Right Ventricular Free Wall Strain and Clinical Outcomes in Transthyretin Amyloid Cardiomyopathy and Effect of Vutrisiran: The HELIOS-B Study

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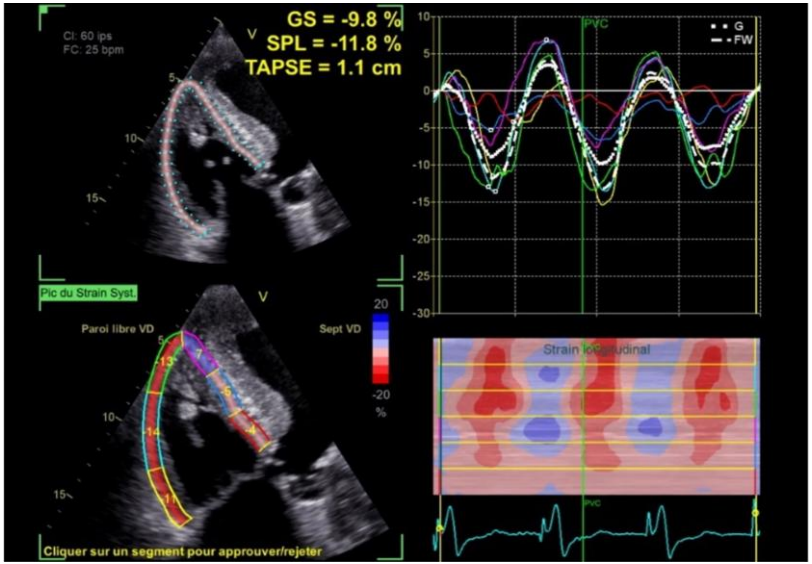
Background

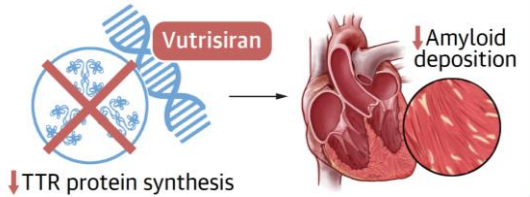
Transthyretin Amyloidosis with Cardiomyopathy (ATTR-CM) and RV Involvement

- Deposition of amyloid fibrils is widespread in ATTR-CM, involving both ventricles.
- Greater right ventricular (RV) involvement and more impaired RV function have been associated with worse prognosis in patients with ATTR-CM.
- RV free wall strain (RVFWS) measures RV deformation and may detect subclinical RV dysfunction.



Vutrisiran

- Vutrisiran, a SC-administered RNAi therapeutic, rapidly knocks down circulating concentrations of transthyretin (TTR).
- We sought to investigate the association of RVFWS with clinical outcomes and the effect of vutrisiran on RVFWS.



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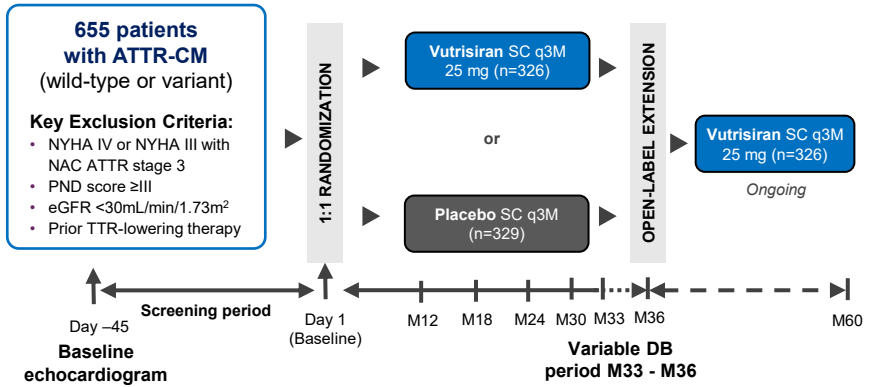
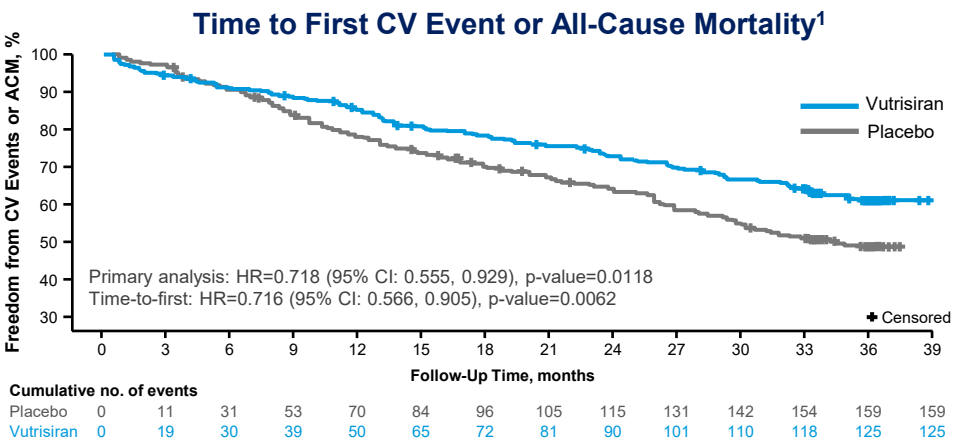
HELIOS-B Study Design and Primary Results

Vutrisiran reduced rates of all-cause mortality and recurrent CV events in HELIOS-B.





Primary endpoint
- Composite of ACM and recurrent CV events up to Month 36

Key secondary endpoint
- ACM up to 42 months

Vutrisiran had favorable effects on cardiac structure and function[2]:
- ➢ Attenuated declines in LV and RV systolic function
- ➢ Improved diastolic function

Abbreviations: ACM, all-cause mortality; ATTR, transthyretin amyloidosis; CI, confidence interval; CM, cardiomyopathy; CV, cardiovascular; DB, double-blind; eGFR, estimated glomerular filtration rate; HR, hazard ratio; NYHA, New York Heart Association; PND, polyneuropathy disability score; SC, subcutaneous.

[1]Fontana M, et al. *N Engl J Med*. 2025 Jan;392(1):33-44; [2]Jering K, et al. *Nat Med*. 2025 Oct;31(10):3560-3568.

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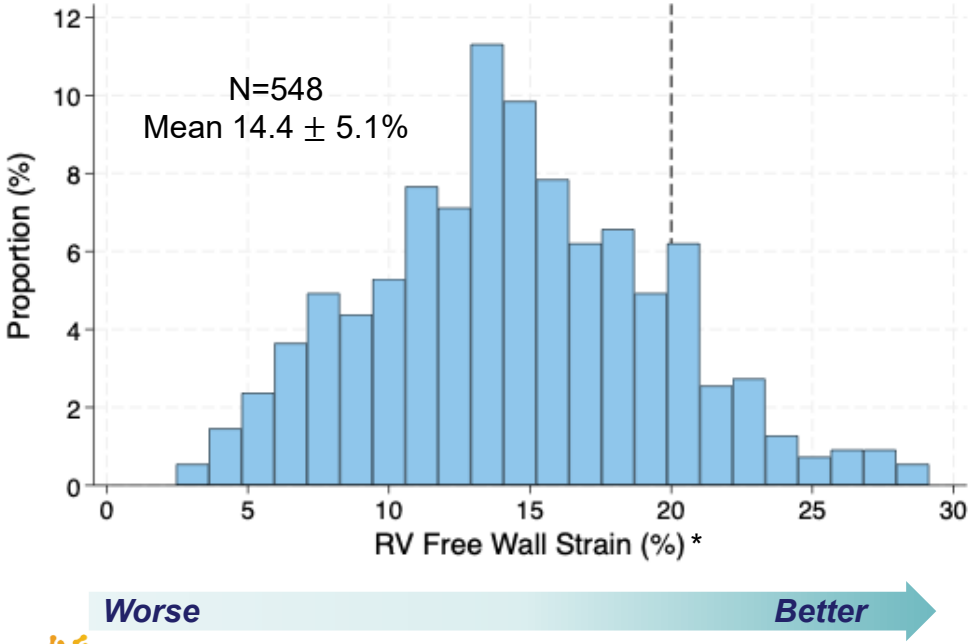
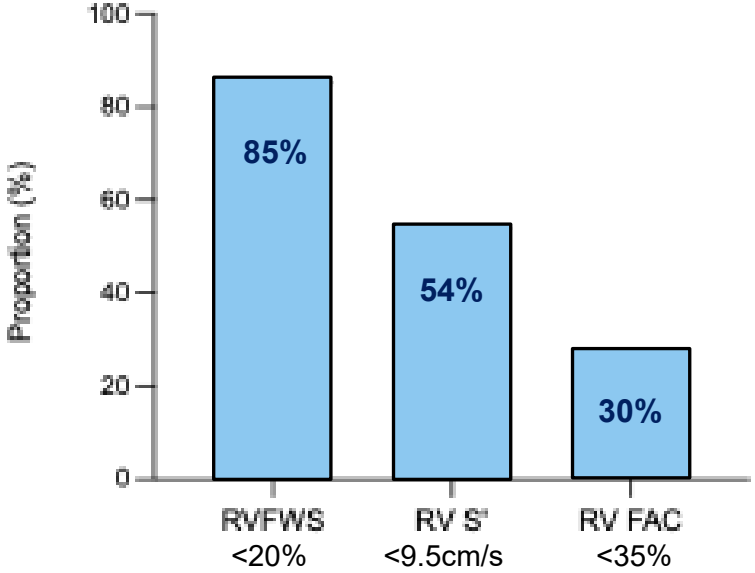
RV dysfunction is common among patients enrolled in HELIOS-B but prevalence differs according to its definition

Distribution of RVFWS



Prevalence of RV Dysfunction



*Shown as absolute value.

Abbreviations: FAC, fractional area change; RV, right ventricular; RVFWS, RV free wall strain, S', systolic myocardial velocity.

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Baseline Characteristics According to RVFWS Quartile

Worse RVFWS → *Better RVFWS*

RV Free Wall Strain	Quartile 1 <10.8% (n=137)	Quartile 2 10.8-14.1% (n=137)	Quartile 3 14.2-17.8% (n=137)	Quartile 4 >17.8% (n=137)	p-value
Age (years)	75 ± 6	76 ± 6	75 ± 7	75 ± 7	0.17
Male sex	96%	94%	91%	88%	0.02
ATTRwt	88%	87%	89%	86%	0.73
NAC ATTR Stage ≥2	49%	33%	24%	22%	<0.001
History of AF/AFl	79%	69%	60%	47%	<0.001
NT-proBNP (ng/L)	2746 [1790, 4465]	2167 [1258, 3167]	1765 [1172, 2589]	1138 [680, 2278]	<0.001
eGFR (mL/min/1.73m^2)	62 ± 19	68 ± 20	70 ± 20	72 ± 25	<0.001
Echocardiographic Characteristics					
LV mass index (g/m^2)	190 ± 47	189 ± 44	182 ± 46	165 ± 39	<0.001
LVEF (%)	49 ± 14	54 ± 12	57 ± 11	63 ± 9	<0.001
Absolute GLS (%)	12 ± 3	13 ± 3	14 ± 3	16 ± 3	<0.001
E/e'	19 ± 6	18 ± 6	18 ± 6	16 ± 6	<0.001
RV EDA (cm^2)	24 ± 7	22± 6	22 ± 5	21 ± 5	<0.001
RV FAC (%)	36 ± 8	38 ± 8	39 ± 8	43 ± 9	<0.001
TR velocity (m/s)	2.5 ± 0.4	2.5 ± 0.4	2.6 ± 0.5	2.6 ± 0.5	0.11

Abbreviations: AF/AFl, atrial fibrillation/flutter; ATTR, transthyretin amyloidosis; A wave, late mitral inflow velocity; E wave, early mitral inflow velocity; e', early diastolic mitral annular tissue velocity; GLS, global longitudinal strain; LA, left atrial; LVEF, left ventricular ejection fraction; NAC, National Amyloidosis Centre; NT-proBNP, N-terminal pro-B-type natriuretic peptide; wt, wild-type.

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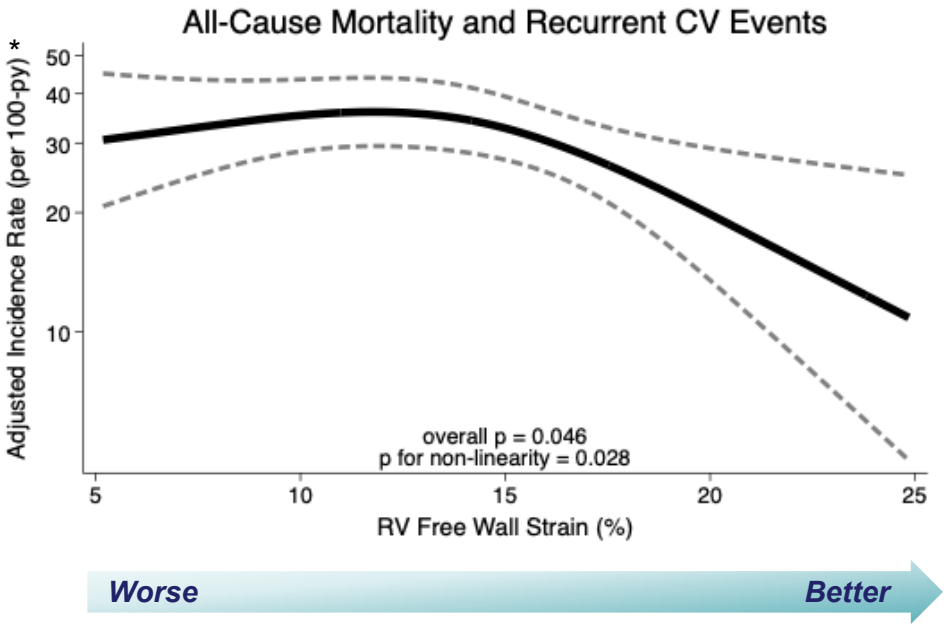
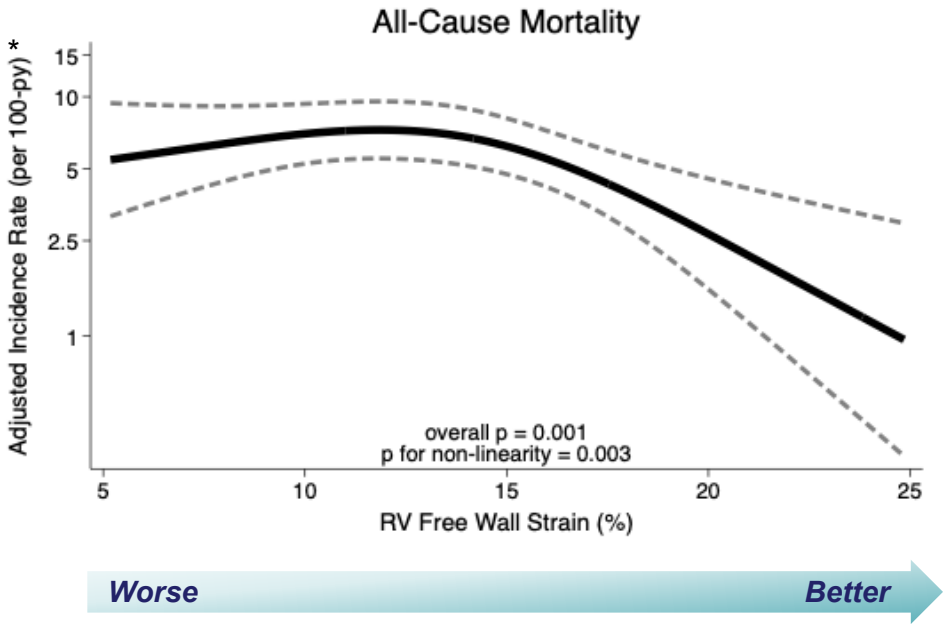
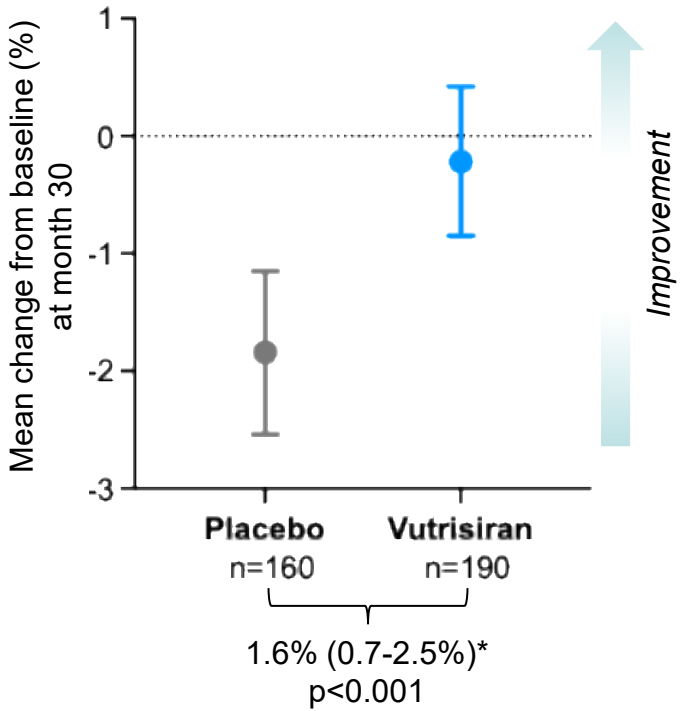
RVFWS is non-linearly associated with all-cause mortality and recurrent CV events





*Adjusted for age, sex, ATTR genotype (wild-type vs variant), NAC disease stage, atrial fibrillation/flutter, treatment assignment, baseline tafamidis use, and LV GLS.

Vutrisiran stabilizes RVFWS at month 30 compared with placebo



The treatment effect of vutrisiran on the primary outcome is not modified by RVFWS (p-interaction =0.41).

*Derived in the overall population using linear regression adjusted for baseline value, age, ATTR genotype (wild-type vs variant), baseline tafamidis use and treatment assignment.

Conclusions

- RV dysfunction by RVFWS is highly prevalent among patients with ATTR-CM enrolled in HELIOS-B. RV dysfunction in ATTR-CM may be underestimated using non-deformation-based echocardiographic parameters.
- RV dysfunction is associated with more advanced disease, greater LV mass, higher estimated filling pressures and worse LV function.
- RVFWS is non-linearly associated with all-cause mortality and recurrent CV events, independent of clinical characteristics and global longitudinal strain.
- Consistent with its beneficial effects on other measures of RV function, vutrisiran stabilizes RVFWS at 30 months compared with placebo.

We thank the patients, their families, investigators, staff, and collaborators for their participation in HELIOS-B.

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