Should Bendamustine Be Considered the Standard Frontline Therapy for Waldenström's Macroglobulinemia? NO!

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Waldenström's Macroglobulinemia (WM) is a low grade lymphoplasmacytoid lymphoma that produces a monoclonal immunoglobulin M (IgM). It accounts for approximately 2% of all of the non-Hodgkin lymphomas (NHL). When treatment is needed, it is important to remember that there is no standard of care for the frontline treatment of WM. One must take into consideration the age of the patient, their comorbid conditions, the disease biology and aggressiveness of it, the patient's preference and quality of life issues. Since this is an indolent lymphoma and the patient may need repeated therapies over the lifetime of the patient and disease, one does not want to over treat.

Single agent rituximab (R) is an active agent for the treatment of WM, and this should be the first consideration for therapy if the patient has a low tumor burden and is symptomatic with fatigue and mild cytopenias. We know that some patients do not respond to R and there are some predictors of response. Low response rates are seen in patients with a serum monoclonal protein level ≥ 40g/L, or serum albumin level is < 35 g/L. Therefore, patients with lower levels of the monoclonal protein and normal albumin are the best candidates for treatment with R.

The reasons why bendamustine-R (BR) should not necessarily be used for frontline therapy is that the data on BR is scanty (only 8% of 514 patients had WM in Dr. Rummel's ASCO 2012 abstract) and there is very little data specific for WM. There are no large, randomized trials and the optimal first line use needs to be determined. There is also no proof that increased quality and duration of response will translate into improved survival. One must remember that WM is a heterogeneous disorder and mainly affects older patients with comorbid conditions.

Many novel agents are available in clinical trials and newer drugs like bortezomib may have less long term side effects such as myelodysplastic syndrome and increased risk of transformation. Promising pathway inhibitors such as the Bruton-tyrosine-kinase inhibitors are effective in relapsed WM and may soon be available for frontline therapy. The mTor inhibitors are showing promise and novel monoclonal antibodies are being evaluated in this disease.

"Physician, do no harm" should be our mantra and less toxic agents are available for a disease that in many patients, is turning into a chronic disease.