Acute Hepatic Porphyria (AHP) Overview

- AHP is a group of rare genetic disorders that cause dysfunction of the liver's ability to produce heme.
- It is characterized by the accumulation of porphyrin precursors, which can lead to pain, neurological symptoms, and organ damage.
- Two main types of AHP are Acute Intermittent Porphyria (AIP) and Variegate Porphyria (VP).

Diagnosis of AHP

- Diagnosis is confirmed through genetic testing.
- Clinical manifestations and laboratory findings can also support the diagnosis.

Approval for AHP Treatment

- Givosiran (GIVLAARI) is approved for treatment of AHP in adults in the US and adults and adolescents aged 12 years and older.
- It is an Investigational RNAi Therapeutic for AHP, in the ENVISION Open-label Extension (OLE) Trial.

Methods

- The study enrolled 94 patients with AHP enrolled in ENVISION at 36 sites in 18 countries.
- Patients completed the 6-month double-blind (DB) period of all eligible patients (n=94) entered the 30-month open-label extension (OLE) period.

Results

- Baseline characteristics were generally balanced between groups (Table 1).

Table 1. Demographics and Baseline Characteristics of Patients in ENVISION (n=94)

| Characteristic            | Givosiran Patients | Placebo Crossover Patients | Ratio
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</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>47 (20–76)</td>
<td>54 (20–76)</td>
<td>1.15</td>
</tr>
<tr>
<td>Gender, M/F</td>
<td>36/58</td>
<td>33/61</td>
<td>1.00</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>76 (48–118)</td>
<td>71 (40–120)</td>
<td>1.07</td>
</tr>
<tr>
<td>Height, cm</td>
<td>165 (139–189)</td>
<td>164 (139–189)</td>
<td>1.00</td>
</tr>
</tbody>
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Givosiran Treatment Led to Sustained and Rapid Reduction of Attacks

- Continuous givosiran treatment led to sustained reductions in hourly pain (with or without IV hemin) compared with the DB period.
- Patients who continued givosiran treatment in the OLE showed a further decrease in attacks compared with the DB period.

Patient Management and Further Recommendations

- Further improvements in patients continuing givosiran treatment compared with the DB period.

Safety Profile of Givosiran Remained Acceptable with No New Safety Concerns

- Throughout the trial, the safety profile of givosiran remained consistent with the known safety profile of givosiran.
- No new safety concerns were identified.

Conclusion

- Givosiran treatment led to sustained reductions in hourly pain in the OLE period, with 70% of patients requiring zero hemin use.
- Patients who continued givosiran treatment showed further improvements compared with the DB period.

Acknowledgments

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- Additional authors and affiliations are listed in the Supplemental Material.