MULTIPLE MYELOMA AND COVID-19

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General Recommendations to Patients

1. Multiple myeloma (MM) is a hematopoietic malignancy exhibiting altered immunity.
2. Given the risk of higher risk of morbidity and mortality with Covid-19 in cancer patients[1], it is important to follow social distancing, proper hand hygiene with frequent hand-washing for 20 seconds, proper cough etiquette, and to avoid going out in crowded places even after the lockdown is released.
3. During treatment, the patient must avoid visiting the hospital frequently, except for response assessments if the tests cannot be performed locally or if there are significant complaints. The patient's attendant/ care-giver can do the medication refill.
4. Patients are encouraged to call their myeloma doctors and nurses for clarification and to avail the option of Tele-medicine if it is available at their treating center.

General Recommendations to Hematologists/ Oncologists for the management of Multiple Myeloma during the ongoing SARS-CoV-2 Pandemic

1. We strongly recommend the setting up of tele-medicine facilities at medical centers. It is especially important to assign duties amongst treating team members as there is a high risk of infection among HCWs.
2. Infection is the most important cause of morbidity and early mortality in multiple myeloma with an increased chance of bacterial infection- 7-fold and viral infections- 10-fold. For a patient undergoing work-up for multiple myeloma, it is advisable to administer the following vaccinations- PCV13 (conjugate pneumococcal vaccine) & annual inactivated influenza vaccine (FV). PPSV23 (pneumococcal polysaccharide vaccine) can be administered 6-12 months after PCV13. (CDC/ACIP, NCCN & IDSA Vaccination guideline for MM)[2]

3. **Newly Diagnosed MM** (based on CRAB only, SLiM can wait)
   a. **Transplant Eligible**
   - If injectable chemotherapy is feasible, first-line: VRd/VTd/ CyBorD (Bortezomib 1.3mg/m^2 D1,8,15,22; oral cyclophosphamide 200-300mg weekly; oral dexamethasone 20-40mg weekly), cotrimoxazole- PCP prophylaxis for all patients. For high-risk cytogenetics, continue therapy for 9-12 cycles. After 4-6 cycles, if on VRd, lenalidomide dose can be decreased to 10 mg or stopped, and the dose of dexamethasone can be decreased to 10-20 mg.
     For standard-risk cytogenetics, dexamethasone can be stopped after 4-6 cycles, provided patient is symptomatically better and has achieved at least

a partial response. Bortezomib, along with IMiD or cyclophosphamide can be continued up to 9 cycles followed by maintenance with IMiD.

- It is advisable to choose oral chemotherapy regimens during the ongoing Covid crisis, especially for patients who need to travel long distances for hospital visits.
  Eg. LCD- Lenalidomide, cyclophosphamide and dexamethasone; CTD- cyclophosphamide, thalidomide and dexamethasone.
- If the facility for stem cell cryopreservation is available, it can be done while autologous stem cell transplantation can be postponed.

b. **Transplant Ineligible**

- Lenalidomide/ Dexamethasone till progression according to FIRST trial is preferred. (3) (Len can be initiated at lower doses- 10-15 mg and gradually escalated, dexamethasone can be initiated at 20mg weekly). Dexamethasone dose can be decreased to 10 mg after 4-6 cycles if the patient has achieved at least a partial response. For high-risk cytogenetics, dexamethasone is preferably continued until progression. For standard-risk cytogenetics, dexamethasone can be stopped after 6 cycles. Other options: MPT, CTD, Thal/Dexa.

4. **Follow-up Strategy**
   - Follow-up biomarkers for disease reassessment- every three months except for symptomatic/ CRAB progression.
   - Follow-up bone marrow for disease reassessment, including MRD assessment, can be minimized. It is sufficient to go by peripheral blood and/or urine biomarkers.

5. **Plasma Cell Leukemia**
   Circulating plasma cells >20% of the differential count or >2000/mm_3- first-line Rx- KRd $\pm$ Daratumumab is preferred.
   During the Covid crisis, less intensive regimens viz., VRd can be administered.
   Palliative treatment if the patient has frailty and multiple co-morbidities.

6. **MM with Renal Failure**
   CyBorD or VTD can be planned. Bortezomib can be administered on D1,4,8,11; dexamethasone 16-40mg weekly and thalidomide 50-100mg daily. Plasmapheresis can be avoided if it is part of the Institutional protocol.

7. **Maintenance Strategy**
   For transplant eligible and ineligible patients, maintenance can be continued until progression. Oral agents are preferred. Maintenance can be switched or stopped if the patient reports toxicities which include frequent infections.
   - High-risk cytogenetics and plasma cell leukemia: Bortezomib +/- Lenalidomide 5-10mg
   - All other risk stratifications: Lenalidomide 5-10mg
   - MM with renal failure: Bortezomib +/- thalidomide

- If transplant is contemplated in future, thalidomide 50mg or bortezomib can be continued
- Maintenance will be given for 3 months until the next follow-up

8. **Relapsed MM**
   - Oral regimens will be preferred- PCD, MPT. Bortezomib-containing regimen if the patient was not exposed at first line.
   - For biochemical relapse, chemotherapy can be switched if front line high-risk characteristics are present.
   - Carfilzomib can be administered as weekly-infusions. Avoid other schedules.
   - Daratumumab can be converted to once monthly regimens.

9. **Transplant Recommendations**
   It is preferable to avoid autologous stem cell transplant until we reach a safer period.

10. **Supportive Care**
    - Zoledronic acid can be administered q3monthly. Beyond 12 months, an individual case-by-case decision can be taken to withhold zoledronic acid if the disease is in remission.
    - For painful bone destructions, single fraction 8 Gy RT is preferable during the Covid crisis.

Availability of medications (e.g. some medications may not be available at some places depending upon the containment zone)

These recommendations will be based on whether patients and hospital falls into a red/ orange/ green zone.

Disclaimer: Consensus-based recommendations

References:

1. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. The Lancet Oncology. 2020 Mar 1;21(3):335–7.
2. Alemu A, Richards JO, Oaks MK, Thompson MA. Vaccination in Multiple Myeloma: Review of Current Literature. Clin Lymphoma Myeloma Leuk. 2016;16(9):495–502.
3. Benboubker L, Dimopoulos MA, Dispenzieri A, Catalano J, Belch AR, Cavo M, et al. Lenalidomide and Dexamethasone in Transplant-Ineligible Patients with Myeloma. New England Journal of Medicine. 2014 Sep 4;371(10):906–17.