touchEXPERT OPINIONS

Advancing the management of adult solid tumours in 2023 and beyond: Unlocking the potential of radiopharmaceuticals

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Addressing diagnostic and treatment challenges with radiopharmaceuticals: Learnings from theranostic approaches in GEP-NETs

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How have radiopharmaceuticals impacted the diagnosis and treatment of GEP-NETs in recent years?

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FDA-approved radiopharmaceuticals in GEP-NETs

^{68}Ga-DOTATATE
^{64}Cu-DOTATATE
^{68}Ga-DOTATOC

Imaging[1,2]

^{177}Lu-DOTATATE as second-line therapy for SSTR-positive GEP-NETs

Therapy[1]

^{68}Ga for PET imaging (diagnostic)/**^{177}Lu** as β-emitter (therapeutic)

Theranostic pairs[2,3]

Advantages

- **High disease control[4]**
- **Overall limited toxicity[4]**

Limitations

- **Possible long-term side effects**
  Nephrotoxicity,[4] haematotoxicity,[4,5] possible hepatotoxicity[6]
- **Defining eligible patients[7]**
  Tolerability to PRRT depends on patient's SSTR avidity, tumour burden, organ function and the patient's functional status

FDA, US Food and Drug Administration; GEP-NET, gastroenteropancreatic neuroendocrine tumour;
PET, positron emission tomography; PRRT, peptide receptor radionuclide therapy; SSTR, somatostatin receptor.

1. NCCN. Neuroendocrine and adrenal tumors. 2022. Available at: https://bit.ly/3OGRDtk (accessed 17 May 2023);
2. Brugarolas P, et al. *J Nucl Med Technol*. 2020;48(Suppl. 1): 34S–9S; 3. Barca C, et al. *Pharmaceuticals (Basel)*. 2021;15:13; 4. Telo S, et al. *Clin Transl Imaging*. 2021;9:423–38;
5. Bergsma H, et al. *J Nucl Med.* 2018;59:452–8; 6. Riff BP, et al. *Clin Nucl Med*. 2015;40:845–50; 7. Burkett BJ, et al. *Radiology.* 2021;298:261–74.

What are the key efficacy outcomes for radiopharmaceuticals in the treatment of GEP-NETs?

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Pivotal clinical trials: Efficacy outcomes

NETTER-1[1]

SSTR positive advanced midgut NETs (N=229)

Phase III trial evaluating **^{177}Lu-DOTATATE 7·4 GBq (200 mCi) every 8 weeks (four cycles) + long-acting octreotide 30 mg** vs **long-acting octreotide 60 mg every 4 weeks**

PFS: 28.4 months vs **8.5** months (HR 0.21, 95% CI 0·14–0.33; p<0.0001)[2]

mOS: 48.0 months vs **36.3** months (HR 0.84, 95% CI 0.60–1.17; two-sided p=0.30)[3]

Clinically and statistically significant improvement in PFS and clinically relevant longer mOS of 11.7 months with ^{177}Lu-DOTATATE[4]

NETTER-R[5]

Pancreatic NETs (N=62 assessed by RECIST v1.1)

Retrospective real-world data (multiple sites) from patients treated with **^{177}Lu-DOTATATE 7.4 GBq at 8 ± 1-week intervals**; median follow-up after first cycle: 24.5 months (range 20–123.4 months)

median PFS: 24.8 months (95% CI 17.5–34.5)
median TTP: 29.5 months (95% CI 21.4–67.6)

ORR: 40.3% (25/62; 95% CI 28.1–53.6)
median DoR: 60.7 months (95% CI 13.1–62.1)

mOS (n=110): 41.4 months (95% CI 28.6–50.2)

Study reinforces the role of ^{177}Lu-DOTATATE for treatment of patients with SSTR-positive pancreatic NETs

CI, confidence interval; DoR, duration of response; HR, hazard ratio; mOS, median overall survival; NET, neuroendocrine tumour; ORR, objective response rate; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SSTR, somatostatin receptor; TTP, time to progression.

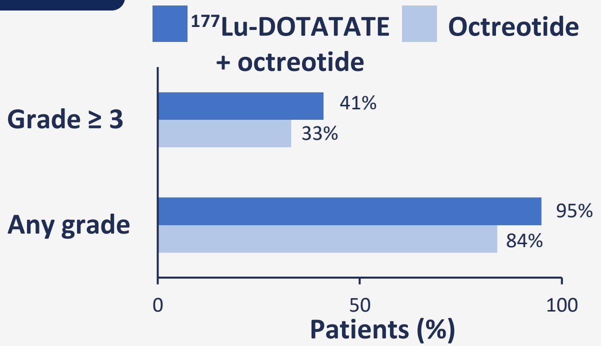
1. Strosberg J, et al. *N Engl J Med*. 2017;376:125–35; 2. Smith-Palmer J, et al. *BMC Cancer*. 2021;21:10; 3. Strosberg JR, et al. *Lancet Oncol*. 2021;22:1752–63; 4. Strosberg JR, et al. *J Clin Oncol*. 2021;39(Suppl.):4112; 5. Clement D, et al. *Eur J Nucl Med Mol Imaging.* 2022;49:3529–37.

What are the key safety considerations for radiopharmaceuticals in patients with GEP-NETs?

Safety of PRRT vs targeted therapy in GEP-NETs

Safety outcomes of PRRT in NETTER-1[1]

^{177}Lu-DOTATATE 7.4 GBq (200 mCi) every 8 weeks (four cycles) + long-acting octreotide 30 mg (n=111)
vs
long-acting octreotide 60 mg every 4 weeks (n=110)



^{177}Lu-DOTATATE grade ≥3 AEs[2]

Incidence ≥4%*

- Lymphopenia
- ↑ GGT
- Vomiting
- Nausea
- ↑ AST
- ↑ ALT
- Hyperglycaemia
- Hypokalaemia

Long-term haematologic AEs

- t-MN, mean (SD): 2.61% (4.38%)[3]
- Persistent haematologic dysfunction: 4%[4]

Safety profile of everolimus in various clinical trials[†]

- **Incidence ≥30%**[5]
- Safety and tolerability was consistent in all studies in advanced NET settings (RADIANT-2, RADIANT-3 and RADIANT-4)[6–8]
- Frequently observed AEs were grade 1 or 2 including stomatitis, diarrhoea, fatigue, infections, rash and peripheral oedema[8]

*With a higher incidence in ^{177}Lu-Dotatate arm; †across various tumour types.
AE, adverse event; ALT, alanine aminotrasferase; AST, aspartate aminotransferase; FDA, US Food and Drug Administration; GEP-NET, gastroenteropancreatic NET; GGT, gamma-glutamyl transferase; NET, neuroendocrine tumour; PRRT, peptide receptor radionuclide therapy; SD, standard deviation; t-MN, therapy-related myeloid neoplasm.

1. Strosberg J, et al. *N Engl J Med*. 2017;376:125–35; 2. FDA. Lutetium Lu 177 dotatate PI. Available at: https://bit.ly/3IAoNqA (accessed 23 May 2023); 3. Sonbol MB, et al. *JAMA Oncol.* 2020;6:1086–92; 4. Bergsma H, et al. *J Nucl Med.* 2018;59:452–8; 5. FDA. Everolimus PI. Available at: https://bit.ly/3OKkw7E (accessed 24 May 2023); 6. Pavel ME, et al. *Ann Oncol*. 2017;28:1569–75; 7. Yao JC, et al. *New Engl J Med*. 2011;364:514–23; 8. Yao JC, et al. *Lancet*. 2016;387:968–77.

How can clinicians best integrate radiopharmaceuticals into the clinical setting to ensure optimal outcomes for patients with GEP-NETs?

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Implementing PRRT in clinical settings

Systematic checklist to be used by the MTB for patient evaluation[1–3]

MTB[1–3]
- Medical/surgical oncologists
- Radiation oncologists
- Nuclear medicine specialists/radiologists
- Gastroenterologists

Therapy appropriateness[1]

Histopathologic findings
- ✓ Proven NET
- ✓ WHO classification

Diagnostic imaging to confirm high somatostatin receptor expression
- ✓ Nuclear imaging for patient selection and estimating treatment response[4]
- ✓ CT/MRI

Patient safety assessment to tolerate therapy[1]

Assess adequate organ function for PRRT
- ✓ Renal → Nephrology
- ✓ Hepatic → Hepatology
- ✓ Bone marrow → Haematology

Assess tumour burden → Cardiology, endocrinology, gastroenterology, pathology (NET specialist)

Review recent/concurrent treatments

Assess patient factors
- ✓ BMI
- ✓ Karnofsky or ECOG performance status score
- ✓ Can follow radiation safety precautions
- × Pregnancy/breastfeeding

BMI, body mass index; CT, computerized tomography;
ECOG, Eastern Cooperative Oncology Group; MRI, magnetic resonance imaging; MTB, Multidisciplinary tumour board; NET, neuroendocrine tumour; PRRT, peptide receptor radionuclide therapy; WHO, World Health Organization.

1. Burkett BJ, et al. *Radiology.* 2021;298:261–74; 2. Mejia A, et al. *Medicine (Baltimore).* 2022;101:(e28970).261–74; 3. Hendifar AE, et al. *Pancreas.* 2022;51:213–8; 4. Puliani G, et al. *Front Endocrinol (Lausanne).* 2022;13:861434.

How might clinical trials help address the key remaining questions about the use of radiopharmaceuticals in GEP-NETs?

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Using the latest data to inform practice

Genetic profiling analysis design of well-differentiated aggressive grade 2 and 3 GEP-NETs in the phase III COMPOSE trial[1]

- Analysis may guide detection of pathogenic mutations in NET patients to inform treatment and surveillance strategies

Prognostic value of TTV with ^{68}Ga-DOTATOC PET/CT in predicting response to ^{177}Lu-DOTATOC treatment in metastatic well-differentiated NETs[2]

- TTV could be considered as an easily accessible and widely available prognostic imaging biomarker

Lack of PRRT prognostic and predictive factors[3]

Emerging RLT options in GEP-NETs beyond ^{68}Ga- and ^{177}Lu-based agents[4]

Need to determine sequence therapy in relation to other drugs[5]

Prospective evaluation of the utility of concurrent ^{18}F-FDG PET/CT and ^{68}Ga-DOTATOC imaging in GEP-NENs: The PETNET study[6]

- A positive FDG PET was significantly associated with reduced OS

ACTION-1 phase Ib/III trial of RYZ101 in SSTR2+ GEP-NETs progressing after ^{177}Lu SSA therapy: Initial safety analysis[7]

- RYZ101 was well tolerated
- 120 kBq/kg declared as RP3D
- Part 2 (phase III) will compare RYZ101 with SOC in pre-treated patients with SSTR2+ GEP-NETs

CT, computerized tomography; GEPNEN, gastroenteropancreatic neuroendocrine neoplasm; GEP, gastroenteropancreatic; NEN, neuroendocrine neoplasm; NET, neuroendocrine tumour; OS, overall survival; PET, positron emission tomography; PRRT, peptide receptor radionuclide therapy; RLT, radioligand therapy; RP3D, recommended phase II dose; SOC, standard of care; SSA, somatostatin analogue; SSTR2, somatostatin receptor subtype 2; TTV, total tumour volume.

1. Halfdanarson TR, et al. *J Clin Oncol*.2023;41(Suppl.): TPS660; 2. Vega-Zolano E, et al. *J Clin Oncol*. 2023;41(Suppl.):e16248;
3. Puliani G, et al. *Front Endocrinol (Lausanne).* 2022;13:861434; 4. Becx MN, et al. *Cancers (Basel).* 2022;14:5792; 5. Albertelli M, et al. *Rev Endocr Metab Disord.* 2021;22:563–79;
6. Vasconcelos JPS, et al. *J Clin Oncol*. 2023;41(Suppl.):4022; 7. Morris M, et al. *J Clin Oncol*. 2023;41(Suppl.):4132.

Advancing outcomes in prostate cancer: Current and future perspectives on theranostics

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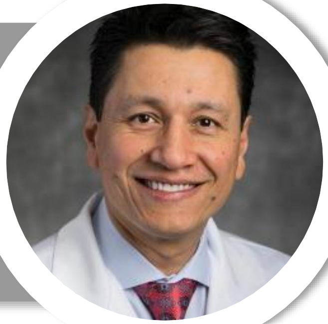

What is the current status and role of radiopharmaceuticals in the management of prostate cancer?

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FDA-approved radiopharmaceuticals in prostate cancer

Imaging

2012 – ^{11}C-choline
targets choline metabolism[1,2]

2013 – Palliative care
$^{223}RaCl_2$
Calcium analogue
(mCRPC bone metastases)[1,2]

2016 – ^{18}F-fluciclovine
L-leucine analogue[1,2]

2020 – ^{68}Ga-gozetotide
targets PSMA[1,2]

2021 – ^{18}F-piflufolastat
targets PSMA[1,2]

Therapy

2022 – ^{177}Lu-vipivotide tetraxetan
targets PSMA
(PSMA+ mCRPC)[1,2]

Imaging

2023 – ^{18}F-flotufolastat
targets PSMA[1,2]

Development of PSMA-targeting radiopharmaceuticals heralds a new era of high-precision theranostics[1]

FDA, US Food and Drug Administration; mCRPC, metastatic castration-resistant prostate cancer; PSMA, prostate-specific membrane antigen.

1. Jia AY, et al. *Prostate Cancer Prostatic Dis.* 2023;doi:10.1038/s41391-023-00670-6; 2. FDA. Prescribing information searchable by agent. Available at: www.accessdata.fda.gov/scripts/cder/daf/ (accessed 19 May 2023).

What have we learned about the value of PSMA-based theranostics in prostate cancer from pivotal trial data?

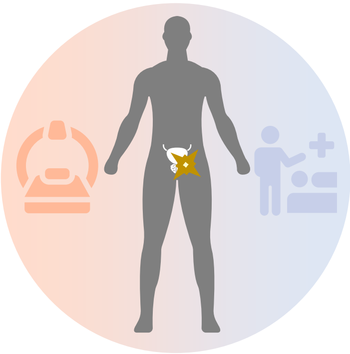
Value of radiotheranostics in mCRPC management

PSMA-targeted imaging

Imaging performance

	^{68}Ga-gozetotide[1]	^{18}F-piflufolastat[2]
Frontline*	PSMA-PreRP 83–96%	OSPREY 95–98%
Recurrence†	PSMA-BCR 82–97%	CONDOR 59–66%

- Superior diagnostic accuracy vs conventional imaging (initial staging and recurrent disease)[3,4]
- May guide ^{177}Lu-PSMA-617 treatment eligibility[4]
- Improved sensitivity at >PSA relative to <PSA[3,4]
- ^{18}F-PSMA-11 non-inferior vs ^{68}Ga-PSMA-11[5]



PSMA-targeted therapy

^{177}Lu-PSMA-617 RLT

vs SoC (VISION)[6]

mPFS (imaging) months

PSMA-RLT + SoC	8.7
SoC	3.4

p<0.001

vs CBZ (TheraP)[7]

mPFS months

	mPFS	PFS at 12 months
PSMA-RLT	5.1	**19%** (95% CI 12–27)
CBZ	5.1	**3%** (95% CI 1–9)

- ^{177}Lu-PSMA-617 (vipivotide tetraxetan) RLT is effective in heavily pre-treated patients with PSMA+ disease[4]

*Specificity; †True positive in ≥1 region(s). CBZ, cabazitaxel; CI, confidence interval; m, median; mCRPC, metastatic castration-resistant prostate cancer; PFS, progression-free survival; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; RLT, radioligand therapy; SoC, standard of care.

1. FDA. ^{68}Ga-gozetotide PI. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2022/212642s002lbl.pdf (accessed 20 June 2023); 2. FDA. ^{18}F-piflufolastat PI. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2021/214793s000lbl.pdf (accessed 20 June); 3. Keegan NM, et al. *Eur Urol Focus*. 2021;7:267–78; 4. Jia AY, et al. *Prostate Cancer Prostatic Dis.* 2023;doi:10.1038/s41391-023-00670-6; 5. De Man, K et al. *Eur Urol.* 2022;82:501–9; 6. Sartor O, et al. *N Engl J Med.* 2021;385:1091–103; 7. Hofman MS, et al. *Lancet.* 2021;397:797–804.

Refining understanding with additional analyses

^{177}Lu-PSMA-617 RLT OS benefit

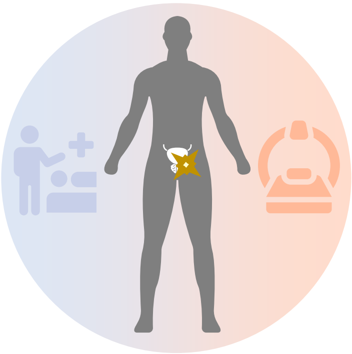
mOS months

VISION[1]	PSMA-RLT + SoC	15.3
	SoC	11.3
TheraP[2]	PSMA-RLT	19.1
	CBZ	19.6

HR 95% CI	VISION	TheraP	
	0.62 0.52–0.74	**0.98** 0.71–1.36	p=0.02 (interaction)

Cross-trial comparison of PSMA-RLT arms[3]

VISION vs TheraP — HR* 95% CI: **0.92** 0.70–1.19



PSMA-PET predictive value

VISION[4]

Whole-body SUV_{mean}

	Highest quartile		Lowest quartile
rPFS months	14.1	vs	5.8
mOS months	21.4	vs	14.5

TheraP[5]

PSA response (PSMA-RLT vs CBZ)

OR 95% CI			
SUV_{mean} ≥10	12.19	3.42–58.76	p=0.039†
SUV_{mean} <10	2.22	1.11–4.51	

*Unadjusted HR;[3] †adjusted p-value (p_{adj}) for treatment-by-SUV_{mean} interaction.[5]

CBZ, cabazitaxel; CI, confidence interval; HR, hazard ratio; m, median; OS, overall survival; OR, odds ratio; PET, positron emission tomography; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; RLT, radioligand therapy; rPFS, median radiographic progression-free survival; SoC, standard of care; SUV, standardized uptake value.

1. Sartor O, et al. *N Engl J Med.* 2021;385:1091–103; 2. Hofman MS, et al. *J Clin Oncol.* 2022;40(Suppl. 16):5000; 3. Soon YY, et al. *J Clin Oncol.* 2023;41(Suppl. 16):5045;
4. Kuo P, et al. *J Clin Oncol*. 2022;40(Suppl. 16):5002; 5. Buteau P, et al. *Lancet Oncol*. 2022;23:1389–97.

What are the key safety considerations when integrating ^{177}Lu-PSMA-RLT into the management of patients with prostate cancer?

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Safety considerations with ^{177}Lu-PSMA-RLT

Dosimetry

- Informed by ^{177}Lu-DOTATATE safety data and EBRT absorbed dose constraints on bone marrow and kidney[1,2]

Key differences EBRT vs RLT[1]

- Prescribing protocols
- Treatment schedules
- Dose rates
- Tissue uptake

Frequent adverse reactions (≥20%)[3,4]

- Fatigue
- Dry mouth
- Nausea
- Anaemia
- ↓ Appetite
- Constipation
- Arthralgia
- Back pain

Common laboratory abnormalities (≥30%)[4]

- Lymphopenia
- Leukopenia
- Thrombocytopenia
- ↓ Calcium
- ↓ Haemoglobin
- ↓ Sodium

- Consider long-term toxicity in risk/benefit assessments for radiolabelled agents[5]
- Prevention is key as some end-organ toxicities may be irreversible[5]
- Consider baseline patient characteristics e.g., pre-treatment haemoglobin,[6] cytopenias[7]

EBRT, external beam radiation therapy; PSMA, prostate-specific membrane antigen; RLT, radioligand therapy; TAT, targeted alpha therapy.

1. Jia AY, et al. *Prostate Cancer Prostatic Dis.* 2023;doi:10.1038/s41391-023-00670-6; 2. Hofman MS, et al. *Lancet Oncol*. 2018;19:825–33;
3. Sartor O, et al. *N Engl J Med.* 2021;385:1091–103; 4. FDA. ^{177}Lu vipivotide tetraxetan PI. Searchable at: www.accessdata.fda.gov/scripts/cder/daf/ (accessed 23 May 2023);
5. FDA. 2020. Available at: www.fda.gov/media/144843/download (accessed 23 May 2023); 6. Nelson AA, et al. *J Clin Oncol.* 2023;41(Suppl. 16):e17065;
7. Abdelrazek AS, et al. *J Clin Oncol.* 2023;41(Suppl. 16):e17057.

What key clinical questions remain, and how are trials aiming to address these?

ASCO 2023 insights: New approaches in mCRPC

New combinations

LuPARP[1] (NCT03874884)

Phase I: ^{177}Lu-PSMA-617 plus PARPi (olaparib)

9-cohort dose escalation study

N=32

- **^{177}Lu-PSMA-617** 7.4 GBq 6 weekly, 6 cycles
- **Olaparib** 50–300 mg BD (3+3 escalation)*

Promising activity across all doses

- **PSA50*** **66%** (n=21/32)
- **PSA90*** **44%** (n=14/32)
- **ORR** **78%** (n=7/9)

Well tolerated combination:

- No DLTs across doses
- No grade 4 TRAEs

G3

Anaemia (7%)
Thrombocytopenia (3%)
Neutropenia (7%)

RP2D: 7.4 GBq ^{177}Lu-PSMA-617 plus 300 mg BD olaparib days -4–18 of each 6-weekly cycle

New agents

TAT + RLT[2] (NCT04886986)

Phase I: ^{225}Ac-J591 plus ^{177}Lu-PSMA-I&T (PNT2002)

Dose escalation study

N=18

- **^{225}Ac-J591** 30, 35 or 40 KBq/kg
- **^{177}Lu-PNT2002** 6.8 GBq

94% experienced PSA decline

- **PSA50†** **61%** (n=11/18)
- **Day 8 SPECT/CT confirmed accurate tumour targeting**

Dual PSMA targeting is feasible and tolerable:

- DLTs at 40 KBq/kg only
- No grade 4 TRAEs

G3

Anaemia (17%)
Thrombocytopenia (11%)
Pain (5%)

RP2D: 35 KBq/kg ^{225}Ac-J591 plus 6.8 GBq ^{177}Lu-PNT2002

*Day: 2–15 or 4–12 or 4–18; †PSA response defined as the proportion of patients achieving either a reduction of 50% (PSA50) or 90% (PSA90) from baseline.

ASCO, American Society of Clinical Oncology; BD, twice daily; Bq, Becquerel; CT, computerized tomography; DLT, dose-limiting toxicity; G, giga; k, kilo; mCRPC, metastatic castration resistant prostate cancer; ORR, overal response rate; PARPi, poly (ADP-ribose) polymerase inhibitor; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; RLT, radioligand therapy; RP2D, recommended phase 2 dose; SPECT, single-photon emission computed tomography; TAT, targeted alpha therapy; TRAE, treatment-related adverse event.

1. Sandhu S, et al. *J Clin Oncol.* 2023;41(Suppl. 16):5005; 2. Tagawa S, et al. *J Clin Oncol.* 2023;41(Suppl. 16):5018.

How might theranostics impact the future management of prostate cancer, now and in the future?

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Evolving role of PSMA-targeted radiotheranostics

Image-guided treatment[1]

^{68}Ga-PSMA-11 (gozetotide)
- EMPIRE II
- PSMA SRT

^{18}F-DCFPyL-PSMA (piflufolastat)
- PSMA-PETgRT
- PATRON

mHSPC[1]

ADT

PSMA+

PSMAddition	^{177}Lu-PSMA-617 + SoC *vs SoC*
UpfrontPSMA	^{177}Lu-PSMA-617 + DTX *vs DTX*

Oligometastatic — without ADT

Bullseye	^{177}Lu-PSMA-617 *vs observation*

mCRPC[1]

PSMA+ → Post-ARSI* → Post-DTX → ^{177}Lu-PSMA-617

PSMAFore	^{177}Lu-PSMA-617 *vs ARSI*†
SPLASH	^{177}Lu-PNT2002 *vs ARSI*
ECLIPSE	^{177}Lu-PNT2002 *vs ARSI*
PR21	^{177}Lu-PSMA-617 *vs DTX*
ENZA-P	^{177}Lu-PSMA-617 + enzalutamide *vs enzalutamide*

New agents, new combinations[1,2]

- α TAT (^{225}Ac; ^{227}Th)
- RLT plus ICI
- RLT plus PARPi

*Progression on prior ARSI; †ARSI not previously used.

ADT, androgen deprivation therapy; ARSI, androgen-receptor signalling inhibitor; ChT, chemotherapy; DTX, docetaxel; ICI, immune checkpoint inhibitor; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; PARPi, poly (ADP-ribose) polymerase inhibitor; PSMA, prostate-specific membrane antigen; RLT, radioligand therapy; SoC, standard of care; TAT, targeted alpha therapy.

1. Jia AY, et al. *Prostate Cancer Prostatic Dis.* 2023;doi:10.1038/s41391-023-00670-6; 2. Jang A, et al. *Ther Adv Med Oncol.* 2023;15:1–12.

Radiopharmaceuticals for adult solid tumours: Challenges and opportunities for implementation

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How can nuclear medicine specialists and oncologists work effectively together to successfully implement radiopharmaceuticals into oncology practice?

Preparation, communication and collaboration are key

Defining roles and responsibilities

- Referring and treating physicians, and AUs administering radiopharmaceuticals, may differ
- Collaboration between oncologic workflows and theranostic centre

Active presence and participation of AUs

- AUs (nuclear medicine specialists and radiation oncologists) are key for awareness, acceptance and consideration of radiopharmaceutical options
- Communication with clinicians managing cancer patients is essential

Coordinating interdisciplinary HCP involvement

- MDT expertise is needed e.g. AUs, nurses, RSOs, medical physicists, radiochemists/pharmacists
- Co-ordinating patient follow-up and care beyond specialist centres

Effective collaboration within and across specialties throughout the patient journey is key to support integration of radiopharmaceuticals into oncology practice

AU, authorized user; HCP, healthcare professional; MDT, multidisciplinary team; RSO, radiation safety officer.

Herrmann K, et al. *Eur J Nucl Med Mol Imaging.* 2022;49:2300–9.

What is the value of radiopharmaceutical theranostics in achieving high-precision medicine in oncology?

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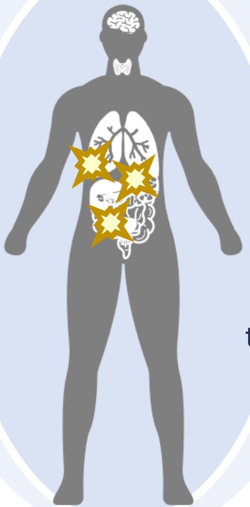
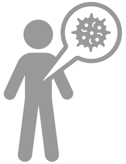
Personalizing the care continuum with theranostics



Personalized management from drug discovery to diagnosis, through to treatment and monitoring

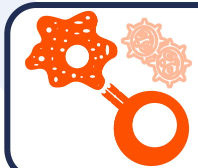
Refined patient selection[1–3]

- Actionable molecular target(s)
- Treatment eligibility evaluation



Molecular imaging[1–3]

- Refined whole-body approach to management
- Prediction and prognostication



Targeted therapy[1–4]

- Ongoing drug and radionuclide development
- Tailoring individualized dosimetry

Theranostic 'pairs'

Radiopharmaceuticals in nuclear medicine are leading the way in theranostics development, offering the potential for high-precision oncology management in adult solid tumours[1–3]

1. Langbein T, et al. *J Nucl Med.* 2019;60(Suppl. 2):13S–9S; 2. Barca C, et al. *Pharmaceuticals (Basel).* 2021;15:13; 3. Gomes Marin JF, et al. *Radiographics.* 2020;40:1715–40;
4. Pini C, et al. *Eur J Nucl Med Mol Imaging.* 2022;49:3613–21.

What are the barriers to the adoption of radiopharmaceuticals as a gold standard treatment in adult oncology?

Identifying needs to support broader adoption

Many practitioners would like to utilize radiopharmaceuticals more actively, but barriers to wider implementation remain[1]

56%* of radiation oncologists surveyed in the US wanted to actively prescribe more RPT[1]

Referral pathways and MDT collaboration[1,2]
- Ill-defined referral pathways
- Not enough individuals for full MDT availability

Workforce and training[1–3]
- Lack of trained HCPs
- Need for RPT expertise and interdisciplinary collaboration

Treatment infrastructure[1–3]
- Variation in approaches between specialist vs community clinics

Logistics and supply chains[1,2]
- Limitations in availability and delivery of RPT to various institutions

Governance and regulation[1,2]
- Clarity needed on licensing requirements and clinical guidelines

*n/N=74/131.

HCP, healthcare professional; MDT, multidisciplinary team; RPT, radiopharmaceutical therapy.

1. Shukla U, et al. *Adv Rad Oncol.* 2022;7:100827; 2. Herrmann K, et al. *Eur J Nucl Med Mol Imaging.* 2022;49:2300–9; 3. Divgi C, et al. *Int J Radiat Oncol Biol Phys.* 2021;109:905–12.

What strategies do you suggest to help overcome the barriers associated with adopting radiopharmaceuticals in oncology?

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Implementing broader adoption

Effective integration and embedding within oncology workflows is needed[1]

Referral pathways and MDT collaboration[1,2]
- Minimum expected caseload
- Partner with referring oncologist/physician(s)
- *'Nuclear medicine champions'*

Workforce and training[1–3]
- Steering committees and MDT implementation
- Nursing capacity and pharmacy support
- Nuclear medicine technologist input

Treatment infrastructure[1–3]
- Type of treatment and institution/centre size
- Appropriate clinical space(s) and protocols
- Outpatient vs inpatient management

Logistics and supply chains[1,2]
- Defined care implementation and coordination
- Radionuclide generation and handling
- Decontamination and waste disposal protocols

Governance and regulation[1–3]
- RAM licensing
- Safety requirements
- Designated RSOs and AUs

Patient support considerations[1–3]
- Educational materials for patients
- Counselling and support
- Transition from trial to real-world settings

AU, authorized user; MDT, multidisciplinary team; RAM, radioactive materials; RSO, radiation safety officer.

1. Herrmann K, et al. *Eur J Nucl Med Mol Imaging.* 2022;49:2300–9; 2. Shukla U, et al. *Adv Rad Oncol.* 2022;7:100827; 3. Divgi C, et al. *Int J Radiat Oncol Biol Phys.* 2021;109:905–12.

Where do you see radiopharmaceuticals within oncology in the next 5 years?

Radiopharmaceuticals: Towards a new standard of care?

Personalized medicine

Data collection and evidence generation to guide practice[1,2]

- Optimize dosimetry
- Innovate trial design
- Long-term follow-up data

Expanding options with new agents and/or indications[2]

- New targets and applications
- New combination regimens
- New radionuclides and constructs
- Use earlier in oncology pathways

Scaling of infrastructure and expertise to support delivery[1,2]

- Update training programs
- Networks of expertise
- Unlock development pipelines

Radiopharmaceuticals and theranostics offer scope for a new standard of personalized management in oncology[1]

1. Herrmann K, et al. *Eur J Nucl Med Mol Imaging.* 2022;49:2300–9; 2. Herrmann K, et al. *Lancet Oncol.* 2020;21:e146–56.