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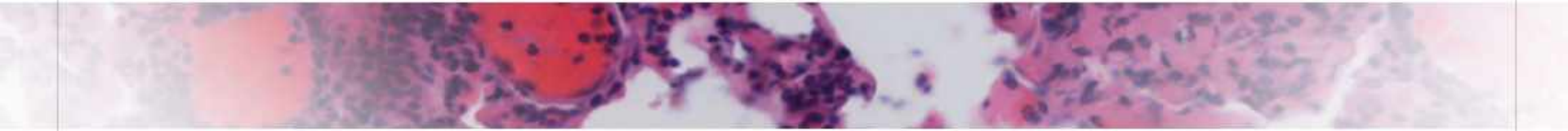

Preliminary results of an ongoing phase 1 dose-escalation study of the novel anti-CD74 antibody drug conjugate, STRO-001, in patients with B-cell non-Hodgkin lymphoma

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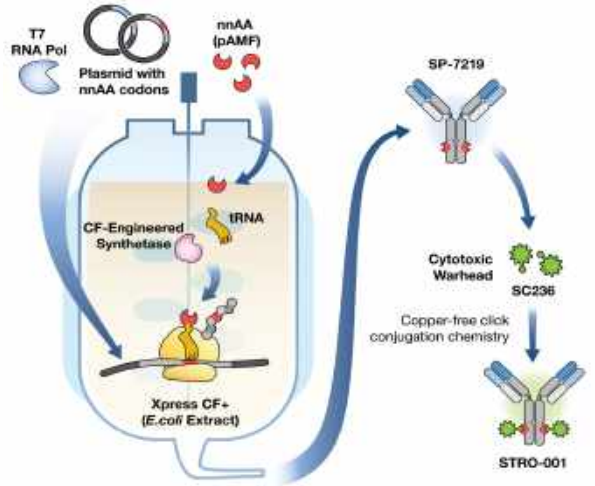
Background

- CD74 is highly expressed on ≈90% of B-cell malignancies, including NHL[1,2]
- STRO-001 is a novel CD74-targeting ADC, containing 2 noncleavable maytansinoid linker warheads per molecule, conjugated to specific nnAA sites[3]
- STRO-001-BCM1 (NCT03424603) is an ongoing first-in-human, phase 1, open-label, multicenter, dose-escalation study evaluating the safety, tolerability, and preliminary antitumor activity of STRO-001 in adults with B-cell malignancies (NHL and multiple myeloma)[4]
- Data presented here are from the NHL cohort

Generation of the CD74-Targeting Antibody and a Novel, Specific, and Homogenous ADC, STRO-001[5]



Using a cell-free expression system, the nnAA pAMF was incorporated at 2 sites in anti-CD74 (SP-7219). Optimal sites were selected based on conjugation efficiency, cell-killing activity, and PK in mice. Anti-CD74 was conjugated at pAMF to the cytotoxic-warhead to generate STRO-001.

ADC, antibody-drug conjugate; NHL, non-Hodgkin lymphoma; nnAA, non-natural amino acid; pAMF, para-azidomethyl-l-phenylalanine; PK, pharmacokinetics.

1. Yu A, et al. *Blood* 2017;130(Suppl 1):573. 2. Zhao S, et al. *J Pathol Clin Res* 2019;5:12-24. 3. Abrahams CL, et al. *Oncotarget* 2018;9(102):37700-37714. 4. Solis W, et al. *Cancer Res* 2018;78(13 Suppl):742. 5. Zimmerman ES, et al. *Bioconjug Chem* 2014;255(2);351-361.

Study Design

Objective

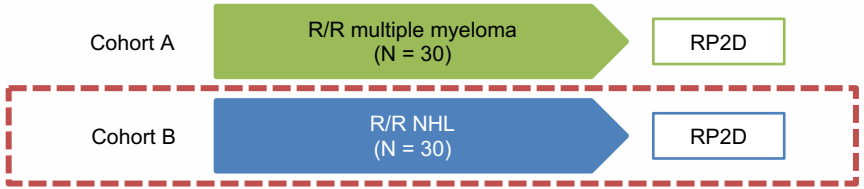
- To evaluate the safety, tolerability, and antitumor activity of STRO-001 in adult patients with NHL enrolled in this ongoing phase 1 dose-escalation study

Study Design

- A modified 3+3 design with accelerated dose titration (N = 1 per cohort until specified AEs or DLT were observed)

Key Eligibility

- Adult patients with R/R multiple myeloma were enrolled in Cohort A
- Adult patients with R/R NHL were enrolled in Cohort B



Study Treatment

- STRO-001 was administered as a 60-minute IV infusion at doses ranging from 0.05 to 2.5 mg/kg
  - Doses of 0.05 to 0.65 mg/kg were administered on day 1 and day 15 of a 28-day cycle
  - Doses of ≥ 0.91 were administered on day 1 of a 3-week cycle
- Treatment was administered until disease progression or unacceptable toxicity

Endpoints

Primary
- Safety and tolerability (AEs)
- Define RP2D (DLTs)

Secondary
- PK and immunogenicity (ADAs)

Exploratory
- Preliminary efficacy
- PK correlation with efficacy
- Biomarkers

AE, adverse event; ADA, antidrug antibody; DLT, dose-limiting toxicity; IV, intravenous; R/R, relapsed/refractory; RP2D, recommended phase 2 dose.

Demographics and Baseline Characteristics

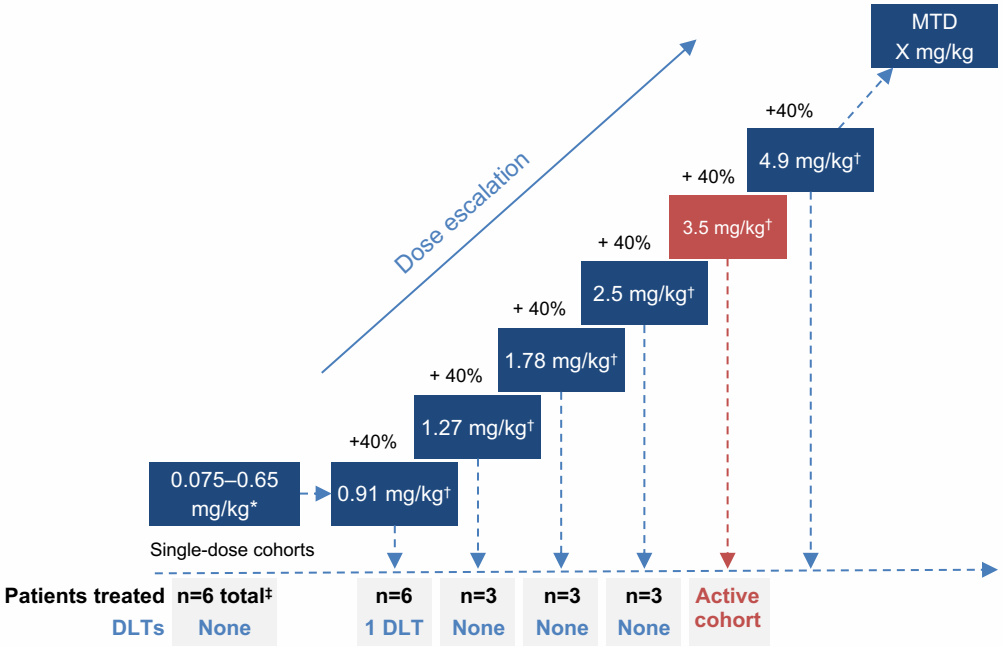
Characteristic	(N=21)*
Age, median (range), years	64.5 (21–82)
Sex, n(%)	
Female	6 (28.4)
Male	15 (71.4)
Time from diagnosis, median (range), years	6.0 (1.0–29.8)
ECOG PS, n (%)	
0	9 (42.9)
1	11 (52.4)
2	1 (4.8)
Race, n (%)	
Black or African American	1 (4.8)
White	19 (90.5)
Other	1 (4.8)

Characteristic	(N=21)*
NHL subtype, n (%)	
DLBCL	7 (33)
Follicular lymphoma	7 (33)
MCL	2 (10)
Marginal zone lymphoma	2 (10)
Burkitt's Lymphoma	1 (5)
Composite DLBCL/FL	1 (5)
Composite DLBCL/CLL	1 (5)
Number of prior therapies, median (range)	5 (1-12)
Prior therapies, n (%)	
Autologous stem cell transplant	2(10)
Unrelated allogeneic stem cell transplant	1 (5)
CAR-T therapy	3 (14)

CAR-T, chimeric antigen receptor T cell; CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; MCL, mantle cell lymphoma.

*21 patients with NHL have been treated with STRO-001 as of October 30, 2020.

Dose-Escalation Status



NHL Cohort

- A total of 21 patients have been treated with STRO-001 (dose range, 0.05-2.5 mg/kg)
- MTD has not been reached
- As of October 30, 2020, 1 DLT of grade 3 pulmonary embolism was observed (patient with bulky lymphadenopathy and concurrent DVT receiving 0.91 mg/kg Q3W)
- Study screening procedures were updated to screen for potential DVT with no subsequent thromboembolic events reported
- Dosing frequency was modified from Q2W (28-day cycle) to Q3W (21-day cycle) for doses ≥ 0.91 mg/kg

MTD, maximum tolerated dose; DVT, deep venous thrombosis; Q2W, every 2 weeks; Q3W, every 3 weeks.
* STRO-001 was administered on day 1 and day 15 of 28-day cycle for doses 0.05 to 0.65 mg/kg (Q2W). † STRO-001 was administered on day 1 of 3-week cycle for doses ≥0.91 mg/kg (Q3W).
‡ In each of 6 single-dose cohorts, 1 patient each received doses of 0.05, 0.075, 0.15, 0.27, 0.43, and 0.65 mg/kg Q2W.

Treatment-Emergent Adverse Events

- Most TEAEs were Grade 1 or 2 (90%)
- No ocular or neuropathy toxicity signals have been observed

TEAE (Any Grade), Occurring in ≥ 15% of Patients With NHL	Patients, n (%) (N=21)
Nausea	9 (42.9)
Fatigue	7 (33.3)
Chills	7 (33.3)
Anemia	6 (28.6)
Headache	6 (28.6)
Dyspnea	5 (23.8)
Abdominal pain	5 (23.8)
Infusion related reaction	4 (19.0)
Decreased appetite	4 (19.0)
Vomiting	4 (19.0)
Pyrexia	4 (19.0)

TEAEs by Grade, Occurring in ≥ 15% of Patients With NHL	Patients With ≥1 Event, n (%)			
	Grade 1	Grade 2	Grade 3	Grade 4
Nausea	5 (23.8)	4 (19.0)	0	0
Fatigue	4 (19.0)	3 (14.3)	0	0
Chills	7 (33.3)	0	0	0
Anemia	3 (14.3)	2 (9.5)	1 (4.8)	0
Headache	2 (9.5)	4 (19.0)	0	0
Dyspnea	1 (4.8)	3 (14.3)	1 (4.8)	0
Abdominal pain	4 (19.0)	1 (4.8)	0	0
Infusion related reaction	1 (4.8)	3 (14.3)	0	0
Vomiting	2 (9.5)	2 (9.5)	0	0
Decreased appetite	3 (14.3)	1 (4.8)	0	0
Pyrexia	3 (14.3)	1 (4.8)	0	0

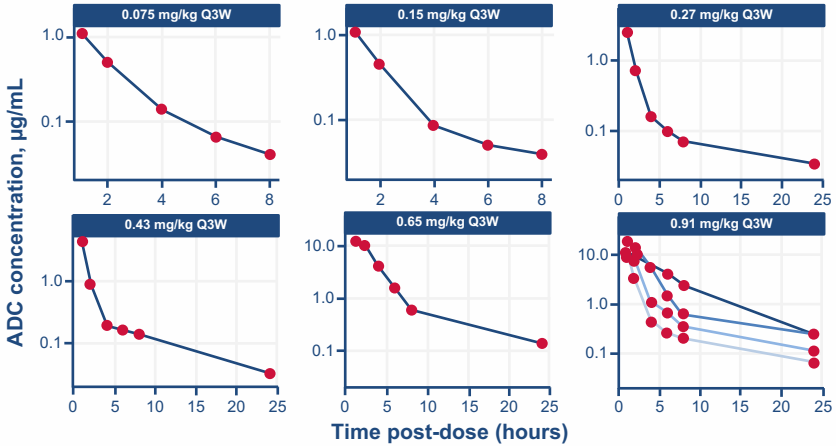
NHL, non-Hodgkin lymphoma; TEAE, treatment-emergent adverse event.

Pharmacokinetics

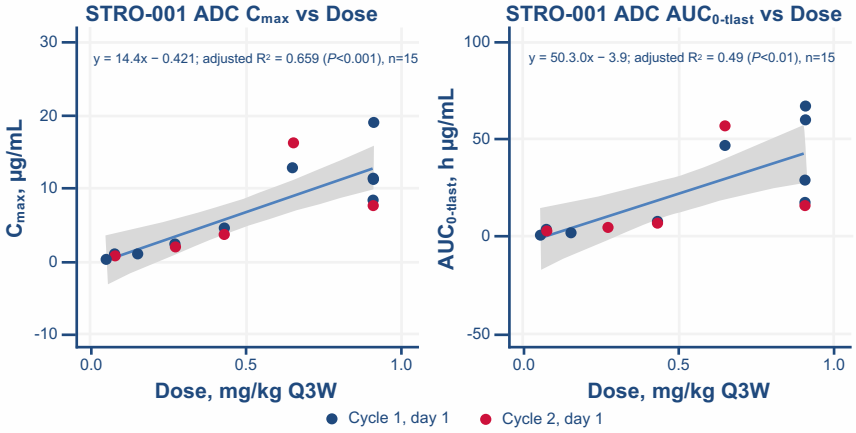
Pharmacokinetics Summary

- Cycle 1 and 2 ADC concentration-time data were available in 15 patients (10 [0.05 to 0.91 mg/kg] and 5 [0.075 to 0.91 mg/kg])
- Maximum concentrations were achieved at the end of infusion
- Following infusion, concentrations exhibited a biphasic decline (lower limit of quantitation by 4 to 24 hours)
- No accumulation was observed
- The half-life estimation is limited by the small sample size
- The exposure (C_{max} and $AUC_{0\text{-tlast}}$)-dose relationship appeared linear

ADC Cycle 1 Concentration-Time Profiles by Dose Group



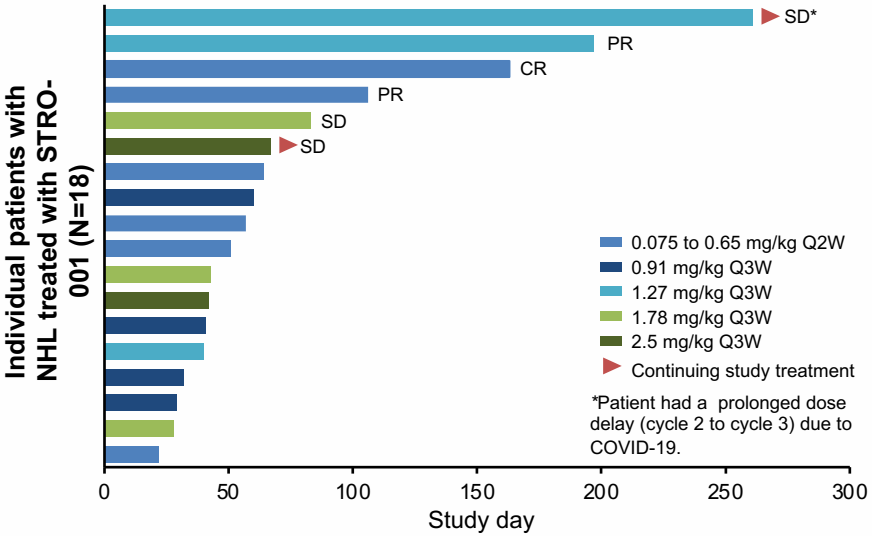
ADC Exposure-Dose Relationship



$AUC_{0\text{-tlast}}$, area under the concentration-time curve from time 0 to time of last measurable concentration; C_{max}, maximum concentration.

Treatment Duration and Responses

Treatment Duration



Response	Patients, n	STRO-001 Dose	NHL subtype
CR	1	0.075 mg/kg	DLBCL
PR	2	0.65, 1.27 mg/kg	DLBCL
SD	3	1.27, 1.78, 2.5 mg/kg	Marginal Zone and Follicular
PD	12	Multiple	

Responses to STRO-001

Dose Level, mg/kg	Demographics and Diagnosis	Prior Therapies	Best Responses	Doses Received	Duration of Treatment
0.075	82-year-old man with Stage III DLBCL, non-GC type diagnosed in 2015	- R-CHOP-R, - Rituximab/lenalidomide - Bendamustine/rituximab - Obinituzumab + gemcitabine + oxaliplatin	CR after 2 cycles (4 doses)	12	24 Weeks (PD after 12 doses)
0.65	64-year old man diagnosed with double-hit Stage IV DLBCL in August 2017	- R-CHOP x 1 and EPOCH X 6 (2017) - RICE with IT prophylaxis (2017/2018) - Rituximab and XRT (2018) - Rituximab, gemcitabine + oxaliplatin with radiotherapy (2018) - Axicabtagene ciloleucel (CAR-T) (May 2018) - Rituximab and lenalidomide (Nov 2018)	PR at cycle 3	8	15 weeks (PD after 8 doses)
1.27	68-year old woman stage IV extranodal DLBCL, non-GC diagnosed in Feb 2018	- R-CHOP - RICE x 2 - DHAP x 2 - CAR-T (May 2019) - Lenalidomide (Nov 2019)	PR at cycle 3	10	27 weeks ongoing (PD at cycle 10)
1.27	51-year old woman, stage III marginal zone lymphoma diagnosed in May 2017	- Obinutuzumab	SD	6	39 weeks ongoing
1.78	36-year old man with stage IIIA follicular lymphoma diagnosed in June 2014	- Flt3L-vaccine immunotherapy - Rituximab - Pneumococcal conjugate vaccine immunotherapy - polyCLC (TLR-3 agonist) – immunotherapy - Pembrolizumab	SD	4	12 weeks (PD after Cycle 4)
2.50	74-year old man with IV follicular lymphoma	- Reituximab/fludarabine/Cytoxan - Ifosfamide/carboplatin, etoposide - Auto SCT	SD	3	9 weeks on active treatment

CAR-T, chimeric antigen receptor T cell therapy; CR, complete response; DLBCL, diffuse large B-cell lymphoma; GC, germinal center; PD, progressive disease; PR, partial response; SD, stable disease.

Summary and Conclusions

- STRO-001 was generally well tolerated in this cohort of patients with R/R NHL
  - Most AEs were grade 1 or 2; no ocular toxicity has been observed
  - A single DLT of pulmonary thromboembolism was observed at 0.91 mg/kg; no further pulmonary thromboembolism events were observed after the protocol was amended to require screening imaging for potential thromboses
  - The MTD has not been reached; STRO-001 is in dose escalation at 3.5 mg/kg
- Antitumor activity was observed in this heavily pretreated patient population
  - The CR and 2 PRs were in patients with DLBCL, including 2 who had previously progressed after CAR-T therapy
- Exposure (C_{max} and $AUC_{0\text{-}tlast}$)-dose relationship appeared to be linear
- Current safety and efficacy data support continued enrollment and further evaluation of STRO-001 in patients with relapsed/refractory NHL