Effect of Vutrisiran in Patients with and without Atrial Fibrillation or Flutter: Analysis from HELIOS-B

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Conclusions

- In participants in the HELIOS-B study, those with evidence of AF/AFL were older, with more symptom burden, and worse health status. Patients with AF/AFL had worse LV and RV systolic function.
- Compared to placebo, vutrisiran lowered the risk of all-cause death and recurrent cardiovascular events in patients with and without evidence of AF/AFL.

Background

- Among patients with transthyretin amyloidosis with cardiomyopathy (ATTR-CM), vutrisiran reduced the risk of all-cause death and cardiovascular (CV) events
- Atrial fibrillation, a sign of advanced heart disease, is common among patients with ATTR-CM. Whether the efficacy of vutrisiran is consistent in patients with and without atrial fibrillation is unknown

Objective

To evaluate the efficacy of vutrisiran in patients with and without atrial fibrillation or flutter (AF/AFL) in the HELIOS-B trial

Methods

- **HELIOS-B** is an international, phase 3, double-blind, placebo-controlled trial of vutrisiran versus placebo in patients with ATTR-CM. Participants were randomized to receive vutrisiran 25 mg or placebo in 1:1 fashion. Baseline AF/AFL was determined by medical history or enrollment ECG
- **Primary outcome:** all-cause death and recurrent CV events
- **Statistics:** Primary endpoint was analyzed using LWYY model. Secondary endpoints were analyzed using Cox proportional hazards models. All models were adjusted for baseline N-terminal pro-B type natriuretic peptide (NT-proBNP) level and stratified by baseline tafamidis use

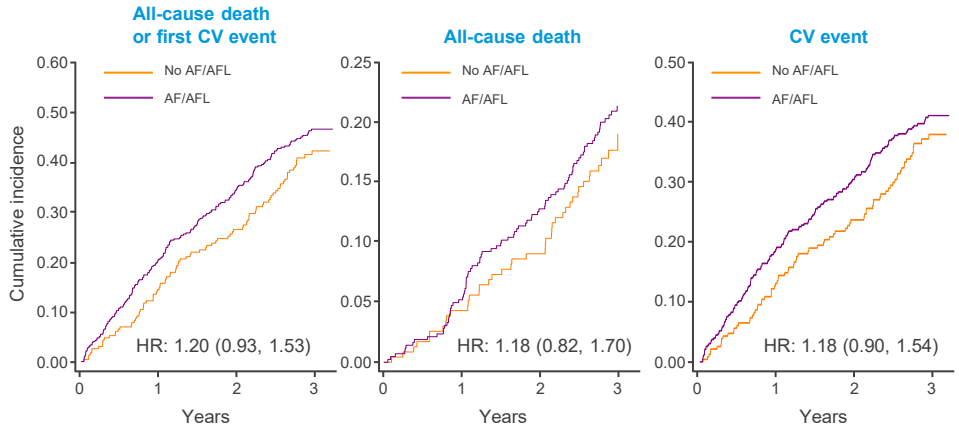
Results

Table. Baseline Clinical and Echocardiographic Characteristics

	No AF/AFL (N=232, 35%)	AF/AFL (N=422, 65%)
Clinical characteristics		
Age, years*	75 ± 8	76 ± 6
Male*	204 (88%)	401 (95%)
NYHA Class III*	14 (6%)	48 (11%)
Wild-type ATTR*	185 (80%)	393 (93%)
Amyloidosis Disease Stage*		
1	185 (80%)	185 (60%)
2	42 (18%)	145 (34%)
3	5 (2%)	25 (6%)
Years since diagnosis*	0.72 [0.25, 1.64]	0.99 [0.35, 2.18]
NT-proBNP, ng/L*	1470 [882, 2454]	2287 [1305, 3692]
Troponin I, ng/L	68 [48, 107]	67 [40, 106]
6-minute walk test distance, m	384 [321, 450]	370 [299, 437]
KCCQ-Clinical Summary Score*	79 ± 19	75 ± 19
KCCQ-Total Symptom Score*	81 ± 20	77 ± 19
KCCQ-Overall Summary Score*	75 ± 19	71 ± 20
Echocardiographic characteristics		
Mean LV wall thickness, cm	1.79 ± 0.26	1.83 ± 0.27
LV end diastolic volume index, mL/m²*	50 ± 13	47 ± 12
LV end systolic volume index, mL/m²	22 ± 11	22 ± 11
LV mass index, g/m²	179 ± 43	183 ± 46
LV ejection fraction, %*	58 ± 12	55 ± 13
GLS, %*	–14.8 ± 3.4	–13.5 ± 3.4
Absolute GLS ≥16%*	81 (34.9%)	98 (23.2%)
Stroke volume index, mL/m²*	28 ± 7	25 ± 7
Left atrial volume index, mL/m²*	36.4 ± 9.7	40.0 ± 10.5
Tricuspid annular S', cm/s*	10.2 ± 2.6	8.9 ± 2.6
RV fractional area change, %	40 ± 9	39 ± 9

*Denotes p-values<0.05.
AF/AFL = atrial fibrillation or flutter; ATTR = transthyretin amyloidosis; GLS = global longitudinal strain; KCCQ = Kansas City Cardiomyopathy Questionnaire; LV = left ventricle; NT-proBNP = N-terminal pro-B type natriuretic peptide; NYHA = New York Heart Association; RV = right ventricle.

Cumulative Incidence of Key Clinical Outcomes



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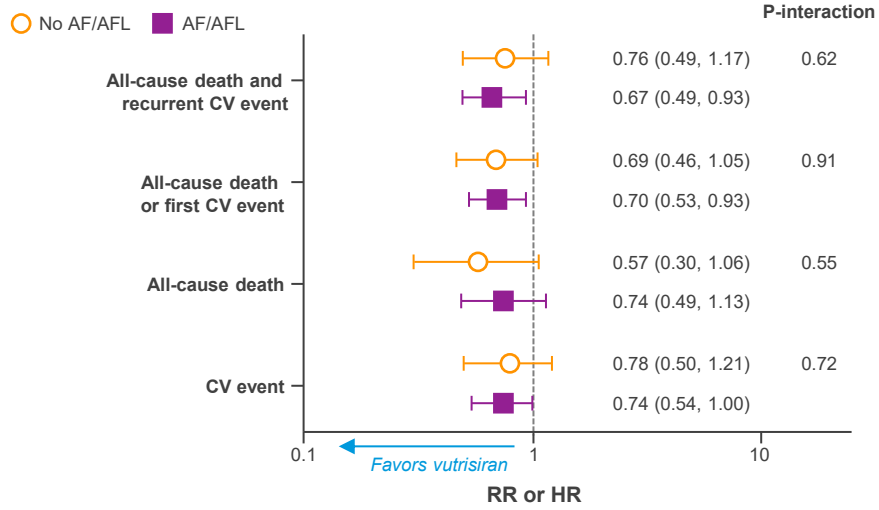

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