Universitätsmedizin Essen
Universitätsklinikum

# Access and basic principles of radiopharmaceuticals

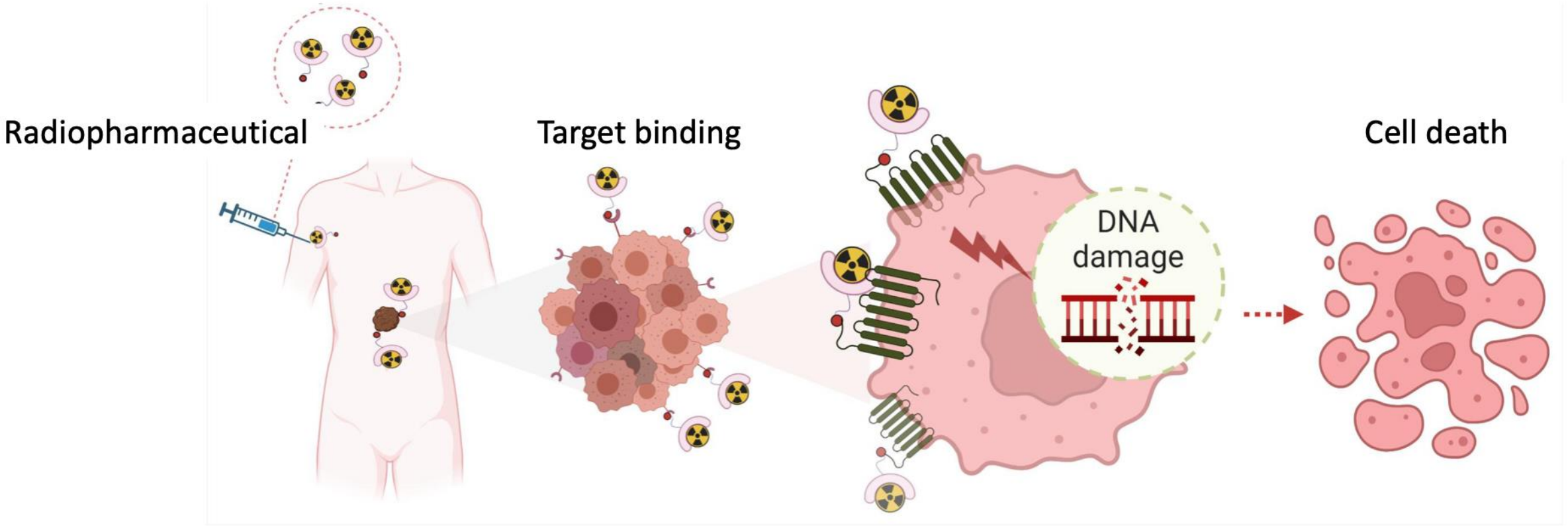
Viktor Grünwald, MD
Professorship for Urologic Oncology

# Conflicts of interest

Financial Interests
Invited Speaker, Personal: Amgen, AstraZeneca, Astellas, BMS, EISAI, Ipsen, Johnson & Johnson, Merck, MSD, Pfizer, Novartis/AAA, Telix Pharmaceutical, Roche
Advisory Board, Personal: BMS, EISAI, Ipsen, Debiopharm, Gilead, Johnson & Johnson, Merck, MSD, Novartis, Oncorena, Recordati, Synthekine
Stocks/Shares, Personal: Amgen, AstraZeneca, BMS, Bicycle Therapeutics, MSD, Genmab
Steering Committee Member: Amgen, BMS, EISAI, Ipsen
Research Grant, Financial interest, Institutional: AstraZeneca, BMS, MSD, Ipsen, Pfizer
Travel support: Ipsen, Johnson & Johnson, Merck, Pfizer

Non-Financial Interests
Membership: ASCO, ESMO, German medical Oncology and Hematology Society
Advisory role: German Cancer Society
Leadership role: Working Group medical oncology (AIO)

# The principle of Radioligand therapy






Jäkel et al. AACR 2024 (Figure adapted from Desai *et al.*, 2022 by using BioRender)

# Radioligand therapy

## chances:

transforming treatment

next generation drugs/regimen

combinations

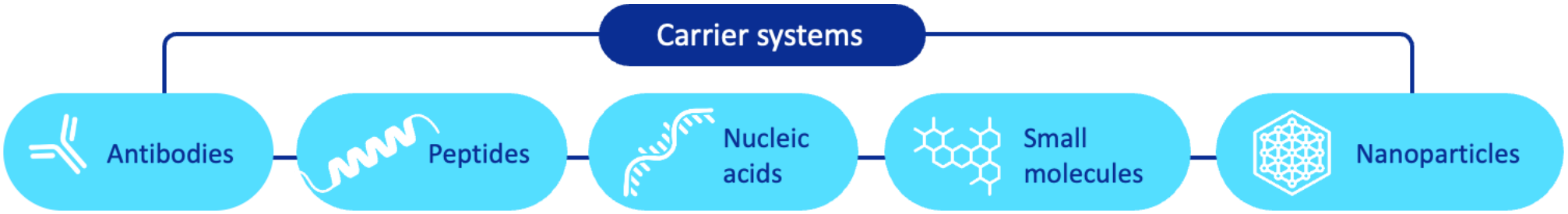
## challenges:

infra structure:
- centers
- qualified employees

health care structure:
- economics
- referrals

guidance for future development

# One target - multiple carrier systems possible



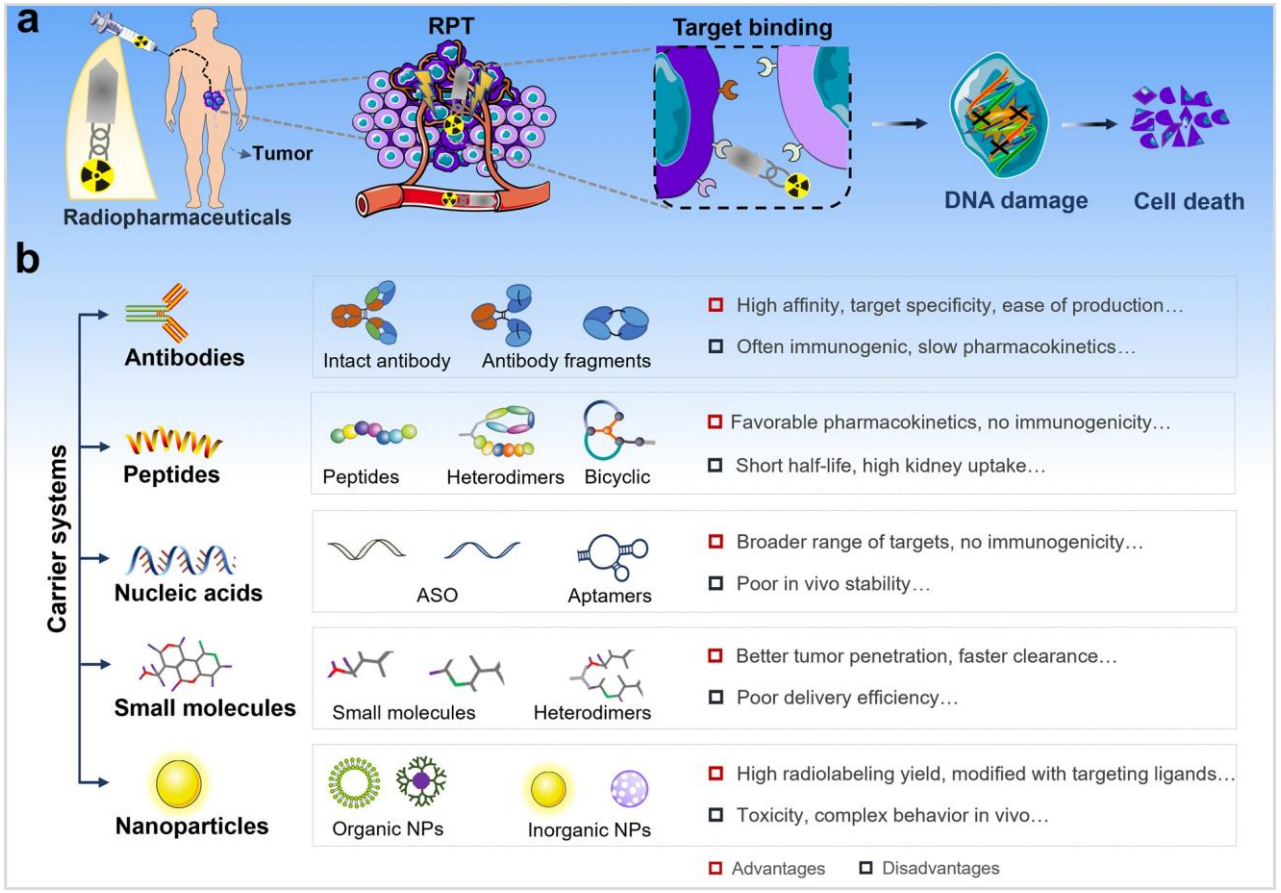

Determining factors for clinical development:

target affinity
bio-distribution
immunogenicity

size & weight
tumor penetration & retention
non-specific binding
metabolism/clearance

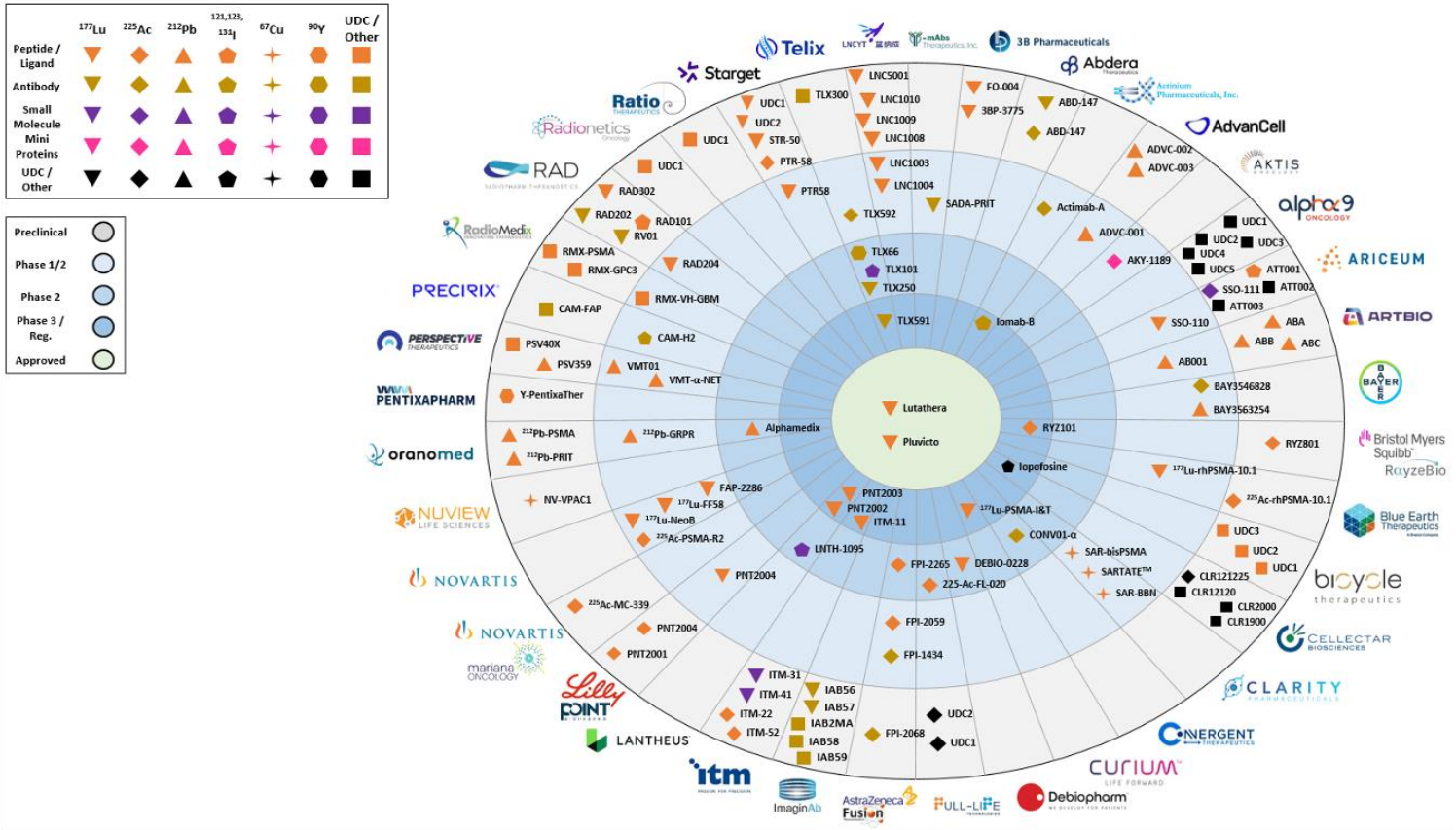
stability
ease of synthesis/labelling
dosing regimen
organ exposure
toxicity

# Carrier systems come with strengths and weaknesses in drug development

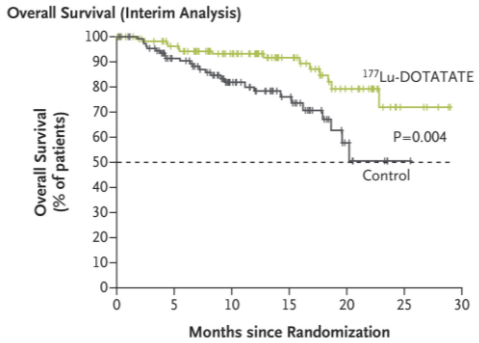



Zhang et al. *Cell Death Discov.* 10, 16 (2024). https://doi.org/10.1038/s41420-023-01778-3

# The pipeline for novel cancer radio-therapeutics is rich and diverse



# Where are we today ? - available licensed agents




Strosberg et al. N Engl J Med 2017;376:125-35. DOI: 10.1056/NEJMoa1607427

NET: Orphant disease

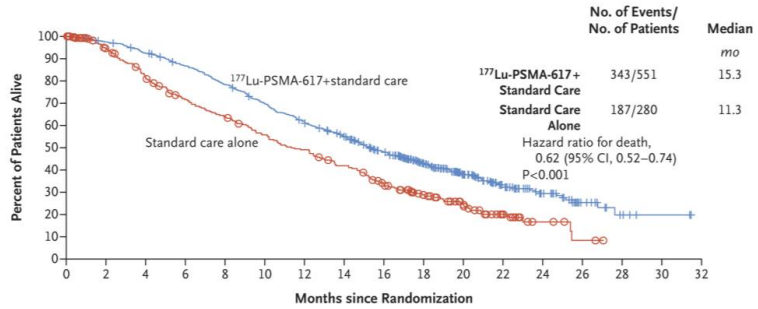
somatostatin receptor (SSTR)

PSMA

$Lu^{177}$ Oxodotreotide

$Y^{90}$ DOTATOC

$Lu^{177}$ PSMA617



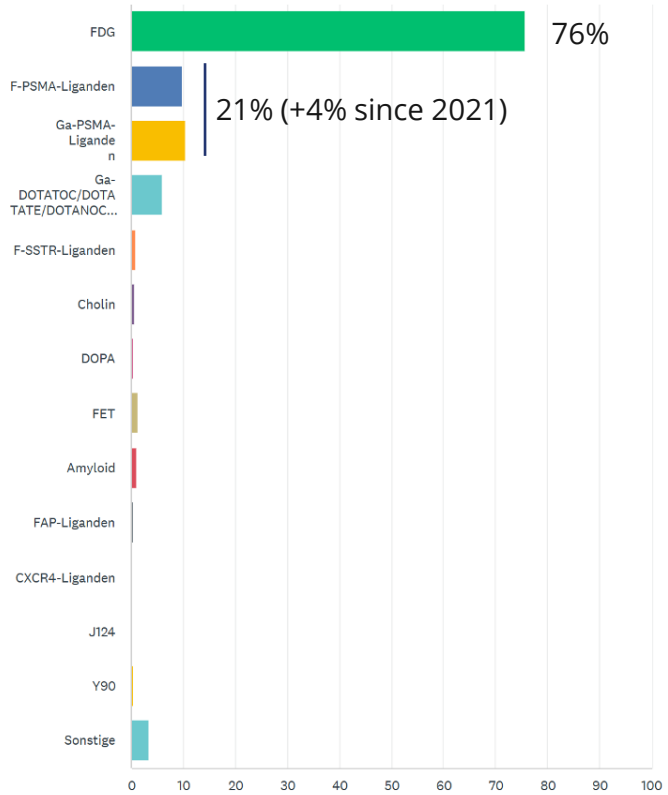

Prostate cancer:
1 467 854 (global incidence)



SmPC: https://www.ema.europa.eu/

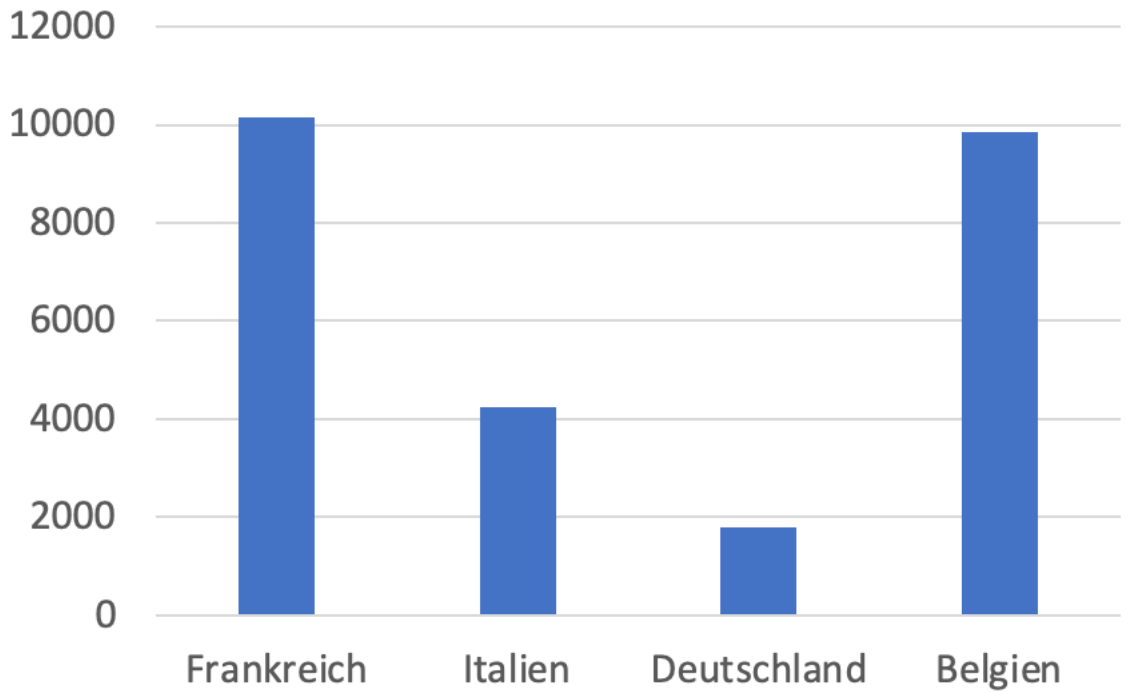
# Use of tracer and PET scans in Germany and EU

Tracer use (Germany 2022)



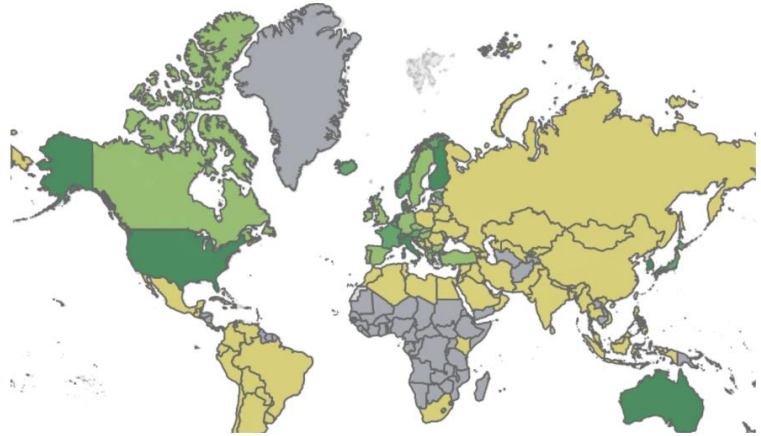

Survey of the DGN/BDN 2022 in Germany

number of PET per 1 Mio inhabitants (2021)




sources:1..SFMN - ACTIVITÉ ET MOYENS DE LA MÉDECINE NUCLÉAIRE FRANÇAISE EN 2021. 2.RIZIV/INAMI - Report on Medical oncology - PET-Scan (radioisotopes) 10 June 20223.Italian Association of Nuclear Medicine and Molecular Imaging (*Daten 2019)

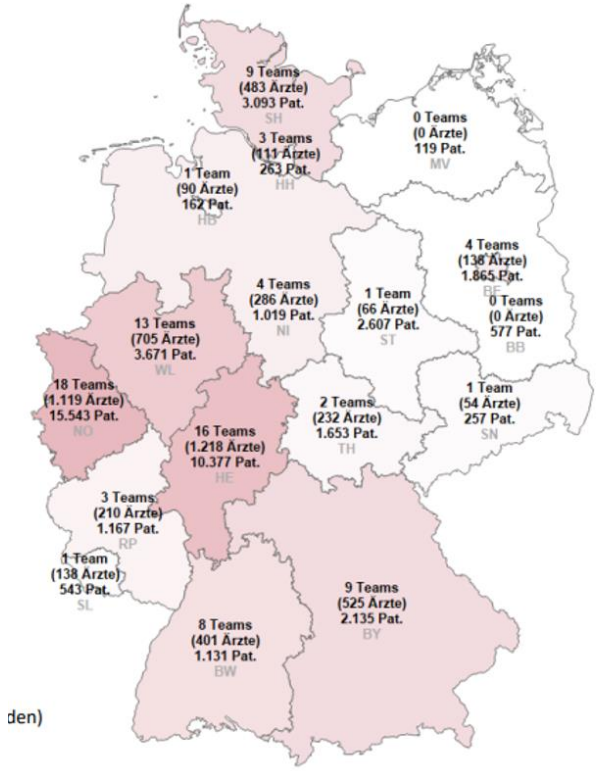
# PET availability and specialized MDT teams




| Income Group | Countries | Countries with PET sca.. | Population (mil) | Number of PET scanners | PET scanners (per 1 mil) |
|---|---|---|---|---|---|
| High Income | 75 | 51 | 1,237M | 4,356 | 3.522 |
| **Germany** | | | **84M** | **≈ 180** | **≈ 2** |
| Upper-Middle Income | 54 | 35 | 2,854M | 860 | 0.301 |
| Lower-Middle Income | 50 | 20 | 2,913M | 451 | 0.155 |
| Low Income | 30 | 1 | 669M | 3 | 0.004 |

Source: IAEA IMAGINE Database

Availability of specialized multidisciplinary GU teams (ASV teams) varies across Germany



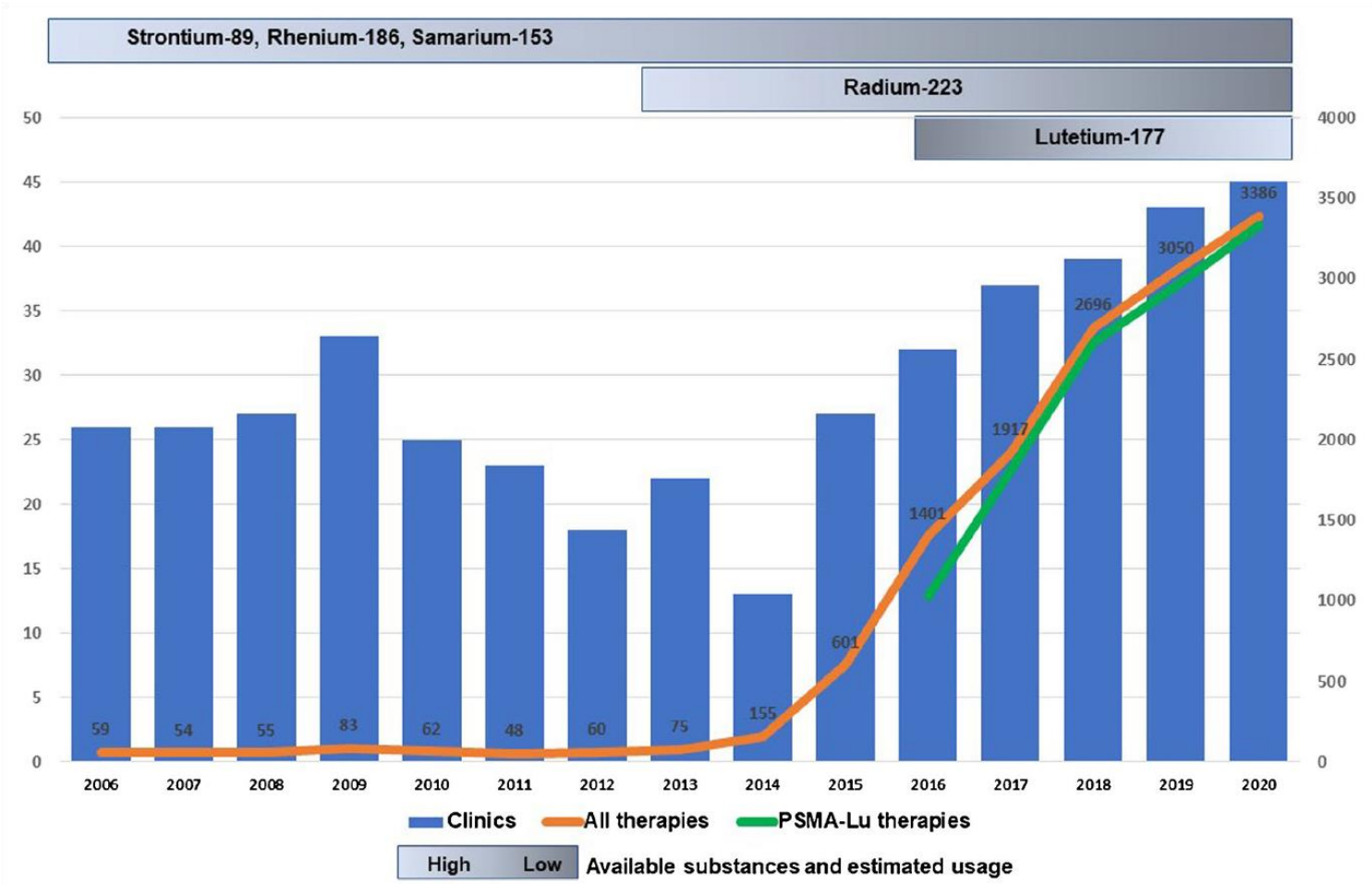

29.03.23

# Nuclear medicine capacity in Germany

- currently approx. 680 beds in Germany available (in 2018: 754)
- minimum duration for each inpatient application: 2 nights
- approx. 120 annual therapies per bed realizable
- 120*680 = 81.600 annual therapies - if perfectly allocated
- better utilization of current capacities necessary


Zippel C et al. Nuklearmedizin 2021; 60: 216–223

# 177Lu-PSMA is a driver of change among radio-pharmaceutical treatments






Flegar C et al. European Journal of Nuclear Medicine and Molecular Imaging (2023) 50:2188–2195

# Which data drives clinical recommendations?

## Clinical trial:

highest quality possible

prospective collection

controls known biases

data only for selected populations available

## Real-World-Data:

retro- or prospective collection

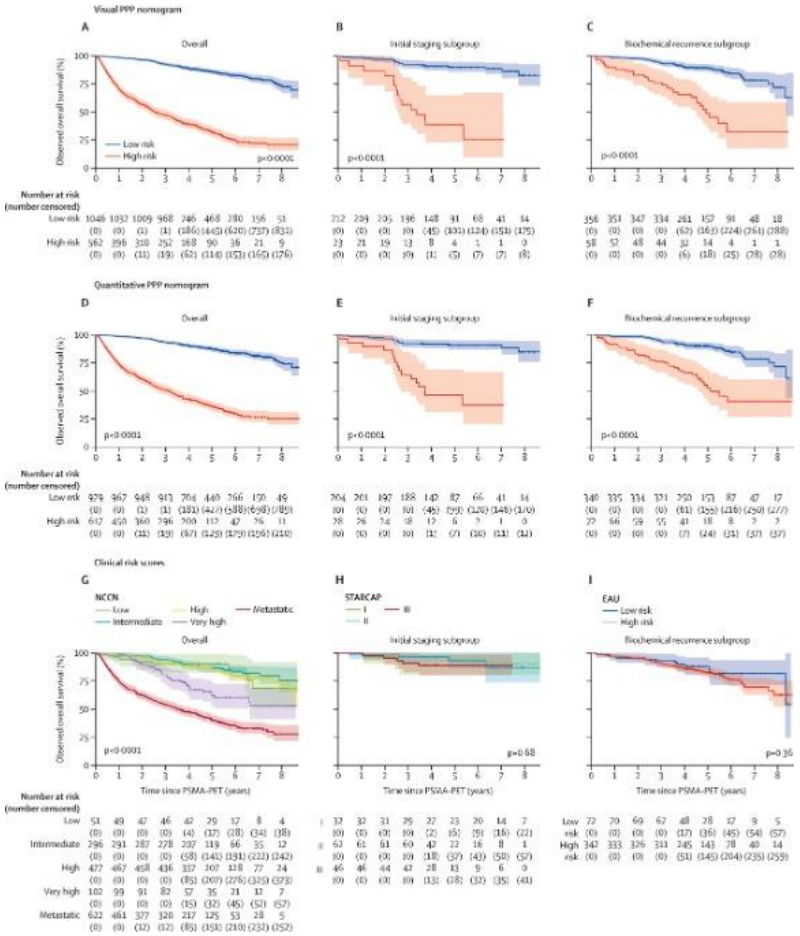
broader population

includes rare subtypes

does not control bias

difficult to compare across treatments

# RWD may lead to novel insights and applications

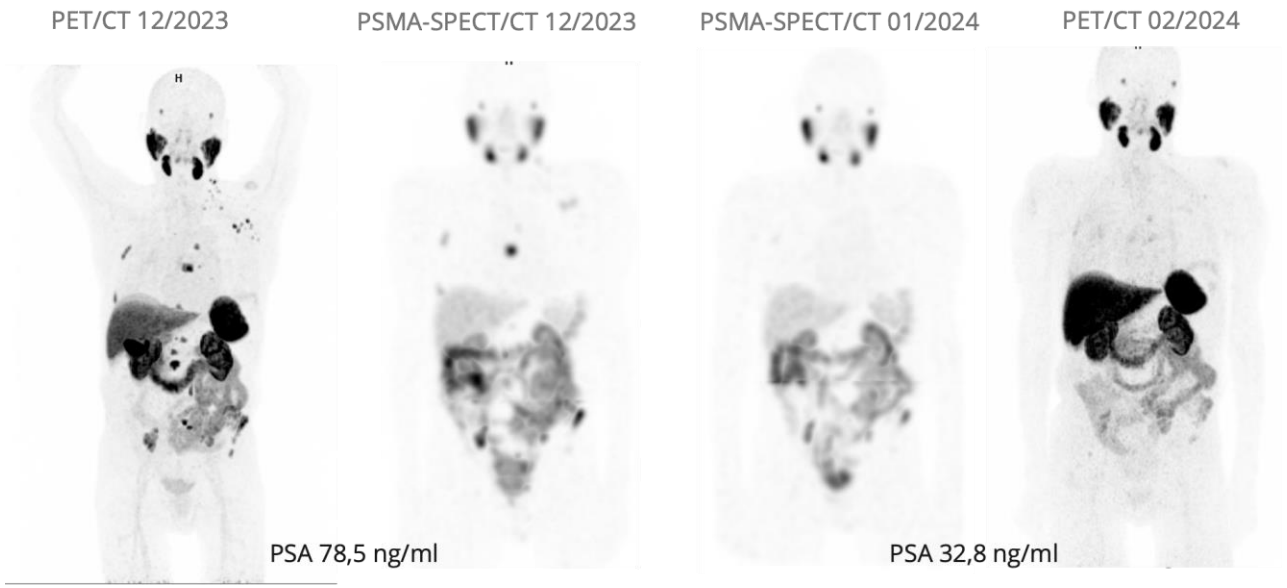



for instance: novel application of PET information on prognostication



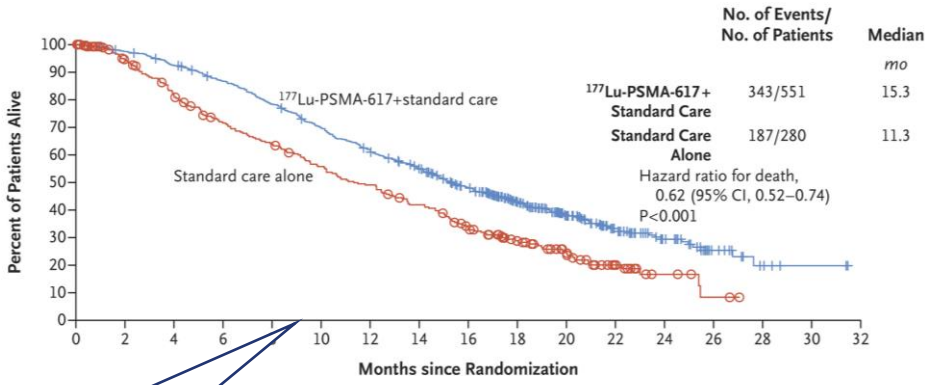
Karpinski et al. Lancet Oncology, Volume 25, Issue 9, 1188 - 1201

# PSMA-RLT - a standard of care in mCRPC patients




permitted continuation of ARPI

Lu$^{177}$-PSMA617

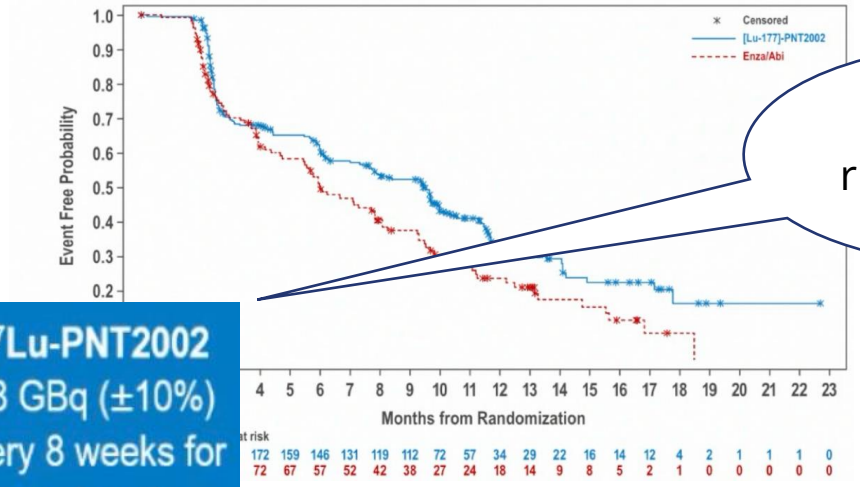



Sartor et al N Engl J Med 2021;385:1091-1103. DOI: 10.1056/NEJMoa2107322

Which is the best dose and regimen?

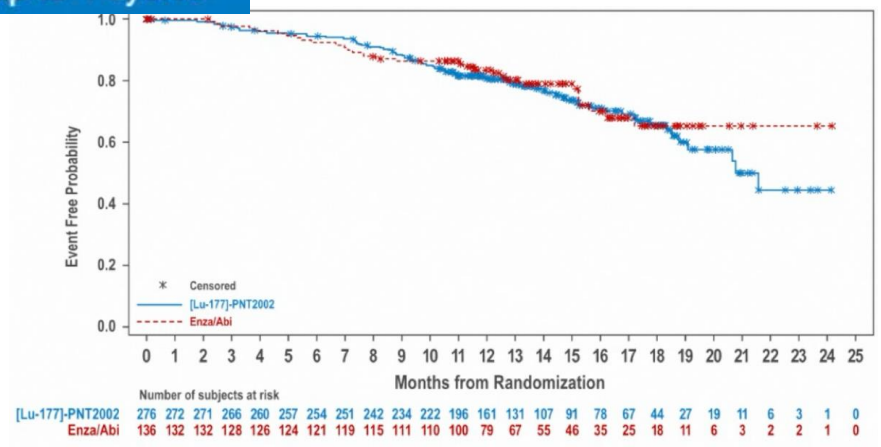
What is the role of combinations?

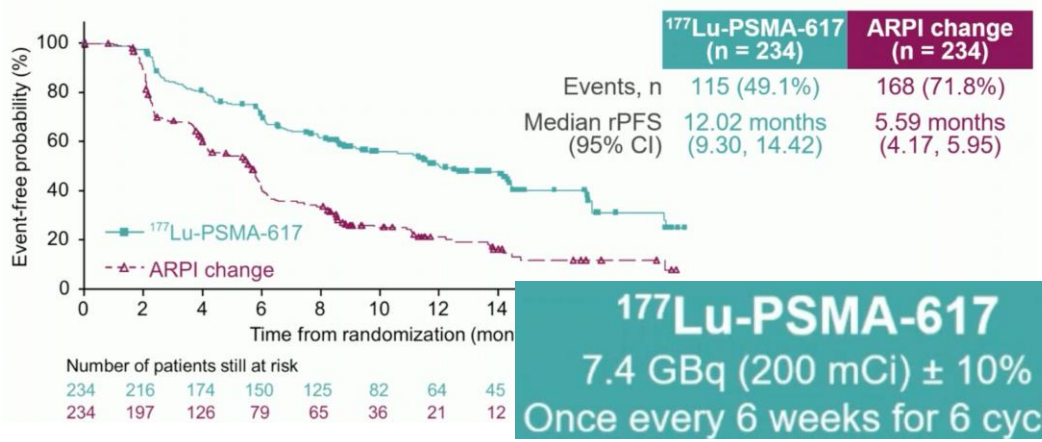
# Other phase III trials did not reported overall survival: SPLASH and PSMAfore in mCRPC




right dose?
right schedule?

**$^{177}$Lu-PNT2002**
6.8 GBq (±10%)
every 8 weeks for
up to 4 cycles

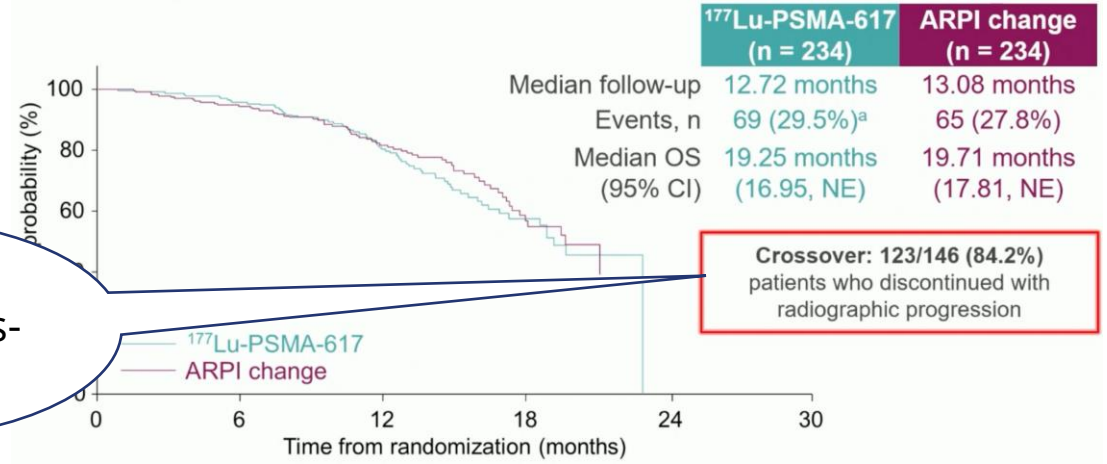



| | $^{177}$Lu-PSMA-617 (n = 234) | ARPI change (n = 234) |
|---|---|---|
| Events, n | 115 (49.1%) | 168 (71.8%) |
| Median rPFS (95% CI) | 12.02 months (9.30, 14.42) | 5.59 months (4.17, 5.95) |

**$^{177}$Lu-PSMA-617**
7.4 GBq (200 mCi) ± 10%
Once every 6 weeks for 6 cycles

what is the effect of cross-over?




| | $^{177}$Lu-PSMA-617 (n = 234) | ARPI change (n = 234) |
|---|---|---|
| Median follow-up | 12.72 months | 13.08 months |
| Events, n | 69 (29.5%)[a] | 65 (27.8%) |
| Median OS (95% CI) | 19.25 months (16.95, NE) | 19.71 months (17.81, NE) |

**Crossover: 123/146 (84.2%)**
patients who discontinued with radiographic progression

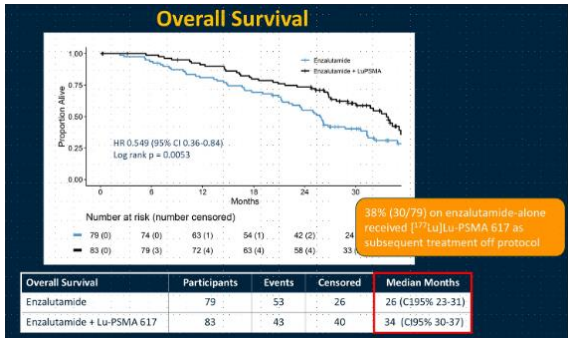


Sartor et al. ESMO24: LBA65

Sartor et al. ESMO23: LBA13

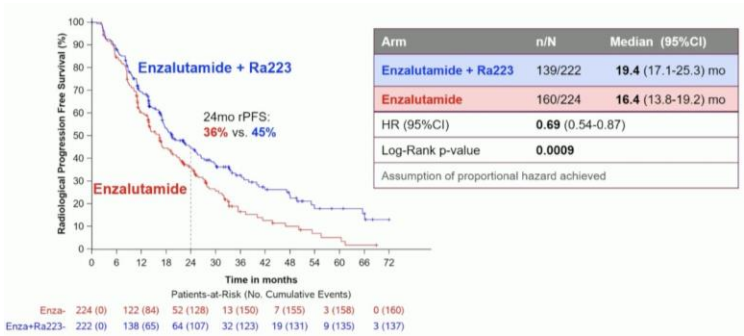
# Are combinations a way forward?

Enzalutamide + Lu$^{177}$-PSMA617




Louise Emmett, ASCOGU 2025: 17

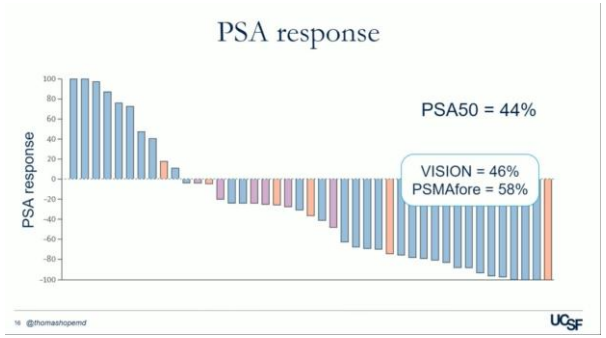
Enzalutamide + Radium223




Gillesen et al. ESMO 2024: LBA1

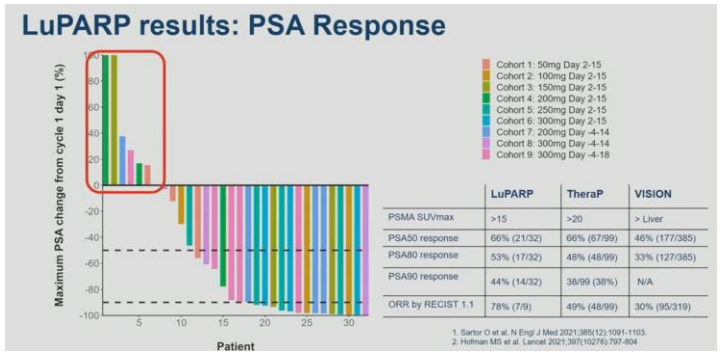
👍 tolerable & safe
👍 additive effects

Lu$^{177}$-PSMA617 + Pembrolizumab




Sandhu et al. ASCO 2022: 5017

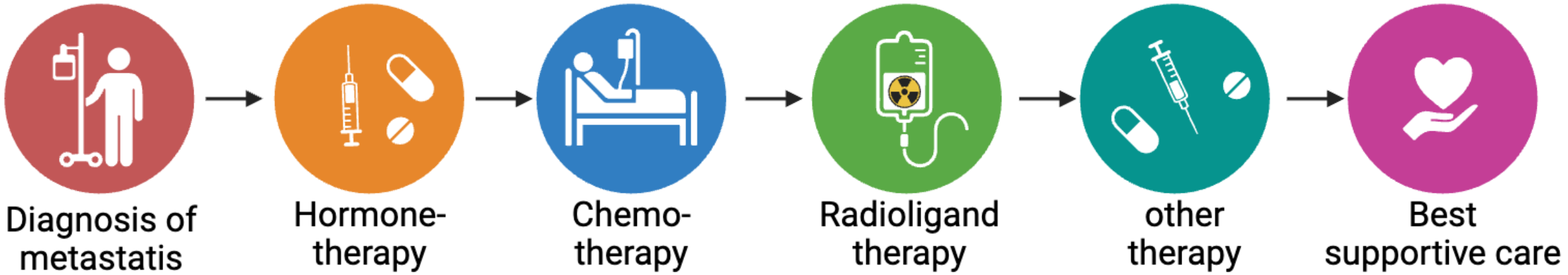
Lu$^{177}$-PSMA617 + Olaparib



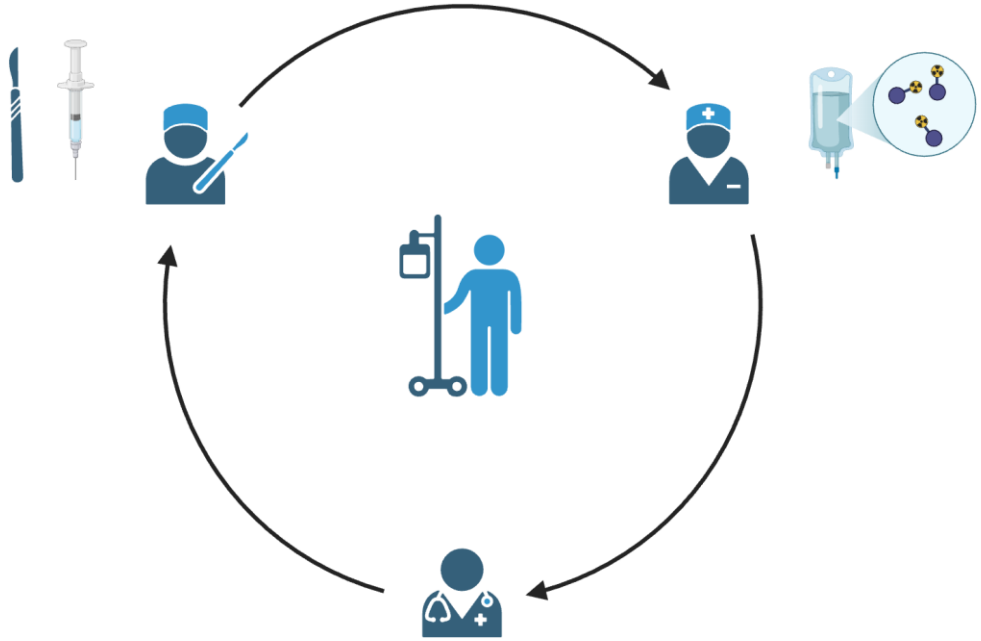

Sandhu et al. ASCO 2023: 5005

✋ no synergism

# Principle therapeutic components in prostate cancer can come in sequence, circles or at the same time



# Patients travel across different specialized disciplines



Urology

Surgery
Hormone-therapy
Supportive care

Nuclear Medicine

Diagnostics
Radio-ligand therapy

Medical Oncology

Medical therapy
Supportive care

created with Biorender

this image is reduced for simplification. The full scope of patient care involve multiple and more stakeholders

# How to connect patients pathways and over-come barriers in patient care?

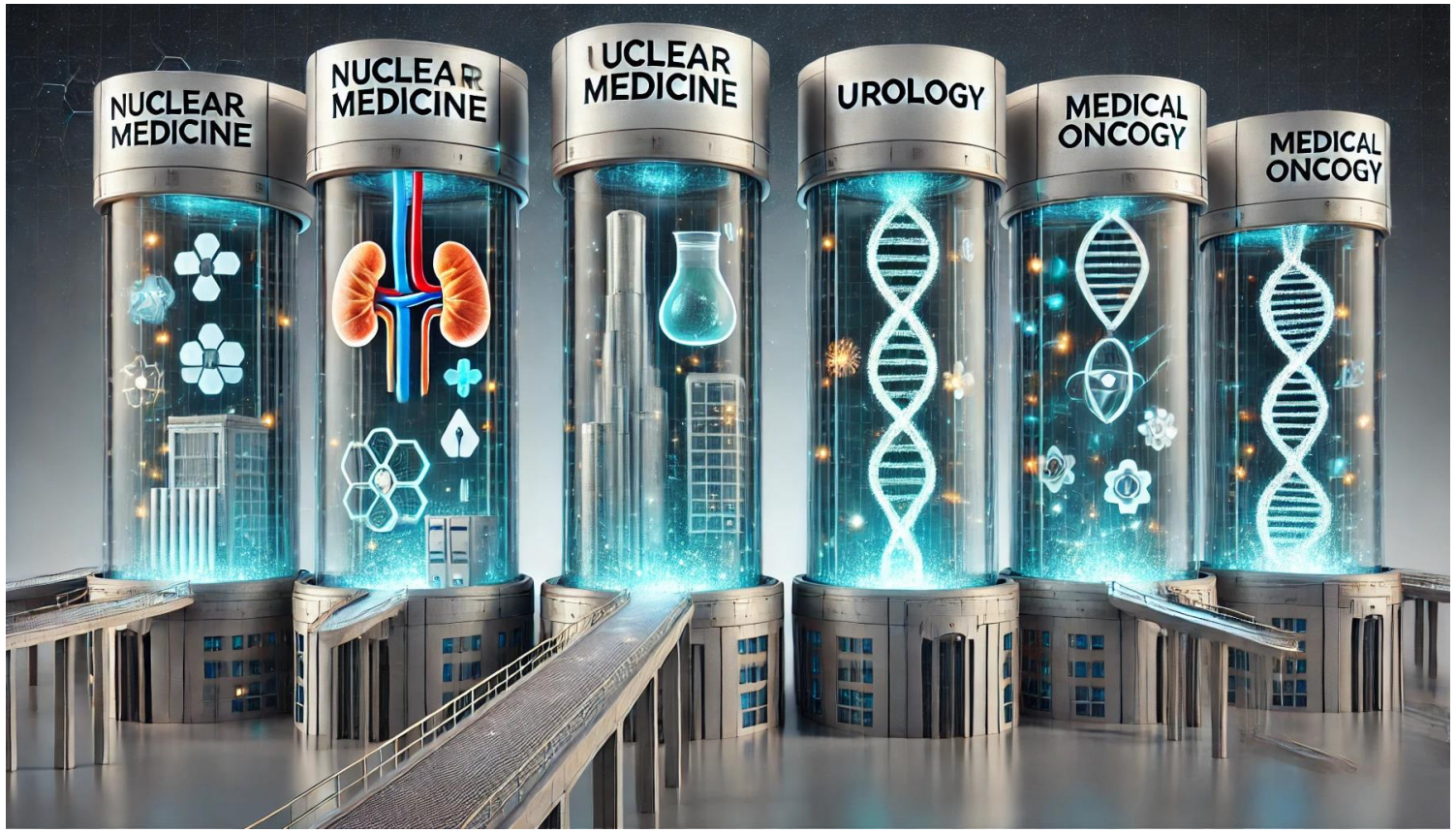



image created by chat GPT

# Chances and barriers for radio-pharmaceuticals

## Access:

- define cross-sectional patient pathways
- provide sufficient hospital facilities
- integrate into the national health care plan

## Authorities:

- build a clear regulatory framework for the use of radio-pharmaceuticals (approval, funding, re-imbursement)
- establish and educate about nuclear waste and disposal policies

## Medical:

- increase awareness and build up national expertise (specialized network)
- integration of nuclear medicine expertise into MDT
- establish RW-registries to assess effectiveness of radio-pharmaceuticals

# Over-coming hurdles in the development - trans-sectoral network

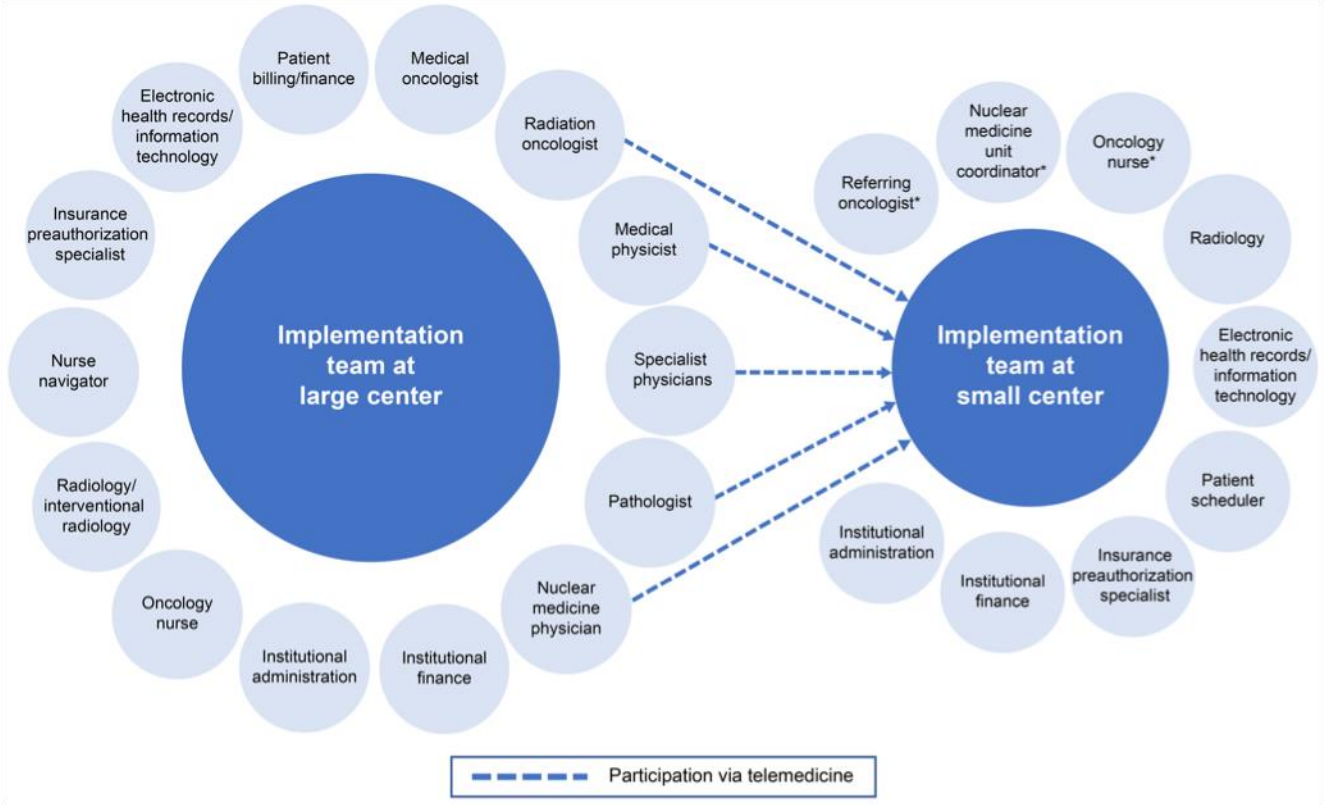
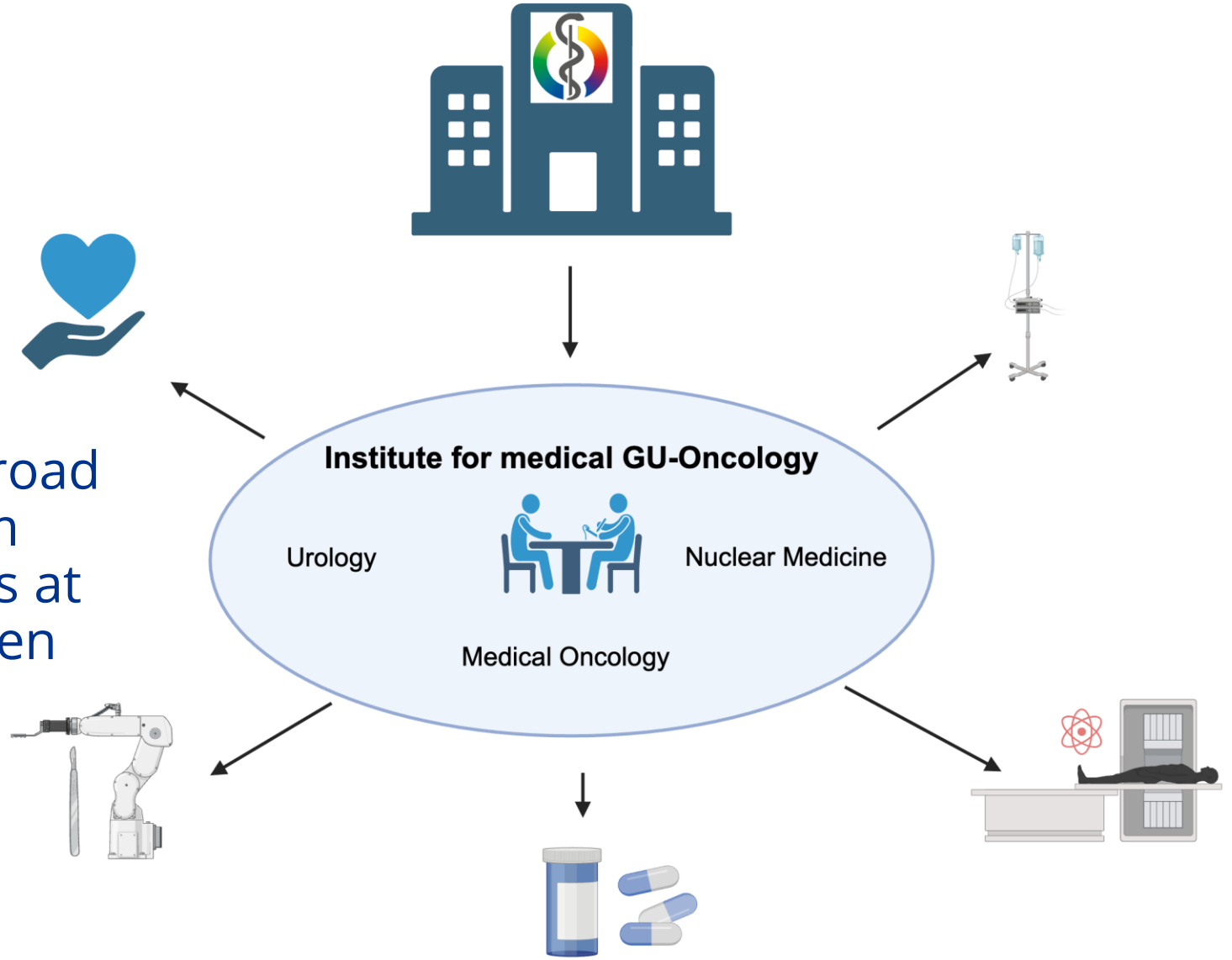




FIGURE 1 Therapy rooms and dedicated restrooms for patients receiving $^{177}$Lu-DOTATATE– and $^{131}$I-MIBG. (A) Treatment room for patients receiving $^{177}$Lu-DOTATATE. The room itself does not need to be shielded. (B) Dedicated restroom for patients receiving $^{177}$Lu-DOTATATE. (C) Treatment room for patients receiving $^{131}$I-MIBG. The room is appropriately shielded (lead-lined). (D) Dedicated, shielded restroom for patients receiving $^{131}$I-MIBG.


Mittra et al. Cancer Medicine. 2024;13:e6780. https://doi.org/10.1002/cam4.6780

# Bridging gaps - teaming a broad multidisciplinary GU team across treating departments at the University Hospital Essen





created with Biorender

# Conclusions

NET and mCRPC are the first indications for radio-nucleotide therapy

Next generation of RLT therapies and combinations are next steps

Changes in the health care structure and networking across disciplines are key

# thank you for your attention

Viktor Grünwald, MD

Professor for Urological Oncology

University Hospital Essen

@ViktorGruenwald