Diagnostic Performance of 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 a prospective study of ^{124}I-evuzamitide cardiac and whole-body PET/MRI to assess the diagnostic accuracy 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 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 1.05±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.
- Ratio of mean LV septum standardized uptake value (SUV) to mean LV blood pool SUV was calculated.

RESULTS

- 97 patients were enrolled from January 2023 through March 2025. All subjects underwent the imaging protocol. Of these, 57 had cardiac transthyretin amyloidosis, 20 had cardiac light chain amyloidosis, 3 had ApoA1 or ApoA4, 8 had systemic amyloidosis but no cardiac involvement, and 17 had no evidence of systemic amyloidosis.
- ^{124}I-evuzamitide was safe without any serious adverse events.
- Time from ^{124}I-evuzamitide injection to whole-body PET was 3.8 ±0.6 hours.
- The baseline characteristics and imaging findings 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 (Figure 3).

Conclusion

In this population of patients diagnosed with or suspected to have cardiac amyloidosis, ^{124}I-evuzamitide PET/MRI had 100% sensitivity and specificity for the diagnosis of cardiac amyloidosis.

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

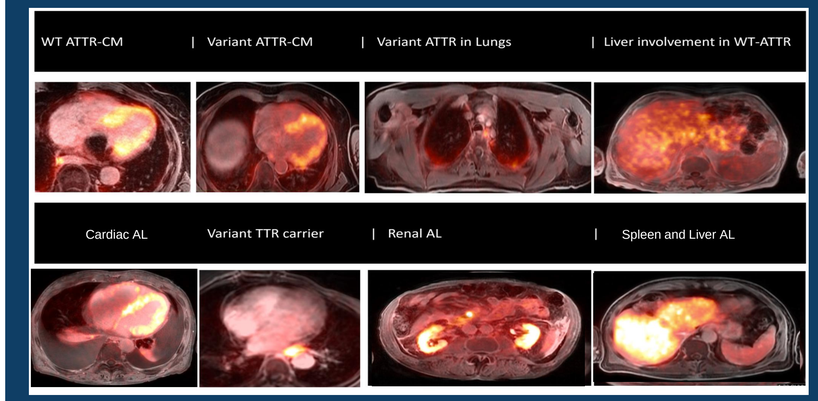

Figure 2: Representative Examples of ^{124}I-evuzamitide uptake in a patients with biopsy-proven wild type ATTR-CM while bone scintigraphy and CMR were not suggestive.

^{124}I-evuzamitide PET/MRI **^{99m}Tc-PYP Scintigraphy**

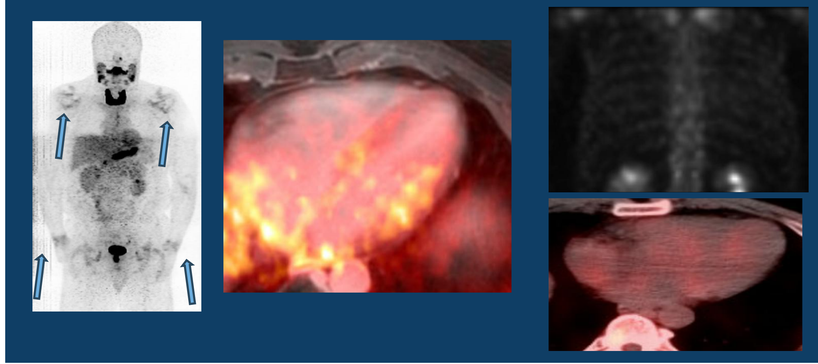

Table 1: Baseline characteristics of patients diagnosed with cardiac amyloidosis vs those without cardiac involvement/controls.

Variable	Cardiac Amyloidosis (N=72)	Controls (N=25)	p-value
Age (years)	74.9±2.4	67.8±8.5	<0.001
Female sex	10 (13.4%)	14 (56%)	<0.001
Controls Underlying Phenotype:			
LVH/HCM		4 (16%)	
Extracardiac AL amyloidosis		6 (24%)	
Transthyretin variant carrier		7 (28%)	
Orthopedic amyloid deposit		4 (16%)	
Systemic amyloidosis without cardiac involvement	0%	8 (32%)	—
Pathogenic transthyretin variant	9 (12.5%)	7 (28%)	0.25
Mean myocardial SUV	7.2 (1.8)	3.3 (0.7)	<0.001
Mean LV blood pool SUV	3.9 (1.1)	3.6 (0.8)	0.001
SUVR (myocardium over LV blood)	1.9 (0.3)	0.9 (0.1)	<0.001
^{124}I-evuzamitide distribution			—
Cardiac	72 (100%)	0 (0%)	
Spleen	15 (20.8%)	2 (8.0%)	
Liver	14 (19.4%)	2 (8.0%)	
Renal	15 (20.8%)	9 (36.0%)	
Lungs	8 (11.1%)	1 (4.0%)	
Orthopedic	30 (41.6%)	10 (40%)	

Figure 3: Diagnostic performance of quantifying ^{24}I-evuzamitide uptake

A mean myocardial/LV blood SUV ratio cut-off of 1.31 yielded:

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

Specificity of 100% (95% CI 87%, 100%)

AUC 1.00, p<0.0001

DISCUSSION

- ^{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, there were no false positive or negatives with ^{124}I-evuzamitide PET/MRI imaging for the diagnosis of cardiac amyloidosis.
- A simple measure of mean myocardial to LV blood pool SUV ≥1.31 yielded a 100% sensitivity and specificity for the diagnosis of cardiac amyloidosis.
- Our participants were a 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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