

Recommendations for anti-Covid-19 vaccination in patients with multiple myeloma (MM) and related conditions, AL amyloidosis and other monoclonal gammopathies of clinical significance

1. Which patients should get vaccinated?

- Data collected by IMS for Covid-19 infection suggest that patients with myeloma are at increased risk of severe infection and higher mortality.
- Based on this and other data, all patients with myeloma or precursor disease (MGUS and smoldering myeloma) should be candidates for Covid-19 vaccine. Vaccine induced immune response may decrease infection rate and decrease severity of the illness.
- These guidelines may be followed also in patients with AL amyloidosis and other monoclonal gammopathies of clinical significance.

2. Type of vaccine to be used

- Currently two mRNA-based vaccines (Pfizer/BioNTech and Moderna) are approved by EMEA and FDA, and both are safe for administration to patients with myeloma. Pending further safety insights, other non-replicating adenoviral vector vaccines (eg. Oxford/Astra-Zeneca, Janssen) and antigen/adjuvant vaccines (eg. Novavax) under approval process should not pose any additional risk to myeloma patients.
- For other vaccines, the principle of avoiding live virus vaccine applies to myeloma patients

3. Timing of administration of the vaccine

- As soon as vaccine is available.
- Prior Covid -19 infection is not a contraindication and does not mean vaccine is not necessary. The expected natural immune response to Covid-19 infection may vary in myeloma patients and the time from Covid-19 infection to vaccination may vary based on local considerations but in general 90 days are commonly considered.
- History of allergy to any vaccine component is a contraindication to vaccination
- Ensure patient is not neutropenic (<500/uL)

- Patients with thrombocytopenia (<50000/uL) and/or on anti-coagulants will require special measure to prevent local bleeding.
- If patient has active progressive myeloma, then vaccination should not hold ongoing therapy.
- If patient's myeloma is stable, and holding therapy is not a concern, then the vaccine should be administered between the courses of therapy. An ideal situation would be to hold treatment 7 days before 1st dose to 7 days after 2nd dose. This would mean holding MM therapy for around 5-6 weeks, depending upon type of vaccine and the interval between doses. Keeping importance of maintaining MM therapy in mind, when such long pause is not possible, consider giving 1st dose of the vaccine 2-7 days after the last dose of MM therapy and up to 10 days before restarting MM therapy, with 2nd vaccination given at the appropriate interval.
- Use of steroid – Hold steroid during both the vaccinations, from 7 days before 1st dose to 7 days after 2nd dose, if possible.
- Maintenance therapy: Lenalidomide monotherapy has been shown to either augment vaccine response or have no adverse effect on vaccine response and does not need to be held for COVID vaccination. Same principle as for myeloma therapy described above applies for other maintenance therapies which can be held as appropriate for both vaccine doses (from 7 days before 1st dose to 7 days after 2nd dose). If Dexamethasone is part of maintenance, then it should be held during vaccination.
- IVIg can blunt immune responses to vaccines, consider giving 14-28 days interval prior to the 1st dose and to delaying IVIG dose to 14 days following the 2nd dose, if feasible.

4. Relationship to transplant and other cellular therapies

- If considering vaccination post-autologous stem cell transplant (ASCT), then wait for 3 months, If pretransplant vaccination then plan to complete vaccination before stem cell collection.
- Patients with already harvested stem cells and having a deferred ASCT it makes sense to vaccinate post-harvest, especially if transplant is delayed for a longer period
- For those patients vaccinated pre-ASCT, data is not currently available about if and when to revaccinate patient after ASCT,

- The 3 months wait following autologous transplant for COVID-19 vaccination should be applicable to all cellular therapies (including CAR T cell) in general.
- We would not recommend delaying the second dose – both dosages should be completed at the recommended interval.

5. Patients on studies

- Recommendations for vaccination of patients on study do not differ from general myeloma patient population. In these patients, vaccination is recommended unless contraindicated by the protocol.
- The investigator should discuss with the Sponsor the plan for vaccination, ensure safe administration with investigational agent and the possibility of treatment interruption to allow effective vaccination.

6. Immune response and its measurement

- Although the vaccine is very effective, the actual benefit to MM patients remains to be determined. Thus protective measures are still very important. Patients should continue to wear a mask and practice social distancing.
- Ideally care giving family members should be considered for the vaccination
- 1st vaccine response in normal individuals is observed after 10 days from initial dose. Kinetics of this response in MM patients remain unclear.
- Measuring vaccine response is not necessary or indicated.
- However, if response to vaccination is to be evaluated then it can be measured in terms of antibody titer. Measurement of immune response should be against the appropriate spike protein and the measurement should provide titer.
- Ideal schedule for testing for antibodies would be before 1st and then 7-21 days after 2nd vaccination. An additional measurement before 2nd vaccination may be considered.
- Currently no plan for additional vaccinations if the response is inadequate.