Targeting CD74 in B-cell non-Hodgkin lymphoma with the antibody-drug conjugate STRO-001

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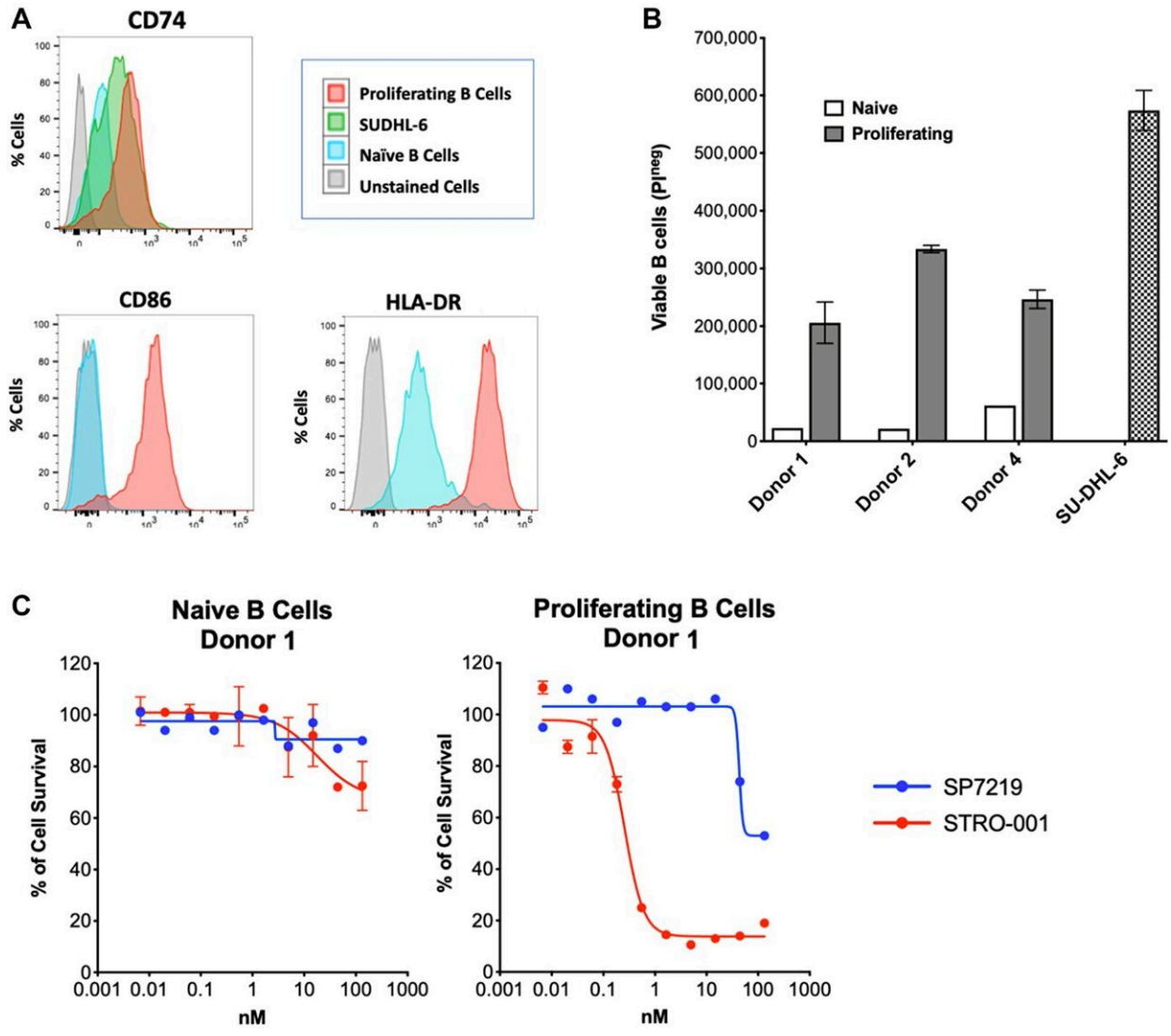

STRO-001 showed potent cell killing activity on proliferating primary human B

cells. (A) In vitro expanded primary B cells showed increased CD86, HLA-DR and CD74 expression compared to naïve B cells. (B) In vitro expanded B cell showed improved proliferation activity compared to naïve B cells. Cell proliferation was analyzed by flow cytometry using propidium iodide exclusion. (C) STRO-001 showed more potent cell killing of proliferating B cells (EC50 = 0.49 nM) than naïve B cells (EC50 = 11 nM). Credit: *Oncotarget* (2023). DOI: 10.18632/oncotarget.28341

A new research paper titled "Targeting CD74 in B-cell non-Hodgkin lymphoma with the antibody-drug conjugate STRO-001" has been published in *Oncotarget*.

Overexpression of CD74, a type II transmembrane glycoprotein involved in MHC class II antigen presentation, has been reported in many B-cell non-Hodgkin lymphomas (NHLs) and in multiple myeloma (MM). STRO-001 is a site-specific, predominantly single-species antibody-drug conjugate (ADC) that targets CD74 and has demonstrated efficacy in xenograft models of MM and tolerability in non-human primates.

In this new study, researchers from Sutro Biopharma reported the results of preclinical studies designed to elucidate the potential role of STRO-001 in B-cell NHL.

The researchers explain, "In order to explore the potential of STRO-001 in NHL, in the present study we investigated CD74 expression in cell types found in bone marrow, evaluated its cytotoxicity in NHL cell lines, and assessed its antitumor efficacy and toxicity in xenograft models of NHL."

STRO-001 displayed nanomolar and sub-nanomolar cytotoxicity in 88% (15/17) of cancer cell lines tested. STRO-001 showed potent cytotoxicity on proliferating B cells while limited cytotoxicity was observed on naïve

human B cells. A linear dose-response relationship was demonstrated in vivo for DLBCL models SU-DHL-6 and U2932. Tumor regression was induced at doses less than 5 mg/kg, while maximal activity with complete cures were observed starting at 10 mg/kg. In MCL Mino and Jeko-1 xenografts, STRO-001 starting at 3 mg/kg significantly prolonged survival or induced tumor regression, respectively, leading to tumor eradication in both models.

"In summary, high CD74 expression levels in tumors, nanomolar cellular potency, and significant anti-tumor in DLBCL and MCL xenograft models support the ongoing clinical study of STRO-001 in patients with B-cell NHL," the researchers conclude.

More information: Xiaofan Li et al, Targeting CD74 in B-cell non-Hodgkin lymphoma with the antibody-drug conjugate STRO-001, *Oncotarget* (2023). DOI: 10.18632/oncotarget.28341

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