens than in corticosteroid monotherapy, mainly because the more rapid platelet recovery in these regimens enabled early tapering or termination of corticosteroids. In this context, these regimens may not be considered as "intensive". Moreover, increases in adverse events were not detected in any rhTPO- or RTX-containing regimens. We suspect these data can work as fair reasons to propose head-to-head RCTs of rhTPO and RTX as first-line treatment.

As for the second comment, we agree that the aim of first-line treatment is to achieve rapid recovery of platelets. Therefore, in our study, we set sustained response (3-6 months) as the main endpoint and overall response (2-4 weeks) and therapy-related adverse events as the secondary endpoints. If we propose new RCTs, then we will set the same outcomes as the study endpoints. However, as the uses of various immune-modulating drugs and antibodies are emerging in the field of ITP, the definition and aim of first-line treatment should be revisited to include the most recent clinical evidence.

Yasuyuki Arai,[1,2] Tomoyasu Jo,[1] Hiroyuki Matsui,[1] Tadakazu Kondo[1] and Akifumi Takaori-Kondo[1]

[1]Department of Hematology and Oncology, Graduate School of Medicine, Kyoto University, Japan; [2]Laboratory of Clinical Immunology and Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA

Correspondence: tadakazu@kuhp.kyoto-u.ac.jp
doi:10.3324/haematol.2018.192385

Information on authorship, contributions, and financial & other disclosures was provided by the authors and is available with the online version of this article at www.haematologica.org.

References

1. Arai Y, Jo T, Matsui H, Kondo T, Takaori-Kondo A. Comparison of up-front treatments for newly diagnosed immune thrombocytopenia -a systematic review and network meta-analysis. Haematologica. 2018;103(1):163-171.
2. Cirasino L, Semeraro S. Need to direct immue thrombocytopenia therapy towards shared goals. Haematologica. 2018:103(6);e268-e269.