Abstract 5580: Phase I, Multicenter, first-in-human (FIH) global study of SIM0505, an anti-CDH6 antibody-drug-conjugate (ADC) in patients with advanced solid tumors.

Xiaohua Wu[1], Rujiao Liu[1], Xiaowei Liu[2], Yan Zhang[3], Dihong Tang[4], Shusuan Jiang[4], Jundong Li[5], Daruka Mahadevan[6], Cesar A. Perez[7], Beryl Manning-Geist[8], Dmitriy Zamarin[9], Miguel Gonzalez-Velez[10], Sarah Premji[11], Hongxia Wang[1], Jiajia Li[1], Rong Sun[12], Qi Fu[12], Haolin Sun[12], Ashley Martz[13], Udayan Guha[13]

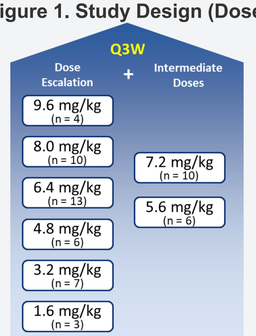
[1]Fudan University Shanghai Cancer Center; [2]Affiliated Hospital of Jining Medical University; [3]Cancer Hospital of Shandong First Medical University; [4]Hunan Cancer Hospital; [5]Sun Yat-Sen University Cancer Center; [6]Univ of Texas Health; [7]SCRI at Florida Cancer Specialists; [8]Emory University; [9]Icahn School of Medicine at Mount Sinai; [10]Hackensack Meridian Health; [11]Sarah Cannon Research Institute; [12]Shanghai Simcere Zaiming Biotech; [13]NextCure, Inc

Background

Cadherin 6 (CDH6) is a transmembrane glycoprotein overexpressed in multiple cancers, including ovarian cancer (OC) and endometrial cancer (EC). SIM0505 is an ADC comprised of an anti-CDH6 humanized IgG1 monoclonal antibody, a stable linker cleaved within tumor cells, and a novel topoisomerase I inhibitor, CPT116. Here, we report initial results from a global FIH study of SIM0505 (NCT06792552).

Methods

Figure 1. Study Design (Dose Escalation)



This is a Phase 1 study using a Bayesian Optimal Interval (BOIN) dose escalation design to evaluate the safety, tolerability, pharmacokinetics, and preliminary anti-tumor activity of SIM0505 in patients (pts) with advanced solid tumors regardless of CDH6 expression. SIM0505 was administered IV every 21 days.

As of 7 Apr 2026, 59 pts were enrolled without preselection for CDH6 expression (46 OC, 10 EC, 3 renal cell cancer) in the dose-escalation (1.6 mg/kg to 9.6 mg/kg). The median duration of follow-up was 5.22 months (range 0.1-10.6).

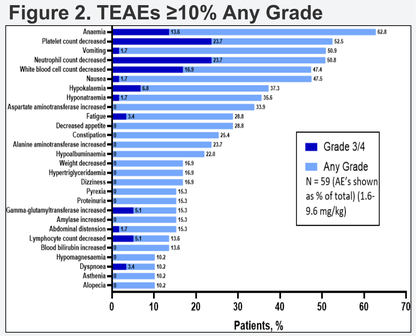
Demographics

Table 1. Study Patient Demographics

Baseline Characteristic	All Patients (n = 59)
Age, years	
Median (range)	58 (42-78)
Sex, n (%)	
Male	2 (3.4%)
Female	57 (96.6%)
Race, n (%)	
Asian	34 (57.6%)
Black or African American	3 (5.1%)
White	20 (33.9%)
Other	2 (3.4%)
Tumor Type, n (%)	
Ovarian	46 (78.0%)
Uterine Serous Carcinoma/Other Endometrial	10 (16.9%)
Renal Cell Carcinoma	3 (5.1%)
ECOG performance status, n (%)	
0	16 (27.1%)
1	43 (72.9%)
Prior systemic anti-cancer regimens	
Median (range)	5 (1-12)
Prior Therapies in Ovarian Cancer, n (%)	
Prior Exposure to Bevacizumab	36 (78.3%)
Prior Exposure to PARP	30 (65.2%)
Prior Exposure to Mirvetuximab soravtansine	11 (23.9%)
FIGO stage (for gynecologic cancers), n (%)	
Stage II	2 (3.6%)
Stage III	12 (21.8%)
Stage IV	42 (75.0%)

Safety Summary

Figure 2. TEAEs ≥10% Any Grade



- TEAEs leading to Dose Reduced (n=12): Predominantly hematological (4.8 – 9.6mg/kg), with majority at 8.0mg/kg. Non-hematological events: fatigue, dyspnoea, and nausea/vomiting (n=1 each)
- TRAEs leading to Dose Discontinued (n=3): Grade (Gr) 2 Interstitial Lung Disease (ILD) and Gr3 fungal pneumonia at 6.4mg/kg, Gr4 thrombocytopenia at 9.6mg/kg
- Adverse Events of Special Interest (AESI): Pneumonitis (n=1, Gr 1 at 5.6mg/kg), ILD (n=1, Gr 2 at 6.4mg/kg)
- No primary prophylaxis for hematological toxicities used

Results

Safety By Dose Levels

Table 2. Overall Safety Summary

Overview of Adverse Events	1.6 mg/kg (n = 3) n (%)	3.2 mg/kg (n = 7) n (%)	4.8 mg/kg (n = 6) n (%)	5.6 mg/kg (n = 6) n (%)	6.4 mg/kg (n = 13) n (%)	7.2 mg/kg (n = 10) n (%)	8.0 mg/kg (n = 10) n (%)	9.6 mg/kg (n = 4) n (%)	Total (n = 59) n (%)
Treatment-emergent adverse events (TEAEs) (%)	3 (100.0)	7 (100.0)	6 (100.0)	6 (100.0)	13 (100.0)	10 (100.0)	10 (100.0)	4 (100.0)	59 (100)
≥Grade 3 TEAEs (%)	1 (33.3)	1 (14.3)	5 (83.3)	1 (16.7)	6 (46.2)	6 (60.0)	9 (90.0)	3 (75.0)	32 (54.2)
TEAEs related to study drug (TRAEs) (%)	3 (100.0)	7 (100.0)	6 (100.0)	6 (100.0)	12 (92.3)	9 (90.0)	10 (100.0)	4 (100.0)	57 (96.6)
≥Grade 3 TRAEs (%)	0	0	4 (66.7)	1 (16.7)	6 (46.2)	5 (50.0)	9 (90.0)	3 (75.0)	28 (47.5)
Serious adverse events (SAEs) (%)	1 (33.3)	1 (14.3)	1 (16.7)	0	3 (23.1)	3 (30.0)	5 (50.0)	2 (50.0)	16 (27.1)
SAEs related to study drug (%)	0	0	0	0	3 (23.1)	2 (20.0)	3 (30.0)	2 (50.0)	10 (16.9)
TEAEs leading to dose interruption (%)	1 (33.3)	0	4 (66.7)	0	6 (46.2)	1 (10.0)	5 (50.0)	3 (75.0)	20 (33.9)
TRAEs leading to dose interruption (%)	0	0	3 (50.0)	0	3 (23.1)	0	5 (50.0)	3 (75.0)	14 (23.7)
TEAEs leading to dose reduced (%)	0	0	2 (33.3)	0	2 (15.4)	1 (10.0)	6 (60.0)	1 (25.0)	12 (20.3)
TRAEs leading to dose reduced (%)	0	0	2 (33.3)	0	2 (15.4)	1 (10.0)	5 (50.0)	1 (25.0)	11 (18.6)
TEAEs leading to dose discontinued (%)	0	0	0	0	2 (15.4)	1 (10.0)	0	1 (25.0)	4 (6.8)
TRAEs leading to dose discontinued (%)	0	0	0	0	2 (15.4)	0	0	1 (25.0)	3 (5.1)
TEAEs leading to death (%)	0	0	0	0	0	1 (10.0)*	1 (10.0)#	0	2 (3.4)
Adverse Event of Special Interest (AESI) [1]	0	0	0	1 (16.7)	1 (7.7)	0	0	0	2 (3.4)
Dose limiting toxicity (DLT) (%) [2]	0	0	0	0	0	1 (10.0)	1 (10.0)	1 (25.0)	3 (5.1)
Prior Regimens of therapy Median (Range)	6 (2-10)	4 (3-11)	4 (1-9)	6.5 (5-11)	4 (1-10)	4.5 (2-12)	4.5 (2-7)	6 (5-8)	5 (1-12)

TEAE: Treatment-emergent adverse event, TRAE: Treatment-related adverse event [1] DLT: 9.6mg/kg- Gr 4 thrombocytopenia, Gr 4 febrile neutropenia and Gr 3 Gastrointestinal (GI) hemorrhage in same patient), 8.0mg/kg- Gr 3 febrile neutropenia, 7.2mg/kg-Gr 2 febrile neutropenia;
* Gr 5: Dyspnoea from disease progression # Gr 5 Urinary tract infection; both unrelated to SIM0505

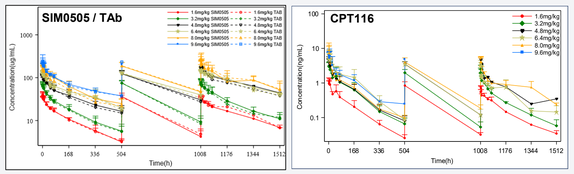
Table 3. Grade ≥ 3* TEAEs Occurring in ≥ 5% of Patients

Overview of Adverse Events	1.6 mg/kg (n = 3) n (%)	3.2 mg/kg (n = 7) n (%)	4.8 mg/kg (n = 6) n (%)	5.6 mg/kg (n = 6) n (%)	6.4 mg/kg (n = 13) n (%)	7.2 mg/kg (n = 10) n (%)	8.0 mg/kg (n = 10) n (%)	9.6 mg/kg (n = 4) n (%)	Total (n = 59) n (%)
With at least one ≥G3 TEAE	1 (33.3)	1 (14.3)	5 (83.3)	1 (16.7)	6 (46.2)	6 (60.0)	9 (90.0)	3 (75.0)	32 (54.2)
Platelet count decreased	0	0	3 (50.0)	0	4 (30.8)	0	5 (50.0)	2 (50.0)	14 (23.7)
Neutrophil count decreased	0	0	1 (16.7)	0	2 (15.4)	3 (30.0)	6 (60.0)	2 (50.0)	14 (23.7)
White blood cell count decreased	0	0	3 (50.0)	0	1 (7.7)	0	3 (30.0)	3 (75.0)	10 (16.9)
Anemia	0	0	0	0	2 (15.4)	0	3 (30.0)	3 (75.0)	8 (13.6)
Hypokalemia	0	0	0	0	1 (7.7)	1 (10.0)	2 (20.0)	0	4 (6.8)
Gamma-glutamyltransferase increased	0	0	1 (16.7)	0	2 (15.4)	0	0	0	3 (5.1)
Febrile neutropenia	0	0	0	0	0	1 (10.0)	1 (10.0)	1 (25.0)	3 (5.1)
Lymphocyte count decreased	0	0	0	1 (16.7)	2 (15.4)	0	0	0	3 (5.1)

*Gr 3-4 only

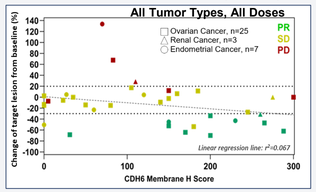
Biomarkers and Pharmacokinetic Profile

Figure 3. Pharmacokinetic (PK) Profile of SIM0505



- SIM0505 (ADC) / Total Antibody (TAb) exposures had similar and dose proportional increase
- No to minimal accumulation of SIM0505 (Rac AUC ~1.3- 1.8) or CPT116 (Rac AUC ~ 0.4-1.3)
- Half life of SIM0505: ~6.6-9.5 days and CPT116: ~4.1-6.0 days

Figure 4. Best % Change in Target Lesion by CDH6 Membrane H-Score (N=35)



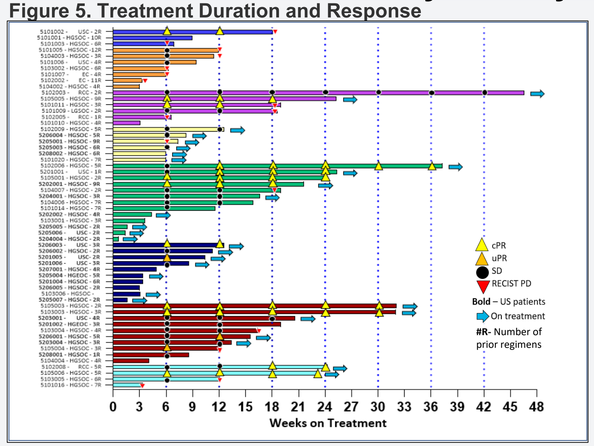
- Reduction of tumor lesion was observed across a range of membrane CDH6 expression

Conclusion

- SIM0505 demonstrated manageable safety and tolerability profile, including at higher dose levels, and showed encouraging antitumor efficacy in OC and USC, supported by a favorable PK profile
- In patients with gynecological cancers (OC, USC, other endometrial) treated at 4.8 – 8.0mg/kg with at least 12 weeks of follow up ORR was 55% using best response (11/20 PR, 1 unconfirmed, 1 pending follow up)
- Data supports Part 2 dose optimization in PROC at 5.6, 6.4, and 7.2mg/kg, currently underway

Preliminary Efficacy

Figure 5. Treatment Duration and Response



- Two intermediate dose levels (5.6 and 7.2 mg/kg) were initiated after evaluation of the highest dose level (9.6 mg/kg).
- Median duration of follow-up was 1.51 months (range 1.1-2.8) for 5.6 mg/kg and 1.18 months (range 0.3 -2.8) for 7.2 mg/kg.
- At data cutoff, median DoR was not estimatable – NE (2.46, NE); follow-up is ongoing.

Figure 6. Best Overall Response

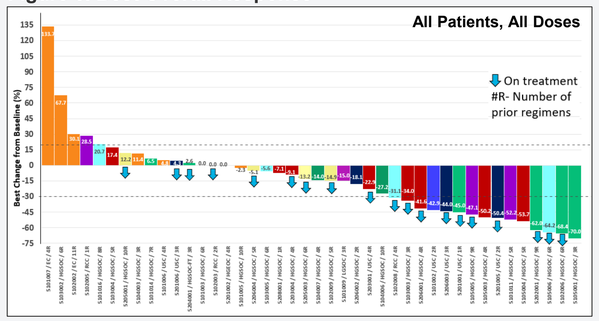
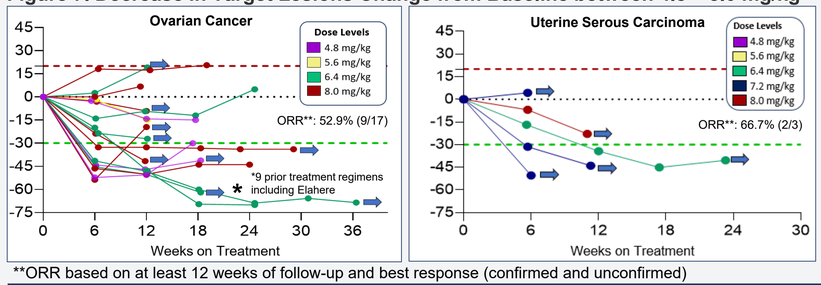


Figure 7. Decrease in Target Lesions Change from Baseline between 4.8 – 8.0 mg/kg



**ORR based on at least 12 weeks of follow-up and best response (confirmed and unconfirmed)

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