[Abstract 42]

CD52 IS EXPRESSED ON HUMAN MAST CELLS AND IS A THERAPEUTIC TARGET FOR THE ANTI-CD52 MONOCLONAL ANTIBODY CAMPATH-1H IN WALDENSTROM'S MACROGLOBULINEMIA AND MAST CELL DISORDERS.

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Campath-1H is a monoclonal antibody used in the treatment of CD52 expressing B-cell malignancies. Recently, we and others have observed that Campath-1H shows unusually high activity in patients with relapsed/refractory Waldenstrom's macroglobulinemia (WM), a B-cell malignancy with excess bone marrow mast cells (BMMC). Importantly, as we have recently shown, BMMC appear to provide direct support for WM tumor cell growth (Tournilhac *et al*, JCO 2004 22:571S), and are therefore a potential therapeutic target in WM. We therefore examined BMMC from patients with WM and other mast cell disorders for cell surface expression of CD52, and targeting by Campath-1H in preclinical studies. Multicolor flow cytometric analysis demonstrated CD52 expression on BMMC ($FceRI^+$, $CD117^+$) from 13/15 WM; 2/2 systemic mastocytosis (SM) patients; 2/4 healthy donors; as well as on the LAD and HMC MC lines. Moreover, RT-PCR analysis confirmed CD52 expression in sorted BMMC from 6/7 WM, along with 6/6 healthy donors. Importantly, Campath-1H induced high levels of antibody dependent cell mediated cytotoxicity (ADCC) actvity against LAD mast cells using activated NK effector cells. No direct cytotoxicity or antiproliferative activity by Campath-1H on LAD cells was observed. These studies demonstrate that CD52 is widely expressed on human MC and provide support for the use of Campath-1H in the treatment of WM and other systemic mast cell disorders.