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Genetic mechanism for the loss of PRAME in B cell lymphomas. Reply.

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Letter to the Editor Hematology Immunology

The authors reply: We thank Dr. Mraz for insightful comments that provide additional context to the findings in our study, in particular bringing to the forefront studies in other B cell malignancies including chronic lymphocytic leukemia (CLL) (1). As pointed out in the Letter by Dr. Mraz and discussed in our manuscript, PRAME deletions were significantly associated with lg- λ rearrangements, and this finding is consistent with a mechanism in which PRAME deletions can occur in the context of rearrangement of variable (V) gene loci on chromosome 22 in a subset of patients (2). For this reason, we studied frequencies and treatment outcomes for PRAME deletions in the context of lg- λ expression, as shown in Figure 1 (2). In particular, we demonstrate that PRAME deletions are independently associated with outcomes in multivariable analysis, making it unlikely that PRAME deletions are a pure surrogate for the prognostic effects of lg- λ usage. As described by Mraz and Pospisilova, the association of PRAME deletion and lg- λ rearrangement and expression is not absolute, and PRAME deletion is likely dependent on the exact V segment usage (3). Consistently, we did not observe PRAME deletions in the majority of patients expressing lg- λ , and, interestingly, a minority of patients with PRAME deletions can occur [...]



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Conflict of interest: CS has performed consultancy for Seattle Genetics, Curis Inc., Roche, AbbVie, Juno Therapeutics, and Bayer and has received research support from Epizyme, Bristol-Myers Squibb, and Trillium Therapeutics Inc.

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