Impact of Vidofludimus Calcium on Serum Neurofilament in Progressive MS: Assessment from the CALLIPER Interim Analysis.

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Background

CALLIPER is a phase 2, multicenter, randomized, double-blind, placebo-controlled trial assessing efficacy and safety of vidofludimus calcium (VidoCa) in progressive MS. VidoCa is an orally available Nurr1 activator (a neuroprotective target in neurodegenerative diseases) and a highly selective 2nd generation DHODH inhibitor, which is being evaluated for its anti-inflammatory and neuroprotective effects.

Objective

Recent data showed that lower Nfl (neurofilament light chain) levels indicate a lower risk of future disability progression in Primary Progressive MS (PPMS)[1]. This interim analysis provided initial data how VidoCa impacts serum Nfl levels in patients with PPMS, non-active Secondary PMS (n-aSPMS) and active SPMS (aSPMS).

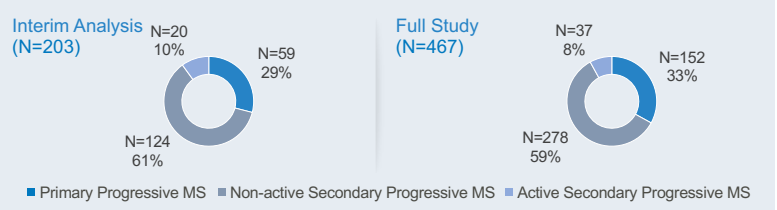
Methods

467 patients with PPMS (35.2%), n-aSPMS (59.5%) and aSPMS (7.9%) were randomized 1:1 to VidoCa or placebo and will be followed for 120 weeks. A pre-planned interim analysis was conducted after approximately half of the study participants completed 24 weeks 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 and 29% PPMS (Figure 1)
- Mean age was 49.7 and mean disease duration was 4.6 years in the full study population
- Compared to placebo, serum Nfl in the overall study population was decreased in the VidoCa group by 22.4% (p=0.01)
- A reduction was seen across all subtypes: -18.8% in PPMS, -20.1% in n-aSPMS and -43.3% in aSPMS against placebo (Figure 2)
- A reduction in Nfl of -38.4% and -15.2% was seen in those with and without activity at baseline (gadolinium-enhancing lesions and/or active SPMS) (Figure 3)

Figure 1: Progressive Disease Subtypes[2]



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/m^2], **median** (min–max)	25.0 [15.8–46.6]
SDMT [points], **median** (min–max)	35.0 [0–180]
EDSS at Visit 1, median (min–max)	5.5 [2.5–6.5]

Figure 2: Improvements in Serum Nfl for Vidofludimus Calcium Consistent Throughout the Overall PMS Population and All Subtypes
Change baseline to Week 24 compared to placebo[4]

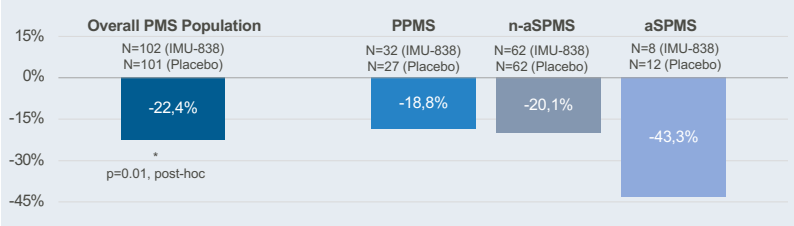


Figure 3: Change in Serum NfL for Vidofludimus Calcium in Patients With/Without Disease or MRI Activity at Baseline
Change baseline to Week 24 compared to placebo[5]

Conclusion

In this interim analysis, Nfl was reduced after 24-week treatment with VidoCa, and the reduction was consistently observed across progressive MS subtypes, including in both patients with baseline disease activity and those without baseline disease activity. The reductions observed in PPMS and n-aSPMS, where little focal inflammation is typically present, supports VidoCa´s neuroprotective potential.

1. *Bar-Or A. et al., EBioMedicine. 2023 Jul;93:104662*
2. Disease subtype information are used as diagnosis entered by the investigator at study entry
3. BMI: Body Mass Index; SDMT: Symbol Digit Modalities Test; EDSS: Expanded Disability Status Scale
4. Standard deviation for change from baseline in % of baseline: CALLIPER week 24: IMU-838 35.7%, PPMS: IMU-838 7.1%, n-aSPMS: IMU-838 14.7%, aSPMS: IMU-838 10.3%, 95% Hodges-Lehmann confidence bound EMPhASIS week 24 for 45mg IMU-838: lower boundary -41.0%, upper boundary -12.0%, includes all randomized patients with available neurofilament data at interim analysis, arithmetic mean value for group averages; aSPMS and n-aSPMS designation as per diagnosis by clinical investigator at study entry RRMS: relapsing-remitting multiple sclerosis; PPMS: primary progressive multiple sclerosis; SPMS: secondary progressive multiple sclerosis; n-a: non-active; a: active
5. Active = any G+MRI lesion at baseline MRI OR/AND active SPMS as defined in the protocol; Non-Active = without G+MRI lesions at baseline.