RESPONSE OUTCOMES, NEUTROPENIA AND INFECTION RISK IN BISPECIFIC ANTIBODY TRIALS - MULTIPLE MYELOMA

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INTRODUCTION

Bispecific antibodies (BiTEs) target both CD3 expressed on the surface of T cells and tumor cell surface marker such as B-cell maturation antigen (BCMA), or G-protein coupled receptor family C group 5 member D (GPRC5d) or Fc receptor homologue 5 (FcRH5).

Phase I/II studies of these agents have shown impressive response outcome results in heavily pretreated patients. Patients included in these trials had progressed on at least 3 lines of therapy, including a proteasome inhibitor (PI), an immunomodulatory imide (IMiD), and an anti-CD38 antibody.

However, there is a concern over emerging data on infection rates with these agents.

We report pooled outcomes of response, infections, and other adverse event rates in bispecific antibody trials in relapsed/refractory myeloma patients.

METHODS

PubMed, EMBASE, Cochrane review, and clinicaltrials.gov databases were searched for phase I/II clinical trials studying Bispecific antibodies in relapsed refractory myeloma patients.

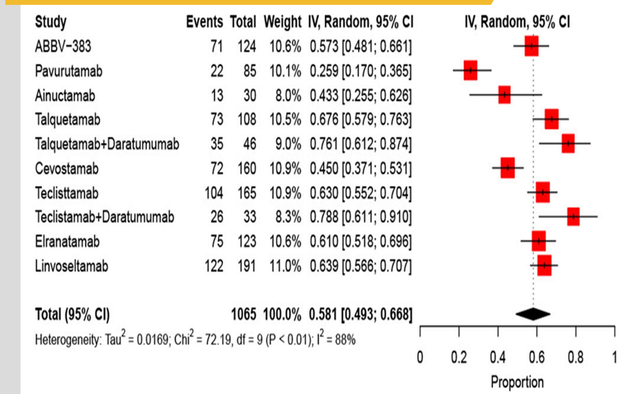
Data were extracted based on Reviews and Meta- Analysis guidelines.

DerSimonian-Laird (DL) random effects model was used to estimate the pooled proportion of patients achieving objective response rate (ORR), very good partial response rate (VGPRR), infections (any grade), grade ≥ 3 infections, neutropenia (any grade), grade ≥ 3 neutropenia, hypogammaglobulinemia and death.

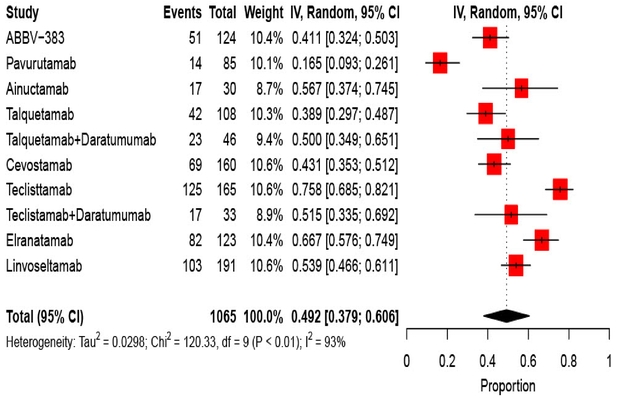
Adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03 or above).

Weights were estimated using inverse variance method. Statistical heterogeneity was calculated using the I^2 and chi-squared test.

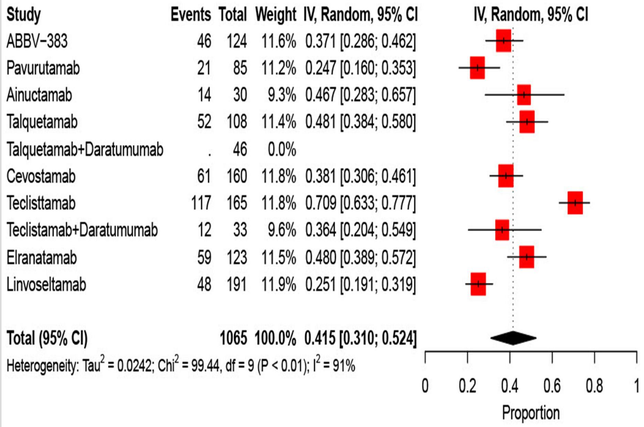
FOREST PLOTS



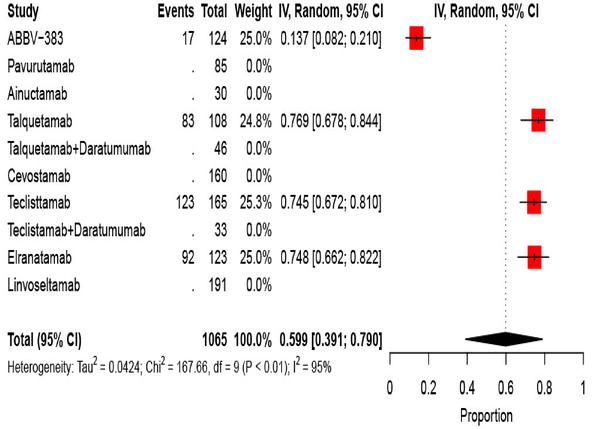
Forest plot of Objective Response Rate (ORR)



Forest plot of infection rate (any grade)



Forest plot of neutropenia (any grade)



Forest plot of hypogammaglobulinemia

RESULTS

Ten studies with 1065 patients who received Bispecific Antibodies in the relapsed or refractory myeloma setting were analyzed.

The pooled proportion of patients who achieved ORR was 58% (95% CI 49% to 67%) and VGPRR was 45% (95% CI 37% to 54%).

The pooled proportion of patients who experienced adverse events were:

- infections (any grade) was 49% (95% CI 38% to 60%)
- grade ≥ 3 infections 24% (95% CI 16% to 32%)
- neutropenia (any grade) 41% (95% CI 31% to 54%)
- grade ≥ 3 neutropenia 40% (95% CI 31% to 51%)
- hypogammaglobulinemia 60% (95% CI 39% to 79%)
- death 4% (95% CI 3% to 7%)

CONCLUSION

Bispecific antibodies resulted in a high rate of deep response in heavily pretreated myeloma patients with significant rates of infections, neutropenia & hypogammaglobulinemia.

The outcomes mentioned above should be interpreted carefully in the context of specific BiTEs, their dosage and other factors involved in the primary disease course such as lines of treatment and prior therapies.

REFERENCES

1. Cliff ERS, Reynolds G, Popat R, Teh BW, Kesselheim AS, Mohyuddin GR. Acknowledging Infection Risk in Bispecific Antibody Trials in the Treatment of Multiple Myeloma. J Clin Oncol. 2023 Apr 1;41(10):1949-1951. doi: 10.1200/JCO.22.02197. Epub 2023 Jan 30. PMID: 36716411.
2. Image credit: clinicaloptions.com

