



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

654.MGUS, AMYLOIDOSIS AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL**Structural and Functional Cardiac Parameters in Patients with AL Amyloidosis Correlate with Uptake of the Amyloidophilic Radiotracer Iodine (¹²⁴I) Evuzamitide**

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Background: The deposition of fibrillar aggregates of monoclonal free light chains in the heart is a characteristic feature of light chain associated (AL) amyloidosis. Cardiac amyloid is the major cause of morbidity and mortality in these patients. Structural and functional sequelae of cardiac amyloidosis can be appreciated clinically using echocardiography, cardiac magnetic resonance imaging, and measurement of serum NT-proBNP and troponins. These measures are not particularly amyloid-specific, and the correlation between parameters derived from these evaluations and amyloid burden remain enigmatic. The iodine-124 labeled peptide (p5+14), iodine (¹²⁴I) evuzamitide, is a novel radiotracer that is being evaluated for the detection of systemic amyloidosis, of any type, by PET/CT imaging. As an amyloid binding peptide, this radiotracer has the potential to serve as a first line diagnostic agent capable of providing whole body semi-quantitative estimation of organ-specific amyloid load. Nascent studies of the relationship between ¹²⁴I-evuzamitide uptake and established clinical parameters in patients with amyloidosis are underway. Here we report a single site, open label pilot study of 18 (*n*=18) patients with AL (*n*=8) and ATTR amyloidosis (*n*=10) that evaluates the cardiac uptake of ¹²⁴I-evuzamitide with contemporaneous echocardiographic and serum biomarkers (NCT05968846).

Methods: The data described herein was collected as part of an open label single site repeat imaging study that plans to enroll up to 20 (*n*=20) patients with AL (*n*=10) and ATTR (*n*=10) amyloidosis. To date, eight (*n*=8) patients with AL and ten (*n*=10) with ATTR amyloidosis have undergone ¹²⁴I-evuzamitide PET/CT imaging with contemporaneous transthoracic echocardiography and assessment of serum NTproBNP within ~30 h of imaging. Patients received 37 or 74 MBq ¹²⁴I-evuzamitide, and PET/CT imaging was performed at ~5 h post injection. Images were interpreted by a single reviewer, experienced in evaluating this tracer, for positive cardiac uptake. A fully manual 2D region of interest (ROI) analysis was performed encompassing the free left ventricular (LV) wall, LV lumen and interventricular septum (IVS). Blood pool was used as a reference tissue to determine standard uptake value ratios (SUVR_{mean}) and to control for the rate of tracer clearance from the central compartment. Cardiac uptake of radiotracer was compared with free LV wall thickness (cm), IVS thickness (cm), global longitudinal strain (GLS, %), and serum NT-proBNP (pg/mL) measurements. Pearson and Spearman correlations were used to test for associations between variables.

Results: Patients with AL amyloidosis were Mayo Stage I (*n*=2/8) or Stage II (*n*=6/8). The mean serum NTproBNP was 672.9±762.4 pg/mL (min=98, max=2327). With singular exception, all patients with AL amyloidosis had visually evident cardiac uptake of ¹²⁴I-evuzamitide in the PET/CT images. In patients with AL amyloidosis (*n*=8), the SUVR_{mean} (encompassing the LV, lumen and IVS) correlated strongly with LV thickness (cm) (Pearson *r*=0.83, *p*=0.011) and GLS (%) (Pearson *r*=0.74, *p*=0.037), but not the IVS thickness (cm) (Pearson *r*=0.57, *p*=0.142). In contrast, in patients with ATTR (*n*=10), there was no significant correlation of SUVR_{mean} with GLS (*p*=0.395), but a moderate significant correlation of SUVR_{mean} with the LV (*p*=0.037) and IVS (*p*=0.017) thickness was observed. Similarly, in this pilot cohort, we observed a strong positive correlation between serum NTproBNP and cardiac SUVR_{mean} (Pearson *r*=0.81, *p*=0.015), but not for patients with ATTR amyloidosis (Pearson *r*=0.58, *p*=0.079).

Conclusion: Serum NTproBNP is a validated and qualified measure of overall survival for patients with AL amyloidosis (PMID: 27416985). Global longitudinal strain, with or without inclusion of other structural parameters such as left atrial volume, is a strong predictor of survival in patients with AL amyloidosis (PMID: 29111123, PMID: 37143609). PET/CT imaging using ¹²⁴I-evuzamitide is a promising technique for diagnosing and monitoring AL and other types of amyloidosis. In light of these

early results that demonstrate a strong relationship between validated metrics of all cause mortality in patients with AL, larger studies should seek to evaluate similar relationships with some metric of ¹²⁴I-ivuzamitide uptake in the heart, and indeed other organs.

Disclosures No relevant conflicts of interest to declare.

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