Early results from a phase 1, multicenter trial of PSCA-specific GoCAR-T cells (BPX-601) in patients with metastatic castration-resistant prostate cancer (mCRPC)

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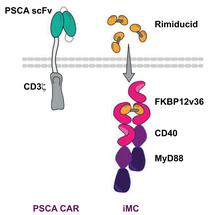
Abstract #140

BACKGROUND

- Prostate stem cell antigen (PSCA) is a cell surface protein expressed in ~80% of prostate cancers[1,2]
- BPX-601 is an autologous PSCA-directed chimeric antigen receptor (CAR)-T cell immunotherapy engineered to co-express a rimiducid-inducible MyD88/CD40 (iMC) co-activation switch to enhance T cell potency and persistence[3,4]

BPX-601: a two-component inducible GoCAR-T cell



1st generation CAR: Directs specificity and cytotoxicity against PSCA-expressing tumors

iMC: Molecular switch that replaces natural T cell costimulation with inducible signaling from MyD88 and CD40

- Increases proliferation, persistence, survival, and cytotoxicity of adoptively transferred CAR-T cells
- Stimulates endogenous immunity (adjuvant effects):
  - Secretion of pro-inflammatory cytokines
  - Upregulation of costimulatory molecules

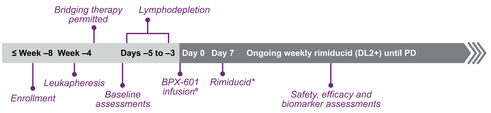
Rimiducid: A synthetic small-molecule dimerizer that mediates the oligomerization of iMC and activation of signaling

Unlike standard 2nd generation CAR-T platforms, iMC co-activation controls GoCAR-T cell proliferation, functional persistence, and production of immunomodulatory cytokines with administration of rimiducid

STUDY OBJECTIVES AND METHODS

- Here we present interim results (data extract Dec 2022) from a Phase 1, multicenter clinical trial of BPX-601 in patients (pts) with mCRPC (NCT02744287). Dose escalation was first initiated in subjects with pancreatic cancer (n=24)
  - Primary objectives: determine safety, tolerability and MTD/RP2D
  - Secondary objectives: characterization of clinical efficacy, PK of rimiducid and long-term safety
  - Biomarkers indicative of GoCAR-T cell expansion, immune cell activity and infiltration into tumor are being monitored
- Eligible mCRPC pts must have measurable disease per RECIST 1.1 or bone only disease per PCWG and progression on ≥2 prior therapies including an androgen deprivation therapy (ADT) and chemotherapy

Timeline for patient enrollment and treatment



[a]Pts received a single infusion of 5 × 10⁸ BPX-601 cells/kg
*Single (DL1, n=3) or weekly (DL2, n=5) doses of 0.4 mg/kg rimiducid were infused beginning 7 days following cell infusion

RESULTS

Baseline Patient Characteristics

	All Patients (N=8)
Age, median (range)–yr	66.5 (56–75)
ECOG performance score, no. (%)	
0	4 (50%)
1	4 (50%)
Site of metastatic disease, no. (%)[a]	
Liver	2 (25%)
Lung	2 (25%)
Lymph nodes	5 (62.5%)
Bone	4 (50%)
Bone only	2 (25%)
PSA level (ng/ml), median (range)	186 (29–331)
Prior lines of treatment, median (range)	6 (5–9)

- All tumors tested (n=5 pts) expressed PSCA mRNA[b]
- All pts received prior ADT[c] and chemotherapy
  - 87.5% received docetaxel
  - 75% received immune-based therapies

[a]Pts included in ≥1 category of site of disease.
[b]As measured by RNAScope; no tumor tissue available for 3 pts
[c]ADT included a standard 17α lyase inhibitor or second-generation anti-androgen therapy.
ECOG, Eastern Cooperative Oncology Group; PSA, prostate-specific antigen

Safety Summary

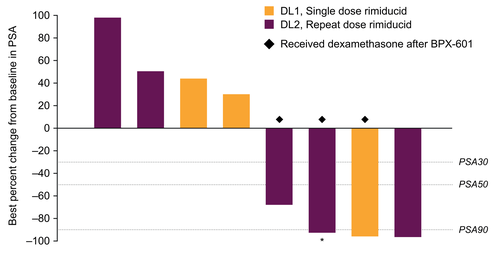
	All Patients (N=8)	
	All grades n (%)	Grade 3+ n (%)
TEAE	8 (100%)	7 (87.5%)
Serious TEAE	5 (62.5%)	5 (62.5%)
Cytokine release syndrome	8 (100%)	2 (25%)
Neurotoxicity/ICANS	2 (25%)	1 (12.5%)
Dose-limiting toxicity	1 (12.5%)	1 (12.5%)*
TEAE leading to death	1 (12.5%)	1 (12.5%)*

TEAEs reported for ≥3 patients

System Organ Class/ Preferred Term	Total n (%)	Grade 3+ n (%)
Subjects reporting ≥1 TEAE	8 (100%)	7 (87.5%)
Anemia	6 (75%)	6 (75.0%)
Back pain	3 (37.5%)	1 (12.5%)
Blood alkaline phosphatase increased	4 (50%)	2 (25.0%)
Blood creatinine increased	3 (37.5%)	0
Cough	3 (37.5%)	0
C-reactive protein increased	3 (37.5%)	0
Diarrhea	3 (37.5%)	0
Fatigue	3 (37.5%)	1 (12.5%)
Hypokalemia	3 (37.5%)	2 (25.0%)
Hypophosphatemia	3 (37.5%)	0
Leukopenia	3 (37.5%)	3 (37.5%)
Neutropenia	5 (62.5%)	5 (62.5%)
Platelet count decreased	5 (62.5%)	1 (12.5%)*
Pyrexia	8 (100%)	0

*Death Day 20 due to sepsis (*Stenotrophomonas maltophilia*)
ICANS, immune effector cell-associated neurotoxicity syndrome; TEAE, treatment-emergent adverse event

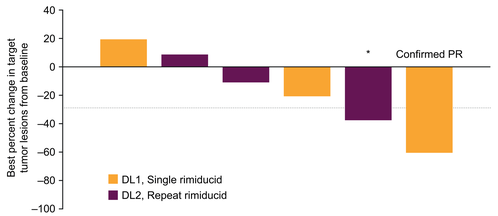
≥PSA50 Response in 50% of Patients



- PSA90 responses in 3 (37.5%) pts within first 28 days
- Marked decreases in PSA despite administration of dexamethasone

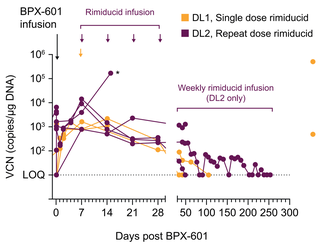
*Death Day 20 due to sepsis; received 1 dose of rimiducid

Radiologic Responses by RECIST



*Death Day 20 due to sepsis.
PR, partial response; RECIST, response evaluation criteria in solid tumors version 1.1.

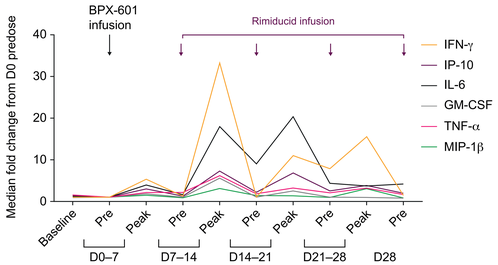
Consistent GoCAR-T Cells Expansion and Long-term Persistence



- BPX-601 expanded in all pts and persistence >40 days was observed in 4/5 evaluable pts
- Pt with GoCAR-T cells in peripheral blood >200 days on study with stable disease by CT at 10 months

BPX-601 cells pharmacodynamics in peripheral blood was tested by qPCR-based detection of CAR sequence in genomic DNA extracted from blood serially collected during the first week after BPX-601 cells infusion, then weekly sampling (prior to rimiducid dosing in cohort DL2) when feasible.
VCN data obtained from whole blood (WB) or PBMCs; PBMC values normalized to WB.
*Death Day 20 due to sepsis; received 1 dose of rimiducid; last VCN data on Day 15 shown.
VCN, vector copy number; LOQ, limit of quantitation; CT, computed tomography.

Weekly Rimiducid Dosing Induces Secretion Of Cytokines and Chemokines Associated with BPX-601 Activation



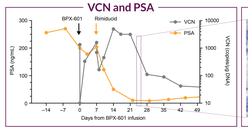
Serum cytokine levels were evaluated at serial timepoints using a multiplex assay. Median values at baseline, predose and weekly peak are presented for pts enrolled in Cohort DL2 (n=5).
D, day.

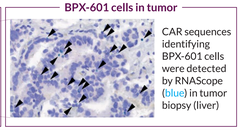
CASE STUDIES

CS1. Confirmed PR observed

68 y/o M with stage IV prostate adenocarcinoma diag. Aug 2019

- Received 5 prior therapies including ADT + docetaxel and PSMA-targeted therapy with disease progression
- CRS grade 2 following BPX-601 and grade 3 CRS following rimiducid resolved
- PSA90 and ~50% reduction in target lesions (liver) at Day 42; confirmed Day 71 with 60% reduction
- Robust BPX-601 cells infiltration in liver metastasis observed at Day 24





CAR sequences identifying BPX-601 cells were detected by RNAScope (blue) in tumor biopsy (liver)

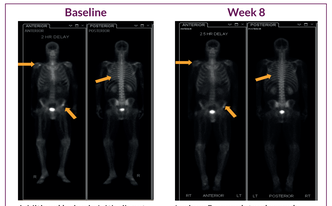
- Treatment-free interval following BPX-601 and a single dose of rimiducid was 4.5 months

CS2. PSA90 response in bone only mCRPC

59 y/o M with bone only mCRPC diag. Jan 2017

- Refractory to 6 prior lines of therapy, including multiple ADTs; prior to enrollment received cabazitaxel
- CRS grade 1 following first rimiducid dose

Study timepoint	PSA (ng/ml)
Baseline	29.4
Day 28	1.1
Day 58	1.0
Day 86	1.2



Additional lesion in L4th rib not easily noted here

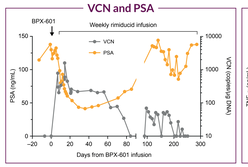
Lesions R upper lateral scapula, posterior L9th transverse and additional L4th rib no longer evident per radiology report

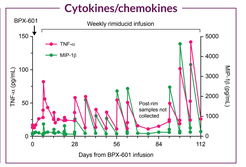
- Decreased enhancement observed in 3 out of 4 lesions at week 8
- PSA90 response at Day 28 (week 4) and ongoing as of Day 86
- Pt continues weekly rimiducid

CS3. Stable disease >10 months

66 y/o M with stage III prostate adenocarcinoma diag. Jul 2012

- Refractory to 5 prior lines of therapy including ADT and investigational PSMA-targeted therapy
- CRS grade 1 following BPX-601 and with first rimiducid dose
- PSA50 response and RECIST response assessment at 10 months confirms best response of stable disease in target lesions (retrocaval and left internal iliac lymph nodes)



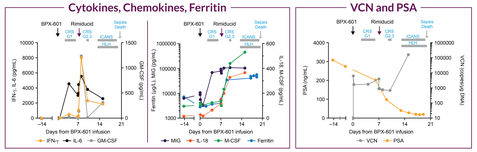


- GoCAR-T cells persisted to low but measurable numbers in peripheral blood >200 days with weekly rimiducid
- Chemokine and cytokine levels reproducibly shows rapid increases following repeated rimiducid

CS4. Hemophagocytic lymphohistiocytosis (HLH)

75 y/o M with stage III prostate adenocarcinoma diag. Jul 2009

- Refractory to 9 prior therapies including Sipuleucel-T and cemiplimab
- Elevated baseline ferritin and CMV re-activation during LD
- Markers of macrophage activation (IL-6, MIG) elevated Day 4 prior to rimiducid
- Select markers of GoCAR-T activity (IFN-γ, GM-CSF) elevated following BPX-601 and rimiducid and decreasing on Day 10 while markers of HLH/MAS further increased. IFN-γ remained elevated with HLH



- PSA90 and tumor shrinkage observed following BPX-601 and rimiducid
- Grade 1 CRS with BPX-601 resolved prior to rimiducid infusion. Grade 3 CRS following rimiducid; resolved. Grade 4 ICANS resolved to grade 1. HLH concurrent with development of ICANS. Grade 5 Sepsis Day 20

CONCLUSIONS

- Most common grade 3+ adverse events were related to myelosuppression. Two pts had grade 3 CRS. 1 dose-limiting toxicity in DL2
- Encouraging preliminary biochemical and radiographic efficacy of BPX-601 PSCA-directed GoCAR-T cells with rimiducid in heavily pretreated mCRPC
- Consistent BPX-601 cell expansion in peripheral blood with persistence >200 days and cytokine secretion responsive to rimiducid
- Evidence of BPX-601 cells infiltration in PSCA-positive tumor
- Exploration of escalating weekly rimiducid doses >0.4 mg/kg planned with next dose cohort

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