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/panel-how-do-we-address-the-unmet-needs-in-mm-with-existing-immunomodulatory-agents/14326/

Released: 08/30/2022
Valid until: 08/30/2023
Time needed to complete: 1h 25m

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

Panel: How Do We Address the Unmet Needs in MM With Existing Immunomodulatory Agents?

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.
Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Lonial:
Hello, I'm Dr. Sagar Lonial from the Emory University School of Medicine in Atlanta, Georgia, and I'm joined by my two colleagues, Dr. Maria V. Mateos from Salamanca, Spain, and Dr. Krina Patel from the MD Anderson Cancer Center in Houston, Texas. And we're going to spend the next few moments talking a little bit about unmet medical needs and how perhaps the next generation of immunomodulatory agents or cell mods may help address some of that. And I think it really is such an exciting time for us in myeloma with so many new drugs and so many new targets understanding how to use these new drugs and compounds together is really important. So, Dr. Mateos, you want to start off with a discussion on sort of your view of some of the unmet needs and where these agents may fit?

Dr. Mateos:
Yeah, sure. Thank you very much, Sagar. Definitely, a majority of the patients we see right now are already exposed to the three main drug classes of drugs. proteasome inhibitors, immunomodulatory drugs antipsychotic H monoclonal antibodies. And while we are facing with these patients earlier and earlier, because of the combination of these three main drug classes as part of the first lines of therapy. When we evaluated the mechanism of in immunomodulatory drugs like, lenalidomide and pomalidomide we see how important is the antitumor effect as well as the immunomodulatory effect together with the possibility of being combined with other drugs. And for me, this is well an actual and MET medical needed. The patients exposed to the three main tract classes and a new population is coming those exposed not only to PI, IMiDs, and the CD38 but also the BCMA targeted therapy from my point of view the new thelmotsa and this is the case for avert imide, as well as the CC-480, are covering this MET medical need.

When we evaluated the efficacy for example of aide in combination just with dexamethasone in the triple plus refractory population we see how this combination is actually effective with an overall resperate around 30%, but important when we evaluate the safety profile it seems to be better in comparison with the data source lenalidomide and pomalidomide because in the case of aide, in combination with dexamethasone, the neutropenia grade three-four is not higher than 30% and important because of the chemical structure the fatigue astenia is much less frequent in comparison with lenalidomide and pomalidomide aide and dexamethasone has been indeed evaluated in a cohort of patients, not only triple drugs, triple class refractory but also exposure to the BCMA targeted therapy.

That from my point of view is the new and MET medical need. We are going to have very soon, and again the efficacy is observed and because of the immunomodulatory affected this, the antitumor effect and the synergistic effect with other partners aide is also being evaluated in combination with bortezomib with carfilzomib and with daratumumab and again we see how this synergistic effect does exist, and the overall resperate is around 60% and what is important with a good safety profile. So from my point of view I think that aide in the future, and because of data activity together with the safety profile either the services to be investigated, even as part of the first line of therapy, and you know that there are some trials ongoing evaluating aide single agent as maintenance after transplant but also in

earlier lines of therapy in combination with bortezomib or with order tracts.

Dr. Lonial:
Yeah, no, I, I think you've, you've hit on a number of really good and important points. Dr. Patel, do you do you have some additional unmet needs to add to that?

Dr. Patel:
Sure. Thank you. I think Dr. Mateos did a great job of reviewing sort of, you know, the biggest unmet needs, I think, yes because myeloma is not curable. We, need therapy consistently and, and continuously. And our goal is to really get better therapies that work for longer, so our patients can live longer. But also, I think a little bit what Mary, we touched on we want better toxicity profiles. So, so far I will say that the majority of my patients when they are penta-refractory triple refractory, you know, penta-refractory they're also having a lot harder time getting through therapies because their neutrophils might be low or you know, their counts are low. They might be getting infections again and again. And I think the immune microenvironment, I'm such an immune therapy person.

So I, I'm going to, I'm going to talk about that. I think the immune microenvironment is so important for myeloma patients, not just an effective, you know for infections and, and side effects, but also in terms of actually killing more myeloma and hopefully fixing the bone marrow environment where it stays in remission longer and maybe one day even a cure, you know, I'm hopeful. And so the, fact that these new cell mods actually give you better activated T cells and NK cells in translational work as well as in some of the clinical studies we've seen I think gives us so much hope for that need of how do we fix the bone marrow and myeloma. And I think the, the combinations that we're going to be able to do in the future. Yes, there's lots of studies right now with PIs and CD-38, but the combinations that in the future we could do potentially with Bispecific CAR-T cells. I mean, all the issues we have right now of manufacturing for CAR-T because these patients, their T cells are just knocked out by the time we do it, you know, that, that that I think the possibilities of how we can improve outcomes with all of these novel therapies is so fantastic. And, and it's really important that we really protect the microenvironment and the other immune cells when we're treating myeloma patients.

Dr. Lonial:
Yeah. I think you both have hit on some really important ideas and that is efficacy in the triple or Penta-refractory class. Refractory patients remains a challenge no matter how good we think we are safety and efficacy and tolerability, particularly with chronic administration continues to remain a problem. I mean, one of the challenges that Dr. Mateos and I both experienced in our smoldering trials was tolerance of lenalidomide beyond two years. That really is tough to do. And so certainly efficacy and safety I think are important pieces. And then in a little bit more abstract way sort of building on what Dr. Patel is discussed. The idea that no single, no single drug or no single class is going to get us to curative therapy and that it really does require combination therapy. And when the direction our field is moving with bispecific and CAR T-cells and ADCs is immune based anything you can do to augment the immune response whether it's anti-tumor or anti-infection or perhaps get to limited duration therapy. And I think many of us in the field now, and, and I'm in that group have said, continuous therapy is what we do. This is how we treat this is why we've made the advances. But recognizing that the infectious complications of continuous therapy are a challenge. The adverse event profile of continuous therapy is a challenge. And so if we can combine drugs in classes and get to limited duration therapy and get the same PFS and maybe even better PFS that ultimately might be a win. And I think that is an unmet need that I think all of us are really hoping to see with these new cell mod classes of drugs. Anybody else have other thoughts?

I know we've, talked about a lot of different things here, but I think, the depth of the discussion has been really, really quite good. You know, I think we're really excited by some of the clinical data that Dr. Mateos reviewed earlier. And then much of what Dr. Patel's been talking about. We hope will come in trials in the next year or two to understand, is there a role, for instance for these new cell mods as maintenance post CAR is there a role for these new cell mods as adjunct therapy before leukapheresis, you know these are all really interesting ideas. And then of course, the partnership with bispecific really, really very interesting. So I, I think we've got a number of different areas and I really appreciate the discussion from both of you on this topic and look forward to data and further discussions either formally or informally with both of you in the future. Thank you.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, Inc. and is part of our MinuteCME curriculum.
To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.