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General AML

CAR T Cell Meeting 2019 | CAR T-cell therapy for acute myeloid leukemia

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On Thursday 14 February 2019, a talk was presented by Elizabeth Budde from City of Hope National Medical Center, Duarte, CA, USA, at the 1st European CAR T Cell Meeting, Paris, France, focusing on targeting CD123 using chimeric antigen receptor T (CAR T) cell therapy for patients with acute myeloid leukemia (AML).

Assistant Professor Budde discussed the high rate of relapsed/refractory (R/R) disease status in patients with AML, with a five-year overall survival (OS) rate of approximately 10% post first relapse, concluding that this calls for an urgent need for novel therapies for these patients. At present, the current targets in AML include CD123, CD33, and fms-like tyrosine kinase 3 (*FLT3*), with Assistant Professor Budde discussing the potential benefits for yet to be identified targets in myeloid-specific expression and leukemic stem cells. Assistant Professor Budde suggested that CAR T-cell therapy for patients with AML presents a high-risk therapeutic option for on-target, off leukemic effects.

It is known that CD123 is over-expressed on AML cells compared to normal adult bone marrow cells, providing a potential therapeutic target, with CD123 CAR T cells providing antigen-specific activation, antigen-driven proliferation, and effective killing of autologous AML blasts with a restricted effect on hematopoiesis.

Assistant Professor Budde outlined the phase I trial (NCT02159495) at City of Hope National Medical Center, which is examining the safety and activity of CD123 CAR T cell therapy via lentiviral gene delivery, with CD28 co-stimulation, in adult patients with R/R AML in one arm of the study. Using allogeneic or autologous T-cell sources for allogeneic stem cell transplantation (allo-SCT), CD123 CAR T cells are engineered for re-infusion at a starting dose of 50M (dose level 0), increasing to 200M (dose level 1) and 500M (dose level 2) if no toxicity is seen. During manufacturing, patients can receive salvage chemotherapy as necessary. The primary objectives of this study were to examine the activity and safety of CD123 CAR T cells and establish the recommended phase 2 dose (RP2D).

To date, 24 patients have been enrolled in the total population:

- Successful manufacture of CAR T cells: 88% (21/24)
- Manufacturing time: 11–16 days
- Patients receiving CAR T cell infusion: 50% (12/24)

Best responses for patients in arm 1 of the study:

- For patients receiving dose level 0 (n = 2): 1 PD, 1 MLFS
- For patients receiving dose level 1 (n = 5): 1 CRi, 2 CR, 2 SD

- For patients receiving dose level 2 (n = 2): N/A (patients did not receive therapy due to low CD123 levels)

Most common grade ≥ 3 adverse events include: lymphopenia (n = 9), thrombocytopenia (n = 8), febrile neutropenia (n = 7)

Assistant Professor Budde concluded that the main goal for CAR T-cell therapy for patients with AML would be the effective targeting of two different antigens. Furthermore, the first-in-human study of CD123 CAR T-cell therapy demonstrated efficacious and safe targeting of CD123 in patients with AML. However, Assistant Professor Budde stated that it will be likely that further optimization is required in order to implement an effective CAR T-cell therapy for AML.

References

1. Budde E.L. Chimeric antigen receptor T-cell therapy for acute myeloid leukemia: targeting CD123. 2019 Feb 14. 1st European CAR T Cell Meeting, Paris, France.