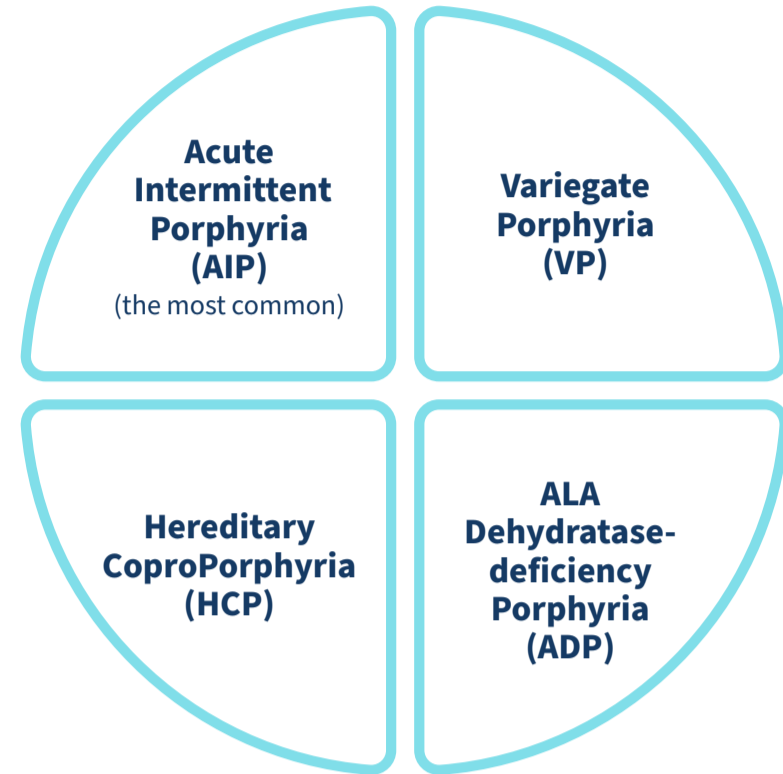


Long-term clinical outcomes of patients with acute hepatic porphyria who were not attack-free after 6 months of givosiran treatment: a subgroup analysis of the phase 3 ENVISION study

1 Introduction

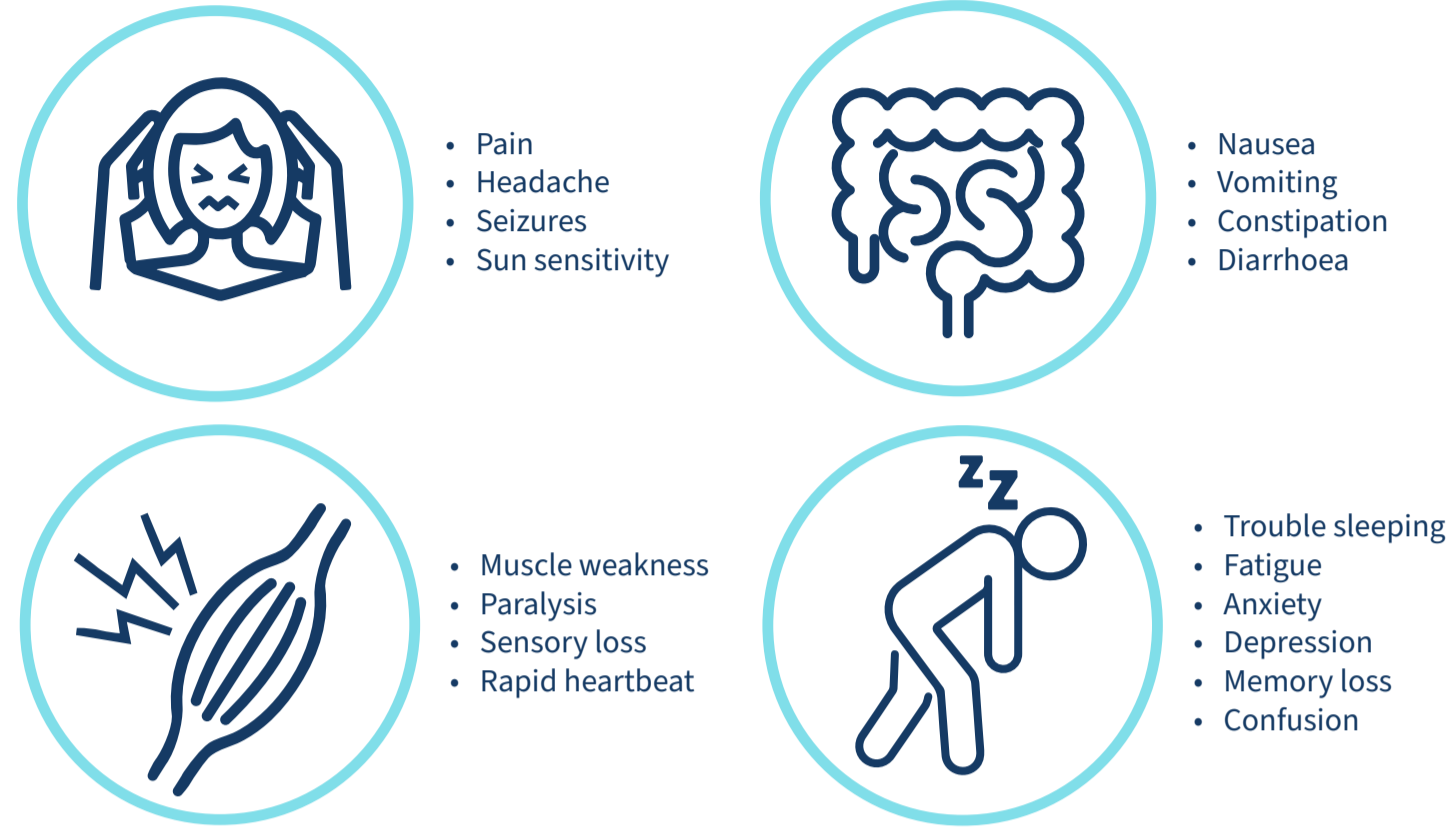
What is AHP?

- Acute hepatic porphyria (AHP) is a term for a group of four genetic diseases that affect the whole body and that if untreated, can get worse with time



- A build-up of delta-aminolevulinic acid (ALA) and porphobilinogen (PBG) in the body can cause:
 - Attacks**
 - Appear suddenly and last a short time
 - Severe and sometimes life-threatening symptoms
 - Chronic symptoms**
 - Appear more slowly and can last a long time
 - Negatively affect day-to-day activities and quality of life

Symptoms of AHP



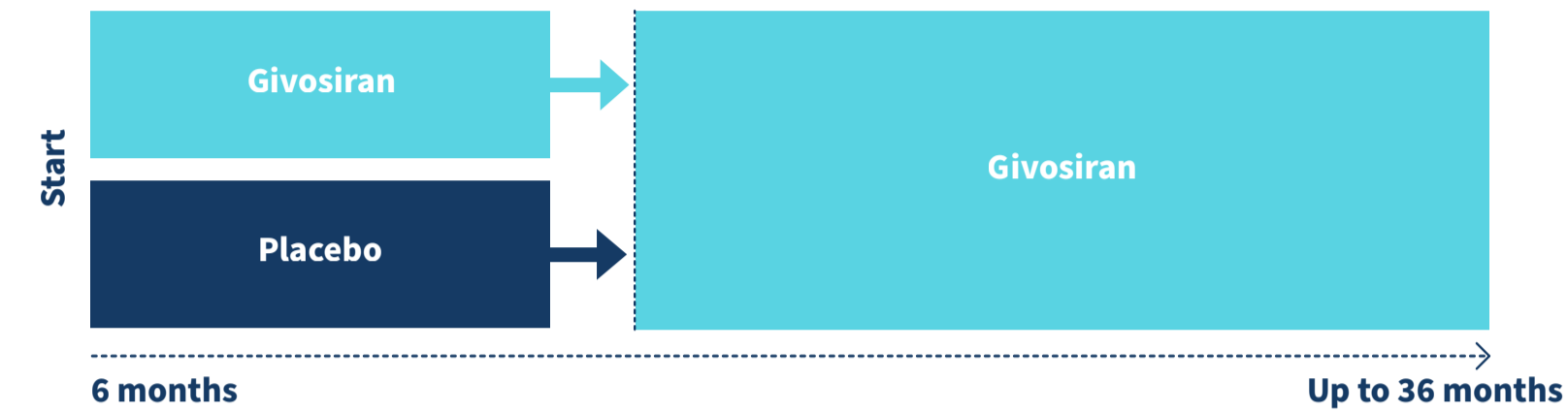
Not all symptoms of AHP shown

What is givosiran?

- A medicine that is used to treat adults with AHP that prevents the build-up of ALA and PBG in the body

What was the ENVISION study?

- ENVISION (NCT03338816) was a Phase 3 clinical study in patients with AHP that evaluated the:
 - effects of givosiran compared with placebo
 - long-term effect and safety of givosiran treatment



- In the 1st 6 months (6M), patients treated with givosiran had fewer attacks than those on placebo
- We investigated the long-term outcomes of patients who completed the study through to month 36 (36M)

- Patients were grouped into:



2 Methods and Results

Annualized attack rate

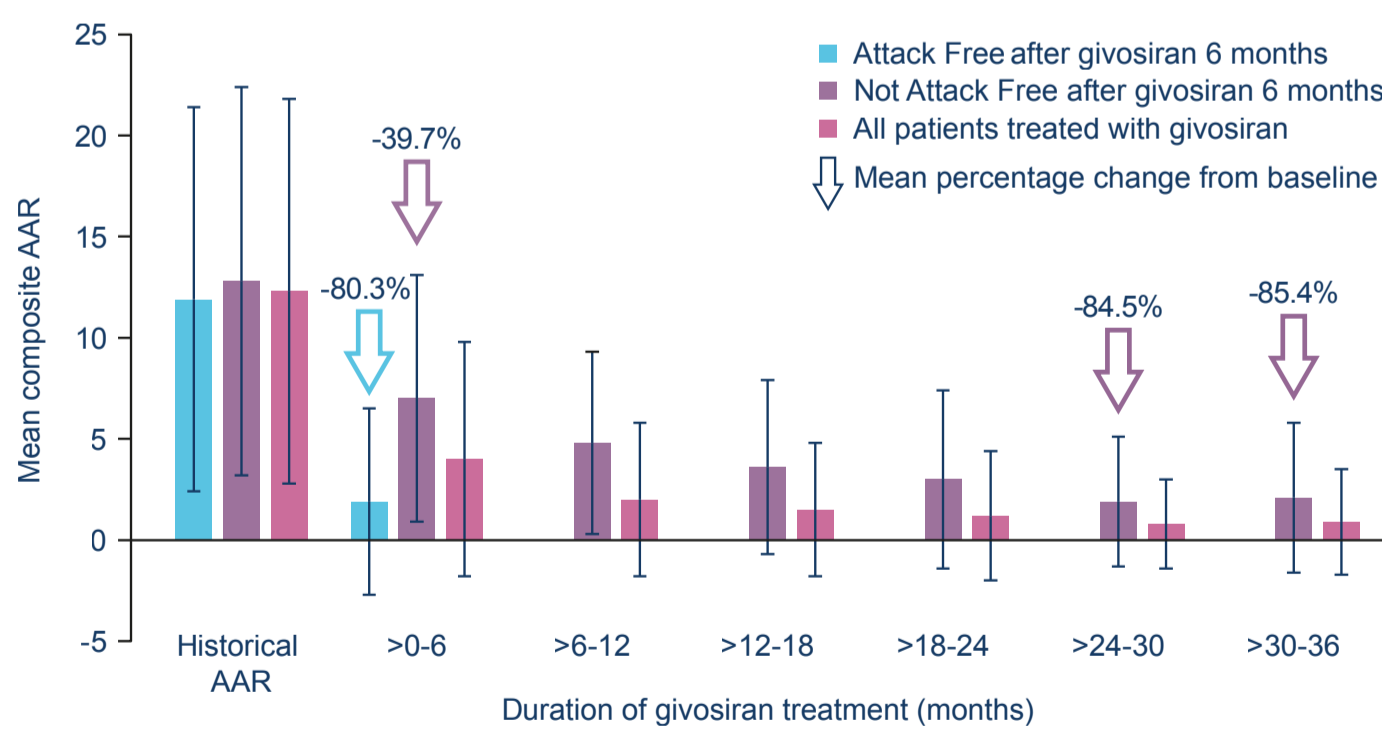
Methods

- Primary endpoint was annualized attack rate (AAR)
- AAR was the average number of attacks per person in a year that required any of the following:



- To calculate the effect of givosiran treatment, AARs were
 - calculated every 6M
 - compared to values before treatment

AAR decreased over time with givosiran treatment



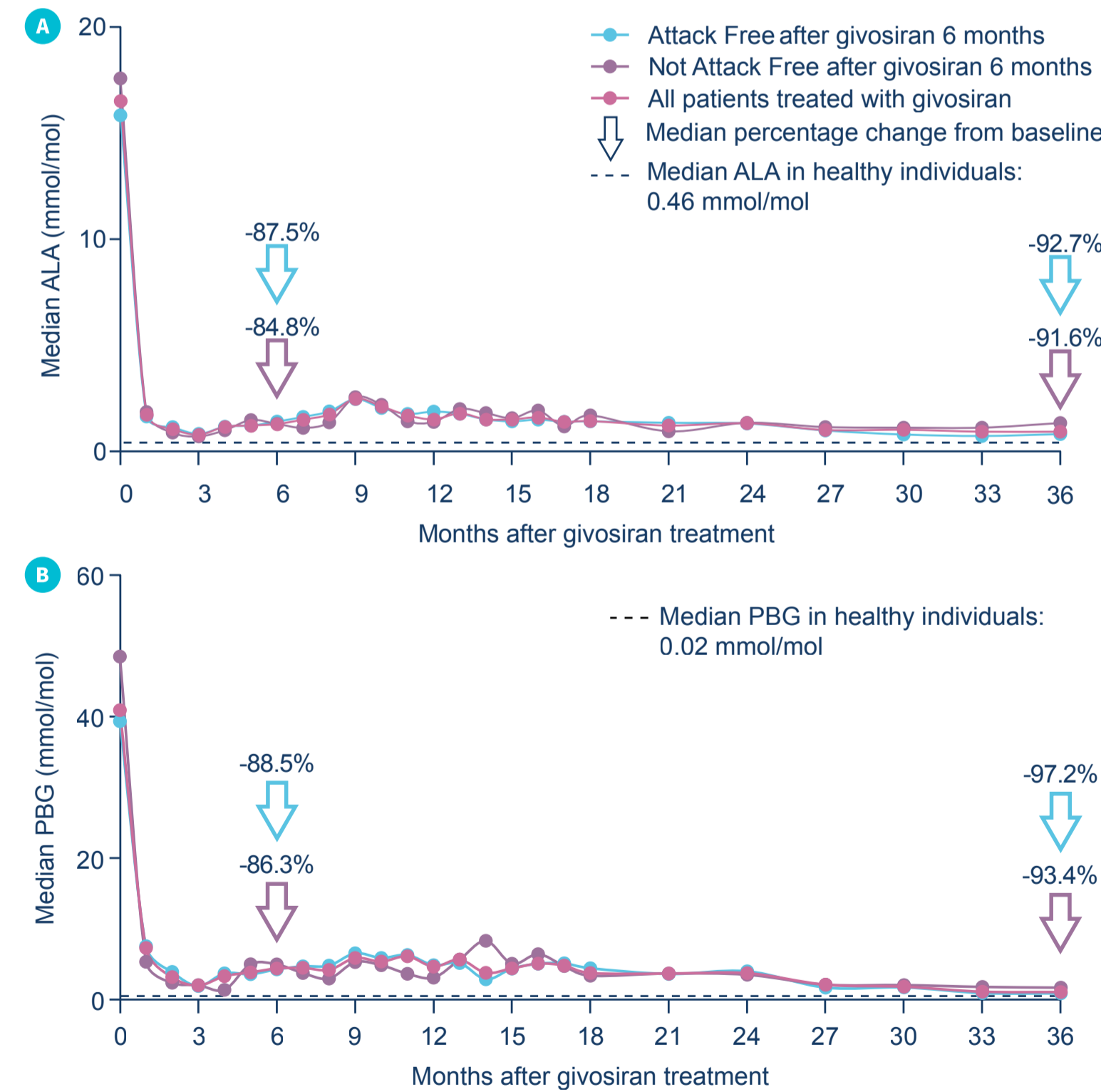
- 1st 6M of treatment: all treated patients had reduced AAR (historical AAR vs >0-6M)
- Continued treatment: AAR decreased further over time in all groups (>6-12M and later)
- Of the Not Attack-Free group, the percentage of patients who were attack-free after the 1st 6M of treatment (during 6M treatment intervals) increased over time:
 - 9% attack-free after >6-12M of treatment
 - 79% after >30-36 M of treatment

ALA and PBG urine concentrations

Methods

- To estimate effect of givosiran, concentrations of ALA and PBG in urine were:
 - measured throughout the study
 - compared to starting values

ALA and PBG concentration decreased over time with givosiran treatment

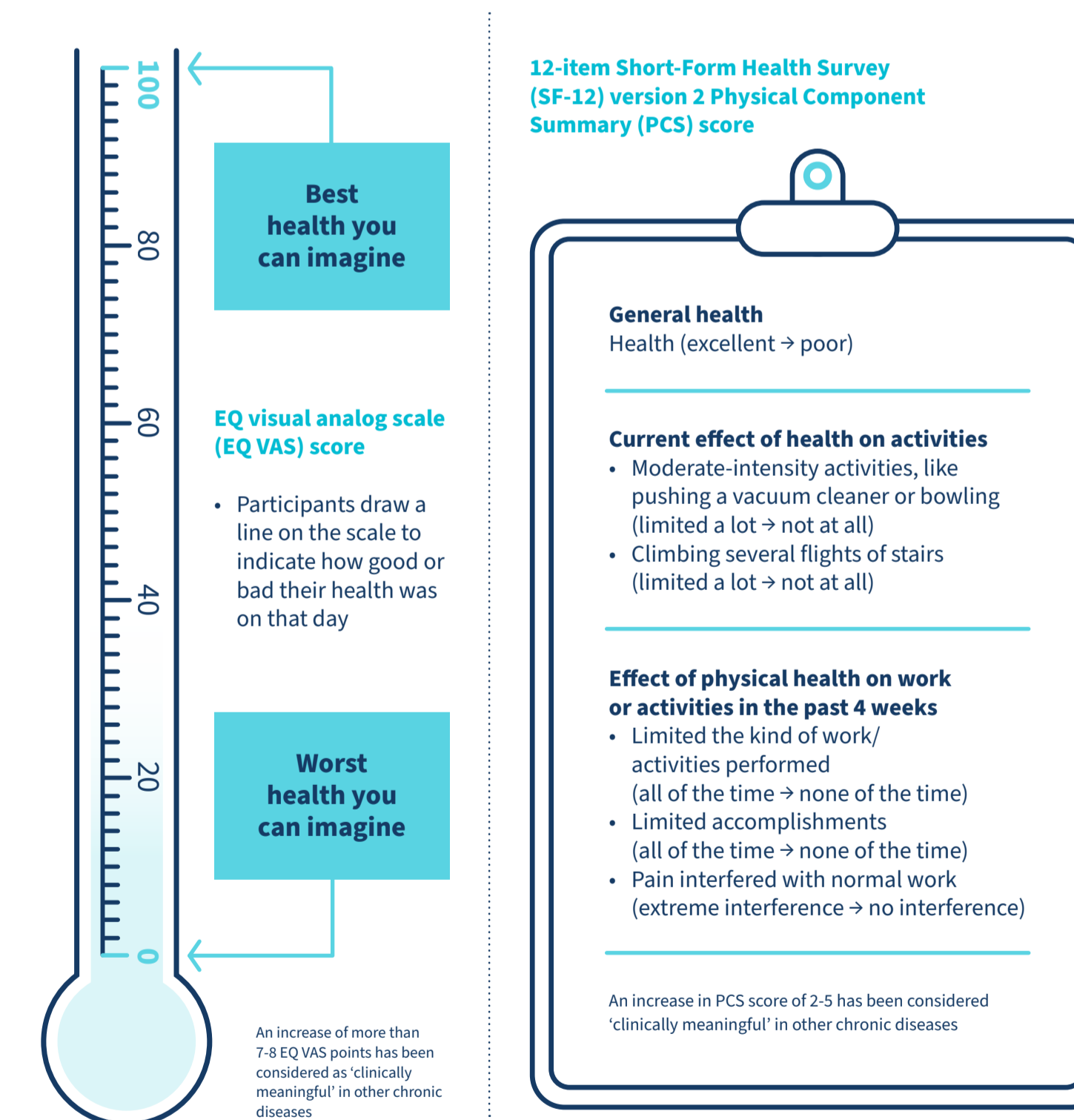


- ALA and PBG reductions were similar in the Not Attack Free and Attack Free groups

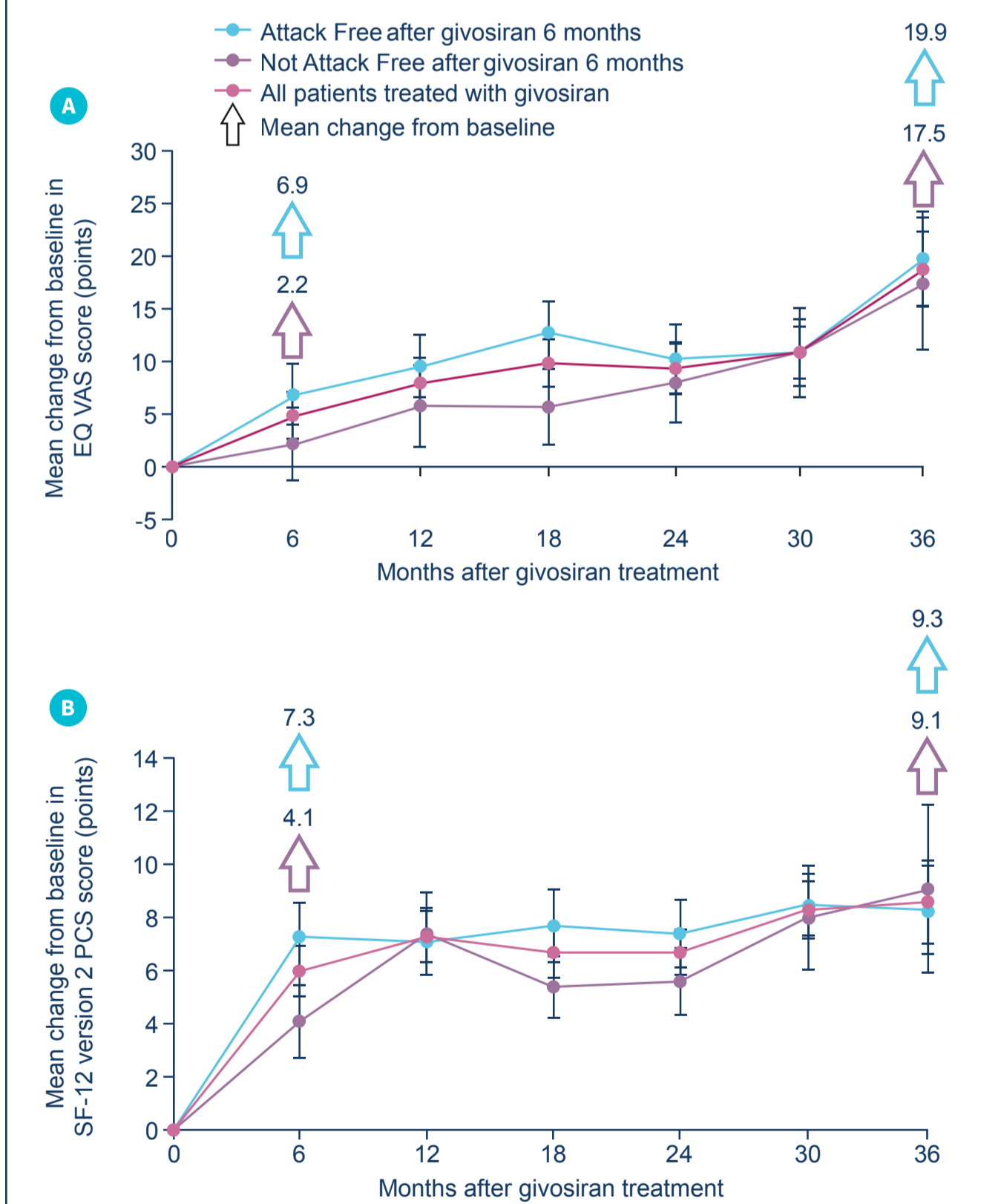
Health-related quality of life (HRQoL)

- Several surveys are used by medical professionals to evaluate health-related quality of life (HRQoL) in people
- These tools can estimate impact of disease on a person's life beyond their symptoms

HRQoL was measured using:



HRQoL improved over time with givosiran treatment



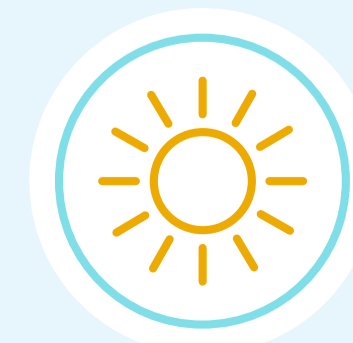
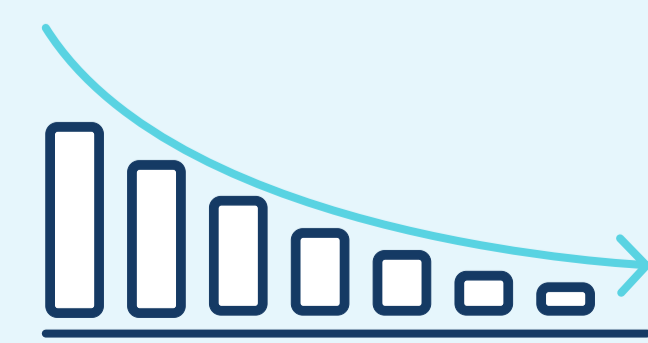
- HRQoL improved in all patients
 - After 6M of treatment (0M vs 6M)
 - After 36M of treatment (0M vs 36M)
- At 36M, HRQoL improvements were similar in the Not Attack Free and Attack Free groups

3 Conclusions

- Results indicate that long-term treatment with givosiran provides sustained clinical and HRQoL benefits to patients who remain attack-free and those who don't



- Both patient groups had reduced attacks and other treatment-related improvements within the 1st 6M of givosiran treatment



Attack-Free group

- Remained attack-free
- HRQoL continued to improve until end of study



Not Attack-Free group

- Further reductions in number of attacks
- HRQoL improved with long-term treatment

Acknowledgements

The authors would like to thank a patient with AIP for reviewing the content of this publication

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