

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Combination Agents for Multiple Myeloma: Comparative Clinical Effectiveness

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Research Questions

1. What is the comparative clinical effectiveness cyclophosphamide + bortezomib + dexamethasone (CyBorD) versus bortezomib + melphalan + prednisone (VMP) for newly diagnosed patients with multiple myeloma where there is no intent for stem cell transplantation?
2. What is the comparative clinical effectiveness cyclophosphamide + bortezomib + dexamethasone (CyBorD) versus lenalidomide + dexamethasone (RD) for newly diagnosed patients with multiple myeloma where there is no intent for stem cell transplantation?

Key Findings

One non-randomized study was identified regarding the comparative clinical effectiveness of CyBorD versus VMP in newly diagnosed patients with multiple myeloma with no eligibility for stem cell transplantation.

Additionally, no relevant health technology assessments, systematic reviews, meta-analyses and randomized controlled trials were identified regarding the comparative clinical effectiveness of CyBorD to VMP or RD.

Methods

A limited literature search was conducted on key resources including Ovid MEDLINE, Ovid Embase, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit retrieval by publication type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and March 12, 2019. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Newly diagnosed patients with multiple myeloma where there is no intent (e.g., not suitable, not eligible, etc.) for stem cell transplantation
Intervention	Bortezomib in combination with cyclophosphamide and dexamethasone (CyBordD)
Comparator	Q1: Bortezomib in combination with melphalan and prednisone (VMP) Q2: Lenolidamine in combination with dexamethasone (RD)
Outcomes	Clinical effectiveness (e.g., overall survival, progression free survival, overall response rate, duration of response, minimal residual disease, quality of life), safety (e.g, side effects, toxicity, adverse events, tolerability).
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first, followed by randomized controlled trials, and non-randomized studies.

One non-randomized study was identified regarding the comparative clinical effectiveness of CyBordD compared to VMP in multiple myeloma patients who are ineligible for a stem cell transplant. No studies were identified regarding the comparative clinical effectiveness of CyBorD versus RD.

No relevant health technology assessments, systematic reviews, meta-analyses and randomized controlled trials were identified regarding the comparative clinical effectiveness of CyBorD to VMP or RD in multiple myeloma patients who are ineligible for a stem cell transplant.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

The non-randomized study¹ identified aimed to understand the safety and effectiveness of CyBorD compared to other bortezomib combination agents, VMP, and bortezomib-dexamethason (VD) in multiple myeloma patients who were considered ineligible for stem cell transplant. Patients received continuous therapy of the bortezomib combination agents with a median of 6 cycle treatments. Overall, the researchers determined that CyBorD had the highest overall response rate among patients and was favoured in terms of progression free survival while all bortezomib combination agents (CyBorD, VMP and VD) had similar median overall survival rates.¹

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

1. Jimenez-Zepeda VH, Duggan P, Neri P, Tay J, Bahlis NJ. Bortezomib-containing regimens (BCR) for the treatment of non-transplant eligible multiple myeloma. *Ann Hematol.* 2017 Mar;96(3):431-439.
[PubMed: PM28074255](#)

Appendix — Further Information

Non-Randomized Studies

'No Intent for Stem Cell Transplantation' Not Specified In Patient Population

2. Djebbari F, Srinivasan A, Vallance G, Moore S, Kothari J, Ramasamy K. Clinical outcomes of bortezomib-based therapy in myeloma. *PLoS ONE*. 2018;13(12):e0208920.
[PubMed: PM30540831](#)
3. Ravi P, Kumar S, Gonsalves W, et al. Changes in uninvolved immunoglobulins during induction therapy for newly diagnosed multiple myeloma. *Blood Cancer J*. 2017 06 16;7(6):e569.
[PubMed: PM28622306](#)
4. Tuchman SA, Moore JO, DeCastro CD, et al. Phase II study of dose-attenuated bortezomib, cyclophosphamide and dexamethason ("VCD-Lite") in very old or otherwise toxicity-vulnerable adults with newly diagnosed multiple myeloma. *J Geriatr Oncol*. 2017 May;8(3):165-169.
[PubMed: PM28256432](#)
5. Alexanian R, Delasalle K, Wang M. High frequencies of response after limited primary therapy for multiple myeloma. *Clin Lymphoma Myeloma Leuk*. 2013 Apr;13(2):119-122.
[PubMed: PM23260599](#)

Review Articles

6. Raza S, Safyan RA, Rosenbaum E, Bowman AS, Lentzsch S. Optimizing current and emerging therapies in multiple myeloma: a guide for the hematologist. *Ther Adv Hematol*. 2017 Feb;8(2):55-70.
[PubMed: PM28203342](#)

Additional References

7. Anderson KC. Progress and paradigms in multiple myeloma. *Clin Cancer Res*. 2016 Nov 15;22(22):5419-5427.
[PubMed: PM28151709](#)
8. Garg A, Morgunskyy M, Belagali Y, Gupta N, Akku SP. Management of multiple myeloma and usage of bortezomib: perspective from India and Ukraine. *Front Oncol*. 2016 21 Nov 21;6:243.
[PubMed: PM27917369](#)
9. Engelhardt M, Terpos E, Kleber M, et al. European Myeloma Network recommendations on the evaluation and treatment of newly diagnosed patients with multiple myeloma. *Haematologica*. 2014 Feb;99(2):232-242.
[PubMed: PM24497560](#)