Theranostics: New frontier of Oncology and Nuclear Med.

Metaphysical analysis

University of the Incarnate Word Nuclear Medicine Science Program

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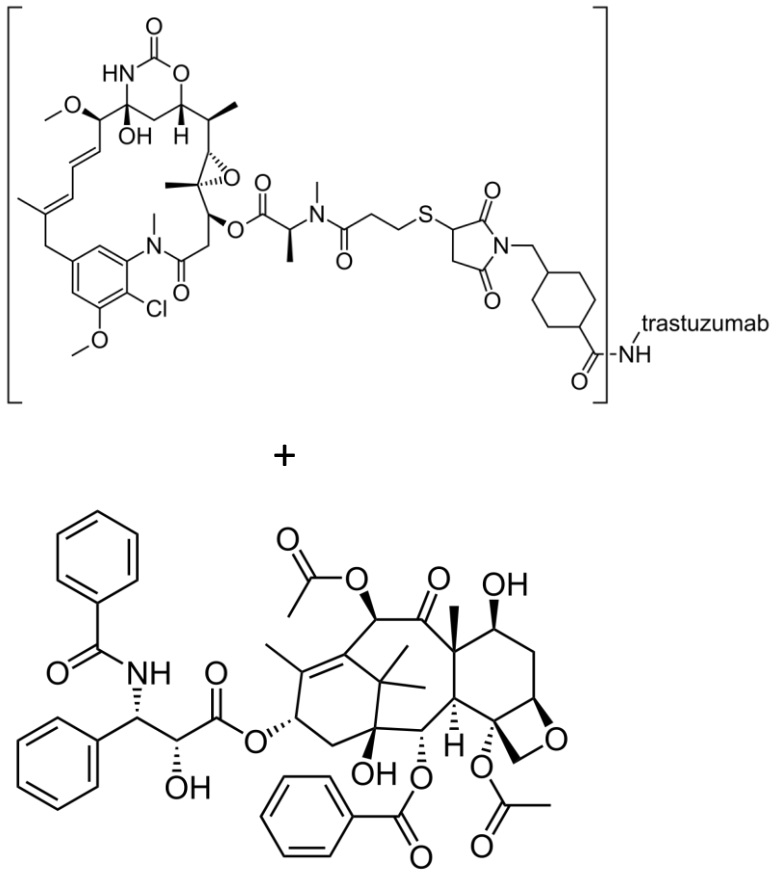
What we know for Theranostics

- Tumors can have different receptors[3]
- Tumors can be killed via the processing of electrochemically active metabolites, bromo-phenazinones, competitive inhibitors, monoclonal antibodies, and antitumor agents[3;7;15]
- Biggest issues: cytotoxicity, radiation exposure, and ineffectiveness[3;10]
- Main treatments:

HER2+(Enhertu)[7;17] **[177Lu]Lu-DOTA-TATE** [3] **[68Ga]Ga-DOTA-TATE**[15]

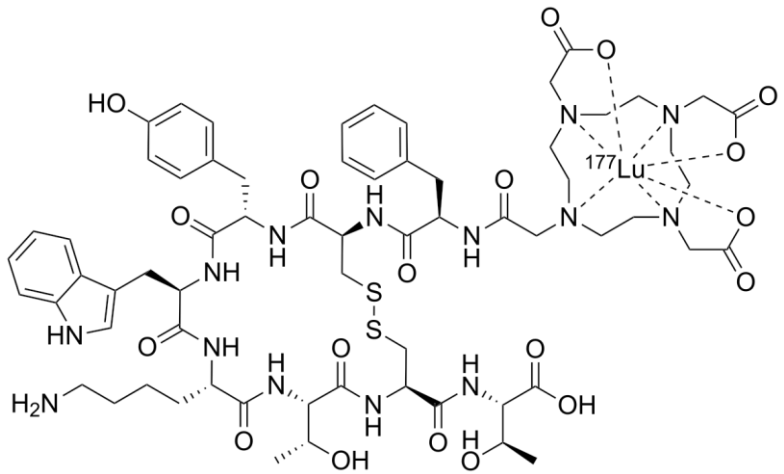
What we know for Theranostics

HER2+(Enhertu)[7;17]



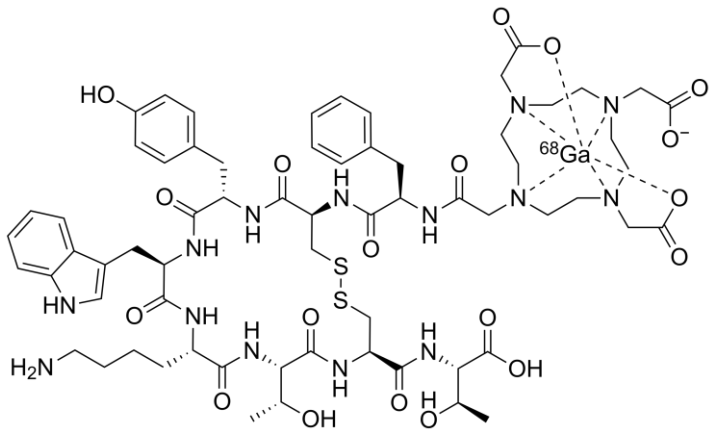
FDA: August 5th, 2022

[177Lu]Lu-DOTA-TATE [3]



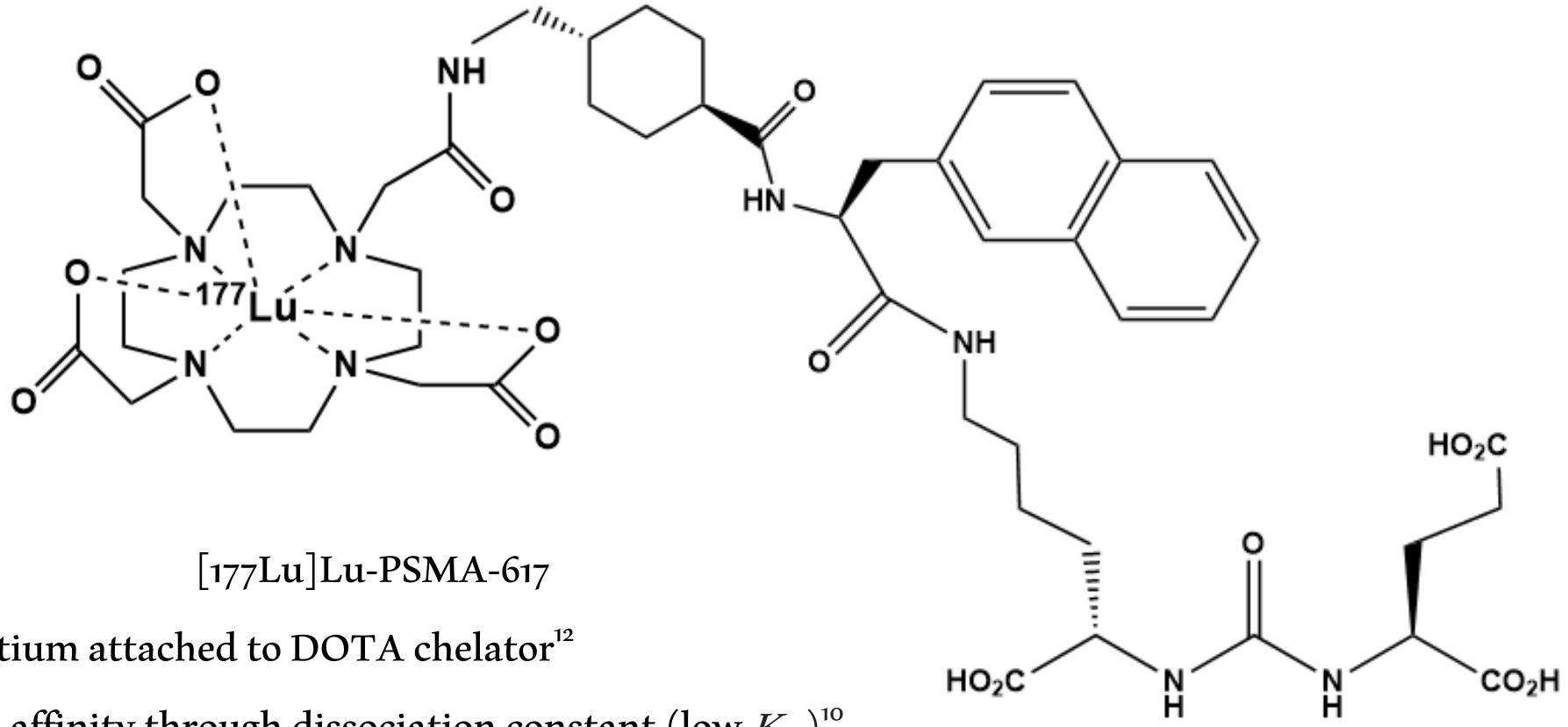
January 26th, 2018

[68Ga]Ga-DOTA-TATE[15]



June 1st, 2016

[177Lu]Lu-PSMA-617

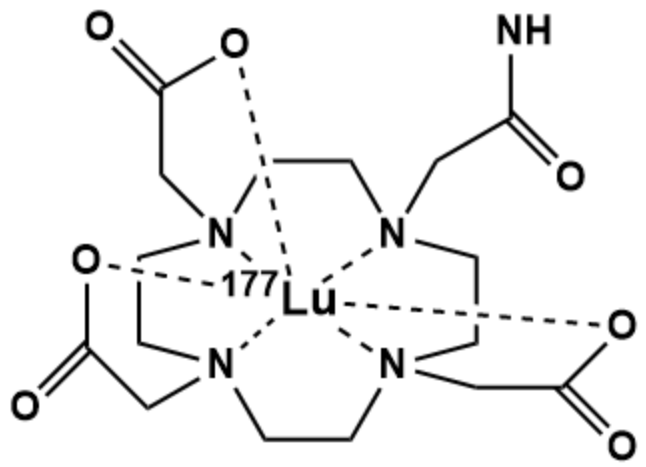


[177Lu]Lu-PSMA-617

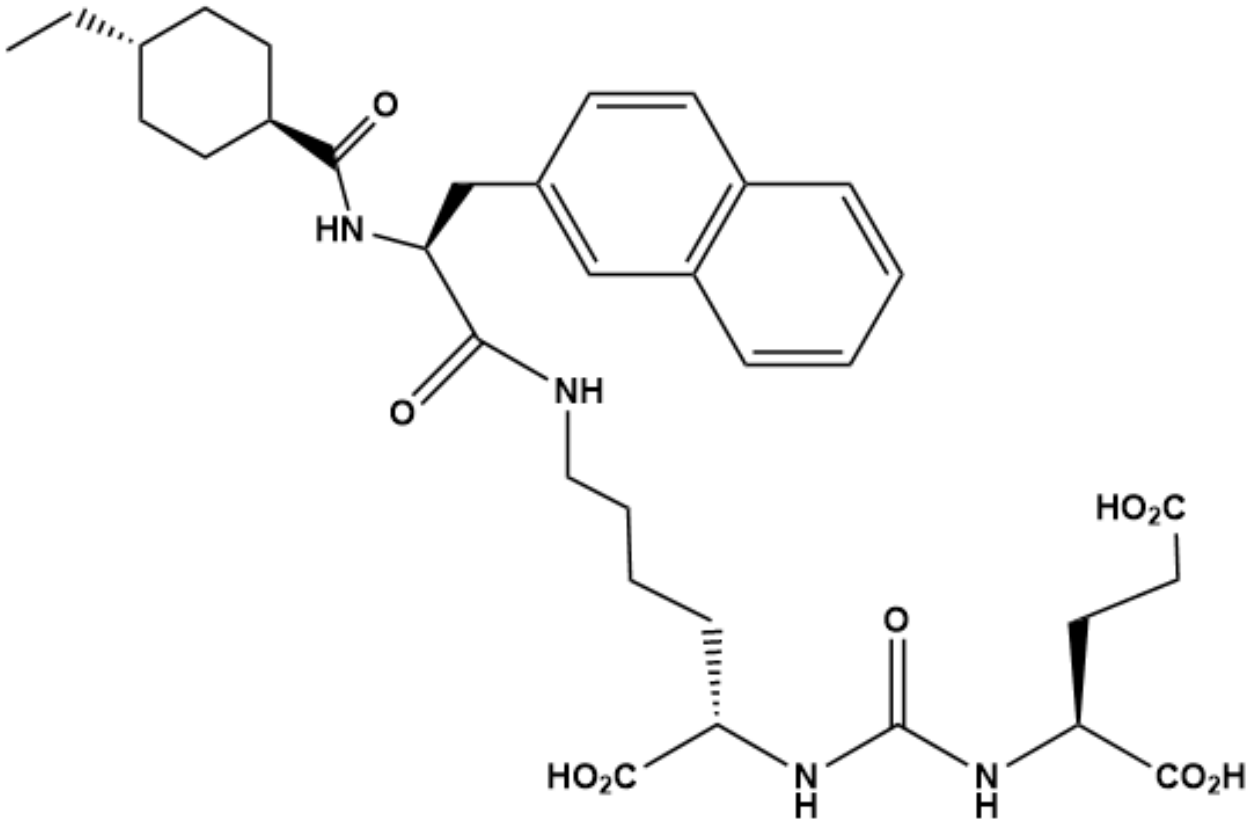
- Lutetium attached to DOTA chelator[12]
- High affinity through dissociation constant (low K_D)[10]
- Though a large attachment, holds promise

[177Lu]Lu-PSMA-617

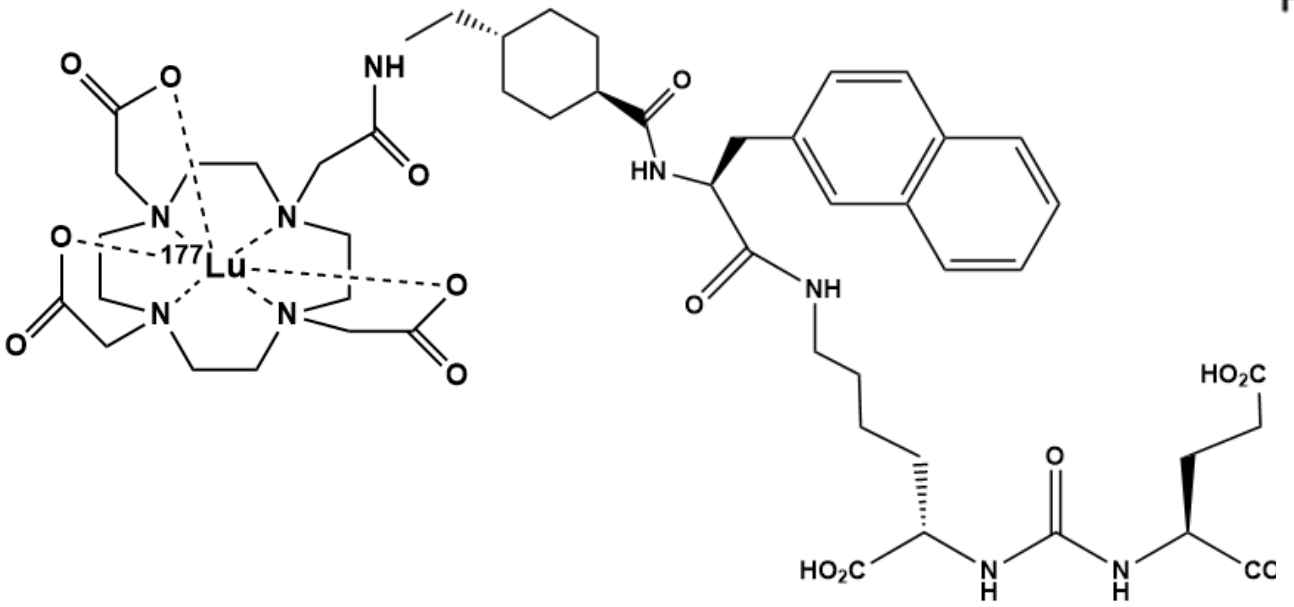
Dolate Chelator

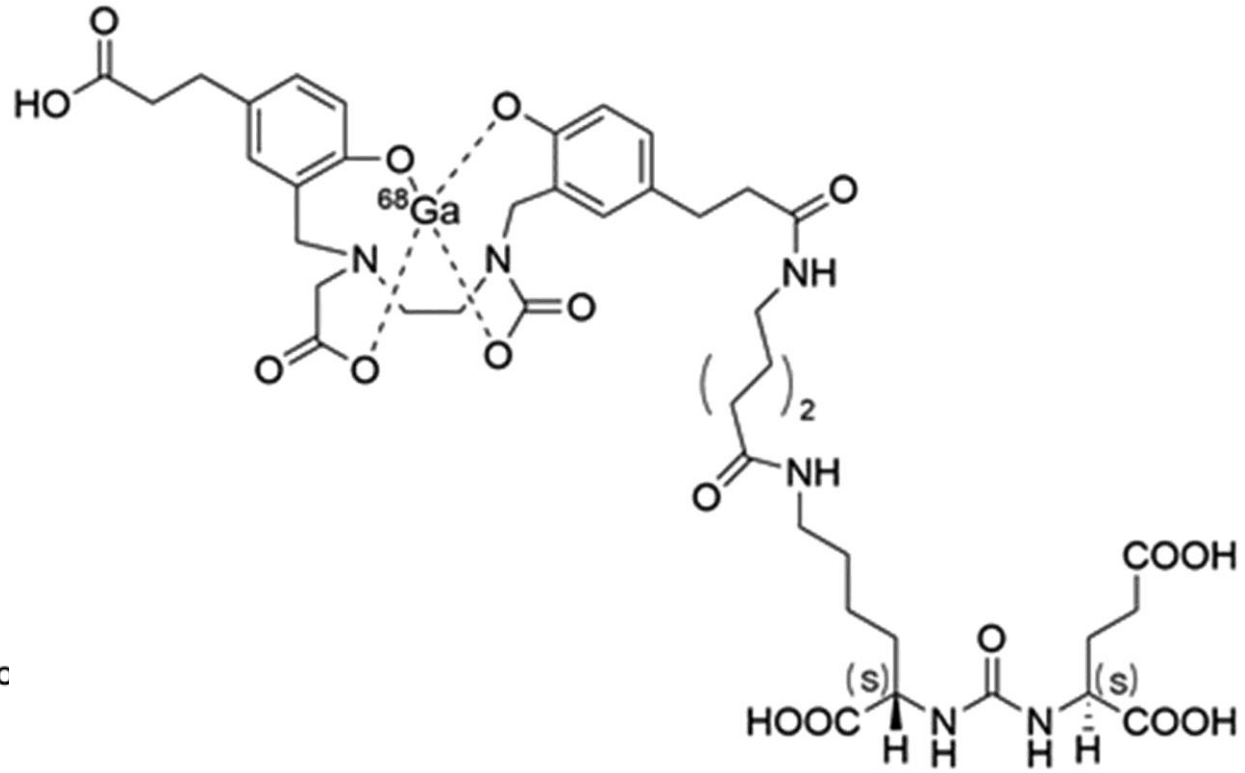


Prostate-specific membrane antigen

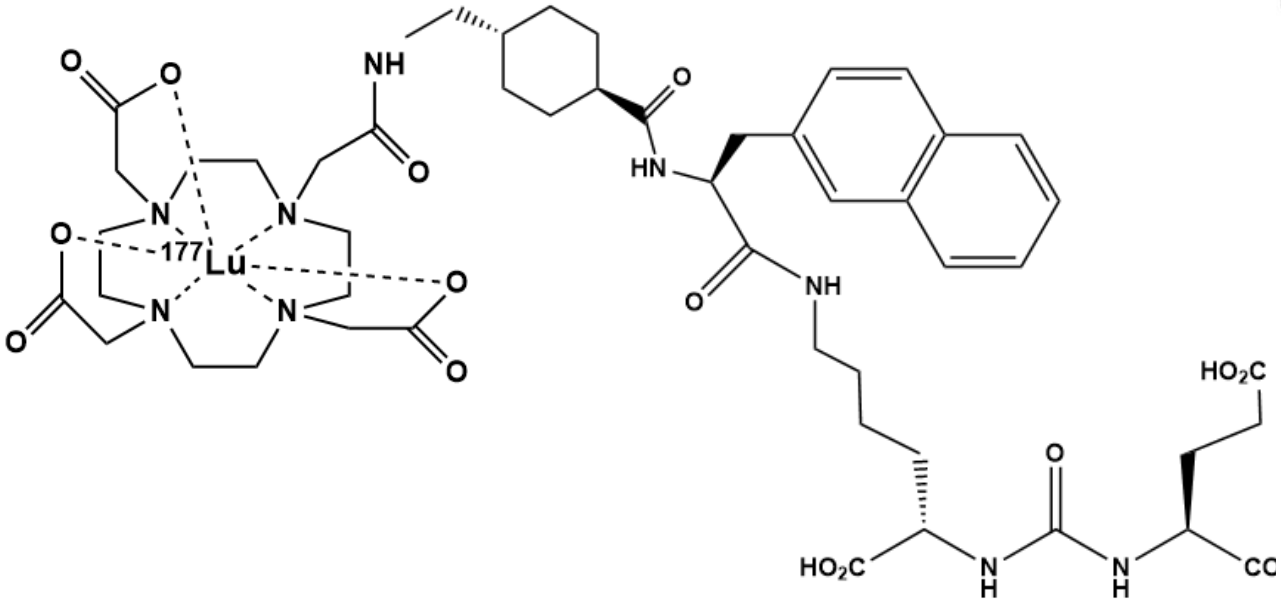


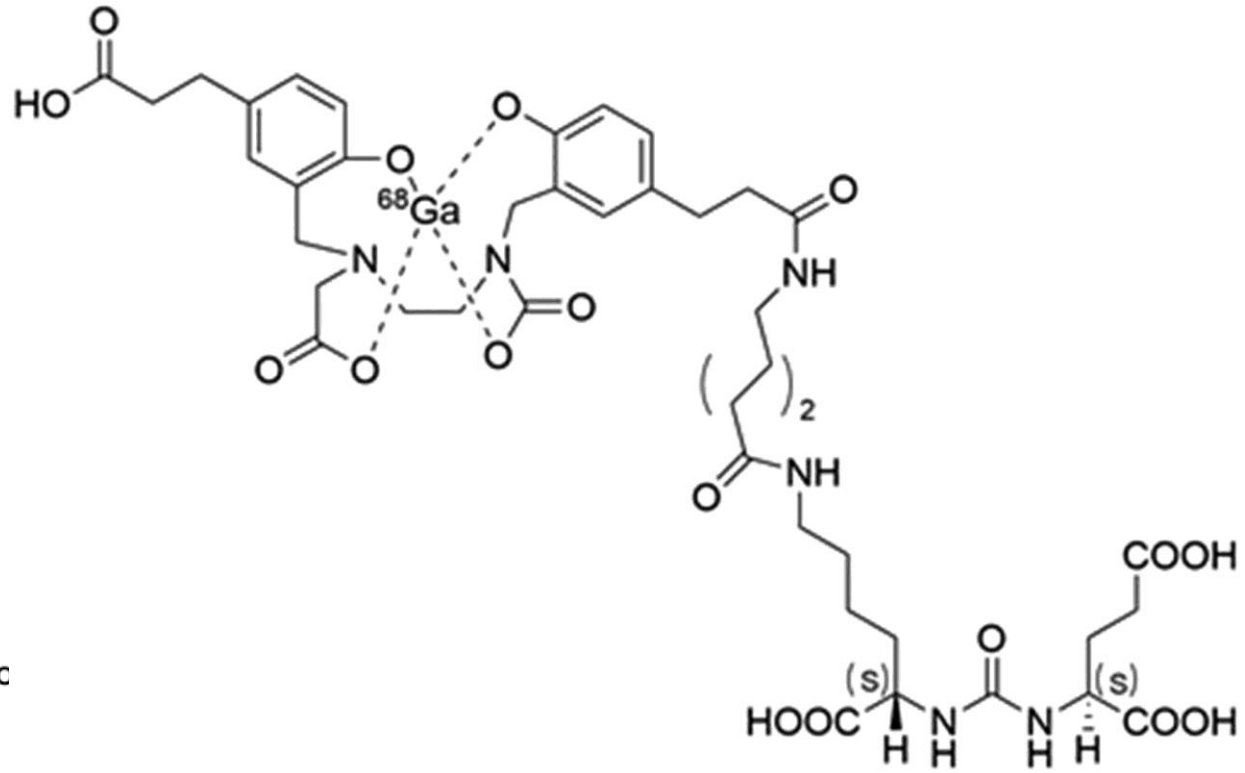
[177Lu]Lu-PSMA-617 & [68Ga]Ga-PSMA-11





[177Lu]Lu-PSMA-617 & [68Ga]Ga-PSMA-11





Granted FDA approval[15]: December 1, 2020

Mechanism for 177Lu-PSMA-617

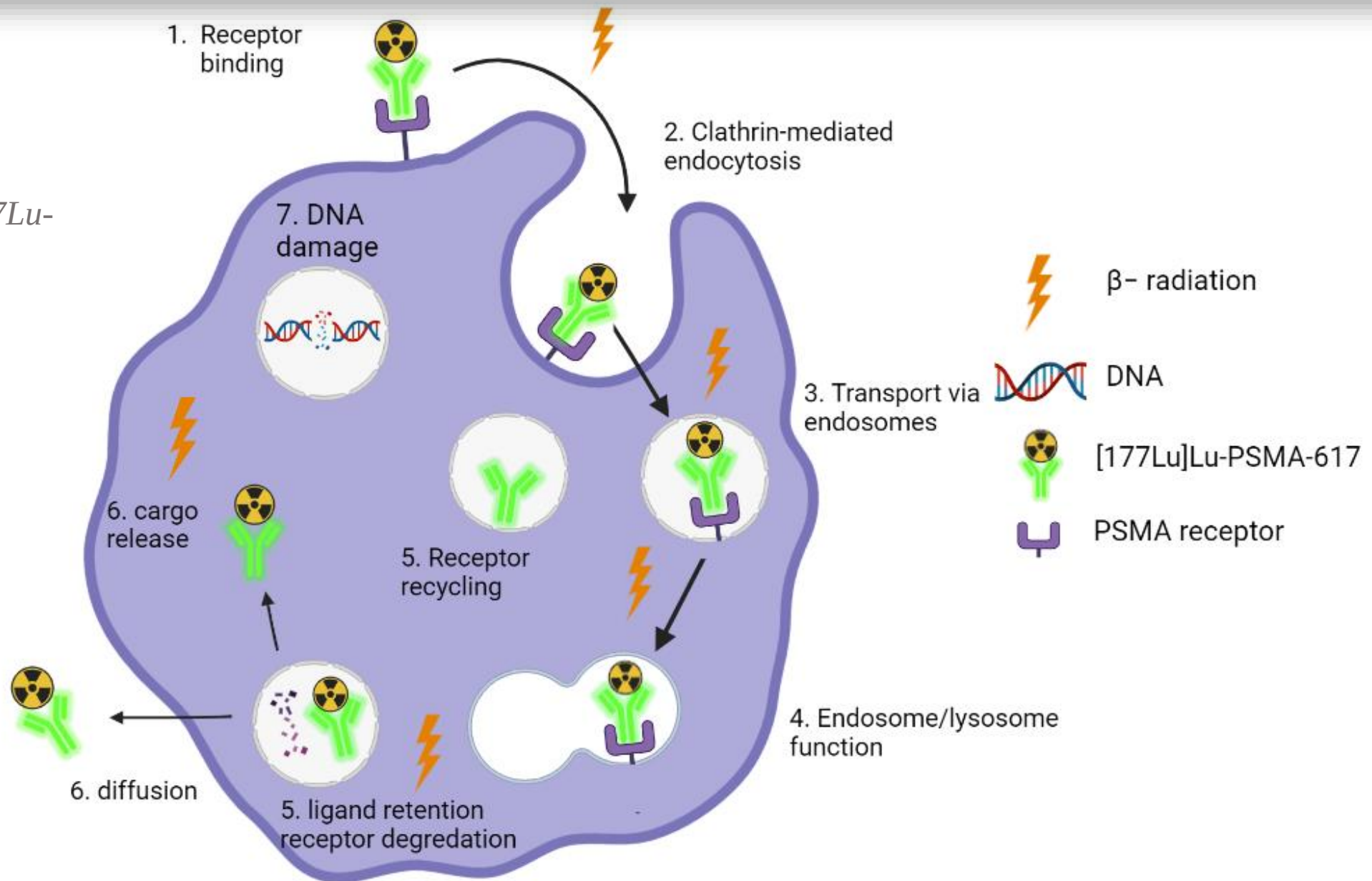


Figure 1: *177Lu-PSMA-617 mechanism*[10]

2016 SNMMI Image of the Year

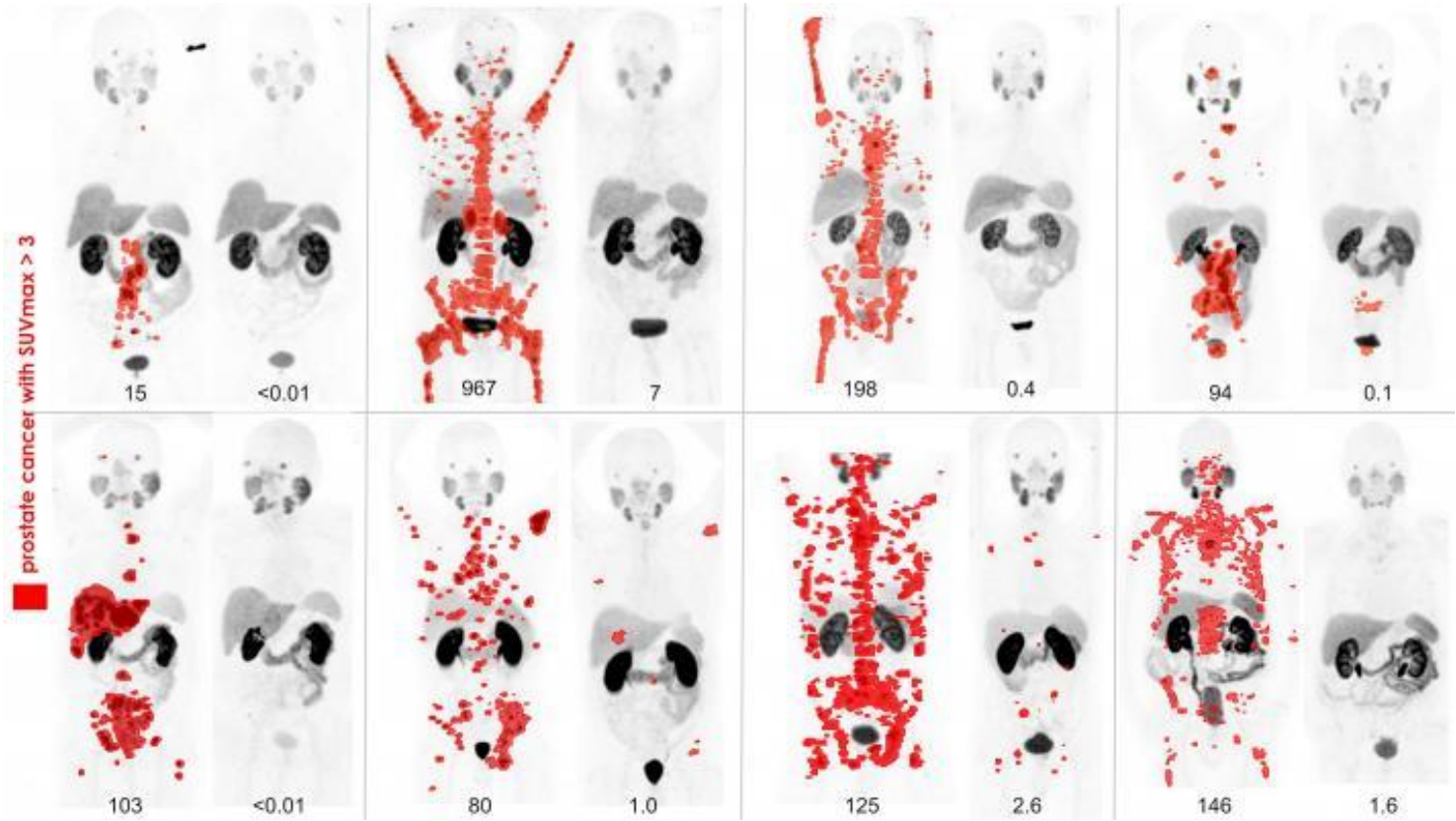


Figure 2: *68Ga-PSMA11 PET maximum intensity projection (MIP) images at baseline and 3 months after 177Lu-PSMA617 in 8 patients with PSA decline ≥ 98 percent in a prospective phase II study. Any disease with SUV over 3 is in red.*[12]

Clinical Trials

- PSA decreased in 47/74 patients (64%)[12]
- PSA decreased by more than 50% in 23/74 patients (31%)[12]
- PSA levels were stable (- 50%-+25%) in 35/74 patients (47%)[12]

University Hospital Münster

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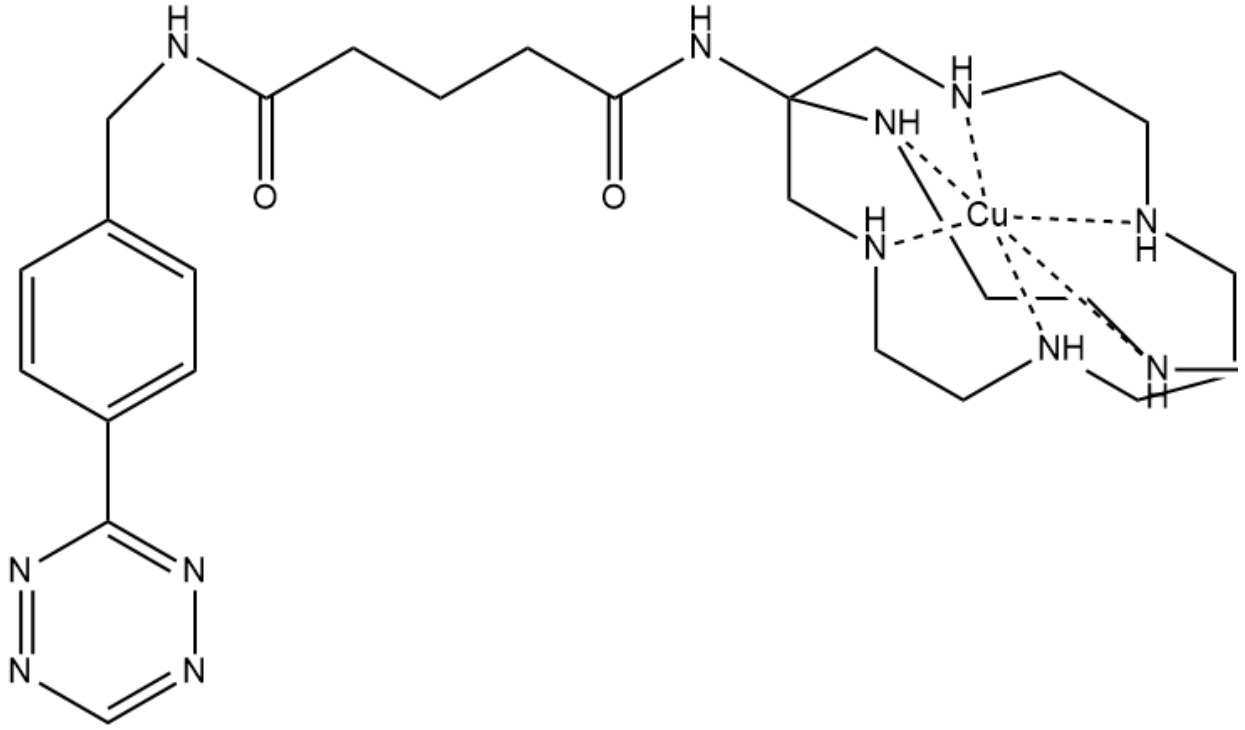
University Hospital Münster

No significant loss of red blood cells, white blood cells, or kidney function mild decline in platelets, but within normal range.[12] Eventual FDA approval in March 2022.

1 vs 2 Treatments

- Relative to their research, PSA decreased in 59% of patients after 1 treatment and in 75% after 2 treatments[12]
- PSA decreased by > 50% in 32% of patients after 1 treatment and in 50% after 2 treatments[12]
- A key point to note is that this study was done on individuals who had exhausted all other options and found no hope with traditional methods (diet and chemotherapy)[12]
- Median survival was 29 weeks, compared to 20 weeks based on medical doctoral expectations[12]

64Cu/67Cu pre-targeted radioimmunotherapy



The presumed base structure of Cu-MeCOSar-Tz[3]

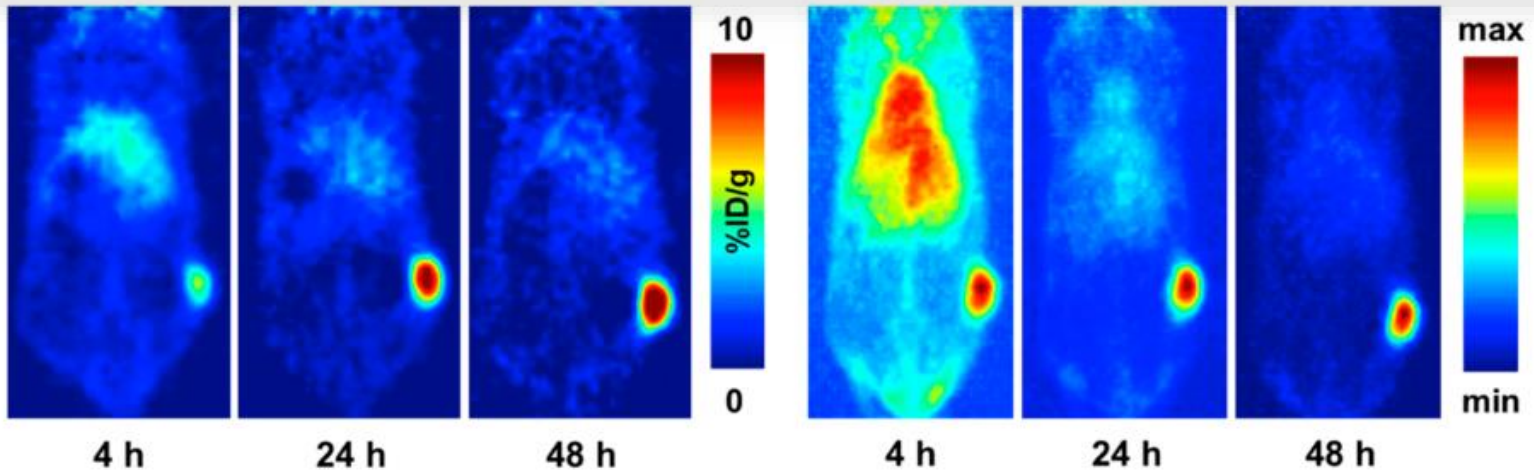
California Institute of Technology

Experimental Trials

- four mice that experienced tumor regrowth had the lowest uptake of [64Cu]Cu-MeCOSar-Tz in the tumor: 3.0, 4.1, 5.6, and 6.8 kBq[3]
- six mice with higher levels of [64Cu]Cu-MeCOSar-Tz in the tumor—all >9.0 kBq—exhibited complete tumor remission[3]
- the SPECT images obtained from [67Cu]Cu-MeCOSar-Tz closely mirror the PET images, reinforcing the Theranostic value of the latter[3]

Experimental Trials

SPECT IMAGES



SPECT/CT IMAGES

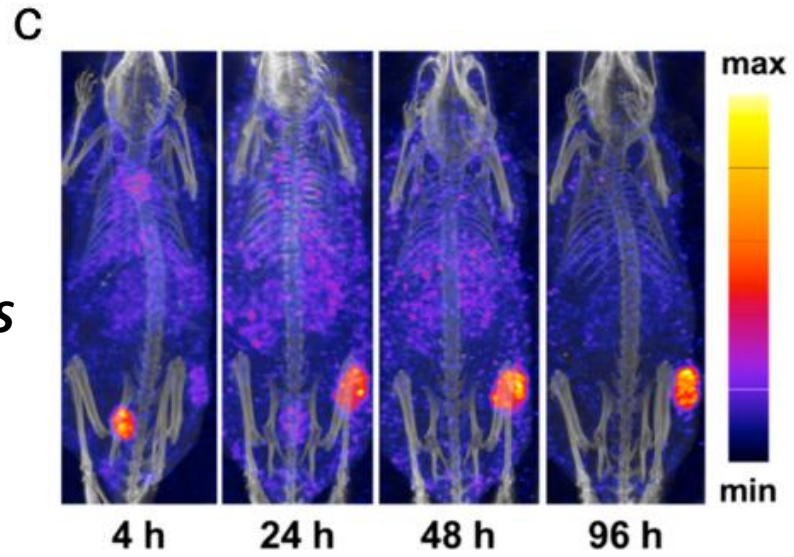
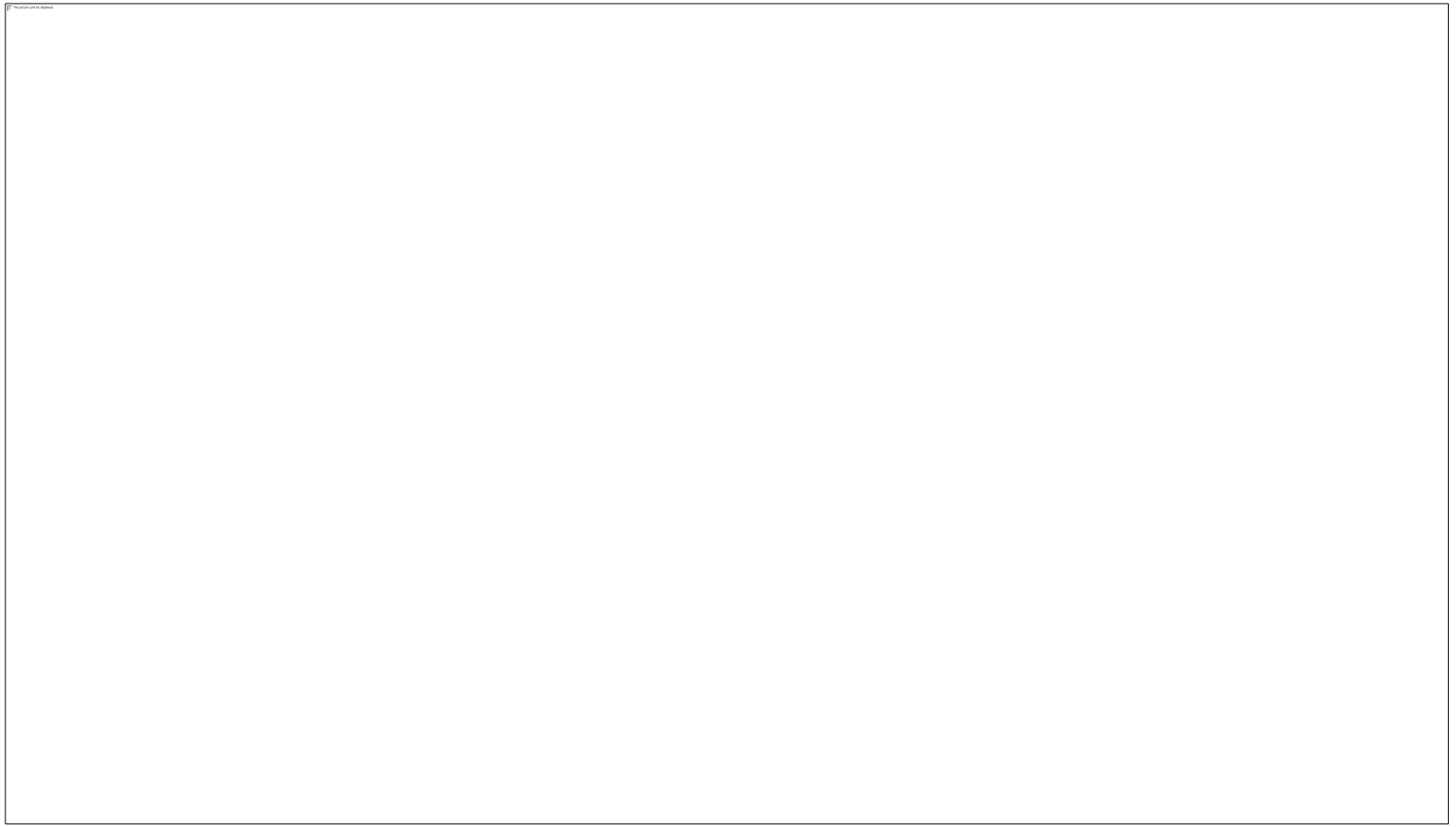


Figure 3: *Coronal slice and MIP PET images of a representative mouse in the theranostic cohort at 4, 24, and 48 h post injection of [^{64}Cu]Cu-MeCOSar-Tz. The coronal slices intersect the center of the tumor. (C) SPECT-CT MIP images of the same representative mouse from the theranostic cohort collected at 4, 24, 48, and 96 h after the administration of [^{67}Cu]Cu-MeCOSar-Tz.*[3]

Alpha DaRT Radiation therapy



Alpha DaRT by Alpha Tau Medical. (n.d.). Www.youtube.com. Retrieved January 1, 2023, from https://www.youtube.com/watch?v=mbhntcM-Oic[1]

Alpha DaRT known Clinical Applications

- Most superficial tumors can be stratified into high- or low-risk groups[11]
- 15% to 25% are at high risk for progression to muscle invasion[11]
- Works particularly well on “Solid” tumors, such as sarcomas, carcinomas, and lymphomas.[16]
- In a first-in-human trial of certain skin cancers or head and neck tumors, Alpha DaRT achieved a 100% overall response rate with over 78% complete response rate, where the tumor completely disappeared.[11]

Summary of Experimental Trials

Cancer	Murine Cells in Mice	Human Cells in Athymic Mice
Squamous Cell Carcinoma	X	X
Lung Squamous Cell Carcinoma		X
Lung Adenocarcinoma	X	X
Pancreas adenocarcinoma	X	X
Prostate Adenocarcinoma	X	X
Breast Carcinoma	X	X
Glioblastoma multiforme		X
B-Cell Lymphoma	X	X
Melanoma	X	X
Colon Carcinoma	X	X

Figure 4: *Experimental models of mouse and human-derived tumors*[5;6;9;11;16]

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Cancer	Murine Cells in Mice	Human Cells in Athymic Mice
Squamous Cell Carcinoma	X	X
Lung Squamous Cell Carcinoma		X
Lung Adenocarcinoma	X	X
Pancreas adenocarcinoma	X	X
Prostate Adenocarcinoma	X	X
Breast Carcinoma	X	X
Glioblastoma multiforme		X
B-Cell Lymphoma	X	X
Melanoma	X	X
Colon Carcinoma	X	X

Figure 4: *Experimental models of mouse and human-derived tumors*[5;6;9;11;16]

RESULTS:

- DaRT achieves a high degree of tumor ablation (destruction) of mouse and human-derived tumor cells of various histological types.[2;5;6]
- DaRT can be combined with chemotherapy to achieve better control of local and metastatic cancer[10]

Points of future research

- Radiolabeling of HER2+[17]
- Mastering of possible Copper/Silver/Gold treatments[4]
- Theranostics with iron oxide core[14]
- Development of efficient attachment molecules[10]

General Discussion/Conclusion

- We must think outside of the box to find better solutions
- We need to learn more about our body and its mechanisms
- Find ways to treat cancers right away
- Maintain hope

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