Lead-203/212 User Group Meeting

PRE-CLINICAL AND CLINICAL EXPERIENCE WITH TARGETED ALPHA-EMITTER THERAPY

Izabela Tworowska, PhD

CSO, RadioMedix

RadioMedix
INNOVATING THERANOSTICS

RADIOMEDIX PIPELINE (selected radiotheranostics agents)

AGENT	TARGET	COLLABORATION	STATUS
AlphaMedix™ ^{212}Pb-somatostatin analog	Neuroendocrine tumors	ORANO MED –business partnership	Phase II multi-center clinical studies
^{68}Ga/^{212}Pb-RMX-VH	GBM, PDAC, Ovarian cancer	Vect-Horus (France) - collaboration	^{68}Ga-RMX-VH (eIND Excel/MDAnderson)
RMX-GPC3	Solid tumors		Pre-clinical
^{225}Ac-PSMA-I&T	Prostate cancer	RadioMedix – CMC/manufacturing	Phase II clinical study

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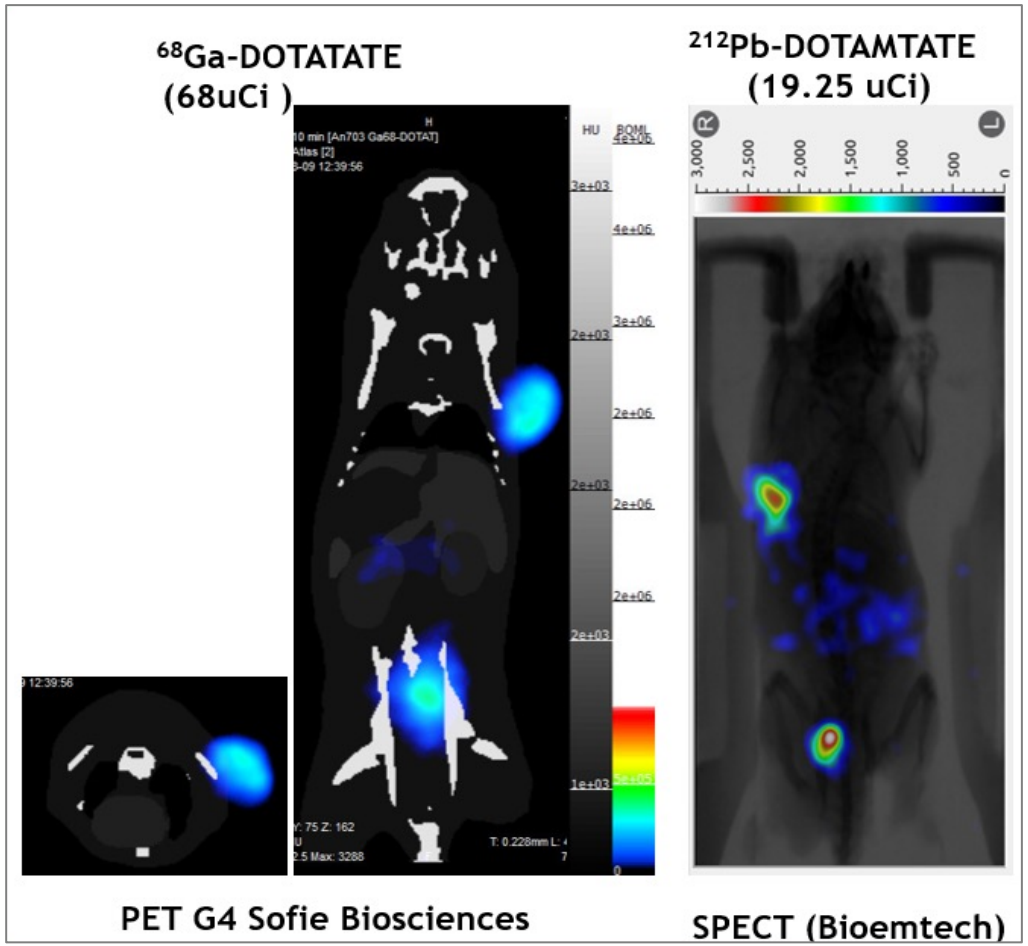
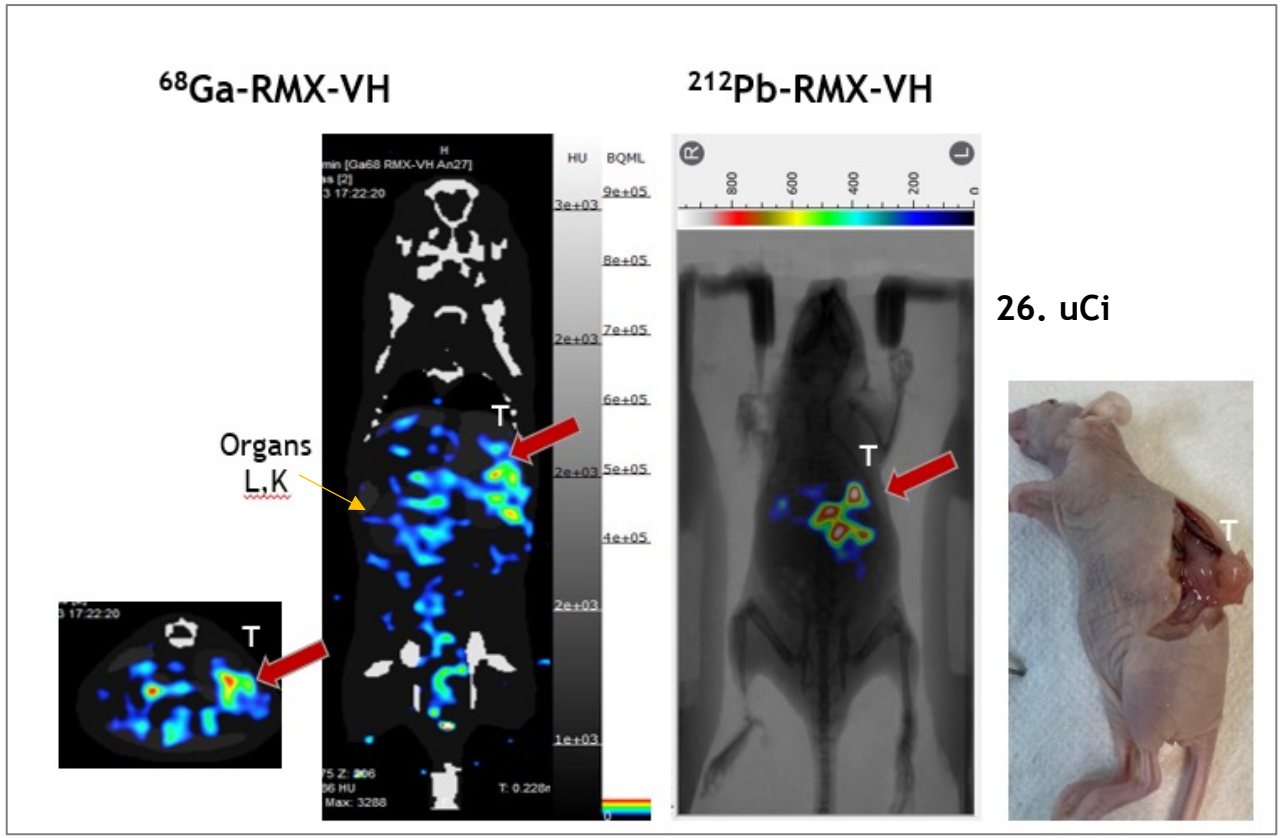
RadioMedix pre-clinical core facility: imaging

Leo G. Flores II, MD, PhD
Xuewei Qu, PhD
Alex Puente



Rafal Zielinski, PhD
MDAnderson Cancer Center



γ-eye™

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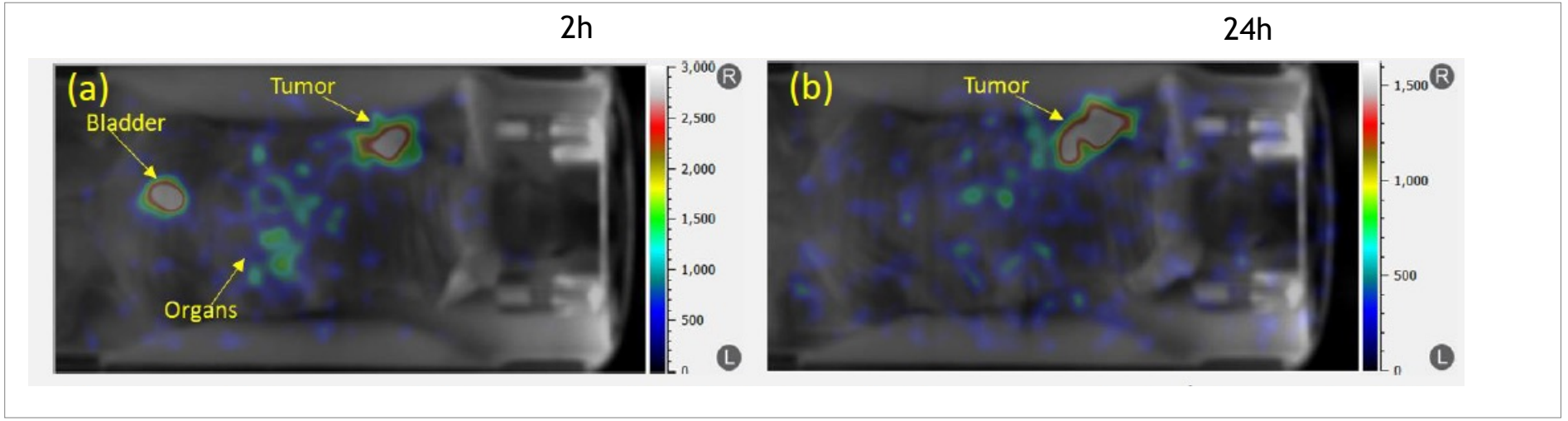
Lead-203/212 User Group Meeting

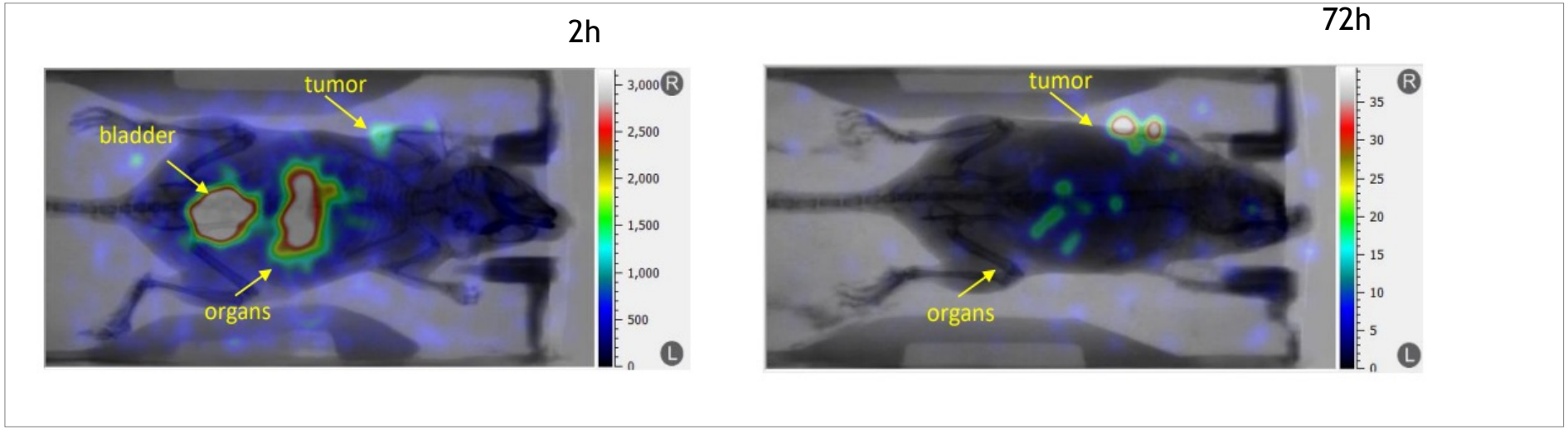
^{212}Pb-RMX-PSMA (19uCi)



BIOEMTECH

γ-eye™

^{225}Ac-RMX-PSMA (3.5uCi)



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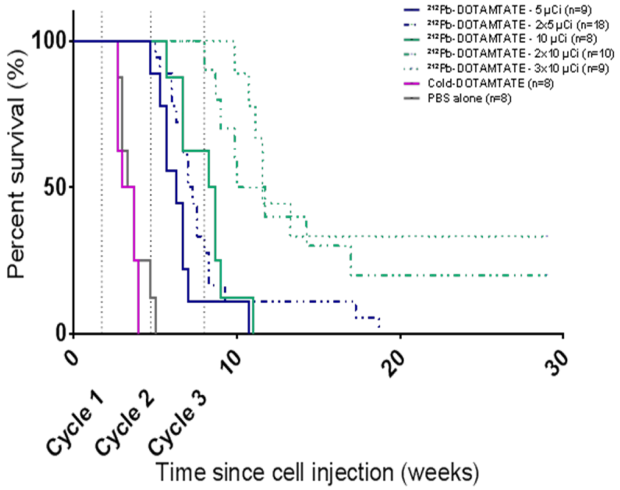
^{212}Pb-DOTAMTATE from bench to bedside

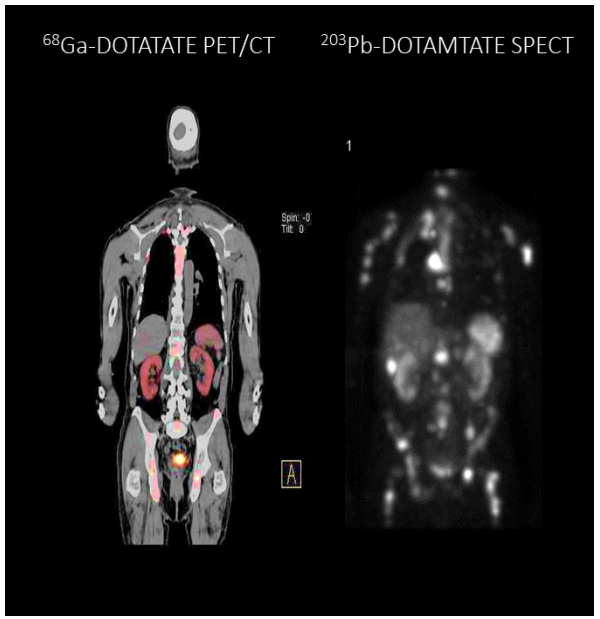
2016 — ^{203}Pb/^{212}Pb-DOTAMTATE pre-clinical studies

2017 — eIND clinical ^{203}Pb-DOTAMTATE

2018 — Phase I dose escalation of ^{212}Pb-DOTAMTATE

2021 — Phase II clinical study





DOSE	MST[week]
5uCi	6.3
2X5uCi	7.1
10uCi	8.5
2x10uCi	10.9 (20%)
3x10uCi	11.6 (33%)
Cold AR-RMX	3.4
PBS	3.5

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oranomed

EXCEL DIAGNOSTICS NUCLEAR ONCOLOGY CENTER

Rapid

^{212}Pb-DOTAMTATE

CENTRALIZED PRODUCTION OF DOSES: ORANOMED

<table>
<tr><td colspan="2">Phase 1
Non-Randomized, Open-Label, Dose Escalation, of
Pb^{212}-DOTAMTATE (AlphaMedix™) in Adult Subjects
with Somatostatin Receptor Expressing
Neuroendocrine Tumors (NET)</td><td colspan="2">Phase II
Open Label Study to Evaluate the Safety and Effectiveness of ^{212}Pb-DOTAMTATE in Subjects with Somatostatin Receptor Expressing Neuroendocrine Tumors</td></tr>
<tr><td>PRRT naïve patients
Dose escalation studies
22 patients
Cohort 1& 2 (SAD1 and 2)
single therapy
DOSIMETRY
Cohort 3
4 patients/ 3cycles
Cohort 4
12 patients/4 cycles</td><td>Patients progressed
after PRRT
11 patients
Dosing as MAD4
4 cycles/8 weeks</td><td>PRRT naïve patients
Multi-center</td><td>Patients progressed
after PRRT
Multi-center</td></tr>
<tr><td colspan="2"></td><td colspan="2">The primary objectives
To evaluate the efficacy of through overall response rate (ORR),
safety and tolerability
Secondary Objectives
To determine median Progression free survival (mPFS), Overall Survival (OS), Time to Tumor Progression (TTP); and the health-related quality of life (HRQL), relative to baseline.</td></tr>
</table>

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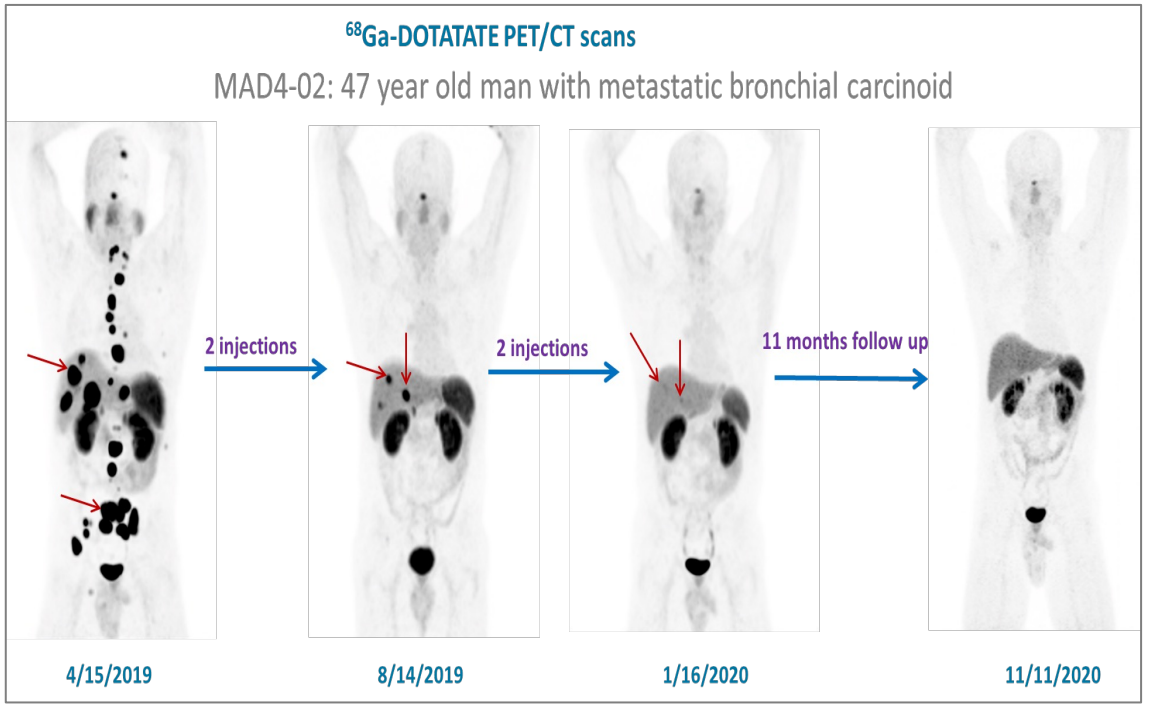
OBJECTIVES AND DEMOGRAPHIC INFORMATION

Subject	Type of NET	Stage	µCi/kg	Cumulative Dose (mCi)
SAD1-01	Midgut	IV	30.7	2.1
SAD1-02	Pancreatic	IV		2.3
SAD1-03	Pancreatic	IV		2.3
SAD2-01	Rectal	IV	40.0	3.3
SAD2-02	Midgut	IV		2.7
SAD2-03	Midgut	IV		3.2
SAD3-01	Midgut	IV	52.0	15.0
SAD3-02[a]	Pancreatic	IV		8.9
SAD3-03	Midgut	IV		7.2
SAD3-04	Pancreatic	IV		12.3
MAD4-01	Midgut	IV	67.6	22.0
MAD4-02	Bronchial	IV		21.6
MAD4-03	Bronchial	IV		19.2
MAD4-04	Rectal	IV		21.8
MAD4-05	Pancreatic	IV		23.6
MAD4-06	Pancreatic	IV		18.4
MAD4-07	Rectal	IV		23.2
MAD4-08	Midgut	IV		18.7
MAD4-09	Bronchial	IV		22.6
MAD4-10	Bronchial	IV		22.9
MAD4-11	Pancreas	IV		22.13
MAD4-12	Pancreas	IV		14.1



[a] SAD3-02 dropped out of the study after the second cycle and was replaced by SAD3-04.

PRRT NAIVE PATIENTS - SUMMARY OF RADIOLOGICAL RESPONSE

9 OUT OF 12 PATIENTS (75%)

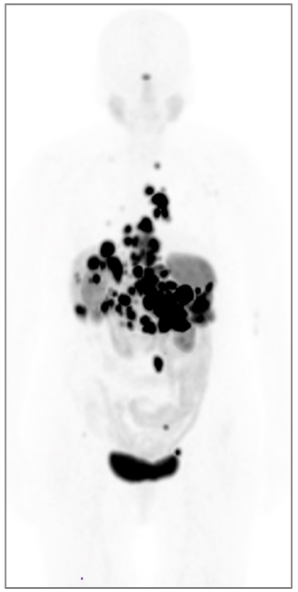
PRRT naïve patients	Last treatment	Response by RECIST v.1.1
MAD4-01	7-Nov-19	**PR**
MAD4-02	19-Nov-19	**CR**
MAD4-03	3-Dec-19	**CR**
MAD4-04	19-May-20	SD
MAD4-05	21-May-20	**PR**
MAD4-06	28-May-20	**CR***
MAD4-07	19-Nov-20	**PR**
MAD4-08	1-Dec-20	SD
MAD4-09	9-Feb-21	SD
MAD4-10	18-Mar-21	**PR**
MAD4-11	20-Jul-21	**PR**
MAD4-12	29-Jul-21	**PR**

PHASE I STUDY IND # 135150 FOR PRRT PROGRESSED SUBJECTS

4 cycles at 67.6 µCi/kg/cycle.

Subject ID	Primary Tumor location	Grade	Cumulative dose
MAD4-R01	Sm. Bowel	G1	19.7
MAD4-R02	Thymus	n/a	23.0
MAD4-R03	Pulmonary	G3	22.3
MAD4-R04	Pancreatic	G2	22.6
MAD4-R05	Sm. Bowel	G2	22.3
MAD4-R06	Pancreatic	G3	23.1
MAD4-R07	Sm. Bowel	n/a	23.1
MAD4-R08	Midgut	n/a	5.7*
MAD4-R09	Sm. Bowel	G2	17.2
MAD4-R10	Pancreatic	G2	15.8
MAD4-R11	Pancreatic	G2	23.2

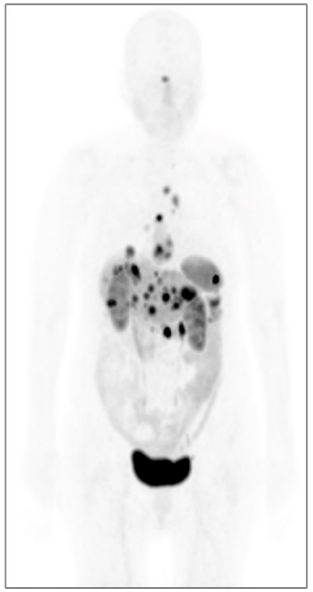
MAD4-R06 71 year old man with refractory G3 pulmonary carcinoid. Treated previously (2017) with ^{177}Lu-DOTATATE



4/6/2021

^{64}Cu-DOTATATE PET/CT scans

Response by RECIST: PR



11/10/2021

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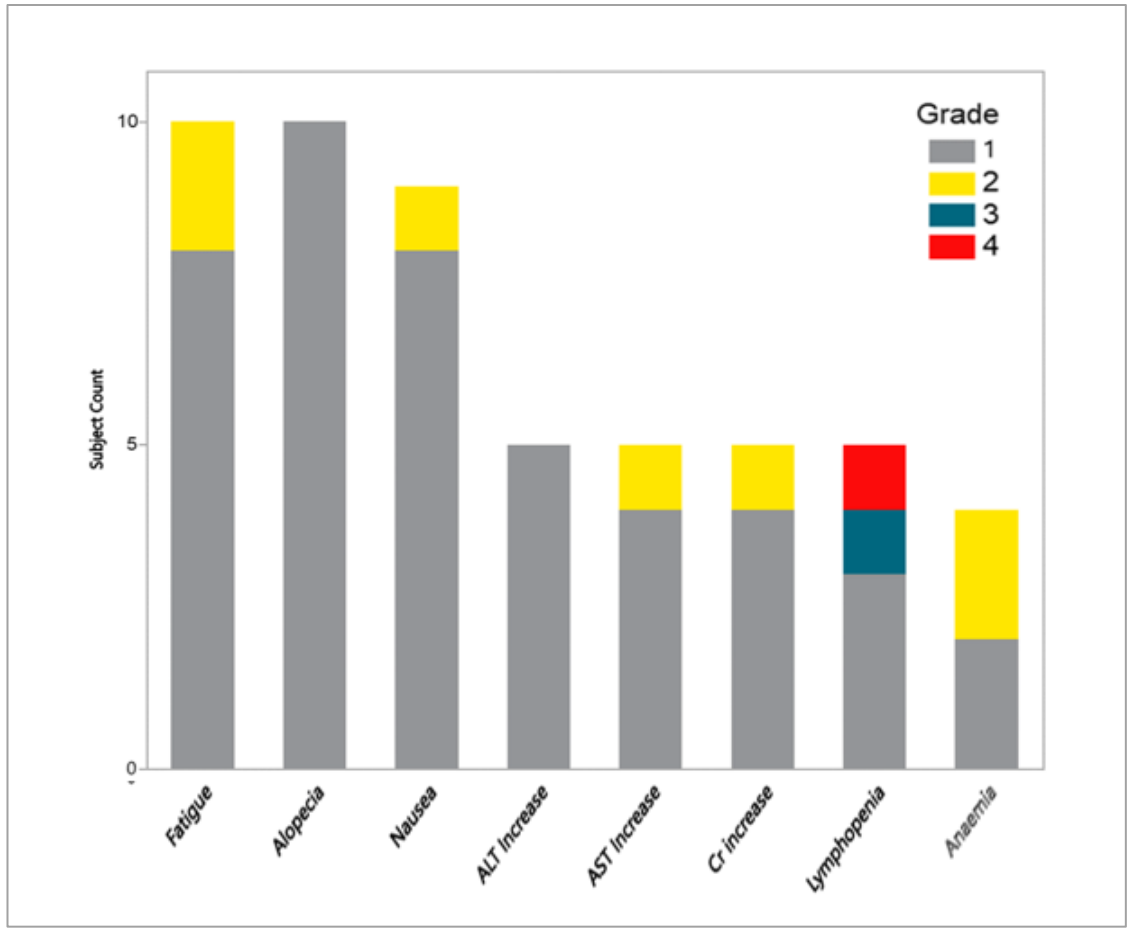
PRRT PROGRESSED PATIENTS- SUMMARY OF RADIOLOGICAL RESPONSE

6 OUT OF 10 PATIENTS

PRRT PROGRESSED PATIENTS	LAST TREATMENT	STATUS	LAST VISIT	RESPONSE BY RECIST V.1.1
MAD4-R01	3-Dec-20	Alive	10 month follow up	SD
MAD4-R02	17-Dec-20	Alive	15 months follow up	**PR**
MAD4-R03	15-Sep-21	Alive	6 months follow up	SD
MAD4-R04	9-Sep-21	Alive	6 month follow up	**CR**
MAD4-R05	23-Sep-21	Alive	3 months follow up	**PR**
MAD4-R06	16-Sep-21	Deceased*	2 months post INV4	**PR**
MAD4-R07	16-Nov-21	Deceased*	2 months post INV4	**PR**
MAD4-R08	1st and last dose: 5/6/2021	Deceased*	0.5 months post INV1	N/A
MAD4-R09	16-Dec-21	Alive	3 months follow up	SD
MAD4-R10	30-Sep-21	Alive	Due to elevated Cr: not completed the last dose.	SD
MAD4-R11	1-Feb-22	Alive	3 months follow up	**PR**

*not drug releated

COMMON ADVERSE EVENTS



SUMMARY

- Progress in the pre-clinical $^{212}Pb/^{225}Ac$ imaging
- Pb^{212}-DOTAMTATE Phase I studies: SAFE and HIGHLY EFFECTIVE DOSE of in patients with metastatic SSTR expressing neuroendocrine tumors regardless of the location and Ki-67 index of the primary tumor

PRRT naive	PRRT progressed
Objective radiological response: 9/12 subjects per RECIST 1.1	Objective radiological response: 6/10 subjects per RECIST 1.1
No clinically significant hematological, renal, or hepatic toxicity.	70% subjects demonstrated response by SSTR PET/CT imaging
No progression : 11 /12 subjects as of April 2022 - up to 4 years after the first treatment	No clinically significant (grade ¾) hematological, renal, or hepatic toxicity
1 subject progressed (PFS: 14 M): FDG (+), SSTR (-).	

- **Phase II study started in December of 2021**

RadioMedix $^{212}Pb/^{225}Ac$ imaging:

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Small Business Technology Transfer (STTR)

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