

Quantitative assessment of changes in cardiac and extracardiac amyloid load in patients with AL and ATTR amyloidosis, measured by PET/CT imaging using the pan-amyloid reactive radiotracer iodine (¹²⁴I) evuzamitide

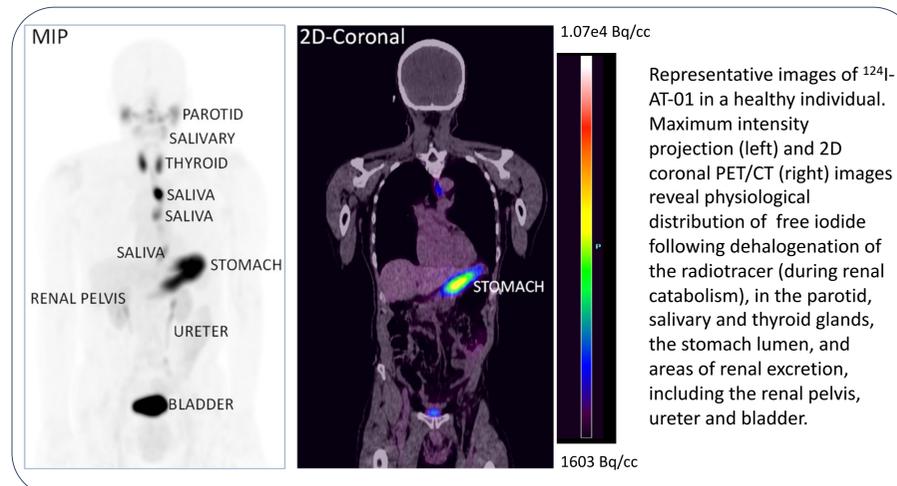
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Introduction

- The early and accurate diagnosis of amyloidosis and an appreciation of the whole-body amyloid burden could improve patient outcomes.
- Therapeutic intervention is most effective when administered early in the course of the disease. Of equal clinical importance is the ability to monitor change in amyloid load to assess response to therapy or progression.
- ¹²⁴I-evuzamitide (¹²⁴I-p5+14), is being developed to diagnose and monitor systemic amyloid deposits by PET/CT imaging.
- PET/CT is an intrinsically quantitative, non-invasive, high-resolution imaging modality, and use of ¹²⁴I-evuzamitide could provide a facile method for diagnosing and monitoring amyloidosis.
- The goal of this study is to quantitatively assess changes in organ-specific ¹²⁴I-evuzamitide uptake in AL and ATTR patients.

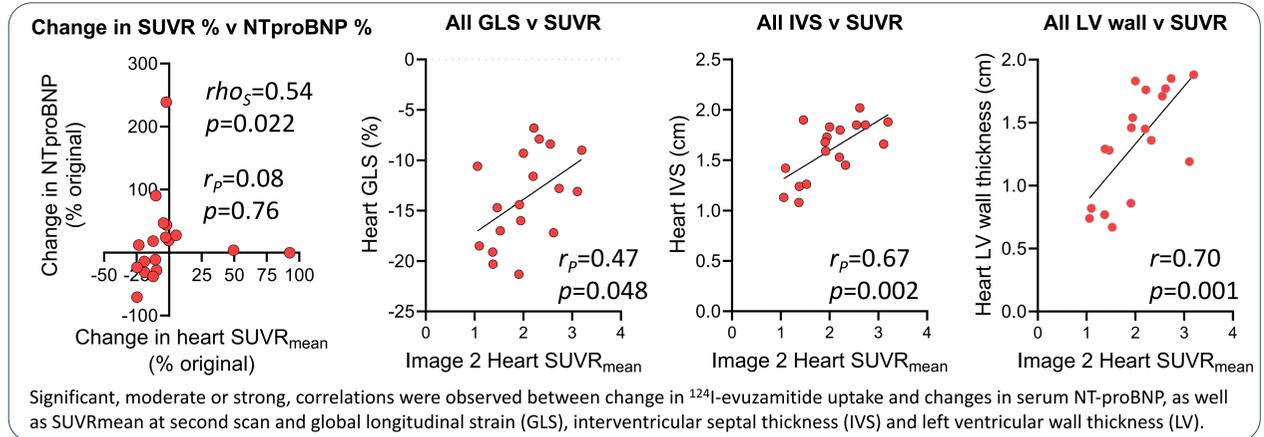
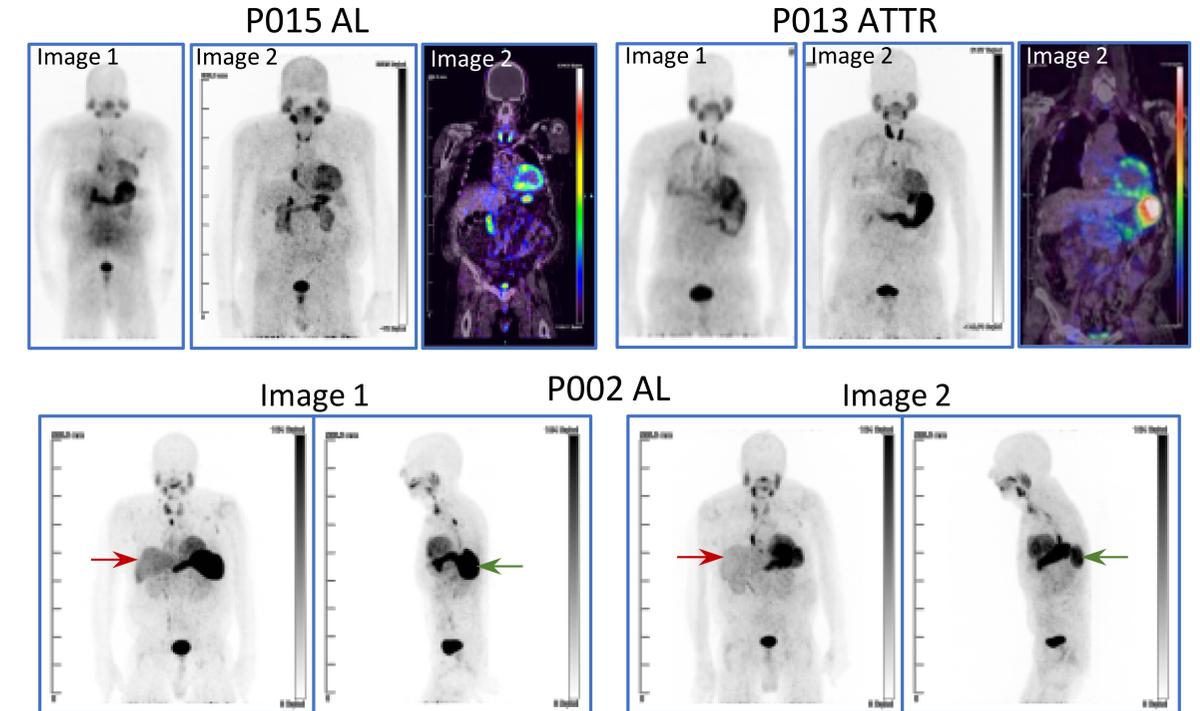
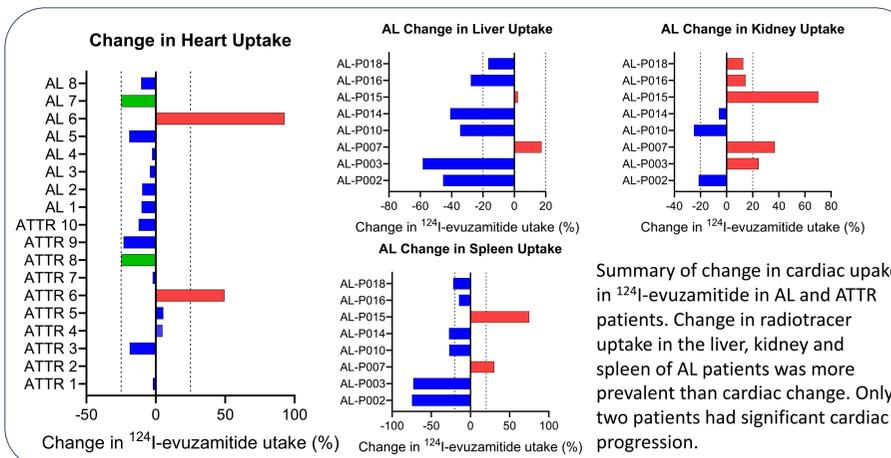
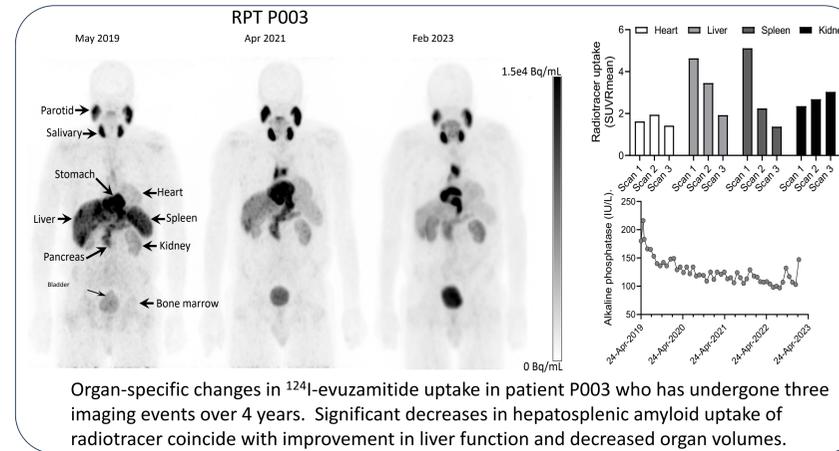
Methods: The study has enrolled 19 patients (AL (*n*=9) and ATTR (*n*=10)) who had positive cardiac uptake of ¹²⁴I-evuzamitide in the Phase 1 (AMY1001 study) (NCT05968846). Patients were re-imaged using 37 or 74 MBq ¹²⁴I-evuzamitide via IV bolus injection with PET/CT imaging performed ~5 h thereafter. Radiotracer uptake in the heart, liver, spleen and kidney was quantified from PET/CT images by fully manual 2D region of interest analysis. The blood pool (thoracic aorta) was used as a reference tissue to determine standard uptake value ratios (SUVR_{mean}). Serum biomarkers were measured, and a transthoracic echocardiographic assessment was performed on the day before imaging. Correlations between cardiac uptake with echocardiography parameters and serum biomarkers were assessed.



Results: The PET images were of high quality and readily interpretable. The mean time between imaging sessions was 3.0±0.9 y. In patients with ATTR amyloidosis (*n*=10) on silencers or stabilizer therapy, cardiac amyloid assessed by ¹²⁴I-evuzamitide uptake changed by -2.4%±21.4% (range -24.7% to +49.5%). Despite therapy, only 1 out of 10 cardiac ATTR patients had a decrease of ≥25%. In patients with AL (*n*=9), cardiac amyloid changed by 1.5%±37.6% (range -24.7% to +92.7%). In contrast, in AL patients the liver and spleen decreased dramatically, -25.5%±25.3% and -16.6%±49.9%, respectively. Significant correlations were observed between echocardiography parameters, serum NTproBNP and cardiac SUVR_{mean} measurements.

Patient ID	Amyloid	Initial Scan Date	Initial Cardiac SUVR	Treatment between scans	Repeat Scan Date	Repeat Cardiac SUVR	Responder* / Progressor* / Stable (Δ%)
RPT P001	ATTR	9/10/19	3.17	Onpattro	12/8/23	3.11	S (-2.01)
RPT P002	AL	7/21/20	3.05	None - hem. remission	12/15/22	2.73	S (-10.19)
RPT P003	AL	4/6/21	1.62	Darzalex	2/2/23	1.46	S (-9.72)
RPT P004	ATTR	9/17/19	1.95	Tegsedi→Onpattro	2/9/23	1.95	S (-0.25)
RPT P005	ATTR	8/24/21	3.14	Vyndamax→Amvuttra	2/16/23	2.55	S (-18.73)
RPT P006	ATTR	6/16/20	2.50	Tegsedi	2/23/23	2.62	S (4.78)
RPT P007	AL	3/5/19	1.44	None - hem. remission	3/2/23	1.38	S (-4.18)
RPT P008	ATTR	11/17/20	2.21	Vyndamax→Acoramidis	3/9/23	2.33	S (5.41)
RPT P009	ATTR	1/21/20	2.14	Onpattro+Vyndamax	3/23/23	3.20	P (49.5)
RPT P010	AL	4/27/21	1.97	None - hem. remission	3/30/23	1.92	S (-2.59)
RPT P011	ATTR	4/13/21	1.95	Vyndamax+Onpattro→Vyndamax+Amvuttra	4/6/23	1.91	S (-2.17)
RP PT012	ATTR	9/22/20	1.41	Diflunisal→Onpattro→Amvuttra	4/13/23	1.06	R (-24.71)
RPT P013	ATTR	8/25/20	2.60	Vyndamax+Onpattro→Vyndamax+Amvuttra	5/4/23	2.00	S (-23.16)
RPT P014	AL	1/22/19	1.89	None - hem. remission	5/11/23	1.53	S (-19.03)
RPT P015	AL	5/11/21	1.15	Darzalex/Lenalidomide	5/25/23	2.22	P (92.69)
RPT P016	AL	11/3/20	1.46	None - hem. remission	6/15/23	1.10	R (-24.67)
RPT P017	ATTR	9/29/20	1.56	Diflunisal+Onpattro→Vyndamax+Onpattro→Vyndamax+Amvuttra	6/22/23	1.37	S (-12.32)
RPT P018	AL	7/30/19	2.46	None - hem. remission	7/13/23	2.20	S (-10.53)
RPT P019	AL	8/6/19	1.92	None - hem. remission	7/20/23	1.68	S (-12.31)

* ≥25% decrease in SUVR from initial scan; † ≥25% increase in SUVR from initial scan



Conclusion: Changes in cardiac amyloid load, based on differential uptake of radiotracer, can be quantified using ¹²⁴I-evuzamitide PET/CT imaging and may be useful for monitoring changes in organ-specific amyloid load. In this small study, TTR silencers, stabilizers, or combinations thereof, had little to no effect on cardiac amyloid load in patients with ATTR amyloidosis.

Disclosure: This work was supported in part by Attralus. AS, SK, EM, SG, and JW co-founded and are shareholders in Attralus. SK and JW are inventors of iodine (¹²⁴I) evuzamitide and its use as an imaging agent.

