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Potency and toxicity in anti-CD19 chimeric antigen receptor T-cell therapy for B-cell non-Hodgkin lymphoma

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Abstract

Chimeric antigen receptor (CAR) T cells have opened up a new model for the treatment of relapsed and/or refractory B-cell non-Hodgkin lymphoma (R/R B-NHL). However, CAR T cell therapy can cause severe or even fatal related toxicity that impairs the survival benefits of patients. Thus, developing and formulating the standardized clinical management of these toxicities are urgent for medics. Of note, potency and toxicity of CAR-T cells therapy are related to patient and disease features, the CAR-T product and escape of tumor cell. However, the optimal patient selection has not yet been well established.

Chimeric antigen receptor (CAR) T cells have opened up a new model for the treatment of relapsed and/or refractory B-cell non-Hodgkin lymphoma (R/R B-NHL). Clinical trials of anti-CD19 CAR-T cells have suggested promising results for treating R/R B cell lymphoma. ZUMA-1 clinical trials indicated 83% of patients had an objective response, and 58% of patients had a complete response (CR) [1]. JULIET study showed 52% patients had overall response; 40% of the large B-cell lymphoma patients had CR, and 12% had partial responses (PR) [2]. TRANSCEND trials suggested 73% and 53% of patients had an objective response and a CR, respectively [3]. However, CAR T cell therapy can cause severe or even fatal related toxicity that impairs the survival benefits of patients. The most common adverse events were neutropenia in 60% patients, anaemia in 37%, and thrombocytopenia in 27%. 2% and 10% of patients respectively occurred grade 3 or worse cytokine release syndrome (CRS) and neurological events [3]. 48% of patients had grade 3 or worse serious adverse events in ZUMA-1 trials [1]. Recent results from the ZUMA7 trials showed grade 3 or higher adverse events happened in 91% of the patients who received anti-CD19 CAR T-cell treatment despite this therapy improved event free survival (EFS) and response rates [4]. Thus, developing and formulating the standardized clinical management of these toxicities are urgent for medics.

As the understanding of CAR T-cell therapy continues to grow, we provide standardized guidelines and recommendations for toxicity diagnosis, prevention, and treatment of patients with B-NHL [5]. In accordance with the guideline, before CAR T-cell therapy, patients should fully perform the essential workup including complete medical history, physical examination, blood laboratory evaluations, and imaging examination, which also will be beneficial to identify high-risk populations. B-NHL has several significant features associated with toxicity, the most notable of which is local CRS. According to the location of CAR T cells and cytokine after infusion CAR-T cells, CRS can be categorized as L-CRS with local inflammatory response, and S-CRS developed from L-CRS with local cytokines spread to the circulatory system. L-CRS, the early stage, usually presents with redness, tissue enlargement, perforation, or bleeding in local or around the lesion site. S-CRS is the following stage, characterized by systemic symptoms (fever, hypotension, and hypoxia, with or without organ dysfunction). CRS can be divided into four grades based on fever (≥38 °C), hypotension (BP < 90 mmHg), hypoxia (oxygen requirement: SaO2 > 90%), and the local manifestations within or around the lesion sites. 1 or 2-grade CRS presents primarily with fever, hypoxemia, and redness/swelling of local tissue, requiring oxygen treatment. Higher than 3-grade CRS has worsening symptoms, accompanied by symptoms arising from compression of neighboring

tissues or serous effusion in the lesion, requiring high-flow oxygen or even mechanical ventilation. Generally, patients with CRS receive therapy with tocilizumab and corticosteroids. When patients had persistent and refractory fever, anti TNF-α can be considered. In addition to the supportive treatment mentioned above, different treatment strategies should be adopted for CRS involving different organs. For example, considering that the patient has tracheal involvement and symptoms of compression, anti TNF can be used- α Treatment and local intervention. The first three weeks after CAR T-cell infusion are a critical period for CRS management. Notably, ICU monitoring is very important for saving patients' lives and early identification of symptoms for treatment, especially if adverse events occur.

CAR T-cell-associated encephalopathy syndrome (CRES) typically occurs within 8 weeks after treatment, mainly represented neurological symptoms like headache, agitation. CRES should distinguish from cerebrovascular events, particularly in patients with a cerebrovascular history. Management strategies for CRES include supportive care and corticosteroids, noteworthy, grade 3 or 4 CRES patients are recommended the ICU monitoring. Other adverse events include hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS), bone marrow suppression, and infection, generally given supportive treatment. Importantly, HLH/MAS and bone marrow suppression may increase the risk of serious infection. Infections are common, with up to 70% of patients reported to be infected; but it should be carefully distinguished from CRS, HLH/MAS, and bone marrow suppression. Timely recognition and early intervention are crucial for patients as infection often occurs in the case of CRS and can exacerbate CRS. In general, empiric broad-spectrum antibacterial therapy is the first choice; at the same time, empiric antifungal therapy is usually added depending on the characteristics of the patient. We recommend CRS supportive care and antimicrobial prophylaxis when CRS and infection are indistinguishable.

Of note, potency and toxicity of CAR-T cells therapy are related to patient and disease features, the CAR-T product and escape of tumor cell. However, the optimal patient selection and sequencing of CAR-T cells therapy has not yet been well established [6]. Recent study provided treatment algorithm for DLBCL in 2022 [7], believing that CAR-T cell therapy as a 2-line treatment that should be preferred for chemo-refractory disease. In patients with active infection, infection should be controlled prior to CAR T cell infusion to reduce the risk of increased morbidity and mortality [8]. In brief, anti-CD19 CAR T-cell therapy have some well-known limitations, including financial costs, limited accessibility. In addition, there is no standard of care and selection of the standard next treatment route.

Declarations of interest

None

References

1. Locke, F. L., Ghobadi, A., Jacobson, C. A., Miklos, D. B., Lekakis, L. J., Oluwole, O. O., ... & Neelapu, S. S. (2019). Long-term safety and activity of axicabtagene ciloleucel in refractory large B-cell lymphoma (ZUMA-1): a single-arm, multicentre, phase 1–2 trial. *The lancet oncology*, *20*(1), 31-42.
2. Schuster, S. J., Bishop, M. R., Tam, C. S., Waller, E. K., Borchmann, P., McGuirk, J. P., ... & Maziarz, R. T. (2019). Tisagenlecleucel in adult relapsed or refractory diffuse large B-cell lymphoma. *New England Journal of Medicine*, *380*(1), 45-56.
3. Abramson, J. S., Palomba, M. L., Gordon, L. I., Lunning, M. A., Wang, M., Arnason, J., ... & Siddiqi, T. (2020). Lisocabtagene maraleucel for patients with relapsed or refractory large B-cell lymphomas (TRANSCEND NHL 001): a multicentre seamless design study. *The Lancet*, *396*(10254), 839-852.
4. Locke, F. L., Miklos, D. B., Jacobson, C. A., Perales, M. A., Kersten, M. J., Oluwole, O. O., ... & Westin, J. R. (2022). Axicabtagene ciloleucel as second-line therapy for large B-cell lymphoma. *New England Journal of Medicine*, *386*(7), 640-654.
5. Li, P., Liu, Y., Liang, Y., Bo, J., Gao, S., Hu, Y., ... & Liang, A. (2023). 2022 Chinese expert consensus and guidelines on clinical management of toxicity in anti-CD19 chimeric antigen receptor T-cell therapy for B-cell non-Hodgkin lymphoma. *Cancer Biology & Medicine*, *20*(2), 129.
6. Sermer, D., Elavalakanar, P., Abramson, J. S., Palomba, M. L., Salles, G., & Arnason, J. (2022). Targeting CD19 for diffuse large B cell lymphoma in the era of CARs: Other modes of transportation. *Blood Reviews*, 101002.
7. Poletto S, Novo M, Paruzzo L, PMM F, Vitolo U. (2022) Treatment strategies for patients with diffuse large B-cell lymphoma. Cancer Treat Rev.

110: 102443.

8. Amini, L., Silbert, S. K., Maude, S. L., Nastoupil, L. J., Ramos, C. A., Brentjens, R. J., ... & Abou-el-Enein, M. (2022). Preparing for CAR T cell therapy: patient selection, bridging therapies and lymphodepletion. *Nature Reviews Clinical Oncology*, *19*(5), 342-355.