INTRODUCTION

Autologous anti-BCMA CAR T cells have been successfully used in clinical trials for the treatment of relapsed refractory Multiple Myeloma (rrMM), achieving high initial response rates (>80%). However, these therapeutic responses are not durable with patients relapsing on average after 12-18 months. Poor T cell fitness, CAR T cell exhaustion, the immunosuppressive effect of the tumour microenvironment and BCMA negative tumour escape are some of the factors contributing to treatment failure. In this study we describe for the first time the activity of an allogeneic anti-BCMA CAR T cell product derived from young healthy donors (HD) against primary MM cells using patient bone marrow (BM) biopsies. In addition, we compare the performance of HD and MM patient-derived anti-BCMA CAR T cells.

RESULTS

1. Allogeneic anti-BCMA CAR T cells become strongly activated upon exposure to MM primary cells.

2. Allogeneic anti-BCMA CAR T cells efficiently target primary MM cells within the BM niche.

3. Allogeneic anti-BCMA CAR T cells efficiently kill MM primary cells irrespective of genomic subgroup and independent of BCMA expression.

4. Allogeneic anti-BCMA CAR T cells from young healthy donors show higher CD4/CD8 ratio and reduced dysfunction compared to MM-derived CAR T cells.

CONCLUSIONS AND FUTURE DIRECTIONS

➢ To our knowledge, this is the first study showing that allogeneic anti-BCMA CAR T cells are therapeutically active against primary MM cells, in a clinically relevant model that includes the BM microenvironment;

➢ HD-derived anti-BCMA CAR T cells were shown to have distinct phenotypic and functional characteristics compared to rrMM-derived anti-BCMA CAR T cells;

➢ This work lends further support to the development of a first-in-human Phase 1 clinical trial for the treatment of rrMM patients using this allogeneic anti-BCMA CAR T cell therapy.

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