Patisiran: Use in Patients with Heart Transplant

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SUMMARY

- Clinical trials to evaluate patisiran treatment in patients who underwent heart transplant have not been conducted to date.
  - An analysis of the efficacy and safety of patisiran in clinical study participants with a past medical history of heart transplant is not available.
- A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any safety concerns regarding the use of patisiran in patients with heart transplant.[1]
- Case reports from published medical literature discuss the use of patisiran in patients with hATTR who underwent heart transplant.[2–6]

INDEX

CLINICAL DATA

Global Open-Label Extension Study

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.[7]

A total of 3 patients with a history of heart transplant (1 patient in the placebo arm and 2 patients in the patisiran arm) completed the APOLLO study and continued into the Global OLE.[8]

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.[9]

In the HELIOS-A study, there was 1 patient (2.4%) in the patisiran reference arm with a past medical history of heart transplant.[10]

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.[11]

Patients were excluded from the study if they had a prior or planned heart, liver, or other organ transplant.[12]

GLOBAL SAFETY DATABASE

A cumulative post-marketing review of Alnylam Pharmaceuticals' global safety database did not identify any safety concerns regarding the use of patisiran in patients with heart transplant.[1]

CASE REPORTS

The following information provides an overview of published case reports regarding the use of patisiran in patients who have underwent a heart transplant. It is not intended to be an all-inclusive list or summary of relevant publications, abstracts, and manuscripts.

Razvi Y, et al. Cardiac transplantation in transthyretin amyloid cardiomyopathy: Outcomes from three decades of tertiary center experience. *Front Cardiovasc Med*. 2023;9. doi:10.3389/fcvm.2022.1075806[2]

- A retrospective study was conducted at two tertiary centers in the UK and Italy to evaluate the long-term outcomes and survival of patients with ATTR-CM who underwent a heart transplant between 1990 and 2020.
- Of the 14 patients included in the study, 2 patients (Patient 2 and Patient 10) received patisiran post-transplant due to the development of mild polyneuropathy.
- Patisiran was initiated 210 months post-transplant in Patient 2 and 6 months post-transplant in Patient 10. Of these 2 patients, neither experienced significant transplant rejection requiring treatment, cardiac amyloid recurrence, or significant infection (requiring hospitalization within 1 month of transplant).
- Patient 2 experienced a temporary renal impairment which required dialysis during the follow up period, and Patient 10 was diagnosed with postoperative CKD. Patient 2 died at month 212 post-transplant. Patient 10 was alive at 29 months post-transplant.

Lyle MA, et al. Heart transplantation in Val142Ile mutation in the modern era: A single center experience. *Clin Transplant*. 2022;36(11):e14780. doi:10.1111/ctr.14780[3]

- A retrospective study of patients with hATTR and Val142Ile variant who either received a heart transplant or were followed post heart transplant at Emory University between January 1, 2014 and February 1, 2022 was conducted.

- Ten patients were identified. All patients were male and were African American. The average age was 63 ± 4 years, and patients were followed an average of 4.5 years post heart transplant. All patients had the Val142Ile mutation (2 homozygous, 8 heterozygous). No patient was on disease modifying therapy prior to receiving a heart transplant. At the time of heart transplant, extracardiac manifestations were present in some of the patients including: 7 patients with carpal tunnel syndrome, 1 patient with mild polyneuropathy and autonomic dysfunction, 1 patient with severe polyneuropathy, and 1 patient with mild lumbar stenosis.
- Following transplantation, 4 patients (40%) were initiated on patisiran post heart transplant for the development of extracardiac disease progression.
  - Two patients developed polyneuropathy; 1 patient at 2 years post heart transplant and 1 patient at 8 months post heart transplant.
  - One patient had progression of severe polyneuropathy.
  - One patient had progression of neuropathic and autonomic dysfunction. The patient developed gastroparesis 3.5 years post heart transplant.
- Patisiran was initiated at an average of 1.7 years post development of the symptoms. No significant adverse events were reported.
- Of the patients on patisiran, the patient with gastroparesis continued to have progressive symptoms despite receiving treatment.

Guendouz S, et al. Heart transplantation, either alone or combined with liver and kidney, a viable treatment option for selected patients with severe cardiac amyloidosis. *Transplant Direct*. 2022;8(7):e1323. doi:10.1097/TXD.0000000000001323[4]

- A retrospective study of patients with cardiac amyloidosis who underwent an orthotopic heart transplant between 2005 and 2018 at the University Hospital Henri Mondor in Creteil, France was conducted to assess patient outcomes.
- Of the 6 patients with hATTR included in the study, 2 patients (Patient 4 and Patient 5) received patisiran post heart transplant.
  - Patient 4 was a male diagnosed with hATTR, heterozygous for the Ser77Tyr variant. The patient received tafamidis since 2015 and underwent a heart transplant in 2016 at the age of 65. He experienced worsening of peripheral neuropathy since 2019, and patisiran was initiated in 2020.
  - Patient 5 was a female diagnosed with hATTR, heterozygous for the Glu89Lys variant. The patient underwent a heart and liver transplant in 2015 at the age of 66. She received tafamidis, and worsening of neuropathy, dysautonomia, and digestive symptoms were reported during follow-up post-transplant. Patisiran was initiated in 2020.
  - Both patients were alive at the conclusion of the analysis.

Seibert K, et al. Progressive multiple mononeuropathy in a patient with familial transthyretin amyloidosis after liver transplantation. *J Clin Neuromuscul Dis*. 2022;23(3):143-147. doi:10.1097/CND.0000000000000368[5]

- A case report detailed a 61-year-old African American male, who presented with advanced biventricular heart failure and progressive numbness from the hands to the feet.
- After an evaluation including but not limited to nerve conduction studies, cardiac magnetic resonance imaging, cardiac biopsy, and genetic testing, the patient was diagnosed with hATTR, homozygous for the V122I variant.

    - Initial cardiac evaluation showed progressive systolic and diastolic heart failure with an ejection fraction of 13% and low amplitude on electrocardiogram.
    - Initial neurological examination showed weakness and atrophy of hand muscles, with normal strength in the lower limbs except for mild weakness in left ankle. The patient's reflexes were trace to absent in the upper extremities and ankles.
- The patient underwent a heart and liver transplant for the management of hATTR less than 1 year after diagnosis.
- Over the 5 years following transplant, the patient developed progressive weakness of the upper limbs, with increasing muscle atrophy in the hands. The patient was started on patisiran about 5.5 years post transplant and has maintained treatment for over 2 years, with reported stabilization of his neuropathy symptoms on serial clinical examination.

Urey MA, et al. Use of patisiran following heart transplant in a patient with hereditary transthyretin cardiac amyloidosis and polyneuropathy. *J Heart Lung Transplant*. 2021;40(4):S477-S478. doi:10.1016/j.healun.2021.01.1973[6]

- A case report detailed a 73-year-old African American male, who presented with new-onset dyspnea. An endomyocardial biopsy confirmed amyloid deposits, and genetic testing confirmed a pathogenic variant in the TTR gene. Nerve conduction studies also revealed a decrease in conduction that was consistent with amyloid polyneuropathy.
- Despite initiation of tafamidis, the patient eventually required inotropes as a bridge to orthotopic heart transplant due to clinical deterioration.
- At 10 months post-transplant, the patient reported worsening symptoms of neuropathy. Patisiran was initiated approximately 1 year after heart transplant. At 18 months, the patient reported stabilization of his polyneuropathy symptoms and no complications from patisiran infusions.

ABBREVIATIONS

ATTR = transthyretin amyloidosis; ATTR-CM = transthyretin amyloidosis with cardiomyopathy; CKD = chronic kidney disease; hATTR = hereditary transthyretin amyloidosis; hATTR-PN = hereditary transthyretin amyloidosis with polyneuropathy; IV = intravenous; OLE = open-label extension; TTR = transthyretin; wtATTR = wild-type transthyretin amyloidosis.

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REFERENCES

1. Alnylam Pharmaceuticals. Data on file. MED-ALL-PATI-2500013.
2. Razvi Y, Porcari A, Di Nora C, et al. Cardiac transplantation in transthyretin amyloid cardiomyopathy: Outcomes from three decades of tertiary center experience. *Front Cardiovasc Med*. 2023;9. doi:10.3389/fcvm.2022.1075806
3. Lyle MA, Brown MT, Morris AA, et al. Heart transplantation in Val142Ile mutation in the modern era: A single center experience. *Clin Transplant*. 2022;36(11):e14780. doi:10.1111/ctr.14780
4. Guendouz S, Grimbert P, Radu C, et al. Heart transplantation, either alone or combined with liver and kidney, a viable treatment option for selected patients with severe cardiac amyloidosis. *Transplant Direct*. 2022;8(7):e1323. doi:10.1097/TXD.0000000000001323
5. Seibert K, Wlodarski R, Sarswat N, et al. Progressive multiple mononeuropathy in a patient with familial transthyretin amyloidosis after liver transplantation. *J Clin Neuromuscul Dis*. 2022;23(3):143-147. doi:10.1097/CND.0000000000000368
6. Urey MA, Topik AL, Saulog JL, et al. Use of patisiran following heart transplant in a patient with hereditary transthyretin cardiac amyloidosis and polyneuropathy. *J Heart Lung Transplant*. 2021;40(4):S477-S478. doi:10.1016/j.healun.2021.01.1973

7. Adams, Polydefkis, González-Duarte, et al. Long-term safety and efficacy of patisiran for hereditary transthyretin-mediated amyloidosis with polyneuropathy: 12-month results of an open-label extension study. *Lancet Neurol*. 2021;20(1):49-59. doi:10.1016/S1474-4422(20)30368-9
8. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTR02-2000110.
9. 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
10. Alnylam Pharmaceuticals. Data on file. MED-ALL-TTRSC02-2200006.
11. 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
12. Protocol for: 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