Abstract

Update on Current Therapeutic Options for Waldenstrom's Macroglobulinemia.

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Alkylating agents (chlorambucil), nucleoside analogues and rituximab are reasonable choices for primary therapy. Oral chlorambucil with or without steroids given in a continuous or intermittent schedule has been the standard treatment for more than 4 decades. Such treatment induces response in 32%-92% of patients in different series and common complication from the treatment is the development of myelodysplasias after prolonged administration. Cladribine and fludarabine induce fast responses in 38% to 100% of the patients with the cost of immunosuppression, predisposing to infections and myelosuppression, limiting the possibility of stem cell collection. Like alkylating agents nucleoside analogues increase the risk for myelodysplasias. Treatment with rituximab induces responses to 20%-50% of the patients. Responses to rituximab may be delayed and extended treatment may be indicated. Rituximab is reasonable option for IgM autoantibody related neuropathy and certain FcγRIIIA receptor gene polymorphisms may affect response to the drug. Transient increases (flare) of IgM may be observed in up to 54% of patients treated with rituximab.

Combination therapy either with nucleoside analogues with alkylating agents and/or rituximab, or rituximab with combination chemotherapy such as CHOP are also reasonable frontline treatment options for WM patients. We treated 72 newly diagnosed patients with the combination of rituximab, cyclophosphamide and dexamethasone and we observed at least a partial response in 74% of the cases with 67% and 80% of the patients surviving without progression or further treatment respectively after 2 years.

Several factors should be taken into account when choosing the most appropriate primary treatment. These factors include the age of the patient and possible co-morbid diseases, the presence of cytopenias and especially thrombocytopenia, the presence of symptoms and signs indicative of hyperviscosity, the need for rapid disease control due to severe symptoms, significant splenomegaly or lymphadenopathy, symptomatic peripheral neuropathy and whether the patient is candidate for autologous stem cell transplantation.

For patients with refractory or relapsing disease, the use of an alternate first-line agent is reasonable. There are cumulative data suggesting that bortezomib is very active in patients with relapsed or newly diagnosed disease. Finally, for patients who develop resistance to all classes of agents, alemtuzumab, thalidomide with or without dexamethasone or other novel agents could be tried. Outside the setting of a clinical trial, the administration of high dose therapy should be reserved only for patients refractory to alkylating agents, purine nucleoside and rituximab. Finally reduced intensity allogeneic transplantation may have a role in the management of selected patients.