ManagingAML

An expert update on the role of CAR T therapy in AML

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Welcome to *Managing AML*, I am Dr. Jae Park. Today, I'd like to provide an update on the role of CAR T therapy in AML. CAR T therapy generated huge interest as a promising cancer therapy, mainly targeting CD19, which is commonly expressed in almost all B-cell hematologic malignancies. As a result of many different clinical trials from several different institutions, there are now two CD19-targeted CAR T products approved for treatment of relapsed/refractory pediatric ALL as well large cell lymphoma. Both of these products use modification of autologous, or patient-derived T-cells, for treatment of this disease. Unfortunately, there is no approved product available for AML patients. The use of CAR T, therefore, in AML remains investigational. One of the reasons it has been challenging to move CAR T therapy toward approval for AML is because the target selection for AML is much more challenging than the target selection for other B-cell hematologic malignancies. The key to success for CAR T-cell therapy is selecting a target that is expressed exclusively/ideally on malignant cells, but not on normal cells, such as hematopoietic stem cells. Finding such a target in AML has been rather challenging. Several clinical trials are ongoing targeting several myeloid markers that are expressed in AML such as the CD33, CD123, and FLT3. Most of these CAR T cells are using either autologous or patient-derived cells, and some are actually using allogeneic or off-the-shelf CAR T cells targeting this approach. However, these CAR Ts are targeting either CD33 or CD123 can potentially also target hematopoietic stem cells that express CD33 and CD123. These clinical trials are being done in conjunction with a bone marrow transplant for the potential concern that if the CAR T-cell therapy were to work well targeting CD33 or CD123, it may eliminate the hematopoietic stem cells and these patients may need to be rescued by subsequent bone marrow stem cell transplant. There remain several obstacles before moving CAR T cell therapy forward in AML but we are hopeful that we can get there in the very near future. In order to do that, we need to find a better target, and maybe a single antigen target may not be the best approach to get the selectivity. Perhaps we need to look for the dual antigen targeting approach, which is already being investigated in CD19 or CD22 targeting B-cell hematological malignancies. Perhaps we need to do something similar for AML patients. One of the challenges also has been getting the right timing for the patient selection for AML because sometimes generation time or the manufacturing for the CAR T can take several weeks, during which time these patients need to be stabilized or their diseases need to be controlled. These are some of the factors in considering making CAR T therapy a success in AML. Thank you for viewing this activity.