Effect of Vidofludimus Calcium, a Novel Nurr1 Activator and Selective DHODH Inhibitor, on MRI Outcomes in Progressive Multiple Sclerosis: Data from the Phase 2 CALLIPER Trial

Poster Download

V. Sciacca
Immunic AG, Gräfelfing, Germany

M. Ondrus
Immunic AG, Gräfelfing, Germany

A. Schreieck
Immunic AG, Gräfelfing, Germany

J. Myles
Immunic AG, Gräfelfing, Germany

F. Ghadiri
Immunic AG, Gräfelfing, Germany

A. Weerage
Immunic AG, Gräfelfing, Germany

N. de Stefano
University of Siena, Siena, Italy

R. J. Fox
Cleveland Clinic, Cleveland, OH, USA

A. Muehler
Immunic AG, Gräfelfing, Germany

Background & Objectives

Vidofludimus calcium (VidoCa) is an orally available direct activator of the transcription factor nuclear receptor-related 1 (Nurr1) and selective inhibitor of dihydroorotate dehydrogenase (DHODH). Nurr1 is a known neuroprotective target and its activation would be hypothesized to result in slowing neurodegeneration. DHODH inhibition is a proven mechanism known to exert selective anti-inflammatory effects on B- and T-cells and antiviral activity.

VidoCa was tested in a Phase 2 study (CALLIPER) in progressive multiple sclerosis (MS) patients, including both SPMS and PPMS patients. The results provided medically meaningful positive trends in confirmed disability worsening in the overall study population as well as across subpopulations and disability endpoints, while not parallelled by changes in brain atrophy. The objective of this abstract is to present more detailed magnetic resonance imaging (MRI) results of the CALLIPER study.

Methods

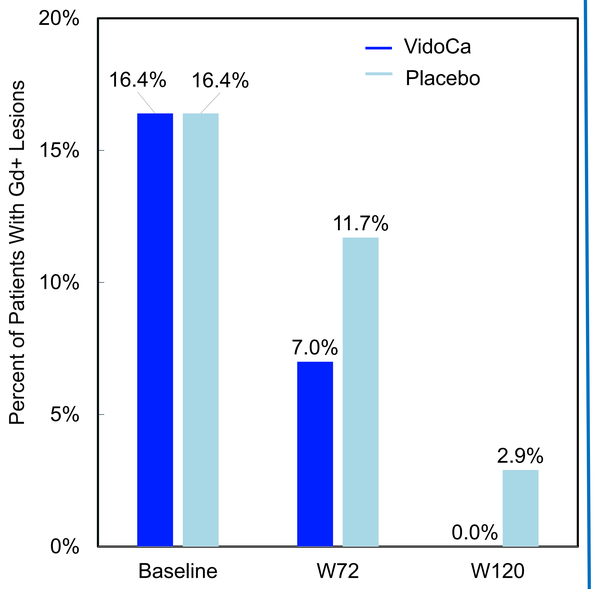
CALLIPER was a randomized, double-blind, placebo-controlled trial, which enrolled 467 participants aged 18 to 65 years with primary progressive MS (PPMS, N= 152) or secondary progressive MS (SPMS; N=315). Eligible participants were randomized 1:1 to receive either 45 mg once daily VidoCa (N=235) or matching placebo (N=232). The duration of double-blind treatment was up to 120 weeks with a minimum of 72 weeks. MRI examinations were performed at baseline and Weeks 24, 48, 72, 96 and 120 (gadolinium [Gd] at baseline and Weeks 72 and 120). The same standardized MRI protocol (allowed field strengths of 1.5 and 3 Tesla) was used at all study centers.

The number of SELs was assessed between baseline and week 96 using a previously established procedure (Elliott C et al., MSJ, 2019). In addition, we report the mean number of SELs at each intermediate time point. Briefly, among lesions classified as SELs at week 96, we retained at each time point only those lesions that both expanded (as determined by the Jacobian) and exhibited a significant, concentric reduction in T1-weighted signal intensity at the lesion rim, consistent with evolving tissue damage.

PPMS = primary progressive multiple sclerosis, SPMS = secondary progressive multiple sclerosis, Gd+ = gadolinium-enhancing on T1-weighted magnetic resonance imaging, DHODH = dihydroorotate dehydrogenase; MRI = magnetic resonance imaging; MS = multiple sclerosis; Nurr1 = transcription factor nuclear receptor-related 1, SEL = slowly expanding lesion; VidoCa = vidofludimus calcium; W = week

Results - Gd+ MRI Lesions

Percent of Patients with Gd+ Lesions



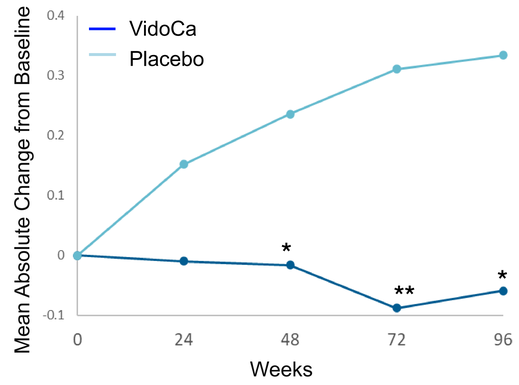
Number of patients included: baseline 464 (VidoCa 232, Placebo 232), W72 366 (VidoCa 186, Placebo 180), W120 80 (VidoCa 45, Placebo 35)

Number of Patients with Any Gd+ Lesion During Study

	N (Gd+)	% (Gd+)	Relative Risk Ratio
VidoCa	15/235	6.4%	0.59
Placebo	25/232	10.8%	

Results - T2 Lesion Load

Mean Volume Change of New/Enlarging T2 Lesions



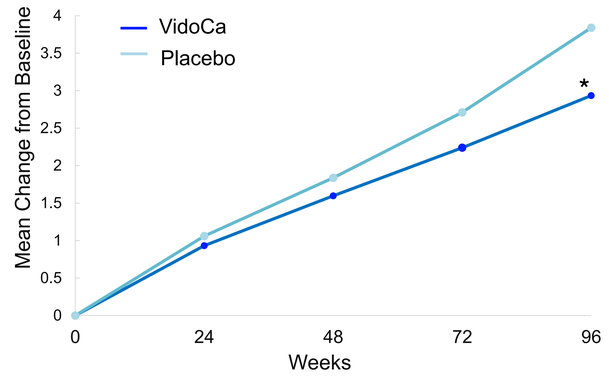
Number of patients included in arithmetic mean change calculation (in cm^3): Baseline 466 (VidoCa 234, Placebo 232),W24 436 (VidoCa 217, Placebo 219), W48 409 (VidoCa 206, Placebo 203), W72 369 (VidoCa 189, Placebo 180), W96 198 (VidoCa 103, Placebo 95)
Ranked ANOVA test with factors for treatment and stratification factors used at randomization and baseline value as a continuous covariate. The test and associated p-value for the test of row mean differences is presented.
***p<0.05 / **p<0.005**

Number of Patients with New/Enlarging T2 Lesions

	VidoCa	Placebo
At any time during study	41.2% (91/221)	50.2% (110/219)
W72	18.5% (35/189)	30.0% (54/180)

Results - Number of SELs

Mean Change from Baseline in Number of SELs



Number of patients included: baseline 418 (VidoCa 209, Placebo 209), W24 411 (VidoCa 204, Placebo 207), W48 401 (VidoCa 200, Placebo 201), W72 360 (VidoCa 183, Placebo 177), W96 196 (VidoCa 103, Placebo 93)
Mixed model for repeated measures (MMRM) estimates are adjusted for stratification factors used at baseline randomization. 2-sided p-value is presented.
***p<0.05**

Least Square Mean Number of SEL Per MRI Examination

Weeks	VidoCa	Placebo
Baseline	0	0
24	0.932	1.060
48	1.597	1.837
72	2.239	2.711
96	2.935	3.840

Conclusion

The MRI results of the phase 2 CALLIPER study show evidence that vidofludimus calcium reduces the MRI hallmarks of acute-focal (Gd+ lesions, T2 lesion load) as well as chronic-compartmentalized inflammation (SELs) in a progressive MS patient population.

VS, MO, AS, JM, FG, AW and AM are employee of trial sponsors.
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.
NdS has received honoraria from Biogen Idec, Bristol Myers Squibb, Celgene, Genzyme, Immunic, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, and Teva for consulting services, speaking, and travel support. He serves on advisory boards for Biogen-Idec, Immunic, the healthcare business of Merck KGaA, Darmstadt, Germany, Novartis, Roche, and Sanofi. He has received research support from the Italian Ministry of University and Research and Fondazione Italiana Sclerosi Multipla. He is the Associate Editor of Neurological Sciences and co-founder of Siena-Imaging S.r.l.