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 2A FINAL RESULTS

Abstract No: 176

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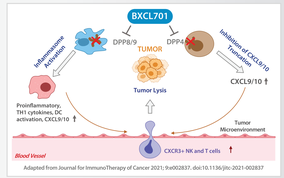
BXCL701 BACKGROUND

- De novo and treatment-emergent SCNC associated with adverse survival outcomes
- BXCL701 modulates 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 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

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

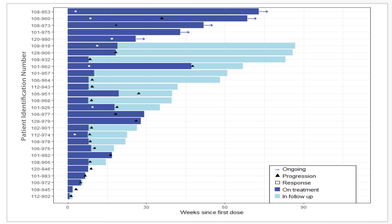
PRIMARY OBJECTIVE: Composite Response Rate, either objective response by RECIST 1.1 criteria, and/or CTC Conversion from ≥5/7.5 mL to <5/7.5 mL, and/or ≥-50% PSA decline from baseline

ADDITIONAL OBJECTIVES: Duration of response, PFS, changes in circulating cytokines, correlation of outcome with baseline tumor characteristics

BASELINE CHARACTERISTICS

Phase 2a Cohort (n = 34)	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 = 30.8 weeks (range 1.9 – 86.9 weeks)

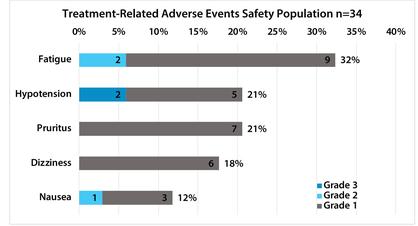
MEDIAN DURATION OF TREATMENT = 9 weeks (range: 0.7 to 73 weeks)

28 Evaluable Patients - Data as of 19-DEC-22

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
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 syndrome ^ Grade 3 colitis



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

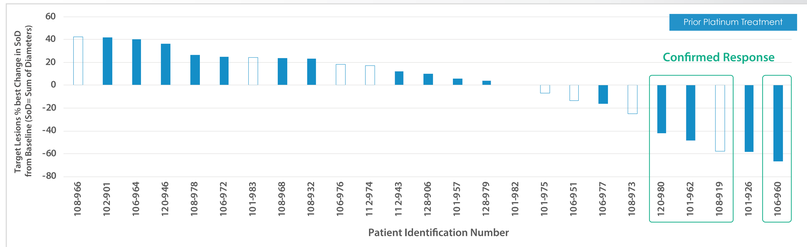
EFFICACY RESULTS - DATA AS OF 19-DEC-22

BEST RESPONSE	SCNC/T-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%)
SD (any duration)	7 (28%)
PD	13 (52%)
Disease Control Rate (CR + 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%
CTC response: 25%
PSA_{50}: 11% 1 patient with PSA -73%
Median DoR* (composite) = 6+ months (range: 1.3 - 17.4 months)
Median DoR* (RECIST 1.1) = 6+ months (range: 1.8 - 9.8 months)

[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 * DoR = Duration of Response

CHANGE IN TUMOR SIZE FROM BASELINE
n = 25 RECIST 1.1 EVALUABLE PATIENTS - DATA AS OF 08-FEB-23
ALL RESPONDERS ARE MSS AND/OR TMB LOW



EFFICACY SUMMARY COMPOSITE RESPONSE – DATA AS OF 19-DEC-2022

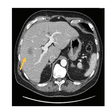
Patient	Prior Systemic Therapies	Duration on Treatment (weeks)	RECIST 1.1 ≥-30%*	CTC ≥5/7.5 ml to <5/7.5 ml*	PSA ≥-50%*	Tumor Biology
106-960	Bicalutamide, Lupron carboplatin, etoposide	65.7	-67% Confirmed		NA	TMB = 3 MSS
108-919#	Degarelix, Lupron	19 (+ 18 off treatment)	-58% Confirmed		NA	TMB = 0 MSS
101-926#	Abiraterone, leuprolide, chemoradiation, abiraterone, prednisone, cisplatin, etoposide	18	-58% Unconfirmed	1 to 0	NA	MSS
101-962	ADT, carboplatin / docetaxel	47	-49% Confirmed		NA	TMB = 4
120-980	Carboplatin, Etoposide, Prostap	24	-42% Confirmed	NA	NA	TMB = 2.9
108-953#	Degarelix, Lupron, carboplatin/docetaxel	70	SD 64 weeks	19 to 4	-73%	MSS PD-L1 low
112-974#	Abiraterone, bicalutamide, docetaxel	7.6	+17%	117 to 47	-50%	TMB = 4 MSS

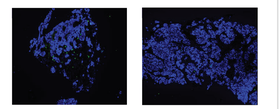
On Treatment | Off Treatment | Response

Tissue used in exploratory biomarker analysis.
*Change from baseline | TMB = Tumor Mutation Burden | MSS = Microsatellite Stable

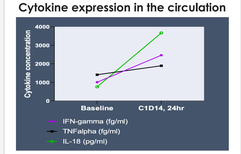
RESPONSE IN A PATIENT WITH TREATMENT-EMERGENT SCNC WITH LIVER METASTASES

- Prior systemic therapies: LHRH agonist, abiraterone + prednisone, cisplatin + etoposide
- Microsatellite stable, low TMB
- 58% reduction in target lesions following 3 cycles of treatment





DPP9 over-expressed (in 101-926) compared to non-responder



CONCLUSIONS

- BXCL701 + pembrolizumab demonstrated encouraging activity with durable responses observed in patients with platinum-resistant, small cell neuroendocrine prostate cancer
  - 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
- Validation of DPP9 over-expression as a predictive biomarker is ongoing
- Phase 2b randomized study in SCNC will commence soon

THANK YOU

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Moses Donkor, Ph.D., Biomarker Lead, BioXcel Therapeutics, New Haven CT

Conflict of Interest Declaration- Primary author Rahul Aggarwal < Rahul.Aggarwal@ucsf.edu > is the Principal Investigator of the multicenter study BXCL701-201 sponsored by BioXcel Therapeutics, Inc. | ClinicalTrials.gov Identifier: NCT03910660

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