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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Response to Mosunetuzumab in Patients with B-Cell Lymphomas Relapsed or Refractory after CAR-T Cell Therapy Is Associated with Changes in Lymphocyte Counts

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Introduction: Mosunetuzumab is a CD20/CD3 bispecific antibody that redirects endogenous T cells to kill malignant B cells by concomitantly binding to CD3 on T cells and CD20 on B cells. A multicenter phase I/II study evaluating mosunetuzumab in relapsed/refractory (r/r) non-Hodgkin lymphomas, including patients r/r after chimeric antigen receptor-modified T-cell therapies (CAR-T), was the basis for FDA approval for mosunetuzumab in follicular lymphoma (NCT02500407; Budde *et al. Lancet Oncol* 2022). We retrospectively assessed the impact of mosunetuzumab on lymphocyte counts and CAR T cells in responding and non-responding patients.
Methods: Samples were collected prospectively from participants enrolled on NCT02500407 and exploratory post hoc analyses were performed on a subset of patients who had received prior CAR-T. P-values unadjusted for multiple comparisons are reported. We examined changes in absolute lymphocyte counts (ALC) and CAR-T transgene levels, as well as CD4 counts and CD8 counts, at baseline (C1D1) and prior to cycle 2 day 1 (C2D1) of mosunetuzumab. We also examined length of time from CAR-T to mosunetuzumab. CAR transgene levels were assessed by quantitative PCR.
Results: 30 patients had cycle 1 day 1 (C1D1) and C2D1 paired samples available for analysis. 27 patients had large B-cell lymphoma (90%) and 3 patients had low-grade follicular lymphoma (10%). The doses of mosunetuzumab received ranged from 6mg - 60mg IV or 1.6mg - 20mg SC. The median time from CAR-T infusion to mosunetuzumab was 161 days (range: 35-1071); 40% of patients (12/30) received mosunetuzumab within 100 days of CAR-T, 43% of patients (13/30) received mosunetuzumab > 100-days to 1 year after CAR-T, and 17% (5/30) of patients received mosunetuzumab > 1 year after CAR-T infusion. We found that patients who responded to mosunetuzumab had a longer time from CAR-T infusion than non-responders (mean 342 days [range: 98-587] vs 110 days [range: 70-150], respectively, $p = 0.02$). Although there was no difference in baseline ALC, we found that responding patients had higher ALCs on C2D1 (p=0.005). For 15 patients with available T-cell subsets, CD4 counts were higher on C2D1 for responders (p=0.05). We also investigated changes in CAR transgene levels. 14/20 patients who received commercially available standard of care CAR-T products had detectable CAR transgene levels vs only 1/10 patients who received an investigational CAR-T due to assay limitations. Thus, we examined changes in CAR transgene levels in those patients who had received commercially available standard of care CAR-T (n=20). No difference was observed between responders and non-responders in CAR transgene copy numbers at baseline; however, on C2D1 after one cycle of mosunetuzumab, non-responding patients had a trend toward decrease in CAR transgene levels while responding patients had persistence or increase in CAR transgene levels (p=0.07).

Conclusions: We observed higher peripheral blood lymphocytes after one cycle of mosunetuzumab in responding patients. Of interest, an increase in lymphocytes in responding patients had previously been described after blinatumomab (Klinger *et al. Blood* 2012). These findings may indicate a class effect of bispecific antibodies in general. We also found that patients who were r/r to CAR-T and responding to mosunetuzumab had a trend towards an increase in CAR transgene levels compared with patients not responding to mosunetuzumab. This suggests an interaction between CAR-T cells and bispecific antibodies. Finally, it is notable that post-CAR patients responding to mosunetuzumab had a longer time from CAR-T infusion, perhaps reflecting recovery from lymphodepletion. Further investigations are needed to understand the mechanism(s) behind these observations.

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