BXCL701—1st-in-class oral activator of systemic innate immunity—combined with pembrolizumab, in patients with metastatic castration-resistant prostate cancer (mCRPC) of small-cell neuroendocrine carcinoma (SCNC) phenotype: Phase 2a interim results

E-POSTER 126

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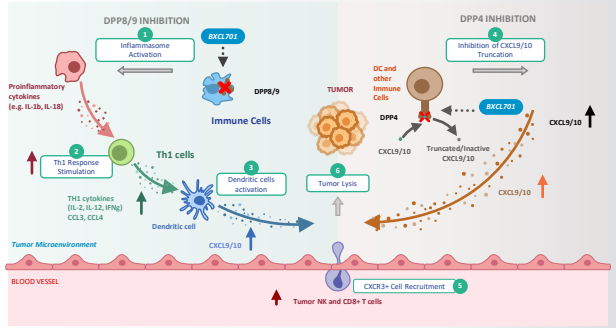
BACKGROUND
Small Cell Neuroendocrine Carcinoma

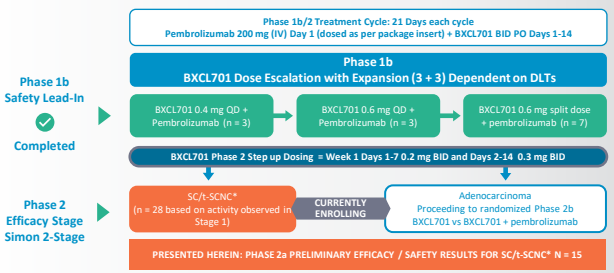
- Treatment of metastatic castration-resistant prostate cancer has evolved rapidly over the past few years:
  - 1st-line treatment with androgen deprivation therapy or one of newer androgen signaling inhibitors (ASI) abiraterone or enzalutamide followed by chemotherapy with docetaxel now standard of care
  - Docetaxel associated with median overall survival <2 years
- Treatment-emergent small cell neuroendocrine prostate cancer (t-SCNC) emerges in ~20% patients resistant to androgen receptor-targeting therapy
- t-SCNC is a histologic subtype that morphologically resembles de novo small cell prostate cancer, highly proliferative and aggressive and does not typically express androgen receptor or PSA
- There is no standard of care for t-SCNC
- BXCL701 immunomodulatory mechanism may turn a "cold" tumor micro-environment into an inflamed "hot" tumor micro-environment, contributing to overcome resistance to immunotherapy

BXCL701 MODULATES TUMOR MICROENVIRONMENT BY ACTIVATING INNATE IMMUNITY FOLLOWED BY ADAPTIVE IMMUNITY, LEADING TO CANCER CELL DEATH



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

METHODS | TRIAL SCHEMATIC AND KEY OBJECTIVES



Primary objective for each Phase 2 Cohort: Composite Response Rate, either objective response by RECIST 1.1 criteria, CTC Conversion from ≥5/7.5 mL to <5/7.5 mL, or ≥-50% PSA decline from baseline
Additional objectives: DoR, PFS, changes in circulating cytokines and correlation of outcome with baseline tumor characteristics
*Small-cell/treatment-emergent small-cell neuroendocrine prostate cancer

KEY INCLUSION AND EXCLUSION CRITERIA

KEY INCLUSION CRITERIA
- Histologically confirmed **SC/t-NEPC**
- Progression as defined by PCWG3 criteria
- At least 1 prior line of systemic therapy for locally advanced or metastatic prostate cancer
- Serum testosterone <50 ng/dL during screening, except for those with de novo small cell prostate cancer
- ECOG performance status of 0-2
- Phase 2 Efficacy Stage only:
  - **For Cohort SC/t-NEPC:**
    - At least 1 prior line of chemotherapy
    - Measurable disease by RECIST 1.1

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

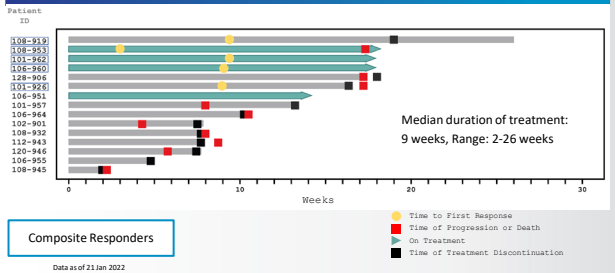
See ClinicalTrials.gov Identifier: NCT03910660 for more details

RESULTS: STUDY POPULATION

Baseline Characteristics		SCNC Cohort N = 18 (%)
Enrolled Patients		18
Age (years)	Mean (SD)	67.3 (7.06)
	Median (Range)	68.5 (54-78)
ECOG Performance Status	0	8 (44)
	1	8 (44)
	2	2 (11)
Bone Only disease		5 (28)
Prior Cancer Therapies	Mean number of prior regimens (SD)	2.3 (1.08)
Evaluable Patients		15
Prior Systemic Therapies	**Previous targeted endocrine therapy**	
	Only enzalutamide	*1 (0.66)*
	Only abiraterone	*2 (1.3)*
	No enzalutumide or abiraterone (ASI)	*12 (80)*
	Platinum chemotherapy	14 *(93)*
	Taxane chemotherapy	7 (21)
	Provenge (sipuleucel-T)	0
	Radiation therapy	10 (66)

Data as of 24-NOV-2021 unless noted otherwise

EXPOSURE DURATION AND SUBJECT DISPOSITION
15 evaluable patients



Composite Responders

Data as of 21 Jan 2022

EFFICACY RESULTS

Best Response	SCNC Patients N = 15 (%) [95% Exact CI]
Composite Response	**5 (33) [11.8 – 61.6]**
Best RECIST 1.1 Response by Investigator Assessment	
RECIST Evaluable[a]	12 (80)
Partial Response	**4 (33) [9.9 – 65.1]**
Confirmed PR	*3 (75)*
Unconfirmed PR	*1 (25)*
SD (any duration) including Minor Response	3 (27)
Non-CR / Non-PD	7 (58)
PD	5 (41)
Disease Control Rate (CR + PR + SD)	**58%**
CTC[b]	
CTC Evaluable[c]	3
CTC Response[d]	**1 (33)**

- Composite response rate: **33%**
- RECIST-defined PR*: **33%**
- Disease control rate: **58%**
- CTC response: **33%**
- Patients typically tend not to be PSA secretors

** Includes confirmed and unconfirmed PRs*

Data cut-off date: 21-JAN-2022

[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

EFFICACY SUMMARY
Data as of 21-JAN-2022

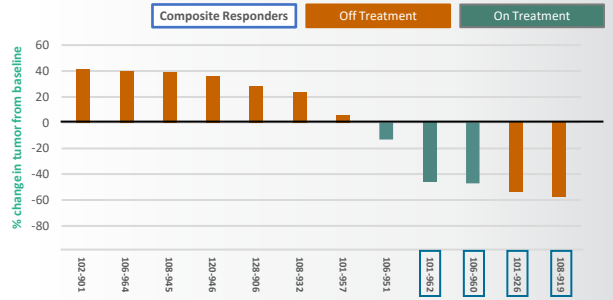
Patient	Prior Systemic Therapies	RECIST 1.1 ≥-30%*	CTC ≥5/7.5 ml to <5/7.5 ml*	PSA ≥-50%*	Tumor Biology
108-919	Degarelix, Lupron	-58% Confirmed 26-week duration		NA	TMB = 0 MSS
101-926	Abiraterone, leuprolide, chemoradiation, abiraterone, prednisone, cisplatin, etoposide	-54% Unconfirmed 10-week duration	1 to 0	NA	MSS
108-953	Degarelix, Lupron, carboplatin/docetaxel	Unavailable	19 to 4	-60%	MSS PD-L1 low
106-960	Bicalutamide, Lupron carboplatin, etoposide	-47% Confirmed 11-week duration		NA	TMB = 3 MSS
101-962	ADT, carboplatin / docetaxel	-46% Confirmed 12-week duration		NA	Unavailable

On Treatment | Off Treatment | Response

Median duration of response: 11.5 weeks

**change from baseline | TMB = Tumor Mutation Burden | MSS = Microsatellite Stable*

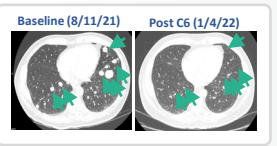
BEST TUMOR RESPONSE (N = 12)

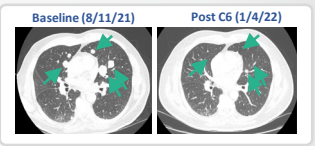


Data as of January 21, 2022

PATIENT VIGNETTE

Patient	Prior Systemic Therapies	RECIST 1.1 ≥-30%*
101-962	ADT, Carboplatin/docetaxel	-46% Confirmed 12-week duration





TOLERABILITY / SAFETY PROFILE

Treatment Related Adverse Events*	N = 18 n (%) Patients	
AE Preferred Term	Any Grade	Grade ≥3
Fatigue	6 (33)	
Hypotension	4 (22)	1 (6)
Cough	3 (17)	
Nausea	3 (17)	
Pruritus	3 (17)	
Acute Kidney Injury	2 (11)	2 (11)
Diarrhoea	2 (11)	
Dry Mouth	2 (11)	

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

- Majority of events were low grade
- AEs consistent with cytokine activation were observed—fever, nausea, chills, fatigue, headache, dizziness
- SAEs experienced by 3 (17%) patients were reported as possibly related to BXCL701 or pembrolizumab: 2 patients with hypotension; 1 patient with acute kidney injury and Grade 5 Tumor Lysis Syndrome
- 4 (22%) patients discontinued therapy due to AEs
- **No evidence that BXCL701 potentiate immune-related AEs related to immune checkpoint inhibitors**

CONCLUSIONS
- BXCL701 + pembrolizumab showed highly encouraging response rates in this aggressive variant of metastatic castration-resistant prostate cancer, for which there is no standard of care:
  - Responses were generally observed in absence of predictive markers for checkpoint therapy response
- Combination of BXCL701 + pembrolizumab demonstrated manageable safety profile:
  - Majority of AEs were low grade
  - No evidence of potentiation of immune-related AEs
- Biomarker work continues and will be presented in a future scientific meeting
- Study continues to enroll patients to completion as per protocol

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 Scott Tagawa < stt2007@med.cornell.edu > is a Principal Investigator in this multicenter study sponsored by BioXcel Therapeutics, Inc. | ClinicalTrials.gov Identifier: NCT03910660