

# Letters

## COMMENT & RESPONSE

### Fitting mSMART Into the Current Clinical Management of Waldenström Macroglobulinemia

**To the Editor** We read with interest the article outlining the 2016 mSMART guidelines for the diagnosis and management of Waldenström macroglobulinemia (WM).<sup>1</sup> We believe that this is a unique opportunity to emphasize important differences that exist with WM therapy.

Under initial therapy, the authors recommend bendamustine and rituximab as preferred regimen in symptomatic treatment-naïve patients with WM when expeditious disease control is desired. The recommendation was based on a small subset analysis of patients who received either RCHOP (rituximab + cyclophosphamide, doxorubicin, vincristine, and prednisone) (n = 19) or bendamustine-rituximab (n = 22).<sup>2</sup> However, other nonalkylating options for rapid disease control exist, which is of particular importance in the treatment of younger patients. Ibrutinib is the only US Food and Drug Administration-approved therapy for symptomatic WM, including previously untreated disease.<sup>3</sup> Two studies evaluating ibrutinib therapy in 94 patients with WM have shown response rates of 90% and a time to response of 4 weeks. In addition, 2 other studies that included 85 patients have shown that bortezomib, dexamethasone, and rituximab can induce responses in more than 85% of patients with a median time to response of 4 to 8 weeks. Therapy with bortezomib or ibrutinib has not been associated with stem cell toxic effects or secondary cancers.

The authors also have recommended that single-agent rituximab be considered in patients with WM who have neuropathy, symptomatic cryoglobulinemia, or hemolytic anemia. One could argue that deeper responses are needed in these patients to prevent further tissue damage. Rituximab can induce an IgM flare in 40% of patients, which could cause a transient worsening of symptoms. Additionally, the response to rituximab in patients with WM ranges between 30% and 50% without complete responses, and time to best response of more than a year.<sup>4</sup>

Another area of concern is the recommendation for observation over maintenance rituximab therapy. The role of maintenance rituximab is an important mainstay in low-grade lymphomas. A large retrospective study that included

248 patients with WM showed significant progression-free survival benefit in favor of maintenance rituximab therapy.<sup>5</sup> The National Comprehensive Cancer Network (NCCN) and International Workshop for WM (IWWM) guidelines consider maintenance rituximab as an option in WM, and a prospective study is under way to further clarify its value. Because many effective salvage regimens exist, the recommendation for stem cell collection in anticipation of autologous transplant should be considered in select circumstances.

In summary, we commend the authors for their efforts in providing direction for the treatment of patients with WM. Readers should be mindful of other consensus approaches, including those published by national and international entities such as the NCCN and the IWWM.

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