

Answer 1:

Bibliographic Information

Recombinant Interleukin-2 Significantly Augments Activity of Rituximab in Human Tumor Xenograft Models of B-cell Non-Hodgkin Lymphoma. Lopes de Menezes, Daniel E.; Denis-Mize, Kimberly; Tang, Yan; Ye, Helen; Kunich, John C.; Garrett, Evelyn N.; Peng, Jing; Cousens, Lawrence S.; Gelb, Arnold B.; Heise, Carla; Wilson, Susan E.; Jallal, Bahija; Aukerman, Sharon L. Biopharma Research and Development, Chiron Corporation, Emeryville, CA, USA. *Journal of Immunotherapy* (2007), 30(1), 64-74. Publisher: Lippincott Williams & Wilkins, CODEN: JOIMF8 ISSN: 1524-9557. Journal written in English. CAN 146:266006 AN 2007:3045 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Recombinant interleukin-2 (rIL-2) is a pleiotropic cytokine that activates select immune effector cell responses assocd. with antitumor activity, including antibody-dependent cellular cytotoxicity (ADCC). Rituximab is an anti-CD20 monoclonal antibody that activates ADCC in non-Hodgkin lymphoma (NHL). The ability of rIL-2 to augment rituximab-dependent tumor responses was investigated. The efficacy of rIL-2 in combination with rituximab was evaluated in 2 NHL tumor xenograft models: the CD20, rituximab-sensitive, low-grade Daudi model and the CD20, aggressive, rituximab-resistant Namalwa model. Combination of rIL-2 plus rituximab was synergistic in a rituximab-sensitive Daudi tumor model, as evidenced by significant tumor regressions and increased time to tumor progression, compared with rIL-2 and rituximab single agents. In contrast, rituximab-resistant Namalwa tumors were responsive to single-agent rIL-2 and showed an increased response when combined with rituximab. Using in vitro killing assays, rIL-2 was shown to enhance activity of rituximab by activating ADCC and lymphokine-activated killer activity. Addnl., the activity of rIL-2 plus rituximab F(ab')₂ was similar to that of rIL-2 alone, indicating a crit. role for IgG1 Fc-Fc γ R-effector responses in mediating ADCC. Antiproliferative and apoptotic tumor responses, along with an influx of immune effector cells, were obsd. by immunohistochem. Collectively, the data suggest that rIL-2 mediates potent tumoricidal activity against NHL tumors, in part, through activation and trafficking of monocytes and natural killer cells to tumors. These data support the mechanistic and therapeutic rationale for combination of rIL-2 with rituximab in NHL clin. trials and for single-agent rIL-2 in rituximab-resistant NHL patients.