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CELMoDs in Multiple Myeloma: Optimizing RRMM Treatment With Potent Immunomodulatory Drugs

Announcer:
Welcome to CME on ReachMD. This activity titled CELMoDs in Multiple Myeloma: Optimizing Relapsed Refractory Multiple Myeloma Treatment with Potent Immunomodulatory Drugs, is jointly provided by Medical Education Resources and PleXus Communications.

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Dr. Lonial:
I'm Dr. Sagar Lonial from the Winship Cancer Institute of Emory University in Atlanta, Georgia, and thank you for joining us today in this Plexus Communications program, *CELMoDs in Multiple Myeloma: Optimizing Relapsed Refractory Treatment with Potent Immunomodulatory Drugs*.

And really, our learning objectives should be to discuss the mechanism of action for CELMoDs and the implications for treatment in the relapsed and refractory setting, propose potential roles for CELMoDs within the therapeutic landscape, critically examine key efficacy and safety data supporting the use of CELMoDs in relapsed/refractory myeloma, and formulate individual treatment strategies for patients with relapsed/refractory myeloma who are suitable candidates for treatment with CELMoDs in the community oncology practice setting. So, these are what our big headings for the next few moments are going to be. We're going to start off with an overview of the therapeutic landscape and unmet medical needs in relapsed and refractory myeloma.

And as you can see in this summary of the therapeutic milestones in myeloma, the last 10 years have been in fact quite busy. The introduction of the immunotherapy approach really began with dara, isatuximab, and even elotuzumab in 2015 and 2016, but really the availability of T-cell engagers and CAR T cells dramatically changed our treatment landscape.

Now, I have for years given talks where I've mentioned that the first actual immune-based approach was the use of thalidomide back in the 1990s, and lenalidomide and pomalidomide continued to build on that immune-enhancing effect of the IMiD category of agents. And what we're going to talk a little bit about today is the next generation of those drugs, which are the CELMoDs, and their potential to further not only kill myeloma but enhance the efficacy of immune-based therapy.

Now, as you know, the outcomes in patients with myeloma have dramatically changed, but there still do remain unmet medical needs. And we know, for instance, that there are certain subsets of patients whose outcomes, despite all of these novel approaches, are suboptimal: older patients, frailer patients, patients with high-risk disease.

There are also subsets of patients perhaps for whom immune therapy is short-lived, and identifying ways to enhance the efficacy in those patients is clearly needed. And finally, patients with extramedullary disease or escape of their normal tumor to typical myeloma-based really do represent many of the unmet medical needs in this field. And so clearly there are subsets of patients that need additional impact through novel therapies.

Now, we know that the modern therapeutic targets for patients with myeloma include a number of important categories. And on the left,

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you'll see the proteasome inhibitors bortezomib, carfilzomib, and ixazomib. You'll see in the middle an agent called venetoclax, which clearly has efficacy in the 11;14 subset of patients. On the right, you'll see the traditional IMiD class that includes thalidomide, lenalidomide, and pomalidomide. But it's really the agents at the bottom right that have had dramatic impacts on outcomes in the last decade, and those include the BCMA- and GPRC5D-directed bispecifics, as well as the BCMA-directed CAR T cells, ide-cel and cilta-cel, as well as the ADC belantamab mafodotin.

The question is, where are there opportunities for us to enhance the efficacy of each of these potential approaches? And as you'll see in the coming few moments, I think CELMoDs represent one of those potential opportunities.

Now, when we talk about selecting treatments for patients with relapsed myeloma, we think about three big categories of patients. We think about patient-specific, disease-specific, and treatment-specific categories. And as you can see listed in these big three lists, there are a number of factors that clearly have important drivers of choosing therapy. For instance, if a patient doesn't have significant caregiver support, then something like a T-cell engager or a CAR T may be a little bit more challenging. On the other hand, if they have significant neuropathy or myelosuppression as a side effect, then there may be certain agents that we want to think less about overall compared to other potential approaches.

But to me, the one in the middle is probably the most important, and that really relates to biology. Are they high-risk patients? And more importantly, what is the opportunity and what is the natural history of this disease, and how do we know these new drugs and targets can offer benefit in those specific patients?

Now we know that there are NCCN guidelines that have now moved up many of these agents, including, for instance, ide-cel and cilta-cel in later lines. Teclistamab and the BCMA-directed bispecifics have historically been late, along with talquetamab. But we do know that there are in fact newer indications for many of these, and CAR T cells have now moved earlier into the potential treatment paradigm in first or second relapse, as has the combination of teclistamab and daratumumab, based on the MajesTEC-3 data, also moved to earlier lines of therapy.

Now, in my mind, historically we've thought about patients in the early relapse setting based on whether they are resistant to bortezomib or resistant to lenalidomide. And as you can see in the len-refractory patients, we think about carfilzomib-based combination or a pomalidomide-based combination. So car in combination with dara or pom in combination with dara or replacing dara with isatuximab. But as I said earlier, we now have additional new therapeutic options such as cilta-cel and ide-cel in first- and second-line therapy, as well as teclistamab and daratumumab in second- and third-line therapy as well.

There are a number of other potential treatment options, but again, a lot of these are beginning to move, and there are a number of phase 3 trials that are currently ongoing, moving many of these late-line therapies to earlier lines of therapy.

Now, where are the unmet medical needs in patients with multiple myeloma? And you can really see three big categories here: additional active treatments needed. Those typically tend to be later lines of patients. But the two that I think are most relevant, particularly in the early relapse setting, are the suboptimal outcomes potentially for frail patients, high-risk cytogenetics, or post-T-cell redirecting therapy in the context of immune exhaustion, or the patient-centered gaps, where caregiver availability, adherence, availability of access to the supportive care necessary for CAR Ts or T-cell engagers, or oral therapies to reduce clinic visits. These are all patient-specific and centered gaps that I think also form unmet medical needs.

Now, what do we historically know about patients with CD38-refractory multiple myeloma? This is a relatively older dataset from 2019 in the MAMMOTH study. But as you can see, if you were penta-refractory, your median overall survival was less than a year. If you were triple- or quad-refractory, your median survival was right at a year. And if you were not triple refractory, your median survival was about 11.2 months. And this is again survival, not progression-free survival. And this is in an era before we had availability of bispecifics and CAR, recognizing that many patients may not get to bispecifics or CAR because of access, supportive care, or caregiver issues. So, how do we enhance outcomes for those patients who may or may not have access to all the new- great new therapies?

And this is another way of looking at that unmet medical need patient population, looking at three different trials: the PREAMBLE trial, the Connect MM trial, and the Flatiron dataset, which all represent, to a certain extent, real-world data from national claims datasets. And what you'll see is that the PFS and OS were longer in patients who received highly effective therapy at second-, third-, or fourth-line therapy, but that once you get beyond second- and third-line therapy, there were not uniform recommendations, and in fact, the outcomes became more and more limited.

Now let's switch gears and talk a little bit about the rationale for using CELMoDs in the relapsed and refractory treatment paradigm. So, we know that the IMiD category of drugs, historically we had complicated drawings that described how they worked, but it turns out in 2010 we identified that their main mechanism of action was binding cereblon. And we subsequently began to understand that it was

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downstream transcription factors, Ikaros and Aiolos, whose downregulation ultimately led to the mechanism of action for cereblon-binding drugs, and those included thalidomide, lenalidomide, and pomalidomide.

What we subsequently identified was that the engineered CELMoDs, and they were engineered to more potently bind cereblon and ultimately have greater immune effects, such as iberdomide, mezigdomide, and golcadomide, these all actually were far superior to the classic IMiD class, and that's why they were given their own designation as CELMoDs, because they did so in a much more effective, efficient, and potent way than what we've seen before.

And just to give you an example, while we know that the target in a myeloma cell is cereblon, and a CELMoD binds cereblon and ultimately causes downregulation of Ikaros and Aiolos, as you can see in the middle of this slide. That then leads to degradation of Ikaros and Aiolos, and in the myeloma cell, it has the effect of downregulating proliferation and increasing apoptosis. But in a T cell and an NK cell, it actually does the opposite. So it's the same target in an immune cell, but a different effect. And what you actually get is upregulation of T cells and NK cells, activating them and making them more proliferative and more antitumor.

And just to give you a sense of relative potency, you can see that if you look at potency here as measured by the closed conformation—and remember, closed conformation results in higher specificity and affinity, resulting in more rapid degradation of Ikaros and Aiolos which ultimately leads not to cytostatic effects on the myeloma cell, but actually leads to cytotoxic effects. So the reason we have to give len and pom continuously is that they don't actually kill the myeloma cell; they just induce growth arrest. Whereas iberdomide and mezigdomide, because of their increased closed fraction of binding cereblon, induce direct tumoricidal effects. So very different effects on myeloma cells than what you see with the IMiD category before.

And just to give you a relative sense of potency, you can see the protein degradation, mezi much faster. In fact, in mezi we see downregulation and absence of Ikaros and Aiolos within just a few hours. iber is a little bit slower, but also relatively far more potent than len or pom. And again, as you'll see here, antiproliferative effects pretty marginal with len and pom because they're cytostatic, whereas in iber and mezi you see pretty potent antiproliferative effects because they are cytotoxic to myeloma cells. Again, very different than what we've seen before.

And a lot of what I've been saying about activation of immune function is not just in cell lines and in models; these are actually T cells from the blood of patients who were on iber on the left and mezi on the right. And what you see in these phase 2 studies is that the number of HLA-DR-positive T cells, or activated T cells, goes up dramatically with the use of iberdomide, and the number of activated NK cells also goes up, and the number of exhausted T cells reduces.

And if you look at mezi, same thing: increase in T-cell activation, increase in NK-cell activation as well. This is in patients receiving drugs on the phase 1 studies for both iber and mezi, so this is not just a laboratory phenomenon. It does translate to patients as well.

And this is really sort of the cartoon version of what I just showed you before: increasing CD8-positive T-cell activation, downregulating the exhausted T-cell phenotype, and the same with NK cells, downregulating TIGIT and KLRG1, which is an exhaustion mechanism, and upregulating CD56, CD16, and Ki-67, resulting in increased activation and proliferation of NK cells.

So let's talk about the efficacy and safety of CELMoDs in the context of relapsed and refractory myeloma. We'll do this first, starting with iberdomide in the CC-220-MM-001. This was the phase 1/2 study of iberdomide that had a number of initial cohorts in phase 1 and then had a couple of dose-expansion cohorts, and then a post-BCMA cohort of patients as well.

And what I really want to focus on is the two expansion cohorts of iber plus dex in cohort D as well as cohort I, which is iber plus dex in BCMA-exposed patients. And what you see in cohort D is an overall response rate of about 27%, median of six prior lines of therapy. All were IMiD refractory. Almost all were PI refractory. All were CD38 refractory. And again, median duration of therapy was about four cycles. But as you can see, we did see responses in the triple-class refractory patient population.

At the same time, in BCMA-exposed, we saw a response rate of about 37% in a median of seven prior lines of therapy. And what this suggests to me is that this by itself certainly is an active drug in this context of late-line relapse therapy.

We then combined them with daratumumab, bortezomib, and carfilzomib, and this led to the response rates that you're seeing here. Again, many of these patients were dara- or bortezomib-resistant coming into this, or even carfilzomib-resistant. And so this to me demonstrates what we know about the IMiD class, that they combine very nicely with the proteasome inhibitors and the anti-CD38 antibodies.

And this ultimately led to the EXCALIBER relapsed/refractory myeloma study, where we did dose optimization. We then took the optimal dose of iber and combined it with dara and dex versus dara-bortezomib-dex. Recall that was the experimental arm in the CASTOR study that had a median progression-free survival of over 18 months and demonstrated, as you saw in a press release, that it met the primary endpoint of MRD negativity. We have not seen additional data, but we do have a PDUFA date for August of 2026 when we

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hopefully—hopefully—based on this trial, will then begin to have access to iberdomide in combination with dara and dexamethasone.

There are other trials looking at iberdomide in combination with ixazomib and dex as an oral second-line therapy in the IFM phase 2 study, and iberdomide plus cyclophosphamide and dex in the phase 2 ICON study, and you can see that listed here in terms of overall efficacy. But this demonstrates the ability of iber to combine with cyclophosphamide, ixazomib, as part of an all-oral regimen, again really guided towards patient adherence and reducing the number of visits to the infusion center.

More recently at ASH this year, we saw a very interesting study from the group in Miami looking at iberdomide in combination with carfilzomib, dara, and dex. So really taking the dara-KRd backbone and replacing the lenalidomide with iberdomide in an early relapse setting. And what you see here is that a substantial fraction of patients achieved MRD negativity relatively early. The overall response rate was 100%, and over time, you can see that safety and efficacy were really quite reasonable. Neutropenia was the most common adverse event. You can see the heme toxicity listed here, and in general, this was a relatively well-tolerated regimen overall.

So, one of the studies worth talking about is the IDEAL trial, and this was a phase 1/2 study of iberdomide as part of a quadruplet for patients with newly diagnosed multiple myeloma. There was a dose escalation of iberdomide, basically replacing lenalidomide as part of the iber-dara-bortezomib-dex regimen. So instead of dara-RVd, it was dara-RId as an alternative way to think about it. And again there were two phases: dose escalation of iberdomide, and 1 mg was the dose that was used moving forward. And then the phase 2 trial evaluated 12 cycles of induction therapy with that quadruplet candidate, followed by maintenance for an additional 24 months with iberdomide as a single agent.

Now, what I think you'll see is that the overall response rate was very, very high, and in fact, over time, the response rate continued to improve, suggesting the immunologic effects of iberdomide that may be deepening response with longer follow-up. Now, one of the details about this is that at the Mayo Clinic, they're no longer using serum protein electrophoresis. They're actually using mass spec, and that might explain part of why it appears on the surface that the CR rate is lower than one would expect, because for them, CR means mass-fix or mass-spec negativity.

If you then look at the progression-free and overall survival, you'll see with limited-duration therapy and a median follow-up of 22 months, the progression-free survival and the overall survival for this small phase 2 study are really quite impressive, and certainly perhaps better than one would see with dara-RVd without the replacement of lenalidomide for iberdomide. So this is certainly very encouraging data moving forward as well.

Now, the other agent that we've talked a little bit about is mezigdomide, or mezi. This is the CC-92480 trial, the 001 trial, a phase 1/2 dose-escalation of mezi plus dexamethasone with different doses and schedules of mezi to identify the optimal dose and schedule. And what was identified at the end of that was mezi 1 mg daily, 21 out of 28 days, in combination with dexamethasone.

And what you'll see in terms of safety from that dose escalation is that again the most common adverse event was hematologic. Not a surprise. That is on target for any drug that binds cereblon potently. But what you'll notice is that the grade 3/ grade 4 adverse events were relatively lower. And in fact, you see that most easily on the right. Many of the traditional IMiD side effects that include things like insomnia, constipation, peripheral neuropathy, DVT, they were low in grade 1, grade 2, and almost nonexistent in grade 3 and grade 4. These, to me, really represent safety enhancements of the CELMoD category over its previous predecessors in the IMiD category.

Now, if you look at overall responses from the phase 1 study, you'll see VGPR rates and PR rates that certainly are reasonable in a late-line relapsed/refractory myeloma patient population. But what I think is most exciting are the expansion cohorts, combining in all patients 101 with a response rate of 40%. Patients with plasmacytomas, 30%, and we're going to take a special look at patients with plasmacytomas in just a moment, and then patients with prior anti-BCMA therapy, small group of only 30 patients, but about 50% overall response rate as well. So this was just mezi plus dex, again demonstrating similar to what I showed you with iberdomide, that you can overcome prior IMiD resistance and that that can translate into meaningful benefit in a number of patients as well.

What you then begin to see is that combining mezi with bortezomib and combining mezi with carfilzomib clearly results in a higher overall response rate, and this can be done safely with a 1-mg mezi dose. And you can see the progression-free survival curves from small expansion cohorts listed here.

And then again, this is a larger expansion cohort of patients looking at mezi plus bortezomib and dex. And again, you can see the two doses are relatively similar at the 0.6 and 1.0 mg, with a median duration of response of about 19 months in this with one median prior line of therapy, so certainly very respectable median progression-free survival and follow-up for the mezi-based combinations overall.

Now, I mentioned the extramedullary disease. We know that that is a big challenge, no matter what class of agents you use in 2026. What I think really struck me was that historically the IMiD class of drugs is not effective at managing patients with extramedullary plasmacytomas. But what we saw in a few patients, and this PET scan is one example, this is a patient with a large liver plasmacytoma

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that got mezi plus dex for two cycles, and as you can see, that liver plasmacytoma is basically gone at the end of two cycles of therapy.

And so, an expansion cohort of extramedullary disease only was looked at, and the response rate in that group was about 30%. Now, recall, len, thal, and pom have a response rate of probably less than 15% to 20% in extramedullary disease, and it's not durable at all. What I think is really encouraging is that certainly mezi seems to have activity at the 1-mg dose in extramedullary disease. And to me the real question is, can you partner this with other drugs that will give you even better efficacy in the context of extramedullary disease at all?

And here's another example of a patient with extramedullary disease at the start of study and 4 months later on just mezi plus dex. So if this is what you get with mezi-dex, imagine what you can get with combinations that include mezi and other highly effective immune-directed therapies.

Now, there were a number of studies that began to look at mezi plus bortezomib or mezi plus carfilzomib, and again you'll see earlier lines of therapy, but certainly response rates of 75, 84 to 90, or 61%, depending upon the specific patient population. One to two to three prior lines of therapy here, again suggesting the combinability is really quite effective, and that this may actually spread not only to the proteasome inhibitors but also to the monoclonal antibodies, where you get mezi plus dara-dex with an overall response rate of 75% and mezi plus elo-dex, where you get a high overall response rate. And again, relatively early, smaller patient population with shorter follow-up, so harder to know the ultimate benefit from this overall as well.

These ultimately led to SUCCESSOR-1. SUCCESSOR-1 is a phase 3 randomized trial of mezi plus bortezomib and dexamethasone versus PVd in one to three prior lines of therapy. And what you see here is a randomized phase 3 trial of mezi plus bortezomib-dex versus PVd. This trial is in progress. Enrollment has completed, and we're waiting on it to hit its primary endpoint of progression-free survival.

And so, as an example, we're going to talk about a case of a patient on SUCCESSOR-1. So this is a patient who initially got RVd times three, had a transplant in 2014, then had RVd consolidation and len maintenance for 10 years as part of the IFM/DFCI trial, and then 10 years later had progression with increased plasma cells, bone marrow plasma cells, fatigue, and bone pain. Was randomized to mezi plus bortezomib-dex as part of the SUCCESSOR-1 trial. You can see the doses of each of the drugs there. Achieved a VGPR with a significant reduction in the lambda light chains and had a negative immunofixation.

In terms of toxicity, she had some anemia and a little bit of thrombocytopenia but otherwise tolerated therapy relatively well.

So, given these options, what would you consider for the next step in managing this patient? Would you continue the current cycle as planned with supportive care, hold treatments due to cytopenias and reassess the marrow, reduce the mezi dose, or discontinue bortezomib to reduce overlapping toxicity?

And the answer in this is continue current cycle as planned with supportive care only. This is a patient who had some mild anemia and mild thrombocytopenia that are manageable and actually are likely on-target effects of both drugs that are being used. This is not a patient that needs to hold treatment and assess marrow because we know they've had a major response. There's no reason to reduce the mezi dose at this time point. It's relatively early in the treatment course. If these heme toxicities persisted for a few more cycles, one could consider that, and certainly not reduce bortezomib, given the fact that they're having such a good and robust response.

Now, one of the largest and most exciting trials presented at both ASCO and EHA this year was the SUCCESSOR-2 trial, and this is a randomized phase 3 trial of mezi in combination with carfilzomib and dex compared to carfilzomib and dex alone. And what we saw was an impressive doubling in the progression-free survival. Remember, this was a later-line group of patients that were treated here, which explains why the KD arm didn't do quite as well as one might expect in an earlier relapse setting. But nonetheless, the addition of mezigdomide clearly had a significant improvement and doubling in progression-free survival.

An endpoint that I think is increasingly more important in myeloma is PFS2. I've advocated for a long time that I don't think overall survival is the right endpoint in one to three prior lines of therapy, but I do think PFS2 is a very important endpoint. And what you'll see here is that the mezi-KD arm had a longer PFS2 than the carfilzomib-dex control arm did, despite the fact that more patients in KD received a bispecific antibody than did patients in the mezi arm. And I think this really does speak to the qualitative and- quantitative benefits of giving mezigdomide in partnership with carfilzomib and dex.

And more importantly, if you begin to look at the subsets of patients who gained significant benefit, you'll see that the benefit was across all major subgroups, particularly those who were both anti-CD38- and len-refractory, patients with extramedullary disease, patients with high-risk genetics, or patients over the age of 75.

And I'll really focus in on this extramedullary disease cohort because we know that this is a challenging group of patients to treat, and this may be a really unique attribute of mezigdomide, that it's able to really be effective in that extramedullary group of patients.

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Again, if you look at the safety summary, neutropenia is an on-target effect, and it can be managed with G-CSF or dose holds. Reduced cardiovascular toxicity. Again, it's oral for the most part, and very high oral deliverability, with only 9.7% of patients that discontinued due to adverse events. So certainly very, very encouraging data from the SUCCESSOR-2 trial.

So, as a second case, let's look at this case as well. This is a patient who got DPD, RVd, cyclophosphamide, VAD, and autotransplant. This tells you how long this patient's been around. They got VAD. They had high-risk features with R-ISS stage III, CKD 3-4, and functional hypogamma. Mezi was given per protocol at 1 with KD given as listed here, and they got monthly IVIG, acyclovir, Bactrim, denosumab, aspirin, and renal monitoring. Cycle 5, day 1, M protein nonquantifiable, and achieved a VGPR, so it was IFX-positive. Stable hemoglobin with a hemoglobin of 10 with an ANC of 1,800. Renal insufficiency was stable with a GFR of 28. A little bit of grade 1 neuropathy and GI intolerance to dex and a little bit of IVIG but otherwise was tolerating treatment well.

So, given this, what would be your next step in managing this patient? Continue current regimen with close monitoring, hold treatment and perform a repeat bone marrow biopsy, discontinue mezi and switch to BCMA-directed therapy, or add G-CSF support and transfusion despite stable counts?

So, the correct answer here is continue current regimen. With an ANC of 1,800, there's no reason to adjust the dose or add G-CSF for support. The patient has had a VGPR, so no reason to switch to BCMA-directed therapy, and we know that they have had significant tumor reduction, and there's no reason to do a bone marrow at this time point.

So, let's look at other mezi combinations and combinations in the future that I think are really quite exciting. This is mezi in combination with an EZH2 inhibitor on the left, with a BET inhibitor in the middle, and with a MEK inhibitor on the right. And what you see is that you can certainly get some level of synergy between the three.

What I think is really quite interesting is the trametinib combination. We know that there may be activity for MEK inhibitors in the context of RAS mutations, and so looking at the ability of mezi to partner with a MEK inhibitor, particularly in patients with RAS mutations, may be a way to look at targeted therapy for patients with specific mutational profiles and certainly is worth follow-up in a larger phase 2 study.

The other drugs that I think make perfect partners for the CELMoDs are the bispecific T-cell engagers. This is MagnetisMM-30, iberdomide plus elranatamab. This is data that was presented at ASCO last year and I think demonstrates really powerful efficacy with response rates that are close to 100%. And on the right, you see the MELT-MM study, which is mezi plus elranatamab. Again, very high overall response rates, and to me represents the best of both classes of drugs: immune efficacy and enhancement with the CELMoDs, T-cell engagement with the BCMA-directed T-cell engagers. Partner them together, you overcome T-cell exhaustion. You enhance the efficacy of both drugs, and you may, in fact, be able to talk about treatment discontinuation over time because of potency of the CELMoD agents together.

And as I showed you early on, this improving CAR T-cell function and overcoming T-cell exhaustion is not just a laboratory phenomenon. This was demonstrated by a number of studies presented at meetings. You can see this data here. This was data at ASH 2024. This was data at EHA 2025. This is data at EHA 2025. You're going to see more data at ASCO and EHA in 2026, further demonstrating the enhancement of efficacy for this class of drugs in combination with CAR T cells as well as T-cell engagers, really rendering these immune therapies even more effective.

So, I think with that, I think it's a great summary. I think the future is obviously very bright for patients with multiple myeloma. Obviously, we are in the era of immune therapy. And as we know, immune therapy is only as effective as the immune system itself. And so, looking at ways to enhance immune efficacy, to use third- and fourth-generation cereblon-binding agents that have been engineered to be more effective, really represents an important next step in the journey. And so hopefully with SUCCESSOR-1, SUCCESSOR-2, and EXCALIBER, we will have access to iber and mezi. These are oral agents that enhance the efficacy of both proteasome inhibitors and immune-based approaches, and these will, in my mind, replace the prior IMiD category of agents, enhance efficacy, and ultimately, I hope, increase the fraction of patients cured with multiple myeloma.

So, with that, I think I will stop. Thank you again for your attention, and hopefully you learned a good deal. And look forward to further questions or discussions in the future. Thank you.

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