



BMT CTN 1502 FREQUENTLY ASKED QUESTIONS (FAQ)

Optimizing Cord Blood and Haploidentical Aplastic Anemia Transplantation (CHAMP)

1. Why conduct a trial of Cord Blood and Haploidentical donors in severe aplastic anemia (SAA)?

SAA is an uncommon but life-threatening condition. Most patients will have standard of care therapy with a matched sibling donor transplant or a trial of immunosuppressive therapy followed by matched unrelated donor transplant if necessary. However, there is a subset of patients who will fail immunosuppression and yet will not have a matched unrelated donor. With an overall incidence of only two cases per million population per year, no single center treats sufficient numbers of patients to completely study this in a reasonable timeframe. Thus, a multi-center network study is required to learn more about alternative donor sources in transplant for patients needing a transplant who do not have matched unrelated donors available. The goal of this trial is to test if optimized approaches can improve engraftment and survival using alternative donors (unrelated cord blood or bone marrow from a mismatched related [haploidentical] donor) so that engraftment and survival are comparable to that after matched unrelated donor bone marrow transplant.

2. Can I put my patient on this protocol as first line treatment for SAA?

No. This trial is designed to increase available donor options for patients who cannot receive the aforementioned standard of care options. If a matched related donor or a matched unrelated donor is available, patients should be treated with those more conventional options. If those donors are not available, the patient should have at least one trial of immunosuppression before considering this study.

3. Is this trial comparing unrelated cord blood to bone marrow from haploidentical donors? Do I need both sources of stem cells available for my patient?

No. This is a parallel, phase II study and eligible patients need to have available only 1 of the donor types specified in this protocol. Each cohort will be analyzed separately.

4. My center had to declare a preferred cohort, cord blood or haploidentical. Can I only enroll on that cohort?

All participating centers have to declare up front their donor source of choice for the trial at their institution (in writing to the Data Coordinating Center). However, a center may enroll to the non-declared cohort if necessary. In that case, the center will have to declare (to the Data Coordinating Center before the trial is opened) their institution's plan for enrolling patients to one arm versus the other. This is done so as to minimize enrollment bias from the center and treating physician.

5. In the haploidentical cohort, why are peripheral blood stem cells (PBSC) not permissible as a donor stem cell source?

This is in part due to standard of care in the matched related and unrelated donor setting for SAA, where transplantation of bone marrow is associated with lower rates of chronic GVHD and higher survival compared to transplantation of PBSC.

6. In the cord blood cohort, why is anti-thymocyte globulin (ATG) being given so early and in such a specific way? Does it have to be the Thymoglobulin[®] preparation?

It **must** be the Thymoglobulin[®] preparation based on data from a retrospective study that showed high exposure *before* transplant with low exposure *after* transplant may lower the incidence of rejection and graft-versus-host disease (GVHD) and lead to better immune reconstitution and survival. Thus, we would not know how to recommend appropriate doses resulting in the best exposure levels of other ATG preparations.

7. What is the dose of Thymoglobulin[®] to give my patient?

In the haploidentical cohort, all patients will receive a total of 4.5 mg/kg spread over 3 days. In the cord blood cohort, doses vary based on the weight of the patient and the baseline lymphocyte count prior to starting the treatment regimen. The dose will be between 3 mg/kg and 15 mg/kg divided over 4 days of administration to be given over 8 hours each day at a constant rate. Prior to starting the first dose, the patient's weight, lymphocyte count, and calculated dose will be entered into AdvantageEDC[™], with the dose being reported back to the treating institution by the coordinating center. Appendix D of the protocol shows how to calculate the dose for any individual patient to allow the treating physician to confirm the dose is correct. If there are any questions about calculating an individual dose of Thymoglobulin[®], please do not hesitate to contact one of the study chairs to discuss as this is a very important part of the protocol treatment.

8. What safety measures are in place for this trial?

There will be continuous monitoring of key safety endpoints including graft rejection and mortality. If either rate significantly exceeds pre-set thresholds, the Data and Safety and Monitoring Board (DSMB) will be asked to advise. The stopping guidelines serve as a trigger for consultation with the DSMB for additional review and are not formal "stopping rules" that would mandate automatic closure of study enrollment.

9. How many patients will be on study? Do you expect to meet this accrual? What are recruitment strategies and plans for monitoring study accrual?

The trial is designed to transplant 30 patients in each cohort for a total of 60 patients. Based on careful analysis of past transplant activity from the CIBMTR, we expect to meet the accrual goal in 3 years. Core clinical centers including PBMTTC centers as well as affiliate centers will participate. Patient information will be made available to centers in electronic form. A summary of projected accrual for this study is attached.