Phase 1 Clinical Trial of BHV-1510, a Next-Generation Trop2 ADC, in Combination with the PD-1 Monoclonal Antibody, Cemiplimab in Patients with Advanced Solid Tumors

Poster 252P

Shiraj Sen[1], I. Micaily[2], C. Perez[3], A. Spira[4], E. Hamilton[5], W. McKean[6], S. Ghamande[7], M. Ahluwalia[8], S. Patel[9], A. Shields[10], S. Puri[11], B. Van Tine[12], B. Levy[13], B. Ma[14], J. Peng[15], N. Khokhar[16], S. Coker[16], C. Chen[17]

[1]Department of Medical Oncology, Early Drug Development, NEXT Oncology, Irving, TX, USA; [2]Gynecological Oncology, Sidney Kimmel Comprehensive Cancer Center at Thomas Jefferson University, Philadelphia, PA, USA; [3]Medical Oncology, Florida Cancer Specialists, Orlando, FL, USA; [4]Research Department, NEXT Oncology at Virginia Cancer Specialist, Fairfax, VA, USA; [5]Drug Development Unit, Sarah Cannon Research Institute, Nashville, TN, USA; [6]Utah Cancer Specialists, START Mountain Region, West Valley City, UT, USA; [7]Gynecologic Oncology, Georgia Cancer Center, MCG WellStar Health, Augusta, GA, USA; [8]Department of Medical Oncology, Miami Cancer Institute - Baptist Health South Florida, Miami, FL, USA; [9]Department of Oncology, UCSD Moores Cancer Center, La Jolla, CA, USA; [10]Medical Oncology, Karmanos Cancer Institute, Detroit, MI, USA; [11]Medicine/Hematology And Oncology Department, Moffitt Cancer Center, Tampa, FL, USA; [12]Medical Oncology Department, Washington University School of Medicine, St. Louis, MO, USA; [13]Medical Oncology, Johns Hopkins Sidney Kimmel Cancer Center, Sibley Memorial Hospital, Washington, DC, USA; [14]Hematology/Oncology Department, New York-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY, USA; [15]Clinical Pharmacology, Biohaven Pharmaceuticals Inc, New Haven, CT, USA; [16]Clinical Development, Biohaven Pharmaceuticals Inc, New Haven, CT, USA; [17]Medical Oncology, Stanford Cancer Center Palo Alto, Palo Alto, CA, USA

BACKGROUND

- Trop2 ADCs have been approved by the US FDA as monotherapy in specific subsets of breast and lung cancer. However, these have limitations with hematologic and gastrointestinal toxicities.
- BHV-1510 is a next-generation Trop2 ADC with a novel topoisomerase I (Topo1) inhibitor, TopoIx, payload and a site-specific, highly stable conjugation linker, that preclinically demonstrated synergy in combination with anti-PD-1 agents.[a]
- BHV1510-101 (NCT06384807) is an ongoing Phase 1/2 first-in-human trial of BHV-1510 in participants with advanced solid tumors as monotherapy or in combination with cemiplimab.
- Our emerging data suggest synergistic potential when combined with immune checkpoint inhibitors, where ADC-induced immunogenic cell death may enhance anti-tumor activity.

Figure 1. BHV-1510 Structure

BHV-1510 consists of a humanized, Trop2 monoclonal antibody with high selectivity and affinity for hTrop2, a stable branched linker, and a unique Topo1 inhibitor, TopoIx, as a payload (DAR4).

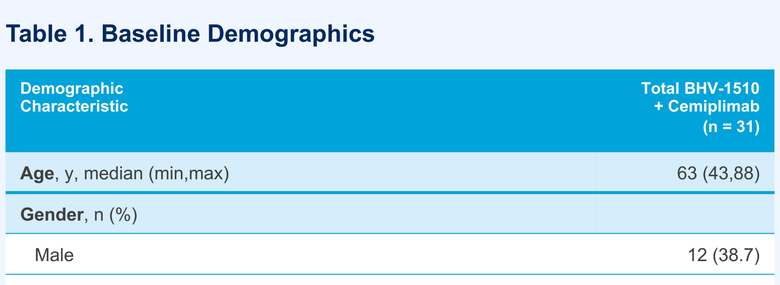


Figure 2. BHV-1510 Demonstrates Excellent Synergy with anti-PD1 Ab Treatment *in vivo*

In combination with anti-PD1 Ab treatment, BHV-1510 exhibits excellent synergy, resulting in significantly greater potency than DS-1062 and anti-PD1 Ab combination treatment.

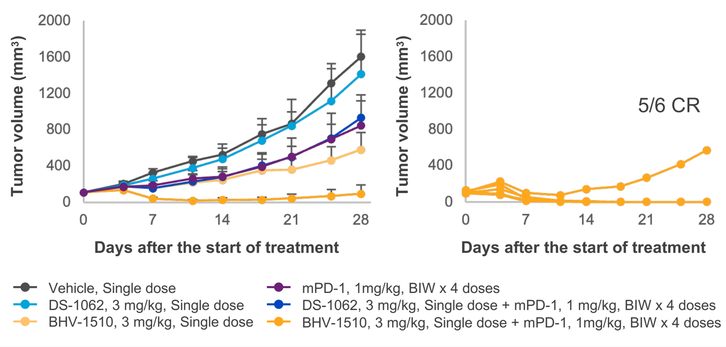
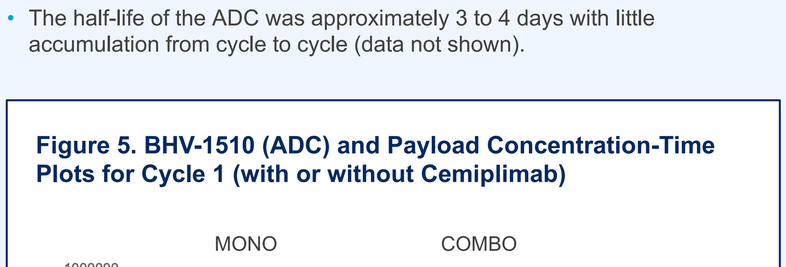


Figure 3. TopoIx Demonstrates Higher *in vitro* Cytotoxicity and Immunogenic Cell Death than DXd/SN38

TopoIx shows superior *in vitro* cytotoxicity compared to DXd and SN38 across diverse cancer cell lines (**Figure A**). TopoIx induces a more potent immunogenic cell death *in vitro*, as evidenced by higher levels of ATP and HMGB1 release (**Figure B, C**), compared to DXd and SN38.



OBJECTIVES

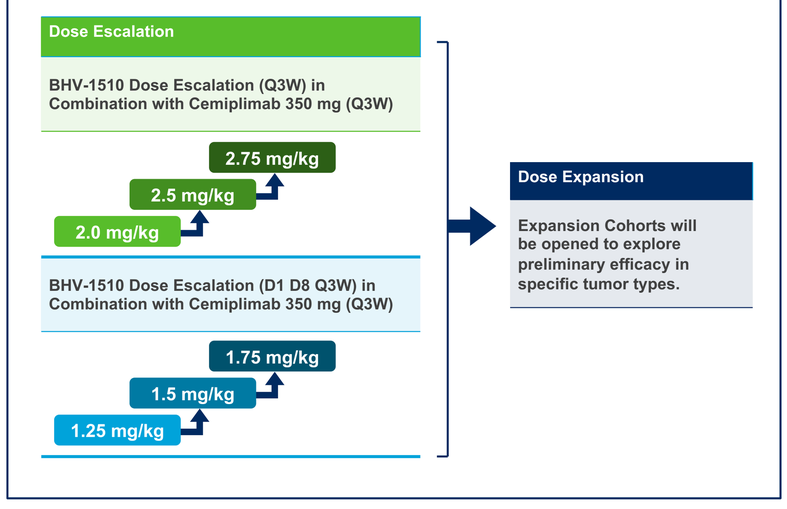
The primary endpoint is safety and tolerability of BHV-1510 in combination with cemiplimab. The secondary endpoints are pharmacokinetics and preliminary efficacy of the combination.

STUDY DESIGN

BHV1510-101 (NCT06384807) is an ongoing Phase 1/2 first-in-human trial of BHV-1510 in participants with advanced solid tumors as monotherapy or in combination with cemiplimab.

Eligible patients were ≥18 years of age and had an advanced or metastatic solid tumor that was refractory to available standard therapies, lacked an approved standard treatment option, or had no standard therapy appropriate for their current stage of disease.

Figure 4. Study Schematic



RESULTS

Enrollment

- As of the clinical cutoff (CCO) date, 10-Oct-2025, 31 participants were enrolled in the combination of BHV-1510 and cemiplimab cohort.
- **Table 1** provides details of the participants demographics and baseline characteristics. Twenty-two participants received BHV-1510 at doses from 2 mg/kg to 2.75 mg/kg Q3W in combination with cemiplimab 350 mg Q3W and 9 participants received BHV-1510 at doses from 1.25 mg/kg to 1.5 mg/kg on Day 1 and Day 8 Q3W in combination with cemiplimab 350 mg Q3W.
- Participants had received not more than 2 prior lines of therapy in the advanced/metastatic setting.
- Of the 31 participants treated in the combination cohort, 27 (87.1%) had prior PD-(L)1 exposure with 16 participants (51.6%) receiving the PD-(L)1 as most recent treatment prior to receiving study treatment.

Table 1. Baseline Demographics

Demographic Characteristic	Total BHV-1510 + Cemiplimab (n = 31)
Age, y, median (min,max)	63 (43,88)
Gender, n (%)	
Male	12 (38.7)
Female	19 (61.3)
Histology, n (%)	
pMMR Endometrial Cancer (EC)	9 (29)
Non-Small Cell Lung Cancer (NSCLC)	19 (61.3)
Urothelial (UC)	2 (6.5)
Triple-Negative Breast Cancer (TNBC)	1 (3.2)
Prior line of therapy for advanced/metastatic disease, median	2
ECOG PS 0, n (%) / **1**, n (%)	8 (25.8) / 23 (74.2)
Prior PD-(L)1 therapy, n (%)	27 (87.1)
Brain metastasis, n (%)	8 (25.8)

pMMR = Mismatch Repair-proficient

Efficacy

- Of 23 efficacy evaluable participants treated with BHV-1510 in combination with cemiplimab, the confirmed objective response rate (ORR) was 52.2%, with confirmed objective responses in 6/14 (42.9%) in NSCLC, 4/6 (66.7%) in endometrial cancer, and 1/2 (50%) in urothelial cancer. A confirmed response was reported in the patient with TNBC.
- The BHV-1510 2.5 mg/kg Q3W combination with cemiplimab had a confirmed ORR in 8/11 participants (72.7%). Confirmed responses were observed in 3/5 (60%) in NSCLC, 4/4 (100%) in endometrial cancer, which included a complete response, and 1/2 (50%) in urothelial cancer.
- Majority of participants had tumor reduction on their first scan, with a median time to response of 11.1 weeks.
- Eighteen participants continue on study treatment at time of CCO.

Pharmacokinetics

- The unconjugated payload concentration was low with a payload-to-ADC molar ratio < 1%, indicating that ADC was highly stable in the circulation.
- There was no marked difference in exposure between the monotherapy and combination therapy for both ADC and payload.
- The half-life of the ADC was approximately 3 to 4 days with little accumulation from cycle to cycle (data not shown).

Figure 5. BHV-1510 (ADC) and Payload Concentration-Time Plots for Cycle 1 (with or without Cemiplimab)

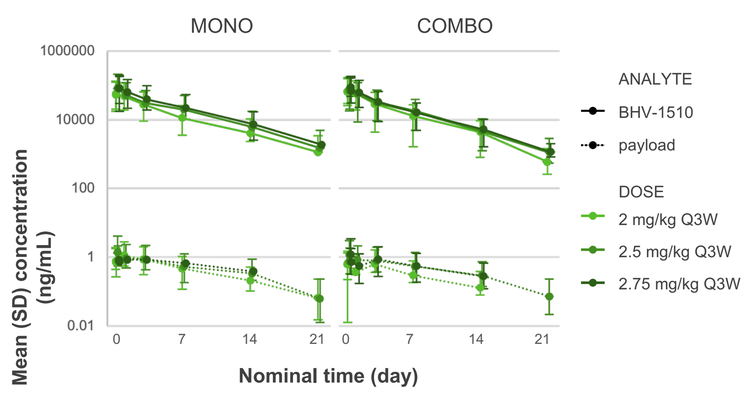


Figure 6. BHV-1510 + Cemiplimab: Percent Change in Target Lesions

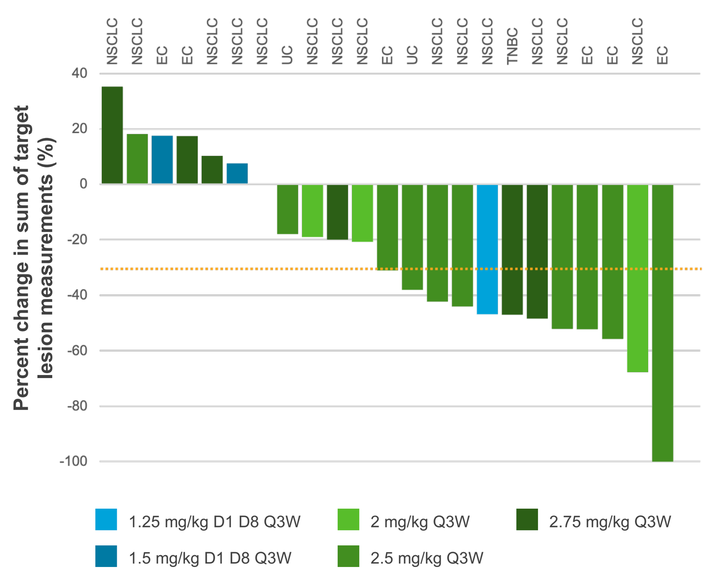


Figure 7. BHV-1510 + Cemiplimab: Treatment Duration

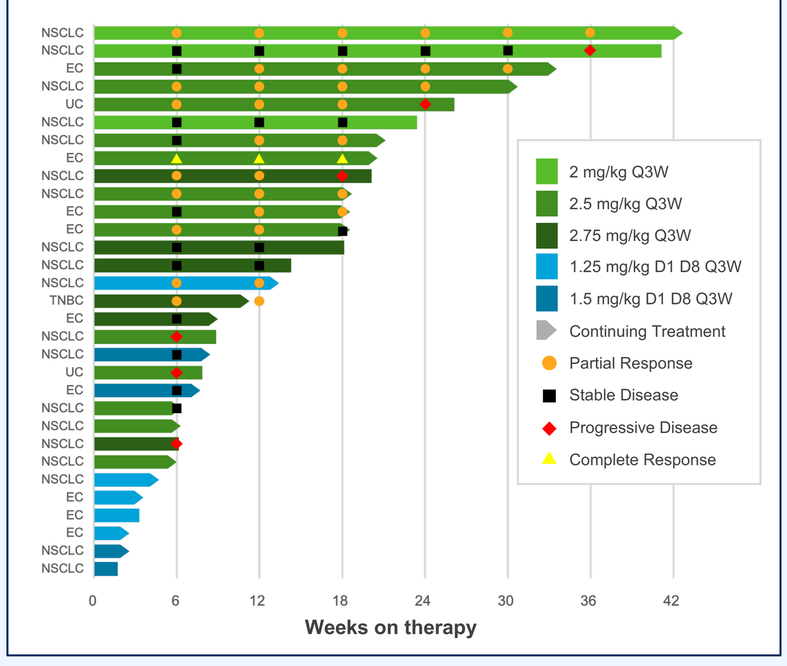
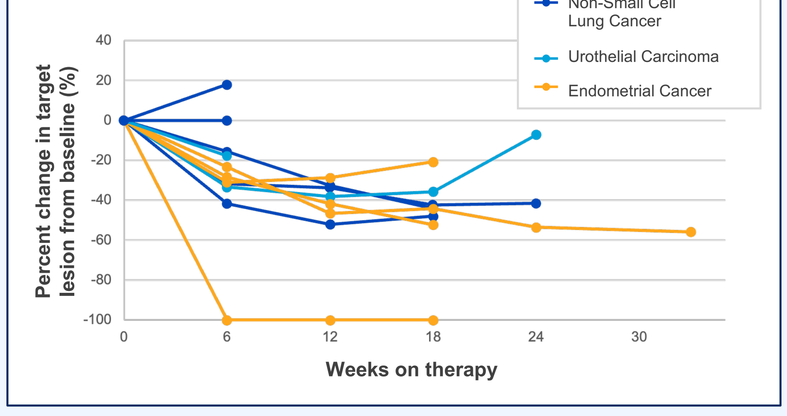


Figure 8. BHV-1510 2.5 mg/kg + Cemiplimab: Target Lesion Change from Baseline



Safety

- The maximum tolerated dose was not reached by the CCO date.
- Only one participant reported a dose-limiting toxicity; Grade 3 stomatitis at the BHV-1510 2.75 mg/kg + cemiplimab 350 mg dose level.
- There were no AEs that led to treatment discontinuation or death.
- Treatment emergent SAEs were reported in 4 participants. All were assessed as not related to study treatment by the investigator.
- Interstitial lung disease/pneumonitis was not reported in any participant.
- The rate of neutrophil count decrease was low and manageable; all grade (Grade ≥3), 12.9% (6.5%). Similarly, the rates of treatment emergent diarrhea and alopecia were low; all Grade (Grade ≥3), 6.5% (0) and 9.7% respectively.
- See **Table 2** for a summary of TEAEs reported in the study.

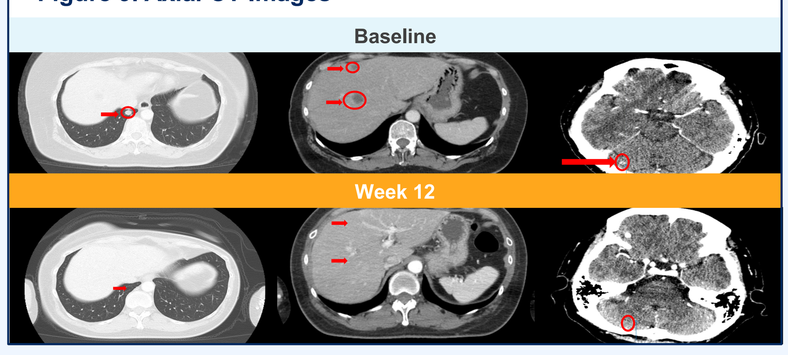
Table 2. TEAEs: BHV-1510 Q3W or D1D8 Q3W + Cemiplimab Q3W in ≥ 10% of Participants

	BHV-1510 Q3W + Cemiplimab Q3W (n = 22)		BHV-1510 D1D8 Q3W + Cemiplimab Q3W (n = 9)	
AE, n (%)	All Grades	Grade ≥3	All Grades	Grade ≥3
Oral mucositis/stomatitis	13 (59.1)	5 (22.7)	3 (33.3)	1 (11.1)
Fatigue	10 (45.5)	1 (4.5)	4 (44.4)	0
Nausea	6 (27.3)	0	2 (22.2)	0
Weight decreased	6 (27.3)	1 (4.5)	0	0
Dysgeusia	6 (27.3)	0	0	0
Candida infection	5 (22.7)	0	0	0
Constipation	4 (18.2)	0	1 (11.1)	0
Decreased appetite	4 (18.2)	0	0	0
Dehydration	3 (13.6)	0	1 (11.1)	0
Neutrophil count decreased	4 (18.2)	2 (9.1)	0	0
Oropharyngeal pain	4 (18.2)	0	0	0

CASE NARRATIVE

- A 57-year-old female with EGFRmt NSCLC treated with amivantamab with best response of stable disease, followed by investigational EGFR/HER2 inhibitor with an objective response in the metastatic setting until progressive disease was documented (**Figure 9**).
- Patient remains on BHV-1510 and cemiplimab Q3W at 42 weeks and tolerating study treatment with a confirmed partial response (cPR).

Figure 9. Axial CT Images



CONCLUSIONS

- Early results of BHV1510-101 show that BHV-1510 in combination with cemiplimab was generally well tolerated and has an acceptable safety profile, both as Q3W and Day1 Day 8 Q3W schedules, notably with low rates of unconjugated payload related hematologic toxicities or diarrhea, and no interstitial lung disease.
- There is encouraging preliminary activity suggesting synergy between BHV-1510 and cemiplimab, with cPRs observed in participants with NSCLC, endometrial, urothelial, and TNBC. Several participants have remained on treatment for 6 months or longer. This builds on the clinical activity observed with BHV-1510 as monotherapy, to be reported separately.

Disclosures:
Ida Micaily: None

References:
a. Sun, Yajun, et al. "Preclinical characterization of GQ1010, a next generation trop2 ADC with the best-in-class potential against diverse trop2+ solid tumors." Cancer Research 83.7_Supplement (2023): 1549-1549.

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