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Anakinra and Siltuximab for Management of Cytokine Release Syndrome Following CAR-T and Bispecific T-Cell Engager Treatment: A Systematic Review

Kunhee Kim, MD[1,a]; Amanda Stroiney, MD[1]; Nicole Sequeira, MD[1]; Mai Salem, MD[1]; Kapil Meleveedu, MD[1]

[1] University of Connecticut School of Medicine, Farmington, CT, USA

Corresponding author
[a] Kunhee Kim, MD, University of Connecticut School of Medicine, Farmington, CT, USA
Email: kunheekim144@gmail.com

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Abstract

Background

CAR-T and bispecific T-cell engager (BiTE) are novel therapies that improve outcomes in hematologic malignancies but can cause cytokine release syndrome (CRS), a life-threatening inflammatory response causing fever, hypotension, and end organ damage. CRS occurs in 79.7% of CAR-T recipients, with 8.9% experiencing grade 3 or higher CRS. Current management consists of corticosteroids and tocilizumab, with anakinra or siltuximab discussed as next line therapy but with limited evidence. We therefore systematically reviewed their use for CRS after CAR-T or BiTE therapy and summarized the available outcome data.

Methods

Embase, Medline, Web of Science, and Scopus were searched for studies published through February 1, 2026, reporting anakinra or siltuximab for CRS in adults receiving CAR-T or BiTE therapy. Prophylactic use and studies reporting tocilizumab alone were excluded. We extracted treatment and CRS characteristics and summarized findings descriptively.

Results

Of 379 records identified, 65 underwent full-text review, and 35 studies including 4483 patients were included. with 3568 patients with CRS. Anakinra was administered for CRS to 541 patients across 31 articles, and siltuximab to 213 patients across 21 articles. Only five articles reported outcomes separately for treated patients. One study reported 33/44 patients experiencing CRS improvement. Another study reported resolution in 6 of 7 patients with CRS after CD22 CAR-T therapy, a median resolution time of 7 days in anakinra cohort with CRS/ICANS, CRS resolution in one siltuximab-treated patient. The remaining articles primarily described treatment exposure, with limited drug-specific outcome.

Conclusion

Anakinra and siltuximab have been used in various settings, including severe or tocilizumab-refractory CRS. However, drug-specific outcomes are inconsistently reported and sometimes combined with ICANS. Current evidence is mostly small observational studies with few comparison groups. Future studies should incorporate comparator groups and consistently report CRS grade, treatment indication and timing, concomitant therapies, and drug-specific outcomes.

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