

Donidalorsen Improves Quality of Life in Hereditary Angioedema Patients in a Phase II Study



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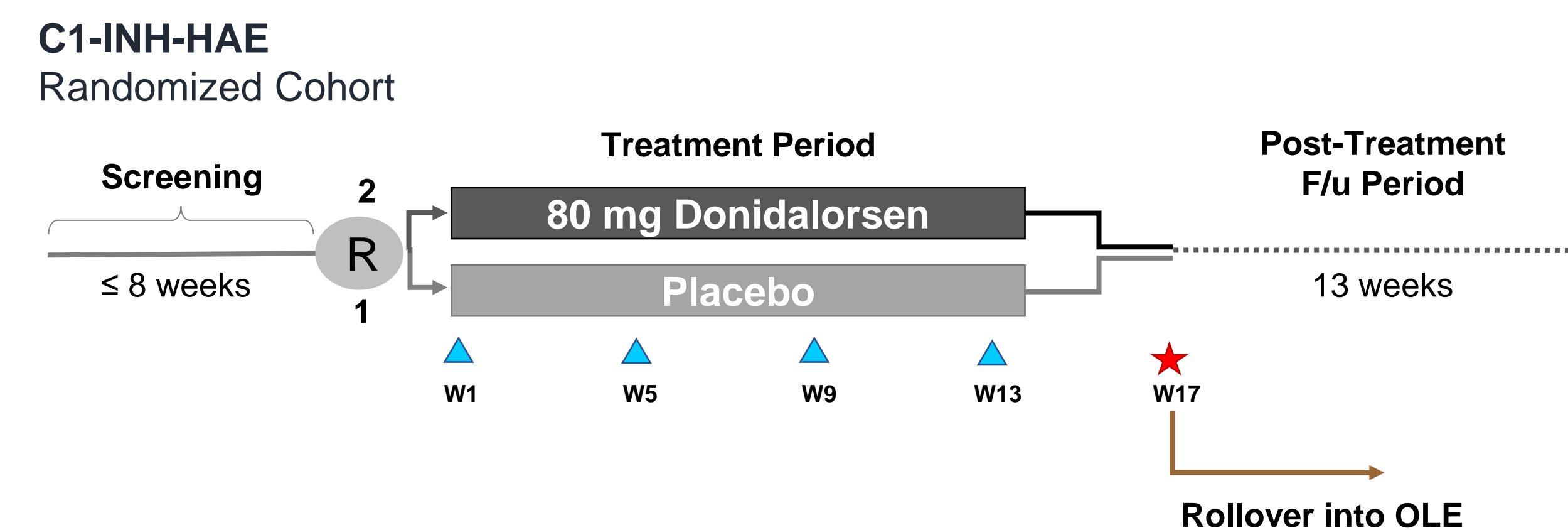
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Rationale

- Patients with hereditary angioedema (HAE) often experience emotional distress and reduced health-related quality of life (HRQoL)
- Improving quality of life has become an important hallmark of disease management of HAE
- Selective inhibition of plasma prekallikrein by antisense oligonucleotide treatment (donidalorsen/ISIS 721744) reduced angioedema attacks by more than 90% in a phase 2 trial
- The impact of this treatment on HRQoL was a predefined end-point in this trial

Methods

- In this phase 2 trial, patients with hereditary angioedema with C1-inhibitor deficiency (HAE type I or II) were randomly assigned in a 2:1 ratio to a 16-week treatment period with subcutaneous dosing of 80 mg donidalorsen or placebo every four weeks
- Quality of life was assessed with the validated angioedema quality of life questionnaire (AE-QoL¹) at randomization and the end of study
- Scores range from 0 – to 100, with higher scores indicating greater impairment
- The minimal clinically important difference is defined as a change of six points

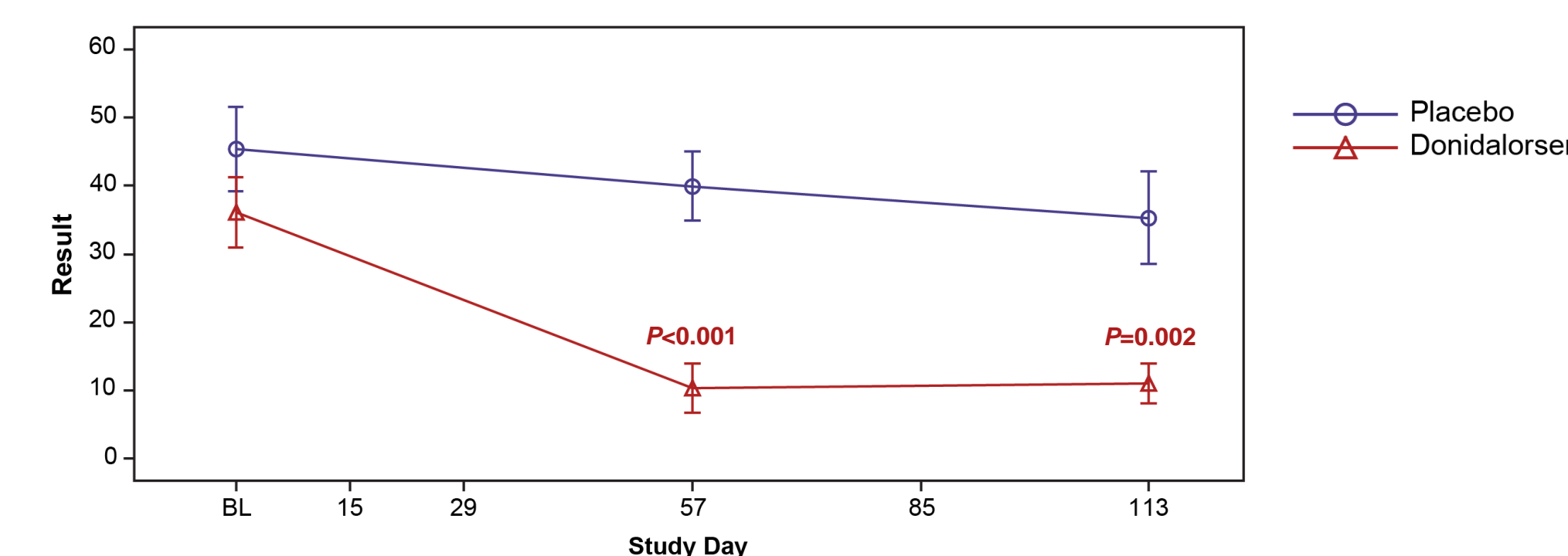


Abbreviations: D, day; F/u, follow-up; OLE, open label extension; R, randomization; SC, subcutaneous; W, week; E, enrollment.
1 Weller et al. *Allergy* 2012

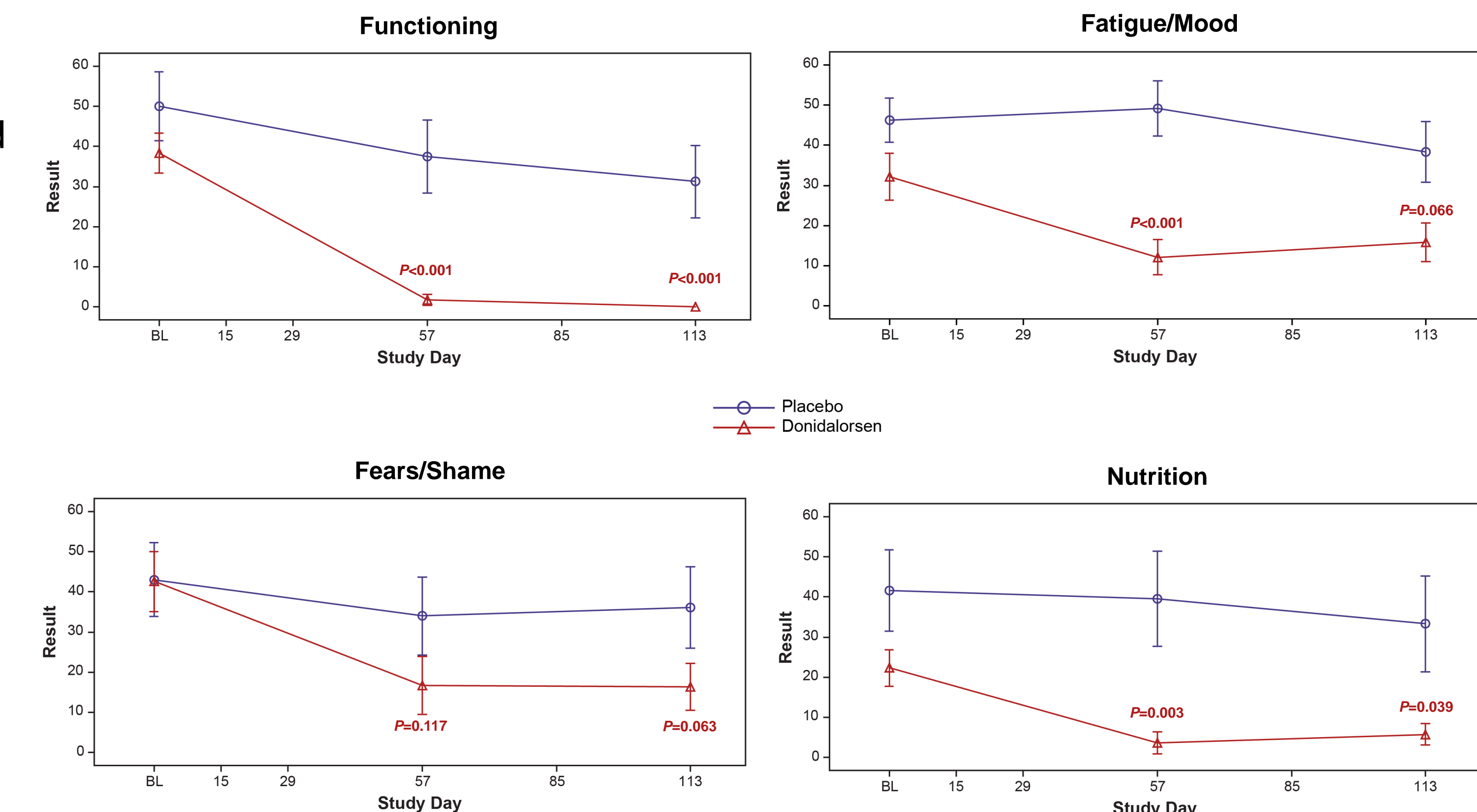
Results

- A total of 20 patients with HAE were enrolled, of whom 14 received donidalorsen and 6 placebo
- Patients reported higher overall HRQoL over 16 weeks in the donidalorsen treatment group compared with placebo
- The mean change in total score of the AE-QoL in HAE patients treated with donidalorsen was -26.85, compared with -6.15 in the placebo group (P=0.002)
- These reductions were also observed across all individual domains of the AE-QoL compared with placebo

Total Score Absolute Value (Mean ± SEM)



Domains Absolute Value (Mean ± SEM)



Conclusion

HRQoL assessment revealed clinically meaningful and sustained improvements from baseline in overall quality of life and across all domains of the AE-QoL questionnaire in HAE patients treated with plasma prekallikrein targeted oligonucleotide antisense therapy