Results of the first-in-human PET/CT imaging study of the amyloid-reactive peptide ^{124}I-AT-01 (^{124}I-p5+14) for the detection of systemic amyloidosis

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Disclosure Information

ISA September 2022

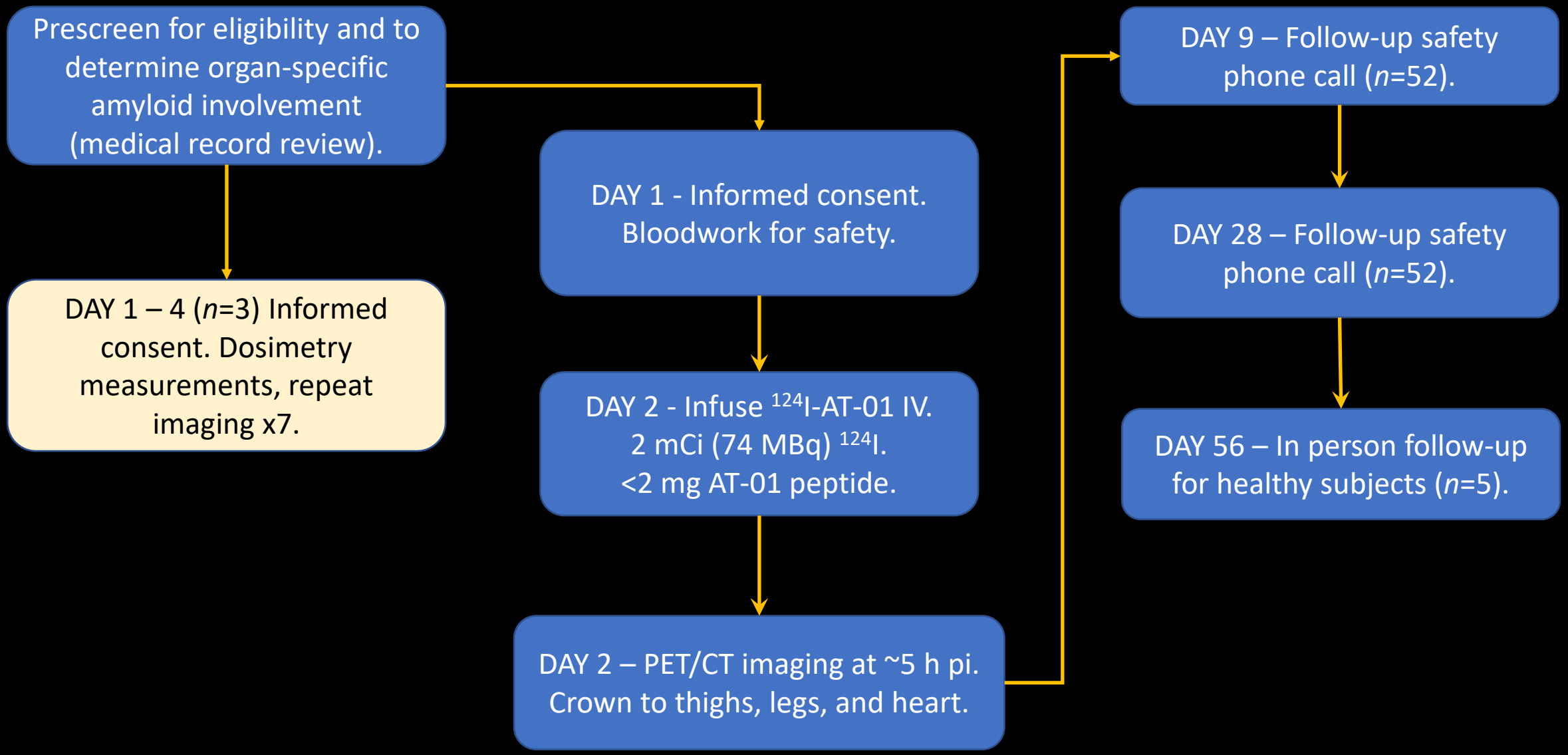
Jonathan Wall, UTGSM

I have the following financial relationships to disclose:

Grant support:	NIH and Pharmaceutical Industry
Support from:	Attralus Inc. (formerly Aurora Bio, Solex, LLC)
Founder, Shareholder, CSO:	Attralus Inc.
Patent rights in:	Amyloid-reactive antibodies and peptides

I will not discuss off-label use in my presentation.

Basic AMY-1001 Study Design (NCT03678259)



^{124}I-AT-01 PET/CT Imaging Phase 1/2 Summary (NCT03678259)

PART 1	*n* = 3	Patients – AL	Dosimetry (7 PET/CT scans in 48 h)
PART 2	*n* = 47	Patients - AL, ATTR, ALECT2, ALys, AGel, AApoA1	Biodistribution and sensitivity
PART 3	*n* = 2	Asymptomatic TTRv carriers (not evaluable)	Early disease screen
PART 4	*n* = 5	Healthy subjects	Specificity
PART 5	*n* = 1	Repeat imaging at least 12 months later	Monitoring response
Total "*n*"	57 (+1)	**Time from diagnosis = 4.4 ± 3.8 y**	

Patients recruited from around the US. Enrolled 29 Males/26 females. All completed the study.

Age	Patients = 65.4 ± 10.0	Healthy subjects = 57.6 ± 8.2
Injected peptide	Patients = 1.4 ± 0.2 mg	Healthy subjects = 1.5 ± 0.1 mg
Injected dose	Patients = 2.01 ± 0.05 mCi (74 MBq)	Healthy subjects = 2.00 ± 0.02 mCi (74 MBq)
Time to imaging post injection = 5.2 ± 0.5 h		
Gender-averaged whole-body effective radiation dose = 0.235 ± 0.02 mSv/MBq		

TRIAL WAS ENDED EARLY TO ALLOW FURTHER DEVELOPMENT

Major Endpoints and Measurements of Interest

- Dosimetry
- Adverse events - safety
- Biodistribution of ^{124}I-AT-01 in patients with diverse types of systemic amyloidosis
- Sensitivity of the ^{124}I-AT-01 in patients with amyloidosis
- Specificity of the ^{124}I-AT-01 in healthy subjects
- Correlation between concentration of the radiotracer (Bq/cc) and serum biomarkers of organ function (e.g., serum NT-proBNP)

Safety – Dosimetry and Adverse Events

Gender-averaged effective dosimetry = 0.235 ± 0.022 mSv/MBq (74 MBq = 17.4 mSv)

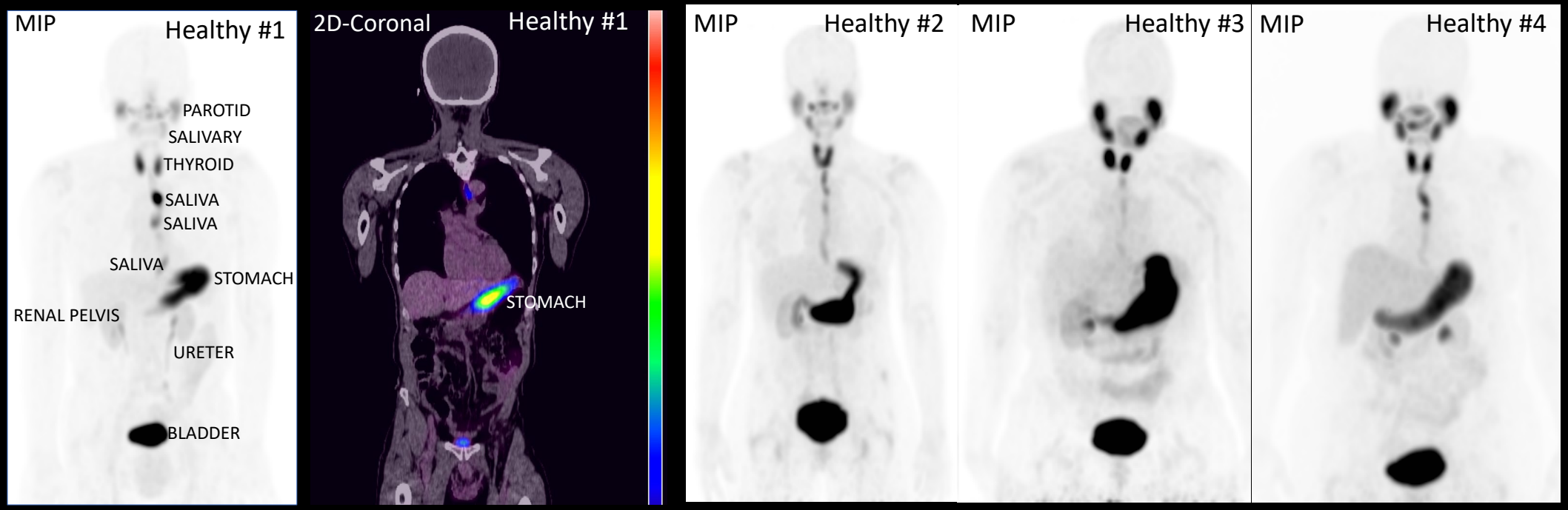
	Subjects with Systemic Amyloidosis [N = 50]	Control[1] [N = 7]	All [N = 57]
Subjects with any Study Drug Related TEAE	1 (2.0%)	0 (0.0%)	1 (1.8%)
Subjects with any SAE	1 (2.0%)	0 (0.0%)	1 (1.8%)
Subjects with any Study Drug Related SAE	0	0	0
Deaths	0	0	0

For patients with systemic amyloidosis, TEAEs that occurred in more than one subject included:

rash (5/50; 10%)
rhinorrhea (3/50; 6%)
chills (2/50; 4%)
nausea (4/50; 8%)
pruritus (2/50; 4%)
anxiety (2/50; 4%)

Overall, ^{124}I-AT-01 was well tolerated, with no deaths or drug-related serious adverse events.

PET/CT Imaging of ^{124}I-AT-01 in Healthy Volunteers



Physiological distribution of radioactivity was observed in the:

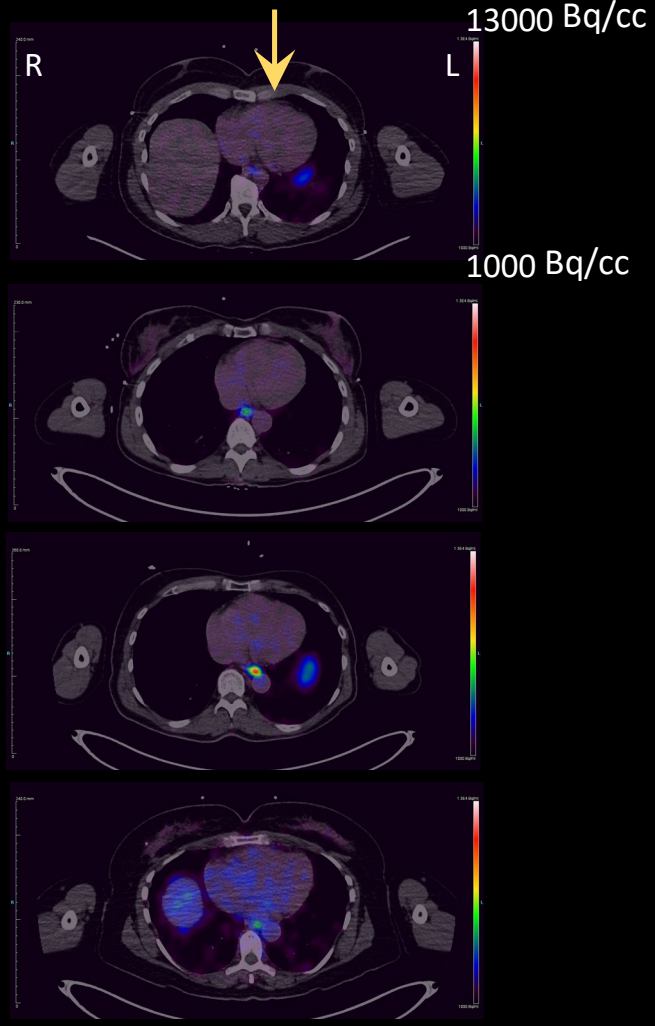
parotid gland	salivary gland	thyroid gland
saliva	stomach lumen	urine
urinary bladder	ureters	

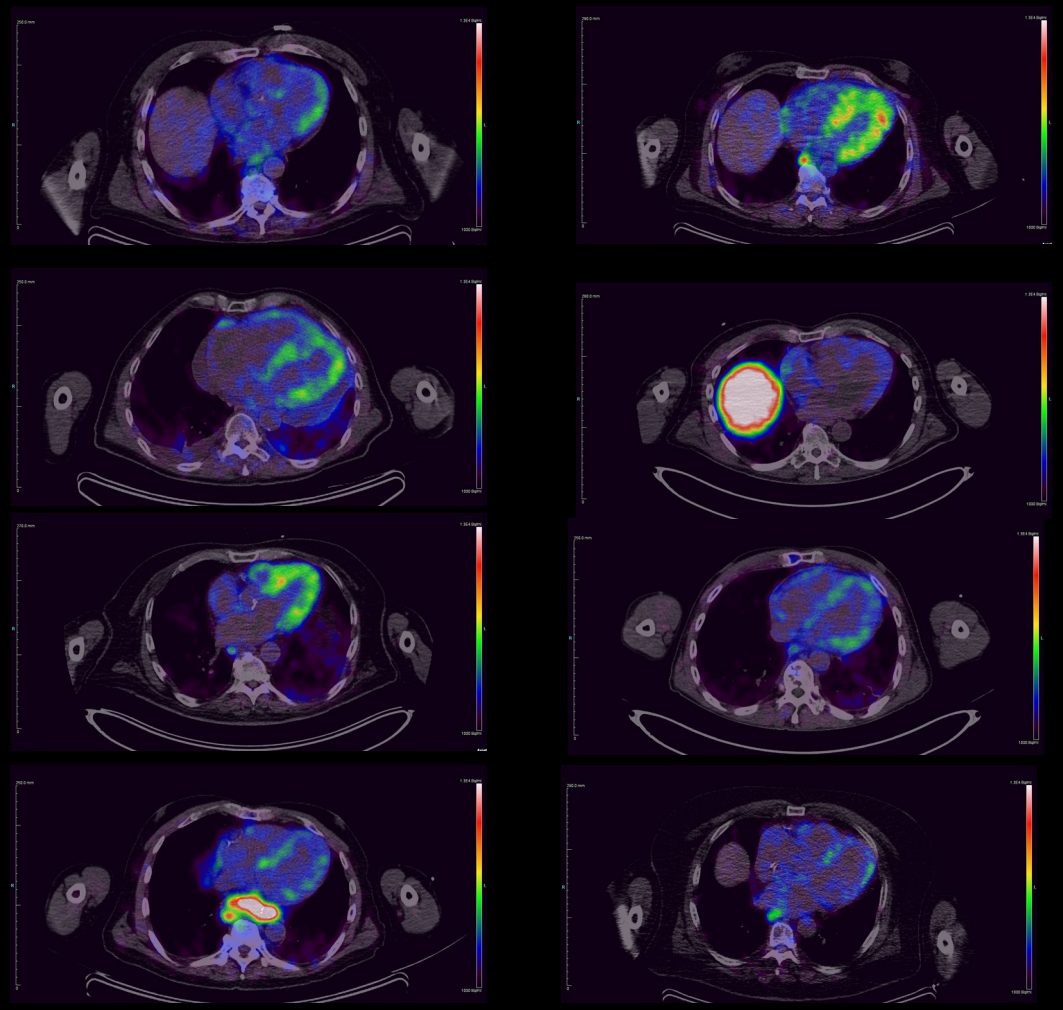
^{124}I-AT-01 Imaging of Cardiac Amyloid in Patients with AL

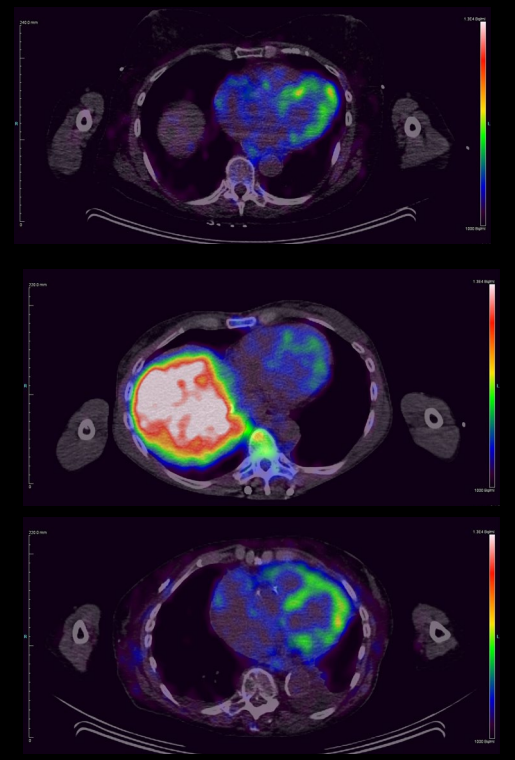
A. Healthy Subjects

B. Clinical + / Imaging +

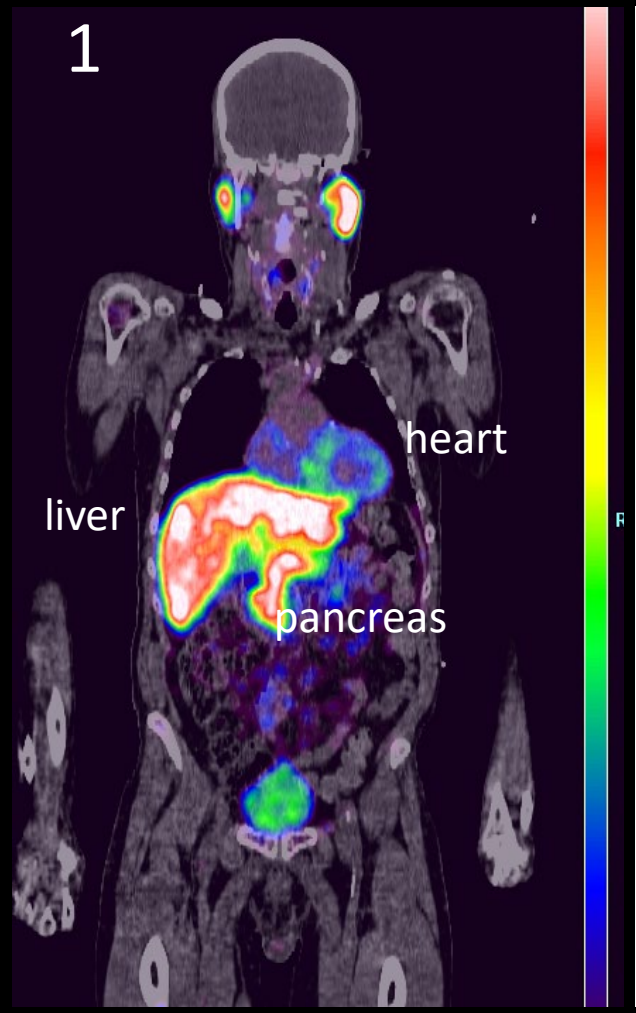
C. Clinical - / Imaging +

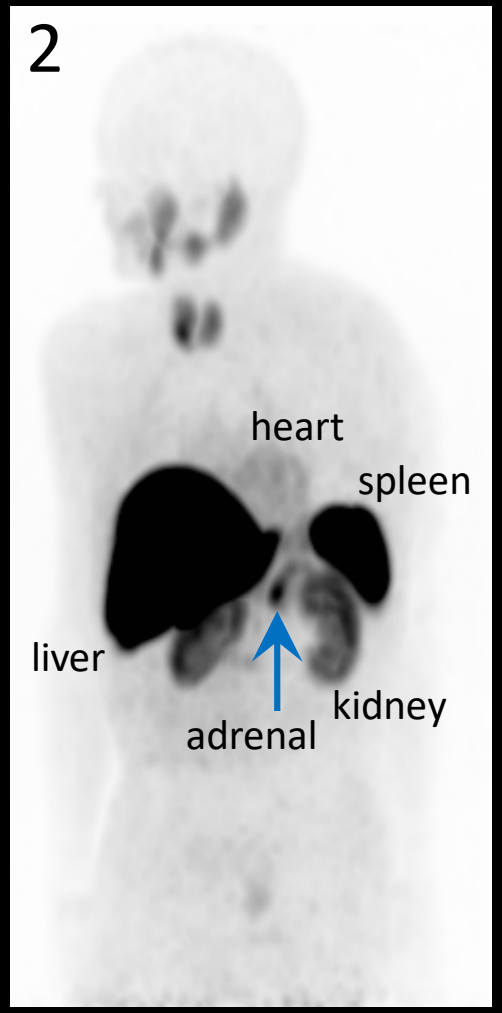


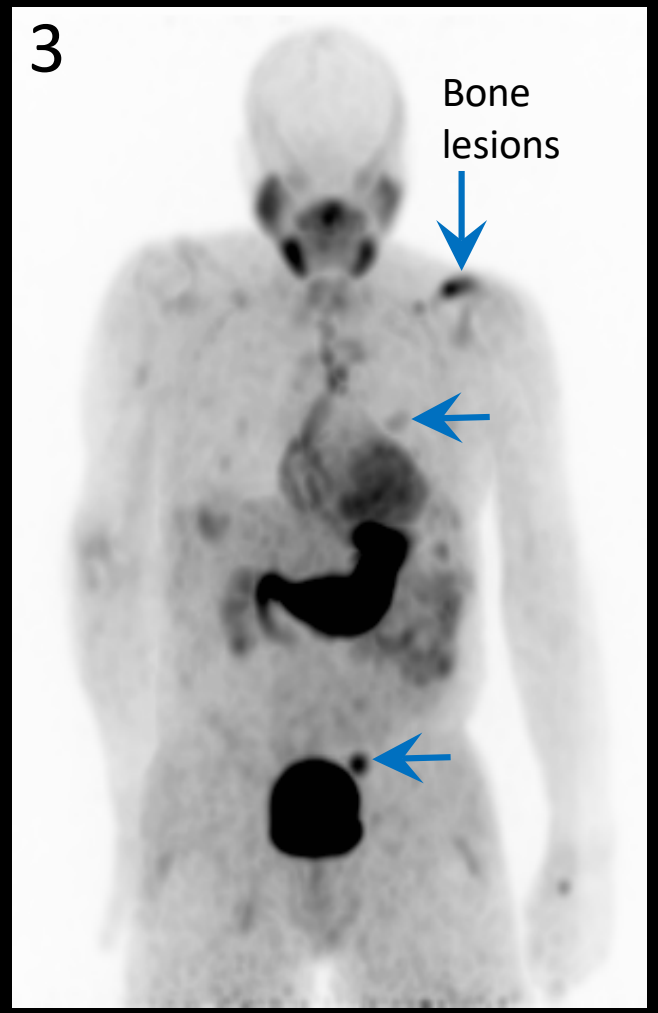


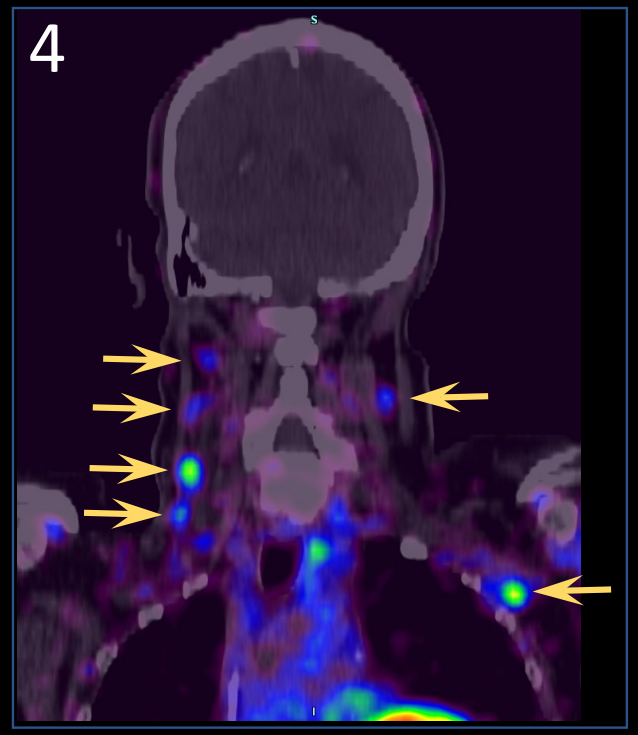


^{124}I-AT-01 Imaging of Extracardiac Amyloid in Patients with AL



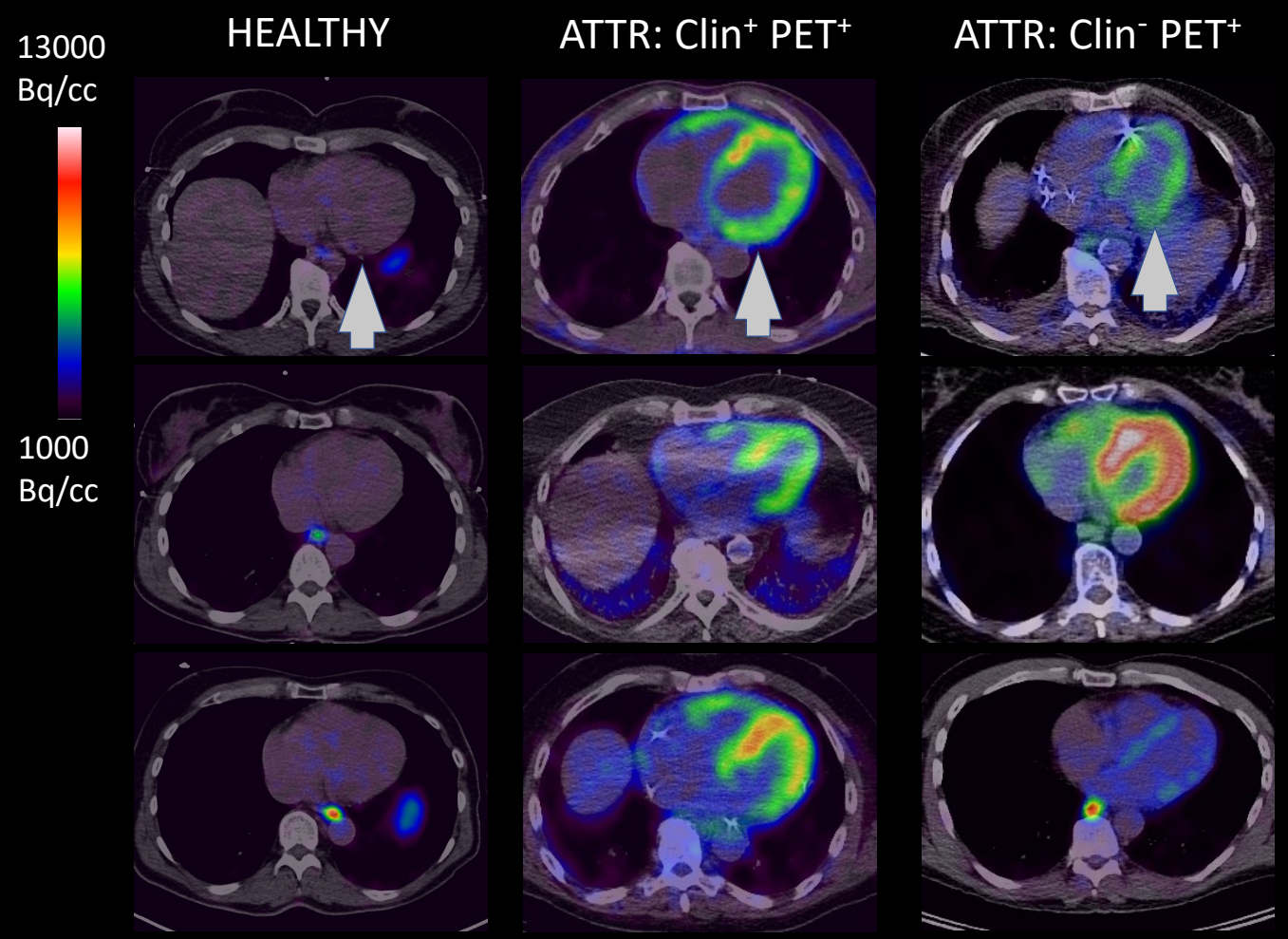






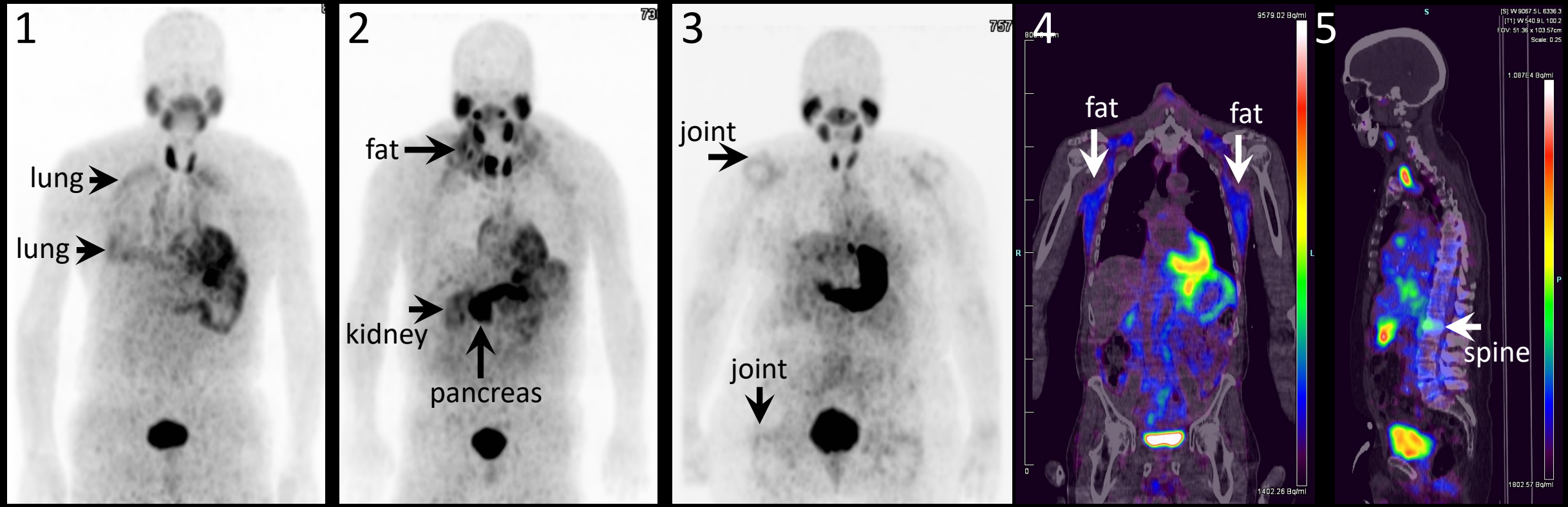
Lymph nodes

^{124}I-AT-01 Imaging of Cardiac Amyloid in Patients with ATTR



Representative transaxial PET/CT images of the heart in heathy subjects and ATTR patients with clinically positive (Clin^{+}) or negative (Clin^{-}) cardiac amyloidosis

^{124}I-AT-01 Imaging of Extracardiac Amyloid in Patients with ATTR



Poster 170

Summary of ^{124}I-AT-01 Uptake in ATTR patients

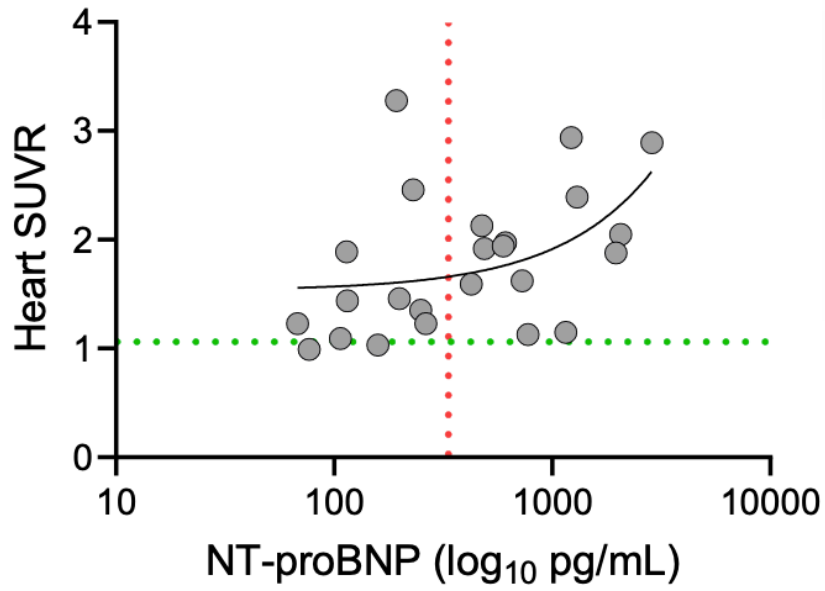
- 20 ATTR patients: 11 diagnosed with cardiomyopathy and 9 diagnosed with polyneuropathy: 15 ATTRv: 5 ATTRwt
- 100% (9/9) patients with elevated NT-proBNP (>333 pg/nL) had positive ^{124}I-AT-01 uptake in the heart
- 100% (5/5) patients with positive ^{99m}Tc-PyP scans had positive ^{124}I-AT-01 uptake in the heart
- 66% (6/9) patients diagnosed ONLY with polyneuropathy had positive ^{124}I-AT-01 uptake in the heart
- 73% (8/11) patients with normal NT-proBNP had positive ^{124}I-AT-01 uptake in the heart
- 80% (4/5) patients with an historical negative ^{99m}Tc-PyP scans had positive ^{124}I-AT-01 uptake in the heart

Potential to identify early pathology (before symptoms and other imaging techniques)

Major ^{124}I-AT-01 Phase 1/2 Study Findings

- Patient-based sensitivity (PPA) = 96% (48/50)
  - 1 ATTRwt patient was diagnosed via a positive laminectomy and neuropathy
  - 1 AL subject was 6 years post successful SCT, and no ongoing symptomology
- ATTR patients Cardiac Sensitivity (PPA) = 100% (11/11)
- AL patients Cardiac Sensitivity (PPA) = 93% (13/14)
- 5 Healthy volunteers were evaluated
  - Cardiac Specificity (NPA) = 100% (5/5)
- AEs were mild and transient

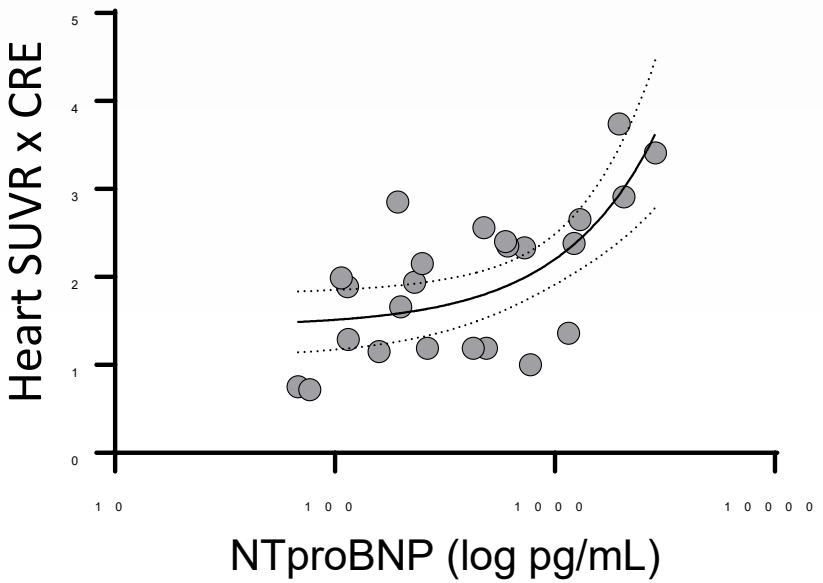
Cardiac Uptake of ^{124}I-AT-01 Correlates with Serum NT-proBNP



AL Patients (*n*=24)

Moderate correlation r_s = 0.478

Significance, p = 0.018



AL Patients (*n*=24)

Strong correlation r_p = 0.679

Significance, p = 0.0003

Conclusion: AT-01 uptake (Bq/cc) in the heart of AL patients correlates significantly with NT-proBNP. Heart SUVR x serum CRE yielded stronger significant correlation.

No correlation between NTproBNP and Heart SUVR in our ATTR cohort: (r_s = 0.281, p = 0.231)

Conclusions

- Diagnosis of systemic amyloidosis continues to be challenging.
- Need for quantitative amyloid-specific imaging agent that can detect amyloid throughout the body that can be used to monitor amyloid burden.
- ^{124}I-AT-01 is a novel pan-amyloid binding imaging agent (*Dr. Martin next talk*).
- High sensitivity in patients with AL and ATTR, particularly in the heart.
- ^{124}I-AT-01 infusion was safe and well tolerated.
- Uptake of radiotracer in the heart correlated with NTproBNP in patients with AL amyloidosis – especially when one adds a measure of renal function.
- Data in patients with ATTR amyloidosis suggest that ^{124}I-AT-01 imaging may be useful in detecting asymptomatic cardiac amyloid.
- ^{124}I-AT-01 is a promising new imaging agent that is currently in planning for a phase 3 pivotal trial.

Amyloidosis and Cancer Theranostics Program

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