Abstract: P1959

Title: THE ROLE OF BISPECIFIC ANTIBODIES AND CAR T CELLS IN THE TREATMENT OF MULTIPLE MYELOMA WITH CENTRAL NERVOUS SYSTEM INVOLVEMENT

Abstract Type: e-Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

Patients with CNS manifestation of multiple myeloma (MM) have a very poor prognosis with overall survival (OS) reported to be < 6 months. Therefore, there is a high medical need to develop new strategies for the treatment of CNS myeloma. There is a lack of efficacy data for the novel immunotherapies, as all clinical trials evaluating CART or bispecific antibodies (bsAbs) excluded patients with CNS manifestations and there are concerns about higher rates of neurotoxicity.

Aims:

First, to evaluate the safety and efficacy of CAR T cells and bsAbs in the treatment of apparent CNS relapse. Second, to evaluate a potential consolidation strategy with CAR-T and bispecifics after chemotherapy in CNS MM relapse.

Methods:

We identified 13 patients in our database who met the criteria for CNS involvement, defined as a radiologic finding on imaging or the presence of clonal plasma cells in the cerebrospinal fluid (CSF), and who were treated with bsAbs or CART during the course of the disease. Specifically, 5 patients were treated with teclistamab (N=3) and talquetamab (N=2) for overt CNS relapse and 8 patients received novel immunotherapies (Teclistamab N=5, Talquetamab N=1, Idecel N=2) as part of a consolidation strategy.

Results:

None of the patients treated with bsAb for overt CNS myeloma showed an objective response, and median overall survival in this group was poor, at 4.8 months from diagnosis of CNS manifestation.

In the consolidation group, CNS involvement was initially treated with a multimodal strategy including PACE-like chemotherapy in all patients and additional intrathecal therapy (N=4) and/or radiotherapy (N=6), followed by novel immunotherapies. Here, the CNS relapse-free survival was 13.4 months (range 5-26 months), supporting the use of immunotherapies in this setting. All patients with bsAbs are still receiving treatment with a median follow-up of 8.8 months. Notably, none of our patients exhibited any ICANS or other signs of neurotoxicity, such as parkinsonism.

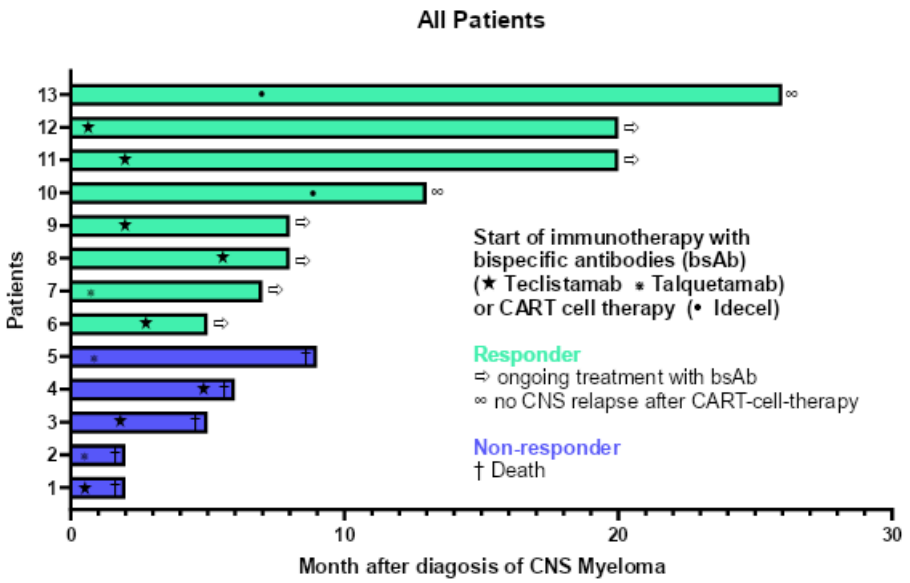
Repeated CFS studies in a patient with meningeal myelomatosis support a direct effect of teclistamab on the control of CNS disease. Despite systemic and intrathecal chemotherapy, this patient had a significant number of residual plasma cells in the CSF at the start of teclistamab. After teclistamab, however, the patient showed a significant increase in CSF T-cells, while the plasma cell count decreased. The patient is in remission and asymptomatic at the time of writing.

Summary/Conclusion:

While treatment with novel T-cell redirection therapies was safe in all of our patients with CNS involvement, clear benefits were seen primarily as a consolidation strategy.

Therefore, we propose a two-step approach with an initial induction with systemic chemotherapy (+/- intrathecal chemotherapy and radiotherapy) followed by consolidative immunotherapy.

While acknowledging our small sample size, our study demonstrates the feasibility of integrating bispecifics and CARTs in the treatment of CNS myeloma.



Keywords: Bispecific, CAR-T, Multiple myeloma, Immunotherapy