Clin Lymphoma Myeloma. 2007 Aug;7 Suppl 5:S199-206.

Novel agents in the treatment of Waldenström's macroglobulinemia.

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Waldenström's macroglobulinemia is a B-cell disorder characterized by bone marrow infiltration with lymphoplasmacytic cells and demonstration of an immunoglobulin M monoclonal gammopathy. Despite advances in therapy, Waldenström's macroglobulinemia remains incurable. As such, novel therapeutic agents are needed for the treatment of Waldenström's macroglobulinemia. In ongoing efforts, we and others have sought to exploit advances made in the understanding of the biology of Waldenström's macroglobulinemia so as to better target therapeutics for this malignancy. Importantly, as part of these efforts, we have prioritized the development of stem cell-sparing drugs because autologous stem cell transplantation remains a viable salvage option in Waldenström's macroglobulinemia. These efforts have led to the development of several novel agents for treating Waldenström's macroglobulinemia, including bortezomib; monoclonal antibodies and/or blocking protein targeting CD40, CD52, or CD70, a proliferation-inducing ligand and B-lymphocyte stimulator; the immunomodulator thalidomide as an enhancer of rituximab activity, as well as agents interfering with stem cell factor, phosphatidylinositol 3-kinase/Akt, phosphodiesterase, cholesterol, and protein kinase C beta signaling. This report provides an update on biologic studies and clinical efforts for the development of these novel agents in the treatment of Waldenström's macroglobulinemia.