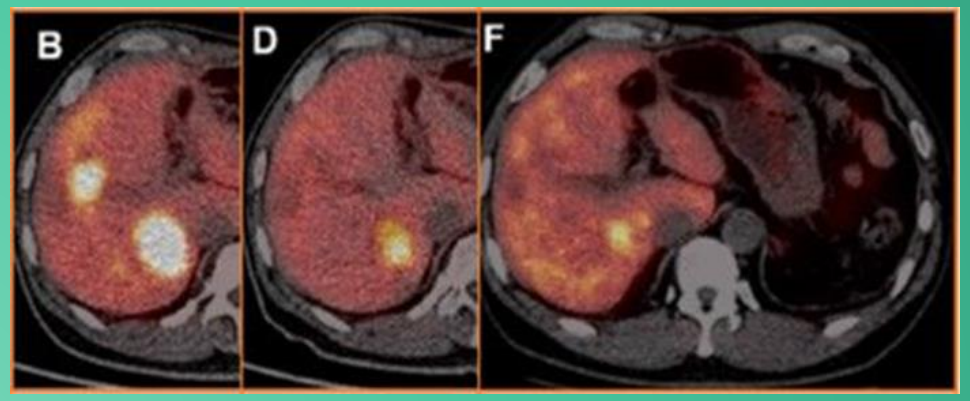
86% GEP-NET Disease Control in a 3-year Follow-up



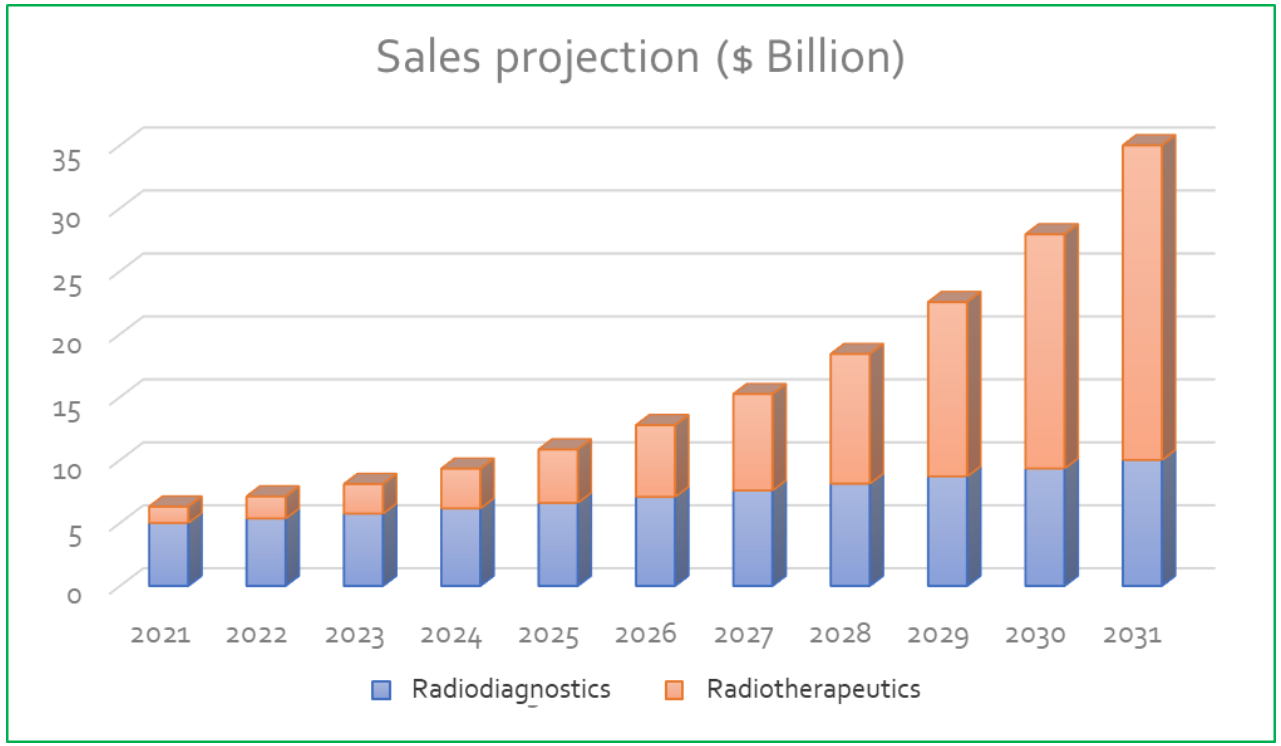
MOLECULAR TARGETING TECHNOLOGIES, INC.

NEXT GENERATION TARGETED RADIOTHERAPEUTICS

M · T · T · I
Molecular Targeting Technologies, Inc.
Advancing Precision Pharmaceuticals

Radiotherapeutics market will grow at 34% p.a. through 2033,

one of the fastest growing sectors in oncology



"Radiopharmaceutical therapeutics are already transforming cancer care…"

- Christopher Boerner, CEO, BMS, Dec 26, 2023

Recent Radiotheranostics Deals

Buyer	Target	Deal	Value ($Bn)	Date
AstraZeneca	Fusion	Acquisition	2.4	Mar-24
BMS	RayzeBio	Acquisition	4.1	Dec-23
Eli Lilly	POINT	Acquisition	1.4	Oct-23
Roche	Peptidream	Acquisition	1.0	Sep-23
RayzeBio	IPO	IPO	0.4	Sep-23
Bayer	Bicycle	Asset Purch.	1.7	May-23
Novartis	Bicycle	Asset Purch.	1.7	Mar-23
Lantheus	POINT	Asset Purch.	1.8	Nov-22

Source: MEDraysintell Nuclear Medicine Report 2022

EvaThera Platform - targeting unmet GBM & NSCLC needs

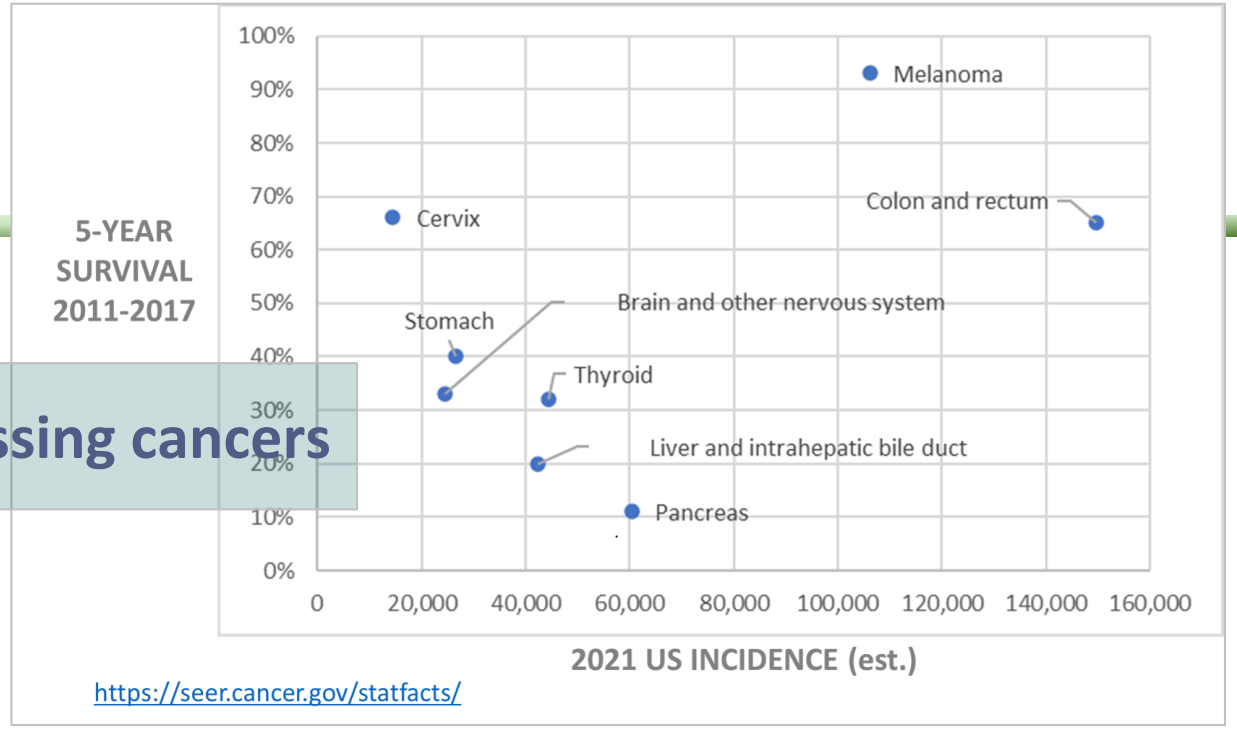
DRUG	TARGET RECEPTOR	INDICATIONS	DEVELOPMENT STAGE	MARKET POTENTIAL
EBTATE® **^{177}Lu-EB-DOTA-TATE**	**Somatostatin receptor type 2 (SSTR2)**	GEP-NET	Preclincal studies showed superiority over other SSTR2 targeting PRRTs 60+ pts treated. Proved safety and higher ORR than ^{177}Lu-DOTATATE	Best-in-class potential
		Iodine resistant & Hürthle cell thyroid cancer (HTC)	Planned Phase I/II	Large
		Nasopharyngeal cancer (NPC)	Planned Phase I/II	Large in SE Asia
		Small cell lung cancer	Preclinical proof of concept	Good PK/PD may enable SCLC efficacy
EBRGD™ **^{177}Lu-EB-DOTA-RGD**	**Integrin αvβ3**	NSCLC - first in class	Strong preclinical efficacy in NSCLC, GBM & CRC.	First, effective integrin αvβ3 targeting therapy with high potential in many cancers
		GBM	Pilot GBM patient study showed robust, focal target engagement	
		Colorectal cancer - first in class		

Broader EvaThera Opportunities

Multiple cancers express therapeutic targets:

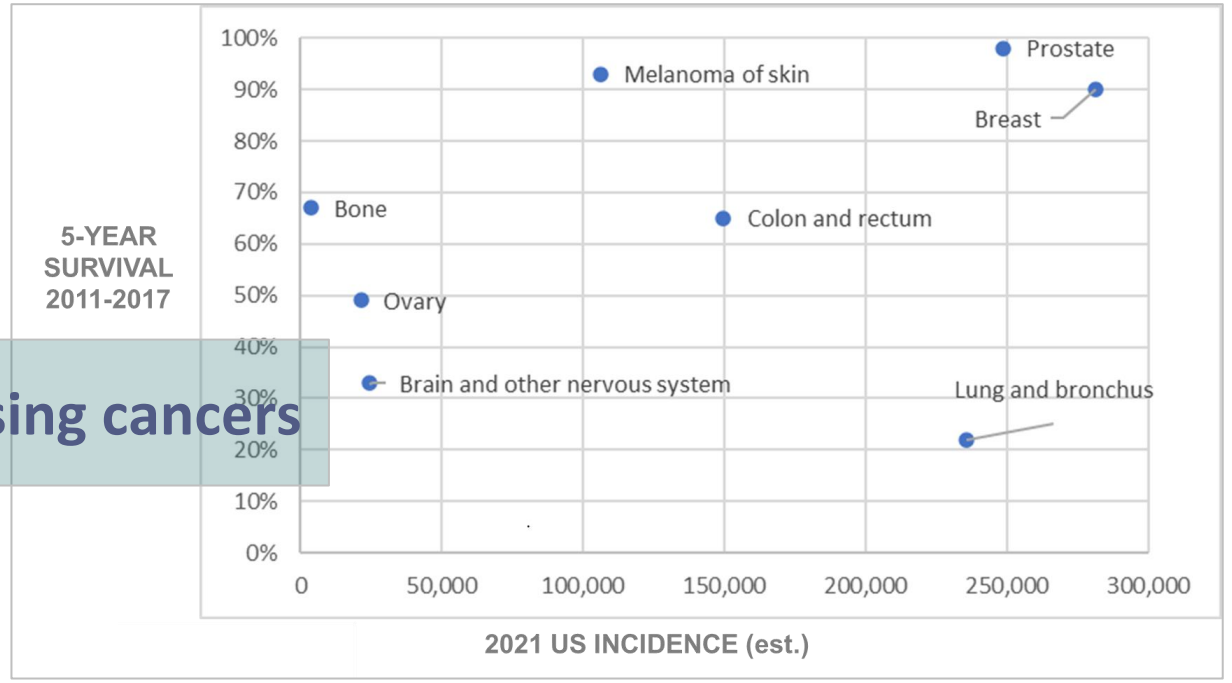
- SSTR2: ~ 500,000 US patients p.a.
- integrin $\alpha_v\beta_3$: ~ 1 million US patients p.a.

SSTR2 expressing cancers



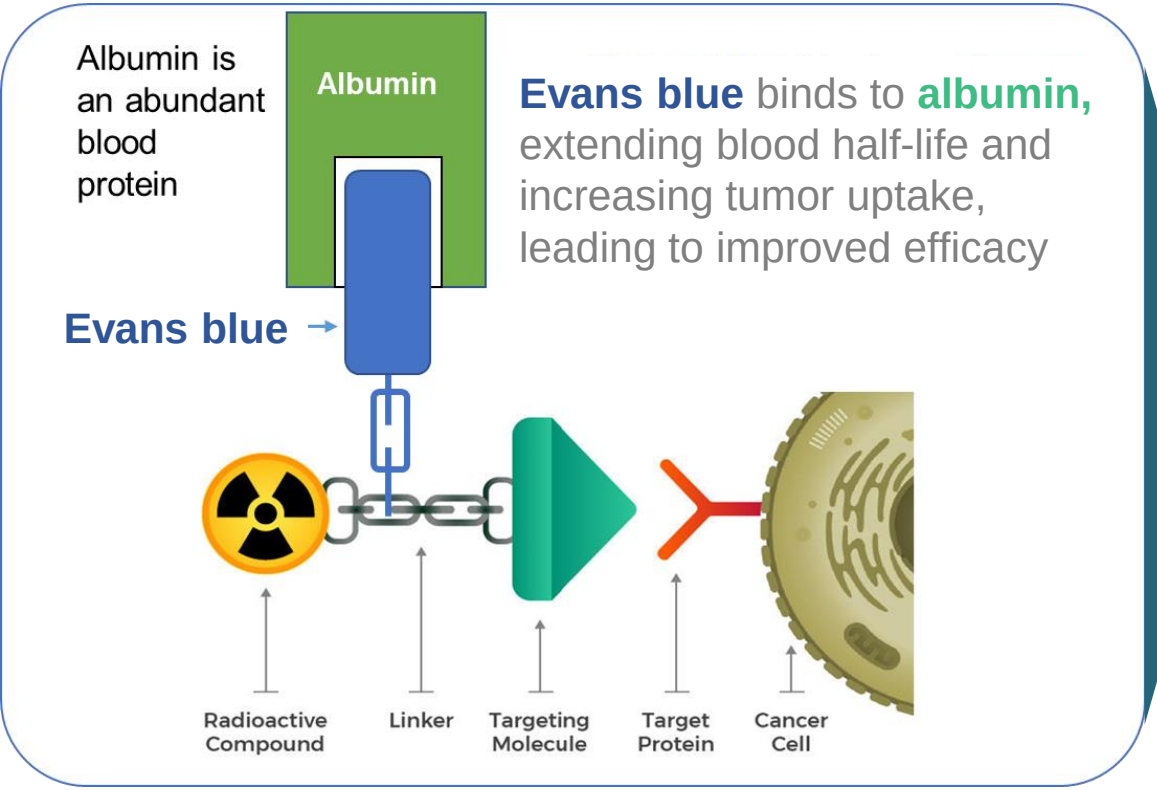
https://seer.cancer.gov/statfacts/

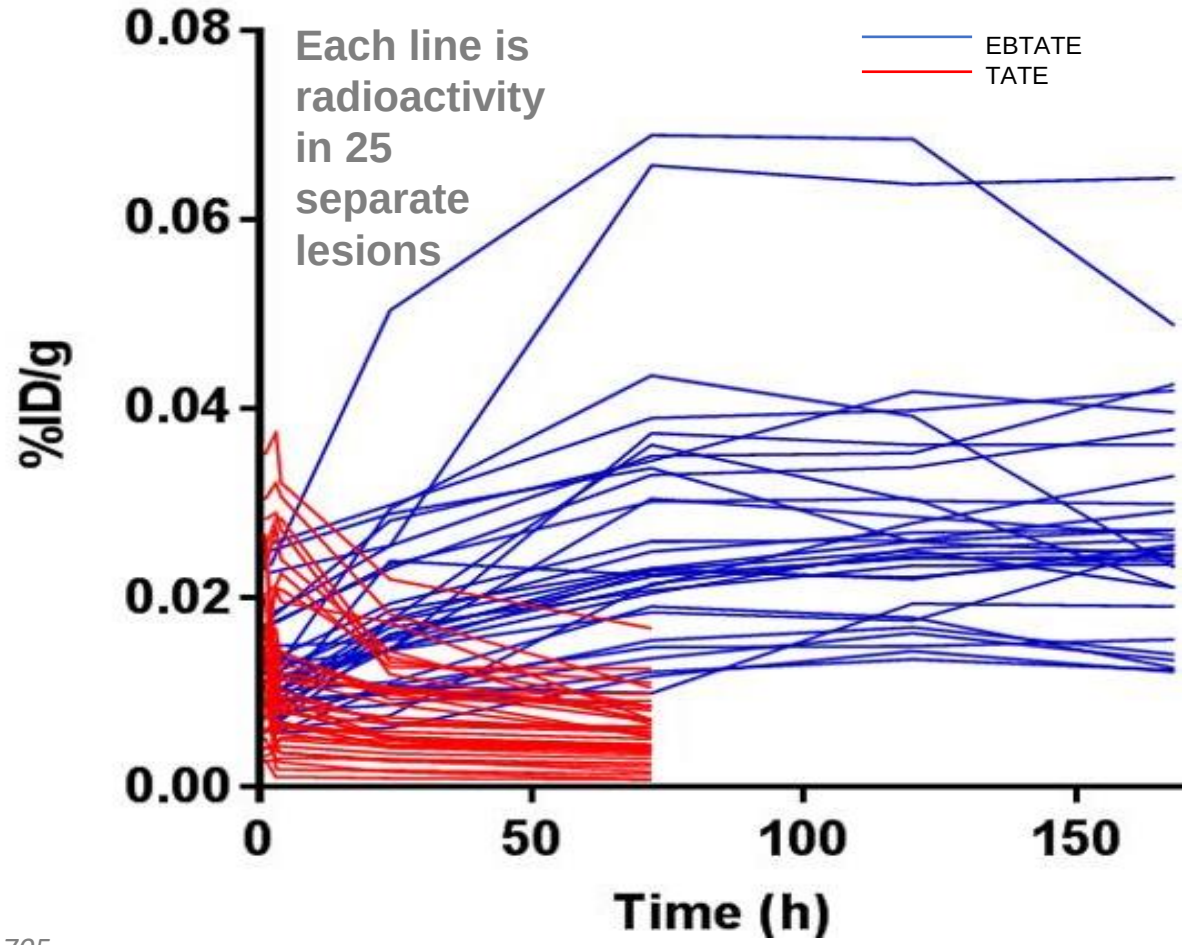
$\alpha_v\beta_3$ expressing cancers



EvaThera platform improves PK/PD vs. other PRRTs

EBTATE sustained tumor absorption in NET patients





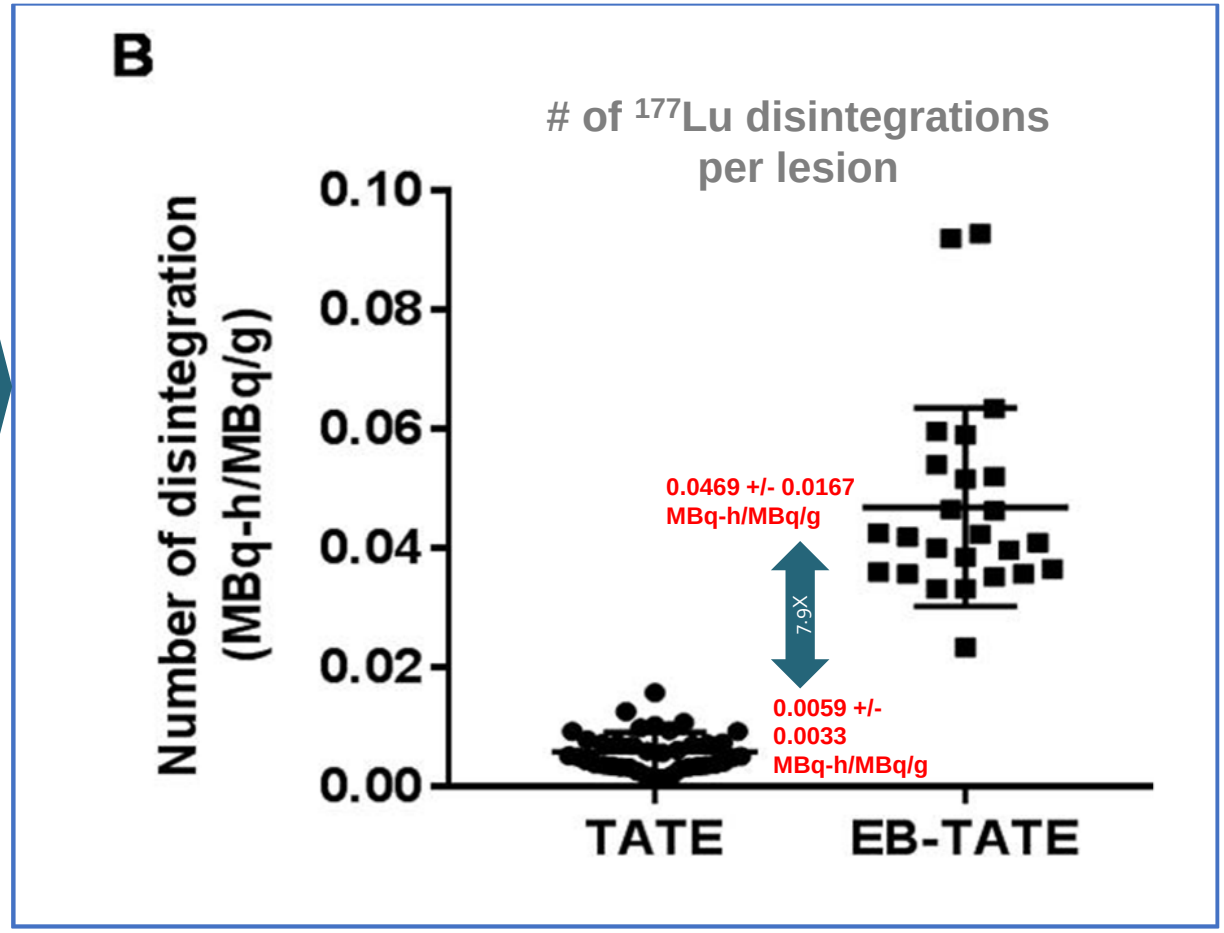
Zhang et al. J Nucl Med 2018; 59: 1699-1705

EvaThera platform has unique advantages

Increased circulation half-life improves tumor uptake and retention

TRT Type	Tumor permeability	Half-life	Manufacturing
Antibody conjugated radiotherapy	+	+++	+
Peptide receptor radionuclide therapy	+++	+	+++
EvaThera	+++	+++	+++

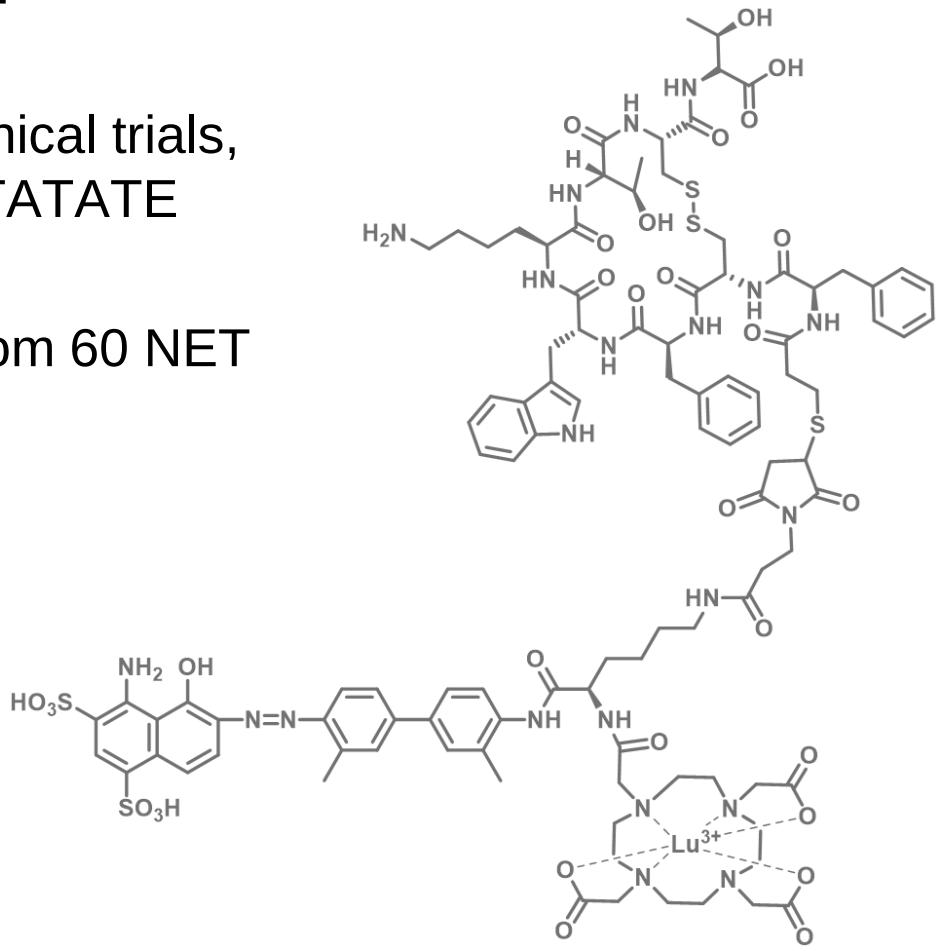
EBTATE shows a 7.9-fold tumor radiation count increase vs. ^{177}Lu-DOTATATE



Zhang et al. J Nucl Med 2018; 59: 1699-1705

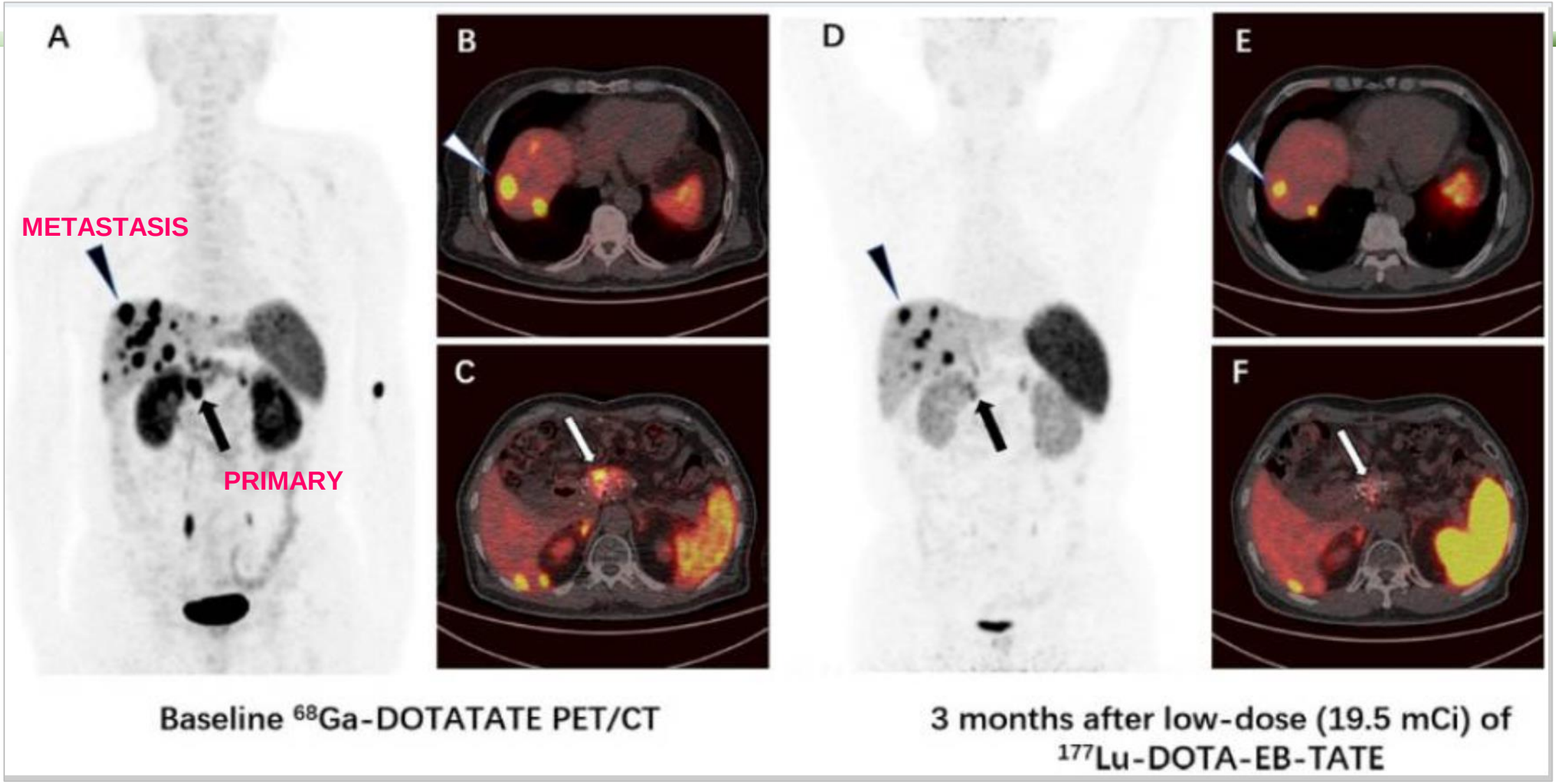
EBTATE: the first and only long-acting PRRT targeting SSTR2 NETs

- **Improved PK/PD**: Evans Blue-albumin binding motif results in a prolonged half-life and **enhances tumor tissue absorption**
- **Superior anti-tumor efficacy**: In preclinical models and clinical trials, EBTATE showed superior anti-tumor efficacy vs. ^{177}Lu-DOTATATE
- **Clinical data support safety and efficacy**: Clinical data from 60 NET patients shows:
  - 86% disease control after 3 years
  - Good safety
  - Amino acid nephroprotection may not be necessary
- **MTTI IP** includes ^{225}Ac and other radionuclides to 2037



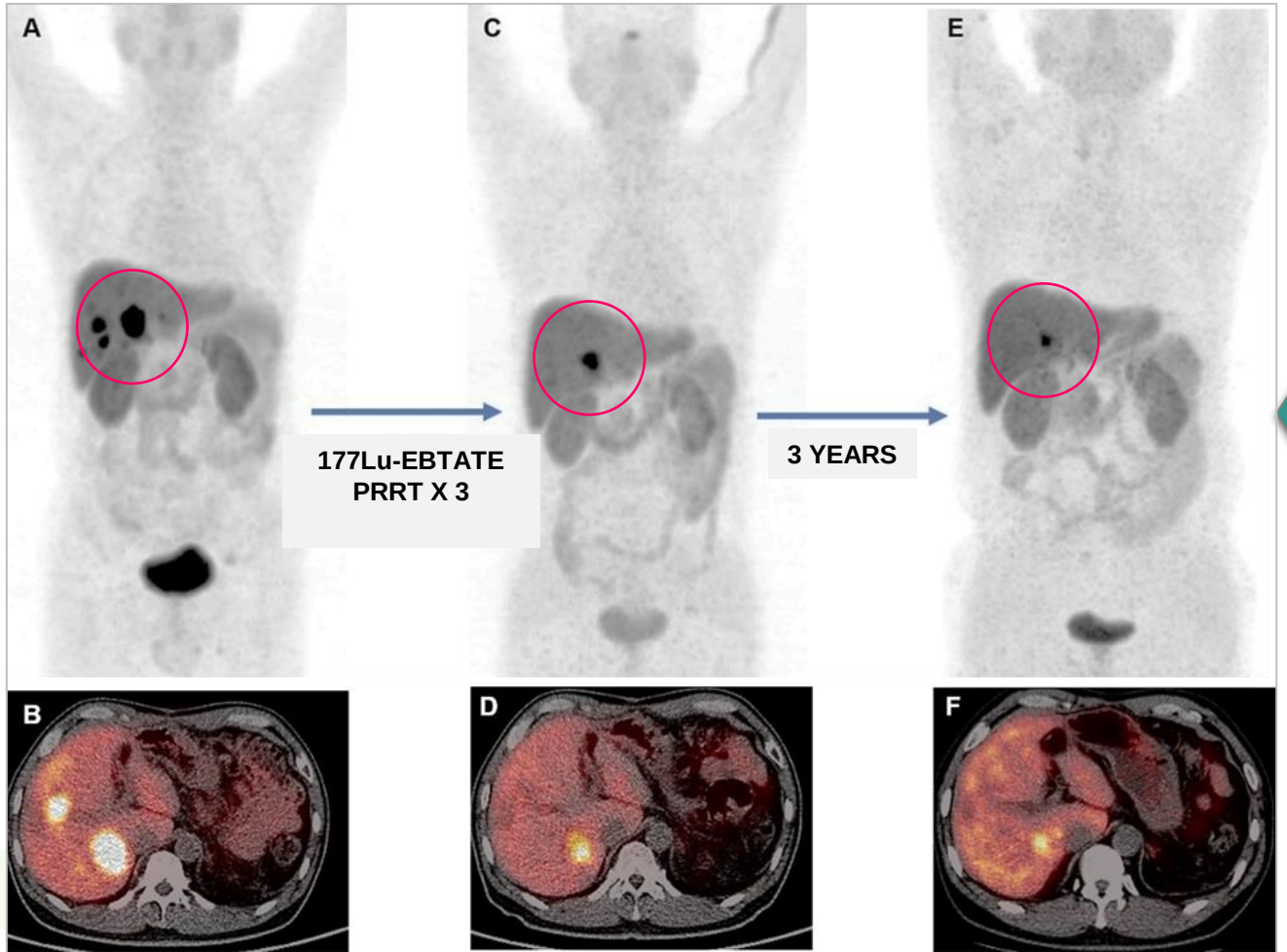
Clinical Outcomes

A single low dose (20 mCi) of EBTATE reduces NET tumor size



Long-Term Efficacy

EBTATE (3 cycles) achieved favorable 3-year follow-up results in 29 NET patients



^{68}Ga-DOTATATE PET/CT diagnostic tracking at 3-year follow-up

Jiang et al. Theranostics 2022; 12(5): 6437-6445

EBTATE Long-Term Efficacy in 29 Patients

^{68}Ga-DOTATATE PET/CT response (EORTC criteria)			
Efficacy(%)	**Group A 1.17 GBq n=12**	**Group B 1.89 GBq n=6**	**Group C 3.97 GBq n=14**
Complete Response	0	3	0
Partial Response	50	50	42.9
StableDisease	16.7	33.3	28.6
Progressive Disease	33.3	16.7	28.6
Disease Response Rate	50	50	42.9
Disease Control Rate	66.7	83.3	71.5

Patients seemed to tolerate ^{177}Lu-DOTA-EB-TATE well, even up to 3.97 GBq/cycle. The overall disease control rate, as well as the percentage decrease in tumor SUVmax, were highest with a 1.89 GBq dose, followed by 3.97 and 1.17 GBq.

Liu et al. J Nucl Med 2021; 62(3): 386-392

EBTATE was safe and well-tolerated in NET patients

Low, long-term toxicity (CTCAE 5.0) in 29 patients

Toxicity	CTC-grade	Baseline	1st cycle		2nd cycle		3rd cycle		Avg.Grade 3&4 AE (%)
			2 wks	4 wks	2 wks	4 wks	2 wks	4 wks	
Leukopenia	Grade-1 & 2	4	6	5	6	10	6	4	0%
	Grade-3 & 4	0	0	0	0	0	0	0	
Thrombocytopenia	Grade-1 & 2	0	3	3	2	4	2	3	13%
	Grade-3 & 4	0	0	2	1	1	1	0	
Anemia	Grade-1 & 2	3	6	4	5	5	4	4	3%
	Grade-3 & 4	1	0	1	0	0	0	0	
Nephrotoxicity	Grade-1 & 2	7	1	2	1	1	1	0	0%
	Grade-3 & 4	0	0	0	0	0	0	0	
Hepatotoxicity	Grade-1 & 2	5	1	3	2	1	1	0	3%
	Grade-3 & 4	0	0	1	0	0	0	0	

Jiang et al. Theranostics 2022; 12(5): 6437-6445

EBTATE benefits vs. ^{177}Lu-DOTATATE

BENEFITS	^{177}Lu-EBTATE	^{177}Lu-DOTATATE
Fewer doses	3 x 100 mCi cycles - shorter treatment duration, better compliance	4 x 200 mCi cycles
Low radiation exposure	Cumulative 11.1 GBq	Cumulative 29.6 GBq
IP	Composition of matter to 2037	Formulation
Patient burden	May not require amino acid treatment	Mandated 4-hour pretreatment (>50% of patients with nausea/vomiting)

EBTATE Overview

- 3-year follow-up showed stable disease with progression-free survival of 43 months after three cycles of ^{177}Lu-EBTATE (N=30 patients)
- Multiple cycles of escalating doses of EBTATE (N=32 patients) seem to be well tolerated and were effective in tumor control
- EBTATE should target Hürthle cell thyroid and nasopharyngeal cancers

Preclinical Results

^{225}Ac, ^{177}Lu, ^{90}Y

Better preclinical tumor uptake and treatment response

Preclinical - xenograft tumor uptake	^{177}Lu-EBTATE	^{177}Lu-DOTATATE
Non-small cell lung cancer (NSCLC)	80% ID/gram	4% ID/gram
Pancreatic cancer AR42J	15.16 SUV	3.53 SUV
Follicular thyroid (Hurthle cell)	4.8 SUV	0.28 SUV
Preclinical - treatment response		
Non-small cell lung cancer (NSCLC)	100% at 18.5 MBq	0% at 18.5 MBq
Pancreatic cancer - AR42J	Protects mice up to 24 days	Mice euthanized in 10 days due to tumor size
Pancreatic cancer AR42J with ^{90}Y	100% survival at 90 days with 3.7 & 7.4 MBq	No survival at 35 days with 7.4 MBq

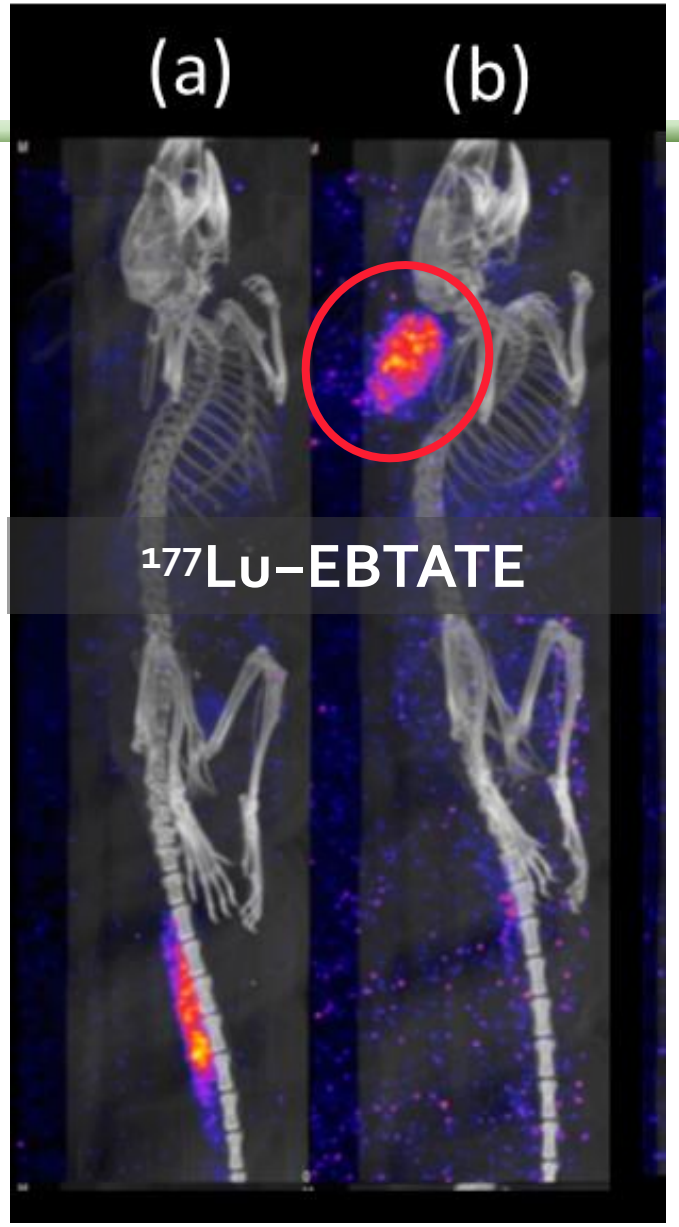
^{177}Lu-EBTATE: Superior tumor uptake

EBTATE uptake

was significantly higher in a

murine NSCLC model (A427-7)

than ^{177}Lu–DOTATATE .

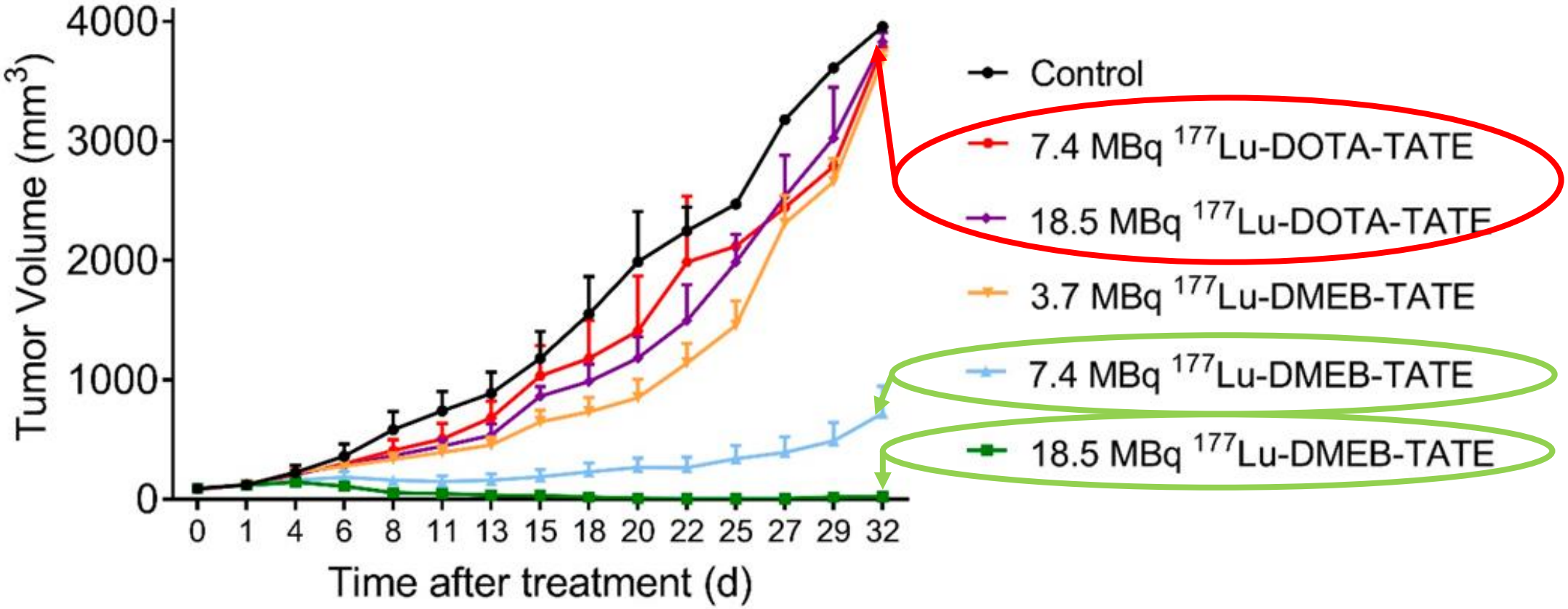


(a & b) at 1 and 24 h post injection

(e & f) at 1 and 24 h post injection

Bandara et al. Bioconjugate Chem 2018; 29(7): 2448-2454

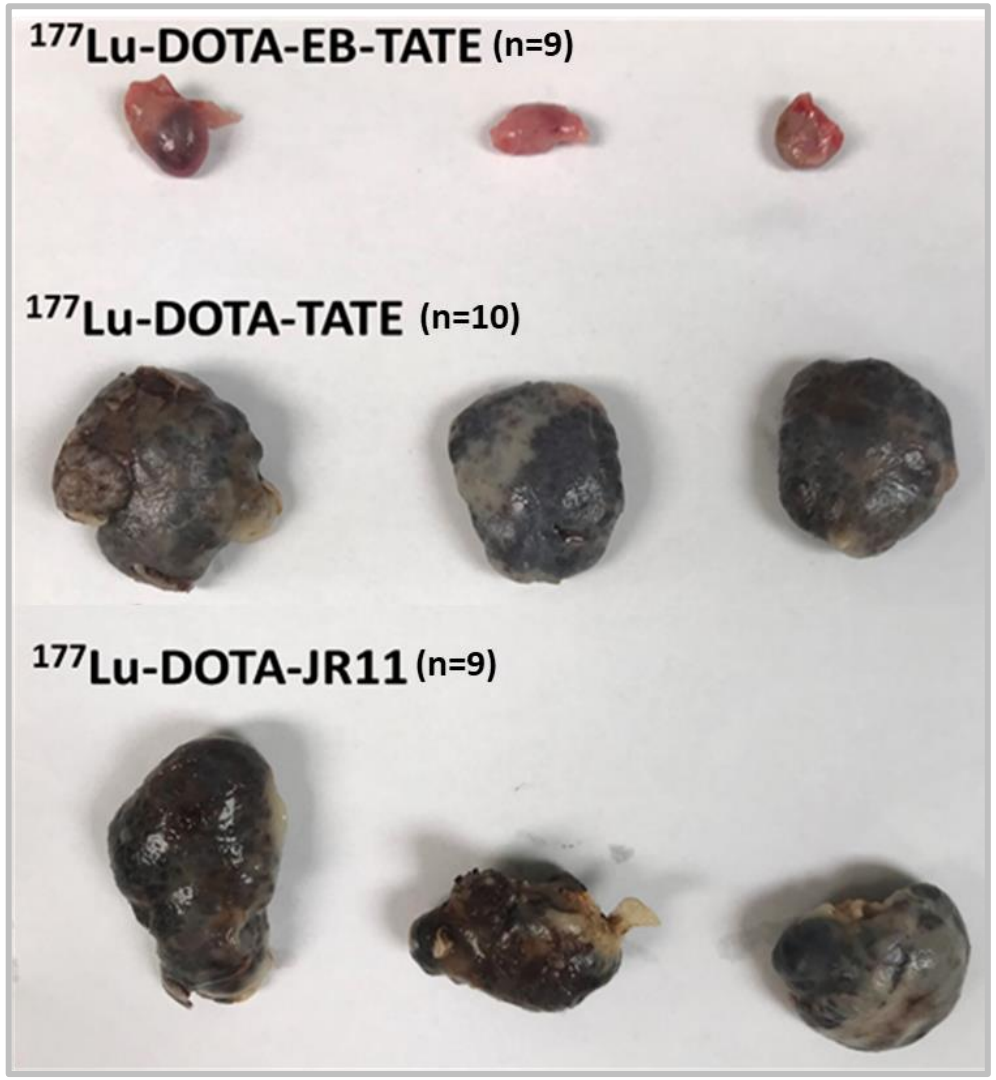
^{177}Lu-EBTATE shrinks NSCLC tumors

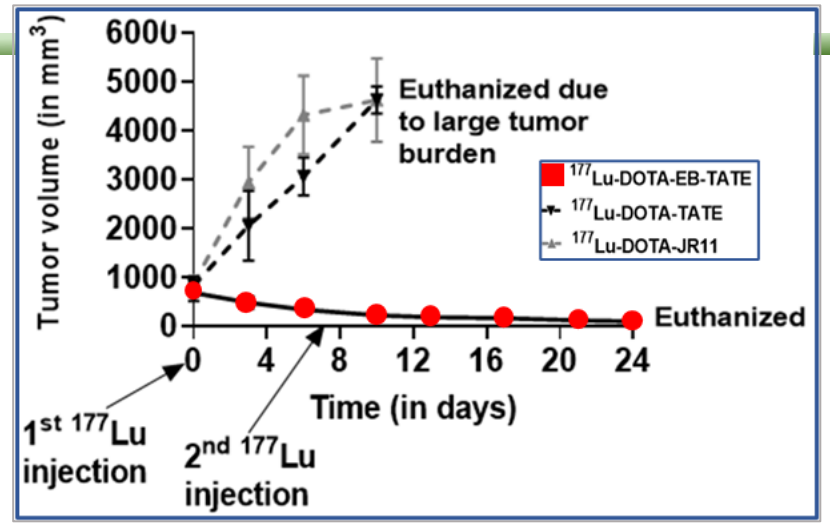


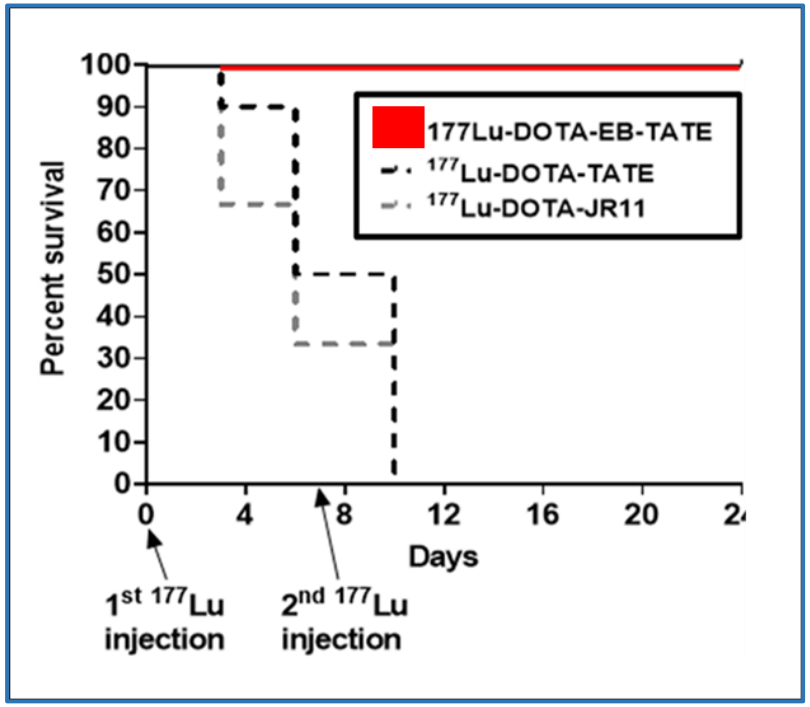
Bandara et al. Bioconjugate Chem 2018; 29(7): 2448-2454

EBTATE vs. other SSTR2 analogs against pancreatic cancer

Greater tumor volume reduction in the AR42J pancreatic cancer mouse model than other SSTR2 analogs :

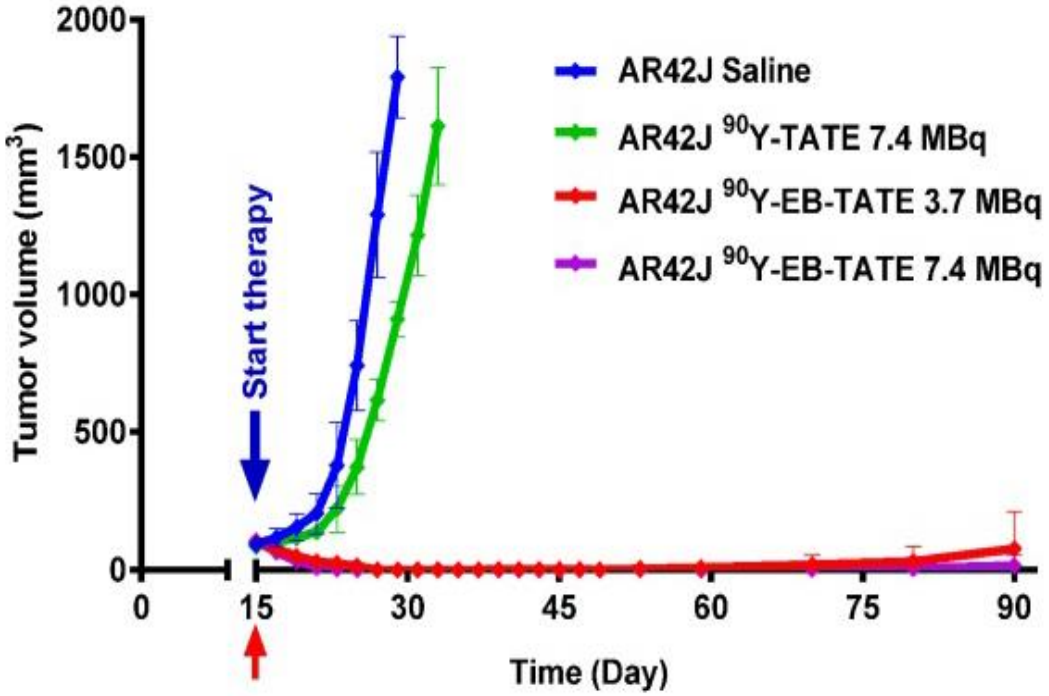


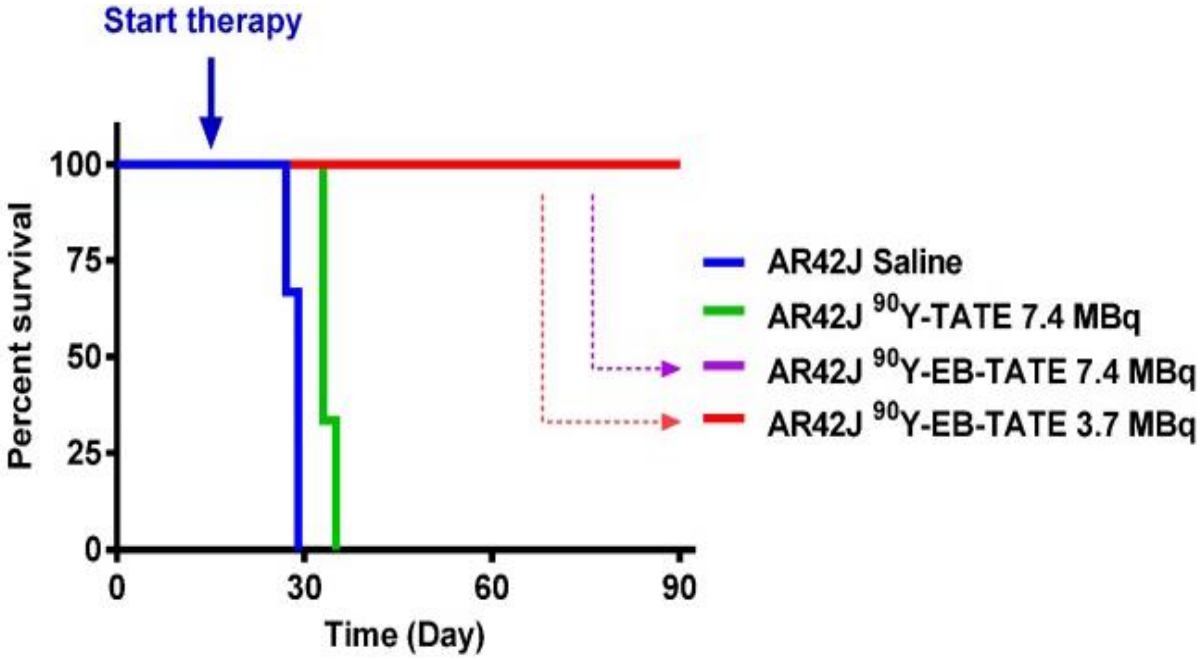




Thakur et al. Clin Cancer Res 2021; 27(5): 1399-1409

^{90}Y-EBTATE shows superior efficacy in pancreatic cancer

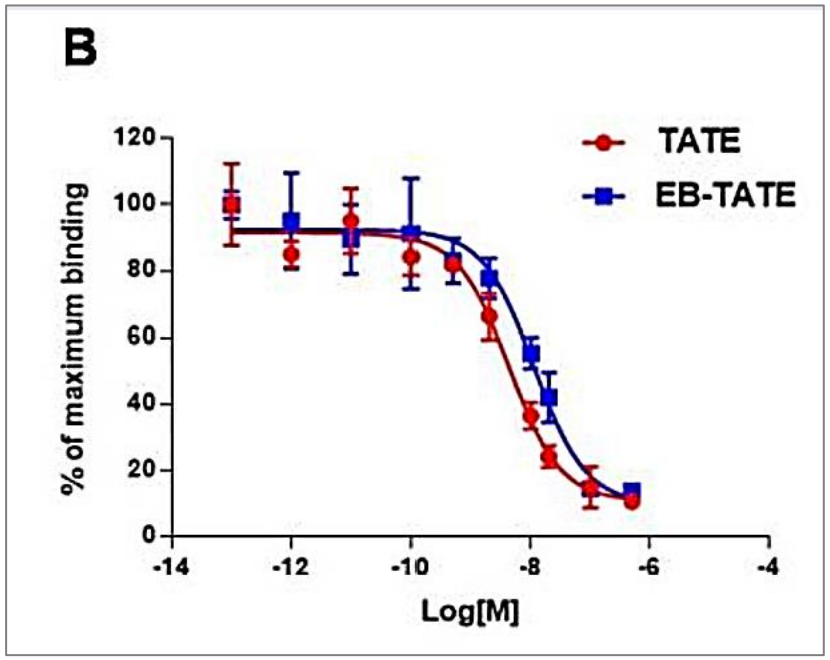




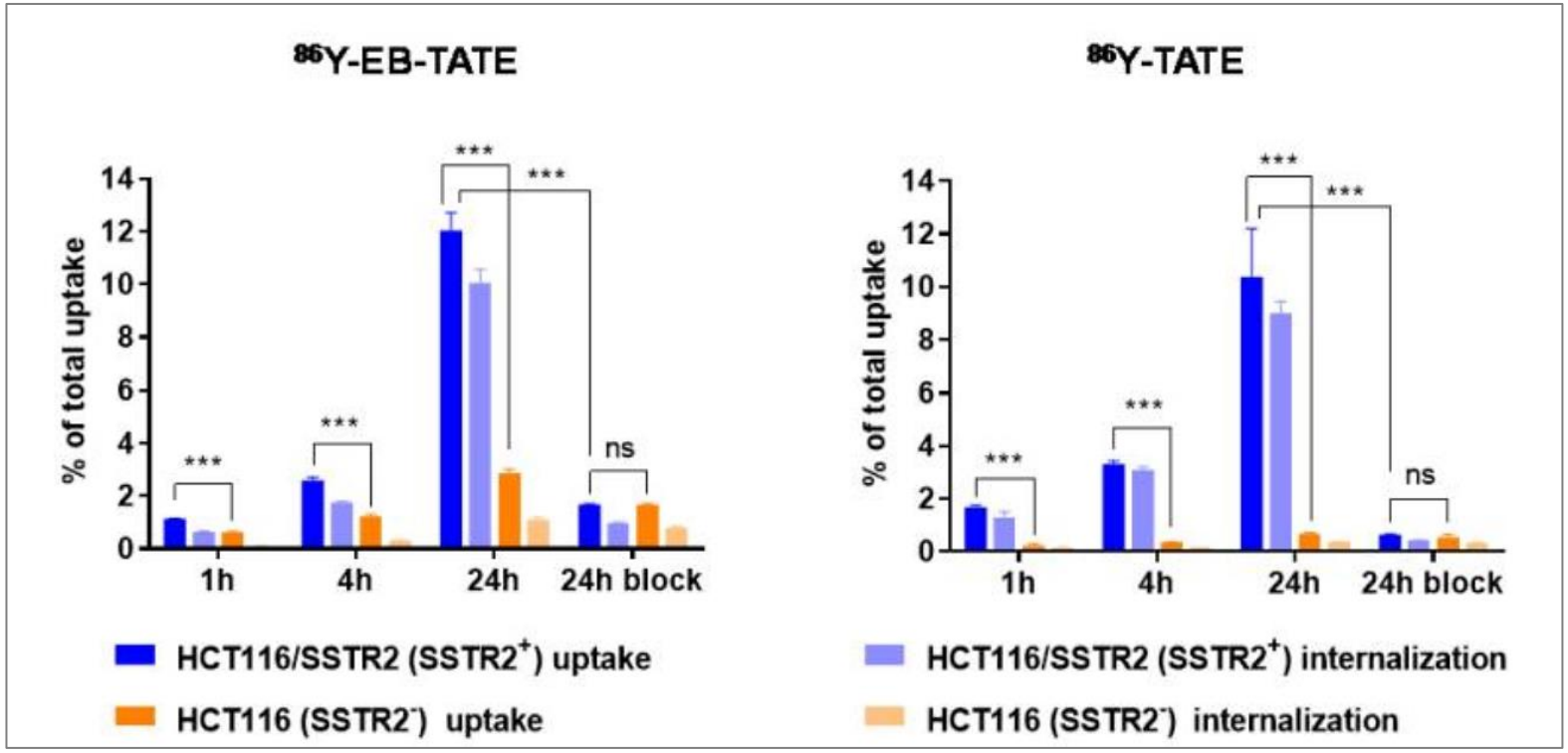
Tian et al. Theranostics 2018; 8:735-745

^{90}Y-EBTATE internalizes in colorectal cancer cells (HCT116)

Similar binding characteristics



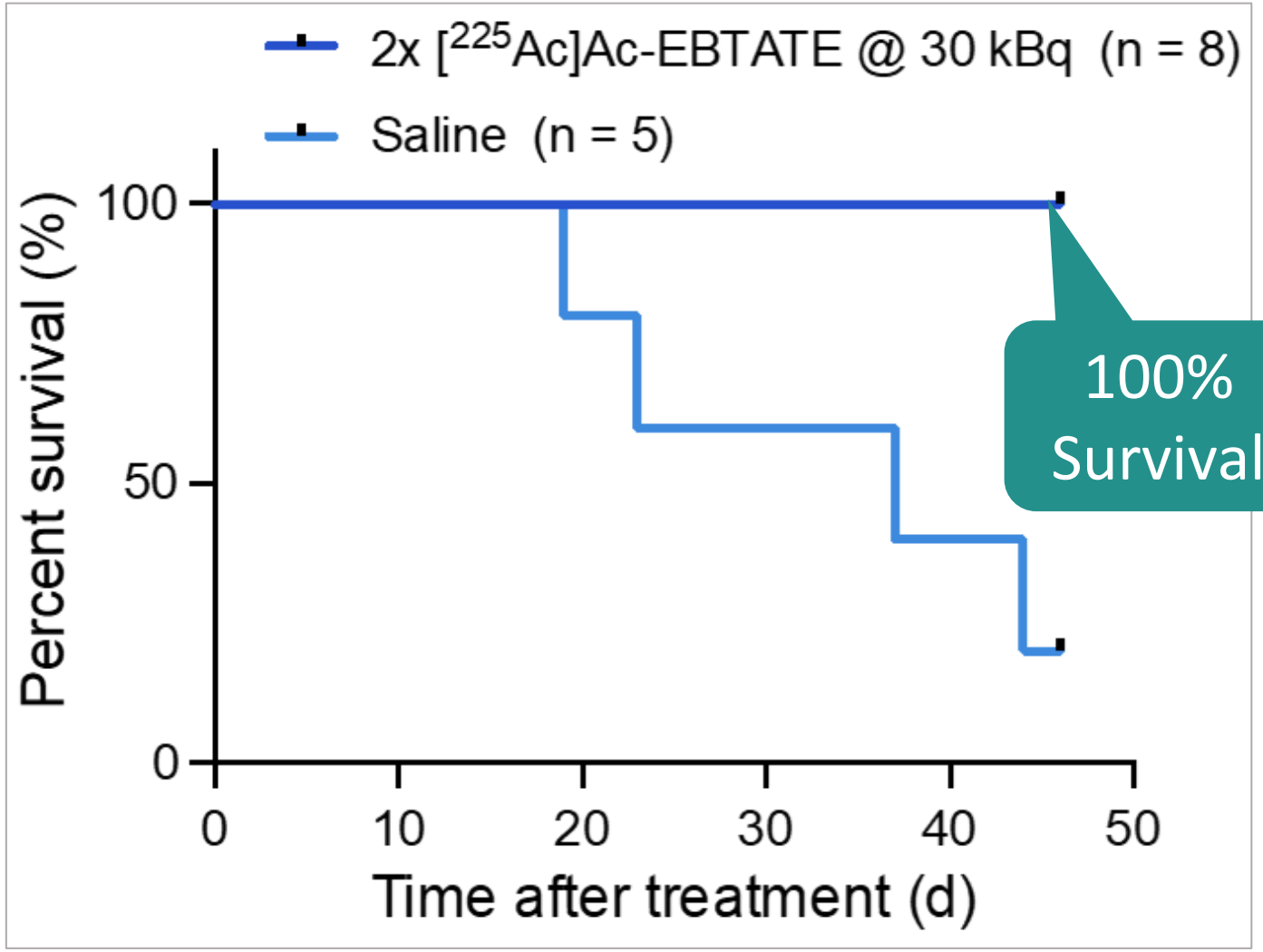
Strong uptake and internalization in SSTR2 positive cells



^{225}Ac-EBTATE

Strong antitumor effect in NCI-H524 xenograft (high SSTR2 expression SCLC)

2x 0.81 µCi (2x 30 kBq) administered 10 days apart for a total of 60 kBq (1.6 µCi) per mouse of [^{225}Ac]Ac-EBTATE



EBRGD

EBRGD™ - unlocking αvβ3 targeting in cancer treatment

Improved tumor uptake and retention

- Conjugation of EB to DOTA-RGD resulted in significant increase in tumor uptake and internalization & retention, as demonstrated with ^{177}Lu/^{90}Y/^{64}Cu.

Strong *In vivo* efficacy in NSCLC and CRC

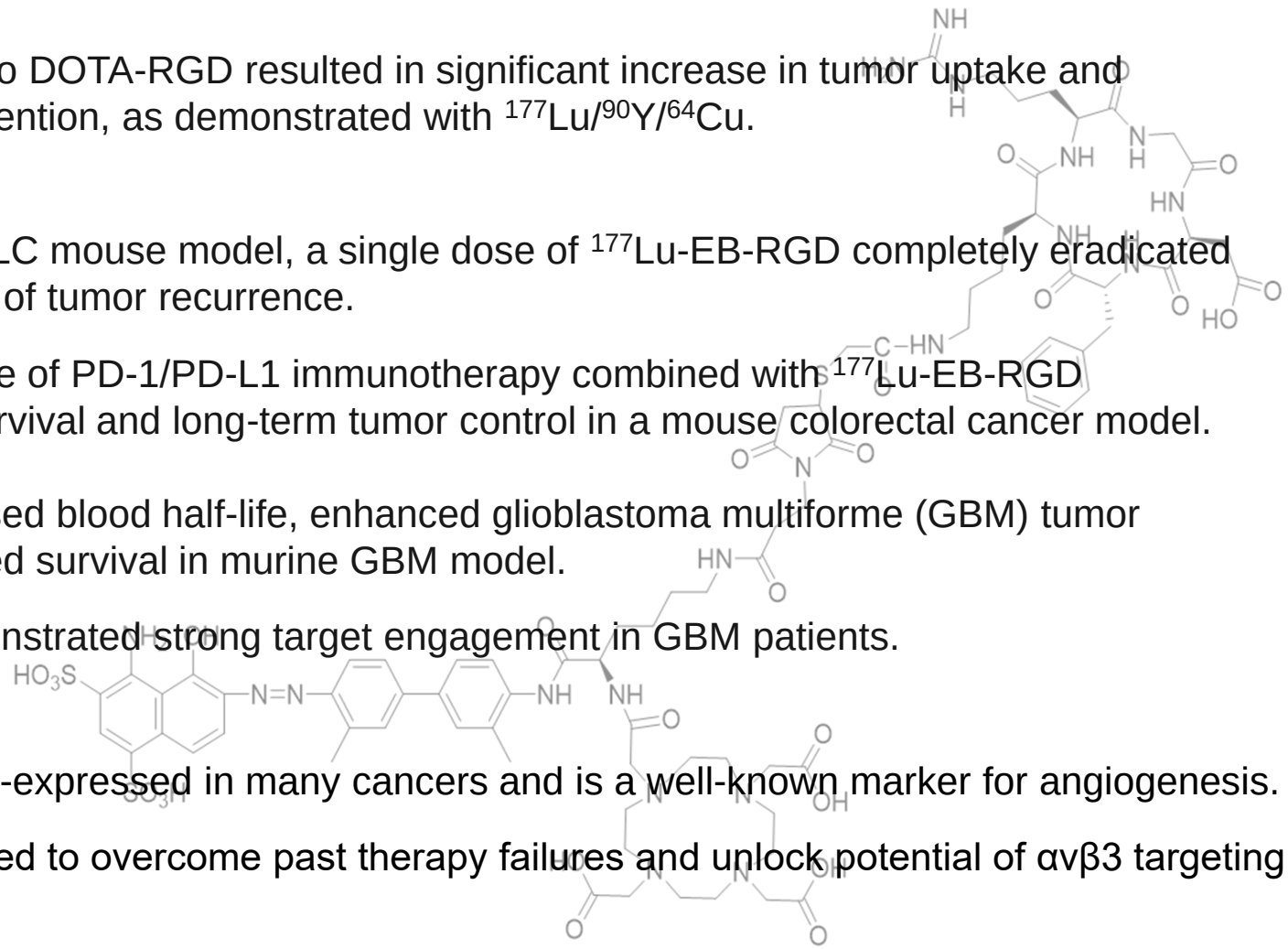
- In a PDX $\alpha_v\beta_3$ NSCLC mouse model, a single dose of ^{177}Lu-EB-RGD completely eradicated tumors with no sign of tumor recurrence.
- Concurrent blockade of PD-1/PD-L1 immunotherapy combined with ^{177}Lu-EB-RGD improved overall survival and long-term tumor control in a mouse colorectal cancer model.

High promise in GBM

- ^{90}Y-EB-RGD increased blood half-life, enhanced glioblastoma multiforme (GBM) tumor uptake, and improved survival in murine GBM model.
- ^{64}Cu-EB-RGD demonstrated strong target engagement in GBM patients.

Potential in a variety of cancers

- αvβ3 integrin is over-expressed in many cancers and is a well-known marker for angiogenesis.
- EBRGD™ is designed to overcome past therapy failures and unlock potential of αvβ3 targeting in cancer treatment.



Integrin αvβ3 integrin is an angiogenesis marker for several cancers

RGD tracer studies validated that integrin αvβ3 is over expressed in most cancers

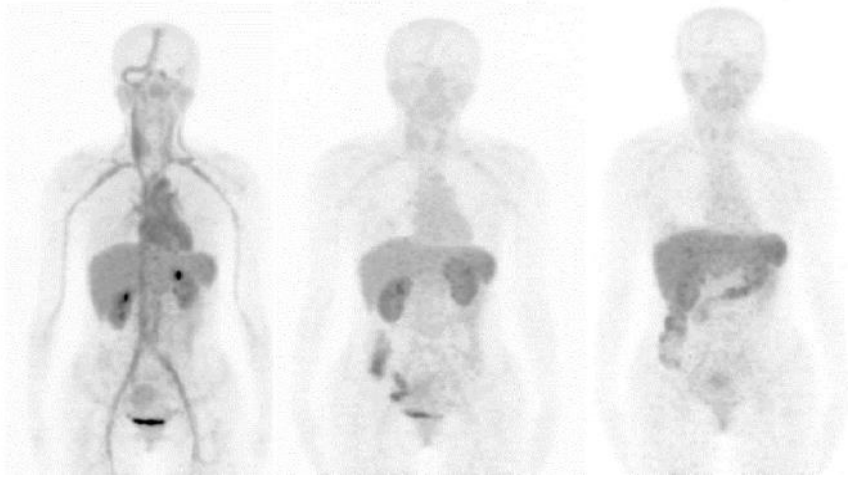
- GBM
- NSCLC
- Breast cancer
- Melanoma
- Sarcoma
- RCC
- SCCHN
- Glioma
- Musculoskeletal cancers
- Rectal Cancer
- Bone metastases

Theranostics 2016; 6(1): 78-92. doi: 10.7150/thno.13242

^{64}Cu-EBRGD – Data from GBM patients demonstrates robust target engagement

Healthy human volunteers

Three healthy volunteers (2 males and 1 female) underwent whole-body PET acquisitions at 1, 8 and 24 h time points after bolus injection of ^{64}Cu-EB-RGD (101.1±9.3, 92.5 -111 MBq).

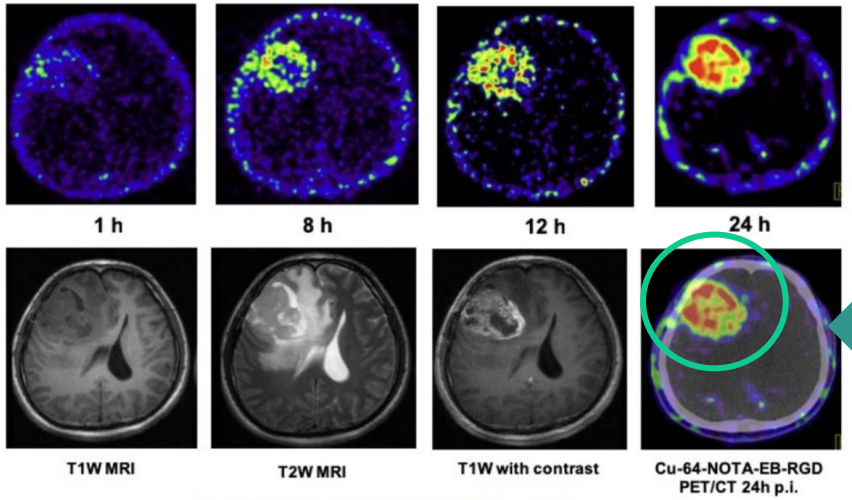


1h **8h** **24h**

Representative coronal PET image of healthy human volunteer injected with ^{64}Cu-EB-RGD at 1, 8, and 24 h p.i.

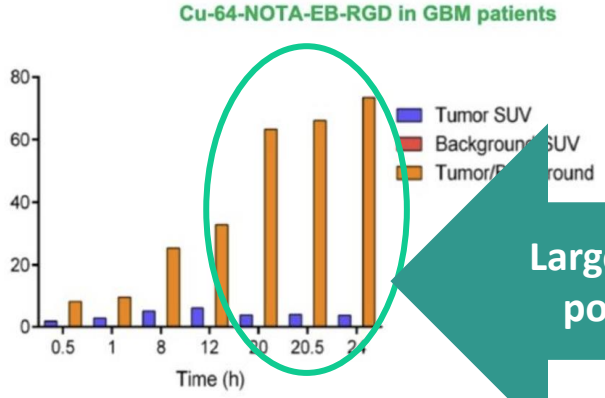
Well Tolerated, no adverse events

Glioblastoma Multiforme Patient

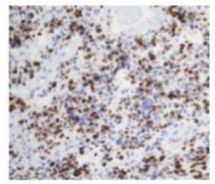


Axial PET slices of glioblastoma patient injected with ^{64}Cu-EB-RGD at different time points p.i.

Target engagement



Quantitative results of Cu-64-NOTA-EB-RGD over time



Immunohistology of integrin $\alpha_v\beta_3$ levels in the tumor

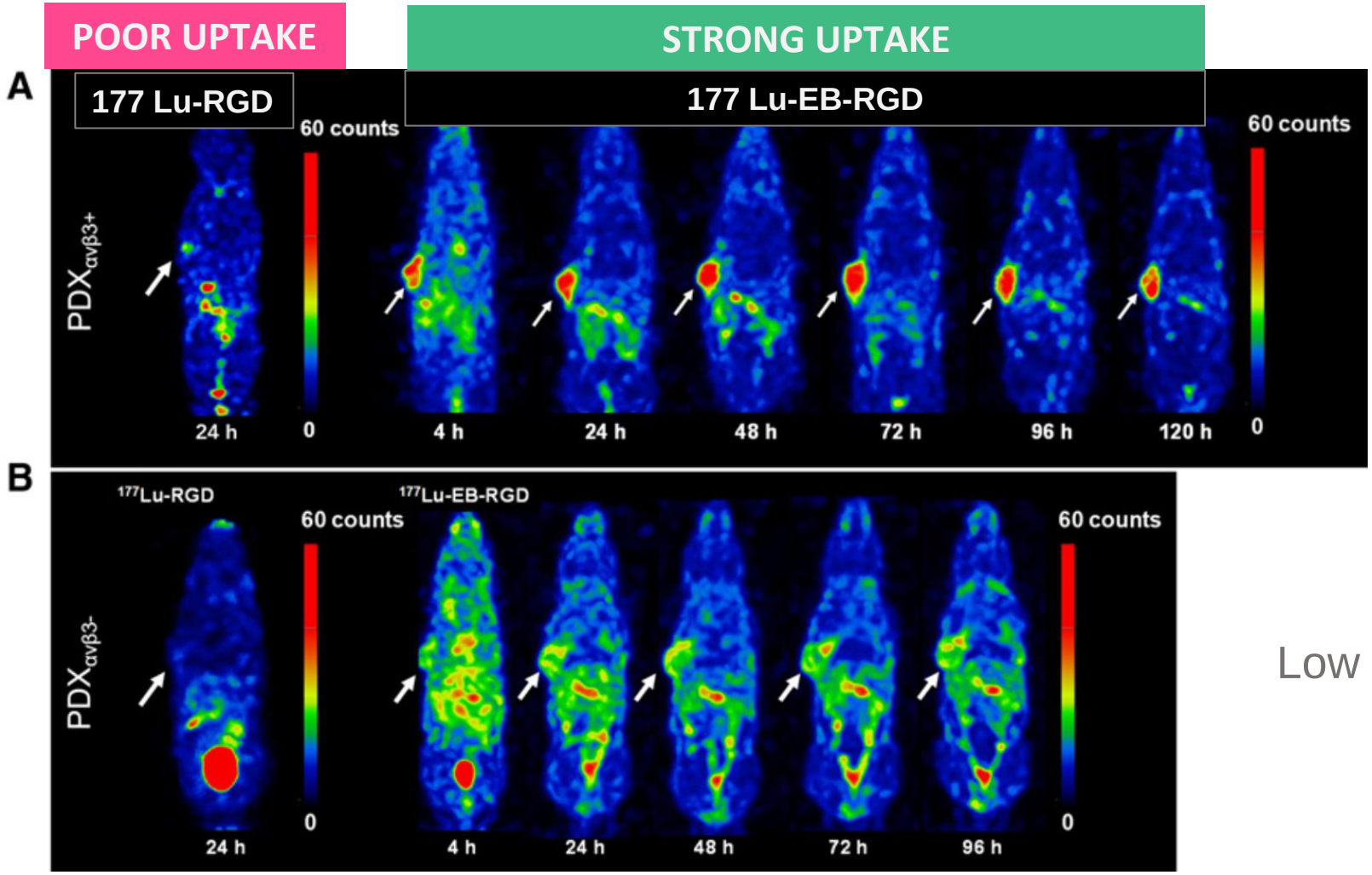
Immunohistology of integrin-$\alpha_v\beta_3$ levels

Large signal/background ratio shows potential for therapeutic efficacy

Preclinical Results
EBRGD

^{177}Lu-EBRGD vs ^{177}Lu-RGD SPECT imaging in $\alpha_v\beta_3$ positive PDX-NSCLC

EBRGD's longer residence time significantly improves uptake



High αvβ3 expressors

Low αvβ3 expressors

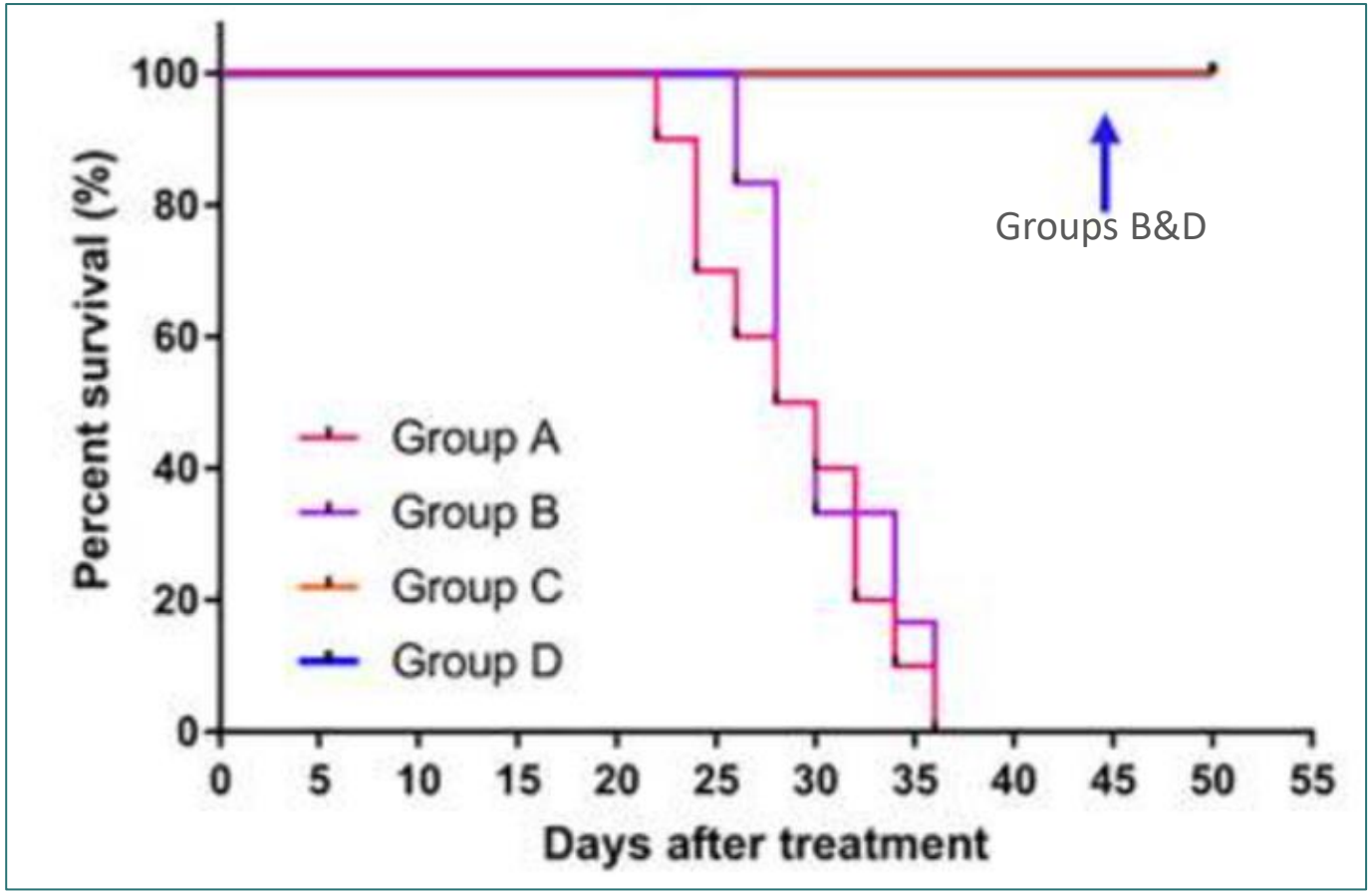
^{177}Lu-EBRGD improved survival of αvβ3+ PDX (NSCLC) mice

Day 0 Group A: Saline

Day 0 Group B: ^{177}Lu-EB-RGD (18.5 MBq)

Day 0 Group C: ^{177}Lu-RGD (29.6 MBq)

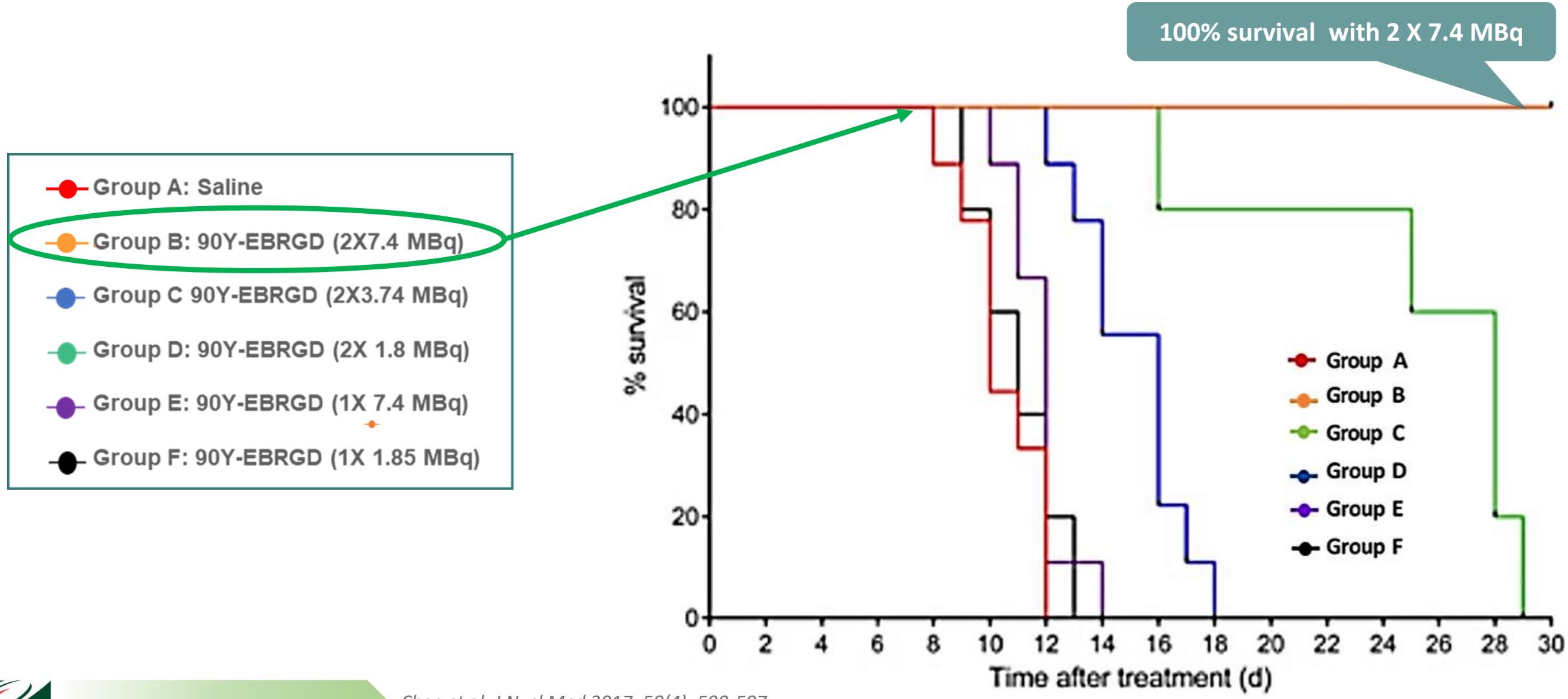
Day 0 Group D: ^{177}Lu-EB-RGD (29.6 MBq)



Zhao et al. Mol Cancer Ther 2020; 19(10): 2034-2043

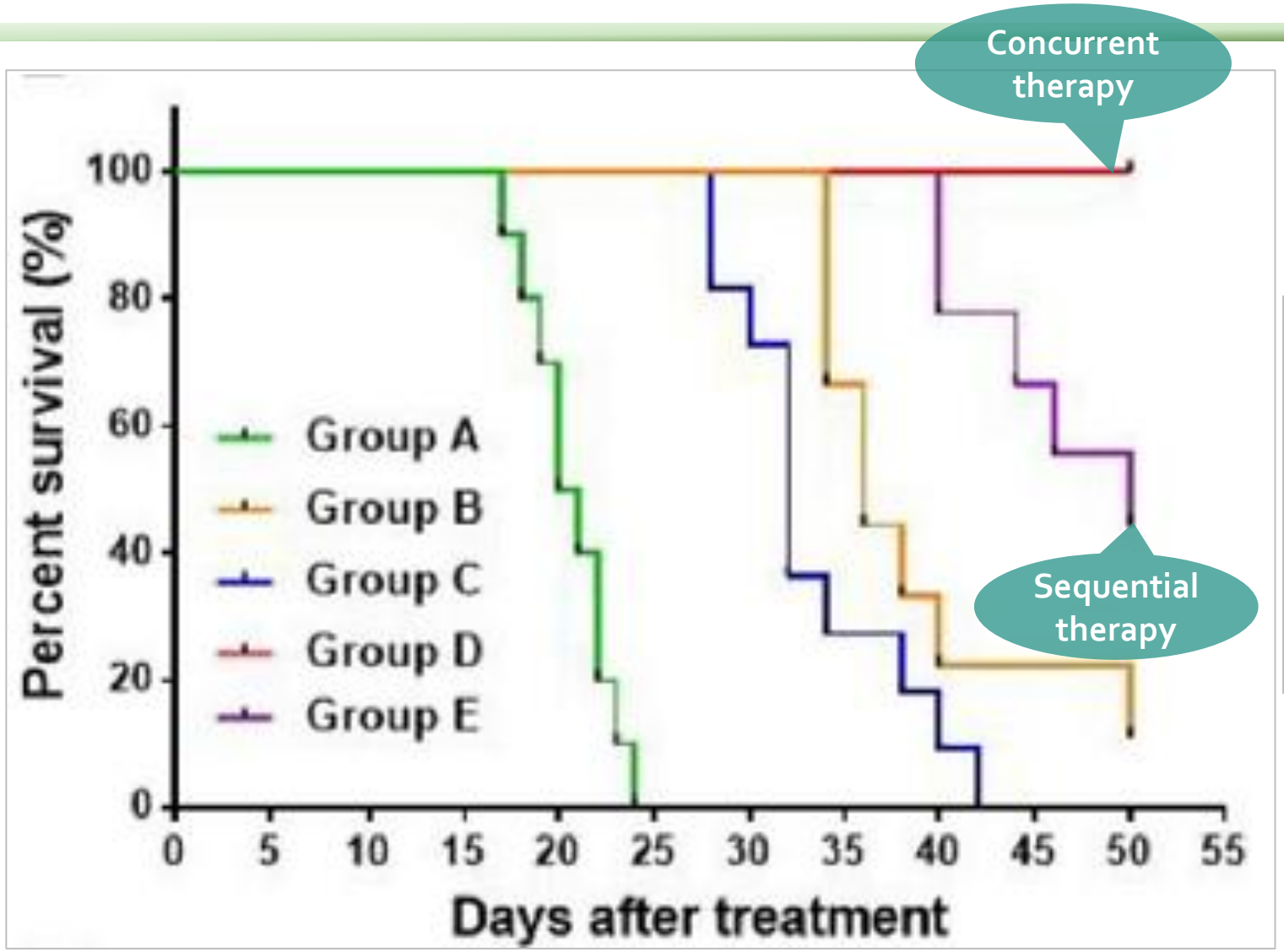
^{90}Y-EBRGD improved GBM survival: complete tumor eradication in mice

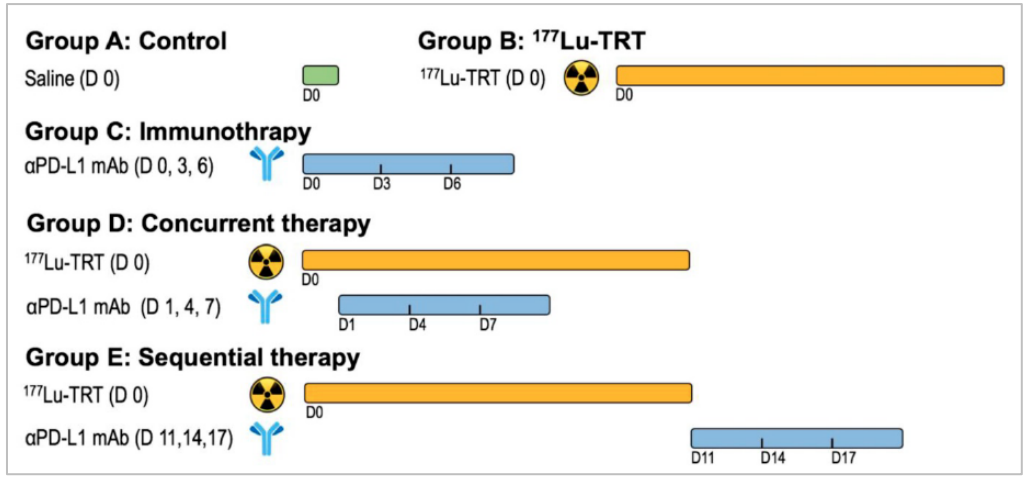
100% survival with 2 X 7.4 MBq



Chen et al. J Nucl Med 2017; 58(4): 590-597

EBRGD enhances immunotherapy efficacy in colorectal cancer

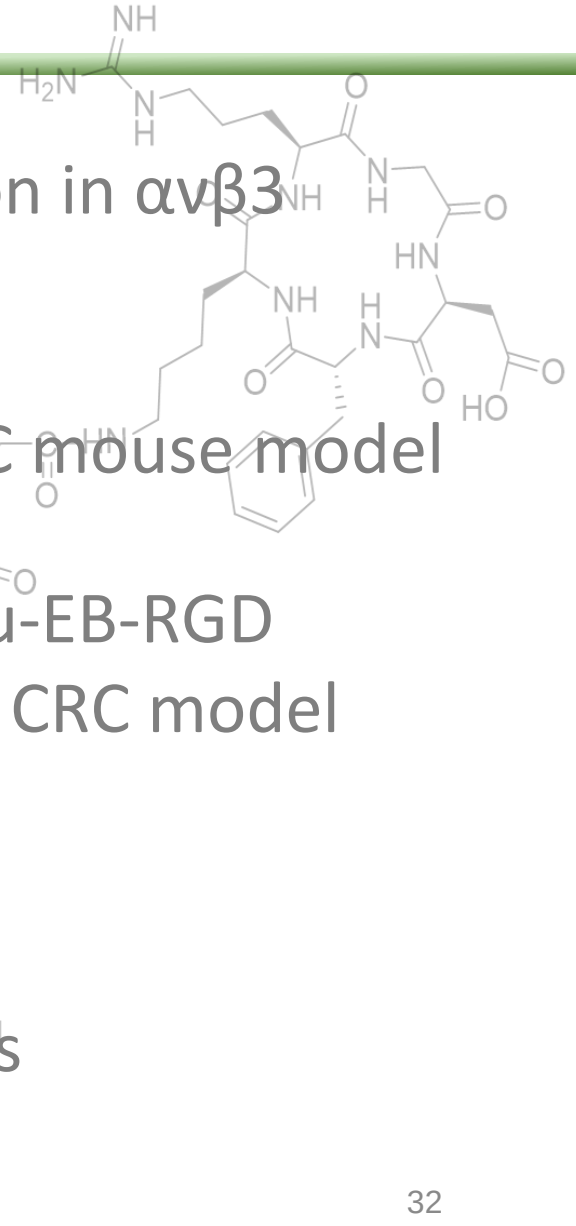




Chen et al. Theranostics 2019; 9(25): 7948-7960

^{177}Lu-EBRGD, a new, rationally designed theranostic

- Delivers strong tumor uptake, internalization & retention in αvβ3 expressing tumors
- A single dose completely eradicated tumors in an NSCLC mouse model
- Concurrent blockade of a checkpoint inhibitor with ^{177}Lu-EB-RGD improved overall survival and tumor control in a mouse CRC model
- ^{90}Y-EBRGD improved survival in murine GBM model
- ^{64}Cu-EBRGD demonstrated focal uptake in GBM patients



Contact Us

Chris Pak, PhD

President & CEO

Email: cpak@mtarget.com

www.mtarget.com

www.evathera.com