OBI-902, a Novel TROP2-Targeted Antibody-Drug Conjugate via GlycOBI® Platform, Has Favorable Pharmacokinetics and Sustained Antitumor Activities in Challenging Solid Tumors

Ren-Yu Hsu[1], Chi-Huan Lu[1], Chi-Sheng Shia[1], Hsin-Shan Wu[1], Lu-Tzu Chen[1], Jhih-Jie Yang[1], Jyy-Shiuan Tu[1], Hui-Wen Chang[1], Shih-Ni Wen[1], Ming-Tain Lai[1], Ya-Chi Chen[1]
[1]OBI Pharma, Inc. Taipei, Taiwan

OBI PHARMA
AACR 2025
4356

BACKGROUND

- Trophoblast cell surface antigen 2 (TROP2) is overexpressed in a variety of solid tumors, including non-small cell lung cancer (NSCLC), pancreatic cancer (PDAC), gastric cancer (GC), and colorectal cancer (CRC), where high expression levels of TROP2 correlate with poor prognosis.
- OBI-902 is a novel site-specific antibody-drug conjugate (ADC) targeting TROP2. It consists of a humanized monoclonal antibody conjugated to a topoisomerase I (TOP1) inhibitor with a drug-to-antibody ratio (DAR) of 4, using OBI's proprietary GlycOBI® glycan conjugation and EndoSymeOBI® dual-enzyme platform. This design aims to improve ADC stability and enhance payload delivery to tumors. (GlycOBI® Poster#1799)

OBJECTIVE

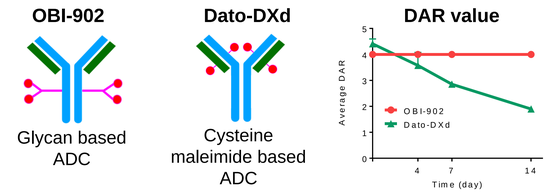
- To provide preclinical evidence that OBI-902 exhibits enhanced linker-payload stability, efficient tumor-targeted payload delivery, and superior, durable antitumor activity across various challenging mouse tumor models compared to benchmarks.

METHODS

- **In vitro stability** of OBI-902's linker-payload was assessed after 14-day incubation with human serum albumin, followed by mass spectrometry analysis.
- **Pharmacokinetics (PK)** of OBI-902 were evaluated over 21 days in a human NSCLC xenograft model following a single IV dose.
- **Biodistribution** of ^{111}In-DTPA-OBI-902 was assessed in a human NSCLC xenograft model, with tissue and organ samples collected at time points ranging from 1 to 168 hours post-injection for gamma counting.
- **Bystander killing effect** of OBI-902 was assessed in NCI-H460-luciferase (TROP2-negative) cells cultured alone or with BxPC-3 (TROP2-positive) cells. Bystander effect was measured by % cell viability indicated by loss of luciferase signal.
- **Antitumor activity** of OBI-902 was evaluated in NSCLC, PDAC, GC, and CRC cell line-derived xenograft (CDX) models, with Dato-DXd, SG, or sac-TMT as benchmarks. Mice received treatments when tumors reached volumes of 200–250 mm³ for standard models and when tumor volume reached 500-700 mm³ for large-tumor models.

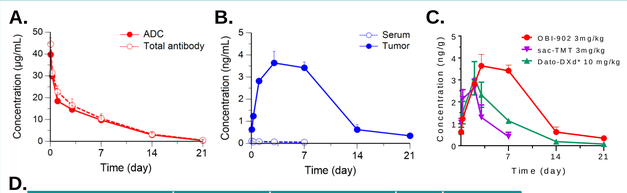
RESULTS

Figure 1. OBI-902 Enhanced Linker-Payload Stability



- OBI-902 conjugated via site-specific glycan linkers maintains a homogeneous DAR in serum albumin, overcoming the limitations of traditional cysteine-based linkers and offering enhanced stability.

Figure 2. OBI-902 Exhibited Excellent ADC Stability in Circulation with Efficient Payload Release at the Tumor



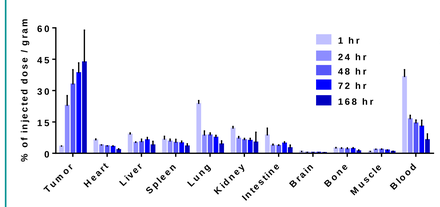
D.

OBI-902 in circulation	C_{max} ± SE (μg/mL)	AUC_{0-t} ± SE (hr*μg/mL)	$T_{1/2}$ (hr)	CL (mL/hr/kg)
ADC	40 ± 1.1	4000 ± 220	88	0.75
Total antibody	45 ± 1.7	4400 ± 230	91	0.67
Tumor free payload	**C_{max} ± SE (ng/g)**	**AUC_{0-t} ± SE (hr*ng/g)**		
OBI-902, 3 mg/kg	3.6 ± 0.30	960 ± 37		
sac-TMT, 3 mg/kg	2.6 ± 0.23	230 ± 26		
Dato-DXd*, 10 mg/kg	3.1 ± 0.44	480 ± 32		

C_{max}, maximum serum concentration; AUC, area under the curve; $T_{1/2}$, half-life; CL, clearance. *:Data was obtained from a separate experiment.

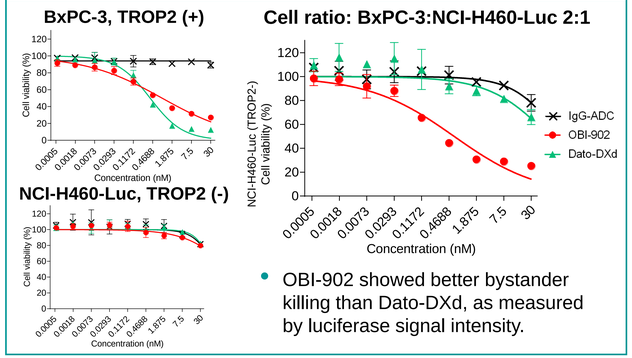
A. OBI-902 showed a favorable PK profile, with stability confirmed by highly overlapping curves of ADC and total antibody in circulation.
B. OBI-902 demonstrated efficient and slow payload release at the tumor site, with minimal payload release into circulation.
C. OBI-902 exhibited higher tumor exposure to free payload compared with sac-TMT and Dato-DXd.
D. Mean pharmacokinetic parameters in circulation and tumor tissue.

Figure 3. OBI-902 Showed Enhanced Tumor Targeting in NSCLC Xenograft Model



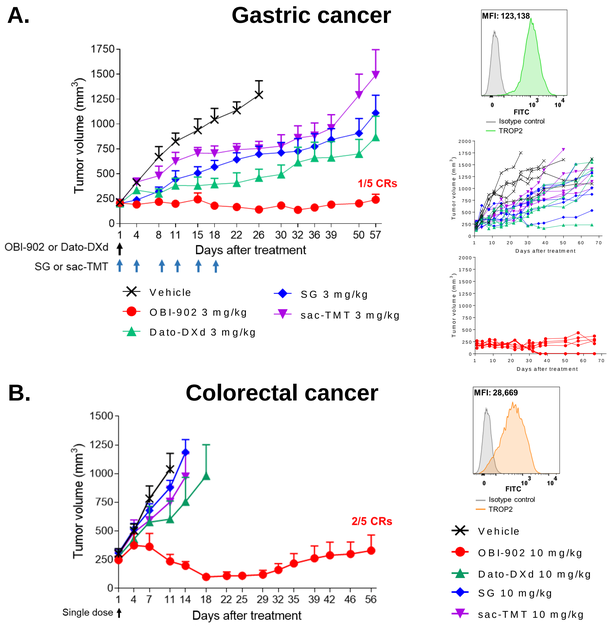
- OBI-902 exhibited time-dependent tumor uptake, achieving high tumor-to-blood ratios at later time points (6.9 at 168 hours).

Figure 4. OBI-902 Demonstrates a Potent Bystander Effect Against TROP2-Heterogeneous Environments



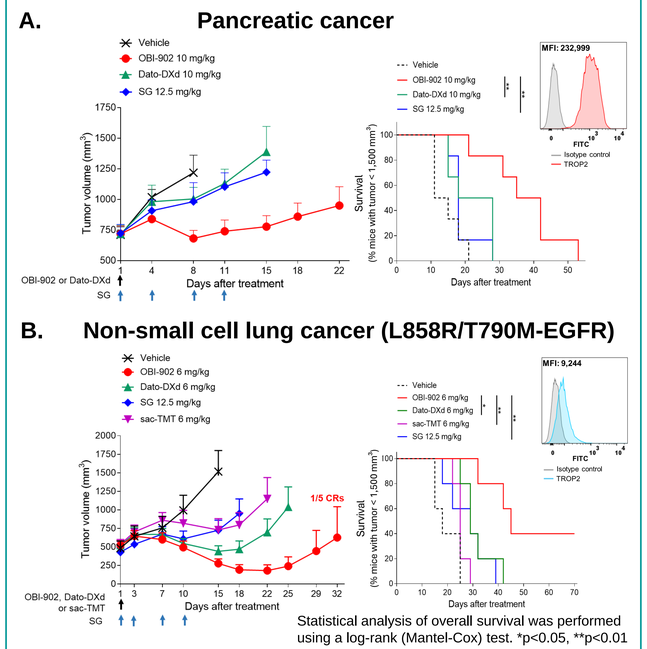
- OBI-902 showed better bystander killing than Dato-DXd, as measured by luciferase signal intensity.

Figure 5. OBI-902 Demonstrates Improved Efficacy and Durable Response in CDX Models



A. In the GC model, tumor volume reductions of OBI-902 were 3.6- to 6.2-fold better compared to benchmarks, by day 57.
B. In the challenging CRC model, OBI-902 sustained tumor suppression by day 56 (330 ± 110 mm³) versus benchmarks exceeding 1000 mm³ before day 18.

Figure 6. OBI-902 Demonstrates Superior Antitumor Activity in Large Tumor CDX Models



Statistical analysis of overall survival was performed using a log-rank (Mantel-Cox) test. *p<0.05, **p<0.01

A. In the PDAC model, OBI-902 extended survival beyond day 50, versus benchmark groups sacrificed by day 28.
B. In the NSCLC model, OBI-902 outperformed benchmarks, with 40% of mice surviving past day 70, while all benchmark-treated mice were sacrificed (tumor volume > 1500 mm³) between days 29-42.

CONCLUSIONS

OBI-902 efficiently delivers and slowly releases its payload to the tumor, achieving desirable drug exposure and sustained antitumor activity across various challenging solid tumors, suggesting its potential as a best-in-class TROP2 ADC.

DISCLOSURE

This study was funded by OBI Pharma, Inc. All authors are employees of OBI Pharma, Inc.

ACKNOWLEDGMENTS

- The TROP2-targeting antibody was in-licensed from Biosion, Inc. OBI Pharma owns commercial rights for OBI-902.
- We are grateful for the support from the National Center for Biomodels (NCB), Taiwan.

Corresponding author: Ya-Chi Chen, yachichen@obipharma.com