

## **When is Treatment Appropriate for Waldenström's Macroglobulinemia?**

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Waldenström's Macroglobulinemia (WM) is defined by the presence of an IgM monoclonal protein regardless of its size and  $\geq 10\%$  bone marrow infiltration by small lymphocytes that exhibit plasmacytoid or plasma cell differentiation. The typical immunophenotype consists of surface IgM<sup>+</sup>, CD5<sup>+/-</sup>, CD10<sup>-</sup>, CD19<sup>+</sup>, CD20<sup>+</sup>, CD23<sup>-</sup> and exclusion of other lymphoproliferative disorders including chronic lymphocytic leukemia and lymphoma. The clinical features include constitutional symptoms consisting of weakness or fatigue, fever, night sweats or weight loss, progressive symptomatic lymphadenopathy or splenomegaly, hemoglobin  $\leq 10$  g/dL or platelets  $< 100 \times 10^9/L$  or complications and including symptomatic hyperviscosity, severe sensorimotor peripheral neuropathy, AL amyloidosis, renal insufficiency or symptomatic cryoglobulinemia. Smoldering WM (SWM) is an asymptomatic disorder defined by the presence of an IgM  $\geq 3$  g/dL and/or  $\geq 10\%$  bone marrow lymphoplasmacytic infiltration but no evidence of end-organ damage such as constitutional symptoms or symptomatic anemia, lymphadenopathy or hepatosplenomegaly. Hyperviscosity may produce oronasal bleeding, blurred vision, headaches, dizziness, retinal vein engorgement with hemorrhages and even papilledema. Stupor and coma rarely develop. Other indications for therapy include the development of constitutional symptoms consisting of weakness, fatigue, night sweats, fever or weight loss. Progressive symptomatic lymphadenopathy or splenomegaly is also an indication for therapy. Anemia defined as a hemoglobin value  $\leq 10$  g/dL or a platelet count  $< 100 \times 10^9/L$  due to bone marrow infiltration also justify therapy. Symptomatic hyperviscosity requires treatment immediately with plasmapheresis. Chemotherapy must be started because plasmapheresis is only a temporary measure to avoid the complications of hyperviscosity. Treatment should not be given based on the size of the IgM monoclonal spike or the degree of lymphoplasmacytic infiltration of the bone marrow.