MAYO CLINIC

ISA
INTERNATIONAL SOCIETY OF AMYLOIDOSIS

XIX INTERNATIONAL SYMPOSIUM ON AMYLOIDOSIS

MAY 26-30, 2024 – ROCHESTER, MN

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INDUSTRY

- Founding shareholder of Attralus Inc.
- ^{124}I-evuzamitide (^{124}I-AT-01) was provided by Attralus.
- Inventor on IP related to amyloid imaging peptides.

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

CHANGES IN ORGAN-SPECIFIC AMYLOID LOAD ASSESSED BY SERIAL PET/CT IMAGING OF IODINE (^{124}I) EVUZAMITIDE

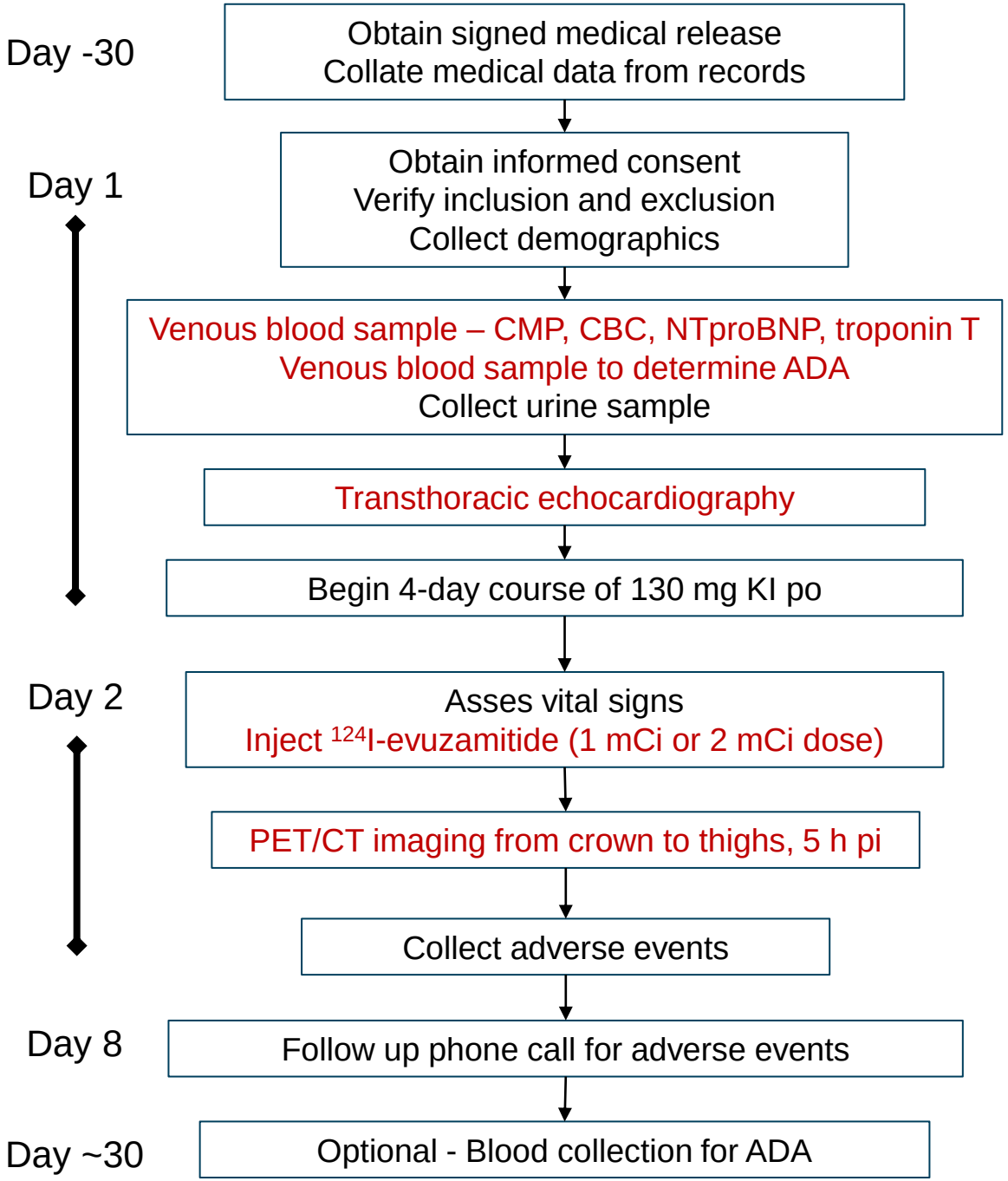
CORRELATION WITH SERUM BIOMARKERS

This was a single center, open-label, single arm PET/CT imaging study in subjects with AL or ATTR amyloidosis who had been previously imaged with ^{124}I-evuzamitide (AT-01).

The primary objective was to measure visual and quantitative changes in organ-specific uptake of ^{124}I-evuzamitide from baseline, in patients with systemic amyloidosis, using PET/CT imaging.

Uptake of radiotracer in the organs was assessed by measuring the standard uptake value ratio (SUVR) – the amount of radioactivity per unit volume scaled by the blood pool radioactivity. Correlations with serum biomarkers were assessed.

REPEAT IMAGING PROTOCOL



POPULATION CHARACTERISTICS

Characteristics	Patient (*N* = 19)
Age (years)	
Median (IQR)	72 (63, 76)
Gender	
Male	11 (58%)
Ethnicity	
Not Hispanic or Latino	19 (100%
Race	
Black or African American	1 (5%)
White	18 (95%)
Time Since SA Diagnosis (years)	
Median (IQR)	7 (6, 9)
Time Since baseline imaging in AMY1001 study	
Mean ±SD (years)	2.9 ± 0.9
Amyloid Type	
AL	9 (47%)
ATTR; Mutation type	10 (53%)
L58H	3 (16%)
T60A	5 (26%)
V30M and V122I	1 (5%)
Wild type	1 (5%)
Amyloid therapy at time of imaging	
AL (% of AL patients; *n*=9)	2 (22%)
ATTR (% of ATTR patients; *n*=10)	10 (100%)
Stabilizer only	1 (10%)
Silencer only	5 (50%)
Stabilizer and silencer	4 (40%)

Clinical Characteristic	AL (*n*=9)[1]	ATTR (*n*-=10)	All (*N*=19)
IVS thickness (cm)	1.5±0.3	1.6±0.3	1.6±0.3
LV wall thickness (cm)	1.3±0.4	1.4±0.5	1.3±0.4
GLS (%)	-14.5±4.0	-13.2±4.9	-13.8±4.4
NTproBNP (pg/mL)	525 (160.5,954)	387 (219,1591) (*n*=9)	456 (164.8,1239) *n*=18)
Troponin T (ng/L)	17.5 (11.5,30.8) (*n*=8)	28.5 (15.8,43.5) (*n*=8)	23.5 (14.3,32.5) (*n*=16)
eGFR (mL/min/1.73)	71.0±17.0	74.5±18.2	72.8±17.3
Cre (mg/dL)	1.1±0.2	1.0±0.4	1.0±0.3
BUN (mg/mL)	21.1±8.4	19.7±6.0	20.4±7.0
Free κ LC (mg/L)	26.4 (17.3,44.1)	15.5 (12.3,24.1)	20.9 (13.2,31.4)
Free λ LC (mg/L)	13.3 (10.8,19.8)	11.4 (8.3,13.8)	11.5 (10.5,15.2)
κ/λ ratio	1.9 (1.0,2.8)	1.6 (1.3,1.9)	1.7 (1.2,2.2)

At repeat imaging:
Six (6/9) AL patients had elevated FLC.
Five (5/9) AL patients had elevated κ/λ ratios

Four (4/10) ATTR patients had elevated FLC (κ).

VISUAL EVALUATION OF IMAGES

		Heart		Liver		Spleen		Kidney	
Amyloid	Patient	Baseline	Repeat	Baseline	Repeat	Baseline	Repeat	Baseline	Repeat
ATTR	P001	Y	Y	N	N	N	N	N	N
AL	P002	Y	Y	Y	N	Y	Y	N	N
AL	P003	Y	Y	Y	Y	Y	Y	Y	Y
ATTR	P004	Y	Y	N	N	N	N	N	Y
ATTR	P005	Y	Y	N	N	N	N	N	N
ATTR	P006	Y	Y	N	N	N	N	N	N
AL	P007	Y	Y	N	N	N	N	N	Y
ATTR	P008	Y	Y	Y	N	Y	N	Y	Y
ATTR	P009	Y	Y	N	N	N	N	N	N
AL	P010	Y	Y	N	N	N	N	Y	Y
ATTR	P011	Y	Y	N	N	N	N	N	N
ATTR	P012	Y	N	Y	N	Y	N	Y	Y
ATTR	P013	Y	Y	Y	N	Y	N	Y	N
AL	P014	Y	Y	Y	N	N	N	Y	Y
AL	P015	Y	Y	N	N	N	N	N	Y
AL	P016	Y	N	Y	N	Y	N	Y	Y
ATTR	P017	Y	Y	N	N	Y	N	N	Y
AL	P018	Y	Y	Y	Y	Y	Y	Y	Y
AL	P019	N	Y	N	Y	Y	Y	Y	Y

Green
Remained positive
Grey
Remained negative
Orange
Became negative
Red
Became positive

Only one patient with increase in visual cardiac uptake

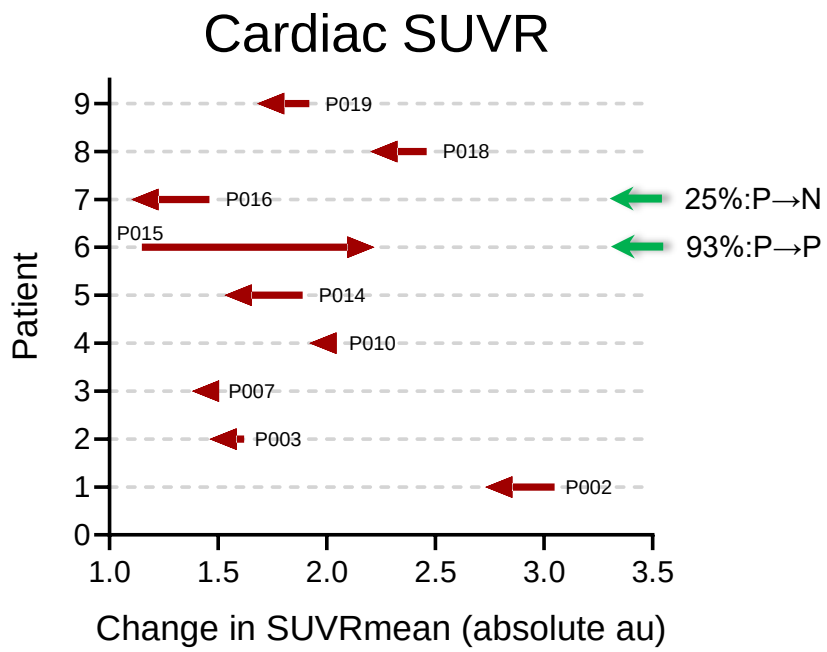
SUMMARY – VISUAL ASSESSMENT OF PET/CT

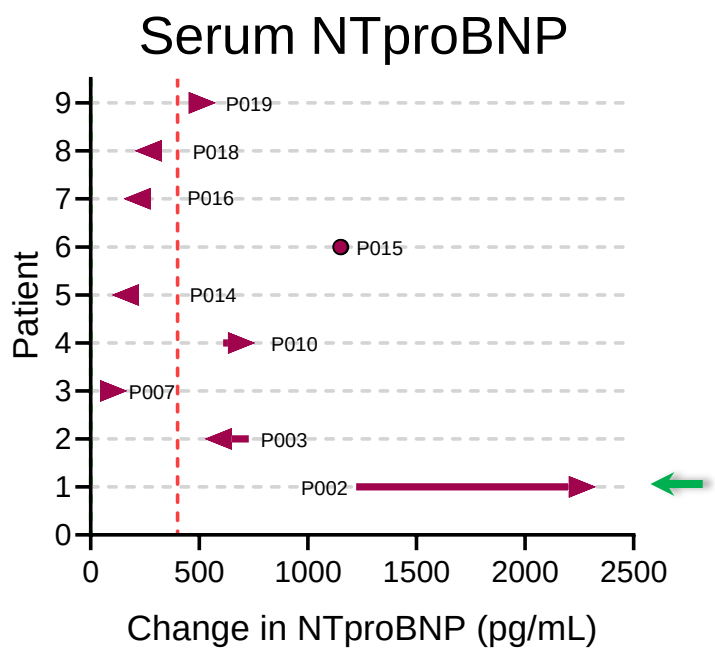
In the all-subject population (*N* = 19):

- 14 patients (*n*=14, 74%) had no increase in ^{124}I-evuzamitide visually positive organs among the heart, liver, spleen, or kidney
- Two patients (*n*=2, 11%) with positive cardiac amyloid at baseline were deemed visually negative at repeat imaging.
  - P012 (ATTR) – vutrisiran: NTproBNP 395→186 pg/mL: SUVR 1.41→1.06
  - P016 (ALκ) – No Tx: κFLC 77→54 mg/L: NTproBNP 199→152 pg/mL: SUVR 1.46→1.10
- Only one patient (*n*=1, 5%), with AL amyloidosis, had positive uptake in the heart that was deemed negative at baseline.
- Five patients (*n*=5, 26%) had a change from negative to positive organ uptake, almost exclusively (4/5; 80%) associated with renal uptake.

CARDIAC UPTAKE WAS STABLE IN THIS POPULATION

AL amyloidosis

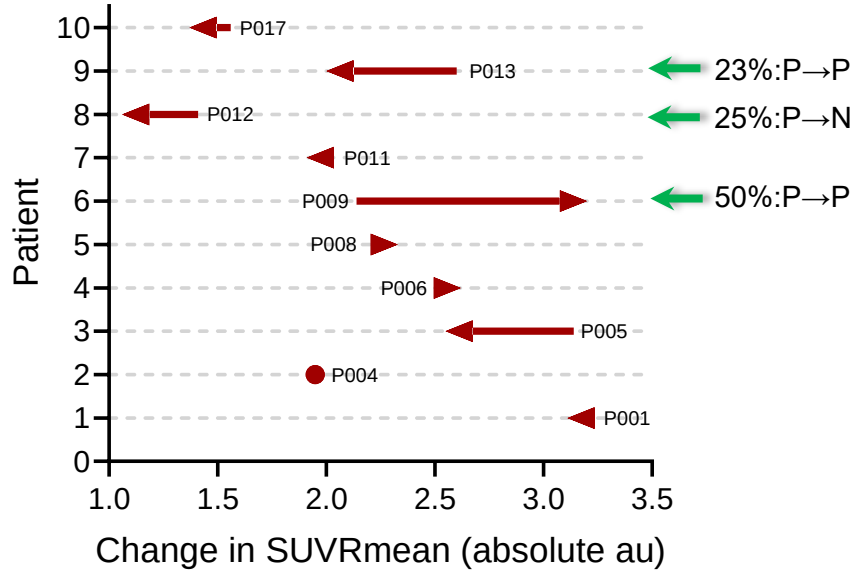


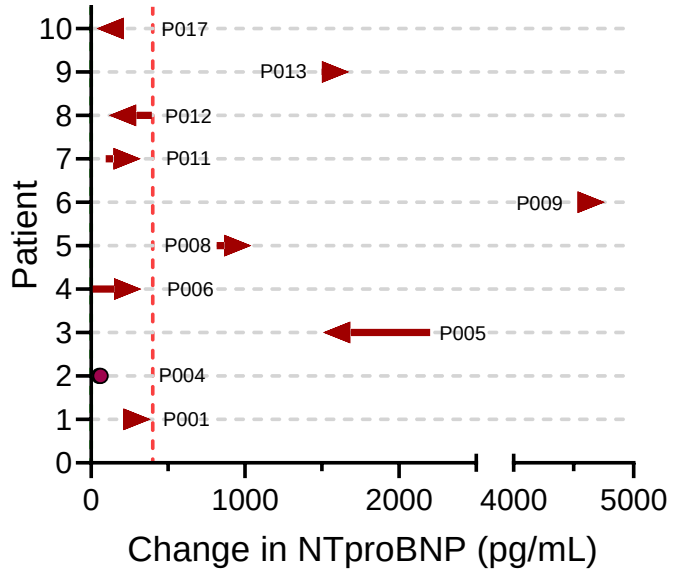


Only one AL patient had an increase in cardiac SUVR.

Only one AL patient had significant increase in NTproBNP – independent of the cardiac SUVR (with increasing FLC).

ATTR amyloidosis





Only one ATTR patient had an increase in cardiac SUVR.

NO patients had significant increase in NTproBNP. Most (60%) patients had normal NTproBNP.

SUMMARY – QUANTITATIVE EVALUATION OF IMAGES

In the AL patient population (*n* = 9):

- 1/9 (11%) – Reduced cardiac SUVRmean to near normal.
- 7/9 (78%) – Stable cardiac SUVRmean.
- 1/9 (11%) – 93% increase in cardiac SUVRmean (no change in NTproBNP).
- 8/9 (89%) – Stable NTproBNP with 1/9 (11%) increasing NTproBNP.

In the ATTR patient population (*n* = 10):

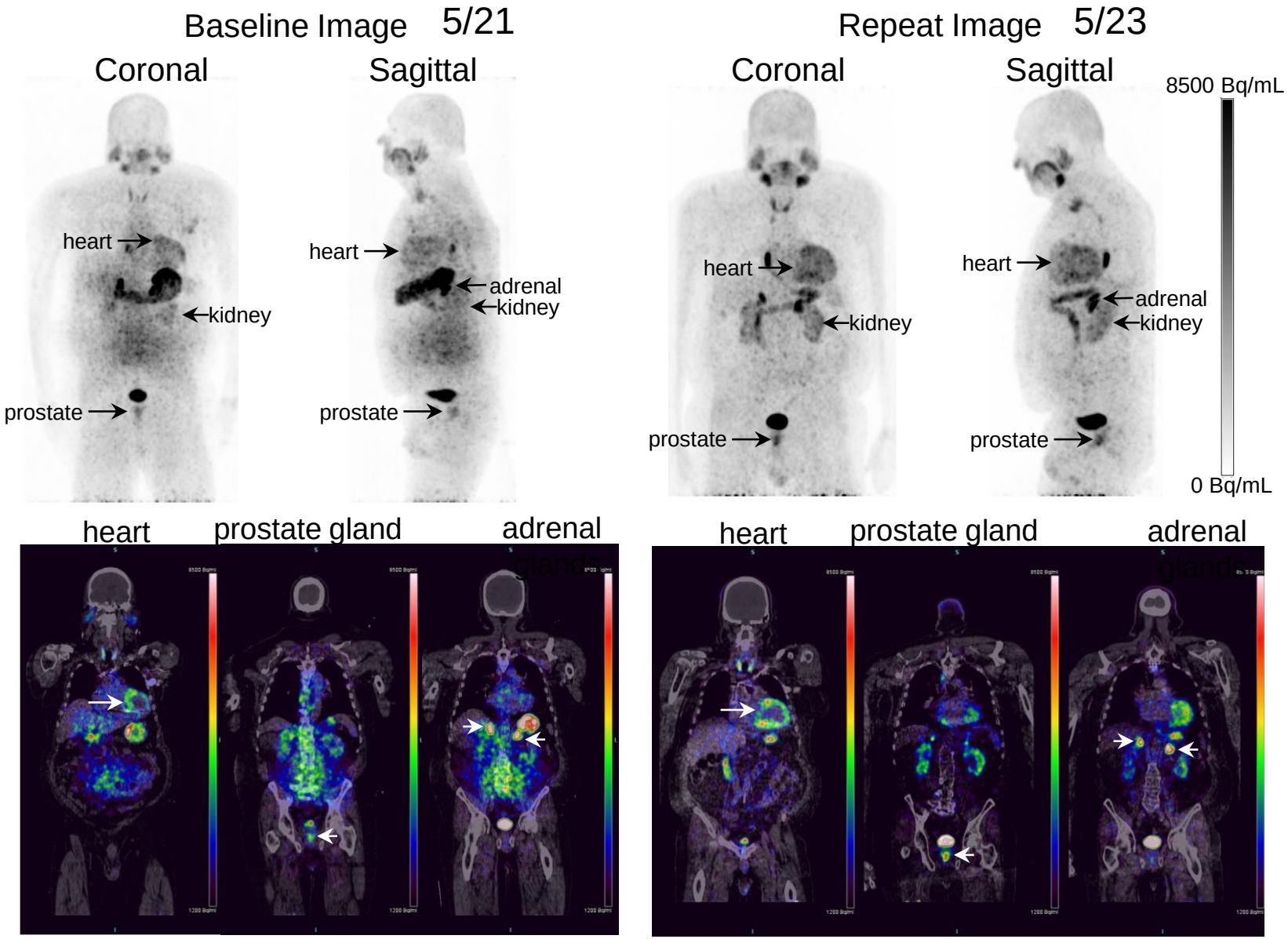
- 2/10 (20%) – Reduced cardiac SUVRmean (>20% decrease).
- 7/10 (70%) – Stable cardiac SUVRmean.
- 1/10 (10%) – 49.5% increase in cardiac SUVRmean (no change in NTproBNP).
- 9/10 (90%) – Stable NTproBNP levels with 1/10 (10%) decreasing NTproBNP.

CASE STUDIES

CARDIAC AMYLOID PROGRESSION - AL

Case 1 [RPT P015]

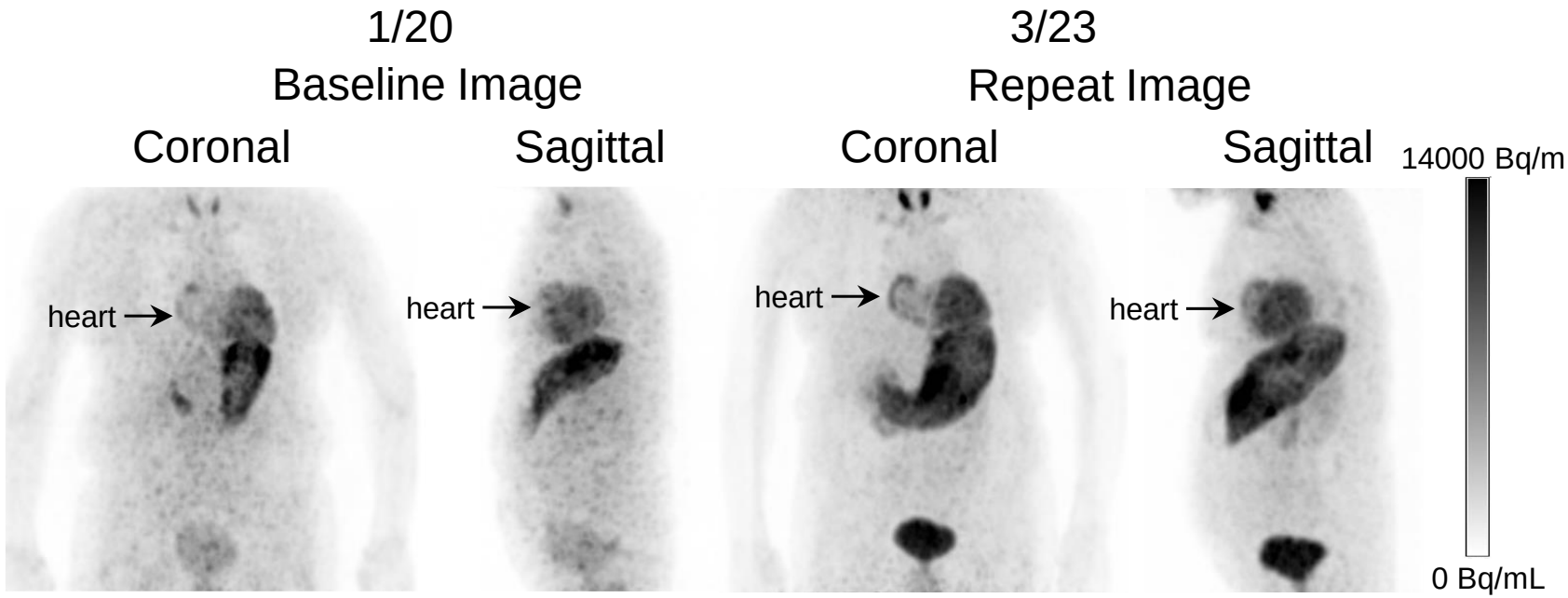
- Male with AL amyloidosis
- Daratumumab/Lenalidomide
- Baseline dFLC = 1.8
- Repeat dFLC = 4.1
- Repeat free λ = 10.5 mg/L
- Baseline SUVR = 1.15
- Repeat SUVR = 2.22
- NTproBNP 1153→1150 pg/mL

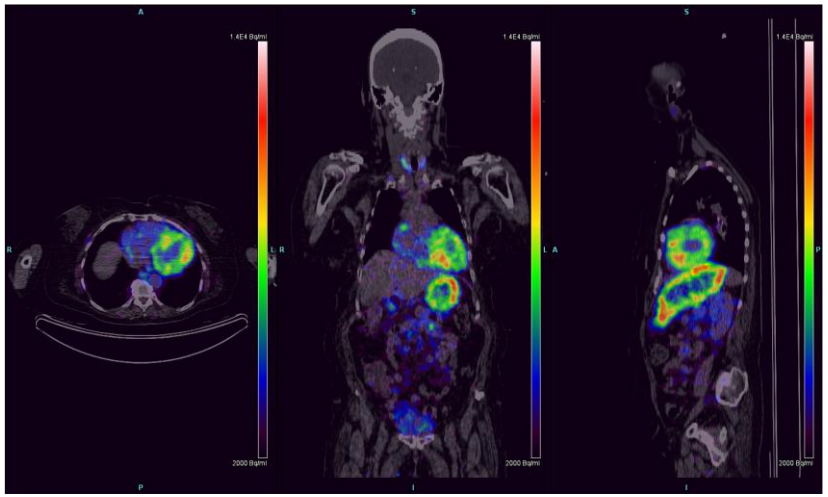


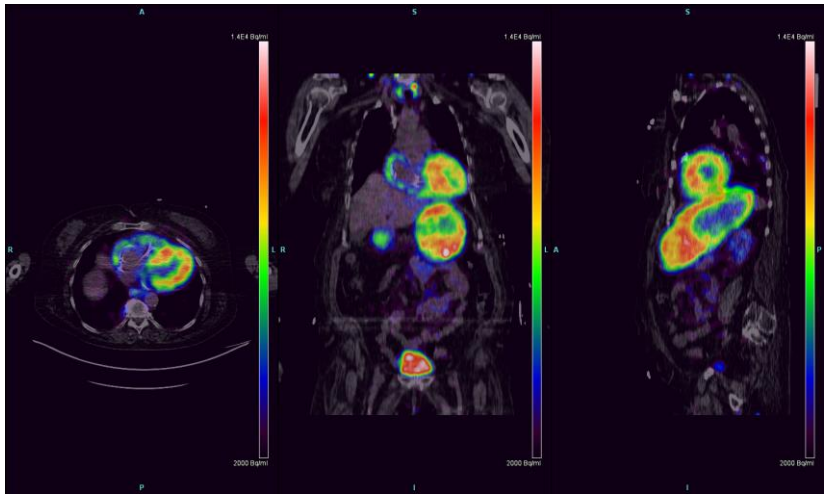
CARDIAC AMYLOID PROGRESSION - ATTR

Case 2 [RPT P009]

- Female with ATTR amyloidosis
- Patisiran + Tafamidis
- Baseline SUVR = 2.14
- Repeat SUVR = 3.20
- NTproBNP 4586→4761 pg/mL



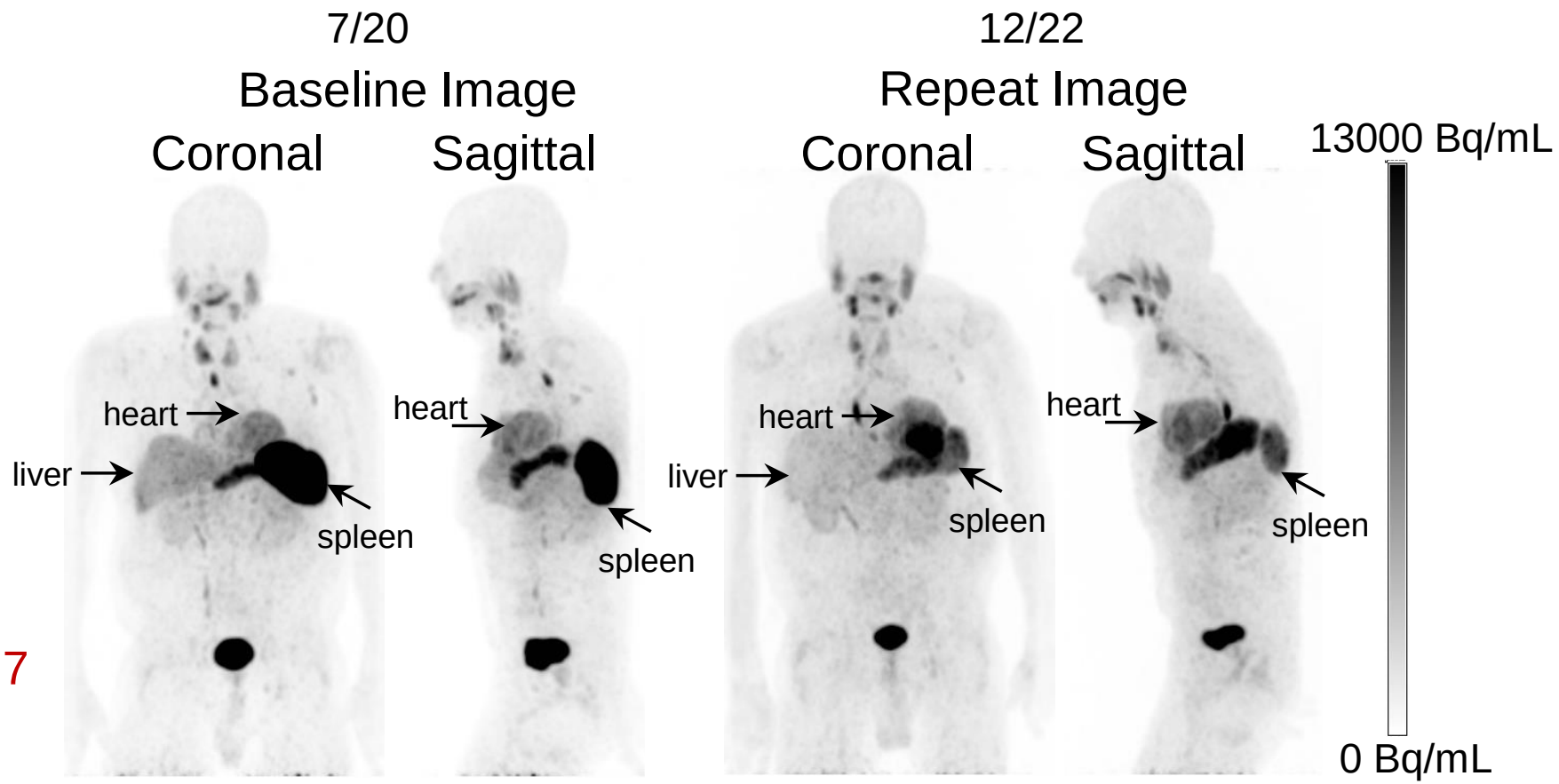




SPLENIC AMYLOID REGRESSION - AL

Case 3 [RPT P002]

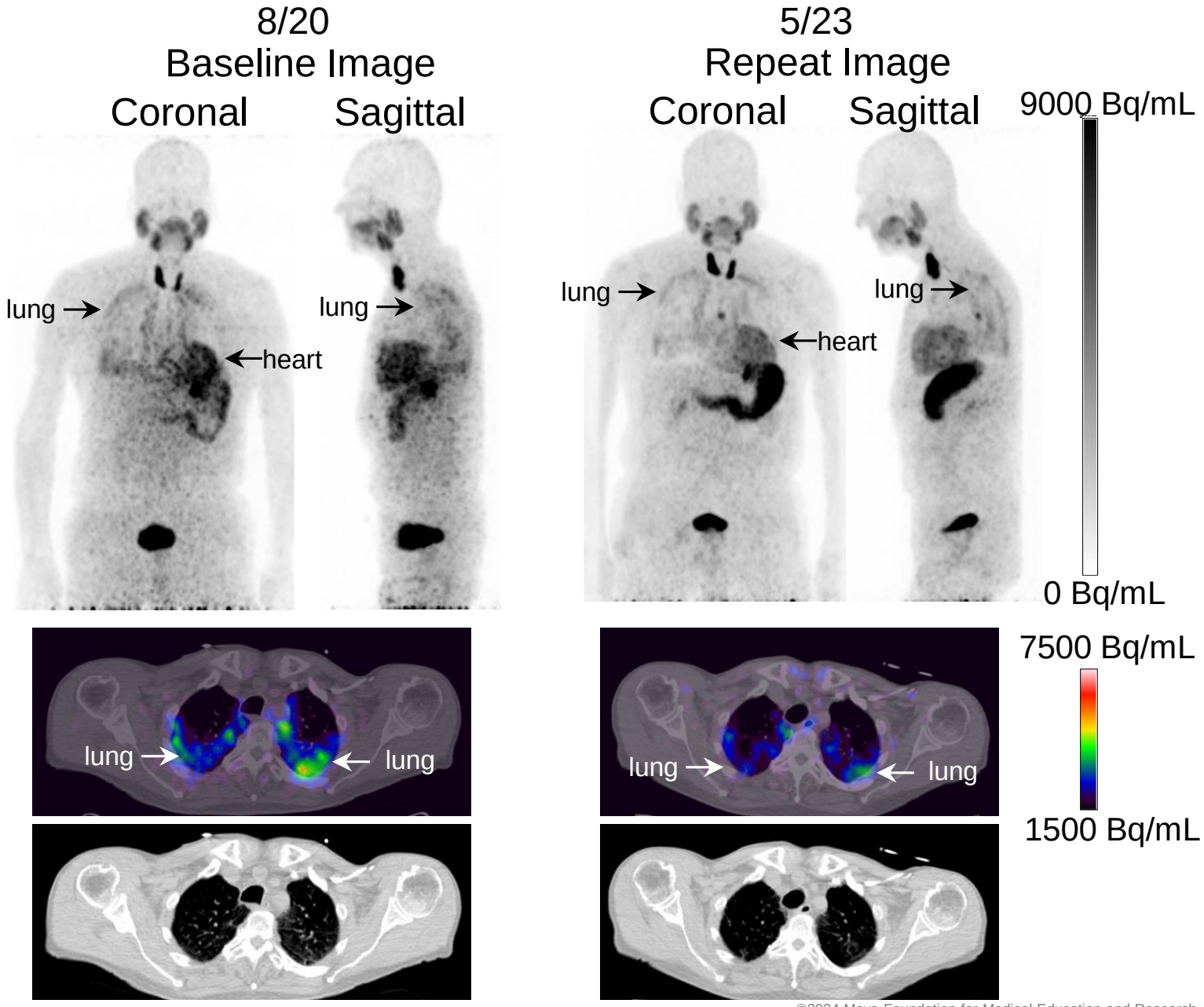
- Male with AL amyloidosis
- No therapy
- Baseline dFLC = 14.3
- Repeat dFLC = 15.8
- Repeat free κ = 26.4 mg/L
  - Increased 6 mg/L
- Baseline Spleen SUVR = 13.7
- Repeat Spleen SUVR = 3.5
- Decreased splenic SUVR (75%) and total organ CT volume -20.5%



CARDIAC AMYLOID REGRESSION – ATTR

Case 4 [RPT P013]

- Male with ATTR amyloidosis
- Tafamidis + Vutrisiran
- Baseline SUVR = 2.60
- Repeat SUVR = 2.00
- Decrease in lung activity
- NTproBNP 1494→1675 pg/mL



CARDIAC AMYLOID REGRESSION – CONFIRMED CLINICALLY

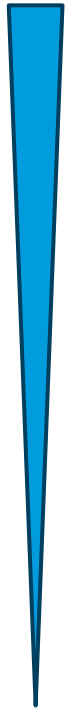
Baseline PET/CT

8/20

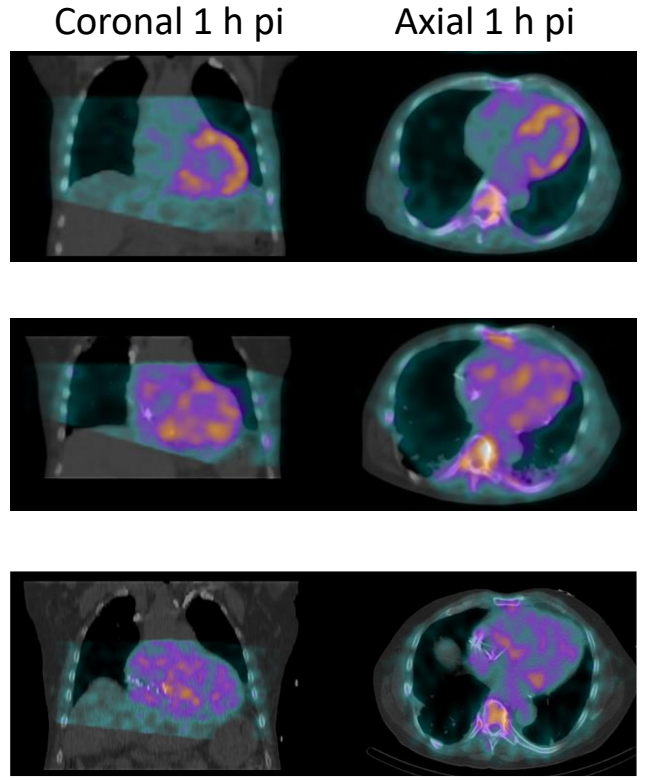
Repeat PET/CT

5/23

^{99m}Tc-PYP uptake



^{99m}Tc-PYP Imaging as SOC

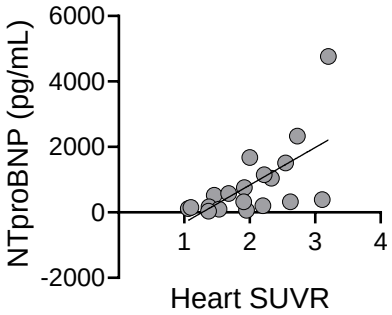


Data kindly provided by Dr. Brett Sperry

Sperry *et al*. Cardiovascular Imaging. 2023;**16**, 514

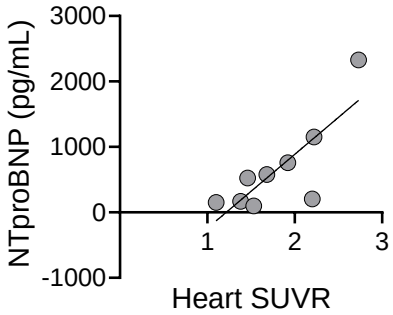
^{124}I-EVUZAMITIDE UPTAKE CORRELATED WITH CERTAIN SERUM BIOMARKERS

All (*N*=19)



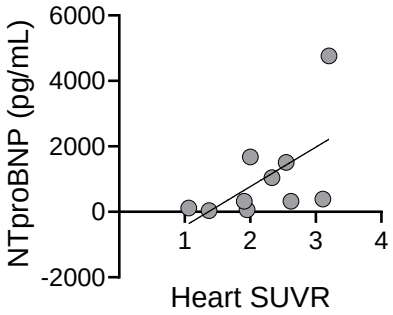
r_S=0.65
p=0.0037

AL (*n*=9)



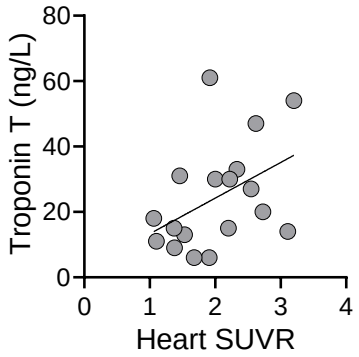
r_S=0.78
p=0.0017

ATTR (*n*=10)



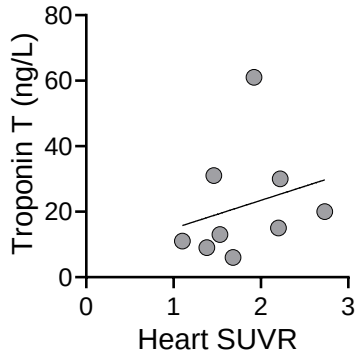
r_S=0.65
p=0.0666

All (*N*=19)



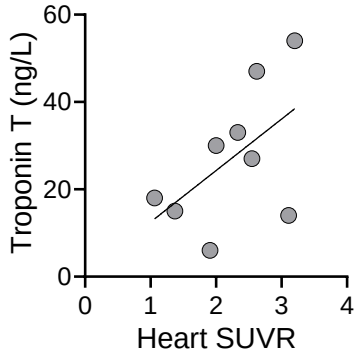
r_S=0.47
p=0.051

AL (*n*=9)



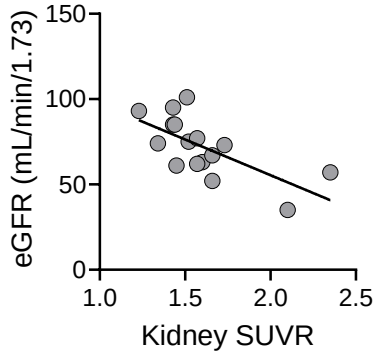
r_S=0.43
p=0.250

ATTR (*n*=10)



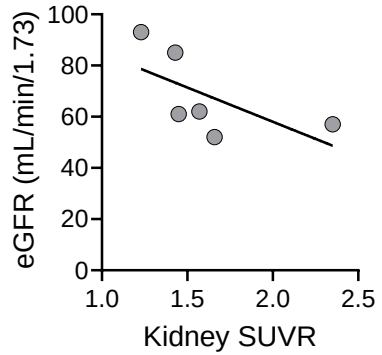
r_S=0.50
p=0.178

All (*N*=16)



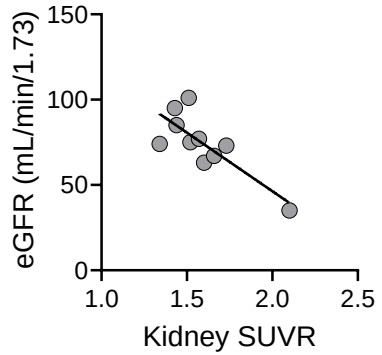
r_S=-0.43
p=0.0665

AL (*n*=6)



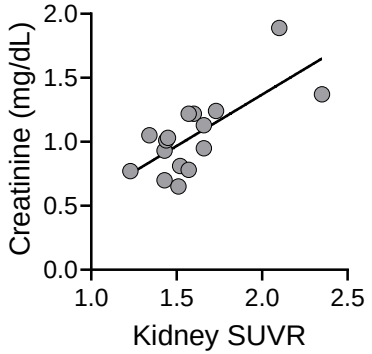
r_S=-0.22
p=0.5719

ATTR (*n*=10)



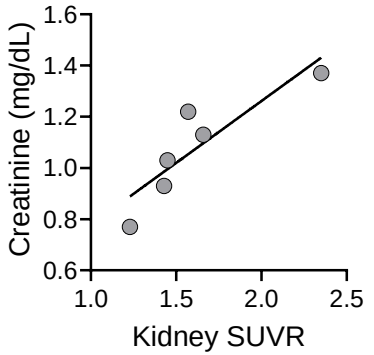
r_S=-0.72
p=0.0234

All (*N*=16)



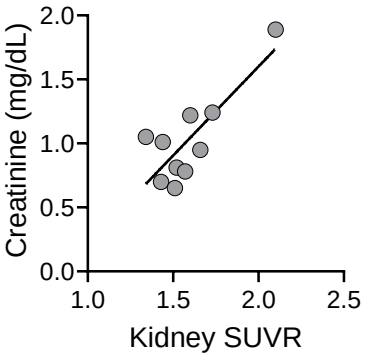
r_S=0.47
p=0.0433

AL (*n*=6)



r_S=0.30
p=0.4366

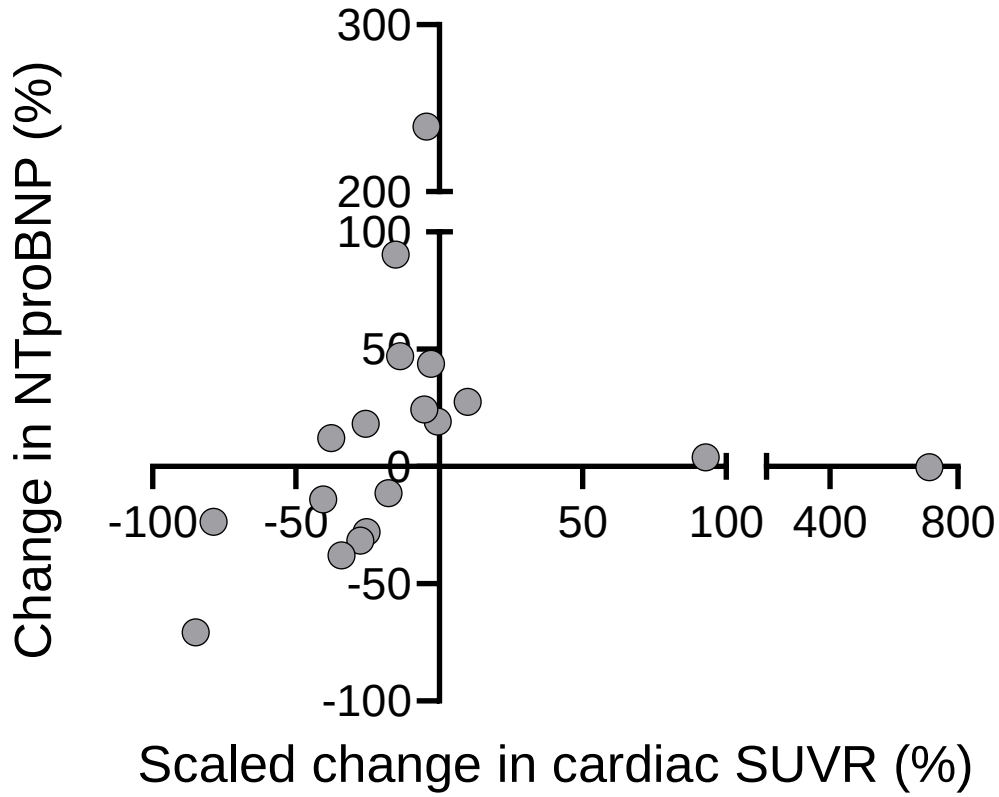
ATTR (*n*=10)



r_S=0.55
p=0.1049

THE CHANGE IN SERUM NTproBNP BETWEEN IMAGING CORRELATES WITH CHANGE IN CARDIAC UPTAKE OF ^{124}I-EVUZAMITIDE

Parameter	Spearman *rho*	Spearman *p*
All Patients (*N*=19)		
ΔCardiac SUVR change (%) vs ΔNTproBNP change (%)	0.57	0.0112*
ΔScaled cardiac SUVR change (%) vs ΔNTproBNP change (%)	0.62	0.0050*



No correlation between changes in serum NTproBNP and change in cardiac uptake of ^{124}I-evuzamitide with:
AL group (*n*=9) or
ATTR group (*n*=10)

SUMMARY

- **Findings**:
  - Changes in the SUVR were consistent with a population with generally stable amyloid, with only two patients (*n*=1 AL and *n*=1 ATTR) exhibiting more than a 1-point change (increase) in SUVR.
  - Two patients with focal tracer uptake at baseline became negative by visual and quantitative assessment.
  - The change in cardiac SUVR from baseline to repeat imaging correlated significantly with the change in serum NTproBNP in the whole population.
  - Uptake of ^{124}I-evuzamitide in organs variably correlated with serum biomarkers, although more work is needed to assess the relevance and underlying physiological changes responsible.
- **Limitations of the Study**:
  - Population could only be recruited from a limited pool of patients who had been previously imaged with ^{124}I-evuzamitide.
  - The returning population was clinically stable: 78% of patients with AL amyloidosis were not on therapy and 100% of ATTR patients were on a stabilizer, silencer or both (40%) – difficult to assess consistent changes in amyloid load in this population.

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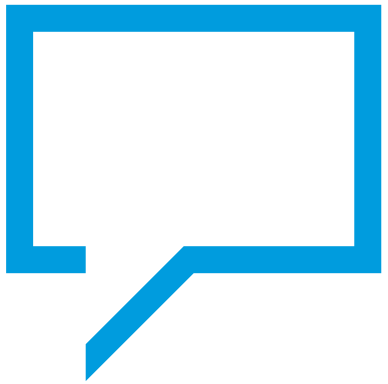
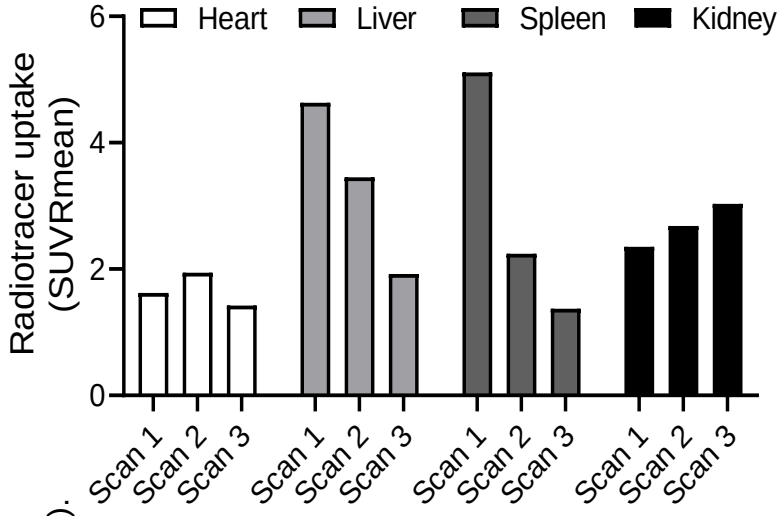
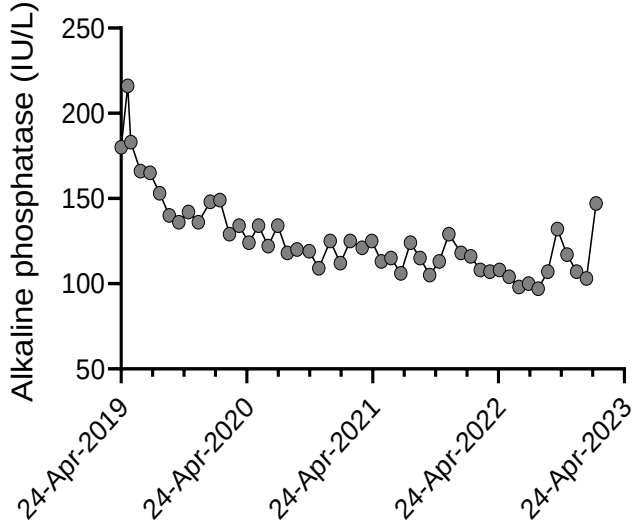
QUESTIONS & ANSWERS



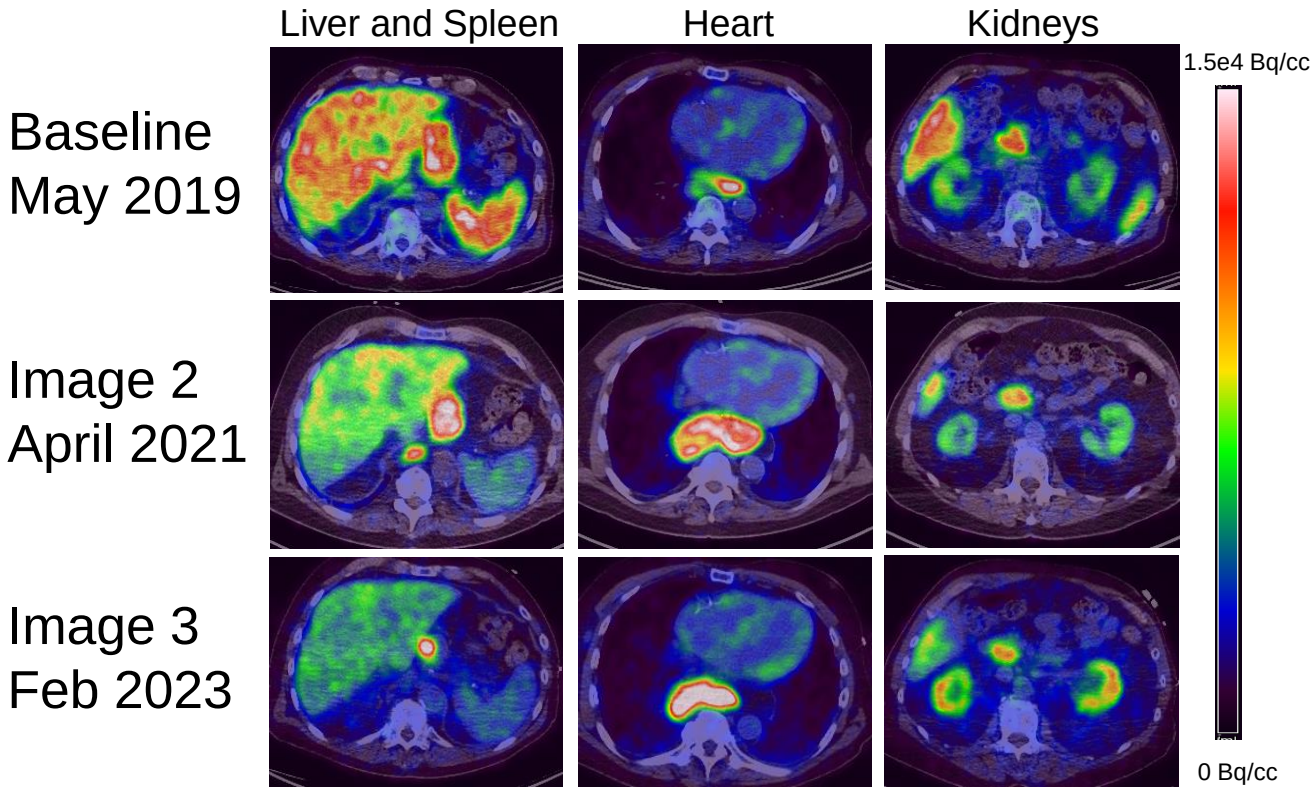
MONITORING CHANGES IN AMYLOID UPTAKE OF ^{124}I-EVUZAMITIDE BY PET/CT IMAGING

Patient with AL amyloid diagnosed by liver biopsy. Dara therapy for 5 years with good hematologic response.





MONITORING CHANGES IN AMYLOID UPTAKE OF ^{124}I-EVUZAMITIDE BY PET/CT IMAGING



Decreases in ^{124}I-evuzamitide uptake could be visualized in transaxial PET/CT images.

Radioactivity in the heart appeared to be stable but increasing in the renal cortex.