SESSION 1: IMPROVING QUALITY of LIFE

PANEL 1.1B: Human health

Mike SATHEKGE
South Africa

Head of Nuclear Medicine, University of Pretoria and Steve Biko Academic Hospital

Mike Sathekge has performed several first-in-human studies and introduced peptide receptor radionuclide therapy and peptide radioligand therapy in Africa, as well as 225AcPSMA for prostate cancer

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energy
Department:
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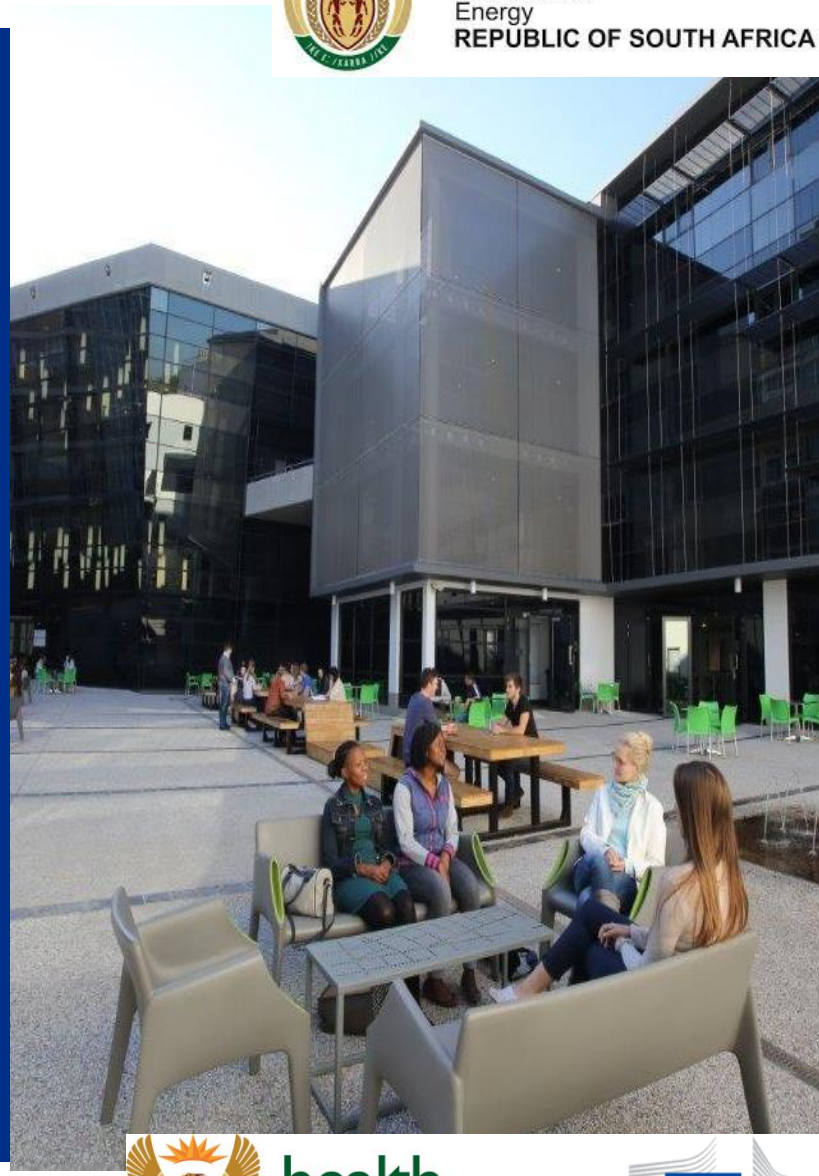
REPUBLIC OF SOUTH AFRICA

Nuclear medicine: Molecular medicine - a unique tool for diagnosis and therapy of diseases (Pt II)

Mike Sathekge, MD PhD

IAEA Ministerial Conference: 29 Nov 2018



health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Joint Research Centre
JRC

Acknowledgments

Morgenstern A, Bruchertseifer F, Betti M

Vorster M, Knoesen O,Reyneke F, Lawal I, Lengana T, Mahapane J, Davis C, Boshomane T, Mokoala K, Mokgoro N, Kaoma C, Cobert C, Kratchowil C, Giesel F, Tautamer, NTP

NM UP/SBAH

Nonjola L, Ebenhan T, Mahlangu Z, D Van Wyk, L Boshoff, R Celliers, AM Koegelenberg, T Pretorius, M Mekwa, Kleynhans J, Zeevaart JR & NECSA radiochemist staff, Maes A, Van de Wiele C, Buscombe J

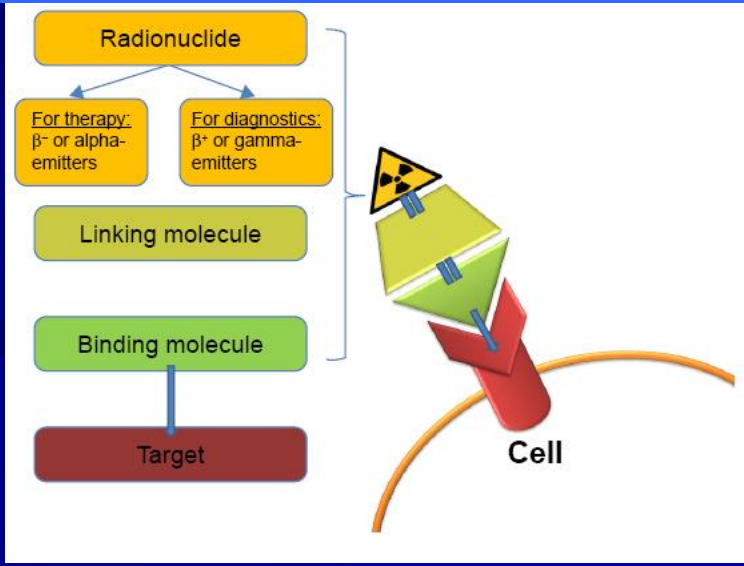
Theranostics: Personalized Medicine

Table 1 Overview of theranostic agents

Theranostic molecule	Iodine	mIBG	SSA	PSMA-ligands	Benzamide/ arylcarboxamide
Target	Thyroid cancer cells	Neurosecretory granules	SSTR, especially the subtype SSTR2	PSMA	Melanin
Planar imaging/ SPECT or	^{131}I and ^{123}I	[^{131}I]I-mIBG, [^{123}I]I-mIBG	SSA labeled with indium-111	[^{123}I]I-MIP-1072	[^{123}I]I-BA52
PET	^{124}I	[^{124}I]I-mIBG	[^{68}Ga]Ga-DOTA-TATE [^{68}Ga]Ga-DOTA-TOC [^{68}Ga]Ga-DOTA-NOC	[^{68}Ga]Ga-PSMA-11 [^{68}Ga]Ga-PSMA-617	[^{18}F]F-ICF15002
Therapeutic agent	^{131}I	[^{131}I]I-mIBG	[^{177}Lu]Lu-DOTA-TATE [^{177}Lu]Lu-DOTA-TOC [^{90}Y]Y-DOTA-TOC [^{90}Y]Y-DOTA-TATE	[^{177}Lu]Lu-J591 [^{90}Y]Y-J591 [^{131}I]I-MIP-1095 [^{177}Lu]Lu-PSMA-617	[^{131}I]I-BA52 [^{131}I]I-ICF15002
Indication	Thyroid cancer	Neuroblastomas, pheochromocytomas, paragangliomas, medullary thyroid carcinomas, and other NEN	NEN, especially GEP-NEN	Metastatic prostate cancer	Metastatic melanoma

Abbreviations: mIBG, metaiodobenzylguanidine; SSA, somatostatin analogs; SSTR, somatostatin receptors; NEN, neuroendocrine neoplasia; GEP, gastroenteropancreatic system; SPECT, single photon emission computed tomography; PET, positron emission tomography.

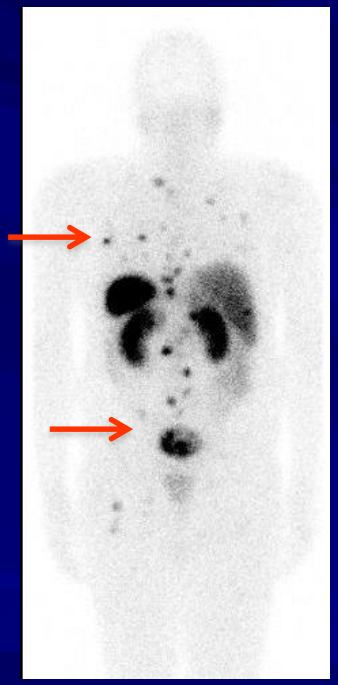
Application of astatine-210: Ikeda H..... Hatazawa J. Appl Radiat Isot 2018



A Yordanova et al. OncoTargets and Therapy 2017

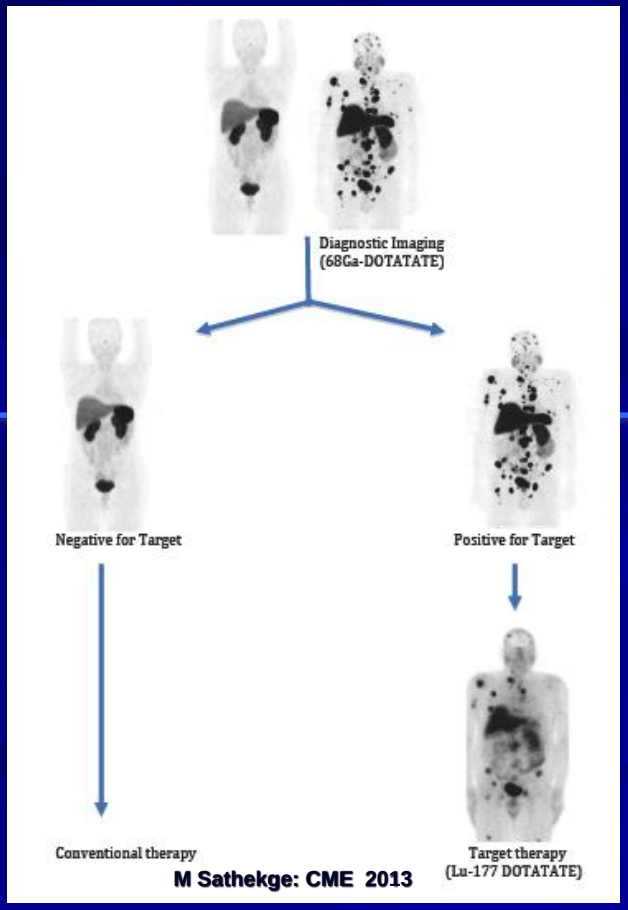
Theranostics

Find



68Ga-DOTATATE/PSMA

Fight



Lu-177/Bi213 DOTATATE/PSMA

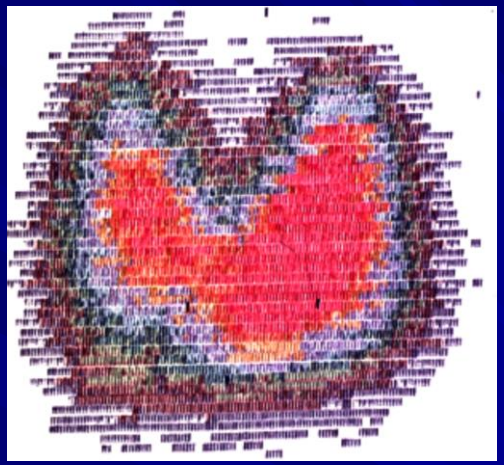
Follow-up

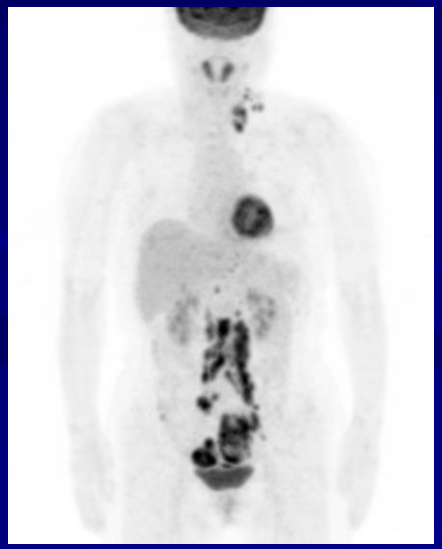
68Ga- DOTATATE/PSMA

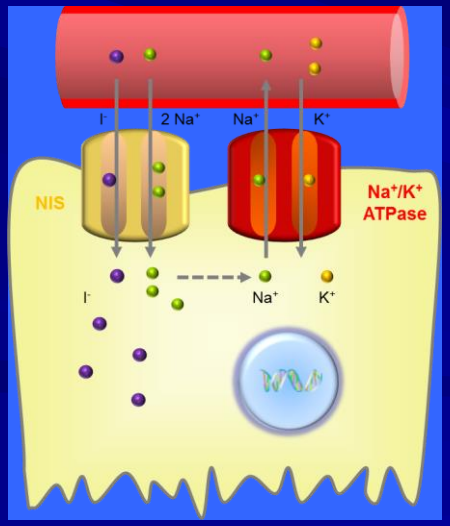
The First Theranostic Paradigm! Thyroid Cancer

Benedict Cassen Invents Rectilinear Scanner
Seeing What Had Previously Been Treated

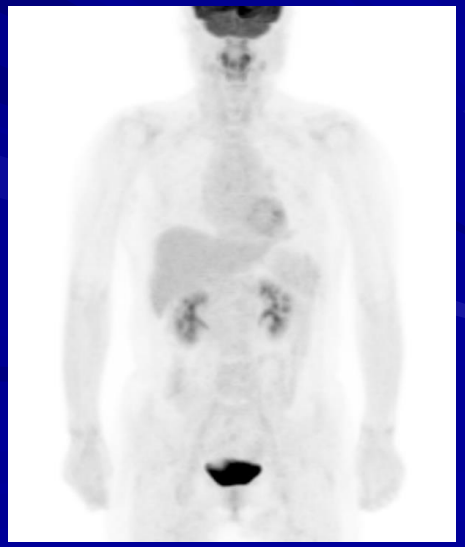
Benedict Cassen (1902-1972) with First "Scanner"



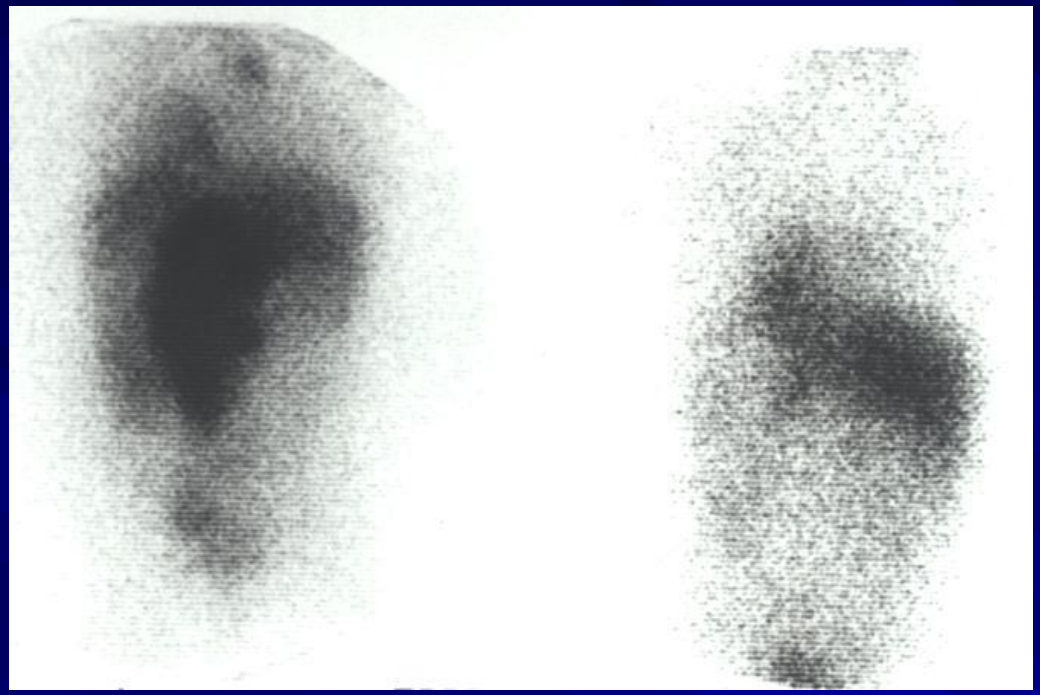

Pre-Treatment



See it, treat it!


Post-Treatment

Neuroblastoma: I-131 MIBG therapy after conventional treatment



1st MIBG therapy

2nd MIBG therapy

Progressive NBL IVs, after VCR/EXN

14 days after 50 mCi I-131 MIBG

Results first 50 patients (1984-1991):
7 CR, 23 PR, 10 SD, 9 PD
1 lost to follow up
excellent palliation

Courtesy: C.A. Hoefnagel

Why ^{188}Re Skin Cancer Therapy

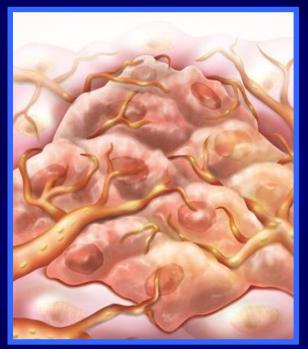
South African Implementation

- Single session (40-120 min)
- Painless
- Non-invasive
- Aesthetic

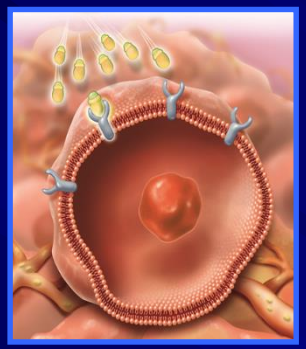
1. Definition of treatment area
2. Protective foil Application
3. Application of Rhenium-188
4. Calculation of treatment time
5. Removal of foil and waste disposal

^{177}Lu-DOTATATE mode of action

1.Injection

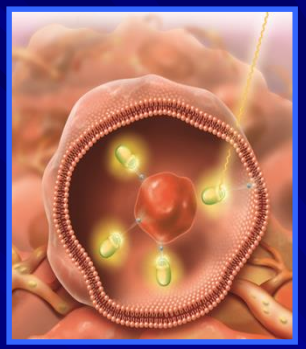


2.Concentration into (NETs) sites

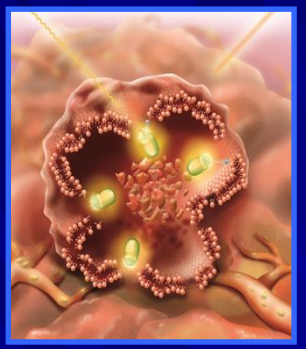


3.The radiopeptide binds to sstr2 overexpressed by NETs

4.The radiopeptide is internalized in the NET cell

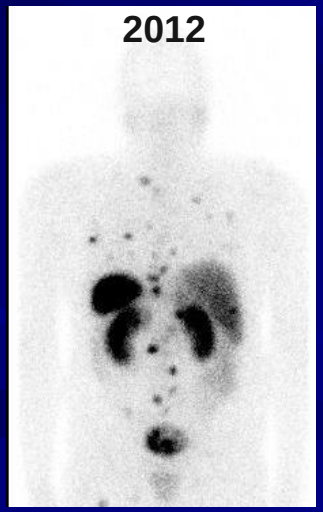


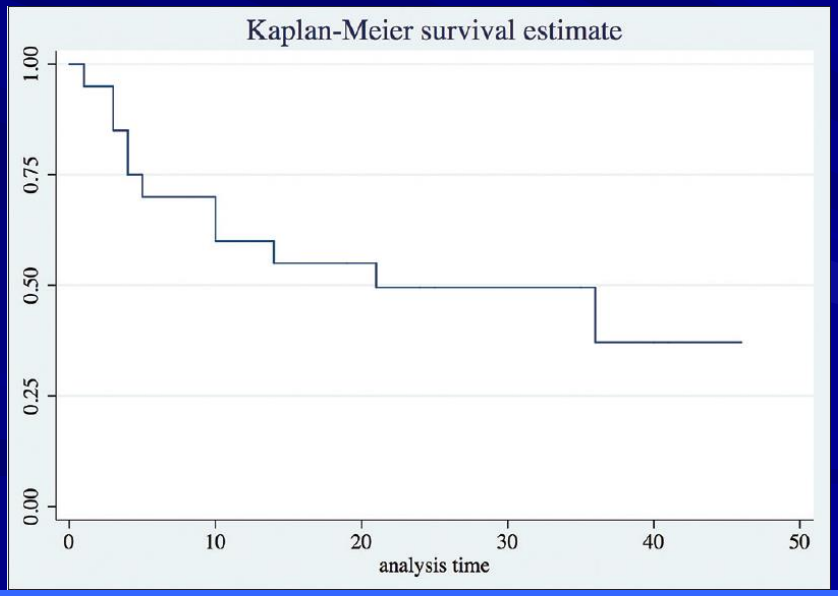
5. The radiopeptide delivers radiation within the cancer cell



6. Radiation induces DNA strands break causing tumor cell death

Kaplan–Meier graph to evaluate the median time to progression (20 months)





First Results and Experience with PRRT in South Africa

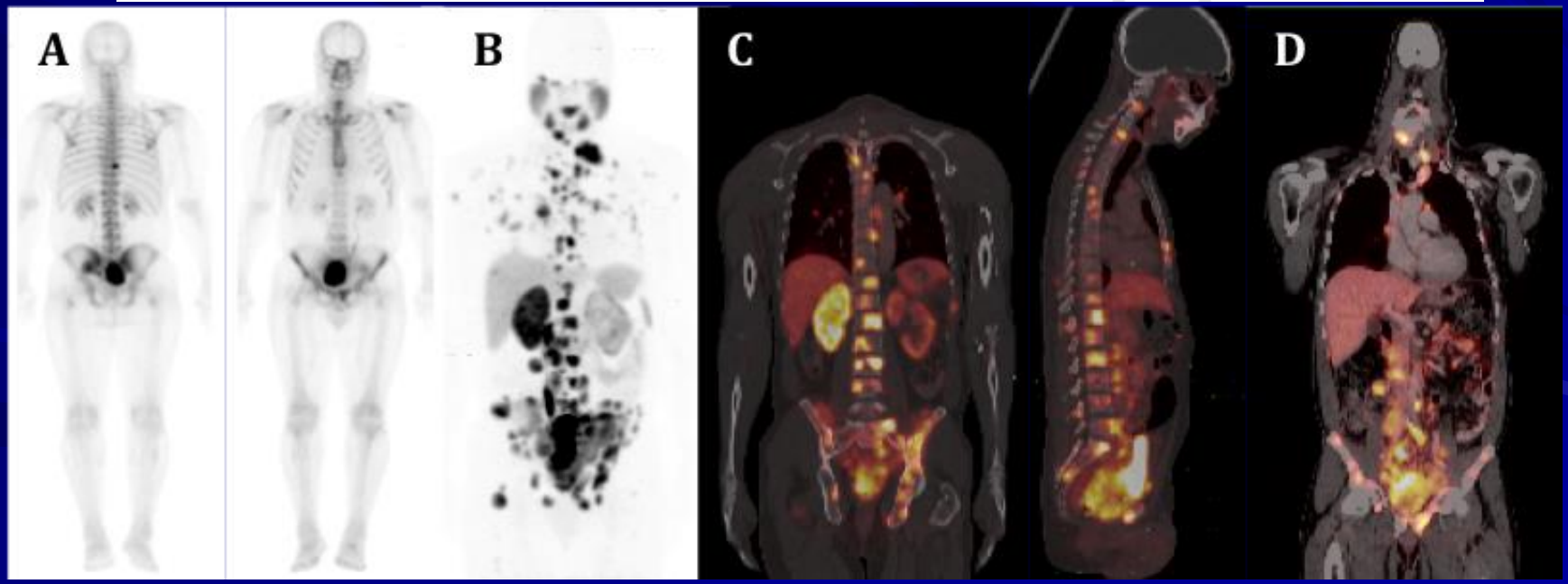
Mariza Vorster, M. R. Modiselle, C. S. Corbett, I. O. Lawal, John R. Buscombe, and Mike M. Sathekge. WJNM 2018

ARTICLE IN PRESS

Original Study

^{68}Ga-PSMA PET/CT Replacing Bone Scan in the Initial Staging of Skeletal Metastasis in Prostate Cancer: A Fait Accompli?

Thabo Lengana,[1] Ismaheel O. Lawal,[1] Tebatso G. Boshomane,[1] Gbenga O. Popoola,[2] Kgomotso M.G. Mokoala,[1] Evelyn Moshokoa,[3] Alex Maes,[1,4] Neo P. Mokgoro,[1] Christophe Van de Wiele,[1,5] Mariza Vorster,[1] Mike M. Sathekge[1]



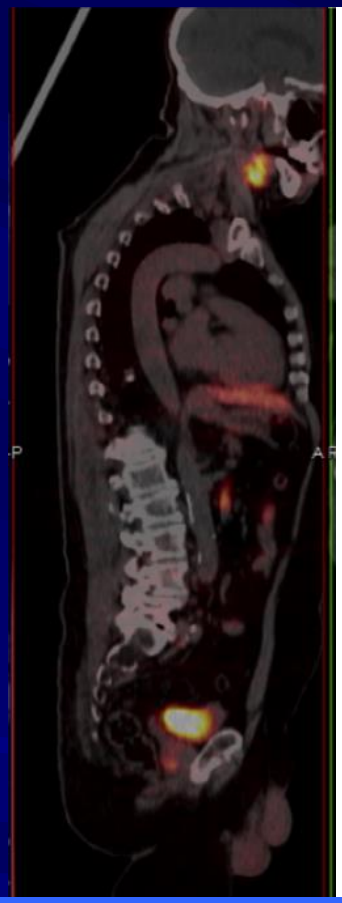
Planned clinical management altered in 52%

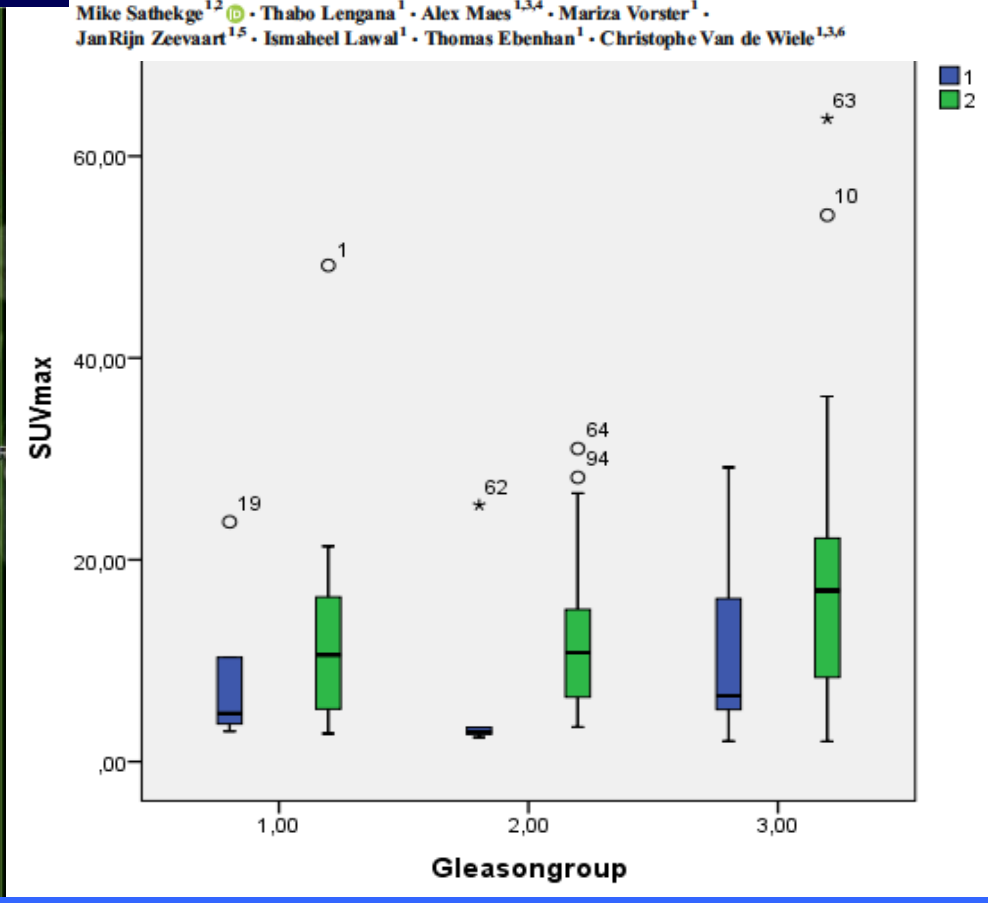
Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-017-3852-8

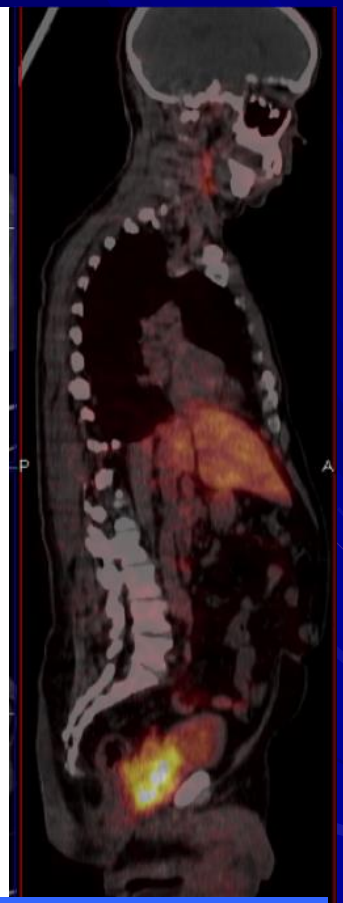
ORIGINAL ARTICLE

^{68}Ga-PSMA-11 PET/CT in primary staging of prostate carcinoma: preliminary results on differences between black and white South-Africans

Mike Sathekge[1,2] · Thabo Lengana[1] · Alex Maes[1,3,4] · Mariza Vorster[1] · JanRijn Zeevaart[1,5] · Ismaheel Lawal[1] · Thomas Ebenhan[1] · Christophe Van de Wiele[1,3,6]





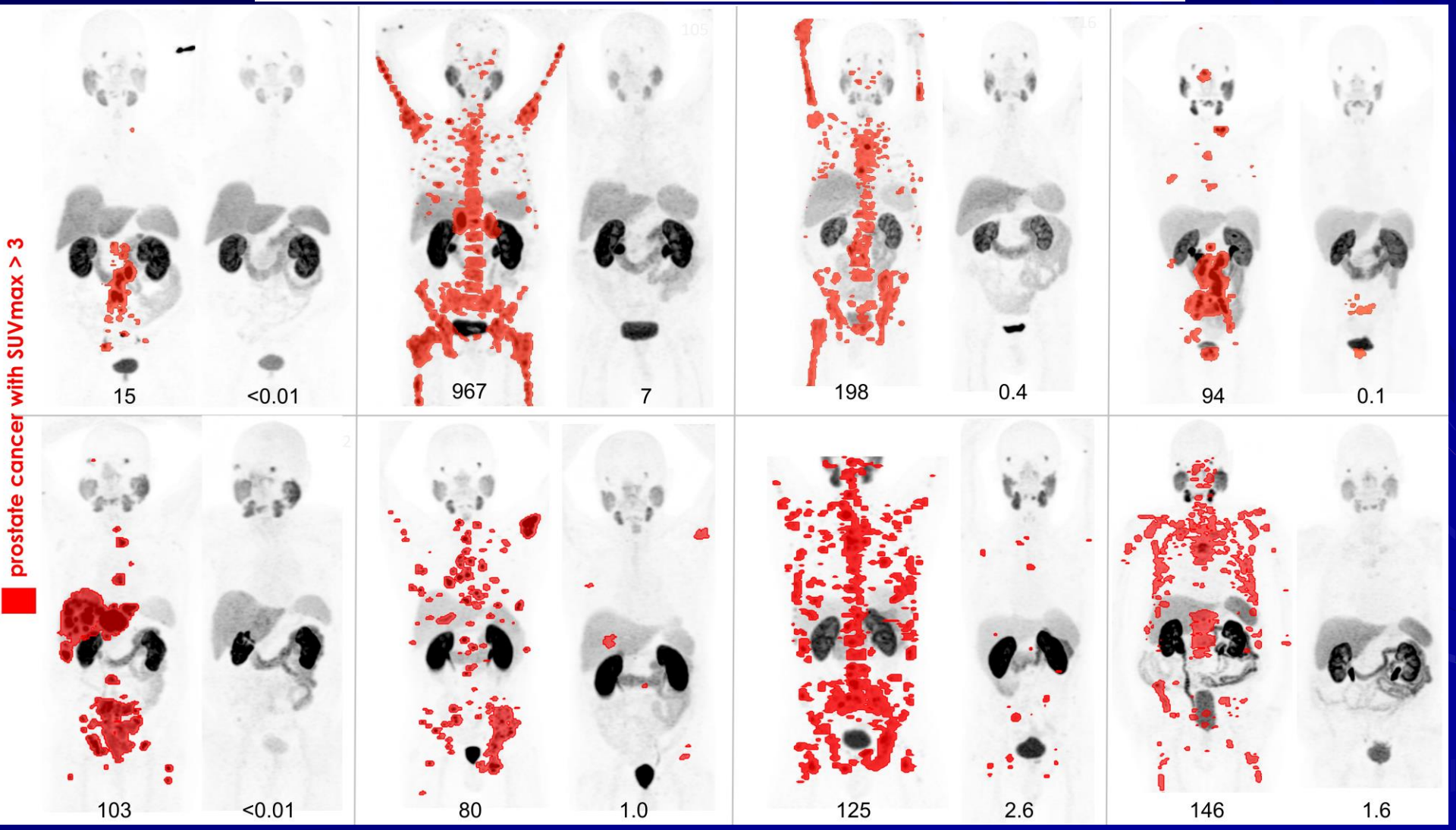


- SUVmax: significantly related to Gleason score group
- SUVmax: significantly higher in Blacks when compared to Whites.
- SUVmax: significantly correlated with PSA values, which was significantly higher in BSAs when compared with WSAs.

[^{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

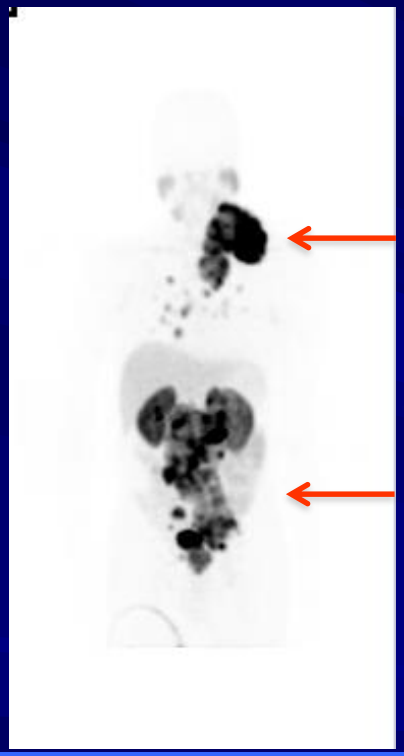
Lancet Oncol 2018; 19: 825–33



SNMMI Image of the Year: PSMA PET Imaging of Theranostic for Advanced

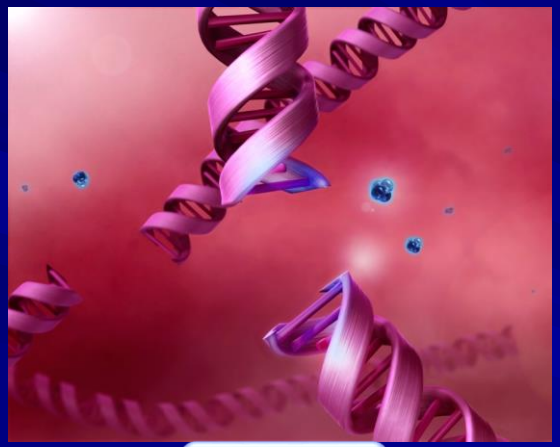
Theranostics

See it



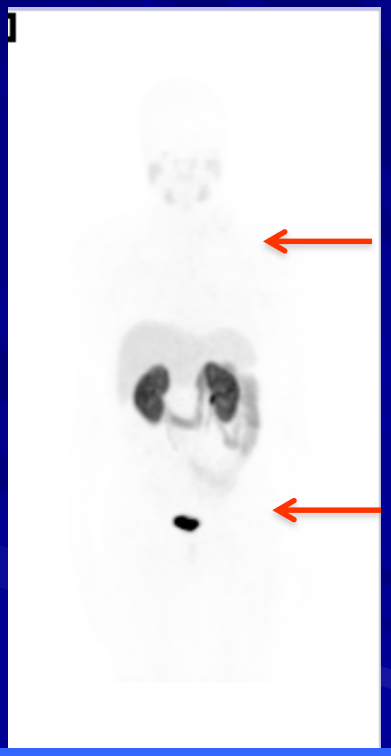
Pre-therapy
PSA = 1300,69 ng/ml

Treat it



α particle
Ac-225 PSMA

Remission



Post-therapy
PSA <0.05 ng/ml

Excellent response on Targeted Alpha Therapy for Prostate Cancer

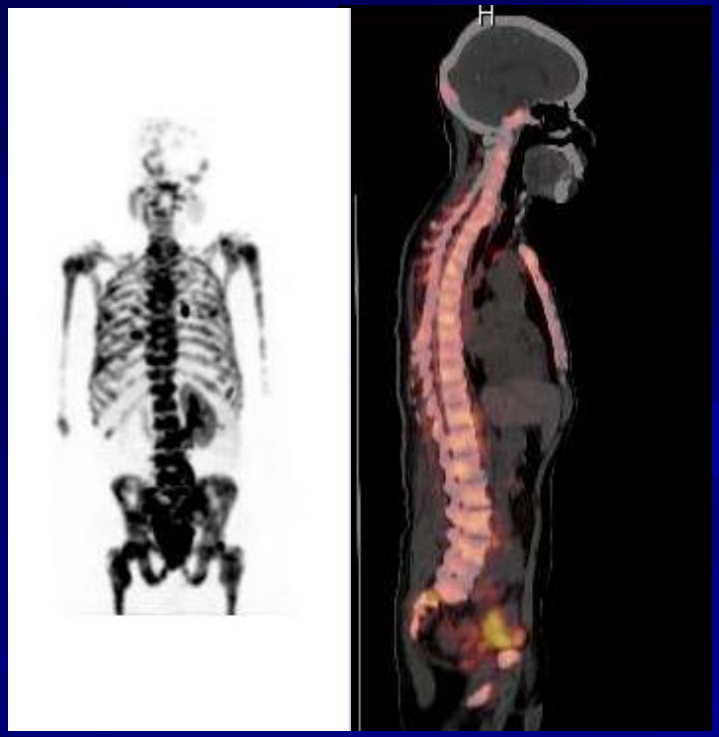
Excellent Response

Bone Mets

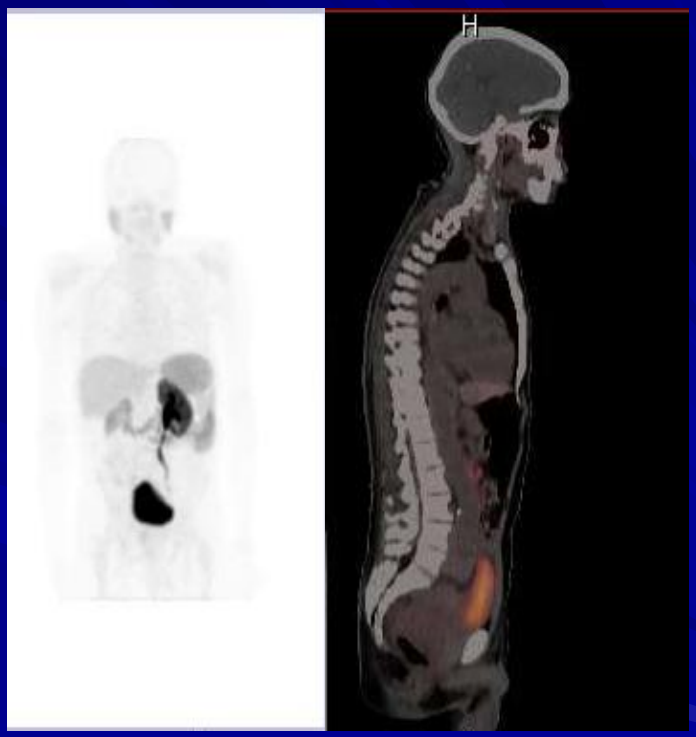
2 x

^{225}Ac-PSMA

March 2018
PSA = 2337 ng/ml



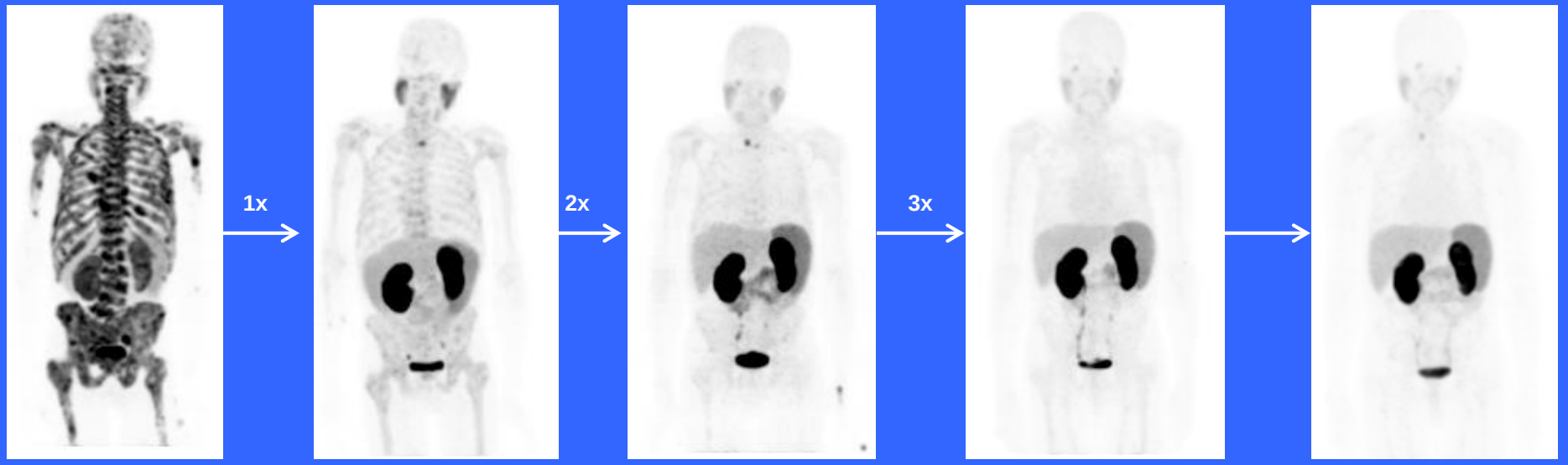
July 2018
PSA = 0.06 ng/ml



Complete Remission

Theranostics
^{68}Ga/^{225}Ac PSMA

^{225}Ac-PSMA-617 RLT of chemotherapy-naïve patients: Remission sustained for >1 year



July 2017
PSA = 782 ng/ml

Sep 2017
PSA = 71 ng/ml

Nov 2017
PSA 0.64 ng/ml

Jan 2018
PSA = 0.07 ng/ml

May 2018
PSA = 0.04 ng/ml

- ✓ ≥90% decline in serum PSA in 82% of patients including 41% of patients with undetectable serum PSA who remained in remission 12 months after therapy.
- ✓ Reduced toxicity to salivary glands due to de-escalation

Sathekge M, et al. Eur J Nucl Med Mol Imaging. 2018

Theranostics: See it, treat it !!!

Summary: Excellent, Promising Results

EFFICACY

- ✓ Tumor shrinkage
- ✓ Symptom relief and QoL improvement
- ✓ Biomarker reduction
- ✓ Impact on survival

TOLERABILITY

- ✓ Nephro and Hematological toxicity well tolerated (limited/none)
- ✓ Xerostomia (mainly G1 due to de-escalation)

Indications and Supply of ^{225}Ac-PSMA617

- ✓ Extensive skeletal metastases – not indicated for ^{177}Lu PSMA
- ✓ MDT – 0nly for patients not qualifying for other therapies or refuse them
- ✓ Determine the activity/dose (de-escalation)
- ✓ Need for a prospective Phase Trial I/II (incorporating it into standard-of-care protocols)
- ✓ Explore cyclotron based production of ^{225}Ac

Nuclear medicine- an ideal conduit for Theranostics

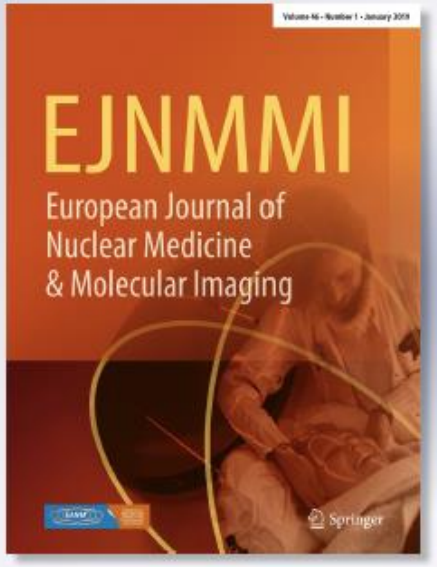
^{225}Ac-PSMA-617 in chemotherapy-naive patients with advanced prostate cancer: a pilot study

Mike Sathekge, Frank Bruchertseifer, Otto Knoesen, Florette Reyneke, Ismaheel Lawal, Thabo Lengana, Cindy Davis, Johncy Mahapane, et al.

European Journal of Nuclear Medicine and Molecular Imaging

ISSN 1619-7070
Volume 46
Number 1

Eur J Nucl Med Mol Imaging (2019)
46:129-138
DOI 10.1007/s00259-018-4167-0



Springer

≥90% decline in serum PSA in 82% of patients including 41% of patients with undetectable serum PSA who remained in remission 12 months after therapy.