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704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

The Efficacy and Safety of Decitabine Combined with Fludarabine and Cyclophosphamide As Conditioning Regimen in Second CD19 CAR-T Infusion

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Background
Chimeric antigen receptor (CAR) T therapy is widely accept for the first line treatment of refractory/relapsed diffuse large B cell lymphoma(DLBCL). However, insufficient remission and short duration of response are the barrier of current CART therapy. More and more patients meet the failure of CD19 CART therapy. Pre-CART condition treatment is an important factor in durable responses. Decitabine, the hypomethylating agent, has been found that it can reduce T cell exhaustion, enhance T cell cytotoxicity and overcome tumor immune escape in the tumor microenvironment. We initiated this study to evaluate the efficacy and safety of decitabine combined with fludarabine and cyclophosphamide as conditioning regimen in 2nd CD19 CART therapy.
Methods
Patients are enrolled in the clinical trail (NCT02537977), inclusion and exclusion criteria are described. Pre-CART conditioning regimen is decitabine 10mg/m2 D-7~-3, fludarabine 25mg/m2 D-5~-3 and cyclophosphamide 300mg/m2 D-5~-3. The dose of second CD19 CART infusion is 5*10^6/kg. Primary outcome is the safety and secondary outcome is the efficacy.
Results
6 patients are enrolled in this trail and all patients are failure of CD19 CART. The media age is 57 year old and median line of treatment is 4. 4 patients(67%) are female. 5 patients(83%) have TP53 mutation/deletion and double expression, 4 patients(67%) have IPI ≥3.4 patients(67%) got complete remission(CR) after the first CD19 CART therapy and 2 patients(33%) got partial remission(PR). The median time of relapse/progression after first CD19 CART is 9 months.
The objective response rate is 50%, 2 patients(33%) got CR and 1 patient(17%) got PR. With median 13 months followup, the 3 patients(50%) maintain remission more than 1 year and are still under follow up. 2 patients(33%) got stable disease for 3 months and undergo salvage therapy. 1 patient(17%) had no response in 1 month and died due to disease progression. Of all 6 patients, only 1 patient(17%) received 2nd CART infusion in 3 months after 1st infusion and had detecable CART cell in peripheral blood.
2 patients(33%) got grade 1-2 cytokines release syndrome(CRS). No sever CRS and Immune effector cell-associated neurotoxicity syndrome(ICANS) were observed. Grade 3-4 adverse events are hematologic toxicity.
Conclusion
Decitabine combined with fludarabine and cyclophosphamide maybe an alternative conditioning regimen in CD19 CART therapy in high risk DLBCL patients. More patients are needed for further study and the trail is undergoing.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Decitabine

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