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Comparison of diagnosis, administration, and treatment-related cost of targeted radiopharmaceutical therapies in patients with metastatic castration-resistant prostate cancer (mCRPC) from a third-party payer perspective

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INTRODUCTION

Prostate cancer (PC) is the second most common cancer and the fifth leading cause of cancer death among men worldwide.[1] Among treatment options for metastatic castration-resistant prostate cancer (mCRPC), an advanced stage of PC, radiopharmaceuticals are an evolving class including therapeutic agents of various radioisotopes which have shown survival benefit in clinical trials.[2] Among them, ^{223}Radium dichloride (^{223}Ra) is a calcium-mimetic alpha emitter (targeted alpha therapy) that initially gained approval in 2013 in the US and subsequently in other global markets.[3,4] Another is ^{177}Lutetium-PSMA-617 (^{177}Lu-PSMA-617), a small-molecule beta emitter binding to prostate-specific membrane antigen (PSMA), which is expressed in prostate cancer tumors but also other tissues in the body. ^{177}Lu-PSMA-617 gained initial approval in the US in 2022.[5] While ^{223}Ra and ^{177}Lu-PSMA-617 are both radiopharmaceuticals, they differ in terms of when they may be used for mCRPC, namely after androgen receptor pathway inhibition and taxane-based chemotherapy unless not medically suitable for 177Lu-PSMA-617, or potentially earlier line for ^{223}Ra.[3-5] These therapies may also differ in the use of products and procedures throughout the treatment journey, including for diagnosis, administration, follow-up, and concomitant medication, thus leading to differences in total cost associated with each therapy. The country in which each therapy is used, the site of care, whether treatment is in- or outpatient, and the funding system for healthcare services, whether as a diagnosis-related group (DRG) lump sum or fee-for-service (FFS), additionally modulate total cost. Currently, there is a lack of direct clinical evidence and treatment guideline instruction on sequencing and selection of therapeutic options for mCRPC patients. As such, it is important to comprehensively consider clinical as well as financial factors from both the patient and health system perspectives when assessing the value of each therapy.

OBJECTIVE

The objective of our research was to estimate and compare the total cost of ^{223}Ra vs ^{177}Lu-PSMA-617 therapy, whenever they may be being used during mCRPC disease, from a third-party payer perspective. An Excel model was developed to generate results for major global countries by accounting for product and procedure costs across the treatment journey and the respective funding systems within each country.

METHODOLOGY

An Excel-based model was developed to calculate the total cost of either ^{223}Ra or ^{177}Lu-PSMA-617 therapy from a third-party payer perspective within major global markets including France, Germany, the UK, Japan, the US.

Step 1: Key stages along the treatment journey and the relevant product(s) and/or procedure(s) within each stage were identified based on available clinical guidelines and product labels for each therapy.[2-11] These sources were largely consistent and formed the basis of the input parameters for the model (Figure 1). Specific inputs could be customized to model individual patient cases and physician choices.

Step 2: For all countries and for all products and procedures, the DRG (or tariff) codes and corresponding remuneration values from a third-party payer perspective were identified and the total cost calculated based on the site of care (in- vs outpatient) and funding system (DRG lump sum vs FFS) of the designated country and therapy (Figure 2 and Figure 3).

DRG funding system calculations included the lump sum linked to the DRG code for the entire treatment journey, plus any additional remuneration where applicable (eg, additional funding for drug treatment specifically, or additional service fee for outpatient follow-up). FFS funding system calculations included the sum of all tariffs and remuneration rates for each product or procedure within each stage of the treatment journey and any additional feeds where applicable (eg, consultation, admission, or administration).[11-34]

The model accounts for the parameters below in estimating the total cost of each treatment:

- **Country** determines most likely therapeutic approach per available guidelines or product label, site of care, and funding system. For Germany, France, the UK, and Japan, the model represents a public payer/budget holder perspective. For the US, it includes the public (Medicare) payer perspective and also the private (commercial) payer perspective (by applying a percentage multiplier to Medicare rates)
- **Diagnosis** enables selection of 1 or more diagnostic procedure(s)
- **Treatment and Administration** enables entry of different dosing schemes and any price discounts, whether assumed or known. Where^{177}Lu-PSMA-617 is not yet approved and pricing information not available (Germany, France, Japan), the US ratio of Pluvicto® to Lutathera® wholesale acquisition cost was applied to the Lutathera® price within each country.
- **Follow-up Monitoring** enables selection of 1 or more imaging procedures within 1 year of follow-up
- **Optional Concomitant Medication** enables addition of optional medications to the primary mCRPC treatment. These agents had been included as options within best standard of care for both the ^{223}Ra and ^{177}Lu-PSMA-617 registrational trials and had shown real-world use.[35-39]

The model shows results for an individual patient and can be scaled up to show budget impact across a population. It also allows for a sensitivity analysis to be performed on the above parameters. It does not, however, account for any potential differences in treatment effect between the 2 therapies.

Figure 1. Model structure reflecting treatment journey

	Diagnosis		Treatment and Administration	Follow-up Monitoring	Optional Concomitant Medications
^{223}Ra dichloride	**One or more of:** • Bone scintigraphy • mpMRI • CT with tracer • CT without tracer	***Bone-only metastasis confirmed***	**Course of ^{223}Ra dichloride**	**One or more of:** • Bone scintigraphy • mpMRI • CT with tracer • CT without tracer	**Any among:** • zoledronic acid • denosumab • androgen deprivation therapy (ADT)
^{177}Lu-PSMA-617	**Either of:** • PSMA PET/CT scan with gallium GA 68 gozetotide tracer • PSMA PET/CT scan with piflufolastat F 18 tracer	***PSMA positivity confirmed***	**Course of ^{177}Lu-PSMA-617**	**One or more of:** • Bone scintigraphy • mpMRI • CT with tracer • CT without tracer	**Any among:** • zoledronic acid • denosumab • androgen deprivation therapy (ADT)

Figure 2. Costs within each treatment journey stage under each funding system

	Diagnosis	Treatment and Administration	Follow-up Monitoring	Optional Concomitant Medication
Products and Procedures	• Imaging procedure(s) • Tracer	mCRPC therapy drug	Imaging procedure(s)	Cost of drug(s) (zoledronic acid, denosumab, ADT)
FFS + Cost	Each of above costs and consultation, admission, or administration fees (if applicable)			
DRG Lump Sum	DRG payment, top-up payment (if applicable), and each of above costs if not yet included			

Figure 3. Site of care and funding system overview

	^{223}Ra dichloride		^{177}Lu-PSMA-617	
	Site of care	**Funding system**	**Site of care**	**Funding system**
France	Outpatient	**Lump Sum**	Inpatient	**Lump Sum**
Germany	Outpatient	**FFS + Cost**	Inpatient	**Lump Sum**
UK	Outpatient	**FFS + Cost**	Outpatient	**FFS + Cost**
Japan	Outpatient	**FFS + Cost**	Outpatient	**FFS + Cost**
US	Outpatient	**FFS + Cost**	Outpatient	**FFS + Cost**

RESULTS

For each of the 5 model countries, input parameters along the treatment journey were set in accordance with available clinical guidelines and product labels, which were consistent across the countries (Figure 4). Treatment doses was set to the median number of doses from the respective registrational trials.[35,36] Goserelin, an established ADT option, was included as a concomitant medication.[38] For the US, commercial reimbursement rates was assumed to be 5% higher for commercial vs Medicare.

Figure 4. Model input procedures and treatment in a likely treatment scenario

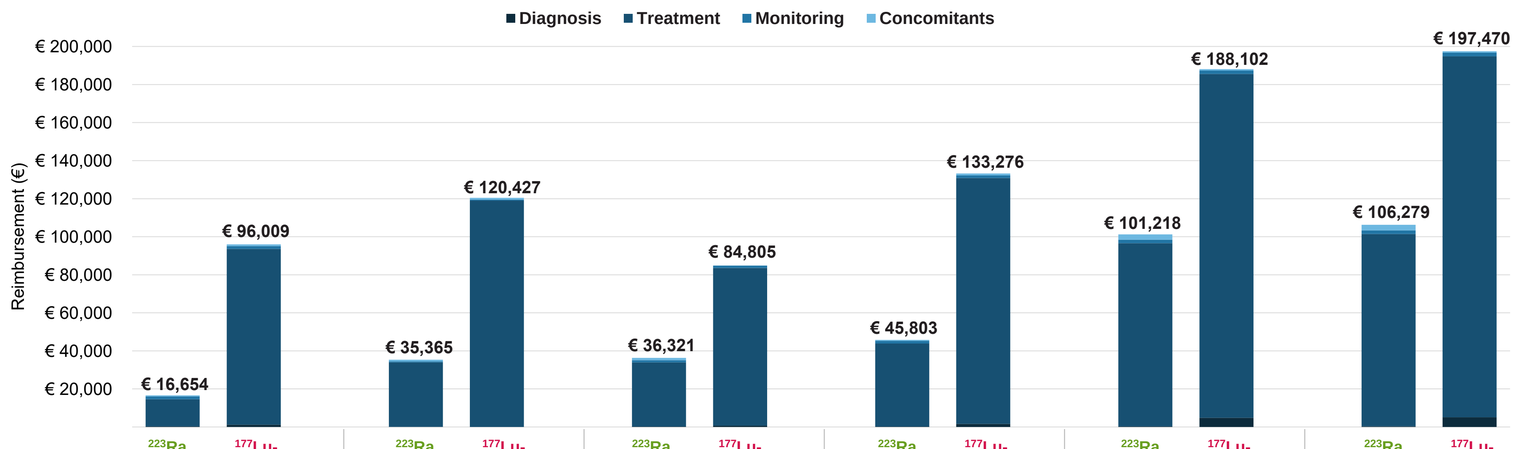
	Diagnosis	Treatment and Administration	Follow-up Monitoring	Optional Concomitant Medication
^{223}Ra dichloride	Bone scintigraphy	6 doses of ^{223}Ra dichloride	6 bone scintigraphy scans	Goserelin
^{177}Lu-PSMA-617	PSMA-PET/ CT and gallium Ga 68 gozetotide	5 doses of ^{177}Lu-PSMA-617	6 bone scintigraphy scans	Goserelin

Results show that across all countries, and their respective sites of care and funding systems, treating mCRPC patients with ^{223}Ra is less costly than with ^{177}Lu-PSMA-617 from a third-party payer perspective (Figure 5). The greatest cost savings (absolute difference) with ^{223}Ra occurred under the US Commercial system (€91,192).* In terms of percent difference in total cost of ^{223}Ra vs ^{177}Lu-PSMA-617, the greatest was observed in European countries: France (141%), Germany (109%), and the UK (98%). Alternatively stated, ^{177}Lu-PSMA-617 is 5.8, 3.4, and 2.9 times as costly as ^{223}Ra in these countries, respectively.

The primary driver of the difference is the cost per dose of ^{177}Lu-PSMA-617. Under FFS, the specific PSMA PET imaging and radioligand tracer elements required to confirm PSMA positivity and thus patient eligibility for ^{177}Lu-PSMA-617 contribute to the higher therapeutic cost vs ^{223}Ra, for which eligibility is confirmable through bone scintigraphy. In contrast with FFS funding systems in which each product and procedure incrementally contributes to total cost, DRG funding systems already include them within a lump sum payment and may thus moderate the total cost differential between the therapies.

*Using 2021 average annual exchange rates, €1=US $1.18; €1=£0.86; €1=¥129 (www.exchangerates.org.uk).

Figure 5. Total cost of therapy comparison of ^{223}Ra and ^{177}Lu-PSMA-617 in mCRPC from a third-party payer perspective for a likely treatment scenario



Absolute difference	€79,355	€85,062	€48,483	€87,472	€86,885	€91,192
Percent difference	141%	109%	80%	98%	60%	60%
^{177}Lu-PSMA-617 cost as a percent of ^{223}Ra dichloride cost	576%	341%	233%	291%	186%	186%

CONCLUSIONS

This detailed coding and reimbursement model, inclusive of product and procedure costs across mCRPC treatment journey stages based on most likely therapeutic approach and agnostic of treatment effect, shows that ^{223}Ra leads to a lower total cost than ^{177}Lu-PSMA-617 from a third-party payer perspective across all 5 countries and their respective care settings and funding systems. Both clinical and financial impact, on patients and health systems would be relevant when assessing therapeutic options. Access to all forms (alpha and beta) of radiotherapeutics is important to ensure that there is physician choice, in turn to ensure individual patient characteristics can be addressed with multiple options in radiotherapy. As a next step, and pending data availability, the model can be further refined to account for any differences in therapeutic benefit between the 2 modalities to gauge cost-effectiveness.

REFERENCES

1. Sung H, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-249. **2.** Henríquez I, et al. Current and emerging therapies for metastatic castration-resistant prostate cancer (mCRPC). *Biomedicines*. 2021;9(9):1247. **3.** Xofigo. Prescribing information. Bayer; 2013. **4.** Xofigo. European assessment report. European Medicines Agency; 2013. https://www.ema.europa.eu/en/medicines/human/EPAR/xofigo **5.** Pluvicto. Prescribing information. Pluvicto. Novartis; 2022. **6.** Marshall CH, et al. Emerging treatments for metastatic castration-resistant prostate cancer: Immunotherapy, PARP inhibitors, and PSMA-targeted approaches. *Cancer Treat Res Commun*. 2020;23:100164. **7.** Tabotta F, et al. Quantitative bone SPECT/CT: high specificity for identification of prostate cancer bone metastases. *BMC Musculoskelet Disord*. 2019;20(1):619. **8.** Leapmann MS. Prostate magnetic resonance imaging (MRI). UCSF Department of Urology. December 2015. https://urology.ucsf.edu/node/2936#.YlPyEcjMKUk **9.** de Bono J, et al. Olaparib for metastatic castration-resistant prostate cancer. *N Engl J Med*. 2020;382(22):2091-2102. **10.** Lantheus Holdings. Lantheus announces collaboration to support prostate cancer clinical development. March 29, 2022. https://lantheusholdings.gcs-web.com/news-releases/news-release-details/lantheus-announces-collaboration-support-prostate-cancer **11.** Cancer ABCs. Which is Better, 177Lu-PSMA-617 (Pluvicto) or Xofigo (Radium-223). August 29, 2022. https://www.cancerabcs.org/advanced-prostate-cancer-blog/2022/8/29/which-is-better-177lu-psma-617-pluvicto-or-xofigo **12.** Nuclear Energy Agency. The supply of medical isotopes: an economic diagnosis and possible solutions. OECD Publishing, November 19, 2019. **13.** National tariff payment system documents, annexes and supporting documents. NHS; November 18, 2020. **14.** National cost collection for the NHS. 2020/21 National cost collection data. https://www.england.nhs.uk/costing-in-the-nhs/national-cost-collection **15.** Drugs, OTCs & Herbals. Medscape Drugs & Diseases. https://reference.medscape.com/drug **16.** MIMS. https://www.mims.co.uk/drugs **17.** Drugs.com. Drug Price Information. https://www.drugs.com/price-guide **18.** Hara T, et al. Prostate cancer detection with Multiparametric MRI: A Comparison of 1 M-Concentration Gadobutrol with 0.5 M-Concentration Gadolinium-Based Contrast Agents. *Curr Urol*. 2018;11(4):201-205. **19.** Centers for Medicare and Medicaid Services. https://www.cms.gov **20.** Codify by AAPC. https://www.aapc.com/codes **21.** Noridian Healthcare Solutions. Fees and News. Updated September 8, 2020. https://med.noridianmedicare.com/web/jfb/fees-news **22.** https://norcalcarcinet.org/news **23.** Hoggo. Trouver mon code CCAM. https://www.hoggo.com/code-ccam **24.** Liens du Coeur. CCAM – radiologie. http://www.ccam-radiologie.fr **25.** Aide au codage. https://www.aideaucodage.fr **26.** Medicalib. https://www.medicalib.fr/blog **27.** http://www.codage.ext.cnamts.fr **28.** https://www.ci-valdesusses.fr/tarifs **29.** SCS Söllner Consulting & Software. https://medizin.soellner.net **30.** https://lto.cgmlauer.cgm.com **31.** Reimbursement.info. DRG - case flat rates. https://app.reimbursement.info/drgs **32.** Pluvicto. NUB application. Novartis. **33.** https://www.ichikawa568.com **34.** Ministry of Health, Labor, and Welfare. https://www.mhlw.go.jp/topics **35.** Parker C, et al. Alpha emitter radium-223 and survival in metastatic prostate cancer. *N Engl J Med*. 2013;369(3):213-223. **36.** Sartor O, et al. Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. *N Engl J Med*. 2021; 385(12):1091-1103. **37.** Bahl A, Khoo V, et. Al. Positioning Xofigo® (radium-223 dichloride) in the metastatic castration-resistant prostate cancer (mCRPC) treatment pathway. *Medicine Matters*. 2020;236. **38.** Gommersall LM, et al. Luteinising hormone releasing hormone analogues in the treatment of prostate cancer. *Expert Opin Pharmacother*. 2002;3(12):1685-1692. **39.** Saad F, et al. The role of bisphosphonates or denosumab in light of the availability of new therapies for prostate cancer. *Cancer Treat Rev*. 2018;68:25-37.

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