Vutrisiran: HELIOS-B Study

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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 including both hATTR and wtATTR.[1]
- The study met the primary endpoint and vutrisiran reduced the risk of all-cause mortality and recurrent CV events compared with placebo during the double-blind period (up to 36 months). The HR was 0.72 (95% CI 0.56, 0.93; P=0.01) in the overall population and 0.67 (95% CI 0.49, 0.93; P=0.02) in the monotherapy population.[1]
- The study met all secondary endpoints with vutrisiran demonstrating statistically significant differences compared with placebo in all-cause mortality through 42 months and 6-MWT, KCCQ-OS, and NYHA class at 30 months.[1]
- In the overall population, the mean trough percent reduction in serum TTR level was 81.0% (95% CI 79.0, 83.0) at month 30.[1]
- There were improvements in exploratory endpoints with vutrisiran compared with placebo for NT-proBNP, troponin I, peak longitudinal strain, and EuroQoL-5D-5L at 30 months.[1]
- The majority of AEs in the trial were mild or moderate and similar between treatment arms.[2]

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, 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 exposure period in the overall population and in the vutrisiran monotherapy population (patients not receiving tafamidis at baseline). After the double-blind treatment period, all eligible patients remaining on the study were allowed to receive vutrisiran in an ongoing OLE.[1]

Primary Endpoint

The primary endpoint was the composite outcome of all-cause mortality and recurrent CV events (CV hospitalizations and urgent HF visits) at Month 33 or 36, which was analyzed using a modified Andersen-Gill model with a robust variance estimator (LWYY model). The primary endpoint was analyzed in both the overall study population and the vutrisiran monotherapy population (patients who were not on tafamidis at baseline). These endpoints were tested in parallel. Heart transplantation or implantation of a left ventricular assist device, or both, were treated as deaths from any cause. Sensitivity analysis was performed using a Mantel-Haenszel-type stratified win ratio method, stratified by baseline NT-proBNP. Predefined subgroups were stratified according to tafamidis use at baseline, ATTR disease type (wtATTR versus hATTR), NYHA class, and age at baseline.[1,3]

Secondary Endpoints

The secondary endpoints were related to functional capacity, patient-reported health status and health-related quality of life, as well as additional assessments of mortality and severity of clinical HF symptoms, including:[1]

- All-cause mortality, including up to 6 months of OLE data (up to Month 42)
- Change from baseline in 6-MWT at Month 30
- Change from baseline in the KCCQ-OS at Month 30
- Change from baseline in NYHA class at Month 30

Exploratory Endpoints

Exploratory endpoints included NT-proBNP level, troponin I level, peak longitudinal strain, and quality of life assessed with the EuroQol 5-Dimension 5-Level questionnaire. Echocardiograms were performed at 12, 18, 24, and 30 months. Serum TTR levels were measured as a pharmacodynamic endpoint. Safety was monitored throughout the trial and included assessments of adverse events, clinical laboratory measures, and vital signs.[1,4]

Inclusion and Exclusion Criteria

Select inclusion and exclusion criteria for HELIOS-B are presented in **Table 1**.[1]

Table 1. HELIOS-B Key Inclusion and Exclusion Criteria.[1]

Inclusion Criteria	Exclusion Criteria
- Age 18-85 years - Documented diagnosis of ATTR-CM (either hATTR or wtATTR) - Medical history of HF with at least 1 prior hospitalization for HF or clinical evidence of HF - Patient meets one of the following criteria: - Tafamidis-naïve and not actively planning to commence treatment with tafamidis during the first 12 months following randomization; or - On tafamidis (Note: must be on-label use of commercial tafamidis per the approved indication and dose in the country of use) - NT-proBNP >300 pg/mL and <8500 pg/mL (or >600 pg/mL and <8500 pg/mL for patients with atrial fibrillation) - Ability to complete ≥150 m on the 6-MWT	- NYHA Class IV heart failure - NYHA Class III with NAC ATTR Stage 3 - PND Score IIIa, IIIb, or IV - eGFR <30 mL/min/1.73 m^2 - Cardiomyopathy not associated with ATTR

Abbreviations: 6-MWT = 6-minute walk test; ATTR = transthyretin amyloidosis; ATTR-CM = transthyretin amyloidosis with cardiomyopathy; CV = cardiovascular; eGFR = estimated glomerular filtration rate; hATTR = hereditary transthyretin amyloidosis; HF = heart failure; NAC = National Amyloidosis Centre; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association; PND = polyneuropathy disability; wtATTR= wild-type transthyretin amyloidosis.

PATIENT DEMOGRAPHICS & BASELINE CHARACTERISTICS

There were 326 patients randomly assigned to the vutrisiran group and 329 patients to the placebo group in the overall population. Of the patients from the overall population, 60% (196 of 326 patients) in the vutrisiran group and 60% (199 of 329 patients) in the placebo group were not taking tafamadis at baseline (monotherapy population). Patient baseline characteristics were comparable between the groups, except for higher NT-proBNP and troponin I values in the vutrisiran group than the placebo group in the monotherapy population as shown in **Table 2**. Baseline demographics and clinical characteristics were not substantially different between the monotherapy population and overall population. Forty-four of 196 (22%) of patients in the vutrisiran group and 41 of 199 (21%) of patients in the placebo group started tafamidis after randomization in the monotherapy population.[1] In the overall population, 3% of patients in both treatment arms were receiving SGLT2 inhibitors at baseline. Eighty percent of patients in the vutrisiran arm and 79% of patients in the placebo arm had use of diuretics at baseline.[3]

Table 2. Baseline Patient Demographics and Clinical Characteristics.[1]

Baseline Characteristics	Overall Population		Monotherapy Population	
	Vutrisiran (n=326)	Placebo (n=328)[a]	Vutrisiran (n=196)	Placebo (n=199)
Age at randomization, years, median (range)	77.0 (45-85)	76.0 (46-85)	77.5 (46-85)	76.0 (53-85)
Male sex, n (%)	299 (92)	306 (93)	178 (91)	183 (92)
Race, n (%)[b]				
White	277 (85)	275 (84)	169 (86)	169 (85)
Asian	18 (6)	19 (6)	12 (6)	15 (8)
Black/African American	23 (7)	24 (7)	10 (5)	11 (6)
Other/Not reported	8 (2)	10 (3)	5 (3)	4 (2)
wtATTR, n (%)	289 (89)	289 (88)	173 (88)	174 (87)
Time since diagnosis of ATTR, years, median (range)	0.86 (0-11.1)	1.03 (0-10.8)	0.50 (0-8.3)	0.63 (0-6.2)
Tafamidis use at baseline, n (%)	130 (40)	129 (39)	-	-
Time on tafamidis prior to trial start, months, median (range)	9.2 (1.1-65.3)	11.3 (1.1-65.5)	-	-
NYHA Class, n (%)				
I	49 (15)	35 (11)	15 (8)	12 (6)
II	250 (77)	258 (79)	172 (88)	169 (85)
III	27 (8)	35 (11)	9 (5)	18 (9)
NAC[c] ATTR stage, n (%)				
1	208 (64)	229 (70)	113 (58)	138 (69)
2	100 (31)	87 (27)	68 (35)	55 (28)
3	18 (6)	12 (4)	15 (8)	6 (3)
Laboratory parameters, median (IQR)				
NT-proBNP, pg/mL	2021 (1138-3312)	1801 (1042-3082)	2402 (1322-3868)	1865 (1067-3099)
High-sensitivity troponin I level, pg/mL	71.9 (44.9-115.9)	65.2 (41.1-105.5)	76.3 (48.4-138.8)	62.2 (39.2-105.6)

Abbreviations: ATTR = transthyretin amyloidosis; IQR = interquartile range; NAC = National Amyloidosis Centre; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association; wtATTR = wild-type transthyretin amyloidosis
[a]One patient withdrew and did not receive study drug.[3]
[b]Race was reported by the patients.
[c]NAC stages are determined on the basis of the levels of the serum biomarkers NT-proBNP and estimated glomerular filtration rate.

Primary Endpoint: All-Cause Mortality and Recurrent CV Events

Treatment with vutrisiran reduced the risk of all-cause mortality and recurrent CV events; HR 0.72 (95% CI 0.56, 0.93; P=0.01) in the overall population and HR 0.67 (95% CI 0.49, 0.93; P=0.02) in the monotherapy population. Prespecified win ratio sensitivity analyses in both populations were consistent with the results of the primary analysis. The time to first CV event or all-cause mortality in the overall population and monotherapy population are shown in **Figures 1 and 2, and Table 3,** respectively.[1]

Table 3. Primary End Point and Patients With At Least One Event.[1]

End Point	Overall Population			Monotherapy Population		
	Vutrisiran (n=326)	Placebo (n=328)	Measure of Effect	Vutrisiran (n=196)	Placebo (n=199)	Measure of Effect
Death from any cause and recurrent CV events – HR (95% CI), P-value			0.72 (0.56 to 0.93), P=0.01			0.67 (0.49 to 0.93), P=0.02
Death from any cause – HR (95% CI), P-value			0.69 (0.49 to 0.98), P=0.04			0.71 (0.47 to 1.06), P=0.12
Recurrent CV events – relative rate ratio (95% CI), P-value			0.73 (0.61 to 0.88), P=0.001			0.68 (0.53 to 0.86), P=0.001
Patients with at least one event – n (%)	125 (38)	159 (48)		76 (39)	105 (53)	
Death from any cause[a]	51 (16)	69 (21)		36 (18)	46 (23)	
Recurrent CV events	112 (34)	133 (41)		66 (34)	87 (44)	

Abbreviations: CI = confidence interval; CV = cardiovascular; HR = hazard ratio

[a]Three patients in the vutrisiran group and four in the placebo group had a heart transplantation. No patients had implantation of a left ventricular assist device.

Figure 1. Time to All-Cause Mortality or CV Event in the Overall Population.[1]
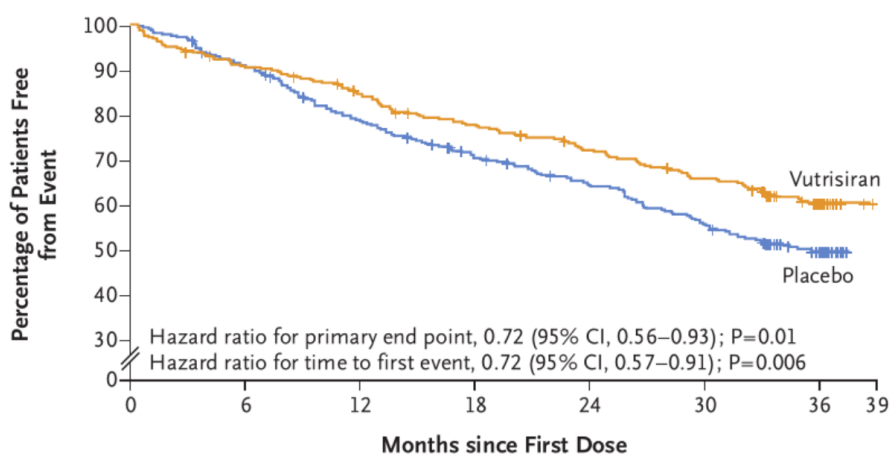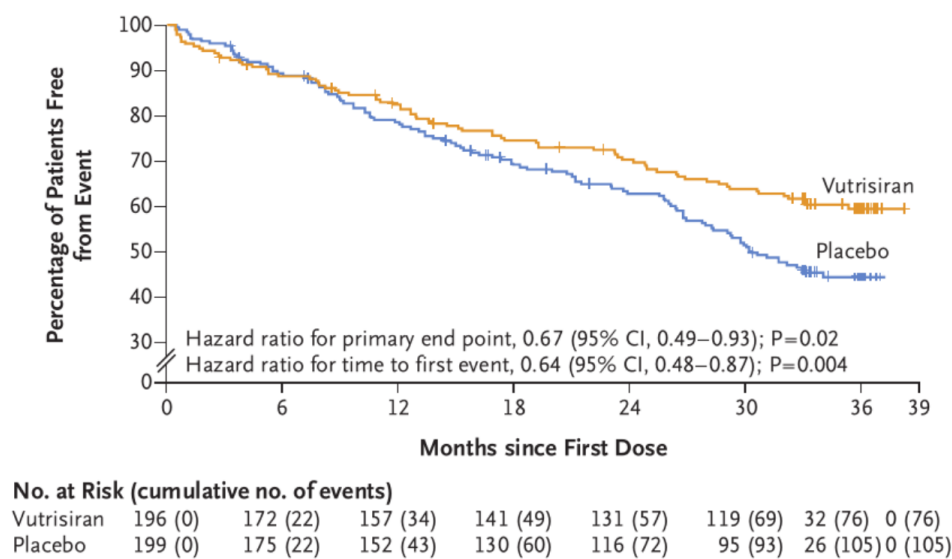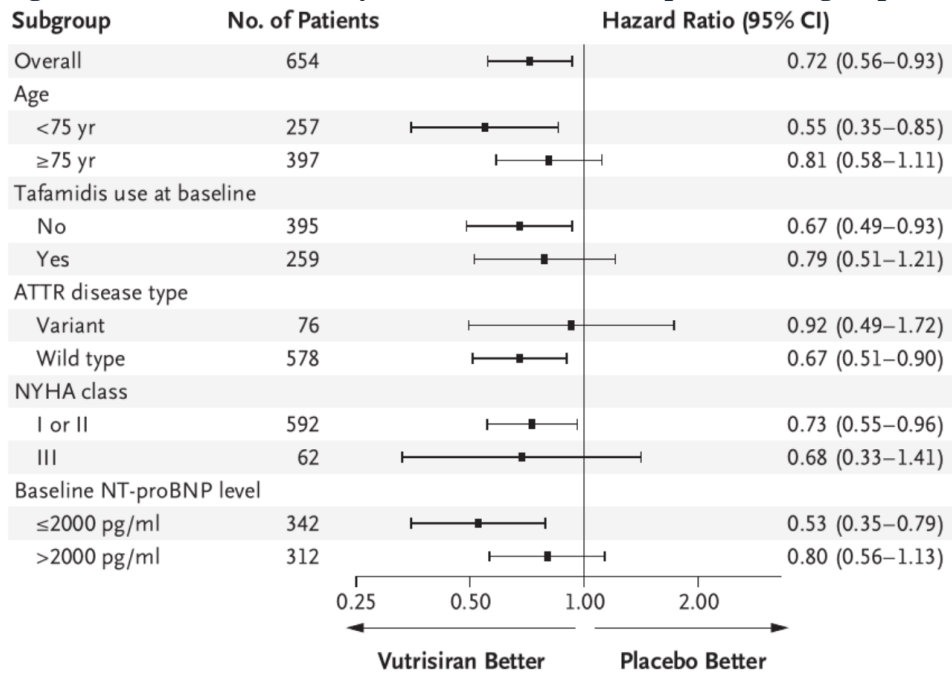

From Fontana et al[1]

Abbreviations: CV = cardiovascular; CI = confidence interval.

Figure 2. Time to All-Cause Mortality or CV Event in the Monotherapy Population.[1]

No. at Risk (cumulative no. of events)

Vutrisiran	196 (0)	172 (22)	157 (34)	141 (49)	131 (57)	119 (69)	32 (76)	0 (76)
Placebo	199 (0)	175 (22)	152 (43)	130 (60)	116 (72)	95 (93)	26 (105)	0 (105)

From Fontana et al[1]
Abbreviations: CV = cardiovascular; CI = confidence interval.

Similar effects were observed in all-cause mortality and recurrent CV events across all prespecified subgroups shown in **Figure 3** and **Figure 4**.[1]

Figure 3. All-Cause Mortality and CV Events in Prespecified Subgroups in the Overall Population.[1]

From Fontana et al[1]
Abbreviations: ATTR = transthyretin amyloidosis; CI = confidence interval; CV = cardiovascular; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association

Figure 4. All-Cause Mortality and CV Events in Prespecified Subgroups in the Monotherapy Population.[1]
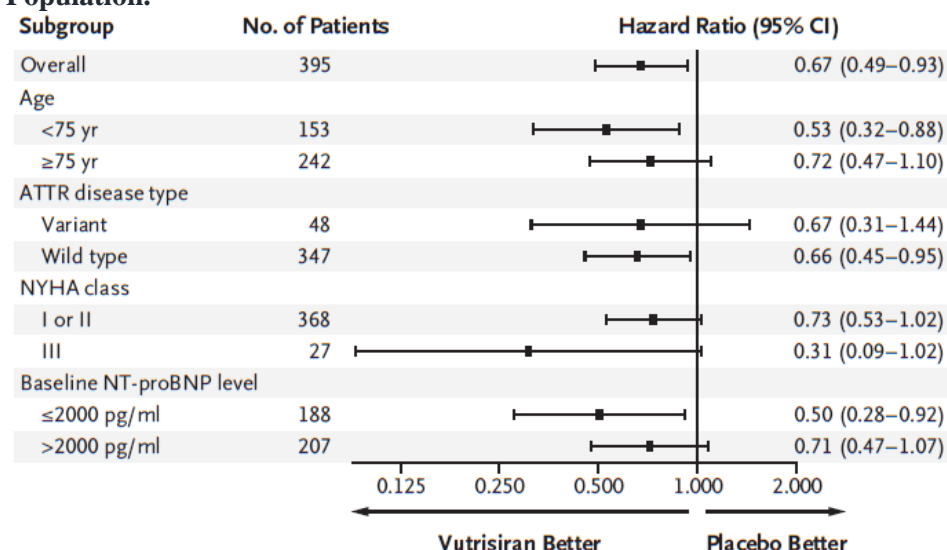
From Fontana et al[1]
Abbreviations: ATTR = transthyretin amyloidosis; CI = confidence interval; CV = cardiovascular; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association

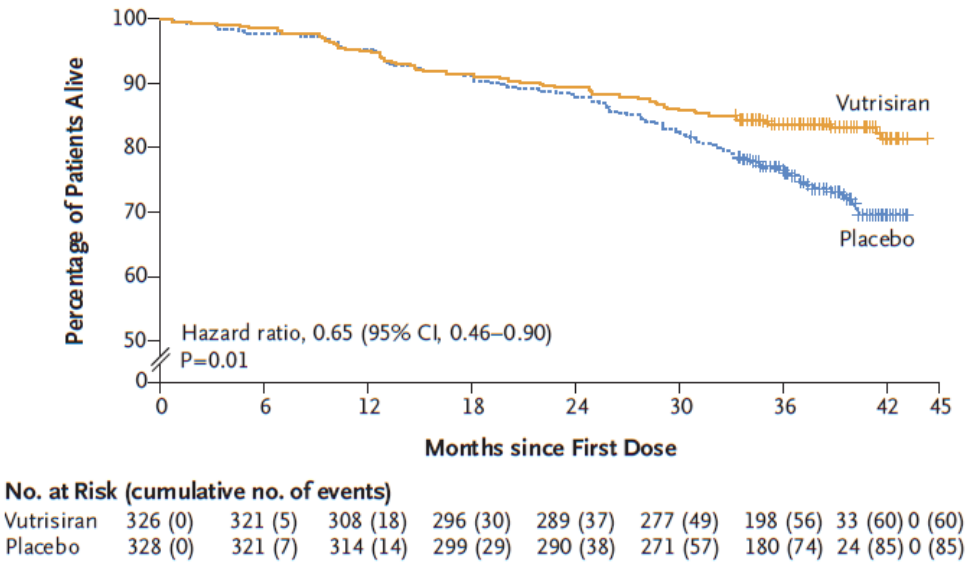### Secondary Endpoints

All-Cause Mortality

Vutrisiran reduced all-cause mortality as shown in **Table 4** through up to 42 months of follow-up vs. placebo in the overall population (HR 0.65 [95% CI 0.46, 0.90], P=0.01; **Figure 5**), and monotherapy population (HR 0.66 [95% CI 0.44, 0.97], P=0.045; **Figure 6**).[1]

Table 4. Secondary End Point and Patients Who Died.[1]

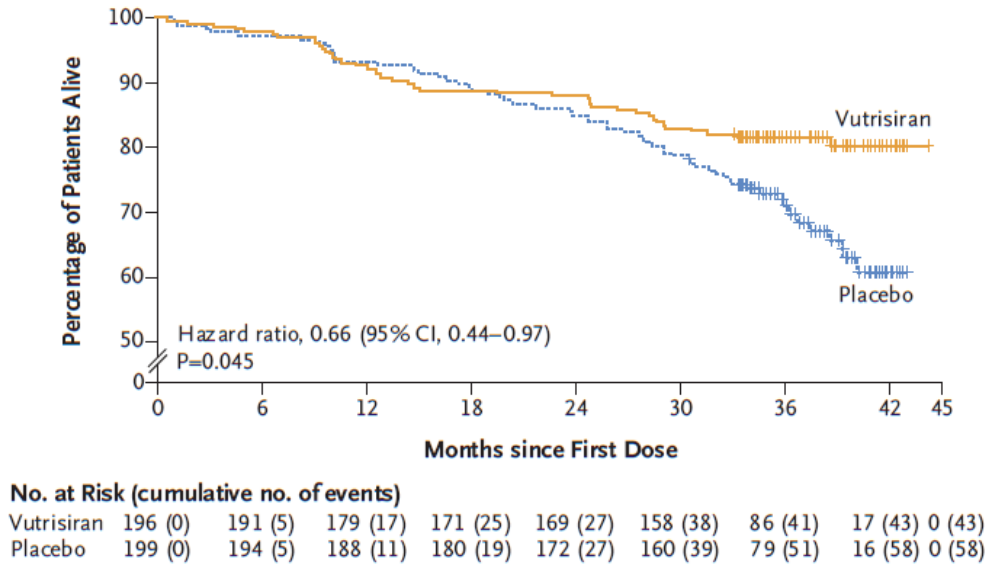| End Point	Overall Population			Monotherapy Population		
	Vutrisiran (n=326)	Placebo (n=328)	Measure of Effect	Vutrisiran (n=196)	Placebo (n=199)	Measure of Effect
Death from any cause through 42 months – HR (95% CI), P-value			0.65 (0.46 to 0.9), P=0.01			0.66 (0.44 to 0.97), P=0.045
Patients who died – n (%)	60 (18)	85 (26)		43 (22)	58 (29)	

Abbreviations: CI = confidence interval; HR = hazard ratio.

Figure 5. Death from Any Cause in the Overall Population.[1]

No. at Risk (cumulative no. of events)

Vutrisiran	326 (0)	321 (5)	308 (18)	296 (30)	289 (37)	277 (49)	198 (56)	33 (60)	0 (60)
Placebo	328 (0)	321 (7)	314 (14)	299 (29)	290 (38)	271 (57)	180 (74)	24 (85)	0 (85)

From Fontana et al[1]
Abbreviations: CI = confidence interval

Figure 6. Death from Any Cause in the Monotherapy Population.[1]

No. at Risk (cumulative no. of events)

Vutrisiran	196 (0)	191 (5)	179 (17)	171 (25)	169 (27)	158 (38)	86 (41)	17 (43)	0 (43)
Placebo	199 (0)	194 (5)	188 (11)	180 (19)	172 (27)	160 (39)	79 (51)	16 (58)	0 (58)

From Fontana et al[1]
Abbreviations: CI = confidence interval

In both populations, similar effects were observed in all-cause mortality across all prespecified subgroups shown in **Figure 7** and **Figure 8**. Sensitivity analyses of the secondary endpoint were consistent with the secondary endpoint analysis.[1]
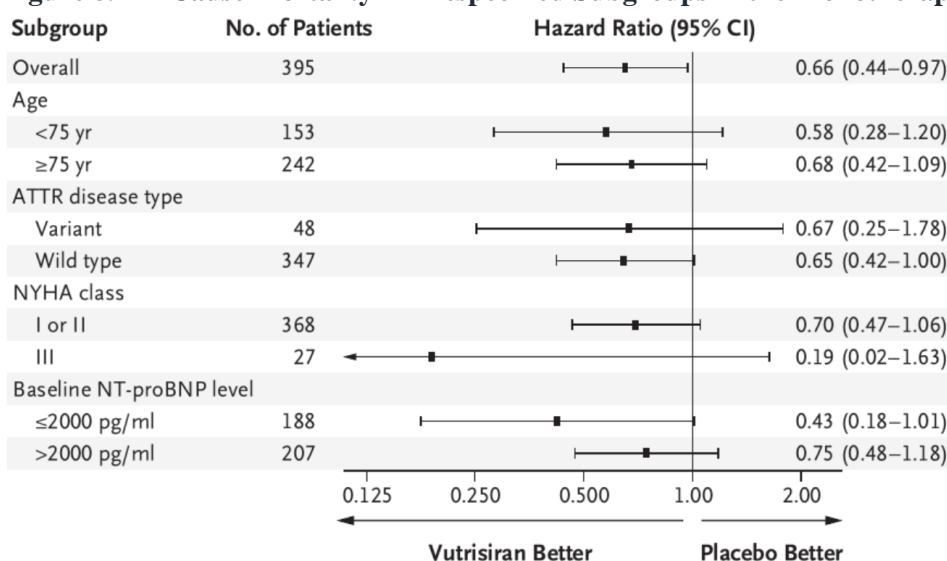
Figure 7. All-Cause Mortality in Prespecified Subgroups in the Overall Population.[1]
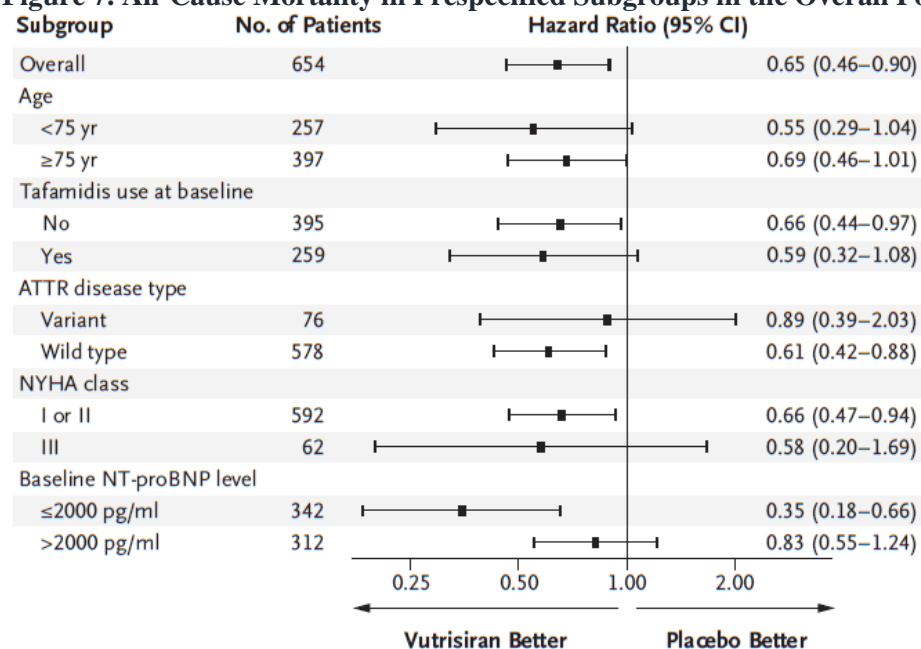
From Fontana et al[1]
Abbreviations: ATTR = transthyretin amyloidosis; CI = confidence interval; CV = cardiovascular; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association

Figure 8. All-Cause Mortality in Prespecified Subgroups in the Monotherapy Population.[1]

From Fontana et al[1]
Abbreviations: ATTR = transthyretin amyloidosis; CI = confidence interval; CV = cardiovascular; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association

Other Secondary Endpoints

Table 5 provides results from other secondary endpoints related to functional capacity, patient-reported health-status and patient-reported health quality of life, and severity of heart failure symptoms.[1]

Table 5. Other Secondary Endpoints.[1]

End Point	Overall Population		Monotherapy Population	
	Vutrisiran (n=326)	Placebo (n=328)	Vutrisiran (n=196)	Placebo (n=199)
6-MWT change from baseline at 30 months, meters				
LS mean (95% CI)	-45.4 (-54.5, -36.3)	-71.9 (-81.3, -62.4)	-59.7 (-72.7, -46.7)	-91.8 (-104.4, -79.2)
LS mean difference (95% CI), P value	26.5 (13.4, 39.6), P<0.001		32.1 (14.0, 50.2), P<0.001	
KCCQ-OS change from baseline at 30 months, points				
LS mean (95% CI)	-9.7 (-12.0, -7.4)	-15.5 (-18.0, -13.0)	-10.8 (-14.1, -7.5)	-19.5 (-22.9, -16.1)
LS mean difference (95% CI), P value	5.8 (2.4, 9.2), P<0.001		8.7 (4.0, 13.4), P<0.001	
NYHA Class change from baseline at 30 months				
Stable or improved, %	68	61	66	56
Adjusted difference in % of patients with stable or improved (95% CI), P value	8.7 (1.3, 16.1), P=0.02		12.5 (2.7, 22.2), P=0.01	

Abbreviations: 6-MWT = 6-minute walk test; CI = confidence interval; KCCQ-OS = Kansas City Cardiomyopathy Questionnaire-Overall Summary; LS = least squares; NYHA = New York Heart Association

Select Exploratory Endpoints

Select exploratory endpoints included levels of cardiac biomarkers NT-proBNP and troponin I, echocardiographic parameters, and quality of life assessed with the EuroQoL-5D-5L questionnaire.[3–5]

Cardiac Biomarkers

In the overall population, vutrisiran treatment led to a 32% relative reduction in NT-proBNP and troponin I (geometric mean fold-change ratio: 0.68) from baseline to month 30 when compared with placebo, as seen in **Table 6.** The treatment effect of vutrisiran on NT-proBNP and troponin I was observed at 6 months and increased over time. NT-proBNP and troponin I results were consistent across all prespecified subgroups in the overall and monotherapy populations.[5]

Echocardiographic Cardiac Structure and Function

Between-group differences in LV diastolic function (as measured by LS mean change from baseline in LV mass index and E/e' ratio) were observed at 12 months, with continued improvement versus placebo through 30 months in patients receiving vutrisiran in the overall population, as seen in **Table 6.** At month 30, the LS mean change from baseline in LV wall thickness, E/A ratio, E/e' ratio, and TDI lateral e' were improved in the vutrisiran treatment group when compared with the placebo group in the overall population.[4]

Between-group differences in LV systolic function (as measured by LS mean change from baseline in LVEF and absolute peak longitudinal strain) were observed at 18 months, with continued improvement versus placebo through 30 months in patients receiving vutrisiran in the overall population. At month 30, the LS mean change from baseline in LV stroke volume was improved in the vutrisiran treatment group when compared with the placebo group in the overall population, as seen in **Table 6.**[4]

Table 6. Change from Baseline at 30 Months for Select Exploratory Endpoints.[3–5]
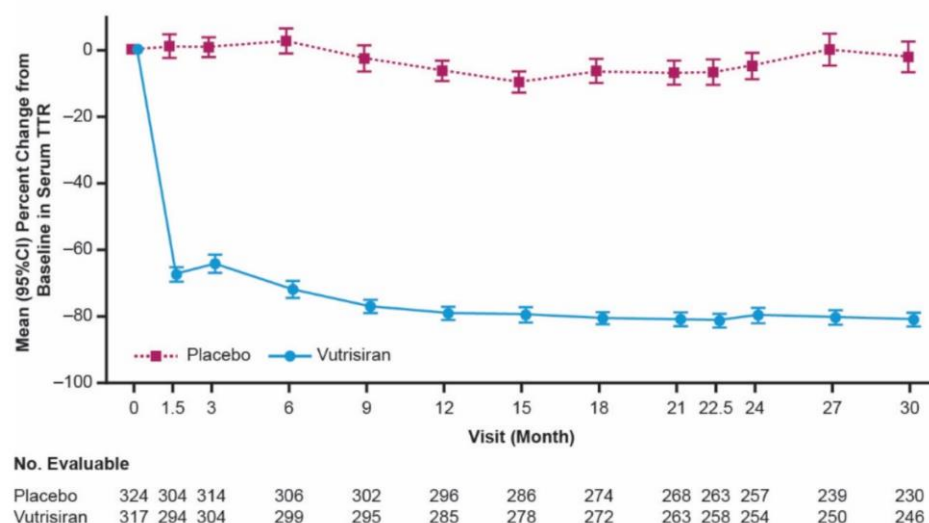
End Point	Overall Population		Monotherapy Population	
	Vutrisiran (n=326)	Placebo (n=328)	Vutrisiran (n=196)	Placebo (n=199)
NT-proBNP fold-change				
Geometric mean (95% CI)	1.19 (1.11, 1.28)	1.75 (1.62, 1.89)	1.30 (1.17, 1.45)	2.28 (2.04, 2.55)
Geometric fold-change ratio (95% CI)	0.68 (0.61, 0.76)		0.57 (0.49, 0.66)	
Troponin I fold-change				
Geometric mean (95% CI)	0.94 (0.88, 1.00)	1.37 (1.28, 1.47)	1.01 (0.92, 1.12)	1.85 (1.68, 2.03)
Geometric fold-change ratio (95% CI)	0.68 (0.62, 0.75)		0.55 (0.48, 0.63)	
Mean LV wall thickness, mm				
LS mean difference (95% CI)	-0.43 (-0.82, -0.03)		-0.8 (-0.14, -0.02)	
Measures of LV diastolic function				
LV mass index (g/m^2)				
LS mean (SEM)	14.83±2.46	25.44±2.82		
LS mean difference (95% CI)	-10.6 (-18.0, -3.3)			
E/A ratio				
LS mean difference (95% CI)	-0.29 (-0.57, -0.01)			
E/e' ratio				
LS mean (SEM)	-1.08±0.27	0.74±0.34		
LS mean difference (95% CI)	-1.82 (-2.67, -0.97)		-2.73 (-3.90, -1.56)	
TDI lateral e', cm/s				
LS mean difference (95% CI)	0.55 (0.24, 0.85)			
Measures of LV systolic function				
LVEF, %				
LS mean (SEM)	-4.12±0.56	-6.15±0.66		
LS mean difference (95% CI)	2.03 (0.34, 3.73)		2.27 (-0.07, 4.61)	
Peak longitudinal strain, %				
LS mean (SEM)	0.95 (0.17)	2.18 (0.19)	1.07 (0.26)	2.37 (0.26)
LS mean difference (95% CI)	-1.23 (-1.73, -0.73)		-1.30 (-2.01, -0.59)	
LV stroke volume, mL				
LS mean difference (95% CI)	4.05 (1.72, 6.38)			
EuroQoL-5D-5L Index change from baseline at 30 months				
LS mean (SEM)	-0.03 (0.008)	-0.06 (0.008)	-0.03 (0.011)	-0.08 (0.011)
LS mean difference (95% CI)	0.03 (0.01, 0.05)		0.05 (0.02, 0.08)	

Abbreviations: CI = confidence interval; E/A = ratio of early to late diastolic transmitral inflow velocities; E/e' = ratio of early mitral inflow velocity to lateral early diastolic mitral annular velocity; EuroQoL-5D-5L = EuroQoL 5-dimensions-5 levels; LS = least squares; LV = left ventricular; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-brain natriuretic peptide; SEM = standard error of the mean; TDI lateral e' = lateral peak early diastolic mitral annular tissue velocity.

Pharmacodynamic Endpoint

In the overall population, the mean trough percent reduction in serum TTR level was 81.0% (95% CI 79.0, 83.0) at month 30 as shown in **Figure 9**.[1]

Figure 9. Mean Percent Change in TTR Level from Baseline.[3]

No. Evaluable

Placebo	324	304	314	306	302	296	286	274	268	263	257	239	230
Vutrisiran	317	294	304	299	295	285	278	272	263	258	254	250	246

From Fontana et al[3]

SAFETY RESULTS

In the overall population, the proportion of patients with at least one AE was similar between treatment arms, and the majority of AEs were mild or moderate. Cardiac AEs occurred at similar or lower rates with vutrisiran than placebo.[2] A summary of the safety results during the double-blind period are presented in **Table 7.**[3] There were no clinically relevant changes in laboratory measures (including hematologic measures, blood chemistry measures, liver function tests, and renal function tests), vital signs, or electrocardiograms in either treatment arm.[1]

Table 7. Safety Summary.[3]

Event, n (%)	Overall Population	
	Vutrisiran (N=326)	Placebo (N=328)
At least 1 AE	322 (99)	323 (98)
AEs occurring in ≥15% of patients in either treatment arm		
Cardiac failure	101 (31)	128 (39)
Covid-19	87 (27)	99 (30)
Atrial fibrillation	69 (21)	68 (21)
Gout	48 (15)	51 (16)
Dyspnea	43 (13)	51 (16)
Fall	42 (13)	69 (21)
Any SAE[a]	201 (62)	220 (67)
Any severe AE[b]	158 (48)	194 (59)
SAEs occurring in ≥5% of patients in either treatment arm		
Cardiac failure	38 (12)	57 (17)
Atrial fibrillation	26 (8)	20 (6)
Cardiac failure acute	13 (4)	18 (5)
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[c]	49 (15)	63 (19)

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

[a]SAEs 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.

[b]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.

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

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REFERENCES

1. Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. August 2024. doi:10.1056/NEJMoa2409134
2. Fontana M, Berk JL, Gillmore JD, et al. Primary results from HELIOS-B, a phase 3 study of vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. Presented at: European Society of Cardiology (ESC) Congress; August 30-September 2, 2024; London, UK.
3. Supplement to: Fontana M, Berk JL, Gillmore JD, et al. Vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. *N Engl J Med*. 2024. doi:10.1056/NEJMoa2409134
4. Jering K, Fontana M, Skali H, et al. Effects of vutrisiran on echocardiographic cardiac structure and function: The HELIOS-B trial. Presented at: Heart Failure Society of America (HFSA) Annual Scientific Meeting; September 27-30, 2024; Virtual.
5. Maurer MS, Berk JL, Damy T, et al. Exploratory biomarker analyses from HELIOS-B, a phase 3 study of vutrisiran in patients with transthyretin amyloidosis with cardiomyopathy. Presented at: Heart Failure Society of America (HFSA) Annual Scientific Meeting; September 27-30, 2024; Virtual.