Preliminary Results from a First-in-Human Phase 1 Study of BA3182, a Dual-Conditionally Binding CAB-EpCAM x CAB-CD3 Bispecific T-cell Engager in Patients with Treatment Refractory Metastatic Adenocarcinoma

Abstract #1581P

Oana Danciu, MD[1], Madison L. Conces MD[2], Devalingam Mahalingam, MD, PhD[3], Michael Cecchini, MD[4], E. Gabriela Chiorean, MD[5], Jennifer B. Valerin, MD, PhD[6], Kyechin Chen, PharmD[7], Judith Llorin-Sangalang, MD[7], Kartik Aysola, MD[7], Jacob S. Thomas, MD[8], and Alexander N. Starodub, MD[9]

[1]University of Illinois Cancer Center, Chicago, IL, USA, [2]University Hospitals Cleveland Medical Center, Cleveland, OH, USA, [3]Northwestern University, Chicago, IL, [4]Yale Cancer Center, New Haven, CT, [5]Fred Hutchinson Cancer Center, Seattle, WA, USA, [6]Chao Family Comprehensive Cancer Center, University of California Irvine Health, Orange, CA, USA, [7]BioAtla, Inc., San Diego, CA, USA, [8]USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA, [9]The Christ Hospital, Cincinnati, OH, USA

Background

EpCAM (epithelial cell adhesion molecule): transmembrane glycoprotein expressed by virtually all epithelia-containing tissues

- Robust expression of EpCAM among adenocarcinomas of the colon, stomach, pancreas, biliary tract, lung, breast, prostate, and thyroid makes it a compelling bispecific T-cell engager (TCE) target when reliably restricting antibody binding-to the tumor microenvironment (TME).[1,2]
- All epithelial tissue express EpCAM, and this broad expression is associated with on-target, off tumor toxicities when targeted by non-conditionally binding TCEs[3]

BA3182 is dual-conditionally active biologic (CAB)-bispecific TCE antibody targeting EpCAM and CD3 (Figure 1)

- CABs are not masked or caged prodrugs and do not require enzymatic cleavage for activation.[4]
- Both CAB-EpCAM and CAB-CD3 binding domains of BA3182 have been designed to bind to their target proteins specifically and reversibly in the acidic TME and have markedly reduced binding outside the TME under normal physiological conditions, thus widening the therapeutic window.[4] **(Figure 1)**
- Selective T cell engagement by BA3182 in the TME has the potential to reduce local T-cell exhaustion and lead to sustained tumor cell killing.[4] **(Figure 2)**
- Preclinical studies using dual CAB BA3182 demonstrated potent antitumor activity in a human CRC xenograft model with a >100-fold improvement in the therapeutic index compared to non-CAB EpCAM x CD3 variants.[1,4]

Figure 1. Structure of BA3182

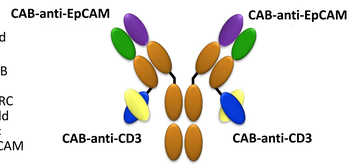


Figure 2. Proposed mechanism of action of BA3182, a dual-CAB EpCAM x CD3 bispecific T-cell engager

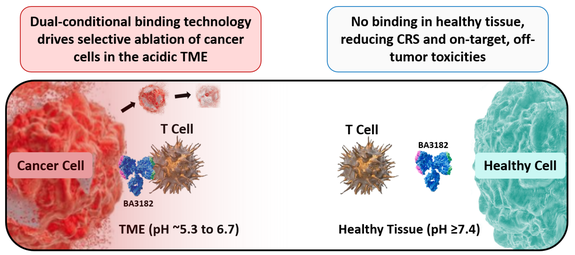
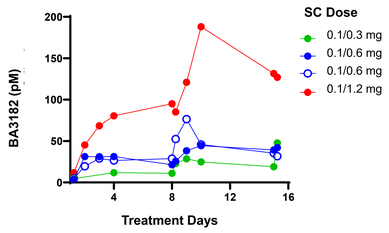


Figure 3. Concentration time profile of BA3182 in human plasma following subcutaneous administration; weekly dosing leads to accumulation of BA3182



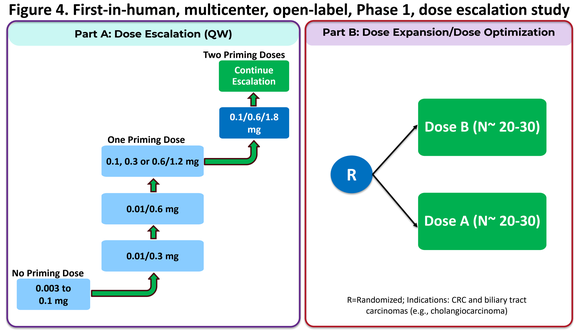
Clinical Trial Identifier

A Phase 1 Multi-center, Open-label, Study Of BA3182 (a Bispecific Epithelial Cell Adhesion Molecule (EpCAM)/CD3 Antibody) in Patients With Advanced Adenocarcinoma.
Clinical Trial Registry Number: NCT05808634

Trial Design

Evaluating safety, tolerability, PK, immunogenicity, and antitumor activity of BA3182 in pts with advanced adenocarcinomas

Figure 4. First-in-human, multicenter, open-label, Phase 1, dose escalation study



Treatment notes:
- Prophylactic acetaminophen and diphenhydramine delivered prior to all doses and prophylactic tocilizumab (no corticosteroids) given prior to Cycle 1 Day 1 treatment dose
- Post treatment ondansetron guided for nausea
- Ongoing weekly treatment dosing continued after DLT observation interval concluded

Key Eligibility Criteria

Age ≥ 18 years, ECOG 0 or 1, unresectable or metastatic adenocarcinoma, standard of care therapy has failed, or no curative therapy is available, or are not eligible, or intolerant to standard therapy.

Study Objectives

Primary:

Assess dose-limiting toxicity (DLT), determine the maximum tolerated dose (MTD) and/or pharmacologically active dose (PAD), and evaluate other safety parameters.

Secondary:

Evaluate preliminary antitumor activity; characterize pharmacokinetics (PK); evaluate immunogenicity.

Preliminary Results

Patient characteristics, disposition, and PK

- As of September 10, 2025, 35 pts were dosed subcutaneously with BA3182 QW with 1 or 2 priming doses 4 to 7 days prior to treatment dosing
- Pts received a mean of 8+ doses (**Figure 7**; between 0.032 mg and 1.2 mg treatment dose)
- BA3182 demonstrated dose-dependent increases in exposure following subcutaneous administration on a once-weekly (QW) schedule (Days 1, 8, and 15 of repeating 21-day cycles)
- Preliminary data suggest that the terminal half-life of BA3182 is equal to or greater than 8 days

Table 1. Patient characteristics

Patient Characteristic	N=35
Age, mean (SD), y	57 (10)
Male (n, %)	19 (54)
Female (n, %)	16 (46)
ECOG performance status	
0 (n, %)	24 (69)
1 (n, %)	11 (31)
Presence of liver metastases (n, %)	22 (63)

Table 2. Tumor histology; prior treatments

Carcinoma Type (n, %)	N=35	Median # of prior treatments
Adenoid Cystic Carcinoma	1 (3)	2
Appendiceal	1 (3)	2
Cholangiocarcinoma	2 (6)	1
Colorectal	22 (63)	4
Gallbladder	1 (3)	3
Ovarian	1 (3)	8
Pancreas	7 (20)	3

Safety

AEs generally transient and readily manageable (Figure 5, Table 3)

- BA3182 priming and first treatment doses were associated with transient and reversible elevations in hepatic analytes, consistent with cholestasis, that resolved with ongoing, higher treatment exposures
- Minimal, transient, low-grade CRS observed to date (G1, N=1; G2, N=1)
- Priming dose of 0.1 mg safely enabled scheduled delivery of higher continuing treatment doses
  - 0.1 mg prime followed by 0.3 mg: G3 non-febrile neutropenia possibly related to tocilizumab (DLT)
  - Priming doses >0.1 mg
    - 0.3 mg prime followed by 0.6 mg treatment dose resulted in transient G4 ALT (DLT)
    - 0.6 mg prime followed by 1.2 mg treatment dose resulted in reversible G3 diarrhea associated with concomitant CMV enteritis (DLT); no diarrhea recurrence upon BA3182 rechallenge
- Treatment maximally tolerated dose not yet defined, and dose escalation continues

Figure 5. Pts who received a single priming dose of 0.1 mg prior to higher treatment doses (n=9) illustrates transient ALT, alkaline phosphatase, and total bilirubin increases that resolved with continued dosing

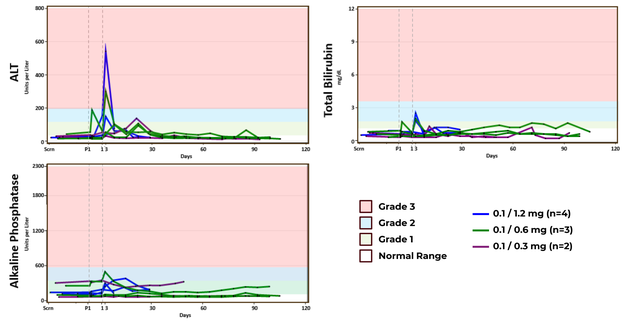


Table 3. Dosing cohort summary of adverse events (AE)

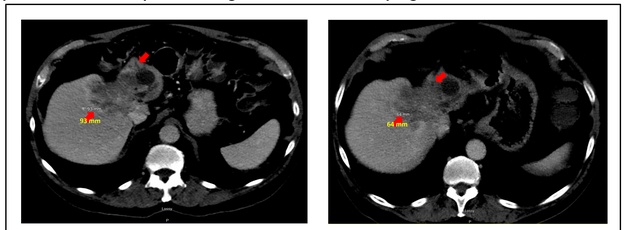
Characteristic	N=35 (n, %)
Any Adverse Events (AEs)	29 (83)
Related AEs of Grade 3-4	14 (40)
Related AEs of Grade 3 hepatic analytes[1]	11 (31)
Related AEs of Grade 4 hepatic analytes[1]	1 (3)
Related AEs of Grade 3-4 non-febrile neutropenia[2]	2 (6)
Related AEs of Grade 3 excluding hepatic analytes[1] and non-febrile neutropenia[2,4]	3 (9)
Any related serious AEs[3]	5 (14)
Related CRS of any grade (per ASTCT grading)	2 (6)
Related AEs leading to death	0
Related AEs leading to treatment discontinuation	1 (3)

[1] Early, transient elevation of hepatic analytes: AST, ALT, bilirubin, and/or alkaline phosphatase
[2] Non-febrile, transient neutropenia, possibly related to tocilizumab
[3] Related SAEs: G2 pancreatitis, G2 atrial fibrillation, G3 diarrhea, G3 acute kidney injury, and G2 CRS
[4] Related AE of G3 excluding hepatic analytes or non-febrile neutropenia: 1 pt @0.03/0.6mg G3 diarrhea; 1 pt @0.6/1.2 mg G3 diarrhea/lymphocyte count decrease; and 1 pt @0.03/0.3mg G3 acute kidney injury/white blood cell count decrease

TRAE >10% (N=35)	TRAE Any (n, %)	TRAE G3+ (n, %)
Alanine aminotransferase increased*	15 (42.9)	7 (20.0)
Aspartate aminotransferase increased*	15 (42.9)	9 (25.7)
Nausea	14 (40.0)	0
Injection site reaction	12 (34.3)	0
Diarrhea	11 (31.4)	2 (5.7)
Fatigue	9 (25.7)	0
Blood bilirubin increased*	8 (22.9)	0
Neutrophil count decreased	7 (20.0)	2 (5.7)
Blood alkaline phosphatase increased*	6 (17.1)	1 (2.9)
Decreased appetite	6 (17.1)	0
Dysgeusia	5 (14.3)	0
Vomiting	5 (14.3)	0
Abdominal pain	4 (11.4)	0
Constipation	4 (11.4)	0

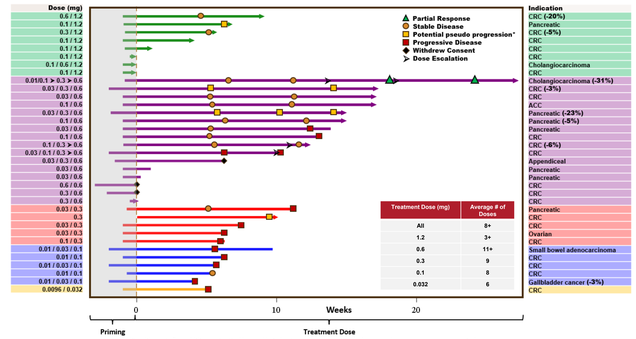
*Transient laboratory changes; resolved

Figure 6. Confirmed partial response (31% tumor reduction) from BA3182 at 0.6 mg in patient with intrahepatic cholangiocarcinoma without progression for >6 months



71-year-old male with intrahepatic cholangiocarcinoma. Previous treatments included gemcitabine, cisplatin, durvalumab as primary therapy and an investigational agent in the 2nd line setting.

Figure 7. Prolonged tumor control with increasing doses of BA3182



*Pts with unconfirmed PD were treated beyond initial progression per protocol when pseudo-progression was suspected

Preliminary assessment of anti-tumor activity among those treated with BA3182 treatment doses of 0.6 mg and higher (N=24)

- 14 CRC pts: among 7 pts who had one scan – 5 achieved SD at 1st scan, 1 pt continued treatment beyond potential pseudo-progression, and 1 discontinued due to PD; among the 7 pts without scans – 2 withdrew consent before the 1st scan and 5 are pending 1st scan
- 6 pancreatic cancer pts: 2 pts had SD at 1st scan and 2 pts continued treatment beyond potential pseudo-progression, and 2 pts died due to progression after less than 2 wks on treatment
- 2 cholangiocarcinoma pts: 1 pt **(Figure 6 and 7)** achieved a confirmed partial response (cPR) and 1 pt is pending first scan
- 1 pt with appendiceal cancer withdrew consent before 1st scans; 1 ACC pt experienced SD
- Among pts treated at higher doses, pts achieved SD at a higher rate and remained on active treatment for prolonged intervals, generally longer than those who received lower doses
- Intrapatient dose escalation was temporally associated with achievement of a confirmed PR, suggesting association of higher BA3182 exposure with increasing antitumor activity

Conclusions

- BA3182, a dual-conditionally binding CAB-EpCAM x CAB-CD3 T-cell engager continues to demonstrate a manageable safety profile with preliminary evidence of antitumor activity
- Early cytokine increases appear to cause reversible cholestasis that resolves with ongoing, higher BA3182 exposures – consistent with tumor-selective targeting
- Prolonged estimated half-life of at least one week associated with dose-to-dose accumulation suggests less frequent dosing will be feasible after response is achieved
- BA3182 treatment achieved an ongoing, confirmed partial response and multiple pts have experienced prolonged tumor control; currently testing 1.8 mg dose level

Abbreviations

ACC = adenoid cystic carcinoma, **AE** = Adverse Event, **ALT** = Alanine Aminotransferase, **ASTCT** = American Society for Transplantation and Cellular Therapy, **CAB** = Conditionally Active Biologic, **CD3** = cluster of differentiation (3), **CRC** = colorectal cancer, **Cmax** = maximum concentration, **CRS** = cytokine release syndrome, **DLT** = dose-limiting toxicity, **ECOG** = Eastern Cooperative Oncology Group, **EpCAM** = Epithelial Cell Adhesion Molecule, **IHC** = Immunohistochemistry, **IUPD** = immune unconfirmed progressive disease, **IV** = intravenous (weight-based dosing), **MTD** = maximum tolerated dose, **NSCLC** = Non-Small Cell Lung Cancer, **PAD** = pharmacologically active dose, **PD** = pharmacodynamics, **PK** = pharmacokinetics, **pM** = picomolar, **pt** = patient, **SAE** = serious adverse event, **SC** = subcutaneous, **TCE** = T-cell engager, **TCR** = T-cell receptor, **TME** = tumor microenvironment.

References

1. Frey G., et al. *mAbs*. 2024;16(1):2322562. doi: 10.1080/19420862.2024.2322562. 2. Went P., et al., *Oncoimmunology*. 2018;7(8):e1450710. doi: 10.1080/2162402X.2018.1450710. 4. Chang HW., et al. *Proc Natl Acad Sci USA*. 2021;118(9):e2020606118. doi:10.1073/pnas.2020606118. 5. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25(4):625-638. doi:10.1016/j.bbmt.2018.12.758

Disclosures

OD: Research funds from Pfizer and Novartis. Site PI of clinical trials for Pfizer, Novartis, Seagen, Sanofi, Regeneron, Puma, BioAlta, Genentech, SystImmune. Scientific Advisory Boards for Novartis, Pfizer, Astra Zeneca, Bayer, Cardinal Health

Acknowledgements and Funding

This study was funded by BioAtla, Inc.

Correspondence: Kartik Aysola, MD
medicalaffairs@bioatla.com
Presenting Author: Oana Danciu, MD
ocdanciu@uic@edu