Lectures

LO8.06  ARGX-110: A NEUTRALIZING, HUMANIZED MONOCLONAL ANTIBODY TO THE HUMAN CD70 ANTIGEN WITH ENHANCED ADCC PROPERTIES

K. Silence, A. Thibault, H. de Haard, T. Dreier, P. Ulrichts, M. Moshir, S. Gabriels
Argen-x BVBA, Zwijnaarde, Belgium

The expression of CD70 is normally restricted to activated B- and T-cells, as well as mature dendritic cells. Overexpression has been documented in a variety of solid and hematological tumors, where it is thought to play a role in evasion of immune surveillance. ARGX-110 is a defucosylated, humanized IgG1 monoclonal antibody that selectively targets and neutralizes CD70, a ligand of CD27. A detailed biological and functional characterization of ARGX-110 was carried out to support its clinical development for the treatment of cancers dependent on signaling through the CD70/CD27 axis. In competitive equilibrium binding experiments, ARGX-110 bound to human and cynomolgus monkey CD70 with affinities of approximately 0.4 nmol/L and 0.6 nmol/L, respectively. ARGX-110 inhibited in a dose-dependent fashion CD70/CD27-induced IL-8 release in Raji cells with IC50 values of 0.1 nmol/L. CD70 is minimally internalized (< 40%) by most hematological cell lines, thus providing a plausible rationale to develop a therapeutic mAb designed to enhance ADCC. In cell depletion studies, ARGX-110 was associated with comparable to better cell lysis compared to rituximab. Cell lysis by ARGX-110 was not dependent on the internalization rate of the ARGX-110/CD70 complex in hematological cell lines. Independence from CD70 copy numbers at the cell surface was also demonstrated. In a Burkitt lymphoma (CD70+ Raji cells) SCID mouse model, ARGX-110 administered intraperitoneally twice weekly at doses ranging from 0.001 to 10 mg/kg starting one day after inoculation resulted in a dose-response effect on animal survival. In cynomolgus monkeys, ARGX-110 did not demonstrate any toxicity upon repeated administration of high doses of 30 mg/kg. B, T and NK cell numbers remained unaltered. ARGX-110 is currently in phase I clinical trial for patients with CD70+ malignancies.

© European Society for Medical Oncology 2013. Published by Oxford University Press on behalf of the European Society for Medical Oncology and NDDO Education Foundation. All rights reserved.