Serum Neurofilament Changes in Progressive MS: Exploring the Impact of Vidofludimus Calcium by Age and Disability – Insights from the CALLIPER Study Interim Analysis

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Introduction

CALLIPER is a phase 2, multicenter, randomized, double-blind, placebo-controlled trial assessing efficacy and safety of vidofludimus calcium in progressive MS, including primary progressive and secondary progressive MS. Vidofludimus calcium is an orally available Nurr1 agonist[1] (a neuroprotective target in neurodegenerative diseases) and a highly selective 2nd generation DHODH inhibitor, which is being evaluated for its neuroprotective effects in progressive MS.

Objective

Explore the impact of vidofludimus calcium on serum neurofilament light chain (NfL) across different baseline disability scores and age groups. Recent data showed that lower NfL levels indicate a lower risk of future disability progression in progressive MS[2].

Method

This study randomized 467 patients with PPMS (32.5 %), n-aSPMS (59.5 %) and aSPMS (7.9 %) to vidofludimus calcium or placebo and they are being followed for up to 120 weeks. A pre-planned interim analysis evaluating serum NfL was conducted after half of the study participants completed 24 weeks of study treatment and had biomarker data available at baseline and Week 24. Serum NfL levels were assessed by the Quanterix Simoa® Assay.

Results

- 203 patients were available for this interim analysis, of which 61% had n-aSPMS, 10% active SPMS and 29% PPMS (Figure 1).
- In the overall study population, average serum NfL was decreased in the vidofludimus calcium group by 22.4% from baseline to week 24 (p=0.01 as compared to placebo).
- A reduction was seen across subgroups by baseline EDSS and Age (Figure 3 and 4).

Baseline Characteristics[3] Full Study Population (N=467)

Age [years], median (min–max)	51.0 (21–65)
Gender (n and % female)	302 (64.7 %)
Race (n and % White)	460 (98.7 %)
BMI [kg/m²], **median** (min–max)	25.0 [15.8–46.6]
SDMT [points], **median** (min–max)	35.0 [0–180]
EDSS, median (min–max)	5.5 [2.5–6.5]

Figure 1: Progressive Disease Subtypes

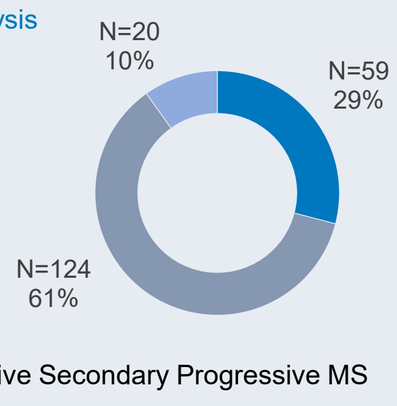


Figure 2: Change in Serum NfL for Vidofludimus Calcium in the Overall Population at Week 24 (Change from Baseline as Compared to Placebo)

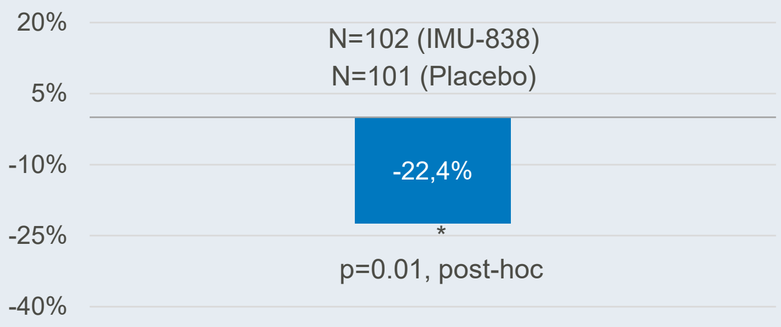


Figure 3: Percent Change in Serum NfL in Vidofludimus Calcium and Placebo Groups from Baseline to Week 24, Presented as Subgroups by Baseline EDSS[4]

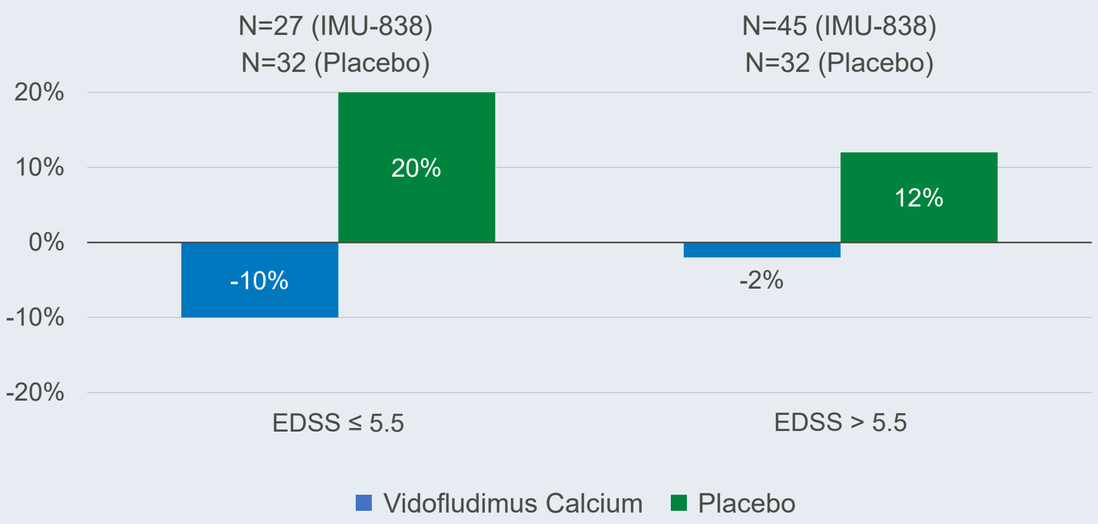
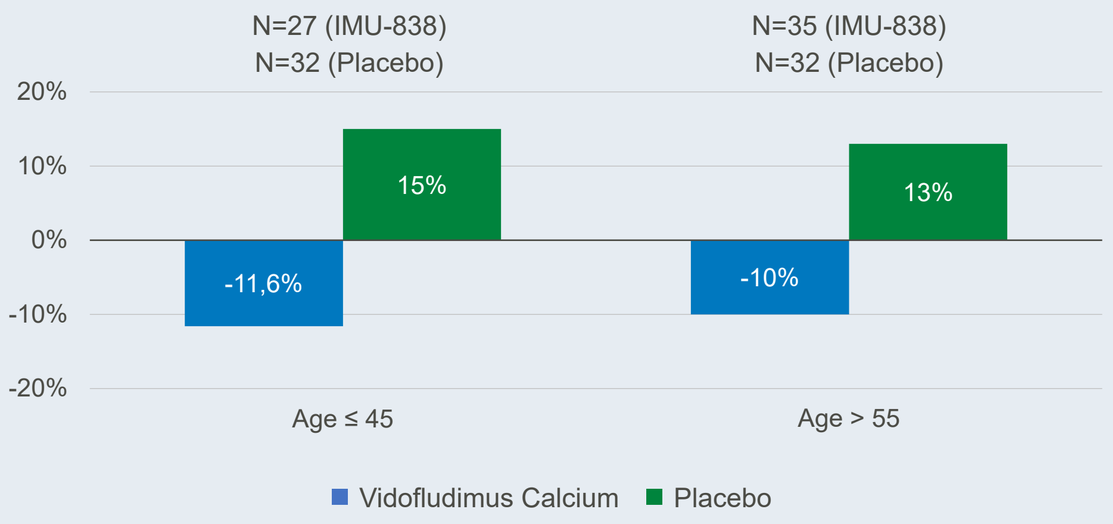


Figure 4: Percent Change in Serum NfL in Vidofludimus Calcium and Placebo Groups from Baseline to Week 24, Presented as Subgroups by Baseline Age[4]



Conclusion

The data suggest that vidofludimus calcium treatment consistently reduces NfL levels compared to baseline across different patient subgroups based on age and disability scores. These observations support the potential effectiveness of vidofludimus calcium in slowing disease progression in progressive MS.

[1] Vietor, J. et al. (2023). Development of a Potent Nurr1 Agonist Tool for In Vivo Applications. Journal of Medicinal Chemistry, 66(9), pp.6391-6402.
[2] Bar-Or, A et al. (2023). Blood neurofilament light levels predict non-relapsing progression following anti-CD20 therapy in relapsing and primary progressive multiple sclerosis: findings from the ocrelizumab randomised, double-blind phase 3 clinical trials. EBioMedicine, 93, 104662.
[3] BMI: Body Mass Index; SDMT: Symbol Digit Modalities Test; EDSS: Expanded Disability Status Scale
[4] Data based on number of patients with non-missing values.