INCIDENCE AND OUTCOMES OF HUMAN HERPESVIRUS-6 INFECTION AFTER CAR-T THERAPY: A SYSTEMATIC REVIEW

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Introduction

- Human herpesvirus-6 (HHV-6) is a known complication after **allogeneic stem cell transplantation**.
- Its role after **chimeric antigen receptor T-cell (CAR-T) therapy** remains poorly defined.
- Neurologic manifestations and overlap with **CAR-T toxicities** complicate recognition and management.

Aim

- To evaluate the **incidence, clinical manifestations, and outcomes** of HHV-6 infection/reactivation after CAR-T therapy.

Objectives

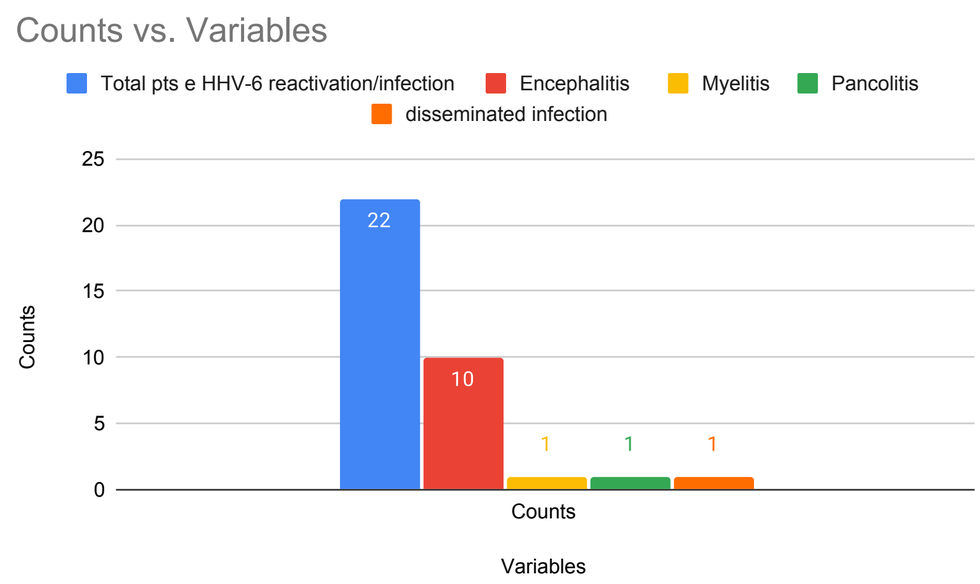
- Systematically review published literature on HHV-6 infection/ reactivation post-CAR-T.
- Summarize patient characteristics, timing, clinical features, and outcomes.
- Highlight overlap with CRS and ICANS to aid clinical suspicion.

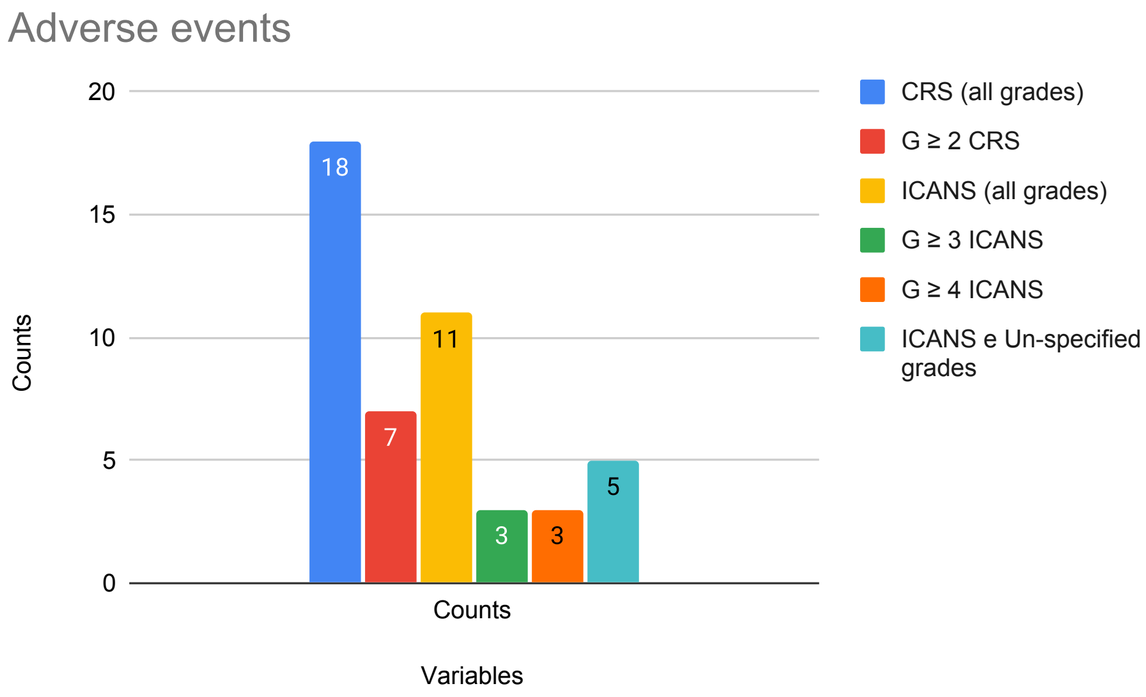
Methods

- Systematic review conducted per **PRISMA 2020** guidelines.
- Databases searched: **PubMed Central, Embase, Cochrane**. Upto March 2025
- **50 records identified → 10 studies included** (9 case reports/ series, 1 cohort).
- Extracted variables: demographics, HHV-6 infection/ reactivation, timing, clinical manifestations, antiviral therapy, CRS/ICANS, and outcomes.
- Descriptive analysis performed.

Results

- **728 CAR-T recipients** included.
- HHV-6 infection/reactivation in **22 patients (3%)**.
- **Median age:** 56 years (18–74); **53.8% male**.
- **Median time to infection:** 21 days (range 16–84).
- **Clinical manifestations:**
  - Encephalitis (n=10)
  - Myelitis (n=1)
  - Pancolitis (n=1)
  - Disseminated infection (n=1)
- **Antivirals used:** 7/22 (foscarnet ± ganciclovir).
- **CRS:** out of 22 pts, we had data available for 18 pts with CRS. Grade 2 in 7/9 with severity data
- **ICANS:** out of 17 pts with available date, 11 pts developed ICANS (3 Grade 3, 3 Grade 4, 5 unspecified).
- **All-cause mortality:** 8/19 (42.1%) with data; **4 deaths attributed to HHV-6**.





Summary

- HHV-6 infection after CAR-T is **uncommon (3%)** but **highly morbid**.
- **CNS involvement predominates** (encephalitis in nearly half of reported cases).
- Clinical overlap with **CRS/ICANS** complicates recognition.
- **Mortality is substantial (42.1%)**, with attributable deaths in a subset.

Discussion

- HHV-6 may be **underdiagnosed** due to overlapping features with CAR-T toxicities.
- Lack of **standardized screening or treatment** protocols in CAR-T recipients.
- Current evidence largely from **case reports/series** → limited generalizability.
- Need for **prospective studies** and potential role for **early PCR monitoring** in high-risk patients.
- Clinical vigilance is critical for timely recognition and management.

References

1.https://ashpublications.org/blood/article/144/5/465/517149

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