MultipleMyelomaHub

General MM, Relapsed/refractory patients

EBMT 2019 | High expansion level and long-term persistence of BCMA CAR T cells contribute to potent anti-tumor activity in heavily treated multiple myeloma patients

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B cell maturation antigen (BCMA) targeted CAR T-cell therapies has shown prominent anti-MM activity in both preclinical and clinical trials. On 27 March 2019, at the 45th Annual Meeting of the European Society for Blood and Marrow Transplantation, in Frankfurt, Germany, Yongxian Hu, from the Bone Marrow Transplantation Centre, The First Affiliated Hospital, Hangzhou, China, presented results of a recent BCMA CAR T trial in relapsed or refractory patients. The trial (ChiCTR1800017404) examined the long-term persistence of a BCMA CAR T-cell product created by lentiviral vector-mediated transduction of activated T cells. These activated T cells express a second-generation CAR with the co-stimulatory receptor 4-1BB for increased efficacy, proliferative capacity, and persistence. Objectives of the trial included the evaluation of toxicity and efficacy.

Patient characteristics

- RRMM patients with at least 3 prior treatment regimens (including proteasome inhibitor, an immunomodulatory agent, anti-CD38 monoclonal antibody, or double/triple-refractory and had over 30% BCMA expression)
- Age <75

Treatment protocol

- Day -4 to -2: Lympho-depleting regimen with Fludarabine (FLU; 30mg/m^2)
- Day -2 to -1: CTX (500mg/m^2)
- Day 0: BCMA CAR T cell infusion (dose range 1 x 10^6kg – 5 x 10^6kg)

Results

- Ongoing trial, data as of 28 November 2018
- N = 17, (median age 61.8 years; range, 49—75)
- Median of 4.9 (range, 0.4—10.8) years since MM diagnosis
- Prior courses of therapy, median = 14 (range, 4—24)
- Median observation period 12 weeks (range, 0.9—40)
- Peak CAR T expansion in CD3+ lymphocytes of peripheral blood (PB) 35%—95%, median 83.5%
- ORR = 100%

- 100% patients MRD negative in bone marrow, 1—2 weeks after BCMA CAR T infusion
- Within 12 weeks, 94% patients ≥very good partial response (VGPR)
- 2% (n = 15) patients had durable responses from 4 weeks post-infusion to data cut-off
- PETCT imaging showed extra-medullary lesions were eradicated after CAR T
- Cytokine release syndrome (CRS) reported in all patients – no patient death from CRS complications
- One patient died from severe infection

Table 1: AEs commonly affecting patients (>20% affected)

Adverse effect	**Patients affected**
Fever	17
Hypoxia	10
Pancytopenia	9
Chills	7
Cough	6
Nausea	6
Heart Dysfunction	5
Fatigue	5
Vomiting	5
Edema	4
Acute kidney injury	4

Key findings

- High levels of BCMA CAR T expression obtained
- High ORR and response rates
- Long-term persistence of BCMA CAR T cells with potent anti-myeloma activity
- CAR T associated AEs can be tolerated

Conclusion

Dr. Hu concluded the presentation by stating that the BMCA CAR T treatment is safe and has prominent efficacy. The main obstacle is relapse, and combination therapy could be used to prevent this. Evidence from this study supports the further development of this anti-myeloma immunotherapy.

Reference

Yongxian H. *et al*. High expansion level and long term persistence of BCMA CAR-T cells contribute to potent anti-tumor activity against heavily treated multiple myeloma patients. 2019 Mar 27. Oral Session 20-3: European Society for Blood and Marrow Transplantation, Frankfurt, Germany.

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