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705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Venous Thromboembolism (VTE) in Post-CAR-T Patients - a Meta-Analysis of Phase 2 & 3 Clinical Trials

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Introduction:
Chimeric Antigen Receptor T- cells (CAR-T) therapy is genetically engineered T cells that provide durable responses for patients with certain hematological malignancies. CAR-T therapy continues to expand as a treatment option for various malignant conditions. ICANS and CRS, a clinical syndrome of neurological symptoms, fever, hypotension, and hypoxia, are potentially serious complications of post-CAR-T. Both of these complications can, in turn, increase the risk of VTE. Only a few case reports and retrospective analyses have described the risk of VTE. The primary objective of this systematic review and meta-analysis is to review the data from phase 2 and 3 clinical trials to determine the incidence and risk of VTE post-CAR-T treatment.
Material and methods:
The National Institute of Health (NIH) library, Cochrane Library, and ClinicalTrials.gov database were scoured for all phase 2 and phase 3 clinical trials, completed by March 7, 2023, on CAR-T cell therapy. Two reviewers independently verified the results. Several data points were extracted. A biostatistician conducted the meta-analysis using the Meta package in the R version 4.1.2 (Balduzzi, Rücker, & Schwarzer, 2019; R Core Team, 2021). The endpoints of interest were the odds ratio and relative risk of developing VTE while in CRS using the Mantel-Haenszel method.
Result:
Nine phase 2 & 3 trials (Seven phase 2 and two phase 3 trials) were identified and were included in our study. The incidence of CRS, ICANS, and VTE was obtained from the toxicity list and supplemental data for analysis. Only KTE-X19 studying Brexucabtagene (Tecartus) for relapsed or refractory adult B-cell acute lymphoblastic leukemia and Relapsed or refractory Mantle-Cell Lymphoma mentioned the incidence of one and three cases of VTE, respectively, in patients getting CAR-T cell therapy.
The total number of patients reviewed from these studies was 1784, of which 1017 received CAR-T cell therapy. The odds of VTE were 99.9995% lower than CRS, OR = 0.0005, 95% CI [0.0001, 0.0017] in patients receiving a CAR-T infusion, $p < .0001$. The Relative risk of VTE was 0.0050, 95% CI [0.0019, 0.0132]. The test of heterogeneity ($p = .0430$) suggests the presence of heterogeneous results. The heterogeneity statistic I2 is 49.86%, indicating moderate heterogeneity (percentage of variation across studies due to heterogeneity rather than chance). The odds of VTE were 99.9999% lower than no VTE, OR = 0.0001, 95% CI [0.0001, 0.0004], $p < .0001$ with a Relative risk of 0.0039, 95% CI [0.0015, 0.0105].
Discussion:
CRS is a known risk factor for VTE. In patients with underlying malignancy undergoing CAR-T therapy, the risk can be much higher than those without malignancy who develop CRS for other reasons. In a retrospective single-center observational study, Hashmi et al. reported an 11% incidence of VTE in lymphoma patients treated with CAR-T directed against the CD-19 receptor. Our systematic review and metanalysis didn't find a statistically increased risk of VTE in the patients getting CAR-T cell therapy despite the risk of CRS/ ICANS and underlying malignancy. The findings suggest that the thrombotic risks are either low or were not reported in the interval specified in the studies. The need for thromboprophylaxis must be made on a case-by-case basis, factoring in other risk factors such as underlying disease, cytopenia, and other medical comorbidities.
Conclusion:
The Incidence of VTE is low following CAR-T therapy despite the risks, and the need for thromboprophylaxis should be based on individual patient characteristics. Patient selection, exclusion criteria, and short follow-up periods following phase 2 trials might impact our study results. In a long-term phase 3 trial, collecting data for VTE may be needed to appropriately stratify patients for their VTE risk so that an appropriate thromboprophylaxis can be recommended to prevent an additional serious complication post-CAR-T.

Disclosures No relevant conflicts of interest to declare.

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