Givosiran: Use in Patients Without an Identified Porphyria-Related Mutation

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SUMMARY

- The phase 3 ENVISION study was a randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of givosiran in patients with a documented diagnosis of AHP.[1]
- Of the 94 patients enrolled in the study, 2 patients had AHP without an identified genetic mutation.[1]
- The efficacy of givosiran in the 2 patients without an identified genetic mutation is provided in **Table 1**.[1,2]
- Additional information regarding the safety of givosiran in the two patients without an identified genetic mutation is not available.

INDEX

CLINICAL DATA

The ENVISION study was a phase 3, randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of givosiran in patients with a documented diagnosis of AHP. Enrolled patients were randomized on a 1:1 basis to receive subcutaneous injections of givosiran 2.5 mg/kg (n=48) or placebo (n=46) once a month for 6 months, followed by an optional 30-month OLE. The primary endpoint was the annualized rate of composite porphyria attacks among patients with AIP at 6 months.[1]

Of the 94 patients enrolled in the study, 2 patients had AHP without an identified genetic mutation. Both patients were subsequently assessed by the investigator as having AIP on the basis of biochemical analysis. Both patients were enrolled in the placebo crossover group, where they switched from placebo to givosiran treatment following the 6-month double blind period.[1]

Efficacy Results

Efficacy results from ENVISION as of July 23, 2019 for these patients are provided in **Table 1.**[2]

Table 1. Efficacy Results in AHP Patients Without Identified Genetic Mutations in ENVISION.[2]

	Patient 1[a]	Patient 2
Exposure		
Number of doses of givosiran received	2	9
Total follow-up on givosiran (days)	56	233

	Patient 1[a]	Patient 2
Efficacy		
Composite AAR[b]		
Historical AAR	10	4
6-month double-blind period	21.6	0
During givosiran treatment	1[c]	0
Secondary Endpoints		
ALA, mmol/mol Cr		
Baseline	23.10	15.68
Month 6	12.12	17.07
Last value	3.93 (Month 7)	1.73 (Month 14)
PBG, mmol/mol Cr		
Baseline	45.52	15.68
Month 6	32.96	17.07
Last value	11.45 (Month 7)	3.38 (Month 14)
Days of hemin use		
6-month double-blind period	0	0
During givosiran treatment	0	0

Abbreviations: AAR = annualized attack rate; ALA = aminolevulinic acid; Cr = creatinine; PBG = porphobilinogen.
Data presented as of data cutoff date of July 23, 2019.
[a]Patient discontinued study drug on Day 197 (Day 29 on givosiran) and withdrew from the study on Day 224 (Day 56 on givosiran).
[b]A composite porphyria attack was defined as an attack that resulted in hospitalization, an urgent health care visit, or intravenous administration of hemin at home.[3]
[c]AAR was calculated for patients who had at least 85 days of follow-up during the OLE period. Patient withdrew from the study before 85 days of follow-up; therefore, number of attacks is presented here.

Safety Results

A summary of AEs reported at the end of the OLE is shown in **Table 2**. The safety results presented below represent the total population of the ENVISION study.[1]

Table 2. Summary of Patients with ≥1 Adverse Event.[1]

Patients with ≥1 Event, n (%)	Placebo Crossover (N=46)	Continuous Givosiran (N=48)	All Patients (N=94)
Any AE	44 (96)	47 (98)	91 (97)
SAE	17 (37)	20 (42)	37 (39)
Severe AE	18 (39)	17 (35)	35 (37)
AE leading to treatment discontinuation	4 (9)	2 (4)	6 (6)
AE leading to study withdrawal	2 (4)	2 (4)	4 (4)
Death	0	1 (2)	1 (1)

Abbreviations: AE = adverse event; SAE = serious adverse event.

Additional information regarding the safety of givosiran in the two patients without an identified genetic mutation is not available.

ABBREVIATIONS

AE = adverse event; AHP = acute hepatic porphyria; AIP = acute intermittent porphyria; OLE = open-label extension.

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REFERENCES

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