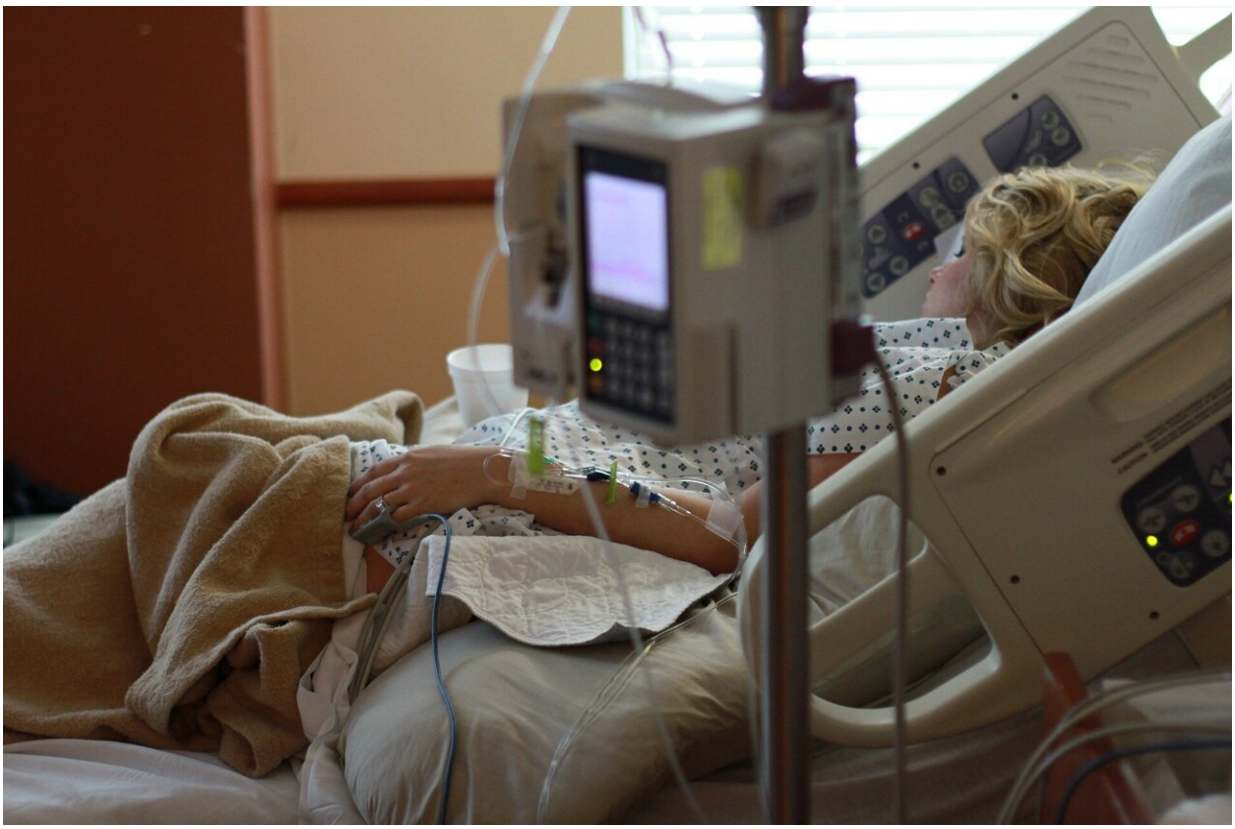
MedicalXpress

Axi-cel CAR T cell therapy shows enhanced responses and continued benefit for high-risk lymphoma patients

December 12 2021



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Three clinical studies led by researchers at The University of Texas MD Anderson Cancer Center demonstrated enhanced responses for patients

with high-risk lymphoma treated with axicabtagene ciloleucel (axi-cel) chimeric antigen receptor (CAR) T cell therapy. These results were reported at the 2021 American Society of Hematology (ASH) Annual Meeting.

Axi-cel is an autologous anti-CD19 CAR T cell therapy manufactured from the patient's own T cells, which have been extracted and then reprogrammed with CAR molecules to help the T cells recognize cancer cells. The reengineered T cells are infused back into the patient to attack the cancer. Based on the pivotal ZUMA 1 study, axi-cel was approved by the FDA in 2017 for the treatment of adults with relapsed or refractory (R/R) large B-cell lymphoma (LBCL) who already have received two or more lines of systemic therapies.

Durable responses after two years for patients with indolent non-Hodgkin lymphoma (Abstract 93)

Follow-up data from the Phase II ZUMA-5 trial showed a long-term survival benefit with axi-cel in patients with R/R indolent non-Hodgkin lymphoma (iNHL) who have failed two or more prior lines of therapy. Principal investigator Sattva Neelapu, M.D., professor of Lymphoma and Myeloma, presented results from the ongoing trial.

"Indolent non-Hodgkin lymphoma is a slow-developing chronic disease in which patients frequently relapse, which leads to the need for new treatment strategies," Neelapu said. "It is encouraging to see that axi-cel provided a continued benefit over two years and may provide a lasting treatment for these patients."

The current analysis includes 110 patients treated on the trial, including 86 with follicular lymphoma (FL) and 24 with marginal zone lymphoma (MZL) after a median follow-up of 30.9 months for FL and 23.8 months for MZL. The treatment was well tolerated, as reported in previous

studies with this therapy.

In the patients with FL, 94% had an objective response, including 79% with a complete response (CR). The estimated duration of response (DOR) and progression-free survival (PFS) medians were 38.6 months and 39.6 months in patients with FL, respectively. Median overall survival (OS) was not reached, but the study reported an estimated 81% OS rate at 24 months. At data cutoff, 57% of eligible patients with FL had ongoing responses.

Among patients with MZL, 83% had an objective response, with 63% achieving a complete response. Median DOR and OS were not reached, but patients had an estimated 70% OS rate at 24 months. Median PFS was 17.3 months. At data cutoff, 50% of eligible patients with MZL had ongoing responses.

In March 2021, data from the ZUMA-5 study led to the first FDA approval of CAR T therapy for follicular lymphoma after two or more lines of treatment.

The abstract can be found here.

Axi-cel demonstrates potential as first-line therapy for patients with high-risk large B-cell lymphoma (LBCL)(Abstract 739)

The Phase II ZUMA-12 trial expands on the ZUMA-1 findings by evaluating the use of axi-cel as first-line therapy for patients with high-risk LBCL. In this study, axi-cel demonstrated a high rate of rapid and complete responses in a population with high, unmet need. Neelapu also presented the results from this study.

"ZUMA-12 is the first study of front-line CAR T cell therapy for high-risk LBCL, and we look forward to confirming the results in a randomized trial," Neelapu said. "Although additional studies are needed, this study shows axi-cel to be effective and suggests patients may receive durable benefit from receiving the treatment before being exposed to other therapies."

High-risk LBCL is a subgroup of the disease in which patients have double- or triple-hit lymphoma or additional clinical risk factors identified by the International Prognostic Index (IPI) or interim positron emission tomography (PET) scan. Historically, around half of these patients do not achieve long-term disease remission with typical treatment approaches like chemoimmunotherapy.

Forty patients with high-risk LBCL were enrolled and treated with axi-cel. Ninety-five percent had stage III/IV disease, 25% had double or triple-hit status per central assessment, and 78% had an IPI score ≥3. The treatment was well tolerated with no new safety signals.

The analysis showed that 89% of patients treated with axi-cel experienced an objective response, and 78% had complete response. At data cutoff, 73% of patients had an ongoing response after median follow-up of 15.9 months. Medians for DOR, event-free survival (EFS), and PFS were not reached; 12-month estimates were 81%, 73% and 75%, respectively. The estimated OS at 12 months was 91%.

The investigators plan to conduct continued follow-up to confirm durability of the patients' responses to the treatment. Additional clinical trials are needed to definitively demonstrate that CAR T cell therapy is superior to existing standard of care with chemoimmunotherapy in these high-risk patients.

The abstract can be found here.

Second-line axi-cel demonstrates improvement in event-free survival for patients with large B-cell lymphoma (LBCL)(Abstract 2)

In the Phase III ZUMA-7 trial, axi-cel showed a clinically significant advantage in EFS relative to standard of care (SOC) high-dose chemotherapy with autologous stem cell transplant. The trial results published today in the New England Journal of Medicine and Frederick Locke, M.D., of Moffitt Cancer Center, will present the results at ASH. Jason Westin, M.D., associate professor of Lymphoma and Myeloma, is senior author of the research.

"For nearly 30 years, the standard treatment for patients with diffuse large B-cell lymphoma (DLBCL) who are refractory to or relapse after initial therapy has been very high-dose chemotherapy and autologous stem cell transplant. This trial aimed to determine if a new therapy, a CAR T cell therapy called axi-cel, could improve outcomes and become a new standard of care," Westin said.

The trial was the first randomized Phase III trial of CAR T cell therapy and enrolled 359 patients with R/R LBLC to receive second-line therapy with either axi-cel (170) or SOC (179).

At 24.9 months median follow-up, median EFS was significantly longer with axi-cel versus SOC. Median EFS was 8.3 months for axi-cel compared to 2 months for SOC treatment. The overall response rate for axi-cel was 83% compared to 50% in SOC, with a corresponding CR rate of 65% and 32%.

The safety of axi-cel was manageable and consistent with third-line therapy. Treatment-emergent adverse events occurred in 155 patients receiving axi-cel and in 140 patients in the SOC cohort. In those treated

with axi-cel, grade 3 cytokine release syndrome occurred in 11 patients and grade 3 neurologic events occurred in 36 patients.

Westin concludes: "This is a paradigm-shifting trial—we are moving from the high-dose chemotherapy era into the targeted therapy era. Our patients will benefit from this change. Axi-cel should be considered as a new standard of care."

The abstract can be found here.

Provided by University of Texas M. D. Anderson Cancer Center