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Abstract #509

Therapeutic targeting of CD74 with STRO-001 antibody-drug conjugate in AML and ALL

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Disclosures

None

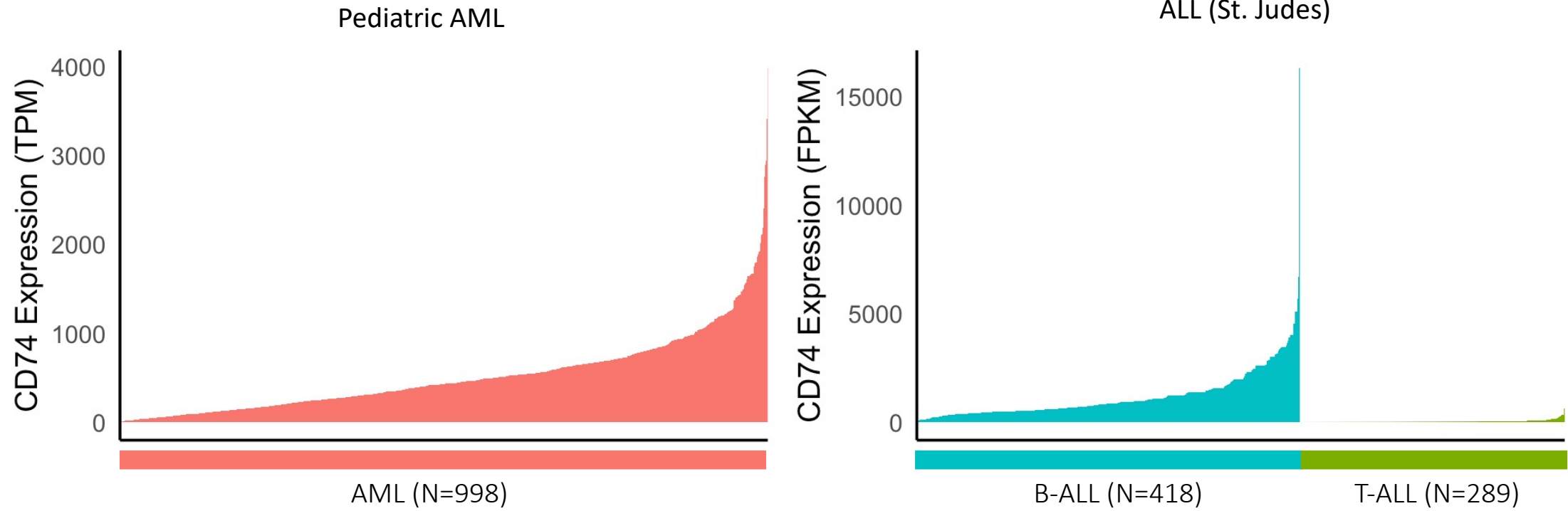
Biological functions of CD74

- Expressed in many immune cells (macrophages, monocytes, B- and T-cells, etc.)
- MHC class II chaperon
- Receptor for migration inhibitory factor (MIF)
- Regulates B cell maturation, proliferation and survival
- Mostly intracellular, and newly synthesized CD74 that gets to the cell surface is rapidly internalized through the endosomal pathway

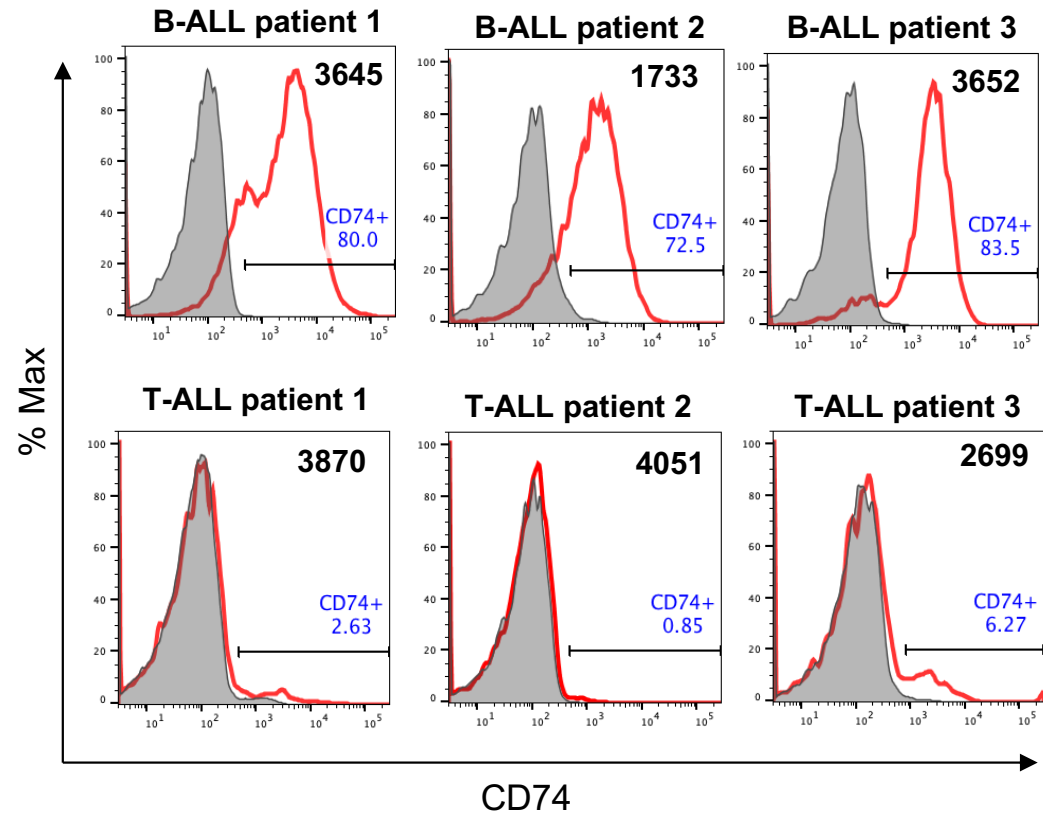
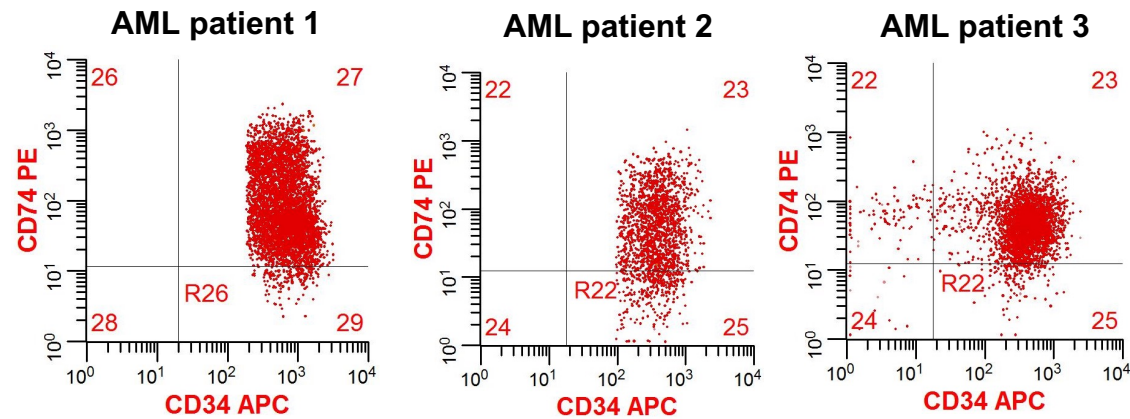
CD74 in cancer

- CD74 is expressed in variety of cancers
(B cell malignancies, multiple myeloma, AML, CML , and many solid tumors)
- Promotes cancer cell survival and progression
- Targeted therapies against CD74 have been developed and are currently being investigated in clinical trials (Milatuzumab and STRO-001)

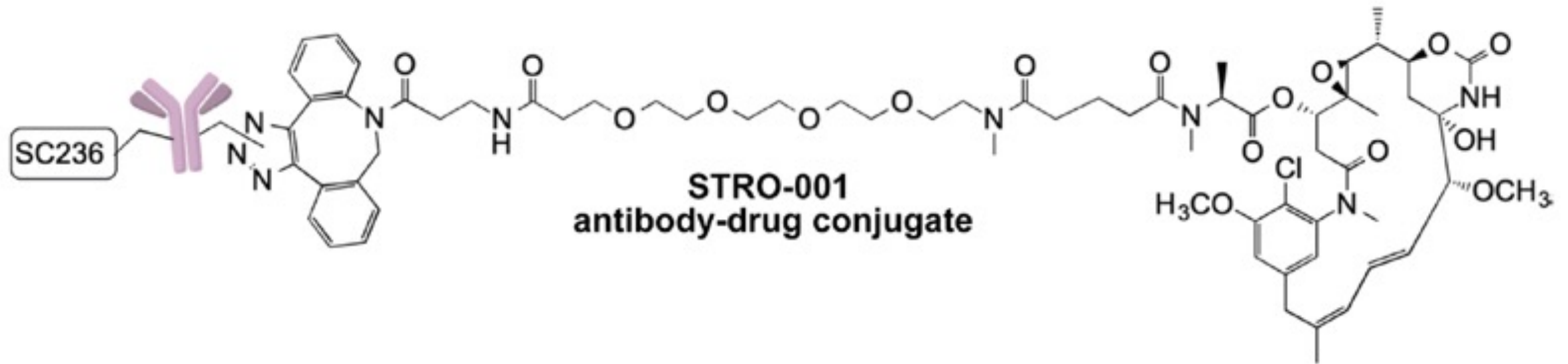
High transcript expression of CD74 in AML and B-ALL but not T-ALL



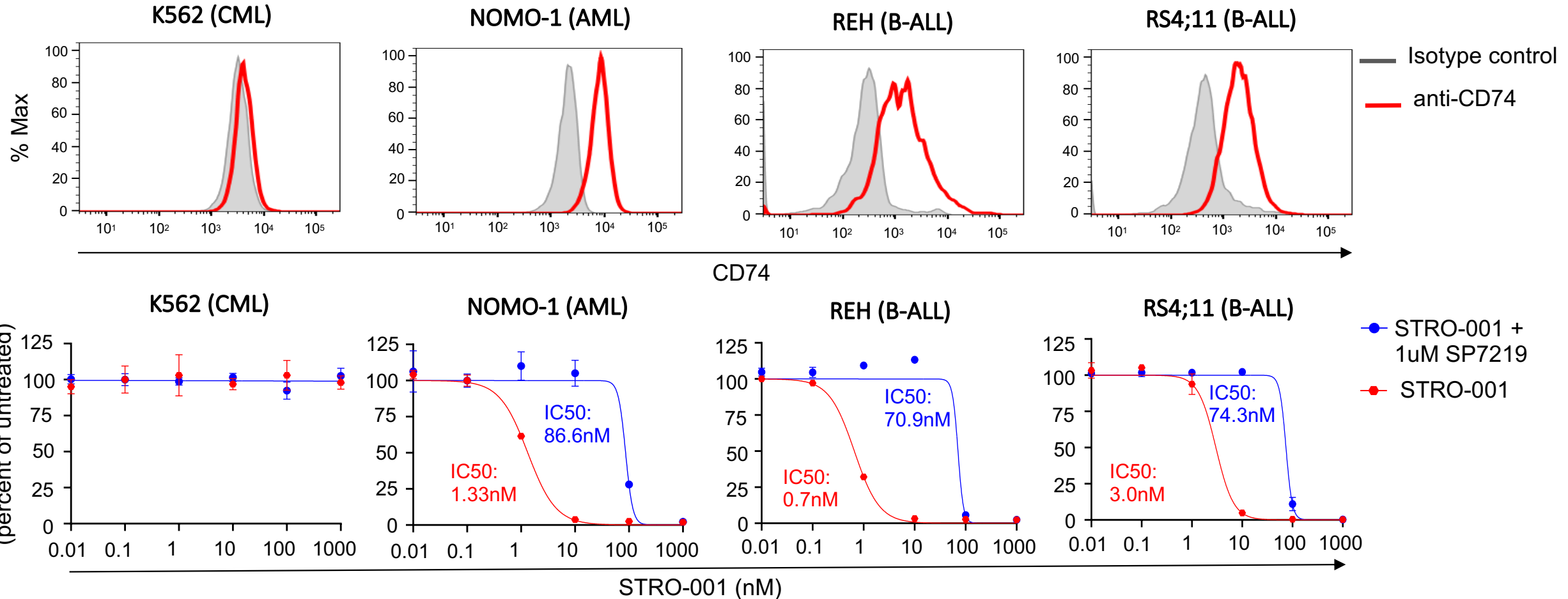
Cell surface expression of CD74 in AML and B-ALL but not T-ALL



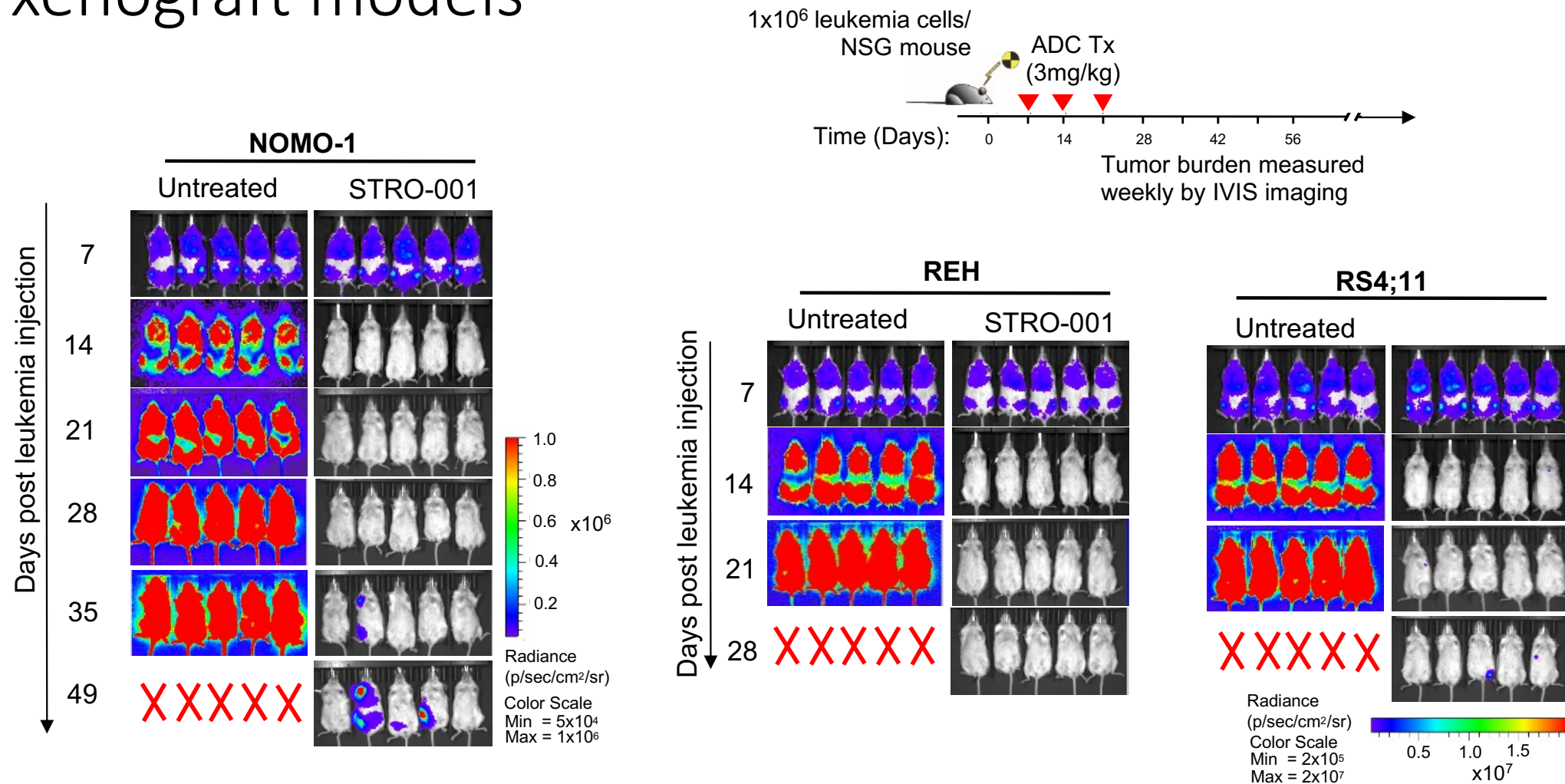
Is STRO-001 effective in AML and B-ALL?



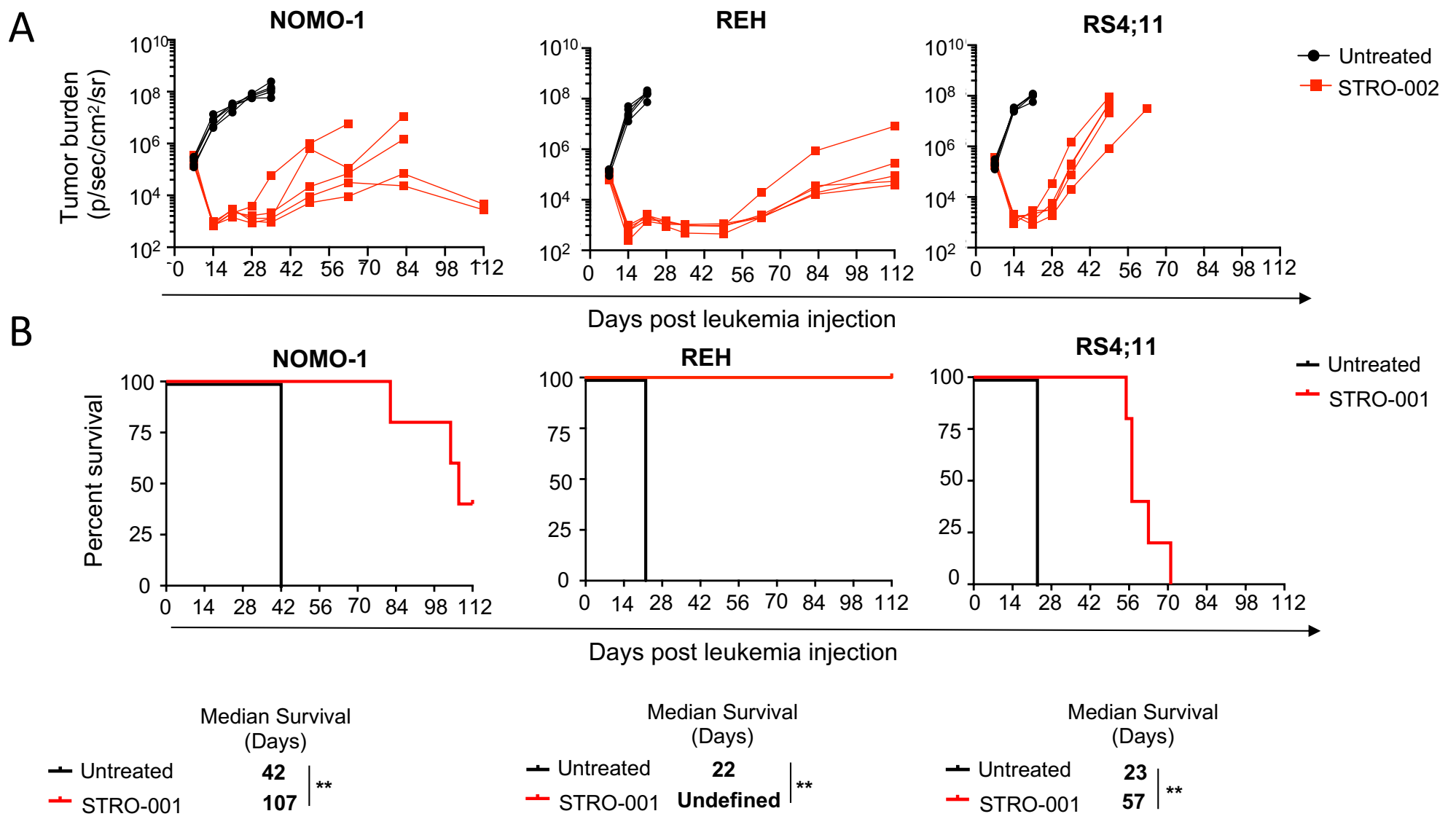
STRO-001 demonstrates target-specific cytotoxicity against CD74-positive AML and B-ALL cells



STRO-001 exhibits in vivo efficacy in NOMO-1, REH, and RS4;11 xenograft models

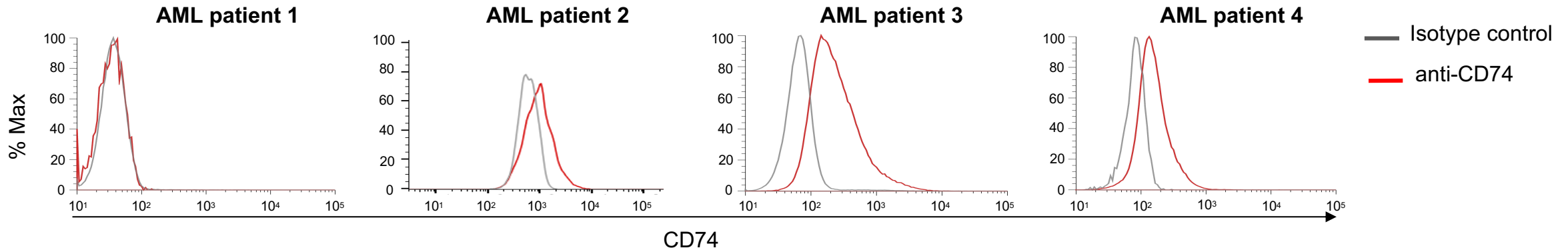


STRO-001 effectively eradicates leukemia cells in vivo and extends survival of leukemia-bearing mice

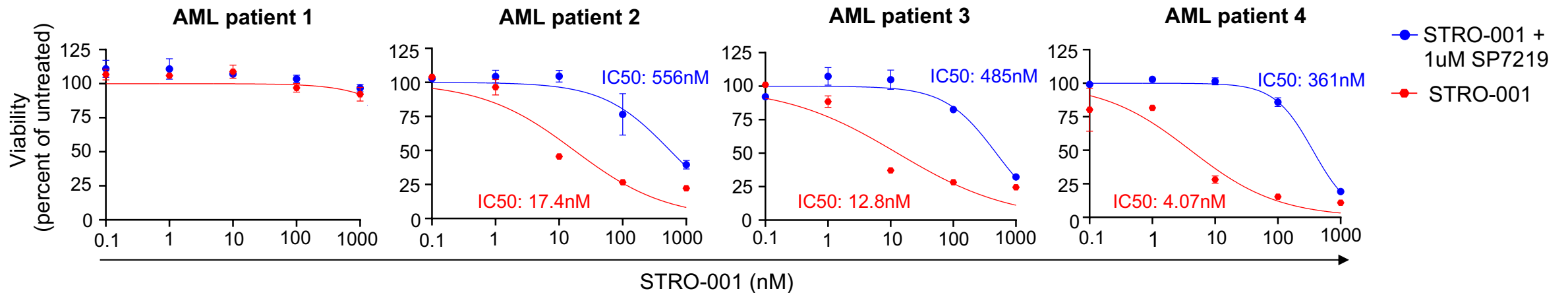


STRO-001 demonstrates potent, target-dependent cytotoxicity against CD74+ but not CD74- primary AML cells

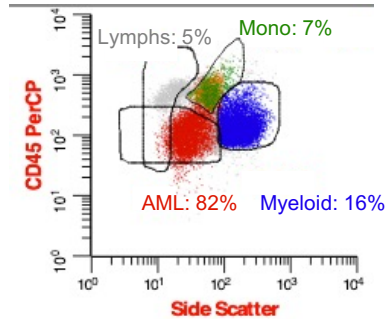
A



B



STRO-001 selectively eliminates primary AML cells in PDX model



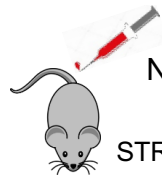
AML patient 4

- NUP98-NSD1
- FLT3/ITD
- WT1

AML patient 4
(7×10^6 cells/
NSG-SGM3 mouse)

Untreated: N = 3 mice
STRO-001 Tx: N = 3 mice

Day 0



Day 7

1st dose

Day 14

2nd dose

Day 21

3rd dose

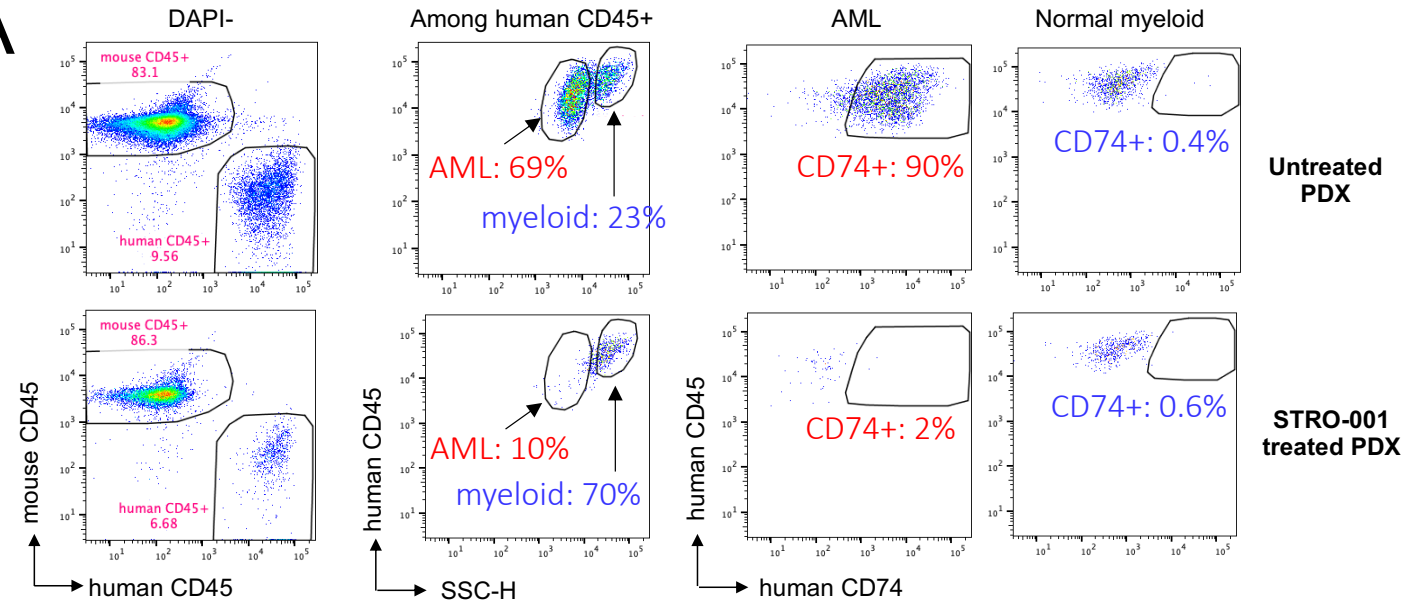
Day 28

4th dose

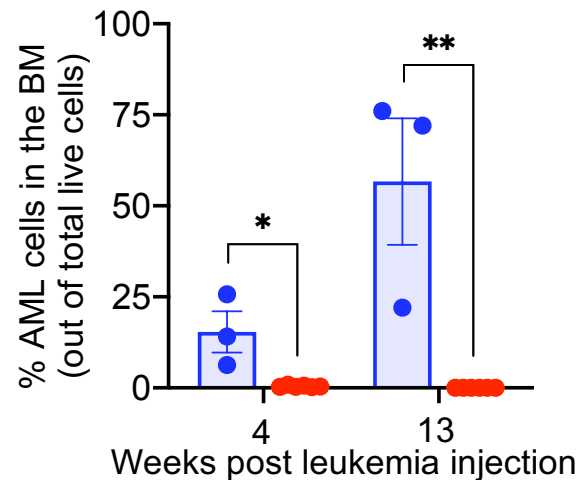
STRO-001 Tx
(3mg/kg)

Monitor survival and disease progression
by retro-orbital bleeds and bone marrow
aspirations

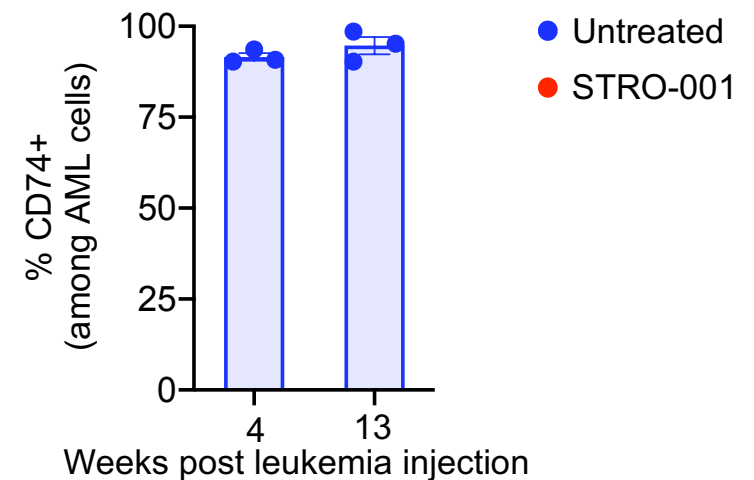
A



B



C



Summary

- CD74 is expressed at the transcript and protein level in AML and B-ALL but not T-ALL
- STRO-001 exhibits target-specific cytotoxicity against AML and B-ALL cells
- STRO-001 demonstrates effective killing of primary high-risk AML in vitro and in vivo

Future Directions

- Evaluate STRO-001 in vitro and in vivo activity in primary B-ALL samples
- Further IND-enabling studies are underway to support transitioning of STRO-001 into clinical testing for refractory/relapse AML and B-ALL

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