



Hospices Civils de Lyon



RIV des ligands du PSMA

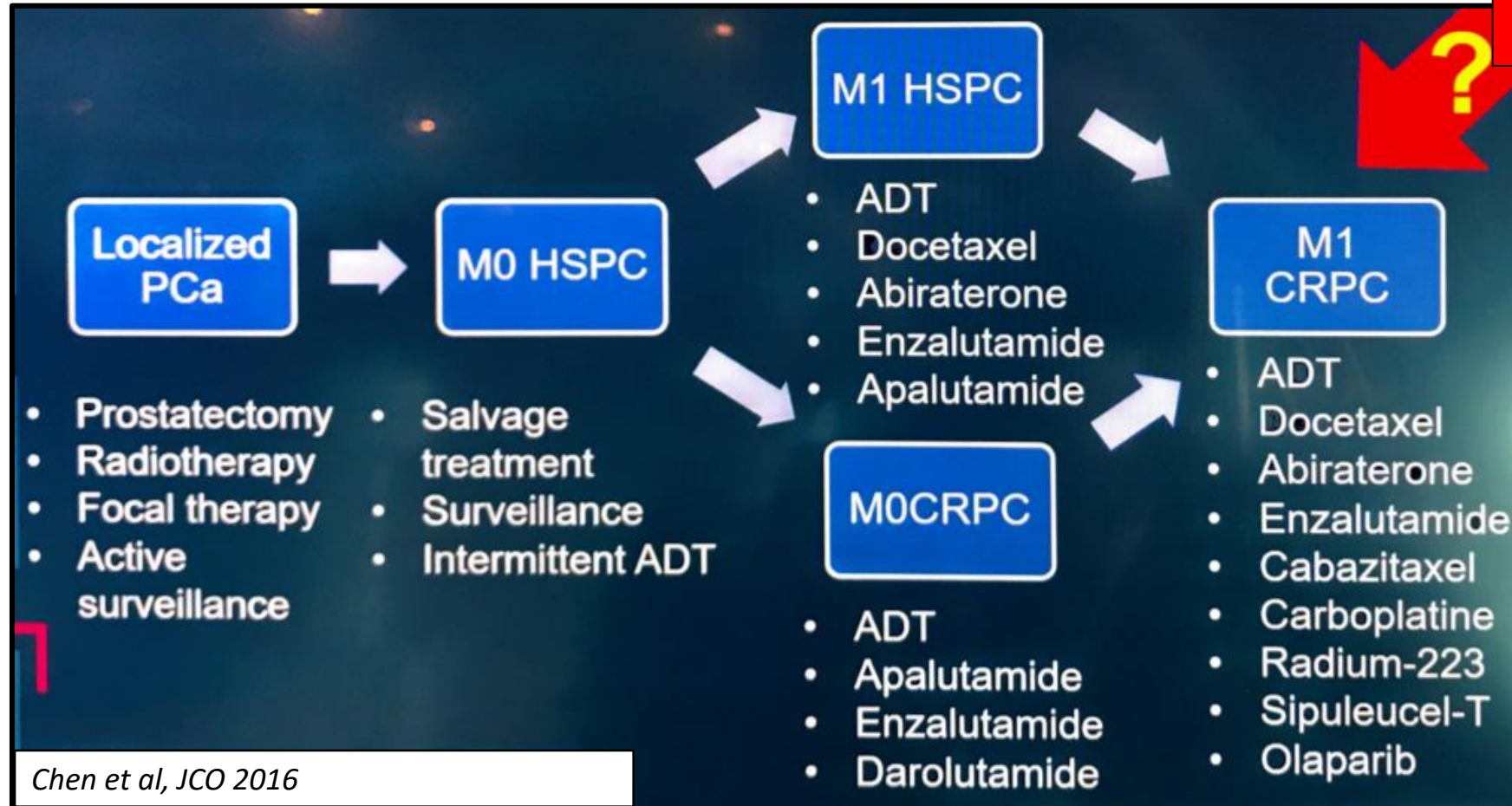
RÉUNION ARA

16 JANVIER 2021

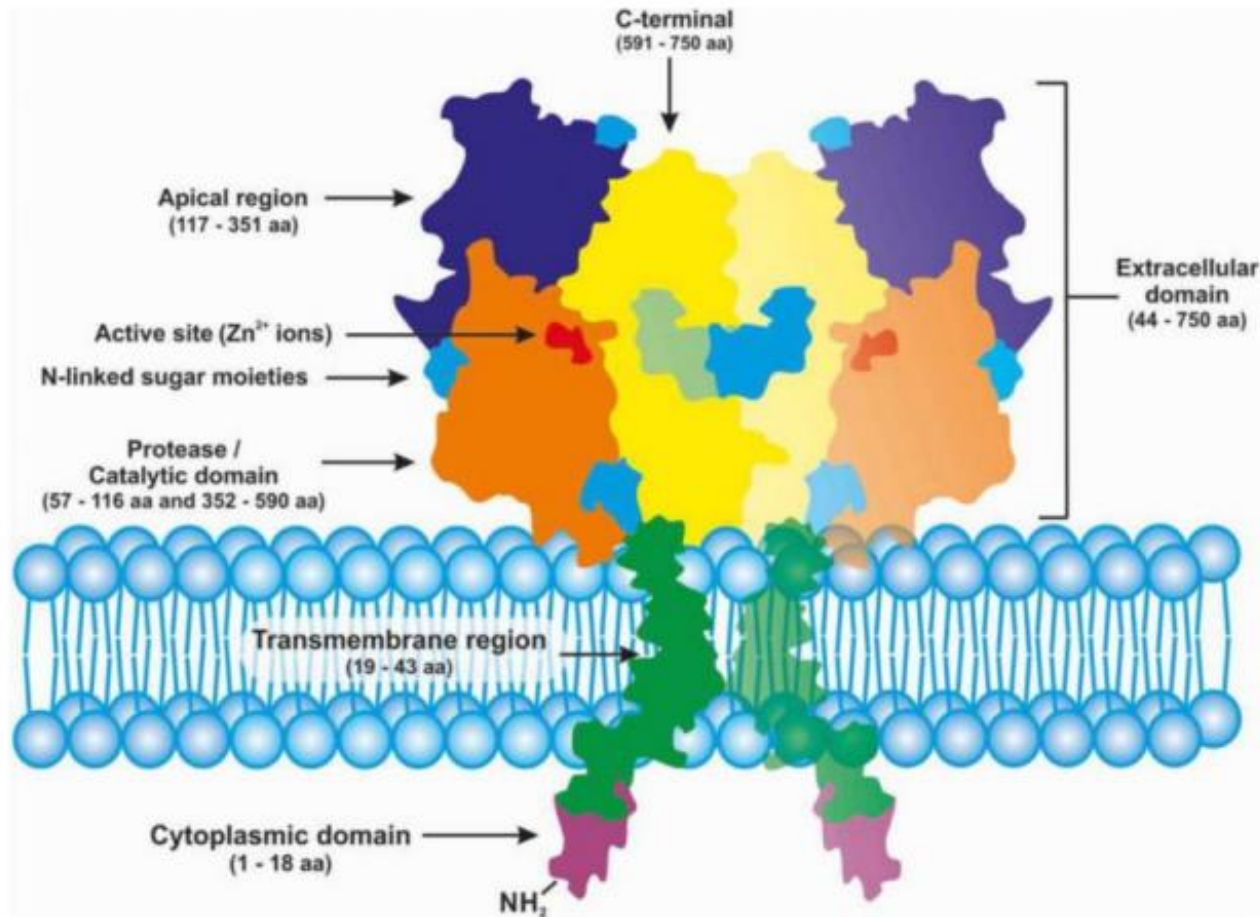
Cancer de la Prostate : Principes Thérapeutiques

- Principes thérapeutiques bien codifiés dans les stades précoces de la maladie
- Dans les stades avancés, développement de résistances aux chimiothérapies actuelles
- Pas de séquence thérapeutique idéale pour les **mCRPC**, pas de consensus

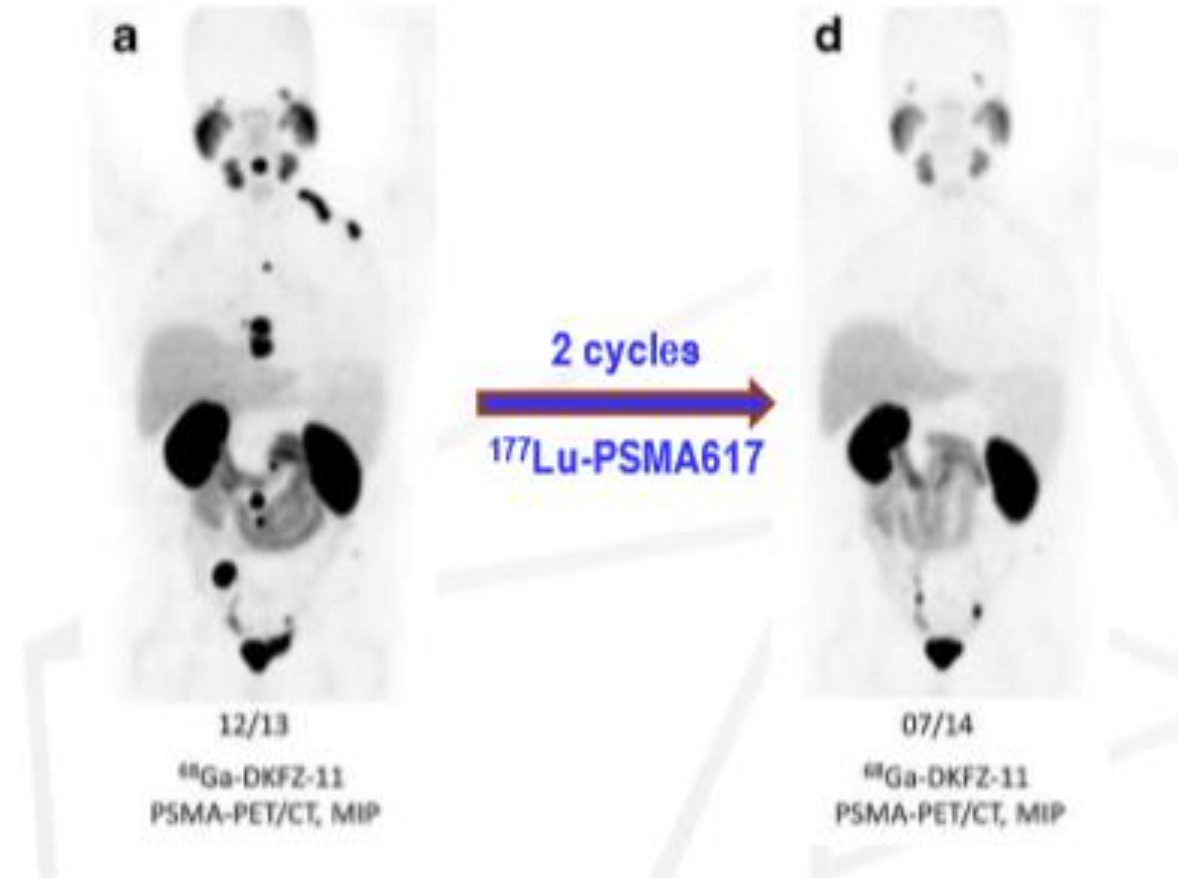
- **Besoin de nouvelles lignes de traitement**
- **Intérêt de la RIV par les ligands du PSMA**



Ligands du PSMA (Prostate Specific Membran Antigen)



O'Driscott C et al, Br J Pharm 2016

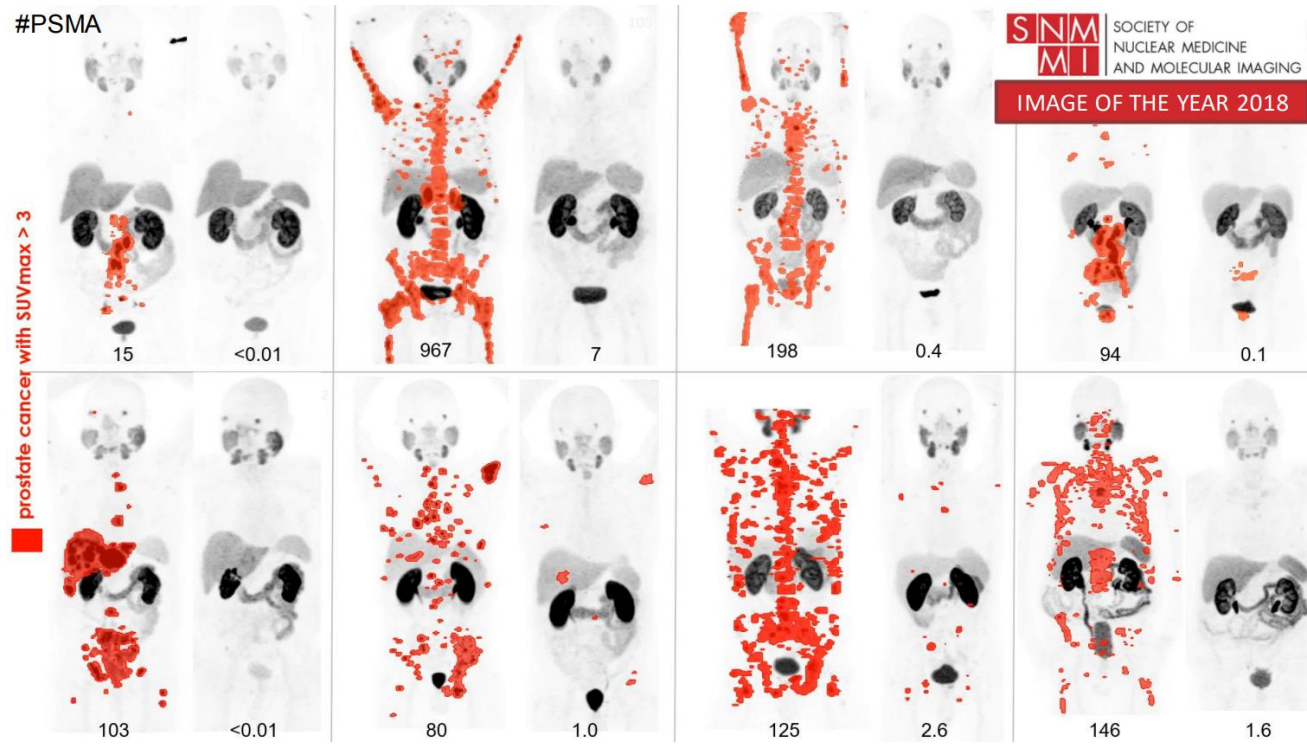


Kratochwil et al, Eur J Nucl Med Mol Imaging 2015

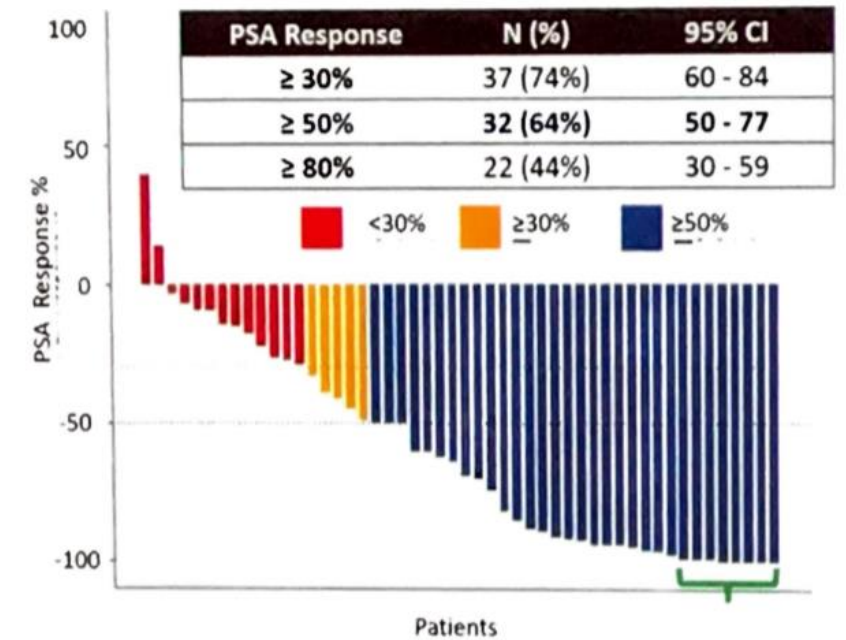
[¹⁷⁷Lu]-PSMA-617 radionuclide treatment in patients with metastatic castration-resistant prostate cancer (LuPSMA trial): a single-centre, single-arm, phase 2 study

Lancet Oncol 2018
Published Online
May 8, 2018

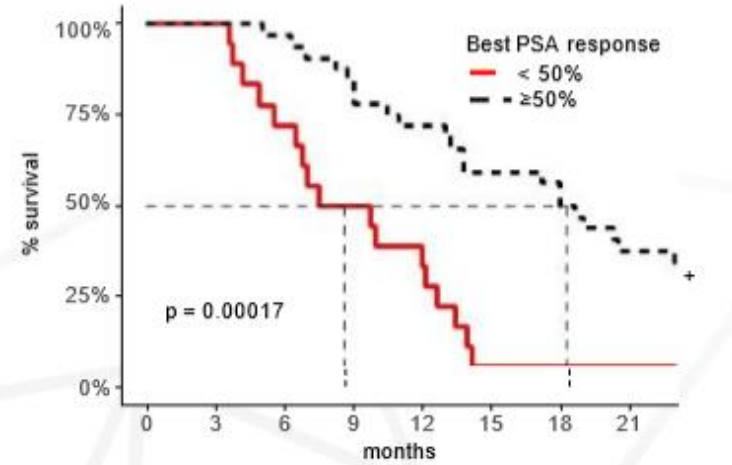
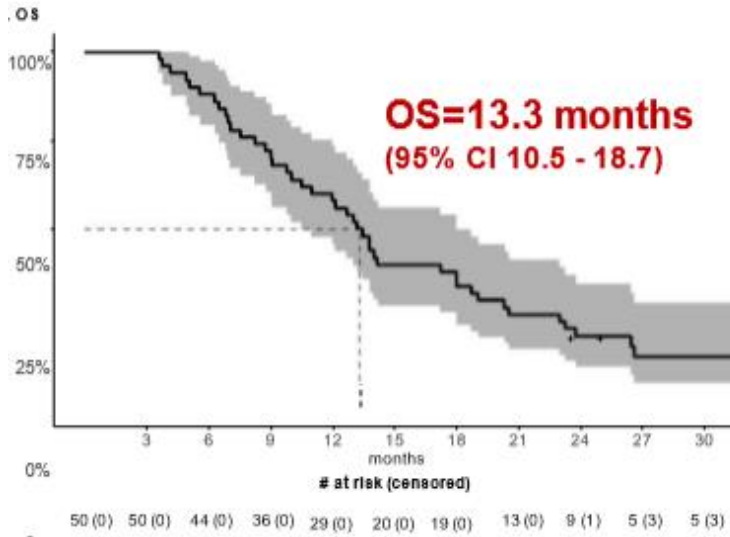
Michael S Hofman*, John Violet*, Rodney J Hicks, Justin Ferdinandus, Sue Ping Thang, Tim Akhurst, Amir Iravani, Grace Kong, Aravind Ravi Kumar, Declan G Murphy, Peter Eu, Price Jackson, Mark Scalzo, Scott G Williams, Shahneen Sandhu



Best PSA Response (N=50)



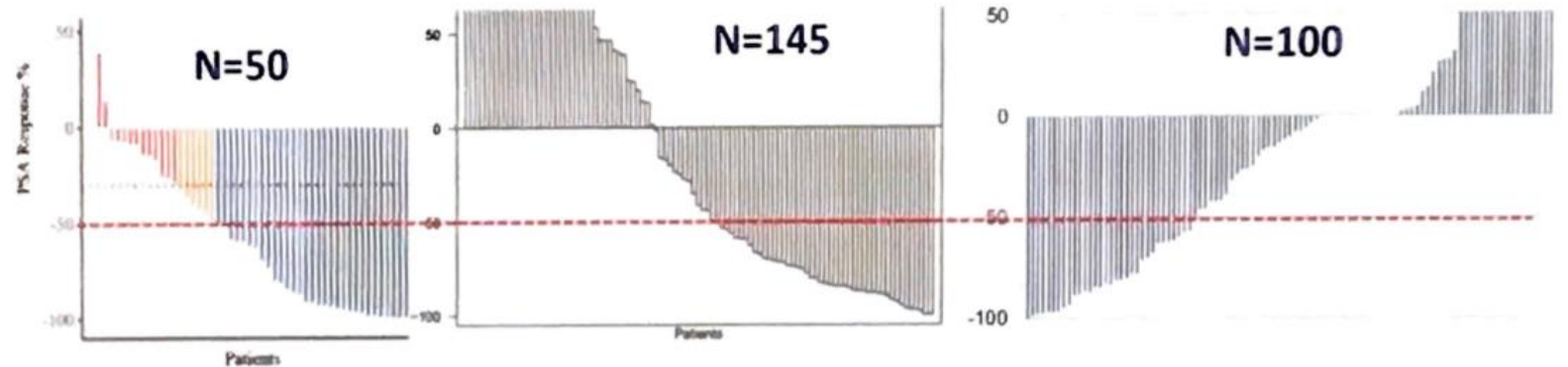
Données actualisées de l'étude Hofman



Hofman MS et al, ASCO GU 2019

PSA ≥ 50%: 18.4 months (95% CI 13.8 - 23.8)
PSA < 50%: 8.7 months (95% CI 6.5 to 13.4)

Comparaison aux autres études ?



PSA ≥ 50% in 64%
Hofman MS et al

PSA ≥ 50% in 45%
Rahbar K et al

PSA ≥ 50% in 32%
Heck et al

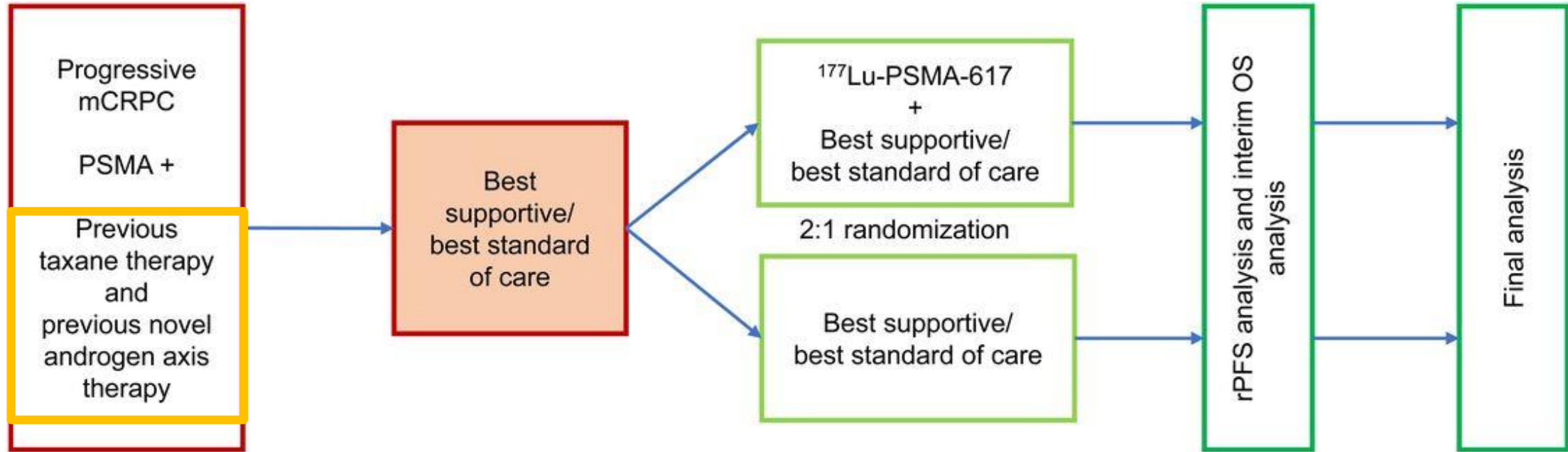
VISION

Pivotal phase 3 VISION trial design



An international, prospective, open-label, multi-center, randomized Phase 3 Study of ^{177}Lu -PSMA-617 in treatment of patients with progressive PSMA-positive metastatic castration resistant prostate cancer

Matériels et méthodes



Stratification Factors

- Serum lactate dehydrogenase (LDH) (≤ 260 IU/L vs. >260 IU/L)
- Presence of liver metastases (yes vs. No)
- ECOG score (0-1 vs. 2)
- Inclusion of NAAD in best supportive/best standard of care (yes vs. no)

Alternative Primary Endpoints

- Overall survival
- Radiographic progression-free survival (rPFS)

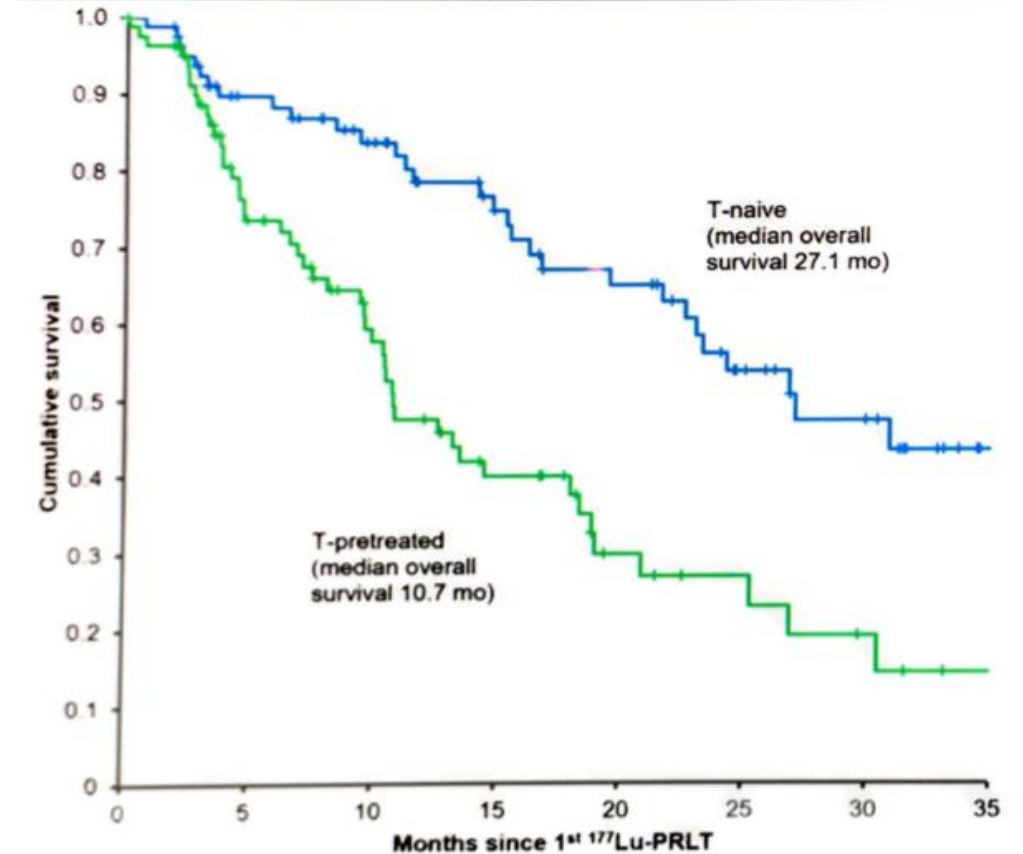
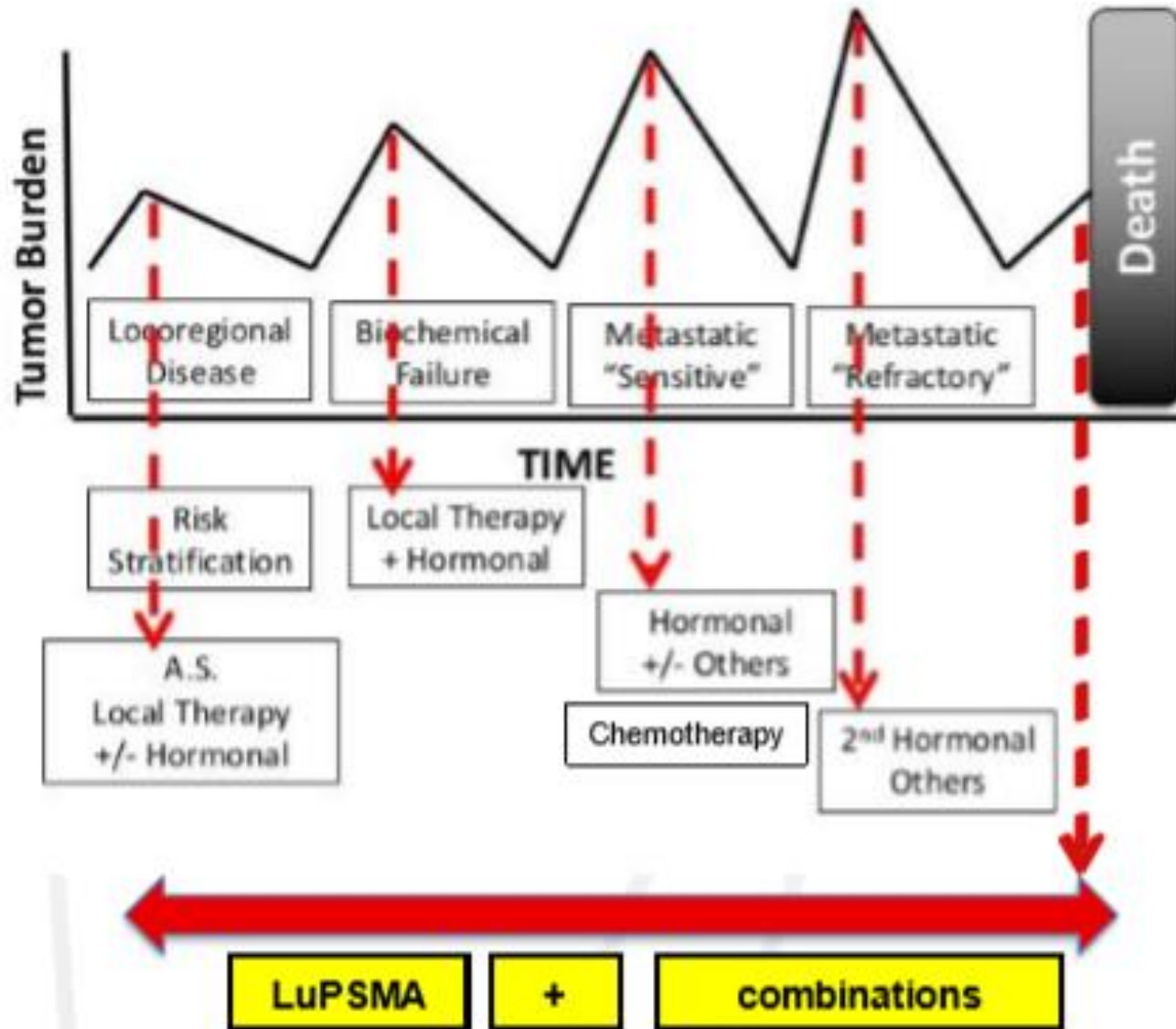
Key Secondary Endpoints (with α control)

- RECIST response
- Time to first symptomatic skeletal event (SSE)

Additional Secondary Endpoints

- Safety and tolerability
- Health-related quality of life (HRQoL; EORTC QLQ-C30 and Brief Pain Inventory – Short Form (PI-SF))
- Health Economics
- Progression-free survival (PFS) (radiological, clinical or PSA progression)
- Biochemical response: PSA levels, alkaline phosphatase levels and lactate dehydrogenase levels

Perspectives futures : Utilisation plus précoce ?



Barber et al, JNM 2019

... et en combinaison avec d'autres traitements ?

TheraP Trial: ^{177}Lu -PSMA-617 vs. cabazitaxel

PRINCE Trial

PSMA-lutetium Radionuclide therapy and **ImmuNotherapy** in prostate CancEr

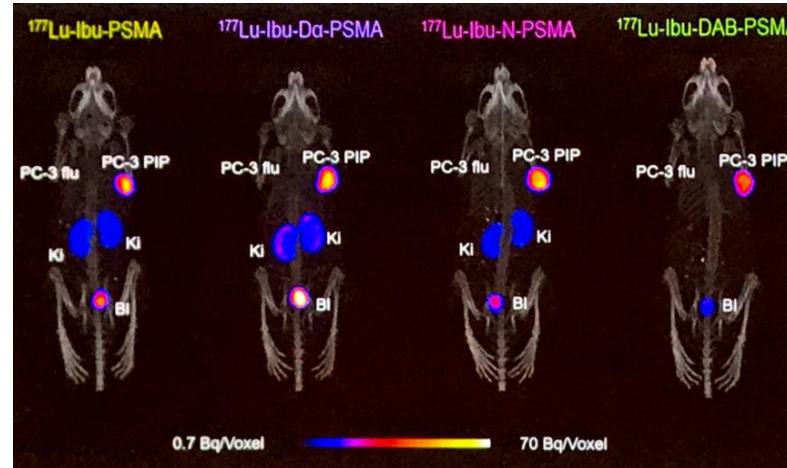
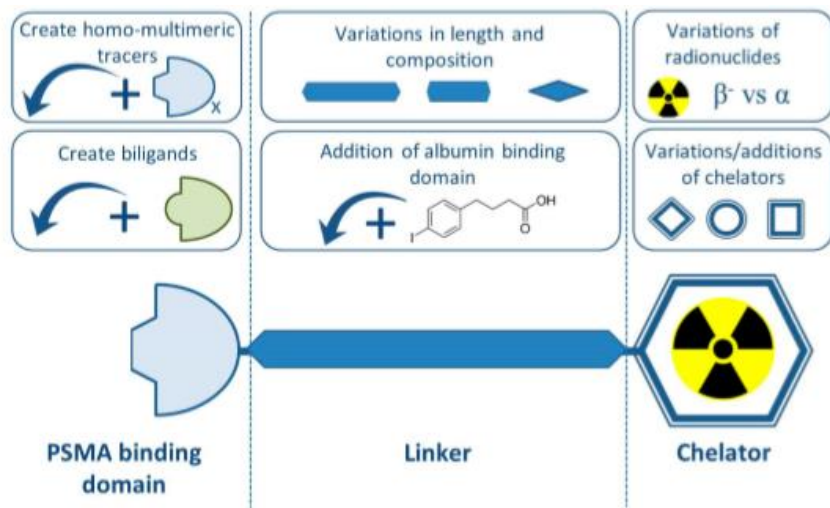
LuPARP Trial

Phase 1 trial of ^{177}Lu -PSMA-617 therapy and Olaparib (PARPi)

#UpFrontPSMA: high-volume metastatic hormone naïve PC

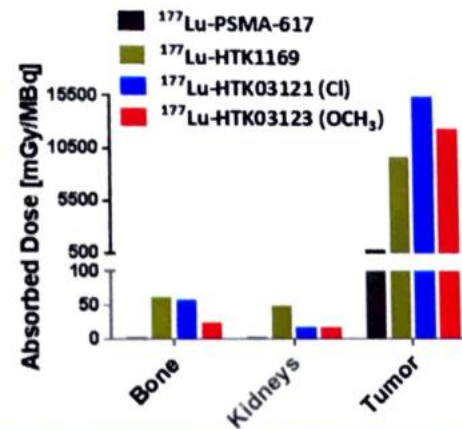
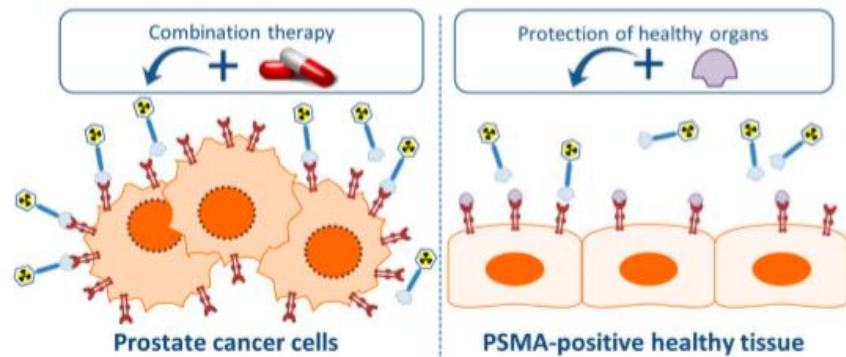
#LuTectomy: ^{177}Lu -PSMA prior to surgery

Le développement de nouveaux ligands PSMA

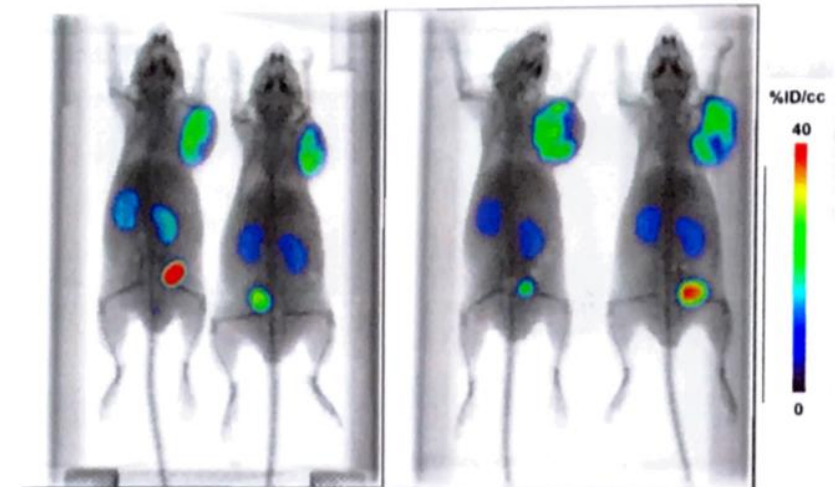


OP-019 Development of a new class of albumin-binding PSMA radioligands, C. Mueller

- Recherche préclinique
- Enjeu : protéger les organes sains exprimant le PSMA et augmenter la captation par les cellules tumorales
- Utilisation d'une nouvelle paire théranostique ?



Tumor dose ration:
¹⁷⁷Lu-HTK03121/¹⁷⁷Lu-PSMA-617= 21.7
¹⁷⁷Lu-HTK03123/¹⁷⁷Lu-PSMA-617= 14.8

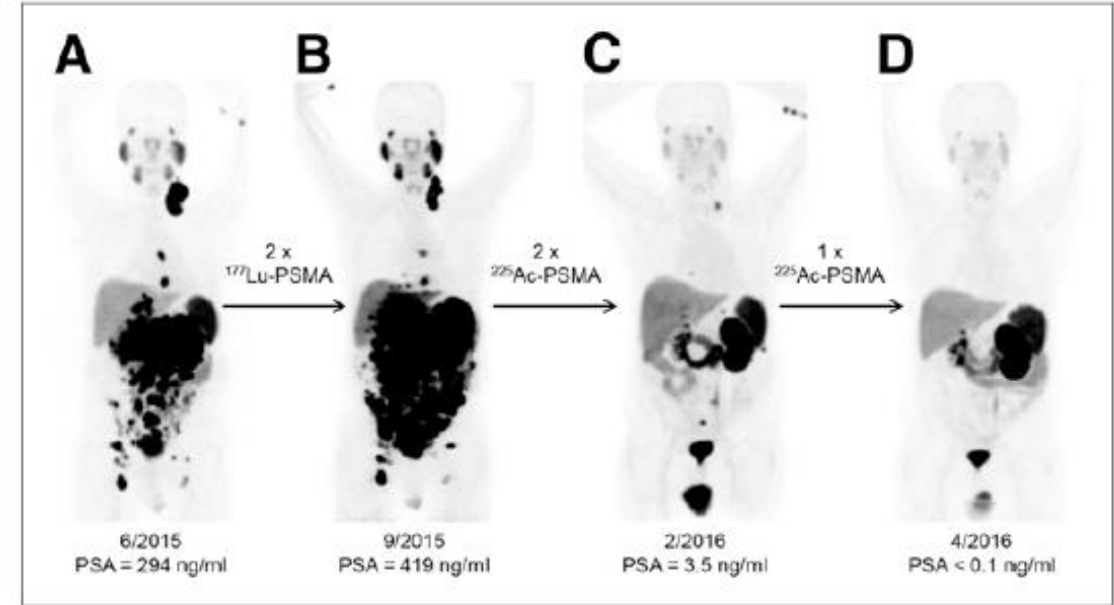
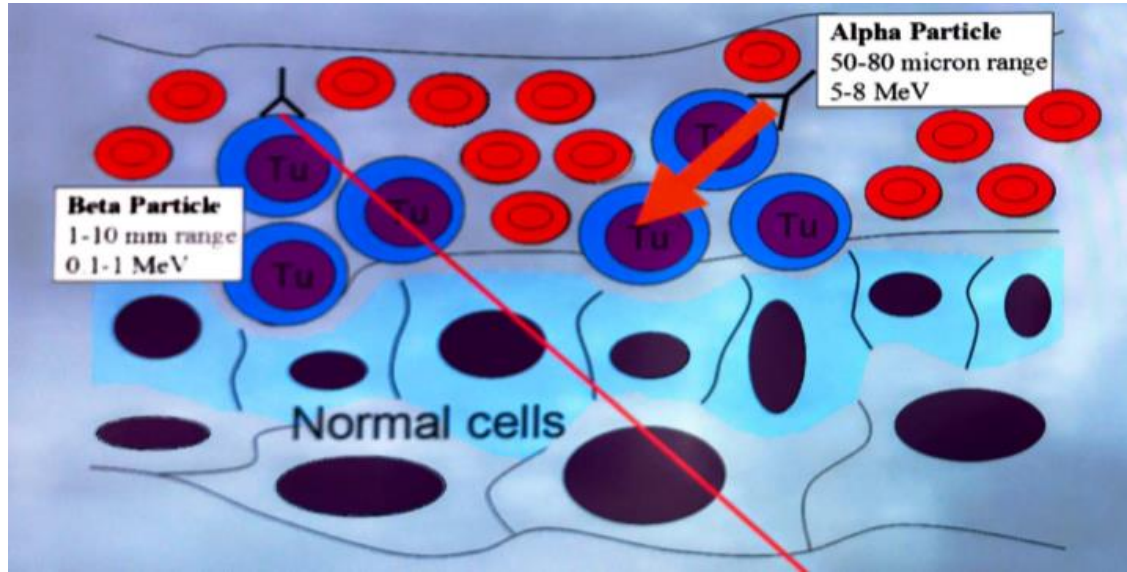


OP-020 A Sarcophagine Containing PSMA Ligand for Targeting Prostate Cancer with 64/67Cu, J. M. Kelly

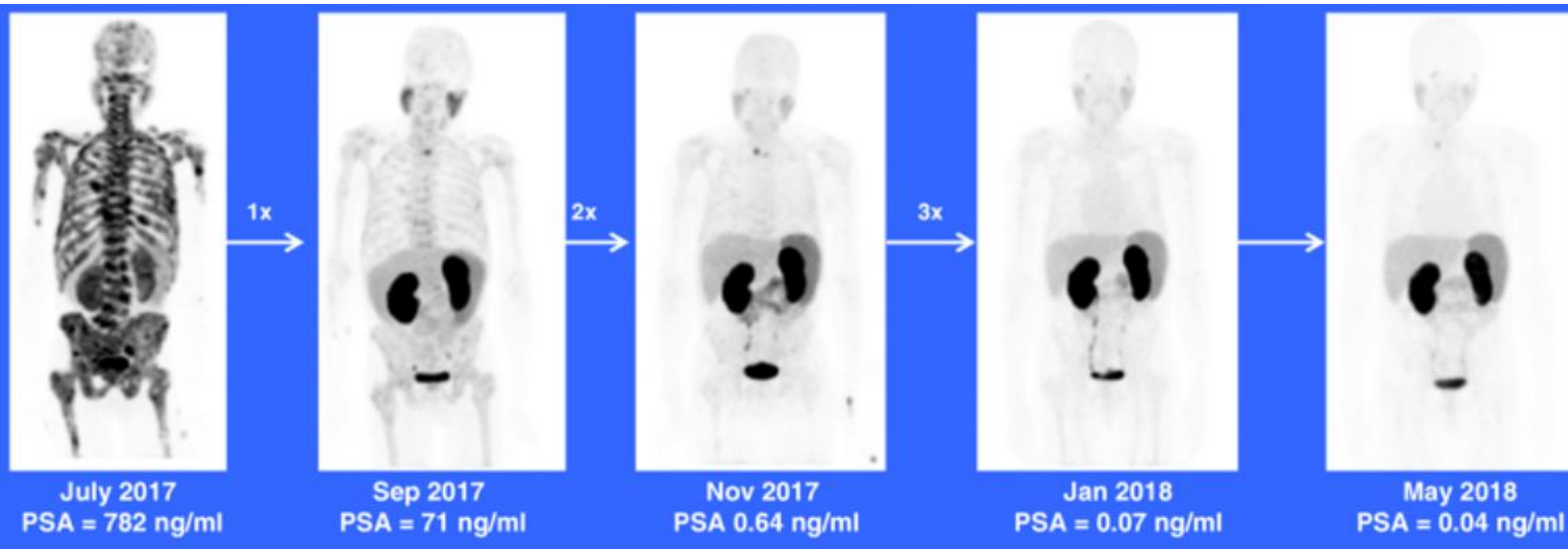
A.M. Ruigrok, *Pharmaceutics* 2019

OP-018 Novel ¹⁷⁷Lu-labeled albumin-binder-conjugated PSMA targeting agents with extremely high tumor uptake and superior tumor-to-kidney therapeutic index, H. Kuo

Alpha-thérapie ?



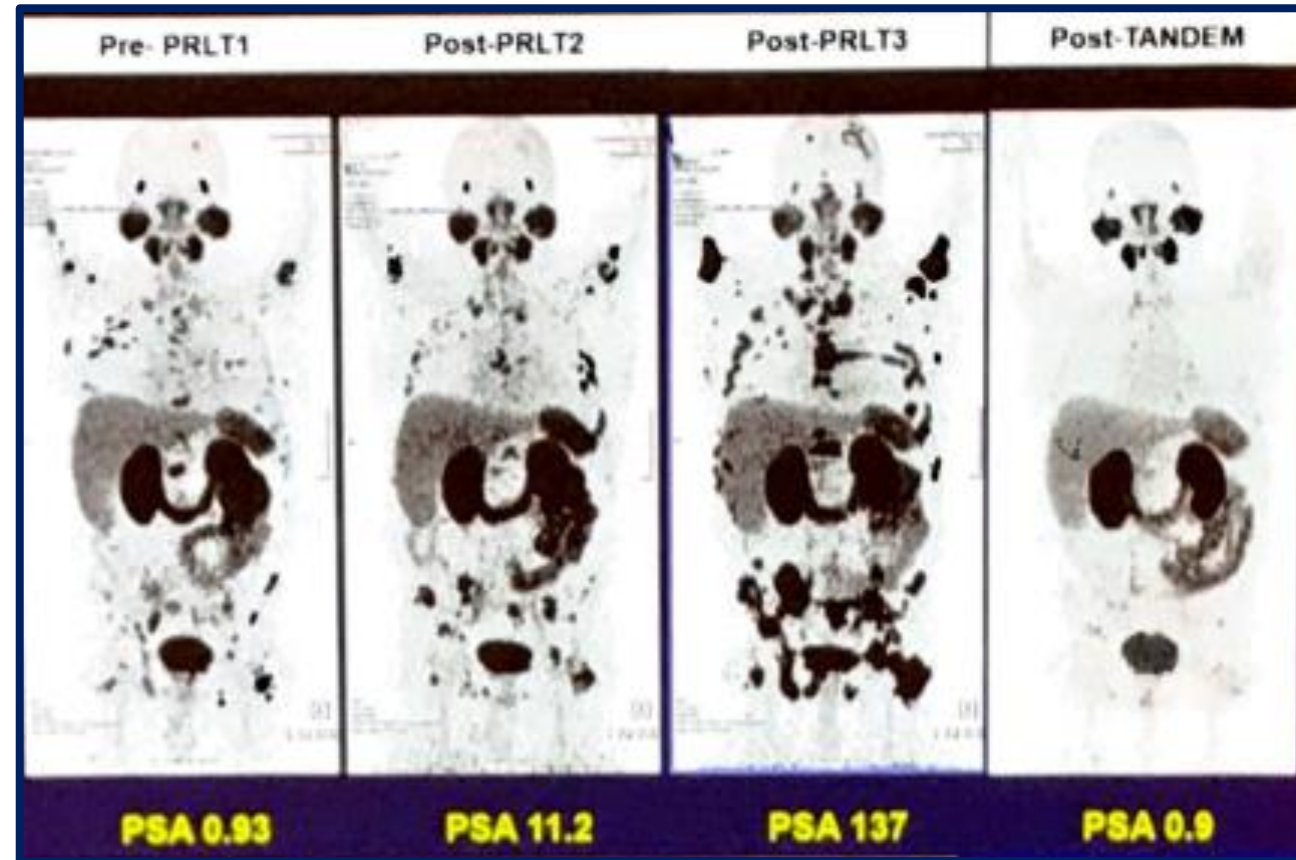
Kratochwil et al, JNM 2016; 57: 1941



A treatment-naïve patient with extensive bone metastasis at primary diagnosis. Complete remission, symptom-free and PSA undetectable after 3 cycles of ^{225}Ac -PSMA-617 on 11-month follow-up.

Sathekge M et al, EJNMMI 2018

Tandem PSMA Radioligand Therapy Using Ac-225 and Lu-177 in advanced Prostate Cancer : Safety and efficacy



- Follow up period : 18m (32% patients died)
- Median PFS : 7,2m, Median OS : not reached
- Meilleure efficacité en limitant les effets indésirables
- Patients réfractaires au traitement par 177Lu-PSMA

Réponse après 4,5GBq 177Lu-PSMA + 5MBq 225Ac-PSMA chez un patient de 58 ans (Gleason 9, hormono, chémo et 177Lu réfractaire)

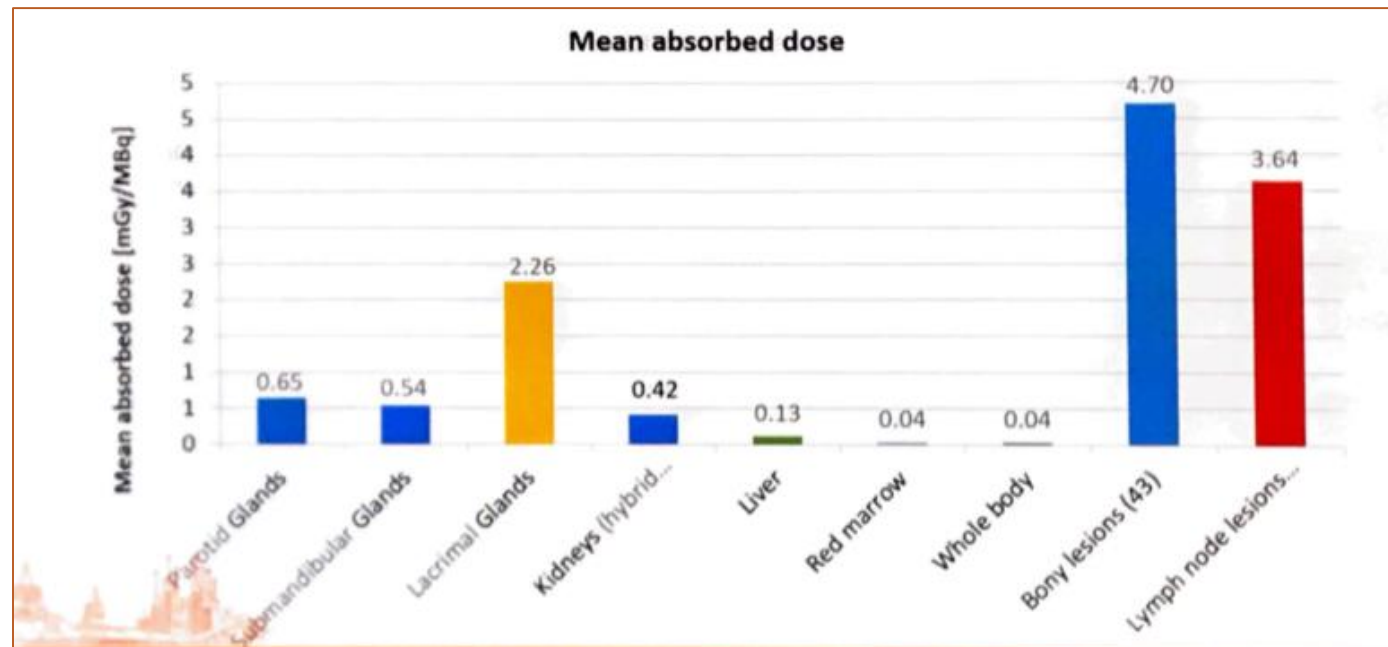
Toxicité et dosimétrie

¹⁷⁷Lu PSMA-617 in advanced castration resistant prostate cancer patients: dosimetry and preliminary evaluation of IRST-IRCCS phase II prospective study (NCT03454750).

M. Sansovini¹, A. Sarnelli¹, S. Severi¹, S. Nicolini¹, E. Tardelli¹, M. Belli¹, F. Matteucci¹, M. Monti¹, F. Foca¹, M. Celli¹, M. Giganti², V. Di Iorio¹, U. De Giorgi¹, G. Paganelli^{1,2}.

¹IRCCS -IRST, Meldola (FC), Italy,

²University of Ferrara, Italy.



- Organes à risque : moelle osseuse, reins et glandes salivaires
- Protection salivaires par des tablettes de polyglutamate folique et rénale par une perfusion de Mannitol à 10%

	N of patients (%)				
	Tot	G1	G2	G3	G4
Renal toxicity	9/43(21.9)	8 (19.5)	0 (0.0)	1 (2.4)	0 (0.0)
Anemia	30/43 (69.7)	20 (48.7)	8 (19.5)	2 (4.8)	0 (0.0)
Thrombocytopenia	2/43 (4.8)	2 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)
Neutropenia	3/43 (6.9)	2 (4.8)	1 (2.4)	0 (0.0)	0 (0.0)
Parotid glands toxicity	3/43 (6.9)	3 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)

Patients can be present more than once, if they have more AE.



Molecular analysis of circulating tumor cells in metastatic castration-resistant Prostate Cancer receiving ^{177}Lu -PSMA-617 Radioligand Therapy

Prognostic biomarkers in men with metastatic castration-resistant prostate cancer receiving ^{177}Lu -PSMA-617

Katharina Kessel¹, Robert Seifert^{1,2,4}, Matthias Weckesser^{1,4}, Wolfgang Roll^{1,4,1}, Schlack^{3,4}, Martin Bögemann^{3,4}, Christof Bernemann^{3*} and Kambiz Rahbar^{1,4*}

Justin Ferdinandus^{1,2} · John Violet³ · Shahneen Sandhu^{4,5} · Rodney J. Hicks^{2,5} · Aravind S. Ravi Kumar^{2,5} · Amir Iravani^{2,5} · Grace Kong^{2,5} · Tim Akhurst^{2,5} · Sue Ping Thang² · Declan G. Murphy^{5,6} · Scott Williams^{3,5} · Michael S. Hofman^{2,5}

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78 results

Improving quality of life in patients with metastatic prostate cancer following one cycle of ^{177}Lu -PSMA-617 radioligand therapy: a pilot study

Verbesserung der Lebensqualität bei Patienten mit metastasiertem Prostatakrebs nach einem Zyklus der ^{177}Lu -PSMA-Radioligandentherapie: eine Pilotstudie

of a score predicting the therapy response of patients with castration resistant **prostate cancer** undergoing radioligand therapy using **prostate**-specific membrane antigen.

Jasch JMM, Lindquist RL, De Santis M, Erber B, Radojewski P, Brenner W,

Authors

Milka Marinova^{1*}, Reza Alamdar^{2*}, Hojjat Ahmadzadehfar^{2,3}, Markus Essler², Ulrike Attenberger¹, Martin Mücke^{4,6}, Rupert Conrad^{5,6}

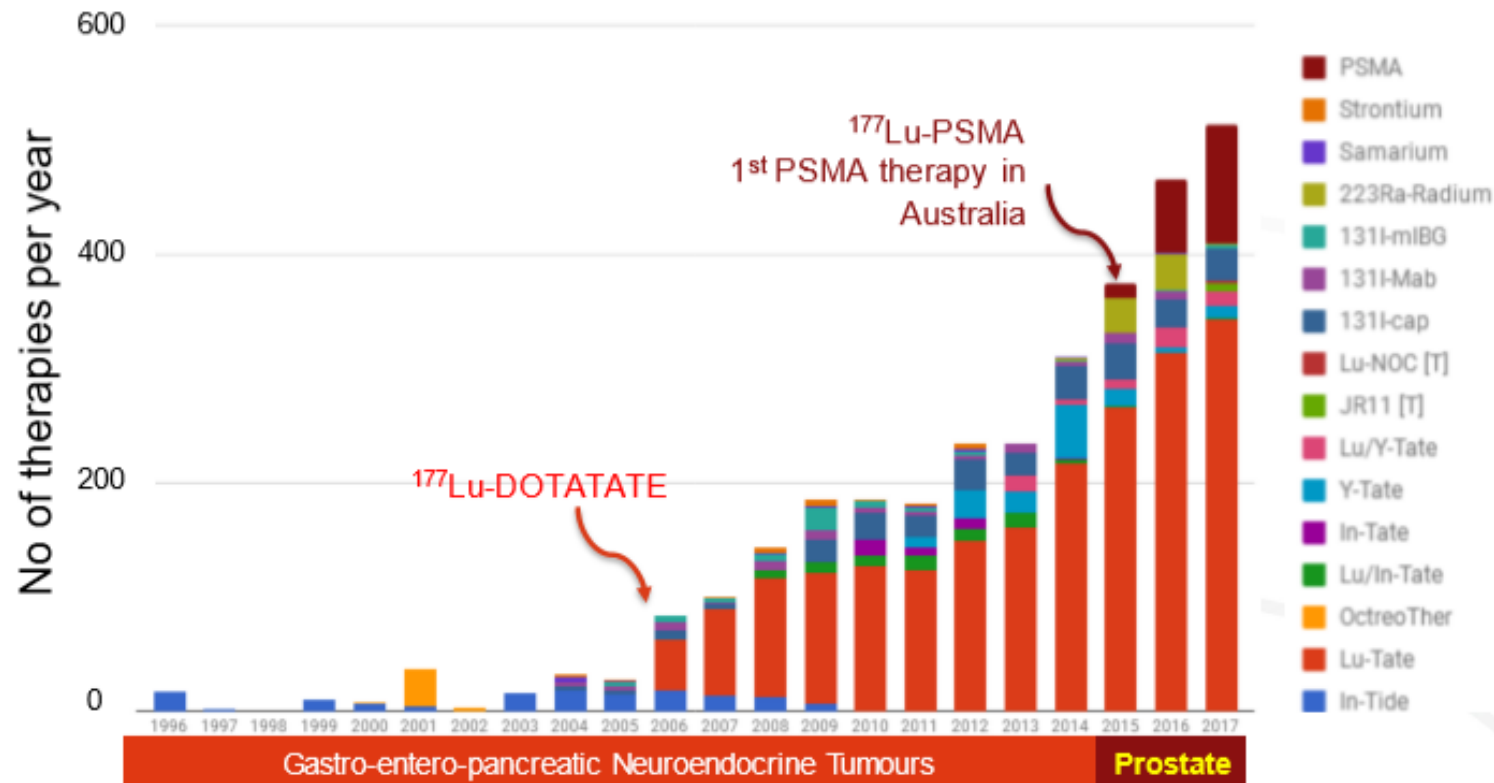
Therapy using ^{177}Lu Lu-PSMA-617 in mCRPC: a pre-VISION single-center analysis

Robert Seifert¹ · Katharina Kessel¹ · Katrin Schlack² · Matthias Weckesser¹ · Martin Bögemann² · Kambiz Rahbar¹



Conclusion : RIV des ligands du PSMA

- Envol des théranostiques depuis une dizaine d'année ...
- Pool de patients +++
- Etude de **phase III VISION**
- Formation nécessaire à la radiothérapie interne vectorisée **dés aujourd'hui !**



Merci pour votre attention & meilleurs vœux pour l'année 2021 !