Quo vaditis, Radiopharmaka?

Michael Hinterreiter / ÖVS-Frühjahrstagung 2024 (Graz)

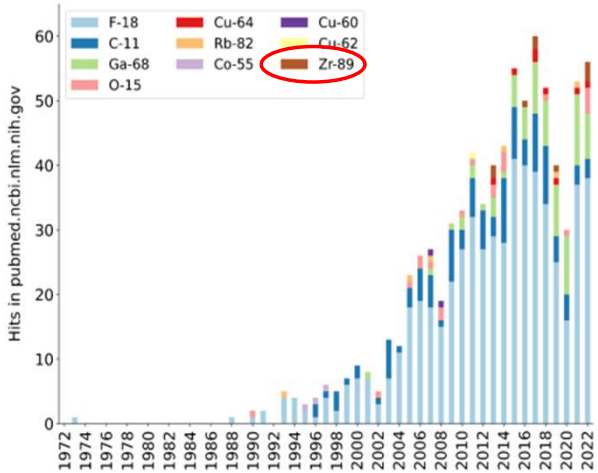
Interessenskonflikt…

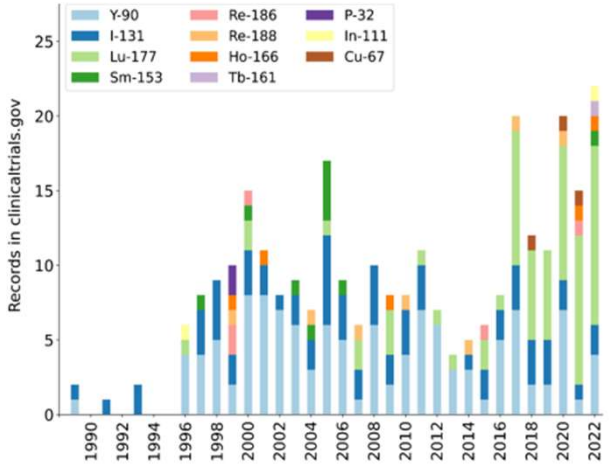
- GE HealthCare - Product Leader Molecular Imaging ACH

Agenda

- Diagnostik
- Therapie
- Thera(g)nostik

Quo vaditis?





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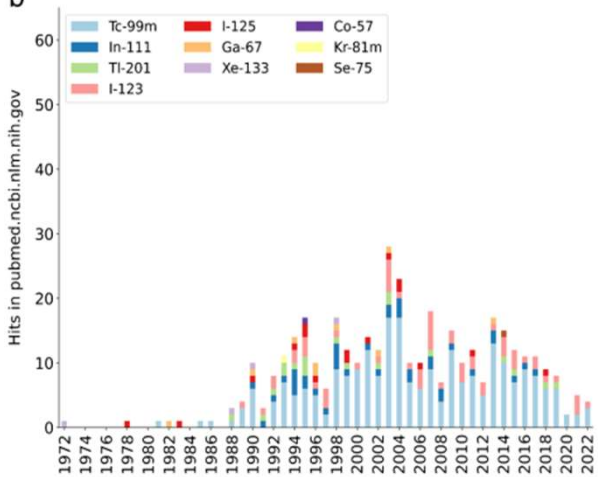

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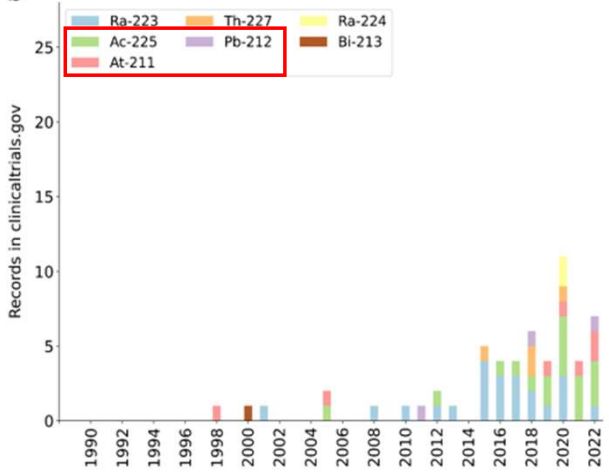
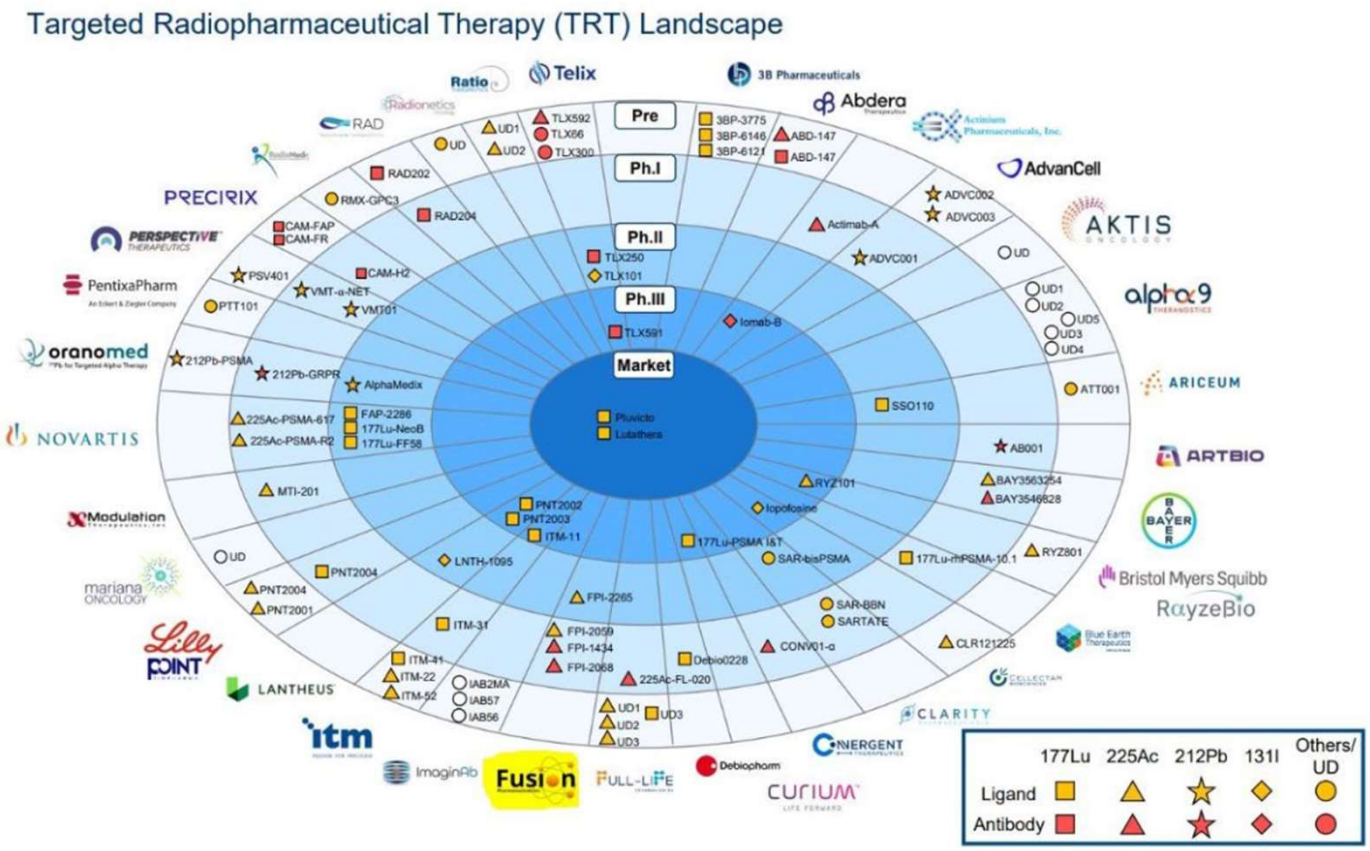


Stokke C. et al., EJNMMI 2024

Quo vaditis?



RBC Equity Research

Quo vaditis?

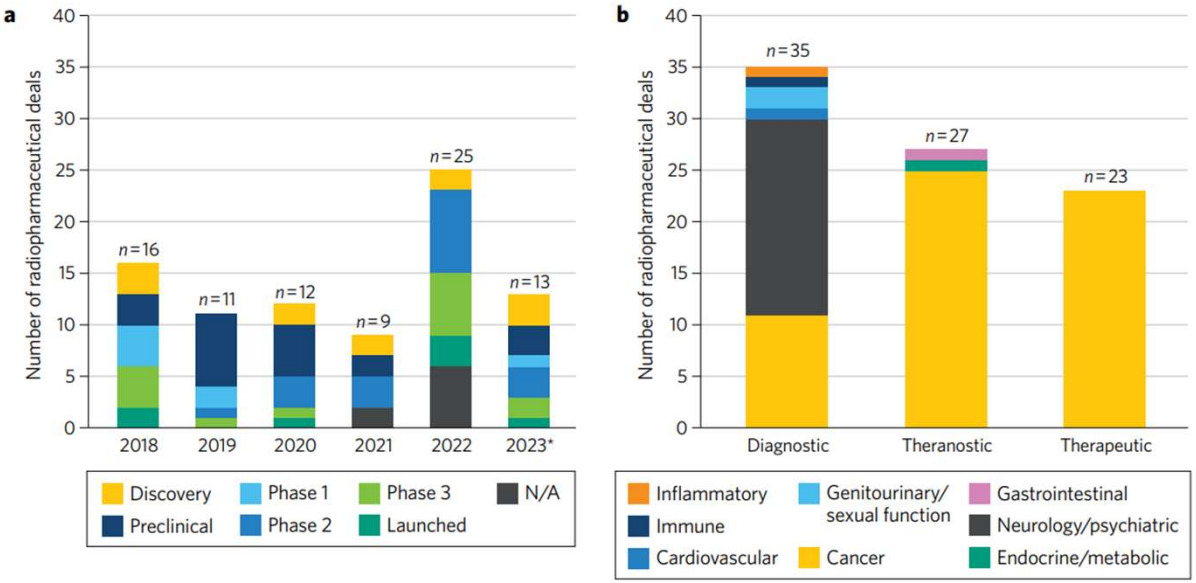


Fig.1 | Biopharma-sponsored deal distribution in the radiopharmaceuticals space: 2018–2023*. a, Number of deals by phase, per year. **b**, Number of deals by indication, per modality. Data source: Cortellis. *Through 3 October 2023. N/A, not available.

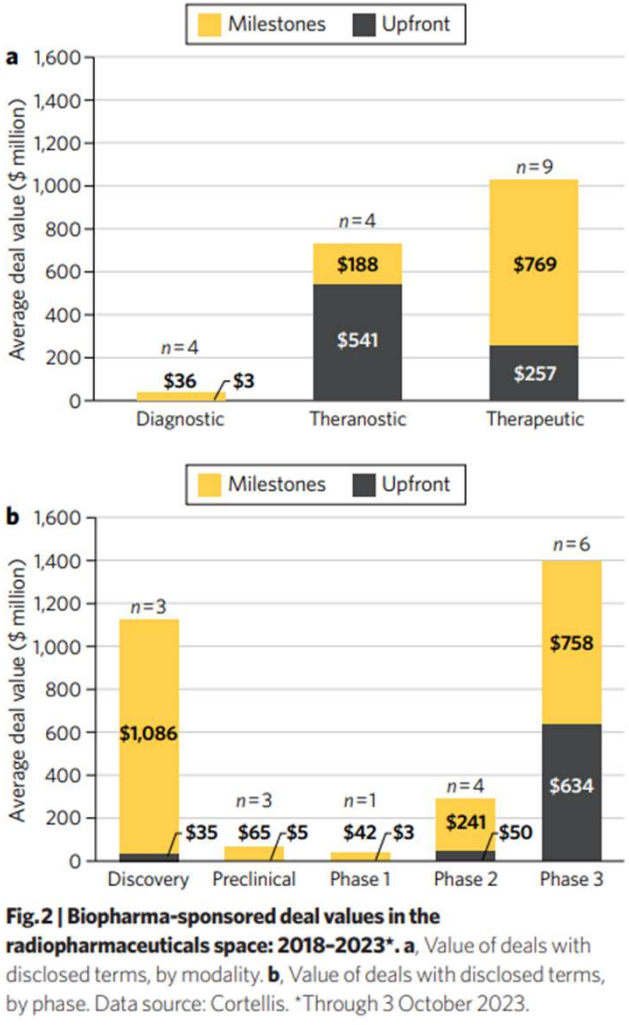


Fig.2 | Biopharma-sponsored deal values in the radiopharmaceuticals space: 2018–2023*. a, Value of deals with disclosed terms, by modality. **b**, Value of deals with disclosed terms, by phase. Data source: Cortellis. *Through 3 October 2023.

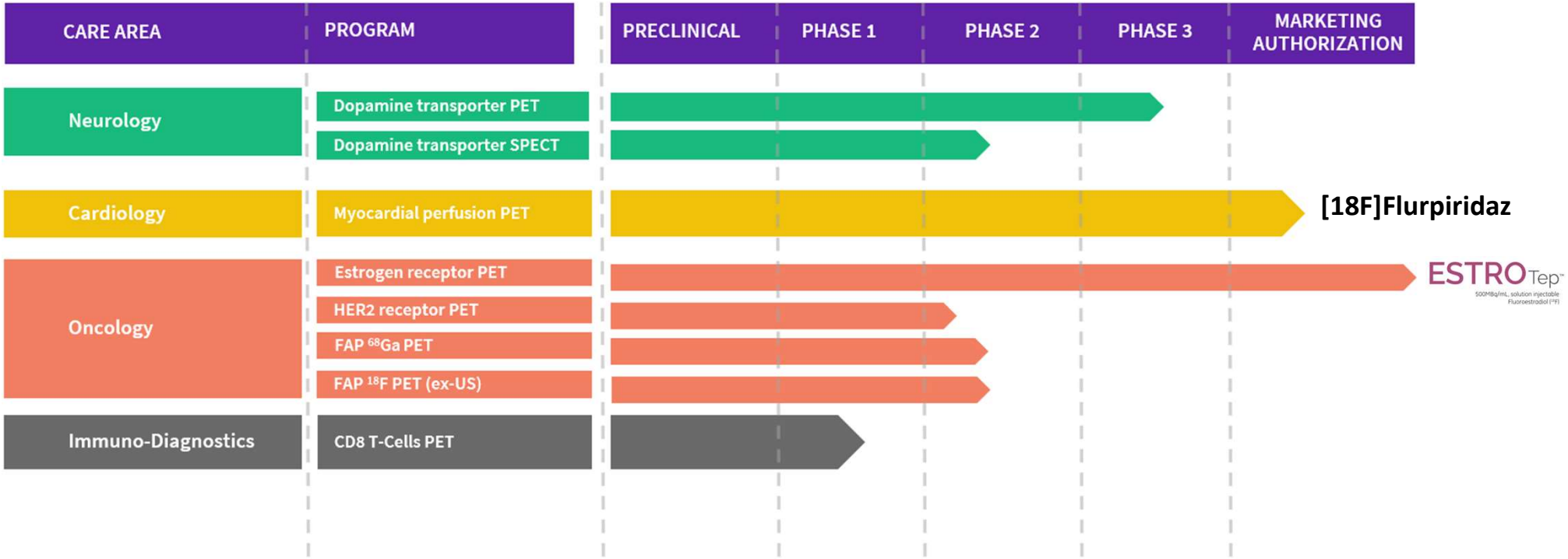
Sullivan B., Davis A., Bak P.: www.nature.com/biopharmdeal | March 2024 | B13-B15

Diagnostik

Michael Hinterreiter / ÖVS-Frühjahrstagung 2024 (Graz)

Diagnostik

GE HealthCare Pharmaceutical Diagnostics: Pipeline



GE HealthCare

Therapie

Michael Hinterreiter / ÖVS-Frühjahrstagung 2024 (Graz)

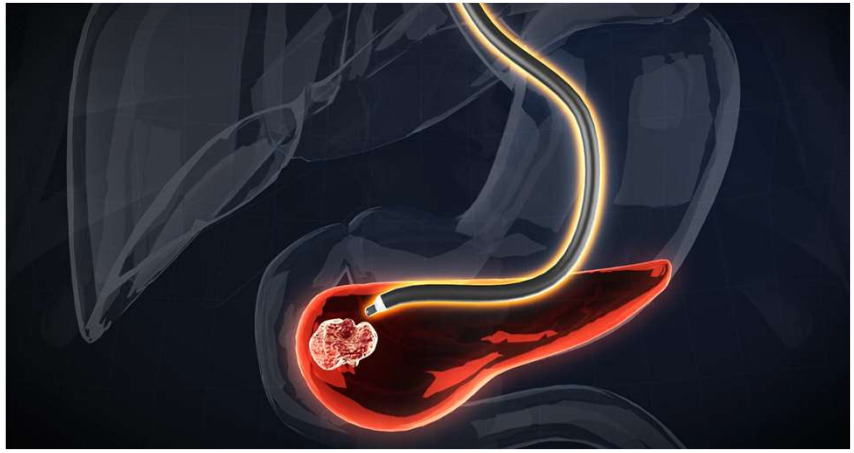
Therapie - ^{32}P

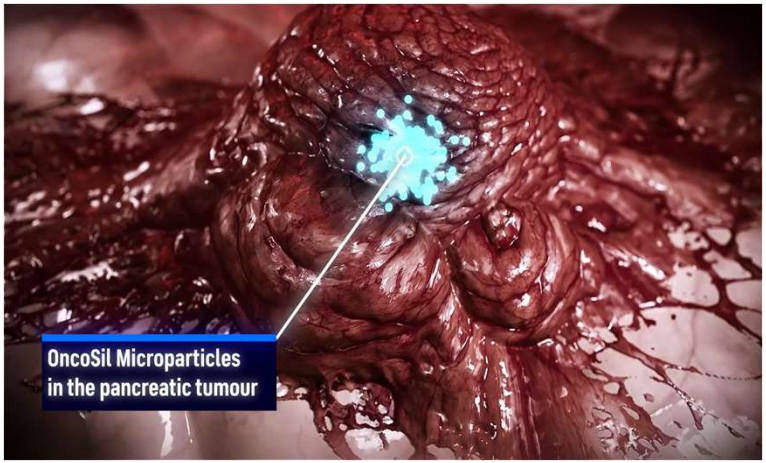
Phosphor-32 (^{32}P)

- **$HWZ_{physikalisch}$:** 14,27 Tage
- **Reine ß$^-$- Emission:** max: 1,71 MeV, Durchschnitt: 0,7 MeV
- **Maximale Reichweiten**
  - Luft: 620 cm
  - Gewebe: 0,8 cm
  - Plexiglas: 0,6 cm
- **Tumordosis von 100 Gy in Form von ^{32}P-markierten Mikropartikeln** (98% innerhalb von 81 Tagen)
- **Appliziertes Suspensionsvolumen = 8% des Tumorvolumens in ml**
- **Aktuell zugelassen bei lokal fortgeschrittenen Pankreastumoren**
- **Medizinprodukt und kein Radiopharmakon**

OncoSil Medical Ltd.

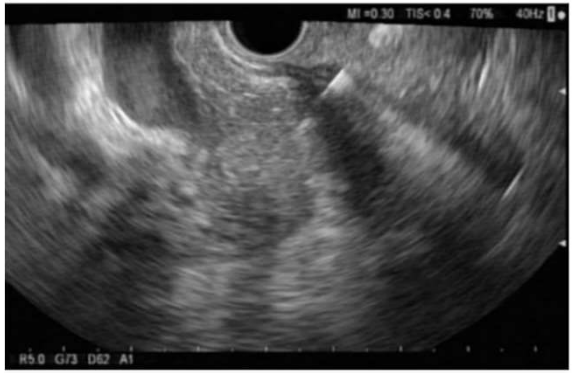
Therapie - ^{32}P



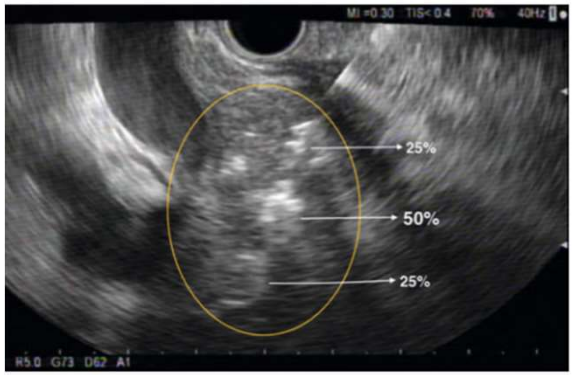


OncoSil Medical Ltd.

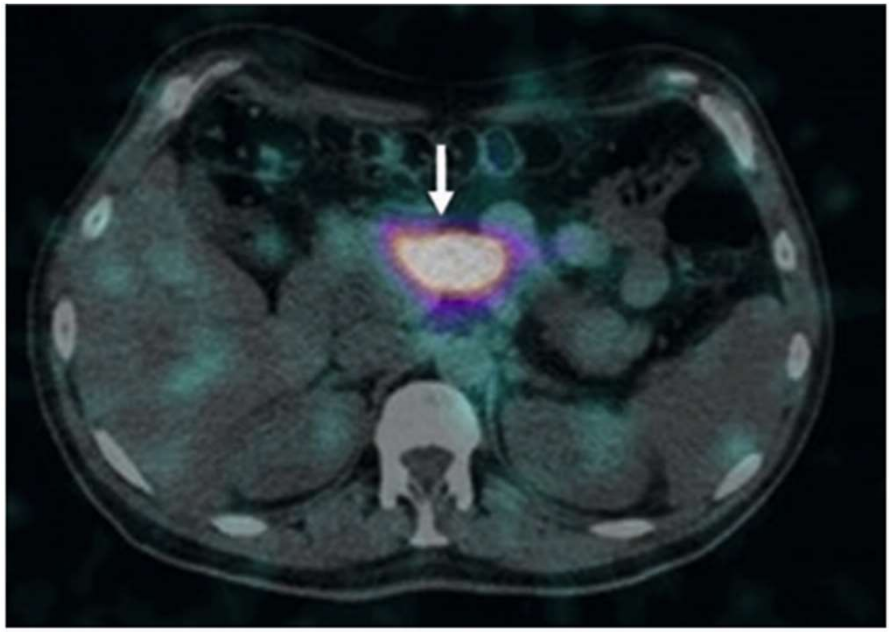
Therapie - ^{32}P



► **Fig. 1** Identification of the pancreatic lesion followed by puncture using a 22-guage fine-needle aspiration needle.



► **Fig. 2** Injection of ^{32}P in a 25%–50%–25% distribution.



► **Fig. 3** Bremsstrahlung single photon emission computed tomography scan 4 hours post ^{32}P injection showing localization into the pancreatic cancer (white arrow).

Jeevinesh N. et al. Endoscopy2021 10.1055/a-1353-0941

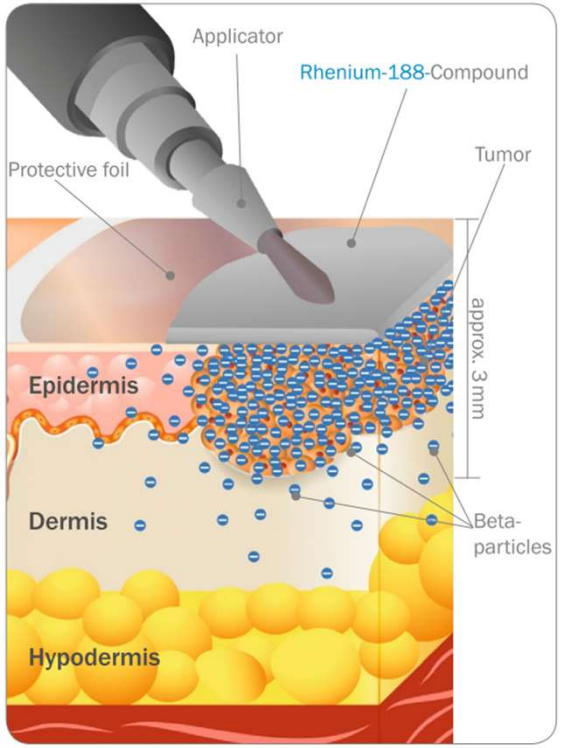
Therapie - ^{188}Re

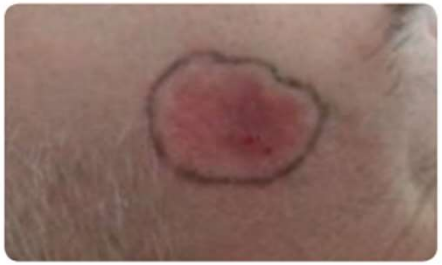
Rhenium-188 (^{188}Re)

- $HWZ_{physikalisch}$: 16,9 h
- Produktion: ^{188}W/^{188}Re-Generator
- Emission von…
  1) $ß^-$ (96,7%, max: 2,1MeV)
  2) γ (15,1%, 155 keV)
- ^{188}Re-markierte Nanokolloide (Exposition 30 min bis 3h)
- Aktuell zugelassen bei nicht-melanozytärem Hautkrebs (NMSC) vom Basalzell- und Plattenepitheltyp
- Maximale Reichweite in der Haut ($ß^-$): 3 mm (92% der Dosis)
- Medizinprodukt und kein Radiopharmakon

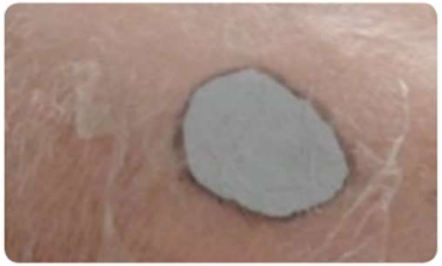
OncoBeta GmbH

Therapie - ^{188}Re

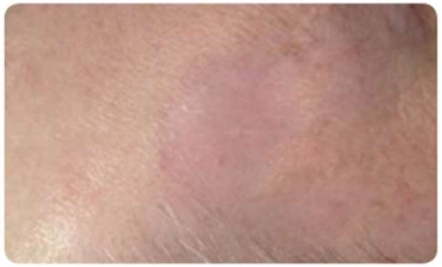




Marking of the lesion and preparation of area to be treated.



Application of **Rhenium-188**-Compound on protective foil; treatment time is generally 45 to 180 minutes.

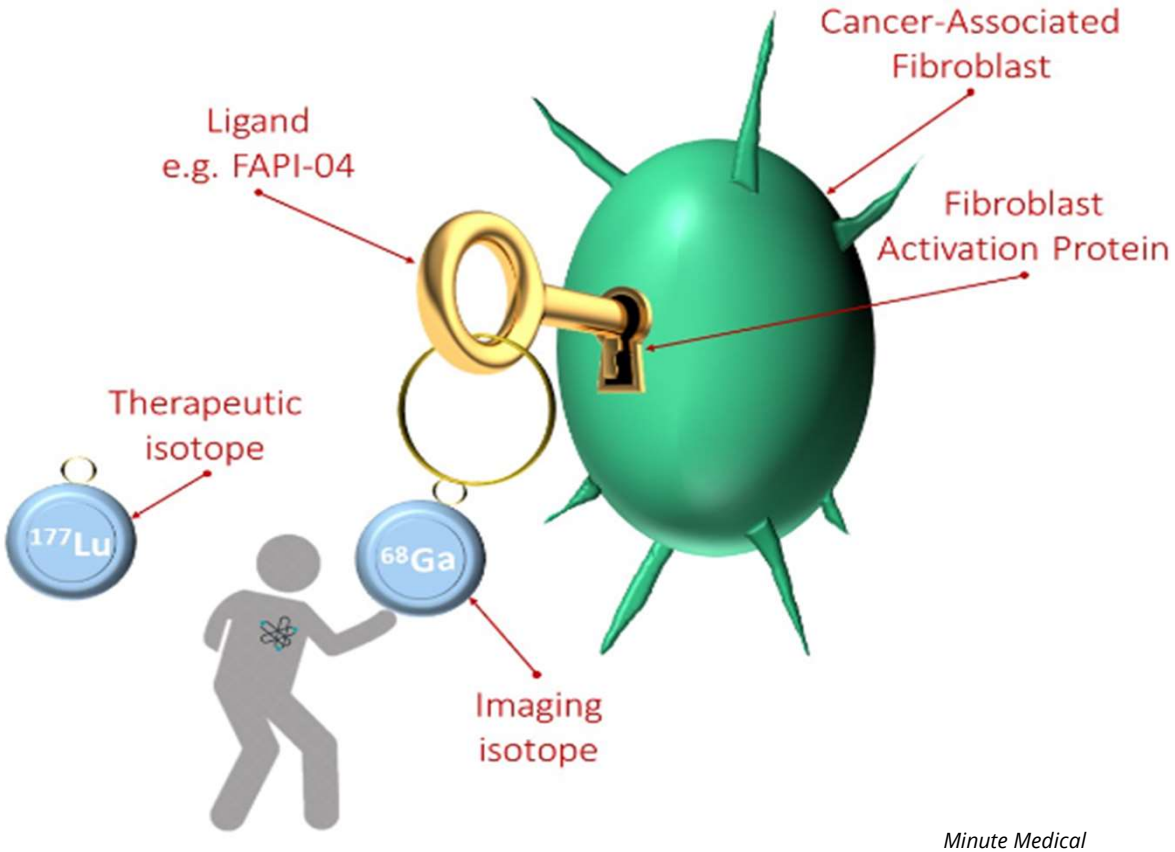


Healing process and growth of new skin tissue after 30 – 180 days.

Thera(g)nostik

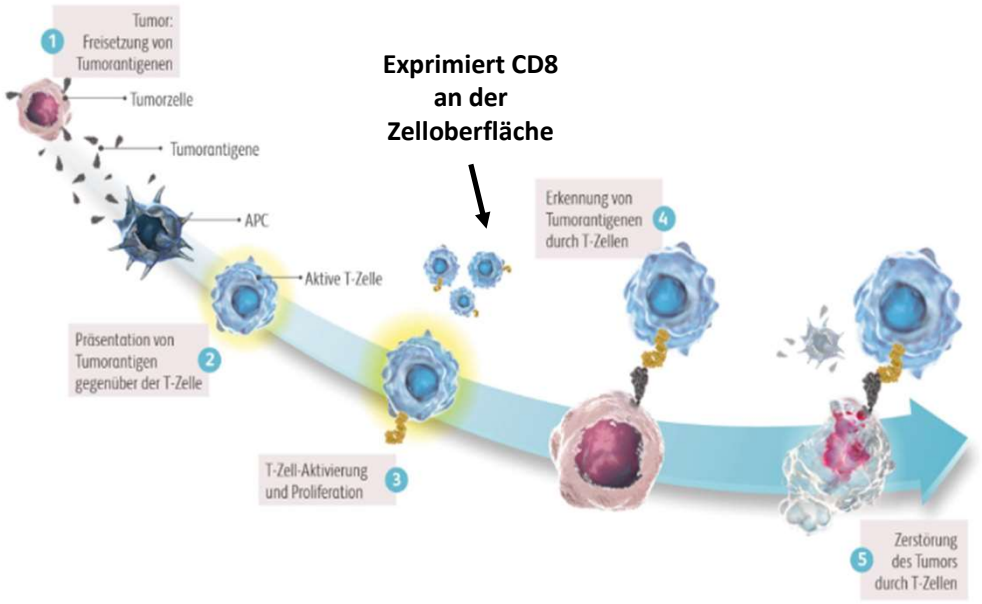
Michael Hinterreiter / ÖVS-Frühjahrstagung 2024 (Graz)

Thera(g)nostik

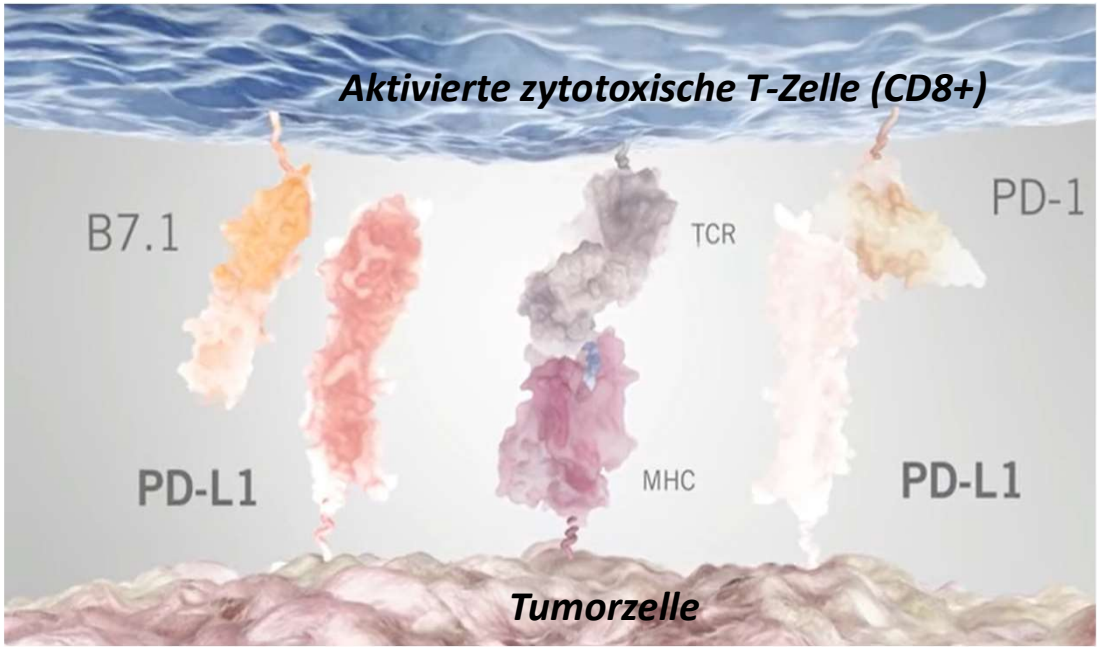


Minute Medical

Thera(g)nostik – Immun(o)therapie

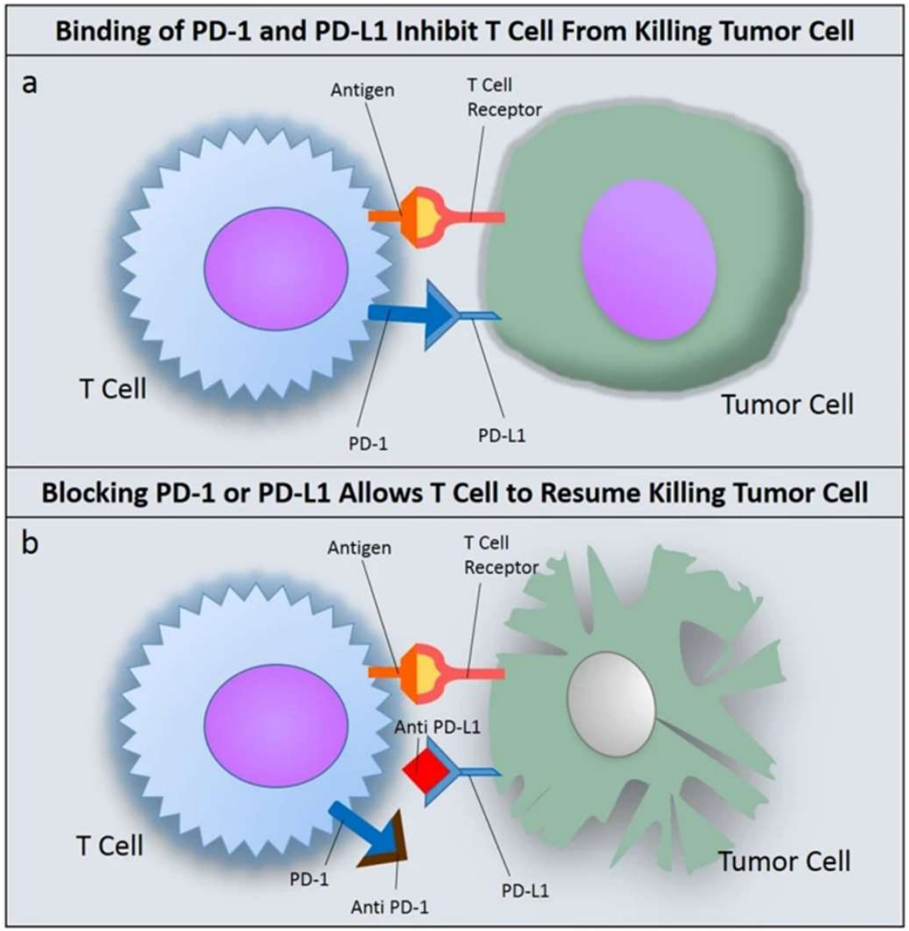


Bristol-Myers Squibb



F. Hoffmann-La Roche Ltd

Thera(g)nostik – Immun(o)therapie

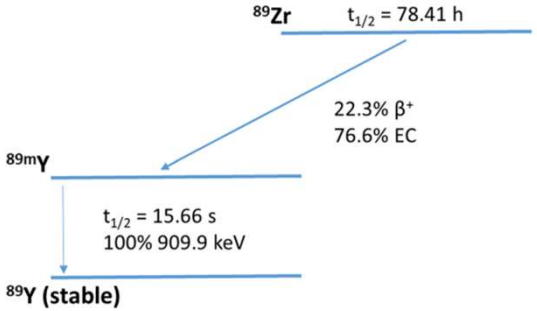


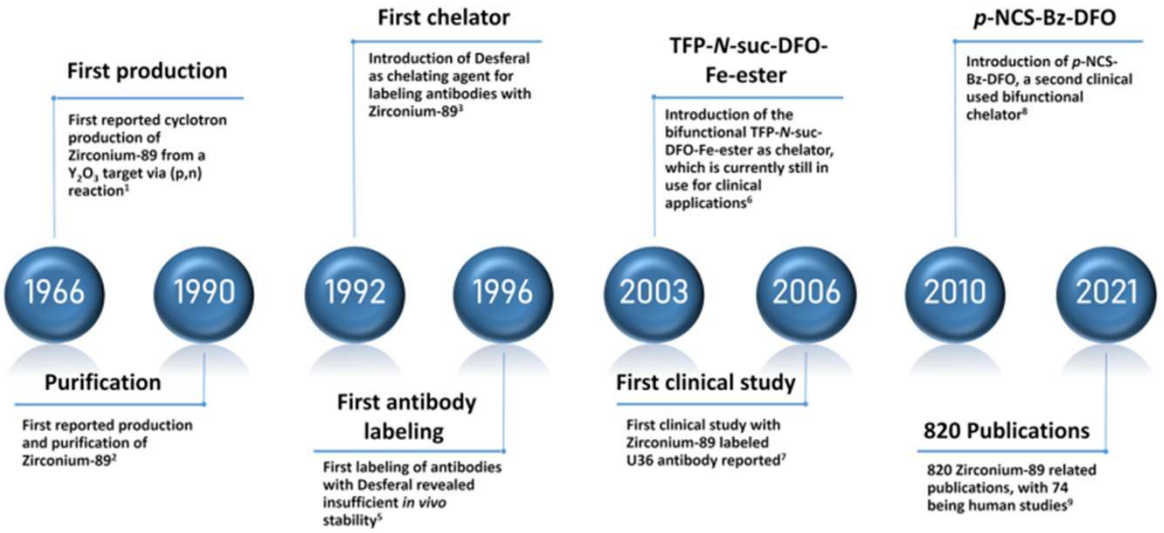
Caldwell C. Jr. et al., Scientific Reports | 7: 13682

Thera(g)nostik – Immun(o)therapie

	^{89}Zr[1]
Half-life	78h
Target reaction	$^{89}Y(p,n)^{89}Zr$
Target Material	^{89}Y
Energy (on target) [MeV]	15
Yield (mCi/µAh) [2]	0.34

IBA Radiopharma Solutions 2024





Wuensche et al. EJNMMI Radiopharmacy and Chemistry (2024)

Thera(g)nostik – Immun(o)therapie

TABLE 1
Patient Characteristics

Characteristic	All patients (n = 15)
Median age (y)	64 (range, 30–81)
Sex (n)	
Male	9 (60)
Female	6 (40)
Tumor type (n)	
Melanoma	8 (53)
Non–small cell lung carcinoma	6 (40)
Hepatocellular carcinoma	1 (7)
Treatment profile at the time of imaging (n)	
On immunotherapy (<2 mo)	3 (20)
On immunotherapy (>2 mo)	5 (33)
On targeted therapy (1–6 mo)	2 (13)
Discontinued prior treatment (>5 mo)	2 (13)
Treatment naïve	3 (20)

- Phase 1 - Studie
- 111 MBq (+/- 20%) ^{89}Zr-Df-IAB22M2C

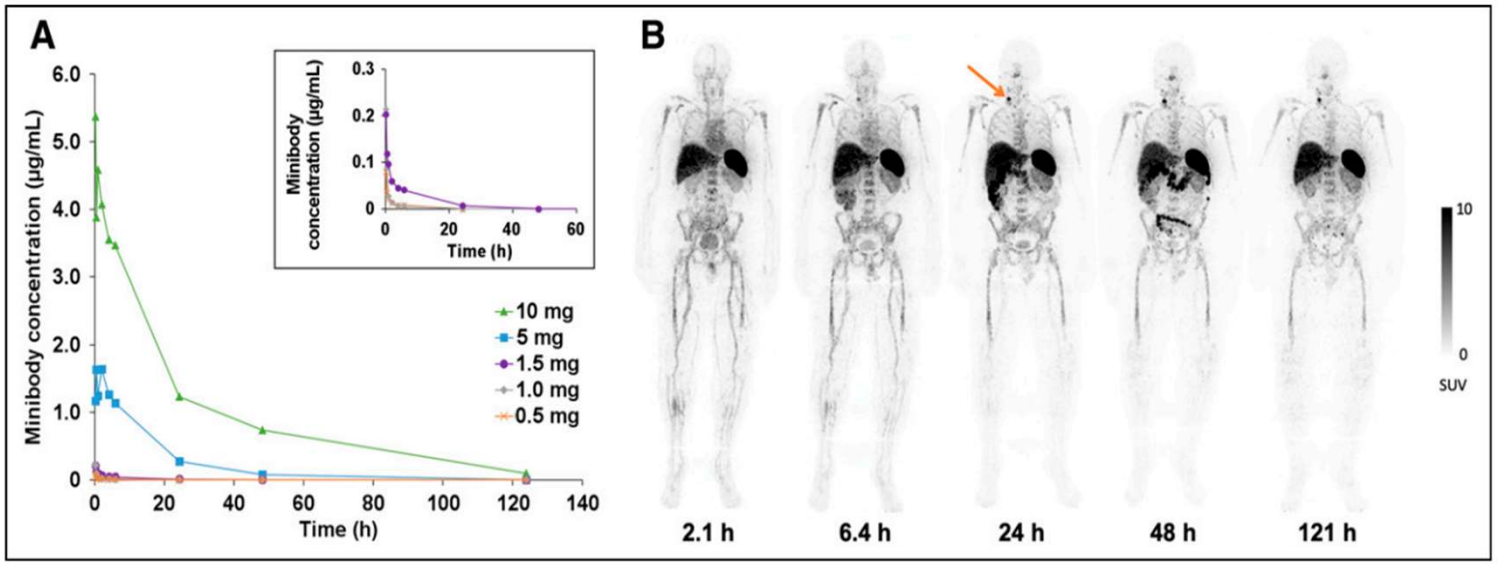


FIGURE 1. Serum clearance and biodistribution of ^{89}Zr-Df-IAB22M2C. (A) Serum clearance of ^{89}Zr-Df-IAB22M2C based on enzyme-linked immunosorbent assay measurements (limit of detection = 5 ng/mL). No minibody was detected in serum at the 0.2-mg dose. (B) Whole-body PET images of a patient at various times after injection of ^{89}Zr-Df-IAB22M2C (1.5-mg minibody dose) demonstrating the distribution of ^{89}Zr-Df-IAB22M2C in normal tissues and uptake in a nodal metastasis in the right neck (arrow), with good visualization of uptake in the nodal metastasis at 24–48 h after injection.

Farwell M.D. et al., J Nucl Med 2022; 63:720–726

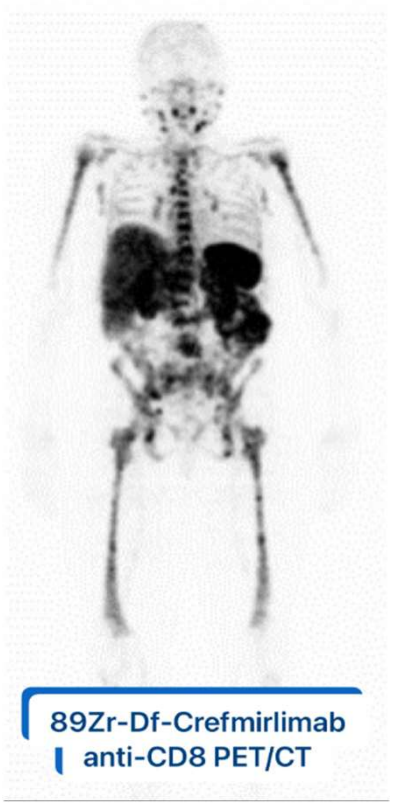
Thera(g)nostik – Immun(o)therapie

Inclusion Criteria Patients must meet all of the inclusion criteria to participate in this study.

1. Patients with incurable malignancies with more than 50% 2-year cancer-associated mortality (as estimated by two physician and where appropriate according to 2014 National Cancer database)

   Diseases include, but are not limited to:

   Ampullary carcinoma Intrahepatic cholangiocarcinoma (IHCC) Appendiceal cancer Melanoma Colorectal cancer (CRC) Non-KIT GIST (gastrointestinal stromal tumor) Extrahepatic cholangiocarcinoma (EHCC) Non-small cell lung cancer (NSCLC) Esophageal adenocarcinoma Ovarian cancer Gallbladder cancer (GBCA) Pancreatic ductal adenocarcinoma (PDAC) Gastric adenocarcinoma Sarcoma (high-grade) Head and neck cancer Small bowel adenocarcinoma (including duodenal) Hepatocellular carcinoma (HCC) Triple-negative breast cancer (TNBC) Urothelial cancer
2. Patients with cancer of unknown primary or a rare tumor (for example, fewer than 15 cases per 100,000 per year) with no approved therapies. (Patients in this inclusion criteria must meet all other exclusion and inclusion criteria except inclusion criteria #1)
3. Patients with incurable malignancies, irrespective of 2-year mortality, who, in the opinion of the investigator have no treatment option expected to yield significant clinical benefit."
4. Patients must have at least one of the following for a diagnosis/disease status:
   1. Unresectable disease
   2. Metastatic disease
   3. Medically unfit for surgical resection but with an expected survival of > 3 months, ECOG < 2 and NYHA status ≤ II (refer to status definitions in tables below)
   4. Disease where no conventional therapy leads to a survival benefit > 6 months in the respective cohort and line of therapy for which the patient is otherwise eligible
   5. Actionable alterations determined by FoundationOneTM



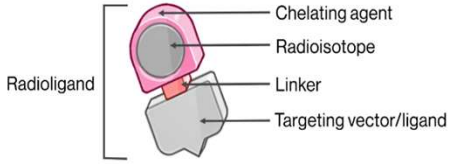
- ^{89}Zr crefmirlimab berdoxam
- ^{89}Zr-Df-IAB22M2C

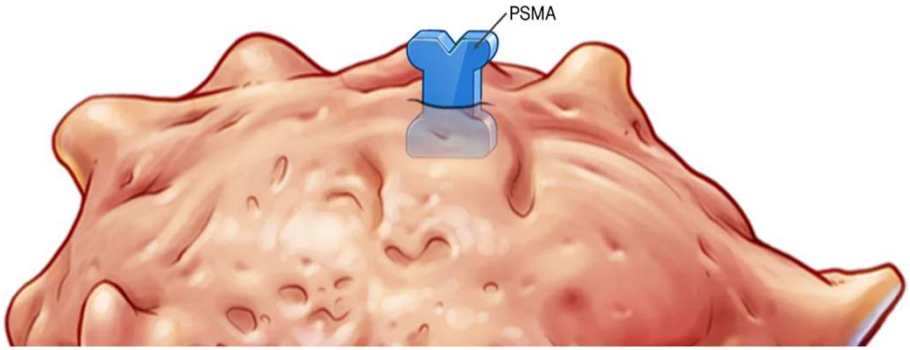
- 2 (3) PET Scans
- Max. 37 MBq ± 20% und 1.5 mg API pro Scan
- i.v. Infusion oder langsame Bolusinjektion

1. PETbaseline innerhalb von 14 Tagen vor Beginn der Immunotherapie
2. 4 bis 6 Wochen nach Start der Immunotherapie und vor dem Beginn des dritten Therapiezyklus
3. Optional bei PD

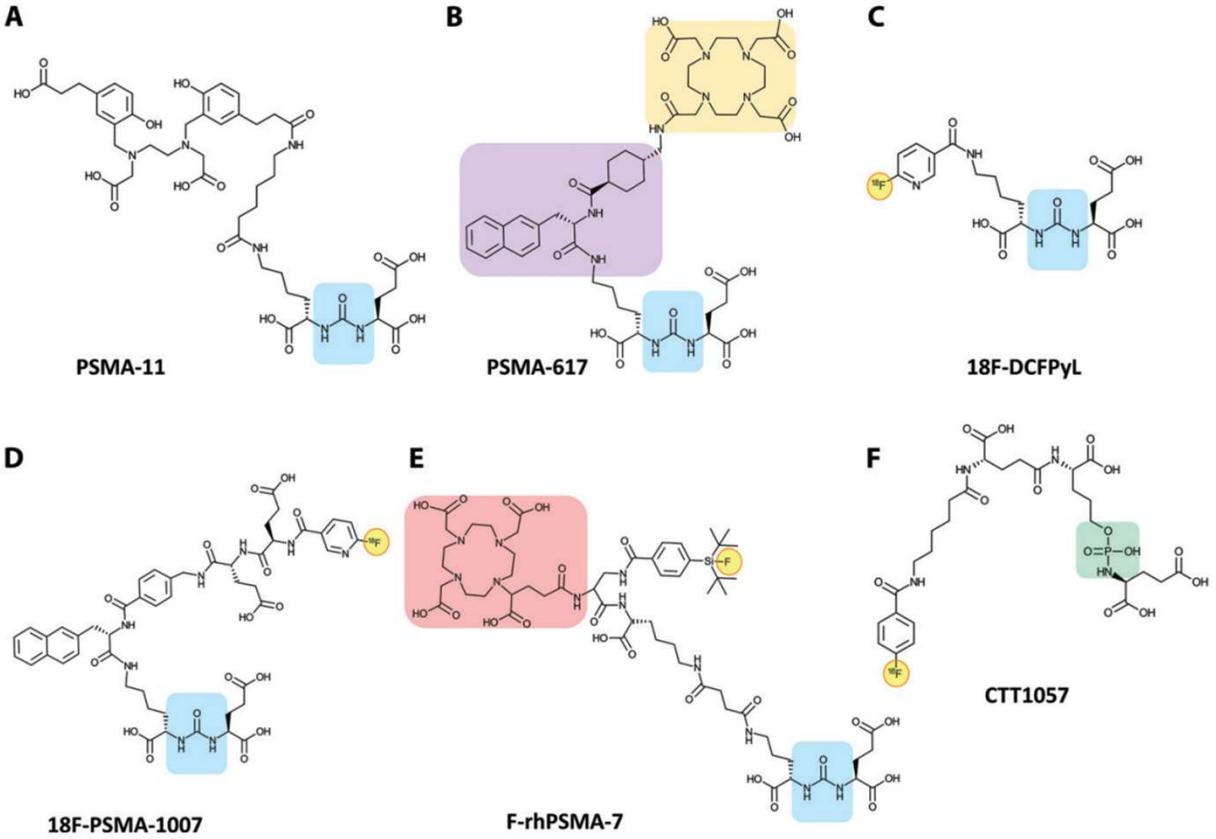
iPREDICT Trail (Phase II) - ClinicalTrials.gov ID NCT05013099

Thera(g)nostik - PSMA



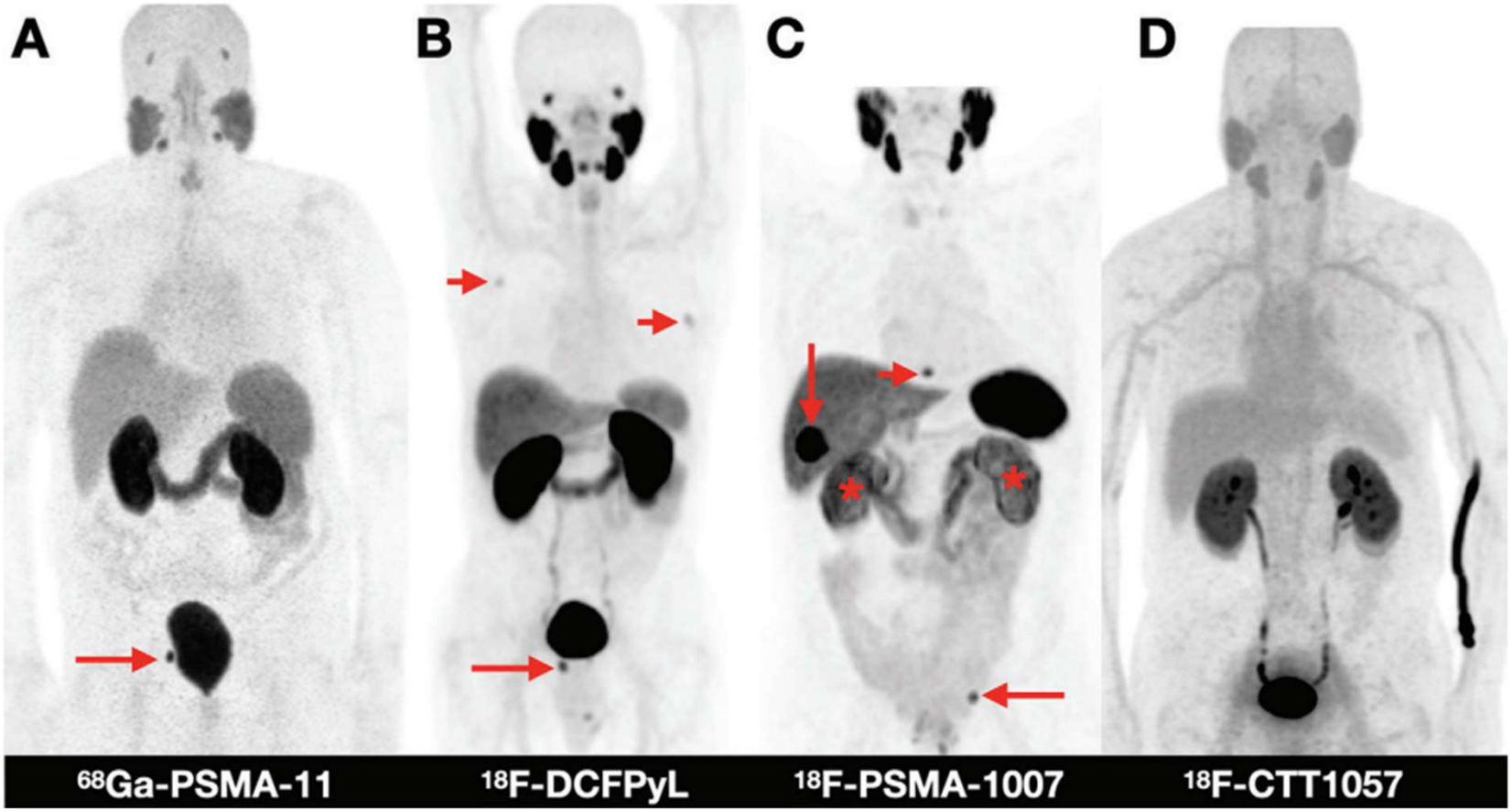


Novartis Pharmaceuticals Corporation



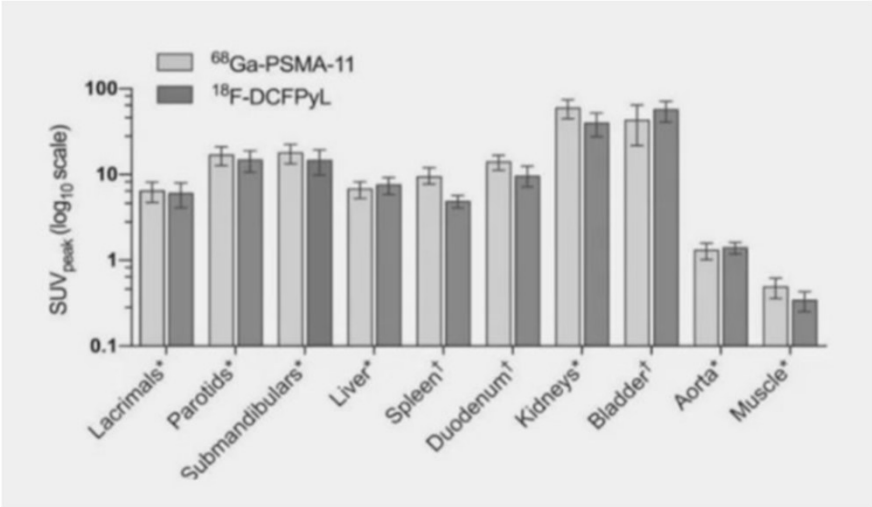
Lawhn-Heath C. et al. Radiology 2021; 000:1–13

Thera(g)nostik - PSMA



Lawhn-Heath C. et al. Radiology 2021; 000:1–13

Thera(g)nostik - PSMA



Hofman M. APCCC 2024

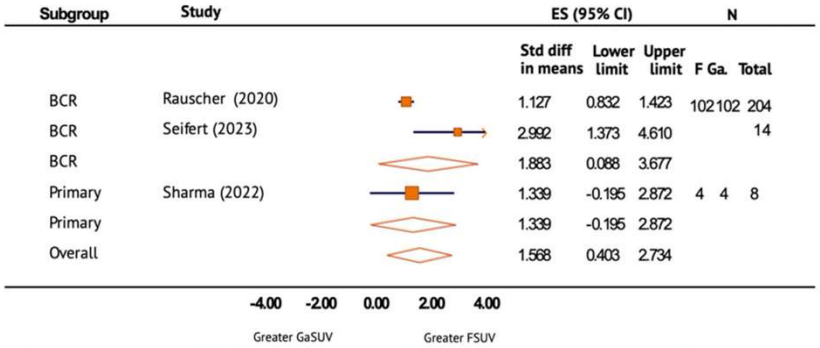


Fig. 4 Benign bone SUVmax of [18F]PSMA-1007 vs [68Ga]Ga-PSMA-11. Forest plot of the standard difference in means and 95% confidence interval of benign bone SUVmax of [^{18}F]PSMA-1007 in comparison with [^{68}Ga]Ga-PSMA-11 on prostate-specific membrane antigen position emission tomography (PSMA PET/CT) by primary staging and restaging after biochemical recurrence (BCR) of prostate cancer. ES effect size.

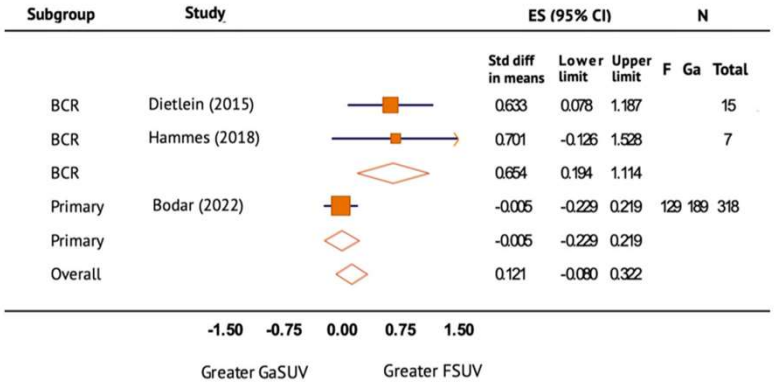
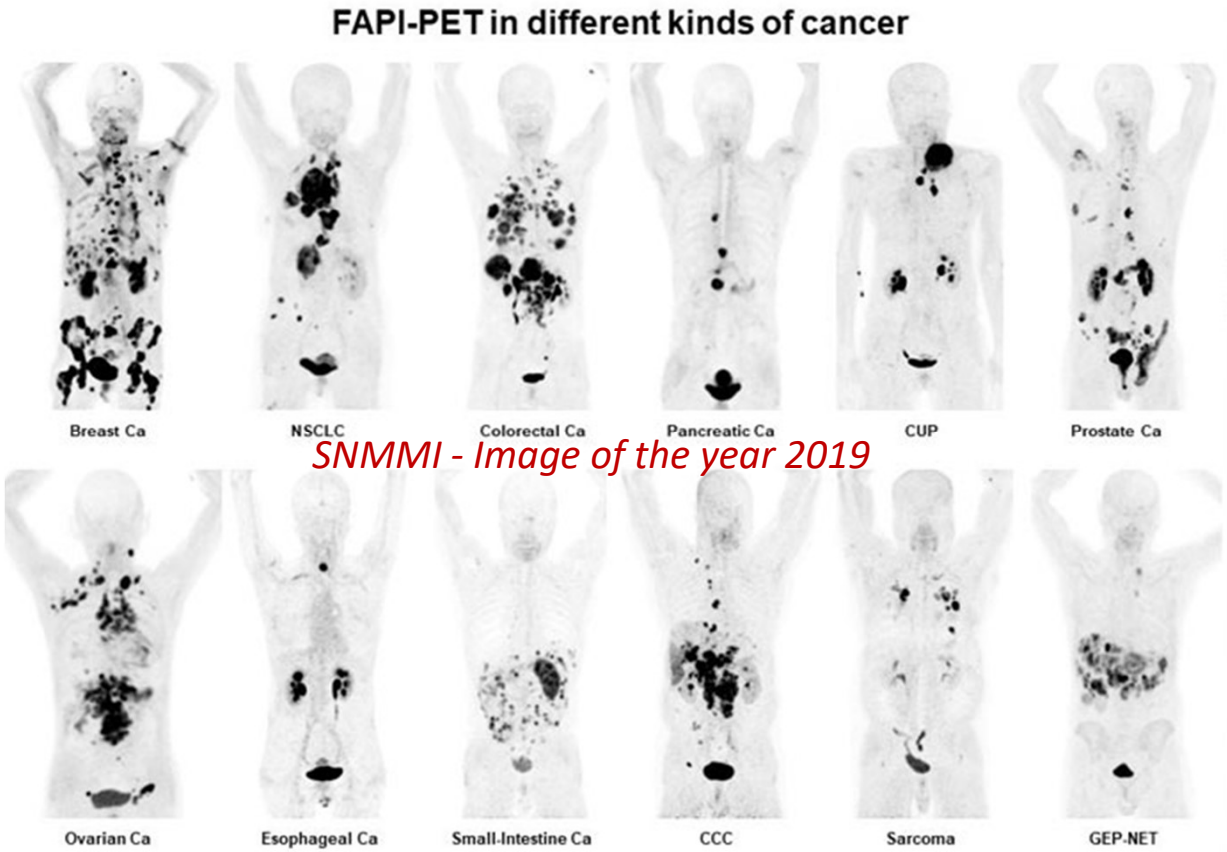


Fig. 5 Lesion SUVmax of [18F]DCFPyL vs [68Ga]Ga-PSMA-11. Forest plot of the standard difference in means and 95% confidence interval of lesion SUVmax of [^{18}F]DCFPyL in comparison with [^{68}Ga]Ga-PSMA-11 on prostate-specific membrane antigen positron emission tomography (PSMA PET/CT) by primary staging and restaging after biochemical recurrence (BCR) of prostate cancer. ES effect size.

Huang S. et al. Prostate Cancer Prostatic (2023)

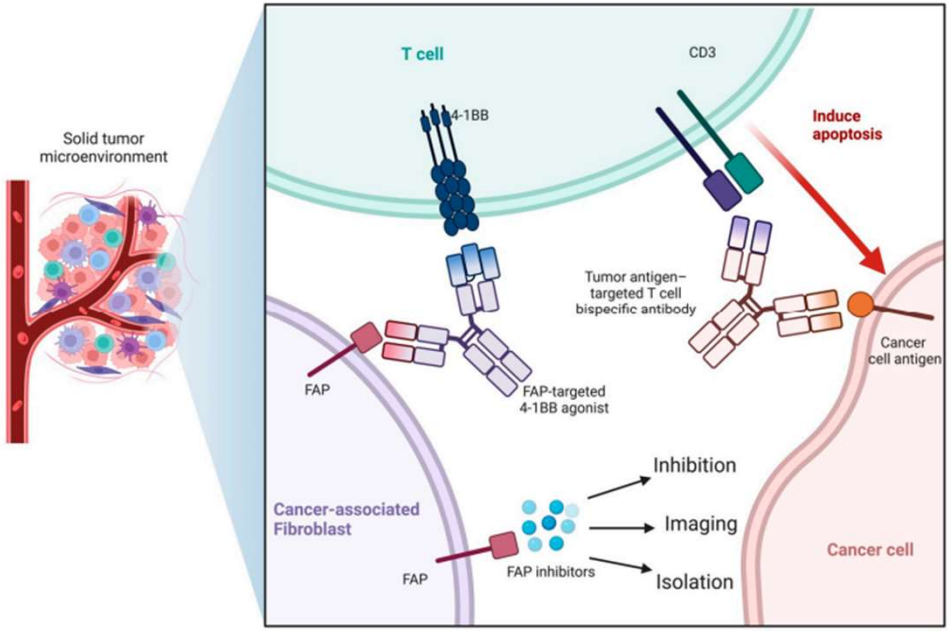
Thera(g)nostik – FAP(I)

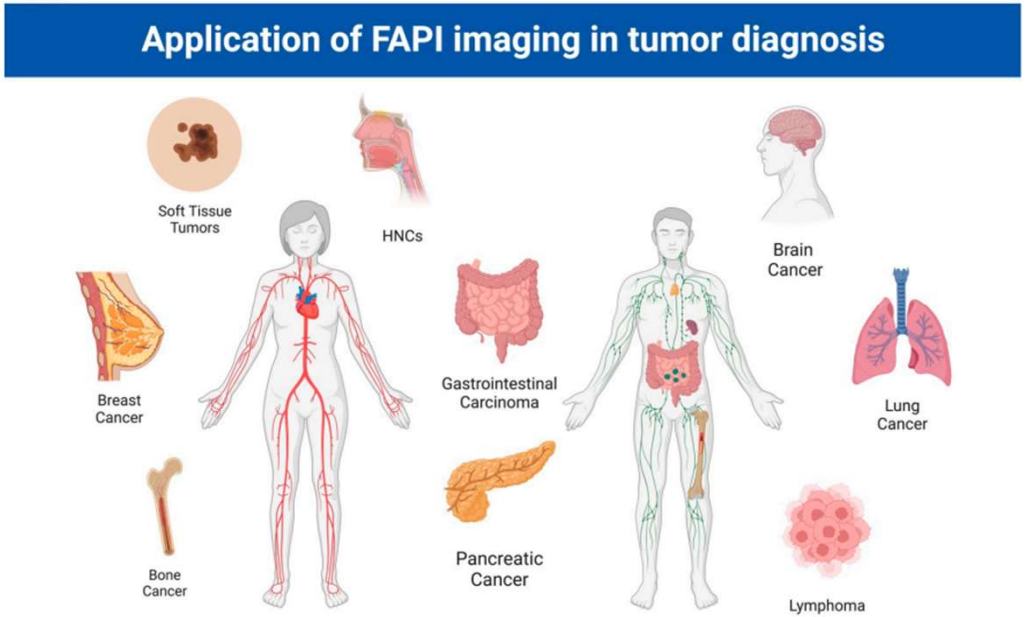


SNMMI - Image of the year 2019

Kratochwil C. et al., University Hospital Heidelberg, Germany.

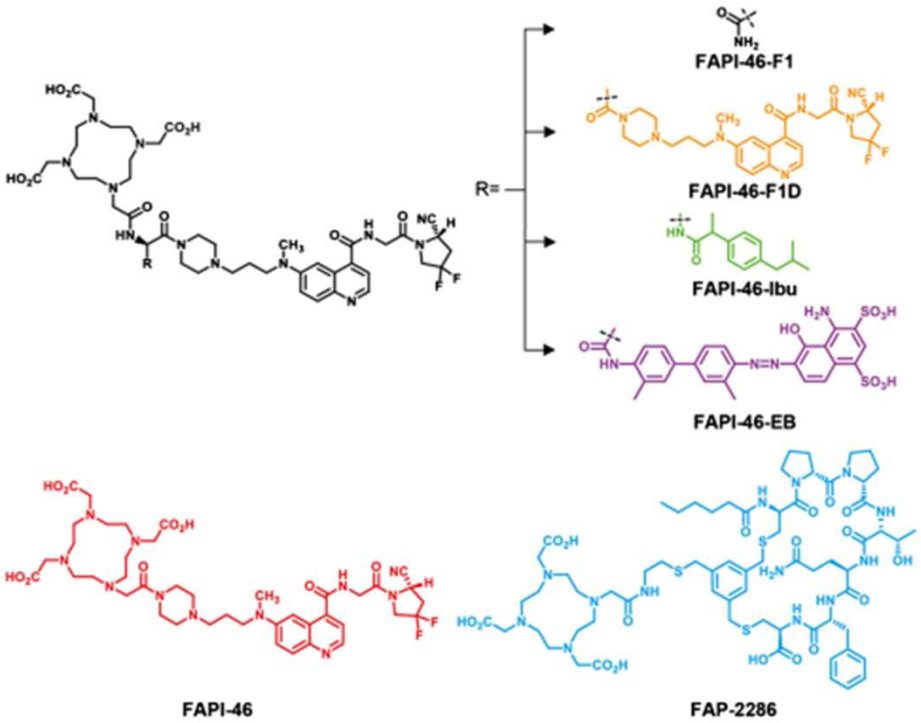
Thera(g)nostik – FAP(I)





Dong Y. et al.; Cancers 2023, 15, 1193

Thera(g)nostik – FAP(I)



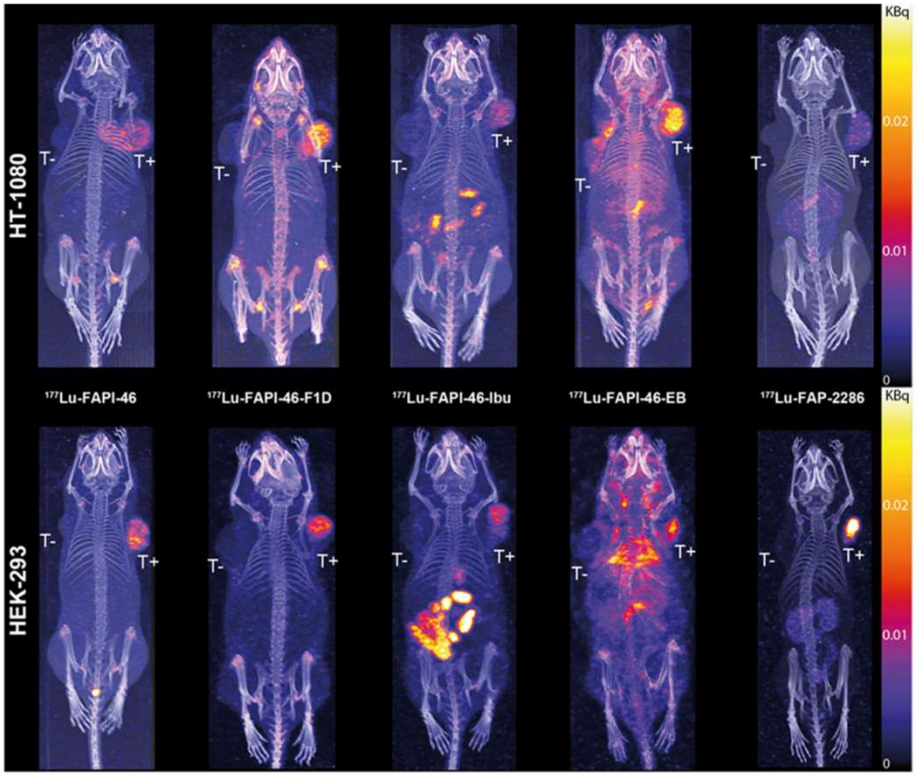
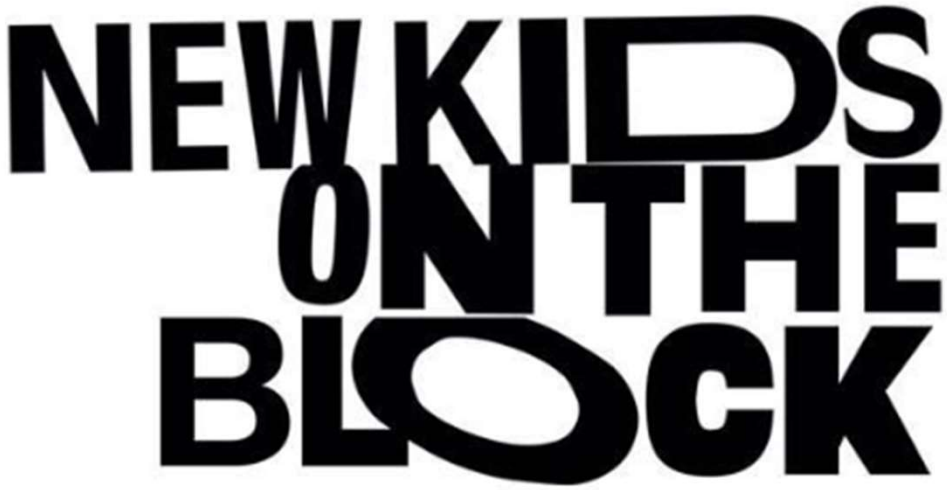


Fig. 2 SPECT/CT images of [^{177}Lu]Lu-FAPI-46, [^{177}Lu]Lu-FAPI-46-F1D, [^{177}Lu]Lu-FAPI-46-Ibu, [^{177}Lu]Lu-FAPI-46-EB, and [^{177}Lu]Lu-FAP-2286 (500 pmol/9–15 MBq) at 4 h p.i. in mice bearing low FAP-expressing model HT-1080.hFAP and the wild type HT-1080.wt (top) or high FAP-expressing model HEK-293.hFAP and the wild type HEK-293.wt (bottom) dual tumors. All radioligands accumulated in the FAP-expressing tumors to different extend and exhibited distinct differences in their total body distribution. T+ = FAP-positive tumor, T− = FAP-negative tumor

Millul J. et al. EJNMMI (2023) 50:3050–3061

Thera(g)nostik



α ist das neue β^-

Thera(g)nostik – Isotope mit Potential

	^{225}Ac
Strahlenart	α (5,8 bis 8,4 MeV) ϒ (150 keV bzw. 188 keV)
$HWZ_{physikalisch}$	9,92 d

Produktion	• Generator: $^{229}Th/^{225}Ac$, Mutter ^{233}U
	• Zyklotron: ^{232}Th; p^+ mit > 100MeV
	  • Verunreinigung mit ^{227}Th
	  • $t_{1/2}$: 21,8 Jahre (99% ß$^-$, 1% α)
	  • Anteil an ^{227}Th: 0,1–0,3% der am Ende des Targetbeschusses vorliegenden ^{225}Ac-Aktivität

Auszug möglicher Liganden	• DOTATATE • PSMA-617 • FAPI-04 • Anti-CD33 (Leukämie)
Limitationen	• Anzahl der global verfügbaren Generatoren [RUS, GER, USA, (CAN), (BEL)] • Maximale Elutionsausbeute/Jahr (55-65 GBq) • Verunreinigung mit ^{227}Th

Thera(g)nostik – Isotope mit Potential

	$^{203}Pb/^{212}Pb$

Strahlenart	• ^{203}Pb: ɣ [EC, 279 keV]
	• ^{212}Pb: ß$^-$, ɣ (79 keV)
	  ○ ^{212}Bi: α (E_{avg}: 6,2 MeV)
	  ○ ^{212}Po: α (E_{avg}:8,9 MeV)

$HWZ_{physikalisch}$	• ^{203}Pb: 51,9 h
	• ^{212}Pb: 10,6 h
	  ○ ^{212}Bi: 60,6 min
	  ○ ^{212}Po: 0.3 µs

Produktion	1) ^{203}Pb: Zyklotron [$^{203Tl}(p^+,n)\rightarrow{}^{203}Pb$] 2) ^{212}Pb: $^{228}Th(^{224}Ra)/^{212}Pb$-Generator
Auszug möglicher Liganden	• DOTATATE/DOTATOC (PSC-PEG2-TOC) • PSMA-617, ADVC001, NG001 • TCMC–trastuzumab (mBC) • TCMC–cetuximab (anti-EGFR)
Limitationen	• Pharmakokinetik (u.a. in Bezug auf ^{212}Bi) • Bindungsstabilität

Thera(g)nostik – Isotope mit Potential

	^{211}At
Strahlenart	α (E_{avg}: 6,2 MeV) ɣ [77 bis 92 keV (^{211}Po)]
$HWZ_{physikalisch}$	7,2 h
Produktion	Zyklotron: ^{209}Bi(α,2n) →^{211}At
Auszug möglicher Liganden	• [^{211}At] NaAt (DTC) • Rituximab (Leukämie) • Meta-benzylguanidine (MABG) • Trastuzumab (mBC)
Limitationen	• Verfügbarkeit • Therapieregime (fraktionierte Applikation)