Vutrisiran: Cardiac Magnetic Resonance Imaging

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SUMMARY

- HELIOS-B was a phase 3, global, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy and safety of vutrisiran in patients with ATTR-CM. CMR was not included as an assessment in the HELIOS-B study.[1,2]
- An analysis of 43 patients with baseline CMR from the UK National Amyloidosis Centre who participated in HELIOS-B and underwent serial CMR as part of their routine clinical care was conducted to evaluate the association between treatment with vutrisiran and changes in cardiac structure, function, and amyloid burden.[3]

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STUDY DESIGN

HELIOS-B

HELIOS-B was a phase 3, global, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy and safety of vutrisiran in patients with ATTR-CM, including both hATTR and wtATTR. Patients were randomized (1:1) to receive either vutrisiran 25 mg (n=326) or placebo (n=329) every 3 months by subcutaneous injection for up to 36 months. The primary endpoint was the composite endpoint of all-cause mortality and recurrent CV events (CV hospitalizations and urgent heart failure visits) at the end of the double-blind period in the overall population and in the monotherapy population (patients not receiving tafamidis at baseline). After the double-blind period, all remaining eligible patients were allowed to receive vutrisiran in an OLE.[1]

CMR Analysis

Per the study protocol, CMR was not included as an assessment as part of the HELIOS-B study.[2] Patients from the UK National Amyloidosis Centre who participated in HELIOS-B and underwent serial CMR as part of their routine clinical care were retrospectively identified to analyze the association between treatment with vutrisiran and changes in cardiac structure, function, and amyloid burden. CMRs were

conducted at baseline and at months 12, 24, and 36. The CMR analysis was conducted by two independent readers, blinded to treatment allocation.[3]

PATIENT DEMOGRAPHICS & BASELINE CHARACTERISTICS

A total of 43 patients from the UK National Amyloidosis Centre who participated in HELIOS-B underwent baseline CMR. A summary of the baseline characteristics and CMR parameters is presented in **Table 1**.[3]

No patients in either treatment group received a TTR stabilizer during the study period. Of the 43 patients, 39 patients (21 patients receiving vutrisiran, 18 patients receiving placebo) completed 1-year CMR, 26 patients (14 patients receiving vutrisiran, 12 patients receiving placebo) completed 2-year CMR, and 17 patients (9 patients receiving vutrisiran, 8 patients receiving placebo) completed 3-year CMR assessments.[3]

Table 1. Baseline Characteristics and CMR Parameters.[3]

Characteristic	Placebo (n=22)	Vutrisiran (n=21)
Age, years, mean (±SD)	75.81 (±6.17)	74.32 (±5.16)
Sex (male:female)	21:1	20:1
NT-proBNP, ng/L, median (IQR)	1915 (940, 2432)	2417 (1210, 3254)
eGFR, mL/min/1.73m^2, median (IQR)	66.0 (59.0, 83.0)	72.5 (59.0, 82.0)
Troponin I, ng/L, median (IQR)	51.6 (40.1, 100.3)	77.6 (54.2, 128.7)
KCCQ Score, mean (±SD)	72.8 (±22.7)	77.7 (±18.6)
Wild-type:variant TTR genotype	18:4	19:2
CMR Parameters, mean (± SD)		
LV EDV, mL	172.83 (±42.29)	164.19 (±35.11)
LV ESV, mL	87.77 (±41.11)	86.83 (±36.27)
LV SV, mL	85.8 (±24.28)	84.90 (±18.89)
LVEF, %	50.62 (±13.32)	51.70 (±11.52)
LVM, g	184.76 (±33.08)	188.91 (±38.32)
RV EDV, mL	178.30 (±36.72)	183.92 (±52.01)
RV ESV, mL	97.18 (±34.03)	99.06 (±43.71)
RV SV, mL	81.07 (±20.61)	85.37 (±19.12)
RVEF, %	46.28 (±10.34)	48.36 (±12.05)
LAA, cm^2	32.60 (±6.21)	32.95 (±7.67)
RAA, cm^2	31.15 (±7.92)	31.63 (±8.25)
Native T1, ms	1135.91 (±44.69)	1137.29 (±40.38)
ECV, %	58.73 (±5.87)	56.05 (±8.71)

Abbreviations: CMR = cardiac magnetic resonance; ECV = extracellular volume; EDV = end-diastolic volume; eGFR = estimated glomerular filtration rate; ESV = end-systolic volume; IQR = interquartile range; KCCQ = Kansas City Cardiomyopathy Questionnaire; LAA = left atrial area; LV = left ventricular; LVEF = left ventricular ejection fraction; LVM = left ventricular mass; RAA = right atrial area; RV = right ventricular; RVEF = right ventricular ejection fraction; SD = standard deviation; SV = stroke volume; NT-proBNP = N-terminal pro-brain natriuretic peptide; SD = standard deviation; TTR = transthyretin.

CMR RESULTS

The differences between the vutrisiran and placebo groups at follow-up were assessed using analysis of covariance with treatment group and baseline CMR values as covariates. The 24- and 36-month data were pooled in a mixed model analysis to assess treatment effect of vutrisiran due to reduced patient numbers at follow-up (**Table 2**).[3]

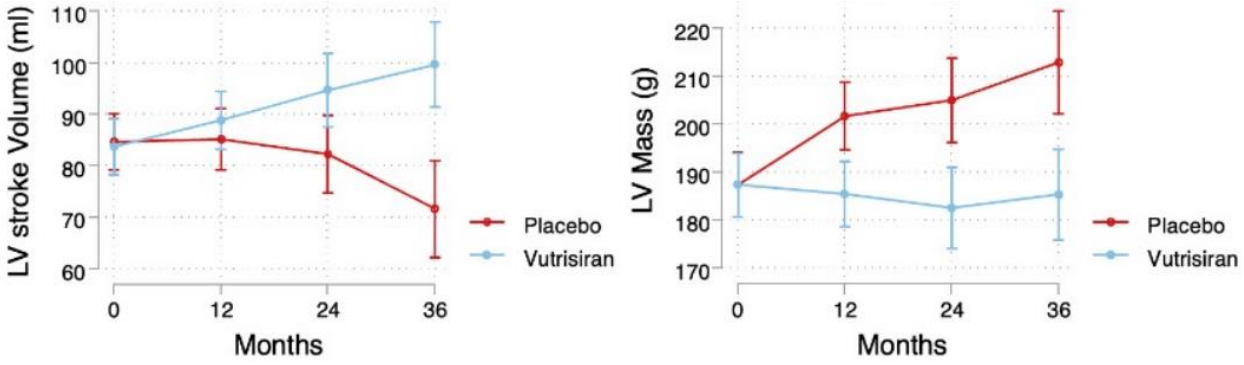
Table 2. Pooled Treatment Effect (Months 24 and 36) of Vutrisiran Compared with Placebo on CMR Parameters.[3]

Parameter	Baseline Value, Mean (SD)	Pooled Treatment Effect (Months 24 and 36), LSMD (95% CI)	Nominal P-value
LV EDV, mL	168.72 (38.82)	-2.66 (-14.11, 8.78)	0.648
LV ESV, mL	87.32 (38.41)	-23.30 (-35.55, -11.04)	<0.001
LV SV, mL	83.47 (21.76)	17.81 (7.34, 28.29)	0.001
LVEF, %	50.66 (12.34)	11.57 (6.00, 17.15)	<0.001
LVM, g	186.74 (35.54)	-22.07 (-34.57, -9.57)	0.001
RV EDV, mL	180.98 (44.24)	-15.12 (-31.96, 1.71)	0.078
RV ESV, mL	98.07 (38.46)	-26.51 (-41.51, -11.52)	0.001
RV SV, mL	83.12 (19.79)	12.94 (2.25, 23.62)	0.018
RVEF, %	47.27 (11.10)	10.51 (5.49, 15.52)	<0.001
LAA, cm^2	32.77 (6.89)	-0.30 (-3.37, 2.76)	0.846
RAA, cm^2	31.39 (7.99)	0.75 (-2.52, 4.03)	0.651
Native T1, ms	1136.58 (42.14)	-18.58 (-35.83, -1.34)	0.035
ECV, %	57.42 (7.43)	-3.42 (-5.98, -0.85)	0.009

Abbreviations: CMR = cardiac magnetic resonance; ECV = extracellular volume; EDV = end-diastolic volume; ESV = end-systolic volume; LAA = left atrial area; LSMD = least squares mean difference; LV = left ventricular; LVEF = left ventricular ejection fraction; LVM = left ventricular mass; RAA = right atrial area; RV = right ventricular; RVEF = right ventricular ejection fraction; SD = standard deviation; SV = stroke volume.

The mean (±SD) LV stroke volume and LV mass observed in the vutrisiran and placebo groups over time are shown in **Figure 1**.[3]

Figure 1. Mean (±SD) LV Stroke Volume and LV Mass Over 36 Months.[3]



Abbreviations: LV = left ventricular; SD = standard deviation.
From Razvi et al.[3]

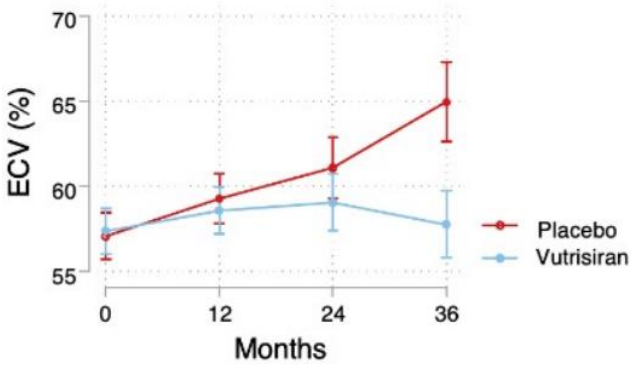
ECV

In the analysis, amyloid progression and regression were defined as an absolute change of ≥5% in ECV. Changes <5% were considered stable.[3]

At 36 months, amyloid regression was observed in 2 out of 9 patients (22%) who received vutrisiran and no patients who received placebo. Conversely, amyloid progression was observed in 5 out of 8 patients (63%) who received placebo and 1 out of 9 patients (11%) who received vutrisiran.[3]

The absolute mean (±SD) change from baseline in ECV at 36 months was -0.10% (±4.72) in the vutrisiran group and +7.86% (±5.67) in the placebo group. The mean (±SD) ECV observed in the vutrisiran and placebo groups over time is shown in **Figure 2**.[3]

Figure 2. Mean (±SD) ECV Over 36 Months.[3]



Abbreviations: ECV = extracellular volume.
From Razvi et al.[3]

ABBREVIATIONS

ATTR-CM = transthyretin amyloidosis with cardiomyopathy; CMR = cardiac magnetic resonance; CV = cardiovascular; ECV = extracellular volume; EDV = end-diastolic volume; eGFR = estimated glomerular filtration rate; ESV = end-systolic volume; hATTR = hereditary transthyretin amyloidosis; KCCQ = Kansas City Cardiomyopathy Questionnaire; LAA = left atrial area; LSMD = least squares mean difference; LV = left ventricular; LVEF = left ventricular ejection fraction; LVM = left ventricular mass; NT-proBNP = N-terminal pro-brain natriuretic peptide; OLE = open-label extension; RAA = right atrial area; RV = right ventricular; RVEF = right ventricular ejection fraction; SD = standard deviation; SV = stroke volume; TTR = transthyretin; wtATTR = wild-type transthyretin amyloidosis.

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REFERENCES

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3. Razvi Y, Sheikh A, Patel R, et al. Effects of vutrisiran on measures of cardiac structure, function and amyloid burden by cardiovascular magnetic resonance from the HELIOS-B trial. Presented at: American Heart Association (AHA) Annual Scientific Sessions; November 7-10, 2025; New Orleans, LA, USA.