Vutrisiran: Safety Results from HELIOS-B

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SUMMARY

- In the HELIOS-B study, the incidence of AEs was similar between the two groups, with 322 patients (99%) and 323 patients (98%) reporting at least one AE in the vutrisiran and placebo groups, respectively. There were no clinically relevant changes in laboratory measures, vital signs, or electrocardiograms observed in either treatment group.[1]

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CLINICAL DATA

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 treatment period in the overall population and in the 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 OLE.[1]

Safety Results

In the overall population, the incidence of AEs was similar between the two groups, with 322 patients (99%) and 323 patients (98%) reporting at least one AE in the vutrisiran and placebo groups, respectively. A summary of the safety results during the double-blind period are presented in **Table 1**. There were no clinically relevant changes in laboratory measures (including hematologic measures, blood chemistry values, liver function tests, and renal function tests), vital signs, or electrocardiograms observed in either treatment group.[1,2]

Table 1. Safety Summary in the Overall Population During the Double-Blind Period.[2]

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.

ABBREVIATIONS

AE = adverse event; ATTR-CM = transthyretin amyloidosis with cardiomyopathy; CV = cardiovascular; hATTR = hereditary transthyretin amyloidosis; OLE = open-label extension; SAE = serious adverse event; wtATTR = wild-type transthyretin amyloidosis.

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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*. 2024. doi:10.1056/NEJMoa2409134
2. 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