Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/multiple-myeloma-newsflash-emerging-data-2020-ash-annual-meeting/12245/

Released: 02/26/2021
Valid until: 02/25/2022
Time needed to complete: 15 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Multiple Myeloma Newsflash: Emerging Data From the 2020 ASH Annual Meeting

Announcer:
You're listening to CME on ReachMD. The following activity is, titled "Multiple Myeloma Newsflash: Emerging Data From the 2020 ASH Annual Meeting."

To access additional activity details and earn CME credit, please visit ReachMD.com/CME.

Dr. Doghramji:
The 2020 American Society of Hematology Meeting was held in December 2020 and nearly 5,000 abstracts were presented. This is CME on ReachMD. I'm Dr. Paul Doghramji and here with me to review several key abstracts presented at the ASH Annual Meeting and how it may directly impact patient care in the field of multiple myeloma is Dr. Joseph Mikhael. Dr. Mikhael is a professor of Applied Cancer Research and Drug Discovery, Translational Genomics Research Institute at the City of Hope Cancer Center, and Chief Medical Officer of the International Myeloma Foundation. Dr. Mikhael, welcome to the program.

Dr. Mikhael:
Thanks, so much, Paul. Great to be with you.

Dr. Doghramji:
Great. So, to start off Joe, let's discuss newly diagnosed multiple myeloma. Can you share details about any key data from the ASH Annual Meeting?

Dr. Mikhael:
Absolutely. Happy to address this topic. You know, it was a very exciting ASH for multiple myeloma. We've seen, over the years, so much change in the world of multiple myeloma and typically, we think of it in the relapse setting, as we're gonna come to in a few minutes. But even in the frontline setting, we've seen significant improvements in what we could do for our patients. And this was particularly highlighted at this annual meeting with the GRIFFIN study we've been following for a little while now and we're quite excited for it to come to fruition… is a randomized phase 2 trial, where we are comparing what is currently the standard of care, using bortezomib, lenalidomide, and dexamethasone versus daratumumab plus bortezomib, lenalidomide, and dexamethasone. So, this randomized trial is very important to us because, although we've developed this very important platform of a triplet, the question is, can quadruplets make our frontline therapy better? And, indeed, we saw in this study, various lessons learned. So, the primary endpoint of this study was to demonstrate an improved stringent complete remission and sure enough, we saw that in the earlier presentations of this study. What was being focused on at ASH this year, was looking to see what would be the effect with continued use of daratumumab in the maintenance setting. So, to help explain this, the triplet versus the quadruplet was not just for initial induction followed by stem cell transplant, but also for two cycles of consolidation and then indeed, in the maintenance setting, where daratumumab and lenalidomide would be compared to just lenalidomide, alone, which is also the standard of care, 'cause most patients will get VRD transplant and lenalidomide maintenance, so that remains the control arm. And the first important result we noted was that with each of these levels of treatment, induction, transplant, consolidation and maintenance, the depth of response was considerably improved in both arms. But at the end of 12 months of maintenance, which was the cutoff for this presentation the rate of complete remission or greater in the intervention arm was 82% versus 61% in the RVD arm, alone. And we're coming to appreciate in myeloma,

more than ever, is the depth of that response considerably more important at the early treatment of our patients. Thankfully, we didn't really see a significant safety signal that was different than what we're used to. And the last point to make about the results was that not only did we see that complete remission depth of difference, but what we're coming to learn is that MRD negativity differences, or Minimal Residual Disease differences, are perhaps even the most important and we saw considerable difference between those two at 62.5% versus 27.2%. It's a little bit early to comment on progressionfree survival or overall survival. So, what does this mean for the practicing clinician? Well, I think as a myeloma community, we are on the verge of moving from triplets to quadruplets and this will likely be the first of those quadruplets where we add daratumumab to VRD in the frontline setting, at least for induction and consolidation and possibly for maintenance. I think we need more time to make that conclusion about maintenance. And I think it will herald other quadruplets that we'll see in the future that include daratumumab with other triplet combinations and even, potentially, other novel antibodies such as isatuximab.

Dr. Doghramji:
Well, thank you for that. So, now, let's turn to early relapsed refractory multiple myeloma. Can you tell us about the important abstracts in this treatment setting?

Dr. Mikhael:
Again, we have seen tremendous advances in myeloma and a lot of these advances in myeloma have not just been in the very heavily relapse setting, but also in the early relapse setting. And this was emphasized in the APOLLO study. This is an open-label, multicenter phase 3 trial and patients that had at least 1 prior line of therapy, and patients were randomized to receive pretty standard pomalidomide and dexamethasone and in the intervention arm, added daratumumab to it and specifically added daratumumab as a subcutaneous injection. The primary endpoint was progression-free survival and sure enough we saw a considerable improvement in median progression-free survival from about 7 months to 12 and a half months. And only about half of these patients were in first relapse. There were patients that were in second and, indeed, third relapse. As we've indicated before, when we add daratumumab, we do tend to see increased infections, specifically pneumonia and respiratory tract infections. But again generally very well managed. And interestingly, in contrast, the older days of IV dara, now giving it subcutaneously, we had significantly fewer what are called "infusional" or, now, "administration" reactions when given subcutaneously. So, this is a very important study for the clinic because it emphasizes, to some degree, what we're already doing. This is already a well-known combination of daratumumab and pomalidomide. It's been available in the community for a few years, by virtue of the NCCN guidelines, but this is now the confirmatory phase 3 study and specifically adds the element of subcutaneous daratumumab, which I think is going to be a very important part of what we do, going forward, because instead of giving patients IV drug for, sometimes, many hours, although there are some accelerated infusions, now we literally give this drug subcutaneously over 5 minutes. So, this has particularly significant implications for the way that we deliver this drug in in the community.

Dr. Doghramji:
Wow, that's pretty great. Is there other pivotal data that was shared at ASH in relapse refractory multiple myeloma?

Dr. Mikhael:
Absolutely, Paul. So, in this same vein of using intense therapies early on in relapse another very important study was the IKEMA, and I actually had the privilege of being part of this study, as well. And this was a little bit of a similar approach that I just described, but in this case, the control backbone was carfilzomib/dexamethasone, which is also a very commonly used combination in early relapse multiple myeloma and this trial was a further update of the phase 3 study in isatuximab/carfilzomib/dexamethasone versus carfilzomib and dexamethasone. So, isatuximab, of course, is a novel CD38 antibody, similar in many respects to daratumumab and so this was a very important randomized, open-label, multicenter phase 3 study, with a little over 300 patients that were randomized in a 3-2 fashion, to isatuximab/carfilzomib/dexamethasone versus carfilzomib and dexamethasone. The primary endpoint, as we would expect, as we saw with APOLLO, was progression-free survival and interestingly, in this case the isatuximab/carfilzomib/dex arm has yet to achieve that. So, it's not yet reached; whereas, in the KD arm, the medium progression-free survival was 19 months.

Really quite a long and good outcome, even in the control arm. As expected, we saw a considerable difference in the response rates between the two; the hazard ratio was 0.53. The safety signal was quite what we would expect with these drugs, although we always have to specifically watch for cardiac effects when patients are receiving carfilzomib. This is not yet an FDA or NCCN guideline approved. We do already have the daratumumab carfilzomib/dex through the CANDOR study having been approved, and we'll likely see with IKEMA a similar approach where we can use this CD38 antibody, isatuximab, in combination with carfilzomib/dex for very deep and durable responses in patients with 1 to 3 prior lines of therapy with myeloma.

Dr. Doghramji:
So, Joe, so we were just talking about some of the key abstracts presented at the ASH annual meeting and I wanna dive into that just a

bit deeper. CAR T-cell therapy is another exciting area in multiple myeloma. What are some of the key takeaways from clinical data presented at ASH that you'd like to share with our listeners?

Dr. Mikhael:
There was a lot of excitement around CAR T-cell therapy as it's not yet approved in myeloma, but the first of them is ide-cel. And so, there was an update at ASH this year of the CRB-401 study, which was a 2-part phase 1 dose escalation and expansion study of this ide-cel product, which is currently under evaluation and may well be the first drug we have available to us in myeloma as a CAR T-cell approach. We saw a response rate of 76% and, again, to put this in context, these are triple-class refractory patients that typically, with the best therapy we have now, may have a response rate of up to 30%. And furthermore the depth of response of seeing nearly 40% of these patients achieve a complete remission is really quite remarkable. Furthermore, the median progression-free survival at least in this smaller cohort was nearly 9 months. Which, if we look at these patients prior to CAR T, that's honestly about their expected overall survival, so, there was a lot of enthusiasm around this. Now, of course, CAR T-cell therapy comes with some challenges and, particularly, we know that by virtue of the conditioning chemotherapy that we give them, patients are gonna have significant cytopenias, including neutropenia, in nearly all of them and also in particular, cytokine release syndrome, although I must say we are getting better at both preventing it and treating cytokine release syndrome. Mostly, thankfully now, they're grade 1 and grade 2, but we still see these in the majority of patients. So, I think my take-home for this first product, the ide-cel product, is that it's clearly demonstrated its ability to demonstrate both depth and duration of response in patients who have very heavily pretreated multiple myeloma. I think we are getting significantly better at managing the toxicities of this therapy and really anticipate that this is going to be something available to the myeloma community in the near future, likely within the year 2021.

Dr. Doghramji:
Very interesting. What about CAR T-therapy cilta-cel? Can you tell us more about this promising data that we have on this agent?

Dr. Mikhael:
Yeah, there was a lot of discussion around this study, as sort of being, if you will, the next major wave of CAR T-cell therapy after we saw ide-cel. The CARTITUDE study, which was a phase 1b/2 study, again, looking at patients that were essentially triple-class refractory, so it had proteasome inhibitors, immunomodulatory drugs, and a CD38 antibody. And so, we saw the results now of 97 patients. And again, a little bit like we saw with ide-cel, we saw that cytokine release syndrome does occur in the majority of patients but again, overwhelmingly, almost all grade 1 and grade 2. And so, that becomes very important for us to be able to manage these patients. But perhaps what was most striking of this study was the overall response rate. So out of the 97 patients, 94 of them responded— that translates to a 97% response rate. And remarkably, 93% had very good partial remission or better and 67% achieved a stringent complete remission. So, the depth of response here is truly unprecedented in myeloma. We're now not just doubling what we've historically seen in triple-class refractory—we're literally tripling it. Little bit early to comment on progression-free survival, but nonetheless, at 12 months, we have just over three-quarters of patients still not having progressed. So I think the take-home message here, similar to what we've seen with ide-cel, is cilta-cel demonstrates particular efficacy, perhaps even greater efficacy, and it's very exciting to see that we can have this sort of depth of response in very heavily pretreated myeloma

Dr. Doghramji:
Excellent. Excellent information. Alright, so as I understand, there were several key abstracts presented on bispecifics. Can you tell us a little bit about this?

Dr. Mikhael:
Perhaps the bispecific that I would highlight the most was the teclistamab study. This was a bispecific that is specific to BCMA, the CD3 target on local T cells, and it was really quite exciting to see this being given in considerably higher numbers of patients, where it was actually initially given IV and now also able to be given subcutaneously. So, in a similar population that we saw with CAR T's with patients that are triple-class refractory, we saw response rates of over 60%—really quite exciting—and at the target dose, a response rate of 73%. Now, there are some safety considerations here, as we would expect, that we do see cytopenias but we also do see some cytokine release syndrome, perhaps not to the same degree as with CAR T, but this is an important point for the community oncologists because these drugs are still given inpatient for the first dose or two by virtue of that risk of CRS, but then ultimately can be given, potentially exclusively, as an outpatient and even given subcutaneously, as I mentioned. So, looking to the future of bispecific therapy, we think this will be a very important treatment strategy going forward. We have other targets now, so there was another abstract of talquetamab, which was using GPRC5D along with T cells and again, similarly, we saw response rates in that 67% to 78% response rates—really quite striking with, again, similarly, some cytokine release syndrome, mostly of grade 1 to 2 quality. So, I think bispecifics are going be a part of what we do in the future. I think we'll continue to work on them to make them more easily accessible in the community, but this modality of not having to go through pheresis that we do with CAR T is likely gonna be very important in the future. And it just speaks to all the great options that our patients are gonna have in the not-so-distant future in multiple myeloma.

Dr. Doghramji:
Wow, well with those great takeaways in mind, I'd like to thank our guest today, Dr. Joseph Mikhael for joining us to review several key abstracts on multiple myeloma presented at the ASH Annual Meeting. Joe, it was great to have you with us today.

Dr. Mikhael:
It was a pleasure to join you, my friend. Thank you for your kindness.

Announcer:
To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. This is CME on ReachMD. Be Part of the Knowledge.