AFM26 – Targeting BCMA for NK cell-mediated immunotherapy of multiple myeloma

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Abstract
Significant progress in multiple myeloma (MM) treatment has been made in recent years and achieving sustained minimal residual disease (MRD) negativity now constitutes a major goal of treatment. High dose melphalan combined with autologous stem cell transplantation (ASCT) is currently regarded the standard of care in first line treatment of MM in eligible patients, but fails to eradicate MRD in the majority of patients ultimately leading to disease relapse. Consequently, novel therapies are needed to target residual disease to delay or prevent potential relapse.

AFM26 is a BCMA-targeting bispecific antibody that selectively engages natural killer (NK) cells to induce myeloma cell lysis. Through its high-affinity binding to BCMA (EGFRxCD16A), AFM26 possesses prolonged NK cell retention (has been shown to be less prone to interference by high levels of circulating IgG than antibody domains). Thus, AFM26 can be used to “arm” NK cells for effective killing of tumor cells. AFM26 also induces markedly lower levels of pro-inflammatory cytokines in peripheral blood mononuclear cell (PBMC) cultures in the presence of target cells compared to BCMA-directed T cell activating approaches. In contrast to other monoclonal antibodies (mAbs) developed in MM such as daratumumab and elotuzumab, AFM26 does not confer target independence. NK cell activation or NK cell depletion.

Retained activity towards BCMA-low target cells

AFM26 does not induce NK cell depletion

Conclusions and Outlook

AFM26 is a first-in-class BCMA-targeting NK cell engager which effectively induces killing of MM cells.

Post-HDT/ASCT may provide optimal conditions for NK cell-based immunotherapy.

AFM26’s anticipated safety profile suggest suitability for early BCMA-directed treatment to target MRD in conjunction with HDT/ASCT.