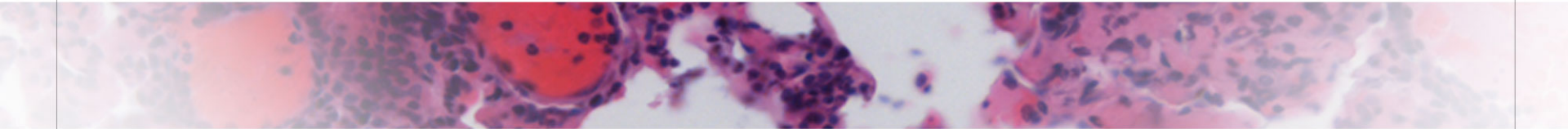




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High Frequency of CD74 Expression in B-cell Non-Hodgkin's Lymphoma (NHL) and Targeting with STRO-001, a Novel Anti-CD74 Antibody Drug Conjugate (ADC) with Potent In Vitro Cytotoxicity and In Vivo Anti-Tumor Activity

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Sutro Biopharma

ASH Annual Meeting

December 11, 2017

Co-Authors & Disclosures

Sutro Biopharma	Abigail Yu, Cristina Abrahams, Millicent Embry, Xiaofan Li, Robert Henningsen, Venita DeAlmeida, Shannon Matheny, Toni Kline, Alice Yam, Ryan Stafford, Trevor Hallam, Mark Lupher and Arturo Molina are employees of Sutro Biopharma
Stanford University	Shuchun Zhao, Yasodha Natkunam – No disclosures.



CD74 Expression in B-cell Lymphoma and Myeloma

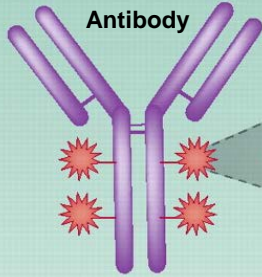
- CD74 is a transmembrane glycoprotein involved in MHC protein formation and transport
- Observed in ~90% of B-cell malignancies evaluated
- Minimally expressed in normal tissue

Immunohistology of patient biopsy specimens		
Diagnosis	No. positive / no. tested	% Target cells stained
Follicular lymphoma	8/9	>95%
Diffuse large B-cell lymphoma	4/4	~80%
Other NHL	31/35	ND
Small lymphocytic lymphoma / CLL	14/14	>90%
Multiple Myeloma	19/22	16/22, >95%; 3/22, ~50%

Stein R, et al. *Clin. Cancer Res.* 2007



Antibody Drug Conjugates: Components and Mechanism of Action



Linker

Drug

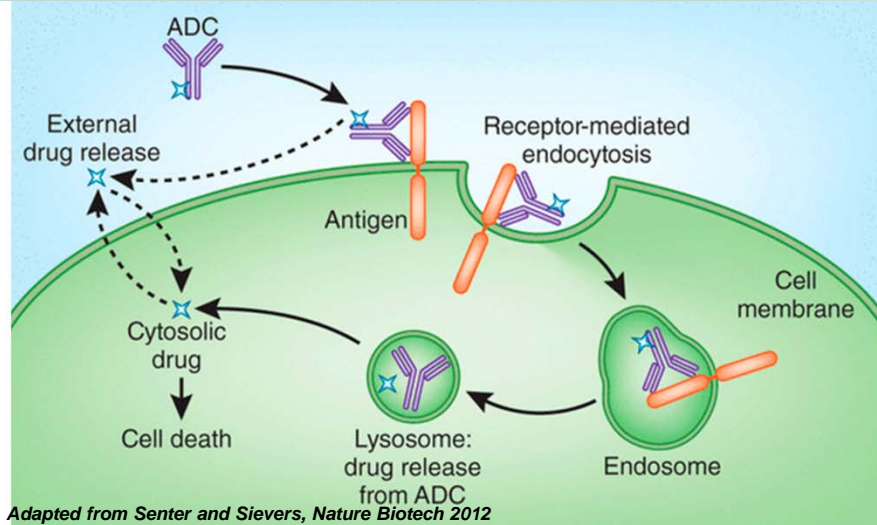
Antibody: Specifically targets the drug to the tumor cell, usually internalized upon binding to target

Conjugation site: Random (lysine) or site-specific

Linker: Cleavable or non-cleavable, stable in plasma

Drug: Cytotoxic with different MOA, tubulin inhibitors, DNA crosslinking agents, RNA pol inhibitors, number of drugs per antibody can vary

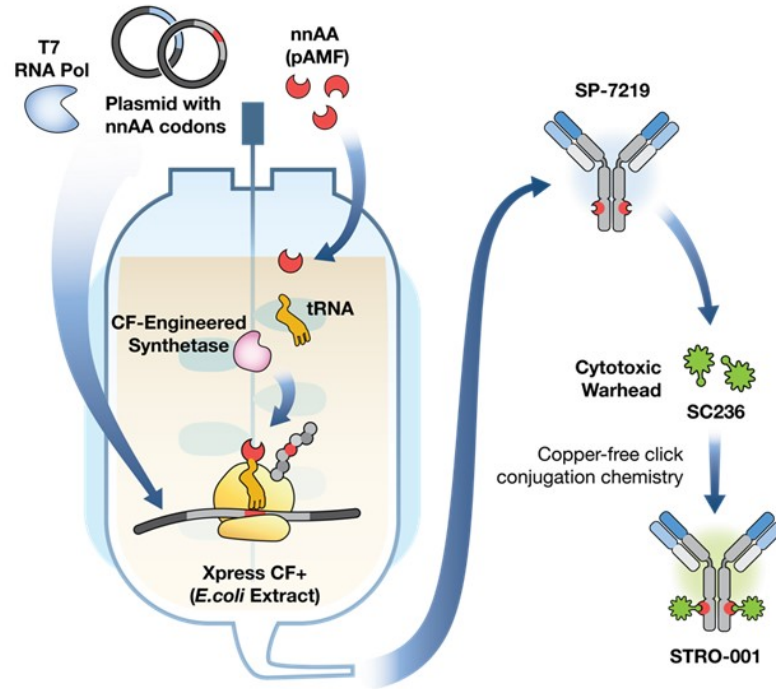
Adapted from Teicher & Chari, Clin Cancer Res 2011



Adapted from Senter and Sievers, Nature Biotech 2012



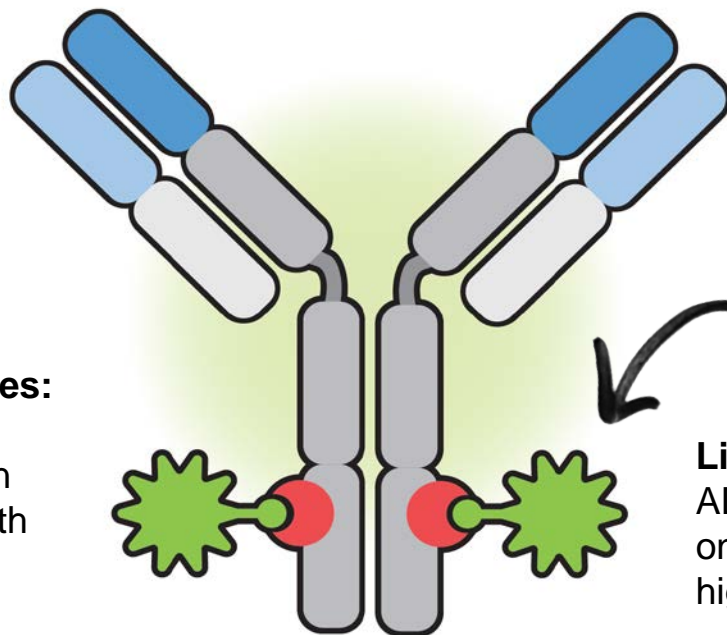
Sutro's CD74-Targeting ADCs: Cell-Free Aglycosylated Antibody Synthesis With Site-Specific Conjugation



STRO-001: Combining Optimized Antibody, Conjugation Sites, Linker and Warhead

Antibody:

Aglycosylated, high affinity and specificity



Warhead:

Non-cleavable maytansinoid linker-warhead. DAR of 2. Major catabolite has limited permeability

Optimized Conjugation Sites:

Specific sites that confer the highest linker drug stability in vivo, resulting in antibody with best activity

Linker:

ADC very stable in plasma, drug only released intracellularly, thereby higher specificity for target cells



Anti-CD74 Antibody SP7219 Binds to Both Human and Cyno CD74 Extracellular Domain with High Affinity

Biochemical Characterization of SP2719 Antibody	Kd
Biacore; recombinant human CD74 ECD	1.74 nM
Biacore; recombinant cynomolgus monkey CD74 ECD	2.70 nM
Biacore; recombinant mouse CD74 ECD	No Binding
FACS cell binding to human CD74 (CHO-huCD74)	0.93 nM
FACS cell binding to cynomolgus monkey CD74 (CHO-huCD74)	1.09 nM
FACS cell binding to mouse CD74 (A20 mouse B cell line)	No Binding

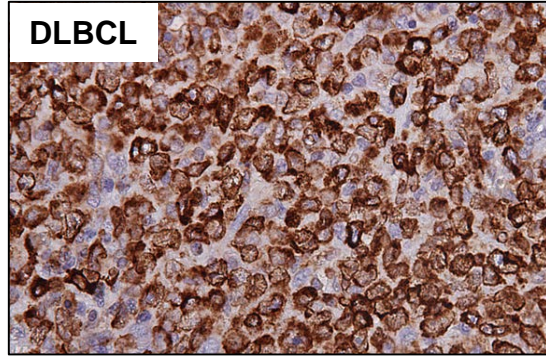


Frequent CD74 Expression in Multiple B-cell NHL Subtypes by IHC

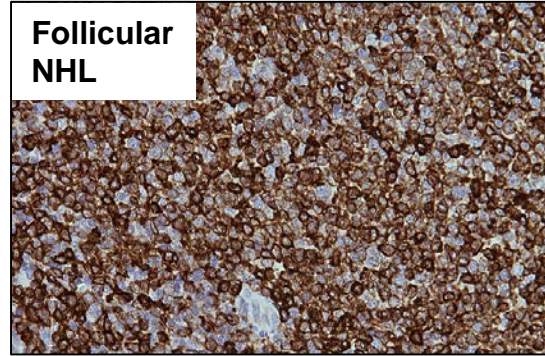
	CD74 positive	%
B cell lymphoma – total samples	404/423	96
Follicular lymphoma	148/151	98
Grade 1 and 2	90/91	99
Grade 3 A and B	58/60	97
Diffuse large B-cell lymphoma	135/140	96
Extranodal marginal zone lymphoma	22/24	92
Splenic marginal zone lymphoma	4/5	80
Nodal marginal zone lymphoma	6/6	100
Mantle cell lymphoma	19/21	90
SLL/CLL	36/36	100
Lymphoplasmacytic lymphoma	5/5	100



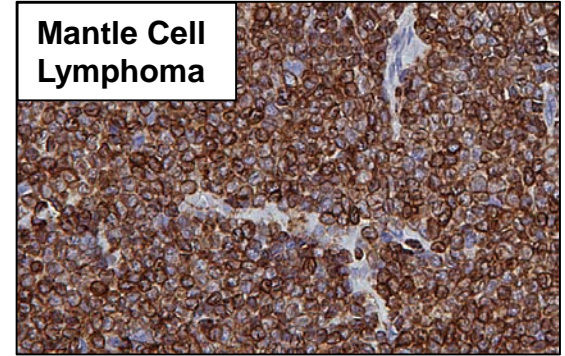
Frequent CD74 Expression in Multiple B-cell NHL Subtypes by IHC



x400



x400



x400



STRO-001 Exhibits Potent *In vitro* Cytotoxicity Across Multiple Cell lines

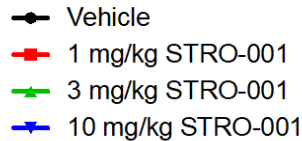
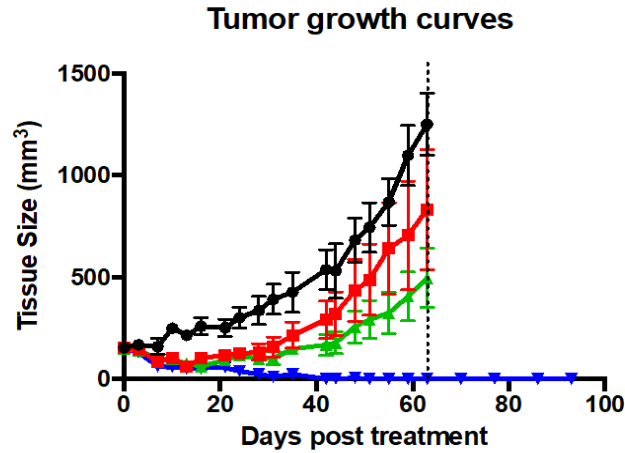
Disease	Cell Line	CD74 Receptor Copy#	STRO-001 Cell Killing	
			EC50 (nM)	Span (%)
Activated B-cell-like Diffuse Large B-Cell Lymphoma (ABC-DLBCL)	OCI-Ly3	77,435	0.54	95
	U2932	10,649	2	79
	RI-1	<4,131	3.7	72
	SU-DHL-2	<4,131	NC	NC
Germinal Center B-cell-like Diffuse Large B-Cell Lymphoma (GBC-DLBCL)	WSU-DLCL2	51,090	0.29	96
	WSU-NHL	49,925	0.8	96
	SU-DHL-4	49,603	0.36	97
	Pfeiffer	47,123	0.54	90
	SU-DHL-6	23,235	0.66	98
	OCI-Ly1	21,529	1	93
	HT	20,788	0.34	61
	NUDUL-1	13,040	0.34	98
Mantle Cell Lymphoma	OCI-Ly19	<4,131	1.4	54
	Mino	28,117	0.68	97
	JVM-2	23,672	1.7	55
	JeKo-1	14,754	0.41	97
	Rec-1	8,247	NC	NC

NC=Not Calculable

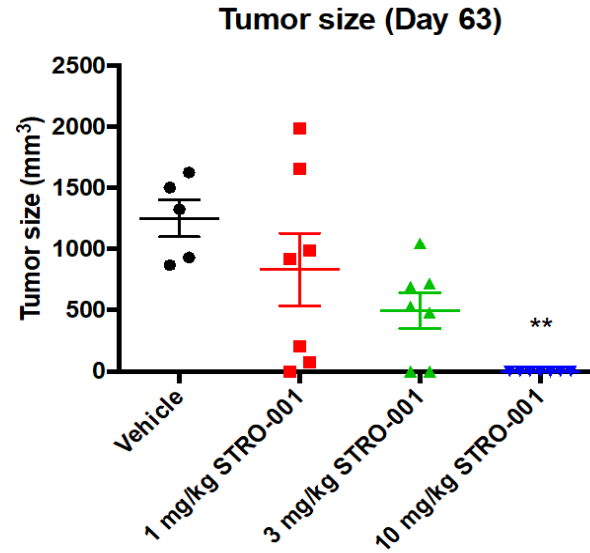


Effect of STRO-001 Treatment on U2932 ABC-DLBCL Xenograft Tumor Growth

A

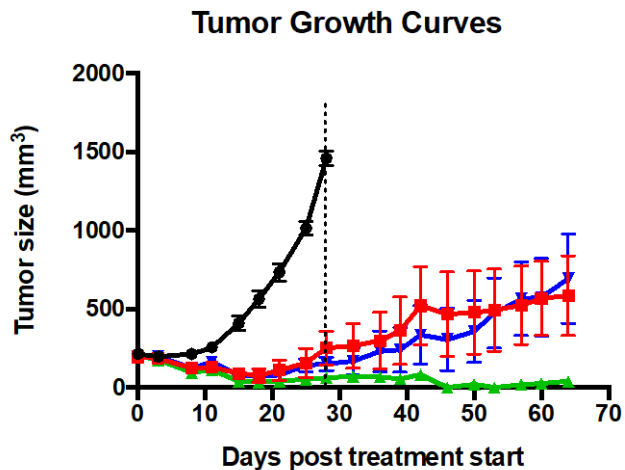


B



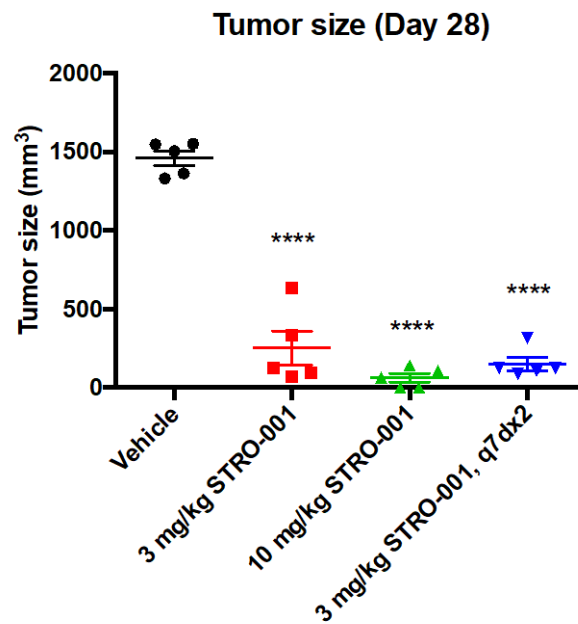
Effect of STRO-001 Treatment on Jeko-1 Mantle Cell Lymphoma Xenograft Tumor Growth

A

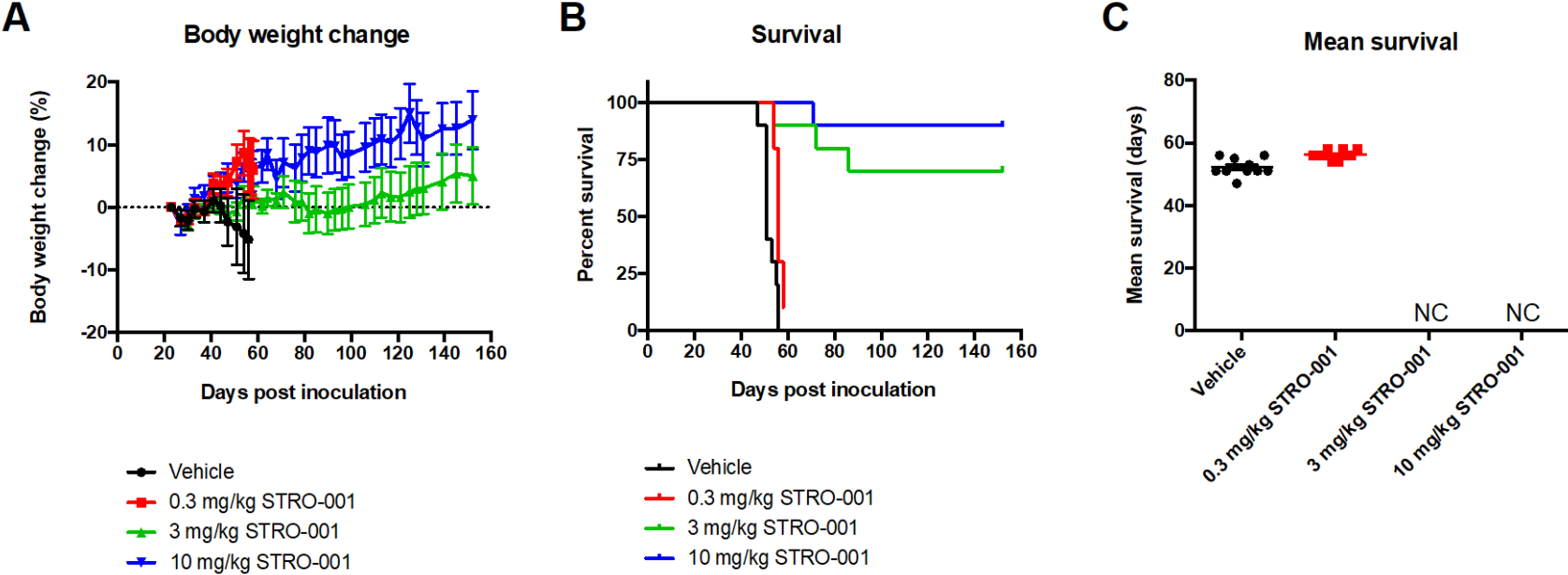


- Vehicle, q7dx2
- 3 mg/kg STRO-001, single dose
- ▲ 10 mg/kg STRO-001, single dose
- ▼ 3 mg/kg STRO-001, q7dx2

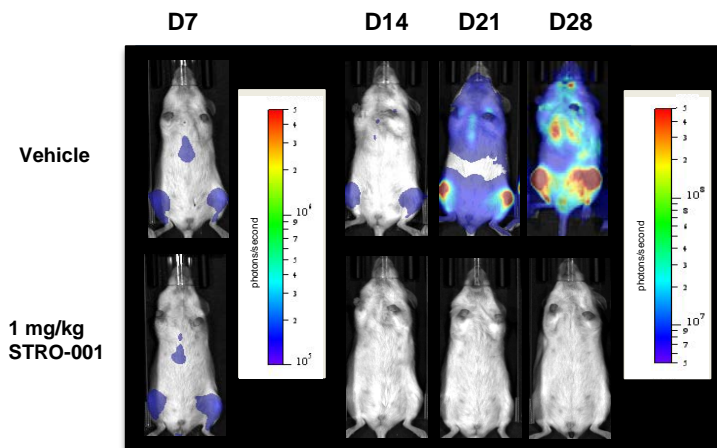
B



Effect of STRO-001 Treatment on Survival in the Disseminated Mino Mantle Cell Lymphoma Xenograft Model

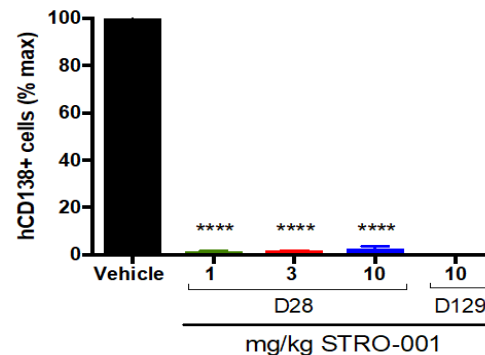
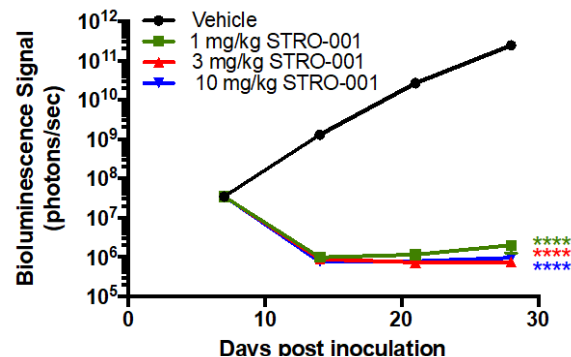


STRO-001 Demonstrates Potent Anti-tumor Activity in Disseminated MM.1S-luc Model



Similar response with 3 and 10 mg/kg STRO-001

- Single dose of 1, 3, and 10 mg/kg STRO-001 results in significant reduction of tumor burden on day 28 based on bioluminescence signal and quantification of CD138+ cells in bone marrow
- Eradication of disease on day 129 based on tumor burden assessment with CD138+ cells



Poster, abstract 4420, Embry M. et al, Monday, Dec 2017 ASH



Conclusions (1)

- Sutro's cell-free antibody synthesis and site-specific conjugation technologies were used to generate STRO-001, an optimized CD74-targeting ADC with a DAR of 2
- CD74 is detected in 404/423 (96%) of B-cell NHL specimens in this large IHC study
- STRO-001 exhibits potent *in vitro* cytotoxicity across multiple NHL cell lines



Conclusions (2)

- STRO-001 exhibits potent *in vivo* anti-tumor activity in NHL and myeloma xenograft models
- STRO-001 produces dose-dependent B cell depletion in the cynomolgus monkey, consistent with the intended pharmacodynamic effect
- STRO-001-BCM1, a phase 1 study of STRO-001 in B-cell NHL and myeloma will start enrollment in 1Q18

