Frequently Asked Questions for

A PROSPECTIVE OBSERVATIONAL STUDY OF THE IMMUNOGENICITY OF VACCINES FOR SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 (SARS-COV-2) VACCINE AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION (HCT), ALLOGENEIC HCT, AND CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY (CAR-T) IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

A CIBMTR/BMT CTN Study

1. **What is the purpose of this study?**

   The purpose of the study is to assess the immune response to COVID-19 vaccines in patients receiving commercial vaccines as part of their standard care after HCT or CAR-T therapy. It will also compare responses in patients who receive the vaccine in the first six months after treatment versus those who received it 6-12 months after treatment. This will give very important and currently lacking information about the protective effects of vaccination in this vulnerable population and, possibly, identify appropriate timing of vaccination.

2. **Can enrolled patients receive the booster?**

   Yes, patients can receive a booster. The date of administration and manufacturer are collected on study forms.

3. **What are the inclusion criteria?**

   - Any Age
   - ≤ 12 months from alloHCT, autoHCT, or CAR-T therapy
   - Previously consented to provide data for research to the CIBMTR with a valid CIBMTR Research Identification Number (CRID)
   - Planned to receive a COVID-19 vaccine as part of routine clinical care
   - Patients with prior COVID-19 are eligible provided the infection was > 3 months before planned vaccine administration
   - Patients who received a COVID-19 vaccine prior to HCT/CAR-T are eligible if re-vaccination following HCT/CAR-T is planned as standard practice
   - Signed a study-specific consent for collection of pre- and post-vaccination blood specimens for submission to the CIBMTR research repository

   Eligibility Notes:

   - No waivers or exceptions to inclusion criteria will be granted.
   - Study sample #1 must be collected prior to vaccine #1, otherwise the patient is ineligible. Additionally, study sample #1 must be ≤12 months from HCT/CAR-T therapy and vaccine #1 could be up to 12 months from HCT/CAR-T +14 days.

4. Why is this study important?

There are very few data available on the response to vaccination in the patients we serve and no data on optimal timing of vaccination. Recent data on solid organ transplant recipients indicate much lower response rates to vaccination than in the general population (Boyarsky et al, JAMA, 2021). Filling this gap in information for HCT/CAR-T patients is important to guide clinical care. The National Comprehensive Cancer Network (NCCN) recently recommended that COVID-19 vaccination be done at least 3 months after cellular therapy, but also stated "Vaccine efficacy in the setting of cancer care and a weakened immune system is unknown." These data may also provide information on whether different vaccine products vary in eliciting immune responses in this setting or whether response is influenced by specific patient and treatment characteristics.

5. Why is it important to activate this study quickly?

As vaccines become increasingly available, all patients will be offered vaccination and the recent NCCN guidelines likely mean that many centers will try to vaccinate patients at about 3 months post-treatment. Additionally, many patients will be vaccinated before they undergo HCT or CAR-T. However, right now, due to varying rates of availability, very few, if any, patients were vaccinated prior to HCT/CAR-T and they are being vaccinated at a wide range of time-points after therapy. This will allow us to better understand the response to post HCT/CAR-T vaccination at varying time-points in the first year after therapy in patients with and without pre-HCT/CT vaccination, and provide guidance for future vaccination strategies.

6. Is there a protocol for this study?

Data collection for this study is being done as part of the CIBMTR "Protocol for a Research Database for HCT, Other Cellular Therapies and Marrow Toxic Injuries". All data requested are data collected as part of routine clinical care. No separate consent is required to submit data for this protocol. Specimen collection for this study is covered by the CIBMTR "Protocol for a Research Sample Repository for HCT, Other Cellular Therapies and Marrow Toxic Injuries". Some patients may have already signed a consent for the CIBMTR Repository to allow collection of pretransplant specimens, but **ALL patients will need to sign a consent for specimen collection for this COVID vaccine study**. This NMDP IRB-approved consent template will be provided (along with age-appropriate assent documents), if your center wishes to participate in the study.

7. Will this study require IRB Submission?

Yes, only the NMDP IRB-approved consents will need to be submitted to your IRB of Record as an amendment to the CIBMTR Protocol for a Research Database for HCT/CAR-T. **Do not submit the 2101 Study plan as a "New Protocol".** Once you receive IRB approval, please submit approval documentation to the Repository IRB.

8. Is this a CIBMTR or a BMT CTN study?

CIBMTR and BMT CTN are collaborating on this study. The study was initially proposed by a BMT CTN State of the Science Committee, which included one of the co-chairs (Dr. Miguel Perales) and the Scientific Director (Dr. Marcie Riches) of the CIBMTR Working Committee for Infection and Immune Reconstitution. Drs. Perales and Riches are, together with Dr. Joshua Hill, co-chairing this Study. The study is being done under IRB-approved CIBMTR protocols and most of the clinical data will come from routine CIBMTR data collection. However, the BMT CTN infrastructure is being used for specimen tracking and for supplemental data collection to enhance efficiency and speed of activation.

9. Will centers get BMT CTN credit for enrolling patients on this study?

Yes, the study is endorsed by the BMT CTN Steering Committee and enrollment credit will be earned.

10. What specimens are being collected?

30 ml of blood will be collected at 4 time-points as described in the table below.
For pediatric patients, where the collection of the full 30 mL sample exceeds the maximum volume allowed per institutional guidelines, the 5 mL serum sample should be prioritized, with the remainder of allowable blood volume dedicated to the PBMC research sample collection.

Schedule for Specimen Collection		
Time-point 1	Baseline: Pre-Vaccine #1	Up to 14 days prior to vaccine administration
Time-point 2	Post Vaccine #1	Single dose vaccines: 14-35 days after vaccination Two-dose vaccines: within 7 days prior to administration of the second dose
Time-point 3	Early Post-Vaccine #2 or similar time frame after a Single Dose Vaccine	Single dose vaccines: Earliest routine clinical visit between 4 and 8 weeks after specimen obtained for Time-point 2 Two-dose vaccines: Between 7 and 35 days post-vaccine #2
Time-point 4	6-7 Months Post-Vaccination	Single dose vaccines: Closest routine clinical visit to 7 months post-vaccination, ideally ± 28 days Two-dose vaccines: Closest routine clinical visit to 6 months post-vaccination, ideally ± 28 days

11. Where are specimens sent?

Specimens will be sent to the National Marrow Donor Program (NMDP) repository. Repository staff will send aliquots, in batches, to LabCorp for antibody testing. The remainder will be stored for future research, including T-cell response assessments and antibody neutralization assays. GlobalTrace, the system used to track specimens in BMT CTN trials, will be used for this study.

12. What antibody test is being used?

LabCorp will assess total antibody against the receptor-binding domain of the Spike protein of SARS-CoV-2 using a semi-quantitative Electrochemiluminescence Immunoassay (ECLIA).

13. Will results of antibody tests be made available to patients?

The serum antibody results will be posted in FormsNet under the subject's CRID. These reports will be posted starting at the end of July 2021. Samples will be batch-shipped from the Repository to LabCorp monthly for testing and results will be available in 3-6 weeks from collection. Each center will determine how results will be shared with their patients.

14. What if patients cannot return to their treatment center for specimen collection?

The study should be offered to patients who are likely to be seen over the next 6 months, and so can have specimens collected. Specimen collection has been arranged through LabCorp. This option is to be reserved for only those cases that truly require an off-site collection to be done for a patient unable to return to the Transplant Center as there are a limited number of spots available for use for this study. This offsite option is ONLY available to patients that are able to have the full 30 mL blood sample collected as allowed per institutional guidelines. **CBC results will not be provided back to centers.**

15. How will supplemental data be submitted?

Data will be entered via the eClinical system managed by the Emmes Corporation. This is the system used for all BMT CTN protocols. It is being used for this CIBMTR/BMT CTN study because of available modules that could be quickly modified to meet the supplemental data needs of this study and so allow timely activation. All data will be transferred and merged with CIBMTR data at the end of the study. The data elements to be submitted at the four time-points are summarized in the table below.

Supplemental Data to be Submitted Pre- and Post-Vaccination	
Baseline	• SARS-CoV-2 Manufacturer • History of prior COVID-19 infection with date (triggers submission of Respiratory Virus Infection Form 2149 in FormsNet, if not already submitted) • History of pre-HCT/CT vaccination with date and manufacturer • Current status of GVHD (alloHCT recipients) • Selected medications, including all potentially immune suppressive medications and posttransplant anti-cancer maintenance therapy • Other post-therapy vaccinations, with dates • Complete blood count • Performance score
All Post-Vaccination Time-points	• Intercurrent COVID-19 infection with date (triggers submission of Respiratory Virus Infection Form 2149 in FormsNet, if not already submitted) • Current status of GVHD for alloHCT recipients • Selected medications, including all potentially immune suppressive medications and posttransplant anti-cancer maintenance therapy • Other intercurrent post-therapy vaccinations, with dates • Complete blood count • Performance score • Grade III-IV patient-reported vaccine-related toxicities

16. Is there reimbursement for submitting data and specimens?

Reimbursement for routine CIBMTR forms submitted through FormsNet (including the Respiratory Virus Infection form) will be per routine CIBMTR reimbursement procedures, under existing Master Healthcare Data and Sample Submission Agreements. Also under these agreements, CIBMTR will automatically reimburse an additional $100 for each specimen *received* (up to a total of 4 specimens) and $100 for each set of supplemental data forms *submitted* to eClinical (up to a total of 4 sets) for this vaccine study, paid quarterly. Centers will not receive reimbursement for samples collected at LabCorp.