Memorial Sloan Kettering Cancer Center

# MSK COVID-19 VACCINE INTERIM GUIDELINES FOR CANCER PATIENTS



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## 1. SCOPE OF THE DOCUMENT

The MSK COVID-19 vaccine interim guidelines are intended to provide clinicians with practical recommendations on using the emergency use authorized (EUA) mRNA COVID-19 vaccines for patients with active and treated cancer.

- There is currently a lack of vaccine efficacy and immunogenicity data, specifically in the cancer population.
- The vaccine is safe for use in cancer patients. The vaccines do not contain live virus.
- Published clinical trials of MRNA vaccine in the general population and existing approaches to other vaccines in cancer patients inform this document's recommendations for using mRNA vaccines in cancer patients.
- The vaccine taskforce constituted by oncology and infectious disease experts has carefully considered potential therapy-related interference with COVID-19 vaccine responses and make practical recommendations to guide clinicians until specific data are available.
- As newer vaccine and scientific studies become available, the task force will regularly update this document.
- Please review the FAQs under section 7 for topic specific special considerations.

The FDA has currently granted emergency use authorization to two vaccines with the following age and dosing interval parameters. Both vaccines are equivalent in efficacy and have comparable adverse effects. *There is no basis for the preferential recommendation of one vaccine over the other under any circumstance.*

| Manufacturer | Technology | Age Recommendation | Interval between doses | Grace Period for 2nd dose* |
|---|---|---|---|---|
| Pfizer | mRNA | ≥ 16 years | 21 days | 17-21 days |
| Moderna | mRNA | ≥ 18 years | 28 days | 24-28 days |

*dose can be administered after the grace period if patient is unable to receive the 2nd dose in the recommended timeframe

Other vaccines in Phase 3 clinical trials **not** currently authorized for use in the United States include:

| Manufacturer | Technology | Safety concerns in immunocompromised hosts | # of Doses |
|---|---|---|---|
| AstraZeneca | Vector vaccine (simian adenovirus) | Replication deficient | Two |
| J & J | Vector vaccine (human adenovirus 26) | Replication deficient | One |
| Novavax | Protein subunit (adjuvanted) | None | Two |

## 2. PATIENTS WITH HEMATOLOGIC MALIGNANCIES

**Authors:** *Tobias Hohl, Santosh Vardhana, David Knorr, Alex Lesokhin*

### Background and Rationale

The rationale to vaccinate MSK patients with hematologic malignancies is to reduce the risk of COVID-19 morbidity and mortality. COVID-19 vaccination will enable receipt of disease-specific therapy and avoid delays in cancer care.

In ideal circumstances, when planning is possible and community rates are low, patients with hematologic disease, particularly patients on B-cell depleting therapies, should undergo shared decision making with their oncologist for recommendations related to optimal timing of vaccination, with the considerations below.

**However, when rates of community transmission of SARS-CoV-2 are high, as they are <u>currently</u>, and if the vaccine is offered to them, it is reasonable for patients to proceed with vaccination, even if they are likely to have a blunted immune response**.

### General considerations for vaccination in hematologic disease

The following considerations should guide eligibility and timing of vaccination:

**1.** Ability to mount a cellular and humoral immune response is paramount [1,2]. Proceed with vaccination in the following patients at the earliest opportunity:

- Patients that have not yet started lymphocyte-depleting therapies and can complete 2-dose schedule 14 days prior to initiation of lymphocyte-depleting therapy.
- Patients that have completed therapy (see below for lymphocyte-depleting therapies).
- Patients with stable lymphocyte counts while on therapy. We define stable lymphocyte counts as an ALC ≥ to 1.0 (normal range: 1.3 - 4.0 x $10^3$ cells/microliter) or B cell counts ≥ 50 cells per microliter. *

For patients that have received lymphocyte-depleting therapy (I.e., rituximab, blinatumomab, anti-thymocyte globulin, alemtuzumab, etc.), it is reasonable to consider deferring vaccination until six months after completion of therapy or until there is evidence of lymphocyte reconstitution (ALC ≥ 1.0 and/or B cell counts ≥ 50) *. This is because patients with B cell aplasia will in all likelihood not mount a humoral immune response. However, given that COVID vaccination generates T-cell memory that may offer at least partial protection, it is reasonable to offer vaccination during times of high community transmission even to patients unlikely to mount a B-cell response. ** Limited data to suggest use of ALC and/or B cell count as a predictive biomarker, can consider use to guide clinical decision making.*

## 2. Therapy- and Disease-specific recommendations for vaccination (in setting of adequate and steady vaccine supply and low community transmission rates) [3,4]

### Lymphoid Malignancies

**CLL** (special consideration of rituximab, venetoclax, ibrutinib)

- If patients are asymptomatic from a CLL standpoint, we would recommend holding B-cell depleting therapy until one month after completion of vaccination (both doses for mRNA vaccination).
- For small molecule therapy in symptomatic patients, we would recommend holding vaccination until 1 month after completion of treatment, once there is evidence of B-cell recovery (ALC ≥ 1.0, B-cell count ≥ 50 cells/ lymph by flow cytometry). When chronic therapy for symptomatic patients is required, vaccination should be considered, as it may still generate T-cell memory responses in the absence of B-cell recovery.

**B- or T-ALL** (Induction/maintenance therapy)

- Induction therapy for newly diagnosed disease should not be delayed for vaccination.
- Vaccine should be given during the maintenance phase at a time patient displays evidence of hematopoietic count recovery. It can also be considered during induction with less intense regimens (e.g. steroids + TKI)

**DLBCL and other aggressive B-cell lymphoma**

- Systemic induction therapy, including anti-CD20 antibodies, for newly diagnosed disease should in general not be delayed for vaccination.
- Vaccine should be given after completion of therapy, assuming patient is in remission and no further treatment is planned, once there is evidence of B-cell recovery from anti-CD20 depletion (ALC ≥ 1.0, B-cell count ≥ 50 cells/microliter lymph by flow cytometry). During times of high community transmission, vaccination should be considered, as it may still generate T-cell memory responses in the absence of B-cell recovery.

**Indolent lymphomas**

- If patients are asymptomatic, we would recommend holding on B-cell depleting therapy until 1 month after completion of vaccination series
- If patients are in need of systemic therapy, we would recommend treating with induction but without maintenance therapy, and vaccinating following completion of therapy, assuming no further immediate treatment is planned and there is evidence of B-cell recovery from anti-CD20 depletion (ALC ≥ 1.0, B-cell count ≥ 50 cells/microliter lymph by flow cytometry). During times of high community

transmission, vaccination should be considered, as it may still generate T-cell memory responses in the absence of B-cell recovery.

**T cell lymphomas**

- Therapy for newly diagnosed and progressive disease should not be delayed for vaccination purposes.
- Vaccine can be given during induction therapy, preferably following count recovery.

**Lymphoma patients with relapsed or refractory disease**

- In the context of disease recurrence or progression, systemic therapy with the potential for therapeutic benefit should not be delayed for vaccination purposes.
- For patients having received B-cell depleting agents, similar considerations apply, as outlined above

**Myeloma**

- With the exceptions of lymphodepleting therapy administration there are no specific disease or treatment related contraindications for vaccination in patients with myeloma.
- Patients treated with lymphodepletion (e.g., high-dose Melphalan with SCT, Cytoxan/Fludarabine or anti-CD52 mAb conditioning for cellular therapy) vaccination can be attempted once lymphocyte recovery is observed, as aligned with HSCT and cellular therapy guidelines.

**Myeloid Malignancies**

- **AML** (induction/consolidation therapy): Induction therapy for newly diagnosed disease should not be delayed for vaccination purposes. Vaccine should not be given during the induction remission phase but should be considered during consolidation therapy. Patients with relapsed disease may be considered for vaccination.
- **MDS**: Patients with MDS on observation or active therapy with HMA should be considered for vaccination.
- **MPNs**: Patients with ET, PV, or MF on observation or active therapy should be considered for vaccination.
- **CML**: Patients receiving TKIs (with or without remission) should be considered for vaccination.

**Therapy specific recommendations**

- **Steroids**: Patients treated with corticosteroids may have diminished responses to vaccination. Corticosteroids are detrimental to patients with mild COVID-19 yet

appear beneficial to patients with severe COVID-19[5]. It is recommended that patients treated with corticosteroids are vaccinated prior to therapy, if feasible.

- **IVIG**: COVID-19 vaccines may be administered to patients receiving plasma therapy not specific to COVID-19 (e.g., IVIG), as these are unlikely to substantially impair development of protective antibody responses.
- **Rituximab**: Patients treated with rituximab clearly have diminished humoral responses to vaccination. Patients treated with rituximab and naturally infected with SARS-CoV-2 appear to be one of the highest risk groups for COVID-19 morbidity and mortality. It is recommended that patients are vaccinated prior to initiation of therapy (e.g., both doses completed ≥ two weeks prior to initiation of B-cell directed therapy), when feasible. If it is not feasible to delay Rituximab-based therapy, it is still reasonable to consider vaccination during times of high community transmission given that vaccination can generate T-cell memory responses even in the absence of humoral immunity.

## Post-vaccination follow-up

At this time, post-vaccine serologies are not recommended in the general population or in patients with hematologic malignancies. Development of and patient enrollment in clinical studies to measure humoral and cell-mediated immunity to COVID-19 vaccination is recommended.

## References


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## 3. HEMATOPOIETIC STEM CELL TRANSPLANT AND CELLULAR THERAPY RECIPIENTS

**Authors:** *Miguel Perales and Zenia Papanicolaou*

### Timing of vaccine administration [1,2]

#### Autologous HCT

- Vaccination may be initiated 2- 3 months after HCT

For patients receiving tandem auto HCT (i.e. GCT) vaccination should be initiated after last planned stem cell infusion

#### Allogeneic HCT

#### Conventional, no severe GVHD, no anti-CD20 antibodies

- Vaccination may be initiated as early as 3 months post HCT (time frame 3-6 months based on local vaccine availability, and rate transmission in the community). COVID19 vaccination should take priority over the regular vaccination schedules.

#### Ex-vivo T-cell depleted and post Cy HCT

- Vaccination may be initiated around 6 months post HCT with confirmed presence of B cells (>50) and CD4+ T-cells (>100).

#### CART cell therapy and receipt of antiCD20 antibodies

- Vaccination may be initiated as early as 3 months if demonstrated IVIG independence and B-Cell count ≥50.

### HSCT patients with GVHD

- Studies with other vaccines with good immunogenicity potential have shown efficacy also in patients with ongoing moderately severe GVHD without obvious risks to result in worsening of the GHVD. These patients should therefore receive the vaccine.
- Although side effects are expected as with any vaccine, there is no example that side effects of non-live vaccines be more frequent or more severe in HCT than in the healthy population of the same age range. So far, there is no data suggesting immune activation of underlying conditions making the likelihood that COVID-19 vaccines will exacerbate GVHD low.

**Reasonable criteria to postpone vaccination with our current knowledge are**:

- Severe, uncontrolled acute GVHD grades III – IV.
- Recipients, who have received anti-CD20 antibodies during the last six months and absolute B-cell count <50.
- CAR T cell patients with B-cell aplasia (absolute B-cell count <50)
- Recent therapy with ATG or alemtuzumab.
- With limited vaccine supply, donor vaccination for passive immunity to HCT recipient is not advised at this time.
- Caregivers are not eligible to receive the vaccine unless they are already in a priority group.

## References


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2. https://www.hematology.org/covid-19/ash-astct-covid-19-and-vaccines

## 4. IMMUNE CHECKPOINT INHIBITORS (ICIs)

**Authors:** *Mini Kamboj and Jedd Wolchok*

### Background and Rationale

- Patients on ICI therapy, particularly lung cancer, are at a higher risk for severe COVID-19. Existing data is mixed but suggests that these findings may be driven by non-therapy related risks and co-existing medical conditions [1-4].
- Patients with lung cancer who have other risk factors for severe COVID-19 infection are also more likely to be treated with ICI. If vaccine supplies are constrained, ICI treated patients with lung cancer should be prioritized to receive the vaccine among other high-risk cancer patients (age>74, multiple co-morbid conditions, hematologic malignancy, active treatment, and metastatic disease) [3,4].
- There is no published data on mRNA vaccines' immunogenicity in cancer patients, including those on ICI.
- Humoral and cell-mediated immune responses to the influenza (flu) vaccine are more robust in patients treated with ICI than those treated with cytotoxic chemotherapy [5-6].
- There is no data to suggest that patients receiving immune checkpoint inhibitors experience complications or exaggerated immune-related adverse (irAE) events from any viral vaccine.
- Multiple studies have demonstrated influenza vaccine safety during ICI treatment without any signal of exaggerated irAE's [7-9].
- COVID-19 outcomes are not specifically worse among those with recent immunotherapy treatment. Although vaccine interaction with ICI is not studied, this finding, and the flu vaccine safety in recently treated patients, inform the recommendation for vaccination regardless of when ICI therapy is initiated.

### Recommendations

1. **Patients on ICI therapy should receive the COVID-19 vaccine. Clinicians should not pause ICI therapy for vaccination.**
2. No specific timing is recommended relative to recent vs. continued therapy.
3. Systemic side effects with the COVID-19 vaccine tend to occur within 2-3 days of the vaccine and may be more pronounced with the second dose. Side effects are also more frequent in those <55 years of age. If possible, avoid scheduling ICI therapy when vaccine side effects are expected [10].

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9. Wijn DH, Groeneveld GH, Vollaard AM, et al. *Influenza vaccination in patients with lung cancer receiving anti-programmed death receptor 1 immunotherapy does not induce immune-related adverse events.* Eur J Cancer 2018; 104:182-187.
10. CDC:https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

## 5. PATIENTS WITH SOLID TUMORS

**Authors:** *Monika Shah and Diane Lagunes-Reidy*

### Overview

Patients with solid tumor cancers should be offered the vaccine if components of the vaccine are not contraindicated. The rationale for COVID-19 vaccination in patients with solid tumor malignancies is to reduce the risk of COVID-19 morbidity and mortality. COVID-19 vaccination will also enable ongoing receipt of disease-specific therapy and avoid delays in cancer care.

### General Background

- Patients with active cancer have a higher risk of morbidity and mortality from COVID-19. [1]
- Data from other vaccine preventable illnesses such as influenza, pneumococcal disease and herpes zoster suggest a protective effect of vaccination in cancer patients. [2]
- For example, influenza vaccination offers protection to cancer patients by reducing influenza-related hospitalizations, interruption of chemotherapy cycles, and risk of death. [3]
- Antibody responses to vaccines are generally lower in patients receiving cytotoxic chemotherapy compared with healthy individuals or cancer patients who are not actively receiving treatment. Several small studies have yielded conflicting results related to generation of immune responses stratified by timing of influenza vaccination in relation to chemotherapy and the nadir/cytopenic period. [4] Recent reports suggest this timing does not seem to matter. [5,6] Precise immune correlates are unknown.
- Given the paucity of data, optimal timing of vaccination in relation to cytotoxic chemotherapy or other cancer directed therapy has not been established. When there is opportunity to choose, vaccination at the furthest possible time point away from the cytotoxic treatment effect (i.e. nadir) during a given cycle is recommended.
- The impact to the humoral and cellular immune responses is variable across solid tumor types and treatment paradigms.

### Additional considerations related to mRNA vaccination in patients with solid tumors

- The dosing schedule recommended for the mRNA vaccines is a two-dose series either 21 days apart (Pfizer) or 28 days apart (Moderna). There are no data to support significant deviations from the recommended vaccine schedule. Given this, precision timing of the 2-dose series is likely not feasible.
- There is no contraindication to receipt of COVID-19 vaccine across the broad range of therapies that patients with solid tumors may receive, inclusive of:

- Cytotoxic chemotherapy
- Radiation therapy
- Hormonal therapy
- Targeted therapies
- Immunotherapy
- Corticosteroids
- Surgical management

**Recommendations for use**

1. **Patients with solid tumors should receive the COVID-19 vaccine, as stratified by factors such as age. There are no additional stratification recommendations related to cancer type or stage of disease at this time.**

2. Clinicians should not hold or pause cancer directed therapy for vaccination.

3. **No specific timing is recommended relative to cancer directed medical or radiation therapy**. Some circumstances to consider are listed below. Vaccination should be offered when made available to the patient.

    a. If feasible, for patients planned for but not yet on immunosuppressive cancer directed therapy, time first dose of vaccine to be given ≥ 2 weeks prior to initiation of therapy.

    b. If feasible, for patients already on cytotoxic chemotherapy, time first dose of vaccine in between chemotherapy cycles, and away from nadir period.

    c. If feasible, for patients completing cytotoxic therapy, time first dose of vaccine to be given after therapy complete and nadir period resolved.

    d. For patients on other cancer directed therapies, including those that may confer additive immunosuppression (i.e. corticosteroids), there is no recommendation related to timing.

4. For patients undergoing cancer related surgery, no specific timing is recommended relative to surgery, except for elective splenectomy. For patients undergoing elective splenectomy as a part of cancer treatment, first dose of vaccination should occur ≥ 2 weeks prior to splenectomy or in the post-surgical period, after recovery [7].

5. Immunotherapy related considerations discussed separately (section 4, page 9-10).

6. Systemic side effects with the COVID-19 vaccine tend to occur within 2-3 days of the vaccine and may be more pronounced with the second dose. Side effects are also more frequent in those <55 years of age. If possible, avoid scheduling immunotherapy or other chemotherapeutic infusions when vaccine side effects are expected.

## References


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## 6. PEDIATRIC CANCERS

**Authors**: *Farid Boulad and Gil Redelman-Sidi*

### Background

1. Currently FDA-approved COVID-19 vaccines include mRNA-1273 (Moderna) and BNT162b2 (BioNTech and Pfizer) and mRNA-1273 (Moderna).
2. Neither of the phase III clinical trials supporting the approval of these vaccines included young children. mRNA-1273 was tested in individuals who were 18 years or older [1], and BNT162b2 in individuals who were 16 years or older [2]. Clinical trials of COVID-19 vaccines including younger individuals are set to begin.
3. COVID-19 is generally mild in children [3, 4], including in children with cancer [5-7].
4. COVID-19–Associated Multisystem Inflammatory Syndrome (MIS-C) is a severe manifestation of COVID-19 that has been described in children. The pathogenesis of this syndrome appears to be immune-mediated and there are theoretical concerns that COVID-19 vaccination could elicit a similar syndrome [8].

### Recommendations

Based on the considerations listed above, and pending additional data on the safety of COVID-19 vaccines in the pediatric population, we recommend the following:

1. **Limit vaccination to the age ranges approved under the current EUAs, specifically ≥16 years of age for BNT162b2 (Pfizer) and ≥18 years of age for mRNA-1273 (Moderna), with prioritization and limitations of patient cohorts harmonized to institutional guidelines and phased distribution plans.**
2. For guidelines for COVID-19 vaccination by specific disease and treatment please see sections 2-5.
3. Decrease in the lower age limits after safety and efficacy data are available from current clinical trials of vaccine in pediatric participants.

### References


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## 7. SPECIAL CONSIDERATIONS AND FREQUENTLY ASKED QUESTIONS

**Authors:** *Mini Kamboj, Monika Shah, and Elizabeth Robilotti*

### General Considerations

1. **Should patients who have recovered from cancer be prioritized to receive the COVID-19 vaccine?**

   Yes, patients who have recovered from cancer should receive the vaccine. Patients with active disease, especially hematologic, thoracic malignancies, and metastatic disease, are at a higher risk for severe disease. Although it is unclear if past cancer treatment similarly increases the risk of adverse outcomes, the COVID-19 vaccine should be offered to these patients.

2. **Can COVID-19 vaccine be administered to patients enrolled in clinical trials at MSK?**

   There are no specific limitations for patients enrolled on clinical studies unless otherwise stated in the protocol inclusion/exclusion criteria. If so, the provider should discuss with the study PI and/or sponsor.

3. **Should patients receive additional doses of vaccine if their second dose was after the recommended time interval?**

   No, third doses are not recommended. Patients should adhere to the recommended dosing interval (see table on page 1).

4. **Should cancer patients get revaccinated if the vaccine was administered during a period of immunosuppression?**

   No, revaccination is not recommended at this time.

5. **Will booster doses of vaccine be needed in the future?**

   The need for and timing of booster doses for mRNA COVID-19 vaccines has not been established. No additional doses beyond the two-dose primary series are recommended at this time.

### Patients with a history of COVID-19

6. **Should patients with a previous history of COVID-19 infection be vaccinated?**

Yes, patients who have recovered from COVID-19 infection should also be offered vaccination. Approximately 2.2 % of patients with prior COVID-19 disease were included in the clinical trials evaluating mRNA vaccines. These patients were able to mount an appropriate response without any increase in adverse events. Reinfection with SARS COV-2 is uncommon in the first 90 days after infection. CDC does not recommend a minimum interval between infection and vaccination in recovered individuals.

**7. Should vaccine be given to patients with positive COVID-19 antibodies?**

Yes, patients with a positive COVID-19 antibody test should be vaccinated. There is not enough experience to correlate antibodies with future protection against COVID-19 infection and immunity duration is not clearly established. Routine serological testing (COVID-19 antibody) before vaccination is not recommended. Serological testing should not be used to guide the timing of vaccination.

## Safety of vaccine in patients with a history of allergy (see section 8 for allergy management)

**8. Should patients with a history of severe allergies, including anaphylaxis, be offered the vaccination against COVID-19?**

The risk of anaphylaxis with the mRNA vaccine (CDC: data from Pfizer) is estimated to be 11 cases per million doses. Patients with a wide variety of common allergies are eligible to get COVID-19 vaccines. This is also true for patients with cancer and an allergy history. The only patients with allergies who should not get the vaccine are those who have a history of anaphylaxis specifically to one of the vaccine components. For example, patients with a known history of anaphylaxis to PEG (polyethylene glycol) should not receive the currently available mRNA products.
Patients with anaphylaxis to other injectable medications should undergo a longer observation period of 30 minutes following receipt of vaccination against COVID-19. Patients with allergies to foods, nuts, animals, latex, or environmental triggers are also eligible to receive an mRNA-based COVID-19 vaccine.

## Adverse effects

**9. What are the common side effects of the COVID-19 vaccines?**

The most common side effects include injection site pain. Other common side effects include fatigue, tiredness, muscle pain, chills, joint pain, and fevers. These side effects were more commonly reported in younger vaccine recipients and following the second shot of the 2-dose series. Side effects typically resolved after one to two days. At times, patients report swelling of the axillary or supraclavicular lymph nodes on the side on which they received the shot. This

side-effect can be associated with a sensation of axillary fullness and pain and is self-resolving.

**10. Should cancer patients pre-medicate before the vaccine to reduce side-effects?**

Premedication is generally not advised. For patients with a history of allergy, premedication may mask early symptoms of life-threatening hypersensitivity and is therefore not routinely recommended.

**11. Is the vaccine safe for patients with a history of Guillain-Barre Syndrome (GBS)?**

There is no epidemiological link between SARS-CoV-2 as a trigger for GBS (Keddie, Brain 2020). No cases of GBS were reported in clinical trials of both mRNA vaccines. Patients with a history of GBS may receive the currently authorized vaccines.

**12. Is the vaccine safe for patients with a history of Bell's palsy?**

In the clinical trials, a numerical difference was observed in the number of Bell's palsy cases between the vaccine and placebo arm. A causal link between Bell's palsy and the vaccine has not been established. Patients with a history of Bell's palsy may receive the vaccine.

## Co-administration of COVID-19 vaccine with other anti-viral therapeutics and vaccines

**13. Can vaccine be given to COVID-19 recovered patients who received the monoclonal antibodies or convalescent plasma (CP)?**

CDC guidelines recommend postponing the vaccine for 90 days after receipt of monoclonal antibody or CP to treat COVID-19 to avoid any interference with vaccine mediated immunity. If antibody therapy is administered between vaccine doses, clinicians should postpone the second dose.

**14. Can COVID-19 specific monoclonal antibodies and other therapeutics be given after mRNA COVID-19 -vaccine?**

For patients with SARS-CoV-2 infection, vaccine status should not alter the decision or timing for the use of monoclonal antibodies, convalescent plasma, corticosteroids, or antivirals.

**15. Is it safe to receive other vaccines with the COVID-19 vaccine?**

The safety and efficacy of mRNA COVID-19 vaccines have not been studied simultaneously with other vaccines. The mRNA COVID-19 vaccine should be administered alone, separate from other routine vaccines. The interval between the mRNA-COVID-19 vaccine and other vaccines should be at least 14 days before and after its administration.

## Infection Control Considerations

**16. Should vaccine be routinely offered to patients after household, community, or hospital-based exposure to SARS CoV-2?**

The vaccine is unlikely to provide clinical protection after exposure to SARS COV-2. The earliest evidence of partial clinical protection is around 12 days after the first dose of the vaccine, which is much longer than the average incubation period for COVID-19 (5-7 days). Routine post-exposure vaccination is not recommended.

**17. When is it safe for patients to receive the vaccine after a significant exposure (for example, COVID-19 in a household contact)?**

Patients may receive the vaccine if they remain asymptomatic and have completed the recommended quarantine period.

**18. Should vaccinated patients follow the current MSK testing protocol for asymptomatic patients?**

Yes, the vaccine's effectiveness in cancer patients is unclear at this time and there is insufficient post-authorization experience in general. Patients should follow testing protocols regardless of the vaccine status. Encourage patients to continue all safety measures, including masking, social distancing and hand hygiene.

**19. Do vaccinated patients pose a transmission risk to others in the household?**

No, mRNA vaccines do not contain live virus and do not pose a transmission risk to others. No special precautions need to be taken around other household members after vaccination.

## Serological Tests

**20. My patient was vaccinated. Should I check for a serological response?**

No, the currently available assay at MSK is an anti-nucleocapsid antibody assay and would not measure vaccine response. Anti-spike antibody assays are in

development but are not yet available for use at MSK. Additionally, serological assays are not recommended to measure vaccine response in the general population nor in patients with malignancies outside of research studies. We will update when these processes are in place.

**21. How should positive serological assays for SARS CoV-2 be interpreted in vaccinated individuals?**

| | Anti-Nucleocapsid * | Anti-Spike antibody |
|---|---|---|
| Prior infection with or without vaccine | + | + |
| Vaccine response only | - | + |

* Assay currently in use at MSK

Some recent reports suggest that humoral immune responses after SARS CoV-2 infection persist for up to 6-8 months and may correlate with clinical protection. The durability of immunity and the precise immune correlates of clinical protection is unclear. Further, cell-mediated immune responses are not measured in these reports. Serological assays should not be used to decide who to vaccinate or to monitor vaccine response outside of a research study.

## 8. MANAGEMENT OF HYPERSENSITIVITY TO m RNA VACCINES

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### Background

- While rare, anaphylactic reactions have been reported following vaccination with mRNA vaccines. Most reactions have occurred within 15 minutes of vaccination. [1]
- If an individual has had a history of an immediate allergic reaction to any ingredient in an mRNA vaccine, that individual should not receive any of the currently available vaccines. [2]
- The ingredient in both mRNA vaccines which is believed to be the allergenic culprit is polyethylene glycol (PEG). Polysorbate, although not in the Pfizer or Moderna vaccine, cross-reacts with PEG.
- Both PEG and polysorbate are found in many injectable cancer therapeutics (appendix table). They are also found in many other injectables, and oral medications, including bowel prep regimens. [3,4]
- **Patients with a history of any type of allergic reaction to food, pets, venom, latex, other drugs (without PEG or polysorbate) or other vaccines (non-mRNA) may proceed with vaccination**; the post-vaccination monitoring period in clinic varies according to spectrum of allergy (anaphylaxis/immediate allergic reaction vs. non-anaphylaxis/immediate allergic reaction) [See Appendix Table]
- Immediate allergic reactions to vaccination are defined as any hypersensitivity-related signs or symptoms such as hives, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis that occur <u>within four hours</u> following administration.

### Contraindication to either mRNA vaccine*

Persons with the following history have contraindications to receiving mRNA vaccine:

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components
- Immediate allergic reaction of <u>any severity</u> to a previous dose of an mRNA COVID-19 vaccine or any of its components, including PEG*
- Immediate allergic reaction of <u>any severity</u> to polysorbate* (due to potential cross-reactive hypersensitivity with PEG)

**may consider allergist consultation to assess and determine if vaccine can be administered safely. For patients who require facilitated referral to an allergist, process to do so with MSK consultants and external partners is in development.*

**References:**


1. *Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine — United States*, December 14–23, 2020 *Early Release* / January 6, 2021 / 70
2. https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html
3. Stone CA, Liu Y, Reiling MV, et al. *Immediate Hypersensitivity to Polyethylene Glycols and Polysorbates: More Common Than We Have Recognized.* J Allergy Clin Immunol Pract. 2019 May-Jun;7(5):1533-1540.e8.
4. Mishra P, Nayak B, Dey RK. *PEGylation in anti-cancer therapy: An overview.* Asian Journ Pharm Sciences 2016; 11:337-348.
5. https://emergency.cdc.gov/coca/ppt/2020/dec-30-coca-call.pdf


**PLEASE NOTE THIS SECTION IS UNDER ACTIVE DEVELOPMENT AND WILL BE UPDATED FREQUENTLY AS INFORMATION COMES IN**

**APPENDIX**

**Figure: Allergy screening and management schema for m RNA vaccines**

**Table: Common parenteral cancer/other drugs that contain PEG and/or polysorbate**

**FIGURE: Allergy screening schema for MSK patients**
**Source: CDC**

| MAY PROCEED WITH VACCINATION | PRECAUTION TO VACCINATION | CONTRAINDICATION TO VACCINATION |
|---|---|---|
| **ALLERGIES**<br>History of allergies that are unrelated to components of an mRNA COVID-19 vaccine†, other vaccines, or injectable therapies, such as:<br>• Allergy to oral medications (including the oral equivalent of an injectable medication)<br>• History of food, pet, insect, venom, environmental, latex, etc., allergies<br>• Family history of allergies<br><br>**ACTIONS**<br>• 30 minute observation period: Persons with a history of anaphylaxis (due to any cause)<br>• 15 minute observation period: All other persons | **ALLERGIES**<br>• History of any immediate allergic reaction‡ to vaccines or injectable therapies (except those related to component of mRNA COVID-19 vaccines† or polysorbate, as these are contraindicated)<br><br>**ACTIONS:**<br>• Risk assessment<br>• Consider deferral of vaccination and/or referral to allergist-immunologist<br>• 30 minute observation period if vaccinated | **ALLERGIES**<br>History of the following are contraindications to receiving either of the mRNA COVID-19 vaccines†:<br>• Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components<br>• Immediate allergic reaction‡ of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components^ (including polyethylene glycol)#<br>• Immediate allergic reaction of any severity to polysorbate^#<br><br>**ACTIONS**<br>• Do not vaccinate#<br>• Consider referral to allergist-immunologist |

† Refers only to mRNA COVID-19 vaccines currently authorized in the United States (i.e., Pfizer-BioNTech, Moderna COVID-19 vaccines)
‡ Immediate allergic reaction to a vaccine or medication is defined as any hypersensitivity-related signs or symptoms consistent with urticaria, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis that occur within four hours following administration.
^ See Appendix A for a list of ingredients. Note: Polyethylene glycol (PEG), an ingredient in both mRNA COVID-19 vaccines, is structurally related to polysorbate and cross-reactive hypersensitivity between these compounds may occur. Information on ingredients of a vaccine or medication (including PEG, a PEG derivative, or polysorbates) can be found in the package insert.
# These persons should not receive mRNA COVID-19 vaccination at this time unless they have been evaluated by an allergist-immunologist and it is determined that the person can safely receive the vaccine (e.g., under observation, in a setting with advanced medical care available)

**TABLE: Common parenteral cancer/other drugs that contain PEG and/or polysorbate**

| Formulary Medications (PARENTERAL ROUTES only) | Polysorbate 80 (PS80) | Polysorbate 20 (PS20) | Polyethylene Glycol (PEG) |
|---|---|---|---|
| Ado-trastuzumab emtansine | | X | |
| ALEMTUZUmab | X | | |
| Alteplase | X | | |
| Atezolizumab | | X | |
| Avelumab | | X | |
| Bamlaniuimab | X | | |
| BEVACIZUmab | | X | |
| blinatumomab | X | | |
| brentuximab | X | | |
| cemiplimab | X | | |
| Cyclophosphamide | | | X |
| Daratumumab | | X | |
| Depomedrol | | | X |
| Depoprovera | | | X |
| Dinutuximab | | X | |
| docetaxel | X | | |
| durvalumab | X | | |
| elotuzumab | X | | |
| etoposide (inj. solution) | X | | |
| fam-trastuzumab | X | | |
| fosaprepitant | X | | |
| Fulvestrant | X | | |
| Gemcitabine | | | X |
| Herceptin | | | X |
| infliximab | X | | |
| ipilimumab | X | | |
| Isatuximab-irfc | X | | |
| LORazepam | | | X |
| mogamulizumab | X | | |
| Neulasta | | | X |
| nivolumab | X | | |
| ofatumumab | X | | |
| PEGaspargase | | | X |
| pembrolizumab | X | | |
| Pertuzumab | | X | |
| Phytonadione | X | | |
| Polatuzumab | | X | |
| ramucirumab | X | | |
| rituximab | X | | |
| sacituzumab govitecan | X | | |
| temozolomide | X | | |
| TRASTUZUmab | | X | |
| ustekinumab | X | | |
| Vancomycin | | | X |