

# Effect of Privosegtor on Plasma Neurofilament-Light and Glial Fibrillary Acidic Protein Levels in the Phase 2 ACUITY Trial in Optic Neuritis

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Trial registration: NCT04762017

## Background

- Acute optic neuritis (ON) is an inflammatory demyelinating disorder of the optic nerve that can result in permanent visual impairment.<sup>1</sup>
- Privosegtor is a novel neuroprotective candidate with broad potential for neuro-axonal diseases.<sup>2</sup>
- In the Phase 2 ACUITY trial, adults with acute unilateral demyelinating ON received intravenous (IV) privosegtor or placebo for 5 days as an add-on to high-dose IV methylprednisolone.<sup>3</sup>
  - Over 6 months, privosegtor was associated with greater low-contrast visual acuity recovery and reduced retinal ganglion cell layer thinning versus placebo, with no safety concerns.<sup>3</sup>

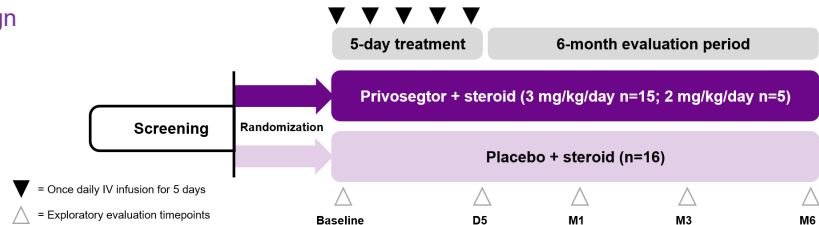
## Objective

To investigate plasma neurofilament light (NfL) and glial fibrillary acidic protein (GFAP) levels, prespecified exploratory biomarkers of neuroaxonal injury and astrocyte response, respectively, following privosegtor treatment in ACUITY.

## Methods

- Design**  
Randomized, double-masked, placebo-controlled trial (NCT04762017; **Figure 1**). Multi-center, 6-month trial with 36 patients randomized (mITT: 33).
- Participants**  
Patients diagnosed with a unilateral acute ON. Onset of visual loss symptoms in the last 12 days before randomization.
- Intervention & comparator**  
Once-daily IV infusion of privosegtor & steroid vs placebo & steroid for 5 days.
- Exploratory analyses**  
Plasma samples were collected at baseline, Day 5, and Months 1, 3, and 6. NfL and GFAP concentrations were measured centrally using Single Molecule Array technology.

**Figure 1.** Trial design



### Statistical Analysis:

- mITT population analyzed using MMRM to estimate LSM change from baseline.
- NfL analyses were not adjusted for age or renal function.
- Analyses focused on privosegtor 3 mg/kg/day because only four participants received 2 mg/kg/day.

**Abbreviations:** LSM: least squares mean; mITT: modified intent to treat; MMRM: mixed model for repeated measures

**Ethics:** The trial was approved by the French Regulatory Authority and French Independent Ethics Committee, in accordance with the Declaration of Helsinki and ICH Good Clinical Practice guidelines. All participants provided written informed consent.

## Results

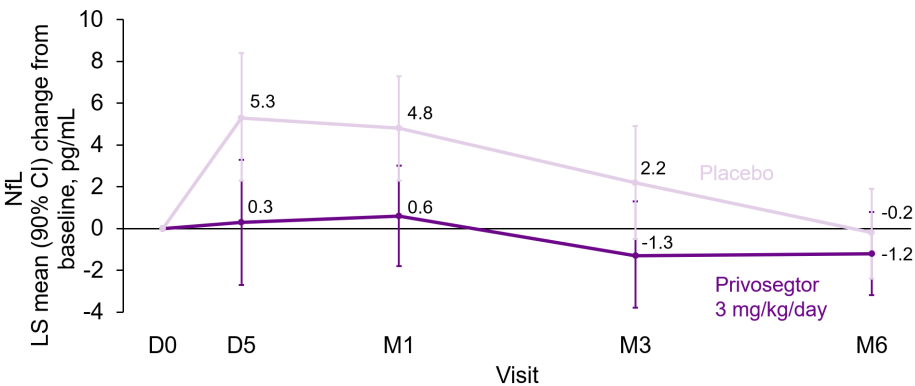
### Baseline characteristics

| Characteristic                                                                | Privosegtor + steroid<br>3 mg/kg/day<br>(N = 15) | Placebo + steroid<br>(N = 14) |
|-------------------------------------------------------------------------------|--------------------------------------------------|-------------------------------|
| Age, years – mean (SD)                                                        | 33.7 (9.8)                                       | 32.7 (10.3)                   |
| Female sex – n (%)                                                            | 9 (60)                                           | 10 (71)                       |
| NfL, pg/mL – mean (SD)                                                        | 6.6 (5.2)                                        | 8.6 (7.4)                     |
| GFAP, pg/mL – mean (SD)                                                       | 104.9 (37.1)                                     | 132.5 (60.2)                  |
| Time since first visual loss symptoms at date of first dose, days – mean (SD) | 9.5 (2.7)                                        | 9.6 (2.5)                     |
| Multiple sclerosis at baseline – n (%)                                        | 10 (66.7)                                        | 9 (64.3)                      |

### Plasma NfL levels

- At Day 5, the mean increase in plasma NfL was higher in the placebo group than the privosegtor group (LSM change: 5.3 pg/mL vs 0.3 pg/mL, respectively; Figure 2).
- NfL levels remained stable in the privosegtor group through Month 6, whereas levels remained elevated above baseline with placebo at Month 1 before returning to baseline by Month 6.

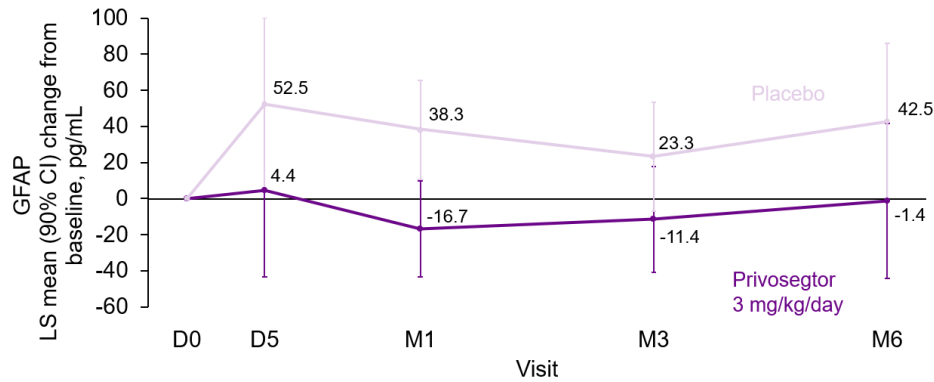
**Figure 2.** Change from baseline in plasma NfL levels



### Plasma GFAP levels

- At Day 5, the mean increase in plasma GFAP was greater in the placebo group than the privosegtor group (LSM change: 52.5 pg/mL vs 4.4 pg/mL, respectively; Figure 3).
- At subsequent time points, the mean GFAP levels declined from baseline in the privosegtor group but remained elevated above baseline with placebo.

**Figure 3.** Change from baseline in plasma GFAP levels



## Conclusions

Increases in plasma NfL and GFAP levels were smaller with privosegtor vs placebo, particularly at early timepoints close to acute ON onset.

These findings, alongside the observed improvements in low-contrast visual function and preservation of retinal structure, provide convergent evidence supporting privosegtor as a potential neuroprotective therapy.

## Key takeaways

- In addition to improving visual function and preserving retinal structure, privosegtor was associated with a lower increase in plasma NfL and GFAP levels versus placebo.**
- PIONEER-1 (NCT07623668) will further evaluate privosegtor as a potential neuroprotective therapy for ON.**

**References.** 1. Bennett J, et al. Lancet Neurol. 2023; 22:89-100; 2. Villoslada P, et al. Neurotherapeutics. 2019;16(3):808-827; 3. Villoslada P, et al. Neurology. 2026;106(11\_Supplement\_1):3177

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