## 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.
- <sup>124</sup>I-evuzamitide (<sup>124</sup>I-p5+14), is being developed to diagnose and monitor systemic amyloid deposits by PET/CT imaging.
- PET/CT is an intrinsically quantitative, non-invasive, highresolution imaging modality, and use of <sup>124</sup>I-evuzamitide could provide a facile method for diagnosing and monitoring amyloidosis.
- The goal of this study is to quantitatively assess changes in organ-specific <sup>124</sup>I-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 <sup>124</sup>Ievuzamitide in the Phase 1 (AMY1001 study) (NCT05968846). Patients were re-imaged using 37 or 74 MBq <sup>124</sup>I-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 (SUVRmean). 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.



Representative images of <sup>124</sup>I-AT-01 in a healthy individual. Maximum intensity projection (left) and 2D coronal PET/CT (right) images reveal physiological distribution of free iodide following dehalogenation of the radiotracer (during renal catabolism), in the parotid salivary and thyroid glands, the stomach lumen, and areas of renal excretion, including the renal pelvis, ureter and bladder.

**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 <sup>124</sup>I-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  $\geq 25\%$ . 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 SUVRmean measurements.

Patient ID	Amyloid	Initial	Initial	Treatment between	Repeat	Repeat	Responder <sup>a</sup> /
		Scan	Cardiac	scans	Scan Date	Cardiac	Progressor <sup>b</sup> /
		Date	SUVR			SUVR	Stable (∆%)
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				Diflunisal+Onpattro→			· · ·
	ATTR	9/29/20	1.56	Vyndamax+Onpattro→	6/22/23	1.37	S (-12.32)
				Vyndamax+Amvuttra			
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)



Organ-specific changes in <sup>124</sup>I-evuzamitide uptake in patient P003 who has undergone three imaging events over 4 years. Significant decreases in hepatosplenic amyloid uptake of radiotracer coincide with improvement in liver function and decreased organ volumes.







Change in <sup>124</sup>I-evuzamitide utake (%)

Summary of change in cardiac upake in <sup>124</sup>I-evuzamitide in AL and ATTR patients. Change in radiotracer uptake in the liver, kidney and spleen of AL patients was more prevalent than cardiac change. Only two patients had significant cardiac progression.

P015 AL







Significant, moderate or strong, correlations were observed between change in <sup>124</sup>I-evuzamitide uptake and changes in serum NT-proBNP, as well as SUVRmean at second scan and global longitudinal strain (GLS), interventricular septal thickness (IVS) and left ventricular wall thickness (LV).

**Conclusion**: Changes in cardiac amyloid load, based on differential uptake of radiotracer, can be quantified using <sup>124</sup>I-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.

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## P013 ATTR









All IVS v SUVR





5

1850