669P: CBX-12-101: Final Results of a Phase 1 Study of CBX-12, a Peptide Drug Conjugate (PDC) in Patients (pts) with Advanced or Metastatic Solid Tumors.

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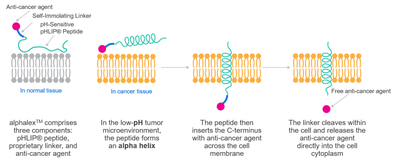
BACKGROUND

- Transformed cells generate energy via aerobic fermentation and create an acidic microenvironment described as the Warburg Effect.
- CBX-12 (alphalex™ - exatecan) contains a pH-low insertion peptide (pHLIP), a stable linker, and a payload [topoisomerase 1 (TOP1) poison exatecan].
- In the acidic environment of tumors, the peptide undergoes a conformational change and preferentially penetrates the tumor cell to deliver exatecan to the cellular cytoplasm while limiting toxicity to healthy tissue.



METHODS

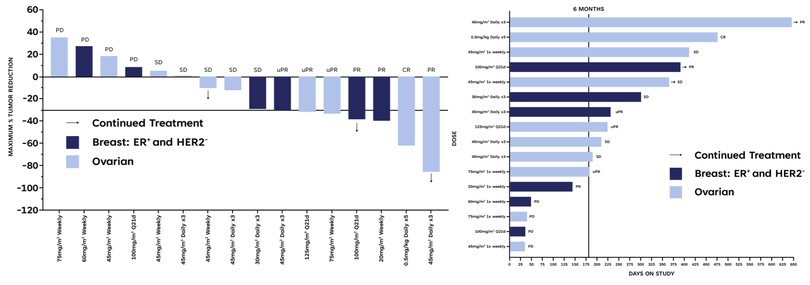
3+3 Phase 1 dose escalation study: 69 subjects

- 69 subjects, refractory solid tumors.
- 3 dose schedules, daily x3 q21d, weekly, and q21 days.
- Primary objectives are safety, tolerability, and to determine the MTD and/or RP2D.

ANTITUMOR ACTIVITY & KEY FINDINGS:

- Objective responses in ovarian, breast, colorectal, and NSCLC.
- Activity in 6 tumor types, including gall bladder and thymic.
- Median PFS: ovarian 7 months, breast 6 months.
- All evaluable breast subjects HER-2 negative HR positive.
- 3 patients (1 ovarian and 2 NSCLC) were not efficacy evaluable as they did not receive a post-baseline scan.

Breakdown of TOP1 Naïve Breast and Ovarian Patients



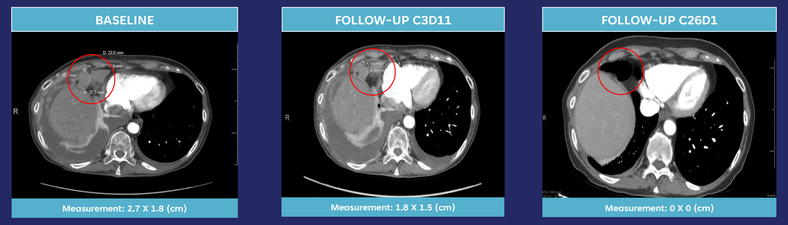
Data cut-off August 13, 2024

ANTITUMOR ACTIVITY & KEY FINDINGS:

- High response rates in TOP1 naïve subjects (40%+).
- CBX-12 demonstrates clinical activity in 6 tumor types.
- CBX-12's antigen agnostic tumor targeting mechanism enables larger patient populations than conjugates that require an antigen for binding.
- Favorable AE profile that is amenable to future combinations.
  - No ILD; No ophthalmic toxicity.
- 2 doses (100 mg/m^2 and 125 mg/m^2 every 21 days) are being studied in an ongoing Phase 2.

CBX-12 Demonstrates Responses in 4 Different Cancers

Tumor	Subjects N	cCR	cPR	uPR	ORR	TOP1 naïve	TOP1 naïve ORR
Ovary	11	1	1	2	36%	10	40%
Breast	16		2	1	19%	7	43%
CRC	7		1		14%	1	100%
NSCLC	2			1	50%	2	50%



A 75-year-old female diagnosed with malignant neoplasm of the fallopian tube who had 3 prior regimens, including carboplatin, paclitaxel, docetaxel, and bevacizumab:

- Showed partial response cycle 3
- Continues treatment at 22 months

FAVORABLE SAFETY PROFILE:

ADRs reported in more than 5% of patients

MedDRA Preferred Term	Phase I Overall (N=69)	
	All	Grade 3-4
Anaemia	37 (53.6)	17 (24.6)
Leukopenia	29 (42.0)	15 (21.7)
Neutropenia	28 (40.6)	19 (27.5)
Nausea	27 (39.1)	0 (0.0)
Fatigue	25 (36.2)	1 (1.4)
Diarrhoea	19 (27.5)	3 (4.3)
Vomiting	17 (24.6)	0 (0.0)
Thrombocytopenia	16 (23.2)	9 (13.0)
Dehydration	7 (10.1)	1 (1.4)
ALT increased	6 (8.7)	0 (0.0)
Hypomagnesaemia	6 (8.7)	0 (0.0)
Alopecia	5 (7.2)	0 (0.0)
AST increased	5 (7.2)	1 (1.4)
Lymphopenia	5 (7.2)	3 (4.3)
Stomatitis	5 (7.2)	1 (1.4)

ADRs leading to dose interruption 14 (20.3%)
ADRs leading to dose reduction 15 (21.7%)
ADRs leading to discontinuation 3 (4.3%)
ADRs leading to death 0

PHARMACOKINETICS:

- CBX-12 PK exhibits linear dose-proportional PK with a mean half-life ranging from 14 to 22 hours for doses ranging from 20 mg/m^2 to 125 mg/m^2.
- Exposure (AUC) ratio of CBX-12 to exatecan was 80-90 fold.
- CBX-12 exposure (AUC) was comparable on all 3 schedules.

SUMMARY AND NEXT STEPS:

- CBX-12 has broad activity, particularly in TOP1 naïve patients with a response rate in ovarian cancer of 40% and breast cancer of 43%.
- CBX-12 had a manageable safety profile, which is amenable to future combinations.
- A Phase 2 study in platinum-resistant ovarian cancer is underway.
- A Phase 2 study in CRC and NSCLC as a monotherapy is planned.
- Multiple combination studies with a PD-1 inhibitor and PARP inhibitor are planned.

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No disclosures specific to this project