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POSTER ABSTRACTS

653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

Prophylactic Tocilizumab to Prevent Cytokine Release Syndrome (CRS) with Teclistamab Administration

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Introduction: Teclistamab is a T-cell redirecting bispecific antibody that targets both CD3 on the T-cell surface and B-cell maturation antigen (BCMA) expressed on myeloma cells. Teclistamab gained accelerated approval for RRMM patients that had previously been treated with 4 prior lines of therapy including a PI, IMID and a CD38 monoclonal antibody. This approval was based on the results of the MajesTEC-1 study demonstrating an ORR of 63%. Cytokine release syndrome (CRS), a known complication of T-cell engaging therapies, occurred in 72% patients which required a REMS program to monitor the patients in hospital for 48 hours post both priming doses and the target dosing. Several approaches are in place to minimize the risk of CRS to allow for the administration of teclistamab safely as an outpatient. We have evaluated the role of administering tocilizumab prophylactically to mitigate the incidence and the severity of CRS.
Methods: A total of 48 patients were admitted to the Emory University hospital from December 2022 until July 2023 as mandated by REMS program for teclistamab step-up dosing followed by the first full dose at least 48 hours apart (0.06, 0.3, and 1.5mg/kg) with premeds per institutional guidelines (Benadryl 50 PO, Tylenol 650 PO, and Dexamethasone 16mg PO 30 minutes prior to each dose). Upon evaluation of our first 15 patients, the median time to CRS from the administration of the first-priming dose was 48 hours. We subsequently administered tocilizumab 8mg/kg IV over an hour (max dose of 800 mg) prophylactically at 44 hours (4 hours prior to the second step-up dose level) for the next 33 patients. CRS was graded per the American Society for Transplantation and Cellular Therapy criteria and managed according to institutional guidelines.
Results: The median age of the patients was 66 years (range, 44-82). All patients were IMID, PI and CD38 mab refractory. The rate of all grade CRS amongst the entire cohort was 21 of 48 patients (43.8%). CRS occurred in 10 of the 33 patients (30.3%) who received prophylactic tocilizumab, compared to 11 of 15 (73.3%) of patients that did not. The majority the events in the prophylactic tocilizumab group are grade 1 [8 (24.2%)]. 1 patient had grade 2 and another had grade 3 CRS (patient with an aggressive relapse at time of teclistamab administration, requiring 3 doses of tocilizumab every 8 hours). The median number of tocilizumab doses was 1 (range, 1-3). The median duration of CRS was 1 day (range, 1-3). 1 dose of steroids (outside of premeds) was administered in the 1 patient who experienced grade 3 CRS but in no additional patients treated with prophylactic tocilizumab. Concurrent immune effector cell neurotoxicity syndrome (ICANS) was also decreased with the incorporation of prophylactic tocilizumab (20% vs 6.1%, respectively). All ICANS in the prophylactic cohort were grade 1 and managed symptomatically. The median duration of ICANS was 1 day. The non-prophylactic cohort experienced 3 of 15 (20%) patients with readmissions, with 1 additional patient going to hospice. None of the patients in the prophylactic cohort were readmitted to the hospital within 14 days of discharge.
Conclusion: Prophylactic tocilizumab prior to the second priming dose has decreased the incidence and severity of CRS in heavily refractory RRMM patients receiving teclistamab. These results are lower in absolute incidence and severity when compared to the MajesTEC-1 trial where CRS was seen in 72% of patients. Prophylactic tocilizumab prevented usage of steroids, prevented dose delays, prevented readmission to the hospital, and possibly reduced the occurrence of ICANS. These

data make a case for early incorporation of prophylactic tocilizumab and support outpatient administration of teclistamab in most patients.

Disclosures Maples: *Pfizer:* Current Employment. **Joseph:** *BMS:* Honoraria; *Janssen Oncology:* Consultancy. **Hofmeister:** *Janssen:* Membership on an entity's Board of Directors or advisory committees; *Sanofi:* Research Funding; *BMS:* Research Funding; *AbbVie:* Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Research Funding. **Dhodapkar:** *Sanofi:* Membership on an entity's Board of Directors or advisory committees; *Bristol Myers Squibb:* Membership on an entity's Board of Directors or advisory committees; *Lava Therapeutics:* Membership on an entity's Board of Directors or advisory committees. **Kaufman:** *Abbvie:* Consultancy; *Incyte:* Consultancy; *BMS:* Consultancy; *Sanofi:* Consultancy. **Lonial:** *TG Therapeutics Inc:* Other: Board of Directors with Stock; *Janssen:* Research Funding; *Novartis:* Research Funding; *AbbVie Inc, Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, Genentech, a member of the Roche Group, GlaxoSmithKline, Janssen Biotech Inc, Novartis, Pfizer Inc, Takeda Pharmaceuticals USA Inc:* Consultancy, Other: Advisory Committee; *Bristol-Myers Squibb Company, Janssen Biotech Inc, Novartis, Takeda Pharmaceuticals USA Inc.:* Other: Contracted Research, Research Funding. **Nooka:** *Adaptive Biotechnologies, Amgen, BeyondSpring, Bristol Myers Squibb, Cellectar Biosciences, GlaxoSmithKline, Janssen, Karyopharm, Oncopeptides, ONK therapeutics, Pfizer, Sanofi, Secura Bio, Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Aduro Biotech, Amgen, Arch Oncology, Bristol Myers Squibb, Cellectis, Genentech, GlaxoSmithKline, Janssen, Karyopharm, Kite Pharma, Merck, Pfizer, Takeda:* Honoraria, Research Funding.

OffLabel Disclosure: Tocilizumab

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