Patisiran Real-World Evidence in hATTR Amyloidosis

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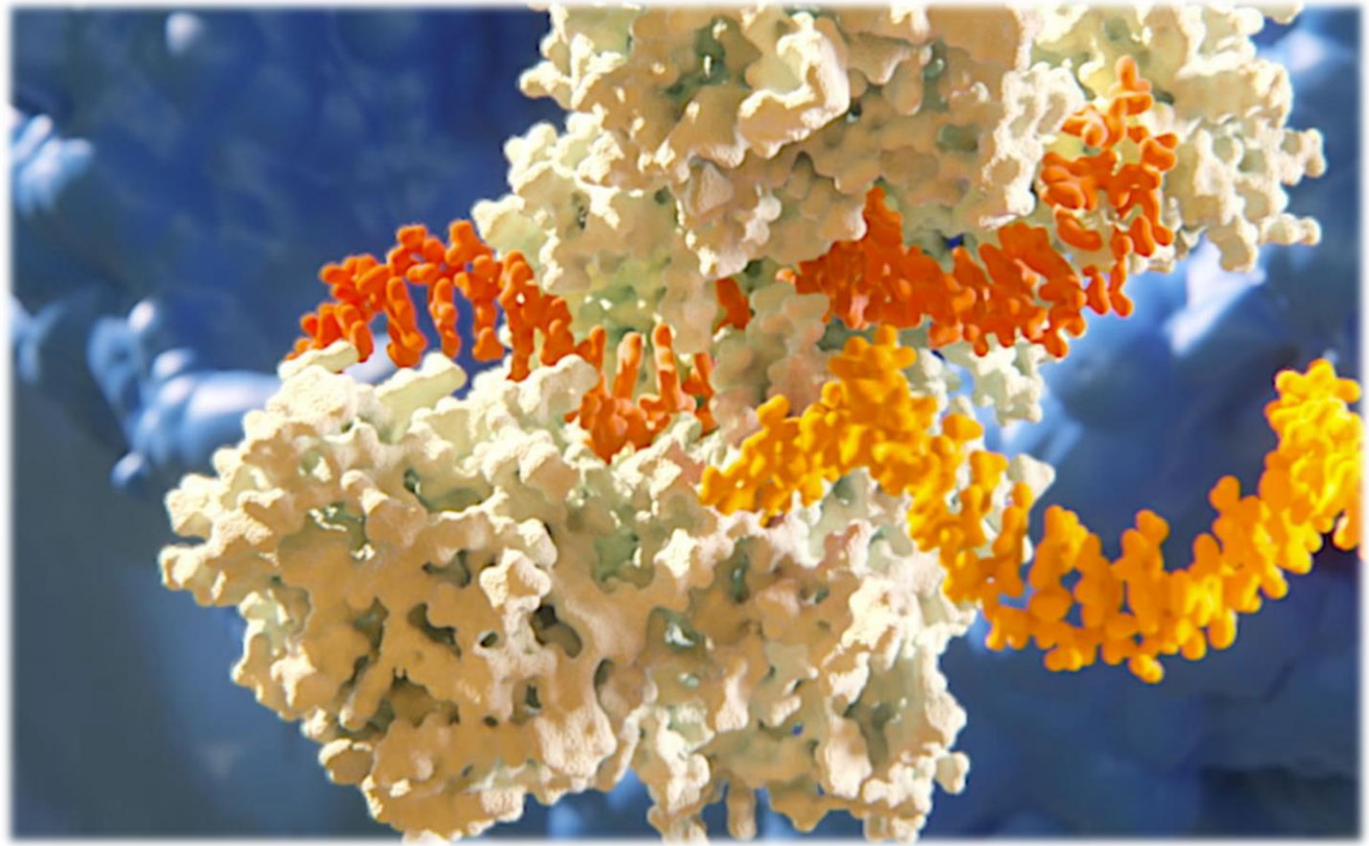
Patisiran Real-World Evidence in hATTR Amyloidosis

Subject area

- Polyneuropathy (N=22)
- Cardiomyopathy (N=4)
- Transplant (N=6)
- Concomitant Treatment (N=5)
- Switching Treatment (N=7)



hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

- **Case Study (N=10)**
- **Retrospective Analysis (N=4)**
- **Single Center (N=8)**

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

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Case Study (N=10)

- 2022 (N=6) >
- 2021 (N=2) >
- 2020 (N=1) >
- 2019 (N=1) >
- **Retrospective Analysis (N=4)** >
- **Single Center (N=8)** >

hATTR, hereditary transthyretin-mediated.

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Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

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Case Study (N=10)

2022 (N=6)

Patisiran for acquired polyneuropathy after domino liver transplant
(Guaraldi et al. *ASNP* 2022)

Late-onset hATTR with polyneuropathy in 77 year old
(Labella et al. *ASNP* 2022)

Polyneuropathy in His110Asn mutation
(Giglia et al. *ASNP* 2022)

Mononeuropathy after liver transplant
(Seibert et al. *J Clin Neuromuscul Dis* 2022)

Early improvement in hATTR with patisiran treatment
(Oginezawa et al. *Clin Neurol* 2022)

Tafamidis to patisiran post-liver transplantation
(Bulinski et al. *J Neurol* 2022)

hATTR, hereditary transthyretin-mediated.

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Case Study (N=10)

2022 (N=6)

Patisiran Treatment in a Patient with Acquired Amyloid Polyneuropathy after Domino Liver Transplant

Study Purpose

To describe patisiran treatment for acquired amyloid polyneuropathy following domino liver transplant

Patient Population

- 2008: 63-year-old male received liver transplant for hepatitis C-related disease (carcinoma and cirrhosis)
- 2017: presented with sensorimotor polyneuropathy, followed by alternating diarrhea and constipation and 15 kg weight loss
- 2020: hospital admission with congestive heart failure; echocardiogram showed signs of amyloid cardiomyopathy

Methods/Assessments

- 2020: echocardiography, 99^{m}-technetium pyrophosphate myocardial imaging
- 2021: NIS, KPS, COMPASS-31, Norfolk QOL-DN, cardiovascular autonomic testing

Genetic Variant(s)

- Liver donor had rare Ser23Asn variant

Effectiveness Assessment

- Within a few months of initiating patisiran, pt reported no further weight loss, with improved gut function, muscle strength, and sensation
- After 22 rounds of patisiran, there was improvement in muscle strength and sensory deficits, and cardiology had stabilized
- NIS improved from 43 to 20

Treatment/Study Duration

- February 2021: patisiran, 0.3 mg/kg q3w (22 rounds)

Adverse Events

- No side effects reported by pt on patisiran treatment

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COMPASS-31, Composite Autonomic Symptom Score-31; hATTR, hereditary transthyretin-mediated; KPS, Karnofsky Performance Status; NIS, Neuropathy Impairment Score; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; pt, patient; q3w, every 3 weeks.

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Case Study (N=10)

2022 (N=6)

Late-onset Hereditary Transthyretin Amyloid Neuropathy: Think About It to Diagnose It

Study Purpose

To highlight the need for awareness of severe late-onset hATTR amyloidosis with polyneuropathy in elderly individuals

Patient Population

- A 77-year-old female
- Repeated neurologic exams for progressive gait disorder over 3 years; no familial history for neurologic disorder; past medical history of hypertension
- Lumbar canal spinal stenosis on MRI; no benefit from decompression surgery

Effectiveness Assessment

- Patisiran treatment stabilized neurologic symptoms

Genetic Variant(s)

- c.250T>C (p.Phe84Leu) heterozygous variant

Methods/Assessments

- Loss of consciousness led to hospitalization
- No acute lesions on brain CT scan; normal EEG
- No major arrhythmias on ECG; signs of mild hypertensive heart disease with septum-basal thickening

Methods/Assessments (cont.)

- Severe distal lower limb weakness with sensory ataxia; milder upper-limb distal weakness
- Lab tests excluded diabetes, B12 deficiency, and endocrinologic/immunologic disorders
- Discharged with diagnosis of vaso-vagal syncope and mild axonal sensorimotor polyneuropathy
- Loss of consciousness led to re-admission
- Detailed medical history revealed chronic vaso-vagal syncope and constipation compatible with autonomic involvement
- Together with dysautonomia, lumbar canal stenosis, and bilateral carpal tunnel, TTR genetic analysis led to a diagnosis of hATTR amyloidosis

Adverse Events

- Not reported

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CT, computed tomography; ECG, electrocardiogram; EEG, electroencephalogram; hATTR, hereditary transthyretin-mediated; MRI, magnetic resonance imaging; TTR, transthyretin.

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Case Study (N=10)

2022 (N=6)

A Case of Polyneuropathy in His110Asn Mutation of TTR Gene Successfully Treated with Patisiran

Study Purpose

To assess the effects of patisiran in a patient with polyneuropathy and a His110Asn variant

Patient Population

- A 56-year-old female referred for a suspected progressive memory decline
- Family history: mother died at 50 years from Guillain–Barré syndrome
- 2021: rapid weight loss, diarrhea, nausea, distal paresthesia
- EMG: sensory axonal polyneuropathy in upper and lower limbs
- Polyneuropathy determined to be FAP stage I
- Normal lab results, including tumor markers, hormonal and vitamin levels
- Brain and lumbosacral MRI unremarkable
- Genetic testing demonstrated TTR variant; salivary gland biopsy: positive Congo red stain

Genetic Variant(s)

- Heterozygous His110Asn variant (considered a variant of uncertain significance)

Methods/Assessments

- Weight, 6MWT, KPS, NIS, NIS-W, COMPASS-31, Norfolk QOL-DN

Treatment/Study Duration

- Patisiran 0.3 mg/kg q3w
- Nine months of follow-up

Effectiveness Assessment

- Weight gain: 6 kg at 6 months; 14.5 kg at 9 months
- Improved neuropathy score on NIS-W scale (19 to 12), speed on 6MWT (148 to 285 m), quality of life (Norfolk QOL-DN score, 95 to 60); autonomic symptoms (COMPASS-31, 12 to 21), and KPS (50% to 70%)

Adverse Events

- Not reported

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6MWT, 6-minute walk test; COMPASS-31, Composite Autonomic Symptom Score-31; EMG, electromyography; FAP, familial amyloid polyneuropathy; hATTR, hereditary transthyretin-mediated; KPS, Karnofsky Performance Status; MRI, magnetic resonance imaging; NIS, Neuropathy Impairment Score; NIS-W, Neuropathy Impairment Score-Weakness; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; q3w, every 3 weeks; TTR, transthyretin.

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Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

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Case Study (N=10)

2022 (N=6)

- **Patisiran for acquired polyneuropathy after domino liver transplant** (Guaraldi et al. *ASNP* 2022)
- **Late-onset hATTR with polyneuropathy in 77 year old** (Labella et al. *ASNP* 2022)
- **Polyneuropathy in His110Asn mutation** (Giglia et al. *ASNP* 2022)
- **Mononeuropathy after liver transplant** (Seibert et al. *J Clin Neuromuscul Dis* 2022)
- **Early improvement in hATTR with patisiran treatment** (Oginezawa et al. *Clin Neurol* 2022)
- **Tafamidis to patisiran post-liver transplantation** (Bulinski et al. *J Neurol* 2022)

Progressive Multiple Mononeuropathy in a Patient with Familial Transthyretin Amyloidosis after Liver Transplantation

Study Purpose

To assess the effects of patisiran in a patient with multiple mononeuropathy after liver transplantation

Patient Population

- A 61-year old African American male
- Initially presented with advanced biventricular heart failure and progressive numbness in hands and feet; findings were consistent with multiple mononeuropathy and concomitant cervical and lumbar polyradiculopathy
- The patient underwent heart and liver transplantation followed by cervical spinal decompression and fusion surgery
- However, the patient showed slowly progressive motor neuropathy symptoms in the upper limbs over the subsequent 5 years

Genetic Variant(s)

- Val122Ile

Effectiveness Assessment

- The patient showed stabilization of neuropathy symptoms during 2 years of follow-up after initiation of patisiran

Treatment/Study Duration

- Patisiran treatment initiated 5.5 years post-transplant.
- Two years of follow-up

Adverse Events

- Not reported

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hATTR, hereditary transthyretin-mediated.

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Case Study (N=10)

2022 (N=6)

ATTRv Amyloidosis with Early Improvement Demonstrated by the 6-minute Walk Test following Patisiran Therapy: A Case Report

Study Purpose

To assess the speed of response to patisiran in a patient with hATTR amyloidosis with polyneuropathy

Patient Population

- A 65-year old male with hATTR amyloidosis
- Numbness in hands, lower-limb muscle weakness and atrophy, progressive weight loss, bilateral carpal tunnel syndrome, orthostatic hypotension, pollakiuria, and constipation
- Severe LV hypertrophy with apical sparing; transthyretin amyloid positive endomyocardial biopsy

Genetic Variant(s)

- Val30Met

Methods/Assessments

- Neurologic exam, 6MWT, BNP, Schellong test sBP, stabilometry (Romberg ratio), new Borg scale score, grip strength, MMT, echocardiography

Treatment/Study Duration

- Patisiran 0.3 mg/kg q3w
- Three months of initial, detailed follow-up (22 months total follow-up)

Effectiveness Assessment

- The 6MWT improved from 217 at baseline to 270 m, 330 m, 366 m, and 378 m at Weeks 3, 6, 9, and 12, respectively
- BNP and ΔsBP did not improve
- The Romberg ratio improved from 53% at Week 3 to 43% at Week 12
- The new Borg scale score improved from breast 2/limb 3 at baseline, 3, 6, and 9 to breast 1/limb 2 at Week 12
- Grip strength increased from 12 kg/16 kg at baseline to 20 kg/24 kg at Week 12; there was no improvement in MMT for four limbs
- LV ejection fraction increased from 50.4% at diagnosis to 57.6% at Week 9
- Nutritional status and body weight was maintained at Month 22

Adverse Events

- Not reported

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6MWT, 6-minute walk test; BNP, brain-type natriuretic peptide; hATTR, hereditary transthyretin-mediated; LV, left ventricular; MMT, manual muscle test; q3w, every 3 weeks; sBP, supine systolic blood pressure; ΔsBP, change in supine systolic blood pressure minus systolic blood pressure upon standing.

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Case Study (N=10)

2022 (N=6)

Clinical Improvement after Change of Therapy from Tafamidis to Patisiran in Progressive TTR Amyloidosis Post-liver Transplantation

Study Purpose

To assess patisiran effectiveness following liver transplantation in a patient with hATTR amyloidosis

Patient Population

- A 36-year-old male diagnosed with TTR-FAP in 2012
- Received tafamidis followed by liver transplantation after 1 year; tafamidis was discontinued
- Symptoms of polyneuropathy gradually worsened after transplantation and continued despite re-initiation of tafamidis in 2018
- Switch to patisiran occurred 6 years post-transplantation

Methods/Assessments

- NCS, mNIS+7, MRI, echocardiography, NYHA class

Genetic Variant(s)

- Glu54Gly

Effectiveness Assessment

- The patient's polyneuropathy symptoms slowly improved on patisiran
- mNIS+7 score decreased from 183.5 to 172.5 after 18 months
- NCS results remained stable
- No change in cardiac amyloidosis, with the caveat that examinations were performed across different centers

Treatment/Study Duration

- Patisiran treatment with 18 months' follow-up

Adverse Events

- Not reported

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hATTR, hereditary transthyretin-mediated; mNIS+7, modified Neuropathy Impairment Score + 7; MRI, magnetic resonance imaging; NCS, nerve conduction studies; NYHA, New York Heart Association; TTR-FAP, transthyretin-familial amyloid polyneuropathy.

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Case Study (N=10)

2021 (N=2)

Patisiran in patient with stage 3 polyneuropathy
(Müschen et al. *Muscle Nerve* 2021)

Patisiran following heart transplant
(Urey et al. *ISHLT* 2021)

hATTR, hereditary transthyretin-mediated.

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Case Study (N=10)

2021 (N=2)

Patisiran in patient with stage 3 polyneuropathy
(Müschen et al. *Muscle Nerve* 2021) >

Patisiran following heart transplant
(Urey et al. *ISHLT* 2021) >

Treatment with Patisiran of a Patient with Hereditary Transthyretin-mediated Amyloidosis with Stage 3 Polyneuropathy

Study Purpose

To assess the effectiveness of patisiran for a 76-year-old male patient with severe polyneuropathy

Patient Population

- A 76-year-old male with hATTR amyloidosis
- FAP stage 3
- Severe left ventricular hypertrophy

Methods/Assessments

- MRC sum score, INCAT, grip strength, R-ODS, serum NT-proBNP, and TTR levels

Genetic Variant(s)

- Val50Met

Treatment/Study Duration

- Patisiran 0.3 mg/kg every 3 weeks
- Study duration of 12 months

Effectiveness Assessment

- 90.5% TTR decrease from baseline at Month 3–12
- Slight grip strength improvement from Month 6, retained at Month 12
- Seven- to 8-point R-ODS improvement to Month 12
- Overall muscle strength (MRC sum score) and INCAT score remained stable over 12 months
- Cardiac function stable over 12 months, but NT-proBNP reduced from baseline to Month 3–12
- Pt reported improved sensation and dysphagia, and less painful dysesthesia

Adverse Events

- Pt did not report any side effects

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FAP, familial amyloid polyneuropathy; hATTR, hereditary transthyretin-mediated; INCAT, inflammatory neuropathy cause and treatment score; MRC, Medical Research Council; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide; pt, patient; R-ODS, Rasch-built Overall Disability Scale; TTR, transthyretin.

Patisiran Real-World Evidence in hATTR Amyloidosis

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Case Study (N=10)

2021 (N=2)

Patisiran in patient with stage 3 polyneuropathy
(Müschen et al. *Muscle Nerve* 2021)

Patisiran following heart transplant
(Urey et al. *ISHLT* 2021)

Use of Patisiran following Heart Transplant in Patient with Hereditary Transthyretin Cardiac Amyloidosis and Polyneuropathy

Study Purpose

To assess the safety and effectiveness of patisiran in a patient with hATTR amyloidosis following heart transplant

Patient Population

- A 73-year-old African American male with hATTR amyloidosis, who had progression of neuropathy following a heart transplant (for cardiac amyloid)

Methods/Assessments

- Patient-reported symptoms

Treatment/Study Duration

- Patisiran treatment beginning 12 months post-transplant
- Eighteen-month follow-up

Genetic Variant(s)

- Val122Ile

Effectiveness Assessment

- Pt experienced improvement in neuropathy within 4–5 months of patisiran initiation
- Pt reported only very mild neuropathy symptoms 12 months post-patisiran initiation

Adverse Events

- Infusions were well tolerated, and pre-infusion dexamethasone was tapered off at pt's request
- Pt maintained normal graft function and did not experience transplant rejection or develop donor-specific antibodies

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hATTR, hereditary transthyretin-mediated; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

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Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

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Case Study (N=10)

2020 (N=1)

Misdiagnosis of anorexia nervosa
(Russo et al. *Amyloid* 2020)

hATTR, hereditary transthyretin-mediated.

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Case Study (N=10)

2020 (N=1)

Misdiagnosis of anorexia nervosa
(Russo et al. *Amyloid* 2020)

From a Misdiagnosis of Anorexia Nervosa to a Dramatic Patisiran-induced Improvement in a Patient with ATTRE89Q Amyloidosis

Study Purpose

To report a case of hATTR amyloidosis misdiagnosis and the subsequent impact of patisiran

Patient Population

- A 46-year-old female
- Presented with abdominal pain, nausea, and weight loss
- Diagnosed with anorexia nervosa by a psychiatrist
- Referred to a neurology unit after MRI highlighted possible cardiac amyloidosis

Methods/Assessments

- BMI, MRC scale, PND score, NCS, NYHA class, NIS, CADT

Genetic Variant(s)

- ATTRE89Q

Treatment/Study Duration

- Patisiran IV 0.3 mg/kg q3w
- Nine months of follow-up

Effectiveness Assessment

- After 9 months of patisiran treatment, pt showed increased weight (from 42.5 kg to 49.5 kg) and BMI (from 15.8 kg/m^2 to 18.4 kg/m^2)
- NIS improved from 126 to 108, and PND score from IIIB to II
- CADT score improved from 7 to 13, with a reduction in GI symptoms such as vomiting
- Significant QOL improvement
- Cardiac function stable

Adverse Events

- Not reported

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BMI, body mass index; CADT, Compound Autonomic Dysfunction Test; GI, gastrointestinal; hATTR, hereditary transthyretin-mediated; IV, intravenous; MRC, Medical Research Council; MRI, magnetic resonance imaging; NCS, nerve conduction studies; NIS, Neuropathy Impairment Score; NYHA, New York Heart Association; PND, polyneuropathy disability; q3w, every 3 weeks; QOL, quality of life.

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Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

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Case Study (N=10)

2019 (N=1)

Patient on long-term patisiran
(Schmidt. *EU-ATTR* 2019)

hATTR, hereditary transthyretin-mediated.

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Case Study (N=10)

2019 (N=1)

Patient on long-term patisiran
(Schmidt. *EU-ATTR* 2019)

Case Report on Long-term Patisiran Treatment

Study Purpose

To assess safety and effectiveness of long-term patisiran treatment in a patient with hATTR amyloidosis

Patient Population

- A 62-year-old male pt with hATTR amyloidosis with polyneuropathy and cardiomyopathy awaiting OLT

Genetic Variant(s)

- Arg54Thr

Methods/Assessments

- Echocardiogram, NT-proBNP, NIS, mBMI, vitamin A

Treatment/Study Duration

- Previously treated with tafamidis 20 mg daily
- Patisiran treatment from June 2013 to 2019 (approx. 6 years)

Effectiveness Assessment

- mBMI improved and NT-proBNP reduced
- NIS stable when measured from 1 year after patisiran treatment initiation to Year 6
- Due to stabilization of disease symptoms, NT-proBNP reduction, and mBMI improvement, liver transplant was not required at the time of publication
- Cardiomyopathy was stabilized, with improvement in left and right atrium dilation, and mild progression of LVCH

Adverse Events

- No AEs recorded
- Pt had normal liver enzymes and renal parameters throughout treatment
- Pt had no febrile episodes, no eye anomalies, and normal thyroid function

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AE, adverse event; hATTR, hereditary transthyretin-mediated; LVCH, left ventricular concentric hypertrophy; mBMI, modified body mass index; NIS, Neuropathy Impairment Score; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide; OLT, orthotopic liver transplantation; pt, patient.

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Alnylam® PHARMACEUTICALS

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

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Retrospective Analysis (N=4)

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Single Center (N=8) >

hATTR, hereditary transthyretin-mediated.

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Retrospective Analysis (N=4)

2023 (N=1)

Belgian retrospective survey on patisiran effectiveness
(De Bleecker et al. *Acta Neurol Belg* 2023)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

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Retrospective Analysis (N=4)

2023 (N=1)

Belgian retrospective survey on patisiran effectiveness
(De Bleecker et al. *Acta Neurol Belg* 2023)

A Belgian Retrospective Survey of Hereditary Transthyretin-mediated (hATTR) Amyloidosis Patients Treated with Patisiran in Real-world Practice

Study Purpose

To assess the epidemiology of hATTR amyloidosis and the impact of patisiran in real-world practice in Belgium

Patient Population

- Thirty-one patients identified, 22 of whom were receiving active treatment (10 tafamidis, 12 patisiran)
- Of the patients initiating patisiran, 7 and 5, respectively, were in FAP stage 1 and 2

Methods/Assessments

- Retrospective study in six Belgian NMRCs based on data collected from medical files
- FAP stage, PND score, NIS-LL, ECG, EMG, NYHA class, % EF

Effectiveness Assessment

- In most of the 9 patients with follow-up data, patisiran led to stabilization or improvement in polyneuropathy assessed by FAP stage, PND score, NIS-LL, and EMG
- Patients showed stabilization of cardiac function assessed by ECG, NYHA class, and % EF
- Results were generally consistent with those seen in the APOLLO trial

Treatment/Study Duration

- Data evaluated: patients treated with patisiran between July 1, 2018 and February 1, 2021

Adverse Events

- Not reported

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ECG, electrocardiogram; EF, ejection fraction; EMG, electromyography; FAP, familial amyloid polyneuropathy; hATTR, hereditary transthyretin-mediated; NIS-LL, Neuropathy Impairment Score-Lower Limb; NMRC, neuromuscular reference center; NYHA, New York Heart Association; PND, polyneuropathy disability.

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Retrospective Analysis (N=4)

2022 (N=1)

Response predictors to patisiran treatment
(Martinez-Vicente et al. PNS 2022)

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Retrospective Analysis (N=4)

2022 (N=1)

Response predictors to patisiran treatment
(Martinez-Vicente et al. *PNS* 2022)

Response Predictors to Patisiran Treatment in Non-endemic ATTRv Patients

Study Purpose

To study factors predictive of response to patisiran in a cohort of non-endemic patients with hATTR amyloidosis

Patient Population

- Twenty-two pts with hATTR amyloidosis:
  - FAP stage 1 (n=10), 2 (n=11)
  - PND score I (n=1), II (n=9), IIIA (n=6), IIIB (n=5)

Methods/Assessments

- Retrospective study with prospective data collection
- Patients classified as good, partial, or non-responders to patisiran
- Pearson correlation used to assess correlation with response

Treatment/Study Duration

- Study duration ≥6 months
- All 22 pts received patisiran; mean duration (SD) of patisiran treatment: 27.6 (18.3) months

Effectiveness Assessment

- Factors predictive of a good response to patisiran were:
  - Male gender (p=0.006)
  - Initial PND score ≤IIIA (p=0.002)
  - Sustained NT-proBNP <300 (p=0.027)
- Non-predictive factors included Val50Met genotype, initial Gillmore stage or NYHA class, serum TTR or % reduction in TTR, carpal tunnel syndrome, spinal stenosis, weight loss, and ophthalmic involvement

Genetic Variant(s)

- Val50Met (n=13), Ser97Tyr (n=2), Gly109Lys (n=2), other (n=5)

Adverse Events

- Not reported

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FAP, familial amyloid polyneuropathy; hATTR, hereditary transthyretin-mediated; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide; NYHA, New York Heart Association; PND, polyneuropathy disability; pt, patient; SD, standard deviation; TTR, transthyretin.

Patisiran Real-World Evidence in hATTR Amyloidosis

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Retrospective Analysis (N=4)

2021 (N=1)

Latency before patisiran effectiveness
(Gentile et al. *Brain Sci* 2021)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

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Retrospective Analysis (N=4)

2021 (N=1)

Latency before patisiran effectiveness
(Gentile et al. *Brain Sci* 2021)

Patisiran in hATTR Amyloidosis: Six-month Latency Period before Efficacy

Study Purpose

To assess the onset of treatment effect with patisiran for patients with hATTR amyloidosis

Patient Population

- Eighteen pts with hATTR amyloidosis:
  - PND score I (n=3), II (n=8), IIIA/B (n=7)
  - Mean NIS, 70.2; Norfolk QOL-DN, 64.2

Methods/Assessments

- PND score, NIS, NIS-LL, Norfolk QOL-DN

Effectiveness Assessment

- Thirteen pts had stable PND score to final assessment, 3 pts improved, and 2 pts worsened
- Mean scores for NIS, NIS-LL, and Norfolk QOL-DN worsened to Month 6, but then improved through Months 12 and 18
- No significant differences in post-treatment results in pts also treated with tafamidis

Genetic Variant(s)

- Phe64Leu (n=7), Glu89Gln (n=5), Val30Met (n=2), Thr49Ala (n=2), Val122Ile (n=1), Ala109Ser (n=1)

Treatment/Study Duration

- All 18 pts receiving patisiran, 4 received tafamidis concomitantly.
- Study duration of 18 months

Adverse Events

- Premedication associated with hyperglycemia (n=1) and hypertension (n=2)
- Three pts temporarily discontinued treatment (severe anemia, fever, diarrhea)
- Three deaths (sudden death, likely cardiac, n=2; severe dehydration, n=1), considered unrelated to patisiran treatment

VIEW POSTER/PUBLICATION ›

hATTR, hereditary transthyretin-mediated; NIS, Neuropathy Impairment Score; NIS-LL, Neuropathy Impairment Score-Lower Limb; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; PND, polyneuropathy disability; pt, patient

Patisiran Real-World Evidence in hATTR Amyloidosis

Alnylam® PHARMACEUTICALS

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

← Back

Retrospective Analysis (N=4)

2019 (N=1)

Patisiran Pre-Approval Access Program
(Hussain et al. *PNS* 2019)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Retrospective Analysis (N=4)

2019 (N=1)

Patisiran Pre-Approval Access Program
(Hussain et al. *PNS* 2019)

Variable Presentation of Hereditary Transthyretin-mediated (hATTR) Amyloidosis: A Single Center Experience with the Patisiran PAAP

Study Purpose

To assess the journey to hATTR amyloidosis diagnosis and the safety and effectiveness of patisiran treatment

Patient Population

- Eight male pts with hATTR amyloidosis, aged 47–75, in the PAAP for pts with unmet medical needs

Methods/Assessments

- Medical and diagnostic history, safety, change from baseline in PND score

Effectiveness Assessment

- Diagnostic delay (up to 10 years from symptom onset) in all pts due to misdiagnoses
- In patisiran-treated patients:
  - One pt improved PND score at 6 months.
  - One pt had stable PND score at 12 months.
  - Two pts had worsened PND score at 6 months (1 pt then had stable PND score to 12 months)

Genetic Variant(s)

- Val122Ile (n=4), Ser77Thr (n=2), Thr60Ala (n=1), Ser50Arg (n=1)

Treatment/Study Duration

- Five of 8 pts received patisiran 0.3 mg/kg every 3 weeks in the PAAP
- Three pts did not meet eligibility criteria or were diagnosed after PAAP had closed
- Study duration of 6 months. Four of 8 pts had 6-month effectiveness assessment

Adverse Events

- All treated pts reported at least one AE (majority mild) and no IRRs
- Three pts each had one severe AE, unrelated to patisiran, but continued with treatment
- No deaths occured

VIEW POSTER/PUBLICATION ›

AE, adverse event; hATTR, hereditary transthyretin-mediated; IRR, infusion-related reaction; PAAP, Pre-Approval Access Program; PND, polyneuropathy disability; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

← Back

Case Study (N=10) >

Retrospective Analysis (N=4) >

Single Center (N=8)

2022 (N=3) >

2019 (N=5) >

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=8)

2022 (N=3)

Clinical experience: Italian center
(Massucco et al. *ASNP* 2022)

Clinical experience: Italian center
(Di Stefano et al. *ASNP* 2022)

Clinical experience: Italian center
(Di Stefano et al. *Pharmgenomic Pers Med* 2022)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=8)

2022 (N=3)

Clinical experience: Italian center
(Massucco et al. *ASNP* 2022)

Clinical experience: Italian center
(Di Stefano et al. *ASNP* 2022)

Clinical experience: Italian center
(Di Stefano et al. *Pharmgenomic Pers Med* 2022)

hATTR-related Polyneuropathy: A Single-center Experience

Study Purpose

To describe the characteristics and outcomes of patients with hATTR amyloidosis-related polyneuropathy at a clinic in Italy

Patient Population

- Twelve pts from a single center in Genoa, Italy
- Baseline PND score: 0, n=2; I, n=4; II, n=3; IIIA, n=1; IIIB, n= 2; IV, n=0

Methods/Assessments

- Routine annual workup, including mBMI, neurologic examination, NIS-244, NIS-LL-88, KPS, CADT, Norfolk QOL-DN, Sudoscan, cardiologic exam with ECG, and echocardiogram

Genetic Variant(s)

- Phe64Leu (n=5, 36%), Val30Met (n=4, 29%), Ile68Leu (n=1, 7%), Tyr98Phe (n=1, 7 %), Arg125Cys (n=1, 7%), Val122Ile (n=1, 7%), Ala140Thr (n=1, 7%)

Treatment/Study Duration

- At the time of the study, 5 pts were being treated with tafamidis, 1 with inotersen, and 4 with patisiran
- Two switched from tafamidis to patisiran, 1 from diflunisal to patisiran, 1 from tafamidis to inotersen, 1 from inotersen to patisiran

Effectiveness Assessment

- All pts receiving patisiran showed stable NIS-244 over time

Adverse Events

- Not reported

VIEW POSTER/PUBLICATION ›

CADT, Compound Autonomic Dysfunction Test; ECG, electrocardiogram; hATTR, hereditary transthyretin-mediated; KPS, Karnofsky Performance Score; mBMI, modified body mass index; NIS-244, Neuropathy Impairment Score; NIS-LL-88, Neuropathy Impairment Score-Lower Limb; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; PND, polyneuropathy disability; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=8)

2022 (N=3)

Clinical experience: Italian center
(Massucco et al. *ASNP* 2022)

Clinical experience: Italian center
(Di Stefano et al. *ASNP* 2022)

Clinical experience: Italian center
(Di Stefano et al. *Pharmgenomic Pers Med* 2022)

Patisiran in hATTR Amyloidosis after 9 Months of Follow-up: A Single Center Real-life Experience

Study Purpose

To assess the impact of patisiran in hATTR amyloidosis in a real-world setting in Italy

Patient Population

- Twelve pts: 6 men, mean age 65.0 years

Methods/Assessments

- Patients enrolled from a clinic in Palermo
- Assessments included PND score, NIS, Norfolk QOL-DN, KPS, COMPASS-31, 6MWT, and body weight

Genetic Variant(s)

- F64L (p.F84L), n=13; E89Q (p.E109Q), n=1; V122I (p.V142I), n=1; H90A (p.H110A), n=1

Treatment/Study Duration

- All pts were prescribed patisiran and followed up for 9 months

Effectiveness Assessment

- PND score: stable (n=13), improved (n=3)
- NIS: reduced (n=6, 50%)
- Norfolk QOL-DN: better QOL (n=8, 67%)
- KPS: improved (n=5, 42%)
- COMPASS-31: reduced (n=4, 33%)
- 6MWT: improved (n=8, 67%)
- Body weight: increased (n=5, 42%)
- All pts were satisfied with treatment, with 1 pt showing mild clinical progression

Adverse Events

- 1 pt reported side effects: hypertension following premedication with steroids

VIEW POSTER/PUBLICATION ›

6MWT, 6-minute walk test; COMPASS-31, Composite Autonomic Symptom Score-31; hATTR, hereditary transthyretin-mediated; KPS, Karnofsky Performance Status; NIS, Neuropathy Impairment Score; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; PND, polyneuropathy disability; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=8)

2022 (N=3)

Clinical experience: Italian center
(Massucco et al. *ASNP* 2022)

Clinical experience: Italian center
(Di Stefano et al. *ASNP* 2022)

Clinical experience: Italian center
(Di Stefano et al. *Pharmgenomic Pers Med* 2022)

Italian Real-life Experience of Patients with hATTR Amyloidosis Treated with Patisiran

Study Purpose

To report nine cases of hATTR amyloidosis managed with patisiran in real-world clinical practice

Patient Population

- Nine pts with hATTR amyloidosis in Italian reference centers
- Eight males, one female
- Several patients received an incorrect diagnosis, leading to diagnostic delay

Genetic Variant(s)

- Phe64Leu (n=3), Glu89Gln (n=2), Ile68Leu (n=2), Val30Met (n=1), Val122Ile (n=1)

Treatment/Study Duration

- All pts were prescribed patisiran; 3 had received prior tafamidis and 1 had received prior tafamidis and inotersen

Effectiveness Assessment

- Most pts had polyneuropathy symptoms, which stabilized or improved following initiation of patisiran
- One pt with Glu89Gln cardiomyopathy showed substantial improvements in cardiac function with patisiran
- Two pts received the COVID-19 vaccine during patisiran treatment, with no adverse events reported; neither patient developed COVID-19

Adverse Events

- Patisiran was generally well tolerated

VIEW POSTER/PUBLICATION

hATTR, hereditary transthyretin-mediated; pt, patient..

Patisiran Real-World Evidence in hATTR Amyloidosis

Alnylam® PHARMACEUTICALS

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

← Back

Single Center (N=8)

2019 (N=5)

Clinical experience: Single German non-endemic center
(Dohrn et al. *EU-ATTR* 2019)

Clinical experience: Spanish center
(Galan Dávila et al. *PNS* 2019)

Clinical experience: French center
(Gendre et al. *PNS* 2019)

First treatment experiences with patisiran
(Grether et al. *EU-ATTR* 2019)

Clinical experience: German center
(Neimeier et al. *EU-ATTR* 2019)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=8)

2019 (N=5)

Clinical experience: Single German non-endemic center
(Dohrn et al. *EU-ATTR* 2019) ›

Clinical experience: Spanish center
(Galan Dávila et al. *PNS* 2019) ›

Clinical experience: French center
(Gendre et al. *PNS* 2019) ›

First treatment experiences with patisiran
(Grether et al. *EU-ATTR* 2019) ›

Clinical experience: German center
(Neimeier et al. *EU-ATTR* 2019) ›

The First Six Months of Patisiran in Hereditary Transthyretin Amyloidosis: Real-life Experiences from a Non-endemic Center

Study Purpose

To assess the effectiveness and safety of patisiran for patients in the first 6 months of treatment

Patient Population

- Three male pts with hATTR amyloidosis, aged 39–73 (1 early onset [<50 years])
- All had sensorimotor and autonomic symptoms, 2 pts had cardiac involvement
- All previously treated with tafamidis but discontinued due to disease progression (n=2) or lack of response (n=1)

Methods/Assessments

- Disease progression assessed every 3 months via symptom history, clinical examination, NCV studies, quantitative sensory testing, Schellong test, Sudoscan, electrocardiogram, laboratory studies

Genetic Variant(s)

- Val50Met (n=2), Glu109Gln (n=1)

Treatment/Study Duration

- Pts receiving patisiran for 2–6 months at time of data collection

Effectiveness Assessment

- All pts had stabilized disease to date on patisiran treatment

Adverse Events

- Patisiran was well tolerated
- One pt had an asthma attack after second infusion, and flush 1 day after infusion

VIEW POSTER/PUBLICATION ›

hATTR, hereditary transthyretin-mediated; NCV, nerve conduction velocity; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=8)

2019 (N=5)

Experience with Patisiran in the Treatment of Hereditary Transthyretin Amyloidosis Neuropathy

Study Purpose

To assess the real-world effectiveness and safety of patisiran treatment for patients with hATTR amyloidosis

Patient Population

- Eight pts with hATTR amyloidosis, aged 57–82
  - Four pts stage II Coutinho
  - Four pts stage I, non-responders to tafamidis

Methods/Assessments

- Norfolk QOL-DN, NIS, TTR reduction

Genetic Variant(s)

- Val30Met (n=6), Ala60Thr (n=1), Glu89Gln (n=1)

Treatment/Study Duration

- 12 months, patisiran treatment, median 14 patisiran infusions (range, 7–37)

Effectiveness Assessment

- Neurologic stabilization (n=4; dysautonomia improvement in 2 pts), neurologic progression (n=4; below natural history in 2 pts, after initial improvement in 1 pt, progression after missing two doses in 1 pt)
- All patients had an 80–90% reduction in TTR
- Seven of 8 pts wanted to continue treatment

Adverse Events

- Patisiran infusion was well tolerated
- One pt had facial flushing
- No severe AEs occured considered related to the study drug
  - One pt suffered an arm fracture that premedication may have worsened
- One pt stopped treatment due to cardiologic progression

VIEW POSTER/PUBLICATION ›

AE, adverse event; hATTR, hereditary transthyretin-mediated; NIS, Neuropathy Impairment Score; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; pt, patient; TTR, transthyretin.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=8)

2019 (N=5)

Clinical experience: Single German non-endemic center
(Dohrn et al. *EU-ATTR* 2019)

Clinical experience: Spanish center
(Galan Dávila et al. *PNS* 2019)

Clinical experience: French center
(Gendre et al. *PNS* 2019)

First treatment experiences with patisiran
(Grether et al. *EU-ATTR* 2019)

Clinical experience: German center
(Neimeier et al. *EU-ATTR* 2019)

Patisiran, a Silencing RNA in Hereditary Transthyretin Amyloid Polyneuropathy: First Experience in Real Life

Study Purpose

To assess safety and effectiveness of patisiran in patients with hATTR amyloidosis with polyneuropathy previously treated with TTR stabilizers

Patient Population

- Twenty-one pts with hATTR, aged 45–86
  - Eleven with PND score ≥IIIA
  - Twenty (95%) with prior stabilizer use
  - NIS (mean [± SD]), 62 ± 31.3

Methods/Assessments

- NIS, PND score, Norfolk QOL-DN, serum TTR, AEs

Genetic Variant(s)

- Val30Met (n=13), unspecified (n=8)

Treatment/Study Duration

- 0.3 mg/kg patisiran every 3 weeks
- Study duration of up to 24 months

Effectiveness Assessment

- Effect of patisiran treatment (post-TTR stabilizer):
  - Mean NIS score unchanged at 6/12 months
  - PND score worsening in 1 pt (1/21)
  - Mean Norfolk QOL-DN score improvement; all but 2 pts improved Norfolk QOL-DN
  - Mean serum TTR reduction of 75% (n=18)

Adverse Events

- No SAEs occured that were considered related to the study drug
- AEs related to patisiran: local erythema or flush (n=5), venous thrombosis (n=1)
- AEs related to premedication: hyperglycemia with prolonged hospitalization (n=1), cardiac failure (n=1)

VIEW POSTER/PUBLICATION ›

AE, adverse event; hATTR, hereditary transthyretin-mediated; NIS, Neuropathy Impairment Score; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; PND, polyneuropathy disability; pt, patient; SAE, serious adverse event; SD, standard deviation; TTR, transthyretin.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=8)

2019 (N=5)

Clinical experience: Single German non-endemic center
(Dohrn et al. *EU-ATTR* 2019)

Clinical experience: Spanish center
(Galan Dávila et al. *PNS* 2019)

Clinical experience: French center
(Gendre et al. *PNS* 2019)

First treatment experiences with patisiran
(Grether et al. *EU-ATTR* 2019)

Clinical experience: German center
(Neimeier et al. *EU-ATTR* 2019)

First Treatment Experiences with Patisiran in Two Patients with Hereditary Transthyretin Amyloidosis

Study Purpose

To assess the onset of treatment effect with patisiran for patients with hATTR amyloidosis

Patient Population

- Two pts with FAP stage II hATTR amyloidosis. Pt 1, 65-year-old male; pt 2, 81-year-old female
- Pt 2 previously received tafamidis, which was stopped due to AEs

Methods/Assessments

- Qualitative case study

Genetic Variant(s)

- Pt 1, Leu58/78His; pt 2, Val30Met

Treatment/Study Duration

- Pt 1 received patisiran, paused treatment for 6 months, and resumed treatment. Pt 2 recently began patisiran treatment

Effectiveness Assessment

- Pt 1 had disease stabilization during patisiran treatment; impairment of clinical symptoms was observed when treatment was paused for 6 months
- Pt 2 had no disease progression during patisiran treatment

Adverse Events

- Both pts tolerated patisiran infusions well with no infusion-related events or AEs

VIEW POSTER/PUBLICATION

AE, adverse event; FAP, familial amyloid polyneuropathy; hATTR, hereditary transthyretin-mediated; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=8)

2019 (N=5)

Clinical experience: Single German non-endemic center
(Dohrn et al. *EU-ATTR* 2019)

Clinical experience: Spanish center
(Galan Dávila et al. *PNS* 2019)

Clinical experience: French center
(Gendre et al. *PNS* 2019)

First treatment experiences with patisiran
(Grether et al. *EU-ATTR* 2019)

Clinical experience: German center
(Neimeier et al. *EU-ATTR* 2019)

Single Center Experience on Patisiran (Onpattro®)

Study Purpose

To assess the effectiveness of patisiran on polyneuropathy and cardiomyopathy outcomes in patients with hATTR amyloidosis

Patient Population

- Thirty-eight pts with hATTR amyloidosis, aged 34–78
  - PND score I (n=24), PND score II (n=6), PND score III (n=8)
  - Mean NIS+7, 46.2

Methods/Assessments

- NIS+7, echocardiogram, mBMI, creatinine, AEs, response. Data collected retrospectively from outpatient records

Genetic Variant(s)

- Val30Met (n=18), Gly47Ala (n=4), other non-Val30Met (n=16)

Treatment/Study Duration

- 0.3 mg/kg every 3 weeks
- Study duration of 72 months (mean treatment duration, 19 months)

Effectiveness Assessment

- NIS+7, septum thickness, mBMI, and creatinine results remained stable in the majority of patients during treatment
- Twelve of 33 pts had overall improvement, 17/33 pts had overall disease stabilization

Adverse Events

- No safety concerns based on laboratory results, NT-proBNP, or patient self-reporting
- Common AEs included IRRs of flushing (n=9) and back pain (n=4)

VIEW POSTER/PUBLICATION ›

AE, adverse event; hATTR, hereditary transthyretin-mediated; IRR, infusion-related reaction; mBMI, modified body mass index; NIS+7, Neuropathy Impairment Score + 7; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide; PND, polyneuropathy disability; pt, patient.

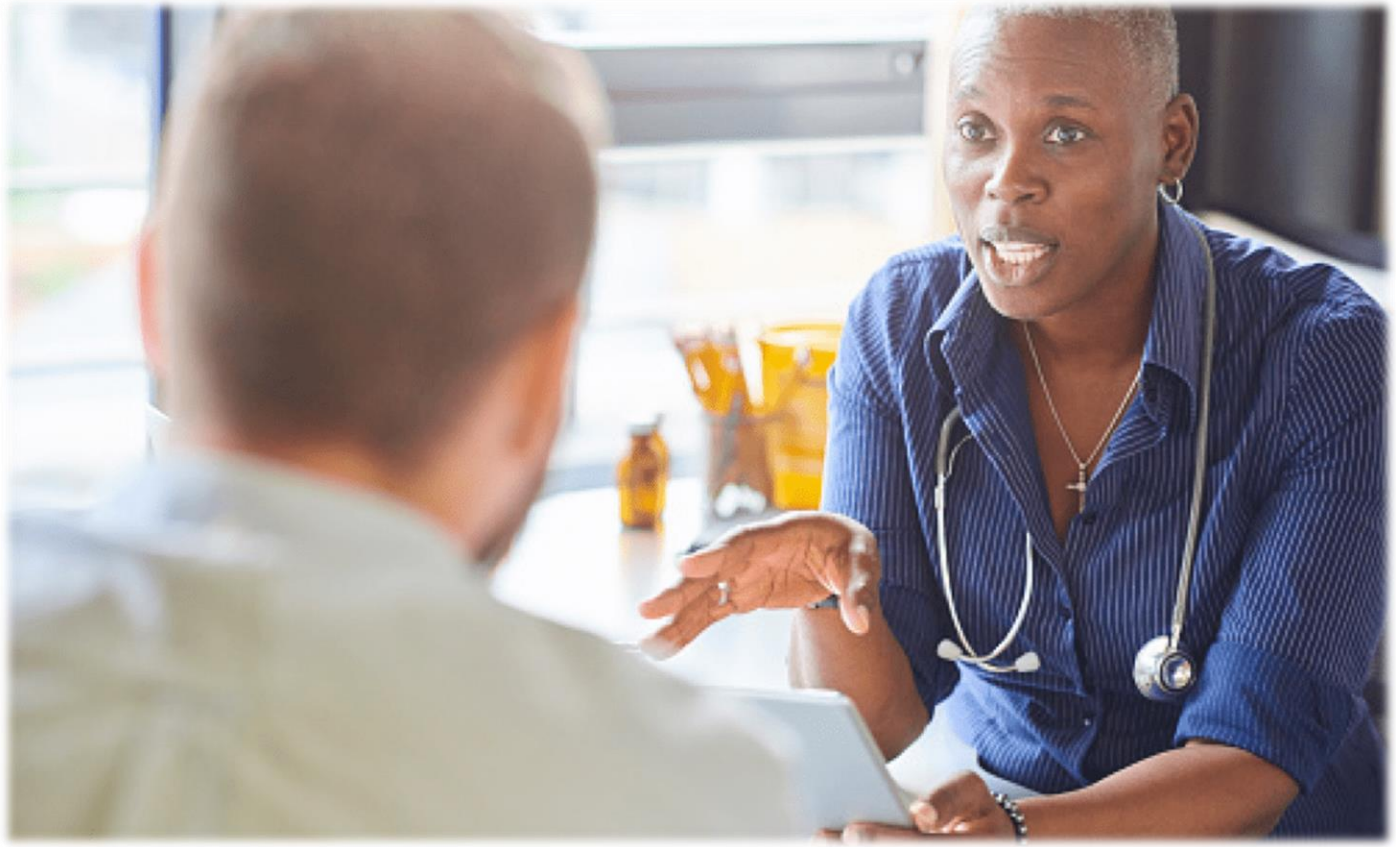
Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

Case Study (N=3)

Controlled Study (N=1)



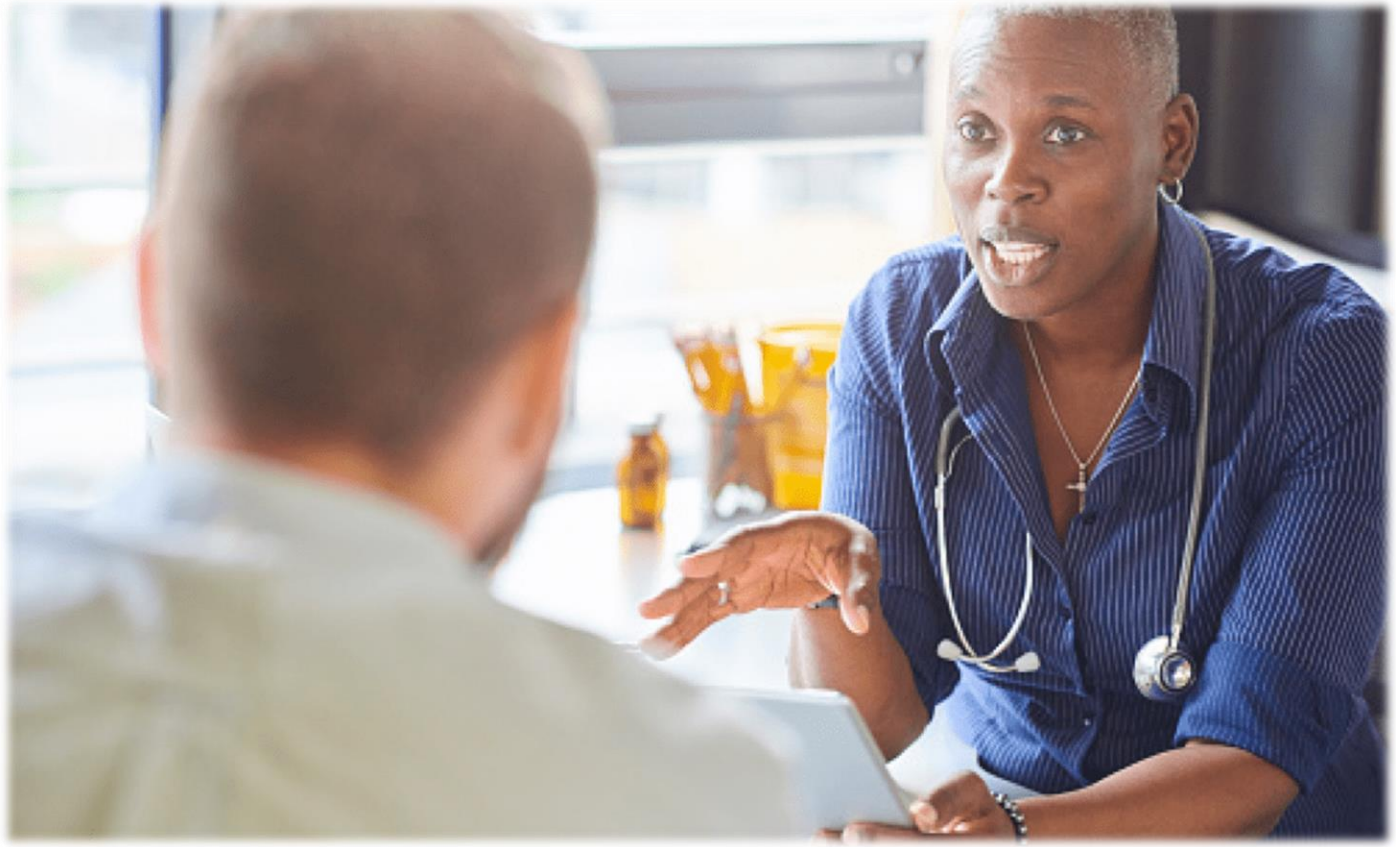
hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=3)

- 2021 (N=2) >
- 2019 (N=1) >
- **Controlled Study (N=1)** >



hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

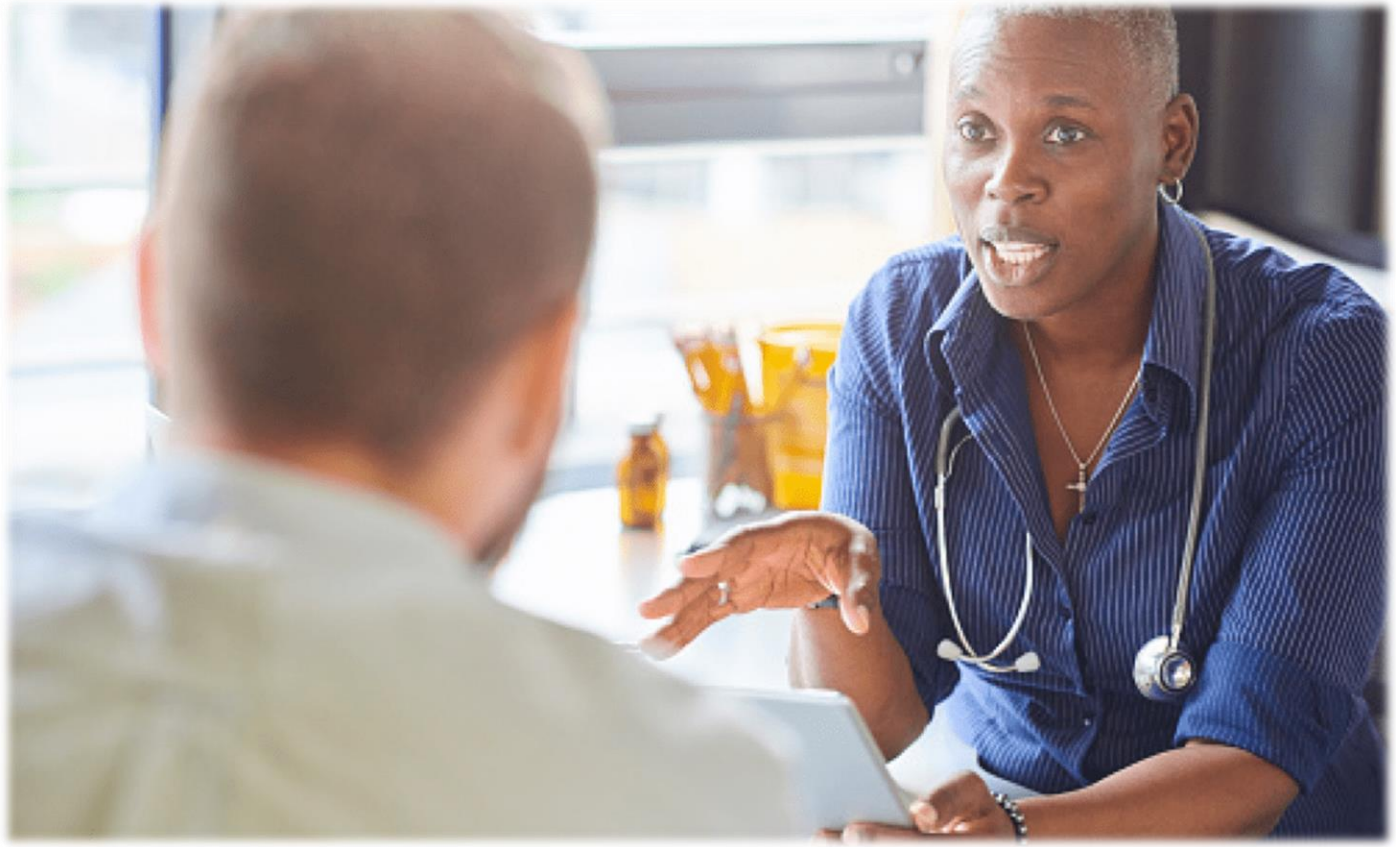
← Back

Case Study (N=3)

2021 (N=2)

Patisiran for advanced heart failure
(Nakamura et al. *J Cardiol Cases* 2021)

Patisiran following heart transplant
(Urey et al. *ISHLT* 2021)



hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=3)

2021 (N=2)

Patisiran for advanced heart failure
(Nakamura et al. *J Cardiol Cases* 2021)

Patisiran following heart transplant
(Urey et al. *ISHLT* 2021)

Patisiran for Advanced Heart Failure with Hereditary Transthyretin Cardiac Amyloidosis

Study Purpose

To assess patisiran effectiveness in a patient with hATTR amyloidosis and advanced heart failure

Patient Population

- A 78-year-old female with hATTR amyloidosis and advanced heart failure refractory to tafamidis

Methods/Assessments

- NT-proBNP, IVS thickness, LVMI, GLS, cardiac uptake during scintigraphy, eGFR

Treatment/Study Duration

- 80 mg tafamidis daily for 12 months, reduced to 20 mg upon patisiran initiation
- Total study duration of 20 months, with patisiran 0.3 mg/kg every 3 weeks initiated at Month 15

Genetic Variant(s)

- Val30Met

Effectiveness Assessment

- Post-patisiran initiation:
  - Reduced NT-proBNP (–38.5%), IVS thickness (–11.8%), and LVMI (–16.6%) at 6 months
  - GLS and eGFR remained stable at 6 months
  - Considerable improvement in cardiac uptake of technetium-99m pyrophosphate

Adverse Events

- No side effects were observed

VIEW POSTER/PUBLICATION ›

eGFR, estimated glomerular filtration rate; GLS, global longitudinal strain; hATTR, hereditary transthyretin-mediated; IVS, interventricular septum; LVMI, left ventricular mass index; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=3)

2021 (N=2)

Patisiran for advanced heart failure
(Nakamura et al. *J Cardiol Cases* 2021)

Patisiran following heart transplant
(Urey et al. *ISHLT* 2021)

Use of Patisiran following Heart Transplant in Patient with Hereditary Transthyretin Cardiac Amyloidosis and Polyneuropathy

Study Purpose

To assess the safety and effectiveness of patisiran in a patient with hATTR amyloidosis following heart transplant

Patient Population

- A 73-year-old African American male with hATTR amyloidosis, who had progression of neuropathy following a heart transplant (for cardiac amyloid)

Genetic Variant(s)

- Val122Ile

Methods/Assessments

- Patient-reported symptoms

Treatment/Study Duration

- Patisiran treatment beginning 12 months post-transplant
- Eighteen-month follow-up

Effectiveness Assessment

- Pt experienced improvement in neuropathy within 4–5 months of patisiran initiation
- Pt reported only very mild neuropathy symptoms 12 months post-patisiran initiation

Adverse Events

- Infusions were well tolerated, and pre-infusion dexamethasone was tapered off at pt's request
- Pt maintained normal graft function and did not experience transplant rejection or develop donor-specific antibodies

VIEW POSTER/PUBLICATION ›

hATTR, hereditary transthyretin-mediated; pt, patient.

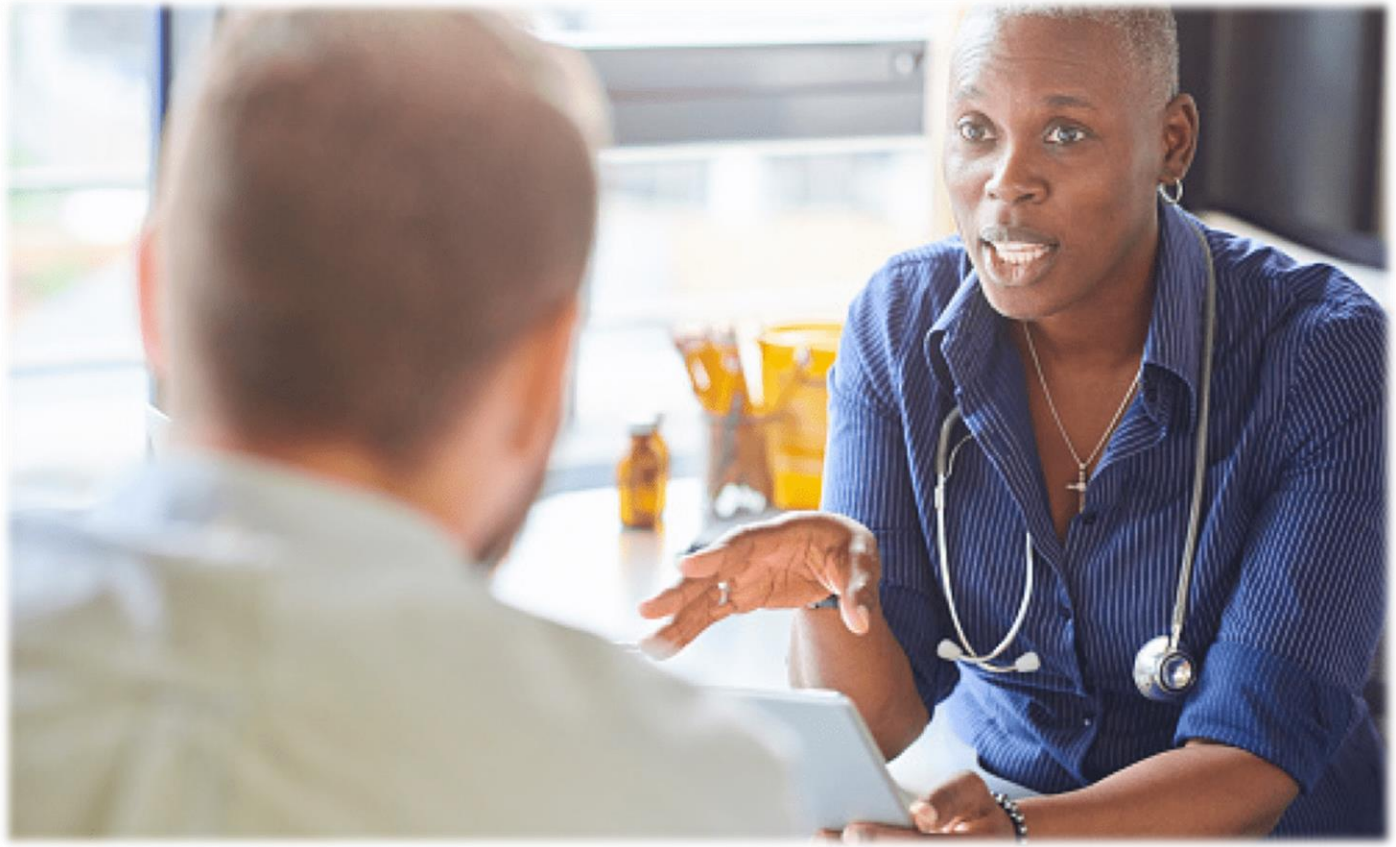
Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=3)

2019 (N=1)

Patient on long-term patisiran
(Schmidt. *EU-ATTR* 2019)



hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=3)

2019 (N=1)

Patient on long-term patisiran
(Schmidt. *EU-ATTR* 2019)

Case Report on Long-term Patisiran Treatment

Study Purpose

To assess safety and effectiveness of long-term patisiran treatment in a patient with hATTR amyloidosis

Patient Population

- A 62-year-old male pt with hATTR amyloidosis with polyneuropathy and cardiomyopathy awaiting OLT

Genetic Variant(s)

- Arg54Thr

Methods/Assessments

- Echocardiogram, NT-proBNP, NIS, mBMI, vitamin A

Treatment/Study Duration

- Previously treated with tafamidis 20 mg daily
- Patisiran treatment from June 2013 to 2019 (approx. 6 years)

Effectiveness Assessment

- mBMI improved and NT-proBNP reduced
- NIS stable when measured from 1 year after patisiran treatment initiation to Year 6
- Due to stabilization of disease symptoms, NT-proBNP reduction, and mBMI improvement, liver transplant was not required at the time of publication
- Cardiomyopathy was stabilized, with improvement in left and right atrium dilation, and mild progression of LVCH

Adverse Events

- No AEs recorded
- Pt had normal liver enzymes and renal parameters throughout treatment
- Pt had no febrile episodes, no eye anomalies, and normal thyroid function

VIEW POSTER/PUBLICATION ›

AE, adverse event; hATTR, hereditary transthyretin-mediated; LVCH, left ventricular concentric hypertrophy; LVEF, left ventricular ejection fraction; mBMI, modified body mass index; NIS, Neuropathy Impairment Score; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide; OLT, orthotopic liver transplantation; pt, patient.

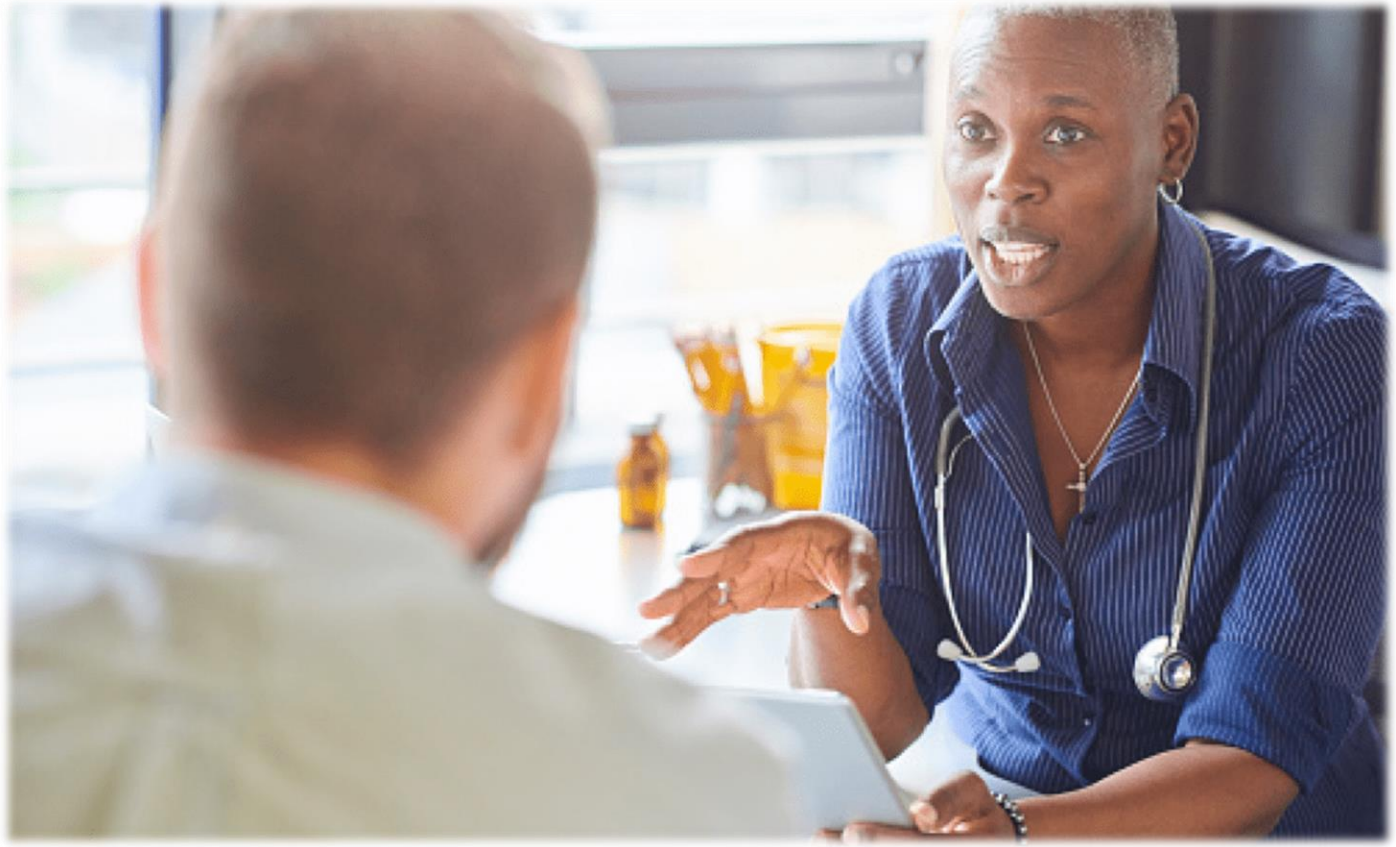
Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=3) >

Controlled Study (N=1)

2021 (N=1) >



hATTR, hereditary transthyretin-mediated.

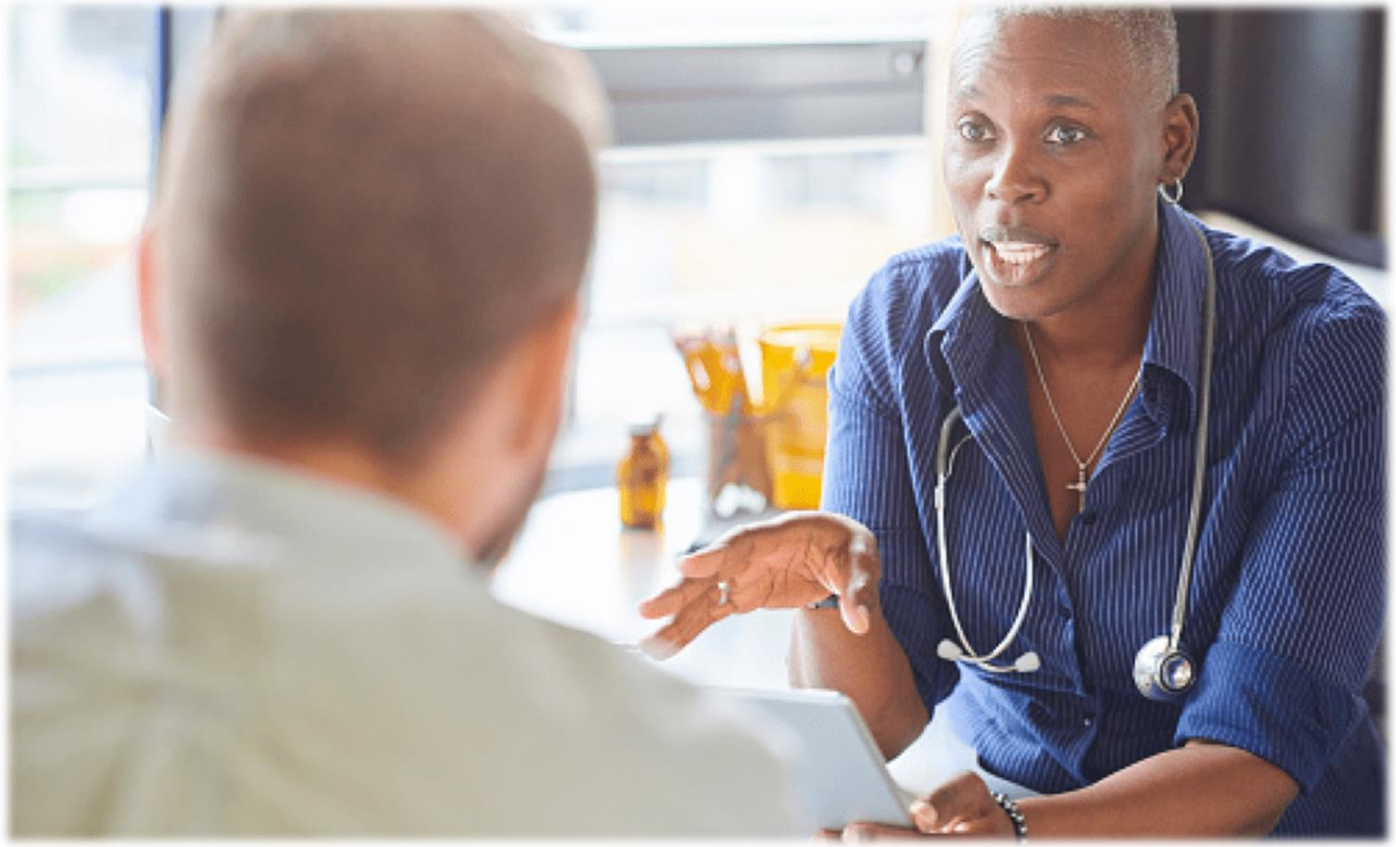
Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Controlled Study (N=1)

2021 (N=1)

Regression of cardiac amyloid
(Fontana et al. *JACC: Cardiovasc Imaging* 2021)



hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Controlled Study (N=1)

2021 (N=1)

Regression of cardiac amyloid
(Fontana et al. *JACC: Cardiovasc Imaging* 2021)

Reduction in CMR Derived Extracellular Volume with Patisiran Indicates Cardiac Amyloid Regression

Study Purpose

To assess the impact of patisiran on cardiac amyloid load in patients with hATTR amyloidosis

Patient Population

- Thirty-two pts with ATTR amyloidosis with cardiomyopathy:
  - Sixteen pts with hATTR amyloidosis treated with patisiran
  - Sixteen untreated pts with hATTR and wtATTR amyloidosis retrospectively matched

Effectiveness Assessment

- Among treated pts at Month 12:
  - Median serum TTR knockdown was 86%
  - Cardiac ^{99}Tc-DPD uptake by bone scintigraphy was reduced in 15 of 16 pts (median 19.6% reduction; unchanged in 1 pt)
- In treated vs untreated pts at Month 12:
  - ECV was significantly lower
- In treated vs untreated pts at Month 12:
  - NT-proBNP levels were significantly lower
  - 6MWT distance improved significantly

Methods/Assessments

- CMR, echocardiography, NT-proBNP, 6MWT, bone scintigraphy

Genetic Variant(s)

- T60A (n=11), V30M (n=3), A97S (n=2), other (n=7), wild-type (n=9, control group only)

Treatment/Study Duration

- Sixteen pts receiving patisiran (12 of 16 receiving diflunisal concomitantly), 16 pts not receiving disease-modifying treatment (control group)
- Pts followed up after 1 year

Adverse Events

- Patisiran was well tolerated and no pts discontinued treatment. Mild IRRs occured in 4 pts. Eight SAEs occured, but were unrelated to patisiran or diflunisal

VIEW POSTER/PUBLICATION >

6MWT, 6-minute walk test; ^{99}Tc-DPD, technetium-99 3,3-diphosphono-1,2-propanodicarboxylic acid; CMR, cardiac magnetic resonance; ECV, extracellular volume; hATTR, hereditary transthyretin-mediated; IRR, infusion-related reaction; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide; pt, patient; SAE, serious adverse event; TTR, transthyretin; wtATTR, wild-type transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Choose a study type

Case Study (N=5)

Single Center (N=4)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Alnylam® PHARMACEUTICALS

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

Case Study (N=5)

2022 (N=4) >

2021 (N=1) >

Single Center (N=1) >

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Alnylam® PHARMACEUTICALS

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

← Back

Case Study (N=5)

2022 (N=4)

Patisiran for aqATTR after domino liver transplantation
(Tsamis et al. *Clin Transplant* 2022)

Patisiran for acquired polyneuropathy after domino liver transplant
(Guaraldi et al. *ASNP* 2022)

Mononeuropathy after liver transplant
(Seibert et al. *J Clin Neuromuscul Dis* 2022)

Tafamidis to patisiran post-liver transplantation
(Bulinski et al. *J Neurol* 2022)

aqATTR, acquired transthyretin amyloidosis; hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=5)

2022 (N=4)

Patisiran for aqATTR after domino liver transplantation (Tsamis et al. *Clin Transplant* 2022) ›

Patisiran for acquired polyneuropathy after domino liver transplant (Guaraldi et al. *ASNP* 2022) ›

Mononeuropathy after liver transplant (Seibert et al. *J Clin Neuromuscul Dis* 2022) ›

Tafamidis to patisiran post-liver transplantation (Bulinski et al. *J Neurol* 2022) ›

Treatment of Acquired Transthyretin Amyloidosis in Domino Liver Transplantation

Study Purpose

To report the management and outcome of a patient with aqATTR, after domino liver transplantation, receiving patisiran

Patient Population

- An 80-year-old male with aqATTR that developed after domino liver transplantation for hepatocellular carcinoma
- History of hepatitis B and coronary heart disease
- After 8 years he developed bradyarrhythmia and 2 years later he developed polyneuropathy and was diagnosed with aqATTR amyloidosis
- Patient had FAP stage 1 and PND score II at diagnosis

Methods/Assessments

- Nerve conduction studies and nerve biopsy led to diagnosis of amyloid polyneuropathy
- FAP stage and PND score reported

Genetic Variant(s)

- Met30

Effectiveness Assessment

- Patient stabilized in FAP stage 2 and PND score IIIB, then improved to FAP stage 1 and PND score II
- Patient remained stable after 2 years of treatment

Treatment/Study Duration

- Tafamidis 20 mg orally once daily from November 2018
- Patisiran 0.3 mg/kg q3w from summer 2020

Adverse Events

- Patisiran treatment was well tolerated; no adverse events reported

VIEW POSTER/PUBLICATION ›

aqATTR, acquired transthyretin amyloidosis; FAP, familial amyloid polyneuropathy; hATTR, hereditary transthyretin-mediated; PND, polyneuropathy disability; q3w, every 3 weeks.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=5)

2022 (N=4)

Patisiran for aqATTR after domino liver transplantation
(Tsamis et al. *Clin Transplant* 2022)

Patisiran for acquired polyneuropathy after domino liver transplant
(Guaraldi et al. *ASNP* 2022)

Mononeuropathy after liver transplant
(Seibert et al. *J Clin Neuromuscul Dis* 2022)

Tafamidis to patisiran post-liver transplantation
(Bulinski et al. *J Neurol* 2022)

Patisiran Treatment in a Patient with Acquired Amyloid Polyneuropathy after Domino Liver Transplant

Study Purpose

To describe patisiran treatment for acquired amyloid polyneuropathy following domino liver transplant

Patient Population

- 2008: 63-year-old male received liver transplant for hepatitis C-related disease (carcinoma and cirrhosis)
- 2017: presented with sensorimotor polyneuropathy, followed by alternating diarrhea and constipation and 15 kg weight loss
- 2020: hospital admission with congestive heart failure; echocardiogram showed signs of amyloid cardiomyopathy

Methods/Assessments

- 2020: echocardiography, 99^{m}-technetium pyrophosphate myocardial imaging
- 2021: NIS, KPS, COMPASS-31, Norfolk QOL-DN, cardiovascular autonomic testing

Genetic Variant(s)

- Liver donor had rare Ser23Asn variant

Effectiveness Assessment

- Within a few months of initiating patisiran, pt reported no further weight loss, with improved gut function, muscle strength, and sensation
- After 22 rounds of patisiran, there was improvement in muscle strength and sensory deficits, and cardiology had stabilized
- NIS improved from 43 to 20

Treatment/Study Duration

- February 2021: patisiran, 0.3 mg/kg q3w (22 rounds)

Adverse Events

- No side effects reported by pt on patisiran treatment

VIEW POSTER/PUBLICATION ›

aqATTR, acquired transthyretin amyloidosis; COMPASS-31, Composite Autonomic Symptom Score-31; hATTR, hereditary transthyretin-mediated; KPS, Karnofsky Performance Status; NIS, Neuropathy Impairment Score; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; pt, patient; q3w, every 3 weeks.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=5)

2022 (N=4)

Progressive Multiple Mononeuropathy in a Patient with Familial Transthyretin Amyloidosis after Liver Transplantation

Study Purpose

To assess the effects of patisiran in a patient with multiple mononeuropathy after liver transplantation

Patient Population

- A 61-year old African American male
- Initially presented with advanced biventricular heart failure and progressive numbness in hands and feet; findings were consistent with multiple mononeuropathy and concomitant cervical and lumbar polyradiculopathy
- The patient underwent heart and liver transplantation followed by cervical spinal decompression and fusion surgery
- However, the patient showed slowly progressive motor neuropathy symptoms in the upper limbs over the subsequent 5 years

Genetic Variant(s)

- Val122Ile

Effectiveness Assessment

- The patient showed stabilization of neuropathy symptoms during 2 years of follow-up after initiation of patisiran

Treatment/Study Duration

- Patisiran treatment initiated 5.5 years post-transplant.
- Two years of follow-up

Adverse Events

- Not reported

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hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=5)

2022 (N=4)

Clinical Improvement after Change of Therapy from Tafamidis to Patisiran in Progressive TTR Amyloidosis Post-liver Transplantation

Study Purpose

To assess patisiran effectiveness following liver transplantation in a patient with hATTR amyloidosis

Patient Population

- A 36-year-old male diagnosed with TTR-FAP in 2012
- Received tafamidis followed by liver transplantation after 1 year; tafamidis was discontinued
- Symptoms of polyneuropathy gradually worsened after transplantation and continued despite re-initiation of tafamidis in 2018
- Switch to patisiran occurred 6 years post-transplantation

Methods/Assessments

- NCS, mNIS+7, MRI, echocardiography, NYHA class

Genetic Variant(s)

- Glu54Gly

Effectiveness Assessment

- The patient's polyneuropathy symptoms slowly improved on patisiran
- mNIS+7 score decreased from 183.5 to 172.5 after 18 months
- NCS results remained stable
- No change in cardiac amyloidosis, with the caveat that examinations were performed across different centers

Treatment/Study Duration

- Patisiran treatment with 18 months' follow-up

Adverse Events

- Not reported

VIEW POSTER/PUBLICATION >

hATTR, hereditary transthyretin-mediated; mNIS+7, modified Neuropathy Impairment Score + 7; MRI, magnetic resonance imaging; NCS, nerve conduction studies; NYHA, New York Heart Association; TTR-FAP, transthyretin-familial amyloid polyneuropathy.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=5)

2021 (N=1)

Patisiran following heart transplant
(Urey et al. *ISHLT* 2021)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=5)

2021 (N=1)

Patisiran following heart transplant
(Urey et al. *ISHLT* 2021)

Use of Patisiran following Heart Transplant in Patient with Hereditary Transthyretin Cardiac Amyloidosis and Polyneuropathy

Study Purpose

To assess the safety and effectiveness of patisiran in a patient with hATTR amyloidosis following heart transplant

Patient Population

- Seventy-three-year-old African American male with hATTR amyloidosis, who had progression of neuropathy following a heart transplant (for cardiac amyloid)

Methods/Assessments

- Patient-reported symptoms

Effectiveness Assessment

- Pt experienced improvement in neuropathy within 4–5 months of patisiran initiation
- Pt reported only very mild neuropathy symptoms 12 months post-patisiran initiation

Genetic Variant(s)

- Val122Ile

Treatment/Study Duration

- Patisiran treatment beginning 12 months post-transplant
- Eighteen-month follow-up

Adverse Events

- Infusions were well tolerated, and pre-infusion dexamethasone was tapered off at pt's request
- Pt maintained normal graft function and did not experience transplant rejection or develop donor-specific antibodies

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hATTR, hereditary transthyretin-mediated; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

Alnylam® PHARMACEUTICALS

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

Case Study (N=5) >

Single Center (N=1)

2019 (N=1) >

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=1)

2019 (N=1)

Single Spanish center
(Gragera-Martínez et al. *EU-ATTR* 2019)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=1)

2019 (N=1)

Single Spanish center
(Gragera-Martínez et al. *EU-ATTR* 2019)

Treatment of Hereditary Amyloidosis Mediated by Transthyretin (hATTR) in Huelva, Spain

Study Purpose

To describe pharmacologic treatment received by patients with hATTR amyloidosis in a Spanish center

Patient Population

- Thirty-nine pts with hATTR amyloidosis

Genetic Variant(s)

- Not reported

Methods/Assessments

- Retrospective study of disease progression and treatment from medical records

Treatment/Study Duration

- Twenty-five pts received OLT; 10 pts on tafamidis, 9 pts on patisiran
- Retrospective study over 6 months

Effectiveness Assessment

- Of the 10 pts on tafamidis, 1 received OLT and 1 switched to patisiran, both due to disease progression
- All 9 pts on patisiran had initiated treatment due to disease progression (with 3 pts having previous OLT)

Adverse Events

- **Not reported**

VIEW POSTER/PUBLICATION ›

hATTR, hereditary transthyretin-mediated; OLT, orthotopic liver transplantation; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

- **Case Study (N=2)**
- **Controlled Study (N=1)**
- **Retrospective Analysis (N=1)**
- **Single Center (N=1)**

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Alnylam® PHARMACEUTICALS

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

Case Study (N=2)

2021 (N=2) >

Controlled Study (N=1) >

Retrospective Analysis (N=1) >

Single Center (N=1)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=2)

2021 (N=2)

Patisiran for advanced heart failure
(Nakamura et al. *JC Cases* 2021)

Splenic regression of amyloid with patisiran and diflunisal
(Patel et al. *Amyloid* 2021)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=2)

2021 (N=2)

Patisiran for advanced heart failure
(Nakamura et al. *JC Cases* 2021)

Splenic regression of amyloid with patisiran and diflunisal
(Patel et al. *Amyloid* 2021)

Patisiran for Advanced Heart Failure with Hereditary Transthyretin Cardiac Amyloidosis

Study Purpose

To assess patisiran effectiveness in a patient with hATTR amyloidosis and advanced heart failure

Patient Population

- A 78-year-old female with hATTR amyloidosis and advanced heart failure refractory to tafamidis

Methods/Assessments

- NT-proBNP, IVS thickness, LVMI, GLS, cardiac uptake during scintigraphy, eGFR

Effectiveness Assessment

- Post-patisiran initiation:
  - Reduced NT-proBNP (–38.5%), IVS thickness (–11.8%), and LVMI (–16.6%) at 6 months
  - GLS and eGFR remained stable at 6 months
  - Considerable improvement in cardiac uptake of technetium-99m pyrophosphate

Genetic Variant(s)

- Val30Met

Treatment/Study Duration

- 80 mg tafamidis daily for 12 months, reduced to 20 mg upon patisiran initiation
- Total study duration of 20 months, with patisiran 0.3 mg/kg every 3 weeks initiated at Month 15

Adverse Events

- No side effects were observed

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eGFR, estimated glomerular filtration rate; GLS, global longitudinal strain; hATTR, hereditary transthyretin-mediated; IVS, interventricular septum; LVMI, left ventricular mass index; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=2)

2021 (N=2)

Patisiran for advanced heart failure
(Nakamura et al. *JC Cases* 2021)

Splenic regression of amyloid with patisiran and diflunisal
(Patel et al. *Amyloid* 2021)

Splenic Regression of Amyloid on Multi-modality Imaging in Response to Treatment with Patisiran and Diflunisal in Hereditary Transthyretin Amyloidosis

Study Purpose

To assess regression of amyloid in a patient with hATTR amyloidosis treated with patisiran and diflunisal

Patient Population

- A 32-year-old female with hATTR amyloidosis, with ocular, cardiac, splenic, and neurologic involvement

Methods/Assessments

- MRI (including CMR), ^{123}I-labelled SAP scintigraphy, serum NT-proBNP

Effectiveness Assessment

- Pt reported gradual improvement in neuropathic symptoms and in functional capacity
- MRI and ^{123}I-labelled SAP scintigraphy indicated regression of splenic amyloid to near-normal levels at 24 months
- NT-proBNP decreased from 419 ng/L at baseline to 102 ng/L (–75.66%)

Genetic Variant(s)

- Phe53Val

Treatment/Study Duration

- Patisiran and diflunisal concomitant treatment
- Twenty-four-month follow-up

Adverse Events

- Pt reported no drug-related adverse effects

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CMR, cardiac magnetic resonance; hATTR, hereditary transthyretin-mediated; ^{123}I, Iodine-123; MRI, magnetic resonance imaging; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide; pt, patient; SAP, serum-amyloid-P component.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

- **Case Study (N=2)**
- **Controlled Study (N=1)**
- 2021 (N=1)
- **Retrospective Analysis (N=1)**
- **Single Center (N=1)**

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

← Back

Controlled Study (N=1)

2021 (N=1)

Regression of cardiac amyloid
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hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Controlled Study (N=1)

2021 (N=1)

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Reduction in CMR Derived Extracellular Volume with Patisiran Indicates Cardiac Amyloid Regression

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  - Sixteen untreated pts with hATTR and wtATTR amyloidosis retrospectively matched

Effectiveness Assessment

- Among treated pts at Month 12:
  - Median serum TTR knockdown was 86%
  - Cardiac ^{99}Tc-DPD uptake by bone scintigraphy was reduced in 15 of 16 pts (median 19.6% reduction; unchanged in 1 pt)
- In treated vs untreated pts at Month 12:
  - ECV was significantly lower
- In treated vs untreated pts at Month 12:
  - NT-proBNP levels were significantly lower
  - 6MWT distance improved significantly

Methods/Assessments

- CMR, echocardiography, NT-proBNP, 6MWT, bone scintigraphy

Genetic Variant(s)

- T60A (n=11), V30M (n=3), A97S (n=2), other (n=7), wild-type (n=9, control group only)

Treatment/Study Duration

- Sixteen pts receiving patisiran (12 of 16 receiving diflunisal concomitantly), 16 pts not receiving disease-modifying treatment (control group)
- Pts followed up after 1 year

Adverse Events

- Patisiran was well tolerated and no pts discontinued treatment. Mild IRRs occured in 4 pts. Eight SAEs occured but were unrelated to patisiran or diflunisal

VIEW POSTER/PUBLICATION ›

6MWT, 6-minute walk test; ^{99}Tc-DPD, technetium-99 3,3-diphosphono-1,2-propanodicarboxylic acid; CMR, cardiac magnetic resonance; ECV, extracellular volume; hATTR, hereditary transthyretin-mediated; IRR, infusion-related reaction; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide; pt, patient; SAE, serious adverse event; TTR, transthyretin; wtATTR, wild-type transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

- **Case Study (N=2)**
- **Controlled Study (N=1)**
- **Retrospective Analysis (N=1)**
- 2021 (N=1)
- **Single Center (N=1)**

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

← Back

Retrospective Analysis (N=1)

2021 (N=1)

Latency before patisiran effectiveness
(Gentile et al. *Brain Sci* 2021)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Retrospective Analysis (N=1)

2021 (N=1)

Latency before patisiran effectiveness
(Gentile et al. *Brain Sci* 2021)

Patisiran in hATTR Amyloidosis: Six-month Latency Period before Efficacy

Study Purpose

To assess the onset of treatment effect with patisiran for patients with hATTR amyloidosis

Patient Population

- Eighteen pts with hATTR amyloidosis:
  - PND score I (n=3), II (n=8), IIIA/B (n=7)
  - Mean NIS, 70.2; Norfolk QOL-DN, 64.2

Methods/Assessments

- PND score, NIS, NIS-LL, Norfolk QOL-DN

Effectiveness Assessment

- Thirteen pts had stable PND score to final assessment, 3 pts improved, and 2 pts worsened
- Mean scores for NIS, NIS-LL, and Norfolk QOL-DN worsened to Month 6, but then improved through Months 12 and 18
- No significant differences in post-treatment results in pts also treated with tafamidis

Genetic Variant(s)

- Phe64Leu (n=7), Glu89Gln (n=5), Val30Met (n=2), Thr49Ala (n=2), Val122Ile (n=1), Ala109Ser (n=1)

Treatment/Study Duration

- All 18 pts receiving patisiran, 4 received tafamidis concomitantly.
- Study duration of 18 months

Adverse Events

- Premedication associated with hyperglycemia (n=1) and hypertension (n=2)
- Three pts temporarily discontinued treatment (severe anemia, fever, diarrhea)
- Three deaths (sudden death, likely cardiac, n=2; severe dehydration, n=1), considered unrelated to patisiran treatment

VIEW POSTER/PUBLICATION ›

hATTR, hereditary transthyretin-mediated; NIS, Neuropathy Impairment Score; NIS-LL, Neuropathy Impairment Score-Lower Limb; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; PND, polyneuropathy disability; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

Choose a study type

- **Case Study (N=2)**
- **Controlled Study (N=1)**
- **Retrospective Analysis (N=1)**
- **Single Center (N=1)**
- 2019 (N=1)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

← Back

Single Center (N=1)

2019 (N=1)

Single Spanish center
(Gragera-Martínez et al. *EU-ATTR* 2019)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=1)

2019 (N=1)

Single Spanish center
(Gragera-Martínez et al. *EU-ATTR* 2019)

Treatment of Hereditary Amyloidosis Mediated by Transthyretin (hATTR) in Huelva, Spain

Study Purpose

To describe pharmacologic treatment received by patients with hATTR amyloidosis in a Spanish center

Patient Population

- Thirty-nine pts with hATTR amyloidosis

Genetic Variant(s)

- Not reported

Methods/Assessments

- Retrospective study of disease progression and treatment from medical records

Treatment/Study Duration

- Twenty-five pts received OLT; 10 pts on tafamidis, 9 pts on patisiran
- Retrospective study over 6 months

Effectiveness Assessment

- Of the 10 pts on tafamidis, 1 received OLT and 1 switched to patisiran, both due to disease progression
- All 9 pts on patisiran had initiated treatment due to disease progression (with 3 pts having previous OLT)

Adverse Events

- Not reported

VIEW POSTER/PUBLICATION ›

hATTR, hereditary transthyretin-mediated; OLT, orthotopic liver transplantation; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

- **Case Study (N=4)**
- **Retrospective Analysis (N=1)**
- **Single Center (N=2)**

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

Case Study (N=4)

- 2022 (N=2)
- 2021 (N=1)
- 2019 (N=1)

Retrospective Analysis (N=1)

Single Center (N=2)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=4)

2022 (N=2)

Tafamidis to patisiran post-liver transplantation
(Bulinski et al. *J Neurol* 2022)

Patisiran for aqATTR after domino liver transplantation
(Tsamis et al. *Clin Transplant* 2022)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=4)

2022 (N=2)

Tafamidis to patisiran post-liver transplantation
(Bulinski et al. *J Neurol* 2022)

Patisiran for aqATTR after domino liver transplantation
(Tsamis et al. *Clin Transplant* 2022)

Clinical Improvement after Change of Therapy from Tafamidis to Patisiran in Progressive TTR Amyloidosis Post-liver Transplantation

Study Purpose

To assess patisiran effectiveness following liver transplantation in a patient with hATTR amyloidosis

Patient Population

- A 36-year-old male diagnosed with TTR-FAP in 2012
- Received tafamidis followed by liver transplantation after 1 year; tafamidis was discontinued
- Symptoms of polyneuropathy gradually worsened after transplantation and continued despite re-initiation of tafamidis in 2018
- Switch to patisiran occurred 6 years post-transplantation

Methods/Assessments

- NCS, mNIS+7, MRI, echocardiography, NYHA class

Genetic Variant(s)

- Glu54Gly

Effectiveness Assessment

- The patient's polyneuropathy symptoms slowly improved on patisiran
- mNIS+7 score decreased from 183.5 to 172.5 after 18 months
- NCS results remained stable
- No change in cardiac amyloidosis, with the caveat that examinations were performed across different centers

Treatment/Study Duration

- Patisiran treatment with 18 months' follow-up

Adverse Events

- Not reported

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hATTR, hereditary transthyretin-mediated; mNIS+7, modified Neuropathy Impairment Score + 7; MRI, magnetic resonance imaging; NCS, nerve conduction studies; NYHA, New York Heart Association; TTR-FAP, transthyretin-familial amyloid polyneuropathy.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=4)

2022 (N=2)

Tafamidis to patisiran post-liver transplantation
(Bulinski et al. *J Neurol* 2022)

Patisiran for aqATTR after domino liver transplantation
(Tsamis et al. *Clin Transplant* 2022)

Treatment of Acquired Transthyretin Amyloidosis in Domino Liver Transplantation

Study Purpose

To report the management and outcome of a patient with aqATTR, after domino liver transplantation, receiving patisiran

Patient Population

- An 80-year-old male with aqATTR that developed after domino liver transplantation for hepatocellular carcinoma
- History of hepatitis B and coronary heart disease
- After 8 years he developed bradyarrhythmia and 2 years later he developed polyneuropathy and was diagnosed with aqATTR amyloidosis
- Patient had FAP stage 1 and PND score II at diagnosis

Methods/Assessments

- Nerve conduction studies and nerve biopsy led to diagnosis of amyloid polyneuropathy
- FAP stage and PND score reported

Genetic Variant(s)

- Met30

Effectiveness Assessment

- Patient stabilized in FAP stage 2 and PND score IIIB, then improved to FAP stage 1 and PND score II
- Patient remained stable after 2 years of treatment

Treatment/Study Duration

- Tafamidis 20 mg orally once daily from November 2018
- Patisiran 0.3 mg/kg q3w from summer 2020

Adverse Events

- Patisiran treatment was well tolerated; no adverse events reported

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aqATTR, acquired transthyretin amyloidosis; FAP, familial amyloid polyneuropathy; hATTR, hereditary transthyretin-mediated; PND, polyneuropathy disability; q3w, every 3 weeks.

Patisiran Real-World Evidence in hATTR Amyloidosis

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Case Study (N=4)

2021 (N=1)

Patisiran for advanced heart failure
(Nakamura et al. *JC Cases* 2021)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=4)

2021 (N=1)

Patisiran for advanced heart failure
(Nakamura et al. *JC Cases* 2021)

Patisiran for Advanced Heart Failure with Hereditary Transthyretin Cardiac Amyloidosis

Study Purpose

To assess patisiran effectiveness in a patient with hATTR amyloidosis and advanced heart failure

Patient Population

- A 78-year-old female with hATTR amyloidosis and advanced heart failure refractory to tafamidis

Methods/Assessments

- NT-proBNP, IVS thickness, LVMI, GLS, cardiac uptake during scintigraphy, eGFR

Effectiveness Assessment

- Post-patisiran initiation:
  - Reduced NT-proBNP (–38.5%), IVS thickness (–11.8%), and LVMI (–16.6%) at 6 months
  - GLS and eGFR remained stable at 6 months
  - Considerable improvement in cardiac uptake of technetium-99m pyrophosphate

Genetic Variant(s)

- Val30Met

Treatment/Study Duration

- 80 mg tafamidis daily for 12 months, reduced to 20 mg upon patisiran initiation
- Total study duration of 20 months, with patisiran 0.3 mg/kg every 3 weeks initiated at Month 15

Adverse Events

- No side effects were observed

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eGFR, estimated glomerular filtration rate; GLS, global longitudinal strain; hATTR, hereditary transthyretin-mediated; IVS, interventricular septum; LVMI, left ventricular mass index; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Case Study (N=4)

2019 (N=1)

Patient on long-term patisiran
(Schmidt. *EU-ATTR* 2019)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

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Case Study (N=4)

2019 (N=1)

Patient on long-term patisiran
(Schmidt. *EU-ATTR* 2019)

Case Report on Long-term Patisiran Treatment

Study Purpose

To assess safety and effectiveness of long-term patisiran treatment in a patient with hATTR amyloidosis

Patient Population

- A 62-year-old male pt with hATTR amyloidosis with polyneuropathy and cardiomyopathy awaiting OLT

Methods/Assessments

- Echocardiogram, NT-proBNP, NIS, mBMI, vitamin A

Effectiveness Assessment

- mBMI improved and NT-proBNP reduced
- NIS stable when measured from 1 year after patisiran treatment initiation to Year 6
- Due to stabilization of disease symptoms, NT-proBNP reduction, and mBMI improvement, liver transplant was not required at the time of publication
- Cardiomyopathy was stabilized, with improvement in left and right atrium dilation, and mild progression of LVCH

Genetic Variant(s)

- Arg54Thr

Treatment/Study Duration

- Previously treated with tafamidis 20 mg daily
- Patisiran treatment from June 2013 to 2019 (approx. 6 years)

Adverse Events

- No AEs recorded
- Pt had normal liver enzymes and renal parameters throughout treatment
- Pt had no febrile episodes, no eye anomalies, and normal thyroid function

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AE, adverse event; hATTR, hereditary transthyretin-mediated; LVCH, left ventricular concentric hypertrophy; mBMI, modified body mass index; NIS, Neuropathy Impairment Score; NT-proBNP, *N*-terminal prohormone of brain-type natriuretic peptide; OLT, orthotopic liver transplantation; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

Alnylam® PHARMACEUTICALS

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

- **Case Study (N=4)**
- **Retrospective Analysis (N=1)**
- 2021 (N=1)
- **Single Center (N=2)**

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

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Retrospective Analysis (N=1)

2021 (N=1)

Latency before patisiran effectiveness
(Gentile et al. *Brain Sci* 2021)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

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Retrospective Analysis (N=1)

2021 (N=1)

Latency before patisiran effectiveness
(Gentile et al. *Brain Sci* 2021)

Patisiran in hATTR Amyloidosis: Six-month Latency Period before Efficacy

Study Purpose

To assess the onset of treatment effect with patisiran for patients with hATTR amyloidosis

Patient Population

- Eighteen pts with hATTR amyloidosis:
  - PND score I (n=3), II (n=8), IIIA/B (n=7)
  - Mean NIS, 70.2; Norfolk QOL-DN, 64.2

Methods/Assessments

- PND score, NIS, NIS-LL, Norfolk QOL-DN

Effectiveness Assessment

- Thirteen pts had stable PND score to final assessment, 3 pts improved, and 2 pts worsened
- Mean scores for NIS, NIS-LL, and Norfolk QOL-DN worsened to Month 6, but then improved through Months 12 and 18
- No significant differences in post-treatment results in pts also treated with tafamidis

Genetic Variant(s)

- Phe64Leu (n=7), Glu89Gln (n=5), Val30Met (n=2), Thr49Ala (n=2), Val122Ile (n=1), Ala109Ser (n=1)

Treatment/Study Duration

- All 18 pts receiving patisiran, 4 received tafamidis concomitantly
- Study duration of 18 months

Adverse Events

- Premedication associated with hyperglycemia (n=1) and hypertension (n=2)
- Three pts temporarily discontinued treatment (severe anemia, fever, diarrhea)
- Three deaths (sudden death, likely cardiac, n=2; severe dehydration, n=1), considered unrelated to patisiran treatment

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hATTR, hereditary transthyretin-mediated; NIS, Neuropathy Impairment Score; NIS-LL, Neuropathy Impairment Score-Lower Limb; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; PND, polyneuropathy disability; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

Alnylam® PHARMACEUTICALS

Polyneuropathy (N=22) | Cardiomyopathy (N=4) | Transplant (N=6) | Concomitant Treatment (N=5) | Switching Treatment (N=7)

Choose a study type

- **Case Study (N=4)** >
- **Retrospective Analysis (N=1)** >
- **Single Center (N=2)**
- 2019 (N=2) >

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=2)

2019 (N=2)

Clinical experience: Single German non-endemic center
(Dohrn et al. *EU-ATTR* 2019)

Single German center
(Hüsing-Kabar et al. *EU-ATTR* 2019)

hATTR, hereditary transthyretin-mediated.

Patisiran Real-World Evidence in hATTR Amyloidosis

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Single Center (N=2)

2019 (N=2)

Clinical experience: Single German non-endemic center
(Dohrn et al. *EU-ATTR* 2019)

Single German center
(Hüsing-Kabar et al. *EU-ATTR* 2019)

The First Six Months of Patisiran in Hereditary Transthyretin Amyloidosis: Real-life Experiences from a Non-endemic Center

Study Purpose

To assess the effectiveness and safety of patisiran for patients in the first 6 months of treatment

Patient Population

- Three male pts with hATTR amyloidosis, aged 39–73 (1 early onset [<50 years])
  - All had sensorimotor and autonomic symptoms, 2 pts had cardiac involvement
  - All previously treated with tafamidis but discontinued due to disease progression (n=2) or lack of response (n=1)

Genetic Variant(s)

- Val50Met (n=2), Glu109Gln (n=1)

Treatment/Study Duration

- Pts receiving patisiran for 2–6 months at time of data collection

Methods/Assessments

- Disease progression assessed every 3 months via symptom history, clinical examination, NCV studies, quantitative sensory testing, Schellong test, Sudoscan, electrocardiogram, laboratory studies

Adverse Events

- Patisiran was well tolerated
- One pt had an asthma attack after second infusion, and flush 1 day after infusion

Effectiveness Assessment

- All pts had stabilized disease to date on patisiran treatment

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hATTR, hereditary transthyretin-mediated; NCV, nerve conduction velocity; pt, patient.

Patisiran Real-World Evidence in hATTR Amyloidosis

← Back

Single Center (N=2)

2019 (N=2)

Clinical experience: Single German non-endemic center
(Dohrn et al. *EU-ATTR* 2019)

Single German center
(Hüsing-Kabar et al. *EU-ATTR* 2019)

Real-life Experiences with Onpattro® and Tegsedi®

Study Purpose

To assess the effect of patisiran and inotersen on serum TTR levels in patients with hATTR amyloidosis

Patient Population

- Thirteen pts, aged 34–77 (10 male, 3 female)

Genetic Variant(s)

- Val30Met (n=7), non-Val30Met (n=6)

Methods/Assessments

- Serum TTR measures

Treatment/Study Duration

- Five pts on patisiran; 3 pts on inotersen; 5 pts with alternating treatment (patisiran, inotersen, patisiran)
- Followed up for 12–18 weeks

Effectiveness Assessment

- Patisiran and inotersen induced robust reduction of serum TTR
- Both compounds appeared equally effective at reducing TTR in the same patients (washout/weaning period between drugs)
- TTR reduction was similar between patients who were naive to treatment or had switched from one treatment to the other

Adverse Events

- Not reported

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hATTR, hereditary transthyretin-mediated; pt, patient; TTR, transthyretin.