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Blood 142 (2023) 2138

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Intrathecal Chemotherapy As Treatment for Chimeric Antigen Receptor T Cell (CAR T) Therapy Associated Neurotoxicity

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Chimeric antigen receptor T cell (CAR T) therapy is offering high remission rates for patients with relapsed and refractory lymphomas, myelomas and acute lymphoblastic leukemias. CAR T therapy causes significant morbidity and mortality associated with its common side effects of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Steroids remain the standard first line treatment for ICANS, however many patients either do not respond or develop rebound symptoms as steroids are tapered. Moreover, patients with severe ICANS who require higher cumulative doses of steroids tend to have worse progression-free survival and overall survival. To mitigate the toxicity associated with steroids use, we have increasingly added intrathecal chemotherapy as part of the treatment algorithm for patients with ICANS who are not responsive to steroids or with grade3-4 ICANS at diagnosis. we hereby report on the outcomes of 12 patients who received intrathecal chemotherapy for the treatment of ICANS at our center between 2017 and 2023.

A total of seventy six patients with Non-Hodgkin's lymphoma (Follicular n=6, Primary mediastinal n=1, DLBCL n=69) received CAR T therapy at our center with a median age of 63.5 years (31, 86). Median follow up for survivors was 16.9 (3.3, 65.9 months)Patients characteristics were male 62%, race (white 83%, black 12%), primary induction failure (44%), received axicabtage ciloleucel (n=24,32%), lisocabtage (n=28, 36%) and tisagenlecluecel (n=24, 32%). Forty-four patients (59%) developed CRS (grade 1/2 in 89% of CRS cases) with a median time to CRS of 3 days (0,15) and a median duration of 3 days (0,36). Thirty-three patients (43%) developed ICANS with a median onset of 5 (0,19) days and median duration of 3.5 (0,28) days. The maximum ICANS grade was grade 1 (n=14, 43%), grade 2 (n=6, 18%), grade 3 (n=11, 33%) and grade 4(n=2, 6%). Twelve patients received intrathecal chemotherapy with 10/12 receiving one dose and 2 patients requiring 2 dosages. Patients who received intrathecal chemotherapy had a median age of 65(47,79) years, male (n=8,67%), Median time from diagnosis to IEC 340(214, 5374 days), and ICANS (grade 1 n=4, grade 2 n=2 and grade 3 n=6). Median time to ICANS was 5 (2,13) days and median ICANS duration was 4(1,25) days. Methotrexate was used in 10 patients and cytarabine in 2 patients. All patients received steroids and 6 patients (50%) received Anakinra as part of ICANS management. Median time for ICANS to receiving intrathecal chemo was 1 (1,25) days with 8 patients receiving intrathecal in the first 24 hours and 2 patients within 48 hours within developing ICANS. Eleven patients had resolution of their ICANS with median time to resolution of 2 days (1,24). Five patients had complete resolution within 24 hours of intrathecal chemotherapy. Five patients had no response to steroids, and all had resolution of their ICANS symptoms after intrathecal chemotherapy.

Our data shows that early administration of intrathecal chemotherapy is feasible and is highly effective in management of ICANS. These findings will need further validation in larger trials to reduce ICANS toxicity and the added adverse events of systemic steroids and immunosuppression.

Disclosures Solh: *Bristol-Myers Squibb:* Speakers Bureau.

https://doi.org/10.1182/blood-2023-186585