# Update on the Assessment of Long-Term Safety and Tolerability of Vidofludimus Calcium in Patients with Relapsing-Remitting Multiple Sclerosis in the Open-Label Extension Period of the Phase 2 EMPhASIS Trial

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## Background

Vidofludimus calcium is a highly selective oral Nurr1 agonist, a neuroprotective target in neurodegenerative diseases, and DHODH inhibitor. In the double-blind phase 2 EMPhASIS trial in relapsing-remitting multiple sclerosis (RRMS), vidofludimus calcium showed a safety and tolerability profile comparable to placebo and a robust reduction in MRI activity versus placebo. A phase 3 program in relapsing multiple sclerosis is currently ongoing (fully recruited with anticipated topline data by the end of 2026).

## Objective

After completion of the double-blind treatment period, study participants had the option to enter the long-term open-label extension (OLE) period. Here we report an update on the long-term treatment persistence as well as safety and tolerability of vidofludimus calcium in patients with RRMS in the OLE period.

## Methods

Of 268 patients with RRMS who started 24 weeks of double-blind treatment with vidofludimus calcium or placebo, 254 patients (95%) completed the blinded treatment period and then continued in the OLE period. Initially, patients in the OLE period were treated with either 30 or 45 mg of vidofludimus calcium given once daily, and with full study results available, all patients were transitioned to 30 mg of vidofludimus calcium once daily.

## Results

As of January 14, 2025, 182 patients remained on open-label treatment with vidofludimus calcium. The annualized discontinuation rate was 6.4%. Using a database cut-off date of January 14, 2025, approximately 952 treatment years were included in the safety analysis. The median treatment duration per patient in the OLE period as of database cut-off was 1667.5 days.

### Subject Disposition

| | Total Number of Patients[a] |
|---|---|
| Randomized in Main Treatment Period | 269 |
| Started Double-Blind Treatment | 268 |
| Discontinued Double-Blind Treatment | 14 |
| Completed Double-Blind Treatment (Week 24) | 254 |
| Started Open-Label Treatment | 254 |
| Discontinued Open-Label Treatment[b] | 72 (of which 11 are due to MS-related clinical events) |
| – Discontinuations Related to War in Ukraine | 3 (2 relocation to other country, 1 lost to follow-up) |
| Continuing Open-Label Extension Treatment[c] | 182 |

**Highlights of subject disposition:**

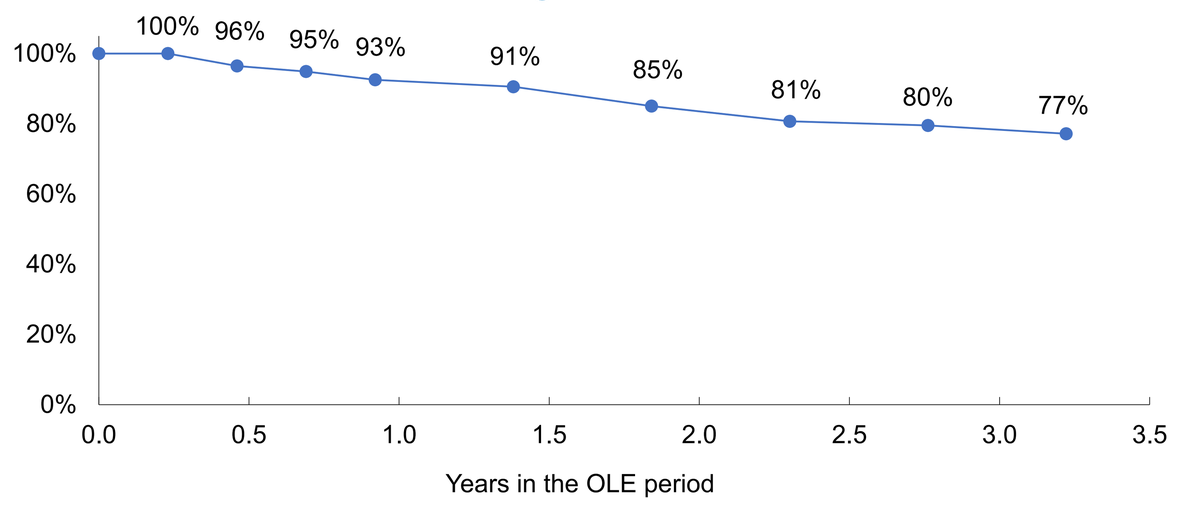
- Data for approximately 952 treatment years in OLE treatment with vidofludimus calcium now available in this study
- Low rate of treatment discontinuations during OLE treatment
  - Per year of study, approximately 6.4% discontinuation rate
- 182 of 254 RRMS patients continuing in OLE as of database cut-off
- Longest continuous treatment period in study: > 5.5 years

a. Includes both patient cohorts and all treatment groups, including placebo, 10, 30 and 45 mg of vidofludimus calcium. b. Between 29-Aug-2019 and 14-Jan-2025. Database cut 14-Jan-2025

### TEAEs Occurring in at Least 3 Patients in the OLE Period

| TEAE by PT | No. of patients (%) |
|---|---|
| COVID-19 | 24 (9%) |
| Nasopharyngitis | 15 (6%) |
| Back pain | 13 (5%) |
| Headache | 12 (5%) |
| Anemia | 6 (2%) |
| Influenza | 6 (2%) |
| Upper respiratory tract infection | 6 (2%) |
| Urinary tract infection | 6 (2%) |
| Cystitis | 5 (2%) |
| Depression | 5 (2%) |
| Fatigue | 4 (2%) |

### Percent of Patients Receiving Vidofludimus Calcium in the OLE Period




### SAEs, Renal Events, and Liver Events

**Rate of SAEs:**

0.02 serious adverse events per treatment year, i.e., 1 SAE for every 59.5 treatment years

**Rate of renal events:**

0.012 renal events per treatment year, i.e., 1 renal event for every 79 treatment years

**Rate of liver events:**

0.010 liver events per treatment year, i.e., 1 liver event for every 95 treatment years

- Five TEAEs led to treatment discontinuation, none of which were considered related to vidofludimus calcium
  - Gilbert syndrome (n=1)
  - Malignant neoplasms (n=3)
  - Deep vein thrombosis (n=1)
- Death: pulmonary embolism (n=1)

Safety analysis set of open-label extension phase: N = 254 patients, approximately 952 treatment years covered, up to >288 weeks of study treatment, and patients treated with 30 mg or 45 mg vidofludimus calcium
Liver and renal events are treatment-emergent adverse events with predetermined preferred terms related to renal function from System Organ Class of 'Renal and urinary disorders' or 'Investigations' or related to liver function from System Organ Class of 'Hepatobiliary disorders' or 'Investigations' are counted.

Gilbert syndrome: relationship to study medication: not related, outcome: not recovered
Malignant neoplasms (invasive lobular breast carcinoma, malignant melanoma stage 1, breast cancer): not related
Deep Venous Thrombosis: relationship to study medication: not related, outcome: recovered
Pulmonary embolism: relationship to study medication: not related, outcome: fatal

## Conclusion

Patients continuing on vidofludimus calcium treatment in the OLE period of the EMPhASIS trial experienced a low discontinuation rate, low rates of adverse and serious adverse events, and no new safety signals. Overall, these results support a favorable safety and tolerability profile for vidofludimus calcium during long-term treatment.

Nurr1 = nuclear receptor related-1; DHODH = dihydroorotate dehydrogenase; MRI = magnetic resonance imaging; MS = multiple sclerosis; PT=preferred term; OLE = open-label extension; RRMS = relapsing-remitting multiple sclerosis; SAE = serious adverse event; TEAE = treatment emergent adverse event

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