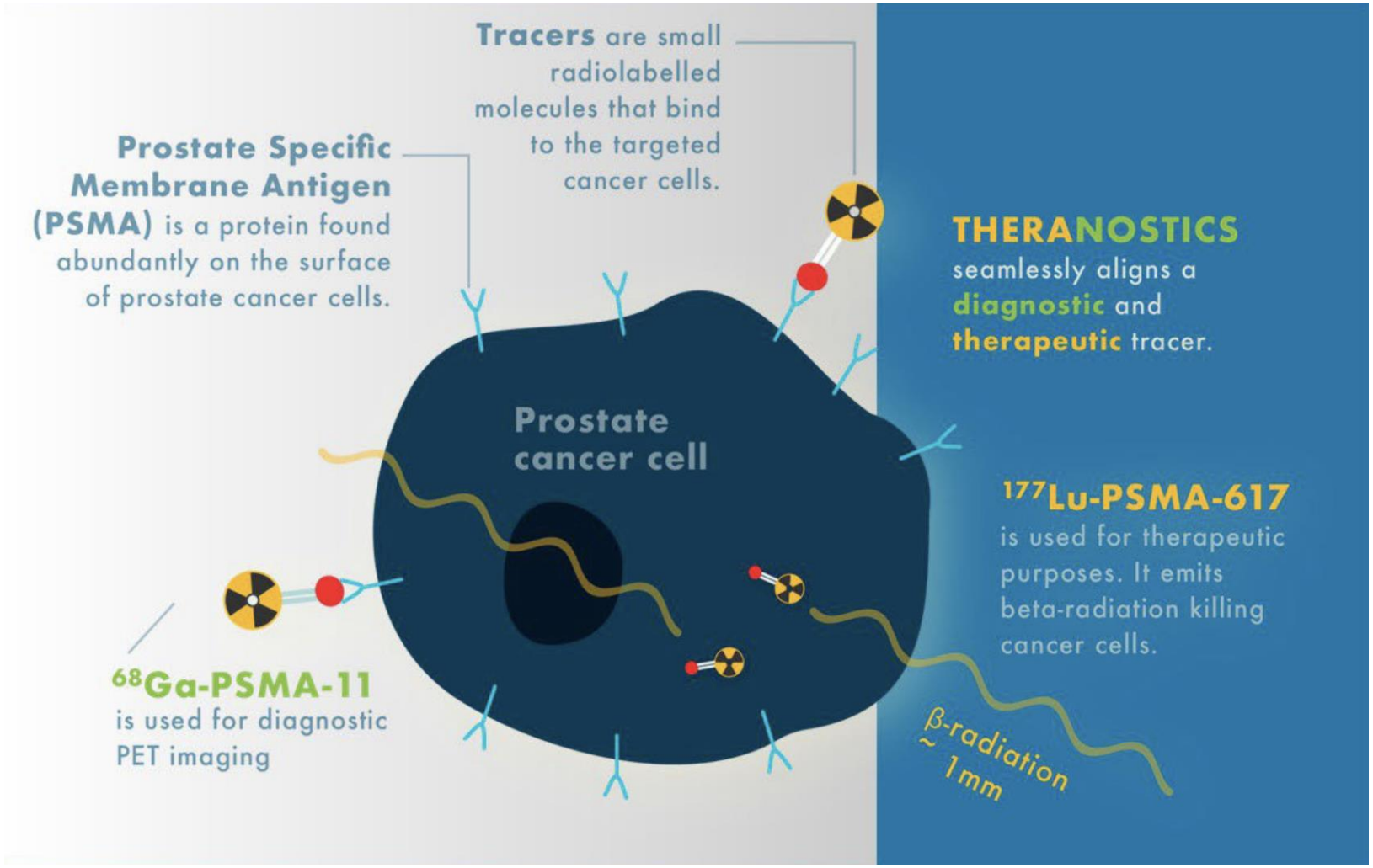
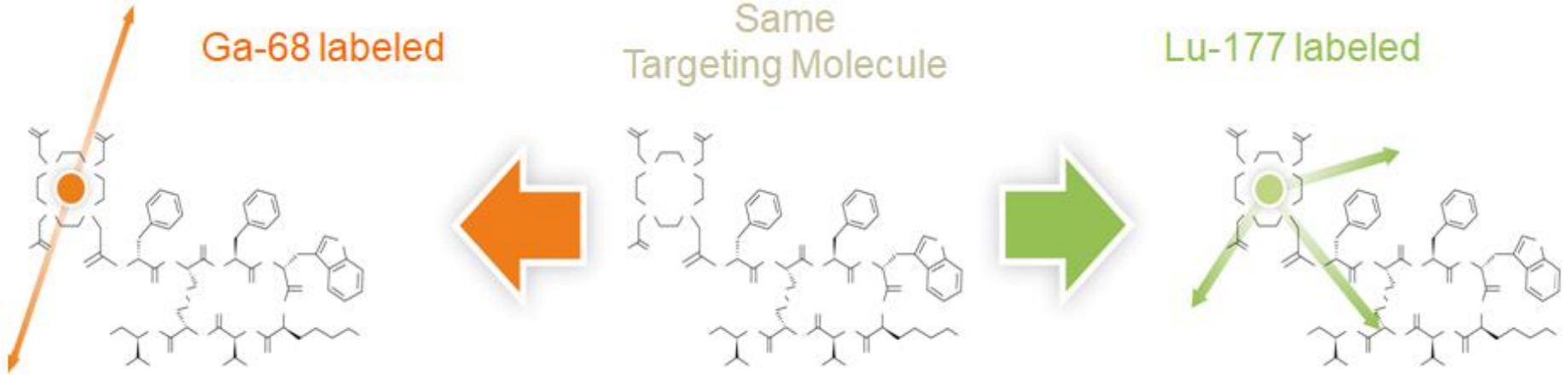
À quel moment et avec quel outil faire intervenir le médecin nucléaire dans la prise en charge des cancers de la prostate ?

Loïc Djaïleb MD, PhD

Praticien Hospitalier Universitaire

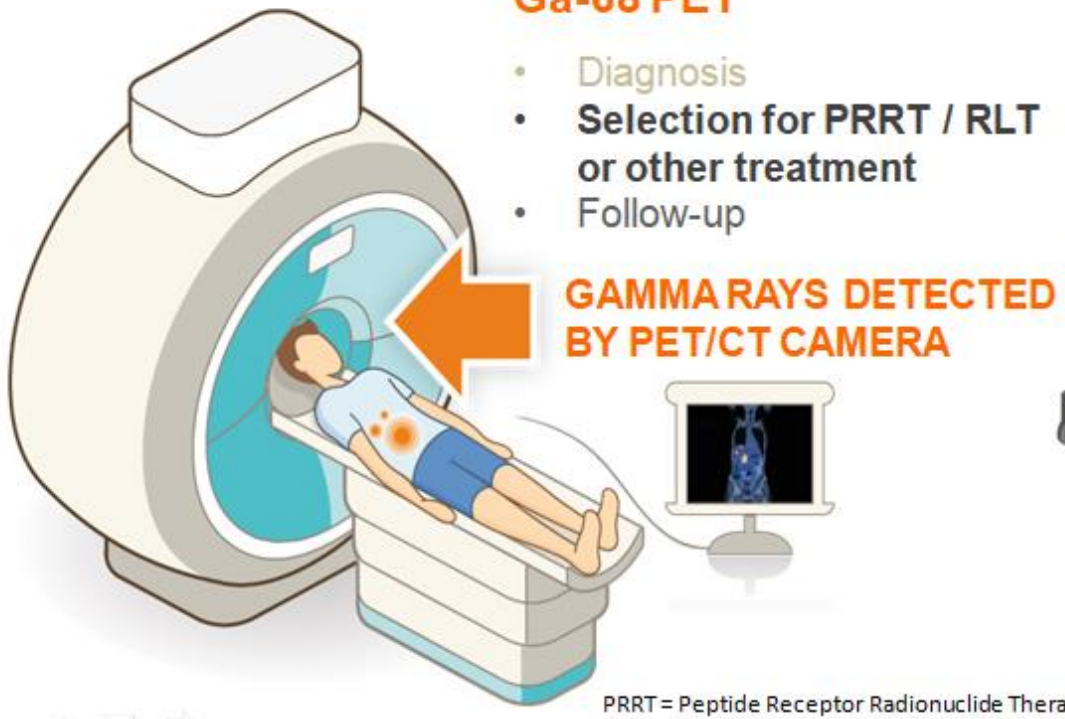
Service de médecine nucléaire, CHUGA, France


Tracers are small radiolabelled molecules that bind to the targeted cancer cells.
Prostate Specific Membrane Antigen (PSMA) is a protein found abundantly on the surface of prostate cancer cells.
THERANOSTICS seamlessly aligns a diagnostic and therapeutic tracer.
Prostate cancer cell
177Lu-PSMA-617 is used for therapeutic purposes. It emits beta-radiation killing cancer cells.
68Ga-PSMA-11 is used for diagnostic PET imaging
β-radiation ~ 1mm



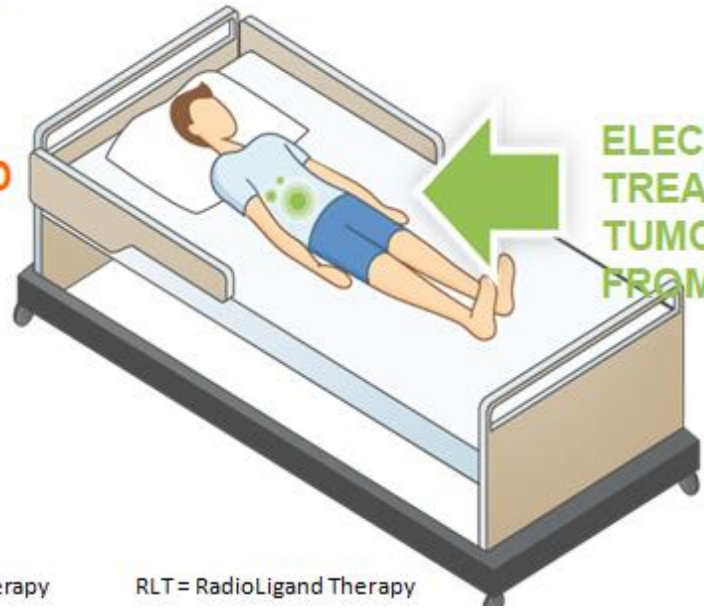
Ga-68 PET

- Diagnosis
- **Selection for PRRT / RLT or other treatment**
- Follow-up



GAMMA RAYS DETECTED BY PET/CT CAMERA

Lu-177 PRRT / RLT



ELECTRONS TREAT TUMORS FROM WITHIN

PRRT = Peptide Receptor Radionuclide Therapy

RLT = RadioLigand Therapy

Plan

- Diagnostic:
  - Bilan extension initial
  - Recidive biologique

- Thérapeutique

Diagnostic: initial

Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study

*Michael S Hofman, Nathan Lawrentschuk, Roslyn J Francis, Colin Tang, Ian Vela, Paul Thomas, Natalie Rutherford, Jarad M Martin, Mark Frydenberg, Ramdave Shakher, Lih-Ming Wong, Kim Taubman, Sze Ting Lee, Edward Hsiao, Paul Roach, Michelle Nottage, Ian Kirkwood, Dickon Hayne, Emma Link, Petra Marusic, Anetta Matera, Alan Herschtal, Amir Iravani, Rodney J Hicks, Scott Williams, Declan G Murphy, for the proPSMA Study Group Collaborators**

Lancet. 2020 Apr 11;395(10231):1208-1216.

Diagnostic: initial

- **Primary outcome** of the trial was accuracy of first-line imaging for identifying either **pelvic nodal or distant-metastatic disease.**

- **Secondary outcomes**
  - proportion of patients with management effect and equivocal findings

Lancet. 2020 Apr 11;395(10231):1208-1216.

Diagnostic: initial

- **Results:**
- **<u>Primary endpoint:</u>**

- **PSMA** : **PLN 30 (20%), M1a (abdominal) 13 (9%),** M1b 15 (10%), M1c 1 (1%)
- **Conventional imaging** : PLN **13** (8.6%), M1a (abdominal) 7 (5%), M1b 17 (11.2%), M1c 1 (1%)

- **PSMA PET-CT** had **a 27% (95% CI 23–31, p<0·0001)** absolute greater AUC for accuracy than conventional imaging (92% [88–95] *vs* 65% [60–69]

- **Conventional imaging** vs **PSMA PET-CT**:

  sensitivity 38% [24–52] vs 85% [74–96]

  specificity 91% [85–97] *vs* 98% [95–100]

Lancet. 2020 Apr 11;395(10231):1208-1216.

ProPSMA diagnostic phase 3 randomised study

Prostate Specific Membrane Antigen (PSMA) PET/CT

for imaging men with newly diagnosed prostate cancer

302 patients *randomised* with untreated prostate cancer

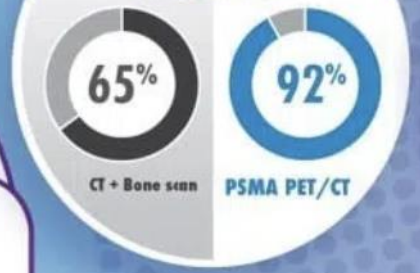
10 sites across Australia

50% current method: **CT + Bone scan**

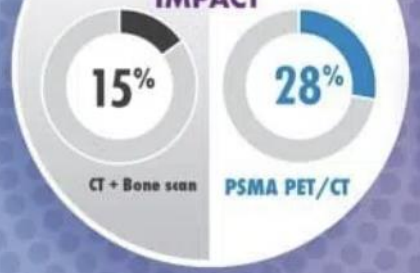
50% studied method: **PSMA PET/CT**

The data supports PSMA PET/CT imaging as a replacement to current standard-of-care CT and bone scan.

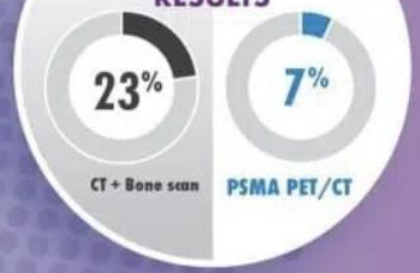
SUPERIOR ACCURACY



GREATER TREATMENT IMPACT

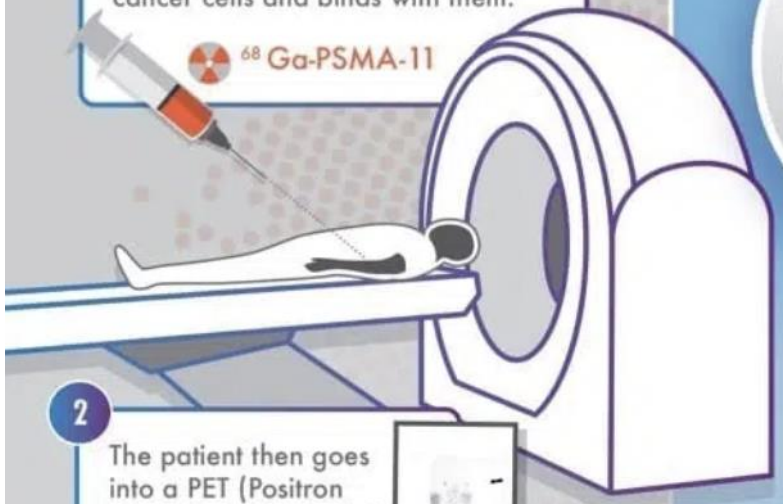


FEWER UNCERTAIN RESULTS

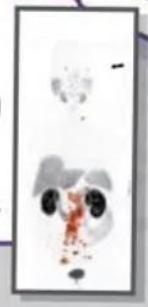


1. A small radioactive molecule is injected into a vein. It finds its way to cancer cells and binds with them.

^{68}Ga-PSMA-11



2. The patient then goes into a PET (Positron Emission Tomography) scanner that images the whole body and shows cancerous cells.



3. Patients were then followed for 6 months to determine accuracy.

OTHER FINDINGS:

- **LESS EXPOSURE TO RADIATION**
- **HIGH REPORTER AGREEMENT**
- **NO ADVERSE EFFECTS SEEN**

Research sponsored by: Peter Mac — Peter MacCallum Cancer Centre Victoria Australia

and proudly funded by: MOVEMBER FOUNDATION; Prostate Cancer Foundation of Australia

Diagnostic: initial

- Conclusion:

PSMA PET-CT is a suitable **replacement** for conventional imaging, providing superior accuracy, to the combined findings of CT and bone scanning

→ TEP Fluorocholine si intention de traitement curatif

Lancet. 2020 Apr 11;395(10231):1208-1216.

Diagnostic: initial

JAMA Oncology | Original Investigation

Diagnostic Accuracy of ^{68}Ga-PSMA-11 PET for Pelvic Nodal Metastasis Detection Prior to Radical Prostatectomy and Pelvic Lymph Node Dissection

A Multicenter Prospective Phase 3 Imaging Trial

Thomas A. Hope, MD; Matthias Eiber, MD; Wesley R. Armstrong; Roxanna Juarez, MD; Vishnu Murthy; Courtney Lawhn-Heath, MD; Spencer C. Behr, MD; Li Zhang, PhD; Francesco Barbato, MD; Francesco Ceci, MD; Andrea Farolfi, MD; Sarah M. Schwarzenböck, MD; Marcus Unterrainer, MD; Helle D. Zacho, MD, PhD; Hao G. Nguyen, MD; Matthew R. Cooperberg, MD; Peter R. Carroll, MD, MPH; Robert E. Reiter, MD; Stuart Holden, MD; Ken Herrmann, MD; Shaojun Zhu, MSc; Wolfgang P. Fendler, MD; Johannes Czernin, MD; Jeremie Calais, MD

Thomas A Hope *et al*, JAMA Oncol. 2021;7(11):1635-1642.

Diagnostic: initial

Inclusion criterion:

NCCN **intermediate- to high-risk histopathology**
proven prostate adenocarcinoma,

PSMA PET

Radical prostatectomy + pelvic lymph node dissection

Initial staging

Thomas A Hope *et al*, JAMA Oncol. 2021;7(11):1635-1642.

Diagnostic: initial

For pelvic nodal metastases:

- Sensitivity: 0.40 (95% CI, 0.34-0.46),
- **Specificity: 0.95 (95% CI, 0.92-0.97)**,
- Positive predictive value 0.75 (95% CI, 0.70-0.80),
- Negative predictive value 0.81 (95% CI, 0.76-0.85),

Thomas A Hope *et al*, JAMA Oncol. 2021;7(11):1635-1642.

Diagnostic: recidive biologique

JAMA Oncology | Original Investigation

Assessment of ^{68}Ga-PSMA-11 PET Accuracy in Localizing Recurrent Prostate Cancer

A Prospective Single-Arm Clinical Trial

Wolfgang P. Fendler, MD; Jeremie Calais, MD; Matthias Eiber, MD; Robert R. Flavell, MD, PhD; Ashley Mishoe, PharmD; Felix Y. Feng, MD; Hao G. Nguyen, MD, PhD; Robert E. Reiter, MD; Matthew B. Rettig, MD; Shozo Okamoto, MD; Louise Emmett, MD; Helle D. Zacho, MD; Harun Ilhan, MD; Axel Wetter, MD; Christoph Rischpler, MD; Heiko Schoder, MD; Irene A. Burger, MD; Jeannine Gartmann; Raven Smith; Eric J. Small, MD; Roger Slavik, PhD; Peter R. Carroll, MD, MPH; Ken Herrmann, MD; Johannes Czernin, MD; Thomas A. Hope, MD

JAMA Oncol. 2019 Jun 1;5(6):856-863.

Diagnostic: recidive biologique

- Biochemical recurrence was defined as a PSA of 0.2 or more ng/mL measured more than 6 weeks after prostatectomy or a PSA of 2 or more ng/mL rise above nadir following radiation therapy (ASTRO-Phoenix consensus definition)

- Patients were enrolled irrespective of prior conventional imaging findings

- All patients were followed up for histopathologic analysis, conventional imaging, or serum PSA after focal salvage therapy acquired during clinical routine

JAMA Oncol. 2019 Jun 1;5(6):856-863.

Diagnostic: recidive biologique

- **The primary endpoint** was positive predictive value (PPV) on a per-patient of ^{68}Ga-PSMA-11 PET for detection of tumor location confirmed by **histopathologic analysis**

- **Secondary endpoints:**
  - per-patient PPV confirmed by composite validation
  - per-patient detection rate stratified by PSA and PSA doubling time

JAMA Oncol. 2019 Jun 1;5(6):856-863.

Diagnostic: recidive biologique

- From September 2016 through October 2017, a total of 635 patients were enrolled (UCLA & UCSF)

- Efficacy cohorts were 223 patients with composite validation and 93 patients with histopathologic validation

JAMA Oncol. 2019 Jun 1;5(6):856-863.

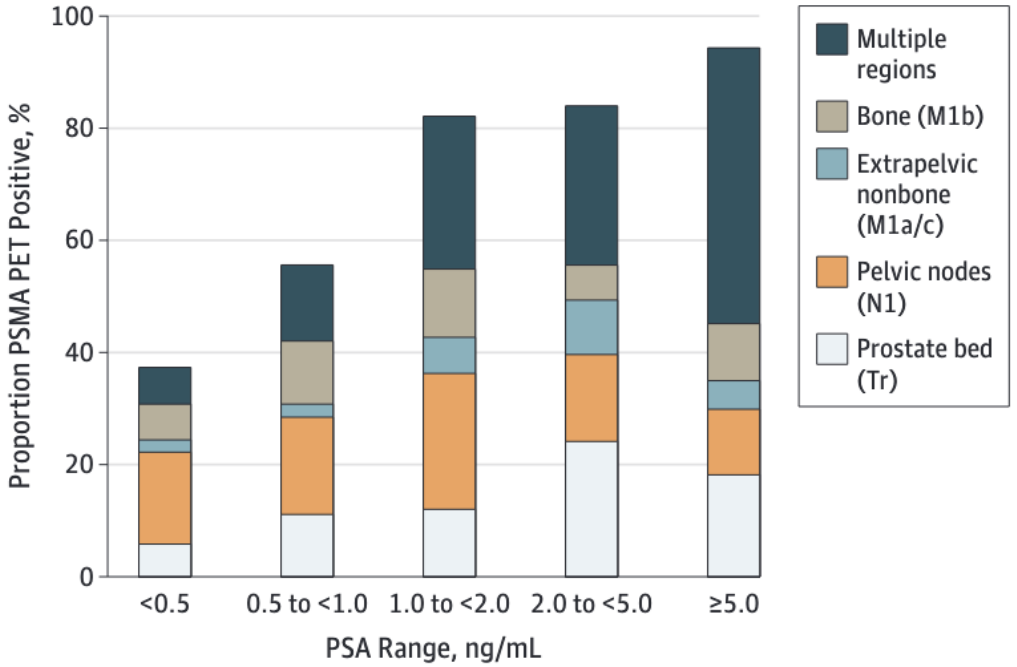
Diagnostic: recidive biologique

- On a per-patient basis, PPV was 0.84 (95% CI, 0.75-0.90) by histopathologic validation (primary endpoint, n= 87)
- On a per-patient basis 0.92 (95% CI, 0.88-0.95) by the composite reference standard (n = 217)
- Inter-reader reproducibility was substantial (Fleiss κ, 0.65-0.78).
- ^{68}Ga-PSMA-11 PET localized recurrent prostate cancer in 475 of 635 (75%) patients

JAMA Oncol. 2019 Jun 1;5(6):856-863.

Diagnostic: recidive biologique

Figure 2. Detection Rate on a Patient Basis Stratified by PSA and Region



Tr indicates prostate bed only; N1, pelvic nodes only; M1, extrapelvic only. Proportion of patients with ^{68}Ga-PSMA-11 PET positive findings were stratified by PSA range and region of disease in accordance with PROMISE.[14]

JAMA Oncol. 2019 Jun 1;5(6):856-863.

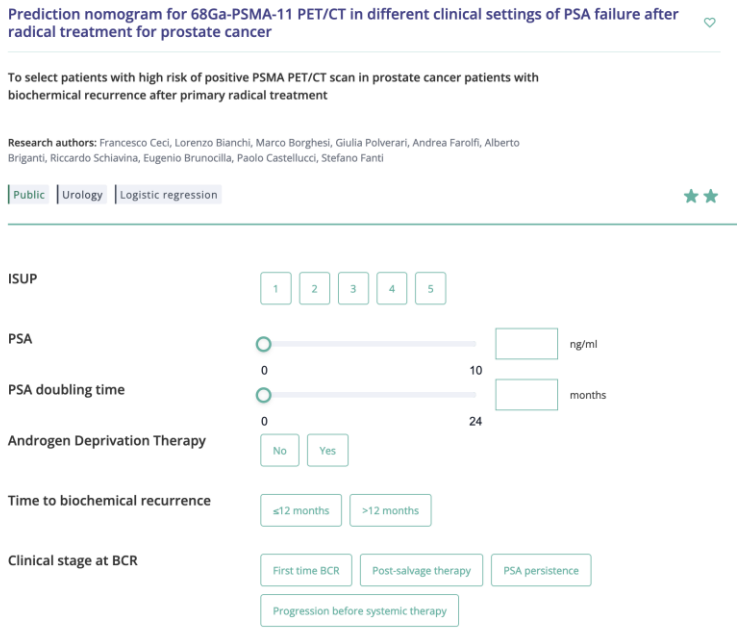
Diagnostic: recidive biologique

- Using blinded reads and independent lesion validation, we establish high PPV for ^{68}Ga-PSMA-11 PET, detection rate and inter-reader agreement for localization of recurrent prostate cancer.

→ TEP Fluorocholine puis ^{68}Ga-PSMA-11

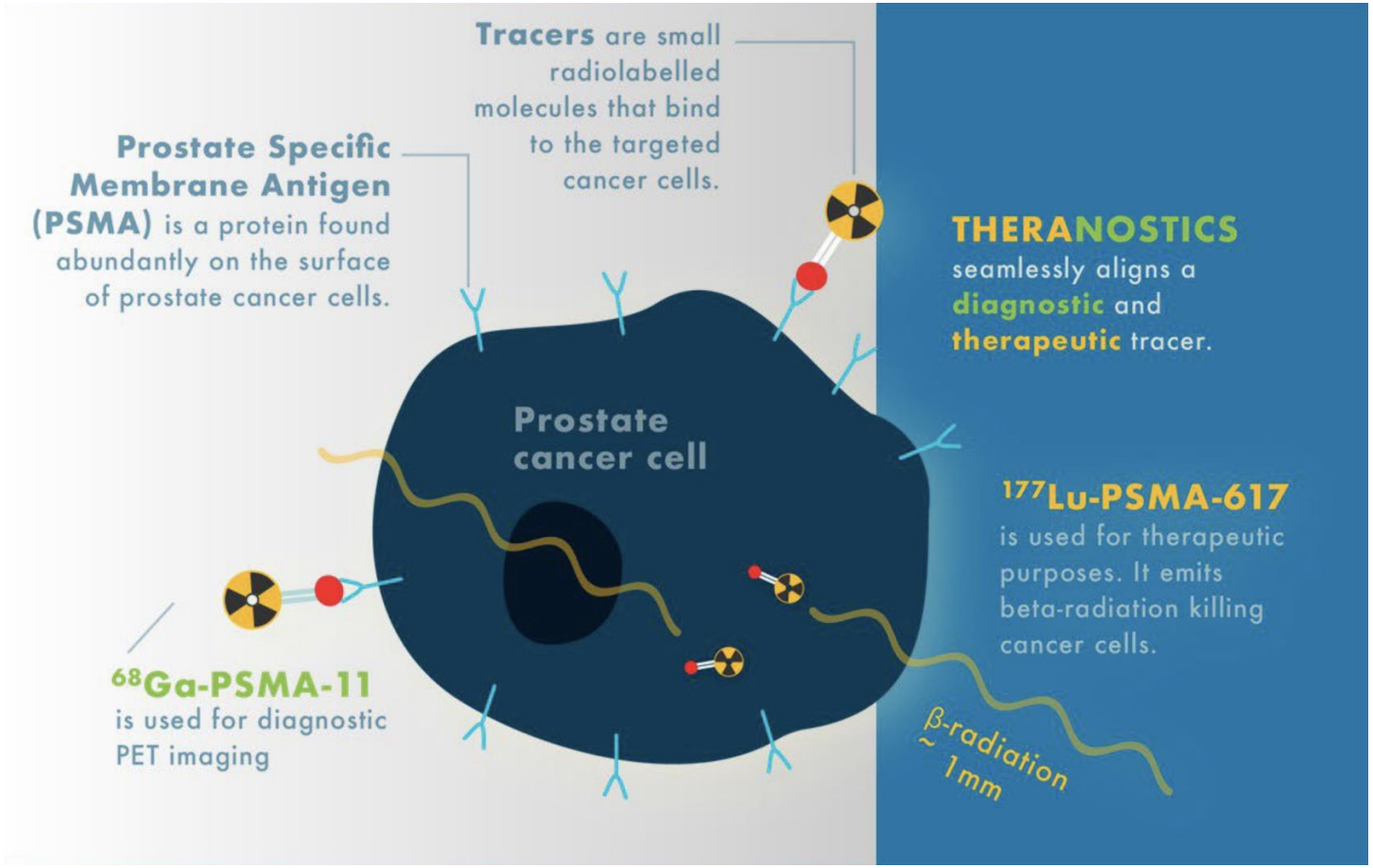
→ ^{18}F-PMSA-1007

https://www.evidencio.com/models/show/2063



Eur J Nucl Med Mol Imaging. 2020 Jan;47(1):136-146

Thérapeutique: 177Lu-PSMA



Lancet. 2021 Feb 27;397(10276):797-804

Thérapeutique: 177Lu-PSMA

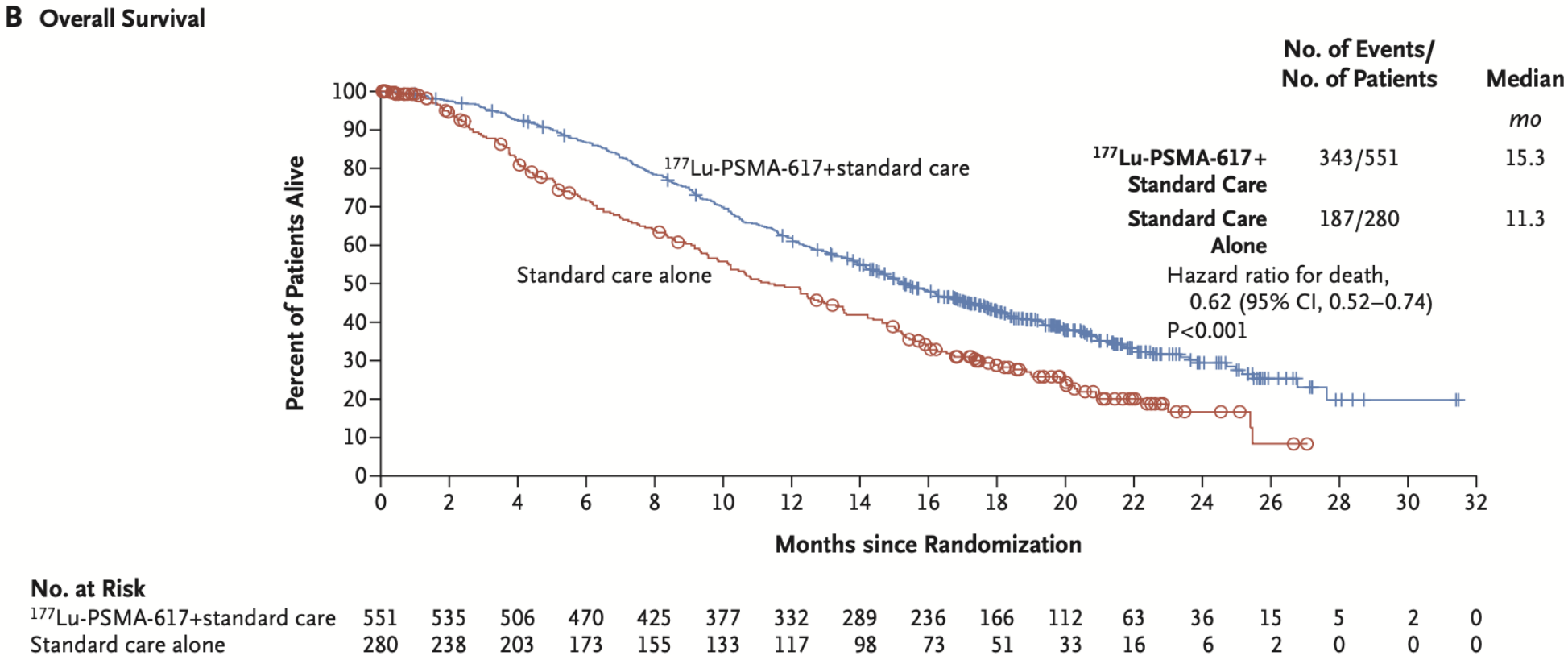
ORIGINAL ARTICLE

Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

N Engl J Med 2021; 385:1091-1103

Thérapeutique: 177Lu-PSMA



N Engl J Med 2021; 385:1091-1103

Thérapeutique: 177Lu-PSMA

[^{177}Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial

Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony M Joshua, Jeffrey C Goh, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedye, Natalie K Rutherford, Andrew Weickhardt , Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, Andrew D Redfern, William Macdonald, Alex Guminski, Edward Hsiao, Wei Chua, Peter Lin, Alison Y Zhang, Margaret M McJannett, Martin R Stockler, John A Violet, Scott G Williams, Andrew J Martin, Ian D Davis, for the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group†*

Lancet. 2021 Feb 27;397(10276):797-804

Thérapeutique: 177Lu-PSMA

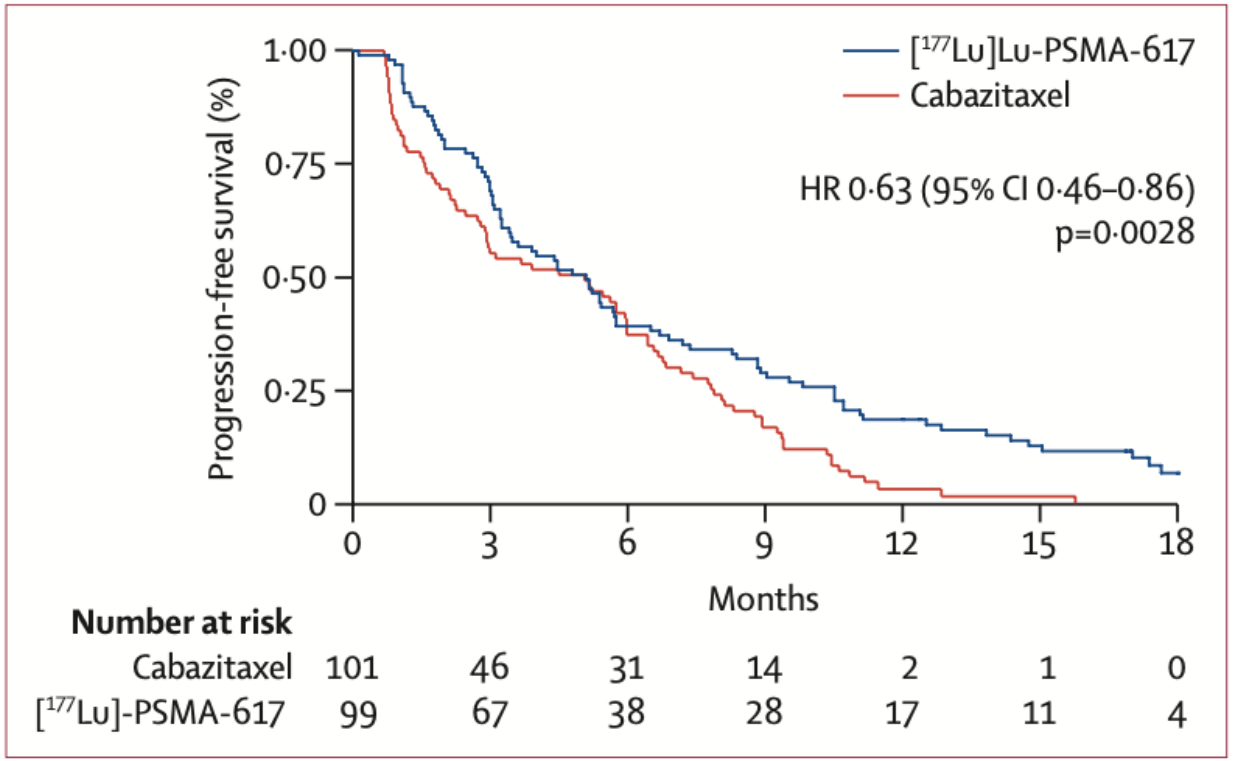
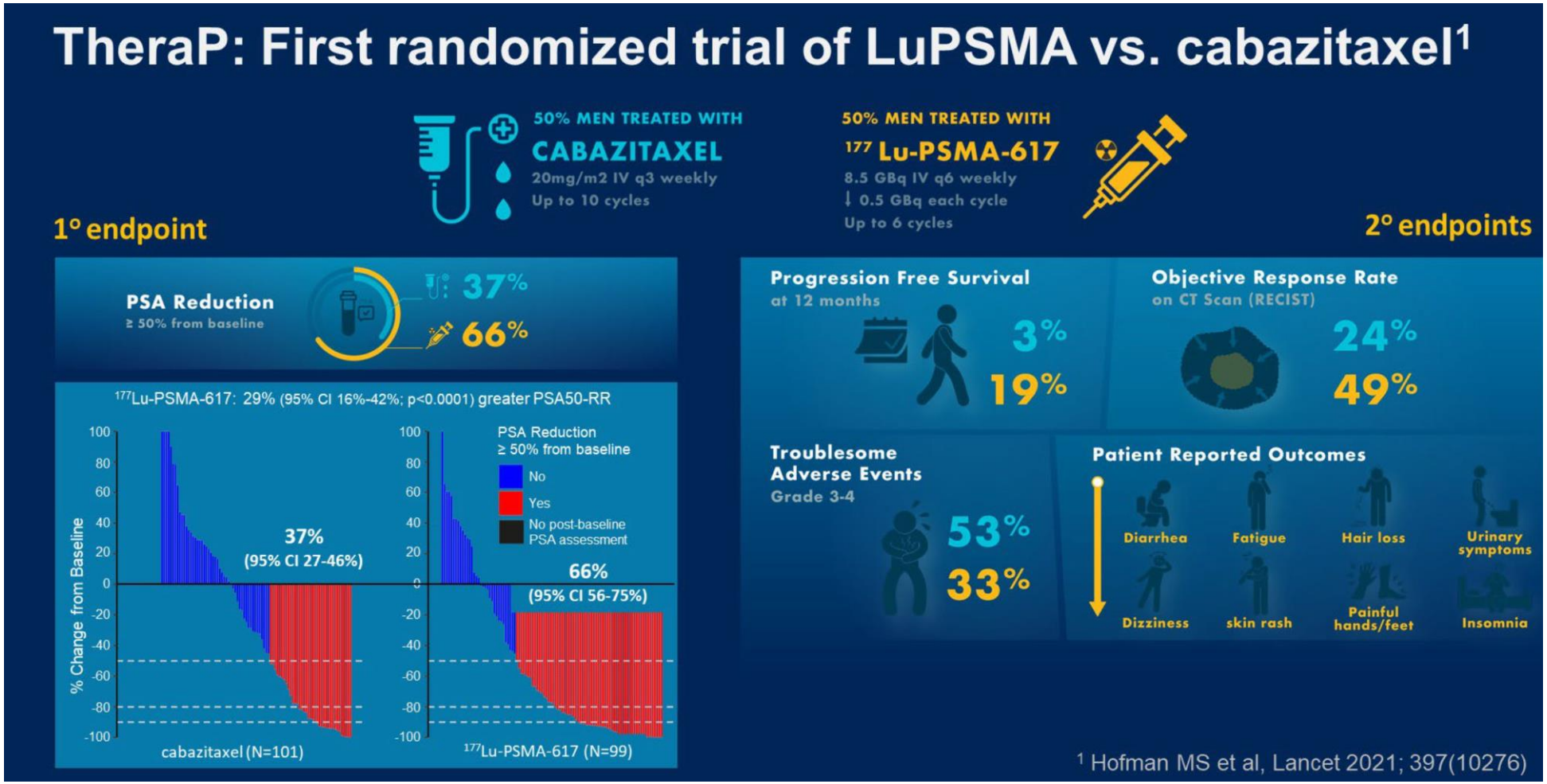


Figure 3: **Radiographic or PSA progression-free survival**
HR=hazard ratio. PSA=prostate-specific antigen. PSMA=prostate-specific membrane antigen. ^{177}Lu=lutetium-177.

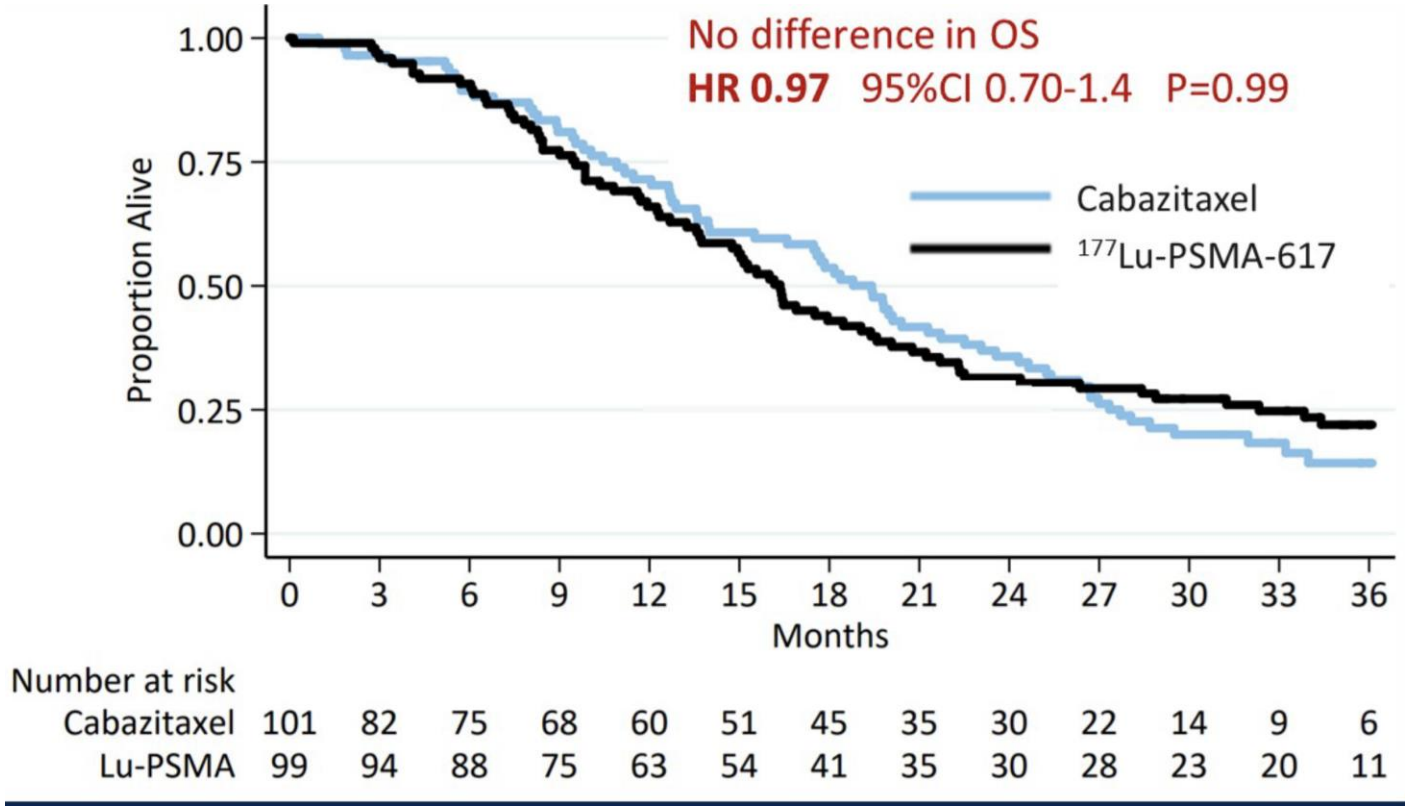
Lancet. 2021 Feb 27;397(10276):797-804

Thérapeutique: 177Lu-PSMA



Lancet. 2021 Feb 27;397(10276):797-804

Thérapeutique: 177Lu-PSMA



ASCO Annual Meeting, 2022

Thérapeutique: 177Lu-PSMA

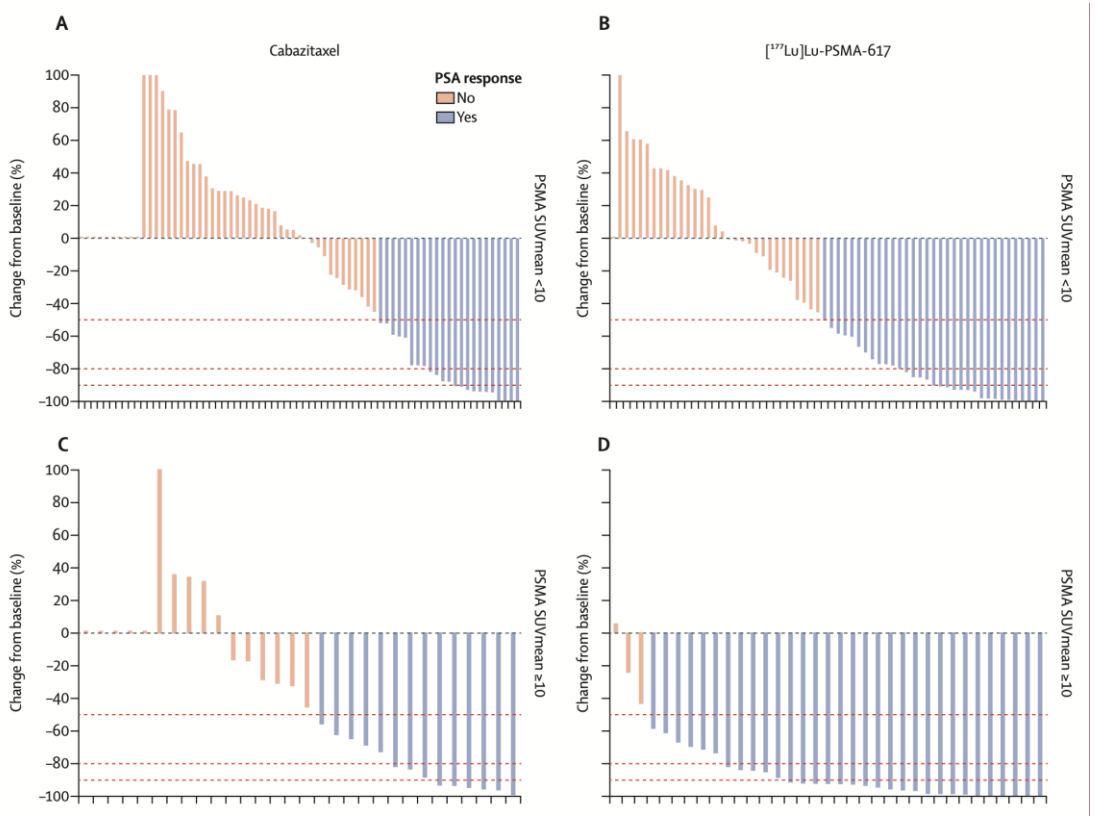
PSMA and FDG-PET as predictive and prognostic biomarkers in patients given [^{177}Lu]Lu-PSMA-617 versus cabazitaxel for metastatic castration-resistant prostate cancer (TheraP): a biomarker analysis from a randomised, open-label, phase 2 trial

*James P Buteau, Andrew J Martin, Louise Emmett, Amir Iravani, Shahneen Sandhu, Anthony M Joshua, Roslyn J Francis, Alison Y Zhang, Andrew M Scott, Sze-Ting Lee, Arun A Azad, Margaret M McJannett, Martin R Stockler, Scott G Williams, Ian D Davis, Michael S Hofman, for the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group**

Lancet Oncol. 2022 Nov;23(11):1389-1397.

Thérapeutique: 177Lu-PSMA

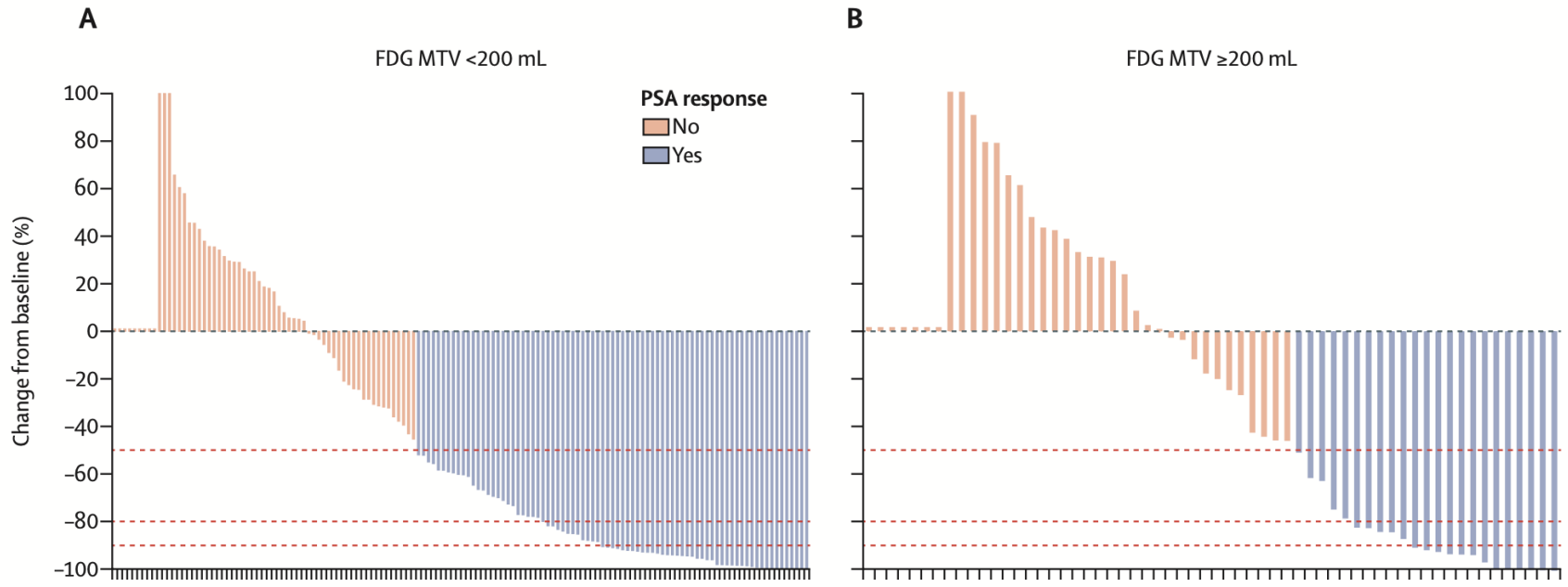
- PSMA SUV mean predictive of PSA response Lu-PSMA



Lancet Oncol. 2022 Nov;23(11):1389-1397.

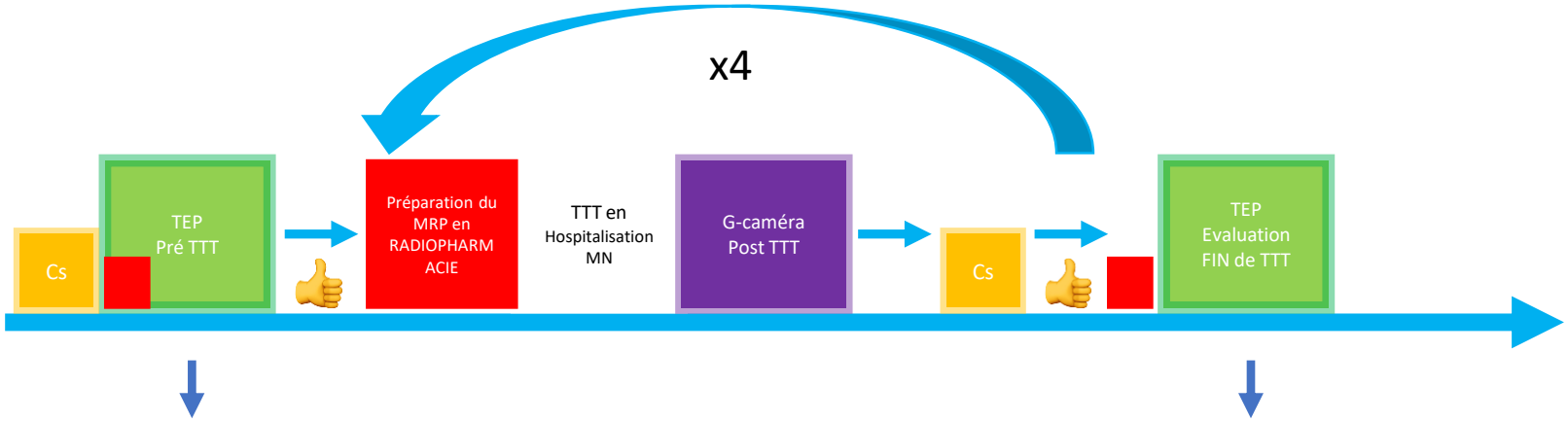
Thérapeutique: 177Lu-PSMA

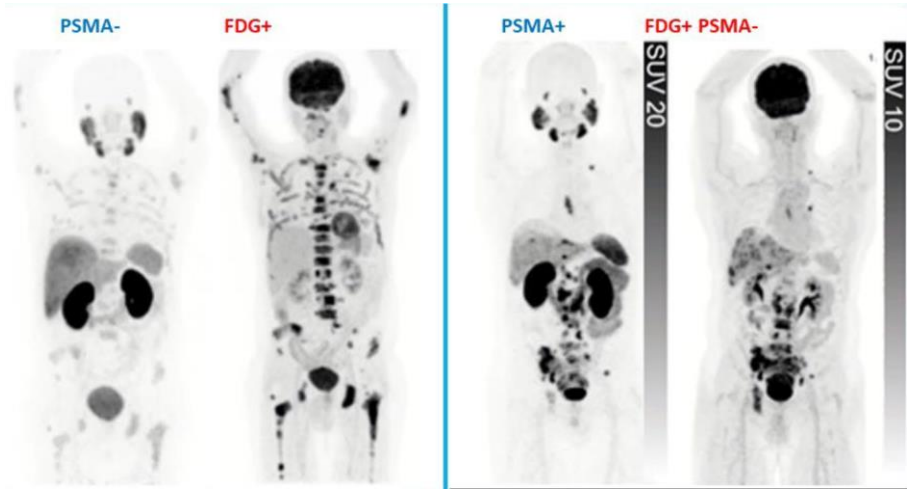
- FDG volume > 200 ml prognostic of PSA response



Lancet Oncol. 2022 Nov;23(11):1389-1397.

Thérapeutique: 177Lu-PSMA





Cs Onco med referent à mi-Traitement et fin de traitement

Thérapeutique: 177Lu-PSMA

- Indication:
- mCRPC
  - Après Hormonothérapie 1ere et 2eme ligne
  - Après DOCETAXEL et CABAZITAZEL

Thérapeutique: Xofigo

- mCRPC
- AMM: mCRPC avec métastases osseuses symptomatiques et sans métastases viscérales connues, en progression après au moins deux lignes antérieures de traitement systémique du CPmRC (autres que les analogues de la LH-RH) ou inéligibles à tous les traitements systémiques du CPmRC disponibles

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^{68}Ga-PSMA-11 PET as a Gatekeeper for the Treatment of Metastatic Prostate Cancer with ^{223}Ra: Proof of Concept