IMPORTANCE OF THE QUESTIONS BEING ADDRESSED
FAQs for BMT CTN PROTOCOL 0803

1. Why conduct a transplant trial in HIV-infected patients with non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma?

The advent and wide-spread availability of highly-active anti-retroviral therapy (HAART) has dramatically changed the life expectancy and disease evolution of patients with HIV/AIDS. It has also permitted HIV-infected patients with NHL and Hodgkin's lymphoma to receive aggressive therapeutic regimens that previously would not have been feasible. Pilot trials at the City of Hope and in the AIDS Malignancy Consortium indicate that autologous transplants are feasible and safe in this patient population, though these are centers with substantial expertise in managing HIV-infected patients. Despite these encouraging, HIV-infection is still considered an exclusion criteria for many autotransplant protocols and care plans. The goal of this trial is to demonstrate the broad applicability of autologous transplantation in HIV-infected patients with lymphoma outside of a few specialized centers. The best avenue for achieving this goal is by conducting the study within the BMT CTN and performing transplants for this patient population in a larger multi-center trial.

2. Why choose one-year overall survival as the primary endpoint?

Overall survival provides an objective end-point for comparing outcomes between HIV-infected patients undergoing autologous transplantation vs. non-HIV-infected patients. Overall survival has been viewed as the "gold standard" for judging the effectiveness (and in this instance the safety) of this intervention. Additionally, most of the concern about doing autologous transplants in HIV-infected patients stems from concern about transplant-related mortality, specifically, risks of infection, and management of anti-retroviral therapy during the early period of cytopenia. Most transplant-related deaths in this setting occur in the first six months after treatment, so a one-year follow-up period should be sufficient to determine whether risks differ in HIV-infected patients.

3. What is the importance of the secondary endpoints of the trial?

In addition to a number of lymphoma-specific end-points, this trial provides a key opportunity for analyzing a number of HIV-specific end-points. These include studies evaluating immunological reconstitution and assessing the impact of transplant upon HIV viral load and viral reservoir. This trial will, for the first time, analyze those HIV-infected transplant patients with undetectable viral loads with the single copy assays in order to ascertain the extent of viral suppression post-transplant.

4. Why was the age range of 15-70 chosen?

The lower age limit was chosen after considerable discussion with pediatric transplanters. It was agreed that the extreme rarity of AIDS-related NHL and Hodgkin lymphoma in younger children would make it difficult, or impossible, to accrue any significant numbers of patients in this age group for the trial. The upper age range was chosen based upon the likely, physiologic limitations to transplantation in patients above this age range.

5. Is our accrual goal feasible?

Yes. We are projecting a modest accrual goal that appears feasible based on a survey of BMT CTN transplant centers based on current referral patterns. We will also be advertising this trial to HIV advocacy groups and research networks.

6. Is there a need for a multi-center network to meet the objectives?

Yes. One of the key goals of this trial is to demonstrate the generalizability of this treatment modality across a broad array of transplant centers. We believe that this can be accomplished only by performing the study in a multi-center network.

7. Accrual estimates – See separate summary of Accrual Estimates.

8. What are the recruitment strategies if applicable, and proposed plans for monitoring study accrual?

Core Clinical Centers and non-Core Centers will participate. Transplant centers will follow their local institutional practices for recruiting patients on research studies. Patient information and educational materials explaining this study will be prepared by the NMDP Office of Patient Advocacy and made available to centers in paper form and on the Web. As noted above, we will conduct an active outreach effort to publicize this study through existing AIDS research networks and advocacy groups.

Monthly accrual reports will be provided to the NIH. Additionally, recruitment reports based on the CIBMTR database will be provided every six months. The screening reports will summarize reasons for non-enrollment and reasons for ineligibility.

9. What are the proposed plans for data acquisition, transfer, management and analysis?

A web-based data entry platform will be used for all BMT CTN supplemental forms. Data are transmitted encrypted using secure socket layer (SSL) technology. SSL is the standard used by banks in their electronic transactions. This platform includes online missing forms reports as well as other reports as deemed useful by the transplant centers. A User's Guide and Data Management Handbook will be developed for reference and training of clinical research associates (CRAs).

Data collected on CIBMTR Initial and Follow-up Report Forms will be transferred electronically from the CIBMTR to EMMES on a regular basis. Any data relevant to real-time monitoring of safety or efficacy endpoints will be collected on BMT CTN supplemental forms, e.g. deaths.

Missing forms reports are updated daily. Queries will be developed to check for missing and inconsistent data. Queries will be distributed to the centers at least monthly.

Analysis files will be prepared prior to each Data and Safety Monitoring Board (DSMB) meeting. Most analyses will be conducted using SAS and following the statistical analysis plans outlined in each protocol.

10. What is the monitoring and overall coordination of protocol management (e.g. brief summary of plans to run the study – initiation, coordination, data collection, and monitoring)?

A protocol coordinator is assigned to each BMT CTN protocol. The protocol coordinator is responsible for the daily operational needs of the study and of the participating transplant centers. The protocol coordinator oversees enrollment and data collection issues and is in regular communication with CRAs at participating transplant centers. The protocol coordinator also works closely with the protocol officer with respect to adverse event reporting and to medically-related protocol questions.

A form submission schedule is developed for each BMT CTN protocol and is included in these materials. A visit schedule will be provided to the transplant centers for every enrolled patient. This schedule will detail the dates of all expected visits and list of forms and/or samples required at each visit.

Initiation site visits will be conducted for all participating centers. These visits will either be in-person visits to the centers or be held via conference call with all transplant center personnel involved with this protocol.

DCC staff, including at minimum the protocol coordinator, will conduct periodic monitoring visits to the participating clinical centers and laboratories. The primary purpose of these visits is to conduct data audits. Other activities include those required to enhance data quality, ensure study integrity, satisfy regulatory requirements, and evaluate site performance. Site visits will occur at variable frequency throughout the course of the studies, depending primarily upon the stage of the study, site performance, and sponsoring agency requirements.

Unexpected serious adverse experiences will be reported according to BMT CTN guidelines. The protocol officer will review all unexpected serious adverse experiences. Expected transplant-related toxicities will be collected on each patient using the calendar-driven reporting system that has been previously reviewed and approved by the DSMB. There is an interim statistical monitoring plan for safety. Treatment-related mortality at Day 30 will be monitored. The DSMB will be notified if TRM rates significantly exceed the expected 5%. The protocol statistician or other DCC statistical staff will ensure that programs are in place to conduct the interim monitoring in accordance with the statistical analysis plans in each protocol.

11. Are there any specific study training plans necessary to accomplish the research goals (e.g. workshops, study certification)?

CRAs will be certified for data submission by the DCC after participating in an in person meeting or in a training session conference call with the protocol coordinator. No other certifications or workshops will be required for this study.