Outlook

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Low CRS and ICANS rates during step up dose reinitiation after prolonged dose delay of bispecific antibodies in multiple myeloma

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Abstract

Abstract Track

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Introduction

Bispecific antibodies are associated with unique side effects including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). To reduce CRS and ICANS risks, step-up dosing (SUD) is required during treatment initiation, either as an inpatient or within proximity to a hospital. CRS occurs in ~60-70% of patients, with ICANS rate of < 10%. SUD is also required for therapy reinitiation after dose delay. Many UK district hospitals do not have facilities for SUD, which can cause delays in delivering or restarting treatment. We evaluated the CRS and ICANS rates of patients following SUD reinitiation (reSUD) after dose delay (>7 days).

Methods

This was a single-centre, retrospective study. We included patients who received teclistamab, elranatamab or talquetamab. Clinical details were obtained via hospital's electronic health record. Disease response was assessed using IMWG criteria. CRS and ICANS were graded according to the ASCTC grading system.

Results

Between Jan 2020 and May 2026, 221 patients received teclistamab, elranatamab or talquetamab. There were 22 dose delays that required reSUD in 18 patients. 12 (67%) were male, median age was 60 (54-79) and the median no. of prior treatment lines was 4 (1-12). The median number of doses received before delay was 12 (1-43). 15 (68%) of the 22 dose delays occurred at ≤4 cycles. The median dose delay interval was 87 days (9-455). 14 (64%) were due to infections, most were respiratory related including COVID-19. 4 (18%) were due to planned procedures. Other reasons included acute kidney injury, unexplained neurological symptoms and cytopenia.

At reSUD, 15 (68%) patients were in VGPR or CR, 1 (5%) was in PR and 6 (27%) had stable disease. 19 (86%) reSUD were given as inpatient, the rest were given as outpatient. The median length of inpatient stay was 6.5 days (3-26). All but 3 reSUD were given as per Summary of Product Characteristics (SPC). Of the 3 cases that were delivered outside of SPC, 2 were teclistamab reinitiated at SUD level 1 (0.06mg/kg) instead of level 2 (0.3mg/kg), and 1 was elranatamab reinitiated at SUD level 2 (32mg) instead of level 1 (12mg). None of these resulted in CRS or ICANS.

There were 2 (9%) grade 1 CRS and 2 (9%) grade 2 CRS during reSUD. These included 3 patients receiving talquetamab and 1

receiving teclistamab. All of these occurred early (< 4 cycles) and in patients in less than VGPR at reSUD. Dexamethasone was given as premedication and all CRS events were treated successfully with 1 dose of tocilizumab. No ICANS were reported.

Conclusions

CRS and ICANS rates were low during reSUD following prolonged dose delay of bispecific antibodies, particularly among patients in VGPR or CR who were well established in treatment. For these patients, reSUD may be safely administered in outpatient settings, avoiding costly inpatient stays. More studies are needed to ascertain the optimal SUD levels after dose delays and ways to mitigate CRS and ICANS risks in these situations.

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