Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/project-oncology/curative-strategies-for-sickle-cell-disease-the-future-of-gene-editing/36489/

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Curative Strategies for Sickle Cell Disease: The Future of Gene Editing

Announcer:
This is *Project Oncology* on ReachMD. On this episode, we'll hear from Dr. Alexis Leonard, who will be discussing the future of sickle cell disease treatment. Dr. Leonard works in the Department of Hematology at St. Jude's Hospital in Memphis, Tennessee.

Here she is now.

Dr. Leonard:
Looking ahead, this is an incredibly exciting time with regards to curative strategies and gene therapy for the care of sickle cell disease. Taking a step back, the fact that we have two FDA-approved gene therapies, one of which was the very first approved CRISPR-Cas9 editing therapy for this disease, is wonderful given the paucity of FDA-approved therapies that we have for sickle cell disease. Right? We have hydroxyurea, which was approved in the nineties for adults; it wasn't approved for kids until 2017. We have chronic transfusions, obviously. That's not an FDA-approved therapy. But then we have these three others: crizanlizumab, glutamine and voxelotor. Voxelotor was withdrawn from the market last fall, so we went from four FDA-approved drugs down to three. And so the addition of curative therapies for sickle cell disease that are FDA approved is exciting.

However, we have a lot more work to do, number one, to make it safer for patients. We are currently using myeloablative chemotherapy to allow maximal engraftment of edited cells in patients, so certainly, that's going to restrict this therapy for some patients who cannot otherwise tolerate myeloablative chemotherapy. So in this current strategy that we call ex vivo—meaning the editing and the modification is all done outside of the body and that we have to give these cells back to the patient after myeloablative therapy—there are many steps along the way that we can improve. We can improve how we collect these stem cells. We can improve how we edit them. We can figure out what's the best target. We can figure out if there are ways to get rid of myeloablative conditioning and use something like, for example, antibody-based conditioning. Or if you could do something fancy like something called multiplex editing, where you not only edit the stem cell to, let's say, induce fetal hemoglobin, but also edit the cell to evade an antibody that would kill the cell, so you could get away with not using any chemotherapy. Instead, you could use an antibody that would get rid of cells that are not edited.

So there are many exciting things in the pipeline for patients that are currently receiving ex vivo therapy. And then really, probably one of the most exciting aspects of this is the pivot and the idea that we could do this all in vivo, meaning we don't have to take the cells out of the body to modify them and give them back, but we could give an injection of editing tools that are encased in, say, a lipid nanoparticle that then find their way to the stem cells in the bone marrow and edit them and you don't need the sort of long, lengthy, complex process that is current ex vivo strategies.

Announcer:
That was Dr. Alexis Leonard talking about the future of sickle cell disease treatment. To access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!