The role of PSMA PET in prostate cancer diagnosis-CGMH experience

Tseng Jing-Ren, MD

Nuclear Medicine and Molecular Imaging Center

CGMH, Linkou

EAU Guideline 2019

Prostate-specific antigen (PSA) recurrence after radical prostatectomy	LE	Strength rating
Perform prostate-specific membrane antigen (PSMA) positron emission tomography (PET) computed tomography (CT) if the PSA level is > 0.2 ng/mL and if the results will influence subsequent treatment decisions.	2b	Weak
In case PSMA PET/CT is not available, and the PSA level is ≥ 1 ng/mL, perform fluciclovine PET/CT or choline PET/CT imaging if the results will influence subsequent treatment decisions.		Weak
PSA recurrence after radiotherapy		
Perform prostate multiparametric magnetic resonance imaging to localise abnormal areas and guide biopsies in patients fit for local salvage therapy.	3	Strong
Perform PSMA PET/CT (if available) or fluciclovine PET/CT or choline PET/CT in patients fit for curative salvage treatment.	2b	Strong

European Association of Urology

EANM European Association of Nuclear Medicine — Biomedical Imaging and Therapy for Personalized Healthcare

European Society of Urogenital Radiology

ESTRO European Society for Radiotherapy & Oncology

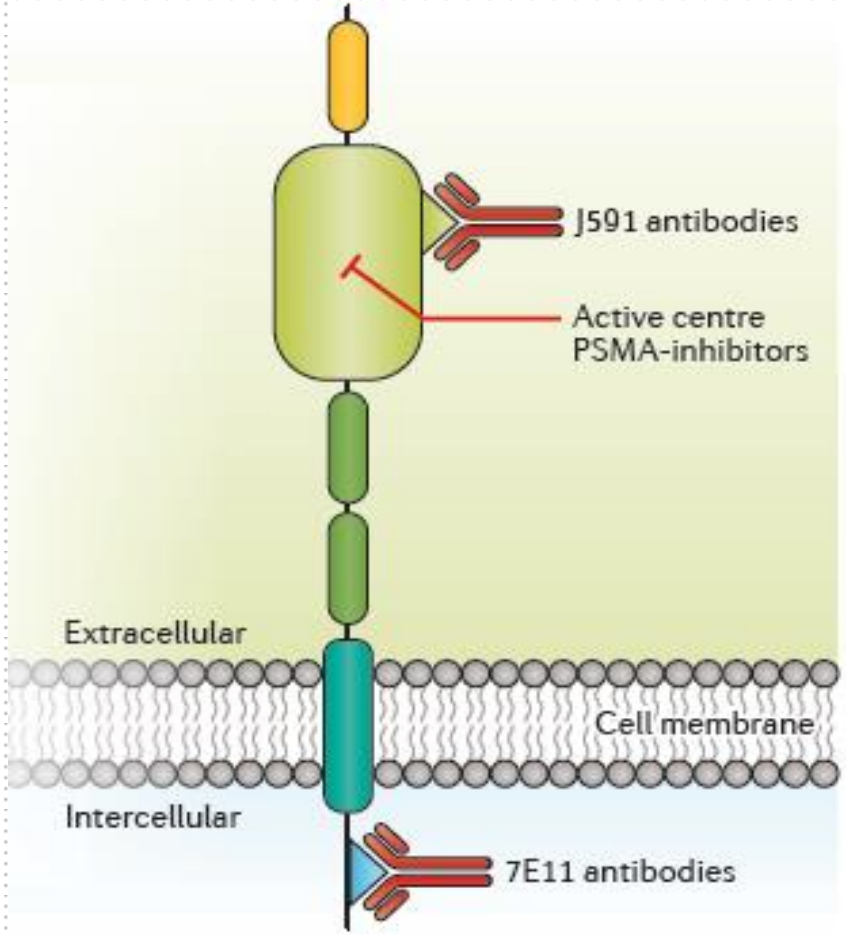
SIOG International Society of Geriatric Oncology

PSMA as target for PCa imaging and therapy

Prostate-**S**pecific **M**embrane **A**ntigen

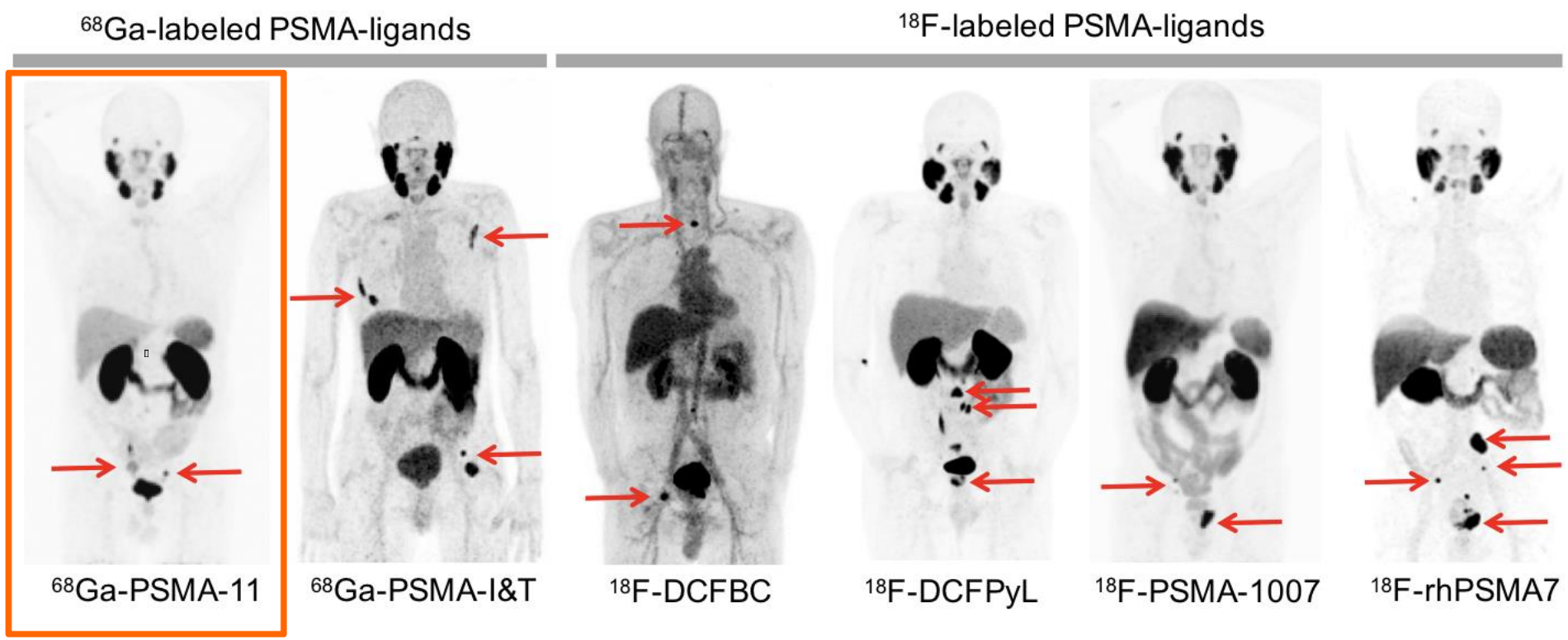
[syn. Glutamate carboxypeptidase II (GCP-II)]

- cell surface protein
- overexpression in >90% of PCa cells
- promising target for imaging and therapy
- development of various PSMA-ligands



Maurer et al., Nat Rev Urol 2016

PSMA-ligands for PET imaging

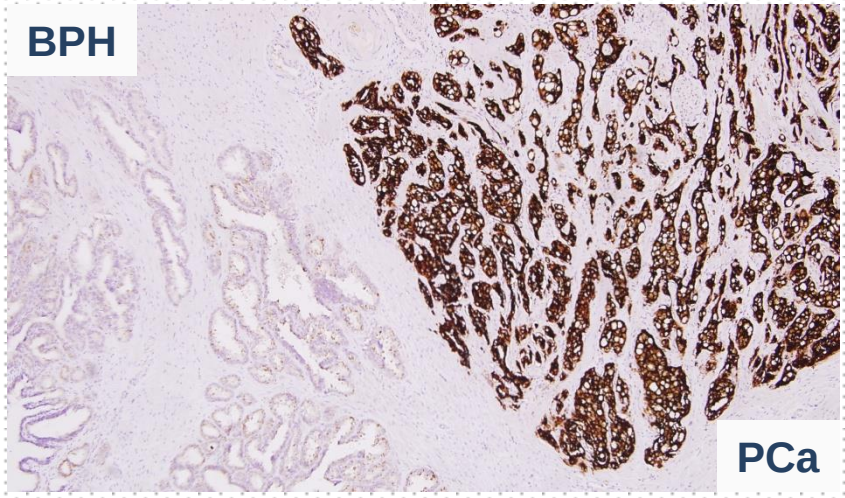


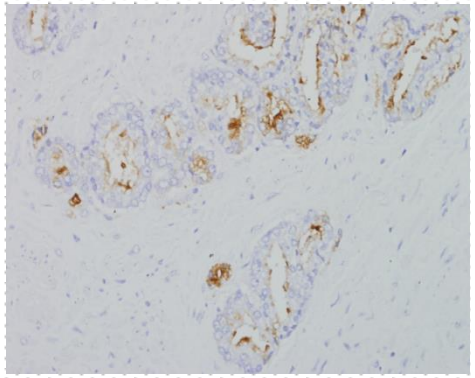
First report of human application:

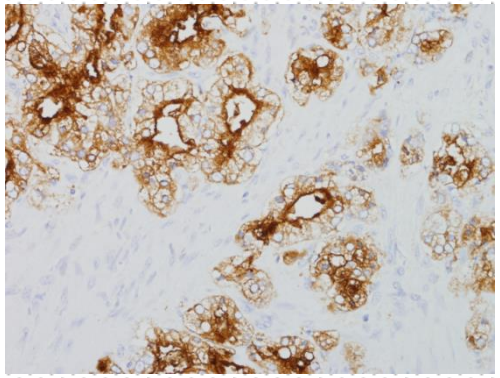
Afshar-Oromieh A al. EJNMMI 2013	Weineisen M et al. JNM 2015	Cho S et al. JNM 2012	Szabo Z et al. Mol Im Biol 2015	Giesel FL et al. EJNMMI 2016

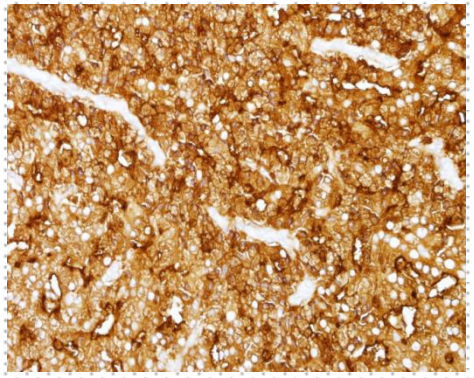
PSMA Expression is Prostate Cancer Specific and Increases with Tumor Grade

# Cases Studied	% Cases Reported to be PSMA Positive	Reference
251	94%	Wright et al
184	100%	Bostwick et al
51	84%	Mannweiler et al
42	88%	Kusumi et al
21	100%	Ananias et al
905	99.9%	Loda et al



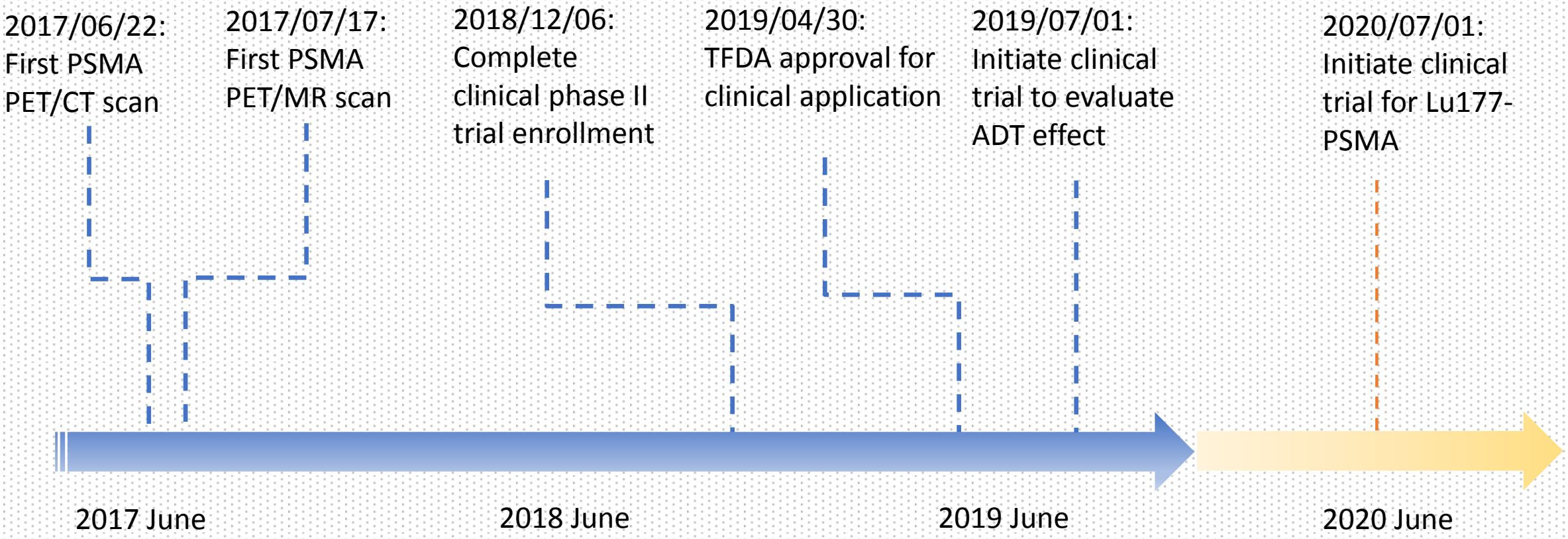






Courtesy of Dr. Neil Bander New York-Presbyterian Hospital

Our study milestones



檔　　號：
保存年限：

林口管理部 2019.04.30 收件章

衛生福利部　函

地址：11558 台北市南港區忠孝東路六段488號
聯絡人：陳孟賢
聯絡電話：02-27877478
傳真：02-33229527
電子信箱：mschen@fda.gov.tw

受文者：長庚醫療財團法人林口長庚紀念醫院

發文日期：中華民國108年4月30日
發文字號：衛授食字第1080005908號
速別：普通件
密等及解密條件或保密期限：
附件：

主旨：貴院為攝護腺癌經治療復發病人林○尚之正子造影需要，申請貴院迴旋加速器中心專案製造「68Ga-PSMA-11(HBED-CC)」一案，本部同意，請查照。

說明：

一、復貴院108年2月26日長庚院林字第1080200212號函。

二、旨揭藥品尚未經衛生福利部核准上市，請相關醫療院所在使用時，必須加強對藥品之不良反應監視及通報，若經發現，請立即通知全國藥物不良反應通報中心，以保障病人權益。

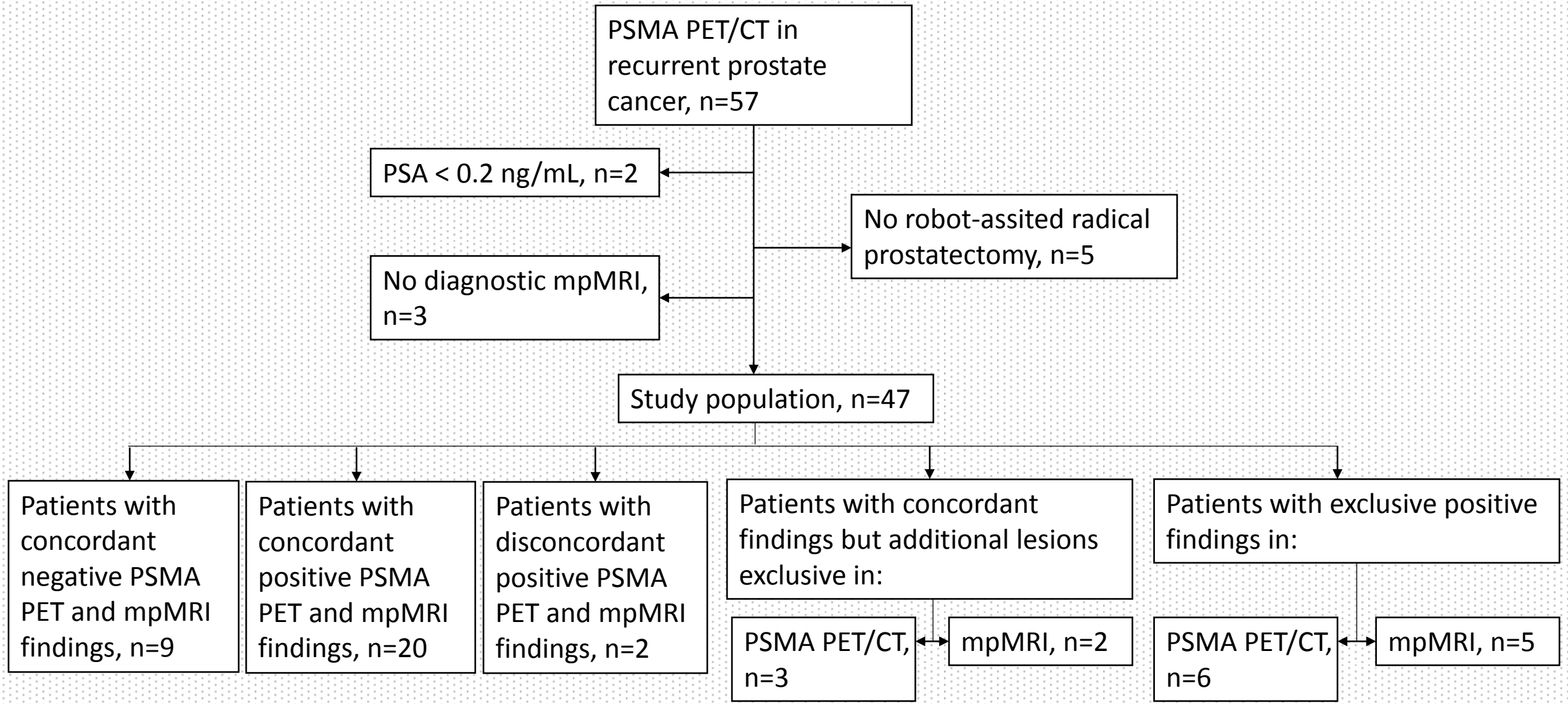
三、案內藥品製造須符合PIC/S GMP藥品優良規範，僅供貴院醫療使用，不得出售、讓轉供他用。

正本：長庚醫療財團法人林口長庚紀念醫院
副本：財團法人藥害救濟基金會全國藥物不良反應通報中心 2019-04-30 09:52:24 收文章

特定藥物專案核准製造及輸入辦法

條　　文	說　　明
第一條　本辦法依藥事法(以下稱本法)第四十八條之二第三項規定訂定之。	本辦法訂定依據。
第二條　區域醫院以上之教學醫院、精神科教學醫院，得檢具下列文件、資料，依本法第四十八條之二第一項第一款向中央衛生主管機關申請特定藥物之專案製造或輸入： 一、診斷證明書。 二、申請醫院之人體研究倫理審查委員會核准申請特定藥物使用之證明。 三、完整治療計畫書及相關文獻依據。 四、病人同意書。 五、所需藥物數量及計算依據。 六、藥物之說明書。 七、藥物之國外上市證明或各國醫藥品集收載影本。 前項第一款及第二款內容，需載明為預防、診治危及生命或嚴重失能之疾病，且國內尚無適當藥物或合適替代療法之意旨。 依第一項申請之藥品，無法檢具第一項第七款資料者，應檢附產品製造品質資料、動物安全性試驗報告、人體使用資料及風險利益評估報告替代之。 依第一項申請之醫療器材，屬我國製造者，得檢附產品結構、規格、性能、用途及圖樣、製造品質資料、安全性試驗報告、人體使用資料及風險利益評估報告替代第一項第七款資料。	一、本法第四十八條之二第一項第一款之特定藥物申請資格及申請時須檢附之文件與佐證資料。 二、本條第一項第二款有關醫院人體研究倫理審查委員會核准係指特定藥物使用之證明，與依人體試驗管理辦法第三條之一申請核准之人體試驗有別。

CGMH Phase II prospective study: PSMA PET/CT v.s mpMRI in biochemical failure Pca patients



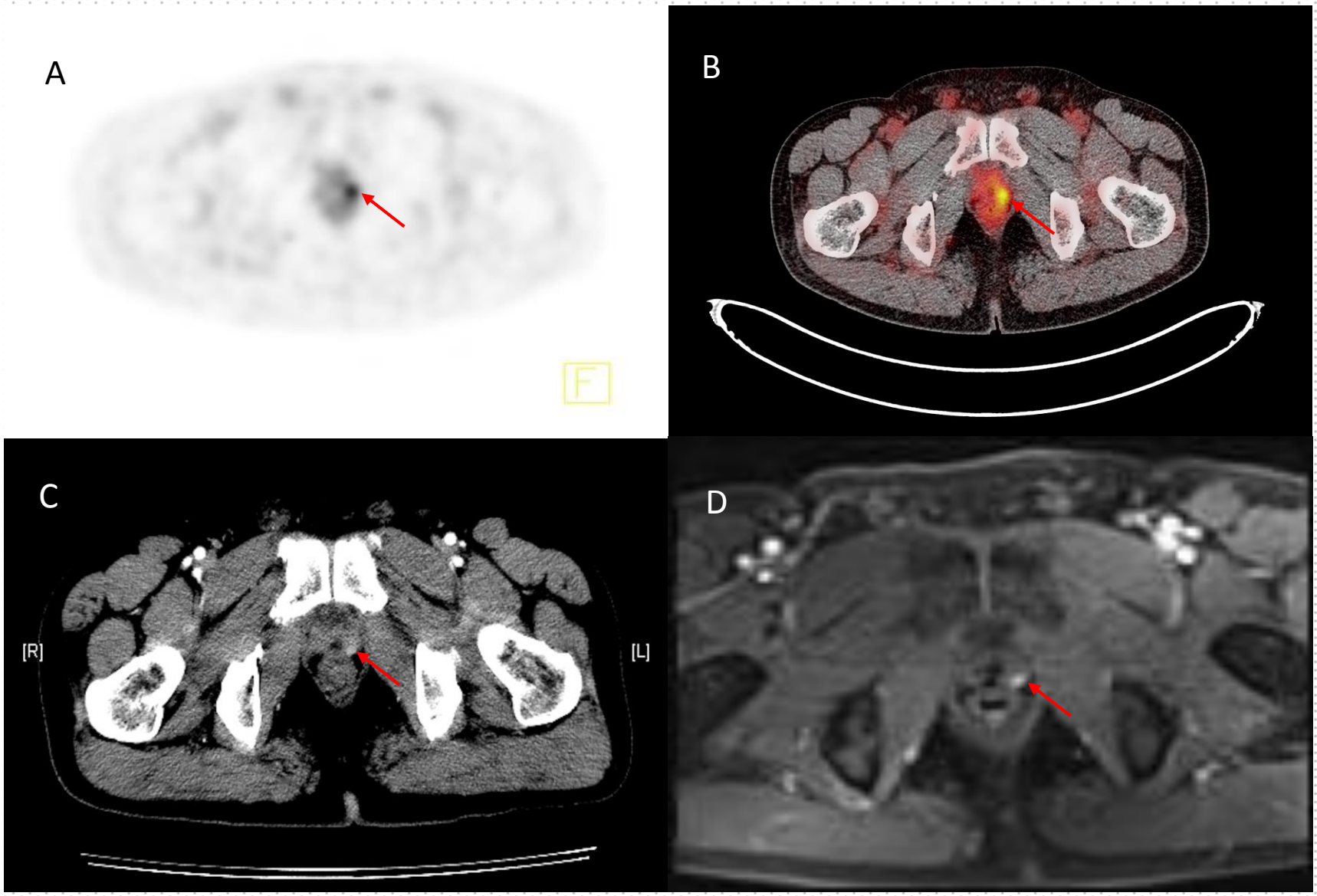
CGMH PHASE II PROSPECTIVE STUDY: PSMA PET/CT V.S mpMRI IN BIOCHEMICAL FAILURE Pca PATIENTS

Table. Malignant lesions detected by PSMA PET/CT or mpMRI

	PSMA PET/CT	*mpMRI*
Local recurrence	21	27
Regional node	16	14
Distant node	1	2
Distant bone	12	4
Total	50	47

	only MRI detected		Consensus		only PET detected	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Local	9	19.2%	34	72.3%	4	8.5%
Node	1	2.1%	43	91.5%	3	6.4%
Distant bone	0	0.0%	42	89.4%	5	10.6%

Sensitivity			
	PET	MRI	p-value
Positive	86.80%	84.20%	1
Local	67.70%	87.10%	0.18
Node	92.30%	76.90%	0.625
Distant bone	100%	44.40%	0.025


A
B
C
[R]
[L]
D

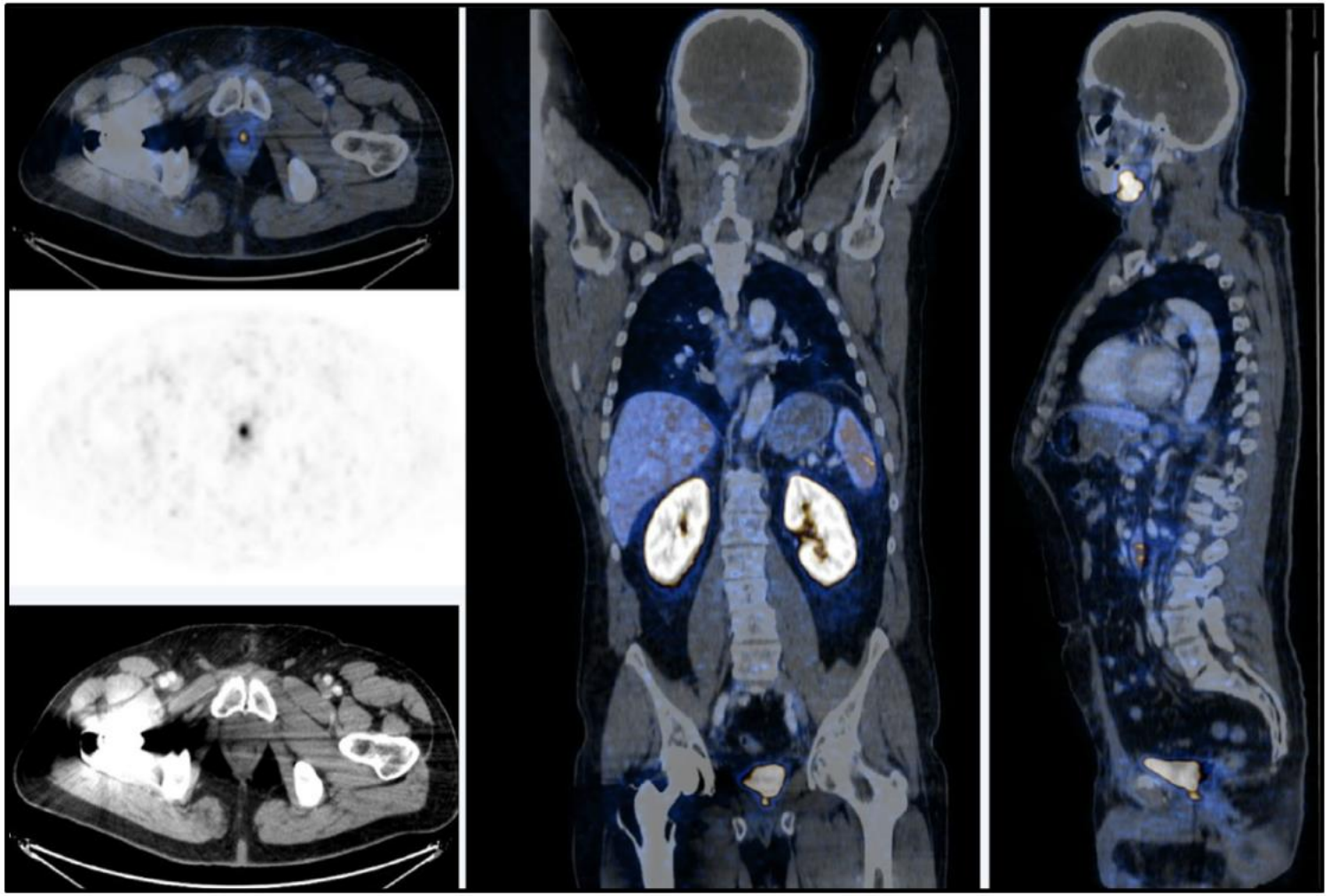


Fig. 5 Case 206: Gleason score 4 + 5 = 9 primary treated with radical prostatectomy in 2016 and a PSA at the time of the scan of 0.94 nm/mL, PSA doubling time 2.2 months. This is a case of persisting disagreement. At first reading, this case was judged not anomalous by four readers, uncertain by one reader, not pathologic by one reader, and pathologic by one reader. According to the study coordinator judgment, the finding was uncertain (probably attributable to radioactive urine uptake) and according the new criteria guidelines should be classified as anomalous, but uncertain. However, final judgment by readers on local relapse was: Not anomalous, 2; Uncertain, 4; Not pathologic, 1

Eur J Nucl Med Mol Imaging (2017) 44:1622–1635
Development of standardized image interpretation for 68Ga-PSMA PET/CT to detect prostate cancer recurrent lesions

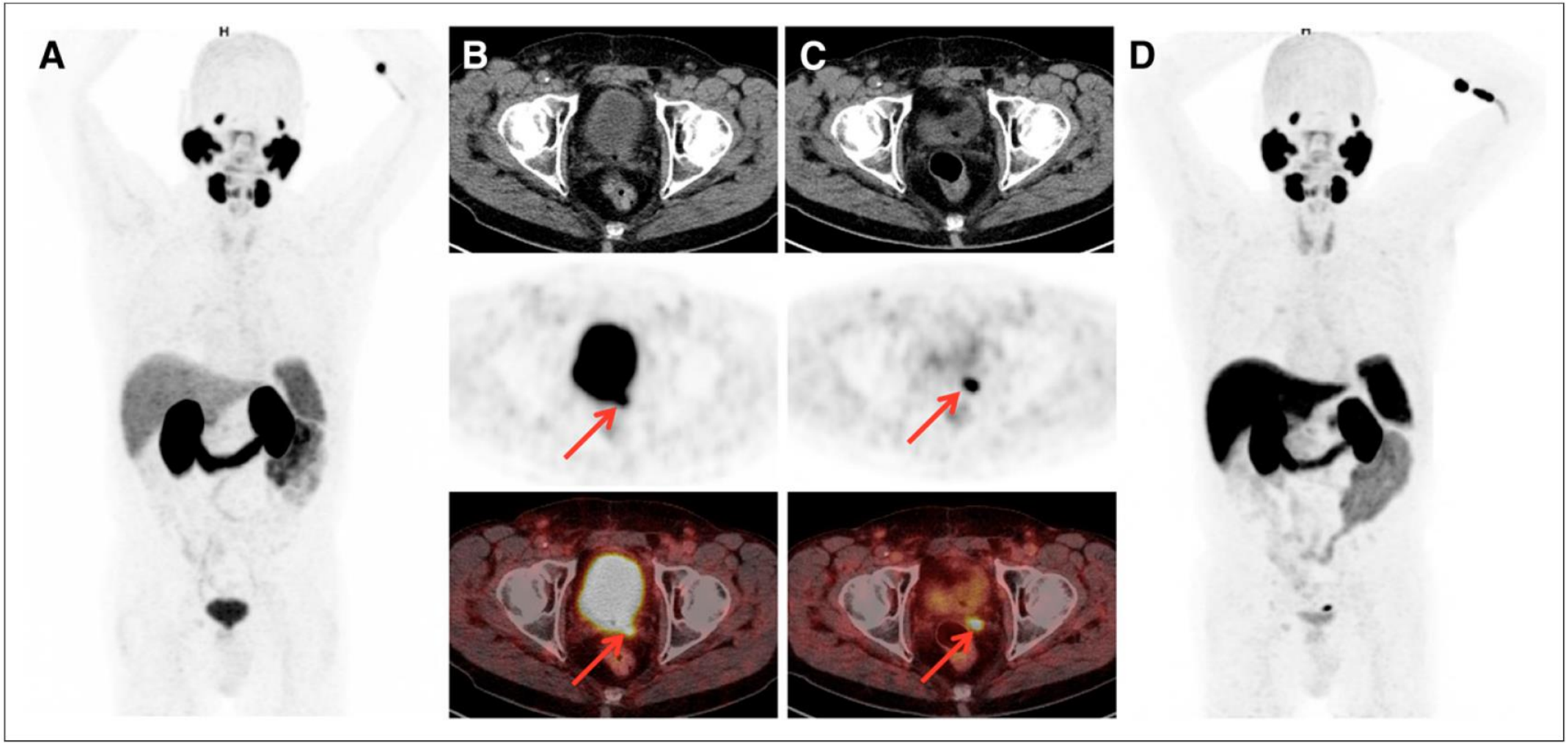


FIGURE 4. Images from 76-y-old patient after radical prostatectomy (2006; Gleason score of 7b; pT3a; pN0) and with PSA level slowly rising to 0.78 ng/mL (October 2017). (A and B) Patient underwent primarily ^{68}Ga-PSMA-11 PET/CT, which resulted in suggestion of local recurrence (arrows). No definite diagnosis could be made on basis of adjacent high activity retention in urinary bladder. (C and D) Subsequent ^{18}F-PSMA-1007 PET/CT 3 mo later clearly depicted PSMA ligand uptake in left seminal vesicle (arrows) with high contrast and very low retention in bladder.

J Nucl Med 2019; 60:362–368 *Detection Efficacy of 18F-PSMA-1007 PET/CT in 251 Patients with Biochemical Recurrence of Prostate Cancer After Radical Prostatectomy*

J Nucl Med. 2019 Sep 27. pii: jnumed.119.234187. doi: 10.2967/jnumed.119.234187. [Epub ahead of print]

Head- to head Comparison of ^{68}Ga-PSMA-11 with ^{18}F-PSMA-1007 PET/CT in Staging Prostate Cancer Using Histopathology and Immunohistochemical Analysis as Reference-Standard.

Kuten J[1], Fahoum I[1], Savin Z[1], Shamni O[2], Gitstein G[1], Hershkovitz D[1], Mabjeesh NJ[1], Yossepowitch O[1], Mishani E[2], Even-Sapir E[1].

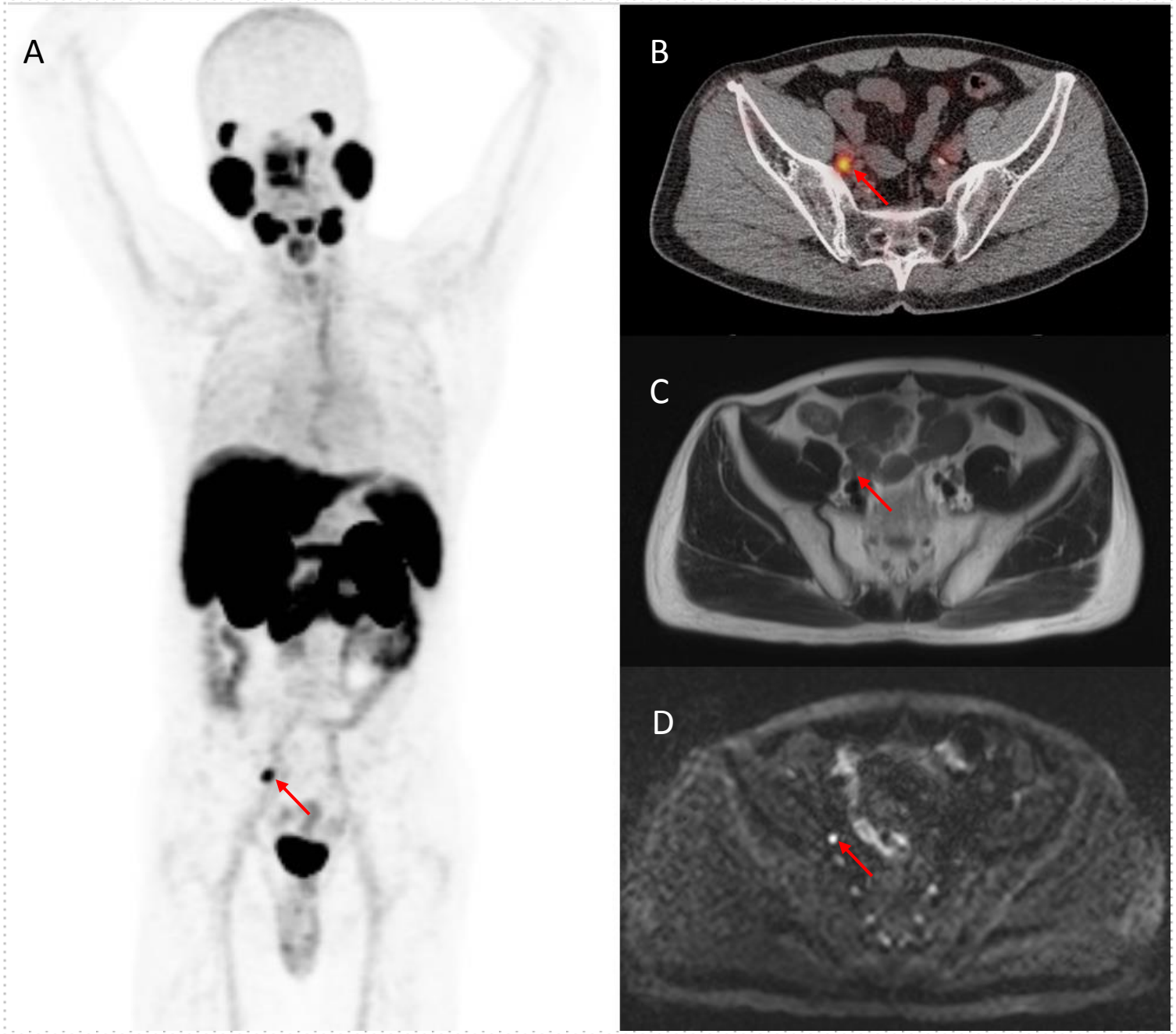
Author information

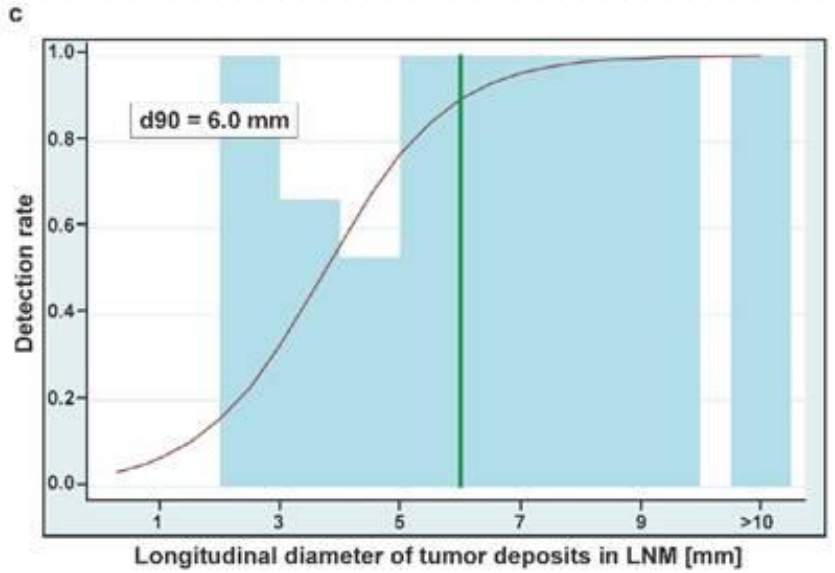
1 Tel Aviv Sourasky Medical Center, Israel.
2 Hadassah Medical Center.

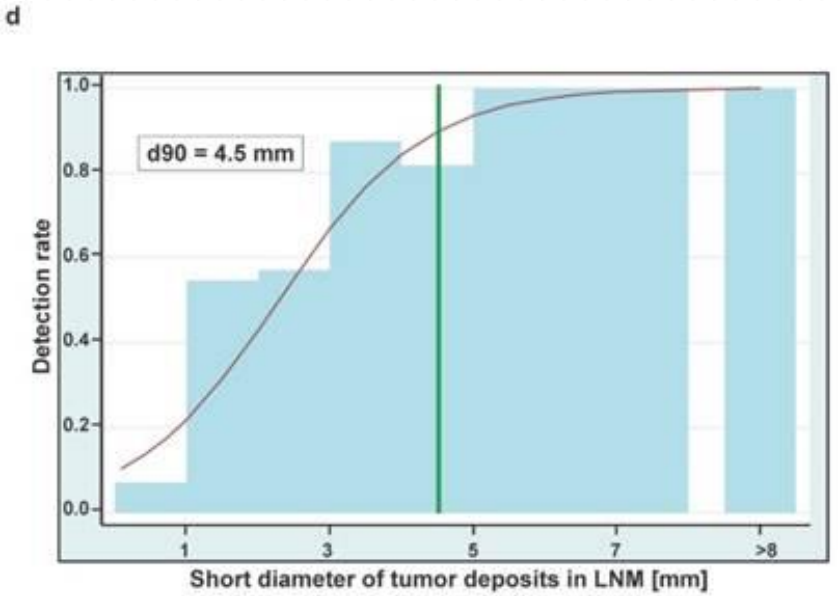
Abstract

^{18}F-PSMA-1007 is a novel prostate-specific membrane antigen (PSMA)-based radiopharmaceutical for imaging prostate cancer. The aim of this study is to compare the diagnostic accuracy of ^{18}F-PSMA-1007 with ^{68}Ga-PSMA-11 PET/CT in the same patients presenting with newly diagnosed intermediate and high-risk prostate cancer. **Methods:** Sixteen patients with intermediate and high-risk PCa underwent ^{18}F-PSMA-1007 and ^{68}Ga-PSMA-11 PET/CTs within 15 days. PET findings were compared between the two radiotracers and to reference-standard pathological specimens obtained from radical prostatectomy. Cohen's kappa coefficient was used to assess the concordance between ^{18}F-PSMA-1007 and ^{68}Ga-PSMA-11 for detection of intra-prostatic lesions. McNemar's test was used to assess agreement between intra-prostatic PET/CT findings and histopathological findings. Sensitivity, specificity, positive predictive value and negative predictive value were reported for each radiotracer. SUV_{max} was measured for all lesions and tumor-to-background activity was calculated. Areas under receiver operating characteristic curves were calculated for discriminating diseased vs. non-diseased prostate segments and optimal SUV-cutoff values were calculated using the Youden's index for each radiotracer. **Results:** PSMA-avid lesions in the prostate were identified in all 16 patients with an almost-perfect concordance between the two tracers (kappa ranged from 0.871 to 1). Aside from the dominant intra-prostatic lesion, similarly detected by both radiotracers, a second less intense positive focus was detected in 4 patients only with ^{18}F-PSMA-1007. Three of these secondary foci were confirmed as Gleason grade 3 lesions whereas the fourth was shown on pathology to represent chronic prostatitis. **Conclusion:** This pilot study shows that both ^{18}F-PSMA-1007 and ^{68}Ga-PSMA-11 identify all dominant prostatic lesions in patients with intermediate and high-risk prostate cancer at staging. ^{18}F-PSMA-1007 however may detect additional low-grade lesions of limited clinical relevance.

Copyright © 2019 by the Society of Nuclear Medicine and Molecular Imaging, Inc.







Theranostics 2017; 7(6):1770-1780. doi:10.7150/thno.18421
Diagnostic Accuracy of Ga-68-HBED-CC-PSMA-Ligand-PET/CT before Salvage Lymph Node Dissection for Recurrent Prostate Cancer

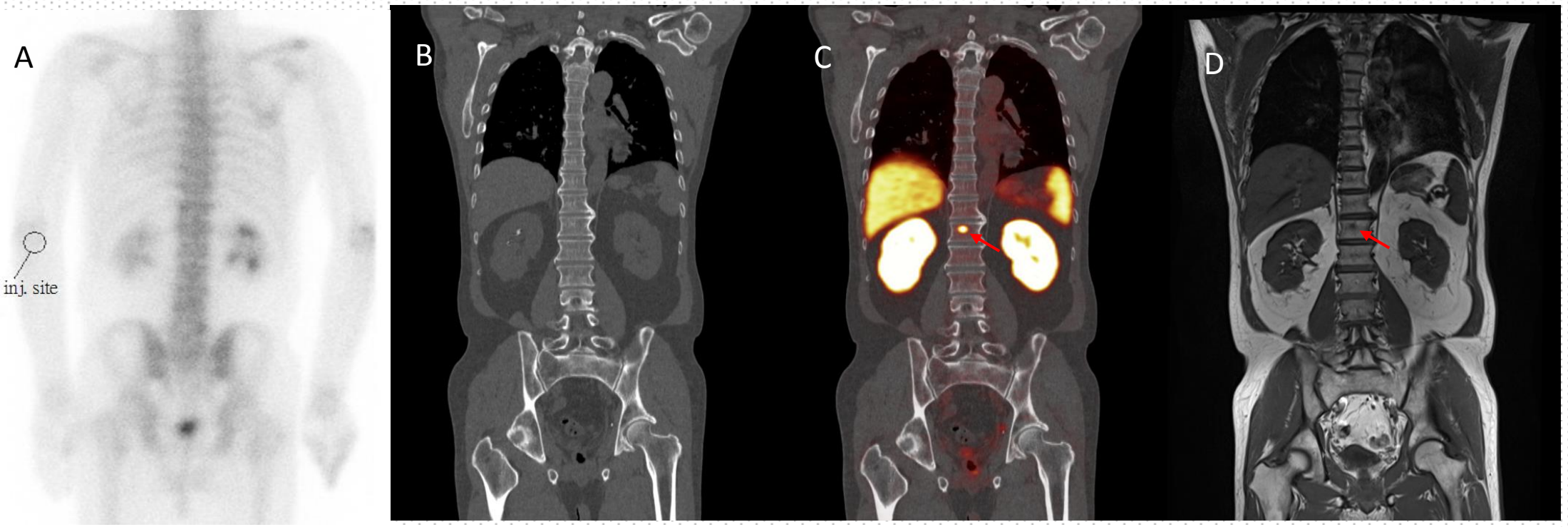
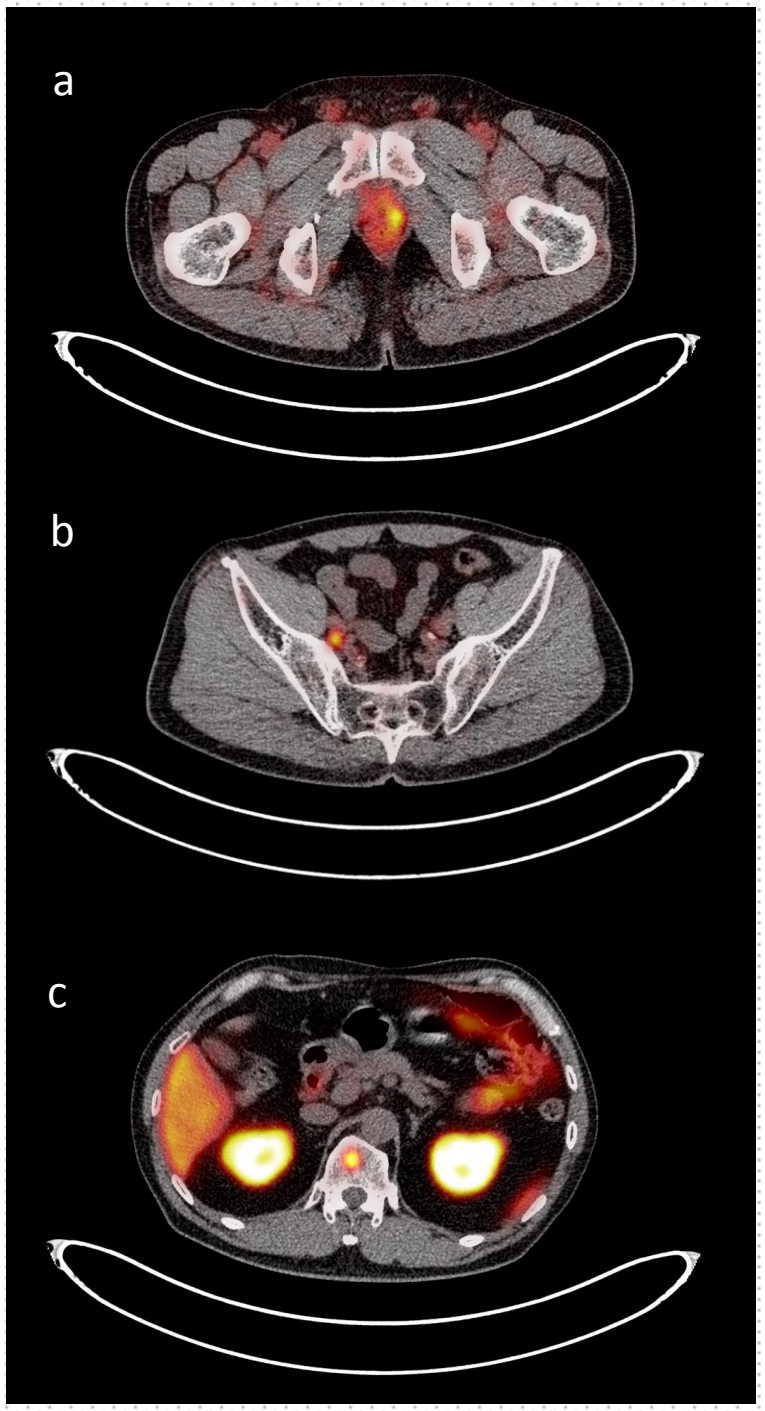


Table 4 Diagnostic properties and receiver operator characteristics for assessment of bone metastases by the index tests compared to the best valuable comparator on a patient level

	M1 by BVC			M0 by BVC							
Imaging modality	M0	Equivocal	M1	M0	Equivocal	M1	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	AUC (95% CI)
PSMA PET/CT ($n = 68$)	2	0	8	57	1	0	0.80 (0.44–0.98) *0.80 (0.44–0.98)*	1.00 (0.94–1.0) *0.98 (0.91–1.0)*	1.00 (0.63–1.0) *0.89 (0.52–1.0)*	0.97 (0.89–1.0) *0.97 (0.88–1.0)*	0.90 (0.89–1.0) *0.89 (0.76–1.0)*
NaF PET/CT ($n = 67$)	1	0	9	51	5	1	0.90 (0.56–1.0) *0.90 (0.56–1.0)*	0.98 (0.91–1.0) *0.90 (0.79–0.96)*	0.90 (0.56–1.0) *0.60 (0.32–0.84)*	0.98 (0.91–1.0) *0.98 (0.90–1.0)*	0.94 (0.84–1.0) *0.90 (0.79–1.0)*
DW-MRI (n = 60)	5	1	2	45	3	4	0.25 (0.03–0.65) *0.38 (0.09–0.76)*	0.92 (0.82–0.98) *0.87 (0.74–0.94)*	0.33 (0.04–0.78) *0.30 (0.07–0.65)*	0.89 (0.77–0.96) *0.90 (0.78–0.97)*	0.59 (0.42–0.75) *0.62 (0.44–0.81)*
DW-MRI (scan field-based, $n = 58$)	4	0	2	45	3	4	0.33 (0.04–0.78) *0.33 (0.04–0.78)*	0.92 (0.82–0.98) *0.87(0.74–0.94)*	0.33 (0.04–0.78) *0.22 (0.03–0.60)*	0.92 (0.82–0.98) *0.92 (0.80–0.98)*	0.63 (0.42–0.84) *0.60 (0.39–0.81)*

BVC best valuable comparator, *M0* no bone metastases, *M1* bone metastasis present, *Equivocal* the patient cannot be categorized as having bone metastasis or not. Optimistic analysis is considering equivocal as M0, pessimistic analysis is considering equivocal as M1 and written in italics. *PPV* positive predictive value, *NPV* negative predictive value, *AUC* area under the curve, *CI* confidence interval

Prospective comparison of 68Ga-PSMA PET/CT, 18F-sodium fluoride PET/CT and diffusion weighted-MRI at for the detection of bone metastases in biochemically recurrent prostate cancer https://doi.org/10.1007/s00259-018-4058-4



What we learned form our patients?

- a. For local recurrent lesion near anastomosis, PSMA PET may be influenced by strong urine radioactivity, mpMRI seems more sensitive.
- b. For small lymph node metastasis, PSMA PET is outperformed without size criteria limitation as used in morphological imaging.
- c. For distant bone metastasis, PSMA PET seems more superior than mpMRI not only by sensitivity but also scan range covering the whole body.
- d. PSMA PET is safe without causing any side effects.

^{18}F-fluciclovine PET-CT and ^{68}Ga-PSMA-11 PET-CT in patients with early biochemical recurrence after prostatectomy: a prospective, single-centre, single-arm, comparative imaging trial

Jeremie Calais, Francesco Ceci, Matthias Eiber, Thomas A Hope, Michael S Hofman, Christoph Rischpler, Tore Bach-Gansmo, Cristina Nanni, Bital Savir-Baruch, David Elashoff, Tristan Grogan, Magnus Dahlbom, Roger Slavik, Jeannine Gartmann, Kathleen Nguyen, Vincent Lok, Hossein Jadvar, Amar U Kishan, Matthew B Rettig, Robert E Reiter, Wolfgang P Fendler, Johannes Czernin

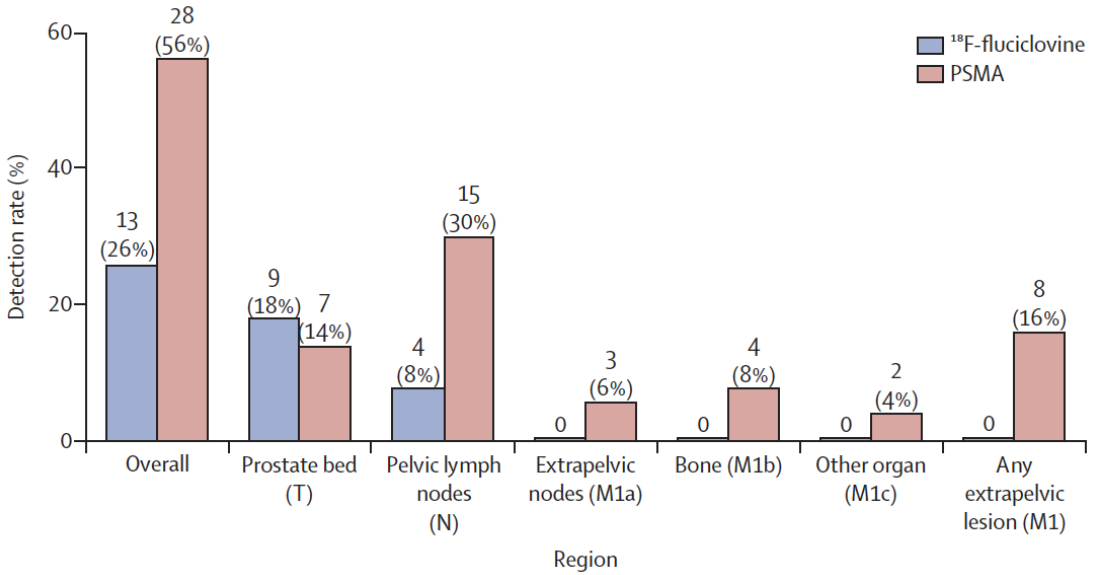
Summary

Background National Comprehensive Cancer Network guidelines consider ^{18}F-fluciclovine PET-CT for prostate cancer biochemical recurrence localisation after radical prostatectomy, whereas European Association of Urology guidelines recommend prostate-specific membrane antigen (PSMA) PET-CT. To the best of our knowledge, no prospective head-to-head comparison between these tests has been done so far. The aim of this study was to compare prospectively paired ^{18}F-fluciclovine and PSMA PET-CT scans for localising biochemical recurrence of prostate cancer after radical prostatectomy in patients with low prostate-specific antigen (PSA) concentrations (<2·0 ng/mL).

Methods This was a prospective, single-centre, open-label, single-arm comparative study done at University of California Los Angeles (Los Angeles, CA, USA). Patients older than 18 years of age with prostate cancer biochemical recurrence after radical prostatectomy and PSA levels ranging from 0·2 to 2·0 ng/mL without any prior salvage therapy and with a Karnofsky performance status of at least 50 were eligible. Patients underwent ^{18}F-fluciclovine (reference test) and PSMA (index test) PET-CT scans within 15 days. Detection rate of biochemical recurrence at the patient level and by anatomical region was the primary endpoint. A statistical power analysis demonstrated that a sample size of 50 patients was needed to show a 22% difference in detection rates in favour of PSMA (test for superiority). Each PET scan was interpreted by three independent masked readers and a consensus majority interpretation was generated (two *vs* one) to determine positive findings. This study is registered with ClinicalTrials.gov, number NCT02940262, and is complete.

Findings Between Feb 26, 2018, and Sept 20, 2018, 143 patients were screened for eligibility, of whom 50 patients were enrolled into the study. Median follow-up was 8 months (IQR 7–9). The primary endpoint was met; detection rates were significantly lower with ^{18}F-fluciclovine PET-CT (13 [26%; 95% CI 15–40] of 50) than with PSMA PET-CT (28 [56%; 41–70] of 50), with an odds ratio (OR) of 4·8 (95% CI 1·6–19·2; p=0·0026) at the patient level; in the subanalysis of the pelvic nodes region (four [8%; 2–19] with ^{18}F-fluciclovine *vs* 15 [30%; 18–45] with PSMA PET-CT; OR 12·0 [1·8–513·0], p=0·0034); and in the subanalysis of any extrapelvic lesions (none [0%; 0–6] *vs* eight [16%; 7–29]; OR non-estimable [95% CI non-estimable], p=0·0078).

Interpretation With higher detection rates, PSMA should be the PET tracer of choice when PET-CT imaging is considered for subsequent treatment management decisions in patients with prostate cancer and biochemical recurrence after radical prostatectomy and low PSA concentrations (≤2·0 ng/mL). Further research is needed to investigate whether higher detection rates translate into improved oncological outcomes.

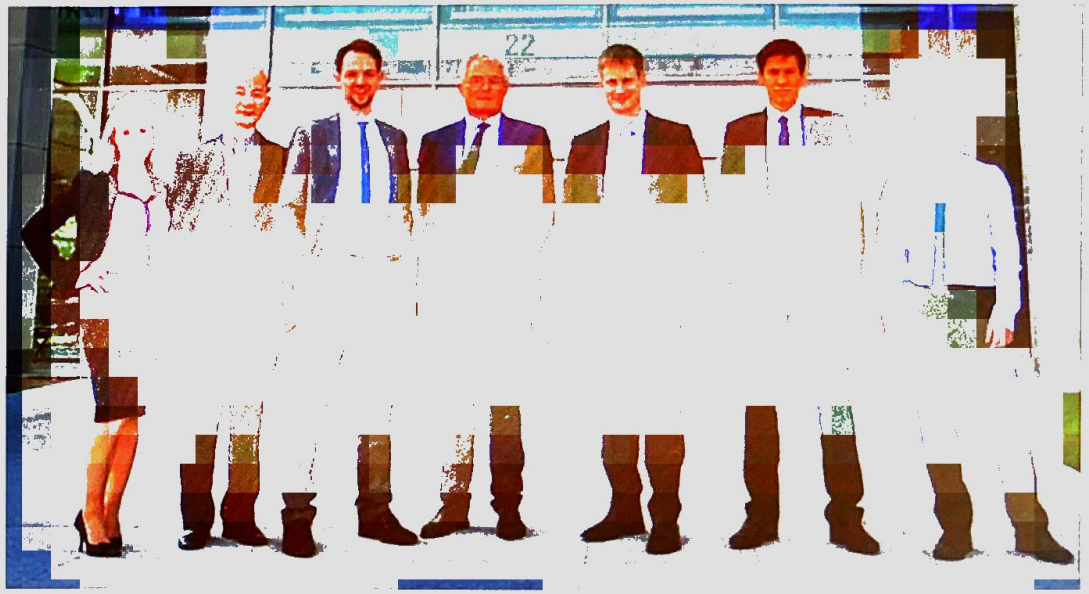


Lancet Oncol 2019; 20: 1286–94

NDA New Drug Application #212642 for ^{68}Ga-PSMA-11

NDA filing	Sept. 6th, 2019
Accepted for filling day-74 letter	Nov. 19th, 2019
NDA approval	
– if priority review	May 6th, 2020
– if standard review	Sept 6th, 2020

Marketing exclusivity was waived:
ANDA after NDA approval !



UCSF UCLA
University of California, Los Angeles

Body of data:

- Two prospective studies at UCSF/UCLA
  - BCR: 635 pts for safety/efficacy, PreRP: 325 pats for safety and efficacy
- Metaanalysis: data from literature with histopathology as standard of truth
  - BCR: 15 papers, 256 patients /Preoperative staging: 5 papers: 266 patients

Is it "Prostate Specific" ?

- An enzyme encoded by the *FOLH1* (folate hydrolase 1) gene at chromosome 11
- Folate dehydrolase, Glutamate carboxypeptidase II (GCP II), N-acetyl-L-aspartyl-L-glutamate peptidase I (NAALADase I).....
- Multifunction as an enzyme, cellular component, and involving several biological process

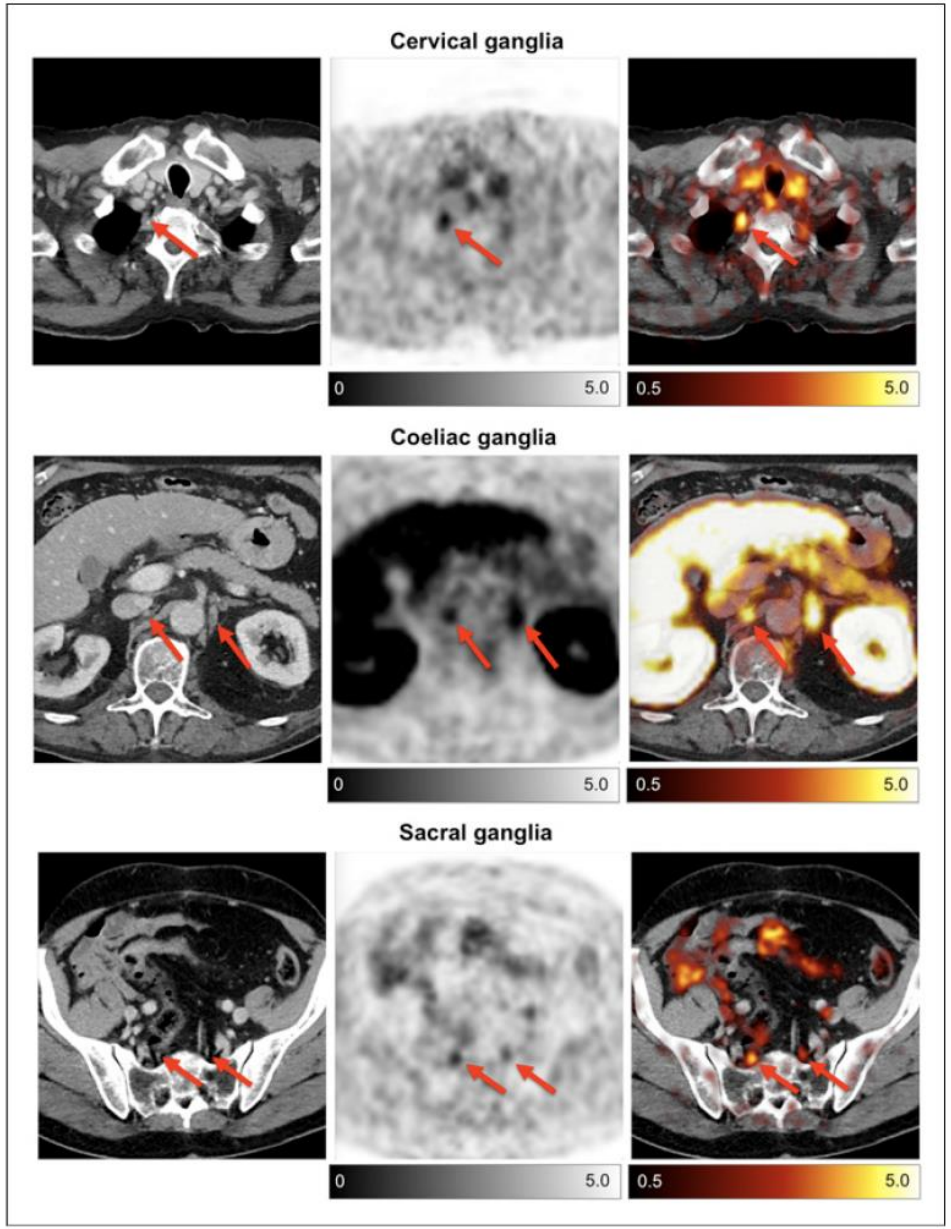
Limitations of PSMA-PET SCAN

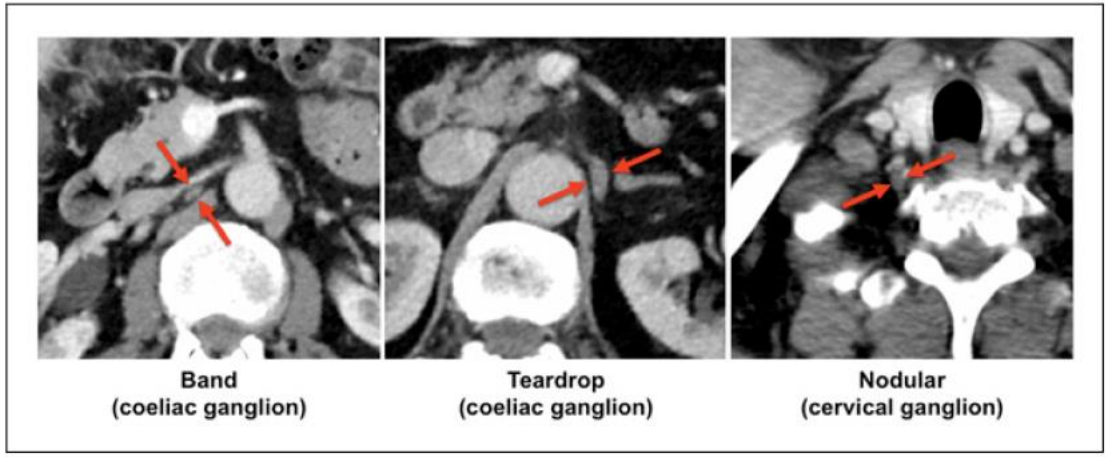
PSMA-PET positive benign lesions:

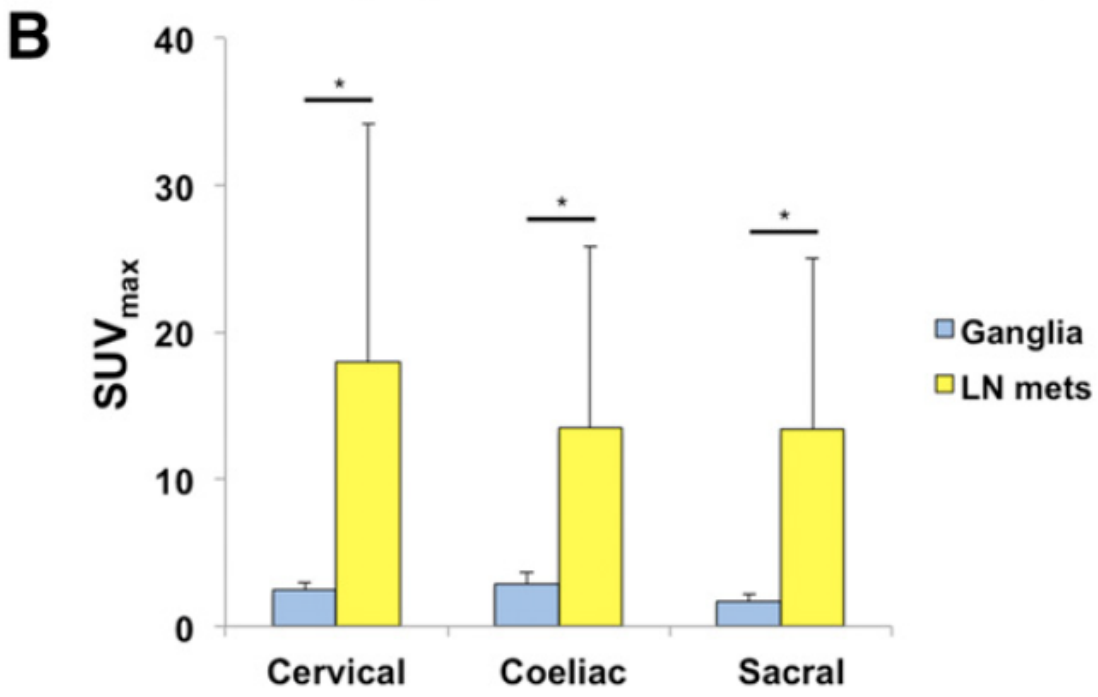
Thyroid adenoma[1], Bone Paget Disease[2], Schwannoma[3], Tuberculosis[3], Incidentaloma[4], Sarcoidosis[5], Ganglia[6,7] …

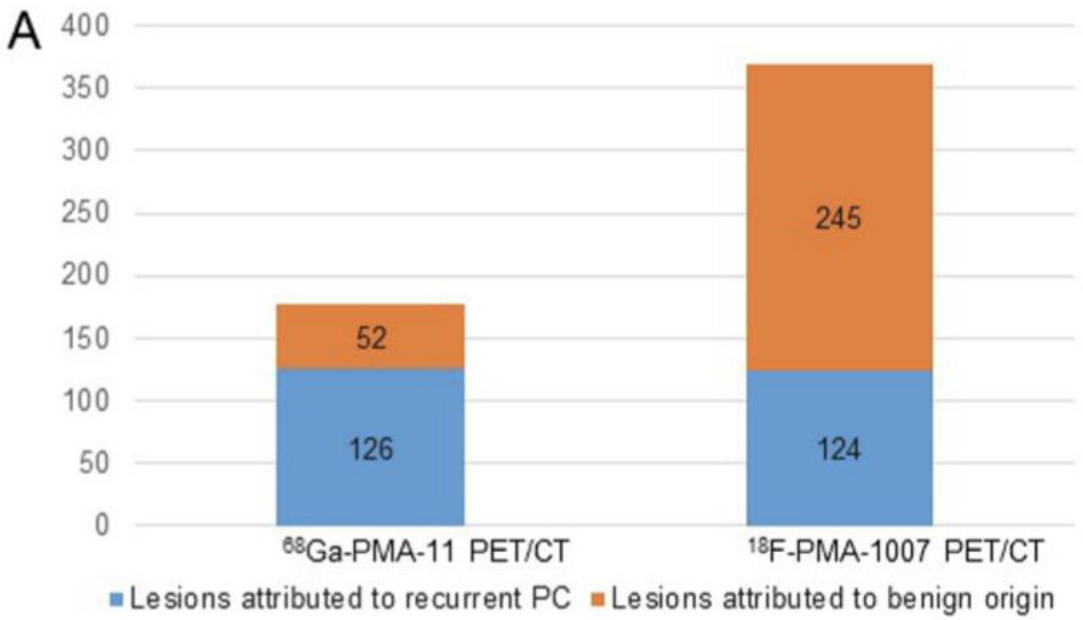
[1]Kanthan et al., Clin Nucl Med 2015, [2]Artigas et al., EJNMMI 2016, [3]Rischpler et al., EJNMMI 2016; [4]Law et al., J Med Imaging Radiat Oncol. 2015; [5]Kobe et al., Clin Nucl Med 2015; [6]Krohn et al., EJNMMI 2015; [7]Matthias et al, JNM 2018

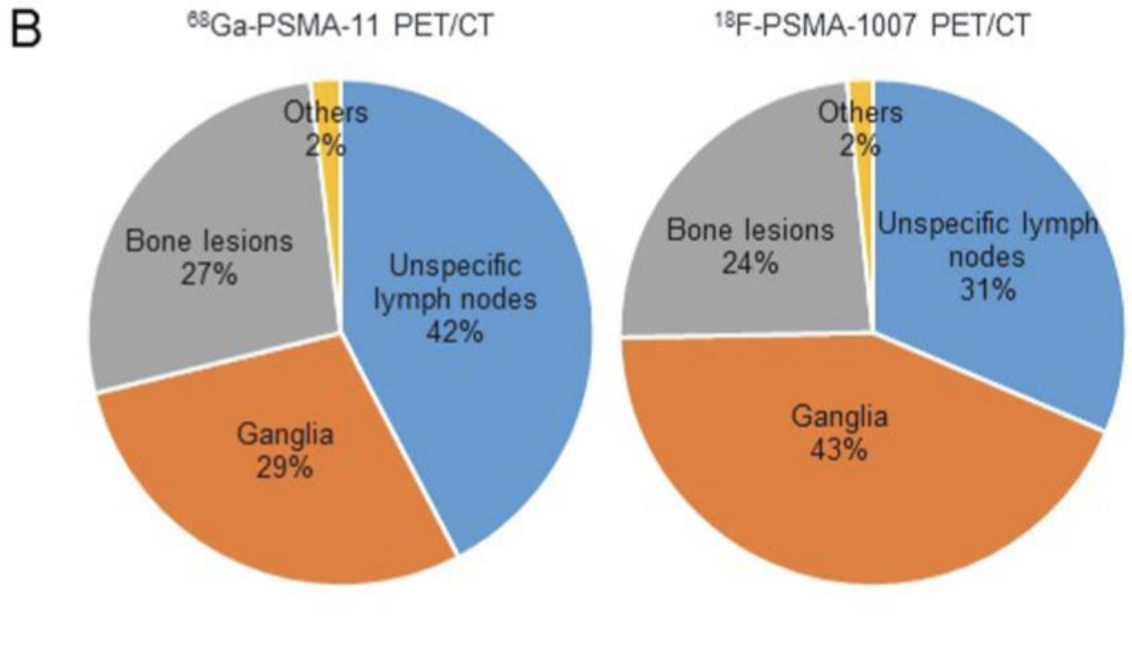
Cervical, Celiac, and Sacral Ganglia











^{18}F-PSMA-1007 PET revealed approximately 5 times more lesions attributed to benign origin compared to ^{68}Ga-PSMA-11 PET (245 vs. 52 lesions, respectively).

This necessitates sophisticated reader training emphasizing known pitfalls and reporting within the clinical context.

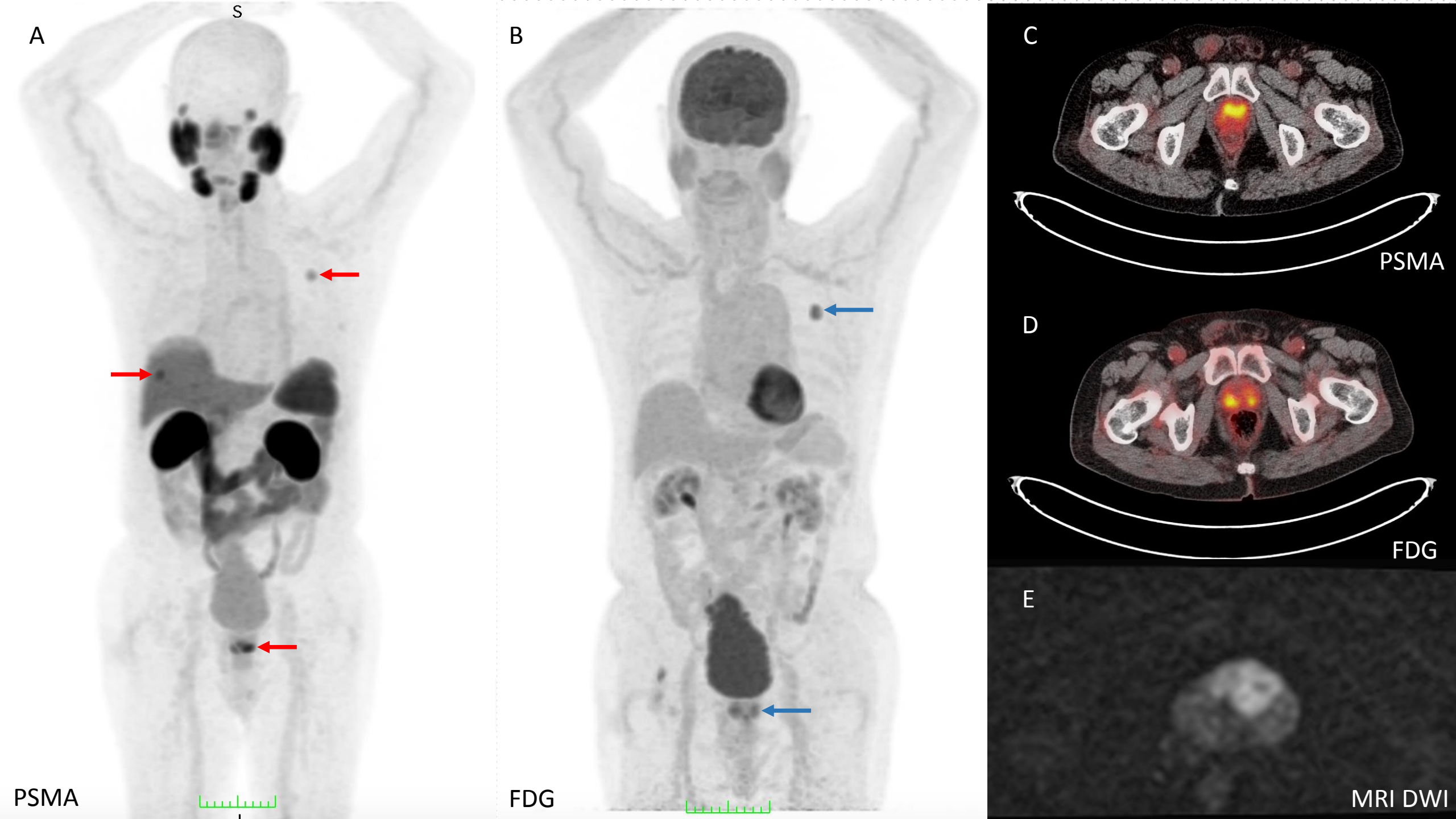
J Nucl Med. 2019 Jun 28. pii: jnumed.119.229187. doi: 10.2967/jnumed.119.229187

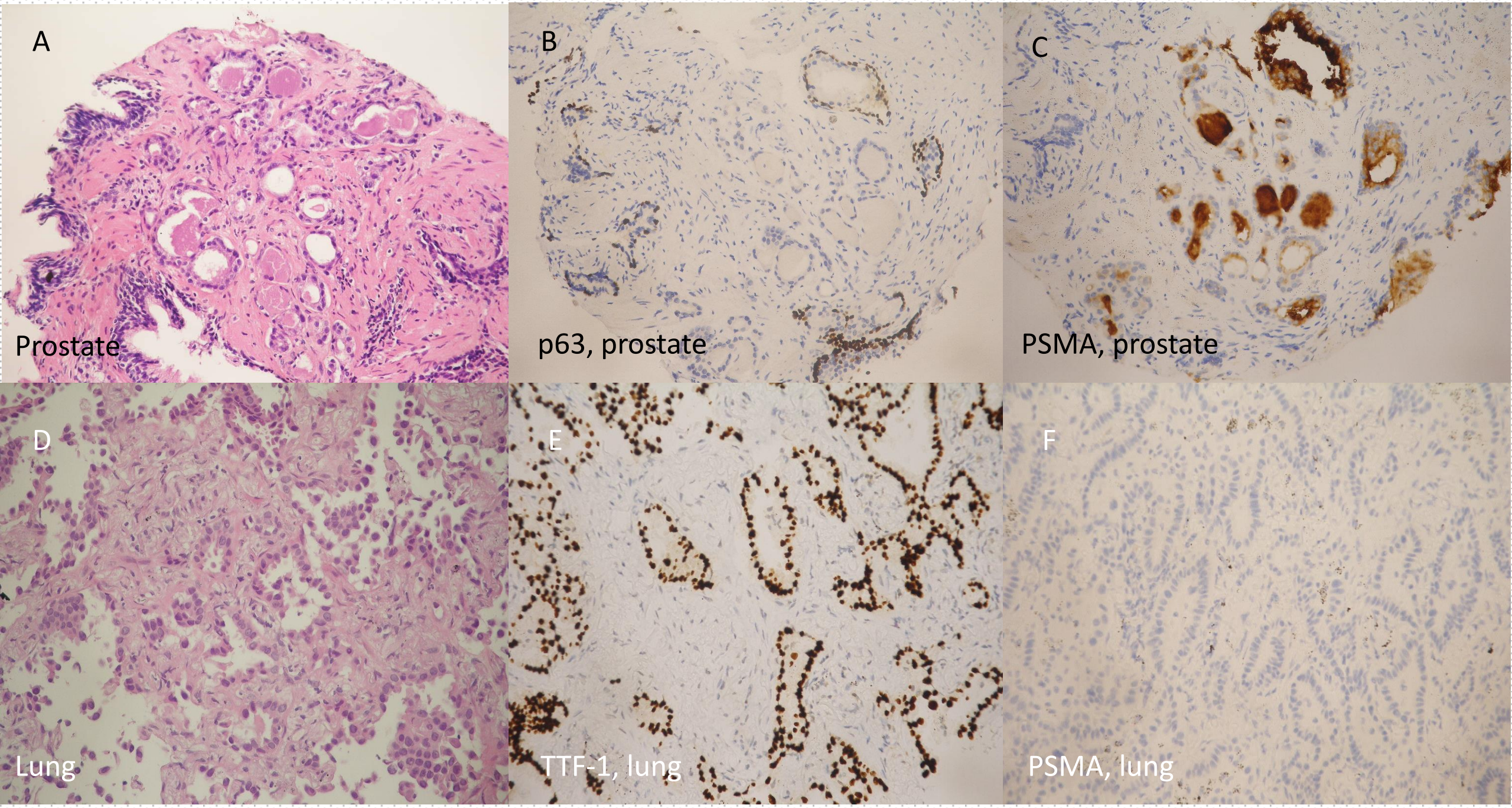
LIMITATIONS OF PSMA-PET SCAN

PSMA-PET positive malignant lesions:

Hepatocellular carcinoma[1], lung cancer[2], renal cancer[3], thyroid carcinoma[4]…

[1]Sasikumar et al., EJNMMI 2016, [2]Pyka et al., JNM 2015; [3]Rowe et al., Clin Nucl Med 2016; [3]Demirci et al., EJNMMI 2014; [4]Verburg et al., EJNMMI 2015;

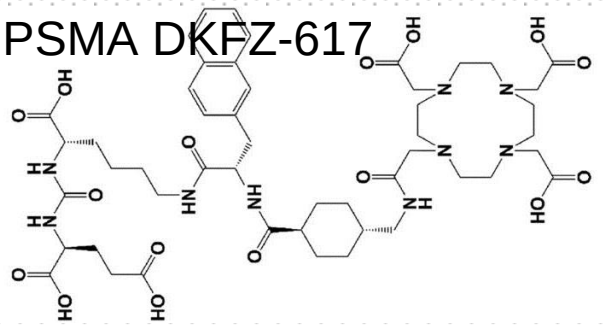

A
S
PSMA
B
FDG
C
PSMA
D
FDG
E
MRI DWI


A
Prostate
B
p63, prostate
C
PSMA, prostate
D
Lung
E
TTF-1, lung
F
PSMA, lung

^{177}Lu-PSMA-radioligand therapy (PRLT)

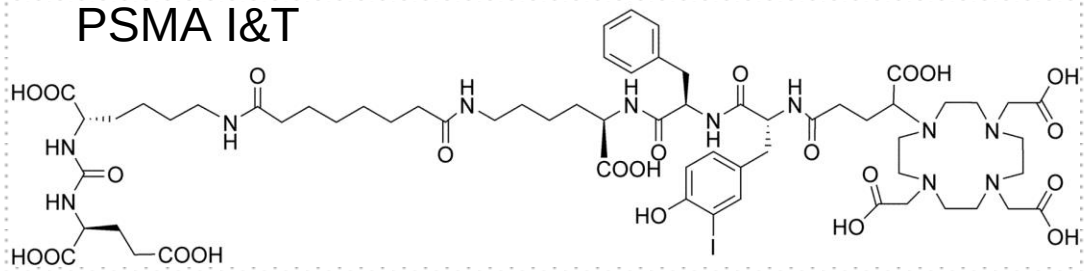
Theranostic PSMA-ligands for endoradiotherapy using ^{177}Lu

PSMA DKFZ-617



Benešová et al., JNM 2015

PSMA I&T



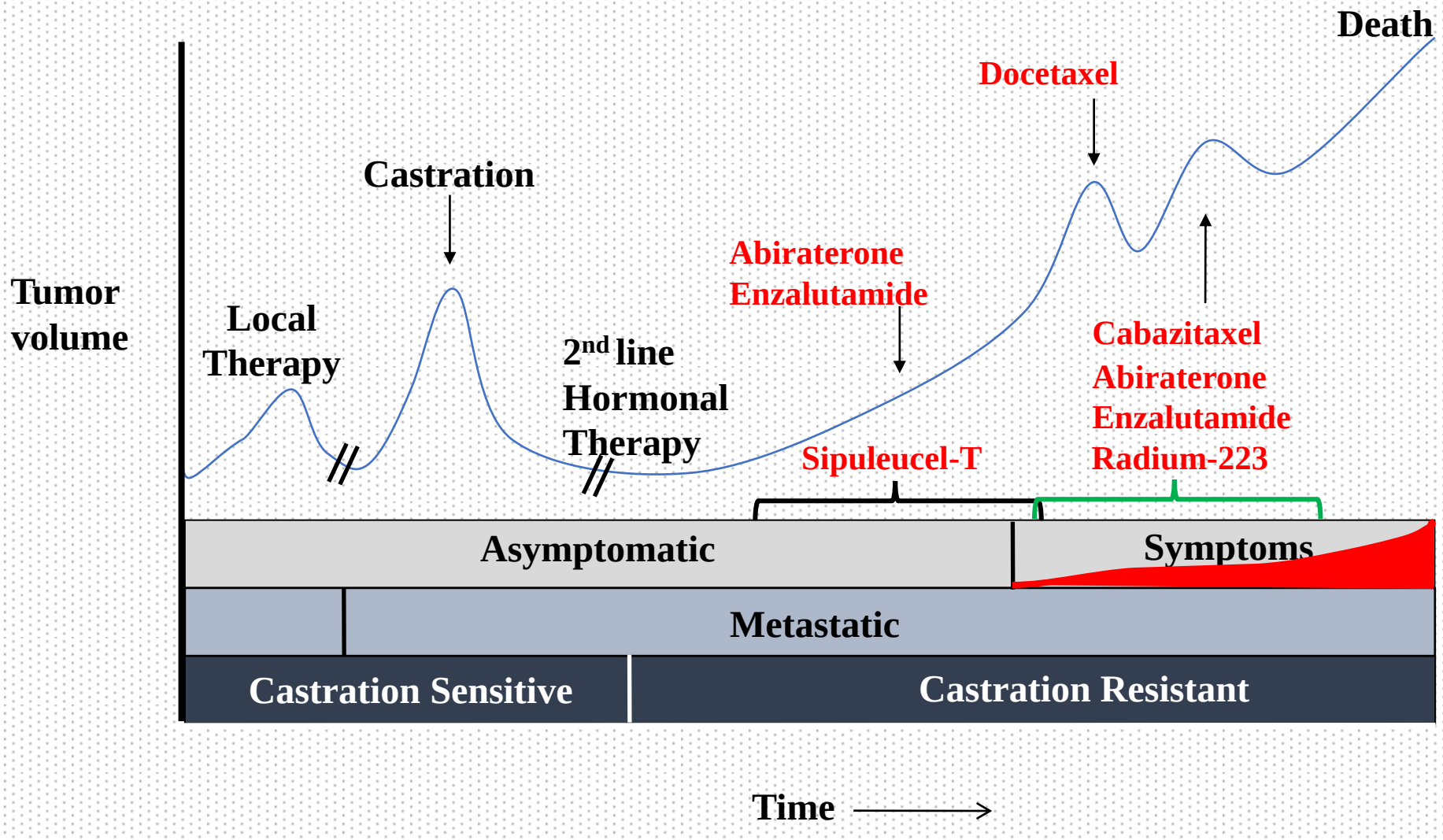
Weineisen et al, JNM 2015

Increasing number of retrospective case series , e.g. [1] [2] [3] [4]

- 50% PSA decline in 30-60% of patients
- rare event of grade III/IV toxicities

- [1] Ahmadzadehfar et al, Oncotarget 2016, [2] Kratochwil et al, JNM 2016, [3] Rahbar et al, JNM 2016, [4] Baum RP et al, JNM 2016

Prostate Cancer - Clinical State and Treatment Options



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

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*

Summary

Background Progressive metastatic castration-resistant prostate cancer is a highly lethal disorder and new effective therapeutic agents that improve patient outcomes are urgently needed. Lutetium-177 [^{177}Lu]-PSMA-617, a radiolabelled small molecule, binds with high affinity to prostate-specific membrane antigen (PSMA) enabling beta particle therapy targeted to metastatic castration-resistant prostate cancer. We aimed to investigate the safety, efficacy, and effect on quality of life of [^{177}Lu]-PSMA-617 in men with metastatic castration-resistant prostate cancer who progressed after standard treatments.

Methods In this single-arm, single-centre, phase 2 trial, we recruited men (aged 18 years and older) with metastatic castration-resistant prostate cancer and progressive disease after standard treatments, including taxane-based chemotherapy and second-generation anti-androgens, from the Peter MacCallum Cancer Centre, Melbourne, VIC, Australia. Patients underwent a screening PSMA and FDG-PET/CT to confirm high PSMA-expression. Eligible patients had progressive disease defined by imaging (according to Response Evaluation Criteria In Solid Tumours [RECIST] or bone scan) or new pain in an area of radiographically evident disease, and were required to have an Eastern Cooperative Oncology Group (ECOG) performance status score of 2 or lower. Eligible patients received up to four cycles of intravenous [^{177}Lu]-PSMA-617, at six weekly intervals. The primary endpoint was PSA response according to Prostate Cancer Clinical Trial Working Group criteria defined as a greater than 50% PSA decline from baseline and toxicity according to CTCAE. Additional primary endpoints were imaging responses (as measured by bone scan, CT, PSMA, and FDG PET/CT) and quality of life (assessed with the EORTC-Q30 and Brief Pain Inventory-Short Form questionnaires), all measured up to 3 months post completion of treatment. This trial is registered with the Australian New Zealand Clinical Trials Registry, number 12615000912583.

Findings Between Aug 26, 2015, and Dec 8, 2016, 43 men were screened to identify 30 patients eligible for treatment. 26 (87%) had received at least one line of previous chemotherapy (80% docetaxel and 47% cabazitaxel) and 25 (83%) received prior abiraterone acetate, enzalutamide, or both. The mean administered radioactivity was 7·5 GBq per cycle. 17 (57%) of 30 patients (95% CI 37–75) achieved a PSA decline of 50% or more. There were no treatment-related deaths. The most common toxic effects related to [^{177}Lu]-PSMA-617 were grade 1 dry mouth recorded in 26 (87%) patients, grade 1 and 2 transient nausea in 15 (50%), and G1–2 fatigue in 15 (50%). Grade 3 or 4 thrombocytopenia possibly attributed to [^{177}Lu]-PSMA-617 occurred in four (13%) patients. Objective response in nodal or visceral disease was reported in 14 (82%) of 17 patients with measurable disease. Clinically meaningful improvements in pain severity and interference scores were recorded at all timepoints. 11 (37%) patients experienced a ten point or more improvement in global health score by the second cycle of treatment.

Interpretation Our findings show that radionuclide treatment with [^{177}Lu]-PSMA-617 has high response rates, low toxic effects, and reduction of pain in men with metastatic castration-resistant prostate cancer who have progressed after conventional treatments. This evidence supports the need for randomised controlled trials to further assess efficacy compared with current standards of care.

Lancet Oncol 2018; 19: 825–33

Published Online
May 8, 2018
http://dx.doi.org/10.1016/S1470-2045(18)30198-0

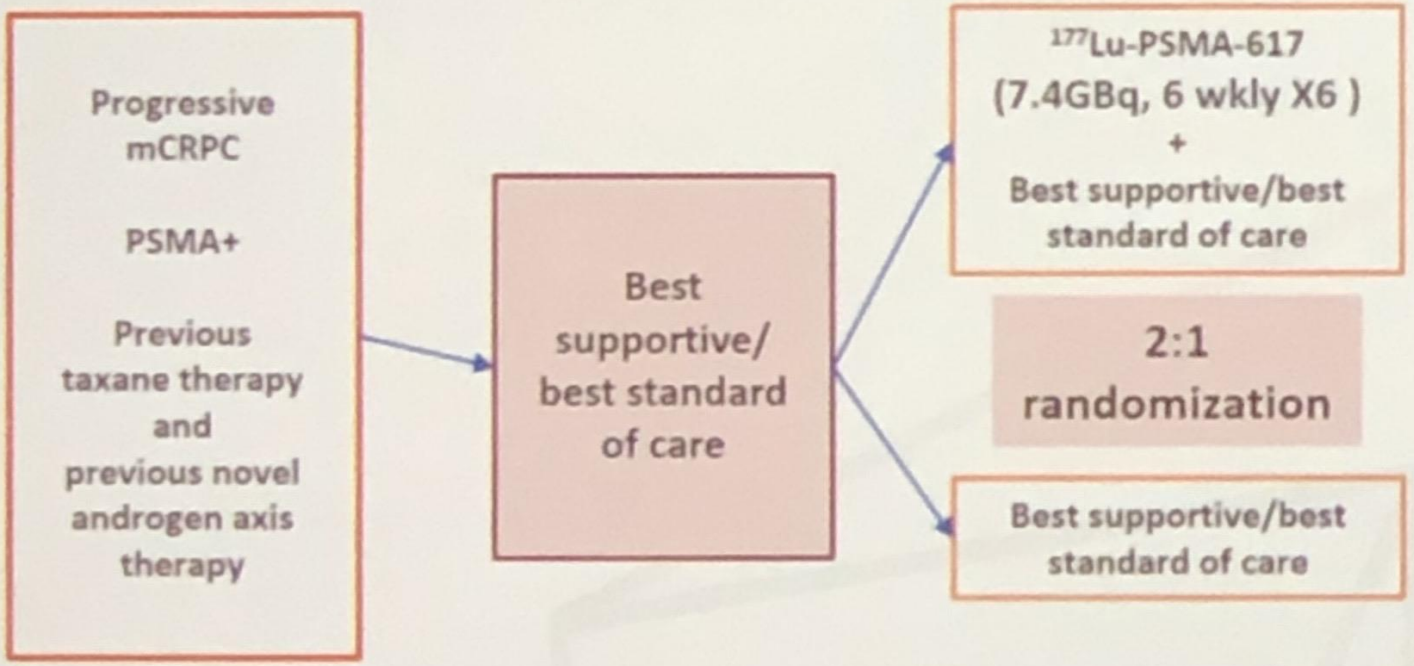
See Comment page 725

*Joint co-authors

Department of Cancer Imaging (Prof M S Hofman MBBS, Prof R J Hicks MD, J Ferdinandus, S P Thang MBChB, T Akhurst MBBS, A Iravani MD, G Kong MBBS, A Ravi Kumar MBBS, P Eu BSc, P Jackson PhD, M Scalzo), **Department of Radiation Oncology** (J Violet MBBS, S G Williams MBBS); **Cancer Surgery** (D G Murphy MB BCh), **Department of Medical Oncology** (S Sandhu MBBS), **Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia** (Prof M S Hofman, Prof R J Hicks, T Akhurst, D G Murphy, S Sandhu)

Correspondence to:
Prof Michael Hofman, Department of Cancer Imaging, Peter MacCallum Cancer Centre, Melbourne 3000, VIC, Australia
michael.hofman@petermac.org

VISION Trial: ^{177}Lu-PSMA versus best supportive care



Primary Endpoint

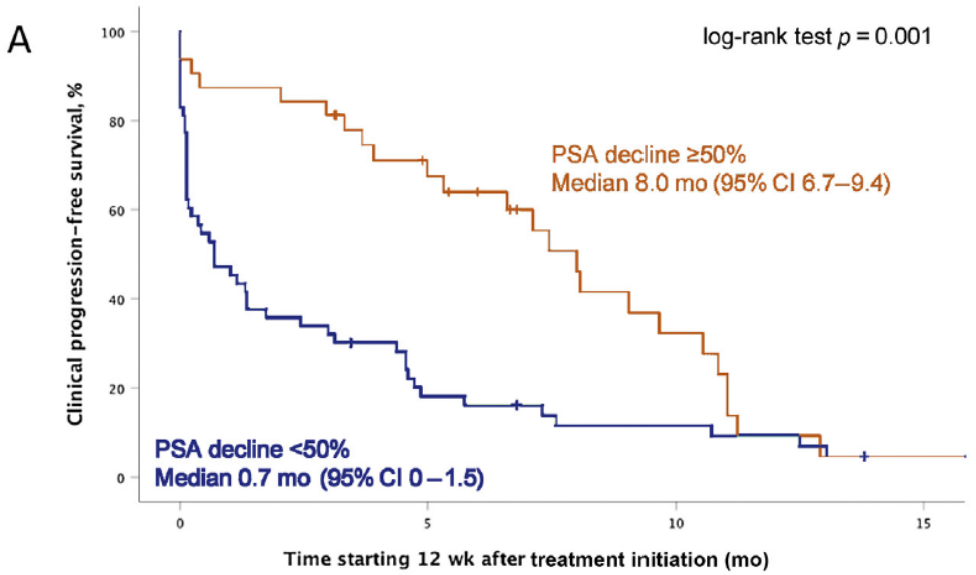
- Overall survival
- Radiographic progression-free survival (rPFS)

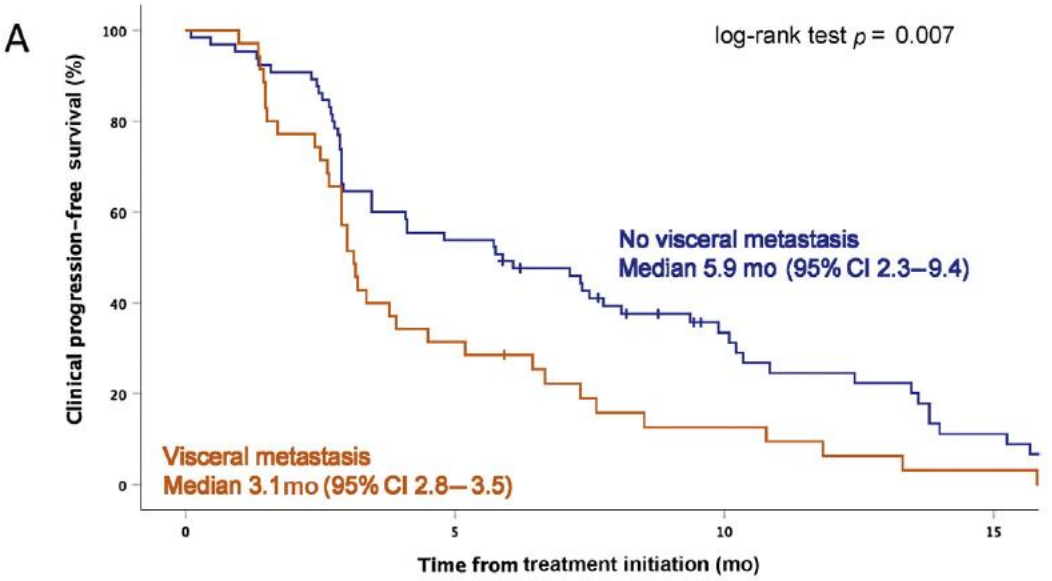
Key Secondary Endpoints

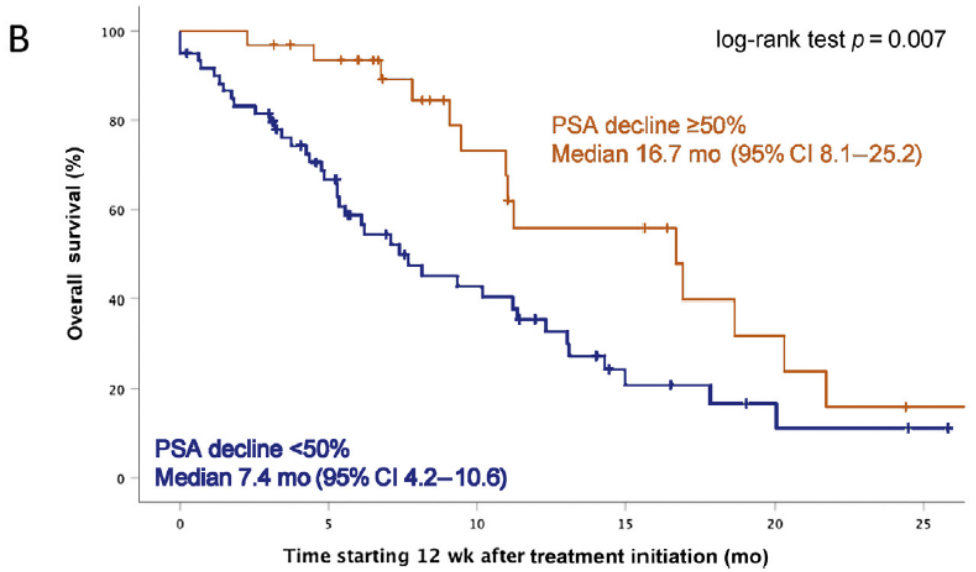
- PSA Response
- RECIST response
- Time to first symptomatic skeletal event (SSE)

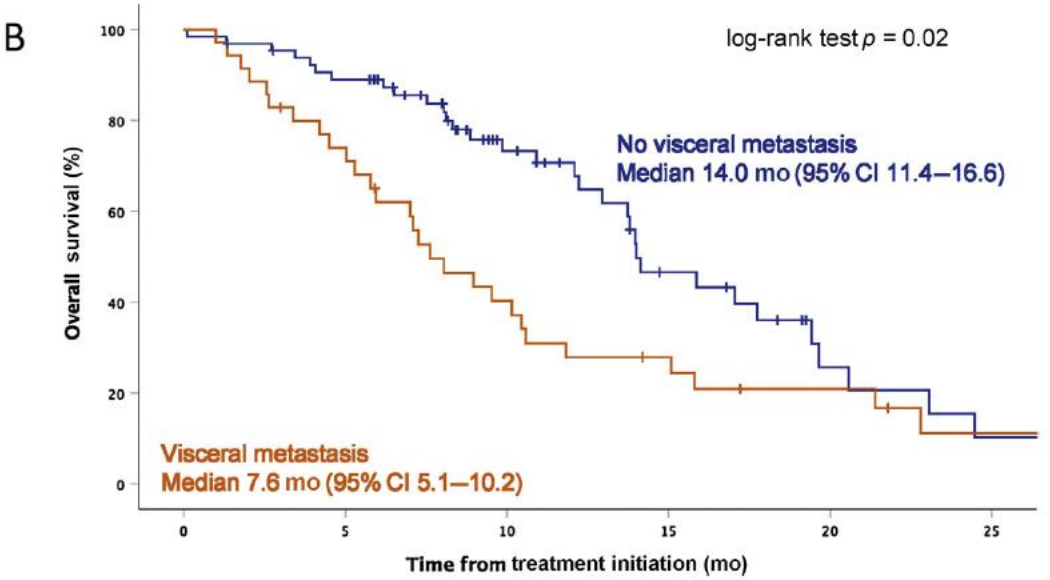
- 9 Countries (NA and EU)
- >750 patients recruited
- 12-14 months FU min 15 month

ENDOCYTE
A Novartis Company


A
log-rank test p = 0.001
PSA decline ≥50%
Median 8.0 mo (95% CI 6.7–9.4)
PSA decline <50%
Median 0.7 mo (95% CI 0–1.5)
Clinical progression-free survival, %
Time starting 12 wk after treatment initiation (mo)


A
log-rank test p = 0.007
No visceral metastasis
Median 5.9 mo (95% CI 2.3–9.4)
Visceral metastasis
Median 3.1mo (95% CI 2.8–3.5)
Clinical progression-free survival (%)
Time from treatment initiation (mo)


B
log-rank test p = 0.007
PSA decline ≥50%
Median 16.7 mo (95% CI 8.1–25.2)
PSA decline <50%
Median 7.4 mo (95% CI 4.2–10.6)
Overall survival (%)
Time starting 12 wk after treatment initiation (mo)


B
log-rank test p = 0.02
No visceral metastasis
Median 14.0 mo (95% CI 11.4–16.6)
Visceral metastasis
Median 7.6 mo (95% CI 5.1–10.2)
Overall survival (%)
Time from treatment initiation (mo)

LuPSMA treatment – basic information

Klinikum rechts der Isar
Department of Nuclear Medicine
Ismaninger Str. 22
81675 Munich, Germany

Inclusion criteria:

- mCRPC
- Previous treatment with
  - novel androgen receptor directed therapy and
  - taxane based chemotherapy or ineligibility
- ECOG PS 0 or 1
- creatinine <1.5 mg/dl
- sufficient bone marrow function (Hb >8 g/dl, Leucos > 2.5 x 10^9/L, Thrombos < 80 x 10^9/L)

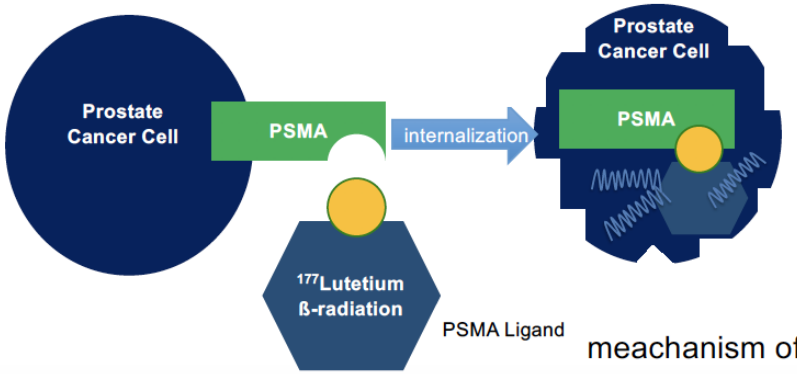
Concomitant medication:

- No contraindication for any supportive treatment
- Continue on basic ADT
- Stop all other active antitumor treatments (chemotherapy, second line ADT, Radium 223)

Most common side effects (Grade III/IV):

- 10-15% hematological toxicitiy
- 5-15% xerostomia
- 5-10% nausea/vomiting

(Rahbar et al JNM 2017,
Heck MM et al Eur Urol 2018)



meachanism of action

LuPSMA treatment – scheme of treatment

Klinikum rechts der Isar
Department of Nuclear Medicine
Ismaninger Str. 22
81675 Munich, Germany

1. Injection ^{177}Lu-PSMA
(3 days in-patient on S2a)

↓ 6 weeks

2. Injection ^{177}Lu-PSMA
(3 days in-patient on S2a)

↓ 4 weeks

PET/CT
(therapy response?)
Send images/labs

↓ 2 weeks

In cases of stable disease/
good response:

Another 2 cycles within 6 weeks
Followed by restaging PET/CT

Up to six cycles possible in a row

Thank You~

Email: drTsengJR@gmail.com