FIRST-IN-CLASS ORAL INNATE IMMUNE ACTIVATOR BXCL701 COMBINED WITH PEMBROLIZUMAB IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (mCRPC) OF SMALL CELL NEUROENDOCRINE (SCNC) PHENOTYPE: PHASE 2 UPDATED EFFICACY RESULTS

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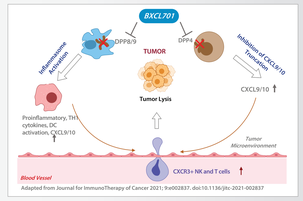
BXCL701 BACKGROUND

- *de novo* and treatment-emergent SCNC are associated with adverse survival outcomes
- 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)



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METHODS

KEY INCLUSION CRITERIA

- Histologically confirmed *de novo* SCNC or treatment-emergent SCNC
- ≥1 prior line of systemic therapy
- Progression as defined by PCWG3 criteria
- Serum testosterone <50 ng/dL during screening, except for patients with de novo SCNC
- ECOG performance status of 0-2

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

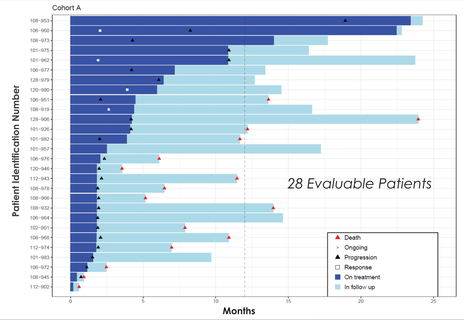
PEMBROLIZUMAB 200 MG IV Q3W DAY 1 + BXCL701 PO BID DAYS 1-14 OF 21-DAY CYCLE
CYCLE 1, BXCL701 STEP-UP DOSING: 0.2 MG BID PO DAYS 1-7 + 0.3 MG BID PO DAYS 8-14
SUBSEQUENT CYCLES: BXCL701 0.3 MG BID PO DAYS 1-14

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 (n = 34 enrolled)	n (%)
Median Age (range)	67.5 years (54 – 80)
ECOG Performance Status (%)	
0	16 (47%)
1	16 (47%)
2	2 (6%)
Visceral Metastases	
Any site	21 (62%)
Liver	11 (32%)
Median lines of prior systemic therapy (range)	3 (1 – 8)
Prior Systemic Treatment	
Androgen signaling inhibitor(s)	25 (89%)
Platinum-based Chemotherapy	19 (68%)
Taxane Chemotherapy	17 (50%)

TREATMENT DURATION



Median duration of follow-up 23.9 months
(range, 11.3 – 38.2)

6 patients (21%) treated beyond progression

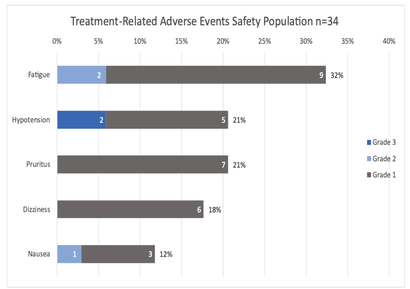
Data as of 06-SEP-23

SAFETY

Treatment-Emergent Adverse Events	n = 34 n (%)
Any Grade	33 (97)
Attributed to BXCL701	*29 (85)*
Attributed to Pembrolizumab	*23 (68)*
Grade 3	16 (47)
Grade 4	0 (0)
Grade 5	1 (3)*
AE Leading to Treatment Discontinuation	6 (18)
Attributed to BXCL701	*6 (18)*
Attributed to Pembrolizumab	*5 (15)*
Immune Related Adverse Events Any Grade	14 (41%)
*Grade ≥ 3^*	*1 (7%)*

** Grade 5 tumor lysis | ^ Grade 3 colitis*

n = number of patients experiencing an AE



TRAEs at least possibly related to BXCL701 or pembrolizumab, occurring in >10% of patients

EFFICACY RESULTS

Best Response	SCNC Evaluable Patients n = 28 (%) [95% Exact CI]
Composite Response *(includes unconfirmed PR)*	7 (25%) [8.3%-41%]
Best RECIST 1.1 Response by Investigator Assessment	
RECIST Evaluable[a]	25 (89%)
Partial Response	5 (20%) [6.8%-40.7%]
Confirmed PR	*4 (16%)*
Unconfirmed PR	*1 (4%)*
Stable Disease (any duration)	7 (28%)
Progressive Disease	13 (52%)
Disease Control Rate (PR + SD)	12 (48%)
CTC[b]	
CTC Evaluable[c]	4
CTC Response[d]	1 (25%) [0.6%– 80.6%]
PSA	
PSA Evaluable[e]	27 (96%)
PSA_{50} Response	3 (11%) [2.4%- 29%]

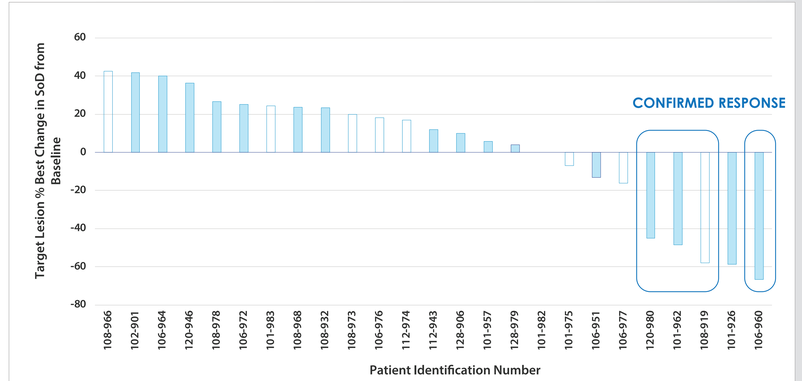
Composite Response Rate: 25%

- **RECIST response rate: 20%**
  - 4 confirmed PR + 1 unconfirmed PR
- Disease control rate: **48%**
- **Median duration of response** for both RECIST confirmed and PSA_{50} responses increased to **7.6 months**

Data as of 06-SEP-23

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

BEST TUMOR RESPONSE n = 25 RECIST 1.1 EVALUABLE PATIENTS



No Prior Platinum Chemotherapy | Prior Platinum Therapy

Data as of 06-SEP-23

CONCLUSIONS

- BXCL701 + pembrolizumab demonstrated encouraging activity with durable responses in patients with platinum-resistant small cell neuroendocrine prostate cancer, for whom there is no FDA approved treatment therapy
  - All responders were MSS and/or TMB low, with low probability of response to pembrolizumab monotherapy
- BXCL701 + pembrolizumab demonstrated manageable safety profile
  - Split and step-up dosing to mitigate cytokine release
  - No evidence of potentiation of immune-related AEs
- Biomarker work continues and will be presented in a future scientific meeting

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.

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