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POSTER ABSTRACTS

622.LYMPHOMAS: TRANSLATIONAL-NON-GENETIC

Impact of Response to Systemic Bridging Therapy on Clinical Outcomes and Cytokine Profiles in Patients Receiving CD19- CAR T-Cell Therapy for B-Cell Lymphoma

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Background: Prior studies have reported that deeper response to bridging therapy (BT) before CAR T cell therapy is associated with improved outcomes in large B cell lymphoma (LBCL) and mantle cell lymphoma (MCL). We report the impact of response to systemic BT on clinical outcomes and cytokine profiles of patients (pts) with LBCL and MCL treated with CD19 CAR-T in the real word setting.
Methods: We included pts with LBCL and MCL treated with systemic BT before receiving commercial CD19-CAR-T at two academic centers, and excluded those who received glucocorticosteroids alone. BT was classified as Polatuzumab (pola) based, intensive chemotherapy, lenalidomide/ Bruton tyrosine kinases inhibitors (len/BTKi), or others. PET/CT scans obtained before and after BT, and after CAR-T therapy were evaluated using Lugano 2014 response criteria. Association between BT and response rates (RR) were examined using Fisher's exact test, and the associations with cytokine levels were examined using Kruskal Wallis tests. The Kaplan Meier method was used to estimate overall (OS) and progression free survival (PFS) from time of CAR T infusion. Cox proportional hazards models were used for univariable and multivariable analyses.
Results: We identified 182 pts (166 with LBCL and 16 pts with MCL),whose median age was 66 (range 23-86). Majority of pts (66%) were male. 35 (21%) had central nervous system (CNS) involvement. BTs included: 75 (41%) pola-based, 58 (32%) intensive chemotherapy, 35 (32%) len/BTKi, and 14 (8%) other BT. 9 (5%) pts received ISRT in combination with systemic BT. Among all pts, 86 (47%) received Axicel, 49 (27%) Tisacel, 36 (20%) Lisocel and, 11 (6%) Brexucel. Median time from apheresis to CAR-T was 38 days (IQR 25-44). RR to BT were:14 (8%) complete responses (CR), 51 (31%) partial responses (PR), 100 (61%) either stable disease (SD) or progressive disease (PD), and 17 were unevaluable. RR did not differ among different BT regimens (p=0.92). At day 100 post-CAR-T, RR were: 96 (55%) CR, PR 29 (17%) and 48 (27%) SD/PD. With a median follow up of 15.5 months, median PFS was 6.2 months (95% CI: 3.5-9.5) **(Figure 1A)** and median (OS) was 16 months (95% CI 12-31). In multivariable analysis, poor response to BT (SD/PD) and elevated LDH prior to CAR-T infusion were associated with worse OS. LDH, ferritin, IL-6, TNF-alfa and CRP **(Figure 1B)** measured prior to lymphodepletion(LD) and at day 0 of CAR-T infusion were significantly higher in pts with SD/PD compared to pts achieving a CR/PR to BT. Ferritin levels prior to LD were higher in pts receiving intensive chemotherapy compared to other BT

Conclusions: Our findings suggest that achieving a response to BT is associated with reduced tumor burden and inflammatory markers pre-LD, reflecting inherent disease biology and treatment-refractoriness. Further studies are required to evaluate which BT strategies may optimize the inflammatory cytokine environment for improved outcomes after CD19 CAR T cell therapy.

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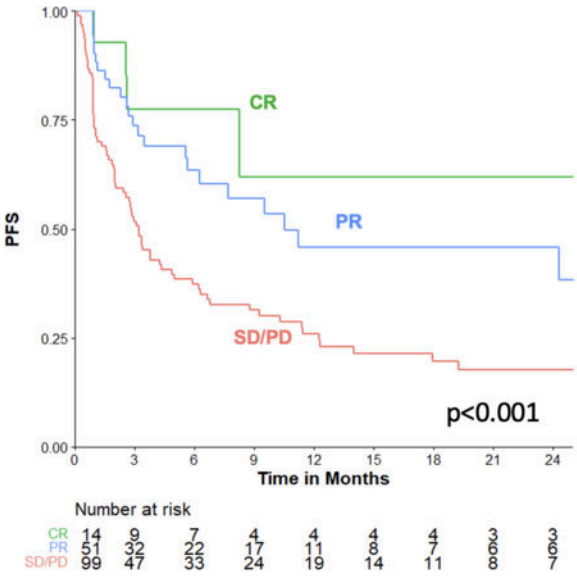

Figure 1A: Progression Free Survival by Bridging Therapy response

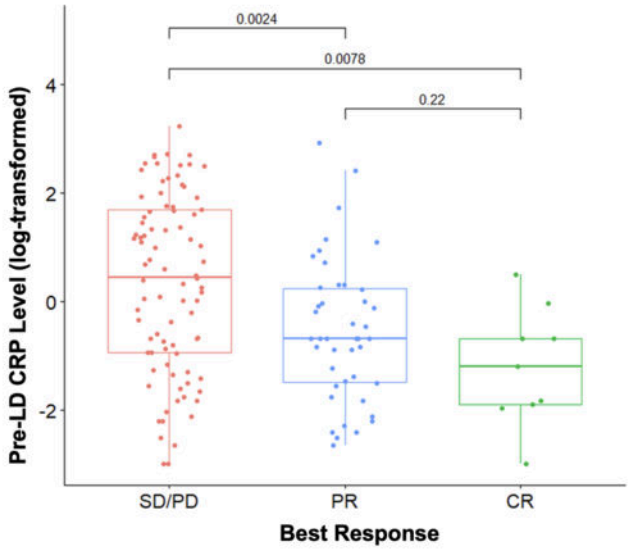

Figure 1B: Successful Bridging Therapy is associated with Reduced Pre-Lymphodepletion CRP

Figure 1

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