Reviewer's report

Title: Prothrombin Complex Concentrate in the Reduction of Blood Loss during Orthotopic Liver Transplantation: PROTON-trial

Version: 2 Date: 6 May 2013

Reviewer: Antoni Sabate

Reviewer's report:

1. Major/Minor Compulsory Revisions

In the Transfusion guidelines section-

• Guidelines for Fresh frozen plasma (FFP) administration are not defined. In fact, in some European teams, the use of FFP is not restricted, which could occasionate confusions. As a result I suggest using PT and PTT data to guide FFP administration because Rotem has a mild or no correlation to conventional coagulation test. Other teams, like ours, does not use FFP unless massive bleeding is noticed which requires also a massive transfusion therapy.

- Guidelines for crystalloids/colloids should be specified. It must be established across centers which fluid therapy policy is used during the surgical procedure. Avoiding different degrees of haemodilution which can interfere with plasmatic fibrinogen values.

In the Sample size section,

the authors considered a mean transfusion requirement of 8 U RBC (SD=4 U). This data was derived from a retrospective data analysis of transfusion requirements during OLT in the UMCG over 2008-2011.

- This figure of RBC requirement (referred to one center) is higher than the mean transfusion registered from other teams (see table, Transplantation Proceedings, 2012, 44 (6): 1523-5). Differences in transfusion rate among participating centers could produce bias, unless the number of patients included by each center is defined previously. On the other hand, if some participating center have less transfusion requirements, the calculated sample size could not be enough to show differences.

2. Discretionary Revisions

Risk of bleeding and transfusion in liver transplantation (LT) is mainly determined by: patient age, severity of liver disease which is related to the diagnosis, surgical technique and preoperative haemoglobin value.1-3


To stratify randomization having in consideration the preoperative hemoglobin value adds some complexity to the study design. The risk of bias related to differences in preoperative hemoglobin value is reduced by considering this point. Even if there is not a clear evidence in regards to surgical technique influences on surgical bleeding, mixed surgical procedures (venovenous bypass or preservation of vena cava) may influence the results obtained.

For safety purpose the author may consider to register one-year retransplantation

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I am involved as coordinator and principal investigator of a multicenter randomized clinical trial on fibrinogen administration in Liver Transplantation