Influence of Vutrisiran on Systolic Blood Pressure in ATTR-CM: Insights From HELIOS-B

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Conclusions

- Lower systolic blood pressure was associated with higher NT-proBNP and identifies a higher-risk phenotype in ATTR-CM
- Patients who died demonstrated progressive SBP decline preceding death
- Vutrisiran attenuated the decline in SBP during follow-up
- Clinical benefits of vutrisiran were consistent across the SBP spectrum, including hypotensive patients

Background

- Transthyretin amyloid cardiomyopathy (ATTR-CM) is characterized by reduced stroke volume and impaired cardiac output
- Declining systolic blood pressure (SBP) may reflect advancing disease
- Vutrisiran, an RNA interference therapeutic, rapidly knocks down circulating concentrations of TTR
- In HELIOS-B, vutrisiran significantly reduced rates of all-cause death and cardiovascular (CV) events among patients with ATTR-CM
- The present analysis sought to evaluate the effect of Vutrisiran on SBP.

Helios-B study
655 patients with ATTR-CM
(wild-type or variant)

R → Vutrisiran SC q3m 25 mg (n=326)
R → Placebo (n=329)

Primary outcome: composite of all-cause death and recurrent CV events during DB period
Secondary outcome: all-cause death through 42 months

Objectives

To assess the association between baseline SBP and outcomes, and the influence of vutrisiran on SBP in patients with ATTR-CM

Methods

- Patients categorized by baseline SBP (<120, 120–129, and ≥130 mmHg)
- SBP measured at baseline (Month 0) and 3-monthly through Month 30

Statistical analysis

- Baseline characteristics and clinical outcomes were compared across SBP categories
- Baseline SBP and NT-proBNP relationship was evaluated using restricted cubic splines
- Temporal SBP trajectories preceding all-cause death evaluated using spline-based longitudinal analysis
- Effect of vutrisiran on longitudinal SBP assessed using linear mixed-effects models, adjusted for age, genotype, log-transformed NT-proBNP, and NYHA class

Disclosures: HELIOS-B was funded by Alnylam.

Results

Table 1. Baseline Characteristics by Baseline SBP Tertile

Characteristic	<120 (n=264)	120 to 129 (n=149)	≥130 (n=241)	P values
Age, years	75 ± 7	73.8 ± 7.7	76.7 ± 5.5	p=0.005
Male sex, n (%)	248 (93.9)	139 (93.3)	218 (90.5)	p=0.14
Wild-type ATTR diagnosis, n (%)	228 (86.4)	129 (86.6)	221 (91.7)	p=0.06
Time from ATTR diagnosis, years	1.06 [0.38–2.15]	0.97 [0.35–2.15]	0.70 [0.70–1.55]	p=0.016
Baseline tafamidis use, n (%)	112 (42.4)	60 (40.3)	87 (36.1)	p=0.15
Hypertension, n (%)	130 (49.2)	86 (57.7)	172 (71.4)	p<0.001
NYHA class III, n (%)	21 (8)	13 (9.5)	28 (11.6)	p=0.64
NAC Stage 2 or 3, n (%)	108 (41)	39 (26.1)	70 (29.1)	p=0.001
NT-proBNP, ng/L	2132 [1236, 3798]	1844 [1096, 2902]	1759 [1017, 2867]	p=0.001
Troponin I, ng/L	71.6 [48, 111.8]	67 [40.4, 112.4]	62.4 [37.9, 105.0]	p=0.05
LV ejection fraction, %	53 ± 14	56 ± 12	59 ± 10	p<0.001
6MWT distance, m	367 ± 103	387 ± 97	375 ± 98	p=0.34
Primary composite outcome	38.3/100py	30.2/100py	32.3/100py	
All-cause mortality	9.1/100py	6.3/100py	6.4/100py	

Figure 1. Association between Baseline SBP and NT-proBNP

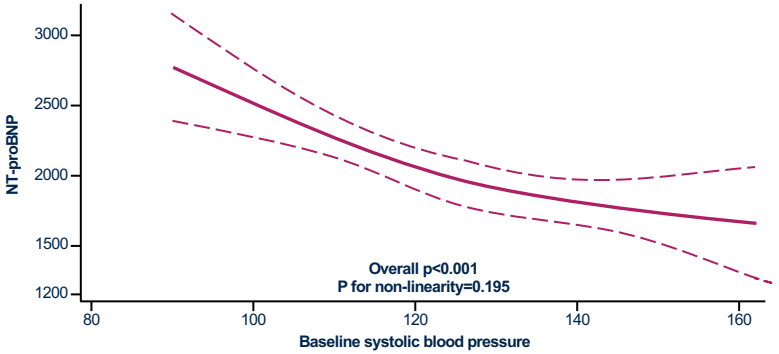


Figure 2. SBP Trajectory Before Death

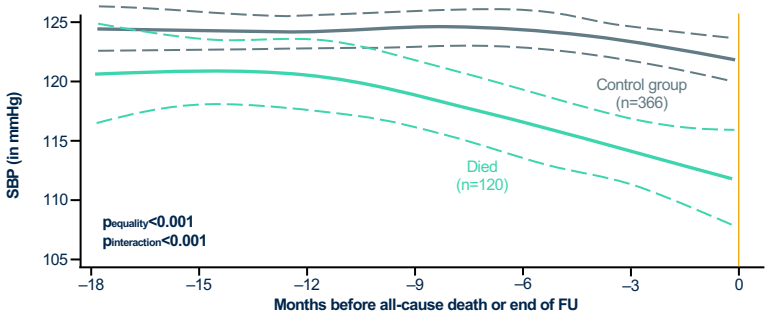
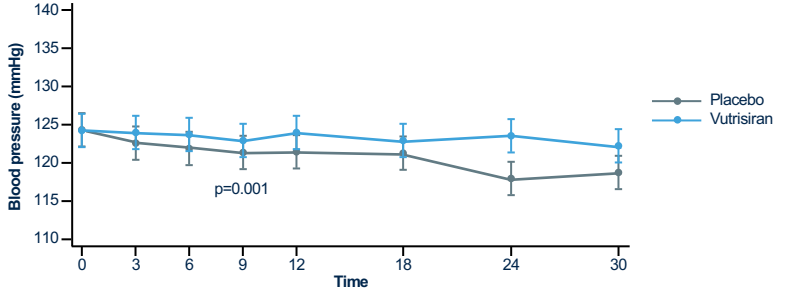


Figure 3. Treatment Effect of Vutrisiran on SBP



Mean systolic blood pressure (SBP) over time (months) in patients receiving vutrisiran (blue) versus placebo (grey) in the HELIOS-B trial. SBP was measured at scheduled visits from baseline to Month 30. Error bars represent 95% confidence intervals from the mixed-effects model.

Figure 4. Treatment Effect of Vutrisiran across Baseline SBP