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care and corticosteroids. More recently, some early clinical data investigated the use of Anakinra as a promising agent in prevention and treatment of severe ICANS.

**Case report:** We report two cases in which Anakinra was used for the treatment of high-grade ICANS concurrently with high dose steroids. A 51-year-old woman with high grade DLBCL and secondary CNS involvement was treated with Tisagenlecleucel CAR-T therapy. On day 2, patient became altered and was diagnosed with ICANS Grade II. High dose steroids were initiated leading to an improvement of symptoms and resolution of ICANS. Patient’s mentation worsened by day 7, rapidly progressing to ICANS Grade IV by day 8. Anakinra 100 mg IV was added to the steroid regimen on the same day. By day 11, after 4 doses of Anakinra, patient’s neurotoxicity completely resolved. Patient was able to achieve a PR by day 30 after CAR-T cell infusion (Figure 1 for detailed timeline). In the second case, a 65-year-old man with DLBCL and leptomeningeal involvement developed ICANS Grade II on day 1 after Tisagenlecleucel CAR-T therapy and was started on high dose steroids. By day 4, neurotoxicity worsened and progressed to ICANS Grade IV. On day 5 patient was transferred to ICU for a mechanical ventilation, and Anakinra 100 mg IV was added and continued daily for 7 days. By day 12, neurotoxicity improved to ICANS grade II and patient was extubated. Meanwhile, high dose steroids were tapered. His condition acutely worsened again by day 19, prompting another transfer to the ICU and re-initiation of Anakinra concurrently with steroids. His family decided against further escalation of care on day 22. In the setting of respiratory failure, patient was transitioned to comfort care and died 23 days post CAR-T cell infusion (Figure 2 for detailed timeline).

**Conclusion:** In both reported cases, ICANS improved following administration of Anakinra, adding support to the notion that Anakinra may be beneficial in treatment of high-grade ICANS. Future studies are needed to better understand the overall efficacy and the ideal timeline for administration of Anakinra.
hypoxic failure due to COVID-19 infection which led to their demise. Their deaths were not attributed to CAR-T cell therapy complications.

It is notable that patient 2 remained asymptomatic for four weeks from the diagnosis of COVID-19. The patient was tested for COVID-19 as part of the routine evaluation prior to a lung biopsy. This was unexpected due to anticipated lower risk of complications from COVID-19 infection after the 14-day milestone. Our experience suggests that patients with immunosuppression due to hematological malignancies and CAR-T therapy may have a delay in manifestation of COVID-19 infection. Vigilance regarding COVID-19 detection and management is advisable for clinical teams taking care of such patients.

Outcomes with Chimeric Antigen Receptor T-Cell Therapy in Relapsed or Refractory Acute Myeloid Leukemia: A Systematic Review and Meta-Analysis

Moazzam Shahzad, MD1,2; Ali Hussain, MD3; Sibgha Gull Chaudhry, MD; Fatima Ali, MD; Ayesha Khalid; Ezza Tariq, MD; Muhammad Usman Zafar, MD; Muhammad Arslan, MD; Iqra Anwar, MBBS5; Rajat Bansal, MD; Peiman Hematti, MD; Tariq Lin, MD; Sunil Abhayankar, MD; Joseph P. McGuirk, DO; and Muhammad Umar Mueen, MD.

1Division of Hematologic Malignancies & Cellular Therapeutics, University of Kansas Medical Center, Kansas city, KS; 2Department of Medicine, St Mary’s Medical Center, Huntington, WV; 3Division of Hematologic Malignancies and Cellular Therapeutics, University of Kansas Medical Center, Westwood, KS; 4Division of Hematology and Oncology, University of Wisconsin School of Medicine and Public Health, Madison, WI

Background: Acute myeloid leukemia (AML) is a clonal hematologic malignancy that generally affects older adults. The prognosis of patients with relapsed/refractory AML (RR-AML) is often poor, and treatment modalities are limited. Chimeric antigen receptor T cell (CAR-T) therapy has shown promising results in lymphoid malignancies and myeloma, and these are now being explored for the management of RR-AML. We aimed to investigate the outcomes of CAR-T therapy in RR-AML patients.

Methods: Following the PRISMA guidelines, we searched PubMed, Cochrane Register of Controlled Trials, and Clinical trials.gov using MeSH terms and keywords for “Leukemia, Myeloid, Acute” AND “Receptors, Chimeric Antigen” OR “adoptive immunotherapy” from the date of inception to April 2021. A total of 673 articles were screened, and original studies reporting patients with RR-AML having CAR-T therapy as the only intervention (8 clinical trials and 2 case reports) were included. Quality evaluation was done using the NIH quality assessment tool. The inter-study variance was calculated using the Der Simonian-Laird Estimator. Proportions along with a 95% confidence interval (CI) were extracted to compute pooled analysis using the ‘meta’ package by Schwarzer et al. in the R programming language (version 4.16-2).

Results: We identified 39 patients in 10 studies who received CAR-T therapy for RR-AML. The median age of patients was 35 (73–80) years, and 59% (n=23) were male. The median follow-up time was 5 (0.7–23) months. (Table 1) Four patients had a history of allologeneic hematopoietic stem cell transplant (HCT) prior to CAR-T therapy, while subsequent HCT was performed in 5 patients. The pooled analysis showed a CR and ORR of 38.5% (95% CI 0.03–0.81, I2 =66%, n=33) and 56% (CI 0.18–0.58, I2 =38%, n=29), respectively. The median duration of response was 5.5 (1–23) months. OS was reported from 1.9 months to 23 months. The pooled incidence of CRS and TN was 42.7% (95%CI 0.06–0.87, I2 =66%, n=28) and 1.3% (95% CI 0.00–0.16, I2 =0%, n=21) respectively. Graft-versus-host disease (GVHD) was reported in 2 patients who had prior and subsequent HCT after CAR-T therapy. First patient developed grade IV GVHD in salvage therapy with donor lymphocyte infusions for relapsed disease six months post-CAR-T and four months post second allo-HCT while the second patient received CAR-T as part of conditioning therapy and developed grade IV GVHD on day 32.

Conclusion: CAR-T therapy has shown favorable results comparable to current salvage therapies for relapsed or refractory AML with an acceptable toxicity profile. However, there are several challenges, including the heterogeneous biology of AML, lack of a targetable antigen expression on malignant cells, and immune escape and exhaustion. Future prospective studies with improved CAR-T constructs will hopefully improve the outcomes in this therapeutically challenging patient population.