POSTER 54

Erythrocyte Alloantibody Sensitization in Daratumumab Immunotherapy: A Retrospective and Systematic Review

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Background: In 2015, daratumumab was approved for use as an immunotherapeutic agent for multiple myeloma. Daratumumab is a CD38-targeting, human IgG1κ monoclonal antibody with efficacy in myeloma due to the uniform expression of CD38 on myeloma cells. However, red blood cells have also been found to express CD38 on their surface, leading to the potential for panreactivity of indirect antibody testing in patients receiving daratumumab. As myeloma patients endure a progressive burden of osteolytic lesions, they frequently undergo orthopaedic oncologic management for skeletal related events. Many such patients may already experience baseline anemia due to their disease and may require a transfusion of blood products perioperatively. As a result, it is important to adequately characterize the risk for alloimmunization in this population to understand the preoperative antibody screens and to mitigate potential adverse perioperative transfusion reactions.

Questions/Purposes: To describe this population, the current analysis aimed to (1) describe the rate of erythrocyte alloimmunization following immunotherapy for multiple myeloma, including the proportion with anti-CD38 alloantibodies specifically; and (2) identify which patients developing alloantibodies underwent prior daratumumab treatment. To accomplish these aims, a retrospective case-control study was performed using a registry of patients receiving immunotherapy at a high-volume tertiary cancer center in addition to a systematic review of literature reporting on alloimmunization and daratumumab use.

Patients and Methods: A retrospective cohort of 339 patients with multiple myeloma bone disease were identified from a registry of 5540 adult patients receiving immunotherapy at a tertiary care center. Inclusion criteria were adult patients (age $\geq$18) with histologic diagnosis of myeloma, identified bone lesions, and alloantibodies detected on an antibody type and screen. Excluded patients were children, those with a non-myelomatous diagnosis or indication for immunotherapy, those with metastatic disease from alternative primary malignancies, and those without evidence of alloimmunization on type and screen. A retrospective review of the electronic medical records including patient demographics, courses of immunotherapy, prior radiotherapy, prior transfusion, prior orthopaedic procedures, and alloantibody type, was completed. Data are presented with descriptive statistics and were subsequently analyzed using multivariable logistic regression modeling.

Results: Of 339 patients undergoing immunotherapy for multiple myeloma, we identified 51 (15%) who developed erythrocyte alloimmunization (mean [standard deviation] age, 68 [12]; 22 female patients [43%]). Of these 51, 37 (73%) had previously been treated with daratumumab and 14 (27%) had not, with a mean (SD) of 3 (2) courses of immunotherapy. The most common courses of non-daratumumab treatment consisted of lenalidomide, nivolumab, pomalidomide, rituximab, carfilzomib, donor infiltrative lymphocytes, and activated marrow-infiltrating lymphocytes. Radiotherapy was performed in 25 patients (49%). All patients had undergone a blood product transfusion with only 1 patient in the 3 months immediately antecedent to type and screen. The most common orthopaedic operations included intramedullary nailing (3 femurs, 1 humerus, 2 patients with both a femur and humerus), 1 wide excision, 1 biopsy, and 1 total shoulder arthroplasty. Anti-CD38 alloantibodies were detected in 34 patients (67%), of which 31 (91%) underwent prior daratumumab immunotherapy ($p = 0.00$). Prior daratumumab treatment conferred 52-times increased odds of developing anti-CD38 alloantibodies when controlling for age, sex, courses of immunotherapy, prior radiotherapy, prior transfusion, and prior surgery ($p = 0.01$).

Conclusion: In the present analysis, we found a non-trivial prevalence of alloimmunization in patients who had received immunotherapy to treat their myeloma, with 3 of 4 alloimmunized patients having been treated with daratumumab during their disease course. In such patients, prior daratumumab immunotherapy confers a risk of developing specifically anti-CD38 antibodies when controlling for potentially confounding variables like previous transfusions. As patients with myeloma frequently undergo an orthopaedic procedure as part of their multidisciplinary care, the presence of anti-CD38 alloantibodies presents unique implications for pretransfusion planning. Subsequent studies may further characterize rates of adverse transfusion reactions in this population or rates of alloimmunization following different immunotherapeutic regimens for multiple myeloma.

Figure 1. Immunotherapeutic strategy of daratumumab for multiple myeloma.

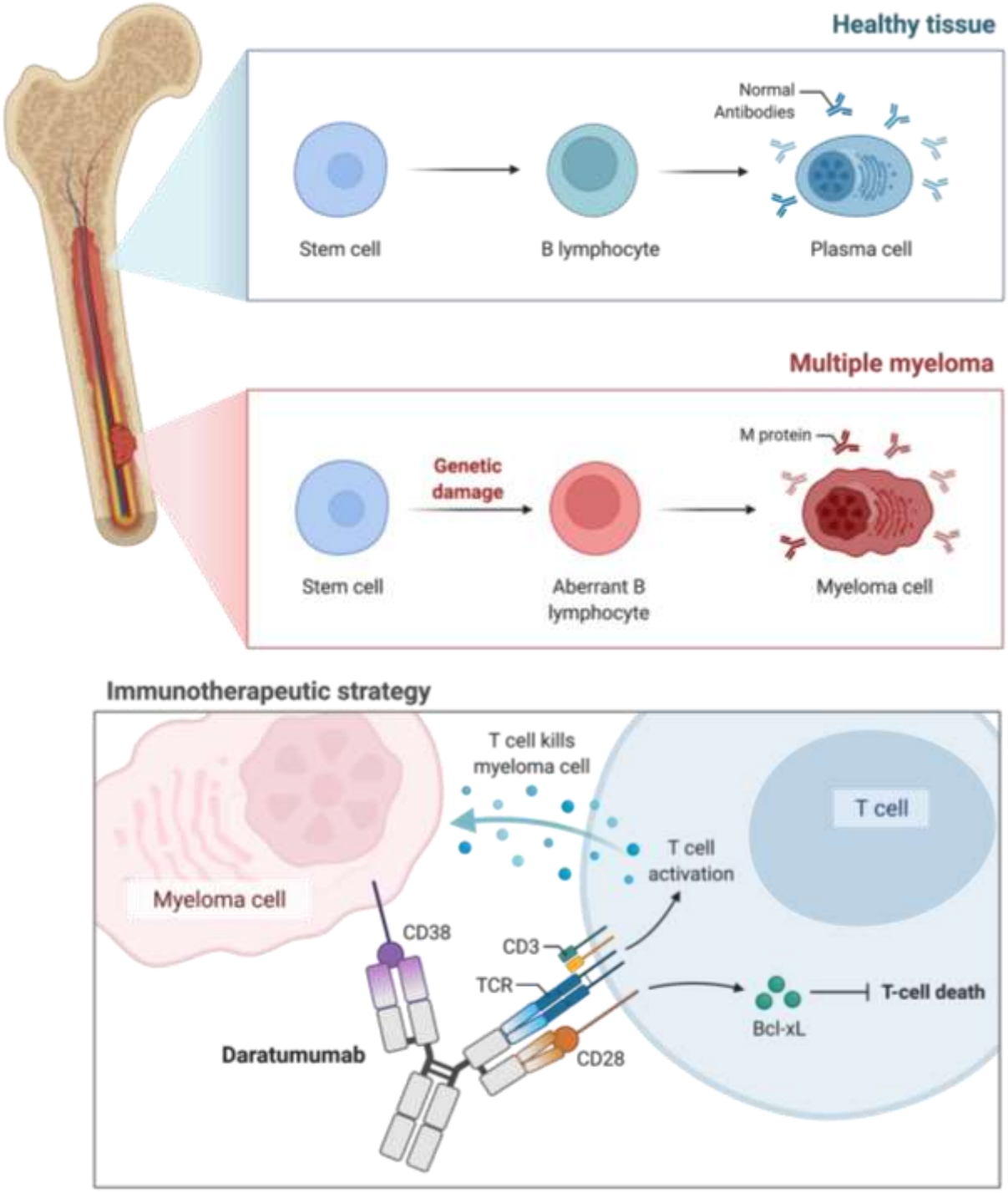

Figure 2. Flow diagram detailing literature search.