IMPACT OF RESPONSE TO HOLDING/BRIDGING THERAPY IN SECOND-LINE DLBCL PATIENTS TREATED WITH AXICABTAGENE CILOLEUCEL: A LYSA STUDY FROM THE FRENCH DESCAR-T REGISTRY

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Abstract

Introduction:

Both axicabtagene ciloleucel (axi-cel) and lisocabtagene maraleucel have demonstrated efficacy over standard of care in phase III trials for second-line (2L) treatment of diffuse large B-cell lymphoma (DLBCL). However, the optimal approach to bridging patients to CAR-T cells remain debated. While the necessity of a holding therapy before leukapheresis and/or bridging therapy after leukapheresis (H/BT) has not been conclusively established, it is evident that, for some patients, H/BT is crucial for maintaining disease control until the infusion. Some retrospective data suggest that in the context of DLBCL beyond 2L, achieving at least a PR with H/BT can improve EFS and OS yet, no large real-word study has been conducted in the 2L setting.

Methods:

We analyzed the impact of H/BT on the outcome of 2L DLBCL patients treated with axi-cel within the French DESCAR-T cohort (NCT04328298). The study included patients diagnosed with DLBCL, high grade B-cell lymphoma, primary mediastinal B-cell lymphoma or transformed indolent lymphoma. These patients had received a H/BT, while awaiting infusion. The primary endpoint was to compare EFS and OS between patients who achieved a CR or PR and those in SD or PD following H/BT. Secondary analysis evaluated vein-to-vein time (V2VT) and its impact on OS. To improve the prediction of outcomes following CAR-T cells, we tested a 3-factor scoring system at lymphodepletion, based on the following criteria: LDH (normal = 0/high = 1); response status (CR = 0/no CR = 1) and disease bulk (< 5 cm = 0/ > 5 cm = 1). We then, analyzed EFS and OS based on these cumulated factors.

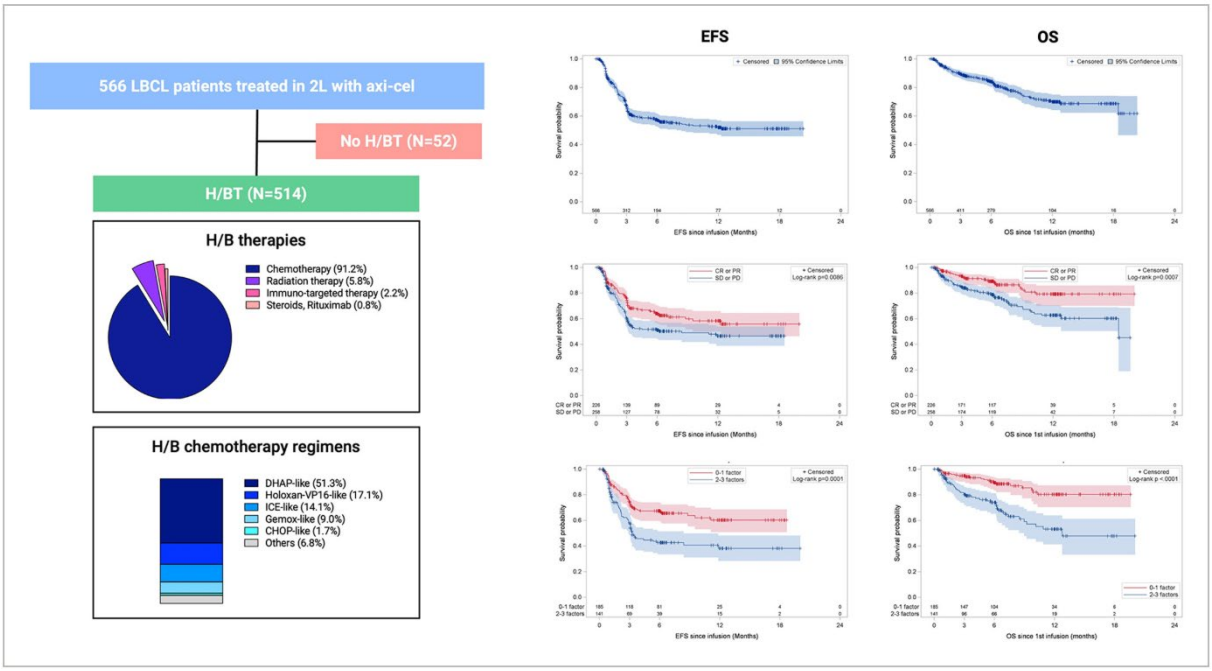
Results:

A total of 566 patients treated between July 2022 and March 2024 were analyzed. Of these, only 52 (9.2%) did not receive a H/BT thus, were excluded from the study. Median age was 61y and median follow-up was 8.5 months. In the entire cohort, 1-year OS and EFS were 69.9% and 52%. CR, PR, SD, PD rates were 14.5%, 29.9%, 11.5%, 38.9%, respectively. Patients achieving CR/PR before CAR T-cell infusion, had better OS and EFS compared to those with SD/PD (hazards ratios [HR] = 0.47, p = 0.0006 and HR = 0.68, p = 0.0084, respectively). Median V2VT was 37 days (min 23; max 242). OS was significantly lower for patients whose V2VT exceeded

46 days (HR = 1.58, p = 0.0345). However, no difference was fund in OS for V2VT of 40 to 46 days versus < 40 days. The 3-factor score allowed to categorize patients in two prognostic groups: those with two or more points had considerably poorer OS and EFS than those with 1 point or 0 (HR = 3.1, p < 0.0001 and HR = 1.94, p = 0.0002 respectively).

Conclusions:

In this extensive nationwide French study involving patients receiving H/BT before axi-cel infusion for 2L DLBCL, better disease control before CAR-T cell infusion was associated with improved OS and EFS. These results suggest that H/BT not only serves as a waiting therapy, but also plays a crucial role in reducing tumor burden, thereby enhancing the effectiveness of CAR-T cells.



Research funding declaration:

French LYSA group

Keywords:

cellular therapies; aggressive B-cell non-Hodgkin lymphoma

No potential sources of conflict of interest.