BACKGROUND

In vivo CAR T-cell expansion and persistence are associated with response, toxicity, and long-term efficacy. As such, the tools used to detect CAR T-cells are fundamental for optimizing this therapeutic approach. Nevertheless, despite the critical value of this essential biomarker, there is significant variability in CAR T-cell detection methods and the frequency and intervals of testing. Furthermore, heterogeneity in the reporting of quantitative data adds layers of complexity that limit inter-trial and inter-construct comparisons.

METHODS

We sought to assess the heterogeneity of CAR T-cell expansion and persistence data in a scoping review using the PRISMA-ScR checklist. Based on 21 clinical trials from the United States featuring a Food and Drug Administration-approved CAR T-cell construct or one of its predecessors, 112 papers were screened and 60 were selected for analysis based on the inclusion of CAR T-cell expansion and persistence data (figure 1A). Paper identifiers, CAR construct and antigen targeted, detection technique(s), detection frequency, expansion data and persistence data were all captured in the analysis.

RESULTS

Across a wide array of CAR T-cell constructs (figure 1B) and based on the first/primary publication, flow cytometry and quantitative polymerase chain reaction (qPCR) were identified as the two primary techniques for detecting CAR T-cells (figure 1C). Despite apparent uniformity in detection techniques, the specific methods used were highly variable. Further, detection timepoints and the number of evaluated timepoints ranged broadly. Additionally, quantitative data for the parameters assessed were often not reported (figure 1D-R). To evaluate whether subsequent papers from a trial resolve this issue, we analyzed all remaining papers reporting on a clinical trial, recording all expansion and persistence data. Flow cytometry and qPCR remained the most common CAR T-cell detection techniques; however, additional methods included droplet digital PCR, NanoString, and single-cell RNA sequencing. Inconsistencies, however, with detection timepoints and frequency remained, and a significant amount of quantitative data was still not readily available (data not shown).

CONCLUSIONS

Our findings highlight the critical need to establish a universal standard for reporting on CAR T-cell detection in patients on early phase studies. The current reporting of non-interconvertible metrics and limited provision of quantitative data make cross-trial and cross-CAR T-cell construct comparisons extremely challenging. While unique attributes of CAR T-cells may limit how they can be detected across various constructs, establishing a standardized approach for collecting and reporting data is urgently needed and would represent a substantial advancement in the ability to evaluate cross-trial outcomes.