Protocol published

We are delighted to inform you that the PREPAReS study protocol was published in the BMJ open (BMJ Open 2016;6:e010156 doi:10.1136/bmjopen-2015-010156)

Below you will find the abstract of this manuscript.

“A study protocol for a randomised controlled trial evaluating clinical effects of platelet transfusion products: the Pathogen Reduction Evaluation and Predictive Analytical Rating Score (PREPAReS) trial” Paula F Ypma, Pieter F van der Meer, Nancy M Heddle, Joost A van Hilten, Theo Stijnen, Rutger A Middelburg, Tor Hervig, Johanna G van der Bom, Anneke Brand, Jean-Louis H Kerkhoffs, for the PREPAReS Study Group

Introduction: Patients with chemotherapy-induced thrombocytopaenia frequently experience minor and sometimes severe bleeding complications. Unrestrictive availability of safe and effective blood products is presumed by treating physicians as well as patients. Pathogen reduction technology potentially offers the opportunity to enhance safety by reducing bacterial and viral contamination of platelet products along with a potential reduction of alloimmunisation in patients receiving multiple platelet transfusions.

Methods and analysis: To test efficacy, a randomised, single-blinded, multicentre controlled trial was designed to evaluate clinical non-inferiority of pathogen-reduced platelet concentrates treated by the Mirasol system, compared with standard plasma-stored platelet concentrates using the percentage of patients with WHO grade ≥2 bleeding complications as the primary endpoint. The upper limit of the 95% CI of the non-inferiority margin was chosen to be a ≤12.5% increase in this percentage. Bleeding symptoms are actively monitored on a daily basis. The adjudication of the bleeding grade is performed by 3 adjudicators, blinded to the platelet product randomisation as well as by an automated computer algorithm. Interim analyses evaluating bleeding complications as well as serious adverse events are performed after each batch of 60 patients. The study started in 2010 and patients will be enrolled up to a maximum of 618 patients, depending on the results of consecutive interim analyses. A flexible stopping rule was designed allowing stopping for non-inferiority or futility. Besides analysing effects of pathogen reduction on clinical efficacy, the Pathogen Reduction Evaluation and Predictive Analytical Rating Score (PREPAReS) is designed to answer several other pending questions and translational issues related to bleeding and alloimmunisation, formulated as secondary and tertiary endpoints.

Ethics and dissemination: Ethics approval was obtained in all 3 participating countries. Results of the main trial and each of the secondary endpoints will be submitted for publication in a peer-reviewed journal.

Trial registration number NTR2106.

Paula Ypma, 4 February 2016
Prevention of viral transmission

Transmission of transfusion-transmissible viruses is rare, as every single donation is tested with advanced screening tests. As an example, the risk of HIV transmission through a blood transfusion is estimated at less than one in 5 million. Therefore, in the PREPARES trial, it is impossible to show whether viral transmission (hepatitis B, C and HIV) can be prevented by the Mirasol pathogen inactivation technique. However, blood transfusion products contain more viruses, but they are generally harmless, and are therefore not tested for. In collaboration with the group of Mike Busch (Blood Systems Research Institute (BSRI), San Francisco, CA), we aim to demonstrate that viral transmission of these ‘commensal’ viruses can be prevented. In the Haga hospital, patient samples and samples of all transfused blood products will be collected, and shipped to BSRI. They will use advanced molecular techniques to identify the various types of viruses, and determine whether transmission can be prevented in the study arm versus the control arm of the trial. The outcome of this sub study in the PREPARES trial will give us insight in the ability of the Mirasol method to prevent transmission of transfusion-transmissible pathogens in general.

Pieter van der Meer, 11 February 2016

For questions concerning PREPARES please contact Pieter van der Meer:
p.vandermeer@sanquin.nl

PREPARES timelines

The outcomes of the PREPARES trial need to be in the public domain as soon as possible after the study is finished. In collaboration with Terumo BCT a timeline has been developed in order to be prepared for what needs to be done. For the short term, finalizing the Statistical Analysis Plan is top priority, we aim to have the final version ready the end of February. Based on this Plan, the tables, listings and figures of the various study reports can be designed. Further, audits are being prepared in March to make sure the trial was conducted according to GCP.

Key date is May 1, when the last patient goes into the trial. With the 56-day follow up, the last blood samples will be collected towards the end of June. In order to have the study database as up-to-date as possible, we will contact the sites in the meantime to send in their CRFs as they are completed. Once all queries are resolved, the database can be locked, which we anticipate to be the end of September. The primary publication should be submitted to a peer-reviewed journal early November. We realize this planning is very ambitious, but we know the milestones, and we try to anticipate all the actions as much as we can. We will work as closely as possible with the sites to make this happen!

Pieter van der Meer, 4 February 2016
Note: Dashed lines indicate projected inclusions till end of study.