Outpatient Heart Failure Worsening in Patients with Cardiac Transthyretin Amyloidosis: Results from the APOLLO-B Trial

Mariana Fontana1, Mathew S. Maurer2, Julian D. Gilmore3, Shaun Bender4, Patrick Y. Jay5, Scott D. Solomon6

1National Amyloidosis Centre, UCL, Division of Medicine, Royal Free Hospital, London, UK; 2Columbia University Irving Medical Center, New York, NY, USA; 3Aryllan Pharmaceuticals, Cambridge, MA, USA; 4Cardiovascular Division, Brigham and Women’s Hospital, Boston, MA, USA.

Conclusions

- This post hoc analysis assessed the prognostic and clinical significance of outpatient worsening heart failure (HF) characterized by oral diuretic initiation or intensification (ODI) in patients with transthyretin amyloidosis (ATTR) with cardiomyopathy (ATTR-CM)
- Overall, patients who experienced an ODI event tended to be at higher risk of all-cause mortality, cardiovascular (CV) hospitalizations, and urgent HF visits.
- Patisiran treatment significantly reduced worsening HF requiring ODI in the overall population, with consistent results in those receiving treatment and not receiving tafamidis.
- A significantly greater increase in daily diuretic usage was observed in the placebo group than the patisiran group at Month 12.

Methods

Patisiran Phase 3 APOLLO-B study

- APOLLO-B is a global, randomized, placebo-controlled study in patients with ATTR-CM (wild-type ATTR, wtATTR) and cardiomyopathy (ATTR-CM), evaluating the efficacy and safety of patisiran in 12-month dosage regimens compared to placebo in patients with Stage 2 or Stage 3A symptomatic ATTR-CM.
- Patients were randomized to receive patisiran (10 mg/kg), placebo, or, in a subset of patients, tafamidis (61 mg) in a 2:1:1 ratio.
- The primary outcome was the percentage of patients with an ODI event (oral diuretic initiation or intensification) during the 12-month period.
- Secondary outcomes included all-cause mortality, cardiovascular hospitalizations, and urgent HF visits.

Results

Baseline Demographics and Disease Characteristics

- Baseline demographics and disease characteristics were generally comparable across the treatment groups (Table 1).

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

References:


Figure 1. APOLLO Study Design

Figure 2. ODI Events Per Patient during the 12M DB period

Figure 3. ODI Events Per Patient over 24 Months in A) Overall Population, B) Patients on Background Tafamidis, and C) Patients Not Receiving Background Tafamidis

Figure 4. Daily Diuretic Dose Increase during APOLLO-B. A) from Baseline to Month 12 (DB Period) and B) from Month 12 to Month 18 (OLE Period)

Figure 5. Kaplan-Meier Plot of Time to ODI over 24 Months in A) Overall Population, B) Patients on Background Tafamidis, and C) Patients Not Receiving Background Tafamidis

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.

Clinical Outcomes in Patients with Outpatient Heart Failure Worsening

- In the overall population, an ODI event was associated with a subsequent increased risk of all-cause mortality, CV hospitalizations, or urgent HF visits (HR 1.357, 95% CI: 0.986, 1.869).

Impact of Patisiran on Daily Diuretic Dosage

- Daily diuretic dose increase was significantly greater in the placebo vs patisiran group at Month 12.