VI Congresso Nazionale di Osteoncologia ISO

14/15 novembre 2017 Padova Palazzo Zacco

L'approccio Teranostico al carcinoma della prostata con 68Ga e 177Lu-Antigene prostata-specifico della membrana (PSMA)

Stefano Severi IRCCS IRST Meldola

ISTITUTO SCIENTIFICO ROMAGNOLO PER LO STUDIO E LA CURA DEI TUMORI

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

Eur J Nucl Med Mol Imaging (2014) 41:1280–1292
DOI 10.1007/s00259-014-2713-y

ORIGINAL ARTICLE

Radiation dosimetry and first therapy results with a $^{124}I/^{131}$ I-labeled small molecule (MIP-1095) targeting PSMA for prostate cancer therapy

Christian M. Zechmann · Ali Afshar-Oromieh · Tom Armor · James B. Stubbs · Walter Mier · Boris Hadaschik · John Joyal · Klaus Kopka · Jürgen Debus · John W. Babich · Uwe Haberkorn

Pharmaceuticals **2014**, *7*, 517-529; doi:10.3390/ph7050517

OPEN ACCESS

pharmaceuticals

ISSN 1424-8247

www.mdpi.com/journal/pharmaceuticals

99mT

Membrane An

Shawn M. Hillier, Kevin P. M
William C. Eckelman, John J

Molecular Insight Pharmaceuti

Article

Synthesis, Radiolabelling and *In Vitro* Characterization of the Gallium-68-, Yttrium-90- and Lutetium-177-Labelled PSMA Ligand, CHX-A''-DTPA-DUPA-Pep

Benjamin Baur [1,†,*], Christoph Solbach [1,†], Elena Andreolli [1,2], Gordon Winter [1], Hans-Jürgen Machulla [1] and Sven N. Reske [1]

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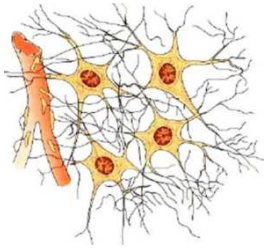
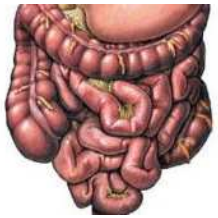
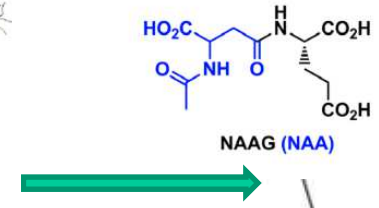
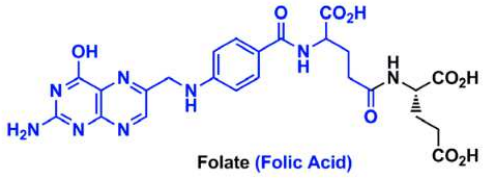
Transmembrane enzyme

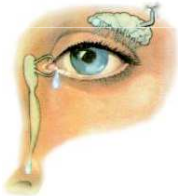
Glutamate carboxypeptidase type II

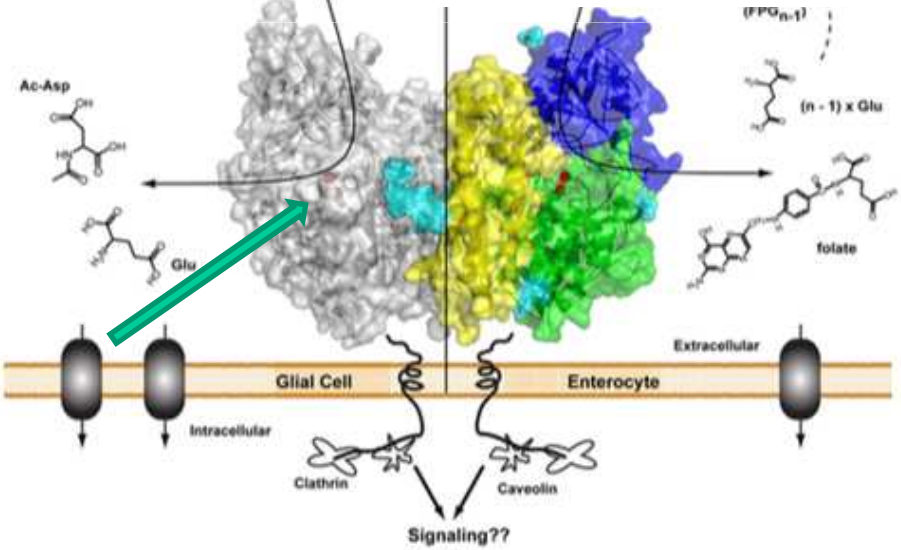


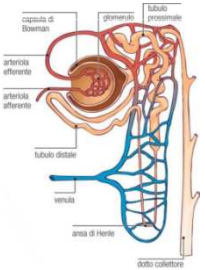


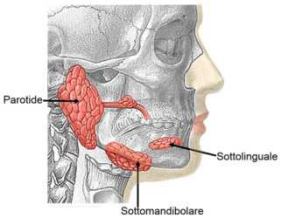


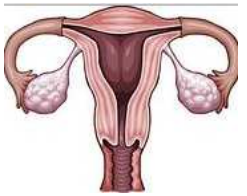


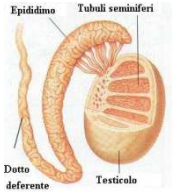












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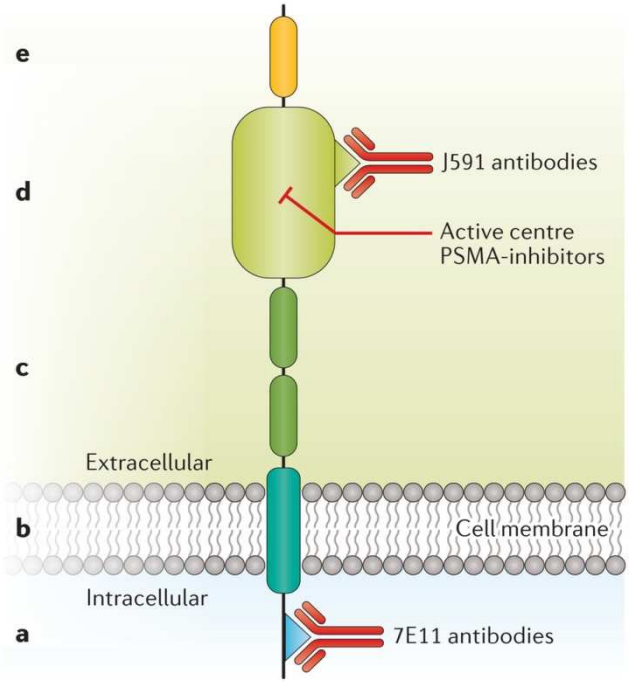
PSMA: Prostate Specific Membrane Antigen



Nature Reviews | Urology

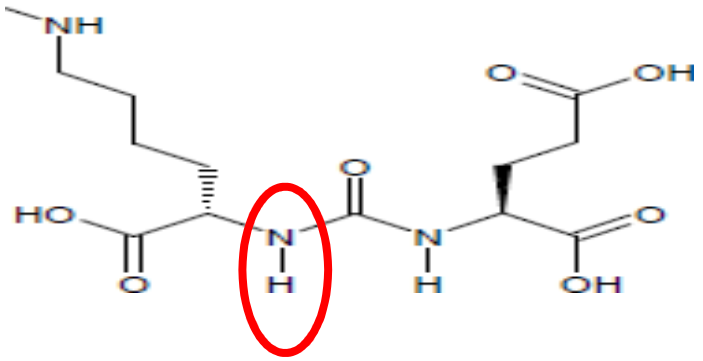
Enzima overespresso in quasi tutti i tumori prostatici,
E' una **glicoproteina** che rappresenta un target ottimale per un anticorpo monoclonale (*Prostascint e J591*)

CARBOSSIPEPTIDASI II (GCPII)

GCPII è una glicoproteina di membrana con attività **zinco-proteasi** che catalizza la reazione di idrolisi del glutammato dal NAAG (N-acetil-aspartil-glutammato)

Lisina- urea- glutammato

Inibitore a base ureidica di GCPII



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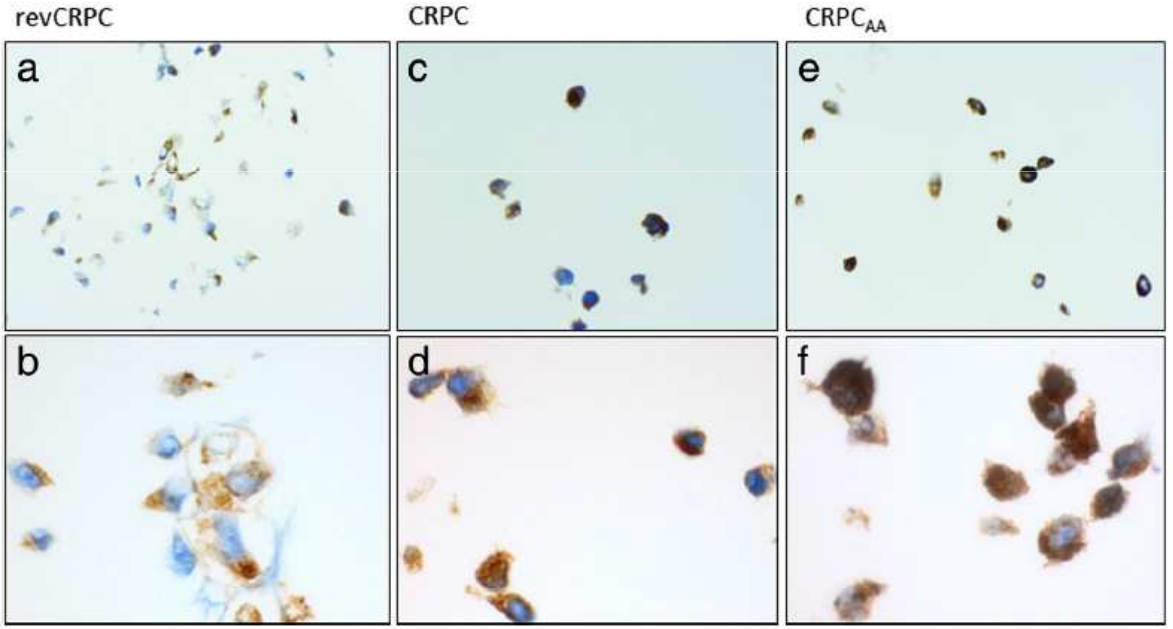
PSMA and ADT

ORIGINAL RESEARCH Open Access

Alterations in androgen deprivation enhanced prostate-specific membrane antigen (PSMA) expression in prostate cancer cells as a target for diagnostics and therapy

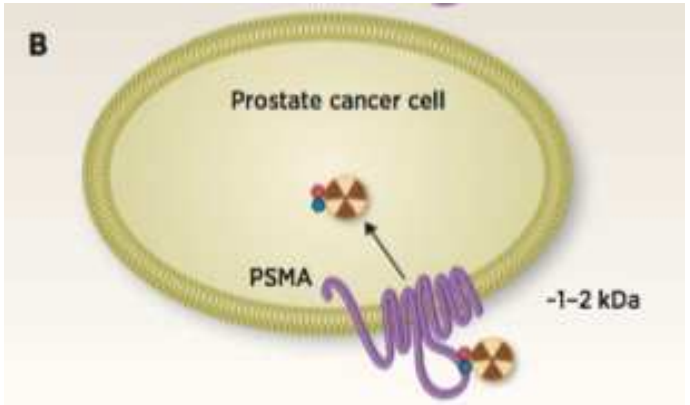


Immunohistological staining of PSMA in the three investigated cell lines subtypes. Cytoplasmic PSMA (*brown signal*) in revCRPC (**a** ×20, **b** CRPCAA (**e** ×20, **f** ×60)

Meller et al. EJNMMI Research (2015) 5:66

PSMA and PCa

- **PSMA increased expression in:**
  - High Gleason Score
  - CRPC (revCRPC < CRPC < $CRPC_{AA}$)
  - On Testosterone withdrawal



- **PSMA overexpressed on CRPC cells membrane:**
  - Highly specific target

- **PSMA internalisation upon binding with inhibitors:**
  - Suitable for PRRT

Limits of Choline PET

Metabolic PET probes ^{11}C- or ^{18}F-Choline fail to detect sites of recurrence in PCa patients with low serum PSA levels (<1.0ng/dl).
In this scenario its use is discouraged by the EAU GL 2015

Guidelines on

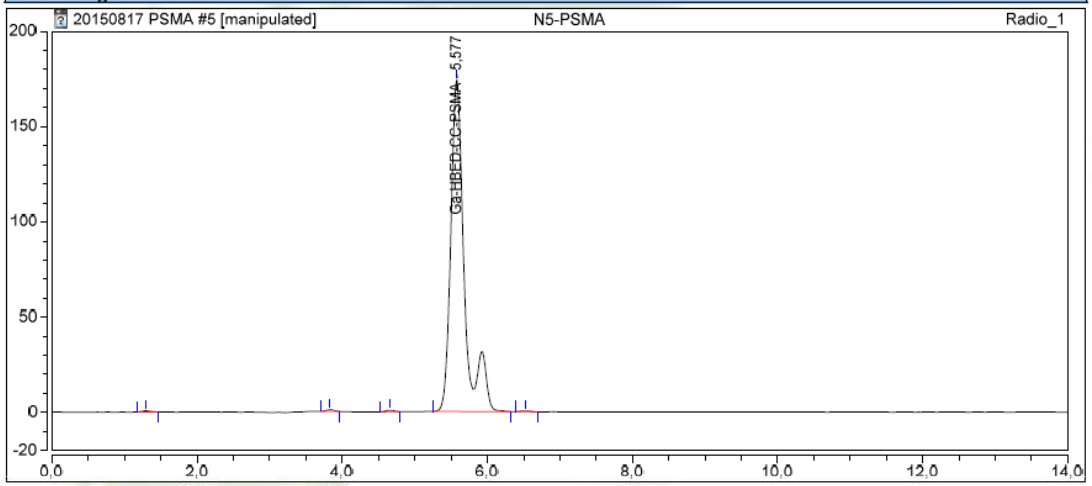
Prostate Cancer

6.10.4.6 Guidelines for imaging and second-line therapy after treatment with curative intent

Biochemical recurrence (BCR) after RP	LE	GR
In the case of BCR, bone scan and abdominopelvic CT should be performed only in patients with a PSA level > 10 ng/mL, or with high PSA kinetics (PSA-DT < 6 mo or a PSA velocity > 0.5 ng/mL/mo) or in patients with symptoms of bone disease.	3	A
A Choline PET/CT is not recommended in patients with BCR and a PSA-level < 1 ng/mL	3	A
Biochemical recurrence after RT		
In patients with BCR who are candidates for local salvage therapy, prostate mpMRI may be used to localise abnormal areas and guide biopsy.	3	C

^{68}Ga-HBED-CC-PSMA-11

Chromatogram



Integration Results

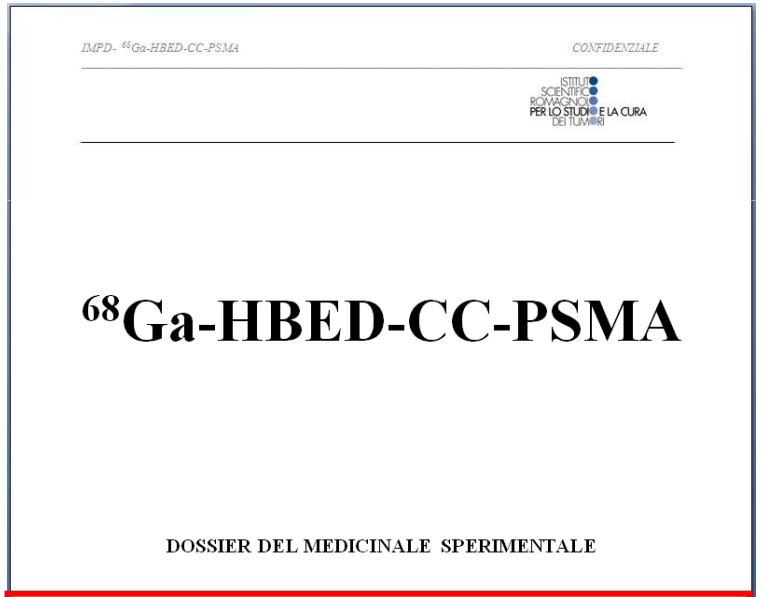
No.	Peak Name	Retention Time min	Area cps-corr*min	Height cps-corr	Relative Area %	Relative Height %	Resolution (EP
1		1,290	0,094	0,676	0,24	0,38	n.a.
2		3,830	0,099	0,854	0,26	0,48	n.a.
3		4,660	0,101	0,802	0,26	0,45	n.a.
4	Ga-HBED-CC-PSMA	5,577	37,991	174,023	99,04	98,43	n.a.
5		6,530	0,074	0,442	0,19	0,25	n.a.
Total:			**38,359**	**176,797**	**100,00**	**100,00**	

12 minuti totali

Purezza radiochimica media: 98%

Resa: 79% ndc

Stabilità: 2 ore


IMPD- ^{68}Ga-HBED-CC-PSMA CONFIDENZIALE

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^{68}Ga-HBED-CC-PSMA

DOSSIER DEL MEDICINALE SPERIMENTALE

INVIATO AIFA LUGLIO

APPROVATO SETTEMBRE

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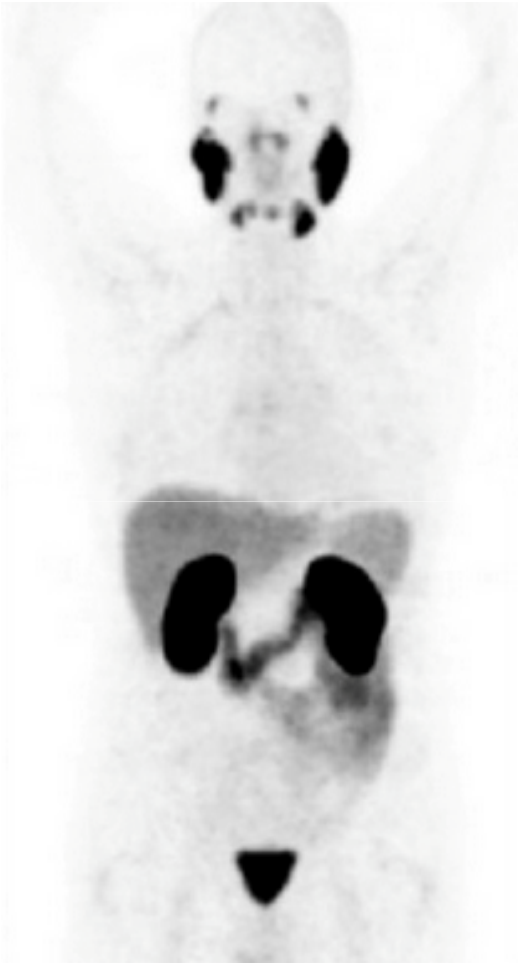
^{68}Ga-PSMA^{HBED}: Biodistribuzione



Attività: 2– 3 MBq/kg (min. 120 MBq)

Sedi di fisiologica captazione/accumulo :

Ghiandole Salivari

Reni / Vescica

Digiuno

Milza - Fegato

Escrezione Urinaria

Dose Effettiva (150MBq): 3 mSv

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Eur J Nucl Med Mol Imaging. 2015 Nov 12. [Epub ahead of print]

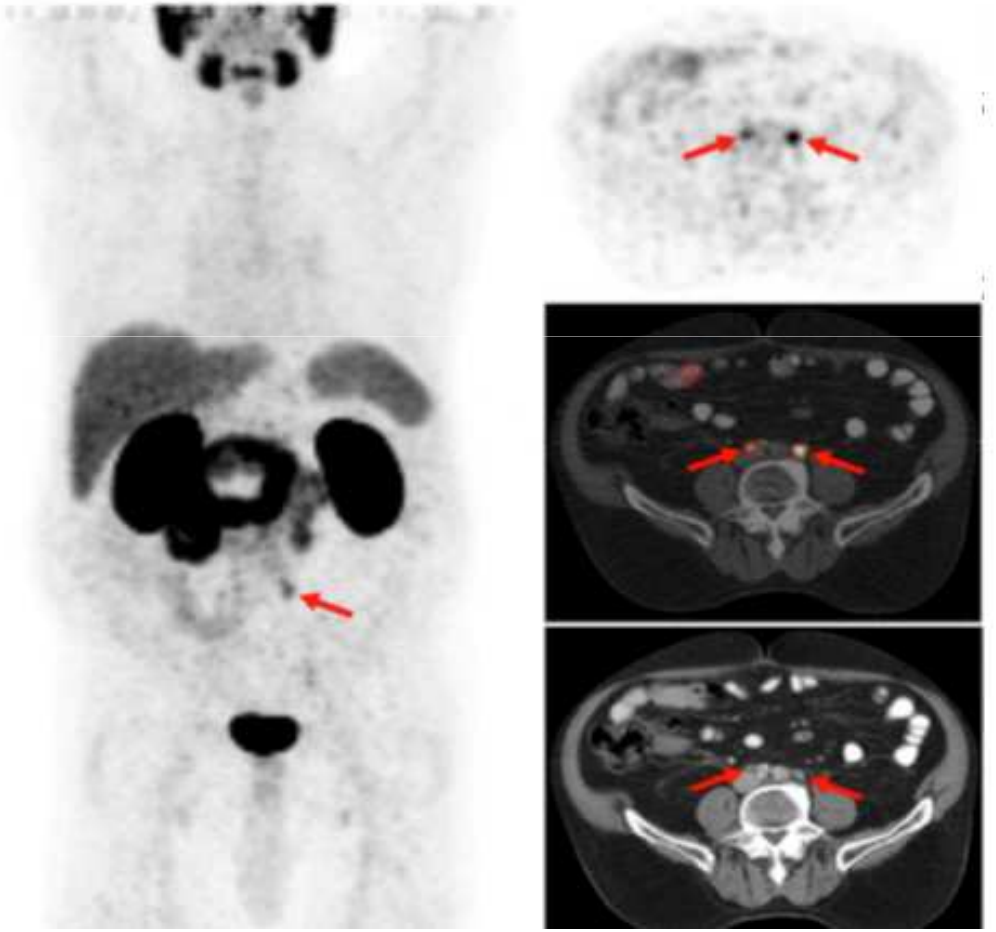
Extent of disease in recurrent prostate cancer determined by [68Ga]PSMA-HBED-CC PET/CT in relation to PSA levels, PSA doubling time and Gleason score.

Verburg FA[1,2], Pfister D[3], Heidenreich A[3], Vogg A[4], Drude NI[4], Vöö S[5], Mottaghy FM[4,5], Behrendt FF[4].

Post-radical prostatectomy
PSA: **0.18 ng/ml**

PET/CT revealed at least two common iliac nodal metastases subsequently subjected to radiotherapy

Post-RT PSA: 0.03 ng/ml



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^{68}Ga-PSMA HBED-PET/CT in the evaluation of the biochemical relapse in patients with a history of prostate cancer radically treated

Protocol Code: IRST185.02

Patients must have histologically or cytologically confirmed prostate cancer;

Radical treatment for prostate cancer (radiotherapy-brachitherapy or surgery);

Patients with PSA progression defined as PSA > 1.0 ng/mL and/or PSA rising defined as 2 subsequent values sho[PSA > 0.2 ng/ml]least 1 week apart;

18F-Choline PET/CT negative or doubtful.

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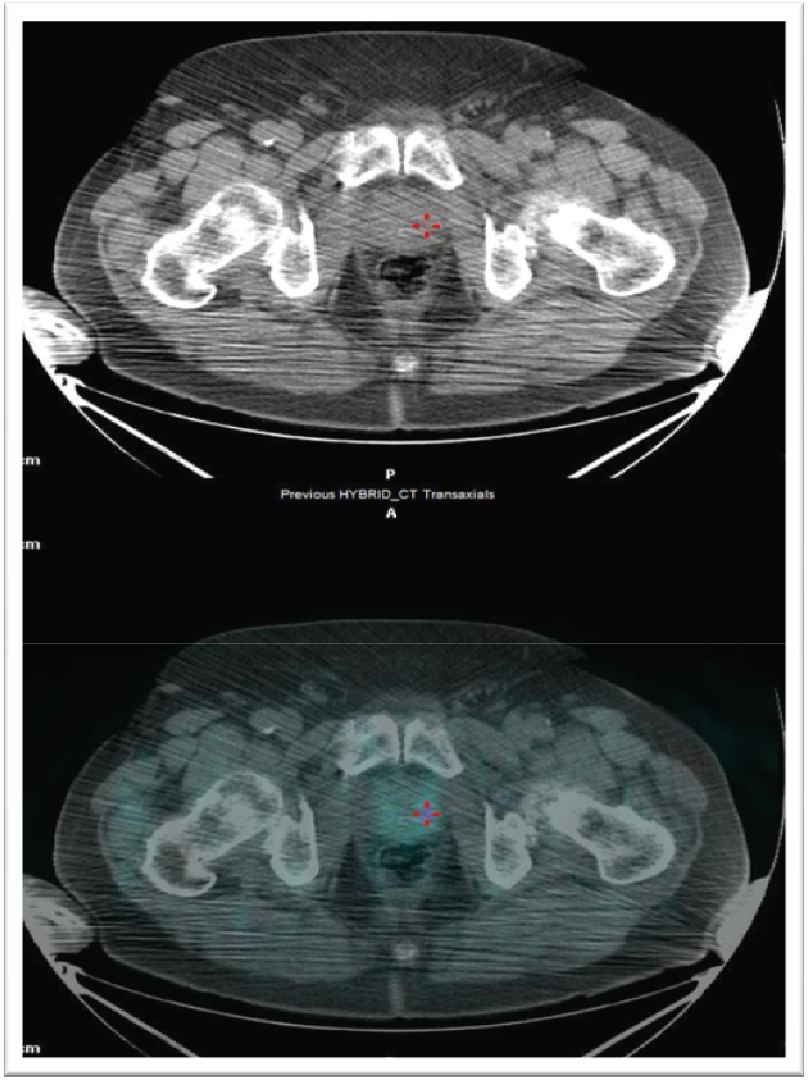
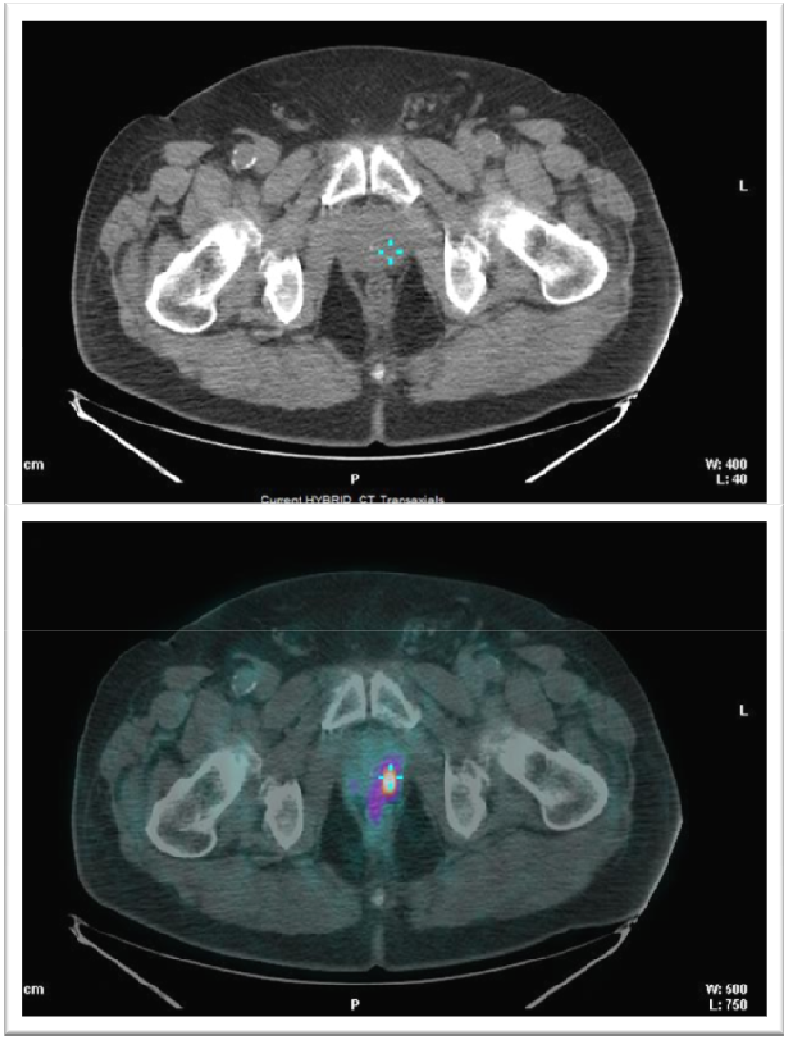


^{18}FMC dicembre 2015



^{68}Ga-PSMA gennaio 2016

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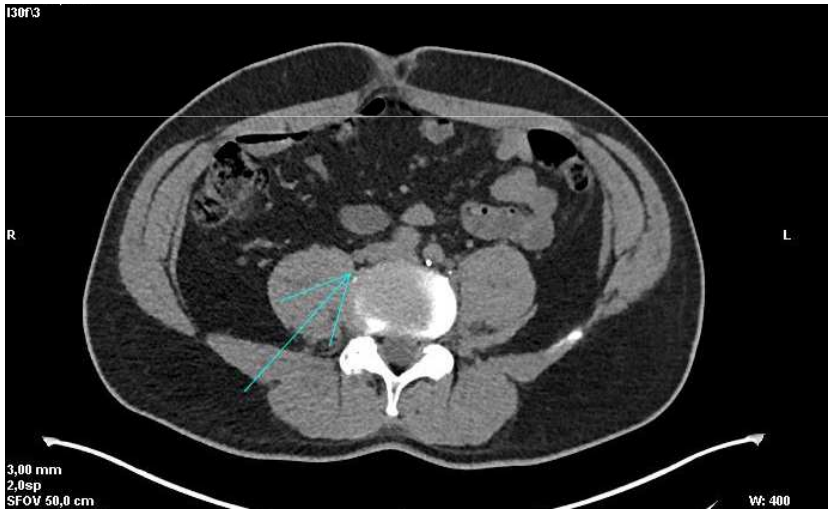
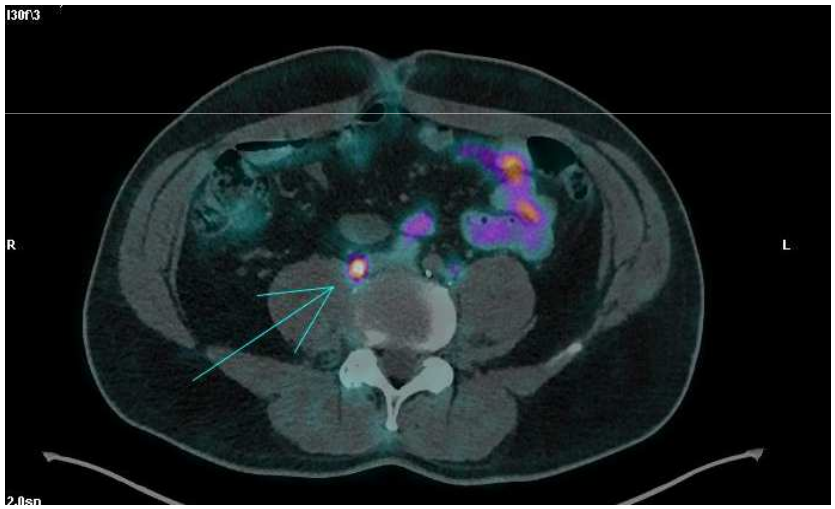
V.D. 60 anni, PSA 66.9 ng/ml all'esordio,

07/2015 prostatectomia, Gleason (4+5), 17/27 ln pos, <u>pT3b pN1</u>
Dopo chirurgia PSA 0.022 ng/ml 08/2015

Recidiva biochimica PSA 0.231 ng/ml 03/2016





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High detection rate of ^{68}Ga-PSMA PET/CT in relapsed prostate cancer patients with low PSA levels and/or negative choline PET/CT: a prospective study

METHODS: 109 patients with biochemical recurrence of PCa and PSA levels <1 ng/ml (group A, n=41) or > 1 ng/ml (group B, n=68) were enrolled in this prospective study.

Table 2: Sensitivity, specificity and diagnostic accuracy, NPV in and PPV of patients studies both groups (A and B)

	Group A (%)	Group B (%)
Sensitivity	60.00	91.80
Specificity	87.50	42.86
Accuracy	70.73	86.76
NPV	58.33	37.50
PPV	88.24	93.30

Clin Physiol Funct Imaging (2017)

doi: 10.1111/cpf.12480

INVITED REVIEW

^{68}Ga-PSMA PET/CT for the detection of bone metastases in prostate cancer: a systematic review of the published literature

Helle D. Zacho[1,2], Julie B. Nielsen[1,2], Uwe Haberkorn[3,4], Louise Stenholt[5] and Lars J. Petersen[1,2]

[1]Department of Nuclear Medicine, Clinical Cancer Research Center, Aalborg University Hospital, [2]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark, [3]Department of Nuclear Medicine, University Hospital of Heidelberg, [4]Clinical Cooperation Unit Nuclear Medicine, German Cancer Research Centre, Heidelberg, Germany and [5]Medical Library, Aalborg University Hospital, Aalborg, Denmark

For primary staging, ^{68} Ga-PSMA PET/CT outperformed bone scans, while the superiority of ^{68} Ga-PSMA PET/CT compared with bone scans with respect to biochemical recurrence and metastatic castration-resistant prostate cancer (mCRPC) remains to be demonstrated.

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Eur Radiol. 2017 Aug 4. doi: 10.1007/s00330-017-4994-6. [Epub ahead of print]

EUROPEAN JOURNAL OF RADIOLOGY

Comparison of hybrid 68Ga-PSMA-PET/CT and 99mTc-DPD-SPECT/CT for the detection of bone metastases in prostate cancer patients: Additional value of morphologic information from low dose CT.

Janssen JC[1], Meißner S[2], Woythal N[3], Prasad V[3], Brenner W[3], Diederichs G[2], Hamm B[2], Makowski MR[2].

	Accuracy	Sensitivity	Specificity
^{8}Ga-PSMA-PET/CT	1.00	97.7%	100%
^{99m}Tc DPD SPECT/CT	0.83	69.4%	98.3%

Ga-PSMA-PET outperforms ^{99m} Tc-DPD-SPECT in skeletal staging in prostate cancer patients

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Cancer of the prostate: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

C. Parker[1], S. Gillessen[2], A. Heidenreich[3] & A. Horwich[4], on behalf of the ESMO Guidelines Committee*

[1]Royal Marsden Hospital, Sutton, UK; [2]Department of Oncology/Hematology, Kantonsspital St Gallen, St Gallen, Switzerland; [3]Department of Urology, Uniklinik RWTH Aachen, Aachen, Germany; [4]Institute of Cancer Research, Sutton, UK

Treatment of relapse after radical therapy

- Following RP, patients should have their serum PSA level monitored. Salvage RT to the prostate bed is recommended in the event of PSA failure. Salvage RT should start early (e.g. PSA <0.5 ng/ml) [III, B].
- Early ADT is not routinely recommended for men with biochemical relapse unless they have symptomatic local disease, or proven metastases, or a PSA doubling time <3 months [IV, B].
- Intermittent ADT is recommended for men with biochemical relapse after radical RT starting ADT [I, B].

Management of advanced/metastatic disease

- Continuous ADT is recommended as first-line treatment of metastatic, hormone-naïve disease [I, A].
- Men starting ADT should be informed that regular exercise reduces fatigue and improves quality of life [30] [I, A].
- ADT plus docetaxel is recommended as first-line treatment of metastatic, hormone-naïve disease in men fit enough for chemotherapy [1, A].

Treatment of castrate-resistant prostate cancer (CRPC)

- Abiraterone or enzalutamide are recommended for asymptomatic/mildly symptomatic men with chemotherapy-naïve metastatic CRPC [I, A].
- Radium-223 is recommended for men with bone-predominant, symptomatic metastatic CRPC without visceral metastases [I, A].
- Docetaxel is recommended for men with metastatic CRPC [I, A].
- Sipuleucel-T is an option in asymptomatic/mildly symptomatic patients with chemotherapy-naïve metastatic CRPC [II, B].
- In patients with metastatic CRPC in the post-docetaxel setting, abiraterone, enzalutamide, cabazitaxel and radium-223 (in those without visceral disease) are recommended options [I, A].

Table 3. Stage-matched therapeutic strategies

Localised disease	
Low risk	Active surveillance Brachytherapy Radical prostatectomy Radical radiotherapy
Intermediate risk	Active surveillance Brachytherapy Radical prostatectomy Radical radiotherapy ± neoadjuvant ADT
High risk	Neoadjuvant ADT + radical radiotherapy + adjuvant ADT Radical prostatectomy + pelvic lymphadenectomy
Locally advanced disease	
	Neoadjuvant ADT + radical radiotherapy + adjuvant ADT Radical prostatectomy + pelvic lymphadenectomy
Metastatic disease	
Hormone-naïve	ADT
Castration-resistant (first line)	Abiraterone Docetaxel Enzalutamide Radium-223 Sipuleucel-T
Second line (post-docetaxel)	Abiraterone Cabazitaxel Enzalutamide Radium-223

Options listed in alphabetical order.
ADT, androgen deprivation therapy.

ADT may cause hot flushes, lethargy, mood changes, osteoporosis, insulin resistance and muscle weakness.

recommendation

- Men on long-term ADT should be monitored for side-effects including osteoporosis (using bone densitometry) and metabolic syndrome [IV, B].

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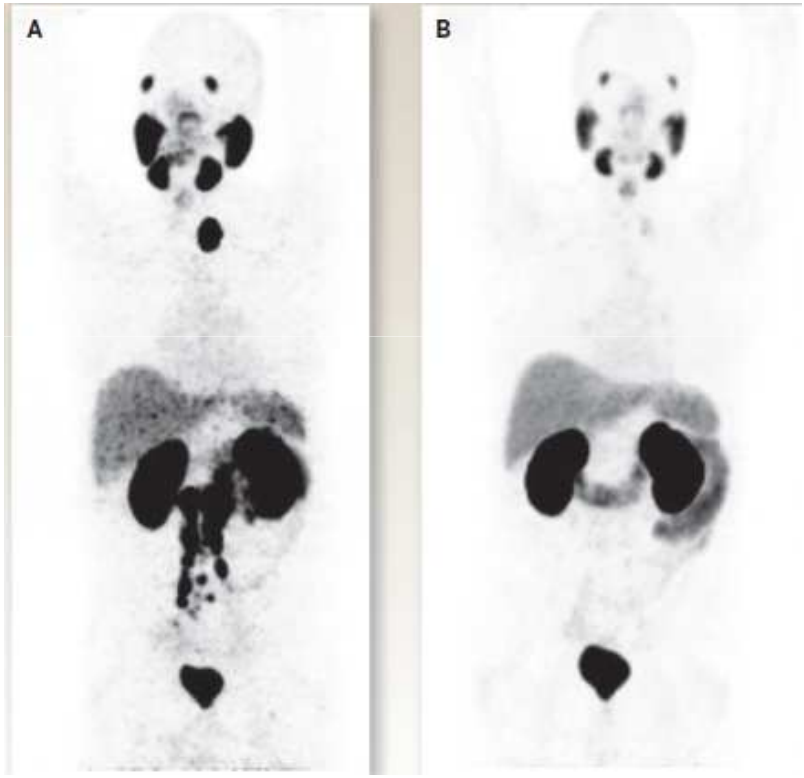
ISTITUTO SCIENTIFICO ROMAGNOLO PER LO STUDIO E LA CURA DEI TUMORI

Lutetium-177 PSMA Radioligand Therapy of Metastatic Castration-Resistant Prostate Cancer: Safety and Efficacy.

Richard P. Baum, Harshad R. Kulkarni, Christiane Schuchardt, Aviral Singh, Martina Wirtz, Stefan Wiessalla, Margret Schottelius, Dirk Mueller, Ingo Klette, Hans-Jürgen Wester. JNM, published on January 21, 2016 as doi:10.2967/jnumed.115.168443



45/56 pz **(80.3%)** demonstrated reduction in PSA levels

Results in 25 patients with at least 2 cycles and 6 months FU

Recist response: PR in 5, SD in 13, and PD in 7 patients. (DCR 72%)
The median PFS was 13.7 months, and the median OS was nr (28 months FU)

all symptomatic patients reported significant improvement in pain and quality of life

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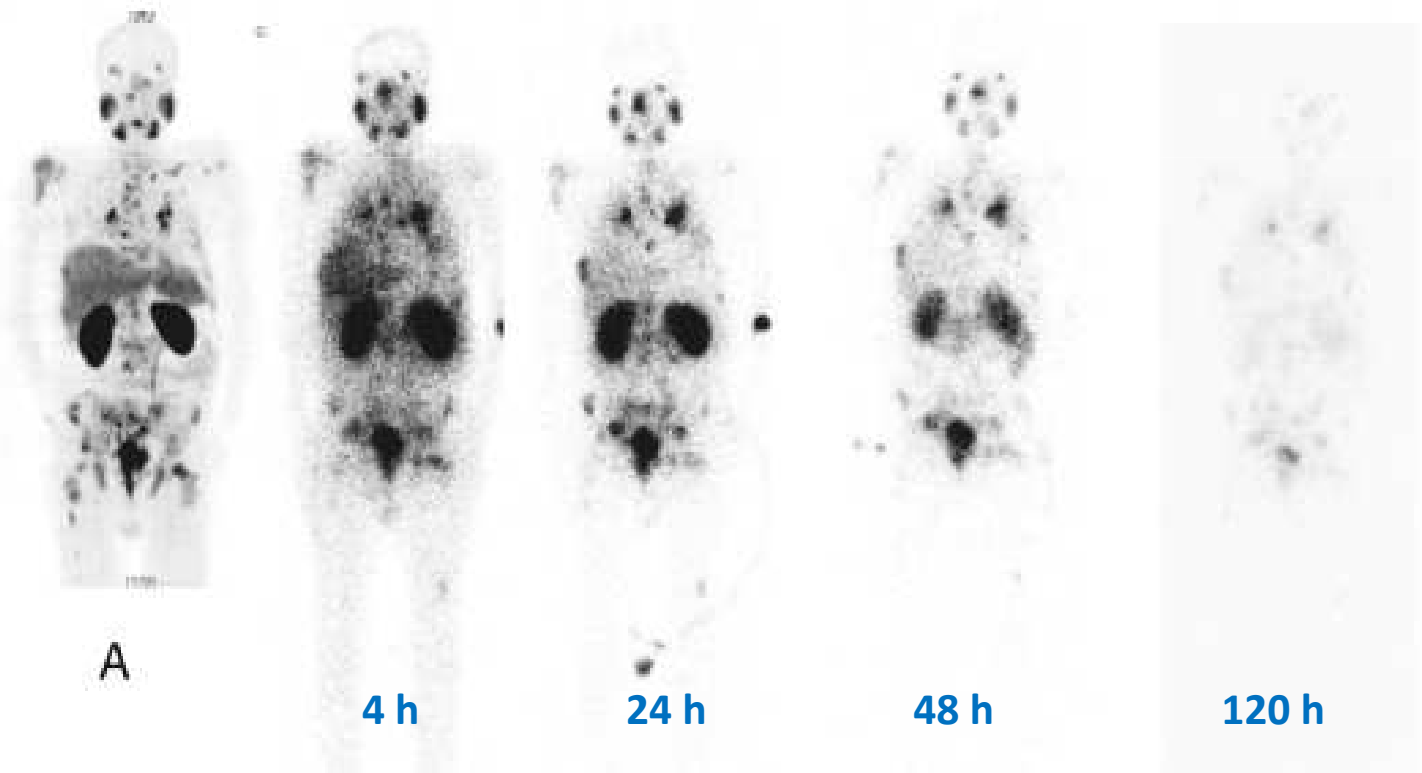
SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

Eur J Nucl Med Mol Imaging (2015) 42:1976–1983
DOI 10.1007/s00259-015-3125-3

ORIGINAL ARTICLE

Pre-therapeutic dosimetry of normal organs and tissues of ^{177}Lu-PSMA-617 prostate-specific membrane antigen (PSMA) inhibitor in patients with castration-resistant prostate cancer

Levent Kabasakal[1] · Mohammad AbuQbeitah[1] · Aslan Aygün[1] · Nami Yeyin[1] · Meltem Ocak[2] · Emre Demirci[3] · Turkay Toklu[4]



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SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

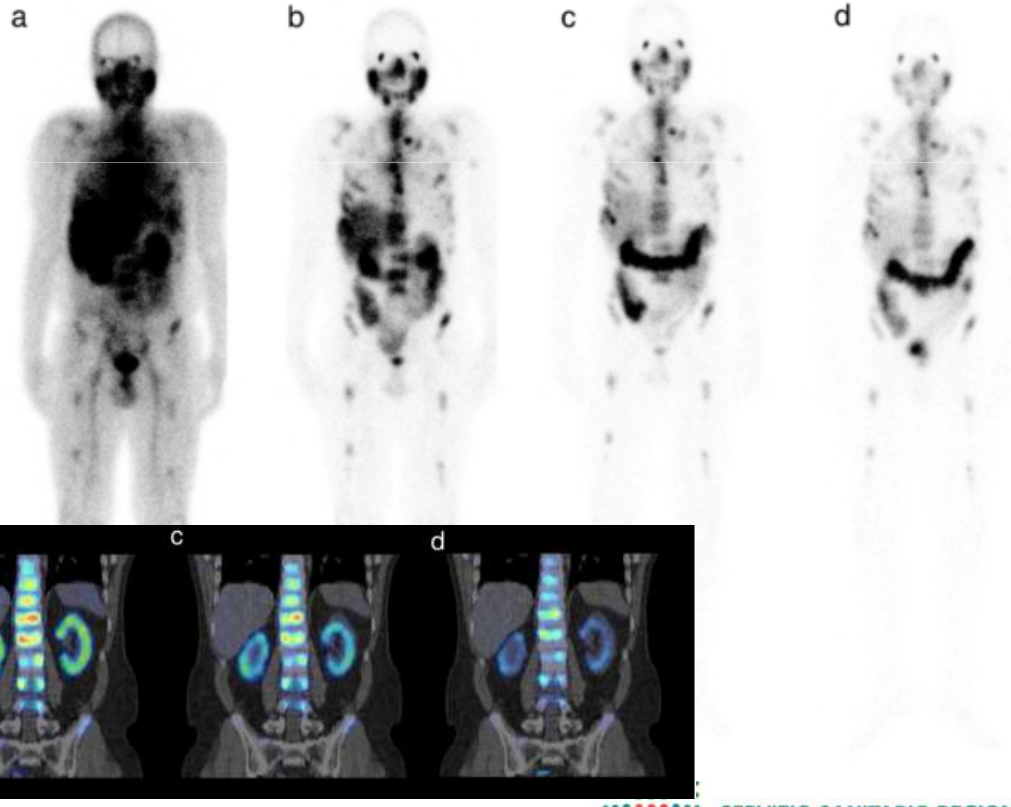
Eur J Nucl Med Mol Imaging (2016) 43:42–51
DOI 10.1007/s00259-015-3174-7

ORIGINAL ARTICLE

Dosimetry for ^{177}Lu-DKFZ-PSMA-617: a new radiopharmaceutical for the treatment of metastatic prostate cancer

Andreas Delker[1] · Wolfgang Peter Fendler[1] · Clemens Kratochwil[2] · Anika Brunegraf[1] · Astrid Gosewisch[1] · Franz Josef Gildehaus[1] · Stefan Tritschler[3] · Christian Georg Stief[3] · Klaus Kopka[4] · Uwe Haberkorn[2] · Peter Bartenstein[1] · Guido Böning[1]

wash –out renale
e salivari
Ritenzione
metastasi ossee



ISTITUTO SCIENTIFICO ROMAGNOLO PER LO STUDIO E LA CURA DEI TUMORI

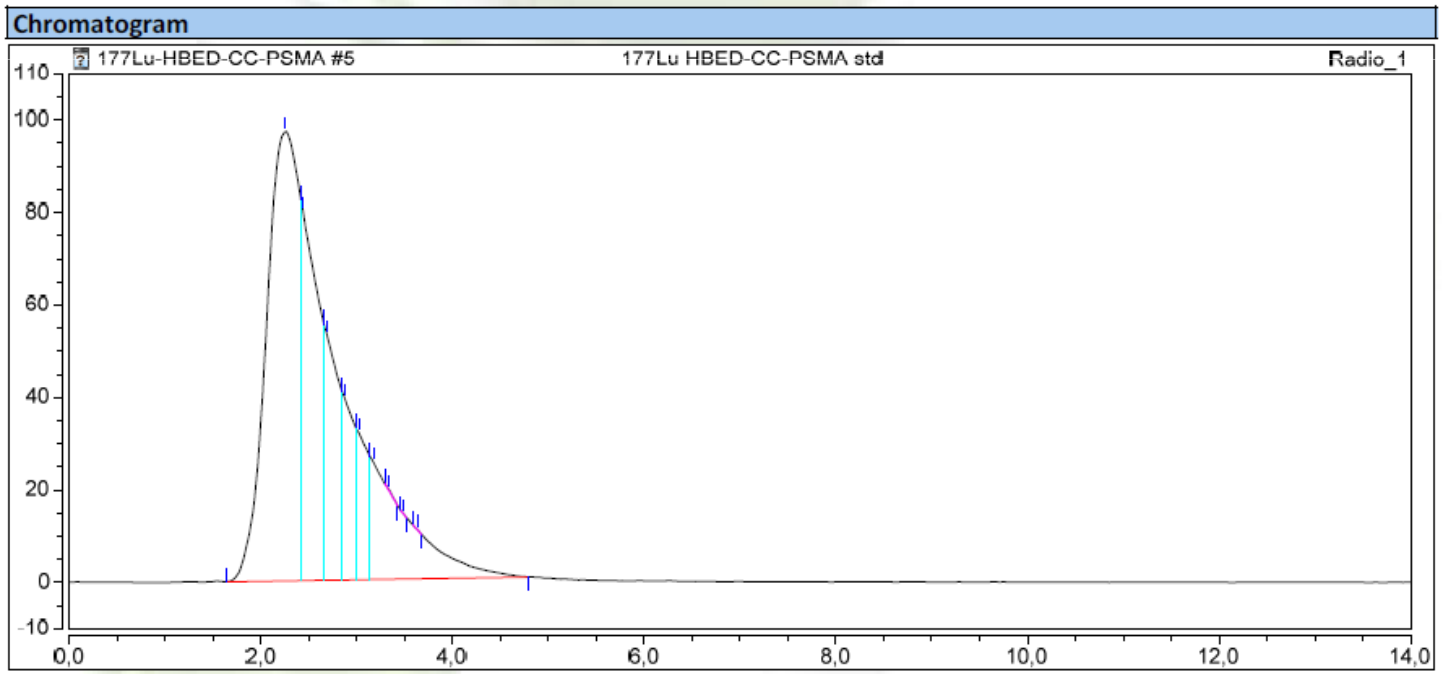
SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA

^{177}Lu-PSMA-11

ISTITUTO SCIENTIFICO ROMAGNOLO PER LO STUDIO E LA CURA DEI TUMORI	BATCH RECORD – PER RICERCA - R02/MQ -	Rev. 1 del 02.01.2014 Pag. 1 di 3
	U.O. Medicina Nucleare - Diagnostica	

Nome del radiofarmaco ^{177}Lu-HBED-CC-PSMA

MARCATURA



ISTITUTO SCIENTIFICO ROMAGNOLO PER LO STUDIO E LA CURA DEI TUMORI

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

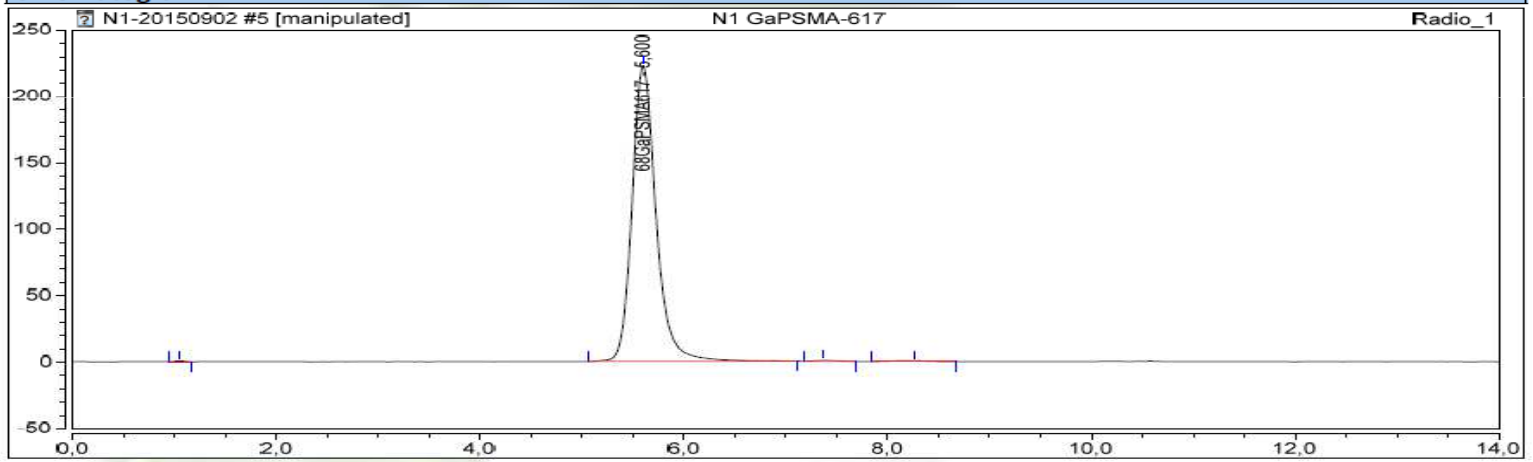
^{68}Ga-PSMA-617

ISTITUTO SCIENTIFICO ROMAGNOLO PER LO STUDIO E LA CURA DEI TUMORI	BATCH RECORD – PER RICERCA - R02/MQ -	Rev. 1 del 02.01.2014 Pag. 1 di 3
	U.O. Medicina Nucleare - Diagnostica	

Nome del radiofarmaco ^{68}Ga-DOTAPSMA (DKFZ-617)

Tempo di sintesi 16 min, purezza radiochimica 99%, resa 70% ndc; stabilità 2 ore

Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area cps-corr*min	Height cps-corr	Relative Area %	Relative Height %	Resolution (EP
1		1,053	0,064	0,587	0,10	0,26	n.a.
2	68GaPSMA617	5,600	60,751	222,955	99,31	99,19	n.a.
3		7,370	0,145	0,626	0,24	0,28	n.a.
4		8,267	0,216	0,604	0,35	0,27	n.a.
Total:			**61,176**	**224,773**	**100,00**	**100,00**	

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Radiometabolic Therapy (RMT) with 177Lu PSMA 617 in advanced castration resistant prostate cancer (CRPC): efficacy and toxicity evaluation

EU trial Number: 2016-002732-32

Protocol Code: IRST185.03

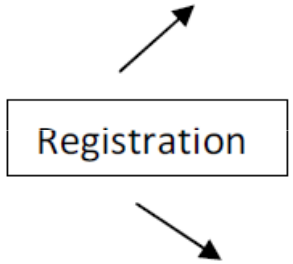
IRST -Identifier Code: L2P1367

Phase	Phase II
Study Design	Single-center, prospective, non controlled, open label, phase II trial

Timelines	Estimated duration for the main protocol: - enrollment period: 24 months - treatment duration: up to 10 months - Follow-up: 12 months after end of treatment.
Objectives	The main objective of this phase II study is to evaluate the Disease Control Rate (DCR) and the safety as co-primary objective. The secondary objectives are: late toxicity, PFS, OS, biochemical response and dosimetry.
Number of Subjects	210
Diagnosis and Main Inclusion Criteria	1. Patients must have histologically or cytologically confirmed prostate cancer 2. Male, aged ≥ 18 years. 3. Metastatic castration resistant prostate cancer 4. 68Ga-PSMA PET/CT positive in known site of disease, documented by CT or MRI or bone scan or 18Coline-PET 5. Patients in progression from previous treatment (according to PCWG3)

STUDY SCHEMA

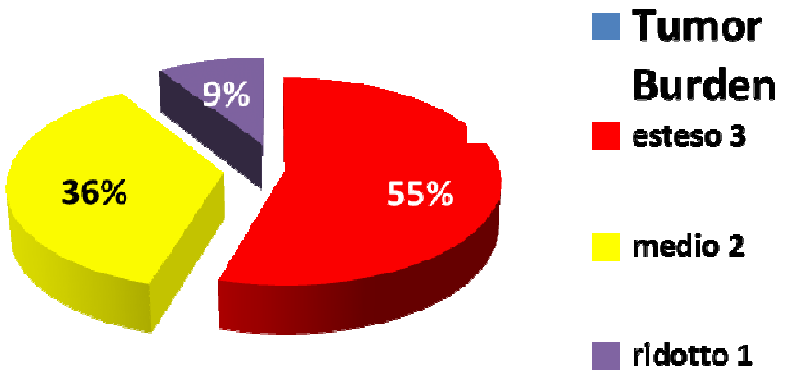
Characteristics	Treatment	
Previous Docetaxel or Age ≥ 75	177 Lu-PSMA 3.7-4.2 GBq every 8-12 wk	+ 1-2 additional cycles **(if no side effect, no evidence of PD and if, based on Investigator's judgment, this could represent a clinical benefit for the patient.)**
No previous Docetaxel or Age < 75	177 Lu-PSMA 5.5 GBq every 8-12 wk x 4	+ 1-2 additional cycles **(if no side effect, no evidence of PD and if, based on Investigator's judgment, this could represent a clinical benefit for the patient.)**

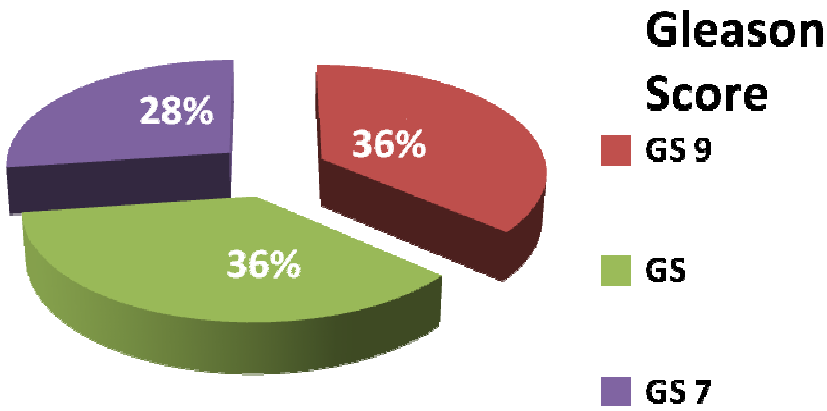


Trattamenti fatti in IRST
con 177Lu-PSMA 617 dal 24/5/2017

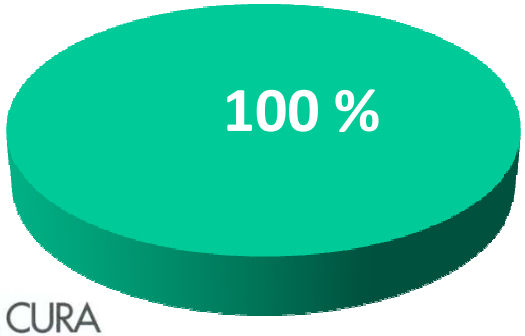
		2 cicli	3 cicli	4 cicli
trattamenti fatti	38			
pazienti arruolati	22	9	2	1
drop-out	1			
non valutabile	1			

2 pz 3,7GBq;
15 pz 4.4GBq;
5 pz 5.5GBq





Metastasi ossee



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www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 33), pp: 55567-55574

Clinical Research Paper

Radioligand therapy of metastatic prostate cancer using ^{177}Lu-PSMA-617 after radiation exposure to ^{223}Ra-dichloride

Hojjat Ahmadzadehfar[1,*], Stefanie Zimbelmann[1,*], Anna Yordanova[1], Rolf Fimmers[2], Stefan Kürpig[1], Elisabeth Eppard[1], Florian C. Gaertner[1], Xiao Wei[1], Stefan Hauser[3] and Markus Essler[1]

The aim of this study was to evaluate the safety of repeated cycles of ^{177}Lu-PSMA-617 after exposure to more cycles of ^{223}Ra. Forty-nine patients were treated with three cycles of Lu-PSMA-617 divided into two groups subjected to a history of therapy with ^{223}Ra. Group 1 included 20 patients, who had received therapy with ^{223}Ra prior to Lu-PSMA-617 therapy. Group 2, which was the control group regarding hematotoxicity, comprised 29 patients without any history of a bone-targeted radionuclide therapy. These results confirmed that performing repeated cycles of Lu-PSMA-617 after ^{223}Ra seems to be safe with a very small probability of hematotoxicity.

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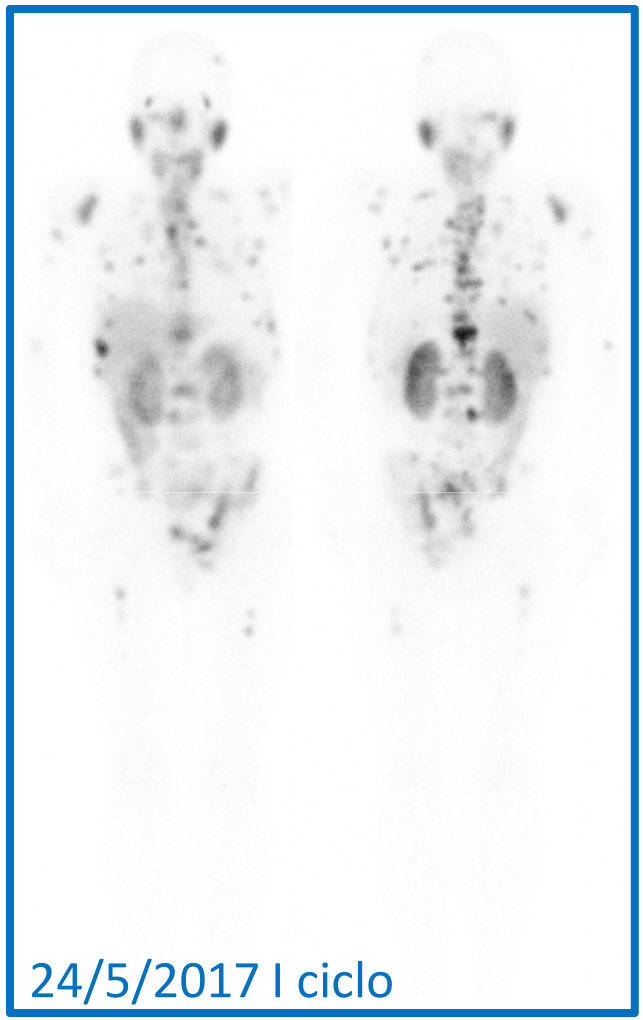
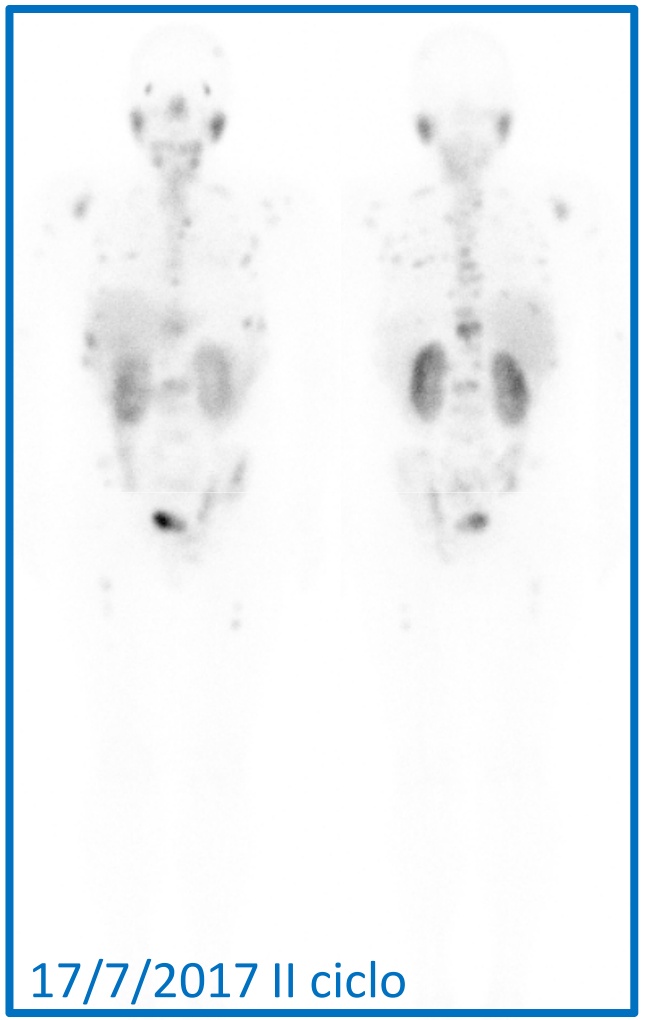
C.G. uomo 60 anni, già trattato con 223Ra (25,5 MBq), Terapia con LU-PSMA 5,5GBq

Non tossicità MIDOLLARE



24/5/2017 I ciclo



17/7/2017 II ciclo

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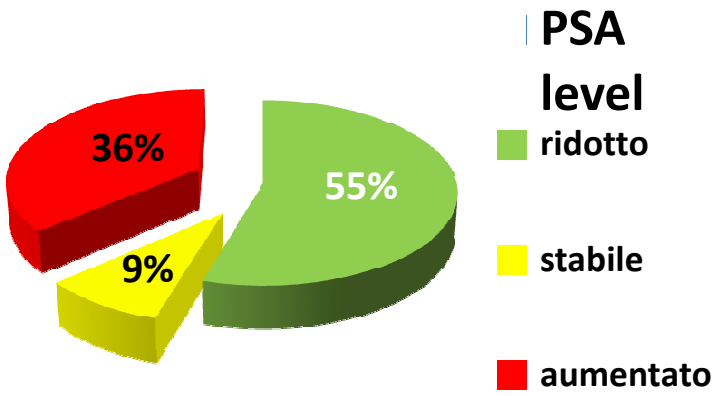
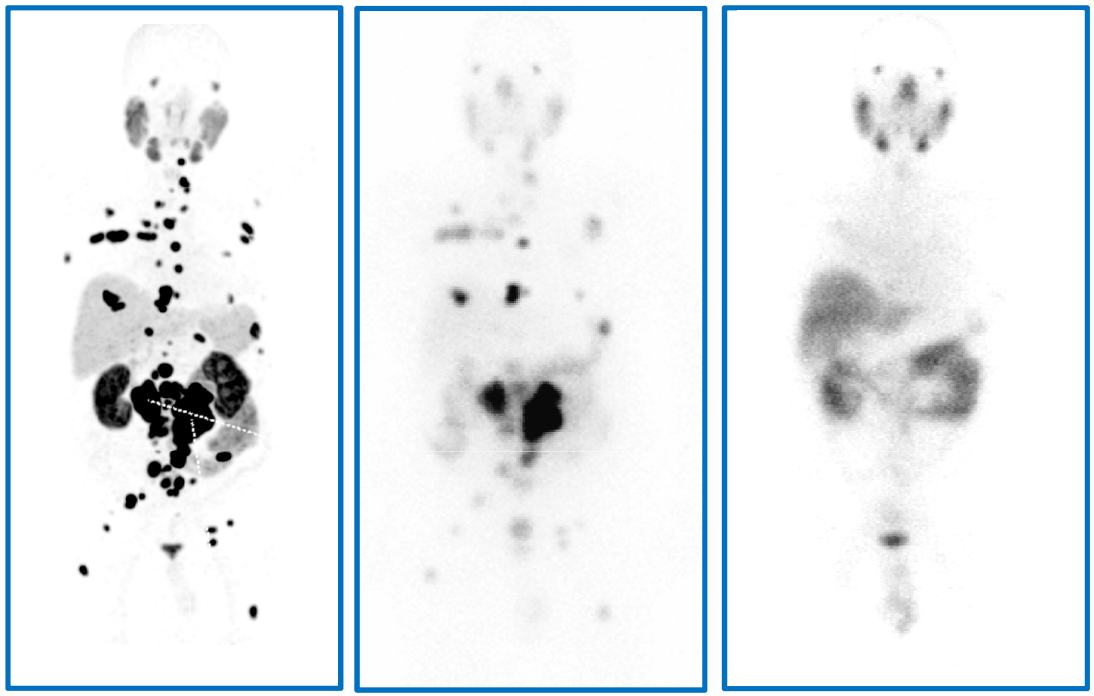
RISULTATI

Dati scintigrafici dopo almeno 2 cicli

DCR 80% 1 RC , 4 PR e 3 SD





Baseline
68Ga PSMA PET

1° cycle
177Lu PSMA PSA
level 14.43

4° cycle
177Lu PSMA PSA
level 1.19

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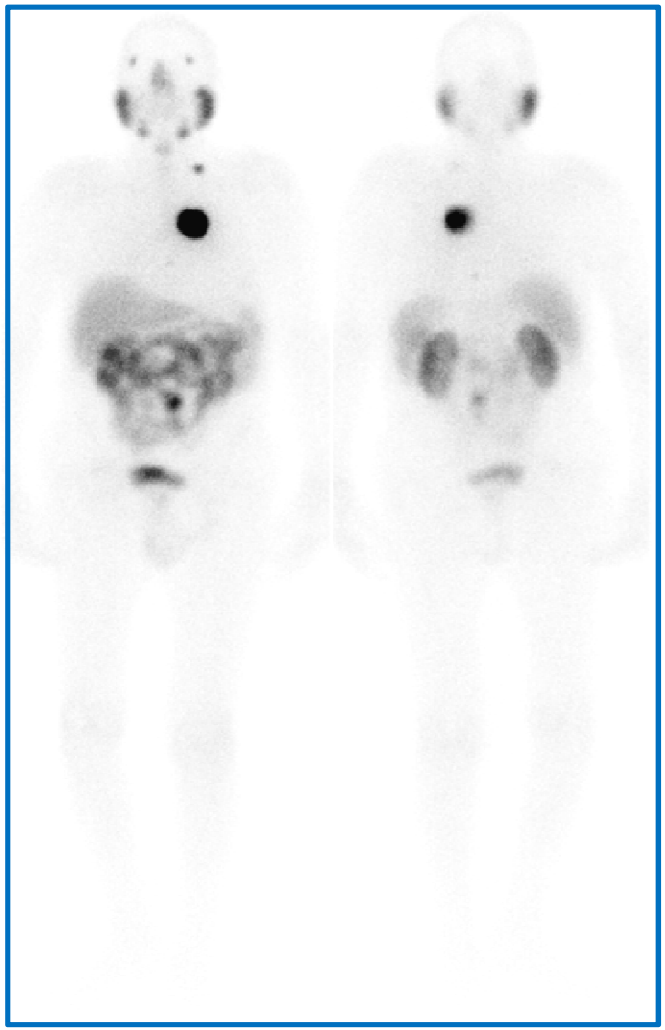
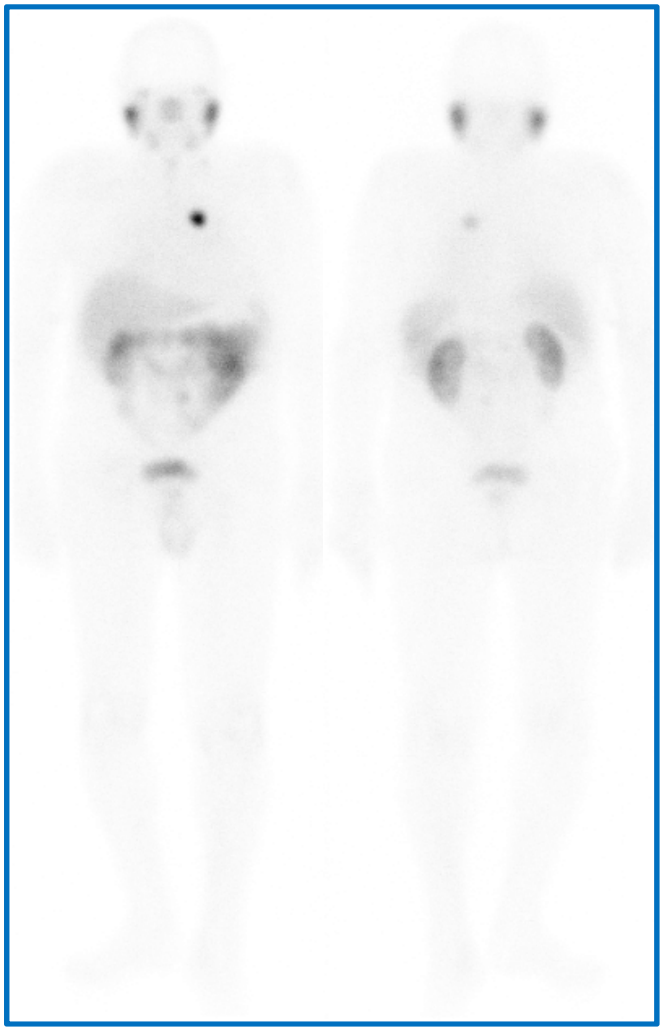


1° cycle 13/9/17
177Lu PSMA 3.7GBq
PSA level 19.35



2° cycle 8/11/17
177Lu PSMA 3.7GBq
PSA level 1.1

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Eur J Nucl Med Mol Imaging
https://doi.org/10.1007/s00259-017-3848-4

ORIGINAL ARTICLE

PSMA targeted radioligandtherapy in metastatic castration resistant prostate cancer after chemotherapy, abiraterone and/or enzalutamide. A retrospective analysis of overall survival

K. Rahbar[1] · M. Boegemann[2] · A. Yordanova[3] · M. Eveslage[4] · M. Schäfers[1] · M. Essler[3] · H. Ahmadzadehfar[3]

Initial PSA decline ≥50%, initial LDH, visceral metastases, second line chemotherapy or prior radium-223 did not have an effect on survival, whereas any initial PSA decline, initial ALP <220 U/L and cumulative injected activity ≥18.8 GBq were associated with a longer survival.

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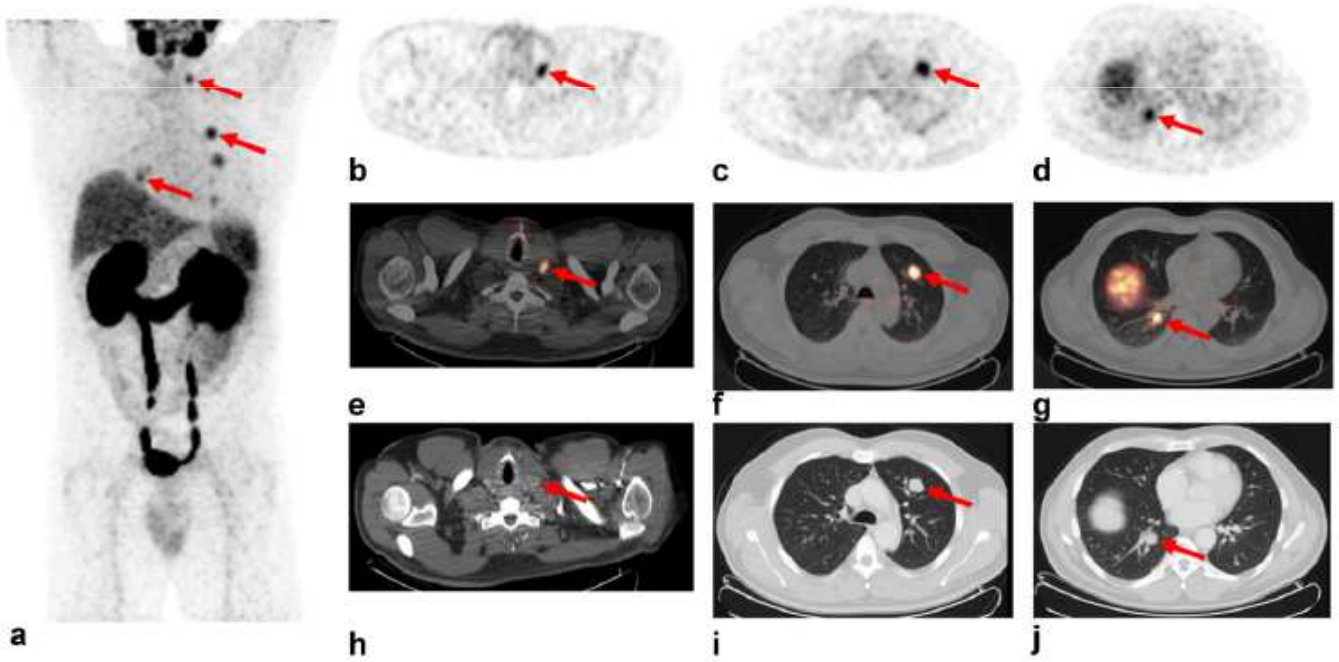
Eur J Nucl Med Mol Imaging (2015) 42:1622–1623
DOI 10.1007/s00259-015-3065-y

IMAGE OF THE MONTH

First evidence of PSMA expression in differentiated thyroid cancer using [^{68}Ga]PSMA-HBED-CC PET/CT

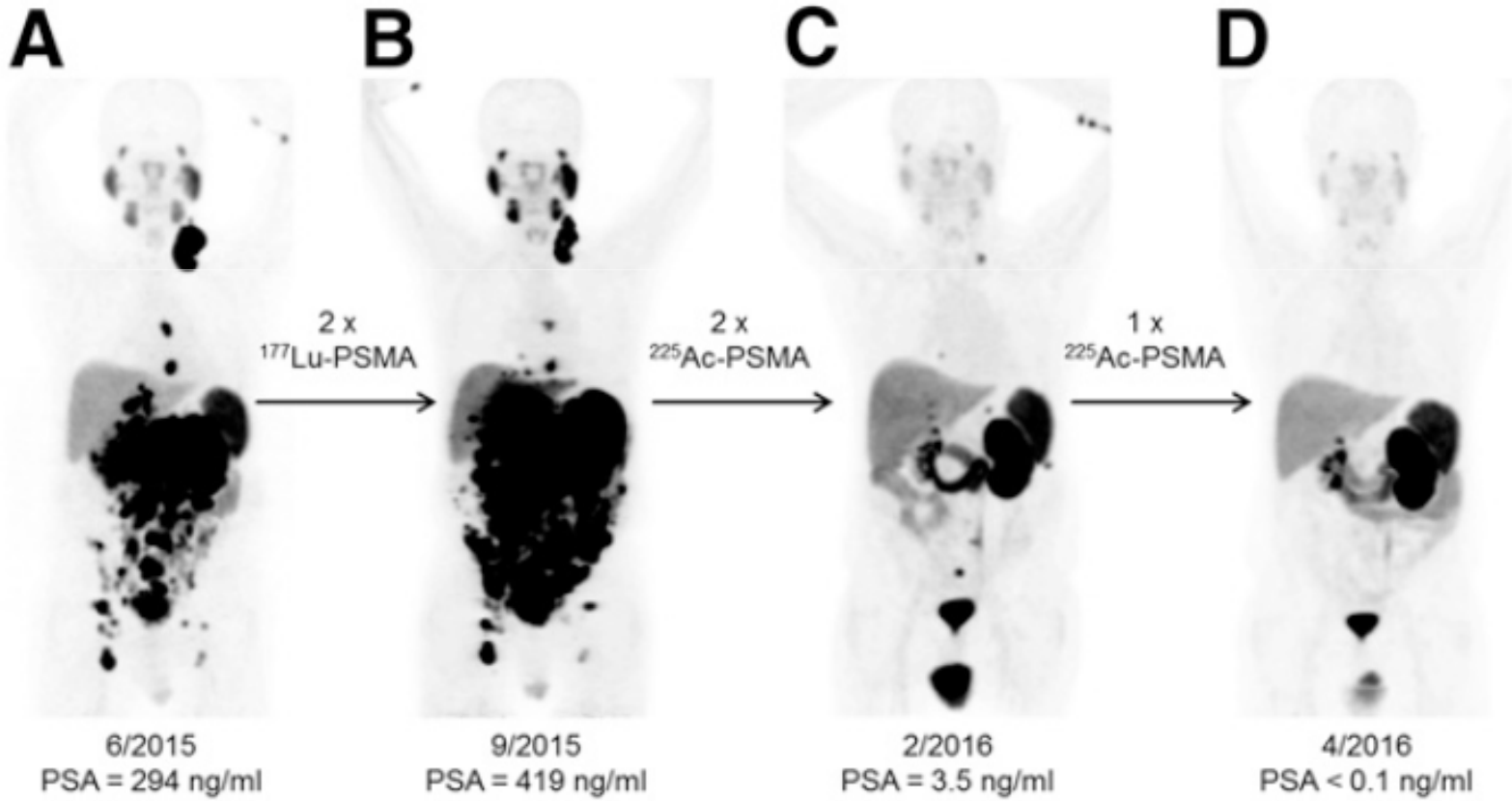
Frederik A. Verburg[1,2] · **Thomas Krohn**[1] · **Alexander Heinzel**[1] · **Felix M. Mottaghy**[1,2] · **Florian F. Behrendt**[1]

cers such as renal cell carcinoma [3, 4], colon carcinoma, neuroendocrine tumours, melanoma or breast cancer [3]. However, to our knowledge no study has yet investigated



^{225}Ac-PSMA-617 for PSMA-Targeted α-Radiation Therapy of Metastatic Castration-Resistant Prostate Cancer

THE JOURNAL OF NUCLEAR MEDICINE • Vol. 57 • No. 12 • December 2016



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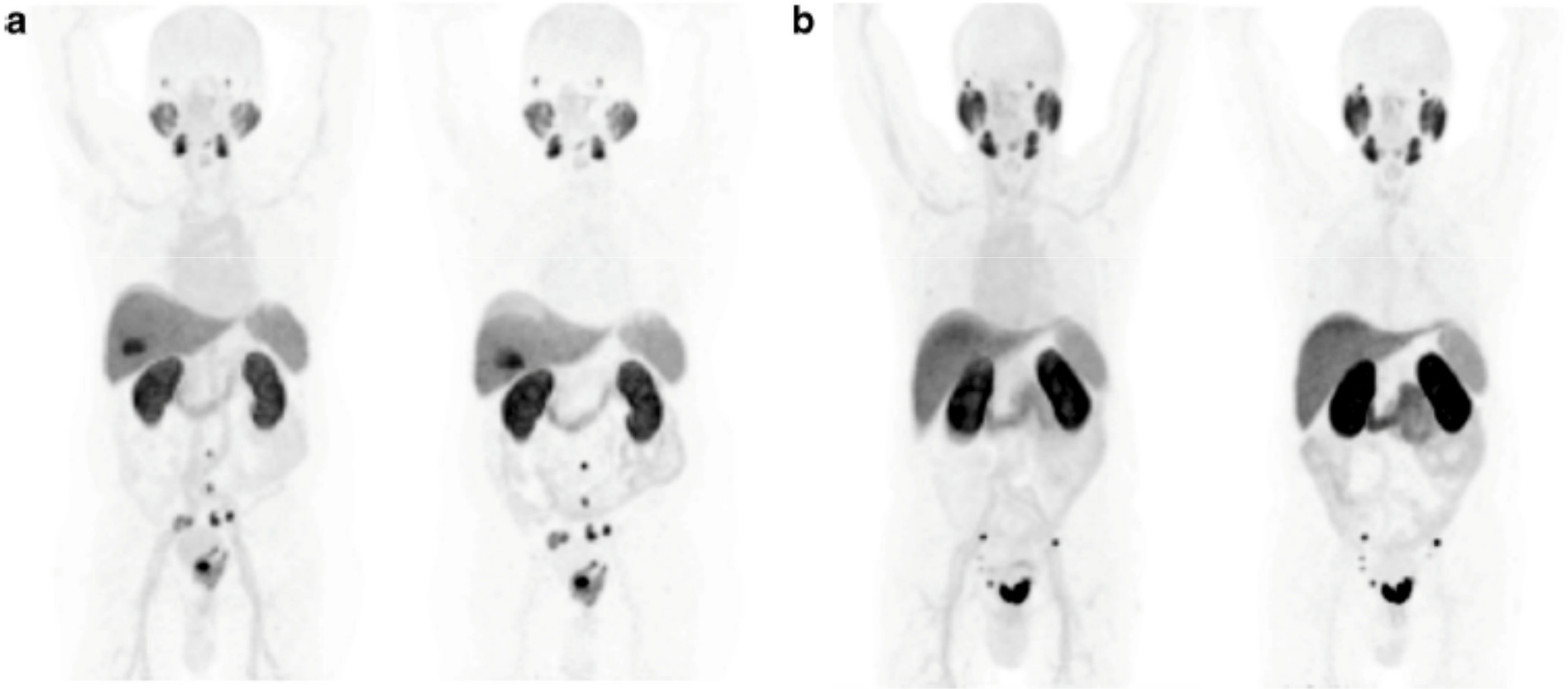
F-18 labelled PSMA-1007: biodistribution, radiation dosimetry and histopathological validation of tumor lesions in prostate cancer patients

Eur J Nucl Med Mol Imaging (2017) 44:678–688



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stefano.severi@irst.emr.it

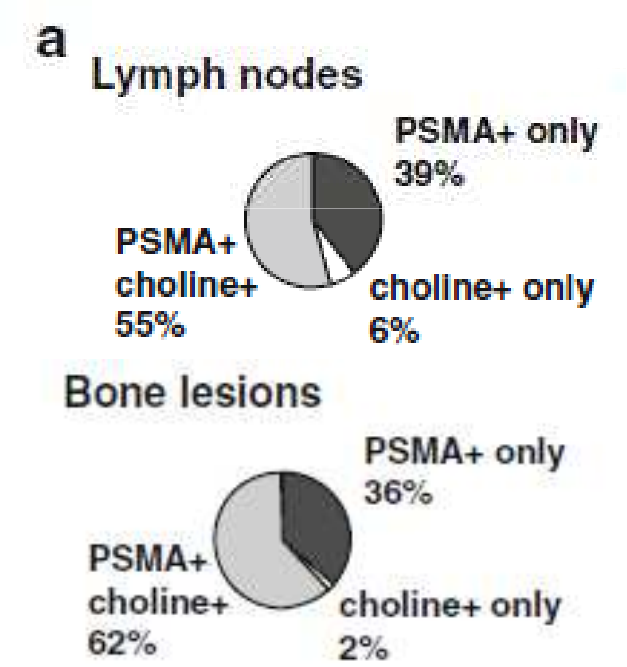
PSMA vs choline

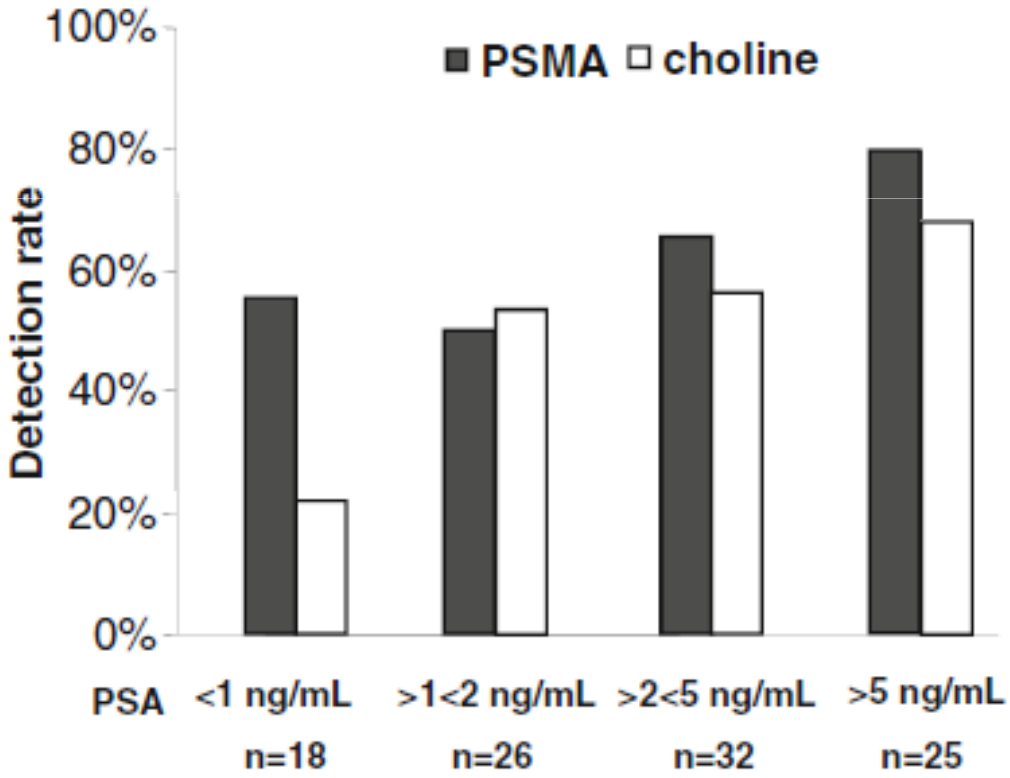
Comparison of ^{68}Ga-labelled PSMA-11 and ^{11}C-choline in the detection of prostate cancer metastases by PET/CT

Johannes Schwenck[1,3] · Hansjoerg Rempp[2] · Gerald Reischl[3] · Stephan Kruck[4] · Arnulf Stenzl[4] · Konstantin Nikolaou[2] · Christina Pfannenberg[2] · Christian la Fougère[1,5]

Eur J Nucl Med Mol Imaging (2017) 44:92–101

101 patients studied with Choline and PSMA





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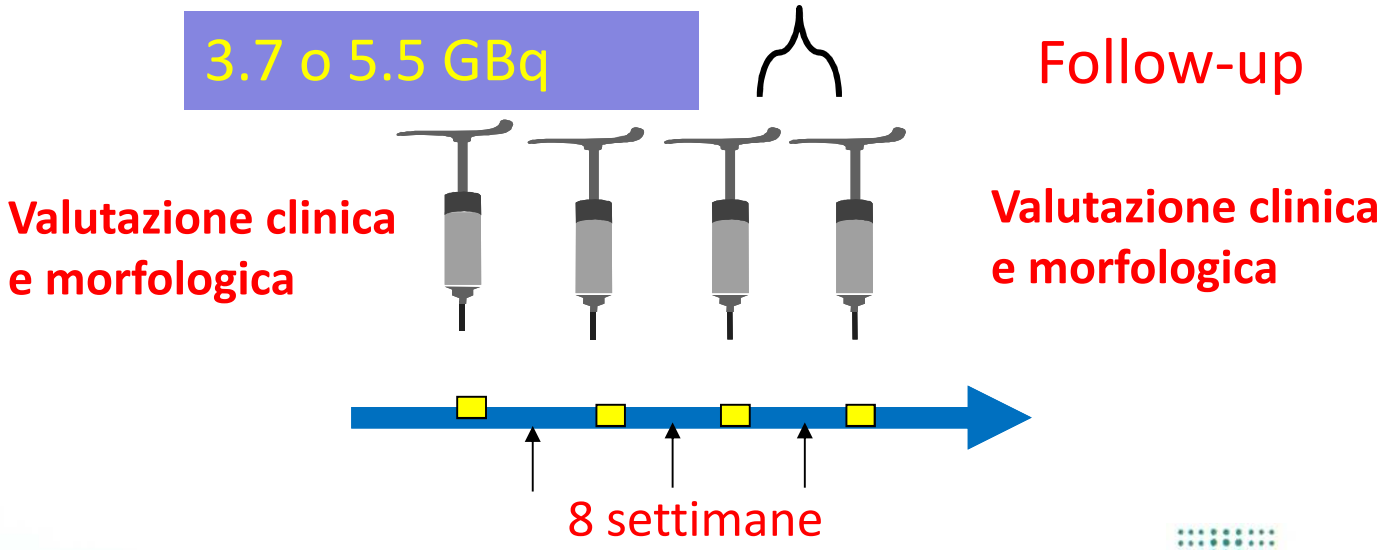
Phase	Phase II
Study Design	Single-center, prospective, non controlled, open label, phase II trial
Back ground and Rationale for study	177Lu PSMA 617 involves selective tumor targeting with the objective of maximizing tumor dose and sparing normal tissue. 177Lu PSMA 617 shows high, specific and rapid uptake in advanced prostate cancer patients. According to Baum et Al. phase II study and others evidences already published, 177Lu PSMA 617 radiometabolic therapy in end-stage progressive mCRPC is safe and effective. The avidity of the tumor target that defines the achievable tumor dose can be demonstrated prior to therapy using 68Ga-PSMA PET/CT, exluding patients that are unfit for such theranostic approach. This novel therapy showed objective responses in patients who have progressed on all standard treatments for prostate cancer with minimal toxicity. Cycles fractionation will also minimize the risk of unreversable toxity even in heavely pre-treated patients.

Study Product, Dose, Route, Regimen and duration of administration	The radiopharmaceutical 177Lu-PSMA 617 will be injected intravenously at the dosage ranging 3.7 - 5.5 GBq repeated 4 times at interval of 8-12 weeks.
Reference therapy	Standard therapy including taxane based CT, abiraterone and/or enzalutamide have to be already done or unfit for the patient
Statistical Methodology	We use Bryant and Day design in order to estimate a sample size who takes in account the activity but also the toxicity. This design is applied at each scheme of therapy and all the analysis will be done separately. If no premature stop will occur, a total of 210 evaluable patients will be enrolled (105 patients in each scheme). To evaluate primary objective the proportion of patients who achieve complete, partial response and stable disease will be calculated. The acute toxicity will be evaluated in the safety population according to the version 4.03. CTC-AE. Overall survival and progression-free survival will be estimated with Kaplan-Meier method and the role of stratification factor will be analyzed with log-rank tests. The Hazard Ratio (HR) for OS and PFS will be estimated according to the Cox model, with its relative 95% confidence intervals.

La terapia si effettua conun **protocollo sperimentale (IRST 185.03)** che richiede un regime di ricovero protetto di tre giorni. Si effettuano 4 cicli di trattamento a 2 mesi uno dall'altro. Il protocollo è attivo dal 29/03/2017 e prevede di **trattare in 3 anni 210 pazienti** con PC ormono resistente ed in progressione di malattia dopo le terapie standard.

Disegno dello studio



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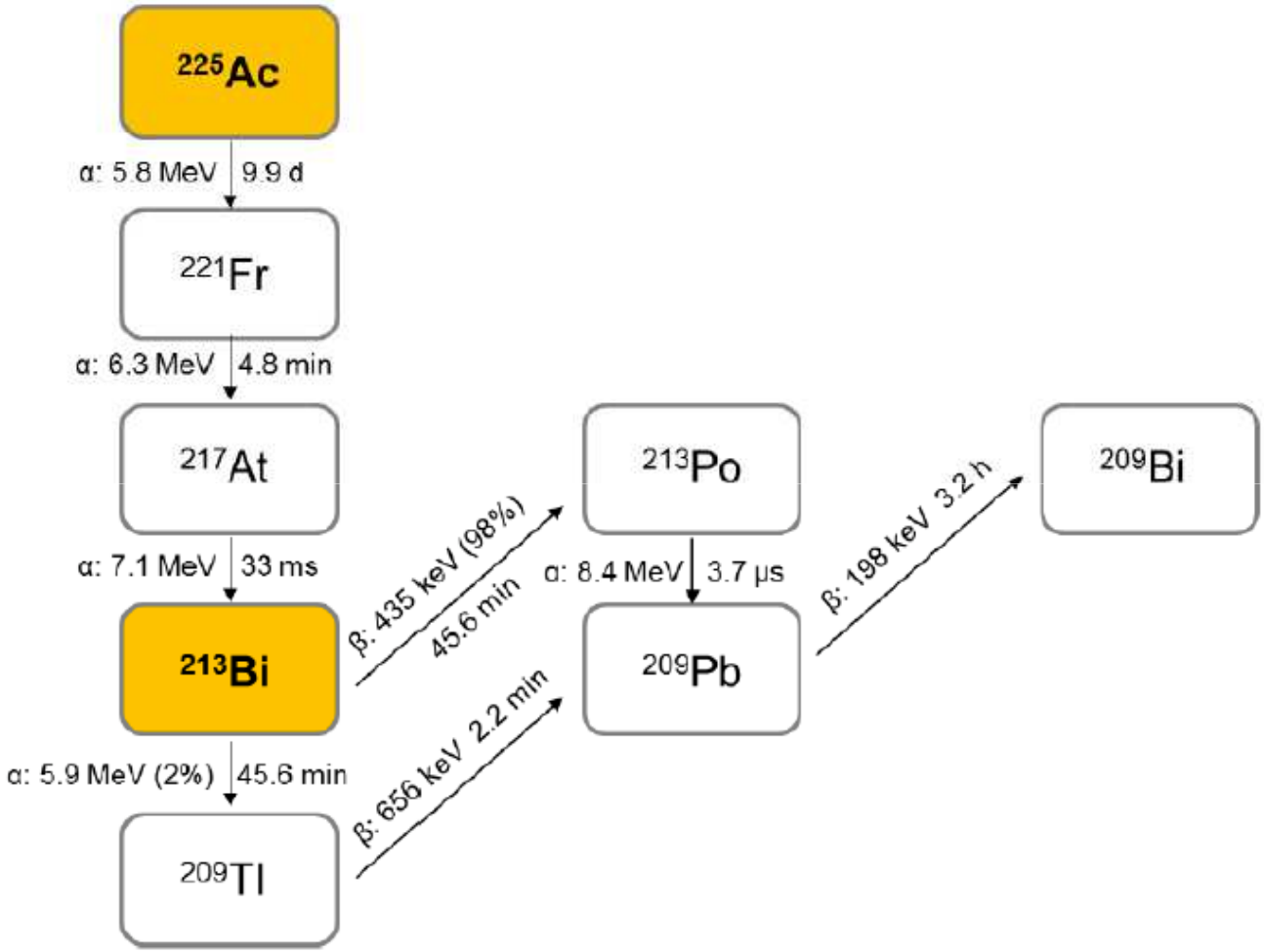
Decay scheme of ^{225}Ac and daughter nuclides



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