Abstract title: Monitoring and Management of CMV and other Viral Reactivations with Bispecific Antibodies (BsAbs) for Patients with Relapsed and Refractory Multiple Myeloma (RRMM)

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Introduction
CMV and other viral reactivations are reported with BsAbs in patients with RRMM. Despite this there are no clear guidelines on the monitoring or management of viral reactivation whilst on treatment leading to variations in practice. We therefore analysed our data to help inform practice.

Methods
This was a retrospective data collection from patients who completed ≥1 cycle of Teclistamab, Elranatamab or Talquetamab between Jan 2022-May 2025. Viral load was measured in blood by PCR at clinical discretion. Overall survival (OS) was estimated using Kaplan-Meier methods.

Results
99 patients (median age 65yrs (44-79)) received Teclistamab (48%), Elranatamab (34%) or Talquetamab (17%) at a median of 5 prior lines (0-11). Median duration of treatment was 6 months (1-40), with a median follow up of 11 months (2-40). 50% received G-CSF, 50% received IVIg replacement (of which 14% started prior to BsAb), at any point. Baseline CMV IgG serology was performed in 78% of patients: 55% positive, 45% negative. 56% patients had >1 CMV PCR test during treatment, 19% 1 PCR, 25% not tested.
For BCMA BsAbs, 60 (73%) patients had CMV PCR tests of which 24 (40%) patients were positive at any point during treatment (all those tested were baseline IgG+), peaking at a median of 2.5 cycles. 54% had a peak viral load (VL) below the limit of quantification (BLQ) and 16% reactivated ≥1 other virus besides CMV. There were no clear cases of CMV end organ disease, although 2 patients received CMV treatment for possible disease. Management of asymptomatic CMV PCR positivity was variable. 3 interrupted treatment (median peak VL 57,980 IU/ml (range 4,452-72,992) for a median 97 days (66–146) with reduction of CMV VL whilst maintaining MM response. 21 patients continued BsAb treatment (peak VL 62% BLQ; 29% < 1,000; 9% >1,000), with either maintenance of low levels, or spontaneous reductions in CMV titres, despite on-going treatment (peak VL range: BLQ-24,087, median: BLQ). 15/21 (71%) had a subsequent CMV PCR test which was also positive. None developed CMV disease. At the time of first CMV positivity, BsAb administration was given Q1W: 14, Q2W: 5, Q4W: 2. The likelihood of developing CMV reactivation was unrelated to age, number of prior lines, baseline lymphocyte count, nadir lymphocyte count, prior T cell immunotherapy status, nadir IgG level or use of IVIG. Other viral reactivations were identified by blood PCR but generally asymptomatic: adenovirus (2), EBV (8), parvovirus (1 case, symptomatic).
17% of Talquetamab patients had viral reactivation (2 CMV (both BLQ), 1 EBV), all were asymptomatic.

OS was not affected by CMV reactivation: median 30m for CMV PCR+ and not reached for CMV PCR -, p=0.5585.

Conclusions

CMV reactivation is common with BCMA BsAbs and occurred early in treatment. Regular blood PCR monitoring for CMV IgG+ patients may be useful as interruption of treatment reduces viral loads, limiting the need for antiviral treatment. CMV disease in our data was rare as were other viral reactivations.