Safety and Tolerability of Vidofludimus Calcium, a Direct Nurr1 Activator and Selective DHODH Inhibitor: Data from Phase 2 CALLIPER Trial

A. Muehler
Formerly Immunic, Inc./AG
USA / Germany

V. Sciacca
Immunic AG,
Gräfelfing, Germany

M. Ondrus
Immunic AG,
Gräfelfing, Germany

J. Myles
Immunic, Inc.,
New York, NY, USA

F. Ghadiri
Immunic AG,
Gräfelfing, Germany

A. Weerage
Immunic AG,
Gräfelfing, Germany

A. Lublin
Immunic, Inc.,
New York, NY, USA

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

Background & Objectives

Nuclear receptor-related 1 (Nurr1) is a transcription factor that regulates genes that enhance neuronal survival and growing evidence supports its protective role in neurodegenerative diseases. Vidofludimus calcium is a direct activator of Nurr1 and selective inhibitor of dihydroorotate dehydrogenase (DHODH). vidofludimus calcium was tested in a Phase 2 study (CALLIPER) in progressive multiple sclerosis (PMS) 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.

The objective of this poster is to present an overview of safety findings from 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). Participants were randomized 1:1 to receive either 45 mg vidofludimus calcium (N=235) or placebo (N=232). The duration of double-blind treatment was up to 120 weeks with a minimum of 72 weeks.

Safety data, such as adverse events, vital signs and blood and urine laboratory tests were collected at baseline and in 12-week intervals.

DHODH = dihydroorotate dehydrogenase, EDSS = expanded disability status scale, MRI = magnetic resonance imaging; MS = multiple sclerosis; n = number, Nurr1 = transcription factor nuclear receptor-related 1, PMS = progressive multiple sclerosis, PPMS = primary progressive multiple sclerosis, SAE = serious adverse event, SPSM = secondary progressive multiple sclerosis, TEAE = treatment-emergent adverse event, ULN = upper limit of normal, yrs = years,

Results

Disposition, demographics, and clinical characteristics

	Placebo	Vidofludimus calcium
Disposition		
Randomized (n)	232	235
Duration of exposure (days)	586.5 (500.0 – 752.0)	591.2 (502.0 – 758.0)
Completed main treatment period	155 (66.8%)	167 (71.1%)
Discontinued main treatment prematurely	77 (33.2%)	68 (28.9%)
Demographics & clinical characteristics		
Female	149 (64.2%)	153 (65.1%)
Age (yrs)	51 (43 – 57)	51 (44 – 58)
White	231 (99.6%)	229 (97.9%)
Baseline EDSS	5.50 (4.50 – 6.00)	5.50 (4.50 – 6.00)
PPMS	75 (32.3%)	77 (32.8%)
Non-active SMPS	135 (57.4%)	133 (57.3%)
Active SPMS	24 (10.3%)	23 (9.8%)

Data expressed as n (%) or median (interquartile range)

TEAEs and SAEs

	Placebo	Vidofludimus calcium
Any TEAE	159 (68.5%)	163 (69.4%)
Urinary tract infection	36 (15.5%)	39 (16.6%)
Back pain	17 (7.3%)	9 (3.8%)
Headache	10 (4.3%)	16 (6.9%)
TEAE leading to discontinuation of study drug	6 (2.6%)	6 (2.6%)
Any SAE	15 (6.5%)	19 (8.1%)
Serious related SAE	2 (0.9%)	0
Death	0	0

Data expressed as n (%)

Liver, renal, and infectious TEAEs

	Placebo	Vidofludimus calcium
Any liver TEAE	12 (5.2%)	13 (5.5%)
AST >3X ULN	5 (2.2%)	5 (2.2%)
AST >5X ULN	5 (2.2%)	1 (0.4%)
AST >10 ULN	1 (0.4%)	1 (0.4%)
ALT >3X ULN	6 (2.6%)	7 (3.0%)
ALT >5X ULN	4 (1.7%)	2 (0.9%)
ALT >10X ULN	4 (1.7%)	1 (0.4%)
ALT/AST >3X ULN and total bilirubin 2X ULN	0	0
Any renal and urinary disorder	14 (6.0%)	14 (6.0%)
Proteinuria	1 (0.4%)	3 (1.3%)
Urinary incontinence	3 (1.3%)	0
Urinary tract inflammation	1 (0.4%)	2 (0.9%)
Infections and infestations	93 (40.1%)	95 (40.4%)
Urinary tract infection	36 (15.5%)	39 (16.6%)
Upper respiratory tract infection	11 (4.7%)	15 (6.4%)
Nasopharyngitis	14 (6.0%)	11 (4.7%)

Data expressed as n (%)

Conclusion

Overall, safety findings from the CALLIPER study demonstrated a similar incidence and spectrum of adverse events in vidofludimus calcium-treated patients with MS compared with placebo, consistent with observations from prior clinical studies of vidofludimus calcium in MS. Collectively, these results further support the favorable safety and tolerability profile of vidofludimus calcium.

AL, VS, MO, JM, FG and AW are employees of trial sponsor. AM is former employee of trial sponsor and holder of patents for the drug under investigation.

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