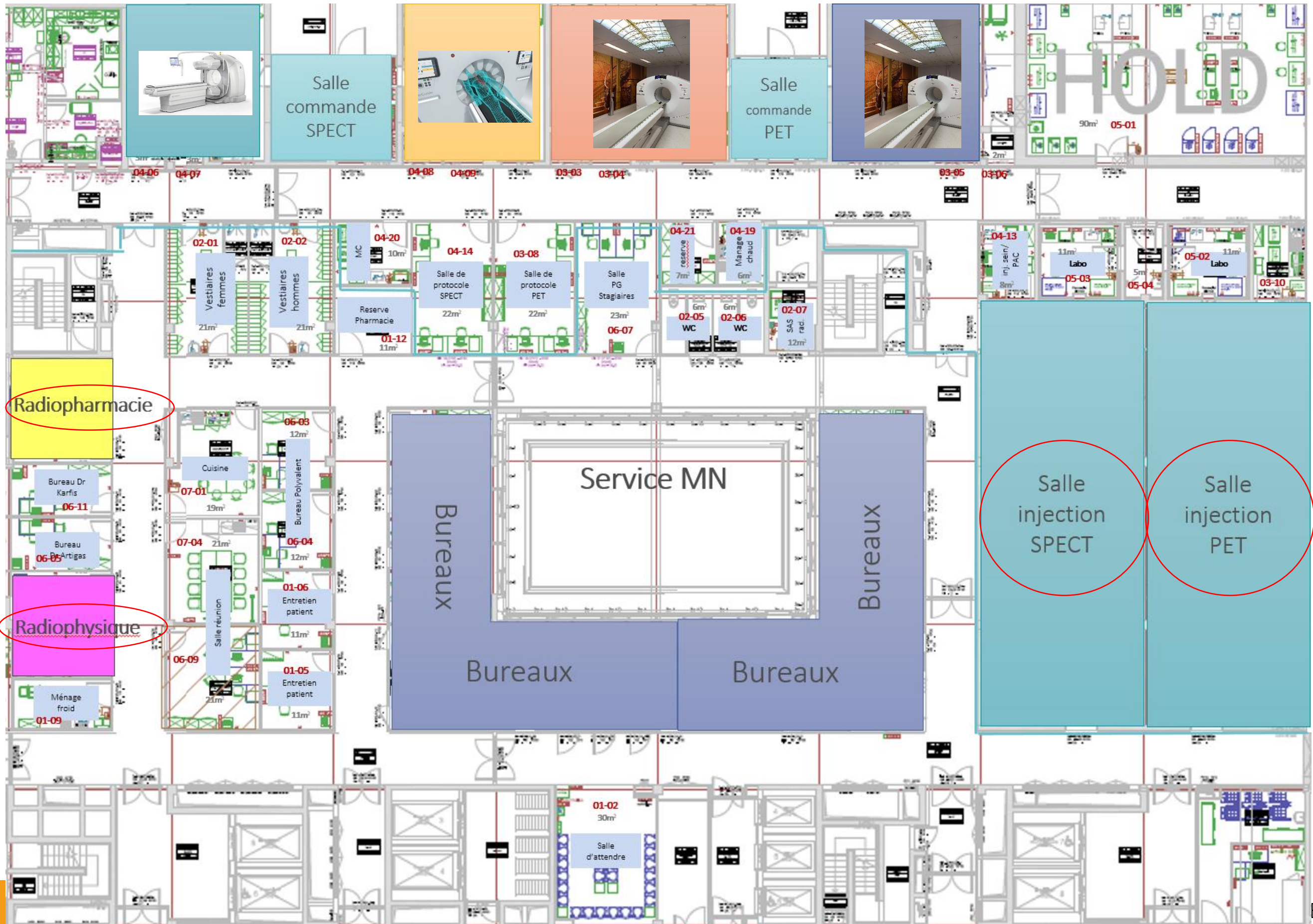


PSMA overview: ^{68}Ga -PSMA, ^{18}F -PSMA, ^{177}Lu -PSMA



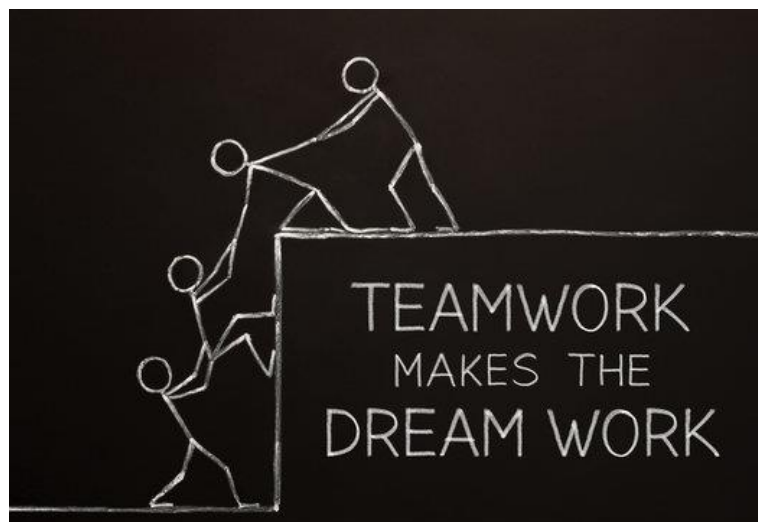
BELNUC TECH DAY
18/11/2023

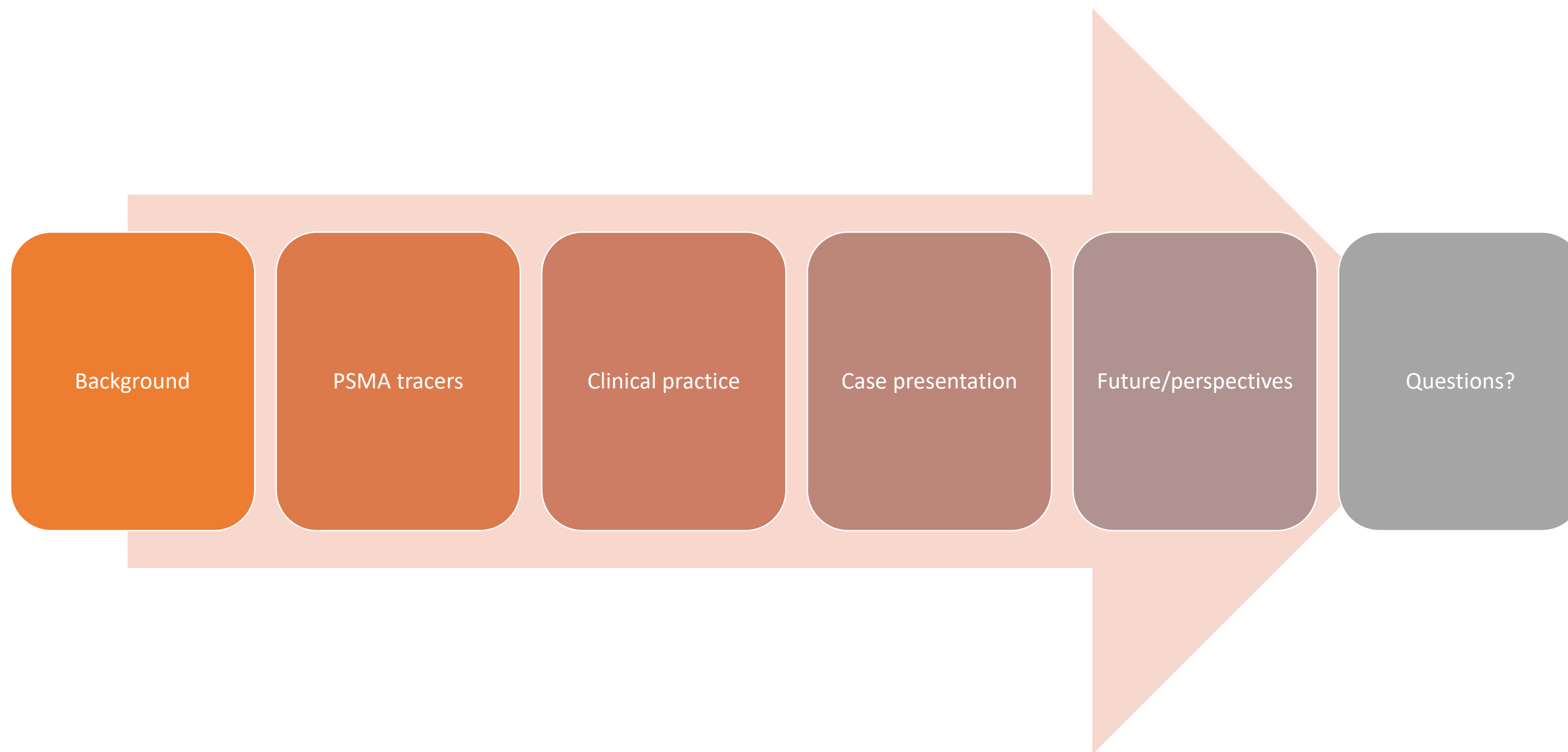


Dpt Nuclear medicine Institut Jules Bordet

Numbers 2023

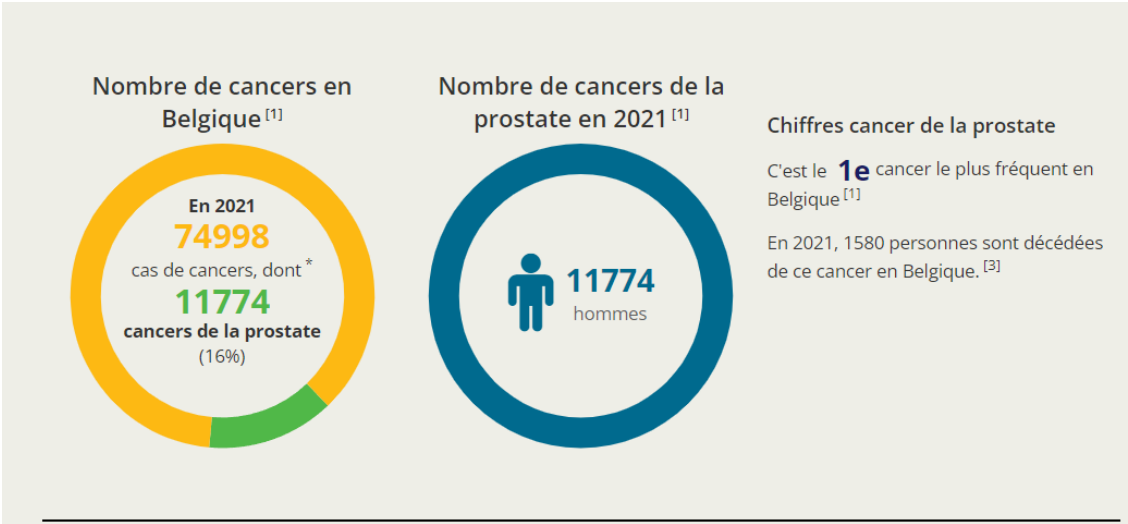
- ^{177}Lu PSMA administrations: 156
- ^{18}F -PSMA PET/CT: 349
- ^{68}Ga -PSMA PET/CT: 256
- Technologists: 13 (Erasme) + 16 (Bordet)





Background: prostate cancer

Incidence



Belgian Cancer Registry 2021, *Belgian Cancer Registry website*,
<<https://www.kankerregister.org/>>

Rank	Cancer	New cases in 2020	% of all cancers
	All cancers*	18,094,716	
1	Breast	2,261,419	12.5
2	Lung	2,206,771	12.2
3	Colorectal**	1,931,590	10.7
4	Prostate	1,414,259	7.8
5	Stomach	1,089,103	6.0
6	Liver	905,677	5.0
7	Cervix uteri	604,127	3.3
8	Oesophagus	604,100	3.3
9	Thyroid	586,202	3.2
10	Bladder	573,278	3.2

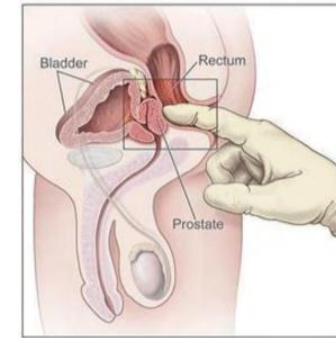
Worldwide Cancer Data 2020, *World Cancer Research Fund International website*, <<https://www.wcrf.org/cancer-trends/worldwide-cancer-data/>>



Background: prostate cancer

Diagnosis

- Clinical exam
- PSA level
- Systematic prostate biopsy
- MRI with PIRADS score +/- targeted biopsy
- Gleason score
- ISUP grading system

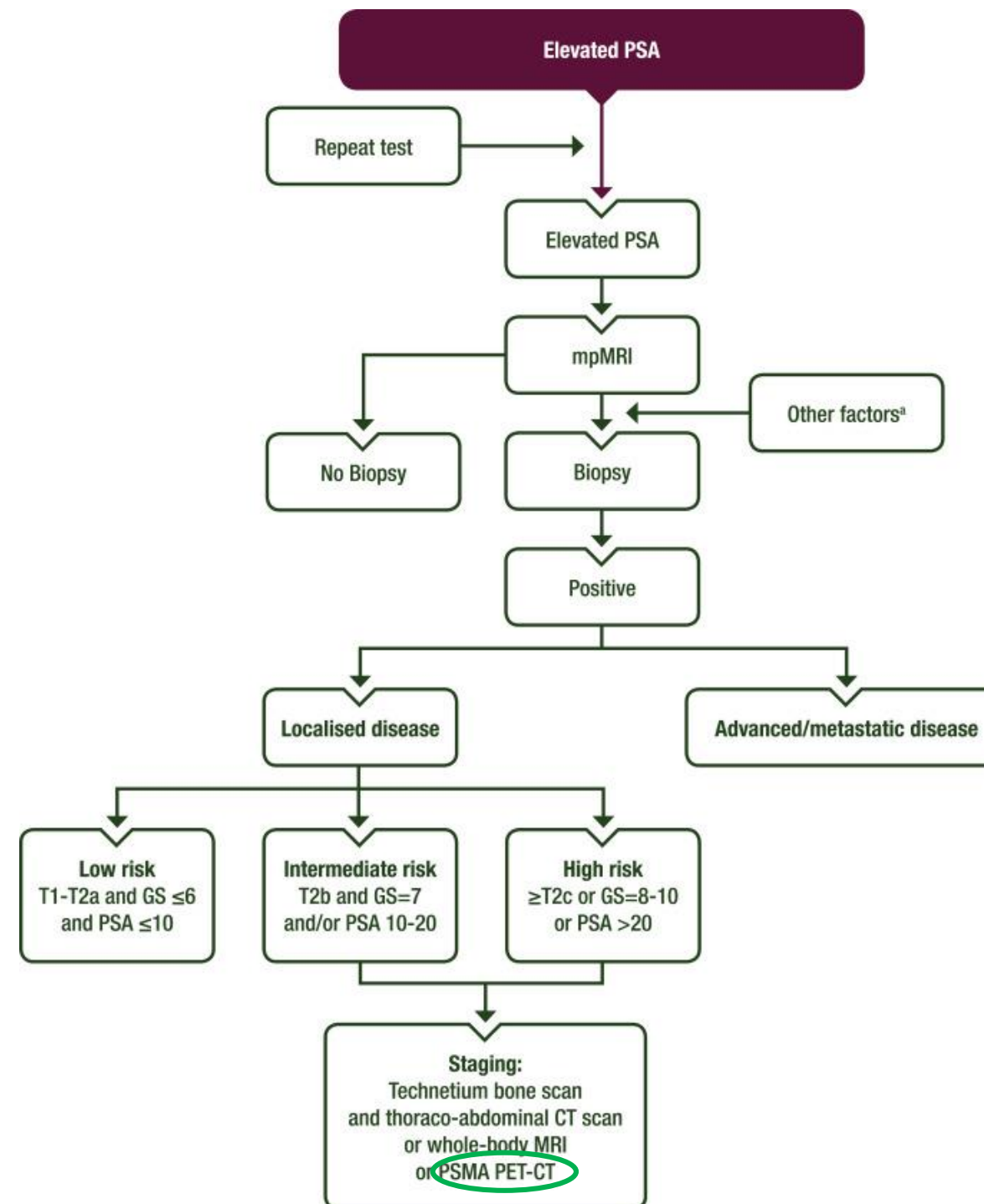


Gleason Score	Grade Group	Characteristics
6	Grade Group 1	• Less aggressive • Very slow growing • Low risk
3 + 4 = 7	Grade Group 2	• Slightly aggressive • Slow growing • Low to Intermediate risk
4 + 3 = 7	Grade Group 3	• Moderately aggressive • Fast growing • Intermediate to High risk
8	Grade Group 4	• Aggressive • Rapidly growing • High risk
9-10	Grade Group 5	• Highly aggressive • Rapidly growing • High risk



Background: prostate cancer

Staging



Parker C, Castro E, Fizazi K, Heidenreich A, Ost P, Procopio G, Tombal B, Gillessen S; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020 Sep;31(9):1119-1134. doi: 10.1016/j.annonc.2020.06.011. Epub 2020 Jun 25. PMID: 32593798.



Background: prostate cancer

Treatments

- Surgery (Radical Prostatectomy +/- pelvic lymphadenectomy)
- Brachytherapy/(radical) radiotherapy
- Androgen Deprivation Therapy (ADT)
- Androgen Receptor Pathway inhibitors (ARPIs)
- Chemotherapies, taxane-based
- ^{223}Ra : symptomatic mCRPC without visceral metastases

Table 1. Stage-matched therapeutic strategies		
Localised disease	Low risk	Active surveillance Brachytherapy RP
	Intermediate risk	Radical RT RP Radical RT ± neoadjuvant ADT Brachytherapy
	High risk	Active surveillance Long-term ADT + radical RT ± neoadjuvant docetaxel RP + pelvic lymphadenectomy
Locally advanced disease		Neoadjuvant ADT + radical RT + adjuvant ADT ± neoadjuvant docetaxel RP + pelvic lymphadenectomy
MO CRPC	High risk	ADT + apalutamide ADT + darolutamide ADT + enzalutamide
Metastatic disease	Hormone-naïve	ADT + abiraterone ADT + docetaxel ADT + enzalutamide ADT + apalutamide RT for low volume ADT alone for frail patients who cannot tolerate the above treatments
	Castration-resistant (first line)	Bone health agent Abiraterone Docetaxel Enzalutamide ^{223}Ra for patients unfit for above treatments (and bone-only metastases)
	Second line or post-docetaxel	Abiraterone Cabazitaxel Enzalutamide ^{223}Ra

^{223}Ra , radium-223; ADT, androgen deprivation therapy; MO CRPC, non-metastatic castration-resistant prostate cancer; RP, radical prostatectomy; RT, radiotherapy.

Parker C, Castro E, Fizazi K, Heidenreich A, Ost P, Procopio G, Tombal B, Gillessen S; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020 Sep;31(9):1119-1134. doi: 10.1016/j.annonc.2020.06.011. Epub 2020 Jun 25. PMID: 32593798.



Background: prostate cancer

Treatments



The NEW ENGLAND JOURNAL of MEDICINE

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*

ABSTRACT

Addition of ¹⁷⁷Lu-PSMA-617 to standard of care in patients with mCRPC and progressive to 1/more ARPIs and 1 or 2 taxanes:

- Survival
- Time to symptomatic skeletal events
- Time to worsening of QoL and pain
- Time to biochemical progression
- Toxic effects of grade 3 or lower



Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer. N Engl J Med. 2021;385(12): 1091-1103.



Background: prostate cancer

Treatments



ESMO GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

Search for Abstracts, G

ESMO > Guidelines > Guidelines by topic > Genitourinary Cancers > Prostate Cancer

eUpdate – Prostate Cancer Treatment Recommendations

Updated treatment recommendations for prostate cancer from the ESMO Clinical Practice Guideline considering treatment intensification and use of novel systemic agents

Published online: 21 March 2023

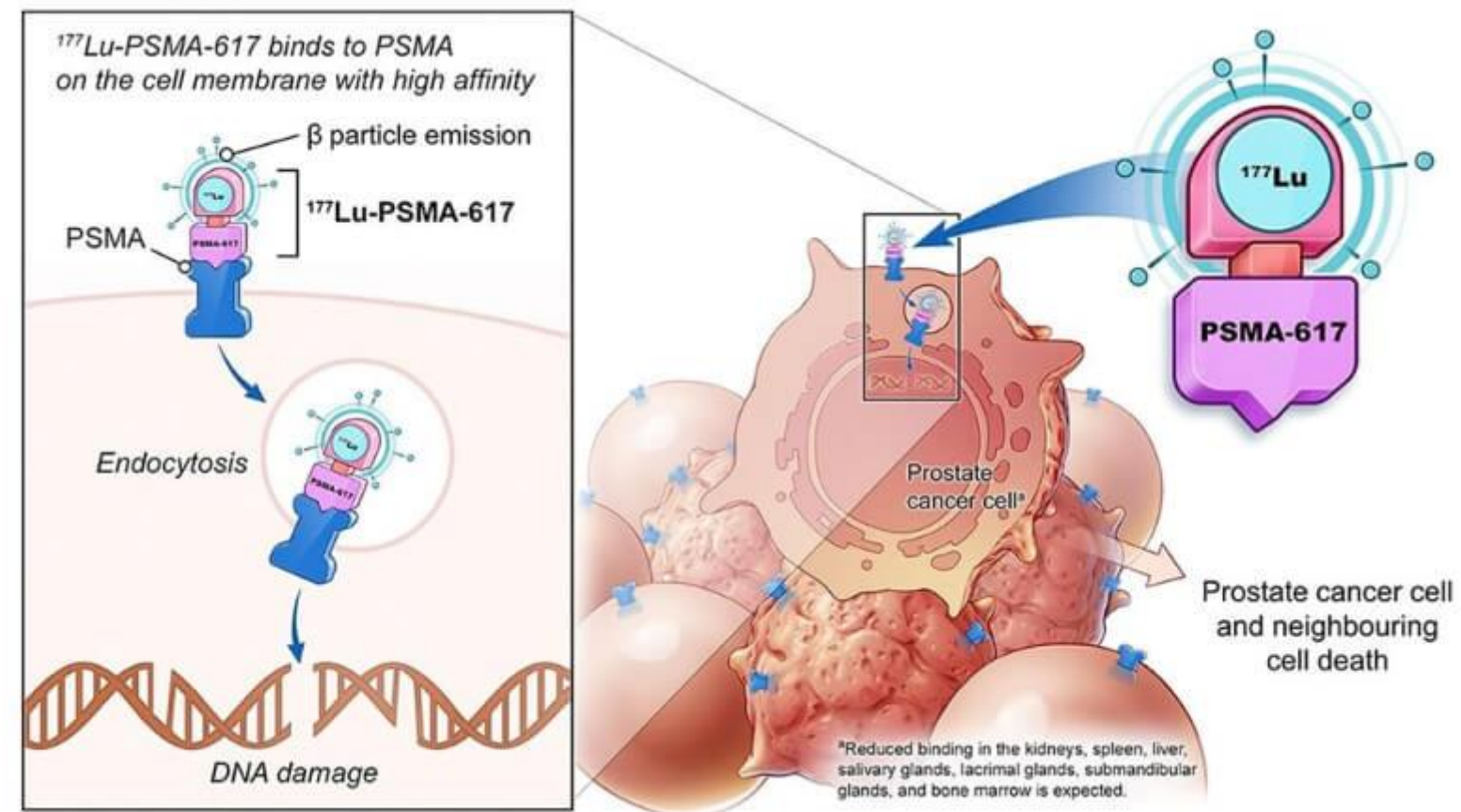
K. Fizazi & S. Giilleisen, et al., on behalf of the ESMO Guidelines Committee

- Abiraterone acetate with prednisone improved MFS and OS for very-high-risk localised prostate cancer undergoing RT and ADT.
- Combining ADT with docetaxel–abiraterone–prednisone in men with de novo mHSPC improved both rPFS and OS versus ADT–docetaxel.
- Combining ADT with docetaxel and darolutamide in men with mHSPC improved OS versus ADT–docetaxel.
- Olaparib improved OS in men with mCRPC and BRCA alterations post-novel androgen receptor axis inhibitor.
- Cabazitaxel in men with mCRPC post-novel androgen receptor axis inhibitor and docetaxel improved both rPFS and OS.
- **¹⁷⁷Lu-PSMA-617 in men with mCRPC post-novel androgen receptor axis inhibitor and taxanes improved both rPFS and OS.**



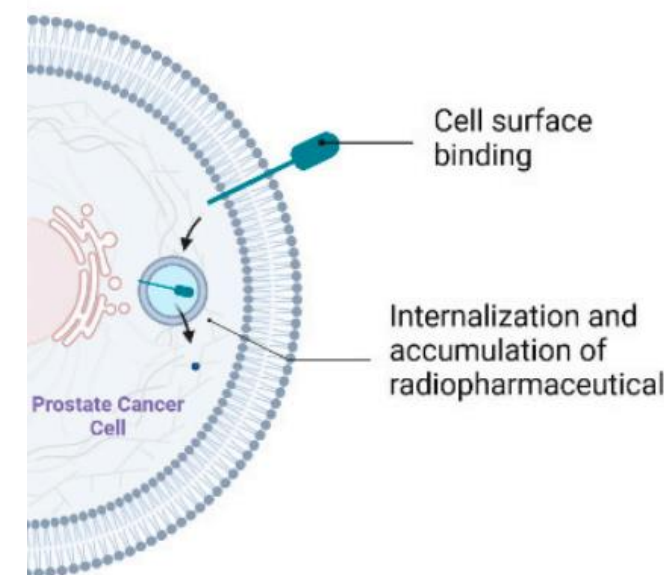
Background: prostate cancer

Treatments



PSMA tracers

- PSMA = transmembrane glycoprotein
- PSMA tracers = small molecules that bind with high affinity to the active extracellular domain of the PSMA protein
- Initially studied in neuronal tissue
- Highly expressed in PCa cells with an accumulation within the cells



PSMA

^{68}Ga
 ^{18}F
 ^{177}Lu
 $^{99\text{m}}\text{Tc}$

Hofman MS, Hicks RJ, Maurer T, Eiber M. Prostate-specific Membrane Antigen PET: Clinical Utility in Prostate Cancer, Normal Patterns, Pearls, and Pitfalls. Radiographics. 2018 Jan-Feb;38(1):200-217. doi: 10.1148/rg.2018170108. PMID: 29320333.

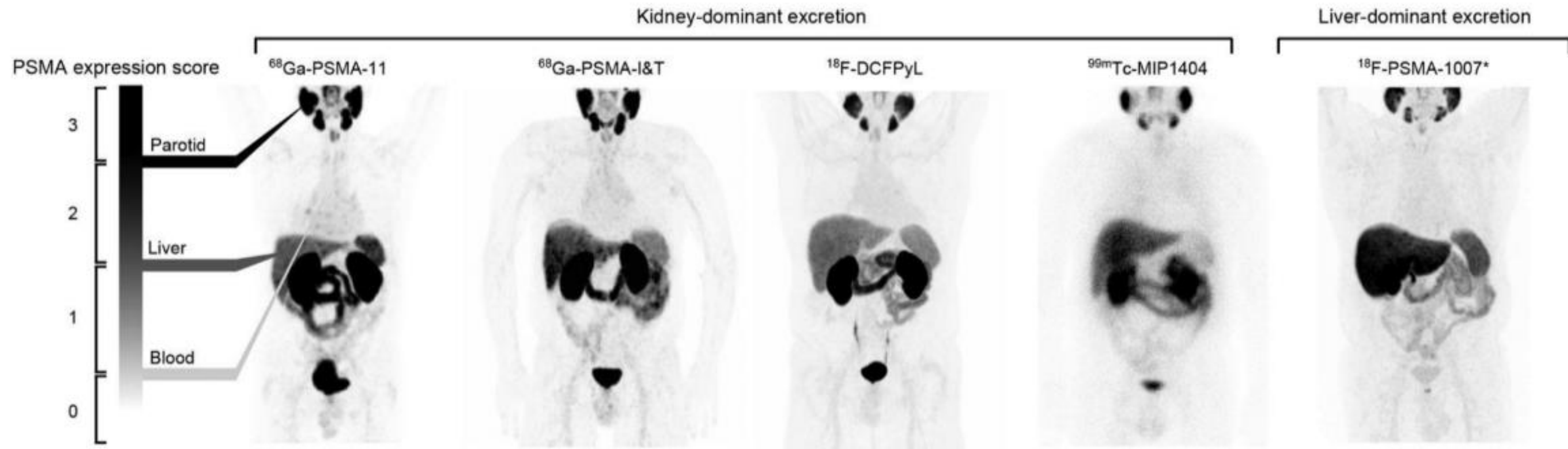
PSMA tracers

- PSMA-11 = HBED-PSMA (^{68}Ga) (Heidelberg, 2012)
- DCFPyI (^{18}F)
- PSMA-1007 (^{18}F)
- DCFBC (^{18}F)
- JK-PSMA-7 (^{18}F)
- rhPSMA-7.3 (^{18}F , ^{177}Lu)
- PSMA-I&T (^{68}Ga , ^{177}Lu , ^{225}Ac)
- PSMA-617 (^{68}Ga , ^{177}Lu , ^{225}Ac)



Hofman MS, Hicks RJ, Maurer T, Eiber M. Prostate-specific Membrane Antigen PET: Clinical Utility in Prostate Cancer, Normal Patterns, Pearls, and Pitfalls. Radiographics. 2018 Jan-Feb;38(1):200-217. doi: 10.1148/rg.2018170108. PMID: 29320333.

PSMA tracers



M. Eiber et al., 2018

Clinical practice

PSMA PET/CT acquisition protocol

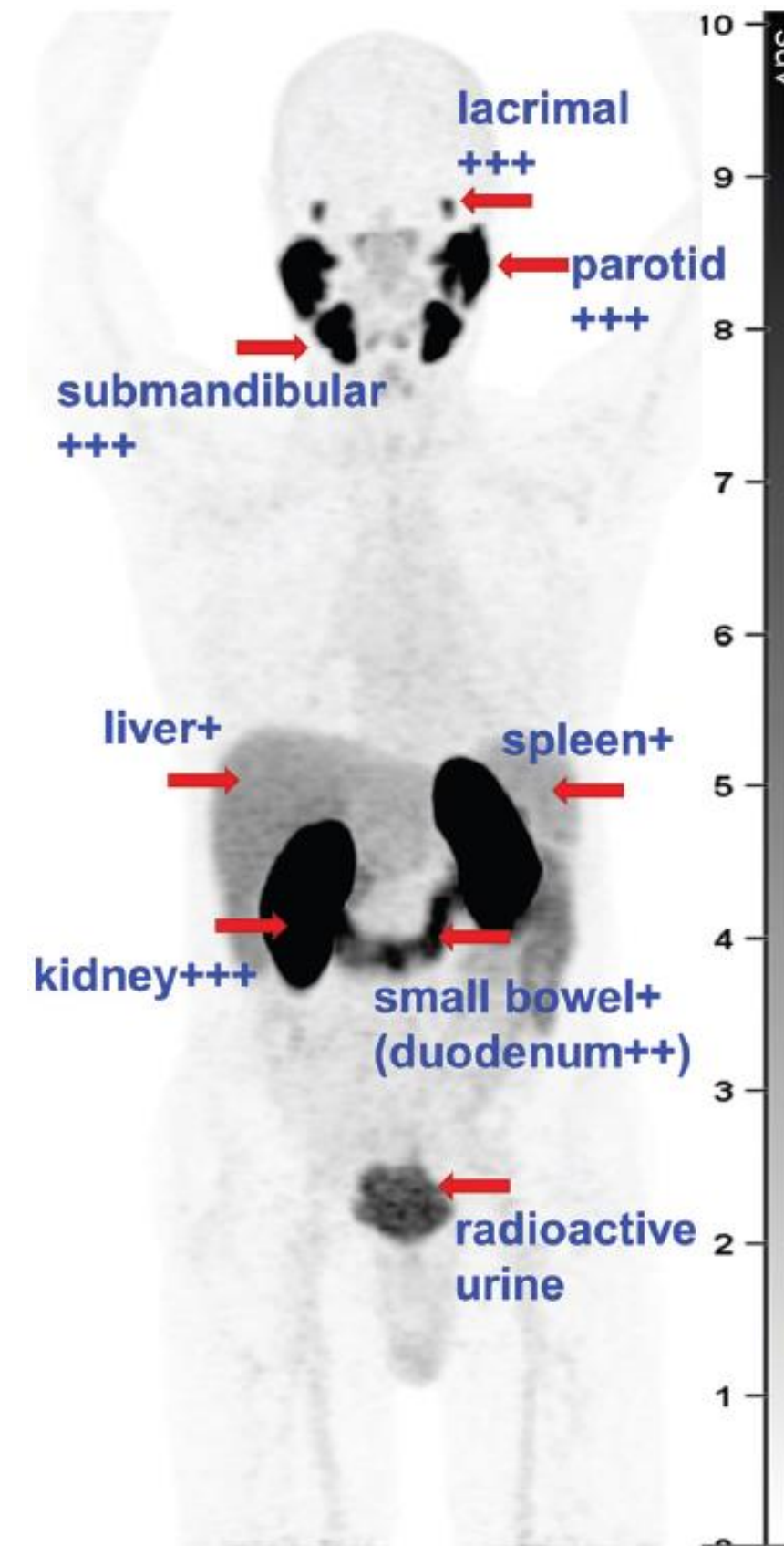
- Patients do not need to fast and may take all their medications
- Administration of the PSMA tracer
- Furosemide administration?
- Imaging 45-75 minutes post injection
- Voiding before imaging
- Patient positioning: supine with both arms elevated above the head, as tolerated by the patient
- Whole-body PET: From the vertex/base of the skull to midthigh
- Pelvis -> head direction
- 1-4 min per bed position



Clinical practice

Physiological uptake PSMA tracers

- Salivary glands
- Lacrimal glands
- Parasympathetic ganglia
- Kidneys & urinary bladder
- Liver (& gall bladder)
- Spleen
- Small intestine & colon



Clinical practice

^{177}Lu -PSMA RLT: indications/contraindications



- mCRPC treated with ADP including a novel ARPi + taxane-based chemotherapy
- PSMA expression > liver (or spleen for ^{18}F -PSMA-1007)



Table 1 Relative contra-indications against ^{177}Lu -PSMA-RLT

Relative contra-indication	Comment
Life expectancy < 3 months	Except the main purpose is palliative (treatment of tumor-related symptoms)
ECOG ≥ 3	High radiation burden to caregivers and relatives, while most likely only prolonging suffering but not quality-life-time
Unmanageable urinary incontinence	A urinary catheter alone is no contra-indication; it should eventually be even considered to improve radiation protection
Acute urinary tract obstruction or hydronephrosis	Patients with diagnosed or risk of urinary retention, [$^{99\text{mTc}}$]Tc-MAG3 or -DTPA renal scintigraphy should be considered a baseline exam [83]
Unmanageable psychiatric comorbidities	Patient unable to be isolated on a nuclear medicine therapy unit (if requested by local radiation protection regulations)
Other severe (e.g., cardiovascular) comorbidities	e.g., patient must be able to tolerate increased hydration
Progressive deterioration of organ function/risk of multiorgan failure	e.g., GFR < 30 ml/min, creatinine > twofold ULN, liver enzymes > fivefold ULN
Acute infections	–
Myelosuppression ^a	WBC < 2.5/nl ANC < 1.5/nl PLT < 75/nl

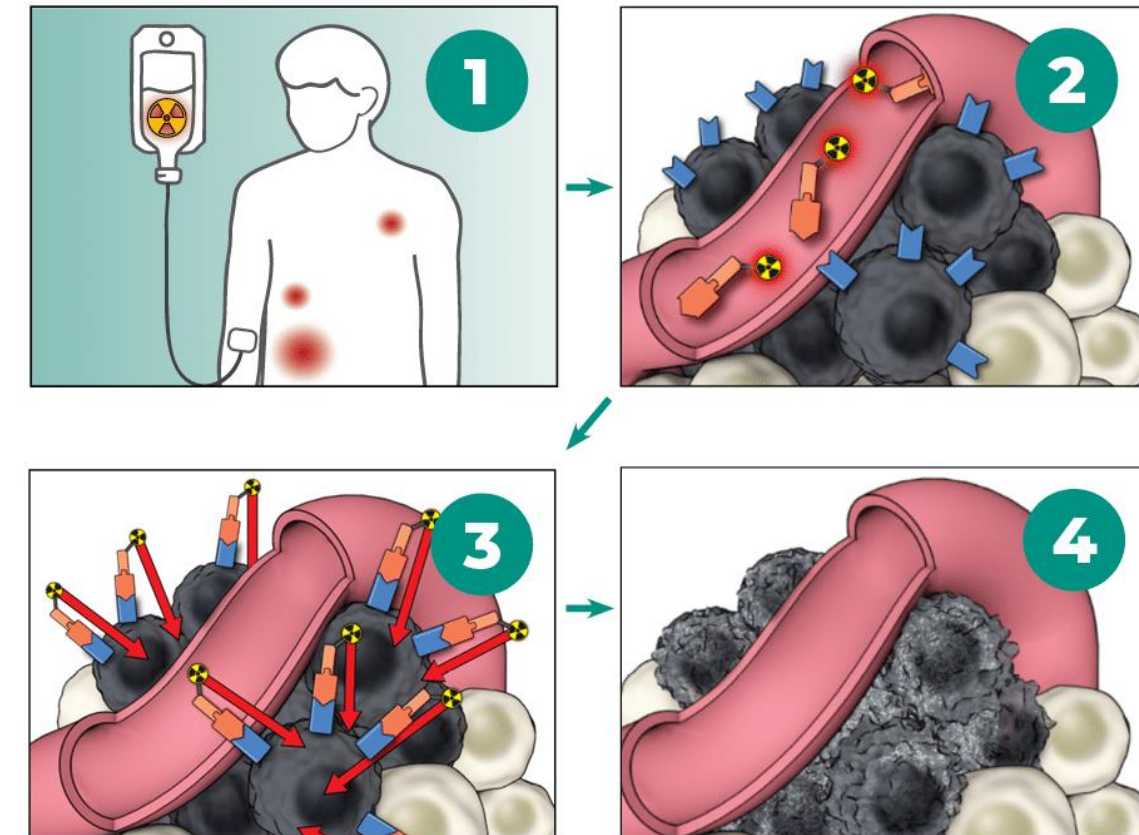
Kratochwil, C., Fendler, W.P., Eiber, M. et al. Joint EANM/SNMMI procedure guideline for the use of ^{177}Lu -labeled PSMA-targeted radioligand-therapy (^{177}Lu -PSMA-RLT). Eur J Nucl Med Mol Imaging 50, 2830–2845 (2023). <https://doi.org/10.1007/s00259-023-06255-8>



Clinical practice

^{177}Lu -PSMA RLT: procedure

- 1) Preparation of the ^{177}Lu -PSMA radiopharmaceutical solution
- 2) Hydration of the patient (no mandatory co-medication)
- 3) Intravenous administration of ^{177}Lu -PSMA-RLT over >30 s
- 4) At least one planar post-therapeutic scan >2 h
- 5) Radioprotection measures



Kratochwil C, Fendler WP, Eiber M, Hofman MS, Emmett L, Calais J, Osborne JR, Iravani A, Koo P, Lindenberg L, Baum RP, Bozkurt MF, Delgado Bolton RC, Ezziddin S, Forrer F, Hicks RJ, Hope TA, Kabasakal L, Konijnenberg M, Kopka K, Lassmann M, Mottaghy FM, Oyen WJG, Rahbar K, Schoder H, Virgolini I, Bodei L, Fanti S, Haberkorn U, Hermann K. Joint EANM/SNMMI procedure guideline for the use of ^{177}Lu -labeled PSMA-targeted radioligand-therapy (^{177}Lu -PSMA-RLT). Eur J Nucl Med Mol Imaging. 2023 Jul;50(9):2830-2845. doi: 10.1007/s00259-023-06255-8. Epub 2023 May 29. PMID: 37246997; PMCID: PMC10317889.

Clinical practice

¹⁷⁷Lu-PSMA RLT: procedure @Bordet



Baseline evaluation

PSMA PET/CT
FDG PET/CT
MAG3 renal scintigraphy
Lab test
Consultation



C1 Lu-PSMA

6-8 weeks

C2 Lu-PSMA

6-8 weeks

C3 Lu-PSMA

6-8 weeks

C4 Lu-PSMA

6-8 weeks

Lab test
PSMA PET/CT
FDG PET/CT
Consultation

Interim evaluation

Lab test
PSMA PET/CT
FDG PET/CT
Consultation

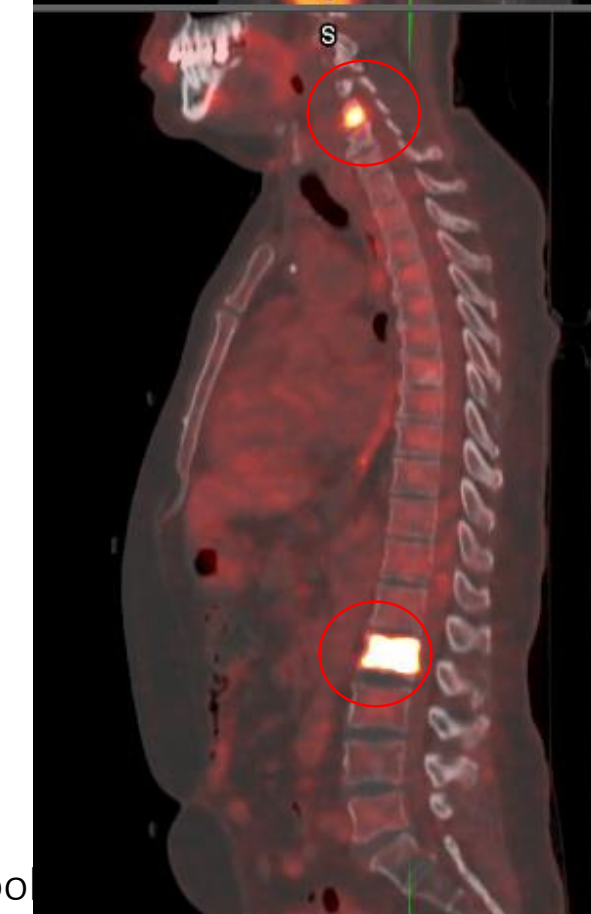
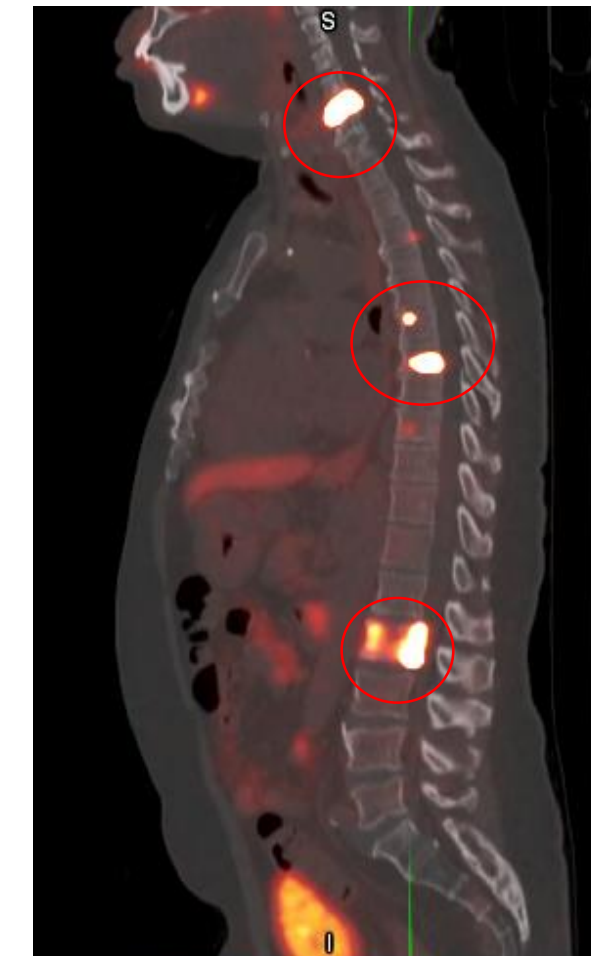
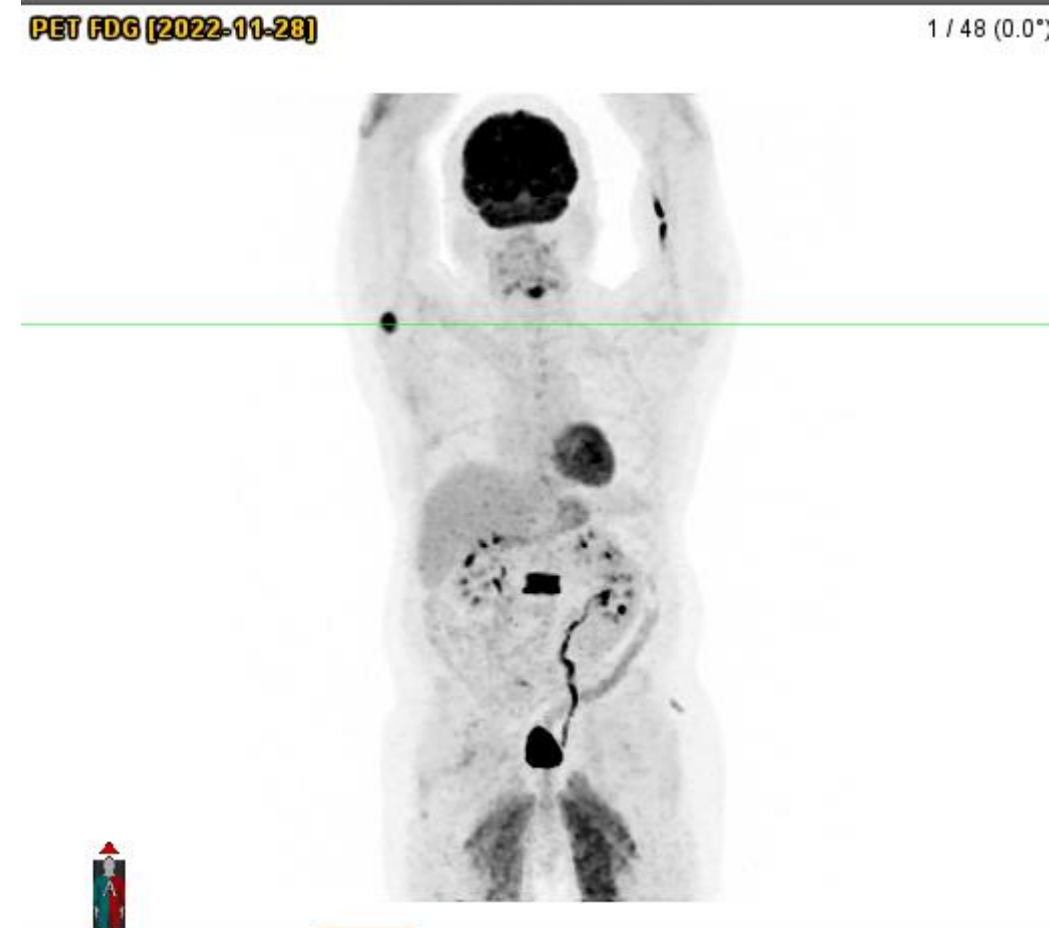
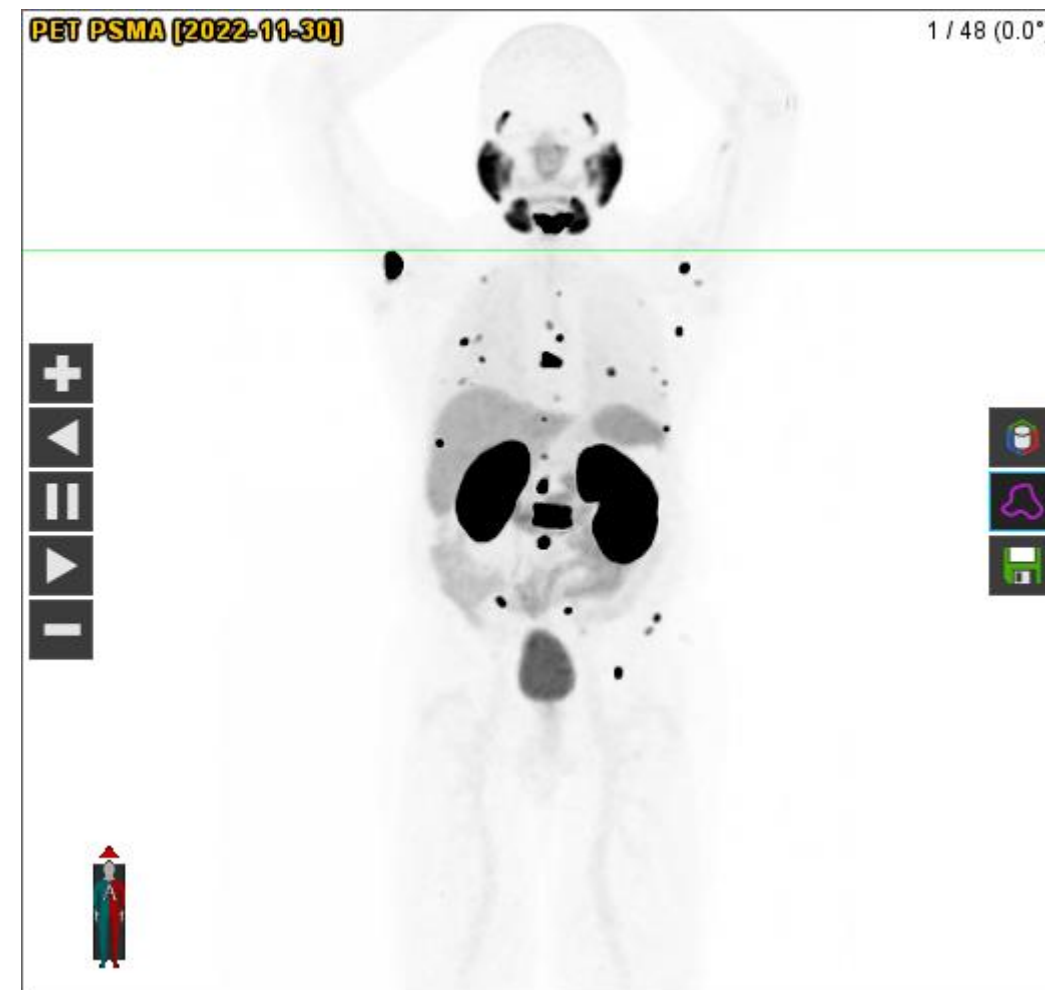
EOT evaluation



Clinical case 1

M, 62Y

- 2018: diagnosis of a Gleason 9 prostate adenocarcinoma with bone and lymph node metastases -> start Decapeptyl + Zytiga + radiotherapy at the prostate level
- 02/2022: progression -> start Taxotere
- 01/2023: progression -> sent to Bordet for Lu-PSMA therapy

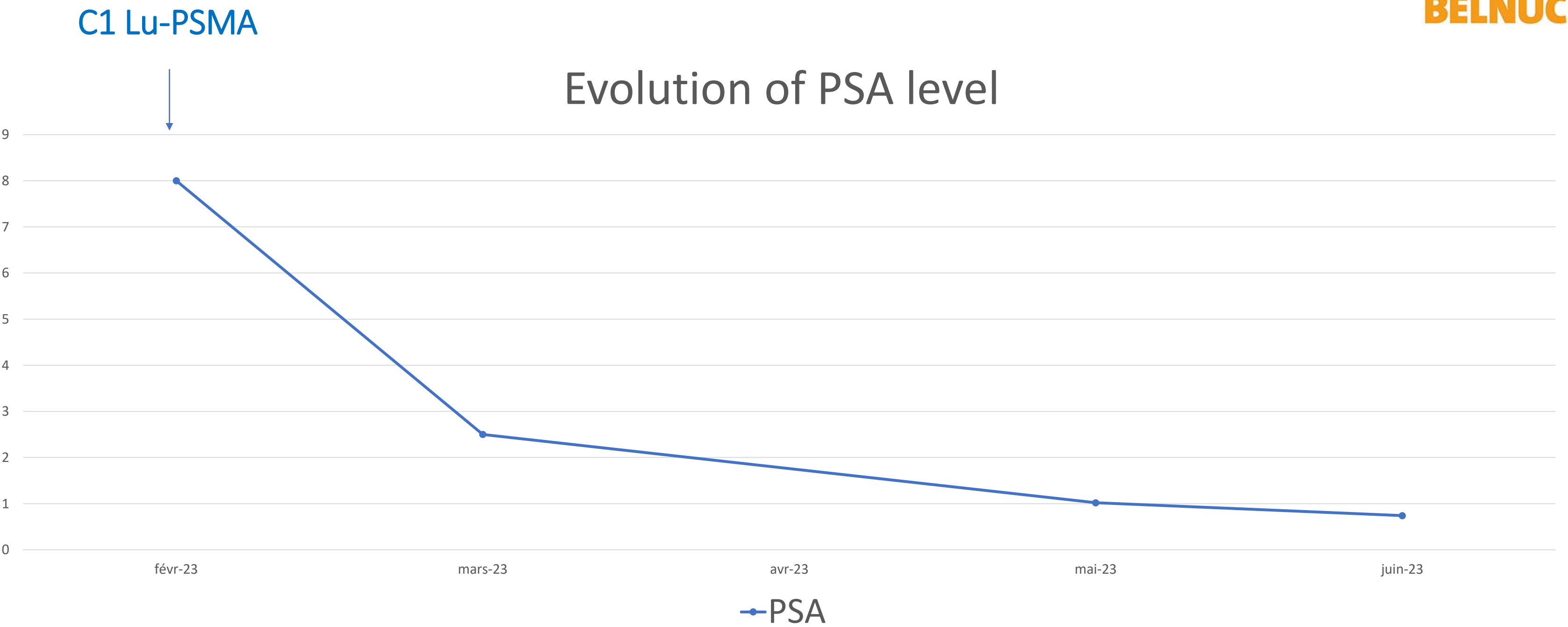


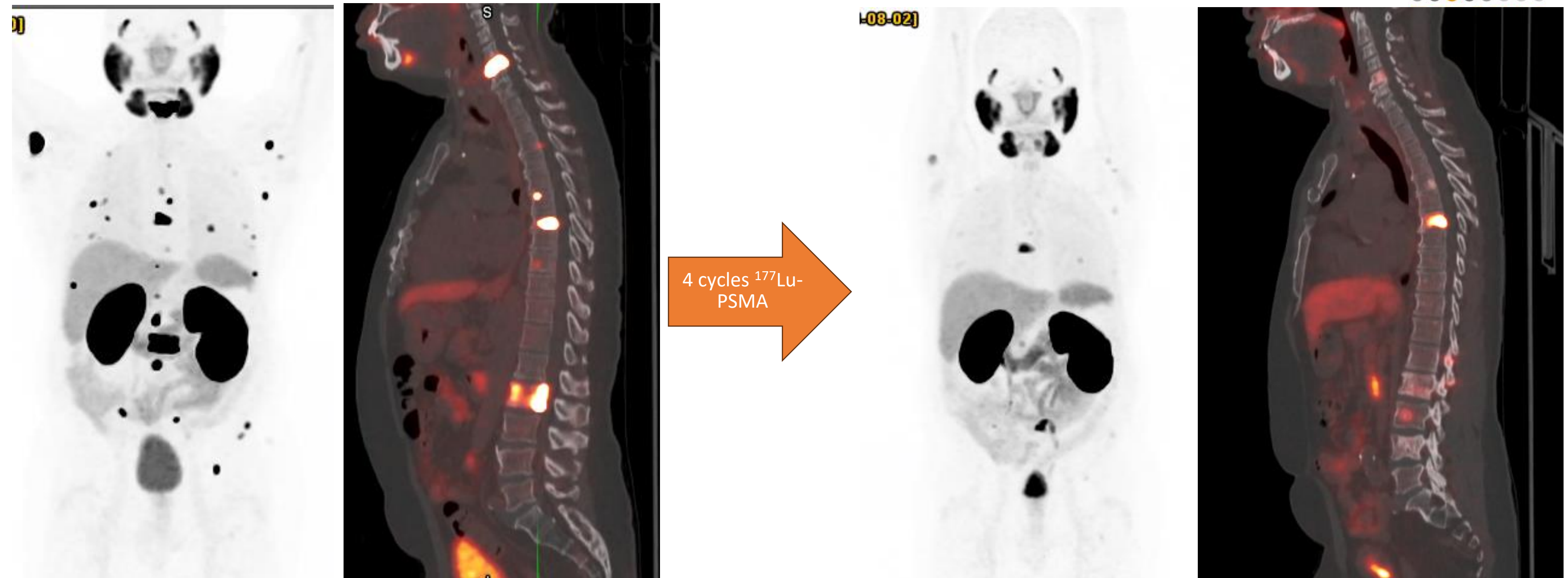
PSMA [2022-11-30]

1

C1 ^{177}Lu -PSMA

Clinical case 1





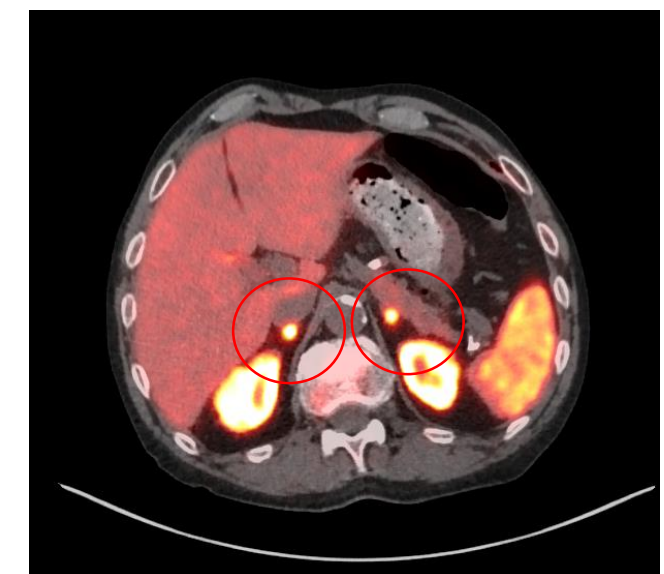
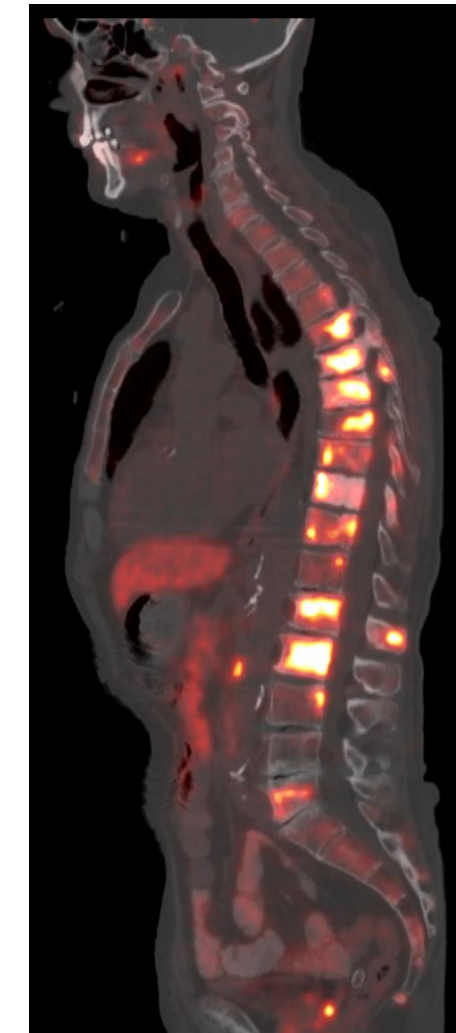
Clinical case 2

M, 80Y

- 2020: diagnosis of a Gleason 9 prostate adenocarcinoma with bone, lymph node and adrenal gland metastases -> start Firmagon
- 04/2021: progression -> start Xtandi
- 11/2021: progression -> start Taxotere
- 04/2022: progression -> start Cabazitaxel
- 08/2022: progression -> sent to Bordet for evaluation of indication for Lu-PSMA



1 / 48 (0.0")



Clinical case 2

M, 80Y



1 / 48 (0.0%)

- Lab test:

HEMATOLOGIE				
Hemoglobine	g/dL	12,6 - 17,4	-	13,8 14,2
Witte bloedcellen	1000/ μ L	4,5 - 11,0	-	7,3 7,0
Trombocyten	1000/ μ L	150 - 400	-	285 296
Nierfunctie				
Ureum	mg/dL	< 49	-	38 44
Creatinine	mg/dL	0,70 - 1,20	-	0,81 0,83
eGFR (CKD-EPI)	mL/min/1,73m ²	> 120	-	84 [1.7] 83 [1.8]
Lever - Pancreas - Hart - Spier				
Bilirubine totaal	mg/dL	0,30 - 1,20	-	1,01 0,78
Bilirubine direct	mg/dL	<= 0,30	-	0,36 0,27
GOT (AST)	U/L	< 40	-	120 96
GPT (ALT)	U/L	< 41	-	127 94
Gamma GT	U/L	8 - 61	-	93 70
Alkalische fosfatase	U/L	40 - 129	-	268 170
LDH	U/L	135 - 225	-	728 514
TUMORMARKERS				
MSH	ug/L	<= 16,3	-	68,3 [1.9] -
MSH herrekend	ug/L	<= 16,3	-	56,3 [1.10] -
PSA totaal	ug/L	< 4,40	-	4,93 4,57

- ¹⁸F-FDG:

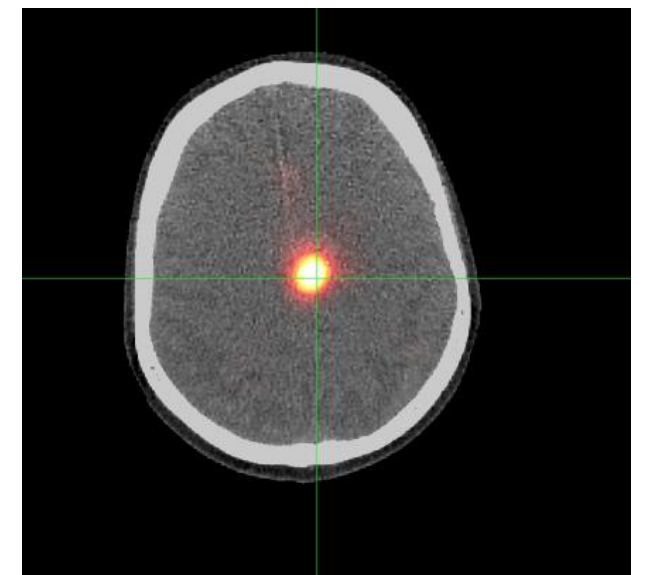
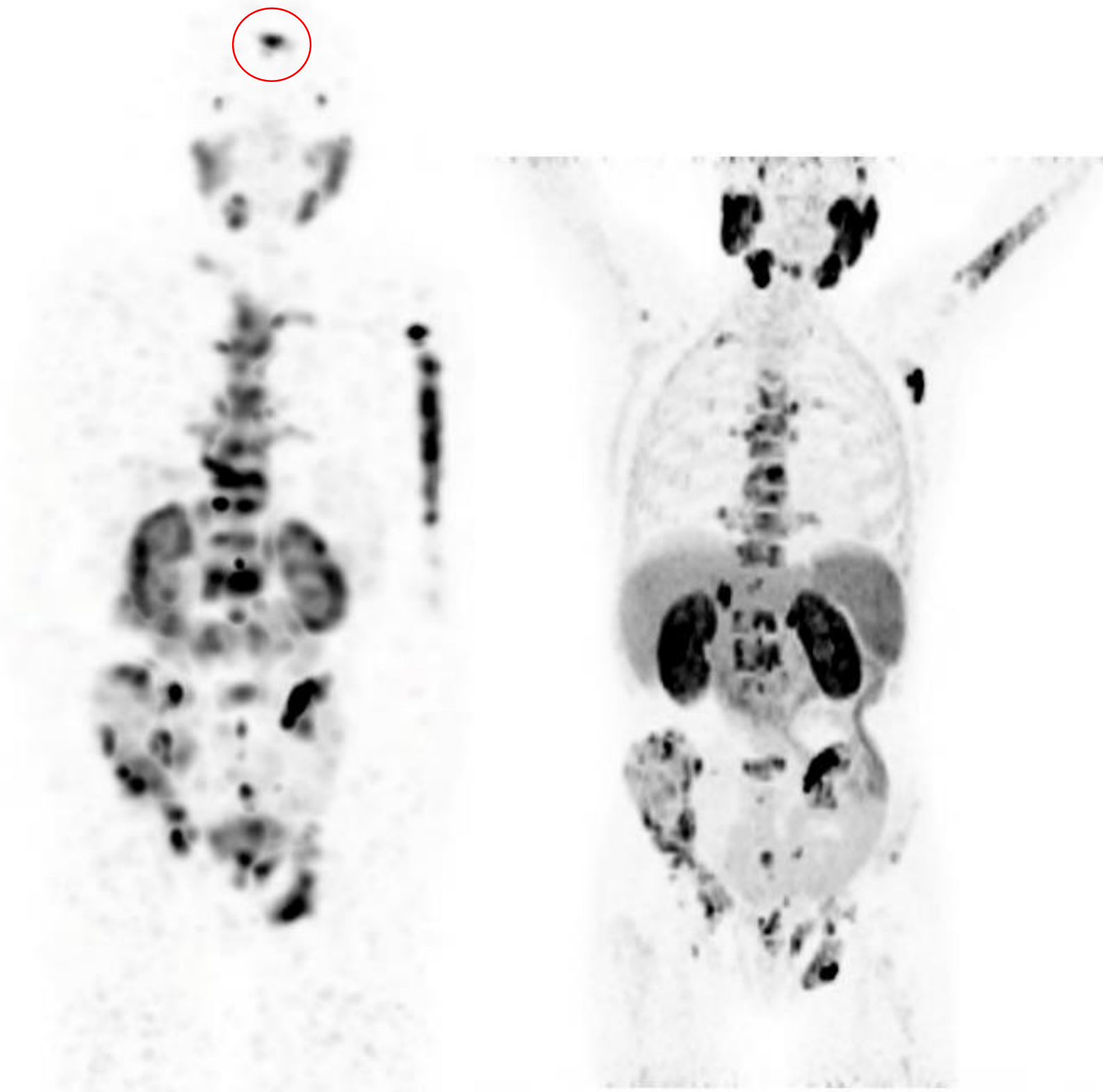


Clinical case 2

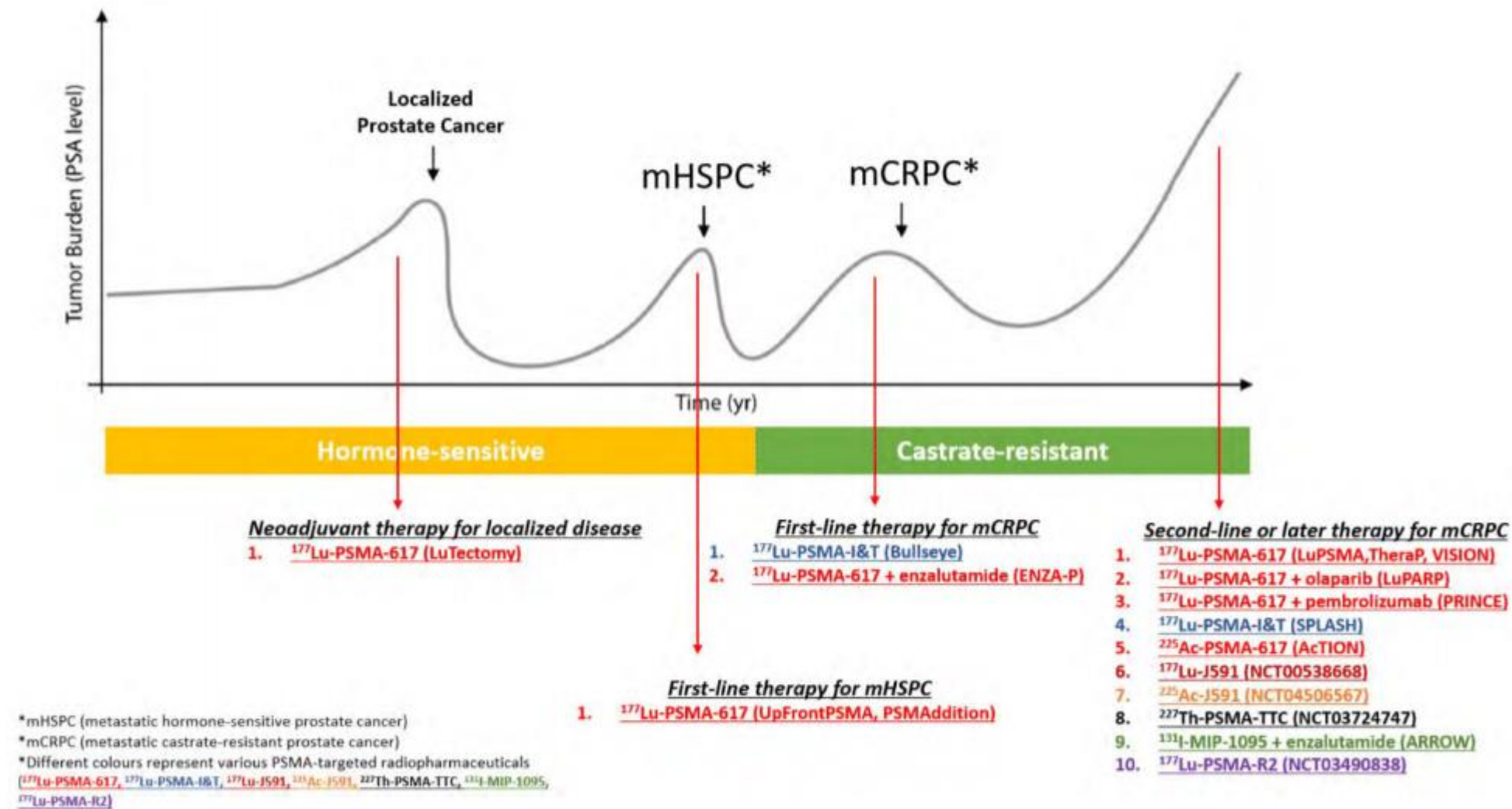
M, 80Y

- 08/2022: C1 Lu-PSMA
- Post treatment scintigraphy:

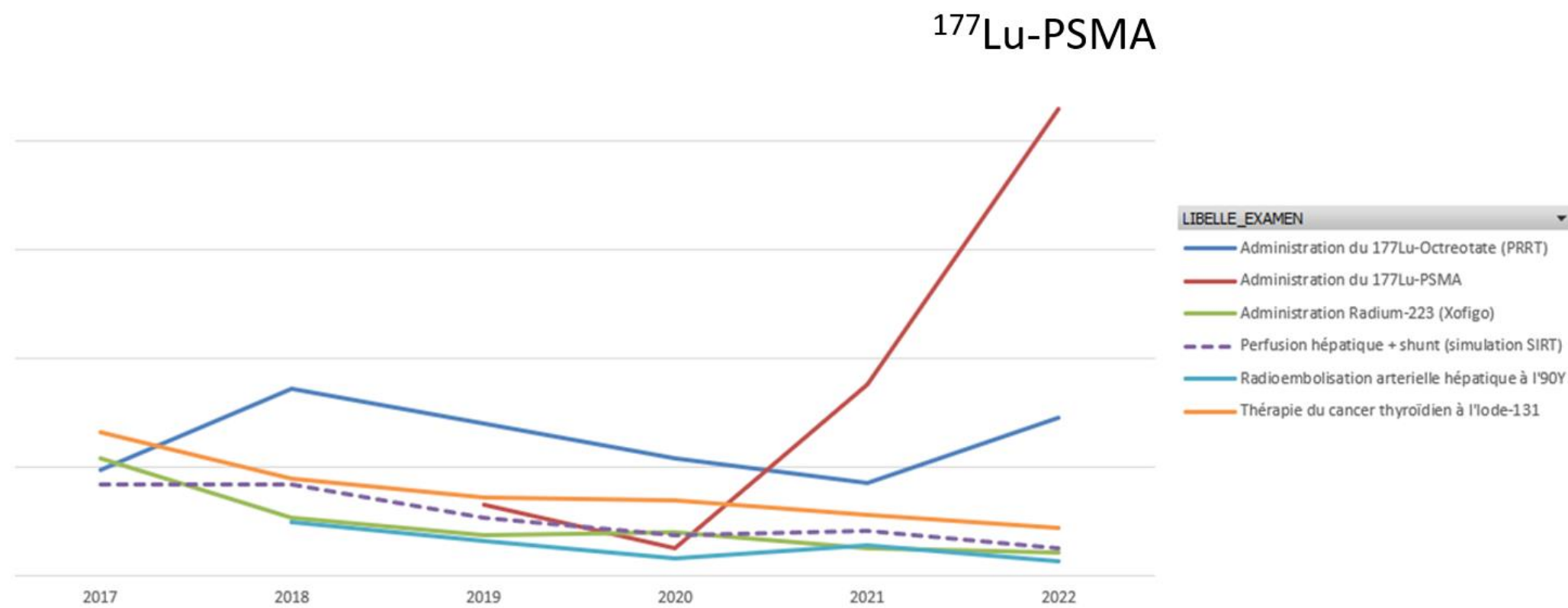
- Don't forget the head!



Future



Future



Questions?

when your lecturer asks if you have any questions



Thank you!

anne-leen.deleu@hubruxelles.be

