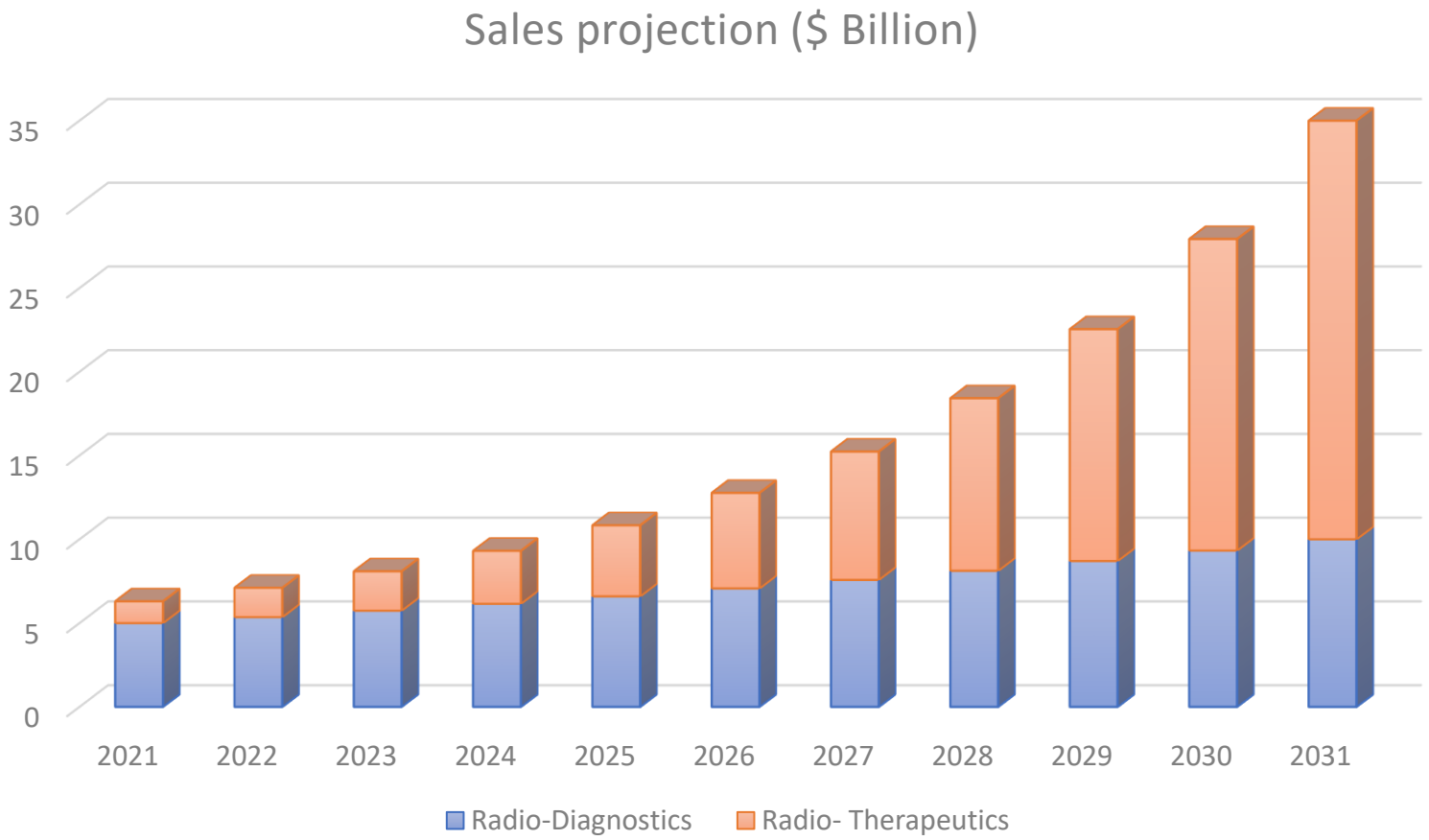
MOLECULAR TARGETING TECHNOLOGIES, INC.

NEXT GENERATION TARGETED RADIOTHERAPIES : SAVING LIVES

EvaThera Platform opportunities – targeting high unmet needs

Platform drug	Target receptor	Indications	Market potential	Radionuclides
EBTATE	Somatostatin receptor type 2 (SSTR2)	• GEP-NET • Hürthle cell thyroid cancer • Nasopharyngeal cancer • Small cell lung cancer	• Best-in-class potential in GEP-NET • Improved PK/PD may enable efficacy in SCLC, which has been challenging to treat by target therapy	• ^{177}Lu emits beta particle - lower energy, emission radius ~2 mm, well-tolerated • Suitable for first-line PRRT
EBRGD	αvβ3 integrin	• GBM – first in class • NSCLC – first in class • Colorectal cancer – first in class	• Potentially the first αvβ3 integrin targeting therapy to be effective • High potential in many cancers	• ^{225}Ac emits alpha particle – high energy, more effective in breaking double stranded DNA, emission radius 40-100 µm • Positive data emerging, but overall safety/efficacy profile not established

Radio-therapeutics market is expected to grow at 34% per year in the next ten years, one of the fastest growing sectors in oncology



	CAGR	2031 sales estimate
Radio-therapuetics	**34%**	**$25 B**
Radio-diagnostics	7%	$10 B
Oncology market	8%	$600+ B

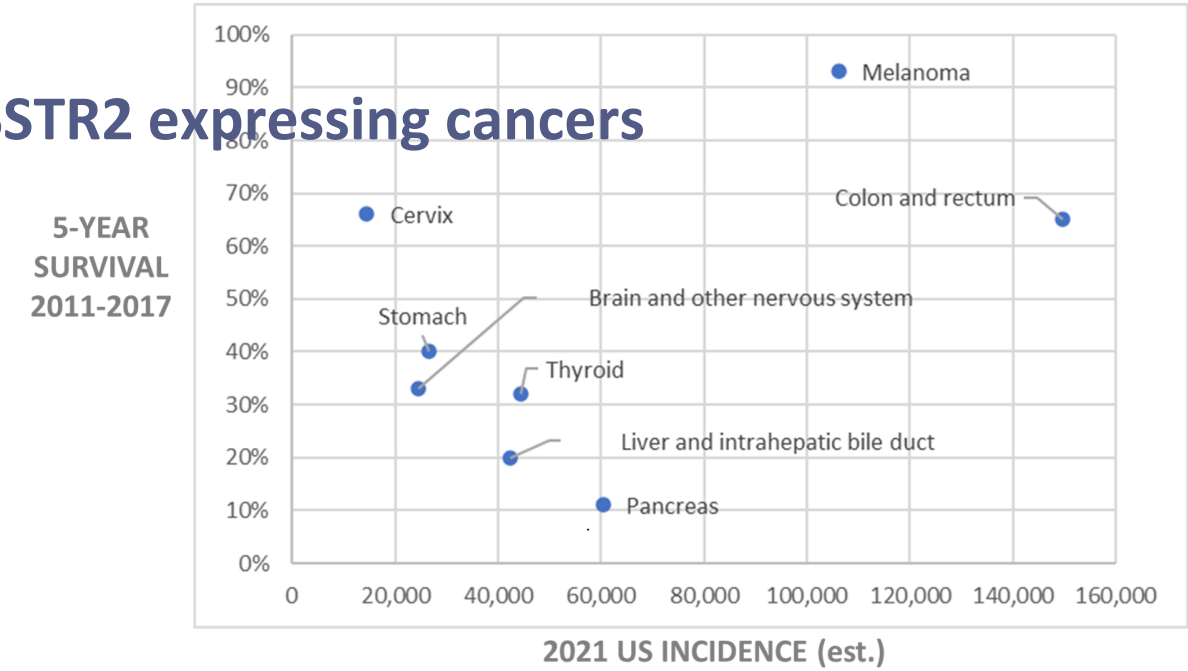
Source: MEDraysintell Nuclear Medicine Report 2022

Broader EvaThera Opportunity

Multiple cancers express therapeutic targets:

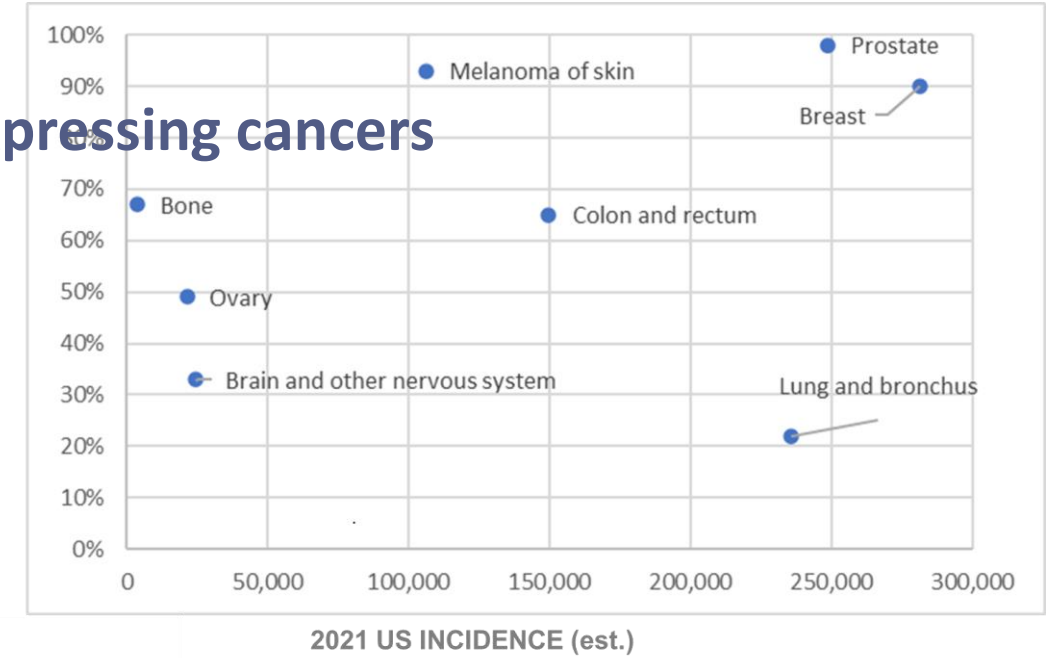
- SSTR2; ~ 500,000 US patients p.a.
- integrin $\alpha_v\beta_3$: ~ 1 million US patients p.a.

SSTR2 expressing cancers



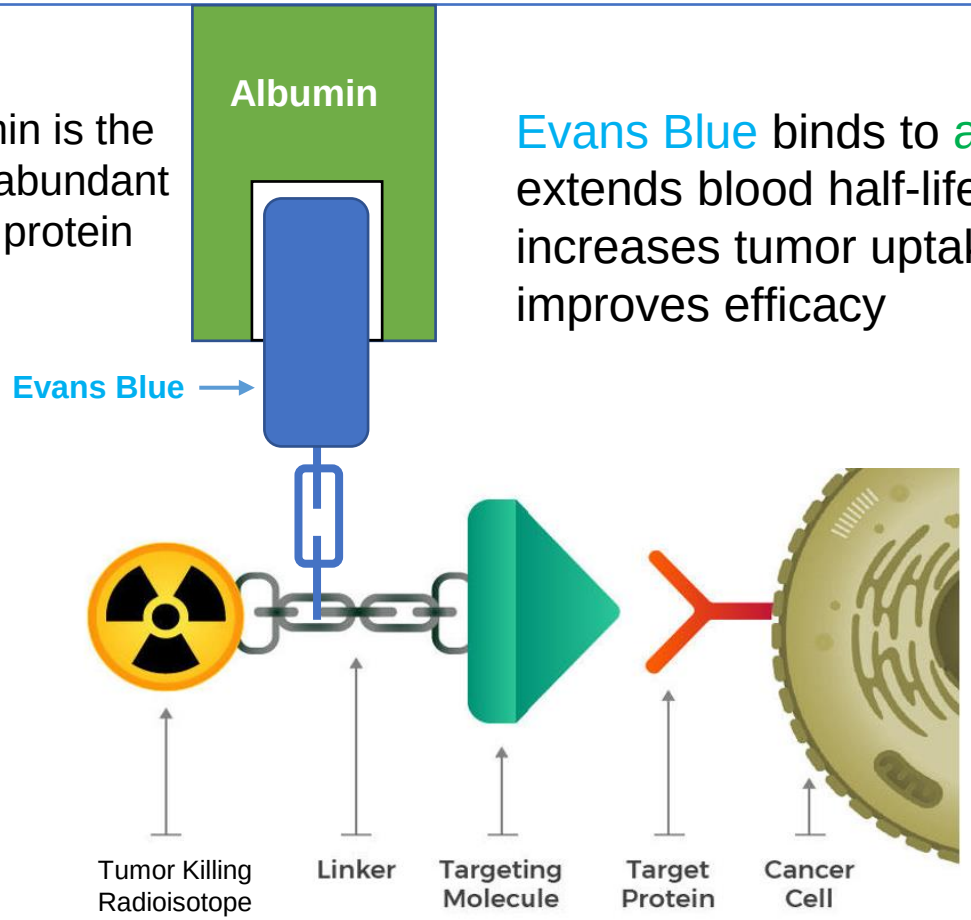
https://seer.cancer.gov/statfacts/

$\alpha_v\beta_3$ expressing cancers



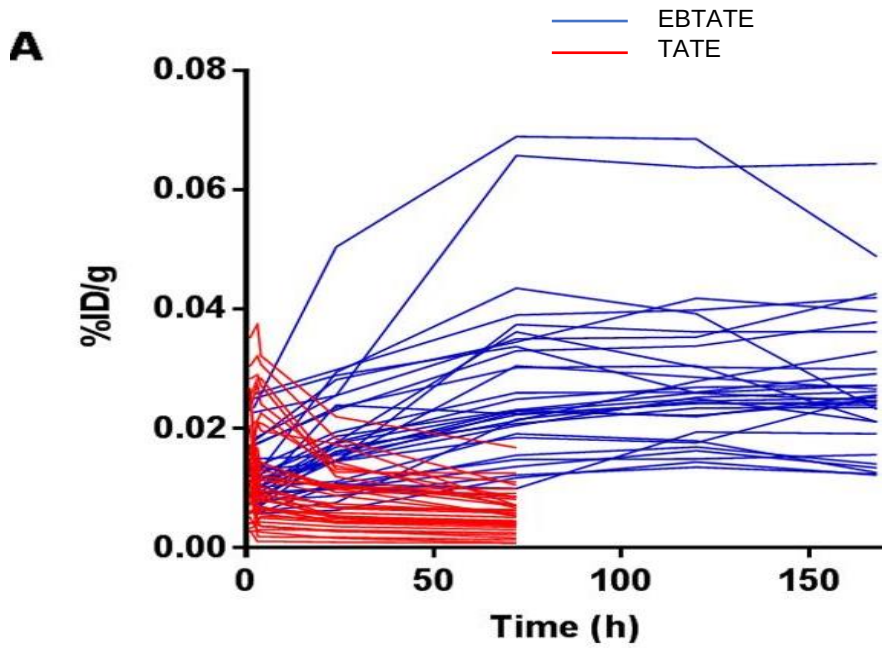
EvaThera platform has improved PK/PD over other PRRTs

Albumin is the most abundant blood protein



Evans Blue binds to albumin, extends blood half-life, increases tumor uptake and improves efficacy

EBTATE sustained tumor absorption in NET patients



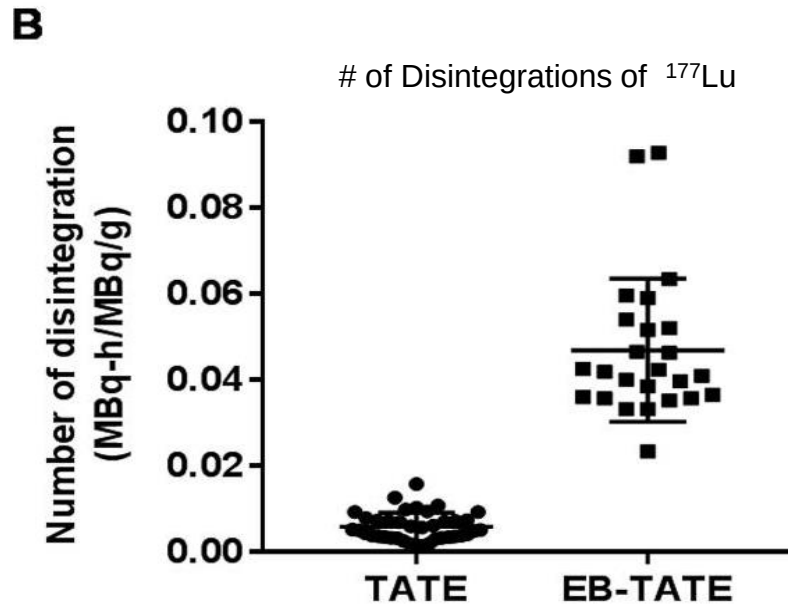
Zhang et al. J Nucl Med 2018; 59: 1699-1705

EvaThera Platform has unique advantages

Increased circulation half-life results in improved tumor uptake and retention

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

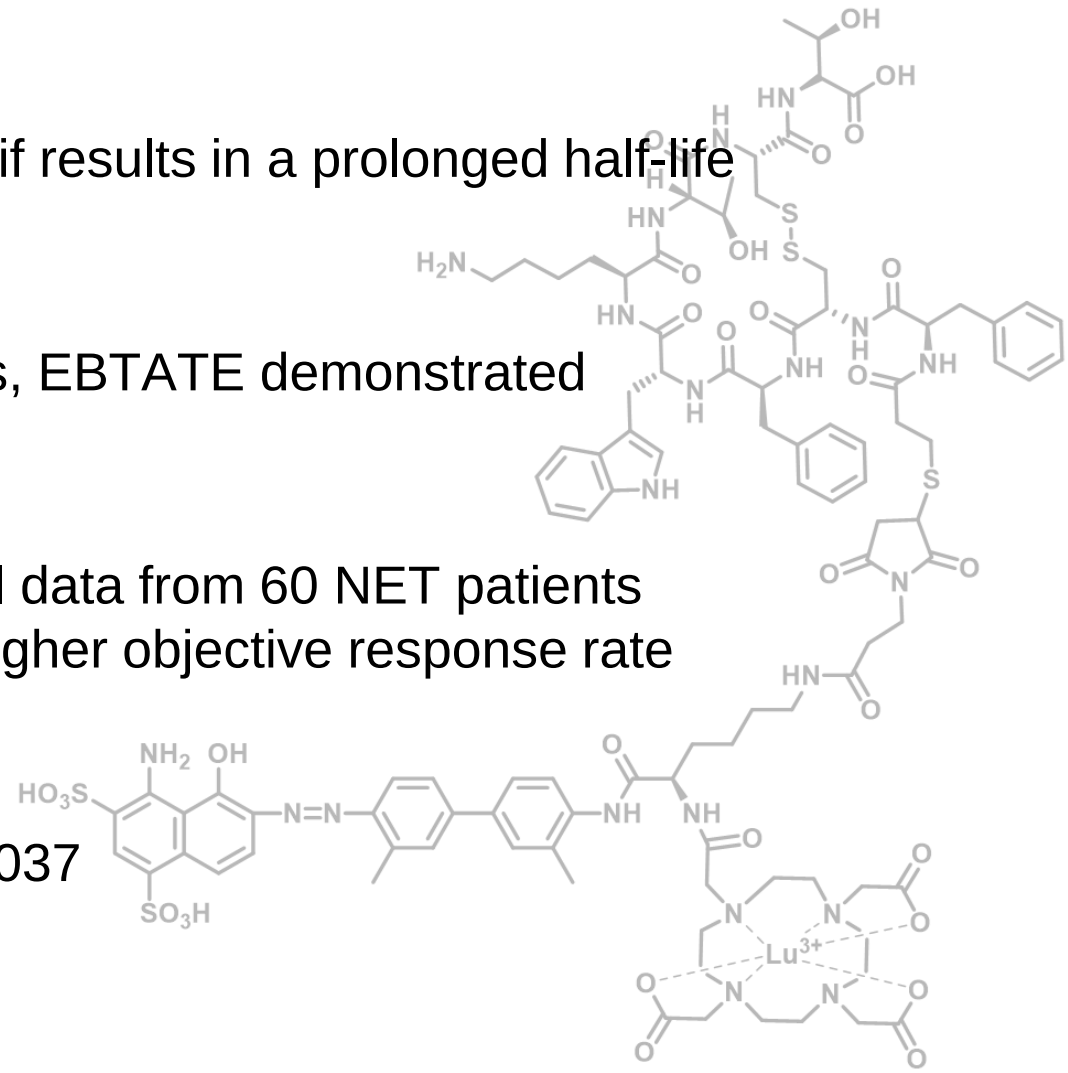
EBTATE showed a 7.9-fold increase in radiation counts in tumor vs TATE



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

EBTATE: The next generation NET radiotherapeutic

- **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, EBTATE demonstrated superior anti-tumor efficacy compared to Lutathera
- **Clinical data support safety and efficacy**: Clinical data from 60 NET patients demonstrate that EBTATE is safe and achieves a higher objective response rate than Lutathera (33% vs 13%)
- **MTTI IP** includes ^{225}Ac and other radionuclides to 2037



EBRGD - unlocks potential of αvβ3 targeting in cancer treatment

Better uptake & retention

- Conjugation of EB to DOTA-RGD significantly increases tumor uptake and tumor retention, as demonstrated with ^{177}Lu/^{90}Y/^{64}Cu

Strong *in vivo* efficacy

- In a PDX$\alpha_v\beta_3$ NSCLC mouse model, a single dose of ^{177}Lu-EB-RGD completely eradicated the tumors with no sign of tumor recurrence during the observation period
- Concurrent blockade of PD-1/PD-L1 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 multiple cancers

- αvβ3 integrin is a marker for angiogenesis and is over-expressed in many cancers
- EBRGD is designed to overcome past therapy failures, unlocking αvβ3 targeting potential in cancer treatment

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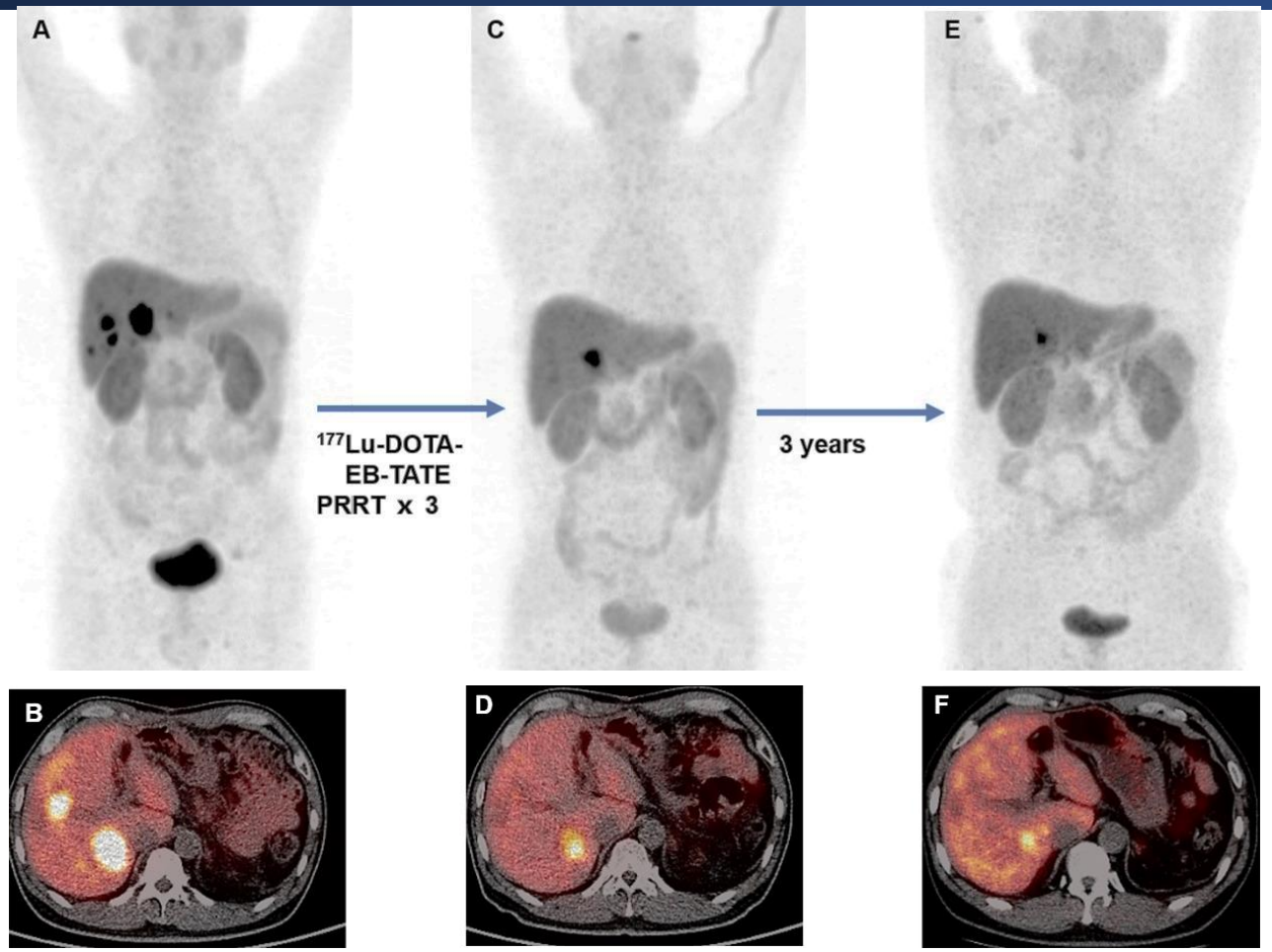
Clinical Outcomes

Long-term efficacy: 3-year follow-up showed EBTATE (3 cycles) delivered favorable sustained benefit



^{68}Ga-DOTA-TATE PET/CT diagnostic tracking at 3-year follow-up showed sustained partial response

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

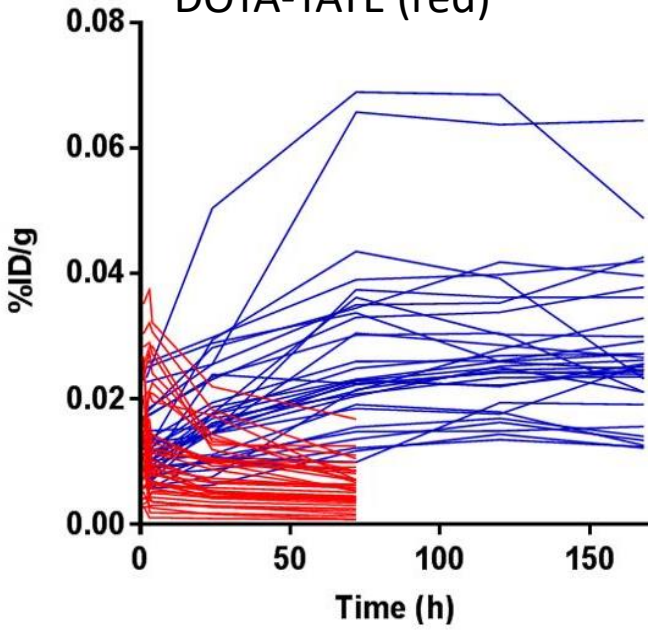
Safety, Pharmacokinetics, and Dosimetry of a Long-Acting Radiolabeled Somatostatin Analog ^{177}Lu-DOTA-EB-TATE in Patients with Advanced Metastatic Neuroendocrine Tumors

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

EBTATE™ reached peak slower, and had a prolonged plateau compared to ^{177}Lu-DOTA-TATE (TATE)

A

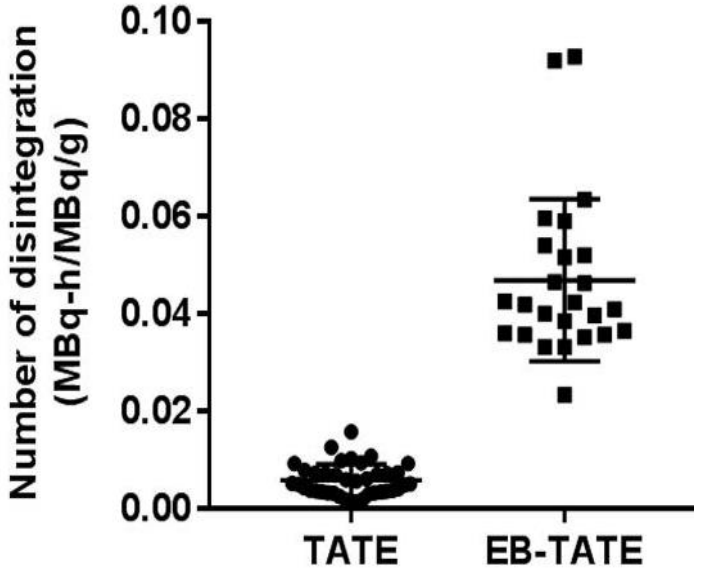
Time Activity
After EBTATE™(blue) & DOTA-TATE (red)



EBTATE™ showed 7.9-fold increase of lesion radiation counts vs TATE

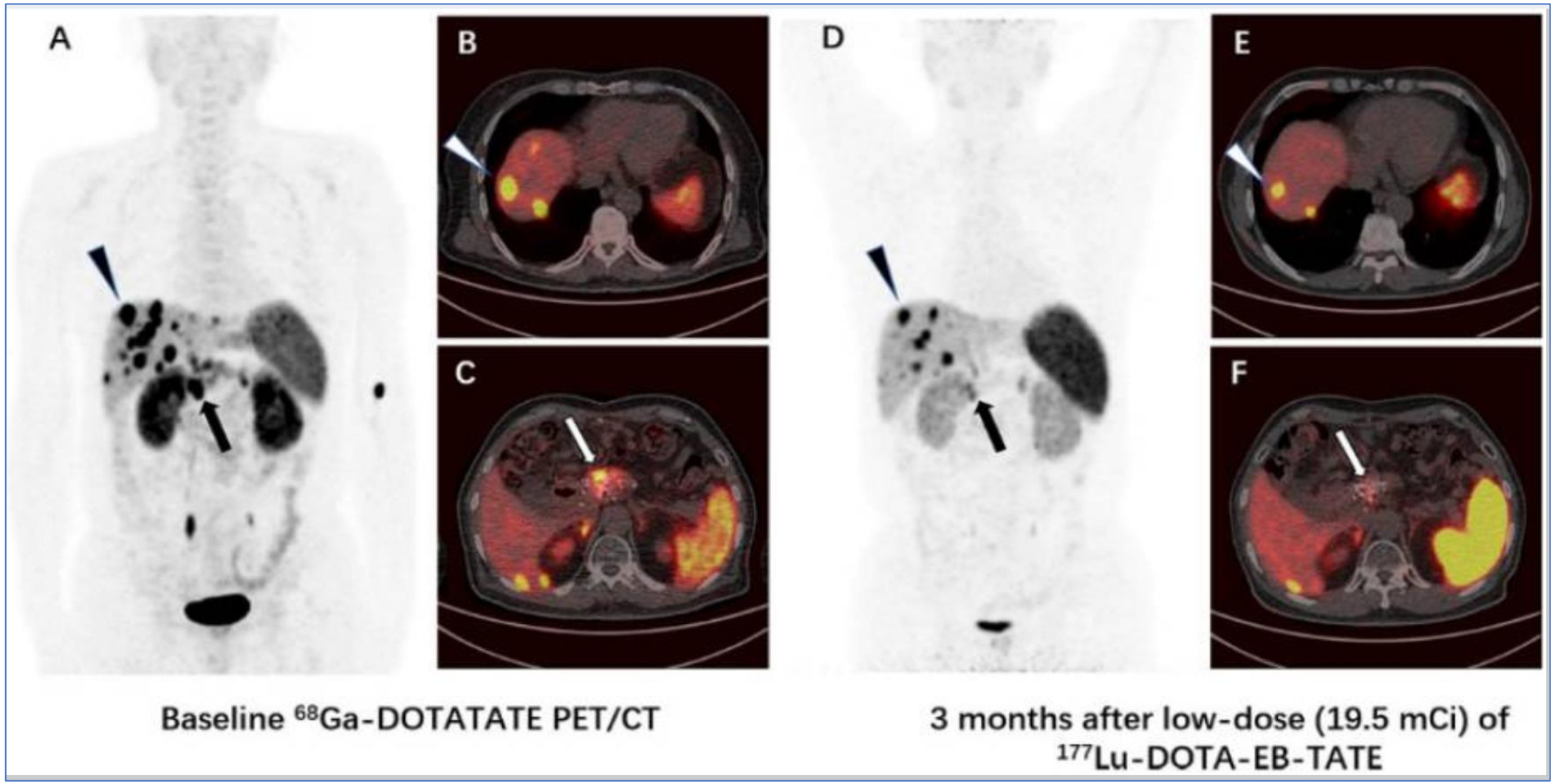
B

# of Disintegrations of ^{177}Lu



Tumor size reduction in patients after a single injection of EBTATE

Wang et al. Theranostics 2018; 8(12): 3308-3316



PET/CT response (EORTC criteria)-^{68}Ga-DOTATATE

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

Efficacy	Group A (1.17 GBq) N=12	Group B (1.89 GBq) N=6	Group C (3.97 GBq) N=14
CR (%)	0	0	0
PR (%)	50	50	42.9
SD (%)	16.7	33.3	28.6
PD (%)	33.3	16.7	28.6
DRR (%)	50	50	42.9
DCR (%)	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.

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EBTATE Safety: Low, long-term hematotoxicity, nephrotoxicity and hepatotoxicity (CTCAE 5.0) among 29 patients similar to SOC*

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

Toxicity	Grade 1 (# of patients)	Grade 2 (# of patients)	Grade 3 (# of patients)	Grade 4 (# of patients)
Leukopenia	1	3	0	0
Thrombocytopenia	1	0	1	0
Anemia	1	2	0	0
Nephrotoxicity	0	0	0	0
Hepatoxicity	1	0	0	0

**Danthala et al. 177Lu-DOTA-TATE therapy in patients with neuroendocrine tumors: 5 years' experience from a tertiary cancer care centre in India. Eur J Nucl Med 2014; 41: 1319-1326*

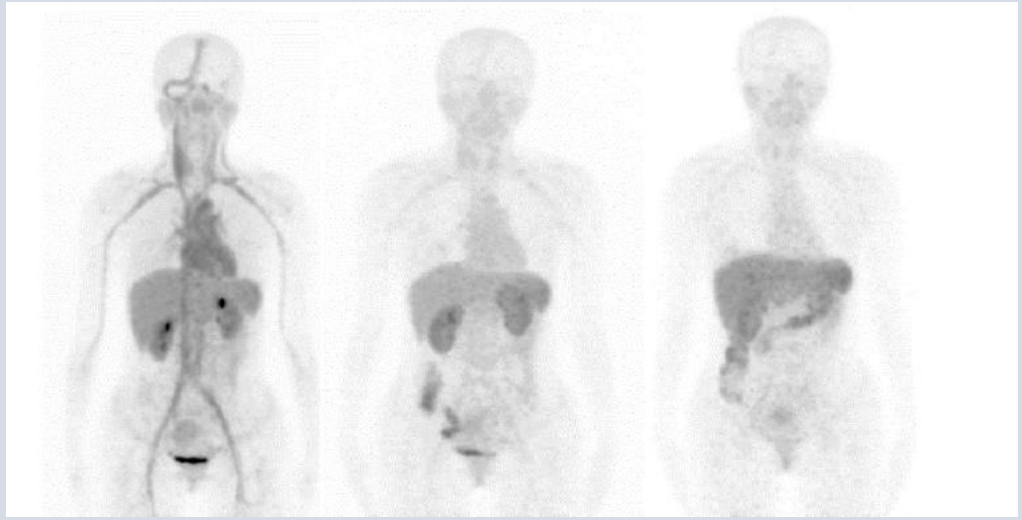
EBTATE Conclusions

- 3-year follow-up showed stable disease with progression-free survival of 43 months after three cycles of EBTATE (N=30 patients)
- In a head-to-head *in vivo* comparison, EBTATE showed improved anti-tumor efficacy versus DOTA-TATE
- Early clinical data showed that EBTATE is safe and achieved objective responses after a single injection
- Multiple cycles of escalating doses of EBTATE (N=32 patients) seem to be well tolerated and were effective in tumor control
- EBTATE should also target Hürthle cell thyroid cancer and nasopharyngeal cancer

^{64}Cu-EBRGD (Glioblastoma targeting & potential therapy)

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).

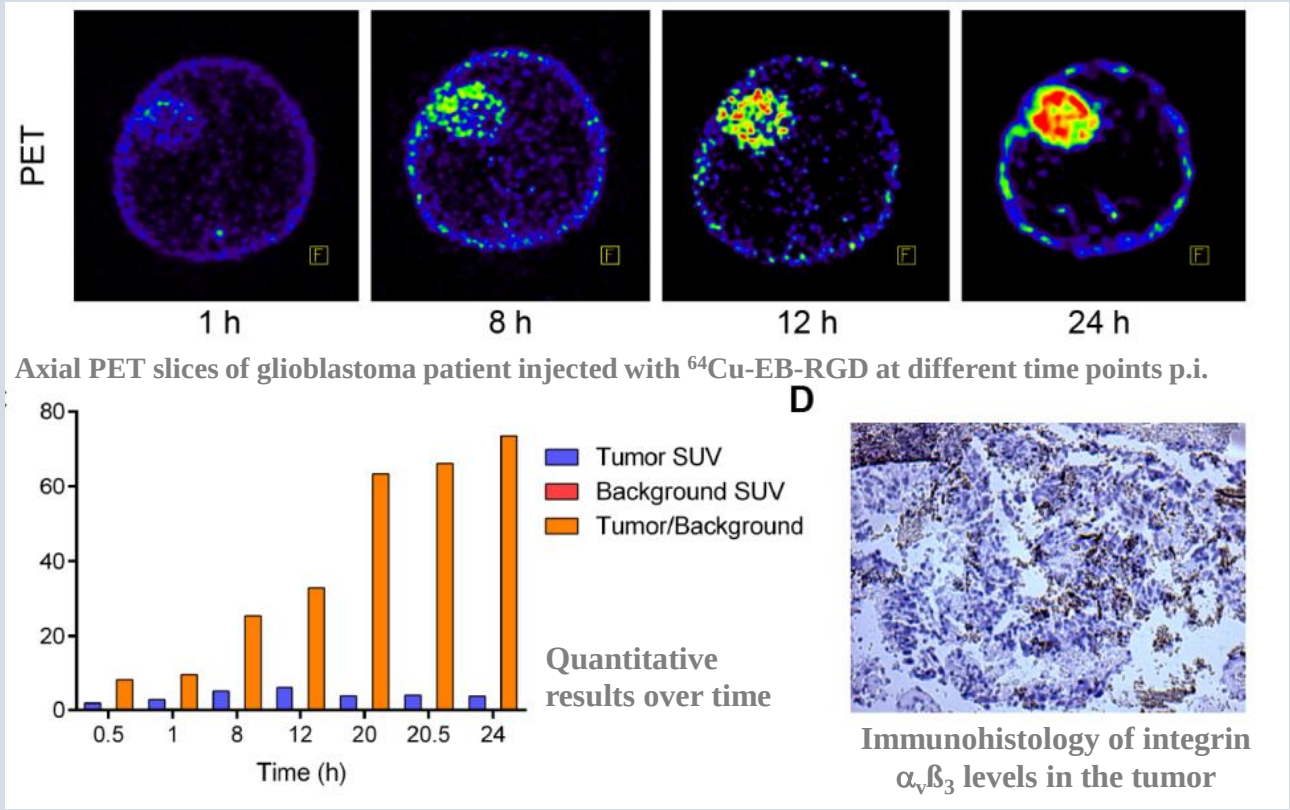


1h **8h** **24h**

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.

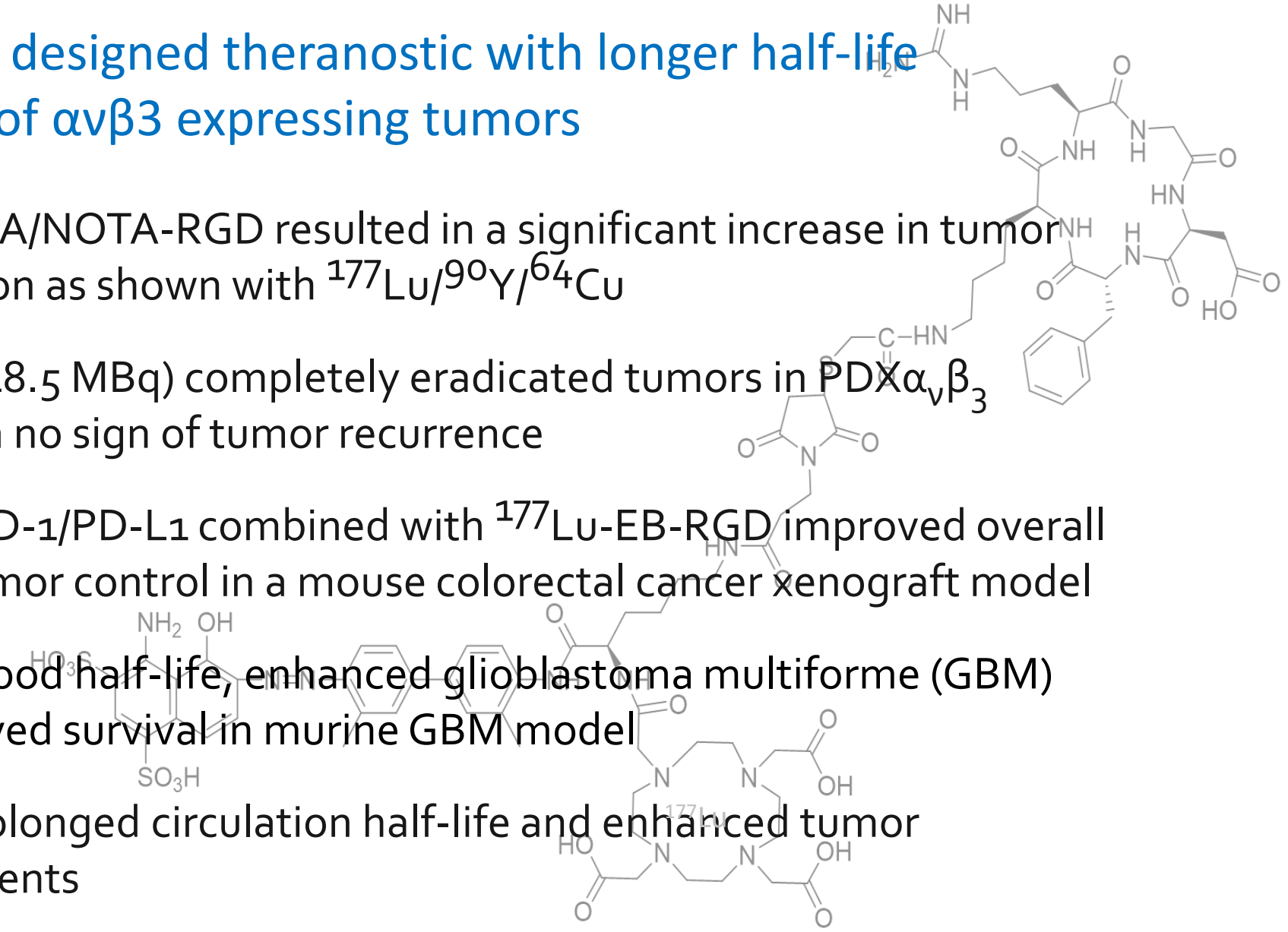
Quantitative results over time

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

Provided by Zhang J, et al, Peking Union Medical College Hospital (PUMCH)

Zhang et al. J Nucl Med 2020; 61(Suppl 1): 349

EBRGD, a new, rationally designed theranostic with longer half-life and improved targeting of αvβ3 expressing tumors



- Conjugation of EB to DOTA/NOTA-RGD resulted in a significant increase in tumor uptake and tumor retention as shown with $^{177}Lu/^{90}Y/^{64}Cu$
- A single dose of EBRGD (18.5 MBq) completely eradicated tumors in PDX$\alpha_v\beta_3$ NSCLC mouse model with no sign of tumor recurrence
- Concurrent blockade of PD-1/PD-L1 combined with ^{177}Lu-EB-RGD improved overall survival and long-term tumor control in a mouse colorectal cancer xenograft model
- ^{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 showed prolonged circulation half-life and enhanced tumor accumulation in GBM patients

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Molecular Targeting Technologies, Inc.

Advancing Precision Pharmaceuticals

Contact

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President & CEO
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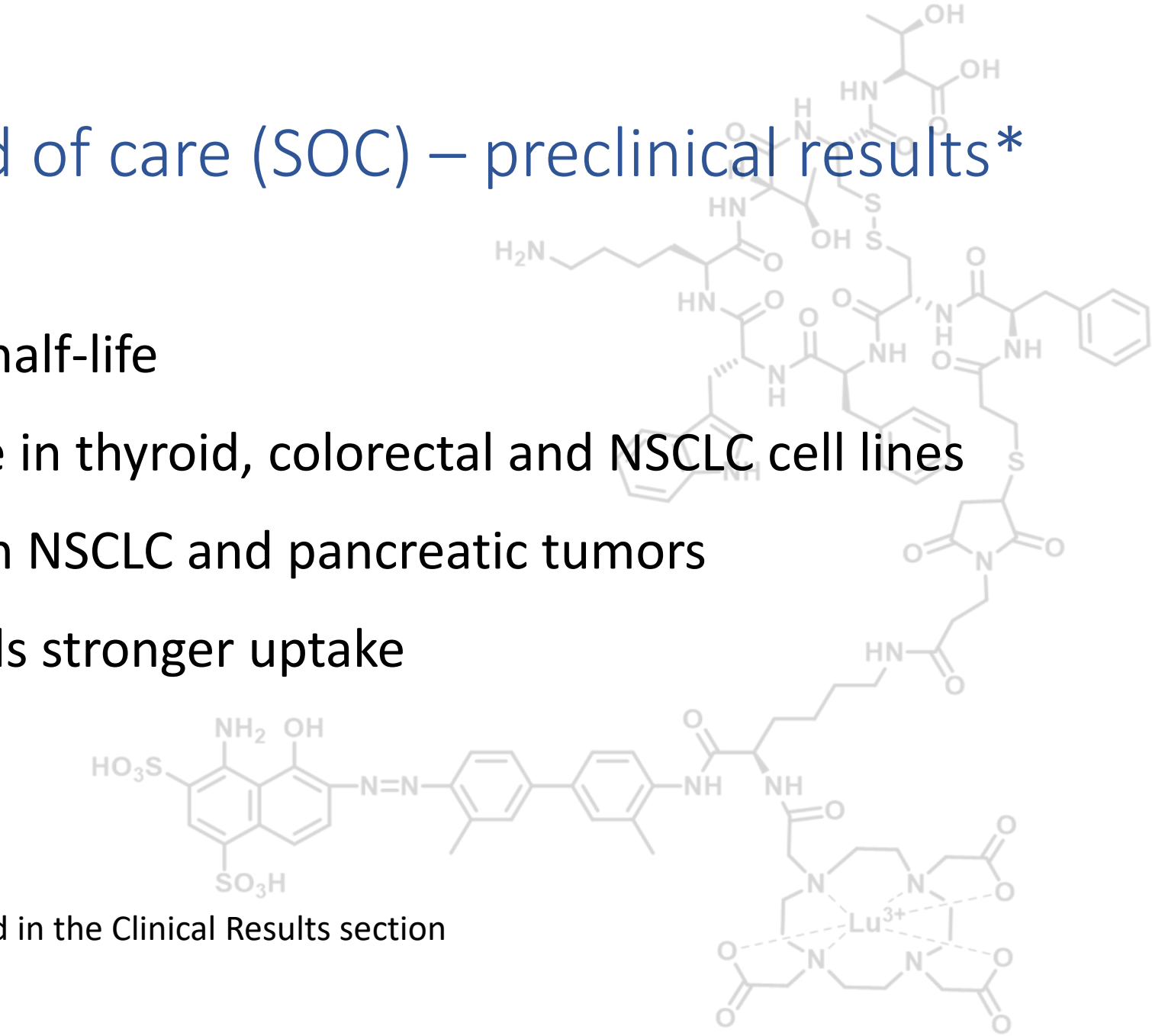
APPENDIX

Preclinical Findings

EBTATE™ vs standard of care (SOC) – preclinical results*

- Prolonged circulation half-life
- Stronger tumor uptake in thyroid, colorectal and NSCLC cell lines
- Better tumor control in NSCLC and pancreatic tumors
- Biodistribution parallels stronger uptake
- Comparable safety



*NET medical benefits are described in the Clinical Results section

Better preclinical tumor uptake and treatment response*

Preclinical – xenograft tumor uptake	EBTATE	SOC
Non small cell lung cancer (NSCLC)-% ID/gram	80%	4%
Pancreatic cancer AR42J-standardized uptake value	15.16	3.53
Follicular thyroid (Hürthle cell)-standardized uptake value	4.8	0.28

Preclinical – treatment response	EBTATE	SOC
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 –AR32J with Y-90	100% survival to 90 days with at 3.7 & 7.4 Mbq	No survival at 35 days with 7.4 Mbq

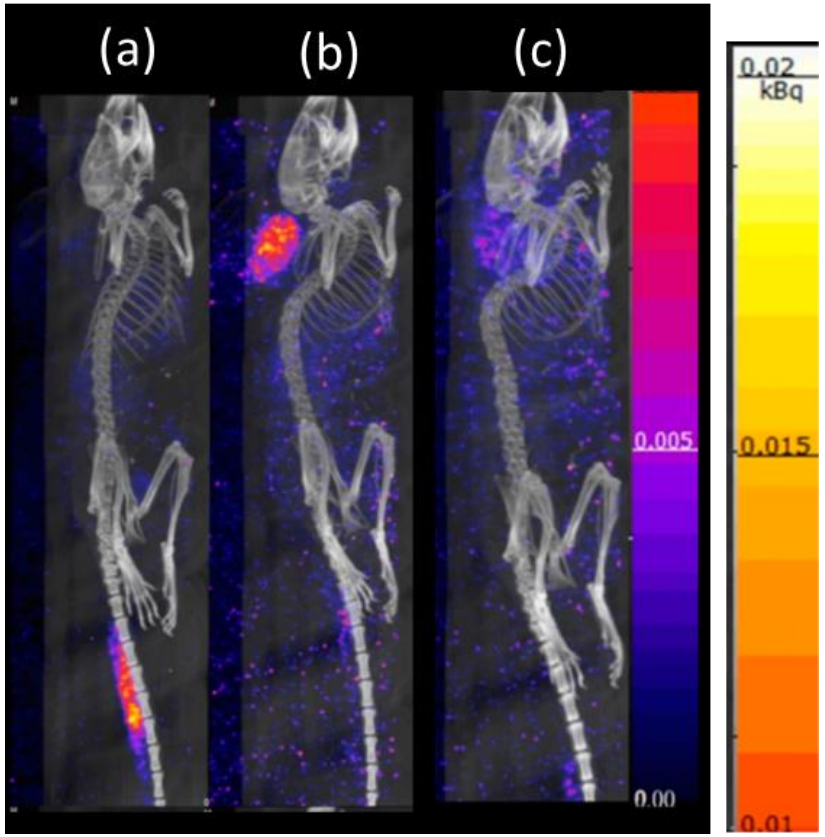
*see the following slides 11 - 15

SUPERIOR TUMOR UPTAKE OF EBTATE -- murine NSCLC model

Results: Uptake of ^{177}Lu–DOTA-EB–TATE

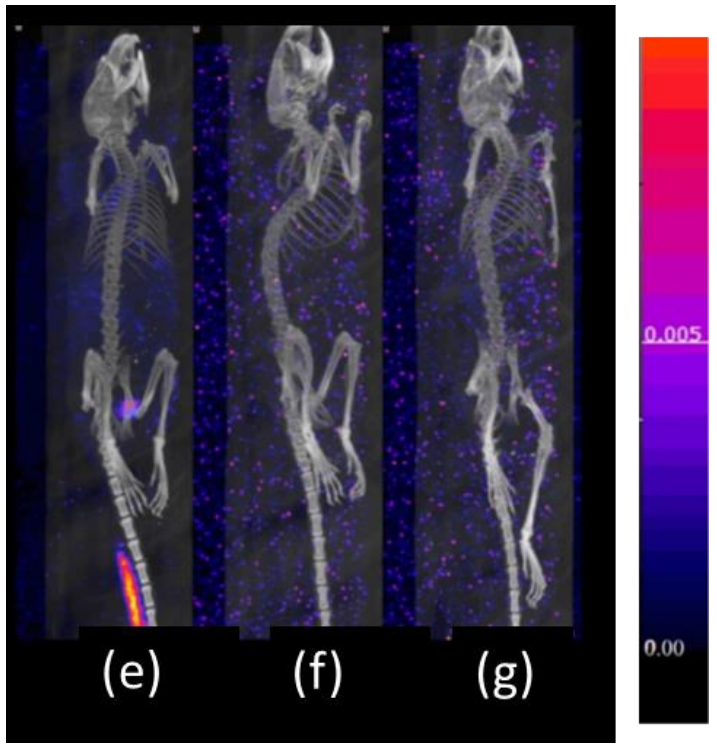
(b) was significantly higher than ^{177}Lu–DOTA–TATE (f) in the tumor.

Uptake at the target was blocked as shown in (c).



(a & b) ^{177}Lu–DOTA-EB–TATE without blocking at 1 and 24 h post injection and (c) with blocking (125 µg of DOTA-EB–TATE co-injected with the dose) at 24 h pi.

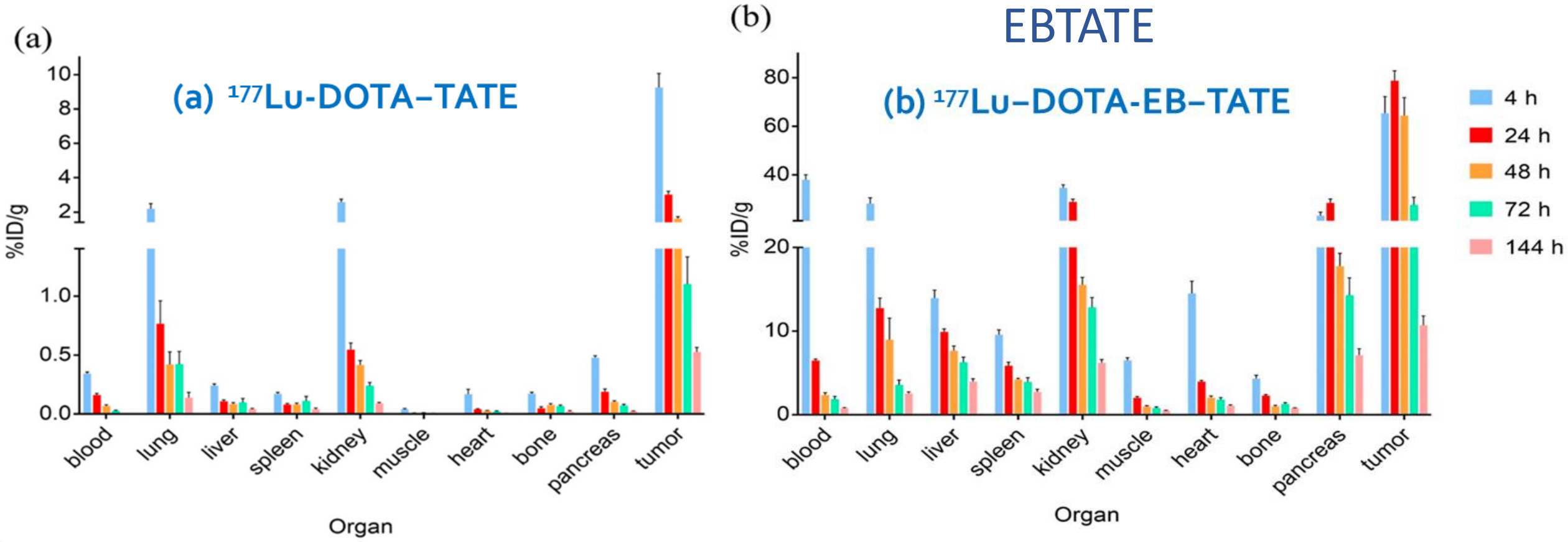
(e & f) ^{177}Lu–DOTA–TATE without blocking at 1 and 24 h post injection and (g) with blocking (125 µg of DOTA–TATE) at 24 h pi.



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

A low dose of EBTATE will clear slowly and stay in the tumor longer

In vivo biodistribution studies in A427-7 (NSCLC) bearing mice

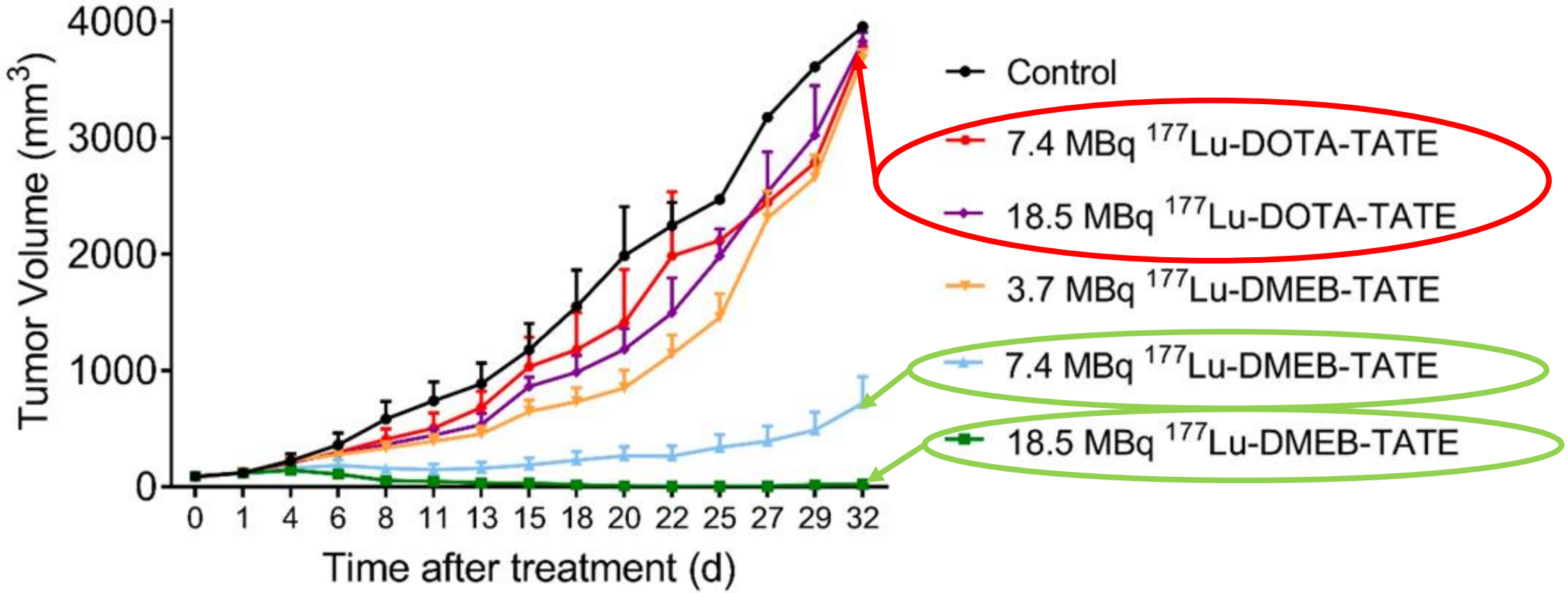


Bandara et al. Bioconjugate Chem 2018; 29(7): 2448-2454

EBTATE shrinks NSCLC tumors, SOC does not

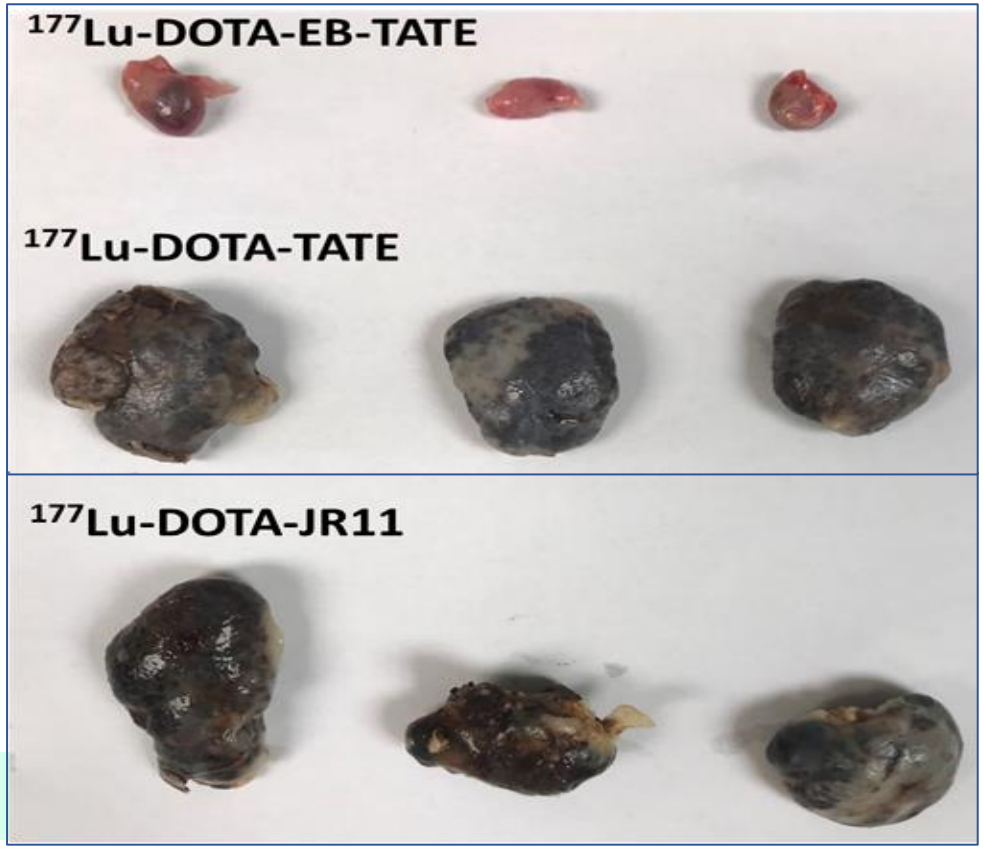
^{177}Lu-DOTA-EB-TATE (^{177}Lu-DMEB-TATE) tumor therapy: tumor growth in athymic nude mice with A427-7 xenografts

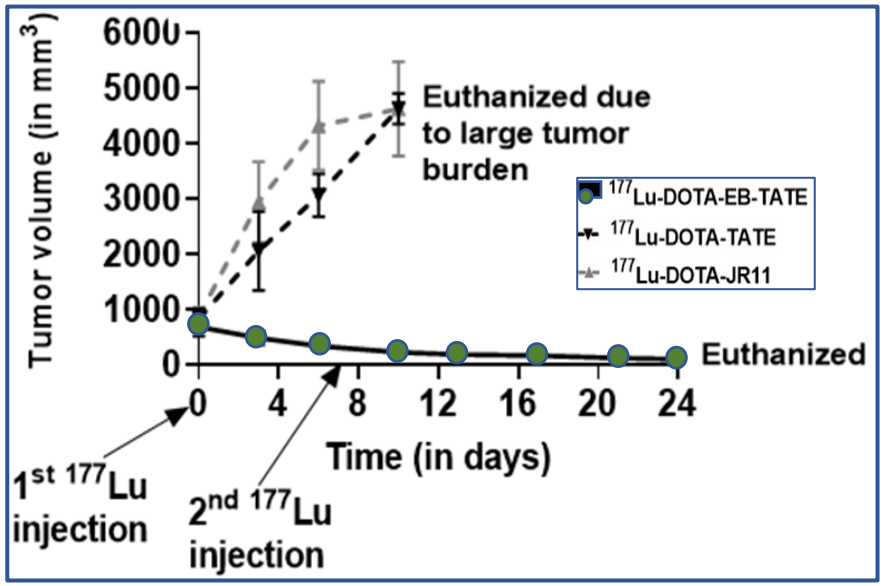
Bandara et al. Bioconjugate Chem 2018; 29(7): 2448-2454

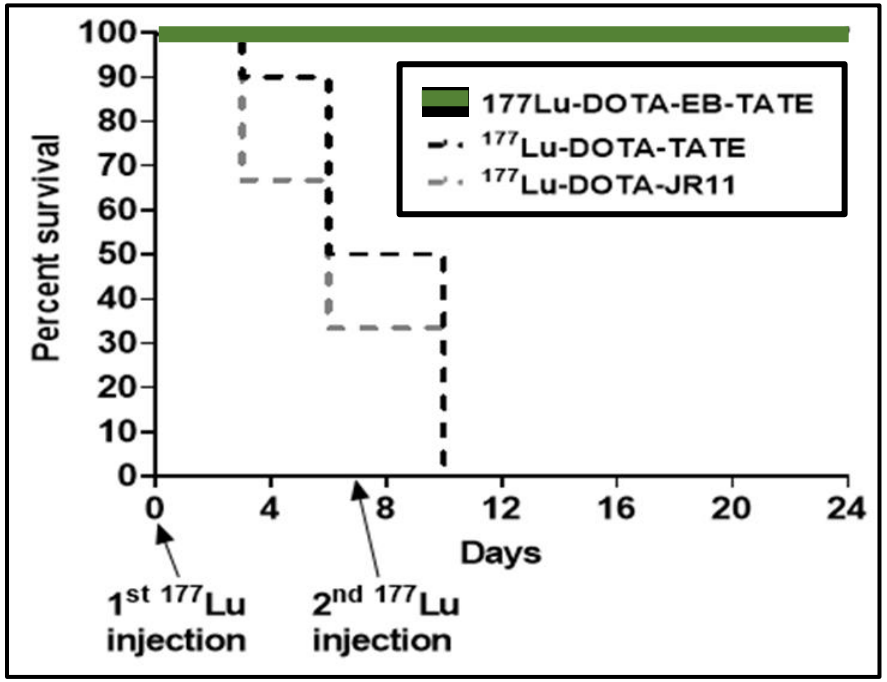


Pancreatic cancer tumors responded to EBTATE, those treated with ^{177}Lu-DOTA-TATE did not

PRECLINICAL EFFICACY OF EBTATE vs. ^{177}Lu-DOTA-TATE in Pancreatic cancer AR42J MOUSE Model *Thakur et al. Clin Cancer Res 2021; 27(5): 1399-1409*







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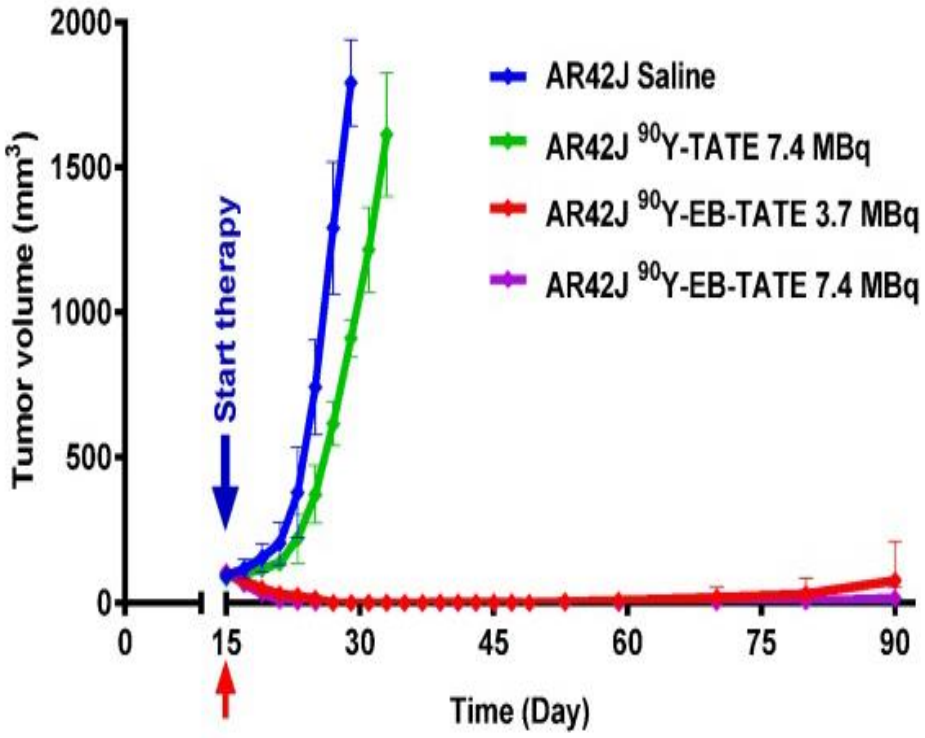
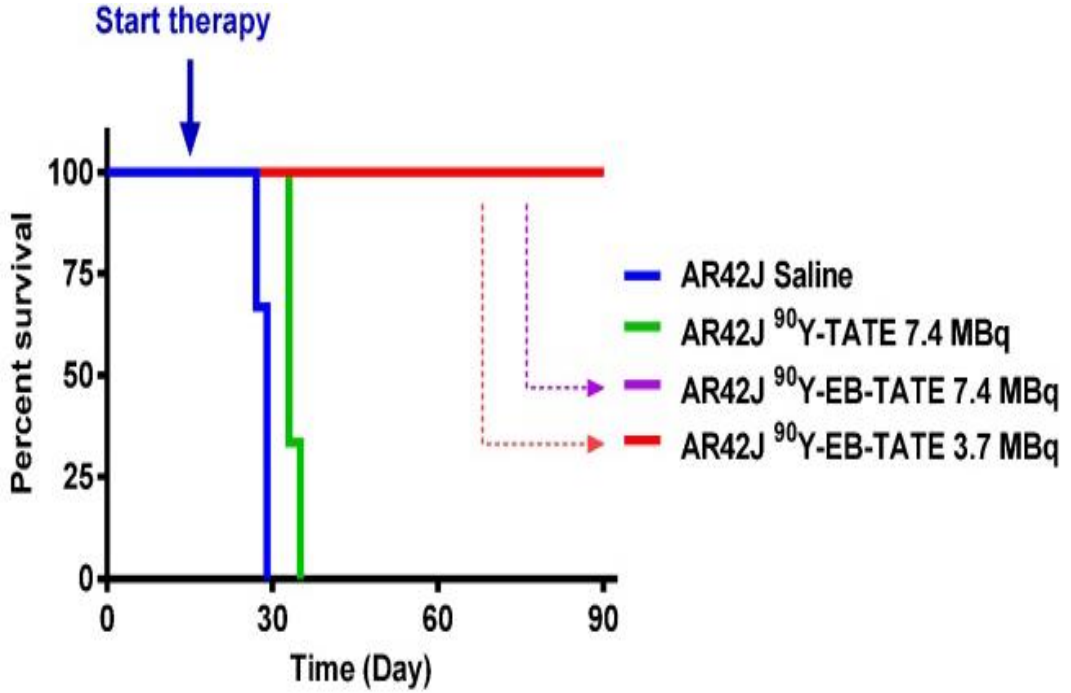
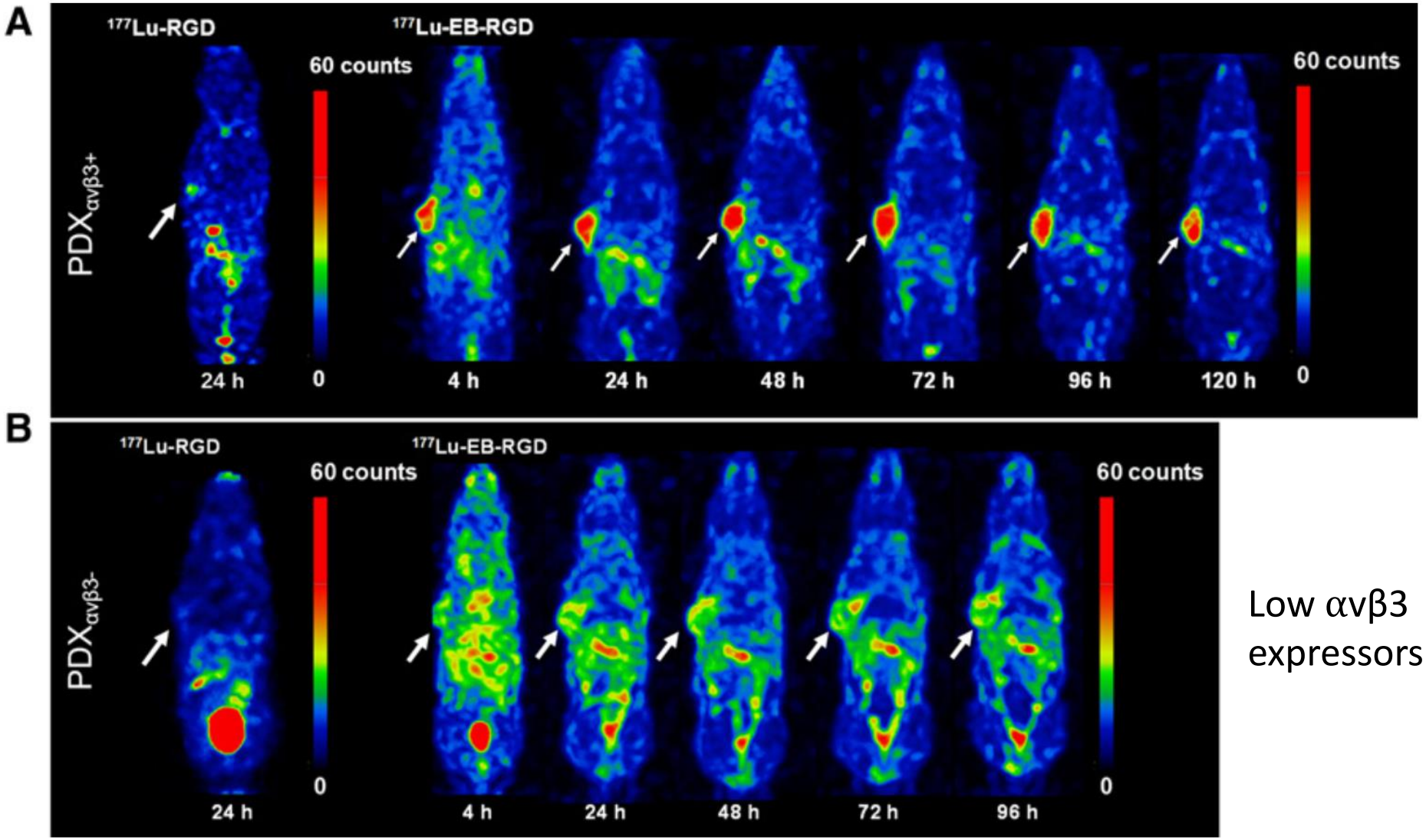
Pancreatic tumor volume and survival of mice injected with ^{90}Y-TATE or ^{90}Y-EB-TATE show superior effect with EB

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





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



High αvβ3 expressors

Low αvβ3 expressors

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

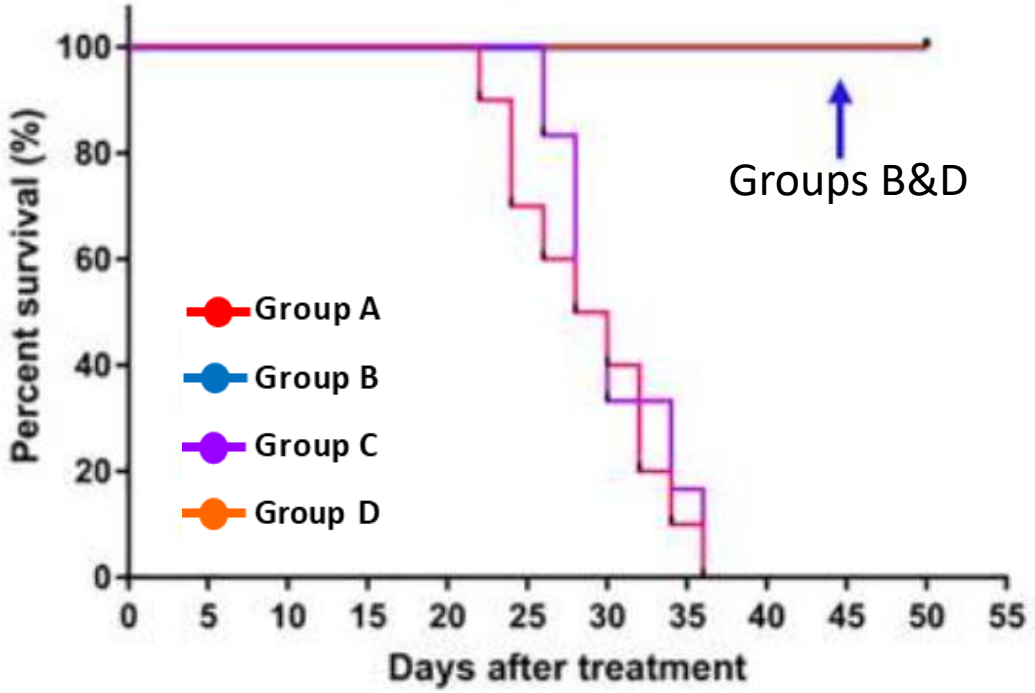
Tumor volume regression and improved survival of αvβ3+ PDX (NSCLC) mice treated with ^{177}Lu-EB-RGD

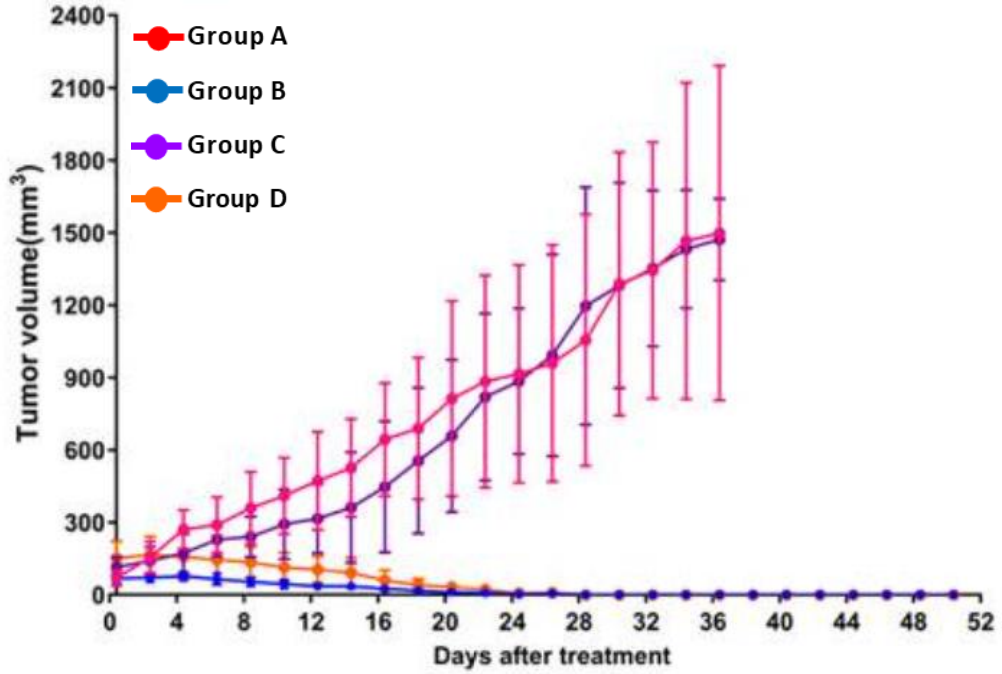
Day 0 — Group A: Saline

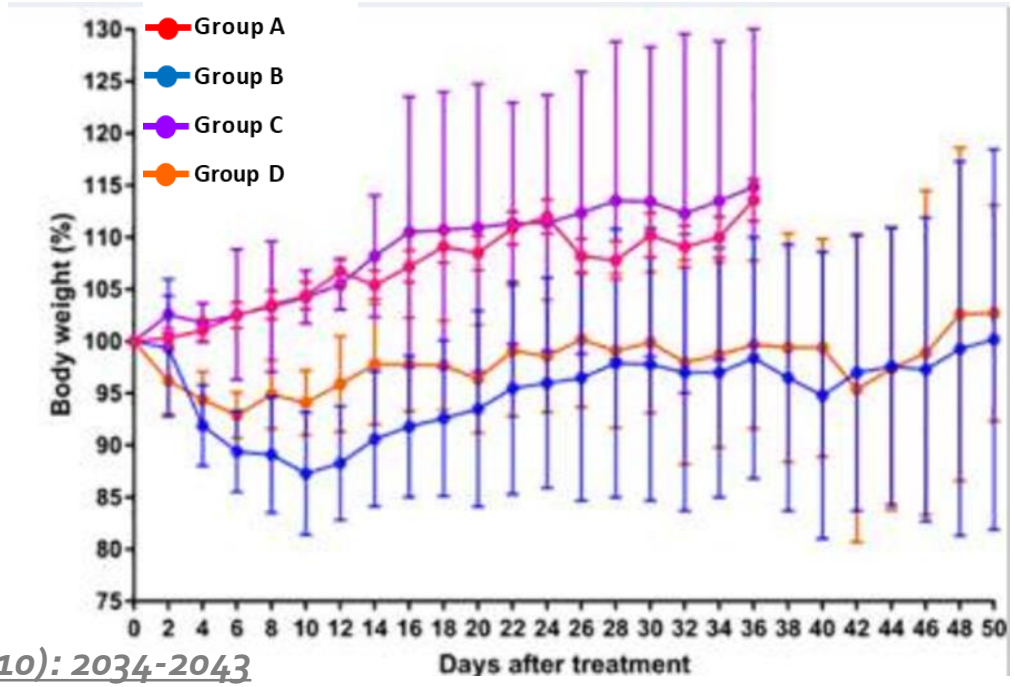
Day 0 — Group B: ^{177}Lu-EB-RGD (18.5 MBq)

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

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

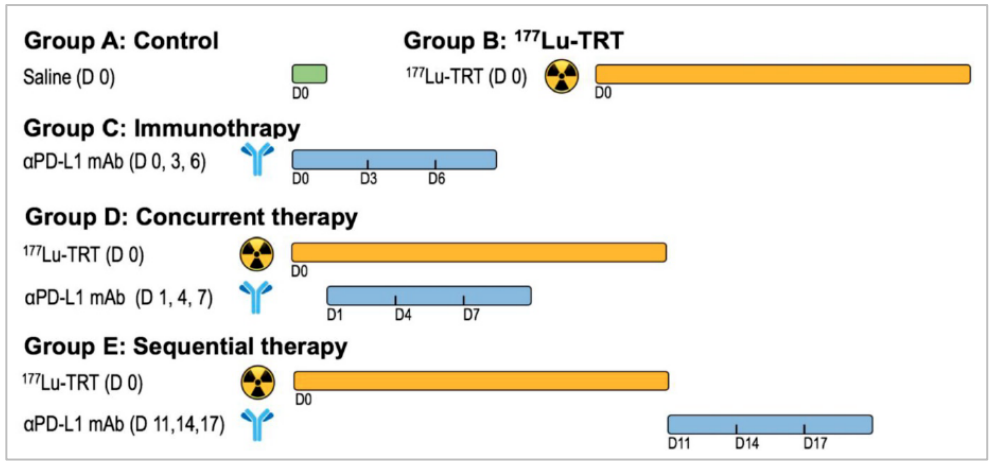


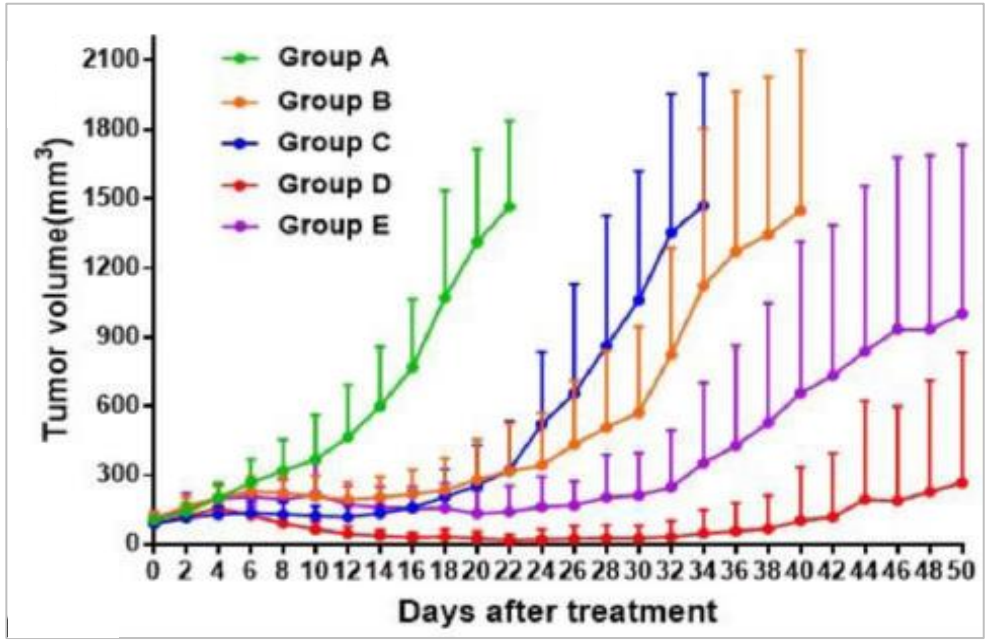


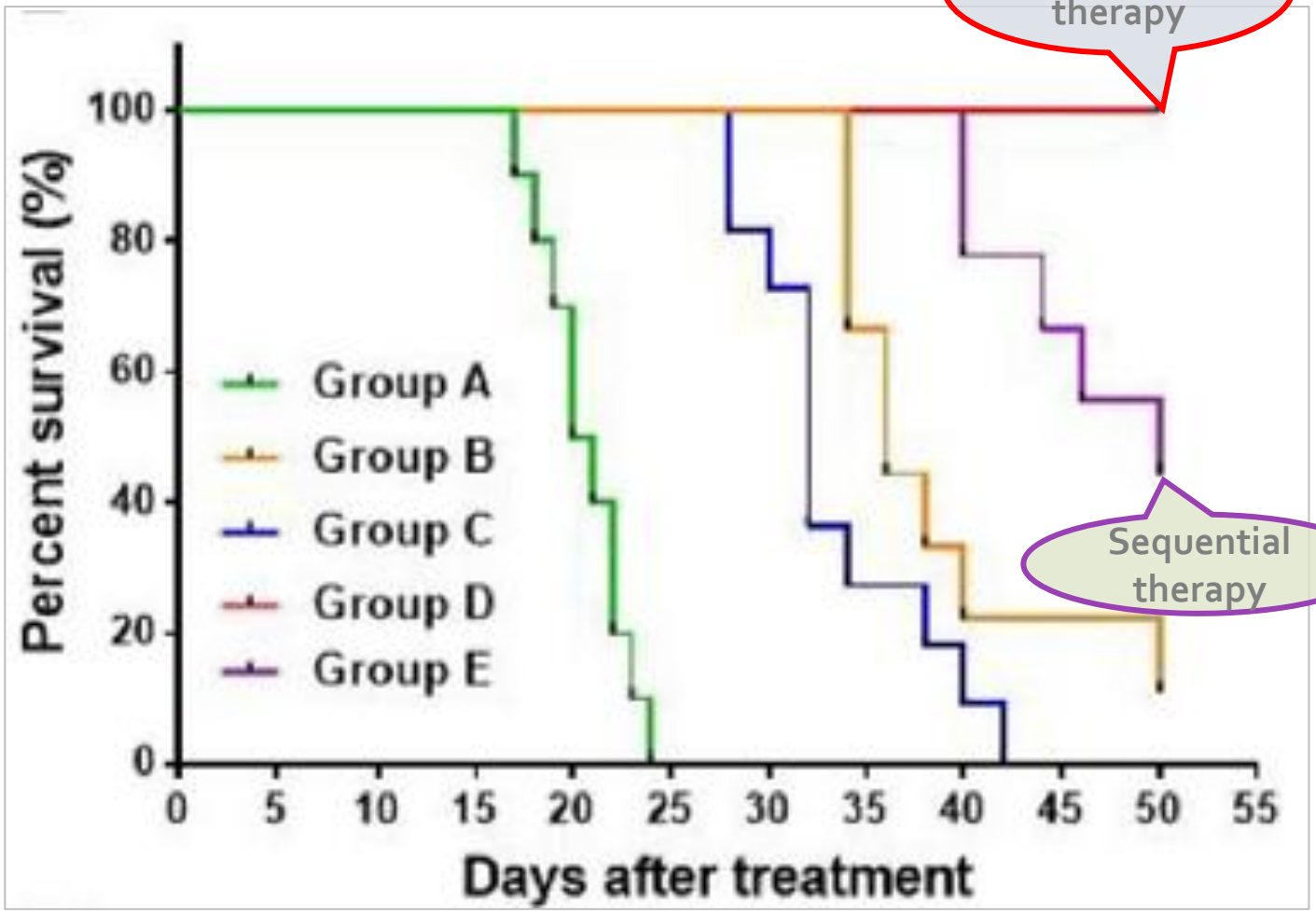


Zhao et al. Mol Cancer Ther 2020; 19(10): 2034-2043

EBRGD enhances immunotherapy efficacy in colorectal cancer







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

GBM tumor volume regression, improved survival of mice injected with increasing dose of ^{90}Y-EB-RGD and complete eradication of tumor at high dose

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