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**Immunotherapeutic strategies for the treatment of plasma cell malignancies.**

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The use of immunotherapy to treat patients with plasma cell dyscrasias (PCD) such as multiple myeloma (MM) and Waldenström's macroglobulinemia (WM) has gained enormous interest in recent years, with considerable efforts being mounted by many investigators. These efforts have included the use of serotherapy (antibody-mediated immunotherapy), vaccination strategies aimed at inducing allogeneic as well as autologous anti-MM immunity, and the use of donor lymphocyte infusions (DLIs). A number of cell surface antigens on malignant plasma cells and/or B cells in MM and/or WM patients have been proposed for use in tumor cell-targeted serotherapy, including immunoglobulin idiotype, CD19, CD20, CD38, CD54, CD138, HM1.24, and MUC1 core protein. Ongoing clinical trials are examining serotherapy targeting CD20 (in MM and WM) and CD38 (in MM), with early reports of responses to the anti-CD20 monoclonal antibody (mAb) Rituximab (Genentech, South San Francisco, CA) in patients with WM and certain patients with MM. The use of agents to induce MM- and WM-selective antigens for targeting in serotherapy has been proposed based on studies demonstrating the upregulation of CD20 by interferon-gamma (IFN-gamma), and of MUC1 core protein by dexamethasone (DEX) on malignant plasma cells. Strategies to induce allogeneic anti-MM immunity have included immunization of the marrow donor to idiotypic protein, as well as DLI. In addition, proposed immunization strategies aimed at inducing autologous immunity include vaccination with dendritic cells pulsed with MM antigens, MM cell-dendritic cell fusions, carrier-linked idiotype protein, catalytic subunit of telomerase, or DNA encoding for single-chain variable fragments (scFv) linked to a carrier protein gene. Whole tumor vaccination strategies are also being examined and include the use of MM cells transfected and/or stimulated with cytokines, costimulatory molecules, or CD40 ligand. Finally, potential obstacles to the use of immunotherapy, including the presence of resistance antigens on MM and WM tumor cells, are discussed.