

# Maintenance or Improvement of Functional Capacity, Health Status, and Quality of Life with Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy: Data from the HELIOS-B Study



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## Conclusions

- Significantly more patients treated with vutrisiran maintained or improved functional capacity, health status, and quality of life over 30 months compared with placebo, across all cutoff values applied
- The benefits observed with vutrisiran were consistent across the prespecified subgroups, and KCCQ-OS subdomains
- These data provide further evidence of the disease-modifying effect of vutrisiran treatment, and demonstrate benefits beyond reduced risk of all-cause mortality and cardiovascular events

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## Introduction

### ATTR with Cardiomyopathy

- ATTR is a systemic, progressive, and fatal disease affecting multiple tissues and organs, and is caused by the accumulation of misfolded amyloidogenic TTR deposits<sup>1-5</sup>
- Extracellular amyloid deposits frequently accumulate in heart tissue, causing cardiomyopathy (ATTR-CM), which leads to heart failure and arrhythmias that result in progressively debilitating symptoms<sup>6,7</sup>
- Disease progression and heart failure in ATTR-CM have major impacts on the functional capacity, health status, and QOL of patients<sup>7-9</sup>

### HELIOS-B Study

- Vutrisiran is an RNAi therapeutic that rapidly decreases circulating levels of the amyloidogenic TTR protein<sup>10</sup>
- Vutrisiran was evaluated in patients with ATTR-CM in the HELIOS-B study (NCT04153149)<sup>11</sup>
  - Vutrisiran reduced the risk of the composite endpoint of all-cause mortality and recurrent cardiovascular events, improved functional capacity and QOL, and prevented worsening of heart failure symptoms versus placebo

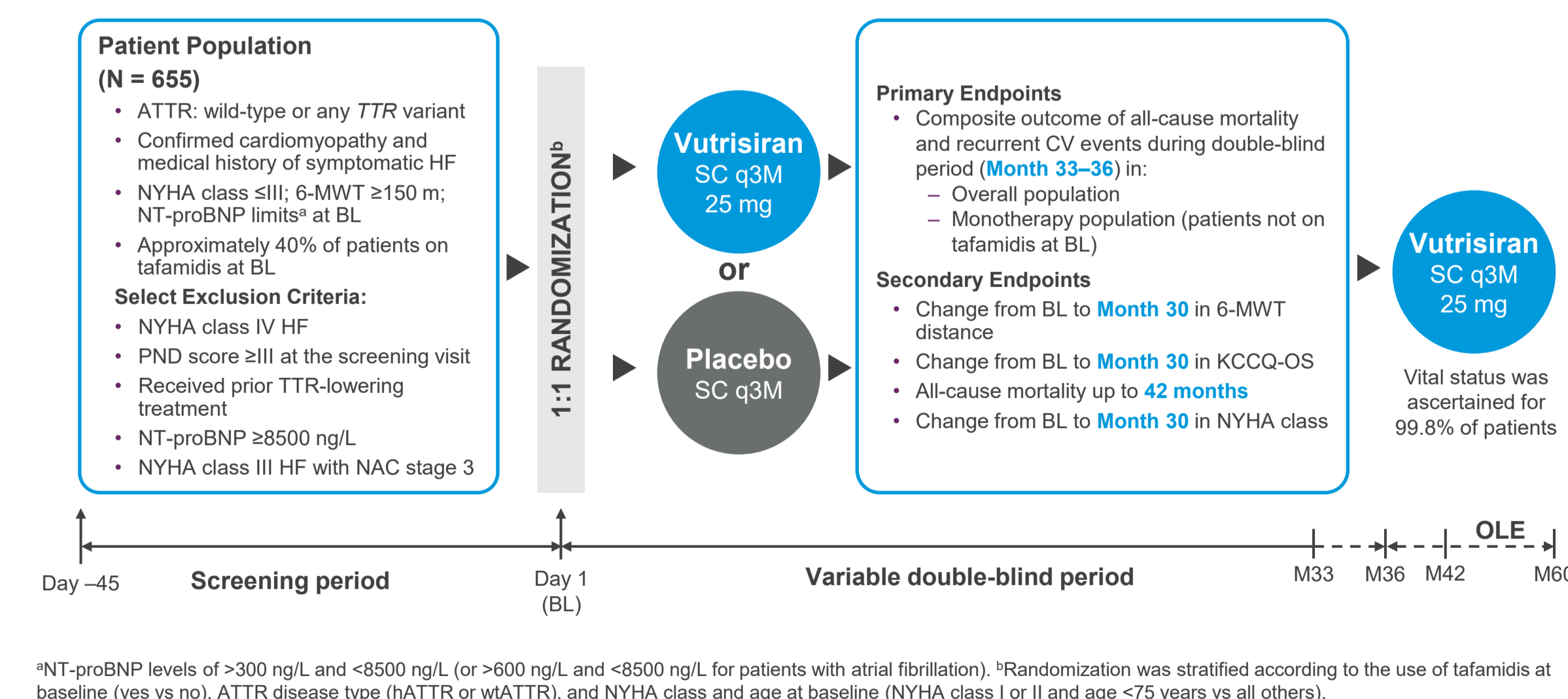
### Objectives

- To further determine the impact of vutrisiran on the functional capacity, health status, and QOL of patients with ATTR-CM in the HELIOS-B trial, by presenting LS mean difference in change from baseline in 6-MWT and KCCQ-OS in prespecified subgroups, and KCCQ-OS subdomains
- To analyze the proportion of patients with maintenance or improvement in the 6-MWT and KCCQ-OS according to multiple clinically relevant cutoffs

## Methods

### Figure 1. HELIOS-B Study Design

Randomized, double-blind study in patients with ATTR-CM<sup>11</sup>



- 6-MWT and KCCQ-OS were assessed at baseline and every 6 months until Month 30
- Maintenance or improvement was defined as not having a decrease from baseline of  $>7$  m,  $>15$  m, or  $>35$  m<sup>12-14</sup> (6-MWT), and  $>5$  points or  $>10$  points (KCCQ-OS)<sup>15</sup>

## Results

Table 1. Baseline Characteristics in the Overall Population Were Similar in the Placebo and Vutrisiran Arms<sup>11</sup>

Parameter	Overall Population	
	Placebo (N = 328)	Vutrisiran (N = 326)
Age, years, median (range)	76 (46, 85)	77 (45, 85)
Men, n (%)	306 (93.3)	299 (91.7)
hATTR amyloidosis, n (%)	39 (11.9)	37 (11.3)
NYHA Class, n (%)	I	35 (10.7)
	II	258 (78.7)
	III	49 (15.0)
ATTR disease stage, n (%)	1	229 (69.8)
	2	87 (26.5)
	3	12 (3.7)
Baseline 6-MWT, meters, mean (SD)	377 (96)	372 (104) <sup>a</sup>
Baseline KCCQ-OS, points, mean (SD)	72.3 (19.9)	73.0 (19.4) <sup>a</sup>
Baseline NT-proBNP, ng/L, median (IQR)	1801 (1042, 3082)	2021 (1138, 3312)
Baseline troponin I, ng/L, median (IQR)	65.2 (41.1, 105.5)	71.9 (44.9, 115.9)

Table 2. Baseline Characteristics in the Monotherapy Population Were Generally Similar in the Placebo and Vutrisiran Arms<sup>a,11</sup>

Parameter	Monotherapy Population	
	Placebo (N = 199)	Vutrisiran (N = 196)
Age (years), median (range)	76 (53, 85)	78 (46, 85)
Men, n (%)	183 (92.0)	178 (90.8)
hATTR amyloidosis, n (%)	25 (12.6)	23 (11.7)
NYHA Class, n (%)	I	12 (6.0)
	II	169 (84.9)
	III	18 (9.0)
ATTR disease stage, n (%)	1	138 (69.3)
	2	55 (27.6)
	3	6 (3.0)
Baseline 6-MWT, meters, mean (SD)	373 (98)	363 (103)
Baseline KCCQ-OS, points, mean (SD)	69.9 (20.8) <sup>a</sup>	70.3 (20.2) <sup>c</sup>
Baseline NT-proBNP, ng/L, median (IQR)	1865 (1067, 3099)	2402 (1322, 3868)
Baseline troponin I, ng/L, median (IQR)	62.2 (39.2, 105.6)	76.3 (48.4, 138.8)

<sup>a</sup>n = 325. <sup>b</sup>NT-proBNP and Troponin I levels were higher in the vutrisiran group compared with the placebo group in the monotherapy population. <sup>c</sup>n = 198. <sup>d</sup>n = 195.

### Difference of LS-mean Change from Baseline (Vutrisiran-Placebo) in the Overall Population<sup>11</sup>

- 6-MWT: 26.46 m (95% CI 13.38, 39.55; p<0.001)
- KCCQ-OS: 5.80 points (95% CI 2.40, 9.20; p<0.001)

Figure 2. Vutrisiran Resulted in Maintenance or Improvement in Functional Capacity in a Higher Percentage of Patients versus Placebo at Month 30 across Multiple Cutoff Values for the 6-MWT

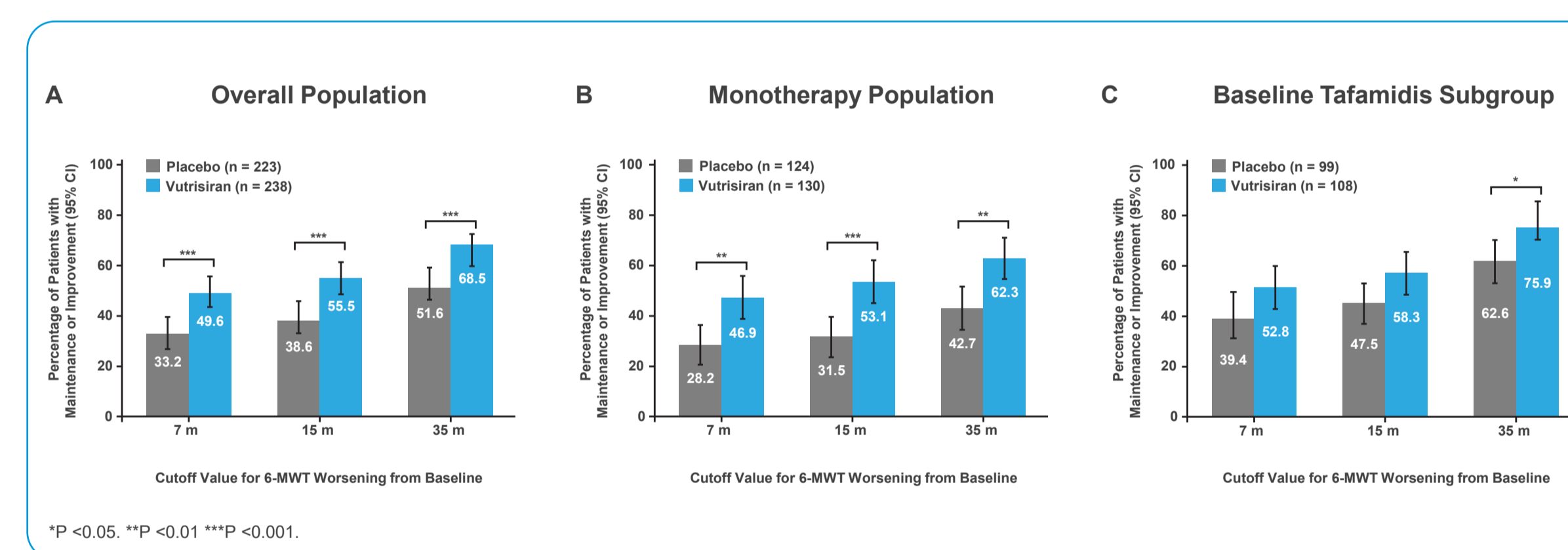


Figure 4. Clinical Benefits with Vutrisiran on Functional Capacity versus Placebo Were Consistent across Prespecified Subgroups

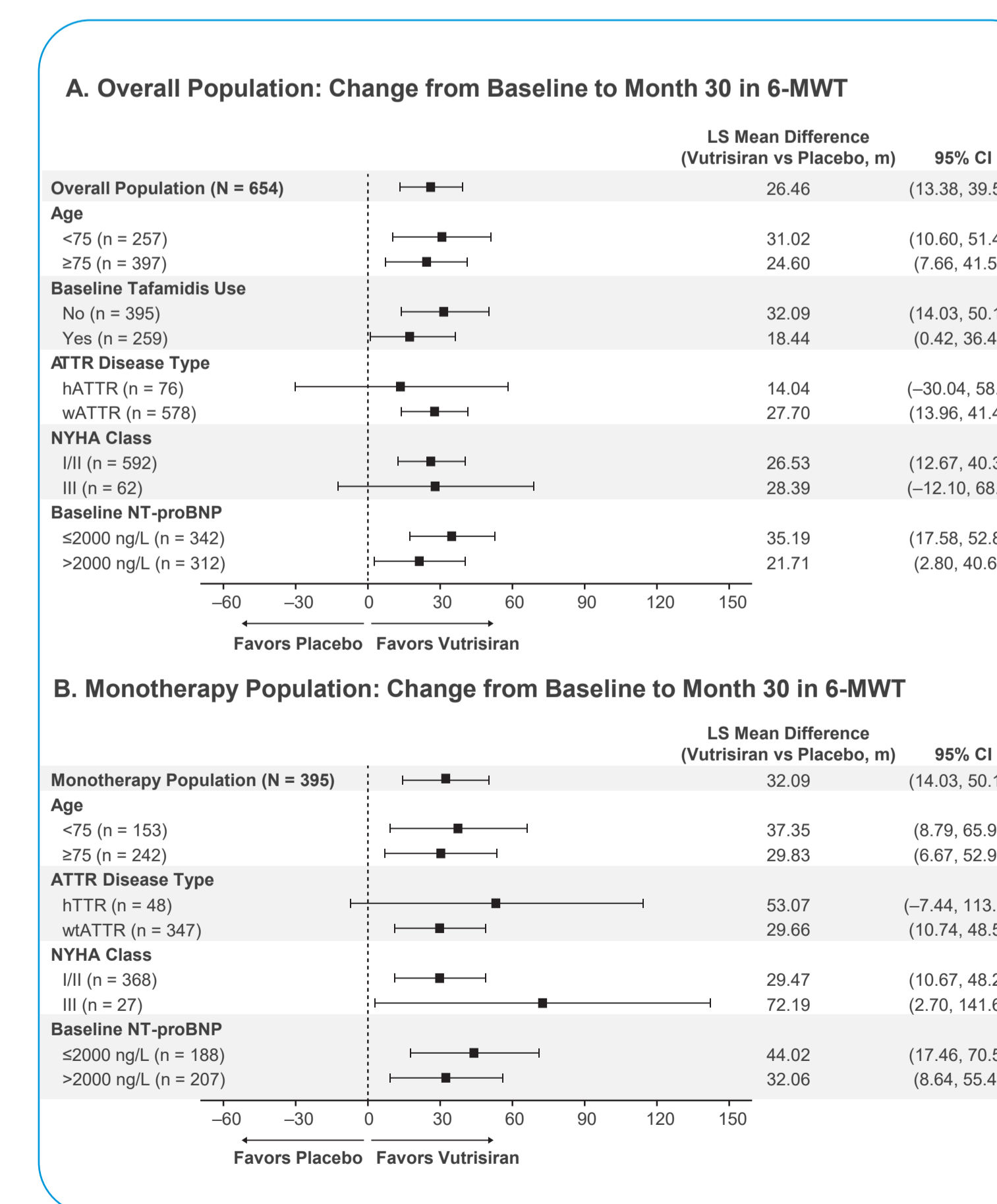


Figure 3. Vutrisiran Resulted in Maintenance or Improvement in KCCQ-OS Score in a Higher Percentage of Patients versus Placebo at Month 30 across Both Cutoff Values

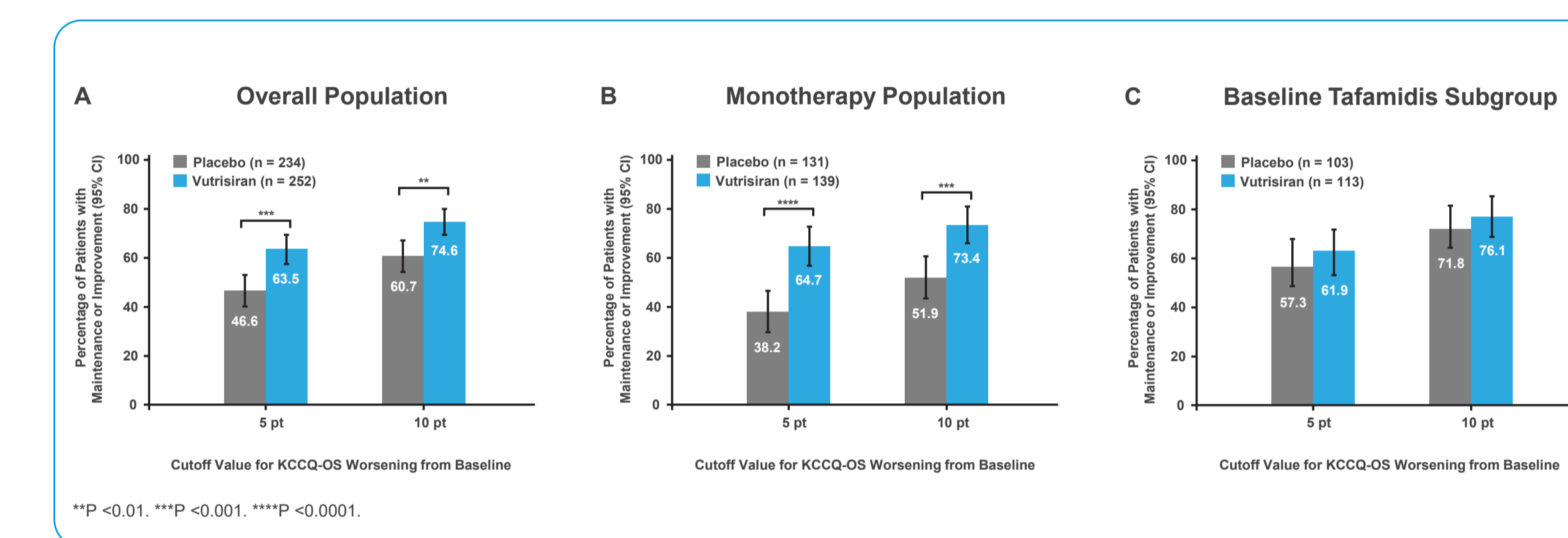


Figure 5. Clinical Benefits with Vutrisiran on Health Status/QOL versus Placebo Were Consistent across Prespecified Subgroups

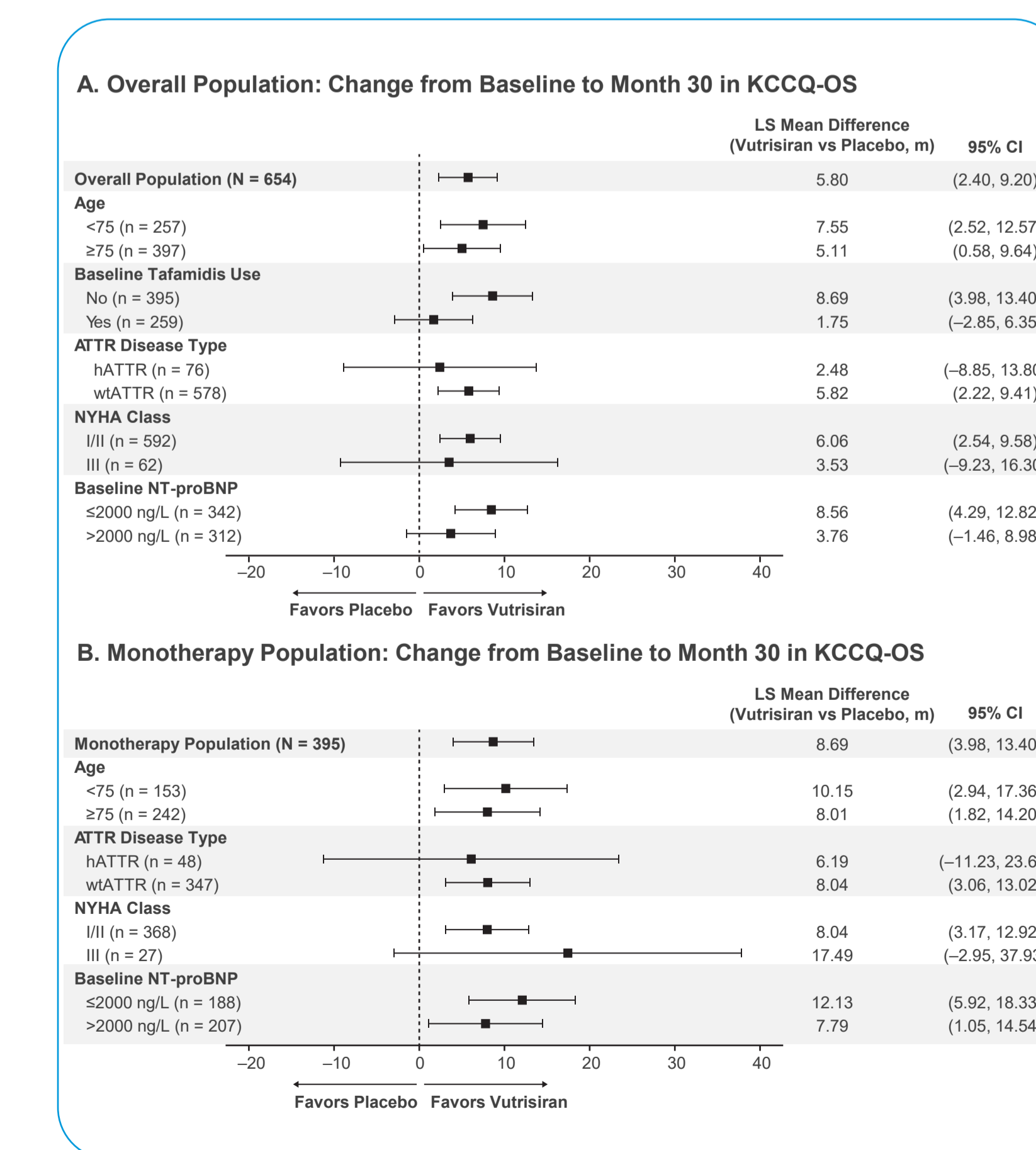
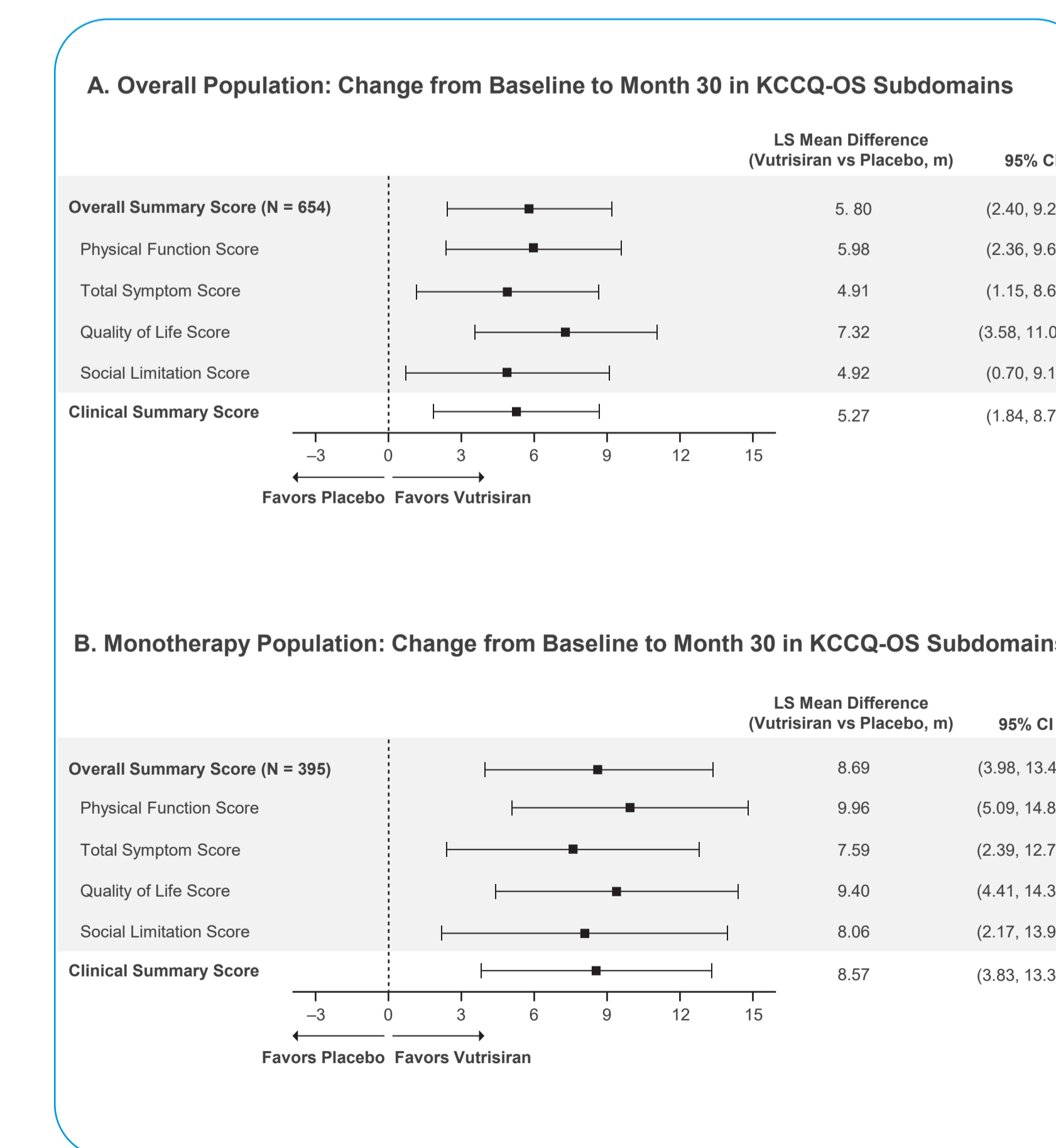


Figure 6. Vutrisiran Improved All Subdomains of the KCCQ-OS Relative to Placebo



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**Abbreviations:** 6-MWT, 6-minute walk test; ATTR, transthyretin amyloidosis; ATTR-CM, ATTR with cardiomyopathy; BL, baseline; CI, confidence interval; CV, cardiovascular; hATTR, hereditary ATTR; HF, heart failure; IQR, interquartile range; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire-Overall Score; LS, least squares; NAC, National Amyloidosis Centre; NT-proBNP, N-terminal prohomone of B-type natriuretic peptide; NYHA, New York Heart Association; OLE, open-label extension; PND, polyneuropathy disability; pt, points; q3M, every 3 months; QOL, quality of life; RNAi, RNA interference SC, subcutaneous; SD, standard deviation; TTR, transthyretin; wATTR, wild-type ATTR.