Assessment of effect of vidofludimus calcium on confirmed disability worsening in the blinded treatment and open-label extension periods of the phase 2 study (EMPhASIS) in relapsing-remitting multiple sclerosis

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Background

Vidofludimus calcium (VidoCa) is a highly selective oral 2nd generation DHODH inhibitor, which in the double-blind phase 2 EMPhASIS trial in relapsing-remitting multiple sclerosis (RRMS) has shown a robust activity against placebo and a safety and tolerability profile comparable to placebo, presumably due to lack of off-target effects on kinases. This summary describes the first interim analysis of the ongoing long-term open-label extension period focusing on disability worsening during the continued treatment with VidoCa in RRMS patients.

Objective

EMPhASIS was a randomized, placebo-controlled phase 2 trial in RRMS, assessing efficacy and safety of 10, 30 and 45mg of VidoCa as compared to placebo for a period of 24-weeks. Upon completion of the double-blind treatment period, the study participants could enter the long-term open-label extension (OLE) period with further monitoring of safety, tolerability, and selected efficacy parameters (such as EDSS). Herein we report the long-term activity of VidoCa on confirmed disability worsening events in RRMS patients.

Methods

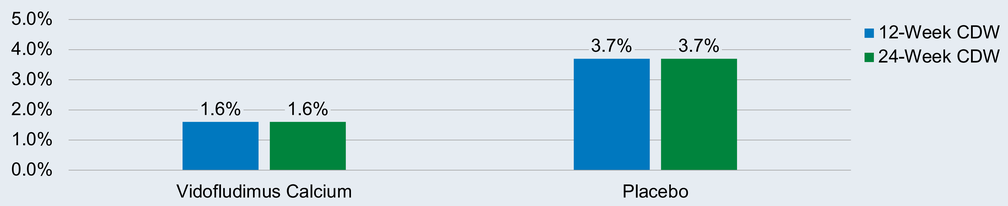
In the EMPhASIS trial, 268 patients with RRMS received study medication with either 10, 30, or 45 mg VidoCa or placebo for a double-blind treatment of 24 weeks. Upon completion of the double-blind period, 254 patients continued in the OLE period. The patients originally randomized to VidoCa 30 and 45 mg continued with the same dose, while the patients originally assigned to placebo or VidoCa 10mg were randomly assigned to either 30 or 45mg of VidoCa. The original treatment allocation was disclosed only after the last patient completed the main treatment period. Subsequently, a transition of all patients in OLE period to 30 mg VidoCa was initiated.

Results

- As of October 2022, 209 patients remained on OLE treatment with VidoCa, with some patients having received more than 180 weeks of active treatment (roughly 3.5 years).
- For the initial 24-week double-blind treatment period, 12-week Confirmed Disability Worsening (12wCDW) and 24-week Confirmed Disability Worsening (24wCDW) events occurred in 1.6% of subjects in the combined VidoCa treatments arms as compared to 3.7% in the placebo group.
- In the OLE period, the proportion of patients free from 12wCDW was 97.2% after 48 weeks and 94.2% after 96 weeks of VidoCa treatment. Similar results were seen for 24wCDW and sustained CDW (i.e. CDW persisting trough last assessment).
- Among VidoCa patients in the OLE period of the trial, 3% experienced one or more relapses within the first year and 6.2% within the first two years.

Confirmed Disability Worsening Events

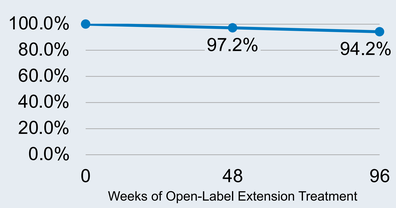
End during the initial 24-week blinded treatment period



Data suggest a possible benefit of VidoCa on **12-week** and **24-week** confirmed disability worsening[1] events as compared to placebo. Confirmatory data will be obtained in the ongoing phase 3 ENSURE clinical program.

Interim analysis regarding 12wCDW events

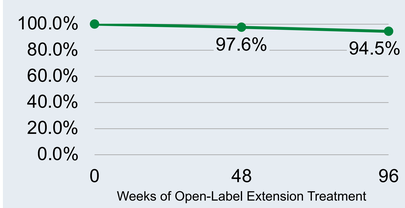
Patients free of 12-week CDW after 1 & 2 years of OLE VidoCa Treatment



Data show that only a few patients on continuous treatment with VidoCa develop **12-week** CDW events over 2 years.

Interim analysis regarding 24wCDW events

Patients free of 24-week CDW after 1 & 2 years of OLE VidoCa Treatment



Data show that only a few patients on continuous treatment with VidoCa develop **24-week** CDW events over 2 years.

Conclusion

Over the 24 weeks of blinded treatment and the open-label extension period, rates of CDW in VidoCa-treated patients were low. These findings provide an initial signal for VidoCa preventing or slowing confirmed disability progression in RRMS.

CDW: confirmed disability worsening; EDSS: Expanded Disability Status Scale

[1]Only disability worsening with a trigger point during the 24-week blinded treatment period are considered. The EDSS increases during the blinded treatment phase were subsequently confirmed during open-label extension phase of the trial. Patients at risk in this analysis are 187 for vidofludimus calcium (pooling 10, 30 and 45 mg data) and 81 for placebo. The trigger event is an EDSS progression defined as an increase in the EDSS compared to Baseline of at least 1.5 points if Baseline EDSS = 0, of at least 1.0 points if Baseline EDSS of 1-5, or of at least 0.5 points if Baseline EDSS ≥ 5.5

12-week CDW: The confirmation event is at least 77 days after the trigger event. At the confirmation event and each assessment between trigger and possible confirmation event, EDSS must be at least as high as at the trigger event.

24-week CDW is defined analogously, the only difference being the time interval between trigger event and confirmation visit, which is at least 161 days.

Full analysis set pooled cohorts 1&2 (N10 = 47, N30 = 71, N45 = 69, NPBO C1 = 69, NPBO C2 = 12)