CORRESPONDENCE

Caplacizumab for Acquired Thrombotic Thrombocytopenic Purpura

TO THE EDITOR: Peyvandi et al. (Feb. 11 issue)[1] found that caplacizumb was associated with a shorter time to normalization of the platelet count — an important marker of disease activity — than was placebo in patients with thrombotic thrombocytopenic purpura (TTP). The numbers of patients in the caplacizumab group and the placebo group who had disease that was refractory to treatment (i.e., who did not have a platelet response after 4 to 7 days) were not specified, but such data would add valuable comparative information because the management of refractory TTP differs greatly from that of TTP that is not refractory to first-line therapies.[2-4] Second, there is a discrepancy between the text and Table 3 of the article with respect to the number of adverse events that were considered by the investigators to be related to treatment and the number of adverse events that were considered to be possibly related to treatment. The text reports 6 adverse events that were considered to be related to caplacizumab and 19 that were considered to be possibly related to caplacizumab, whereas Table 3 reports 20. Similarly, the text reports 4 adverse events that were considered to be related to placebo and 3 that were considered to be possibly related to placebo, whereas Table 3 reports 5.

Finally, we would ask the authors to clarify whether the 11 patients in the caplacizumab group who had a relapse during the 12-month follow-up included 8 patients who had a relapse during the 1-month follow-up. If not, over the 12 months of follow-up, the patients who received caplacizumab had more episodes of recurrent thrombocytopenia than the placebo group (22 patients vs. 14) rather than an equal number (14 vs. 14).

Mazin T. Abdelghany, M.D.
Meridale V. Baggett, M.D.
Massachusetts General Hospital
Boston, MA
mabdelghany@partners.org

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THE AUTHORS REPLY: Refractoriness is an indicator of a poor prognosis for survival in patients with acquired TTP.[1] Table 1 provides data regarding refractory TTP in our phase 2 study of capla-

Table 1. Post Hoc Analysis of Refractoriness to Treatment in the Safety Population of the TITAN Study.*

Definition of Refractoriness	Caplacizumab (N=35)	Placebo (N=37)
	number (percent)	
No platelet response after 7 days, despite daily plasma-exchange therapy†	2 (6)	8 (22)‡
Absence of platelet-count doubling after 4 days of standard treatment, with lactate dehydrogenase level >ULN§	0	4 (11)

* ULN denotes upper limit of the normal range.
† Definition is from Sayani and Abrams.[2]
‡ Two patients in the placebo group who discontinued the study prematurely (<7 days) without reaching the platelet-count criterion (i.e., platelet count, <150×10^{9} per liter) were counted as having disease that was refractory to treatment.
§ Definition is from Soucemarianadin et al.[3]

cizumab according to two definitions of refractoriness.[2,3] Regardless of the definition, a lower percentage of patients in the caplacizumab group than in the placebo group had disease that was refractory to treatment, which suggests that caplacizumab might prevent refractory TTP and its associated worse outcomes.[1]

To clarify, Table 3 of our article reports the cumulative number of patients with at least one adverse event that was considered to be related or possibly related to the investigational medicinal product, whereas the text separately reports the number of patients with at least one adverse event that was considered to be either related or possibly related to treatment. We confirm that the data regarding patients with relapse during the 12-month follow-up include those with relapse during the 1-month follow-up: 11 patients in the caplacizumab group, as compared with 3 in the placebo group, had a relapse during the entire follow-up period. Overall, 13 patients in each treatment group had at least one recurrence of TTP (exacerbation or relapse).

Flora Peyvandi, M.D., Ph.D.
University of Milan
Milan, Italy

Filip Callewaert, Ph.D.
Ablynx
Zwijnaarde, Belgium
filip.callewaert@ablynx.com

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Convalescent Plasma for Ebola Virus Disease

TO THE EDITOR: In their study, van Griensven et al. (Jan. 7 issue)[1] found no significant survival benefit of using convalescent plasma with unknown levels of neutralizing antibodies in patients with Ebola virus disease (EVD). Survivors of EVD donated plasma anywhere from 2 months to 6 months or more after they had recovered. Substantial immune activation and robust B-cell and T-cell responses have been observed in patients with acute EVD and in some patients during convalescence,[2] although humoral response has not been thoroughly studied in EVD. We have found that in convalescent patients, specific neutralizing activity against Ebola virus glycoprotein (EBOV-GP) increases over time (≥9 months after infection), which suggests that affinity maturation of antibodies takes place long after clinical recovery.[3]

The time that has elapsed after recovery from EVD may be a proxy for the level of activity of EBOV-GP–specific neutralizing antibodies. Given these data, we would be interested in whether patients who received plasma that had been donated 6 months or more after recovery from EVD had a survival advantage over controls and over patients who had received plasma from survivors at earlier time points.

Jose R. Arribas, M.D.
Instituto de Investigación Hospital La Paz
Madrid, Spain
joser.arribas@salud.madrid.org

Joanna Luczkowiak, Ph.D.
Rafael Delgado, M.D.
Instituto de Investigación Hospital 12 de Octubre
Madrid, Spain