Monitoring patisiran and inotersen treatment with quantitative SPECT/CT in hereditary transthyretin amyloid cardiomyopathy

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Background: Novel ribonucleic acid interference (RNAi) therapeutics such as patisiran and inotersen have been shown to benefit neurologic disease course and quality of life in patients with hereditary transthyretin amyloidosis (ATTRv).

Purpose: We aimed to determine treatment effects on myocardial amyloid load determined by quantitative single photon emission computed tomography/computed tomography (SPECT/CT) in patients with ATTRv-related cardiomyopathy (ATTRv-CM) and to identify nuclear imaging biomarkers to quantify and monitor response to therapy.

Methods: ATTRv-CM patients underwent [99mTc]-radiolabeled diphosphono-1,2-propanodicarboxylic acid ([99mTc]-DPD) scintigraphy and SPECT/CT imaging before and after 12 months of treatment with patisiran (n=5) or inotersen (n=4).

Results: Patisiran-treated patients had a significant reduction in cardiac uptake as measured by standardized uptake values (SUVpeak: 7.98 g/mL ± 0.87 vs. 6.50 g/mL ± 1.59, p=0.025, Figure 1A; SUVmax: 8.80 g/mL ± 0.94 vs. 6.96 g/mL ± 1.59, p=0.009, Figure 1B; SUVmean: 5.64 g/mL ± 1.01 vs. 4.42 g/mL ± 1.26, p=0.016, Figure 1C). Patients treated with inotersen showed evidence of stabilization in cardiac SUV uptake (SUVpeak: 8.56 g/mL ± 2.25 vs. 7.99 g/mL ± 1.90, p=0.665; SUVmax: 9.29 g/mL ± 2.39 vs. 8.79 g/mL ± 2.03, p=0.719; SUVmean: 5.07 g/mL ± 1.46 vs. 4.86 g/mL ± 0.95, p=0.834) but had significant deterioration in left ventricular (LV) function (LV cardiac index: 3.39 L/min/m2 ± 0.04 vs. 2.94 L/min/m2 ± 0.01, p=0.028, Figure 1D). Comparison of cardiac SUV uptake and longitudinal cardiac function revealed significant correlations between longitudinal changes in cardiac SUVpeak and LV global longitudinal strain (r=-0.658, p=0.027, Figure 1E) and right ventricular free wall longitudinal strain (r=-0.771, p=0.008, Figure 1F).

Conclusions: In conclusion, using serial quantitative SPECT/CT imaging, we demonstrated that patisiran treatment significantly reduces cardiac SUV uptake in ATTRv-CM patients, indicating regression of cardiac TTR amyloid. Our data suggest that quantitative SPECT/CT imaging may be a valid tool to quantify and monitor response to disease-specific RNAi therapeutic agents in ATTRv-CM patients.
Figure 1. Longitudinal Changes in Nuclear Imaging and Cardiac Magnetic Resonance Imaging Parameters and Correlation with Longitudinal Cardiac Function.

Figure 1
Graphical Abstract