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14. ABSTRACT

The study aims include investigating specific mechanisms of adverse effects related to RBC storage age in critically ill patients. To ensure consistent sample and data collection in this multi-site study and to launch subject enrollment, we have standardized the procedures that are followed at each of the clinical sites. This includes coordinating IRB submissions, training clinical staff in study procedures related to sample collection, processing, and shipping. IRB approvals for the clinical sites participating in this study have been approved, and patient enrollment began in March 2011. Thus far, we have enrolled 38 patients, from whom samples have been collected, processed, shipped from Canada to San Francisco. A repository of plasma, PBMCs and whole blood samples is being built at Blood Systems Research Institute (BSRI). As we are still collecting patient samples, we have not begun cytokine testing. These tests will be performed in batches once enough samples have been obtained to minimize batch-to-batch variability in the testing results.

15. SUBJECT TERMS
RBC storage age; subject enrollment; IRB approval; repository

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Adverse Effects of RBC Storage in Critically Ill Patients

INTRODUCTION

Combat casualties are specifically at risk of adverse effects resulting from the use of RBCs of increased storage age. A large multicenter randomized controlled trial in 30 Canadian centers of 2500 critically ill patients called the Age of Blood Evaluation (ABLE) trial has been funded. In this trial of critically ill patients, which includes patients with traumatic injuries, study groups will be randomized to either RBCs of < 8 days storage time or standard RBC storage time (mean 21 days). The primary outcome of this trial is 90 day mortality. Secondary outcomes include severity of multiple organ dysfunction syndrome, serious thrombotic events and nosocomial infections, and ICU and hospital length of stay. Prospective clinical studies investigating the mechanisms and clinical outcomes associated with increased or decreased RBC storage age in critically ill patients including traumatic injury have not been performed. The ABLE study presents a unique and probably one-time opportunity to investigate mechanisms in the context of clinical outcomes for well-characterized study groups. This study is designed to determine specific mechanisms of adverse effects related to the RBC storage age in transfused critically ill patients enrolled in the ABLE study. This ancillary study will specifically determine if the RBC unit storage time affects patient's immune function, inflammation, coagulation, microparticle concentrations and microchimerism.

Hypotheses

1.) Increased storage time of transfused RBC units will affect both inflammation and coagulation factors in critically ill patients and these parameters will be positively associated with measured clinical endpoints including increased morbidity (sepsis, serious thrombotic events, multi-organ failure) and mortality.

Aims

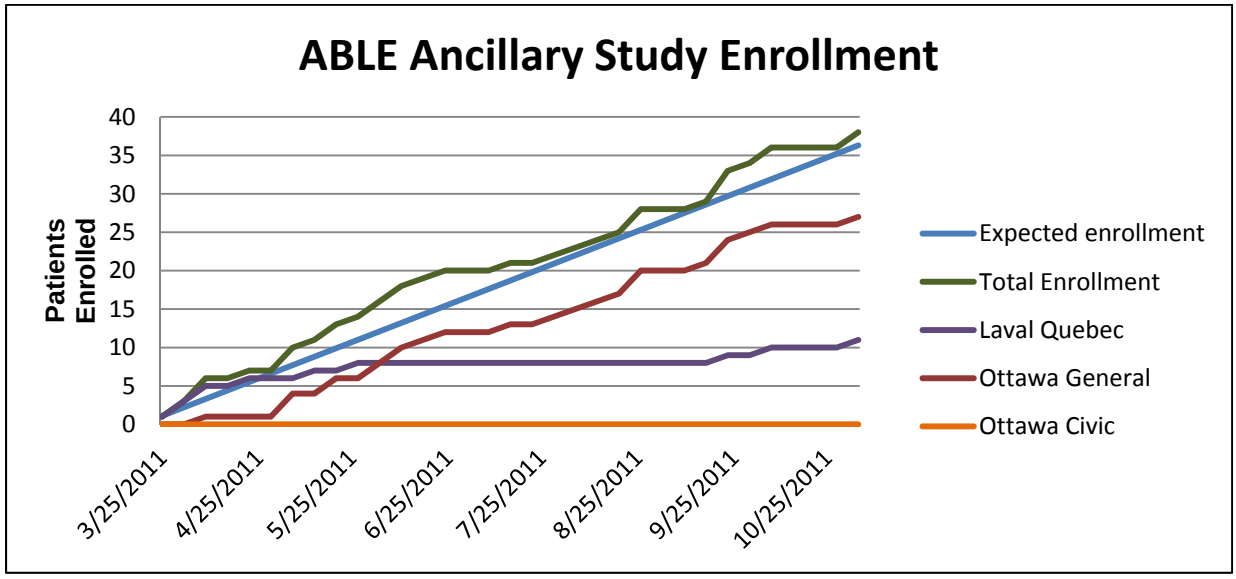
1.) To determine how RBC unit storage time affects inflammation and coagulation in critically ill patients, how these effects change over time after transfusion and if these parameters correlate with clinical outcomes.
    1a. Measure the levels of pro-and anti-inflammatory cytokines and coagulation factors in serum from transfused subjects longitudinally using multiplex assays (high and standard sensitivity).
    1b. Quantify levels of markers associated with cardiovascular disease including cellular adhesion molecules and growth factors using multiplex bead-based assays.
    1c. Correlate patterns of cytokine and inflammatory marker secretion and measures of coagulation with receipt of blood stored for short vs. long periods.
    1d. Correlate patterns of cytokine and inflammatory marker secretion and coagulation with all clinical outcomes.
2.) To develop a patient sample repository for future analysis of additional effects of RBC storage age in critically ill patients.

BODY

Research Ethics Board (REB) approvals were obtained for all the Canadian clinical sites, Blood Systems Research Institute (BSRI) through University of California San Francisco Institutional Review Board (UCSF IRB) and from Human Research Protection Office (HRPO). The manual of procedures was finalized and all site coordinators were informed of the processing methods. We began enrollment in March 2011. As

of November 8th 2011, we have enrolled a total of 38 patients in this study. Evaluable samples have been collected, processed and shipped from the clinical sites to BSRI. These samples are being stored at BSRI until they are ready to be analysed. Cytokine analysis will be performed in batches in order to avoid variability of test results due to testing procedures and/or reagents used. Since we are still enrolling patients, and have not performed any lab analysis on these samples, we do not have any results to report at this time.

Graph below shows total enrollment versus expected enrollment (as of November 8, 2011). Graph also shows actual enrollment for each of the sites.



In order to increase the rate of enrollment we are currently in the process of enrolling another clinical site in Quebec, Canada. This will not affect the budget of the study, but will help meet enrollment targets. This has not been approved by HRPO yet, and will be submitted soon.

KEY RESEARCH ACCOMPLISHMENTS

- We have begun patient enrollment and sample collection at the clinical sites in Canada
- The samples are being processed, shipped and stored.
- To date, 38 patients have been enrolled, which is at the expected rate of enrollment.

REPORTABLE OUTCOMES

As mentioned above, we have begun sample acquisition. As a result, we have started building a repository of plasma, PBMCs and whole blood samples.

CONCLUSION

The ABLE ancillary study has launched and is accruing patients at the rate expected. In addition to managing current study accrual, new sites are actively being explored to enhance the pace of subject enrolment. The sample repository is being built, and cytokine analyses will be performed when a sufficient sample size has accrued to allow batch processing, to maximize the quality of the data generated.

REFERENCES

None

APPENDICES

None