Preliminary Dosimetry Results from a First-in-Human Phase 1 Study Evaluating the Efficacy and Safety of [225Ac]-FPI-1434 in Patients with IGF-1R Expressing Solid Tumors

Ac-225 Users Group Meeting

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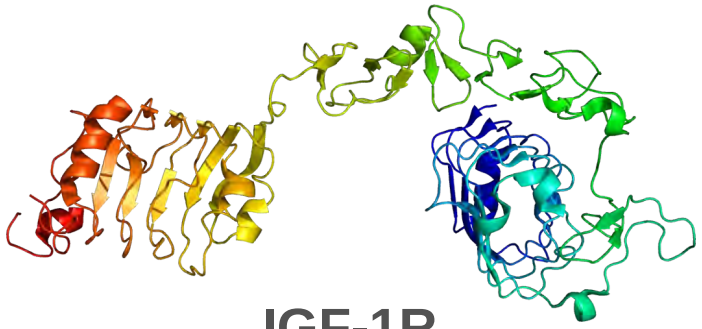
[^{225}Ac]-FPI-1434 Background

Type I insulin-like growth factor receptor (IGF-1R) is a transmembrane protein which is overexpressed in solid tumors



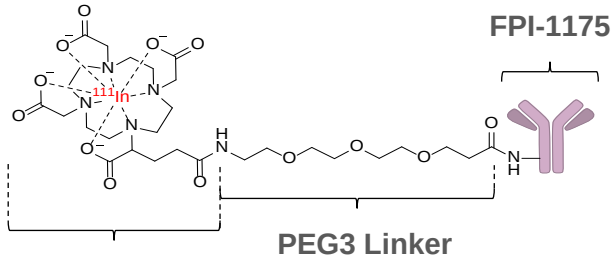
IGF-1R

Implicated in:

- Increased cellular proliferation
- Metastatic potential
- Cell survival
- Chemotherapy and radiotherapy resistance

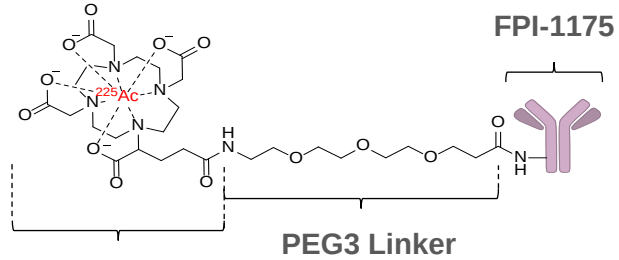
IGF-1R Expression in Solid Tumors	
100%	Ovarian
100%	Bladder
90%	Sarcomas
62%	Head & Neck
62%	Prostate
59%	NSCLC
57%	Pancreatic
50%	Colorectal
50%	Liver
47%	Breast
43%	Small Cell Lung
40%	Esophagus
36%	Renal
36%	ACC

[^{111}In]-FPI-1547



Imaging

[^{225}Ac]-FPI-1434



Therapy

[^{225}Ac]-FPI-1434 Key Study Objectives / Design

First-in-Human Phase 1 Study FPX-01-01 (NCT03746431)

- Primary Objective: Evaluate the safety and tolerability of [^{111}In]-FPI-1547 Injection and [^{225}Ac]-FPI-1434 Injection in patients with advanced refractory solid tumors
- Patient selection and individualized patient dosimetry based on imaging with [^{111}In]-FPI-1547
- 3+3 dose-escalation
- Identify maximum tolerated dose / recommend Phase 2 dose of [^{225}Ac]-FPI-1434
- Single dose escalation completed, enrollment into multi-dosing cohorts and cold antibody sub-study ongoing

[^{225}Ac]-FPI-1434 Study Population / Therapeutic Administrations

[^{225}Ac]-FPI-1434 Administration (kBq)

	Mean	Min	Max
Cohort 1 (10kBq/kg) N=4	884	797	984
Cohort 2 (20kBq/kg) N=4	1840	1290	2290
Cohort 3 (40kBq/kg) N=4	3394	2400	4179

Key eligibility criteria

- IGF1R-expressing advanced solid tumors
- TBR >2:1 relative uptake to compared to skeletal muscle
- ECOG 1-2 and adequate end-organ function
- Prior therapeutic radiopharmaceuticals >6 mos of enrollment
- Prior radiation to large areas of bone marrow <20 Gy
- Safety Review Committee review following each cohort

Patient Characteristics Safety Population Treated with [^{225}Ac]-FPI-1434 (N=12)

Median Age (range)	61.0 (36-78) years
Gender, n (%)	
Male	9 (75%)
Female	3 (25%)
Race, n (%)	
White	10 (83%)
Asian	1 (8%)
Not reported	1 (8%)
Tumor type, n (%)	
Prostate cancer	6 (50%)
Colorectal cancer	3 (25%)
Adrenocortical carcinoma	1 (8%)
Fibromyxoid sarcoma	1 (8%)
Ovarian cancer	1 (8%)
Baseline ECOG, n (%)	
0	7 (58%)
1	5 (42%)

[^{225}Ac]-FPI-1434 Safety Assessments

Most Common FPI-1434-related AEs Cohorts 1-3

All Grades (≥2pts) , n (%)	
Thrombocytopenia	5 (42%)
Neutropenia	4 (33%)
Fatigue	4 (33%)
Lymphocyte count decrease	3 (25%)
White blood cell count decrease	3 (25%)
Nausea	2 (17%)
Grade 3, n (%)	
*Neutropenia	1 (8%)
*Lymphocyte count decrease	1 (8%)
*White blood cell count decrease	1 (8%)
No Grade 4 AEs observed	

* Gr 3 WBC decrease , neutropenia, lymphopenia were attributed to the same patient

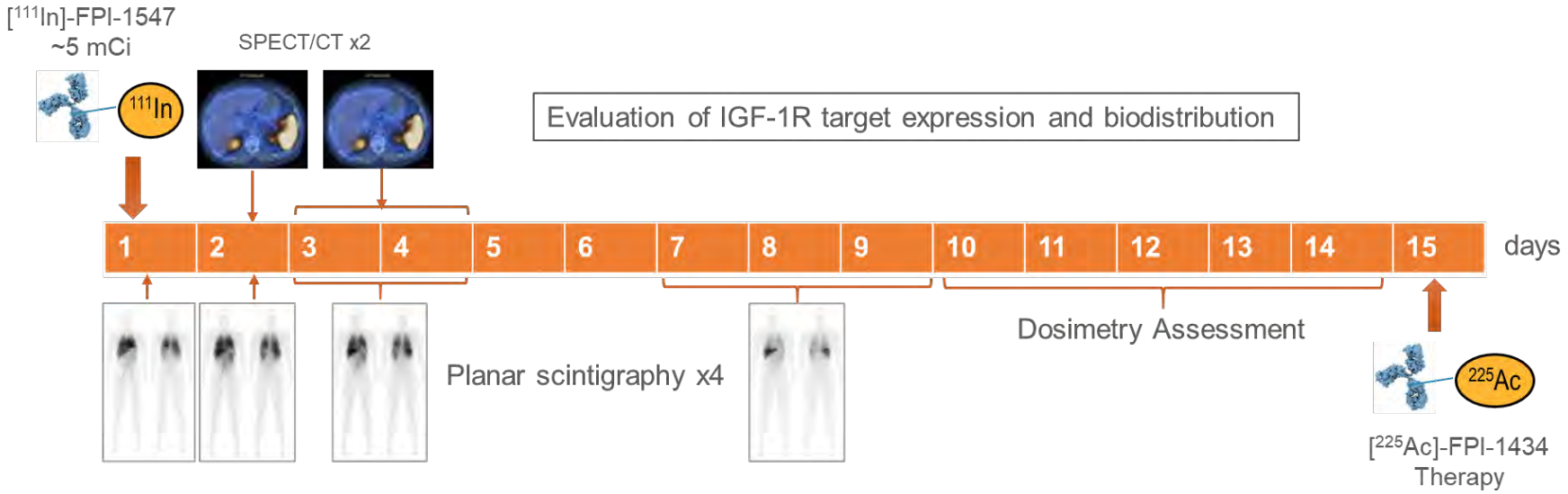
Post-Treatment Safety Events
Safety Population – Cohorts 1-3 (N=12)

Patients, n (%)	
Any Adverse Events (AEs)	12 (100%)
Serious Adverse Events (SAEs)	1 (8%)
FPI-1434-related AEs	8 (67%)
FPI-1547-related AEs	1 (8%)
FPI-1434-related SAEs	0 (0%)
FPI-1547-related SAEs	0 (0%)

56-day DLT evaluation period following therapeutic administration for dose-limiting toxicity assessment through single-administration dose-escalation.

No DLTs, treatment-related SAEs, or dose interruption/modification were reported in Cohorts 1-3

[^{225}Ac]-FPI-1434 Imaging Procedure and Dosimetric Methodology

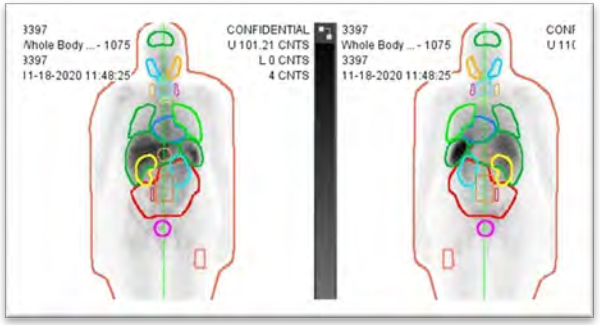


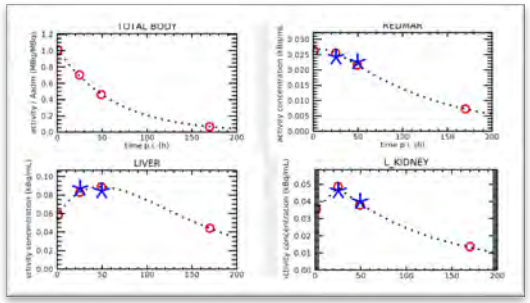
Planar Regions of Interest
CT-based organ volume

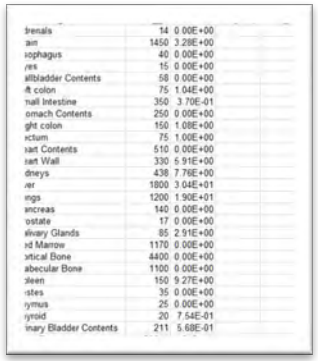
Time Activity Curves and
Time-integrated Activity

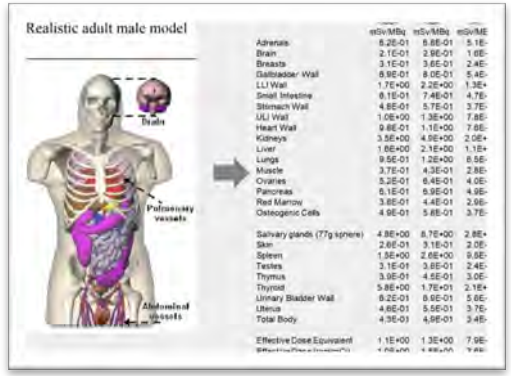
Residence Time Calculation
In-111 to Ac-225 values

OLINDA/EXM 2.1-2.2
(Hermes Medical Solutions)





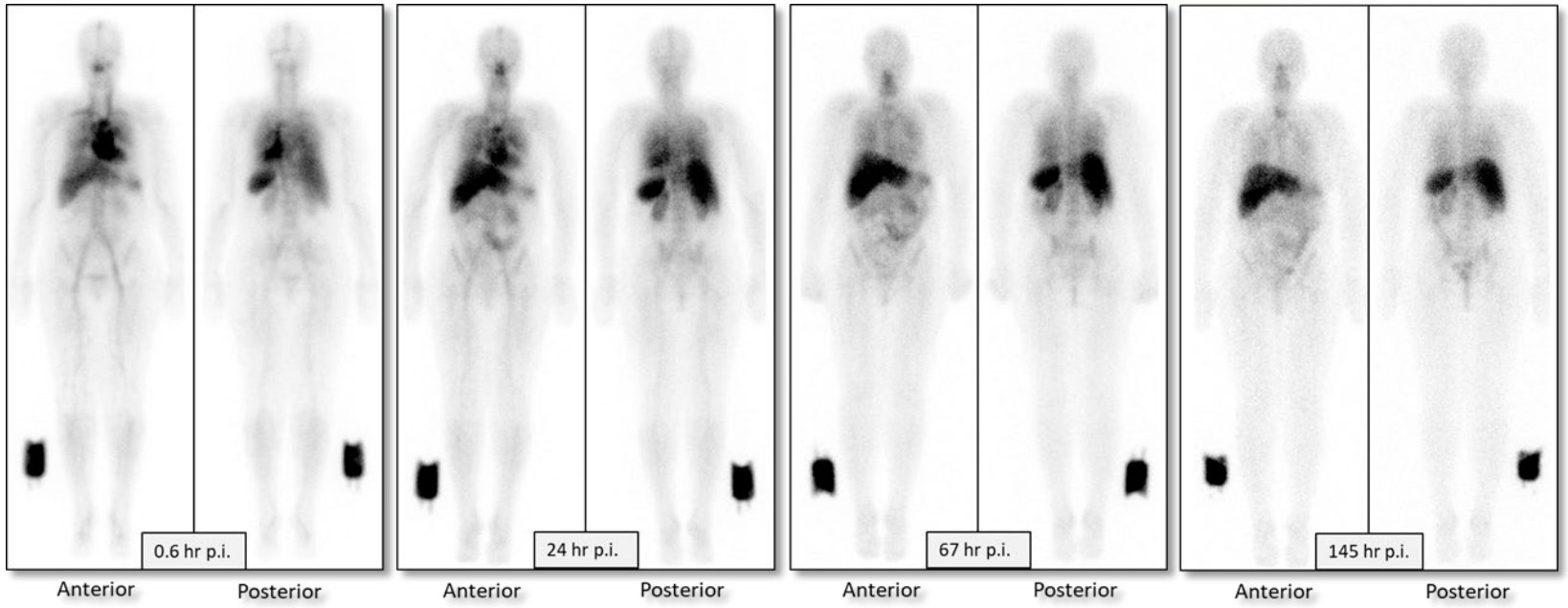


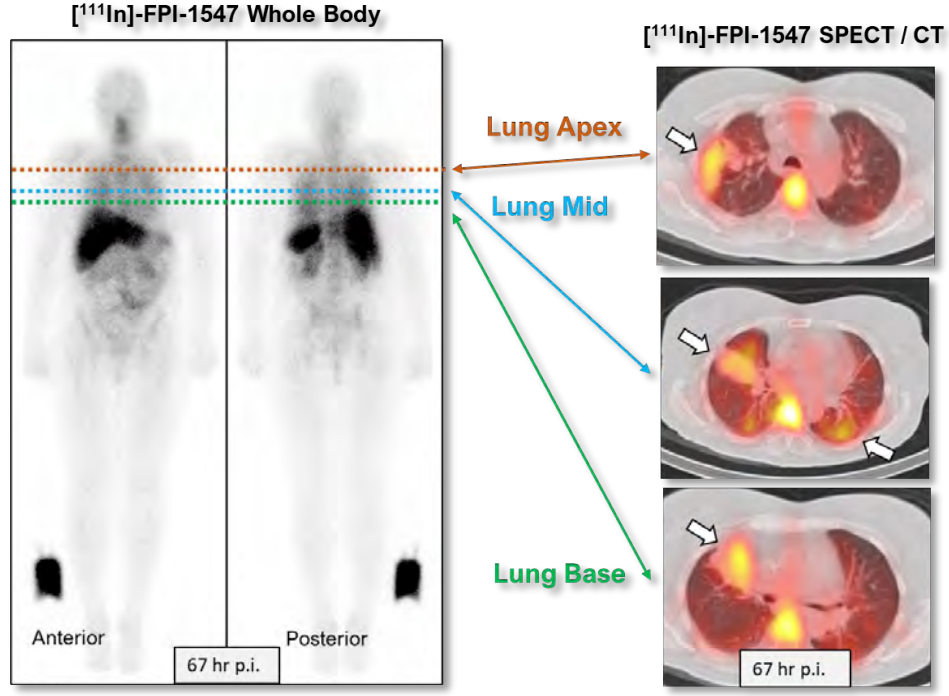


[^{225}Ac]-FPI-1434

Subject 204-007

65 y.o. female with Ovarian Cancer

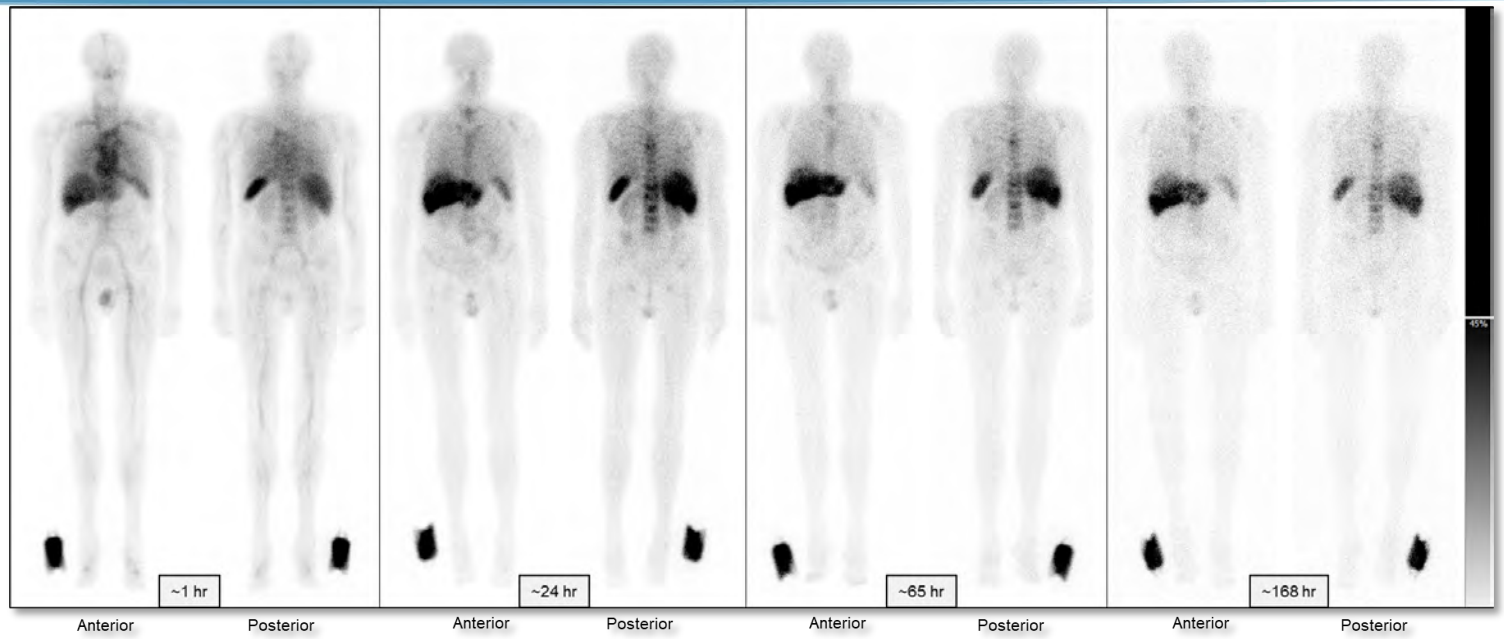


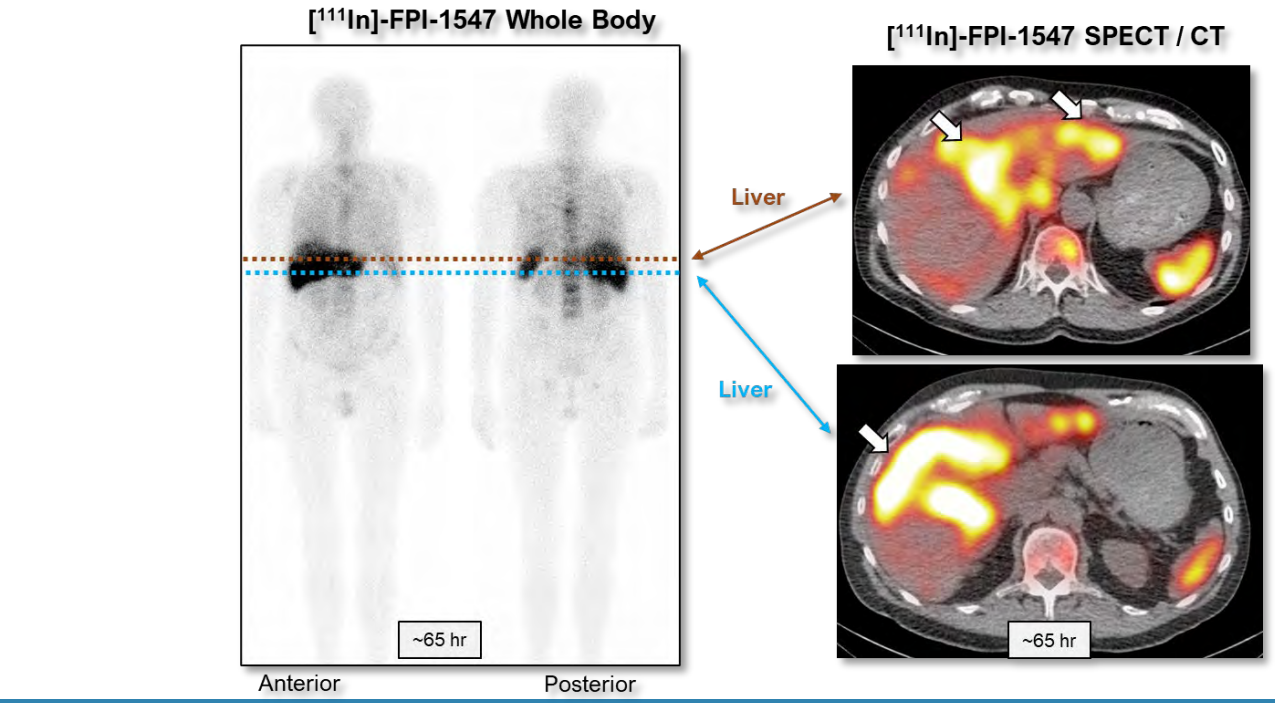


[^{225}Ac]-FPI-1434

Subject 202-008

69 y.o. male with Castrate-resistant Prostate Cancer





[^{225}Ac]-FPI-1434 Radiation Absorbed Dose Estimates

Target Organ	Mean* (mGy-Eq/MBq)	Minimum* (mGy-Eq/MBq)	Maximum* (mGy-Eq/MBq)	Standard Deviation* (mGy-Eq/MBq)
Adrenals	78	56	102	14
Brain	94	56	169	34
Esophagus	75	54	99	14
Eyes	74	53	98	14
Gallbladder Wall	77	55	100	14
Left colon	81	59	104	14
Small Intestine,	75	54	99	14
Stomach Wall	76	54	99	14
Right colon	78	57	102	14
Rectum	81	59	104	14
Heart Wall	1,190	690	2,040	392
Kidneys	988	615	1,820	305
Liver	934	556	1,660	319
Lungs	626	328	910	175
Pancreas	76	54	99	14
Salivary Glands	1,520	900	2,370	452
Red Marrow	807	398	1,450	303
Osteogenic Cells	1,280	922	1,860	227
Spleen	3,668	1,740	9,060	1881
Thymus	75	54	99	14
Thyroid	693	315	1,510	347
Urinary Bladder Wall	76	55	99	14
Total Body	*140*	*111*	*167*	*16*

N=13
Patients with evaluable [^{111}In]-FPI-1547 Image Data for Dosimetry

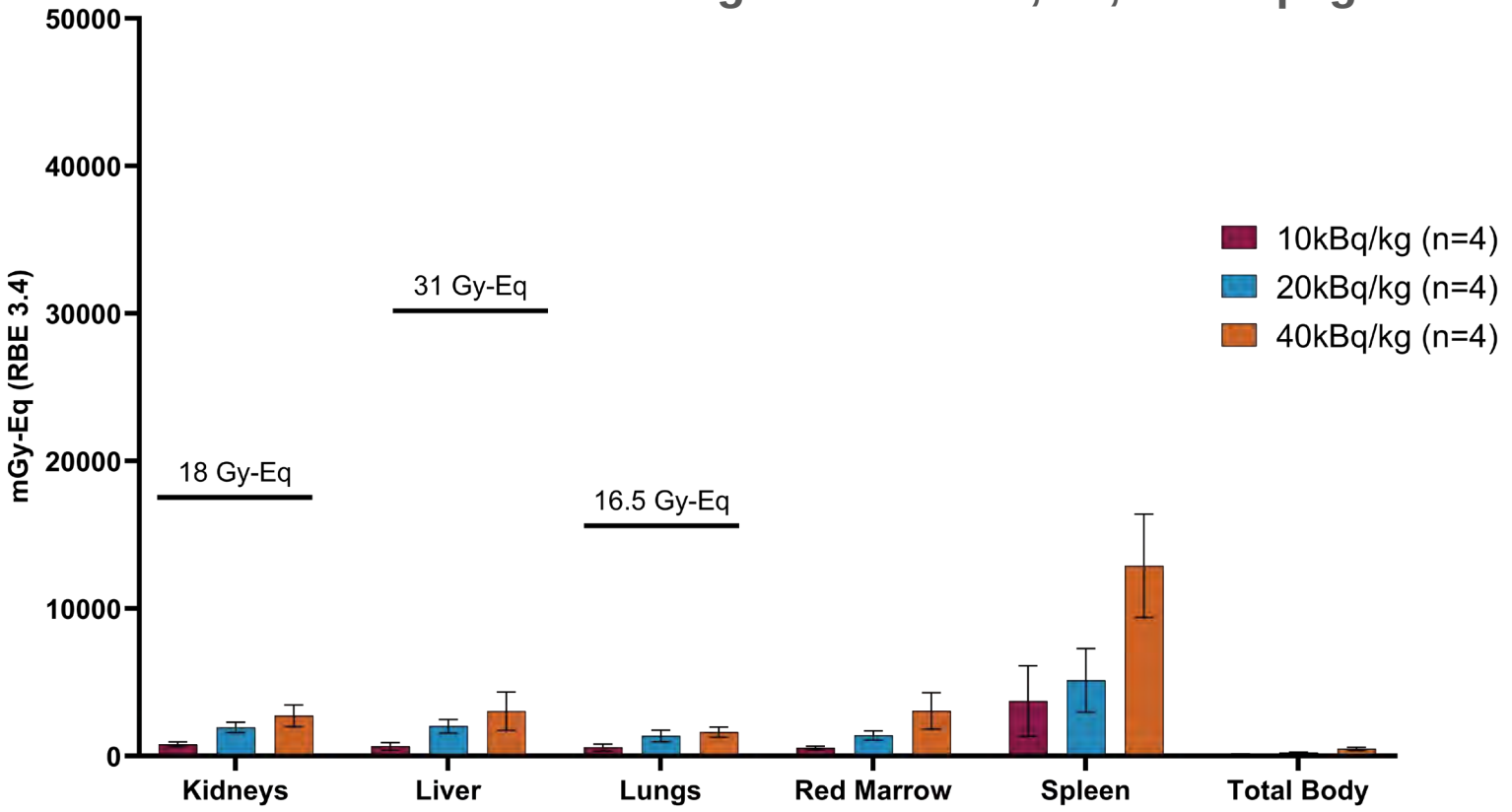
N=12
Patients received therapy with [^{225}Ac]-FPI-1434

N=1
patient eligible per imaging but not treated due to rapid disease progression

Administered therapeutic activity was not to exceed protocol-defined thresholds of **18 Gy (kidneys), 31 Gy (liver), and 16.5 Gy (lungs)** using an RBE value of 3.4 for all calculations

[^{225}Ac]-FPI-1434 – Dose Escalation Cohorts

Dosimetry for the first 3 cohorts of [^{225}Ac]-FPI-1434 administered as a single dose at 10, 20, 40 kBq/kg



Radiation Dose Estimates per Unit of Administered Activity (mGy-Eq/MBq) N=13

Target Organ	Mean	±SD
Kidneys	988	305
Liver	934	319
Lungs	626	175
Red Marrow	807	303
Spleen	3,668	1881
Total Body	*140*	*16*

[^{225}Ac]-FPI-1434 Conclusions

- 100% of patients imaged were eligible based on imaging to receive [^{225}Ac]-FPI-1434.
- Prospective and personalized treatment planning for targeted alpha therapy of IGF-1R expressing tumors is an important safety checkpoint to estimate risks to critical organs.
- Dosimetric results well within pre-specified limits in a single-dose regimen up to 40 kBq/kg.
- [^{225}Ac]-FPI-1434 demonstrated a manageable safety profile with no drug-related serious adverse events and/or dose limiting toxicity in administered activity up to 40 kBq/kg body-weight.
- Recruitment to multi-dose and cold antibody cohorts ongoing.