

MEET OUR EXPERT



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Ajai Chari, MD, Talks Diversity in Multiple Myeloma Research

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Novel treatment regimens are prolonging life in patients with multiple myeloma, both those who are eligible and ineligible for transplant. However, as new research results emerge, clinicians are learning to manage the real-world considerations associated with these therapies, from effects on the immune system to concerns surrounding therapy sequencing.

Ajai Chari, MD, spoke with *ONCOLOGY®* about the rapidly evolving field of multiple myeloma. He began by discussing how he first became interested in this therapeutic area and why it is so rewarding to work with these patients each day.

Chari also specifically explained the need for diversity among patients with multiple myeloma who are enrolled on clinical trials. In addition, he spoke about how COVID-19 can severely impact and impair the immune systems of patients with multiple myeloma who are undergoing treatment.

Q: Why did you get into the oncology field?

CHARI: No one in my family has ever been a physician. I didn’t know what I was getting into. When I got to medical school, I enjoyed it. I enjoyed internal medicine, but my eyes lit up in oncology. It was a combination of amazing relationships with patients—the depths and continuity of relationships you get from [patients with] cancer is unprecedented—and the intellectual stimulation. The challenge of the complexity of the care is exciting. There are

so many unanswered questions, and so, from an intellectual perspective, there’s so much research to be done.

What [drew me to] myeloma was, first, that the diagnostic testing can be so complicated. It’s almost like a scientific equivalent of a Wordle because you have to understand the light chains, the urine proteins, and the imaging of the marrow; there are a lot of data to integrate. I find it interesting that no 2 patients are the same. What drives me is the medicine, and I feel like we should be providing the same care that we would to our loved ones. When that is your benchmark, we get amazing results. What’s more gratifying than people who are alive in complete remission for years beyond [what we originally] thought? For the newly diagnosed patients, you have patients who are bedridden or bedbound, who within a few months are back to their previous quality of life because the therapeutics are so effective and the symptoms of myeloma can be so rapidly reversed. It’s really gratifying.

Q: What challenges do community oncologists face with the introduction of new therapies?

CHARI: With the T-cell redirection [therapies come] a steep learning curve and the management of cytokine release syndrome [CRS]. It needs to be recognized and treated properly, and it’s an interdisciplinary effort. It starts with the nurses; we need them to know if the patient is having a fever or if they’re

getting confused, and [if they are, to] alert the frontline provider. Then the provider needs to activate the treatment of CRS. The pharmacy needs to realize this as a high priority, so drugs such as tocilizumab [Actemra] [are administered]. Then, the recognition of neurologic issues needs to be very high sensitivity [as well], and so that's one setting. Patients [can also] show up in the emergency [department]. Neurologists and infectious disease doctors need to be trained on this. The T-cell [redirecting therapies] require quite a bit of experience and learning, and that will take some time.

[Chimeric antigen receptor] T-cell therapy will likely be done only at transplant centers because of the specialized nature of that process. Bispecific [antibodies] have the benefit of being off the shelf, so a specialized center isn't required to collect T cells. This means that community doctors will need to learn how to do these bispecific [antibodies].

Currently, many of these T-cell redirections are done in the hospital, for initial treatments for the bispecific [antibodies]. If we start doing them as outpatient procedures because of COVID-19—that is a big issue. For one, fevers can easily be misattributed to anything other than the study drug or the bispecific [antibody]. The other issue is that some of the T-cell redirections are affecting outcomes with COVID-19, as we've seen in deaths in patients with myeloma and COVID-19. It will be important for community doctors to use the full arsenal of COVID therapeutics that are now available, because myeloma patients are compromised. Specifically, drugs that target B-cell maturation antigen [BCMA] [can make patients] particularly vulnerable to COVID-19, [possibly causing] death. Those patients need [very] thoughtful COVID-19 management.

Q: Can you discuss your recent paper on the effects of COVID-19 on patients with multiple myeloma?

CHARI: I was the lead author [analyzing] a global data set; it was a very collaborative effort looking at COVID-19 outcomes in late 2020.¹ We found that the risk factors for worse outcomes in myeloma were older age, renal failure, higher-risk myeloma, and uncontrolled myeloma. Interestingly, at that point, we didn't find any differences [due to myeloma] treatment. Now, subsequent work from our institution has shown that treatments can [indeed] affect vaccine responses to particular BCMA-directed therapy, and that C38 antibody therapy doesn't [allow] response to COVID-19 vaccines. Those patients should be getting booster shots, and [they should receive] the COVID-19 therapeutics [if they contract the virus], because of their impaired immune system. In some ways, myeloma is a canary in the coal mine, because our patients [may have] immunoparesis, [meaning] their plasma cells don't work. We have unfortunately seen adverse outcomes from COVID-19. The outcomes [in general] have gotten much better with the vaccine therapeutics, but we're [still] in the trenches with COVID-19.

Q: What are some unmet needs in myeloma, specifically for those who are older or frail?

CHARI: Our youngest patient at Mount Sinai was diagnosed when he was aged 18 years and our oldest is [aged more than] 100 years, so it's a very heterogeneous disease. You can't have a one-size-fits-all [approach] because there's no way that somebody [aged more than] 80 [years] will be able to tolerate therapy just as well as somebody who's in their 20s or 30s. People come to the table as they get older with more medical problems, and [these can] affect not only their overall lifespan but also

their tolerance to therapies and [adverse effects]. The problem with older patients is that they don't always get to the umpteenth line of therapy. Sometimes you get [only] 1 or 2 [attempts to reach the best outcome possible].

One of the biggest advancements for that population is the regimen of daratumumab [Darzalex], lenalidomide [Revlimid], and dexamethasone, from the MAIA study [NCT02252172].² In that study at current follow-up, the remission duration for newly diagnosed patients with a median age of 73 years is more than 4 years. These are not patients who are getting transplanted; they're just getting this cocktail of drugs. That's tremendous progress and an improvement in survival as well. We still need more therapies for this population because the truly frail and elderly aren't necessarily coming to academic medical centers. They're being treated in the community. One of the limitations of myeloma research, and oncology research in general, is that the patients in clinical trials don't capture the real world. We have huge gaps in outcomes between study-eligible [patients] and real-world patients. To narrow that gap, academia, pharmaceutical companies, the FDA, nonprofits, and patient advocacy groups need to work together collaboratively. We need to collectively work together to change these very restrictive eligibility criteria and try to make [study eligibility] more permissive and real-world friendly.

REFERENCES

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