New York esophageal squamous cell carcinoma 1 (NY-ESO-1)–specific T cells (letetresgene autoleucel) (LTEC) have been demonstrated to have clinical activity in patients with NY-ESO-1–positive tumors. We investigated the impact of lymphodepleting regimen (LDR) on lymphocyte recovery and cytokine production in response to LTEC.

**Objective**

Study design. LTEC was manufactured in a Phase I clinical trial of the safety and efficacy of lete-cel in hematologic malignancies. In this Phase I trial, 45 patients with advanced solid malignancies were enrolled.

**Methods**

Patients were randomized to receive 1 of 4 regimens based on different effector lymphocyte doses and LDR prior to lete-cel infusion (Cohorts 1 and 2: high doses of fludarabine and cyclophosphamide; low LDR; Cohorts 3 and 4: high doses of fludarabine and cyclophosphamide; high LDR).

**Results**

- **Higher T-cell expansion (peripheral blood T cells) and increased cytokine production were seen in responders**. Patients with higher peak cytokine levels (IL-2, IL-4, IL-6, INF-γ) and higher peak lymphocytes post-leter-cel infusion were more likely to respond.
- **Increased tumor cell death and cytokine production were seen in responders**. Patients with higher peak cytokine levels (IL-2, IL-4, IL-6, INF-γ) and higher peak lymphocytes post-leter-cel infusion were more likely to respond.
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**Conclusions**

- **Higher T-cell expansion (peripheral blood T cells) and increased cytokine production were seen in responders**. Patients with higher peak cytokine levels (IL-2, IL-4, IL-6, INF-γ) and higher peak lymphocytes post-leter-cel infusion were more likely to respond.
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**References**

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