

## Patisiran: Serum Transthyretin Levels

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### SUMMARY

- In patisiran clinical studies, serum TTR levels were evaluated as a biomarker for PD assessment and were assessed using ELISA.<sup>1-4</sup>
  - In the Phase 2 OLE study, a mean percent reduction in serum TTR level of 82% was observed over 24 months in patients treated with patisiran.<sup>1</sup>
  - In the APOLLO study, a median percent reduction in serum TTR level of 81% (range, -38% to 95%) was observed over 18 months in patients treated with patisiran.<sup>2</sup>
  - In the Global OLE study, a reduction in median serum TTR levels was observed by the first measurement timepoint, decreasing by 84.3% at Week 26 (range, 97.4% to 6.3%) and 88.2% by Week 52 (range, 97.0% to 25.9%), in the APOLLO-placebo group.<sup>3</sup>
  - In the APOLLO-B study, a mean percent reduction in serum TTR level of 86.8% (SD, 13.6%) was observed at 12 months in patients treated with patisiran.<sup>4</sup>
  - In the HELIOS-A study, a mean steady-state peak percent reduction in serum TTR level of 86.0% (SD, 10.0%) was observed at 18 months in patients treated with patisiran.<sup>5</sup>

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### CLINICAL DATA

#### Phase 2 OLE

The Phase 2 OLE study (N=27) was a multicenter, international study in patients with hATTR-PN. Patients who previously received and tolerated patisiran in the Phase 2 study were eligible to enroll in the Phase 2 OLE study. Patients received IV patisiran 0.3 mg/kg every 3 weeks for approximately 2 years.<sup>1</sup>

In the Phase 2 OLE, serum TTR was used as a biomarker for PD assessment. Over 24 months, the mean percent reduction from baseline in serum TTR level was 82%, with a mean maximal reduction of 93%.

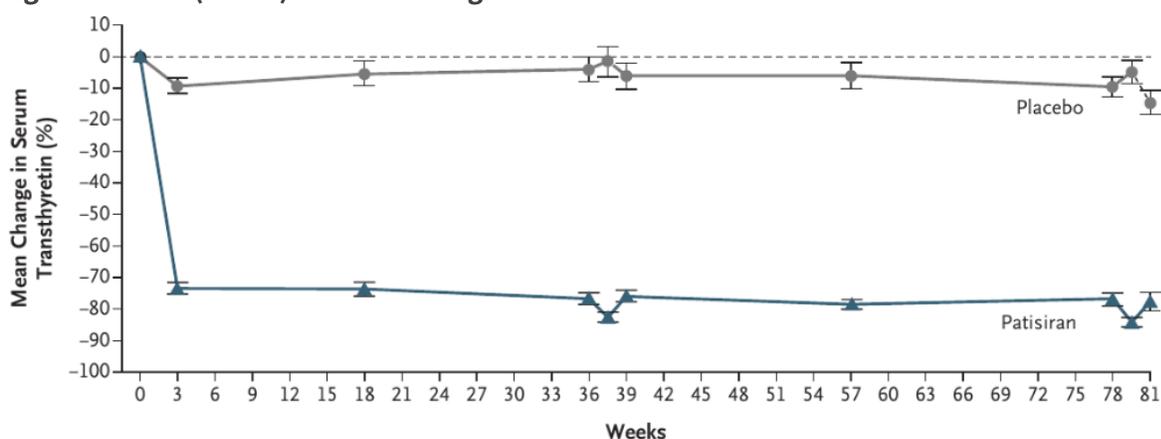
Concomitant TTR stabilizer use (patisiran and TTR stabilizer or patisiran alone), TTR genotype (V30M or non-V30M), sex, and age (<65 or ≥65 years) did not affect the PD activity of patisiran.<sup>1</sup>

### APOLLO Study

APOLLO was a multicenter, international, randomized (2:1), double-blind, placebo-controlled, phase 3 study designed to assess the efficacy and safety of IV patisiran 0.3 mg/kg every 3 weeks (n=148) versus placebo (n=77) in patients with hATTR-PN. The primary endpoint was the change from baseline in the mNIS+7 at 18 months.<sup>2</sup>

In the APOLLO study, serum TTR was used as a biomarker for PD assessment. In the patisiran group, a reduction in serum TTR was observed from baseline to Week 3 and sustained over a period of 18 months (**Figure 1**), and the median percent reduction from baseline in serum TTR level during the 18 months was 81% (range, -38% to 95%) and was similar across age, sex, or genotype.<sup>2</sup>

**Figure 1. Mean (± SEM) Percent Change from Baseline in Serum TTR Over Time in APOLLO.<sup>2</sup>**



Abbreviations: SEM = standard error of the mean; TTR = transthyretin.

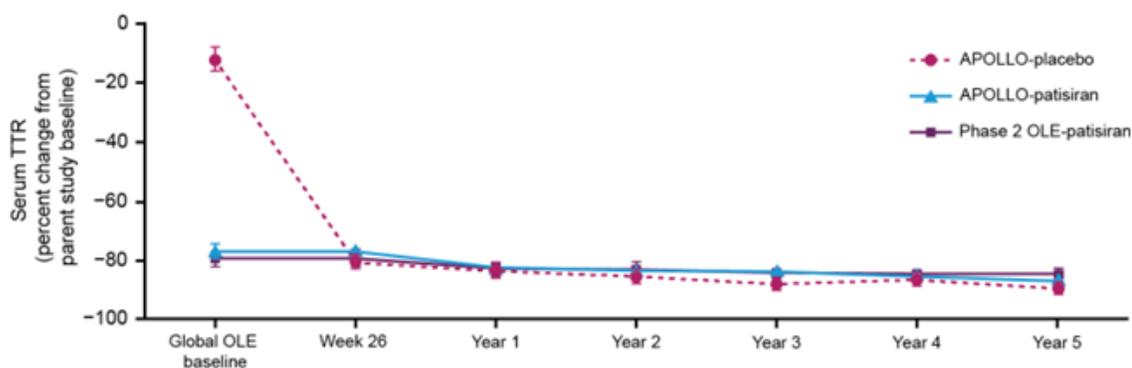
I bars represent standard error. The nadirs in TTR reduction at 9 and 18 months correspond to the predose and postdose assessments. From Adams et al.<sup>2</sup>

### Global OLE

The Global OLE study (N=211) was a multicenter, international study designed to evaluate the long-term safety and efficacy of IV patisiran in patients with hATTR-PN. Patients with hATTR-PN who completed the patisiran Phase 2 OLE study or phase 3 APOLLO study and met eligibility criteria were able to start or continue IV patisiran 0.3 mg/kg every 3 weeks for up to 5 years. The study enrolled 25 patients from the patisiran Phase 2 OLE study (Phase 2 OLE-patisiran group), 137 patients from the APOLLO-patisiran arm (APOLLO-patisiran group), and 49 patients from the APOLLO-placebo arm (APOLLO-placebo group).<sup>6</sup>

In the Global OLE study, serum TTR was used as a biomarker for PD assessment. A reduction in median serum TTR levels was observed by the first measurement timepoint, decreasing by 84.3% at Week 26 (range, 97.4% to 6.3%) and 88.2% by Week 52 (range, 97.0% to 25.9%) in the APOLLO-placebo group (**Figure 2**).<sup>3</sup>

**Figure 2. Mean ( $\pm$  SEM) Percent Change from Parent Study Baseline in Serum TTR Over 5 Years in the Global OLE.<sup>3</sup>**



APOLLO-placebo n =	39	39	37	33	26	19	19
APOLLO-patisiran n =	102	127	126	119	102	98	82
Phase 2 OLE-patisiran n =	20	24	25	25	24	22	22

Abbreviations: OLE = open-label extension; SEM = standard error of the mean; TTR = transthyretin

Observations collected within 21 days of the last dose date are included.

From Adams et al.<sup>3</sup>

### APOLLO-B Study

APOLLO-B was a multicenter, randomized (1:1), double-blind, placebo-controlled, phase 3 study designed to evaluate the efficacy and safety of IV patisiran 0.3 mg/kg every 3 weeks (n=181) versus placebo (n=179) in patients with ATTR-CM, including both hATTR and wtATTR. The primary endpoint was the change from baseline in the 6-MWT at 12 months. After the 12-month double-blind treatment period, all patients received patisiran in an OLE period.<sup>4</sup>

In the APOLLO-B study, serum TTR was used as a biomarker for PD assessment. At baseline, the mean serum TTR level was 235.32 mg/L (SD, 68.05 mg/L) in the patisiran arm and 244.77 mg/L (SD, 73.17 mg/L) in the placebo arm. At 12 months, the mean serum TTR level was 30.93 mg/L (SD, 33.60 mg/L) in the patisiran arm and 229.40 mg/L (SD, 77.15 mg/L) in the placebo arm. In the patisiran arm, the mean percent reduction from baseline in serum TTR level was 86.8% (SD, 13.6%) at 12 months.<sup>4</sup>

### HELIOS-A Study

HELIOS-A was a phase 3, global, randomized, open-label study designed to evaluate the efficacy and safety of vutrisiran in patients with hATTR-PN. Patients were randomized (3:1) to receive either vutrisiran 25 mg every 3 months by subcutaneous injection (n=122) or patisiran 0.3 mg/kg every 3 weeks by IV infusion (as a reference group, n=42) for 18 months. This study used the placebo arm of the APOLLO study as an external control arm (n=77) for the primary endpoint and most other efficacy endpoints. The primary endpoint was the change from baseline in mNIS+7 at 9 months.<sup>7</sup>

In the HELIOS-A study, serum TTR was used as a biomarker for PD assessment. Noninferiority of the percent reduction from baseline in serum TTR levels over 18 months in the vutrisiran arm compared with the within-study patisiran arm was evaluated as a secondary endpoint.<sup>7</sup> In patients treated with

patisiran, the steady-state peak and trough mean percent reduction from baseline in serum TTR levels over 18 months was 86.0% (SD, 10%) and 74.7% (SD, 14.7%), respectively.<sup>5</sup>

## ONPATTRO PRESCRIBING INFORMATION – RELEVANT CONTENT

For relevant labeling information, please refer to the following sections of the [ONPATTRO Prescribing Information](#)<sup>8</sup>:

- CLINICAL PHARMACOLOGY Section 12.1 Mechanism of Action
- CLINICAL PHARMACOLOGY Section 12.2 Pharmacodynamics

## ABBREVIATIONS

6-MWT = 6-minute walk test; ATTR-CM = transthyretin amyloidosis with cardiomyopathy; ELISA = enzyme-linked immunosorbent assay; hATTR = hereditary transthyretin amyloidosis; hATTR-PN = hereditary transthyretin amyloidosis with polyneuropathy; IV = intravenous; mNIS+7 = modified Neuropathy Impairment Score +7; OLE = open-label extension; PD = pharmacodynamic; SD = standard deviation; SEM = standard error of the mean; TTR = transthyretin; wtATTR = wild-type transthyretin amyloidosis.

Updated 25 September 2025

## REFERENCES

1. Coelho T, Adams D, Conceição I, et al. A phase II, open-label, extension study of long-term patisiran treatment in patients with hereditary transthyretin-mediated (hATTR) amyloidosis. *Orphanet J Rare Dis*. 2020;15(1). doi:10.1186/s13023-020-01399-4
2. Adams D, Gonzalez-Duarte A, O’Riordan WD, et al. Patisiran, an RNAi therapeutic, for hereditary transthyretin amyloidosis. *N Engl J Med*. 2018;379(1):11-21. doi:10.1056/NEJMoa1716153
3. Supplement to: Adams D, Wixner J, Polydefkis M, et al. Five-year results with patisiran for hereditary transthyretin amyloidosis with polyneuropathy: A randomized clinical trial with open-label extension. *JAMA Neurol*. 2025;82(3):228-236. doi:10.1001/jamaneurol.2024.463
4. Maurer MS, Kale P, Fontana M, et al. Patisiran treatment in patients with transthyretin cardiac amyloidosis. *N Engl J Med*. 2023;389(17):1553-1565. doi:10.1056/NEJMoa2300757
5. Supplement to: Adams D, Tournev IL, Taylor MS, et al. Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. *Amyloid*. 2023;30(1):18-26. doi:10.1080/13506129.2022.2091985
6. Adams D, Wixner J, Polydefkis M, et al. Five-year results with patisiran for hereditary transthyretin amyloidosis with polyneuropathy: A randomized clinical trial with open-label extension. *JAMA Neurol*. 2025. doi:10.1001/jamaneurol.2024.4631.
7. Adams D, Tournev IL, Taylor MS, et al. Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. *Amyloid*. 2023;30(1):18-26. doi:10.1080/13506129.2022.2091985
8. ONPATTRO (patisiran) Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc.