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MANAGEMENT OF VIRAL INFECTIONS IN RELAPSED REFRACTORY MULTIPLE MYELOMA (R/R MM) PATIENTS ON BISPECIFIC ANTIBODIES

SINGLE UK ACADEMIC CENTRE EXPERIENCE AND 2 CASE STUDIES

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Introduction

Bispecific antibodies (BsAbs) have revolutionised the treatment landscape in multiple myeloma. Nevertheless, they pose a significant risk of infective complications driven by cytopenias, hypogammaglobulinaemia and T cell exhaustion. The sequelae of viral infections in this highly immunosuppressed patient cohort are linked with increased morbidity and mortality, particularly SARS-CoV-2. Clinical practice for routine surveillance of CMV/EBV/Adenovirus with viral PCR panels is variable; as a result there is currently limited data regarding the incidence of viral reactivation and management in this cohort[1]. Monitoring for viral infection and reactivation should be based on symptoms and clinical presentation[1] but routine surveillance should be considered to help guide future practice .

Aims

To audit the incidence of viral infections and viral reactivation and their management in our cohort of BsAb treated patients.

Methods

We retrospectively evaluated all relapsed refractory myeloma patients treated between October 2022 and January 2025 with BsAbs in our centre. We defined infection as positive respiratory viral panels or CMV/EBV/Adenovirus PCR results, and CMV reactivation as CMV DNA >1000IU/ml. We summarise management strategies from review of clinical notes.

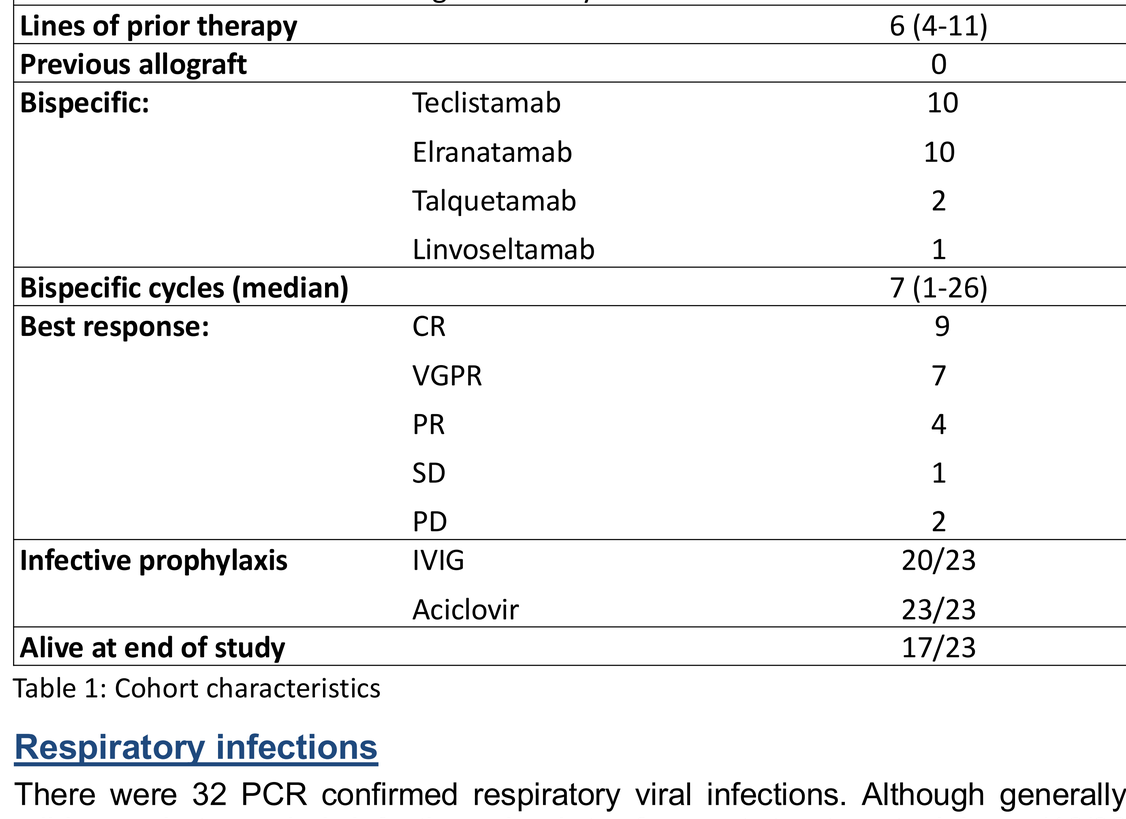
Results

Total patients		23
Age (median)		61 (50-80yrs)
Sex (male)		18
Ethnicity:	White British	11
	Black	10
	Asian	2
Paraprotein:	IgG	14
	IgA	4
	Light chain myeloma	5
Lines of prior therapy		6 (4-11)
Previous allograft		0
Bispecific:	Teclistamab	10
	Elranatamab	10
	Talquetamab	2
	Linvoseltamab	1
Bispecific cycles (median)		7 (1-26)
Best response:	CR	9
	VGPR	7
	PR	4
	SD	1
	PD	2
Infective prophylaxis	IVIG	20/23
	Aciclovir	23/23
Alive at end of study		17/23

Table 1: Cohort characteristics

Respiratory infections

There were 32 PCR confirmed respiratory viral infections. Although generally mild, respiratory viral infections lead to frequent treatment delays (16/32 infections) with median duration of delay of 17 days (range 2-38 days) and hospital admissions 7/32 cases. 5/9 patients with SARS-COVID-19 infection received antiviral therapy. 1 patient died from complications of severe COVID-19 infection despite antiviral treatment.



Viraemias

8/23 patients had a positive blood virology PCR test. There were 10 positive blood PCR test episodes in total (4 CMV reactivation, 4 EBV viraemias, 2 adenovirus viraemias) of which there was only 1 symptomatic infection (see case 1).

Testing for CMV/EBV/adenovirus was conducted for a mixture of asymptomatic monitoring and screening of symptomatic patients. Of the 4 CMV reactivations 2 received antiviral therapy. 1 pre-emptively and 1 during a complex admission with general decline despite multiple antimicrobial therapies (unclear if CMV active infection).

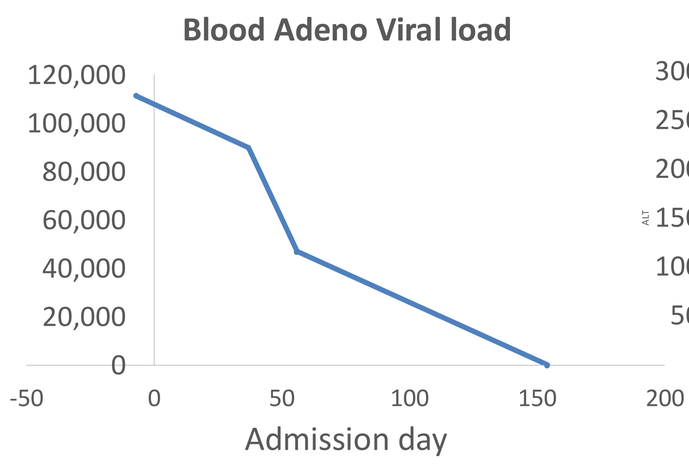
6/10 viraemias lead to associated treatment delay. There were no patients that lost their treatment response following a treatment delay because of a viral infection. There were no deaths due to CMV/EBV/adenovirus infection.

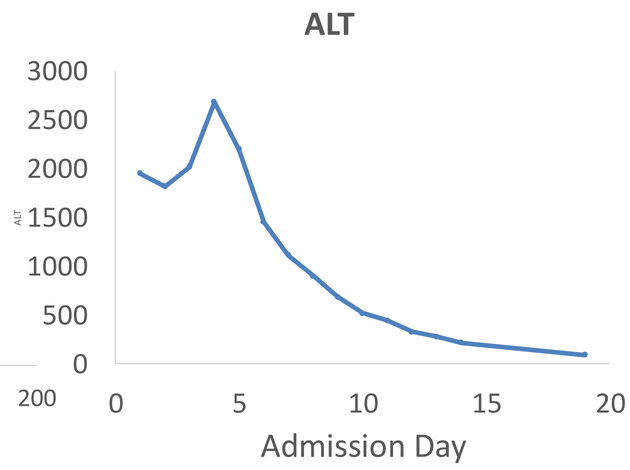
Case Study 1

58M. Lambda light chain myeloma. 6 prior lines of chemotherapy. Triple class refractory. Commenced Teclistamab 7th line November 2022. Had completed 8 cycles and was in serological complete response. Was admitted June 2023 with fevers, myalgia, malaise and cough. Initial bloods showed G4 neutropenia, raised inflammatory markers (CRP 215, ferritin 94000) and marked transaminitis with ALT of 2679.

Patient was commenced on broad spectrum antibiotics. CT Chest/Abdomen/Pelvis showed mild tree in bud abnormality in the lungs bilaterally but normal liver appearances. Subsequent infection screen results showed positive respiratory swab PCR, blood PCR and urine PCR for adenovirus raising suspicion of disseminated adenovirus infection with associated acute hepatitis.

The adenovirus infection was managed by holding Teclistamab. IVIG was given at a prophylactic dose. Consideration was made for treatment with Cidofovir but given concerns about nephrotoxicity and spontaneous improvement in transaminitis this was not required. Teclistamab was successfully restarted after a prolonged delay. Patient remains in CR.





Case Study 2

64F IgGK myeloma due to start Linvoseltamab 4th line on clinical trial. Was noted on screening bloods prior to commencing BsAb to have CMV reactivation (1713 iU/ml), and asymptomatic. As was about to commence further immunosuppressive treatment was treated with valganciclovir with rapid resolution of CMV reactivation with negative viral loads on 2 occasions. Subsequently commenced BsAb with regular monitoring of CMV PCR viral loads. Treatment ongoing, in PR.

Conclusion

Our real-world data confirm that viral infections are common in R/R MM patients treated with BsAbs; few required anti-viral treatment but most resulted in BsAb treatment delays.

This data set is likely an under-representation of the incidence of viral reactivation as routine screening was not carried out systematically. Aciclovir for HSV/VZV prophylaxis, IVIG for secondary hypogammaglobulinaemia, and screening for Hepatitis B reactivation and prophylaxis remain key strategies to reduce the burden of viral infections in this cohort.

We emphasise the need to consider early respiratory viral panels including SARS-CoV-2 as well as CMV/EBV/Adenovirus PCR panels in all symptomatic cases and suggest that, as these treatments become more widely accessible, there may be a role for routine surveillance of CMV/EBV/Adenovirus PCR. This will inform on the incidence of viral reactivation and help guide our management decisions.

References

1. Raje, N., Anderson, K., Einsele, H. *et al. Monitoring, prophylaxis, and treatment of infections in patients with MM receiving bispecific antibody therapy: consensus recommendations from an expert panel. Blood Cancer J.* **13**, 116 (2023). https://doi.org/10.1038/s41408-023-00879-7

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