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HuMax-CD38, a new human CD38 monoclonal antibody, effectively mediates killing of multiple myeloma and plasma cell leukemia cells



Multiple myeloma (MM), a malignant disorder of the B cell lineage is characterized by neoplastic proliferation of plasma cells in the bone marrow. Current treatment regimens exhibit moderate response rates. However, only marginal changes in overall survival are observed and the median survival is approximately 3 years. There is – thus - a critical unmet medical need for treatment of MM. All malignant MM tumor cells demonstrate high CD38 expression, and as such CD38 represents a potential target for immunotherapy.

HuMax-CD38, a human IgG1 antibody, was generated by immunizing human Ig transgenic mice. Immuno fluorescence studies showed binding of HuMax-CD38 to CD38-transfected CHO cells, several CD38-expressing cell lines and freshly isolated MM tumor cells. In addition, the ability of HuMax-CD38 to induce tumor cell death via several mechanisms such as antibody-dependent cell-mediated cytotoxicity (ADCC), and complement-dependent cytotoxicity (CDC)

was tested. Using mononuclear cells as effectors, HuMax-CD38 induced ADCC of several CD38-expressing B cell lines, and MM cell lines. More importantly, HuMax-CD38 mediated ADCC of tumor cells freshly isolated from bone marrow of MM patients, and also triggered ADCC of freshly isolated tumor cells from a patient with a rare CD38/CD138 – positive, chemotherapy-refractory, plasma cell leukaemia. In addition, HuMax-CD38 induced CDC of primary MM cells, freshly isolated from a cohort of 13 MM patients. The ability of HuMax-CD38 to reduce outgrowth of human lymphoma cells was tested *in vivo* in a SCID mouse xenograft model. HuMax-CD38 effectively inhibited tumor growth, both in a preventive as well as a therapeutic setting.

In conclusion, Humax-CD38 effectively mediated killing of CD38-positive tumor cells *in vitro* and *in vivo*. HuMax-CD38, therefore, represents a promising candidate for the development of antibody therapy of MM and plasma cell leukaemia.