Effect of Vidofludimus Calcium, a Direct Nurr1 Activator and Selective DHODH Inhibitor, on Patient-Reported Outcomes (PRO) in Progressive MS: Data from Phase 2 CALLIPER Trial

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Background & Objectives

- Nuclear receptor-related 1 (Nurr1) is a transcription factor that regulates pathways involved in neuronal survival, with emerging evidence supporting a protective role in neurodegenerative disease.
- Vidofludimus calcium (VidoCa) is a direct Nurr1 activator and selective dihydroorotate dehydrogenase (DHODH) inhibitor.
- In the placebo-controlled Phase 2 CALLIPER study in progressive multiple sclerosis (PMS), VidoCa showed clinically meaningful trends in reducing confirmed disability worsening and increasing confirmed disability improvement across the overall population and subgroups during the double-blind period.
- This analysis reports patient-reported outcomes (PROs) from the CALLIPER study.

Methods

CALLIPER was a randomized, double-blind, placebo-controlled Phase 2 trial that enrolled 467 participants aged 18–65 years with primary (PPMS; n=152) or secondary progressive multiple sclerosis (SPMS; n=315).

Participants were randomized 1:1 to receive vidofludimus calcium (VidoCa) 45 mg once daily (n=235) or placebo (n=232).

The double-blind treatment period ranged from 72 to 120 weeks.

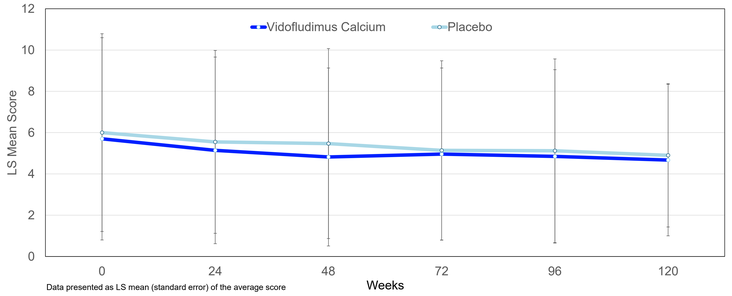
Patient-reported outcomes (PROs), including depressive symptoms (Patient Health Questionnaire-9 [PHQ-9]) and treatment satisfaction (Treatment Satisfaction Questionnaire for Medication), were assessed every 24 weeks.

These endpoints were exploratory, and the study was not powered for formal statistical comparisons.

DHODH = dihydroorotate dehydrogenase; MRI = magnetic resonance imaging; MS = multiple sclerosis; Nurr1 = transcription factor nuclear receptor-related 1, PHQ-9 = Patient Health Questionnaire-9, PMS = progressive multiple sclerosis, PRO = patient-reported outcome, SPSM = secondary progressive multiple sclerosis, TSMQ = Treatment Satisfaction Questionnaire for Medication, VidoCa = vidofludimus calcium

Results

Patient Health Questionnaire-9 (PHQ-9)



Data presented as LS mean (standard error) of the average score

Change from Baseline in PHQ-9 – Total Score

	Baseline	Week 48	Week 72	Week 120
Vidofludimus Calcium	0	-0.786 (0.268)	-0.568 (0.273)	-1.777 (0.456)
Placebo	0	-0.347 (0.268)	-0.609 (0.277)	-0.525 (0.487)

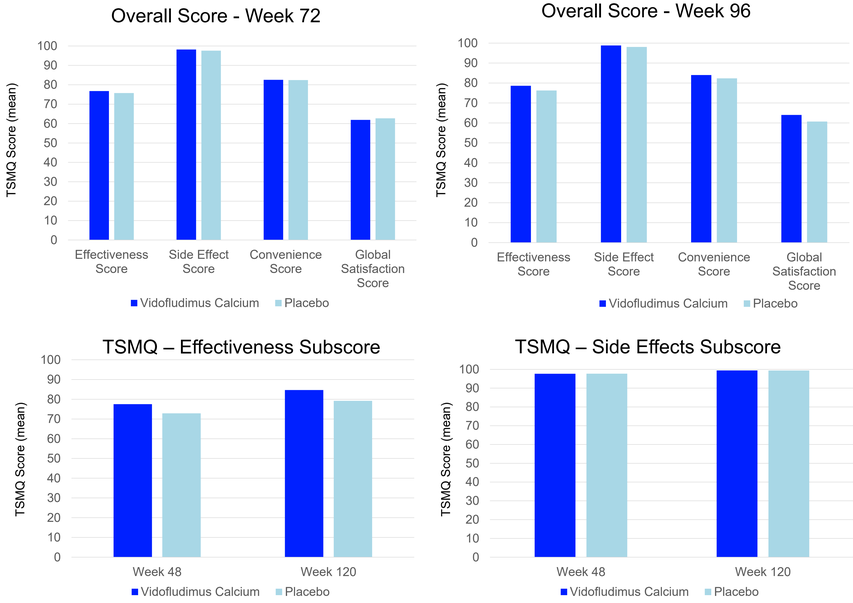
Data presented as LS mean (standard error) of the change from baseline

Change from Baseline in PHQ-9 – Question 9: Thoughts You Be Better Off Dead

	Baseline	Week 48	Week 72	Week 120
Vidofludimus Calcium	0	-0.071 (0.01)	-0.064 (0.11)	-0.044 (0.031)
Placebo	0	-0.07 (0.01)	-0.074 (0.11)	-0.05 (0.034)

Data presented as LS mean (standard error) of the change from baseline

Treatment Satisfaction Questionnaire for Medication (TSQM)



Conclusion

Treatment with vidofludimus calcium (VidoCa) was not associated with worsening depressive or suicidal thoughts compared with placebo.

Patient-reported treatment effectiveness was numerically higher with VidoCa, while reported side effect burden was similar between treatment arms.

Overall, these findings suggest a favorable patient-reported profile for VidoCa.

VS, MO, JM, FG and AW are employees of trial sponsor.

AM is a shareholder and former employee of trial sponsor and a holder of patents for the drug under investigation.

RJF reports personal consulting fees from Astoria Biologica, Biogen, Bristol Myers Squibb, Cognito, EMD Serono, Galvani, Immunic, INmune Bio, Kiniksa, Novartis, Sanofi, Siemens, and TG Therapeutics and has served on advisory committees for AB Science, Biogen, Immunic, Novartis, and Sanofi, and received clinical trial contract and research grant funding from Biogen, Novartis, and Sanofi.