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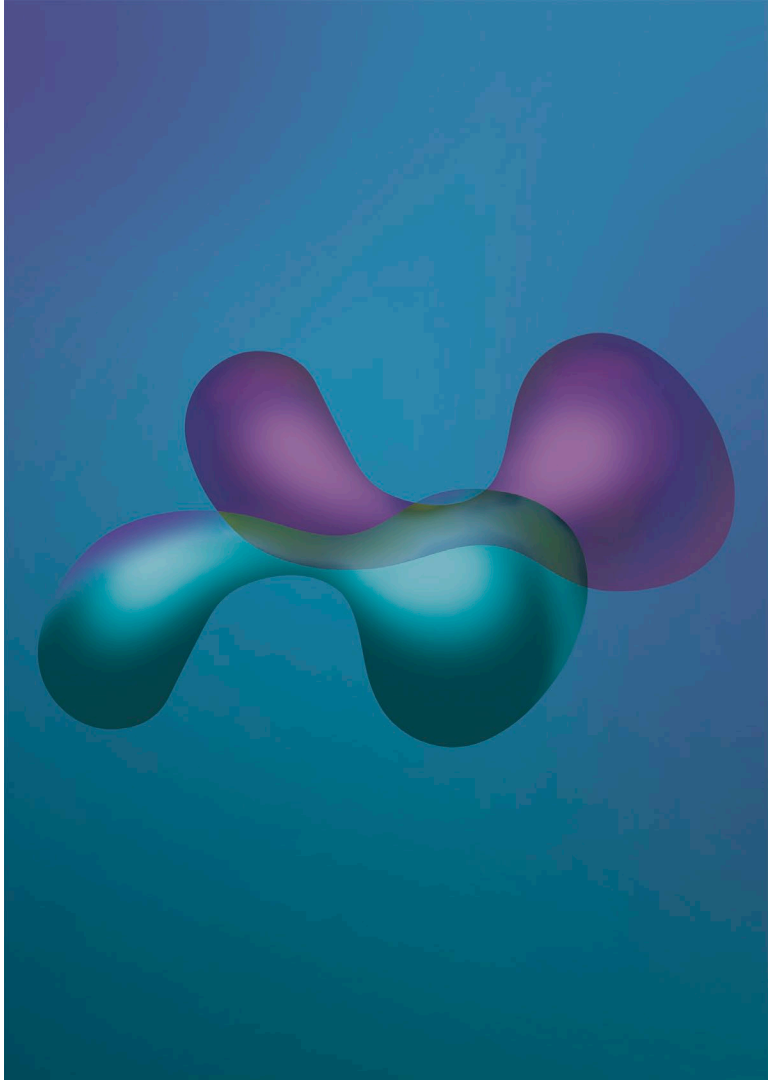
LIGAND-INDUCIBLE, PROSTATE STEM CELL ANTIGEN (PSCA)-DIRECTED GoCAR-T® CELLS IN ADVANCED SOLID TUMORS: PRELIMINARY RESULTS FROM A DOSE ESCALATION STUDY

Carlos R. Becerra,[1] Pamela Hoof,[1] Scott Paulson,[1] Gulam A. Manji,[2] Olivia Gardner,[3] Aditya Malankar,[3] Joanne Shaw,[3] Devin Blass,[3] Brandon Ballard,[3] Xiaohui Yi,[3] Madhavi Anumula,[3] Aaron Foster,[3] Joseph Senesac,[3] Paul Woodard[3]

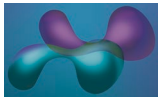
[1]Baylor University Medical Center, Dallas, TX, USA;
[2]Columbia University Medical Center/New York Presbyterian Hospital, New York, New York, USA; [3]Bellicum Pharmaceuticals, Houston, TX, USA.



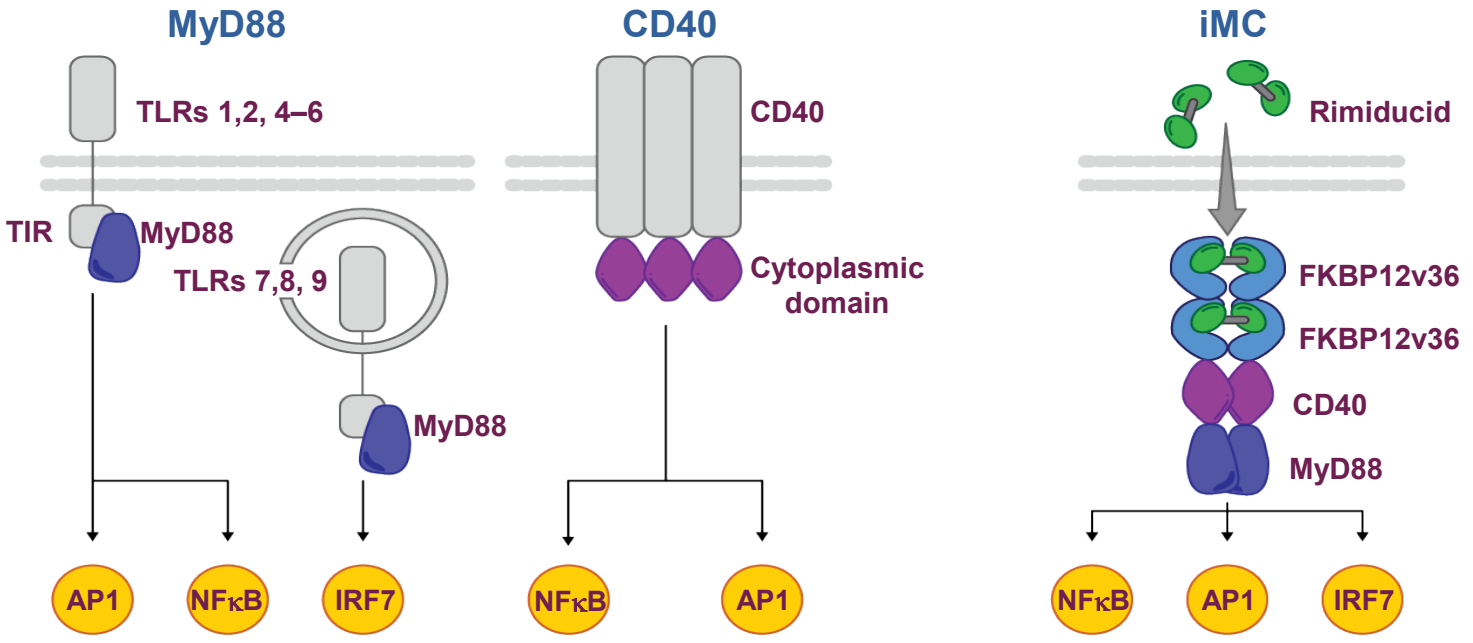
DISCLOSURE SLIDE

Dr. Becerra has received honoraria from Taiho Pharmaceutical; has consulted for Agenus, Bayer, Heron, Ipsen, SOBI, and Takeda; and has participated in speakers' bureaus for Bristol-Myers Squibb, Celgene, Merck Serono, and Taiho Pharmaceutical

This study was sponsored by Bellicum Pharmaceuticals



INDUCIBLE MYD88/CD40 (iMC)

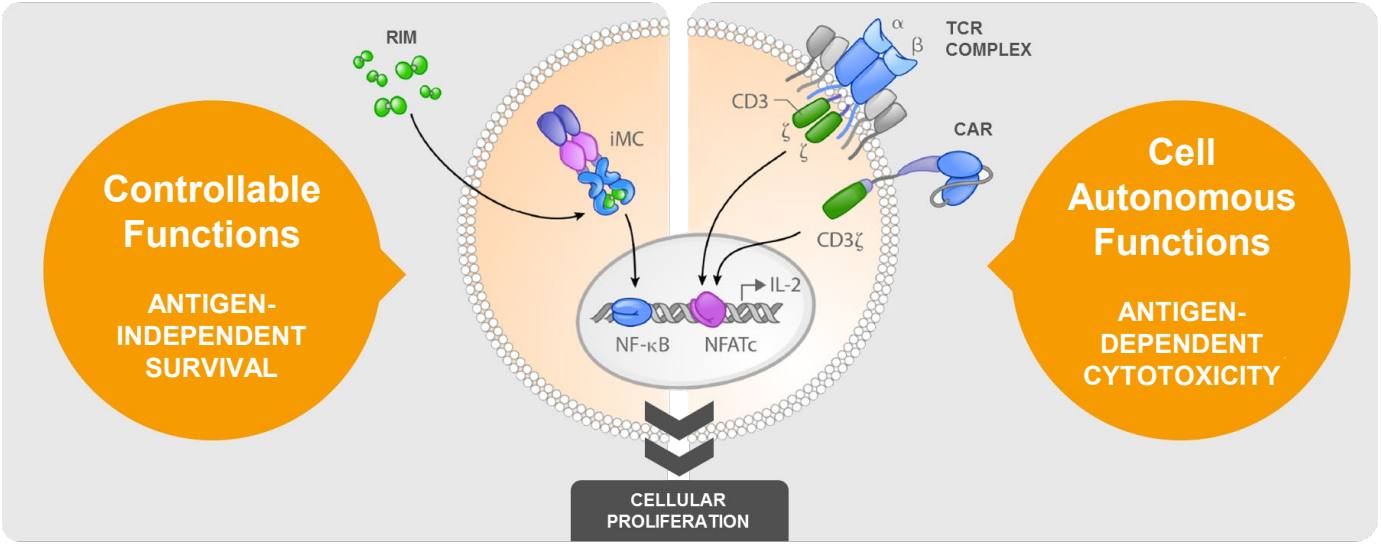


Proinflammatory cytokines, Type I IFNs, T Cell Proliferation and Persistence
Other immune functions

IFN, interferon; iMC, inducible MyD88/CD40; TIR, toll/interleukin-1 receptor; TLR, toll-like receptor.

GoCAR-T®: BPX-601 OVERVIEW

- Autologous T cell product candidate
- Antigen-specific activation through PSCA-CD3ζ CAR
- Rimiducid-dependent costimulation through inducible MyD88/CD40 domain

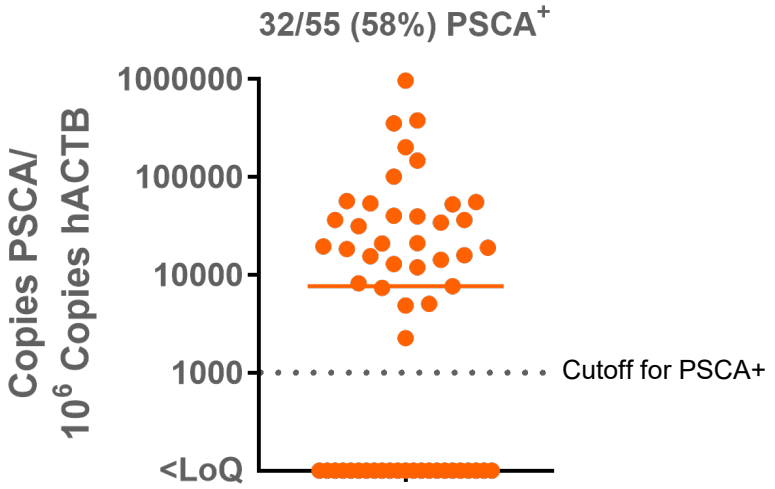


Hypothesis: GoCAR-T design optimizes BPX-601 for antigen-directed and -independent T cell activation, proliferation, and persistence, which may afford BPX-601 enhanced clinical activity relative to traditional CAR-T cell therapies for solid tumors

CAR, chimeric antigen receptor; iMC, inducible MyD88/CD40; PSCA, prostate stem cell antigen; Rim, rimiducid; TCR, T cell receptor.

PROSTATE STEM CELL ANTIGEN (PSCA) TARGET RATIONALE

PSCA screening of pancreatic tumors[1]

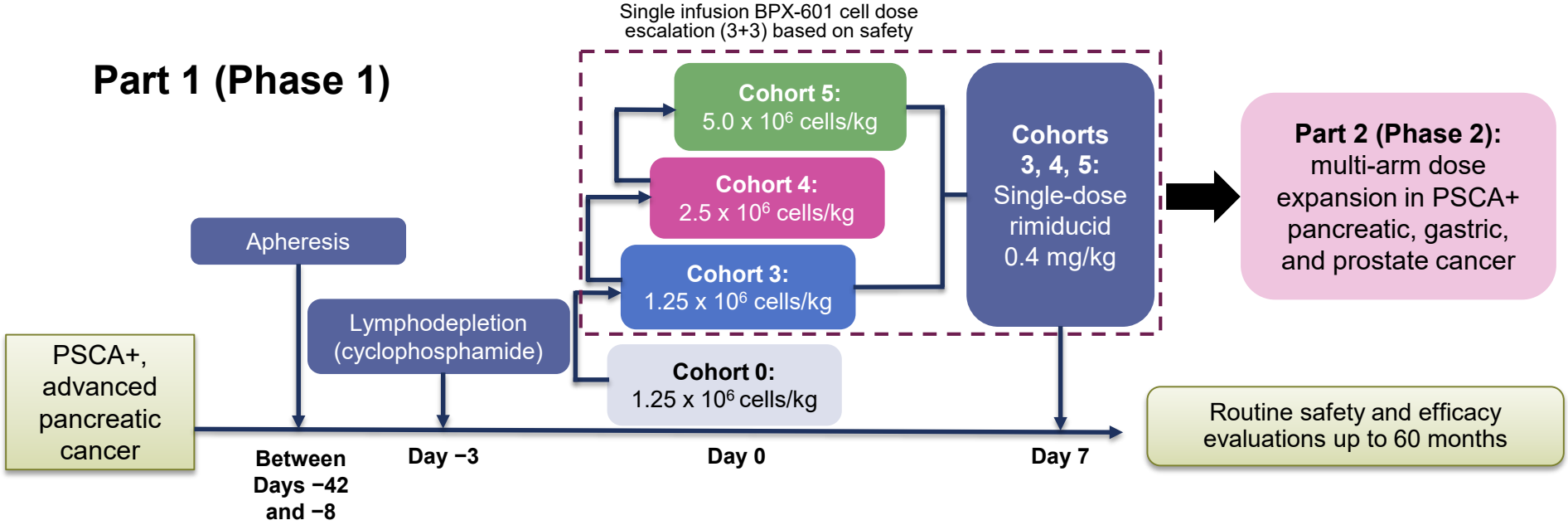


- Small, GPI-anchored cell-surface protein of the Thy-1/Ly-6 family[2]
- Expressed in 60–80% of pancreatic ductal adenocarcinomas[3,4]
- Also expressed in prostate, bladder, gastric, and other solid tumors and correlates with disease stage[5]
- Low basal expression on normal prostate epithelium, urinary bladder, kidney, esophagus, stomach, and placenta[1]
- Low toxicity profile with PSCA-targeted antibodies in prostate and pancreatic cancer[6,7]

GPI, glycosylphosphatidylinositol; hACTB, human beta-actin; LoQ, limit of quantification.

1. Bellicum data on file; 2. Saeki N, et al. *Clin Cancer Res*. 2010;16:3533–3538; 3. Argani P, et al. *Cancer Res*. 2001;61:4320–4324;
4. Wente MN, et al. *Pancreas*. 2005;31:119–125; 5. Abate-Daga D, et al. *Hum Gene Ther*. 2014;25:1003–1012;
6. Morris MJ, et al. *Ann Oncol*. 2012;23:2714–2719; 7. Wolpin BM, et al. *Ann Oncol*. 2013;24:1792–1801.

BP-012 PHASE 1/2 STUDY DESIGN



- Part 1 objectives: safety, tolerability, MTD and/or RDE for use in Part 2
- Part 1 status: enrollment ongoing in Cohort 5

NCT02744287

MTD, maximum tolerated dose; PSCA, prostate stem cell antigen; RDE, recommended dose expansion.

PATIENT DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

Cohort	Patient	Age	Sex	Tumor Type	BPX-601 Dose (10^6 cells/kg)	Rim (Y/N)	LD Regimen*	# Prior Systemic Therapies	PSCA (copies)†
0	0A	50	F	Pancreas	1.25	N	CTX only	1	5,000
	0B	58	F	Pancreas	1.25	N	CTX only	3	377,000
	0C	65	F	Pancreas	1.25	N	CTX only	5	15,000
3	3A	59	F	Pancreas	1.25	Y	CTX only	2	34,000
	3B	70	M	Pancreas	1.25	Y	CTX only	1	7,000
	3C	58	F	Pancreas	1.25	Y	CTX only	1	31,000
4	4A	71	F	Pancreas	2.5	Y	CTX only	2	7,686
	4B	65	M	Pancreas	2.5	Y	CTX only	4	8,243
	4C	60	F	Pancreas	2.5	Y	CTX only	2	354,730
5	5A	61	M	Pancreas	5.0	Y	CTX only	3	14,238
	5B	64	M	Pancreas	5.0	Y	CTX only	1	19,533
	5C	59	M	Pancreas	5.0	Y	CTX only	5	969,094

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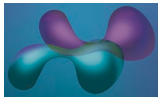
* Cytoxan 1 g/m^2 by IV infusion on Day −3; † PSCA (copies per 10^6 copies hACTB) was measured at screening.
CTX, cyclophosphamide; hACTB, human beta-actin; LD, lymphodepletion; PSCA, prostate stem cell antigen; Rim, rimiducid.



SAFETY SUMMARY

Most common AEs reported by > 1 patient	Total (N=12)
Any Event, n (%)	12 (100)
Fatigue	4 (33)
Abdominal pain upper	3 (25)
Hypotension	3 (25)
Abdominal pain	2 (17)
Back pain	2 (17)
Diarrhea	2 (17)
Flatulence	2 (17)
Nausea	2 (17)
Pyrexia	2 (17)

- No DLTs, neurotoxicity, or events of cytokine release syndrome were observed
- Pyrexia is the only treatment-related AE reported by >1 patient (n=2)
  - Grade 1–2 on Day 0 following BPX-601 infusion
  - Both events resolved within 24–36 hours with supportive care

AE, adverse event; DLT, dose-limiting toxicity.

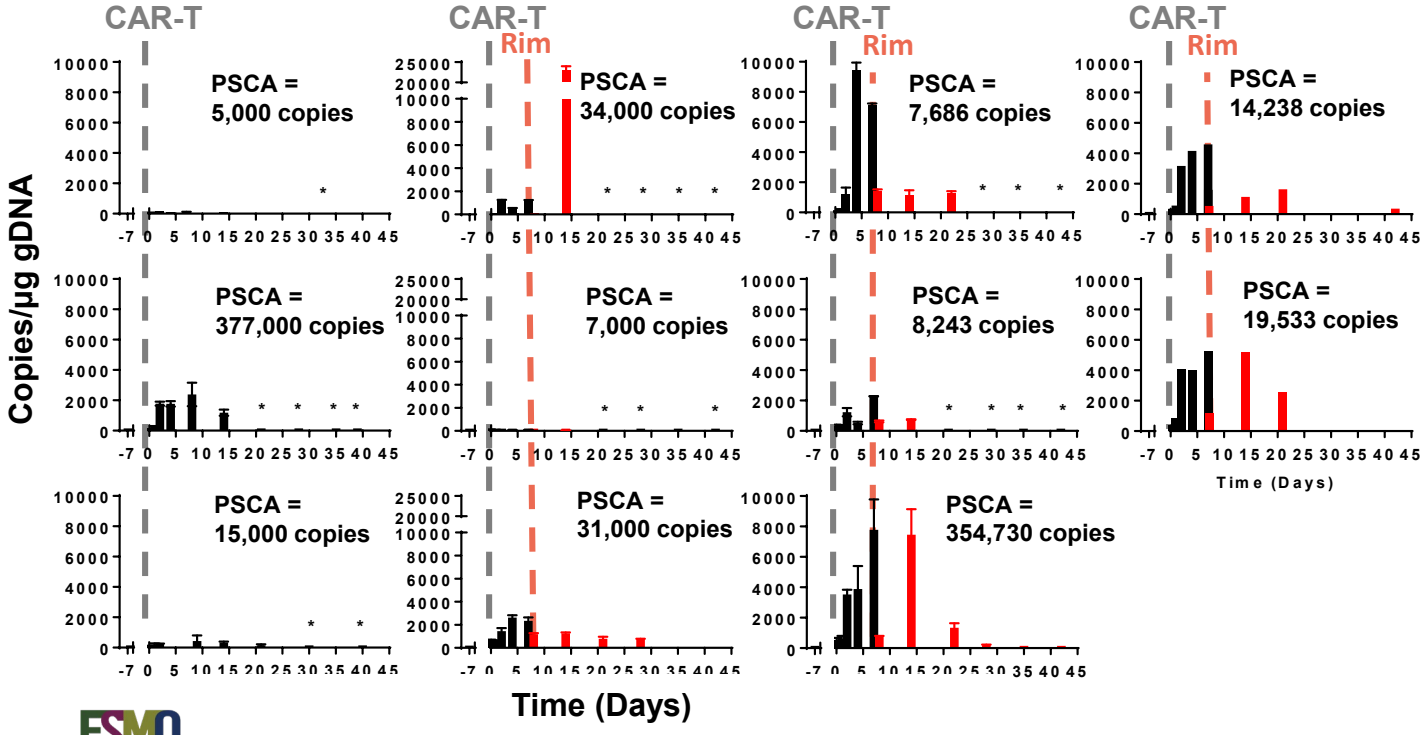
BPX-601 T CELL EXPANSION AND PERSISTENCE

Cohort 0
1.25x10⁶/kg

Cohort 3
1.25x10⁶/kg + Rim

Cohort 4
2.5x10⁶/kg + Rim

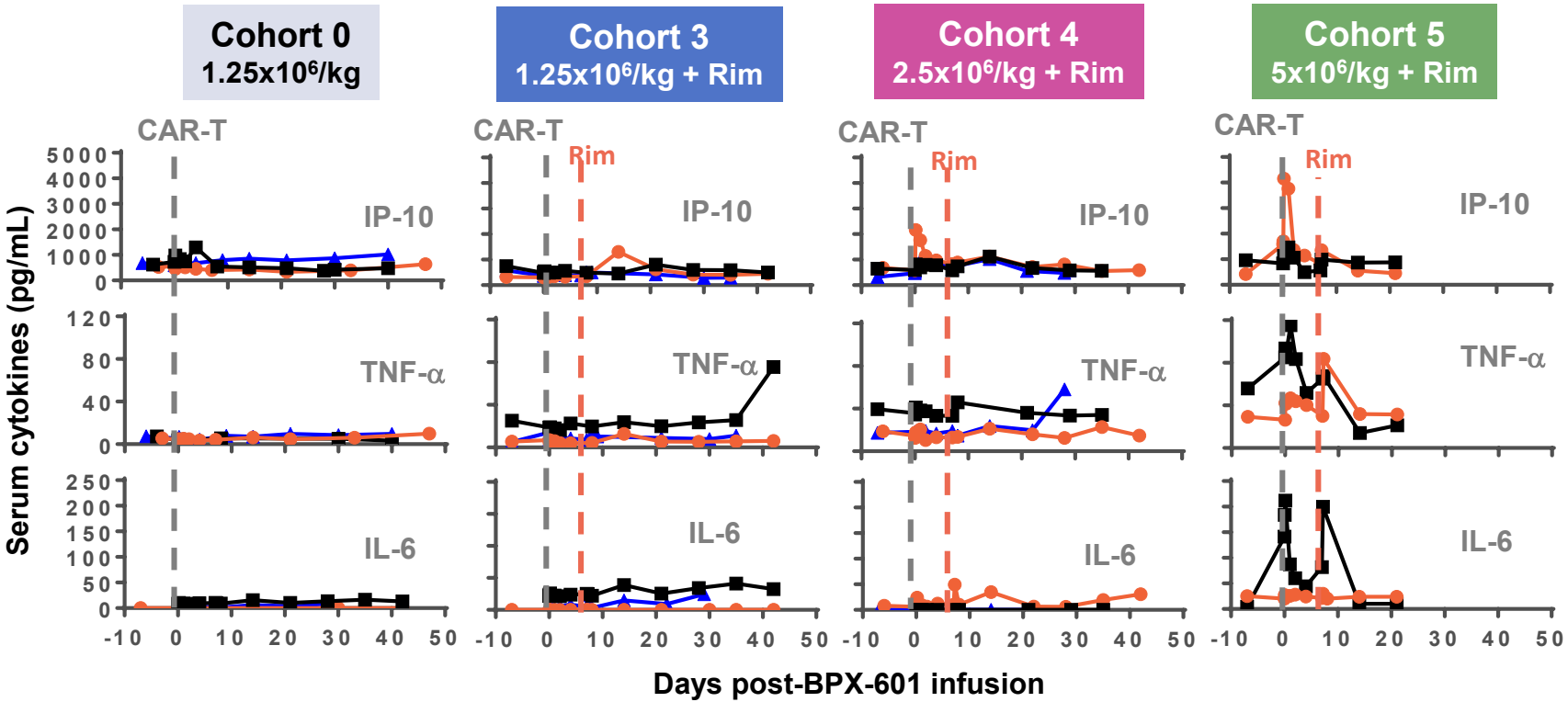
Cohort 5
5x10⁶/kg + Rim



- Limited evidence of LD with CTX-only regimen (79% ± 25% of cells remained)
- Rapid cell expansion by Day 4, but no persistence without Rim
- With single-dose Rim:
  - Cell expansion of 3- to 20-fold within 7 days in 4 patients
  - Cell persistence of >3 weeks in 3 patients

* Vector copy number < limit of quantification.
CTX, cyclophosphamide; LD, lymphodepletion; PSCA, prostate stem cell antigen; Rim, rimiducid.

PERIPHERAL CYTOKINE PROFILES OVER TIME



The orange, black, and blue lines represent data for an individual patient in the indicated cohort for multiple cytokines.
Rim, rimiducid.

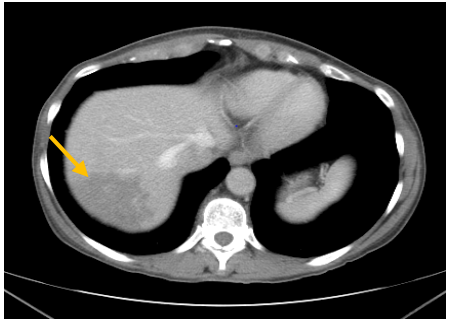
EVIDENCE OF ANTI-TUMOR ACTIVITY IN BPX-601–TREATED PATIENTS

Cohort	Best Response (RECIST)			
	CR	PR	SD	PD
0	0	0	1	2
3	0	0	2	1
4	0	0	2	1

Two patients with SD had tumor shrinkage >20%

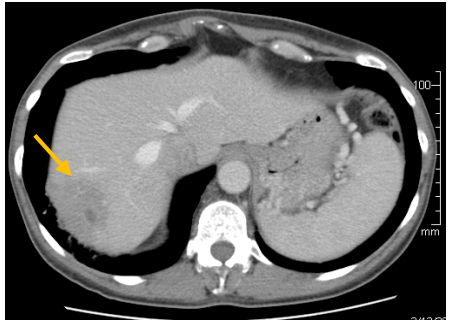
Patient 3A: 2 prior therapies; PSCA = 34,000 copies

Baseline



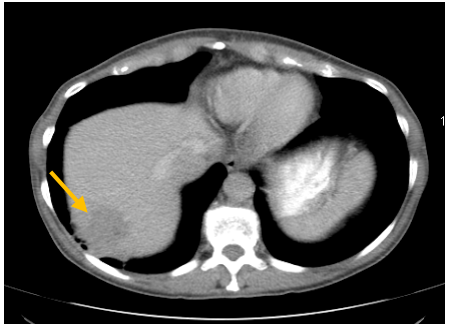
- Lesion longest diameter: 70 mm
- **CA19-9: 294**

Month 1



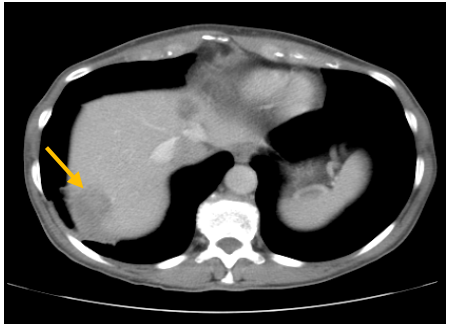
- Lesion longest diameter: 57 mm
- **CA19-9: 152.6**
- Overall response: SD (−15%)

Month 2



- Lesion longest diameter: 49 mm
- **CA19-9: 207.2**
- Possible new lesion
- Overall response: SD (−25%)

Month 4



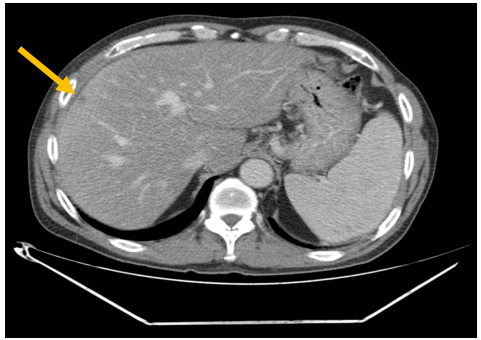
- Lesion longest diameter: 40 mm
- **CA19-9: 641.4**
- New lesion confirmed
- Overall response: PD

CA19-9, cancer antigen 19-9; CR, complete response; PD, progressive disease; PR, partial response; PSCA, prostate stem cell antigen; SD, stable disease.

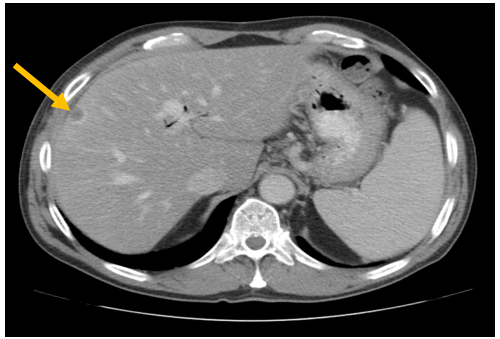
EVIDENCE OF ANTI-TUMOR ACTIVITY IN BPX-601–TREATED PATIENTS

Patient 4B: 4 prior therapies; PSCA = 8,243 copies

Baseline

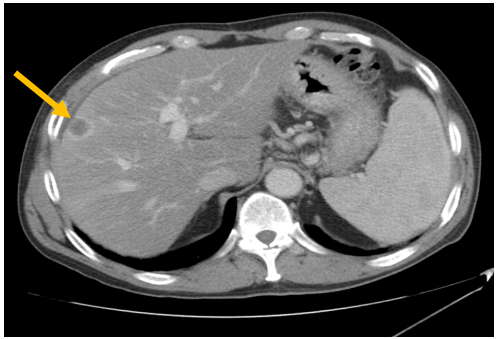


Month 1



- Slightly enlarged lesion with ring enhancement characteristic of pseudoprogression

Month 2

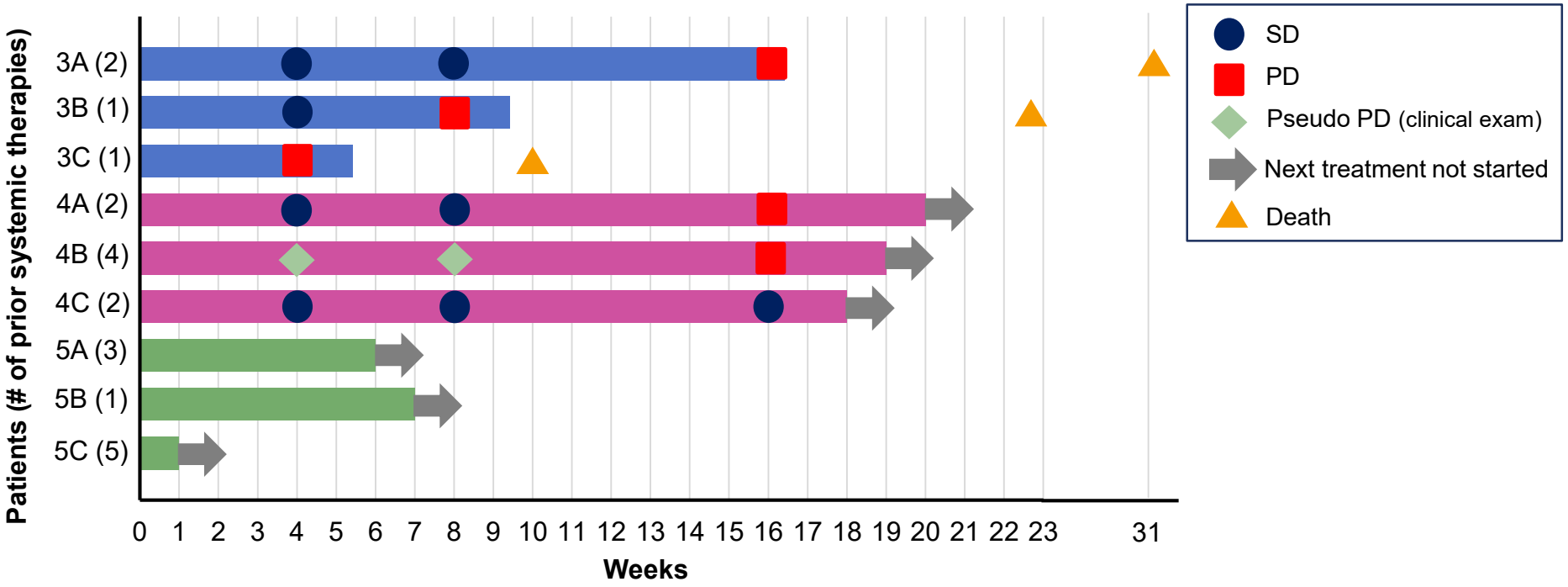


- Similar lesion size
- Increased density
- Continued ring enhancement

- At Month 4, no clinical symptoms of worsening disease
- Ongoing treatment-free interval >19 weeks

PSCA, prostate stem cell antigen.

SWIM PLOT AFTER BPX-601 ADMINISTRATION



Disease control without new therapy was 16 and >18 weeks (ongoing) in 1 and 3 patients, respectively

PD, progressive disease; pseudo PD, pseudoprogression, progressive disease; SD, stable disease.

SUMMARY AND CONCLUSIONS

- Administration of BPX-601 with single-dose rimiducid was well tolerated
  - No observed cytokine release syndrome or neurotoxicity of any grade
  - Most frequent AEs were consistent with those experienced by advanced cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies
  - Treatment-related AEs were limited, mild to moderate in intensity, and resolved with supportive care
- Despite inadequate lymphodepletion with cyclophosphamide alone, BPX-601 displayed enhanced expansion and prolonged persistence in some patients treated with rimiducid
- Evidence of biological activity/stable disease have been observed in this heavily pre-treated patient population
- Part 2 (opening soon) will include more intense lymphodepletion with cyclophosphamide/fludarabine, a repeat-dose rimiducid infusion schedule, and gastric and prostate cancer patients

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