Study Plan List of Changes

CIBMTR SC21-07/BMT CTN 2101 COVID v5.0

Dated: 26JAN2022

The following changes, and the rationale for the changes, were made from Version 4.0 to Version 5.0 of the **Study Plan**. Additionally, there were a few administrative changes, including corrections to typos and formatting.

#	Section number, title, and page number of original	Original text:	Changed to:	Rationale
1.	1. Background Page 1	As of September 2021, the FDA has approved the Pfizer-BioNTech (BNT162b2) mRNA vaccine for people over the age of 12, while the other 2 vaccines are approved for use under emergency use authorization (EUA). Furthermore, the FDA and CDC now recommend a third dose of mRNA vaccines for certain immunocompromised patients, which includes recipients of HCT and/or CAR-T.	As of November 2021, the FDA has approved the Pfizer-BioNTech (BNT162b2) mRNA vaccine for people over the age of 5, while the other 2 vaccines are approved for use under emergency use authorization (EUA). Furthermore, the FDA and CDC now recommend a third dose of mRNA vaccines, including recipients of HCT and/or CAR-T.	Updated to reflect the changing COVID-19 vaccine landscape.
2.	2.1 Study Overview Page 4	**Figure 2.1. Study Schema** (Note: If the vaccine is administered as a single dose, an eight-week specimen will still be collected for comparability to the evaluation time point after two-dose vaccines. Additionally, if patients receive a third SARS-CoV-2 vaccine dose (booster), an additional visit and sample will be collected after that dose, generally expected to be at about week 12.	**Figure 2.1. Study Schema** (Note: If the vaccine is administered as a single dose, an eight-week specimen will still be collected for comparability to the evaluation time point after two-dose vaccines. Additionally, if patients receive a third SARS-CoV-2 vaccine dose, an additional visit and sample will be collected after that dose, generally expected to be at about week 12.	References to boosters were removed throughout the Study Plan to avoid confusion as some patients are receiving more than 3 shots.

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3.	2.3 Specific Objectives Page 5	• Assess the change in antibody titers following the second dose of the vaccine and the booster dose, for patients receiving booster	• Assess the change in antibody titers following the second dose of the vaccine and the third dose, for patients receiving a third dose	References to boosters were removed throughout the Study Plan to avoid confusion as some patients are receiving more than 3 shots.
4.	2.4.1 Inclusion Criteria Page 6	• ≤ 12 months from alloHCT, autoHCT, or CAR-T therapy	• ≤ 12 months from alloHCT, autoHCT, or CAR-T therapy • **Only pediatric patients (≤ 18 years old), racial/ethnic minority patients (i.e., patients other than those identified as non-Hispanic White), and/or patients with non-malignant disease may be enrolled on the alloHCT cohort as of November 29, 2021.**	The allo cohort completed accrual and now only certain underrepresented groups are allowed to be enrolled on that cohort.
5.	2.4.1 Inclusion Criteria Page 6	• Patients with prior COVID-19 are eligible provided the infection was > 3 months before planned vaccine administration	• Patients with prior COVID-19 are eligible once symptoms from the acute infection have resolved	The required minimum time frame since COVID infection was removed as this is no longer a CDC recommendation.
6.	2.5 Study Treatments and Sample and Date Collection Page 6	The choice and timing of booster is at the discretion of the institution.	The choice and timing of the third dose is at the discretion of the institution.	References to boosters were removed throughout the Study Plan to avoid confusion as some patients are receiving more than 3 shots.

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<tr><th>Visit</th><th>Visit Description</th><th>Visit Window*</th></tr>
<tr><td>Time-point 1</td><td>Baseline: Pre-vaccine #1</td><td>Within 14 days prior to vaccine administration</td></tr>
<tr><td>Time-point 2</td><td>Post-vaccine #1</td><td>Single dose vaccines: 14-35 days after dose #1

Two-dose vaccines: within 7 days prior to dose #2</td></tr>
<tr><td>Time-point 3</td><td>Post-vaccine #2 (or similar time frame after a single dose vaccine) / Pre-vaccine dose #3 (Booster)</td><td>Single dose vaccines: 4-8 weeks after specimen obtained for Time-point 2

Two-dose vaccines: 3-8 weeks after dose #2. If vaccine dose #3 (booster) is planned, the sample should be drawn within 7 days prior to booster administration if the booster is administered ≤ 8 weeks after the dose #2.</td></tr>
<tr><td>Time-point 3b
(only required for patients receiving a booster >8 weeks after dose #2)</td><td>Pre-vaccine dose #3 (booster)
This sample is obtained only if there are >8 weeks between dose #2 and booster dose</td><td>Obtain sample within 7 days prior to booster administration only if there are >8 weeks (56 days) between dose #2 and booster dose</td></tr>
<tr><td>Time-point 4
(only required for patients receiving booster)</td><td>Post-vaccine #3 (booster)
This sample is obtained only if the patient is receiving a booster dose</td><td>Obtain sample between 7 – 35 days following the booster</td></tr>
<tr><td>Time-point 5</td><td>Final post-vaccine</td><td>7 – 9 months after dose #1, ideally at 8 months ± 28 days</td></tr>
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This sample is obtained only if there are >8 weeks between dose #2 and ~~booster~~ dose #3</td><td>Obtain sample within 7 days prior to dose #3~~booster~~ administration only if there are >8 weeks (56 days) between dose #2 and ~~booster~~ dose #3</td></tr>
<tr><td>Time-point 4
(only required for patients receiving dose #3~~booster~~)</td><td>Post-vaccine #3 ~~(booster)~~
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<tr><td>8.</td><td>Table 2.2 Schedule for Specimen Collection Page 7</td><td>[N/A text added]</td><td>†For centers planning to give a 4th dose following the 3-dose series, Time-point 5 should be drawn prior to dose #4 if the timing is consistent with the visit window above. However, if Time-point 5 cannot be completed prior to dose #4, the dose #4 information should be collected on the Time-point 5 visit forms. No additional samples/data are collected after Time-point 5 irrespective of additional vaccine doses after that time-point.</td><td>Clarification of data collection for patients who receive 4 doses.</td></tr>
<tr><td>9.</td><td>Table 2.3 Supplemental Data to be Collected Pre- and Post-Vaccination</td><td>
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<tr><td>Baseline</td><td>• SARS-CoV-2 Manufacturer
• History of prior COVID-19 infection with date*
• Current status of GVHD (allos)
• 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</td></tr>
<tr><td>All Post-Vaccination Time-points</td><td>• Intercurrent COVID-19 infection with date*
• 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</td></tr>
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• Current status of GVHD (alloHCT recipients)
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10.	Section 3.2 Definition and Analysis of Endpoints for Secondary and Exploratory Objectives Page 9	• For patients receiving vaccine dose #3 (Booster), the distribution of the maximum RBD immunoglobulin titer will be described for each cell therapy cohort based on the GMT with 95% CI and range. Within each HCT/CAR-T stratum, the maximum titers will be compared between patients receiving a booster and vaccinated 6-12 months after HCT/CAR-T and those vaccinated < 6 months after HCT/CAR-T using Wilcoxon rank sum tests.	• For patients receiving vaccine dose #3, the distribution of the maximum RBD immunoglobulin titer will be described for each cell therapy cohort based on the GMT with 95% CI and range. Within each HCT/CAR-T stratum, the maximum titers will be compared between patients receiving a third dose and vaccinated 6-12 months after HCT/CAR-T and those vaccinated < 6 months after HCT/CAR-T using Wilcoxon rank sum tests.	References to boosters were removed throughout the Study Plan to avoid confusion as some patients are receiving more than 3 shots.
11.	3.3 Accrual Page 10	Based on these data, it is anticipated that accrual to this observational trial will be completed within 9 months of activation.	Based on these data, it is anticipated that accrual to this observational trial will be completed within 12 months of activation.	The expected accrual period has been lengthened.
12.	4. Significance Page 10-11	To date, there is no information regarding efficacy of SARS-CoV-2 vaccines following HCT/CAR-T treatments and no information on the efficacy of any mRNA vaccine in this population.	To date, there is limited information regarding efficacy of SARS-CoV-2 vaccines following HCT/CAR-T treatments and limited information on the efficacy of any mRNA vaccine in this population. Most of these data are in allogeneic HCT patients.	Updated to reflect the changing COVID-19 vaccine landscape.