ASCO® Genitourinary Cancers Symposium

Phase 1 Study of P-PSMA-101 CAR-T Cells in Patients With Metastatic Castration-Resistant Prostate Cancer (mCRPC)

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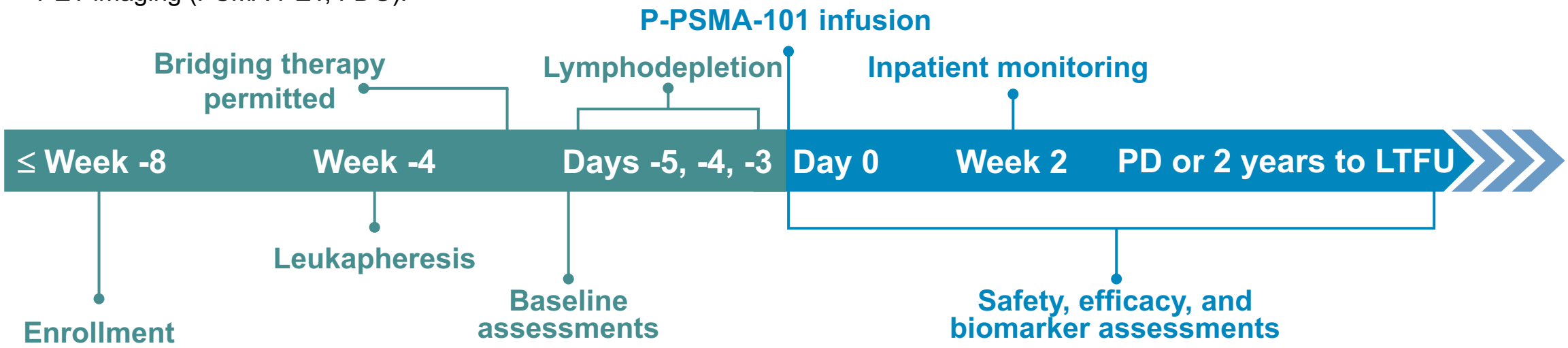
Phase 1 mCRPC Clinical Trial: P-PSMA-101-001

- P-PSMA-101 is an autologous CAR-T therapy targeting PSMA and is made using a unique non-viral transposon system (piggyBac®) that results in a CAR-T product composed of a high percentage of stem cell memory T cells (T_{SCM}).
- Open label, 3+3 design, dose escalation + recommended Phase 2 dose expansion, 60 patients.
- Standard 3-day lymphodepletion regimen: fludarabine 30 mg/m^2 and cyclophosphamide 300 mg/m^2.
- Standard response criteria as per PCWG3: PSA, bone scans/CT, and exploratory biomarkers and novel tumor-targeted PET imaging (PSMA-PET, FDG).
- PET imaging was dependent on institutional availability.
- Key inclusion criteria: mCRPC, measurable disease, received a CYP17 inhibitor or second-generation anti-androgen therapy and a taxane, and adequate organ function.
- Key exclusion criteria: second malignancy, active infection, or significant autoimmune, central nervous system, cardiac, ocular, or liver disease.
- 17 patients have been treated, with 14 by the Dec 31, 2021 data cutoff for this presentation



CAR = chimeric antigen receptor; CT = computed tomography; FDG = fluorodeoxyglucose; LTFU = long-term follow-up; mCRPC = metastatic castration-resistant prostate cancer; PCWG3 = Prostate Cancer Working Group 3; PD = progressive disease; PET = positron emission tomography; PSA = prostate-specific antigen; PSMA = prostate membrane-specific antigen.

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Treatment-Emergent Adverse Events

TEAEs (n=14)

TEAE, n (%)	Overall	Grade ≥3
Dose-limiting toxicity (at dose 0.75 x 10^6 cells/kg)	1 (7)	1 (7)
CRS[a]	8 (57)	2 (14)
ICANS	2 (14)	1 (7)
Neutropenia/neutrophil count decreased[b]	5 (36)	5 (36)
Thrombocytopenia/platelet count decreased[b]	5 (36)	4 (27)
Anemia	5 (36)	5 (36)
Infection		
Overall	2 (14)	1 (7)
First month	2 (14)	1 (7)

TRAEs (n=14)

TRAE, n (%)	With >20% incidence	Grade ≥3
CRS	7 (50)	2 (14)
Headache	7 (50)	0 (0)
Fatigue	6 (43)	1 (7)
Chills	5 (36)	0 (0)
AST increased	5 (36)	3 (21)
Vision blurred	4 (29)	0 (0)
ALT increased	4 (29)	1 (7)
Pyrexia	3 (21)	0 (0)
aPTT prolonged	3 (21)	0 (0)

[a] Grade ≥3 events were 2 cases of macrophage activation syndrome/CRS, one fatal after non-compliance in follow-up. CRS was frequently associated with transaminitis and intermittently with ocular symptoms/inflammation.
[b] Patient counted once for either term.
ALT = alanine aminotransferase; aPTT = activated partial thromboplastin time; AST = aspartate aminotransferase; CRS = cytokine release syndrome; ICANS = immune effector cell–associated neurotoxicity; TEAE = treatment-emergent adverse event; TRAE = treatment-related adverse event.

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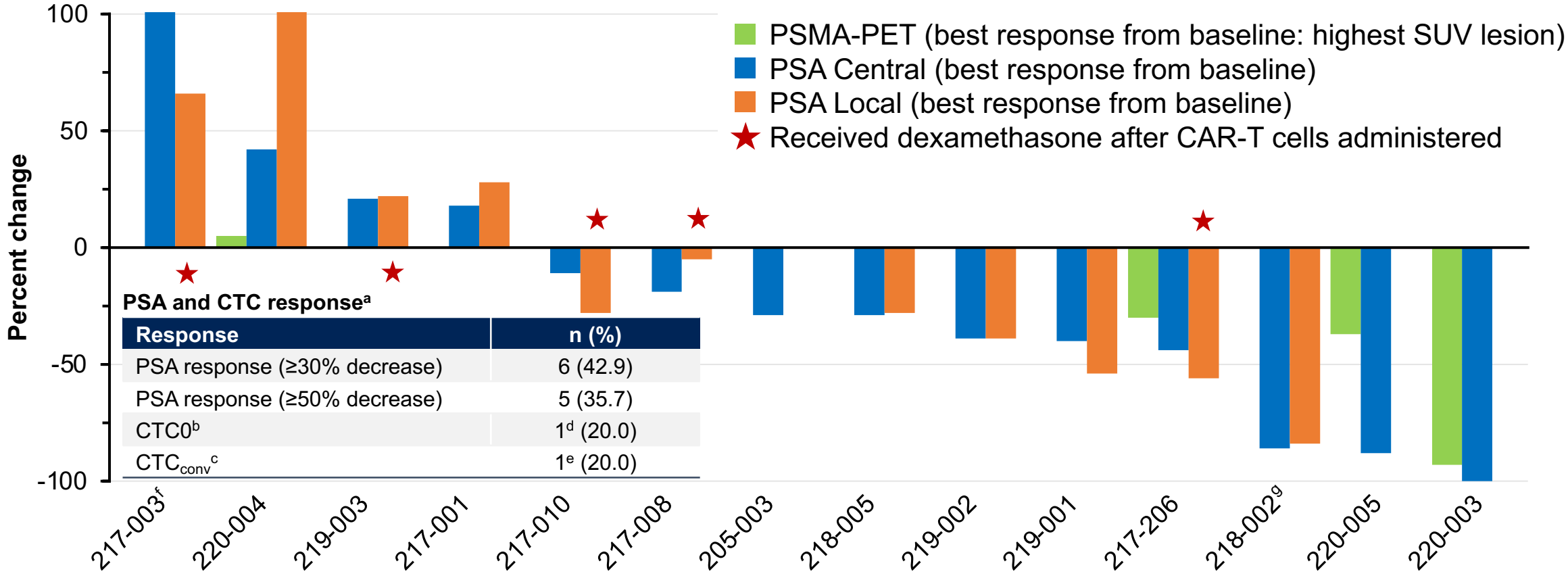
Efficacy: Exceptional Antitumor Responses at the Lowest Dose Levels

Marked decreases in PSA and PSMA-PET SUVs



PSA and CTC response[a]

Response	n (%)
PSA response (≥30% decrease)	6 (42.9)
PSA response (≥50% decrease)	5 (35.7)
CTC0[b]	1[d] (20.0)
CTC_{conv}[c]	1[e] (20.0)

[a] Central or local results. [b] CTC0 (n=5) defined as patients with CTCs >0 at enrollment and CTC = 0 at a post-infusion CTC assessment (12–13-week follow-up). [c] CTC_{conv} (n=5) defined as patients with CTCs ≥5 at enrollment, then CTCs ≤4 measured at a post-infusion assessment. [d] Patient 219-001. [e] Patient 217-206. [f] Only 1 PSA timepoint obtained from patient. [g] Patient 218-002 received dexamethasone 2 mg BID starting at month 3 post–P-PSMA-101 infusion due to bone pain; steroid was tapered to 0.5 mg QD and is currently ongoing. BID = twice daily; CAR = chimeric antigen receptor; CTC = circulating tumor cells; PET = positron emission tomography; PSA = prostate-specific antigen; PSMA = prostate membrane-specific antigen; QD = every day; SUV = standardized uptake value.

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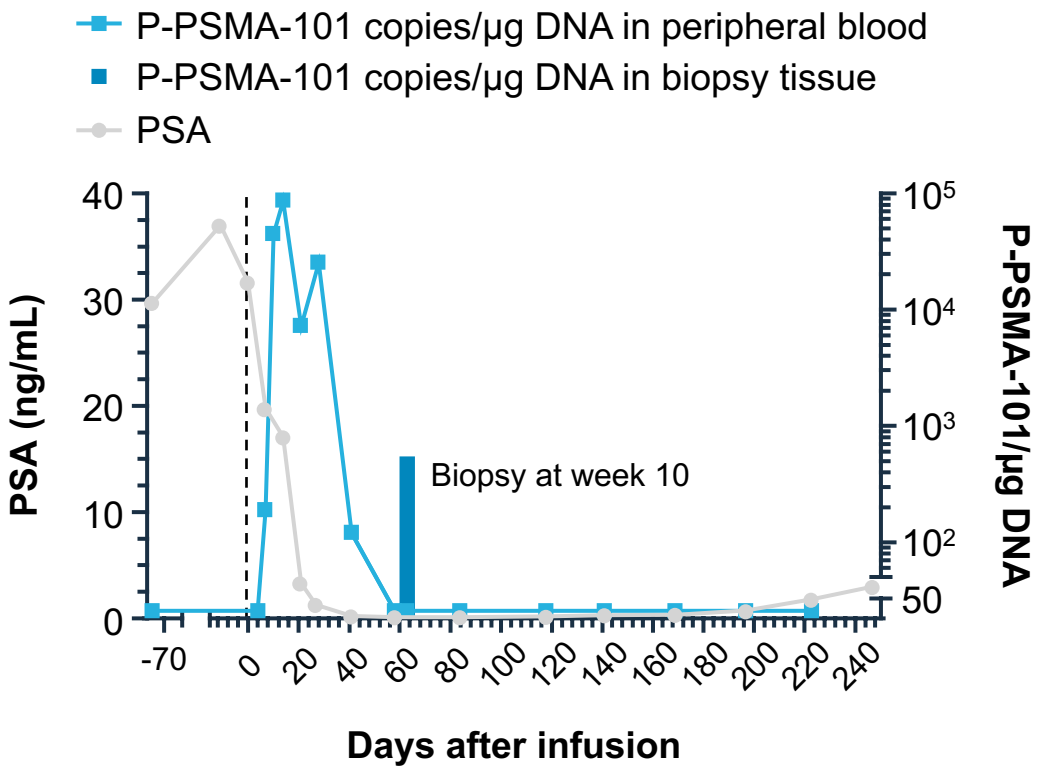
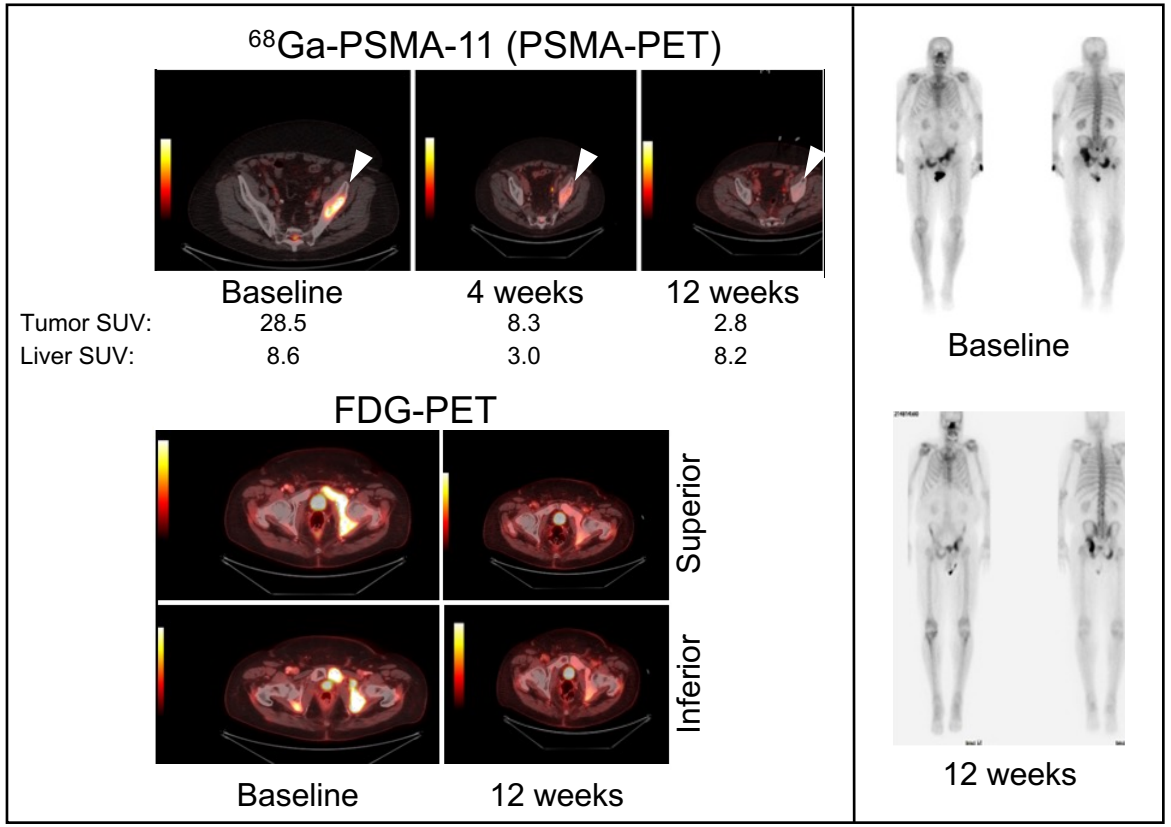
Patient 220-003: Evidence of Near-Complete Tumor Elimination

PK, PSA, PSMA-PET, FDG-PET, bone scan, and pathology correlate in response





Biopsy at week 10 of prior bone metastasis showed CAR-T cells, bone remodeling, and bone marrow but no tumor cells.

CAR = chimeric antigen receptor; FDG = fluorodeoxyglucose; PET = positron emission tomography; PK = pharmacokinetics; PSA = prostate-specific antigen; PSMA = prostate membrane-specific antigen; SUV = standardized uptake value.

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Conclusions

- This interim update shows the exceptional efficacy of novel anti-PSMA CAR-T-cell product.
- P-PSMA-101 at very low doses induced durable biochemical, radiographic, and functional radiographic responses in heavily pretreated patients with mCRPC, including a pathologic complete response, with notable PFS and OS, and significant CAR-T-cell expansion to the 10^4 to 10^5 copies/µg DNA range.
- 10 of 14 patients (71%) demonstrated PSA declines, with 5 of 14 patients (36%) showing PSA declines of ≥50%.
- T_{SCM} had elevated bone and inflammation homing markers and demonstrated trafficking to bone tumor biopsies, highly relevant in bone-avid disease like prostate cancer.
- CRS rate was 57% and ICANS rate was 14%, which was manageable when treated rapidly with anticytokine agents (29% treated with tocilizumab) and/or steroids.

CAR = chimeric antigen receptor; CRES = CAR-T–related encephalopathy syndrome; CRS = cytokine release syndrome; ICANS = immune effector cell–associated neurotoxicity; mCRPC = metastatic castration-resistant prostate cancer; OS = overall survival; PFS = progression-free survival; PSMA = prostate membrane-specific antigen; T_{SCM} = stem cell memory T cells.

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