BMT CTN PROTOCOL #1903 (HIV T-cell)

Frequently Asked Questions (FAQs)

V 4.0

1. Why is this clinical trial meaningful to conduct?

Based in part on a study conducted by the BMT CTN (BMT CTN 0803) the recent clinical experience with high dose chemotherapy and autologous stem cell transplantation (ASCT) in patients with HIV and relapsed or refractory lymphoma has been very encouraging with regard to tumor outcomes, remission duration, and safety of the procedure. The investigators believe that ASCT may also provide a platform for interventions that might have added impact on HIV disease and provide insights into cure strategies. Preliminary data from studies of ex-vivo expanded multi HIV antigen (gag, pol and nef) -specific T-cells targeting conserved epitopes of gag and pol (HST-NEETs) suggest that the use of HST-NEETs may be an effective strategy for targeting HIV. With this in mind, we seek to assess their effect on the long-term retroviral reservoir following ASCT. This is potentially an ideal setting to test HST-NEETs as the lymphodepletion induced by high dose chemotherapy may promote greater in-vivo expansion of T-cells following adoptive transfer. In the past, the standard approach to assessing this HIV reservoir has been the viral outgrowth assay. The assay requires a very large blood draw and is labor intensive, requiring in vitro culture for 2-3 weeks. In addition, evidence has emerged that the assay misses a large part of the reservoir. A new assay, the intact proviral DNA assay (IPDA), is more sensitive and does not require a large volume blood draw or in vitro cultures. We will use the IDPA to assess the HIV-reservoir in this study.

2. Why was the HST-NEETs administration window of 3 to 7 days post ASCT chosen?

The administration window of 3-7 days post-transplant was chosen as there should be “space” for the T-cells to expand during this time, and it should not interfere with engraftment. Although this is the ideal window, we will allow for cells to be administered up to 30 days post-transplant.

3. Why was the BEAM conditioning regimen selected?

BEAM is the most common high dose conditioning regimen used worldwide prior to ASCT for all forms of lymphoma and was the sole conditioning regimen used in BMT CTN 0803 which forms the backbone for this study.

4. Why was the sample size of 12 selected and is the accrual goal feasible?

We have designed this study as a safety and feasibility study primarily due to the low numbers of patients currently receiving ASCT for HIV-related lymphoma (HRL). In the past 6 years, the average number of patients undergoing ASCT for HRL has been seven annually. We believe therefore that it will be feasible to accrue 12 participants over 4 years as the trial will be conducted through the BMT CTN, allowing access to the majority of centers performing ASCT for HRL.

5. Are there any plans in place to stop enrollment if the manufacturing of the product within the protocol specified window does not appear to be feasible?

Given the small number of participants planned for enrollment, there are no specific stopping rules for halting the trial if there are problems with the feasibility of manufacturing the HST-NEETs within the specified window.

However, since accrual is not expected to be rapid, the protocol team will be monitoring the feasibility of manufacturing on an ongoing basis and will be reporting this to the DSMB. If there are clear problems with product manufacture, it will likely become apparent quickly to the protocol team as well as the DSMB.

6. Can you use a pump to infuse the HST-NEETs?

The Children's National staff would recommend against using a pump and suggest infusing as an IV push over 1-2 minutes.

7. What if the participant's HIV subtype is unknown?

The Exclusion Criteria #2: "Participant is known to have an HIV subtype other than B." was clarified that it is intended to exclude participants whose subtype is known to be something other than B. If the participant was not tested or the result is not known, then they would not be ineligible under this criterion.

8. Sterility Testing of the HST-NEETs?

Each individual site need only test sterility to confirm that aseptic technique was maintained during thaw and dilution. Sterility of the product is already tested at CTL prior to freezing.

9. What HLA Resolution is required?

High resolution is preferred but low resolution is acceptable.

10. When to report AEs on participants who have not received the HST-NEETs?

Before a participant receives the investigational product, only AEs related to protocol required specimens should be reported. Additionally, only AEs related to protocol required specimen collection should be reported for participants who are transplanted, but do not receive the investigational product.

Please note, no adverse events should be reported for patients who have not enrolled onto the protocol.

For all other AE related questions, reference Section 4.5 of the Protocol.

11. When is the best time to draw the manufacturing sample?

This collection should occur at least 6-8 weeks prior to ASCT due to the time required to manufacture the HST-NEETs.

The peripheral blood for manufacturing should be collected when the ALC is over 800 and before GCSF. This is easier to accomplish if the CBC with differential is performed earlier in the screening process.

12. What is the timeframe for shipping the manufacturing sample?

This collection should be shipped for overnight delivery on the day of collection. If shipment is not possible on the day of collection the sample must be shipped for delivery first thing the following morning as the sample must be processed within 48 hours of collection.

13. When is apheresis used vs peripheral blood to obtain the manufacturing sample?

- ✓ If the participant's ALC is greater than or equal to 800/uL the collection will occur through a peripheral blood collection.
- ✓ For participants with an ALC lower than 800/uL but greater than or equal to 400/uL the collection will occur via apheresis.
- ✓ If a re-collection is required, the manufacturing sample will be collected using apheresis.