Managing Myeloma

The what, how, and when of CAR-T therapy in multiple myeloma

Paul G. Richardson, MD
R.J. Corman Professor of Medicine
Harvard Medical School
Dana-Farber Cancer Institute
Boston, Massachusetts

Welcome to *Managing Myeloma*. My name is Dr. Paul Richardson, and it's my pleasure today to discuss where CAR-T therapy may fit in the myeloma treatment paradigm in the future, and also describe briefly some of the adverse events and the toxicities that have been seen in clinical trials and how these may be best minimized.

First and foremost, CAR-T therapy has shown tremendous promise in highly refractory patients in whom other potential treatment modalities have been exhausted. To see the high quality of responses together with the durability of these responses has been particularly encouraging. CAR-T therapy as a modality has been particularly exciting in leukemia and lymphoma. What has been recognized in myeloma patients is that while we see very high quality responses, durability remains an area of challenge. At the recent ASCO meeting my colleague, Dr. Noopur Raje, gave a wonderful presentation where she described very elegantly the response data. She also mapped out for us the progression-free survival median, which clearly shows that while the therapy is remarkable in its effect, the median progression-free survival for the study cohort in her particular trial is about a year. We clearly have to do more thinking to the future as to how we may make this more durable in its benefit. The promise for that, though, is very real; various targets such as BCMA are now comprehensively under study. There are other CAR-T modalities that seek to improve upon the existing strategies by incorporating greater memory. Additionally, none of these approaches to date have been coupled with a formal maintenance strategy, and that would be an obvious way forward to improving outcome.

I think there is great promise for CAR-T therapy, particularly in younger, fit patients because like all of these cellular therapies – especially in the immune space, there are some important toxicities to be aware of. What about these adverse events? One of the hallmarks of the approach is the so-called cytokine release syndrome which reflects immune activation. Some of this may be helpful; too much, of course, isn't. In that regard, there could be some life-threatening toxicities associated with CAR-T therapy that have been recognized for some time now, particularly in the context of leukemia and lymphoma therapy. In myeloma we have seen these toxicities as well. They've proved manageable in the vast majority of cases, but they are important. This may mean that the approach has to be only performed in the context of highly specialized centers and as part of clinical trials for the present. I am certainly hopeful, though, that in the future we'll see CAR-T therapy being advanced earlier into the treatment paradigm as its efficacy becomes confirmed. Indeed, I'm very hopeful that in the future we will see also approval for these particular strategies in the same way as we've seen them for both leukemia and lymphoma.

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