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Comment to "Sequencing of cellular therapy and bispecific antibodies for the management of diffuse large B-cell lymphoma": chimeric antigen receptor T-cell therapy remains effective after exposure to bispecific antibodies

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Comment to "Sequencing of cellular therapy and bispecific antibodies for the management of diffuse large B-cell lymphoma": chimeric antigen receptor T-cell therapy remains effective after exposure to bispecific antibodies

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Author contributions

Gilles Crochet and Roch Houot wrote this comment

Disclosures

- G. Crochet received honorary/travel grant from Gilead, Roche, Sobi, BMS and AbbVie.

- R. Houot received honoraria from Bristol Myers Squibb, Celgene, Gilead Sciences, Incyte, Janssen, Kite, Merck Sharp & Dohme, Novartis, and Roche.

Dear Editor,

In this issue of Haematologica, Melody and Gordon provide a comprehensive review of sequential immunotherapies in patients with relapsed or refractory (R/R) large-cell B lymphoma (LBCL). The authors claim that the efficacy of CAR T-cell therapy in patients previously exposed to bispecific antibodies (BsAbs) is currently unknown [1]. However, we recently reported the efficacy and safety of CD19 CAR T-cells in patients with R/R LBCL previously exposed to CD20/CD3 or CD22/CD3 BsAbs [2]. The relatively similar mechanism of action of BsAbs and CAR T-cells has raised concerns about potential resistance to immune-killing after progression to BsAbs, along with T-cell exhaustion that could affect subsequent CAR T-cell results [3]. However, our results are reassuring. Out of 47 patients, we found that the overall (ORR) and complete response rate (CRR) after CAR T-cells were 85% and 43%, respectively. The 1-year progression-free survival (PFS) and overall survival (OS) were 42% and 55%, respectively. After propensity score matching analysis, we found that the efficacy was similar between BsAb-exposed and BsAb-naïve patients. Furthermore, CAR T-cells efficacy was similar between BsAb-resistant and BsAb-sensitive patients. Finally, we found no cross-toxicities between BsAb and CAR T-cells [2].

To date, given the current approvals, CAR T-cells are usually given before BsAb in R/R LBCL patients. However, several ongoing trials are evaluating CD20/CD3 BsAbs as part of first-line therapy in LBCL patients. If these trials are positive, BsAbs may be given upfront in the future and thus most R/R LBCL patients will have been previously exposed to BsAb. Our study, although preliminary, suggests that prior exposure to BsAb may not preclude CAR T-cell efficacy in LBCL. The absence of cross-resistance between CD19 CAR T-cells and BsAb targeting different antigens in this population does not favor a particular sequence over another.

References

1. Melody M, Gordon LI. Sequencing of cellular therapy and bispecific antibodies for the management of diffuse large B-cell lymphoma. Haematologica. 2024 xxx.
2. Crochet G, Iacoboni G, Couturier A, et al. Efficacy of CAR T-cell therapy is not impaired by previous bispecific antibody treatment in large B-cell lymphoma. Blood. 2024;144(3):334-338.
3. Philipp N, Kazerani M, Nicholls A, et al. T-cell exhaustion induced by continuous bispecific molecule exposure is ameliorated by treatment-free intervals. Blood. 2022;140(10):1104-1118.