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 Trial (EMPhASIS)

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Background

Vidofludimus calcium is a highly selective oral 2nd generation DHODH inhibitor, which in the double-blind phase 2 EMPhASIS trial in relapsing remitting multiple sclerosis (RRMS) showed a safety and tolerability profile comparable to placebo and a robust benefit on MRI activity versus placebo. A Phase 3 program in relapsing MS is currently ongoing.

Objective

Upon completion of the double-blind treatment period, the study participants could enter the long-term open-label extension (OLE) period. Here we report the first interim analysis of the OLE period regarding safety and tolerability of vidofludimus calcium in RRMS.

Methods

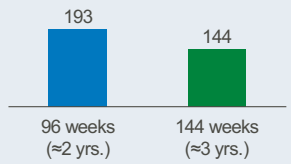
Of 268 patients with RRMS who started the double-blind treatment of 24 weeks, 254 patients completed the blinded treatment period and then continued in the OLE period with either 30 or 45 mg of vidofludimus calcium given once daily. Using data from the October 16, 2022 data lock, approximately 519 treatment years were included in this interim analysis.

Results

As of October 16, 2022, 209 patients remained on OLE treatment, with some patients having received more than 180 weeks of active treatment. 193 patients were treated in OLE at least 96 weeks and 144 patients at least 144 weeks. The annualized discontinuation rate was 5.3%.

Patients on OLE Treatment

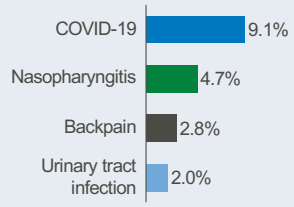
As of October 16, 2022



Annualized discontinuation rate **5.3%**[1]

Most Common Treatment-Emergent Adverse Events (TEAEs)

% Number of Patients



- The overall rates of renal and liver TEAEs per treatment year were 0.023 and 0.015, respectively.
- Four TEAEs lead to treatment discontinuation.
- 14 serious adverse events (SAEs) were reported, yielding an SAE rate of 0.027 per patient per treatment year.

- No SAEs were considered related to IMP.
- No new safety signals were observed.
- No signal for changes in hematology parameters were seen.

EMPhASIS Interim Analysis OLE Period

Exposure Data (Database Extraction: October 16, 2022)

	Total Number of Patients[2]
Randomized	269
Started Blinded Treatment	268
Discontinued Blinded Treatment	14
Completed Blinded Treatment (Week 24)	254
Started Open-Label Treatment	254
Discontinued Open-Label Treatment[3]	45 (of which 10 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[4]	209

Highlights:

- Data for approximately 519 treatment years in OLE treatment with vidofludimus calcium now available in this study
- Low rate of treatment discontinuations during open-label treatment
  - Per year of study, approximately 5.3% discontinuation rate
- 193 patients treated more than 96 weeks (≈2 yrs.)
- 144 patients treated more than 144 weeks (≈3 yrs.)
- Longest continuous treatment period in study: >180 weeks (≈ 4 yrs.)

Summary of Safety & Tolerability in OLE Period[5]

Patients Treated with 30 or 45 mg Vidofludimus Calcium, No Control Arm

Rate of serious adverse events (SAE):

0.027 serious adverse events per treatment year, i.e. 1 SAE for every 37 treatment years

Rate of renal events:

0.023 renal events per treatment year, i.e. 1 renal event for every 43 treatment years

Rate of liver events:

0.015 liver events per treatment year, i.e. 1 liver event for every 64 treatment years

- Patients with adverse events related to increases in transaminase levels: 4
- All events of mild severity, only 1 patient had transaminase levels >5x ULN[6]
- Outcome for all 4 patients: fully recovered, no drug discontinuation

Conclusion

The OLE period of EMPhASIS experienced a very low discontinuation rate, low rates of adverse events and serious adverse events, and no new safety signals. Overall, this data suggests a favorable safety profile in long-term treatment with vidofludimus calcium.

1) Of the 209 that continued in open-label extension treatment
2) Including both patient cohorts and all treatment groups, including placebo, 10, 30 and 45 mg of vidofludimus calcium
3) Between 29-Aug-2019 and 16-Oct-2022
4) By database cut 16-Oct-2022
5) Safety analysis set of open-label extension phase: N = 254 patients, approximately 519 treatment years covered, up to >180 weeks of study treatment
6) ULN: upper limit normal