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Annex 2: a transcript of the case-based panel discussion under treatment, monitoring and stem cell transplant
Part A: choice of initial treatment regimen
Question 1: what is the proposed first line treatment on the background of affordability, accessibility, and availability? Remember most of our patients cannot afford transplant so is it wise to continue on a triple regimen indefinitely or would you transition them to maintenance? **Response: Prof Riyat:** at least a triple regimen upfront but in elderly patients 2 - drug regimen. Continuous treatment should be given in patients not eligible for transplant. **Response: Prof Chite:** if the patient is transplant-ineligible, the patient should continue on the triple regimen if they are doing well until toxicity is no longer tolerable or if there is disease progression despite the drug they are using. In my practice I have treated a standard risk patient for over a year with satisfactory response even after 4 - 5 years treatment-free. Sometimes we give the patient a drug holiday the problem comes in because we are not able to risk stratify them. If a patient has high risk disease giving a drug holiday may give opportunity to residual myeloma cells to proliferate and the disease may become difficult to control. Therefore, it is best to establish risk status before choosing treatment and then balance treatment with toxicity to obtain the optimal aggressiveness of treatment required.
Question 2: what is recommended as 1st line regimen for patients with renal disease? **Response: Prof Riyat:** Bortezomib is a safe drug to use on patients with renal disease. Lenalidomide is toxic and needs dose adjustment and sometimes stopped completely. If using a three-drug regimen, cybordex is recommended and quite a good upfront.
Questions 3: what is the role of surgery or radiotherapy in the management of bone lesions, cord compression? **Response: Prof Riyat:** surgery doesn't have much role, radiotherapy is purely palliative for pain control and on patients with pathological fractures and for management of cord compression. **Response: Prof. Chite**: for patients who have spinal cord lesions with compression and likely cord collapse, surgical intervention will be helpful to stabilize the spine.
Part B - Drug administration and adverse events
Question 1: what is the experience of giving Bortezomib-IV/SC with regards to adverse effects? **Response: Dr. Caroline Wafula:** if you give it through SC the adverse effects are less specifically nausea, vomiting, lower blood count, compared to giving it via IV. The preferred mode of administering wold be SC. **Response: Prof. Chite:** I agree SC has a much better adverse effect profile. I have seen patients in our setting with grade 4 peripheral neuropathy secondary to bortezomib. So, if we could have access to carfilzomib it would serve well as a replacement for bortezomib in case of neuropathy.
Question 2: how strongly would you recommend prophylaxis against infections? **Response: Prof. Chite:** infection prophylaxis is not always given throughout MM treatment. In our initial years we saw many patients presenting with infection even before treatment, their outlook was poor and some of them passed on due to sepsis not myeloma. When we aggressively treated the infections then they performed well. Therefore, we should treat the infections first. **Response: Dr. Caroline Wafula:** some of the antimyeloma drugs being used are myelosuppressive such as IMIDS and PIs therefore they place the patient at risk of infections. Consider using abroad spectrum antibiotics to prevent infections. This decision is patient dependent since some patients could be carrying resistant bugs. Use targeted antibiotics if you can obtain cultures if an infection is already established. Where protocols for empirical treatment have been developed for oncology units these can be used in place of targeted treatment.
Question 3: what anti-myeloma drugs are responsible for PN? **Response: Caroline Wafula:** angiogenesis inhibitors, proteasome inhibitors: the PN is always dose-dependent. You may want to reduce the dose or stop treatment to avoid PN.
Question 4: are there recommendations to dose adjust Dexamethasone on the background of its S/E?

Response: Dr. Caroline Wafula: it is a steroid, we will monitor blood sugar levels, obesity levels, it is a liver enzyme inducer, and hence it should be adjusted based on the S/E it presents with.

Response: Prof. Chite: longtime S/E or short-term S/E. Adjust based on the type of SE. We need to increase the availability of other agents to create room for options if you have to drop one drug over the other. This is an opportunity for a multidisciplinary care approach whereby patients with other comorbidities consultations with their primary consultants are crucial to ensure that changes in antidiabetic therapy and steroid dose adjustments don't result in patients having hypoglycaemia possibly resulting in death.

Response: Mercy Oduor: diabetes occurrence on patients put on steroid therapy is not a common occurrence although there are patients who already have diabetes at MM diagnosis and the steroids may interfere with their blood sugar control.

Response: Roselyn Yatich: nurses need to do their daily assessment to ensure patients do not suffer from disease or drug toxicity as well as ensure that they are meeting the set therapeutic goals. When it comes to neuropathy, there is a need to evaluate for pain, motor function, bowel function, and sensory function so that spinal cord function is detected early. A delay in identifying these red flags a patient may slip into complete paralysis. Observe strict infection prevention and control practices for MM patient keeping in mind that steroids may compromise patient immunity. Patients should also be educated on how to observe hygiene and comply with infection prevention and control. Patient safety concerns should take priority in offering care to MM patients. MM patients are prone to pathological fractures therefore nurses need to have an awareness of this to facilitate comfortable stay and avoid falls.

Question 5: how safe is it to use factor Xa inhibitors in MM where anticoagulation is indicated?

Response: Prof. Riyat: all MM patients are not equal risk for VTE. IMIDs are notorious for VTE. Determine patients who are at high risk and low risk. Patients at low risks use low dose aspirin. For high-risk use full dose prophylactics e.g. rivaroxaban (10-20 mg) depending on the risk factors.

Response: Caroline Wafula: risk assessment is important. Factor Xa inhibitors present a challenge for patients with bleeding tendencies because we may not be able to reverse bleeding if it occurs. Therefore, we can put all these factors into consideration before selecting the anticoagulant to use be it aspirin, LMWH, warfarin or rivaroxaban. The factor Xa inhibitors are the newer agents in the market and are attractive because they need less monitoring as compared to LMWH and warfarin.

Question 6: how is Bortezomib prepared for subcutaneous use in terms of volume in milimeters?

Response: Dr. Caroline Wafula: SC Bortezomib administration: 2.5mg/ml: add 1.4ml of 0.9% NaCl to a final concentration of 2.5mg/ml.

Part C: stem cell transplant

Question 1: most patients are not able to proceed for SCT should the induction period be longer?

Response: Dr. Mishra: patients ineligible for transplant should be treated for at least 6 cycles of induction chemotherapy followed by indefinite maintenance chemotherapy. Sometimes for the patient who has entered remission, whether they have achieved complete remission or not, check on their SFLC? We might extend it from 6 to 8 cycles. For patient's ineligible for transplant, I give at least 8 cycles of induction chemotherapy followed by indefinite maintenance.

Question 2: in case a patient is scheduled for SCT but there is a delay, is it recommended to add two more cycles as you wait for SCT?

Response: Dr. Mishra: we take patients for transplant after 4 cycles of chemotherapy that will be after 4 induction cycles approximately four months, in case you are not able to take them for transplant, like now because of the CIVID-19 pandemic we advise they continue with chemotherapy for another 2 to 3 cycles until they can go for the transplant. For those cases who are willing, we recommend the collection of their stem cells and then they continue with the induction chemotherapy. We can collect stem cells after four cycles of VRD cryopreserve then continue with VRD.

Question 3: how best can we start SCT in the country?

Response: Prof. Riyat: in terms of transplant, we can do it, we have the human capacity, but deficiency is still in terms of administrative constraints, but in terms of performing the process we are capable of starting soon.

Part D: access to antimyeloma agents

Question 1: what challenges do you face in procuring anti-myeloma drugs in your facility?

Response: Dr. Caroline Wafula: challenges we face is cost and limitation and that means we have been referring our MM patients to MTRH for treatment because we don't have the drugs. Under usual circumstance the allocated funds are not sufficient to procure antimyeloma drugs but we just learn that bortezomib is supported under the UHC program so with time we will be able to obtain it for our patients. We also order it through KEMSA but sometimes it is not supplied even though the order list shows that it is available. We think that through this forum perhaps we will be able to lobby so that we can be considered to receive the drugs in the next cycle. Unfortunately, it is only bortezomib that is UHC supported, we do not have access to thalidomide and lenalidomide so that also presents a challenge.