■ Incorporating Real-World Evidence and Patient Value Criteria into Value-Based Frameworks for Relapsed/Refractory Multiple Myeloma

In the article “Evaluating Oncology Value-Based Frameworks in the U.S. Marketplace and Challenges in Real-World Application: A Multiple Myeloma Test Case,” published in the *JMCP* January 2018 issue, Djatche et al. report on their evaluation of 3 U.S. value-based frameworks for comparing carfilzomib, elotuzumab, and ixazomib plus lenalidomide-dexamethasone as triplet regimens for relapsed/refractory multiple myeloma. This timely analysis highlights a number of important shortcomings of currently available value-based frameworks, and the authors provide valuable constructive recommendations for future modifications to these tools. Notably, they highlight the limitations of the value-based frameworks in terms of consistency of treatment evaluations and with regards to adaptability to address multiple targeted stakeholder perspectives.

This latter point is of particular relevance in relapsed/refractory multiple myeloma. As the authors highlight, the value-based frameworks mainly rely on evidence from randomized clinical trials and do not necessarily capture other aspects and value criteria of importance to the patient perspective in the real-world setting, such as convenience and preference. In this context, an additional important recommendation may be the inclusion of real-world evidence within value-based framework evaluations, particularly in clinical settings in which there is divergence between the efficacy reported from phase 3 trials and the effectiveness reported in real-world patient populations. Such a scenario has been reported recently in multiple myeloma, highlighting notable discrepancies between real-world effectiveness and clinical trial efficacy for a number of approved regimens, particularly those incorporating agents administered via intravenous or subcutaneous injection.^{1,2}

This gap between effectiveness and efficacy may be related to the convenience and patient preference associated with oral therapy, as reported recently in multiple myeloma.^{3,4} The importance of these aspects is magnified in myeloma because they contribute to the feasibility of long-term treatment, and evidence is emerging of a correlation between real-world treatment duration and overall survival.⁵ In order to achieve this real-world surrogate endpoint for survival, namely long-term treatment duration, regimens are likely to need to fulfill the value criteria of importance to patients, supporting the inclusion of real-world evidence and patient perspectives within revised value-based framework methodologies.

Acknowledging the limitations of the present value-based frameworks, Djatche et al. draw conclusions from their framework evaluations that rank carfilzomib-based therapy as most valued, followed by elotuzumab-based and ixazomib-based therapy. However, recent real-world data in relapsed/refractory myeloma patients indicate that those receiving ixazomib-based therapy have a longer duration of therapy and prolonged time to next therapy compared with those

receiving carfilzomib- or bortezomib-based therapy. In addition, the discrepancy between these real-world findings and respective clinical trials appears most striking for carfilzomib-based therapy.² Considering these findings and the recent reports on patient preference for oral versus injectable therapies,^{3,4} it may be hypothesized that the ranking of the regimens would be altered if evaluated using a value-based framework incorporating real-world evidence and value criteria related to patient perspective. Because of its oral route of administration and its similar effectiveness and efficacy,^{1,2} ixazomib-based therapy could possibly be valued more highly in such a comprehensive value-based framework.

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