SOFIE
From start to clinic

Current Status of Clinical Trials on FAP Targeted Radiopharmaceuticals

Gordon Research Conference-Radionuclide Theranostics for the Management of Cancer

7/19/22

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Disclosures

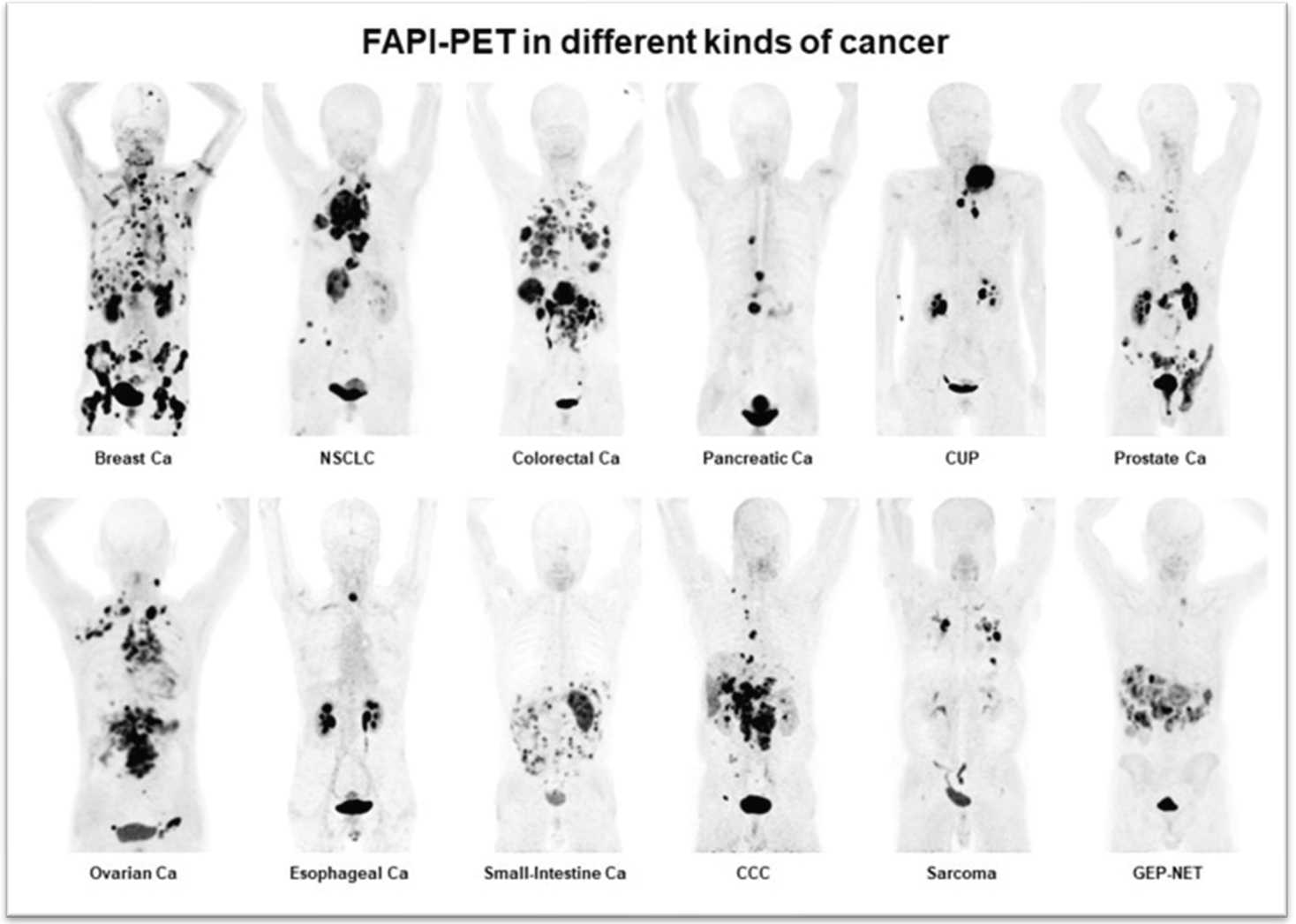
I serve as the Chief Scientific Officer for SOFIE

SOFIE has global commercial rights for diagnostic use of FAPI family of compounds from Heidelberg University

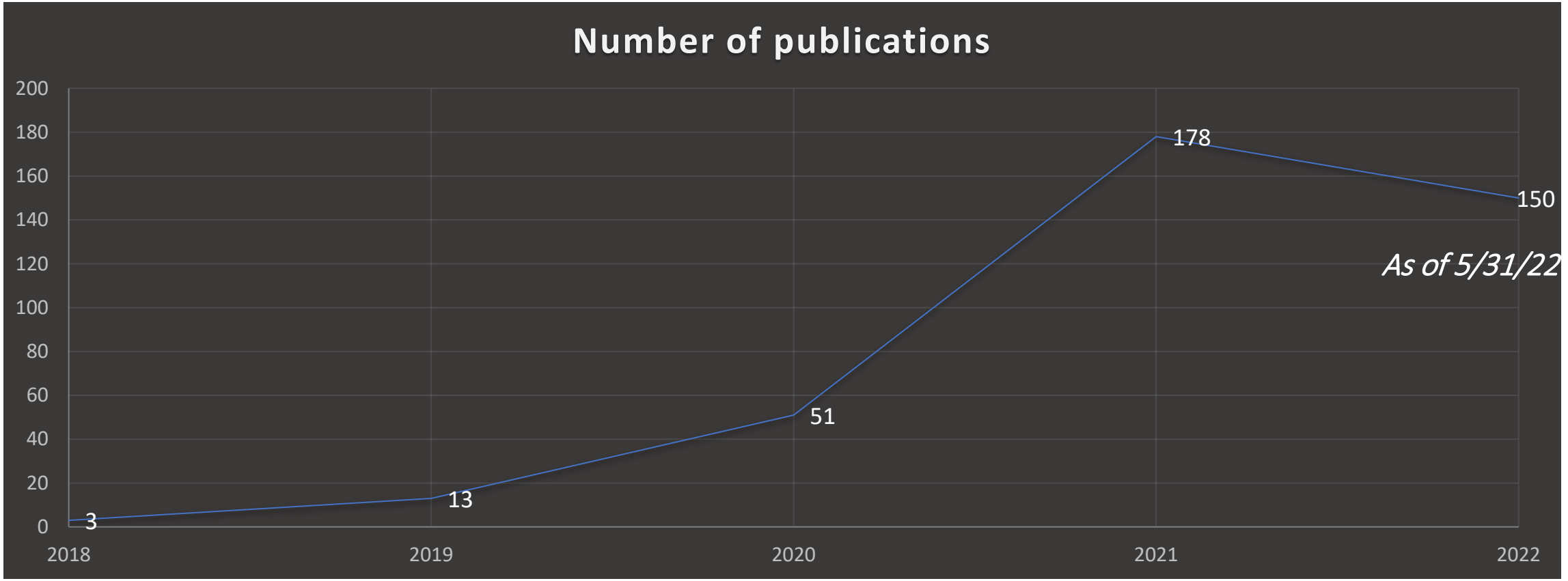
FAP as a target for radiopharmaceuticals

SNMMI Image of the Year 2019

"A single radiotracer can identify nearly 30 types of cancer, allowing for new applications in noninvasive diagnosis, staging and treatment, according to research presented at the 2019 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI). This honor goes to a team of researchers at University Hospital Heidelberg, Germany, showcasing the efficacy of the FAPI radiotracer."



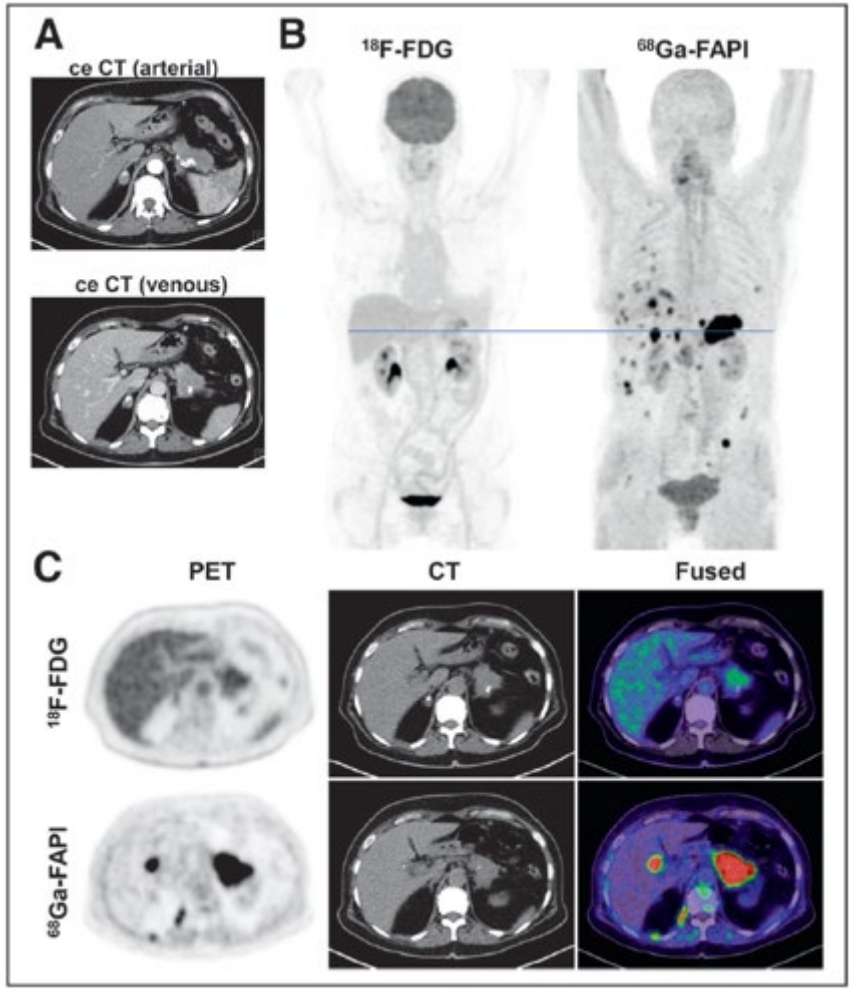
Mounting interest in FAP targeted radiopharmaceuticals



JNM Best Clinical Article in 2021

Impact of 68Ga-FAPI PET/CT Imaging on the Therapeutic Management of Primary and Recurrent PDAC

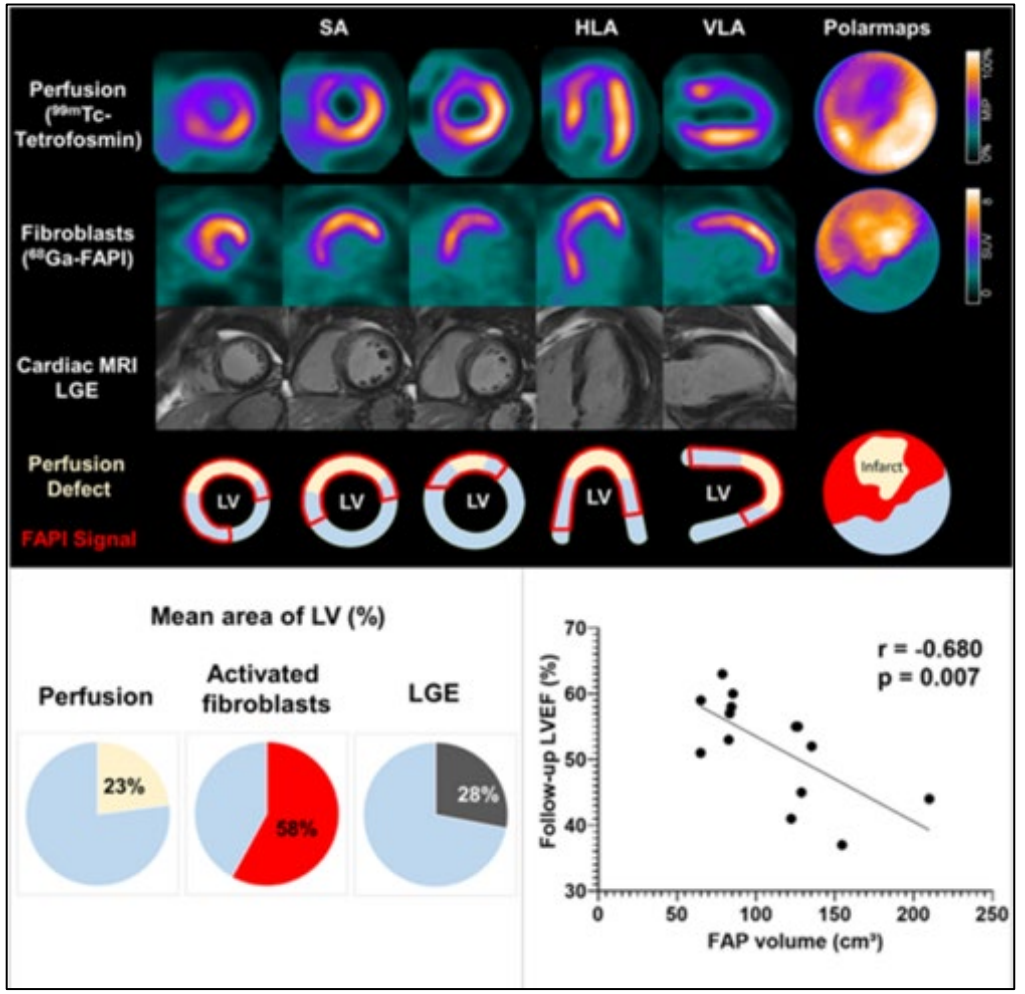
[^{68}Ga]FAPI PET/CT results led to changes in TNM staging in 10 of 19 patients



Röhrich M, Naumann P, Giesel FL, Choyke PL, Staudinger F, Wefers A, Liew DP, Kratochwil C, Rathke H, Liermann J, Herfarth K, Jäger D, Debus J, Haberkorn U, Lang M, Koerber SA. Impact of 68Ga-FAPI PET/CT Imaging on the Therapeutic Management of Primary and Recurrent Pancreatic Ductal Adenocarcinomas. J Nucl Med. 2021 Jun 1;62(6):779-786

SNMMI Image of the Year 2022

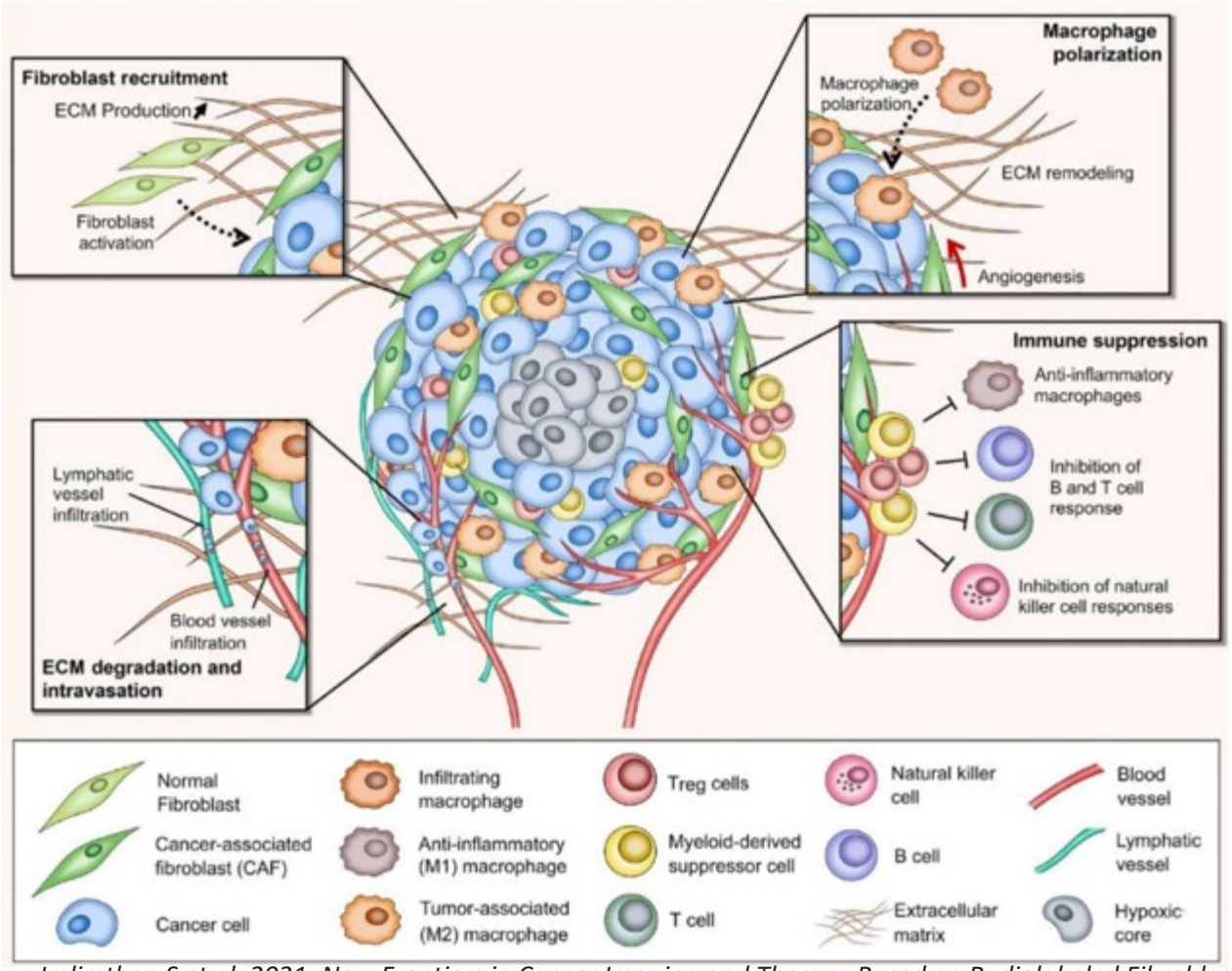
Representative case with acute anterior wall myocardial infarction: [^{68}Ga]FAPI-46



Johanna Diekmann, James Thackeray, Thorsten Derlin, Christoph Czerner, Tobias Ross, and Frank Bengel, Department of Nuclear Medicine, Hannover Medical School, Hannover, Niedersachsen, Germany; and Tobias Koenig, Jonas Neuser, Andreas Schaefer, Jochen Tillmans, and Johann Bauersachs, Department of Cardiology and Angiology, Hannover School of Medicine, Hannover, Niedersachsen, Germany.

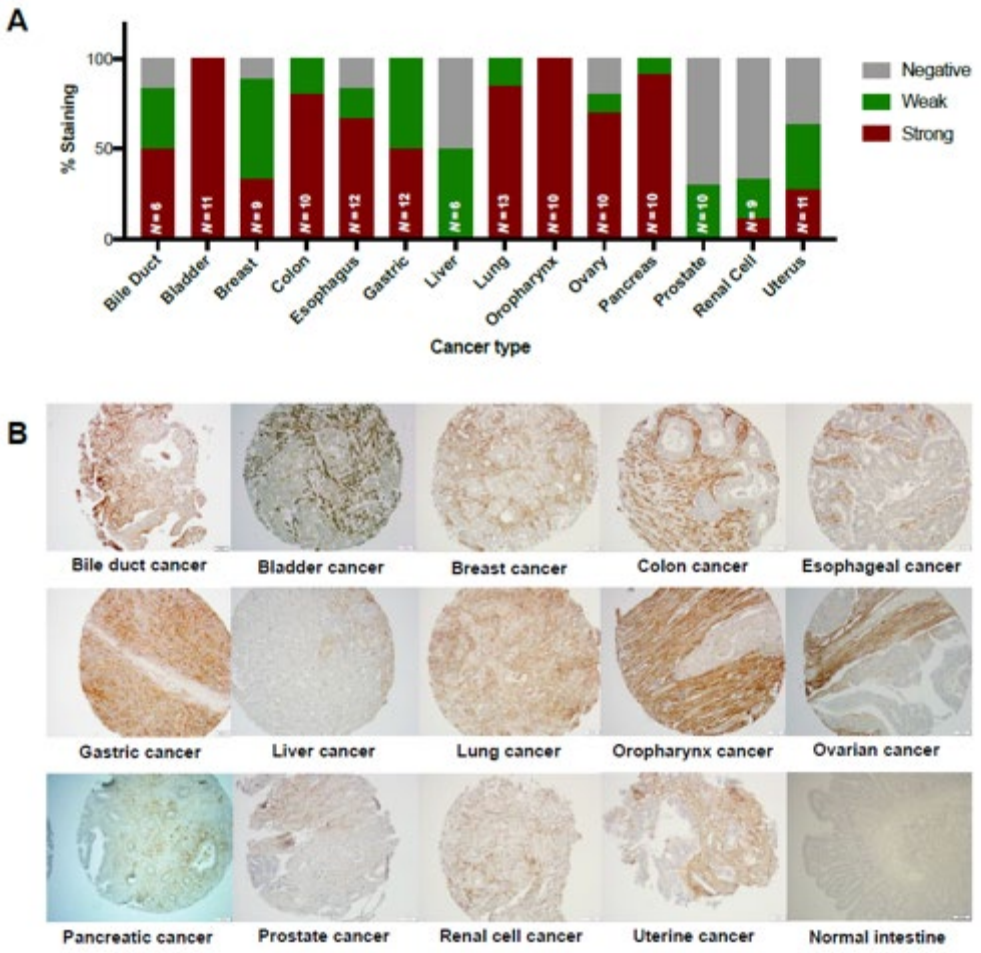
FAP and CAFs

- Among all the stromal cells, **cancer-associated fibroblasts (CAFs)** are dominant populations in the tumor microenvironment
- Fibroblasts become activated during wound repair and regeneration. Malignant tumors are recognized as **“wounds that do not heal”**
- **FAP** is highly expressed on the surface of CAFs
- When looking at markers of CAFs, FAP has received interest as a potential biomarker for CAF identification
- FAP is a great target due to its overexpression in most of the cancer types (90%)

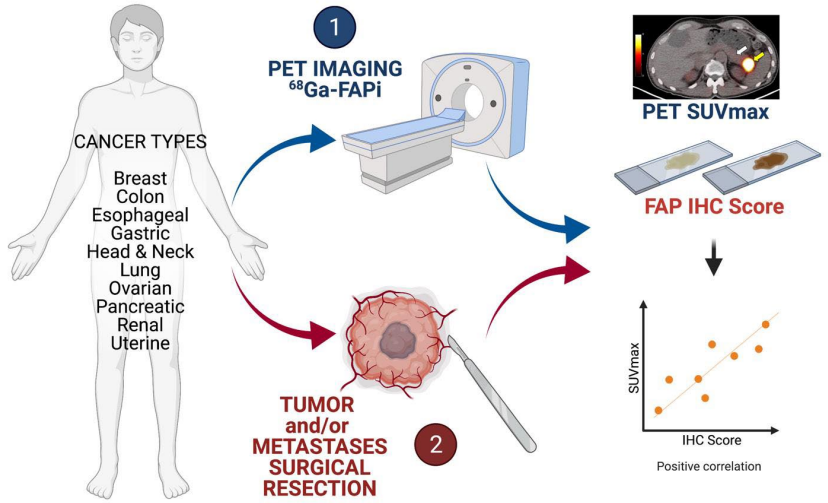


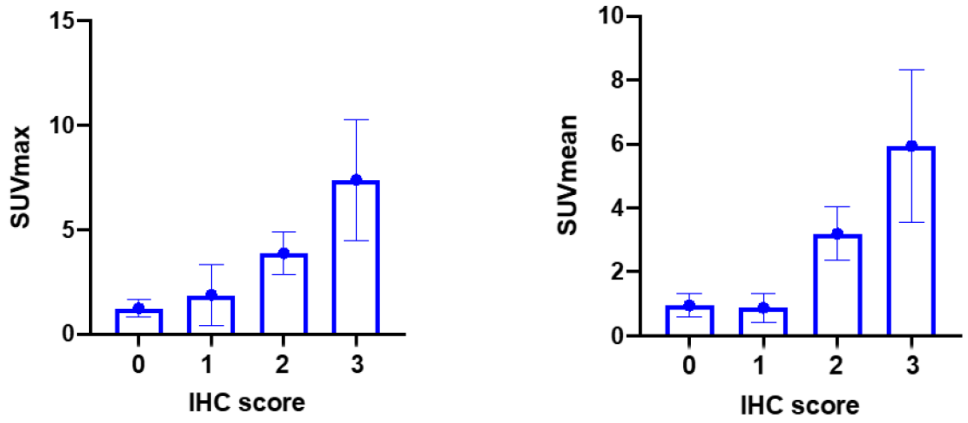
Imlimthan S et al. 2021. New Frontiers in Cancer Imaging and Therapy Based on Radiolabeled Fibroblast Activation Protein Inhibitors: A Rational Review and Current Progress. Pharmaceuticals (Basel).

FAP expression and PET signal validation

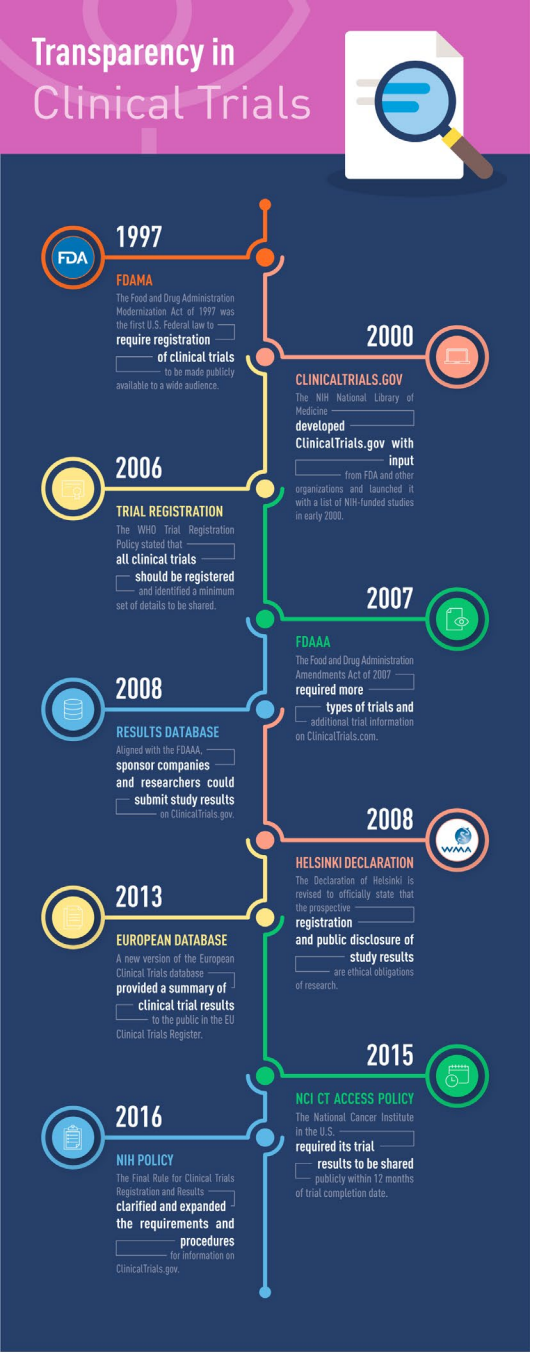


Correlation between FAP immunohistochemistry score and ^{68}Ga-FAPI-46 PET SUVs across cancer and non-cancer issues





Mona et al. doi: 10.2967/jnumed.121.262426



NIH U.S. National Library of Medicine

ClinicalTrials.gov

ClinicalTrials.Gov is the Largest clinical trials database, holding registrations from over **329,000** trials from **209 countries**

1997 — The Food and Drug Administration Modernization Act of 1997 mandates a clinical trials registry

2000 — ClinicalTrials.gov comes online

2007 — Food and Drug Administration Amendments Act of 2007 section 801 mandates registration and penalty for noncompliance

2009 — Reporting results as mandatory

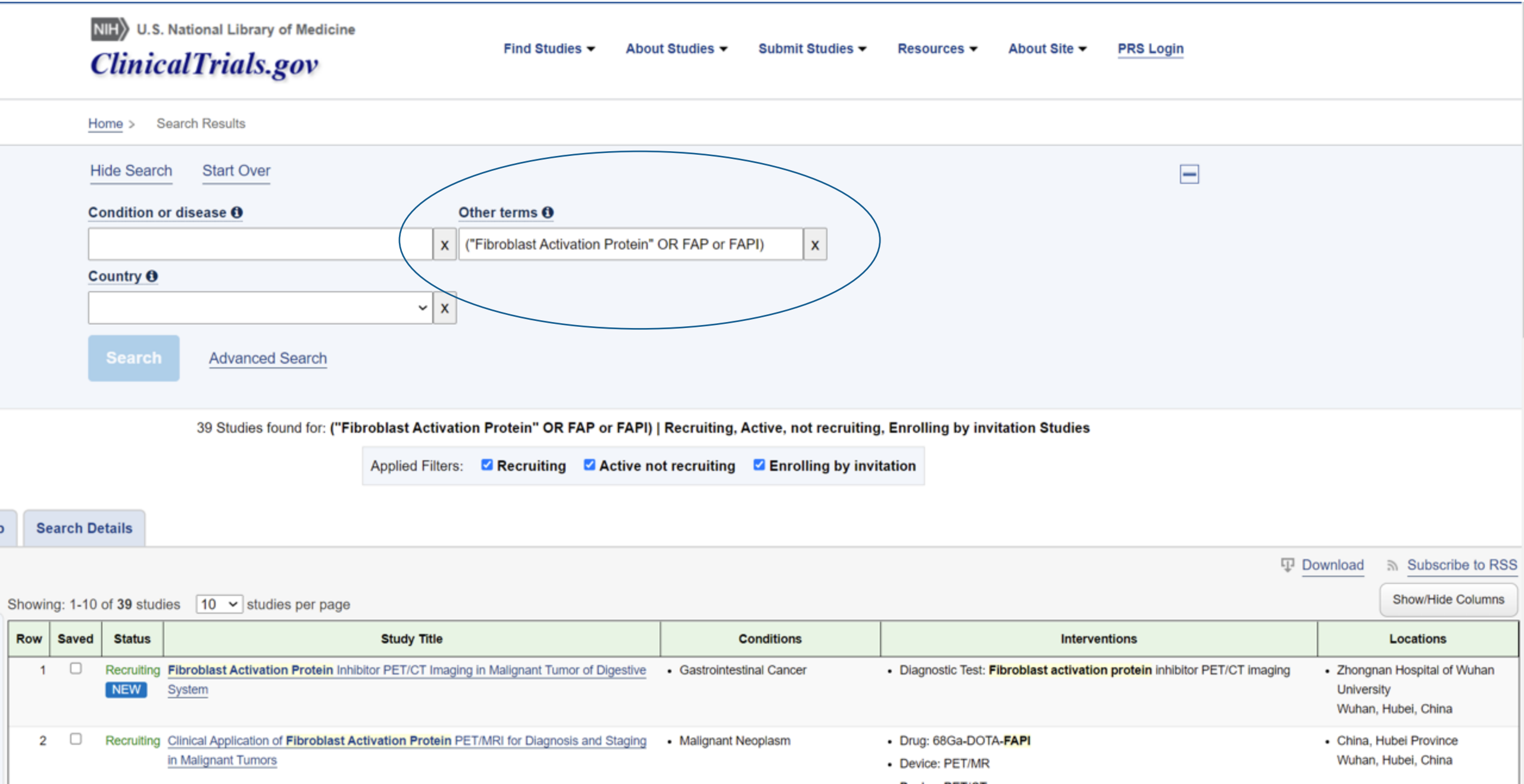
Reference:

https://blog.lillytrialguide.com/clinical-trial-history-transparent-research/

ClinicalTrials.gov- What must be registered?

- Registration is required for studies that meet the definition of an "applicable clinical trial" (ACT) and either were initiated after September 27, 2007, or initiated on or before that date and were still ongoing as of December 26, 2007.
- Controlled clinical investigations (***other than phase 1 investigations***) of any FDA-regulated drug or biological product for any disease or condition
- Controlled trials with health outcomes of FDA regulated devices and pediatric postmarket surveillance (***excludes small feasibility studies***)
- ACTs generally include interventional studies that **meet one** of the following conditions:
    - The trial has one or more sites in the United States
    - The trial is conducted under an FDA investigational new drug application or investigational device exemption
    - The trial involves a drug, biological, or device product that is manufactured in the United States or its territories and is exported for research

Studies on ClinicalTrials.gov



Active Studies on Clinicaltrials.gov by Industry

Non-Radiopharmaceuticals

- Avacta Life Sciences Ltd

AVA6000- FAP activated pro-drug of doxorubicin

- Roche

Multiple FAP targeted non RLT

RO7300490

RO7122290

RO6874281

RO6874281

- Molecular Partners AG

MP0317, a tri-specific fibroblast activation protein (FAP) x

CD40 DARPinÂ® drug candidate

Radiopharmaceuticals

- Clovis Oncology

^{68}Ga-FAP-2286 (Imaging)

^{177}Lu-FAP-2286 (Therapeutic)

- SOFIE

[^{68}Ga]FAPI-46 (Imaging)

Other FAP targeting radiopharmaceuticals in development (not on ClincialTrials.gov)

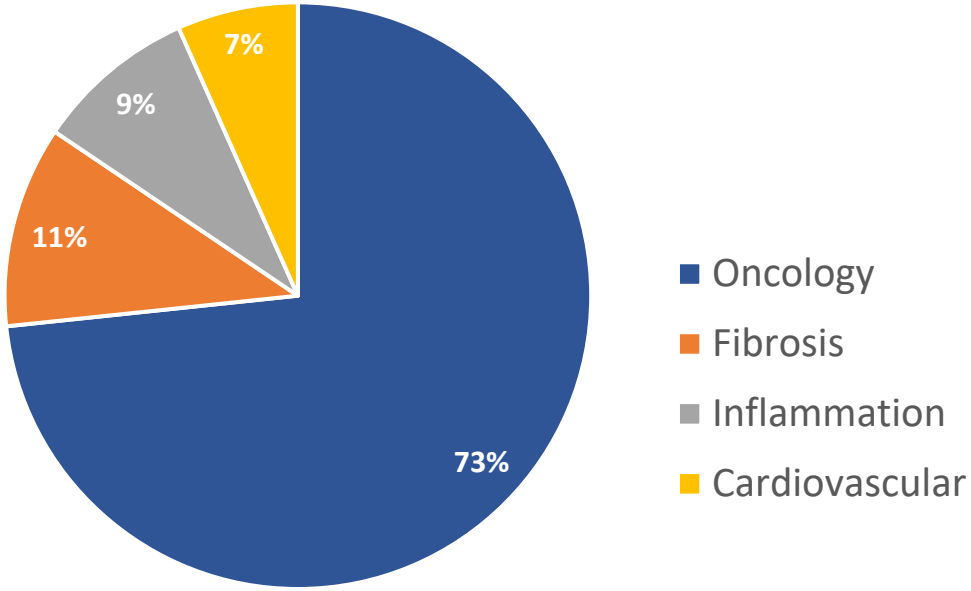
Company	Program	Radioisotope (Imaging and or Therapy)	Status
Noria/Lantheus/Ratio	NTI-1309	Imaging	Preclinical
Noria/Ratio Therapeutics	RPS-309	Theranostic (68Ga, 177Lu)	Preclinical
Philogen	OncoFAP	68Ga	Phase 1
Point Biopharma	PNT6555	177Lu or 225Ac	Preclinical/Phase 1
3B Pharmaceuticals	3BP-3940	Theranostic (177Lu, 225Ac, 90Y, 68Ga)	Preclinical/Phase 1 (compassionate use)
Novartis	FAPI-46	177Lu	Preclinical

^{177}Lu-EB-FAPI is currently under academic use. Expected to be industry sponsored in the upcoming months

^{177}Lu-SA.FAPI family of compounds under academic use

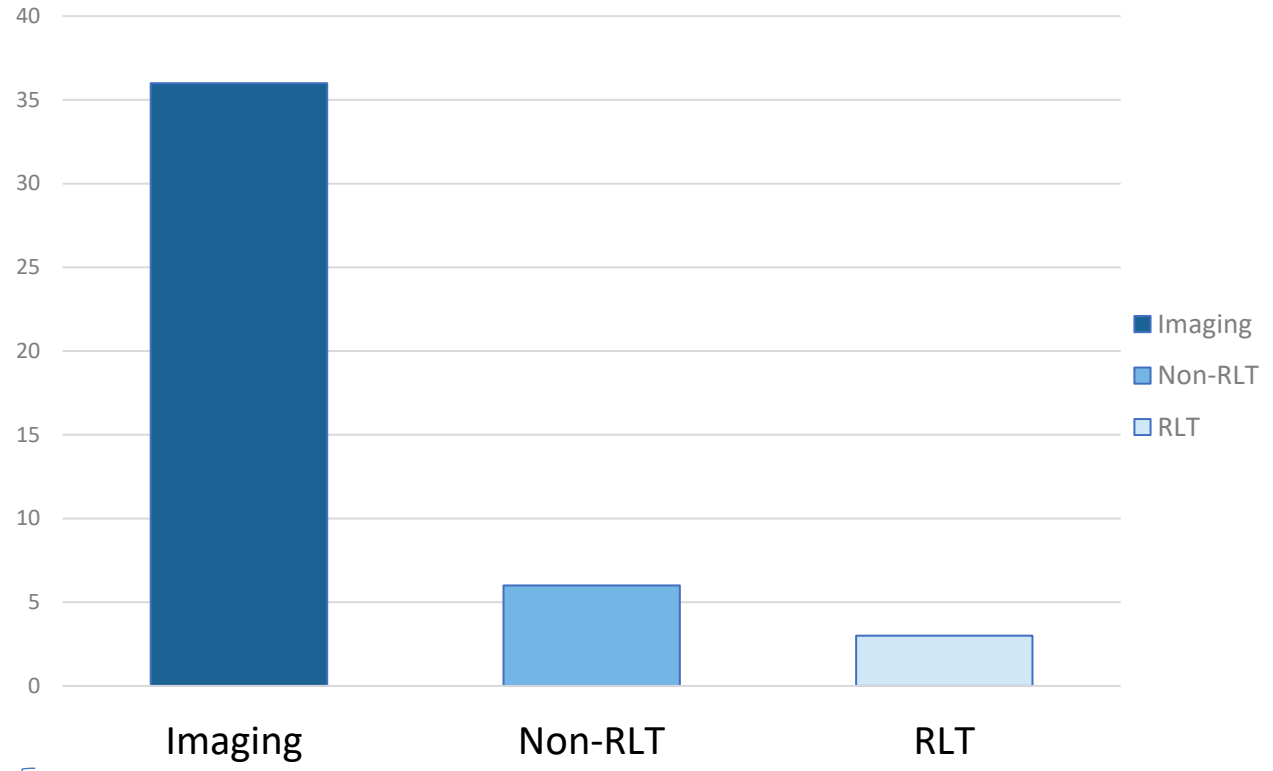
Clinical research by indication and study type

Studies by indication



RLT: Radioligand Therapy
Non-RLT: Non-Radioligand Therapy

Studies by type (Imaging, RLT or non-RLT)

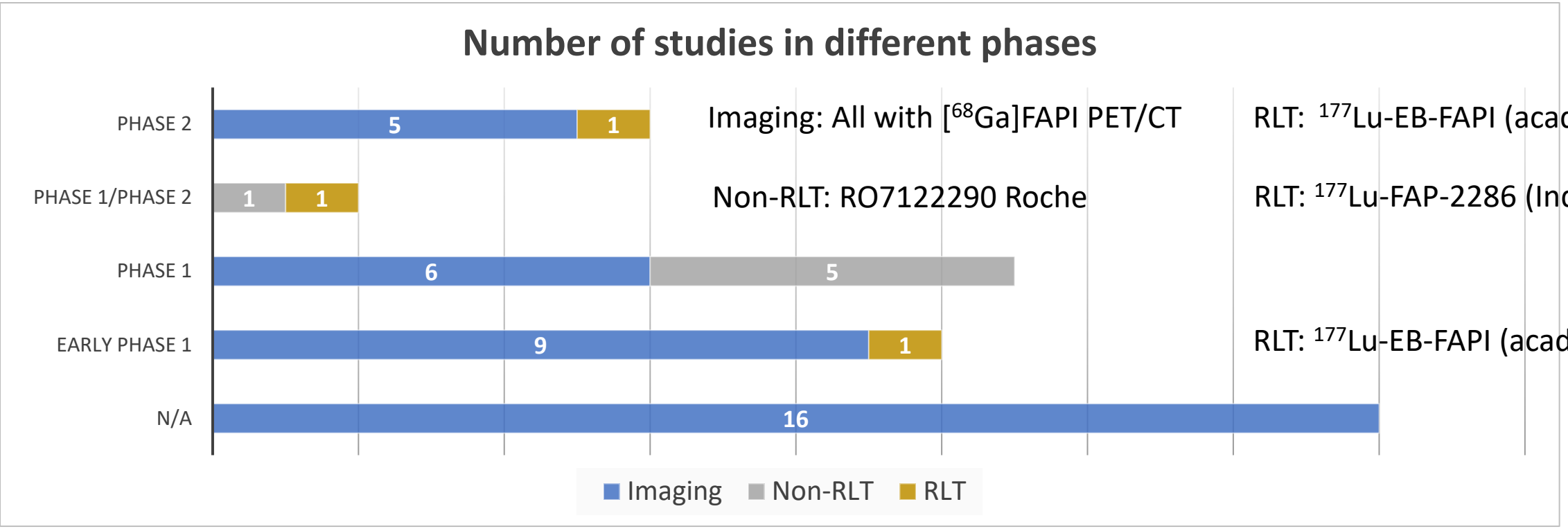


83% [^{68}Ga]FAPI (46 or 04)
[^{18}F]FAPI

17% ^{68}Ga-FAP-2286

^{177}Lu-FAP-2286
^{177}Lu-EB-FAPI

Clinicaltrials.gov studies by Phase of trial



IMAGING

- Majority of the studies are in Imaging
- Most of the imaging studies are exploratory and in Phase 0/NA/or Phase 1
- Phase 2 imaging studies are with [^{68}Ga]FAPI PET/CT

Therapeutic

- Non-RLT studies are in early phases (Phase 1 or Phase 1 / 2)
- RLT studies are with ^{177}Lu-EB-FAPI and ^{177}Lu-FAP-2286

Taking a closer look at the Clovis and SOFIE products

Radiopharmaceuticals

- Clovis Oncology

^{68}Ga-FAP-2286 (Imaging)

^{177}Lu-FAP-2286 (Therapeutic)

- SOFIE

[^{68}Ga]FAPI-46 (Imaging)

[^{18}F]FAPI-74 (Imaging)

TARGETED RADIONUCLIDE THERAPY

https://www.clovisoncology.com/pipeline/pipeline-overview/

CLOVIS ONCOLOGY

FAP-2286 (Fibroblast activation protein)

LuMIERE
Advanced solid tumors

DISCOVERY | PRECLINICAL | PHASE I

ISOTOPE(S)

Lu Lutetium (177) Ga Gallium (68)

Imaging Using ^{68}Ga FAP-2286
Solid tumors

Sponsored by UCSF

DISCOVERY | PRECLINICAL | PHASE I

ISOTOPE(S)

Ga Gallium (68)

2nd Generation Alpha-emitter
TBD

DISCOVERY | PRECLINICAL

ISOTOPE(S)

Ac Actinium (225)

Combination Program
TBD

DISCOVERY | PRECLINICAL

NIH U.S. National Library of Medicine

ClinicalTrials.gov

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NCT04939610

Home > Search Results > Study Record Detail

Save this study

Trial record **3 of 65** for: clovis oncology

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A Study of 177Lu-FAP-2286 in Advanced Solid Tumors (LuMIERE) (LuMIERE)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT04939610

Recruitment Status : Recruiting
First Posted : June 25, 2021
Last Update Posted : June 3, 2022

See Contacts and Locations

Sponsor:
Clovis Oncology, Inc.

Study Description

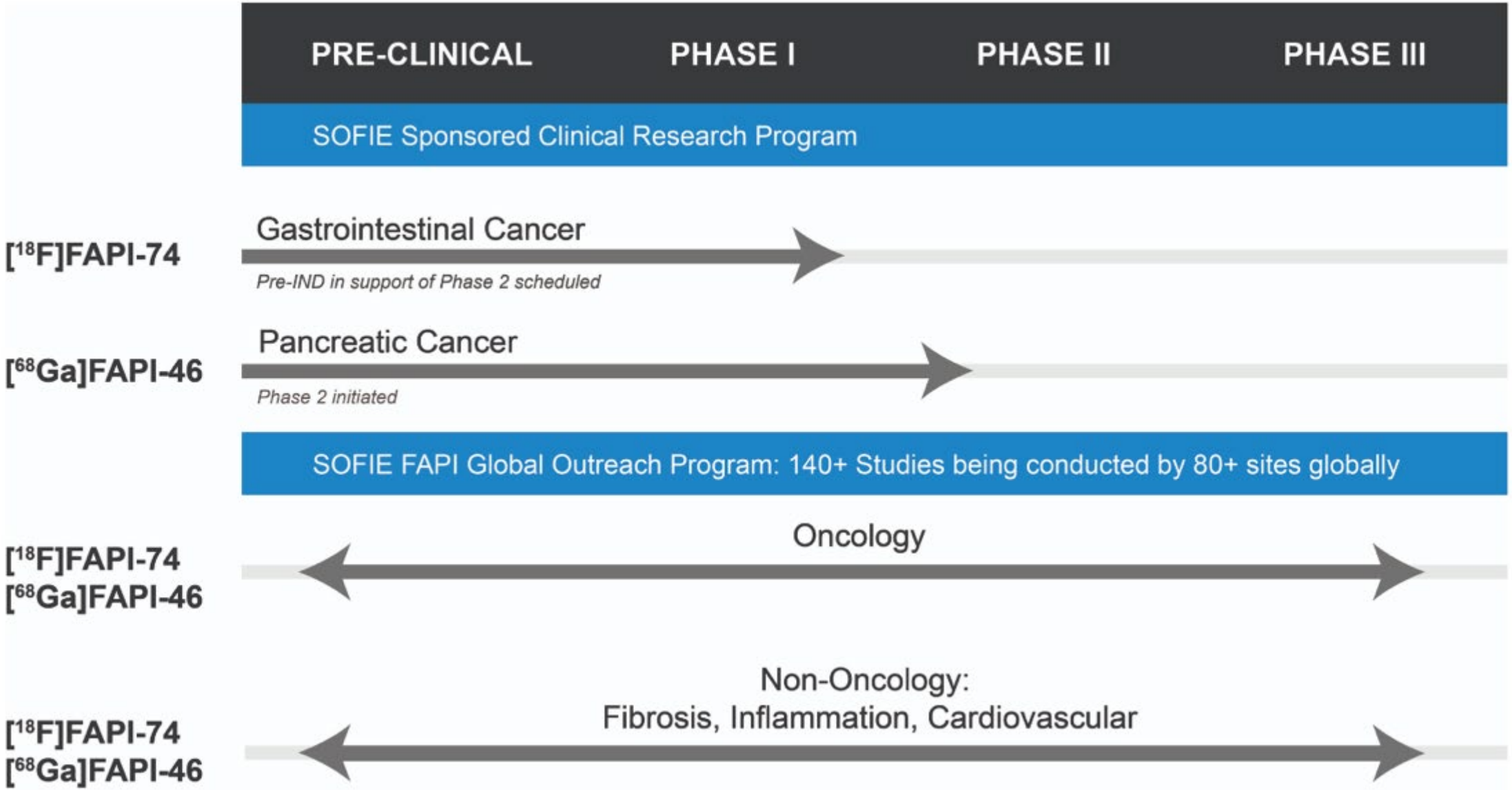
Go to

Brief Summary:
Phase 1 of this study will evaluate the safety and tolerability of 177Lu-FAP-2286 and determine the recommended Phase 2 dose (RP2D) in patients with advanced solid tumors. Phase 2 of this study is designed to evaluate objective response rate (ORR) in patients with specific solid tumors.

Condition or disease	Intervention/treatment	Phase
Solid Tumor	Drug: 68Ga-FAP-2286 Drug: 177Lu-FAP-2286	Phase 1 Phase 2

LuMIERE: A Phase 1/2, Multicenter, Open-label, Non-randomized Study to Investigate Safety and Tolerability, Pharmacokinetics, Dosimetry, and Preliminary Activity of 177Lu-FAP-2286 in Patients With an Advanced Solid Tumor

SOFIE's Product Pipeline



Family of compounds

[^{68}Ga]-FAPI-46

Gallium isotope

Number 46
Specific compound

- Lead **gallium** labeled compound
- DOTA chelator in the molecular structure allows coupling of the FAPI molecules for theranostic use
- SOFIE has obtained an **IND** for [^{68}Ga]-FAPI-46 for a Phase 2 study
- A **Phase 2**, Multicenter, Single Arm, Open Label, Non-Randomized Study of [^{68}Ga]FAPI-46 PET in Patients with Resectable or Borderline Resectable **Pancreatic Ductal Adenoarcinoma**
- Total number of patients: **60**
- Study launch: **May 2022**
- First site activated: **NYU**
- 2nd site to be activated: **Mayo Clinic** end of August

Family of compounds

[^{18}F]-FAPI-74

Fluorine isotope

Number 74
Specific compound

- Lead **Fluorine 18** compound
- Allows for broader applicability of FAP PET through 18-F radiolabeling
  - Provides advantage of a longer half life (2 hours)
  - Meeting the capacity to support larger studies with high patient throughput
- **Automated synthesis** consumables available through Trasis for MiniAIO and AIO
- Pre-IND meeting scheduled with FDA for **July 19th 2022**
- Positive response from FDA to proceed to Phase 2 in **Gastrointestinal cancers**
- IND enabling data completed
- IND to be filed and activated by end of Fall 2022

SOFIE's FAPI Global Outreach Program

Gain access to GMP grade precursor and reference standard in support of investigator-initiated trial

Technical manufacturing assistance to get the sites started

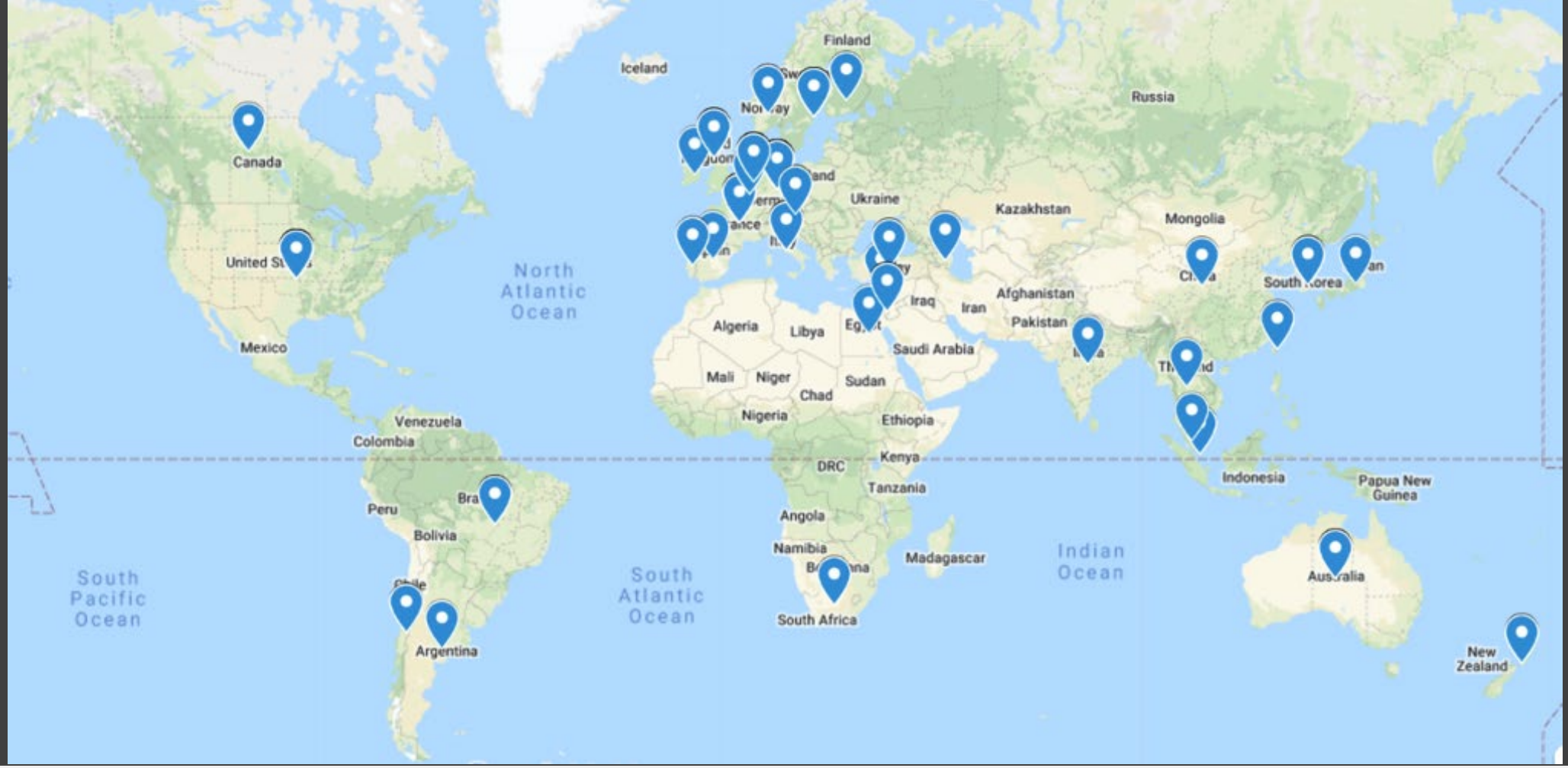
Cross Reference to SOFIE's IND(s) or IND content to pursue investigator-initiated trial

Allows sites to expand their research program and grant opportunities

Process for access to FAPI precursor

Introductory Call → Application Completion → Application Approval → MTA Signature → Material Shipment

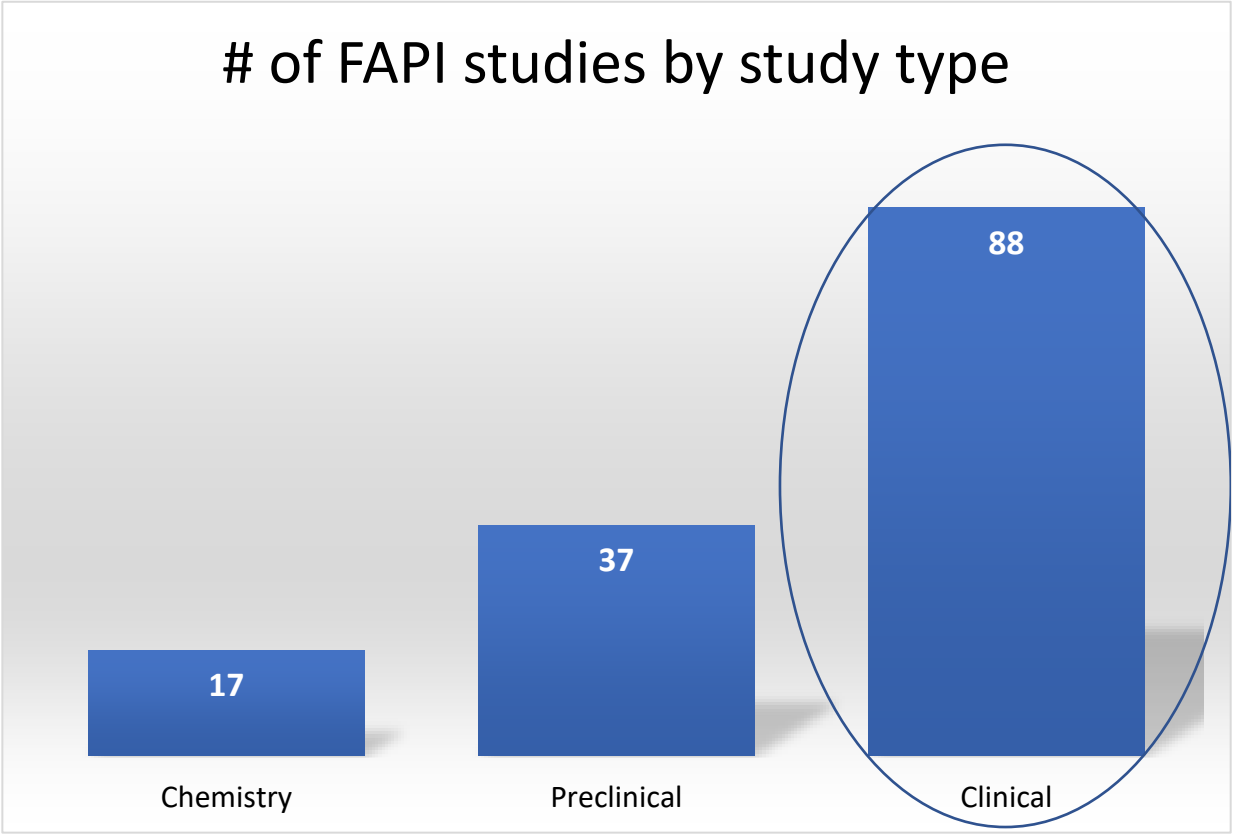
Complete application on our website: https://sofie.com/pipeline/access/



SOFIE's FAPI Global Outreach Program

- 34 Countries
- 140+ research studies
- Studies include: Chemistry, pre-clinical, clinical, oncology and non-oncology
- 80+ unique institutions
- Compounds: [^{18}F]-FAPI-74 and [^{68}Ga]-FAPI-46

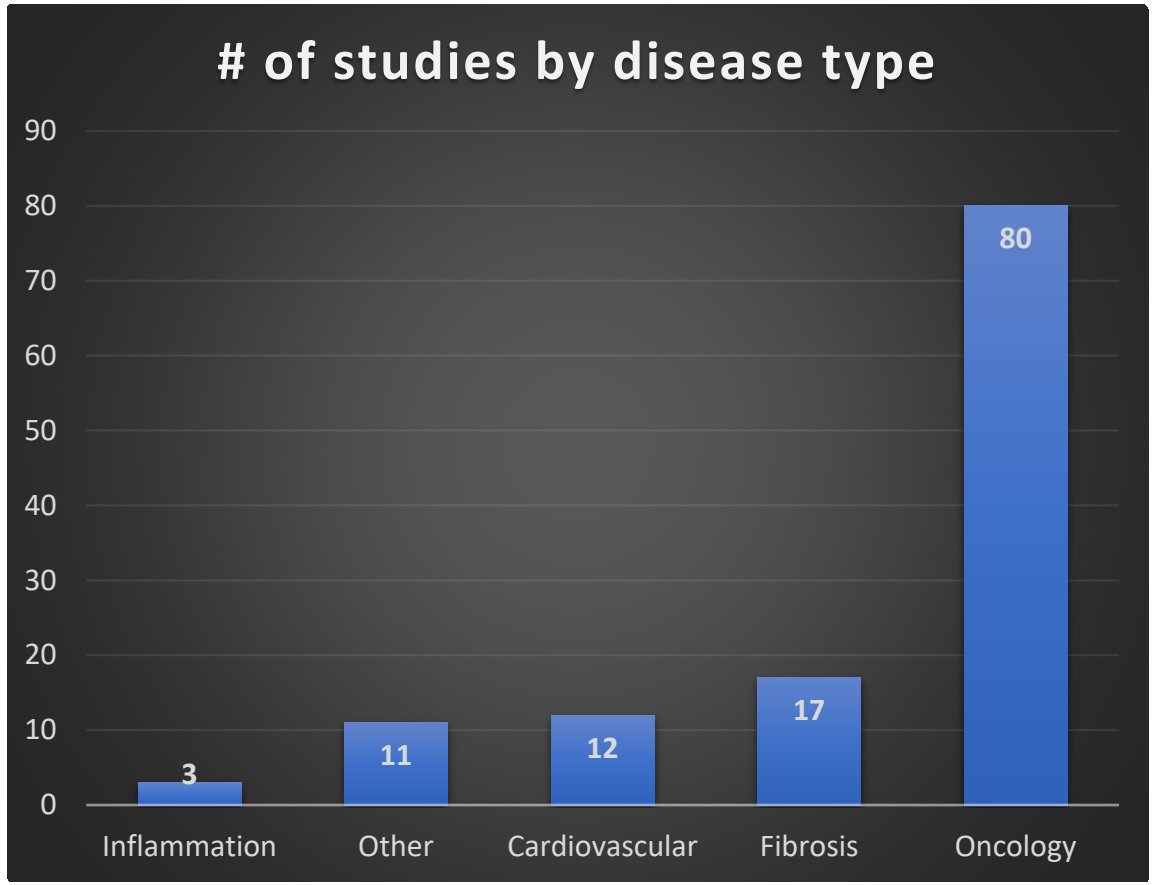
FAPI Global Outreach Program- Statistics

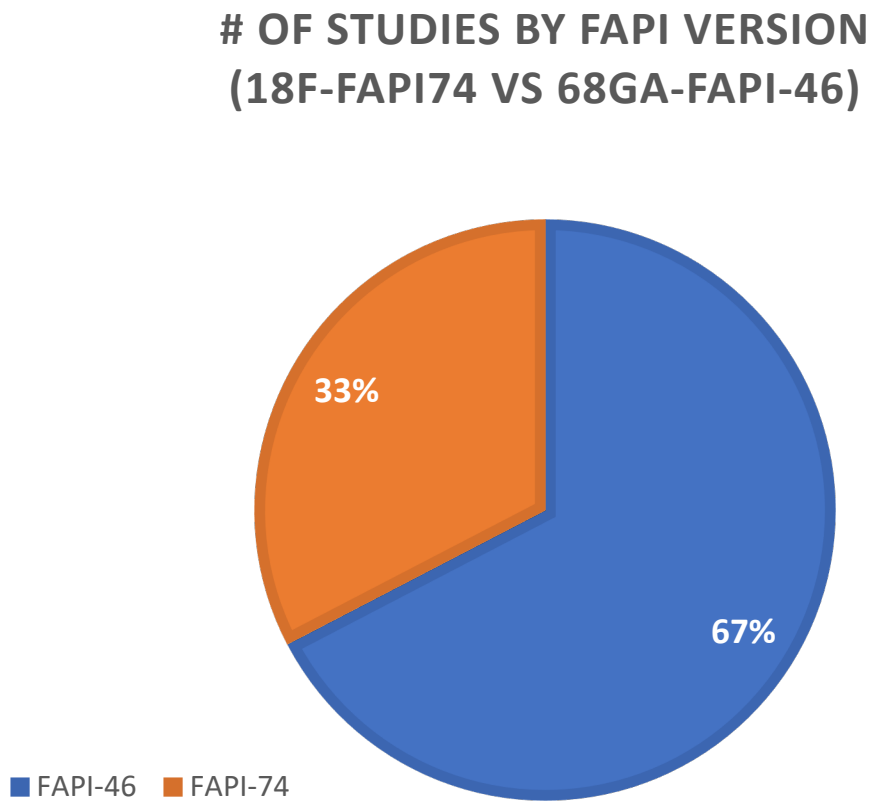


4034 Patients

88 clinical studies globally underway with 4000+ patients

FAPI Global Outreach Program- Statistics Continued





- Majority of the studies are in Oncology. Cardiovascular, Fibrosis and other diseases are being explored as well
- Galium studies are currently at 67% but this has decreased in favor of 18F-FAPI studies over the past 6 months
- 18F-FAPI studies expected to grow

What is to come for FAP targeting in Diagnostics?

- Equal or superior detection performance of FAP targeted radioligands compared to FDG in various cancers. Preliminary results in the following cancers look promising for detection FAP targeted radioligands:
  - Gastrointestinal (liver, pancreatic, colorectal, gastric etc)
  - Esophageal
  - Head and Neck/CUP
  - Breast
  - Lung
- Seeing superior performance compared to FDG in metastatic lesion detection

- Utility of FAP radiotracers will need to be evaluated in specific indications and tumor state (primary, nodal and distant metastasis) under prospective trials
- Identifying unmet clinical need
- FDG and FAP targeted radiopharmaceuticals image different critical biological processes in tumorigenesis. Each add respective value informing us of biology of disease. Important to focus on biology of disease information provided by each probe

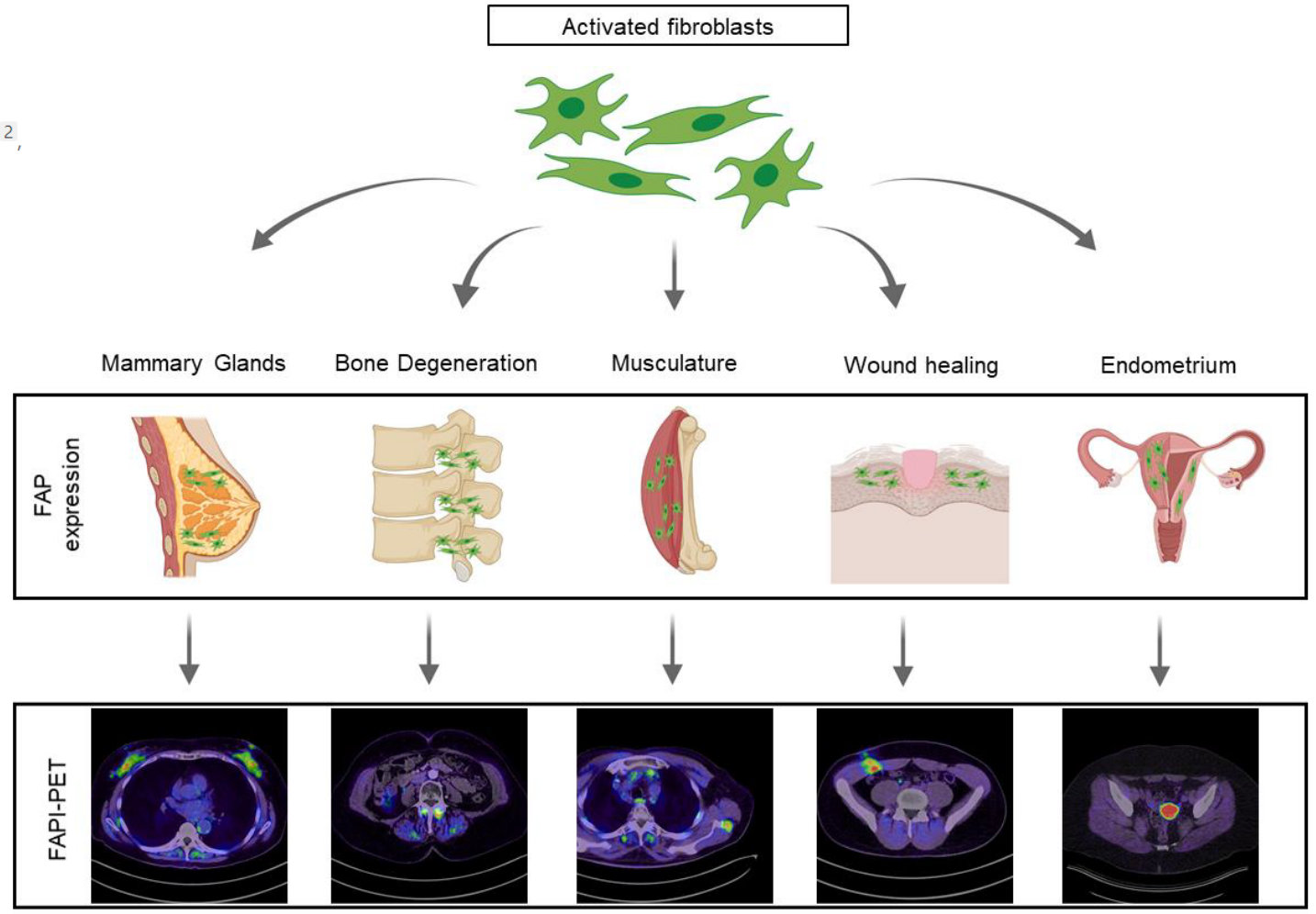
Pitfalls- Considerations to be made in FAP targeting image interpretations

Pitfalls and common findings in ^{68}Ga-FAPI-PET – A pictorial analysis

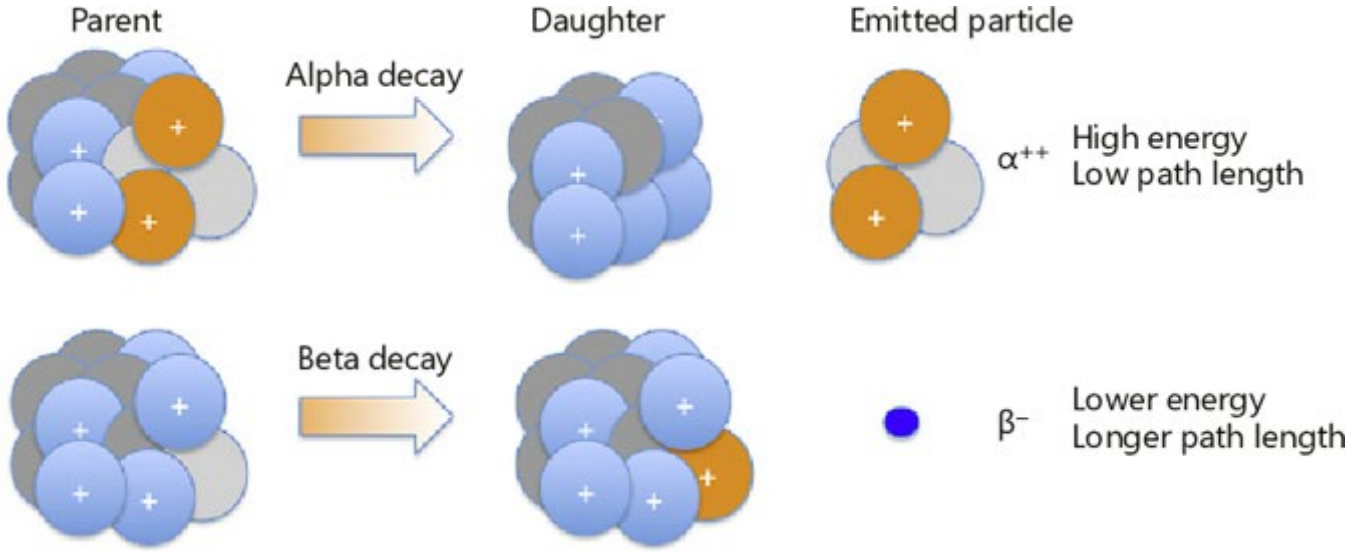
Lukas Kessler [1], Justin Ferdinandus [1], Nader Hirmas [1], Fadi Zarrad [1], Michael Nader [1], David Kersting [1], Manuel Weber [1], Sandra Kazek [1], Miriam Sraieb [1], Rainer Hamacher [2], Katharina Lueckerath [1], Lale Umutlu [3], Wolfgang P Fendler [1], Christoph Rischpler [1]

University Hospital Essen

- 91 patients underwent whole-body PET/CT. Findings were rated in a consensus session of two experienced readers
- Non-tumor specific [^{68}Ga]-FAPI uptake in degenerative lesions, muscle, head-and-neck, scarring, mammary glands or uterus
- Common pitfall findings were **degenerative lesions** mostly associated to joints and vertebral bones



Radioligand therapy: Considerations to be made



DOI:10.1159/000494760

Radionuclide	Half life	Type of damage
^{225}Ac	T1/2 = 10 days	dsDNA damage
^{212}Pb/^{212}Bis*	T1/2 = 1 h	
^{177}Lu	T1/2 = 6.7 d	ssDNA damage
^{90}Y	T1/2 = 64 h	
^{212}Pb	T1/2 = 10.6 h	

*^{212}Pb, by itself is a β-emitter, but acts as an in vivo generator for its short-lived α-emitting daughters.

- Assessment of RLT utility of FAP targeted radioligands is in early clinical investigation
- Alpha vs beta emission vs both
- Monotherapy vs Combination therapy (RLT followed by non RLT)

THANK YOU!

Questions? Please reach out to
sherly.mosessian@SOFIE.com