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Keeping Pace in Hematologic Malignancies: Updates from ASCO 2022

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Keeping Pace in Hematologic Malignancies: Updates from ASCO 2022” is provided by Prova Education.

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Dr. Kumar:
A lot of new data were presented recently at ASCO 2022. Let’s find out what this means for clinical practice today. This is CME on ReachMD, and I am Dr. Shaji Kumar.

Dr. Mateos:
I am Dr. María-Victoria Mateos.

Dr. Kumar:
Let’s get to it. First, there was some exciting news for newly diagnosed multiple myeloma, with the results of the long-awaited DETERMINATION trial. Can you tell us about that?

Dr. Mateos:
DETERMINATION trial evaluated the role of transplant as part of the first line of therapy after induction with RVd versus RVd 8 cycles, and both arms will continue with maintenance with lenalidomide until progressive disease. The first take-home message is transplant does continue being the standard of care, because of the significant benefit in terms of progression-free survival. However, it is true that this trial with a very long follow-up didn’t report any benefit in terms of survival. This means that we can potentially consider the patient preferences in order to proceed or in order to autologous stem cell transplantation as part of the first line of therapy. And the second consideration is the incorporation of the undetectable measurable residual disease, because when it is negative, the outcome for patients who receive and who didn’t receive autologous stem cell transplantation was comparable.

Translocation 11;14 is the emerging as a predictive biomarker. What is the effect of this mutation on progression-free survival, in patients receiving triple induction therapy?

Dr. Kumar:
Yes, the translocation 11;14, is one of those translocations in myeloma that can be present in up to 20% of patients. Previous studies have demonstrated that the outcomes of patients with 11;14 translocation appears to be intermediate between the other standard – multiple myeloma and patients with high-risk disease. But most of the older data had been in the context of previous injection therapies. And this particular abstract from Emory University looked at the outcomes of patients with translocation 11;14 in the context of __2:12, lenalidomide and dexamethasone triplet.

They were able to show that the progression-free survival was inferior to patients with standard multiple myeloma, confirming some of the earlier findings. And these findings are important because we have a drug, venetoclax, which is a BCL-2 inhibitor, that has

demonstrated significant activity among the patients with translocation 11;14, and this potentially opens up an avenue for us to improve the outcomes of patients with translocation 11;14.

We also have some new data for the transplant-eligible patients with newly-diagnosed myeloma. The GRIFFIN trial looked at quadruple therapy with daratumumab, and its effect on minimal residual negativity in this patient population. María, what can you tell us about that data?

Dr. Mateos:
Yeah, in the GRIFFIN study, DARA-VRd followed by transplant in consolidation with the DARA-VRd and maintenance with the dara/lenalidomide was compared with the standard of care RVd transplant, RVd and then maintenance. The addition of daratumumab to VRd improved the quality of the proportion of patients achieving complete response, but when the minimal residual disease was evaluated, the addition of DARA resulted in a higher rate of undetectable measurable residual disease. But in addition, on trying to generate surrogate markers predicting outcome in this population, the sustained and detectable measurable residual disease was evaluated at 6 months and in 1 year. And, almost 50% of the patients treated with DARA-RVd, greater sustained undetectable measurable disease or disease at 6 months, and at 1 year, versus 12 or 14% of patients in the control arm. And the important information is those patients with sustained undetectable measurable residual disease presented an excellent outcome. In terms of progression-free survival, few patients have so far progressed. So definitely, from my point of view, this is going to be an important surrogate marker, predicting outcomes in multiple myeloma.

Dr. Kumar:
That's an important point, and I think the daratumumab-RVd regimen is likely to be a very commonly used quadruplet regimen going forward, given the efficacy that we have seen so far. The high rates of MRD negativity we hope will translate to a better progression-free survival, which hopefully we will see with more mature data, and which will then support increased use of this quadruplet regimen in this patient population.

For those just tuning in, you are listening to CME on ReachMD. I am Dr. Shaji Kumar, and here with me today is Dr. María-Victoria Mateos. Together we are discussing the emerging data from ASCO 2022, and what it means for your clinical practice.

Turning now to the relapsed disease, teclistamab looks to be a promising new agent. What were the key new data presented at ASCO?

Dr. Mateos:
At ASCO, we had the opportunity to see another data efficacy and safety data from the MajesTEC-1 clinical study, in which teclistamab, a BCMA/CD3 bispecific monoclonal antibody was evaluated in 165 relapsed and refractory myeloma patients, after the median of 5 prior lines of therapy, and majority of the patients __5:47 class refractory. In this sub data, we've seen how the overall response rate was 63%, with almost 40% of the patients achieving at least complete response, and the median durability of the response was proportionately one and a half year, with a median progression-free survival in the intent-to-treat patient population of approximately 1 year. Safety profile is quite acceptable, although we have to assume that the majority of the patients will develop CRS, hematological toxicity, but especially infections. And maybe in the clinical practice, we have to start with adequate prophylaxis, in order to protect our patients from CRS infections. But definitely, the updated data for MajesTEC-1 supported the use of teclistamab in the future, when this drug is approved in relapsed and refractory myeloma patients, and the next step is to move to randomized studies. One of the major benefits for teclistamab, as well as other bispecific monoclonal antibodies is the possibility of it being combined with other drugs, like the monoclonal antibody daratumumab. And this is what it is going to be evaluated in the MajesTEC-3 clinical study. Phase 3 randomized study, conducted in relapsed and refractory myeloma patients after 1-3 prior lines of therapy. The experimental arm will be teclistamab plus daratumumab, and the control arm is going to be either DARA-PD or DARA-VD. And the trial is ongoing, and the primary endpoint is progression-free survival. In addition, one additional consideration about the MajesTEC-1 and the efficacy data reported for teclistamab, single-agent because when we compared these efficacy data with triple-class exposed, relapsed and refractory myeloma patients included in the LocoMMotion study, an observational and prospective clinical study – we see how the incorporation of this BCMA-targeted therapy throughout the use of the bispecific monoclonal antibody, teclistamab, resulted into a better efficacy in terms of response rate, as well as in terms of durability of the response, and complete response rate.

Shaji, let's move on now to cell therapy. And we now have two approved CAR T-cell therapy. Can you highlight the new data around cilta-cel and ide-cel for us?

Dr. Kumar:
Absolutely, María. I think we saw some exciting updates with respect to the CAR T-cell therapy. As you mentioned, we have ide-cel that is already approved, and there was a real-world data that was presented at ASCO, which looked at a cohort of 196 patients who were treated with ide-cel. Interestingly, the data showed that the overall response rate was about 84% – quite similar to what was seen in the pivotal KarMMa study. The progression-free survival for this cohort was about 8.9 months, and the median overall survival was not

reached. All these numbers appear to be quite identical to what we saw with the pivotal KarMMa study. Interestingly, they also looked at patients who met the criteria for the KarMMa trial, and those who did not. Certainly, it seems like the patients who did not meet the criteria for the trial did not have as good an outcome as the ones who met the criteria for the trial, again highlighting the differences or the importance of looking at real-world evidence in comparison to what we see in the clinical trials.

There was an interesting analysis looking at patients who are receiving the ide-cel in the clinical trials and looking at some of the coordinated studies. In particular, the investigators wanted to look at clinical characteristics that may predict for an inferior outcome, both in terms of manufacturing the CAR T, as well as the clinical outcomes. They found that patients with a higher tumor burden, or patients with lower starting lymphocyte count – these are the patients who are more likely to have a poor outcome. This kind of correlated studies would be important for us if we tried to select the right patient for these therapies. Now, the other CAR T-cell that is approved is the cilta-cel, and there are ongoing studies that are looking at different patient populations. The CARTITUDE-2 is a multi-cohort study that is looking at a variety of different patient populations. The results from the cohort A, that look at patients who had 1-3 prior lines of therapy and were lenalidomide-refractory, showed that the overall response rate was quite comparable, at about 95% with almost 90% of patients getting a complete response. Now this is important data, because the ongoing phase 3 trial is looking at the comparison of cilta-cel with standard of care combinations, like daratumumab, pomalidomide and dexamethasone, or pomalidomide, bortezomib, and dexamethasone, particularly in this patient population. Now the cohort B is an interesting cohort, because that looked at the functional high-risk patient population, and these are patients with disease that relapsed very early after the initial therapy. And even in this high-risk patient population, the overall response rate was quite comparable, with almost all patients responding to the therapy, with majority of them getting to be minimal residual disease negative. So I think as we continue to learn more from these studies we will be able to select the appropriate therapy for our patients, based on the underlying clinical characteristics.

Dr. Mateos:
There is not any doubt that BCMA/CAR T-cell will move to earlier lines of therapy. The information in the real-world experience will contribute to improve the outcomes of our patients treated with CAR Ts in the clinical practice.

Dr. Kumar:
Well, it's been great catching up on the latest information from ASCO with you. María-V. before we go, what is one take-home message for our listeners today?

Dr. Mateos:
The treatment landscape for patients with multiple myeloma is rapidly evolving. At the moment of the relapse, we see earlier and earlier, patients already exposed to the three main drug classes: proteasome inhibitors, IMiDs, and anti-CD38 monoclonal antibodies. We've just had the opportunity to see at the ASCO, how the BCMA-targeted therapy is able to cover this unmet medical need, with excellent data reported with bispecific monoclonal antibodies, as well as a third therapy. It is logical to see how this BCMA-targeted therapy will rapidly move to earlier lines of therapy.

Dr. Kumar:
And I will add, the treatment of newly-diagnosed myeloma also continues to evolve, with mature data from GRIFFIN trial demonstrating the high rates of MRD negativity for the quadruplet regimens, which will likely lead to better long-term outcomes. And we also have data at the ASCO, which supports the continued use of autologous stem cell transplantation as part of the usual therapy of multiple myeloma, in the transplant-eligible patient population. Unfortunately, that's all the time we have today, so I want to thank our audience for listening in, and thank you, María-V., for joining me today. It was a pleasure speaking with you.

Dr. Mateos:
Thank you very much, Sadji.

Announcer:
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