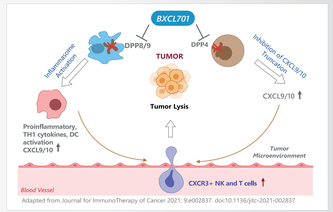
A PHASE 2 STUDY OF THE FIRST-IN-CLASS ORAL INNATE IMMUNE ACTIVATOR BXCL701 WITH PEMBROLIZUMAB IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (MCRPC): LONG-TERM FOLLOW-UP

Abstract No: 2436

Rahul R. Aggarwal, Hematology/Oncology, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, United States of America; Scott T. Tagawa, Hematology and Medical Oncology, Weill Cornell Medicine, New York, NY, United States of America; Paul Monk, Medical Oncology, The Ohio State University, Columbus, OH, United States of America; Xinhua Zhu, Zuckerberg Cancer Center, Northwell Health Cancer Institute, New Hyde Park, NY, United States of America; Rob Jones, Beatson West of Scotland Cancer Centre, University of Glasgow, Glasgow, United Kingdom; Mark Linch, University College London Cancer Institute & UCL Hospital Foundation Trust, London, United Kingdom; Dan Costin, Center for Cancer Care, White Plains Hospital, White Plains, NY, United States of America; Johann de Bono, The Royal Marsden Hospital, London, United Kingdom; Lawrence I Karsh, Urology Department, The Urology Center of Colorado, Denver, CO, United States of America; Daniel Petrylak, Medical Oncology department, Yale University School of Medicine, New Haven, CT, United States of America; Pascal Borderies, Medical & Scientific Affairs, BioXcel Therapeutics, Inc., New Haven, CT, United States of America; Rashmi Deshpande, Clinical Scientist, BioXcel Therapeutics, Inc., New Haven, CT, United States of America; Vincent O'Neill, Head Oncology Unit, BioXcel Therapeutics, Inc., New Haven, CT, United States of America; Jingsong Zhang, Medical Oncology, Moffitt Cancer Center, Tampa, FL, United States of America

BXCL701 BACKGROUND

- 299,010 men diagnosed with prostate cancer in U.S. in 2024
- ~20% (~59,802) expected to progress to more aggressive mCRPC
  - ~80% adenocarcinoma (~47,842)
  - ~20% will develop SCNC (~11,960)
- BXCL701 modulates the tumor microenvironment by activating innate immunity followed by adaptive immunity leading to cancer cell death
- Phase 1b safety lead-in tested 2 total daily doses of BXCL701 (0.4 mg and 0.6 mg) [SITC 2020]
  - On-target AEs consistent with cytokine activation seen at highest daily dose (0.6 mg)
  - Splitting daily dose + step-up dosing improved tolerability (no reported DLTs and lower rates of AEs of interest hypotension and peripheral edema)



Adapted from Journal for ImmunoTherapy of Cancer 2021; 9:e002837. doi:10.1136/jitc-2021-002837

METHODS

KEY INCLUSION CRITERIA

- Histologically confirmed adenocarcinoma
- Measurable disease by RECIST 1.1 or bone metastases
- Progression as defined by PCWG3 criteria
- Serum testosterone <50 ng/dL during screening
- ECOG performance status of 0-2
- 1 or 2 androgen signaling inhibitors (ASI) + ≥1 prior line of taxane containing chemotherapy

KEY EXCLUSION CRITERIA

- >2 cytotoxic chemotherapy regimens for mCRPC
- Prior treatment with anti-PD-1, anti-PD-L1, anti-programmed death-ligand 2 (PD-L2) agent or with agent directed to another co-inhibitory T-cell receptor
- History of symptomatic orthostatic hypotension within 3 months prior to enrollment

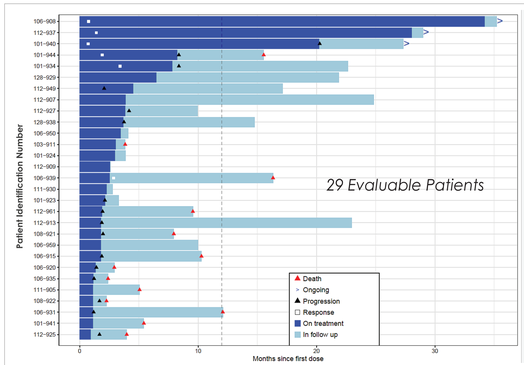
Pembrolizumab 200 mg IV q3w Day 1 + BXCL701 PO BID Days 1-14 of 21-day cycle
Cycle 1, BXCL701 step-up dosing: 0.2 mg BID PO Days 1-7 + 0.3 mg BID PO Days 8-14
Subsequent cycles: BXCL701 0.3 mg BID PO Days 1-14

Primary objective: Composite Response Rate, either objective response by RECIST 1.1 criteria, and/or CTC Conversion from ≥ 5/7.5 mL to <5/7.5 mL, and/or ≥-50% PSA decline from baseline
Secondary objectives: DoR, OS, PFS, changes in circulating cytokines and predictive biomarker identification

PATIENTS BASELINE CHARACTERISTICS

Phase 2a Cohort (n = 42 enrolled)	n (%)
Median Age (range)	**69.5** (51-87)
ECOG Performance Status (%)	
0	**13** (31)
1	**25** (60)
2	**3** (7)
Bone Only disease	**17 (40)**
Median lines of prior systemic therapy (range)	**5** (1 –11)
Prior Systemic Treatment	
Previous targeted endocrine therapy	
Enzalutamide only	**5** (17)
Abiraterone only	**6** (21)
Enzalutamide and abiraterone	**17** (59)
Taxane Chemotherapy	**29** (100)
Provenge (sipuleucel-T)	**7** (24)
Radiation Therapy	**12** (41)

TREATMENT DURATION



Median duration of Treatment
3 months
(range, 1 – 37)

Median duration of follow-up
29 months
(range, 22 – 34)

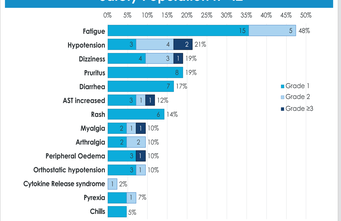
Data as of 30-AUG-23

SAFETY

Treatment-Related Adverse Events (TRAE)	n = 42 n (%)
Any Grade	**42** (100)
Attributed to BXCL701	***41*** *(98)*
Attributed to Pembrolizumab	**36** *(86)*
Grade 3	**27** (64)
Grade 4	**1** (2)
Grade 5	**1*** (2)
AE Leading to Treatment Discontinuation	**2** (5)
Attributed to BXCL701	**2** *(5)*
Attributed to Pembrolizumab	**2** *(5)*

** Grade 5 Disease Progression Not Related to Drug Treatment*
n = number of patients experiencing an AE

TRAE of Special Interest for the Combination Safety Population n=42



AEs consistent with cytokine activation

Data Extract 18-Jul-2024

EFFICACY RESULTS

Best Response	Phase 2a Adenocarcinoma Patients N = 29 (%) [95% Exact CI]
Composite Response	**6 (21) [8.0– 39.7]**
Best RECIST 1.1 Response by Investigator Assessment	
RECIST Evaluable[a]	18 (62)
Partial Response	**5 (28)** [9.7– 53.5]
Confirmed PR	*4 (80)*
Unconfirmed PR	*1 (20)*
SD (any duration)	7 (39)
PD including 2 bony progressions	6 (33)
Disease Control Rate PR + SD)	**67%**
PSA	
PSA Evaluable[b]	29 (100)
PSA_{50} **Response**	**5 (17) [5.8– 35.8]**
CTC[c]	
CTC Evaluable[d]	**11 (38)**
CTC Response[e]	2 (18)

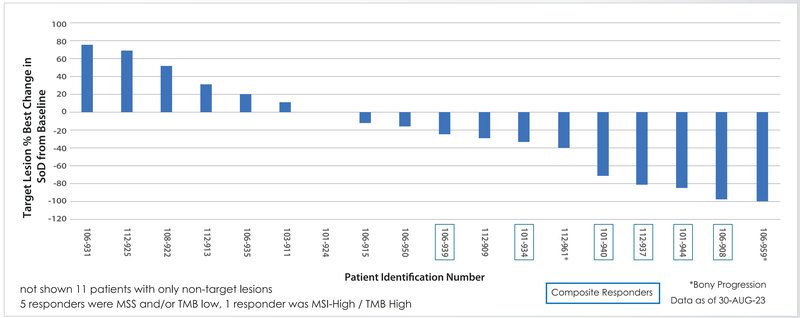
Composite response rate: **21%**
- RECIST-defined PR*: **28%**
- Disease control rate: **67%**
- PSA_{50}: **17%**—including 5 patients with -100% to -57% PSA decrease
- Median duration of response for both RECIST confirmed and PSA_{50} responses increased to **19 months**
- CTC response: **18%**

** Includes confirmed and unconfirmed PRs*

Data as of 30-AUG-23

a *Patients who received ≥2 cycles of study therapy and had 1 on-treatment tumor assessment* **b** *Baseline PSA >4 ng/mL and 1 on-treatment PSA assessment* **c** *Circulating tumor cell* **d** *Baseline CTC value ≥5/7.5 mL and 1 measurable on-treatment assessment* **e** *CTC conversion from ≥5/7.5 mL to <5/7.5 mL*

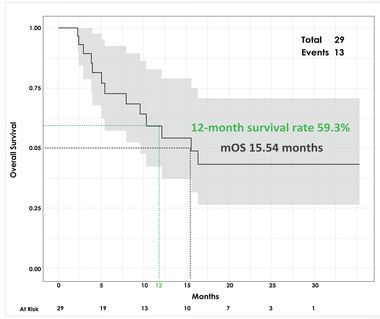
BEST TUMOR RESPONSE n = 18 RECIST 1.1 EVALUABLE PATIENTS

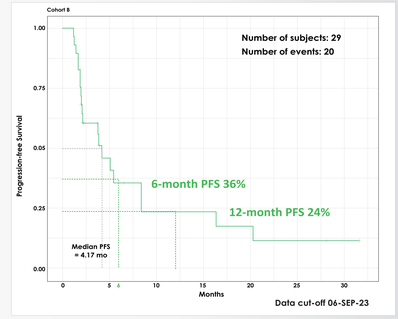


not shown 11 patients with only non-target lesions
5 responders were MSS and/or TMB low, 1 responder was MSI-High / TMB High

*Bony Progression
Data as of 30-AUG-23

ADENOCARCINOMA PATIENTS OVERALL SURVIVAL & RADIOGRAPHIC PFS KAPLAN-MEIER CURVES





Pembrolizumab KEYNOTE-199 Study Efficacy Comparison*

- Three cohorts of patients with mCRPC treated with docetaxel and one or more targeted endocrine therapies (n=258; 199 with measurable disease enrolled in cohorts 1 and 2)
- Microsatellite status unknown
- ORR in RECIST measurable disease 3-5% (Cohorts 1 & 2)
- mPFS 2.1mo (3 cohorts)
- mOS 9.6mo (3 cohorts)

**Antonarakis ES, Piulats JM, Gross-Goupil M, Goh J, Ojamaa K, Hoimes CJ, Vaishampayan U, Berger R, Sezer A, Alanko T, de Wit R, Li C, Omlin A, Procopio G, Fukasawa S, Tabata KI, Park SH, Feyerabend S, Drake CG, Wu H, Qiu P, Kim J, Poehlein C, de Bono JS. Pembrolizumab for Treatment-Refractory Metastatic Castration-Resistant Prostate Cancer: Multicohort, Open-Label Phase II KEYNOTE-199 Study. J Clin Oncol. 2020 Feb 10;38(5):395-405. doi: 10.1200/JCO.19.01638. Epub 2019 Nov 27. PMID: 31774688; PMCID: PMC7186583.*

CONCLUSIONS

Combination of BXCL701 + pembrolizumab demonstrates encouraging response rates and median survival times in a genomically unselected late-line mCRPC patient population with limited standard of care treatment options, coupled with an acceptable safety profile

- Results appear favorable to those expected with pembrolizumab monotherapy
- Split and step-up dosing to mitigate cytokine release
- No evidence of potentiation of immune-related AEs
- Further evaluation in a randomized trial is warranted

Thank You

BioXcel Therapeutics, Inc. would like to thank all patients, their families, and caregivers who made this study possible. BioXcel Therapeutics, Inc. would also like to thank the participating investigators and their staff for their support on this study and their dedication to their patients, despite the additional challenges as a circumstance of the COVID-19 pandemic.

CONFLICT OF INTEREST DECLARATION

Primary author Rahul Aggarwal <Rahul.Aggarwal@ucsf.edu> is the Principal Investigator of this multicenter study sponsored by BioXcel Therapeutics, Inc.

ClinicalTrials.gov Identifier: NCT03910660