Preliminary Evaluation of ^{99m}Tc-Labeled Peptide p5+14 (AT-05) for the Detection of Cardiopulmonary Amyloidosis Using SPECT/CT and Planar Gamma Scintigraphic Imaging

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BACKGROUND

- Early and accurate detection of cardiac amyloidosis is critical but can be challenging.
- Novel therapies for ATTR amyloidosis are most effective in early-stage disease.
- A novel technetium-99m labeled pan-amyloid reactive peptide p5+14 (the basis of ^{124}I-evuzamitide) may prove useful in the community cardiology setting as a facile, early screen for cardiac amyloidosis.
- Here we present data from the first-in-human study (NCT05951816) on the use of ^{99m}Tc-p5+14.

METHODS

In this Phase 1, single-center, open-label study, a total of 35 subjects will be recruited - five (*n*=5) healthy volunteers and 30 (*n*=30) recently diagnosed patients with AL or ATTR cardiac amyloidosis. Subjects were administered ≤22 mCi of ^{99m}Tc-p5+14 intravenously and, at 1h and 3h post-injection, were imaged using planar scintigraphy and SPECT/CT imaging. Standard ^{99m}Tc-pyrophosphate imaging was performed on most patients at 72h after ^{99m}Tc-p5+14 imaging.

RESULTS

The planar and SPECT/CT images were of high quality and readily interpretable at both 1 h and 3 h post-injection. No cardiac uptake was observed in healthy subjects. In contrast, patients with cardiac amyloidosis had significant uptake of ^{99m}Tc-p5+14 in the heart evidenced in planar and SPECT/CT images. Preliminary assessment of the myocardium-to-blood ratio at 1 h post injection in patients was approximately 3:1. Pulmonary lesions were also ^{99m}Tc-p5+14 avid. Hepatosplenic uptake of the radiotracer was observed in a patient with AL amyloidosis.

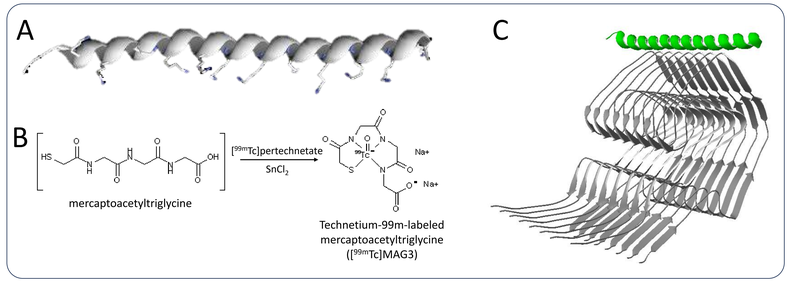

Figure 1. Peptide p5+14 is a 45-amino acid synthetic reagent that has a predicted α-helical structure in the presence of its ligand (A). The amino sequence ensures that the 12 charged lysine side chains align on one face of the helix. Tc-99m is hypothesized to coordinate through the three N-terminal glycine residues akin to MAG3 (B). ^{99m}Tc-evuzamitide is thought to bind amyloid fibrils by aligning along the long axis through electrostatic interactions (C).

Current Phase 1 Study	Primary Outcome	Activities
Part 1 – Dosimetry measurements for ^{99m}Tc-p5+14 in AL patients (*n*=5)	Safety – whole body effective radioactivity dose measurement	20 mCi ^{99m}Tc-p5+14-CMP-TE PGS and SPECT/CT x 6 over 24h
Part 2 – Biodistribution of ^{99m}Tc-p5+14 in patients with ATTR (*n*=10) and AL (*n*=5) with ACM	Positive percent agreement in patients with ACM and comparison with ^{99m}Tc-PYP	20 mCi ^{99m}Tc-p5+14-CMP-TE PGS and SPECT/CT at 1h and 3h pi 20 mCi ^{99m}Tc-PYP-PGS and SPECT/CT at 1h and 3h pi
Part 3 - Biodistribution of ^{99m}Tc-p5+14 in Healthy Subjects (*n*=5)	Negative percent agreement for heart in healthy volunteers	20 mCi ^{99m}Tc-p5+14-CMP-TE PGS and SPECT/CT at 1h and 3h pi
Part 4 - Biodistribution of ^{99m}Tc-p5+14 in patients with ATTR patients with ACM who are PYP negative (*n*=10)	Positive percent agreement with biopsy proven ACM in PYP-negative population	20 mCi ^{99m}Tc-p5+14-CMP-TE PGS and SPECT/CT at 1h and 3h pi 20 mCi ^{99m}Tc-PYP-PGS and SPECT/CT at 1h and 3h pi

Figure 2. Schematic representation of the four-part Phase 1 pilot clinical study of ^{99m}Tc-p5+14 in patients with cardiac AL or ATTR amyloidosis. ACM, amyloid cardiomyopathy; CMP, complete metabolic panel; TE, transthoracic echocardiography; PGS, planar gamma scintigraphic imaging; SPECT/CT, single photon emission computed and x-ray computed tomography.

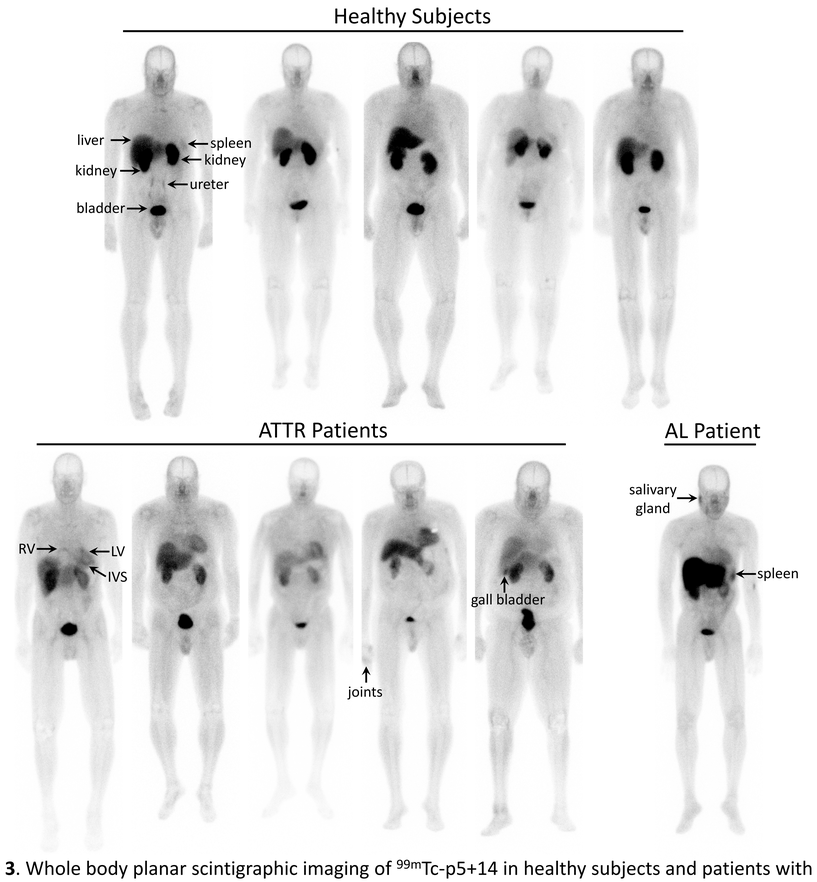

Figure 3. Whole body planar scintigraphic imaging of ^{99m}Tc-p5+14 in healthy subjects and patients with amyloidosis. Physiologic radioactivity was seen in the liver, kidney, ureter, and urinary bladder. Uptake in patients was seen in the right and left ventricular walls (RV and LV), interventricular septum (IVS), joints and spleen and salivary gland of the patient with AL amyloidosis.

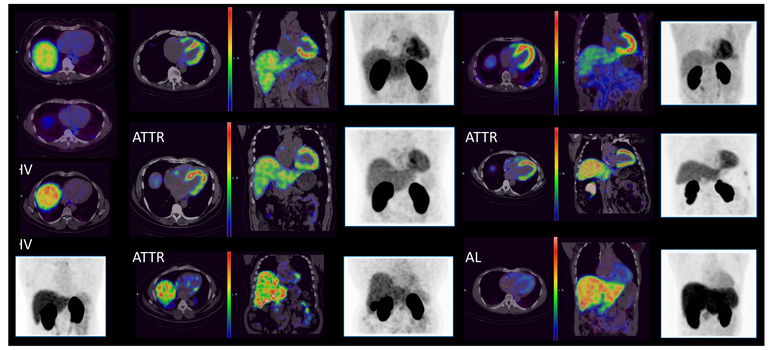

Figure 4. Cardiac amyloid SPECT/CT imaging using ^{99m}Tc-p5+14 in healthy volunteers (HV) and patients with ATTR or AL amyloidosis imaged at 1 h post injection (pi). No uptake was seen in the heart of HV. In contrast, the LV, IVS, and RV were imaged in axial, coronal and maximum intensity projections (MIP).

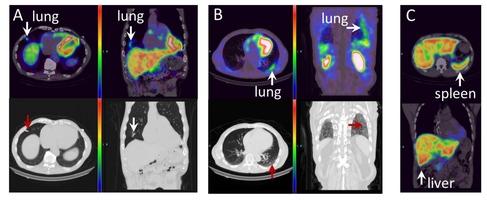

Figure 5. Extracardiac uptake of ^{99m}Tc-p5+14 in patients with ATTR or AL amyloidosis imaged at 1 h pi. Uptake was observed in the lung of patients with ATTR (A, B) and liver and spleen of a patient with AL amyloidosis (C).

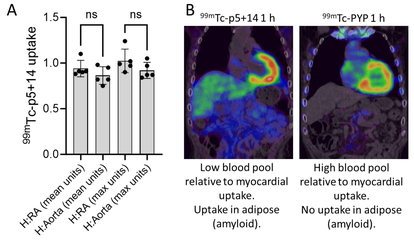

Figure 6. Analysis of cardiac uptake of ^{99m}Tc-p5+14 in HV and patients with amyloidosis at 1 h pi. (A) The heart (LV and IVS)-to-right atrium (RA) or aorta (blood) ratio in HV was <1 using the mean or max uptake values. In this cohort, cardiac uptake of ^{99m}Tc-p5+14 relative to blood was greater than for ^{99m}Tc-PYP with no evidence of extracardiac uptake.

CONCLUSION

^{99m}Tc-p5+14 is a promising new reagent for the facile detection of ATTR and AL cardiac amyloid using gamma imaging and may serve as a useful tool for the early detection of amyloidosis by community cardiologists.

DISCLOSURE

JSW: Co-founder, interim CSO, and shareholder in Attralus Inc. Research funding from Attralus Inc.
EBM and AS: Founding shareholder in Attralus Inc.
SJK: Founding shareholder in Attralus Inc.
SJK and JSW: Patent rights in peptides used for amyloid imaging, licensed to Attralus.

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