

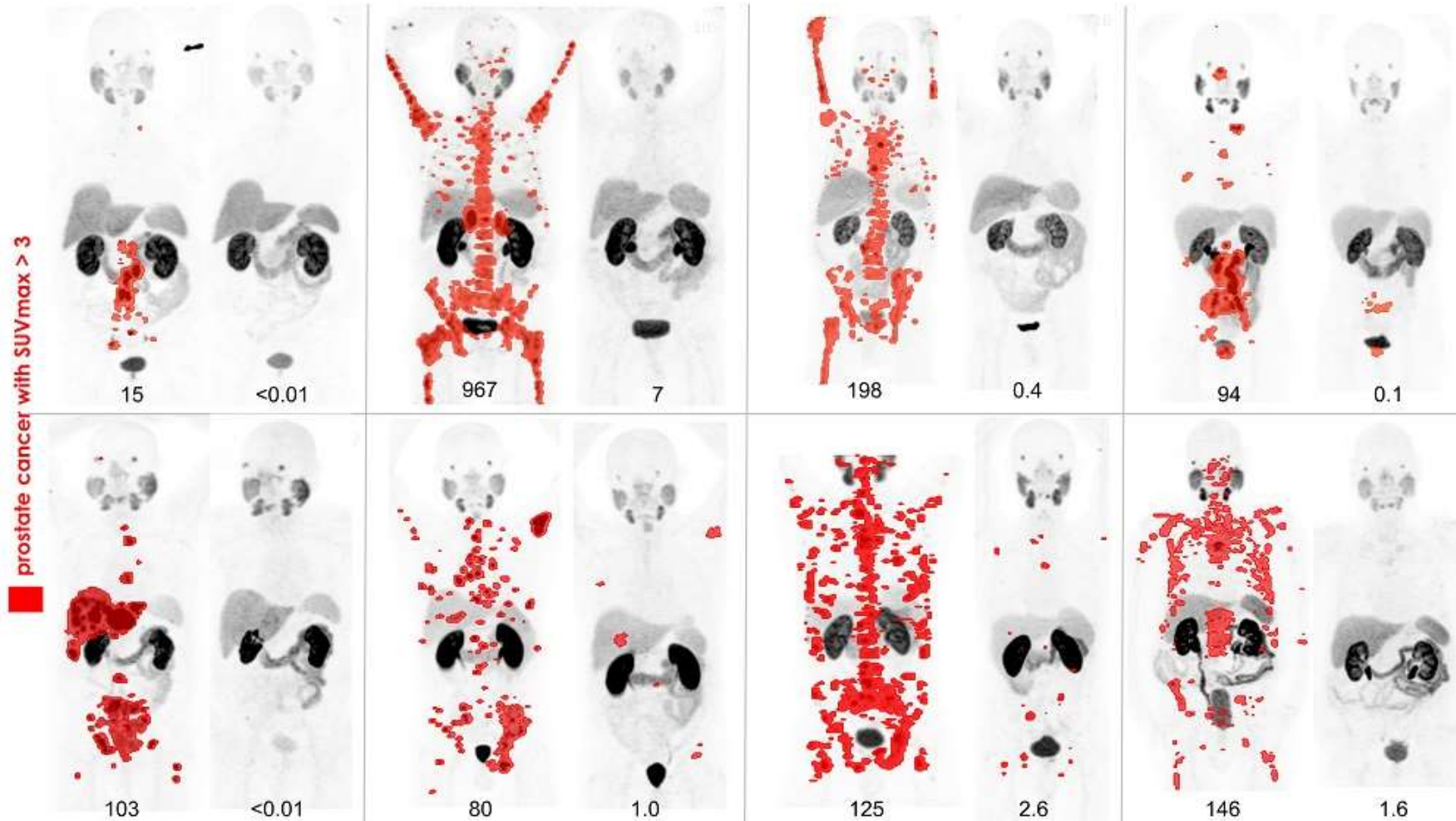
Theranostics

The Foundation of
Precision Cancer Care



#caringforthegoodlife

Nebraska Cancer Specialists



Precision Cancer Medicine

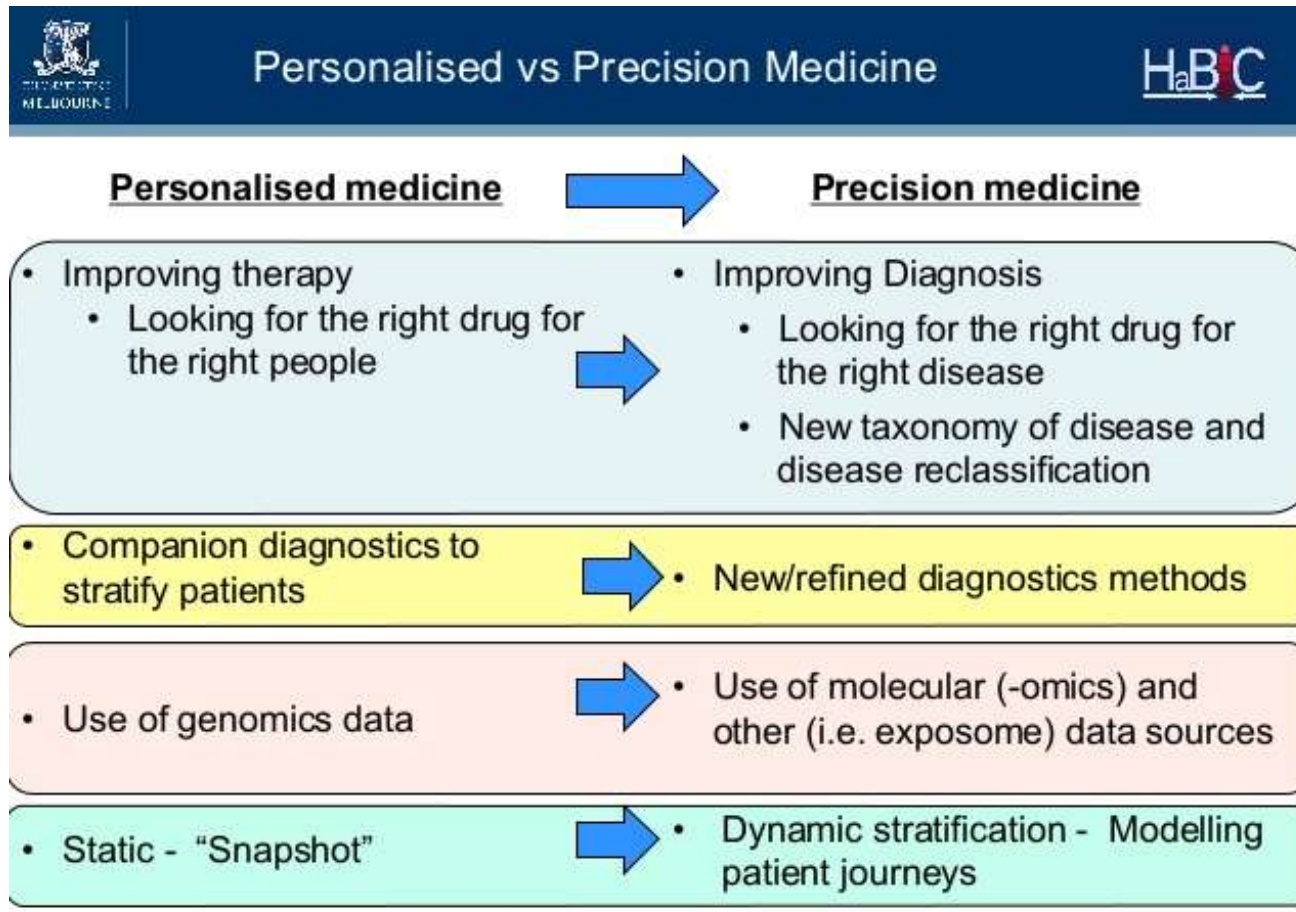
What is Precision cancer medicine

It is an evolving approach to cancer care that aims to leverage new knowledge regarding the pathogenesis of cancer to

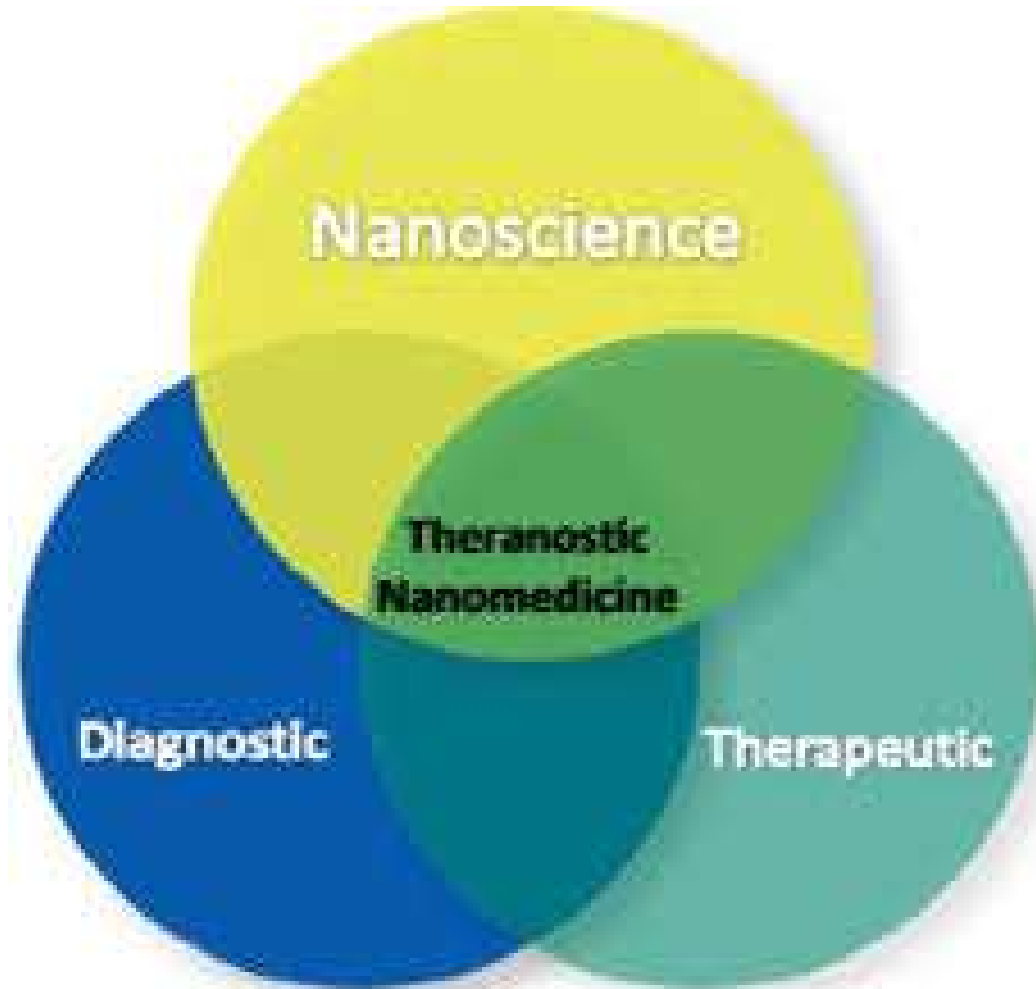
- more precisely target therapy and
- spare normal cells/tissues



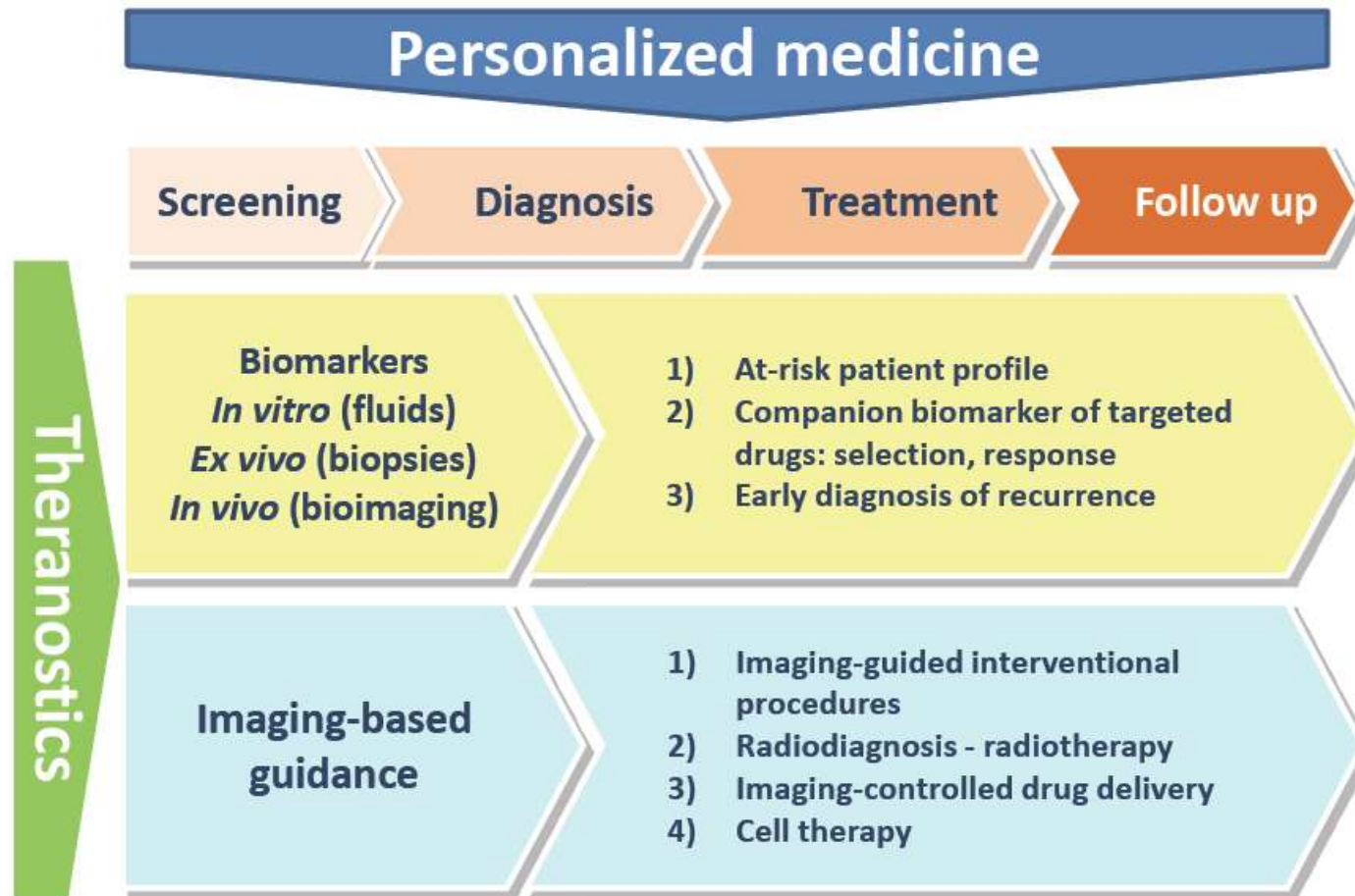
Personalized Evolves to Precision



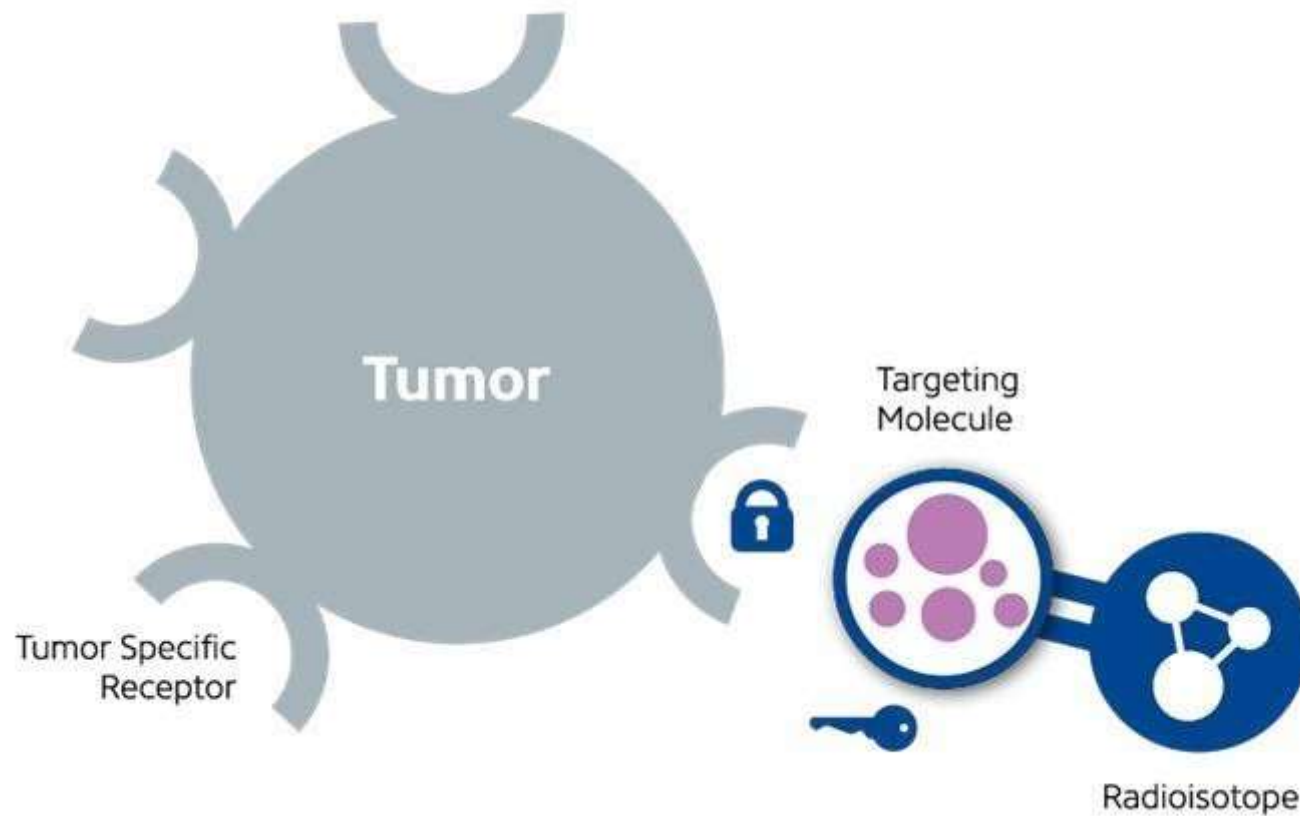
Precision Medicine



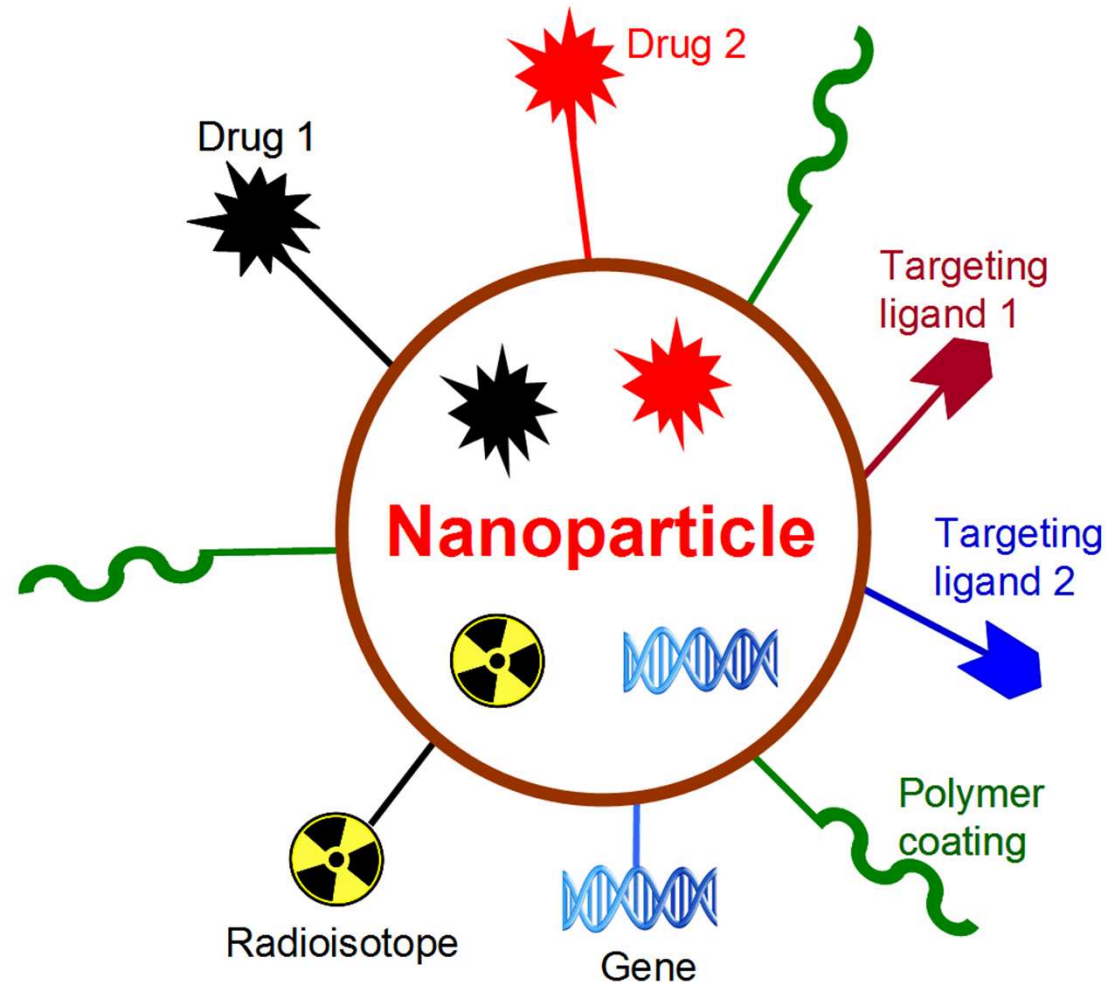
What is Theranostics?



Theranostics: Mechanism



Why is Radio-Targeting Preferred?



Theranostics - 2018

¹⁷⁷Lu-Dotatate Significantly Improves Progression-Free Survival in Patients with Midgut Neuroendocrine Tumours: Results of the Phase III NETTER-1 Trial

Jonathan Strosberg¹, Edward Wolin², Beth Chasen³, Matthew Kulke⁴, David Bushnell⁵, Martyn Caplin⁶, Richard P. Baum⁷, Erik Mittra⁸, Timothy Hobday⁹, Andrew Hendifar¹⁰, Kjell Oberg¹¹, Maribel Lopera Sierra¹², Philippe Ruszniewski¹³, Dik Kwekkeboom¹⁴ on behalf of the NETTER-1 study group

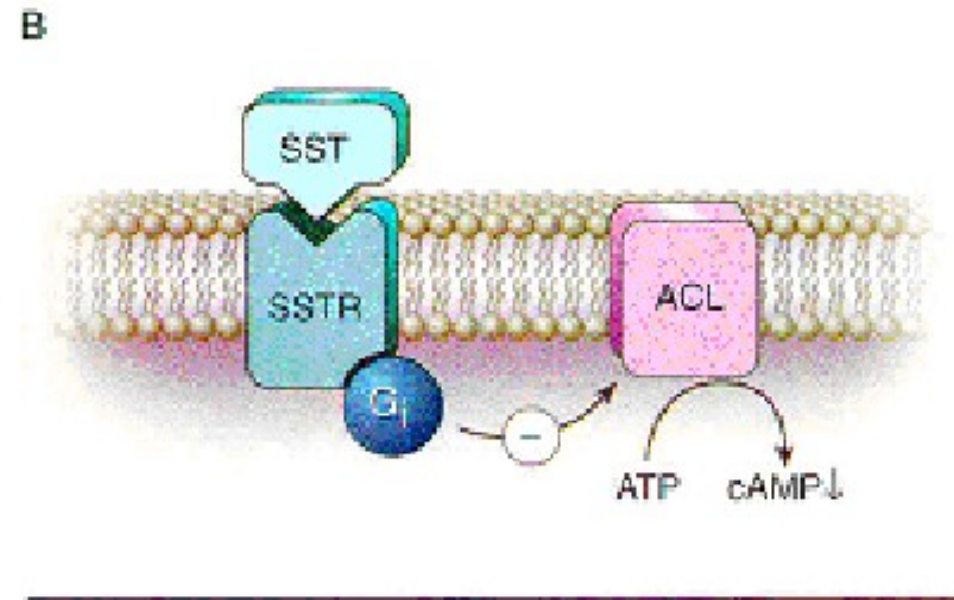
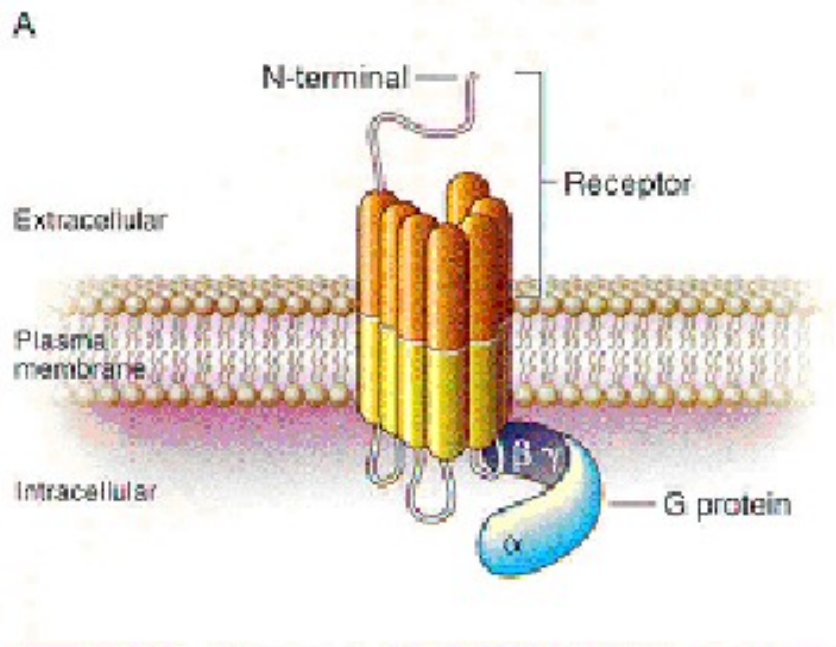
¹ Moffitt Cancer Center, Tampa, FL 33612, USA; ² Markey Cancer Center, University of Kentucky, Lexington, KY 40536-0093, USA; ³ University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA; ⁴ Dana-Farber Cancer Institute, Boston, MA 02215, USA; ⁵ University of Iowa, Iowa City, IA 52242, USA; ⁶ Royal Free Hospital, London, United Kingdom; ⁷ Zentralklinik, Bad Berka, Germany; ⁸ Stanford University Medical Center, Stanford, CA 94305, USA; ⁹ Mayo Clinic College of Medicine, Rochester, MN 55905, USA; ¹⁰ Cedars Sinai Medical Center, Los Angeles, CA 90048, USA; ¹¹ University Hospital, Uppsala University, Uppsala, Sweden; ¹² Advanced Accelerator Applications, New York, NY 10118, USA; ¹³ Hopital Beaujon, Clichy, France; ¹⁴ Erasmus Medical Center, Rotterdam, Netherlands

Presentation Presidential Session II of the 18th ECCO – 40th ESMO – European Cancer Congress 2015, 27 September 2015, abstract 6LBA, Vienna

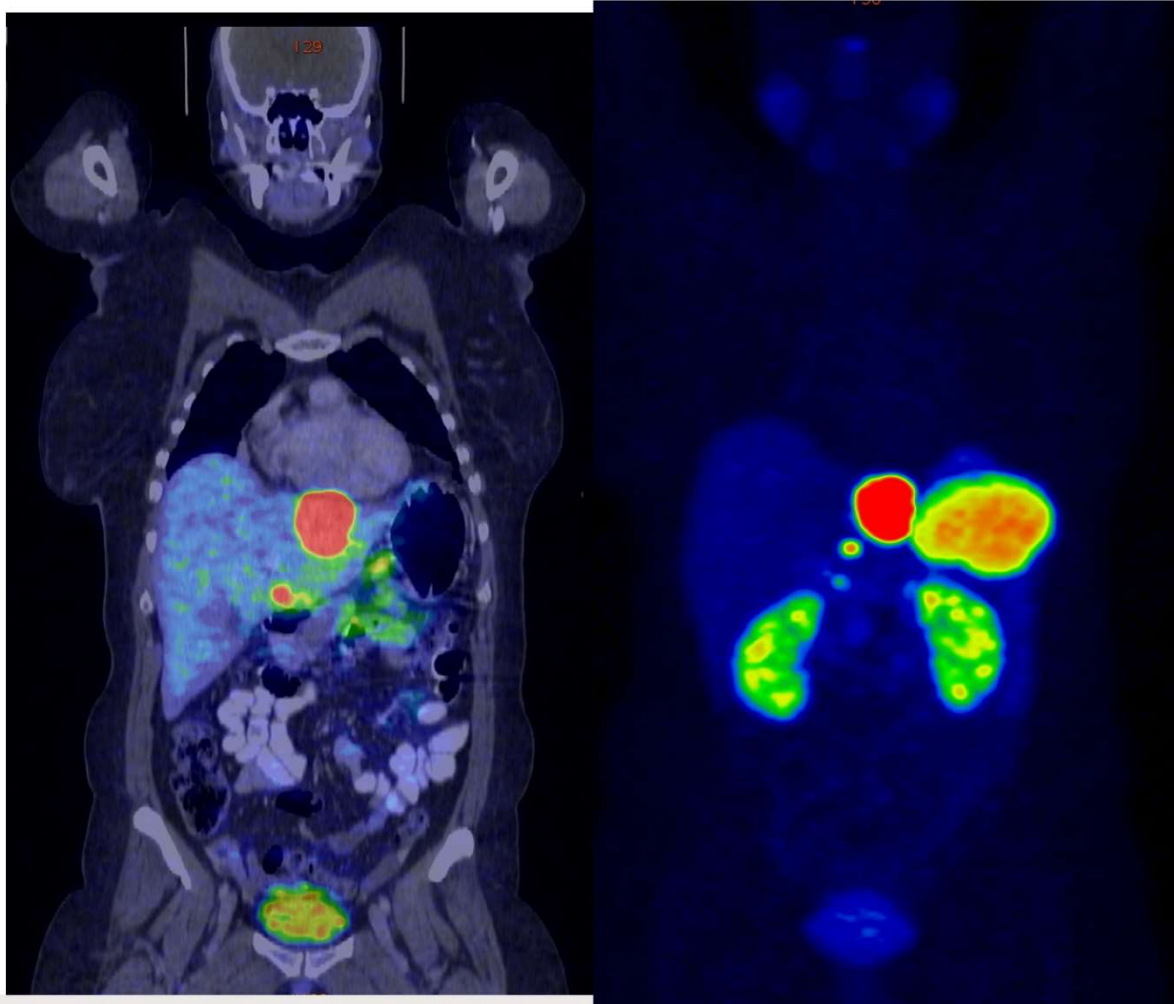
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Neuroendocrine Theranostics – DOTATATE Somatostatin Receptor



Neuroendocrine Theranostics



Neuroendocrine Theranostics: PFS

Progression-Free Survival

N = 229 (ITT)

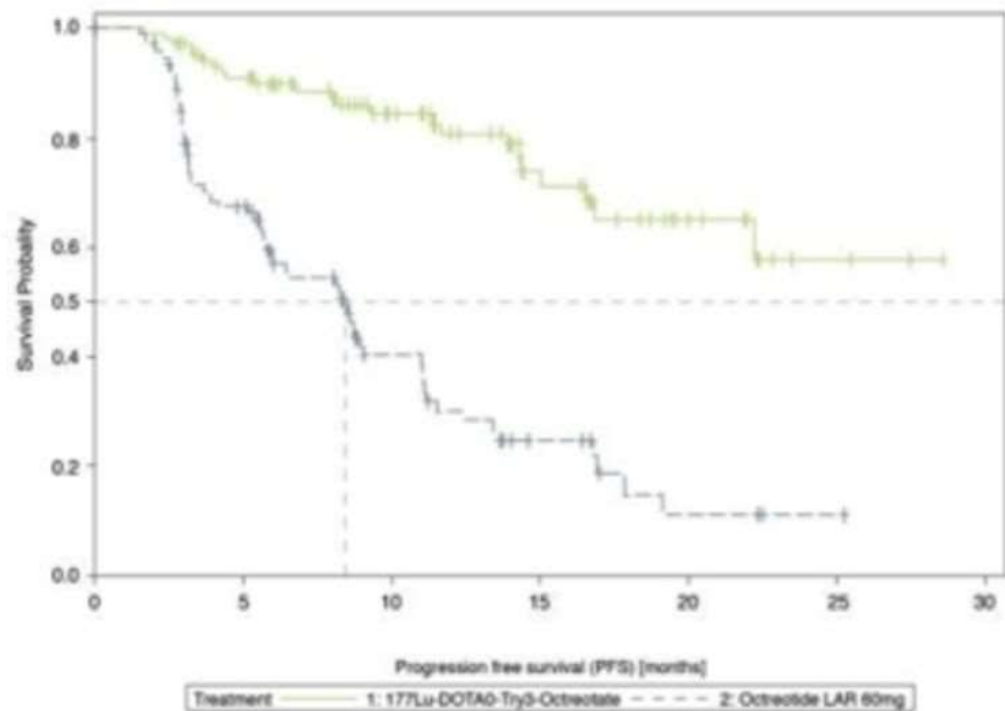
Number of events: 90

- ^{177}Lu -Dotatate: 23
- Oct 60 mg LAR: 67

Hazard ratio: **0.21**
[0.129 – 0.338] **p < 0.0001**

79% reduction in the risk of
disease progression/death

Estimated Median PFS in the
Lu-DOTATATE arm
≈ 40 month



All progressions centrally confirmed and independently reviewed for eligibility (SAP)

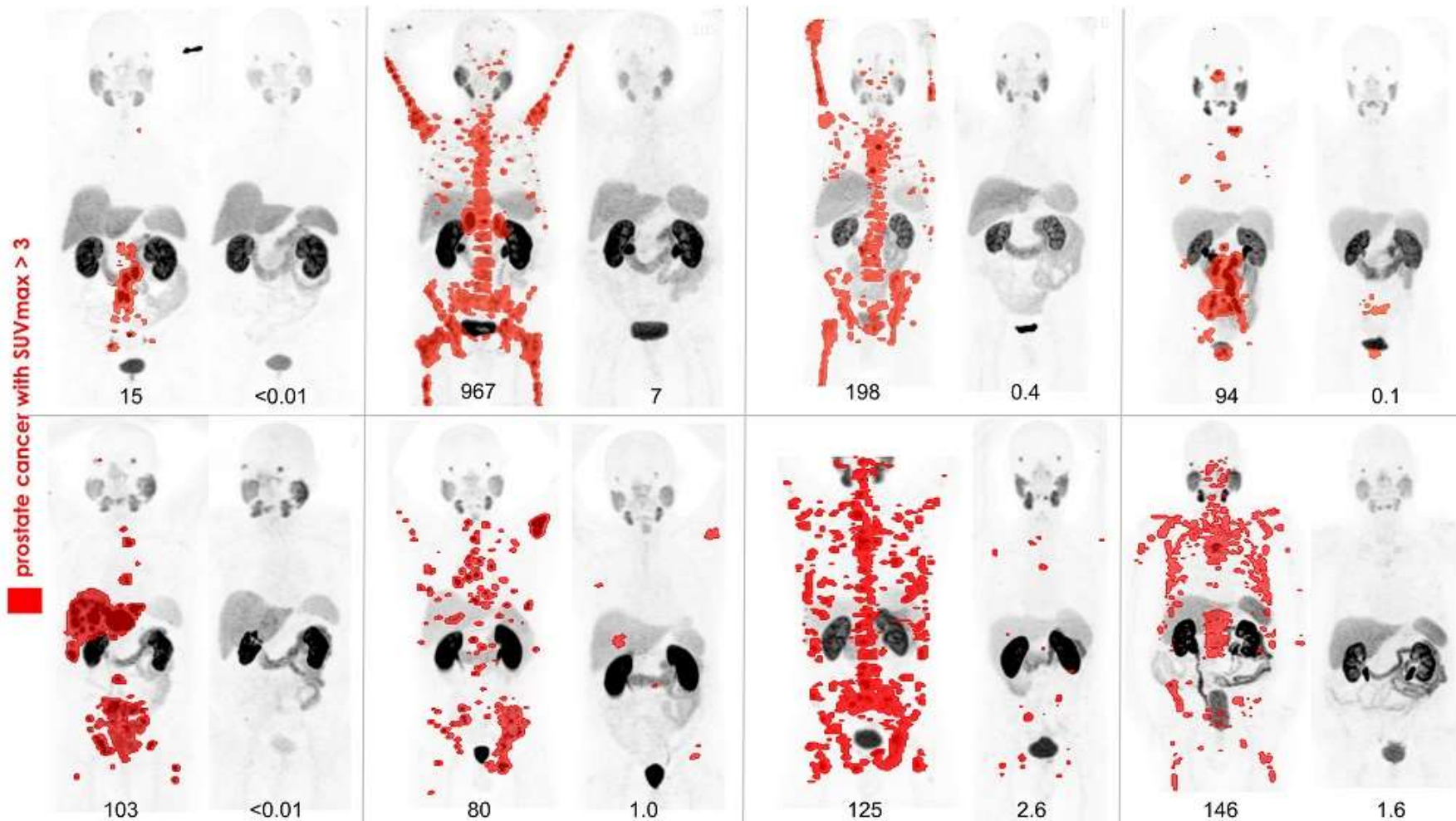


Theranostics in Development

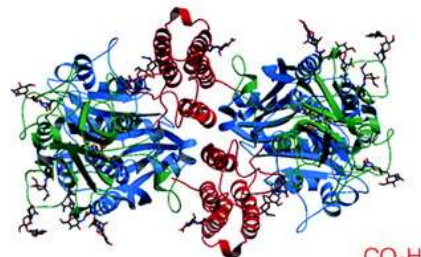
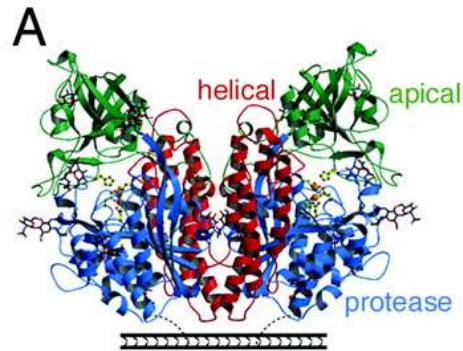
- Prostate
- Breast
- Lung
- CNS
- Melanoma
- Colorectal
- GIST
- Apoptosis and Necrosis (Diagnostic)



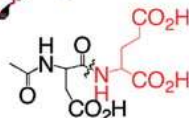
Prostate Cancer Theranostics



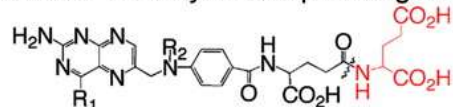
Prostate-Specific Membrane Antigen (PSMA)



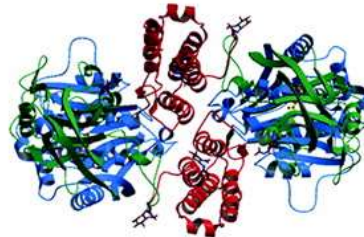
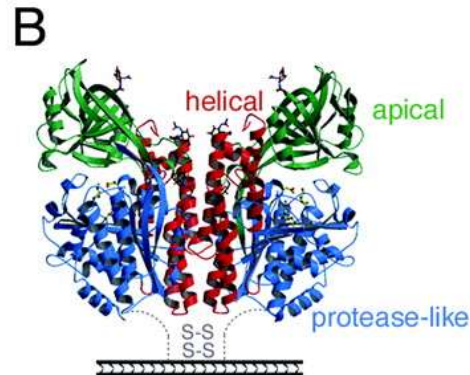
Substrates:



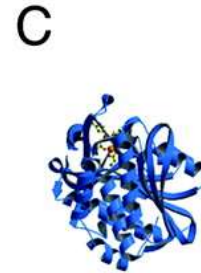
α -NAAG=N-acetylated aspartate glutamate



mono- γ -glutamated folate/methotrexate



Substrates: None



Substrates:
Proteins/polypeptides
with large hydrophobic
N-termini



Substrates:
Folate/methotrexate



Difference in Ligands

Ligands are distinguished by

1. Target Affinity
2. Non-Target Affinity
3. Efficacy
4. Adverse Effects

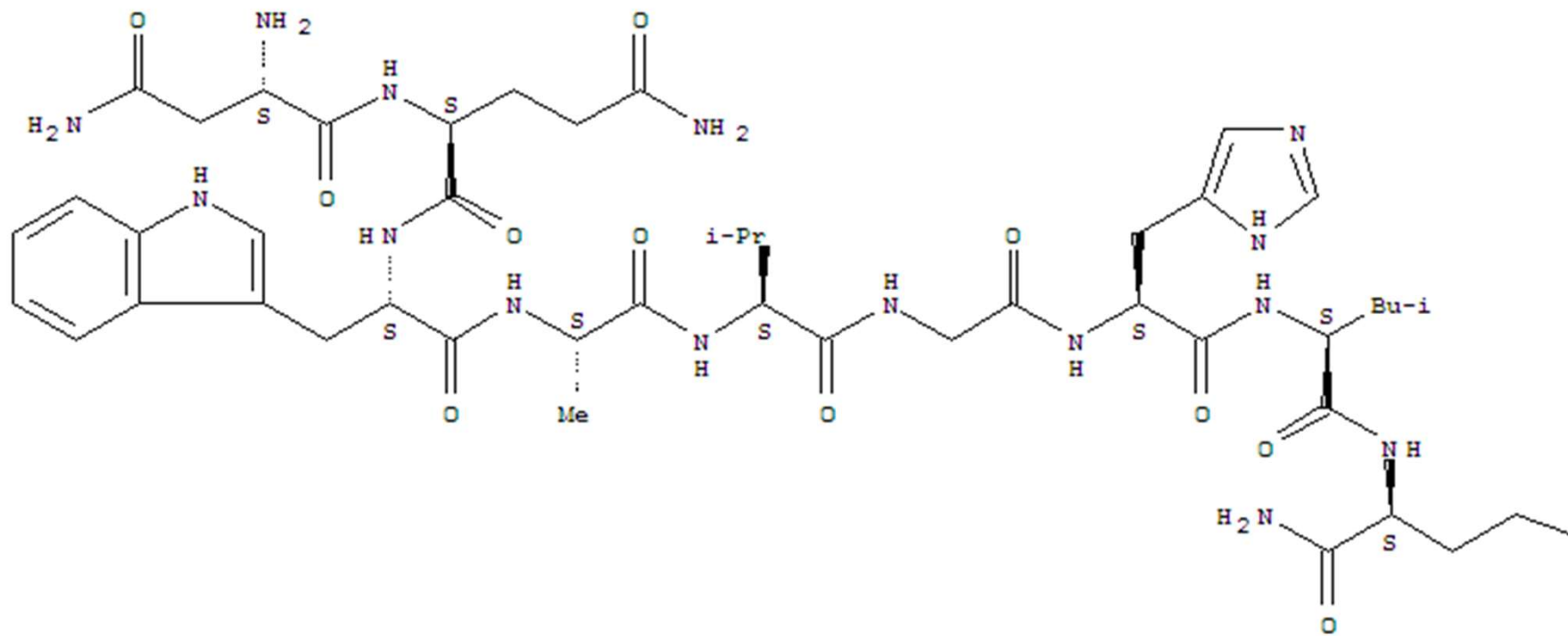


European Fire-bellied Toad



Bombesin

PAGE 1-A



Tumors with Bombesin Receptor Expression

- Head/Neck Squamous Cell 100%
- Small Cell Lung 85%-100%
- Prostate 62%-100%
- Non-small Cell Lung 74%-78%
- Breast 38%-72%





Questions or Comments?