International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Ixazomib- versus bortezomib-based proteasome inhibitor triplet regimens in older transplant-ineligible newly diagnosed multiple myeloma: A scoping review of real-world evidence

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ADMINISTRATIVE INFORMATION

Support - Takeda Pharmaceuticals Company.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202690014

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 3 September 2026 and was last updated on 3 September 2026.

INTRODUCTION

Review question / Objective This study compared the real-world effectiveness and safety of ixazomib- versus bortezomib-based triplet regimens as first-line treatment in older (≥65 years) transplant-ineligible newly diagnosed multiple myeloma patients.

Background Frontline therapy for older patients with transplant-ineligible newly diagnosed multiple myeloma (TIE-NDMM) remains challenging in real-world clinical practice. Given their advanced age, frailty, and multiple comorbidities, a substantial proportion of patients face barriers to healthcare access and exhibit limited tolerance to continuous therapy. Although bortezomib-based triplets are widely used, their long-term use is often constrained by cumulative toxicities, most notably peripheral neuropathy (PN), and the burden of parenteral administration.

Rationale To date, no comprehensive synthesis has directly compared the real-world effectiveness and safety of I- versus V-based PI triplets specifically in older transplant-ineligible (TIE) NDMM patients. Therefore, this study systematically reviewed and synthesized the available real-world evidence comparing I- and V-based triplet regimens in older TIE-NDMM patients, thereby delineating more tolerable and feasible continuous treatment regimens.

METHODS

Strategy of data synthesis The primary outcomes (progression-free survival and duration of treatment) will be summarized as median times and ranges. Secondary outcomes (adverse event, serious adverse event, discontinuation, and peripheral neuropathy rates) will be summarized as proportions depending on data availability. These outcomes will all be presented as median values derived from the included studies.

Eligibility criteria Real-world studies are eligible if they reported efficacy or safety outcomes for TIE-NDMM patients with median age ≥65 years who received I- or V-based triplet regimens.

Source of evidence screening and selection A comprehensive literature search will be conducted in PubMed, Embase, and Cochrane Library from database inception until April 18, 2025. The search strategy will combine controlled vocabulary (MeSH/Emtree) with free-text terms. The reference lists of the included studies and relevant reviews will be manually screened for additional records. All retrieved records will be imported into EndNote for deduplication. Two reviewers will independently screened the titles and abstracts for relevance, followed by a full-text review of potentially eligible studies. Discrepancies will be resolved through discussion or adjudication by a third reviewer if necessary. A PRISMA 2020 flow diagram will be used to document the study selection process.

Data management A standardized data extraction form will be created. The following information will be collected: study characteristics (author, year, country, study design, and trial ID/registry); patient characteristics (sample size, median/mean age, sex distribution, frailty status, and follow-up time); treatment regimens (composition, dosage, and treatment duration); efficacy outcomes (PFS and DOT); safety outcomes (incidence of grade ≥3 AEs, SAEs, and treatment discontinuation—overall and toxicity-related). Data will be extracted independently by two reviewers, with cross-checks to ensure accuracy. Disagreements will be resolved by consensus.

Language restriction No limitation.

Country(ies) involved China.

Keywords Ixazomib, Bortezomib, Older, Multiple Myeloma, Scoping Review.

Contributions of each author
Author 1 - Yan Wang.
Author 2 - Sha Liu.
Author 3 - Jiian-qiing Mi.