Donor-Derived Anti-CD19 Chimeric-Antigen-Receptor-Expressing T Cells Cause Regression Of Malignancy Persisting After Allogeneic Hematopoietic Stem Cell Transplantation

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Abstract 151 (James Kochenderfer) Donor-Derived Anti-CD19 Chimeric-Antigen-Receptor-Expressing T Cells Cause Regression of Malignancy Persisting After Allogeneic Hematopoietic Stem Cell Transplantation Clinically Relevant Abstract

**Anti-CD19 Chimeric Antigen Receptors (CARs)**

- T-cell activation domain
- Co-stimulatory domain
- Hinge and transmembrane region
- Antibody-derived recognition moiety
- CAR genes inserted into T cell via vector
- CAR-expressing T cell
- Anti-CD19 CAR protein
- CD19
- Cancer cell

Background

- Relapse of malignancy is a leading cause of death in patients undergoing allogeneic stem cell transplantation.

- B-cell malignancies persisting despite allogeneic stem cell transplantation are often treated with unmanipulated donor lymphocyte infusions.

- Donor lymphocyte infusions have inconsistent efficacy and are associated with significant morbidity and mortality from graft-versus-host disease.

- We aimed to improve treatment of B-cell malignancies after allogeneic transplantation by infusing allogeneic T cells that were genetically modified to express an anti-CD19 chimeric antigen receptor (CAR).
Trial design

- Patients with any CD19+ B-cell malignancy persisting after allogeneic transplantation and at least one standard DLI are potentially eligible.

- Patients must have minimal or no GVHD and must not be receiving any systemic immunosuppressive drugs.

- Patients receive a single infusion of anti-CD19-CAR-transduced T cells without any other interventions (no chemotherapy is given).

- The CAR-transduced T cells are derived from the original transplant donor.

- Phase I dose-escalation.
Summary of results

- 10 patients have been treated.

- 3 patients obtained substantial regressions of their malignancies.

- A patient with CLL obtained a complete remission that is ongoing after 12 months.

- Another patient with CLL had tumor lysis syndrome as his CLL regressed in bone marrow, blood, and lymph nodes.

- A third patient with mantle cell lymphoma obtained a partial remission.

- Toxicity was manageable and consisted mainly of fever, hypotension, and B-cell depletion.
Patient 5, who obtained an ongoing complete remission had been extensively treated before enrolling on the anti-CD19 CAR trial

- Diagnosed with CLL in 1996
- Multiple lines of chemotherapy
- Two matched sibling allogeneic transplants
- Unrelated donor transplant in 2009
- Multiple lines of chemotherapy for relapse post-transplant
- 5 unrelated donor lymphocyte infusions
Regression of adenopathy leading to complete remission in Patient 5 after infusion of allogeneic anti-CD19 CAR T cells

Before treatment

1 month after infusion

9 months after infusion
Allogeneic anti-CD19 CAR T cells have significant anti-malignancy activity when administered without prior chemotherapy.

Allogeneic anti-CD19 CAR T cells caused regressions of malignancy in patients who were not lymphocyte depleted.

Malignancies that were resistant to standard donor lymphocyte infusions regressed after administration of allogeneic anti-CD19 CAR T cells.

No patient developed GVHD after infusion of anti-CD19 CAR T-cells.

There is significant patient to patient variation in efficacy and toxicity.