Abstract #48 | Poster

# Comprehensive analysis of bridging to CAR T-cell therapy in large B-cell lymphoma with conventional treatment or CD3xCD20 bispecific antibodies

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**Background:**
Bispecific antibodies (bAbs) are increasingly used as holding or bridging therapy prior to CAR T-cell treatment, but their impact on safety and efficacy remains unclear. While T-cell–redirecting therapies may

impair T-cell fitness, preclinical data also suggest potential synergistic effects of bAb and CAR T-cells.

**Aims:**
To evaluate safety and efficacy of bAb-based holding/bridging with epcoritamab or glofitamab compared with conventional chemotherapy or no bridging prior to CAR T-cell therapy in relapsed/refractory large B-cell lymphoma (r/r LBCL), including analysis of immune and CAR T-cell subsets.

**Methods:**
We assessed patient characteristics, prior treatments, progression-free (PFS) and overall survival (OS), and safety outcomes, including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). In a subset, peripheral blood mononuclear cells were analyzed by flow cytometry before and after bridging and after CAR T-cell infusion. CAR copies were quantified by PCR.

**Results:**
A total of 112 patients from nine German centers were included: 67 receiving bAb-based bridging (BisCAR; 47% female; median age 66 years [25–85]) and 45 receiving conventional or no bridging (ConCAR; 33% female; median age 60 years [24–84]). Severe cytopenia during bridging was less frequent in BisCAR (3.0% vs 17.8%, p=0.0082), while post–CAR T-cell toxicity was comparable (CRS 71.5% vs 73%, p=1.0; ICANS 26.9% vs 28.9%, p=0.832). Treatment-related mortality was 3.0% vs 8.9%. Overall response rates after bridging and at month 1 post–CAR T-cell therapy trended higher in BisCAR (70.1% vs 61.1% and 80.6% vs 72.1%). Glofitamab-based bridging induced transient immune activation with enhanced CAR T-cell activation without evidence of terminal exhaustion, reflected by higher $CD25^{+}$ CAR T-cell MFI (p=0.0225) and similar $PD\text{-}1^{+}TIGIT^{+}$ frequencies (p=0.350). Early CAR T-cell activation correlated with response and toxicity.

**Conclusion:**
bAb-based bridging prior to CAR T-cell therapy is feasible, safe, and effective in r/r LBCL, showing favorable toxicity and signals of improved efficacy compared with conventional approaches. Transient immune activation without detrimental effects on CAR T-cell function supports bAb bridging as a promising strategy.

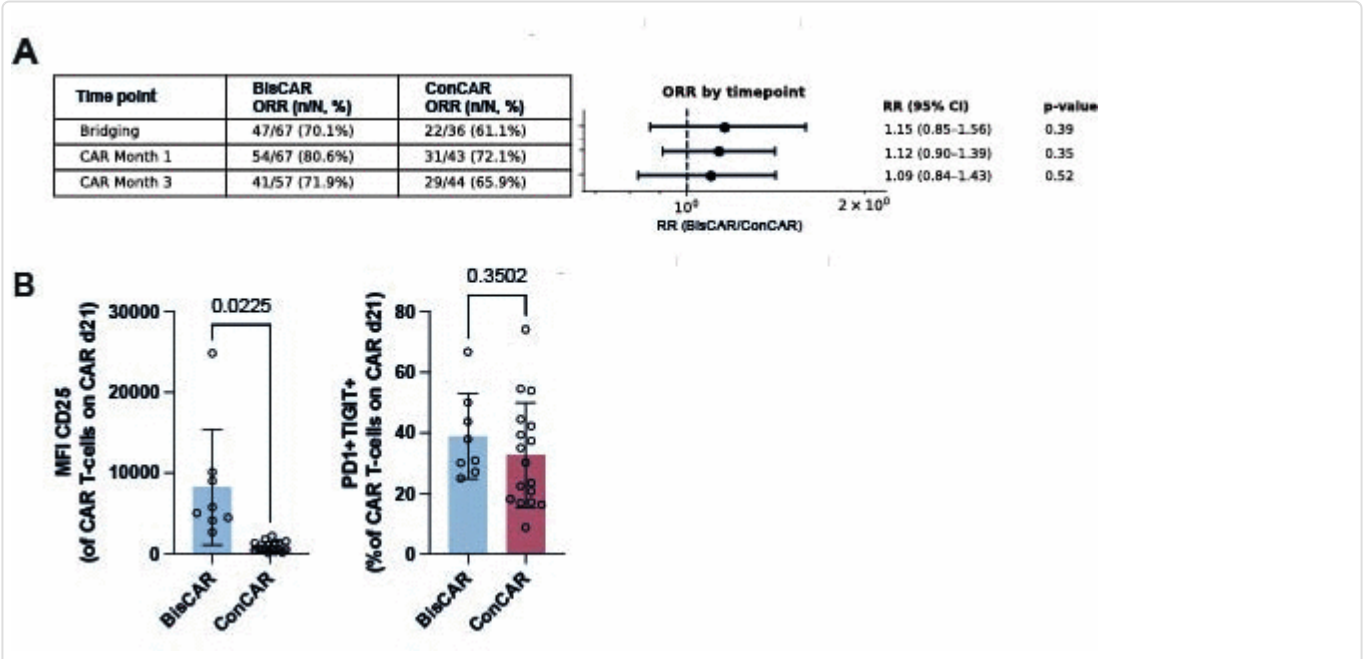


**Figure 1**
(A) Overall response rate (ORR) of BisCar and ConCAR patients to bridging and following CAR T-cell treatment. (B) Activation (MFI of CD25) and overt exhaustion (% PD1+TIGIT+) of CAR T-cells in BisCAR and ConCAR patients at 21

days post CAR infusion