First-in-Human Cardiac and Whole-Body ^{124}I-evuzamitide (AT-01) PET/MRI in Systemic Amyloidosis

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BACKGROUND

- Cardiac magnetic resonance imaging (CMR) is currently considered the gold standard imaging modality to assess cardiac structure, function, and surrogates of amyloid load.
- ^{124}I-evuzamitide (AT-01) is a novel pan-amyloid PET radiotracer.
- We conducted the first-in-human study of ^{124}I-evuzamitide cardiac and whole-body PET/MRI to assess the feasibility and tracer distribution in patients suspected to have or diagnosed with systemic amyloidosis.

METHODS

- The study was approved by the OHSU IRB and conducted under an FDA-approved IND.
- Cardiac amyloidosis was suspected or diagnosed in all patients prior to enrollment. The study was not designed to evaluate ^{124}I-evuzamitide PET/MRI in an intention-to-diagnose population. Rather, we designed the study, the first using hybrid PET/MRI to evaluate the performance of ^{124}I-evuzamitide in high risk patients or those diagnosed through other means according to the guidelines and compare its performance to controls.
- Patients were diagnosed by standard clinical, laboratory, biopsy, and imaging criteria. ^{124}I-evuzamitide diagnostic performance was judged against comprehensive clinical evaluation (gold standard)
- All patients underwent hybrid cardiac PET/MRI followed by whole-body (WB) PET/MRI with ^{124}I-evuzamitide (mean administered activity 1.04±0.02 mCi, average 5-6 minutes per bed). All patients received potassium iodide 130 mg for 3 days, first dose at least 30 minutes prior to ^{124}I-evuzamitide administration.
- Images were analyzed for tracer distribution and organ involvement.
- Ratio of mean LV septum standardized uptake value (SUV) to mean LV blood pool SUV was calculated, as well as mean LV septum SUV subtracted from mean LA SUV.

RESULTS

- 50 patients were enrolled from January through August 2023. All subjects completed the study protocol.
- ^{124}I-evuzamitide was safe without any serious adverse events and no tracer-related adverse events. There was a mild AE of redness at the site of peripheral line in one subject and the AE resolved in less than 24 hours.
- Time from ^{124}I-evuzamitide injection to start of cardiac PET and whole-body PET were 3.1±0.6 hours and 4.0±0.6 hours
- The baseline characteristics are shown in Table 1.
- ^{124}I-evuzamitide PET/MRI had 100% sensitivity and specificity in detecting cardiac amyloidosis. No false positive or false negative cases were observed.

Table 1: Baseline characteristics of patients diagnosed with cardiac amyloidosis vs those without cardiac involvement/controls.

Variable	Cardiac Amyloidosis (N=34)	Controls (N=16)	p-value
Age (years)	74.7±8	66.44±9	0.002
Male sex	31 (91%)	6 (37.5%)	<0.001
Cardiac Amyloidosis subtype			—
Light chain	7 (20.6%)	-	
Transthyretin	27 (79.4%)	-	
Controls Underlying Phenotype:			
LVH/HCM		4 (25%)	
Extracardiac AL amyloidosis		5 (31%)	
Transthyretin variant carrier		5 (31%)	
Orthopedic amyloid deposit		2 (13%)	
Systemic amyloidosis without cardiac involvement	0%	7 (43.8%)	—
Pathogenic transthyretin variant	4 (11.8%)	5 (31.3%)	0.250
Left ventricular hypertrophy (basal LV septum ≥12 mm)	33 (97%)	10 (62.5%)	0.366
^{124}I-evuzamitide administered activity (mCi)	1.05 (0.02)	1.04 (0.01)	0.124
Mean time from ^{124}I-evuzamitide to start of cardiac PET (hours)	3.15	3.05	0.571
Mean time from ^{124}I-evuzamitide to start of Whole-body PET (hours)	4.00	3.85	0.405
Mean myocardial SUV	7.58 (2.12)	3.43 (0.75)	<0.001
Mean LV blood pool SUV	4.28 (1.20)	3.39 (0.63)	0.001
SUVR (myocardium over LV blood)	1.76 (1.67, 1.93)	0.94 (0.87, 1.06)	<0.001
Mean LA blood pool SUV	3.67 (0.95)	3.52 (0.85)	0.602
Mean Myocardium SUV – LA SUV	3.4 (2.58, 3.36)	0 (0, 0.55)	<0.001
^{124}I-evuzamitide distribution			—
Cardiac	34 (100%)	0 (0%)	
Spleen	5 (14.7%)	2 (12.5%)	
Liver	4 (11.8%)	2 (12.5%)	
Renal	3 (8.8%)	6 (37.5%)	
Lungs	4 (11.8%)	1 (6.3%)	
Orthopedic	12 (35.3%)	5 (31.3%)	

Figure 1: Representative Examples of ^{124}I-evuzamitide uptake or lack of in various organs

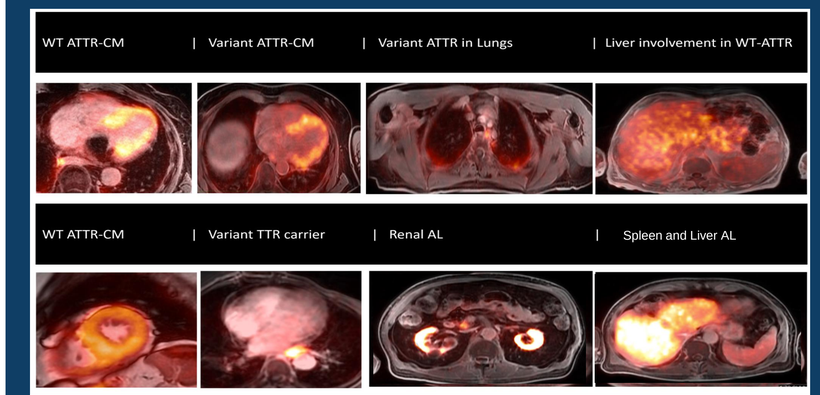
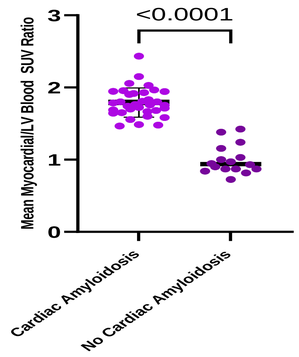


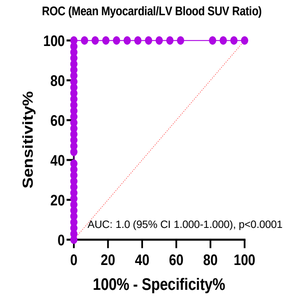
Figure 2: Diagnostic performance of quantifying ^{24}I-evuzamitide uptake

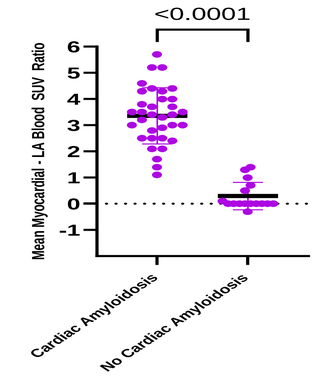


A mean myocardial/LV blood SUV ratio cut-off of 1.45 yielded:

Sensitivity of 100% (95% CI 90%, 100%)

Specificity of 100% (95% CI 81%, 100%),

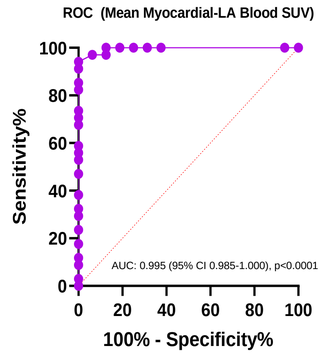




A mean myocardial-LA blood SUV ratio cut-off of 1.55 yielded:

Sensitivity of 94% (95% CI 81%, 99%)

Specificity of 100% (95% CI 81%, 100%),



CONCLUSIONS

- ^{124}I-evuzamitide PET/MRI is feasible and provides comprehensive diagnostic evaluation and organ survey of patients suspected to have or diagnosed with systemic amyloidosis.
- In this population of patients diagnosed with or suspected to have cardiac amyloidosis, ^{124}I-evuzamitide PET/MRI had a 100% sensitivity and specificity for the diagnosis of cardiac amyloidosis.
- A simple measure of mean myocardial to LV blood pool SUV ≥1.45 yielded a 100% sensitivity and specificity for the diagnosis of cardiac amyloidosis.
- Our participants were a highly selected group of patients, and as such, an intention-to-diagnose phase III multicenter trial of ^{24}I-evuzamitide in patients suspected to have cardiac amyloidosis is needed to confirm our findings.

DISCLOSURES and FUNDING

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