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.
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
Acknowledgments

Morgenstern A, Bruchertseifer F, Betti M


NM UP/SBAH

Theranostics: Personalized Medicine

Table 1 Overview of theranostic agents

<table>
<thead>
<tr>
<th>Theranostic molecule</th>
<th>Iodine</th>
<th>mIBG</th>
<th>SSA</th>
<th>PSMA-ligands</th>
<th>Benzamide/arylcarboxamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target</td>
<td>Thyroid cancer cells</td>
<td>Neurosecretory granules</td>
<td>SSTR, especially the subtype SSTR2</td>
<td>PSMA</td>
<td>Melanin</td>
</tr>
<tr>
<td>Planar imaging/SPECT or PET</td>
<td>$^{131}$I</td>
<td>$^{[13]I}$-mIBG, $^{[125]I}$-mIBG</td>
<td>SSA labeled with indium-111</td>
<td>$^{[13]I}$-MIP-1072</td>
<td>$^{[13]I}$-BA52</td>
</tr>
<tr>
<td>Indication</td>
<td>Thyroid cancer</td>
<td>Neuroblastomas, pheochromocytomas, paragangliomas, medullary thyroid carcinomas, and other NEN</td>
<td>NEN, especially GEP-NEN</td>
<td>Metastatic prostate cancer</td>
<td>Metastatic melanoma</td>
</tr>
</tbody>
</table>

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

M Sathekge: CME 2013

68Ga-DOTATATE/PSMA

Follow-up

Lu-177/Bi213 DOTATATE/PSMA

68Ga-DOTATATE/PSMA
The First Theranostic Paradigm! Thyroid Cancer

Benedict Cassen Invents Rectilinear Scanner
Seeing What Had Previously Been Treated

Pre-Treatment

See it, treat it!

Post-Treatment
Neuroblastoma: I-131 MIBG therapy after conventional treatment

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

1st MIBG therapy 2nd MIBG therapy

Progressive NBL IVs, after VCR/EXN

14 days after 50 mCi I-131 MIBG

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
177Lu-DOTATATE mode of action

1. Injection
2. Concentration into (NETs) sites
3. The radioligand binds to sstr2 overexpressed by NETs
4. The radioligand is internalized in the NET cell
5. The radioligand 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
Planned clinical management altered in 52%
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.
[\textsuperscript{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 Nicks, Justin Ferdinandus, Sue Ping Thang, Tim Akhurst, Amir Irawani, Grace Kong, Aravind Ravi Kumar, Declan G Murphy, Peter Ec, Price Jackson, Mark Scalzo, Scott G Williams, Shashleen Sandhu

Lancet Oncol 2018; 19: 824-33
Excellent response on Targeted Alpha Therapy for Prostate Cancer

Pre-therapy PSA = 1300.69 ng/ml

Post-therapy PSA < 0.05 ng/ml

α particle Ac-225 PSMA

 Fifteen patients with locally advanced or metastatic prostate cancer were treated with targeted alpha therapy. The treatment resulted in excellent response with a reduction in PSA levels.
Excellent Response

Bone Mets

March 2018
PSA = 2337 ng/ml

July 2018
PSA = 0.06 ng/ml

2 x
$^{225}$Ac-PSMA

Excellent Response

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

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

- **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

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 – only 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
≥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.