RaPTR: Early Real-World Patterns of Treatment Cycle Completion in Radiopharmaceutical Therapy

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Background & Objectives

Background

- ^{177}Lu-PSMA-617 (Pluvicto®) and ^{177}Lu-DOTATATE (Lutathera®) are established radiopharmaceutical therapies (RPTs)
- ^{177}Lu-PSMA-617: 6 planned cycles | ^{177}Lu-DOTATATE: 4 planned cycles
- Limited real-world data on treatment cycle completion rates
- SNMMI established RaPTR (Radiopharmaceutical Therapy Registry) — multi-center, standardized data collection

Objectives

- Describe early real-world patterns of treatment cycle completion
- Identify areas for further investigation into factors associated with incomplete therapy

Methods

- Descriptive analysis of RaPTR registry data
- ^{177}Lu-PSMA-617 cohort: 100 patients, 2 institutions (53 + 47 patients)
- ^{177}Lu-DOTATATE cohort: 132 patients, 1 institution (UT Southwestern)
- Registry captures >200 structured data fields per patient:
  - Demographics, treatment administration, laboratory monitoring, adverse events
  - Data stored in REDCap (clinical) and MIM Cloud (imaging)
- Completed cycles compared between institutions using Wilcoxon rank-sum test

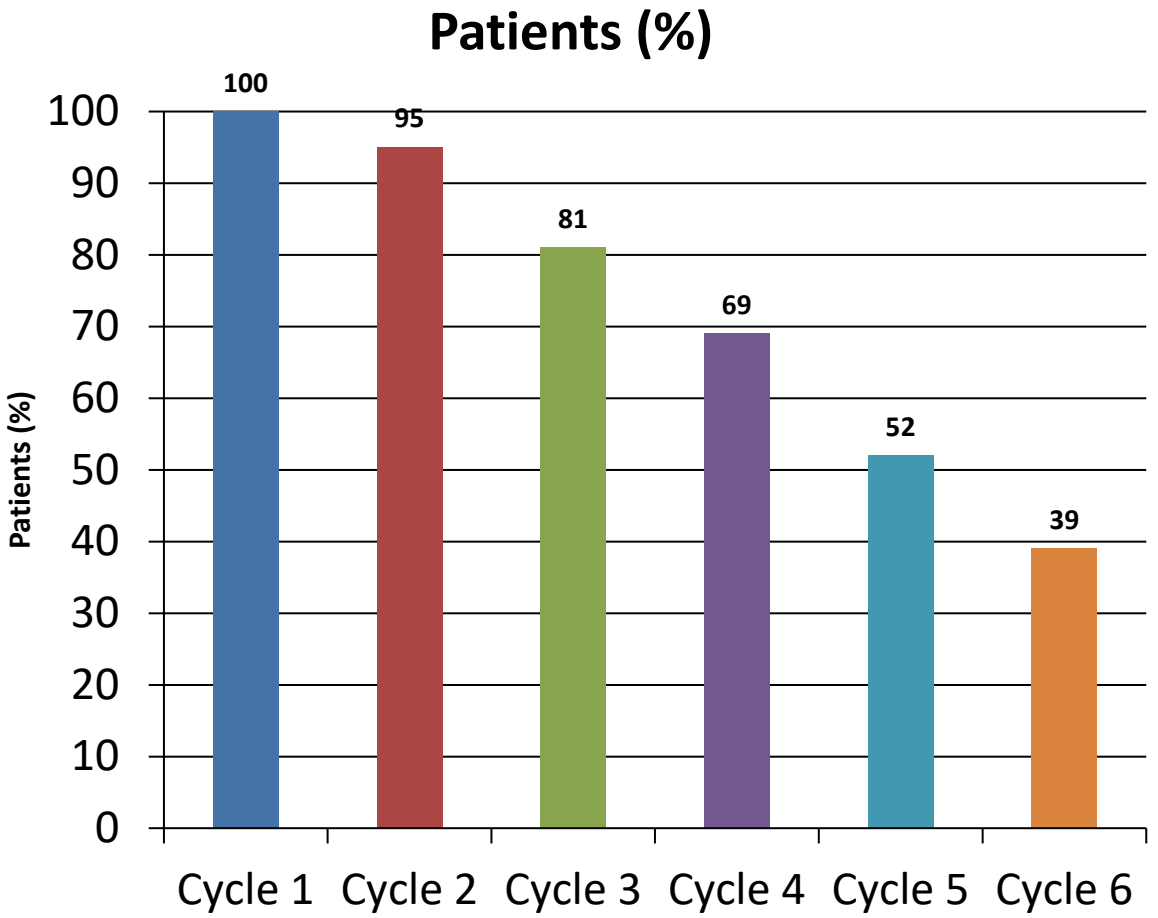
Results: ^{177}Lu-PSMA-617 Cycle Completion

- N = 100 patients | 436 total cycles

- Cycle 2: 95% received
- Cycle 3: 81% received
- Cycle 4: 69% received
- Cycle 5: 52% received
- **Cycle 6: 39% completed all 6 cycles**

- **61% discontinued before completion**

- No difference between institutions (p = 0.30)



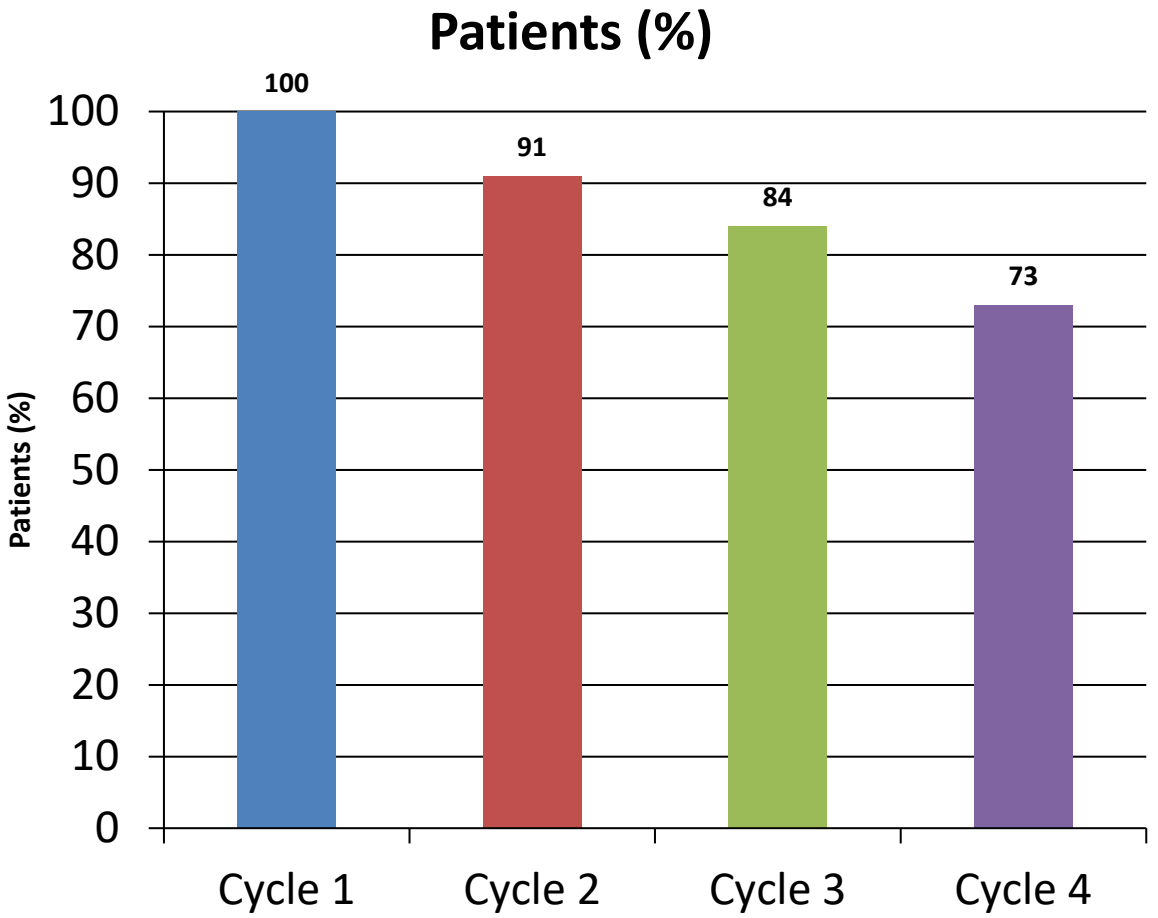
Results: ^{177}Lu-DOTATATE Cycle Completion

- N = 132 patients | 460 total cycles
- Single institution (UT Southwestern)

- Cycle 2: 91% received
- Cycle 3: 84% received
- Cycle 4: 73% completed all 4 cycles

- **Higher completion vs. PSMA (73% vs. 39%)**

- Possible explanations:
  - — Fewer total cycles (4 vs. 6)
  - — Different toxicity profile
  - — Less heavily pre-treated population



Discussion

- **RaPTR provides scalable infrastructure for future analyses:**
  - — Inter-institutional disease response, treatment discontinuation, toxicity, and dosimetry
  - — May capture outcomes of diverse ethnic/racial groups

- **Notable difference in completion: 39% (PSMA, 6 cycles) vs. 73% (DOTATATE, 4 cycles)**

- **Contributing factors may include:**
  - — Fewer DOTATATE cycles required (4 vs. 6) — fewer opportunities for dropout
  - — Potential differences in toxicity profiles between agents
  - — mCRPC patients receiving PSMA are more heavily pre-treated
  - — Disease progression is inevitable even after initial excellent response

- **Lu-177 PSMA-617 therapy is not curative:**
  - — VISION trial: median OS benefit of ~4 months
  - — Heterogeneous PSMA expression within/among tumors
  - — Both primary and acquired resistance mechanisms

Limitations

- Early descriptive snapshot of RaPTR data
- Reasons for treatment discontinuation were not assessed in this analysis
- Data completeness and follow-up duration vary across sites
- Cannot distinguish between:
  - Discontinuation due to toxicity
  - Discontinuation due to disease progression
  - Patients who had not yet completed therapy at time of data extraction
- Single institution for DOTATATE data limits generalizability
- Registry is still growing — statistical power will increase over time

Case Report: Lu-177 PSMA-617 Therapy Failure

71-year-old male with metastatic Castration-Resistant Prostate Cancer (mCRPC)

- Illustrates the clinical reality of treatment discontinuation
- Representative of the 61% who do not complete all 6 planned PSMA therapy cycles
- Demonstrates discordance between PSA response and radiographic progression
- Highlights challenges of treating heavily pre-treated mCRPC patients

Case 1: 71 y/o mCRPC — Treatment Timeline

- 11/2021: PSA 13.0 — Gleason 4+4 (Grade Group 4)
- 12/2022: PSA 0.3 — After XRT + ADT + enzalutamide
- 10/2023: PSA 5.81 — Confirmed PSA progression → Started ARPI (Darolutamide)
- 11/2023: PSA 12.8 — Prior to Cycle 1 Docetaxel
- 03/2024: PSA 59.84 — POD to Docetaxel (6 cycles) → Started Abiraterone

Key Points:

→ Multiple lines of therapy prior to Pluvicto

→ Progressive disease through ARPI, chemotherapy, and novel hormonal agents

→ PSMA PET confirmed PSMA-avid disease (test <12 at all timepoints)

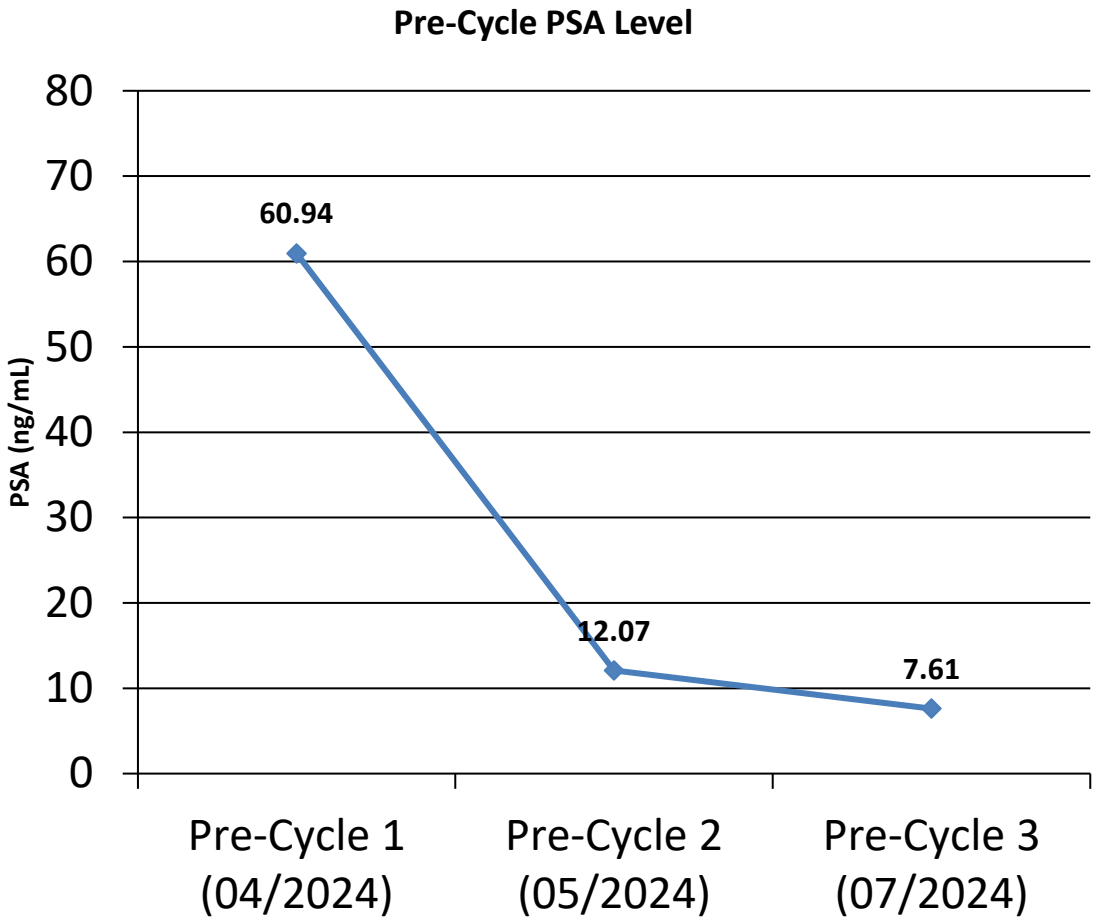
Pluvicto (Lu-177 PSMA-617) — Initial Response

Pluvicto Treatment:

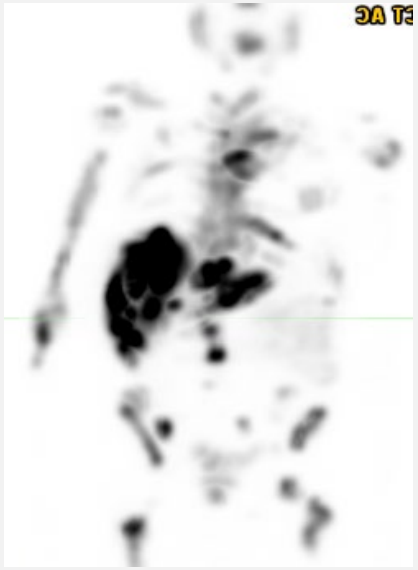
- 04/26/2024: PSA 60.94 (Pre-Cycle 1) — PSMA test <12
- 05/28/2024: PSA 12.07 (Pre-Cycle 2) — PSMA test <12
- 07/09/2024: PSA 7.61 (Pre-Cycle 3) — PSMA test <12

88% PSA Reduction from Baseline

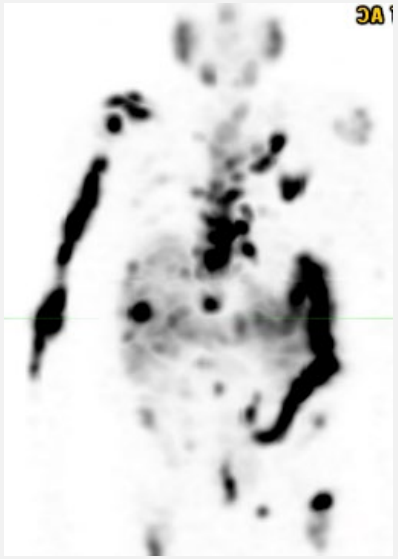
Initially appeared to be excellent biochemical response...



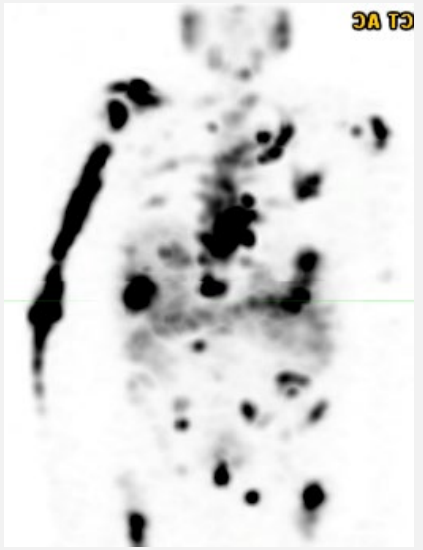
PSA 60.94



PSA 12.07

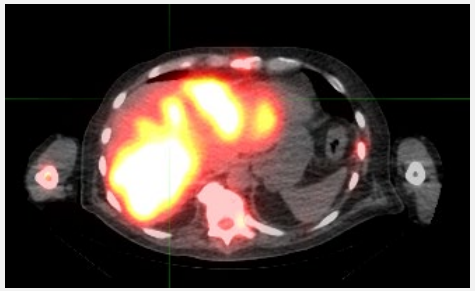


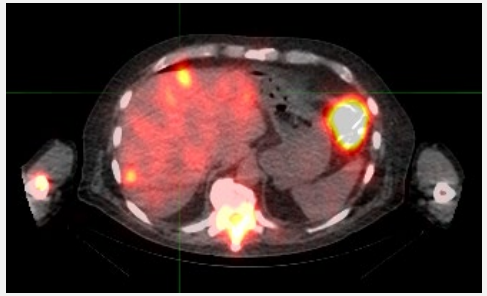
PSA 7.61

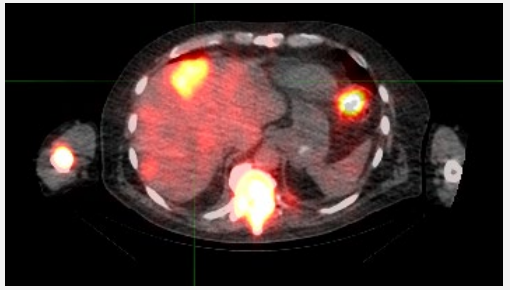


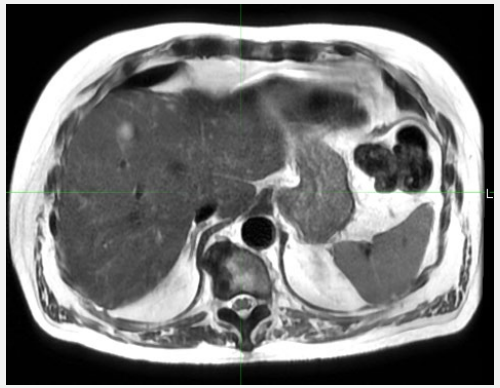
Therapy stopped patient started on Cabazitaxel

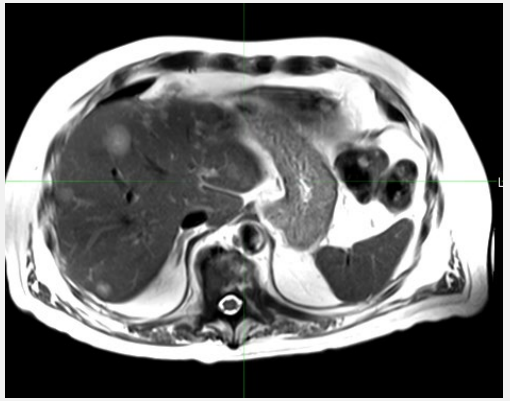
Post cycle 3 therapy PSA 19.09











PSA88%

Evidence of radiographic progression on MRI

Therapy Failure & Disease Progression

Despite 88% PSA Decline — Radiographic Progression

- Post-Cycle 3 PSA: 19.09 (rebounding from nadir of 7.61)
- Serial PSMA PET/CT showed decreasing PSMA-avid disease burden
- MRI confirmed hepatic metastatic progression
- Evidence of radiographic progression despite PSA decline

- **THERAPY STOPPED after 3 cycles (of 6 planned)**
- Patient transitioned to Cabazitaxel

Key Lessons:

→ PSA response alone does NOT guarantee durable disease control

→ Hepatic metastases associated with worse OS regardless of PSMA expression

→ Multimodal monitoring essential (PSA + imaging)

→ This patient represents the 61% who discontinue PSMA therapy early

Conclusions & Future Directions

Conclusions

- Only 39% complete all 6 cycles of ^{177}Lu-PSMA-617
- 73% complete all 4 cycles of ^{177}Lu-DOTATATE
- No inter-institutional difference ($p = 0.30$)
- RaPTR provides scalable national infrastructure
- Case illustrates PSA-imaging discordance and therapy failure

Future Directions

→ Identify predictors of treatment discontinuation

→ Optimize patient selection (FDG PET, visceral disease)

→ Combination strategies (ENZA-p, LuPARP, UpFrontPSMA)

→ Novel radionuclides (Ac-225, Tb-161, Cu-67)

→ Rechallenge therapy (RE-LuPSMA trial)

→ Expand RaPTR participation for more statistical power

Thank You

Questions?

RaPTR: Radiopharmaceutical Therapy Registry

University of Arizona | UT Southwestern | SNMMI