Risk of gastrointestinal toxicities and health-related quality of life events in patients with multiple myeloma treated with daratumumab

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INTRODUCTION

- Context:** Daratumumab (D), a human monoclonal antibody which targets CD38, has shown survival benefits in patients with multiple myeloma with notable safety concerns.
- Objective:** To determine the risk of gastrointestinal toxicities and health-related quality of life events

METHODS

Literature search

- We performed a comprehensive literature search using MEDLINE, EMBASE databases, and meeting abstracts through April 30, 2018.
- The references of all potential studies were also reviewed for any additional relevant studies.
- All databases and meeting abstracts were systematically searched with the keywords 'Daratumumab' AND 'multiple myeloma'.
- We limited the search to 'humans' and 'randomized controlled trials'.
- All studies written in English or non-English languages were obtained.

Eligibility criteria

- The randomized controlled trials (RCTs) that were eligible to be included in the meta-analysis had to conform with the following characteristics:
- 1. Phase III RCTs comparing daratumumab based regimen and a control group in patients with multiple myeloma; and
- 2. Phase III RCTs that mention gastrointestinal toxicities and health-related quality of life events as adverse effects.

Data extraction

- Three authors screened independently for eligibility and conducted data extraction from each eligible study. Disagreements were resolved by other two reviewers.

Study outcome measures

- The endpoints of our meta-analysis were gastrointestinal toxicities and health-related quality of life events as adverse effects.

Data synthesis and analysis

- Mantel-Haenszel method was used to calculate the estimated pooled risk ratio (RR) with 95% confidence interval (CI).
- Heterogeneity was assessed using I² statistic.
- Random effects model was applied.
- P value less than 0.05 were considered significant.

RESULTS

- Patients or other participants:** Three phase III RCTs with a total of 1744 patients with multiple myeloma were eligible.
- Interventions:** Studies compared D + bortezomib (V) + melphalan (M) + prednisone (P) vs VMP, D + lenalidomide (R) + dexamethasone (Dex) vs RDex and DVdex vs VDex. The randomization ratio was 1:1 in all studies. Daratumumab was utilized in relapsed and refractory multiple myeloma in the POLLUX study (n= 564) and the CASTOR study (n= 480) and as first-line treatment for patients with multiple myeloma who were ineligible for stem-cell transplantation in the ALCYONE study (n= 700). Figure 1 demonstrates the comprehensive steps of study selection. The characteristics of the studies were demonstrated completely in Table 1.

Fig. 1 Flow diagram of the study selection process

Table. 1 Characteristics of the studies included in the meta-analysis

Study	Author/Year	Study Type	Study Phase	Line of Treatment	Number of Patients		Treatment	
					Daratumumab	Control		
ALCYONE	Mateso/2018	Multicenter, Randomized, open-label, active-control	III	Untreated patients who are ineligible for stem cell transplantation	346	354	DVMP	VMP
POLLUX	Dimopoulos /2016	Randomized, open-label, multicenter	III	Relapsed or refractory	283	281	RDex	RDex
CASTOR	Palumbo/2016	Multicenter, Randomized, open-label, active-control	III	Relapsed or refractory	243	237	DVDex	VDex

RESULTS

Meta-analysis results

- The RR of all-grade side effects were as follows: nausea, 1.26 (95% CI: 0.73 – 2.18; p = 0.39); diarrhea, 1.33 (95% CI: 0.93 – 1.90, p = 0.11); fatigue, 1.07 (95% CI: 0.74 – 1.54; p = 0.70); asthenia, 0.84 (95% CI: 0.38 – 1.85, p = 0.66); and insomnia, 1.05 (95% CI: 0.80 – 1.36; p = 0.71).
- The RR of high-grade adverse effects were as follows: nausea, 1.92 (95% CI: 0.17 – 21.60; p = 0.59); diarrhea, 1.43 (95% CI: 0.75 – 2.74, p = 0.27); fatigue, 1.87 (95% CI: 0.99 – 3.52; p = 0.051); asthenia, 0.81 (95% CI: 0.30 – 2.14, p = 0.67); and insomnia, 0.30 (95% CI: 0.04 – 1.93; p = 0.20).

CONCLUSION

- Addition of daratumumab did not increase the risk of gastrointestinal toxicities and health-related quality of life events in patients with multiple myeloma compared to control arm, while contributing substantial survival benefits.

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