Vutrisiran: Use in Patients with Atrial Fibrillation or Flutter

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SUMMARY

- In a post hoc analysis of the HELIOS-B study, the efficacy of vutrisiran in patients with and without AF/AFL was evaluated.[1]
  - Treatment with vutrisiran compared with placebo resulted in a RR of 0.76 (95% CI 0.49, 1.17) for the composite endpoint of all-cause mortality and recurrent CV events in patients with baseline AF/AFL and a RR of 0.67 (95% CI 0.49, 0.93) in patients without baseline AF/AFL.[1]
  - In the overall population of the HELIOS-B study, the incidence of AEs was similar between treatment groups.[2]

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STUDY DESIGN

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. 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).[2]

A post hoc analysis of the HELIOS-B study was conducted to evaluate the efficacy of vutrisiran in patients with and without AF/AFL. Baseline AF/AFL was determined by medical history or ECG at enrollment.[1]

PATIENT DEMOGRAPHICS & BASELINE CHARACTERISTICS

Baseline characteristics between patients with AF/AFL and those without AF/AFL are shown in **Table 1**.[1]

Table 1. Baseline Patient Demographics and Clinical Characteristics.[1]

Baseline Characteristics	No AF/AFL (N=232, 35%)	AF/AFL (N=422, 65%)
Age, years, mean ±SD [a]	75 ±8	76 ±6
Male sex, n (%) [a]	204 (88)	401 (95)
NYHA Class III (%) [a]	14 (6)	48 (11)
wtATTR, n (%) [a]	185 (80)	393 (93)
Amyloidosis Disease Stage (%) [a]		
1	185 (80)	185 (60)
2	42 (18)	145 (34)
3	5 (2)	25 (6)
Years since diagnosis [IQR] [a]	0.72 [0.25, 1.64]	0.99 [0.35, 2.18]
NT-proBNP, ng/mL [IQR] [a]	1470 [882, 2454]	2287 [1305, 3692]
Troponin I, ng/mL [IQR]	68 [48, 107]	67 [40, 106]
6MWT, m [IQR]	384 [321, 450]	370 [299, 437]
KCCQ-Clinical Summary Score [a]	79 ±19	75 ±19
KCCQ-Total Symptom Score [a]	81 ±20	77 ±19
KCCQ-Overall Summary Score [a]	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/m^2 [a]	50 ±13	47 ±12
LV end systolic volume index, mL/m^2	22 ±11	22 ±11
LV mass index, g/m^2	179 ±43	183 ±46
LV ejection fraction, % [a]	58 ±12	55 ±13
GLS, % [a]	-14.8 ±3.4	-13.5 ±3.4
Absolute GLS ≥16% (%) [a]	81 (34.9)	98 (23.2)
Stroke volume index, mL/m^2 [a]	28 ±7	25 ±7
Left atrial volume index, mL/m^2 [a]	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

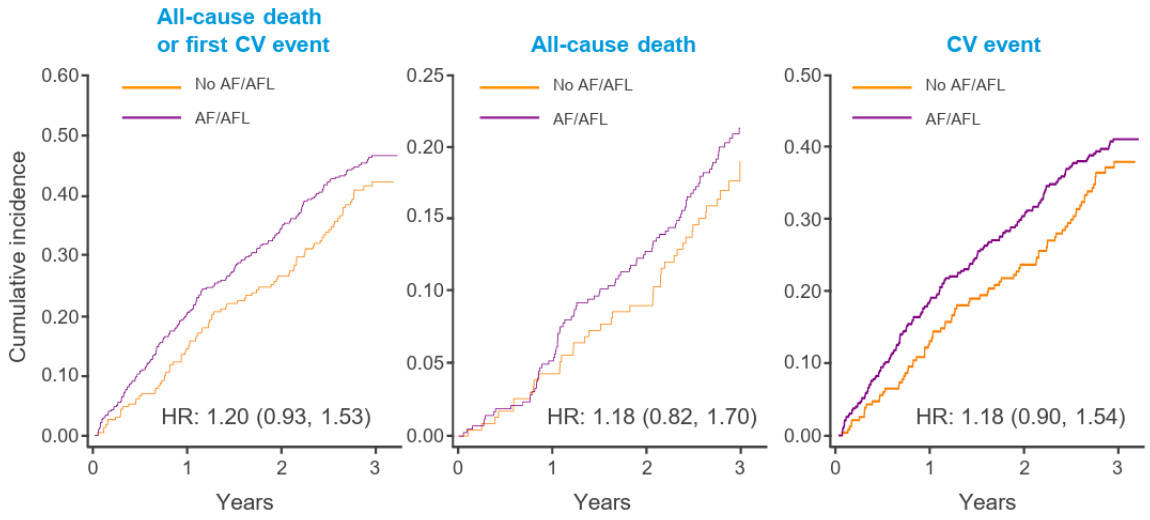
Abbreviations: AF/AFL = atrial fibrillation or flutter; ATTR = transthyretin amyloidosis; GLS = global longitudinal strain; IQR = interquartile range; KCCQ = Kansas City Cardiomyopathy Questionnaire; LV = left ventricle; NT-proBNP = N-terminal pro-B type natriuretic peptide; NYHA = New York Heart Association; RV = right ventricle, SD = standard deviation.

[a]p-value <0.05

EFFICACY RESULTS

The cumulative incidence of clinical outcomes in patients with and without baseline AF/AFL are shown in **Figure 1**.[1]

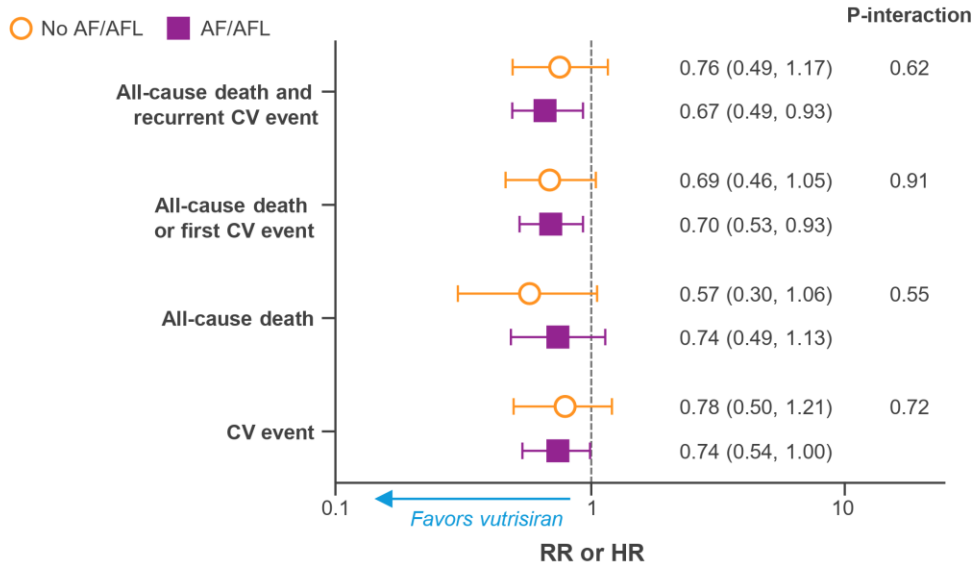
Figure 1. Cumulative Incidence of Clinical Outcomes in Patients with and without AF/AFL.[1]



Abbreviations: AF = atrial fibrillation; AFL = atrial flutter; HR = hazard ratio
From Wang, et al.[1]

The effect of vutrisiran on the primary composite endpoint of all-cause death and recurrent CV events and secondary endpoint of all-cause death in patients with and without AF/AFL is shown in **Figure 2**.[1]

Figure 2. Effect of Vutrisiran in patients with and without AF/AFL.[1]



Abbreviations: AF = atrial fibrillation; AFL = atrial flutter; CV = cardiovascular; HR = hazard ratio; RR = risk ratio
From. Wang, et al.[1]

SAFETY RESULTS

In the overall population, the proportion of patients with at least one AE was similar between treatment groups, and the majority of AEs with vutrisiran were mild or moderate. A summary of the safety results

during the double-blind period are presented in **Table 2**.[2,3] An analysis of AEs stratified by baseline AF/AFL is not available.

Table 2. HELIOS-B Safety Summary.[3]

Event, n (%)	Overall Population	
	Vutrisiran (n=326)	Placebo (n=328)[a]
At least 1 AE	322 (99)	323 (98)
Any SAE[b]	201 (62)	220 (67)
Any severe AE[c]	158 (48)	194 (59)
Cardiac AEs	227 (70)	242 (74)
Cardiac SAEs	116 (36)	124 (38)
Any AE leading to treatment discontinuation	10 (3)	13 (4)
Any AE leading to death[d]	49 (15)	63 (19)

Abbreviations: AE = adverse event; SAE = serious adverse event.

[a]Of the 329 patients randomized to receive placebo, 1 patient withdrew from the study and was not dosed.

[b]Serious AEs were defined as AEs that resulted in death, were life-threatening, resulted in inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were important medical events as determined by the investigators.

[c]Severe AEs were defined as AEs for which more than minimal, local, or noninvasive intervention was received; which had a severe effect on limiting self-care activities of daily living; or which had the potential for life-threatening consequences or death.

[d]Deaths that occurred after the end of study visit or after the data cut-off date were not included.

ABBREVIATIONS

AE = adverse event; AF/AFL = atrial fibrillation or flutter; ATTR = transthyretin amyloidosis; GLS = global longitudinal strain; HR = hazard ratio; IQR = interquartile range; 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; RR = risk ratio; SAE = serious adverse event; SD = standard deviation.

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REFERENCES

1. Wang X, Fontana M, Claggett B, et al. Effect of vutrisiran in patients with and without atrial fibrillation or flutter: Analysis from HELIOS-B. Presented at: the Annual Meeting of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC); May 9-12, 2026. Barcelona, Spain.
2. Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. 2025;392(1):33-44. doi:10.1056/NEJMoa2409134
3. Supplement to: Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. 2025;392(1):33-44. doi:10.1056/NEJMoa2409134