

Exploring the Potential of Vidofludimus Calcium to Reduce Fatigue in Multiple Sclerosis by Preventing Epstein-Barr Virus Reactivation

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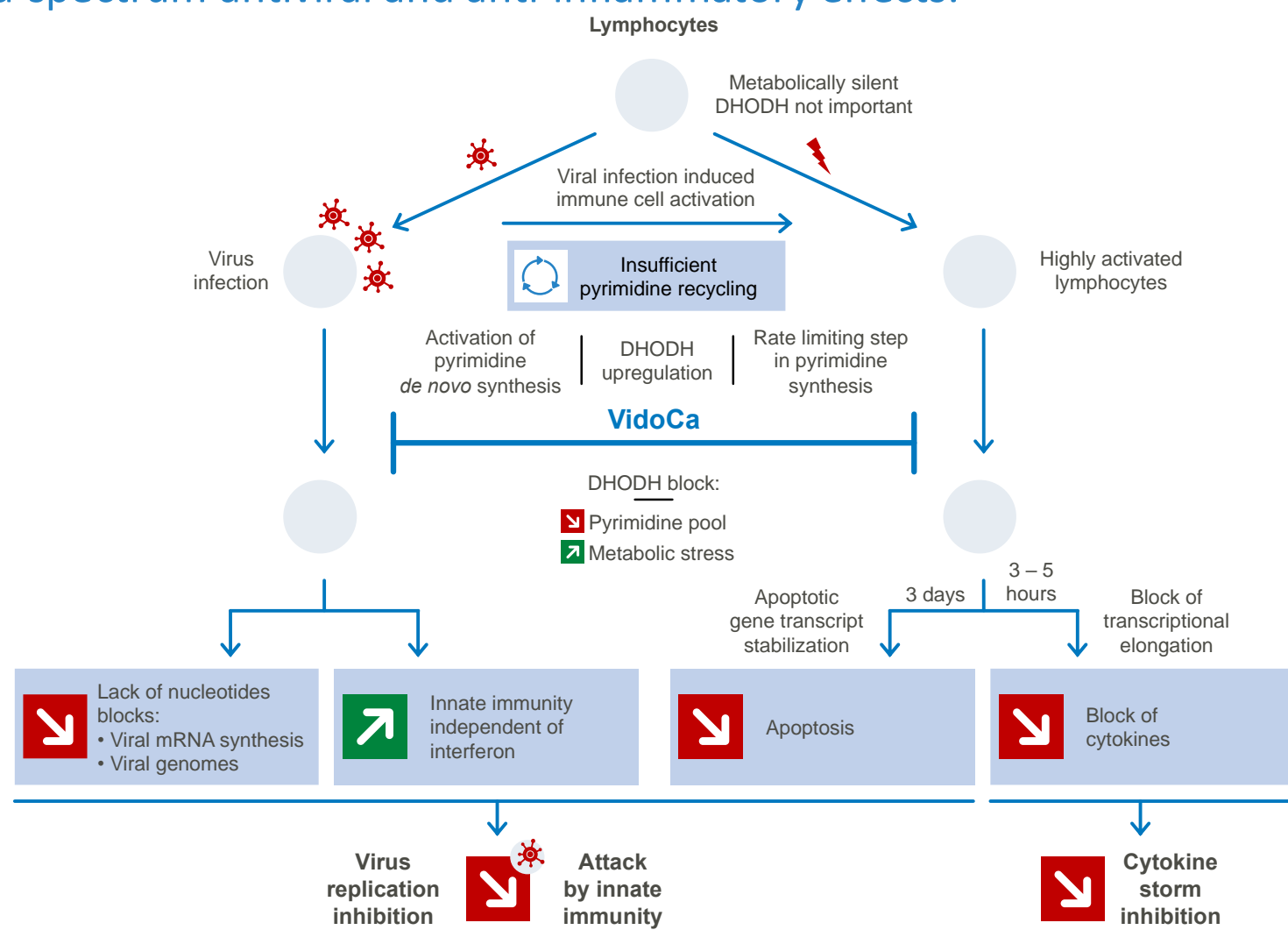


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Background

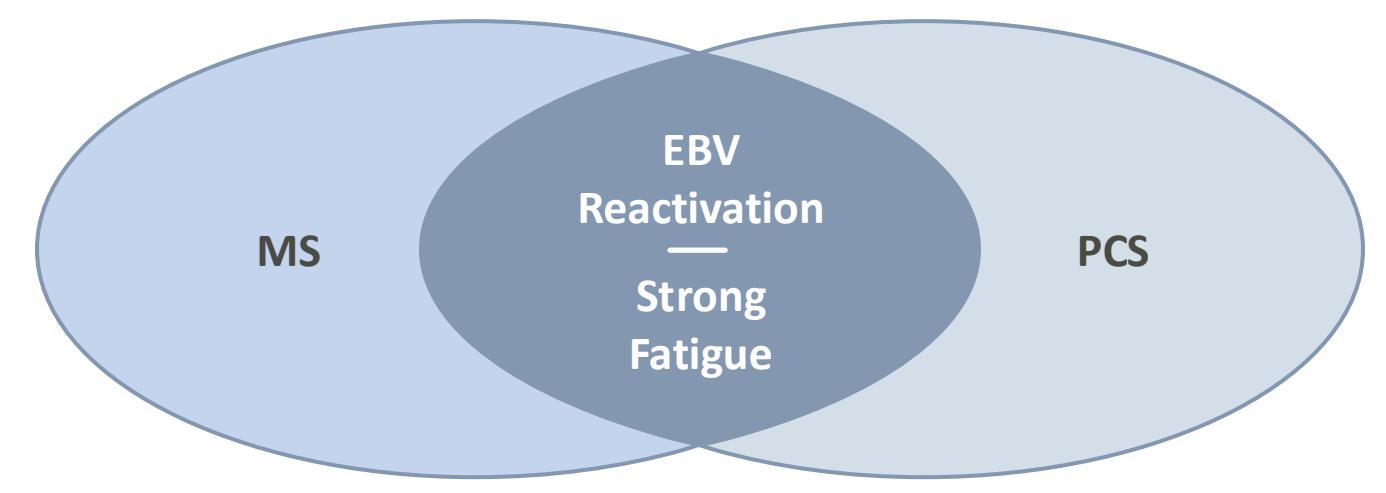
Vidofludimus calcium (VidoCa) is an orally bioavailable Nurr1 activator, which is related to neuroprotective effects, and DHODH inhibitor, which mediates broad-spectrum antiviral and anti-inflammatory effects.



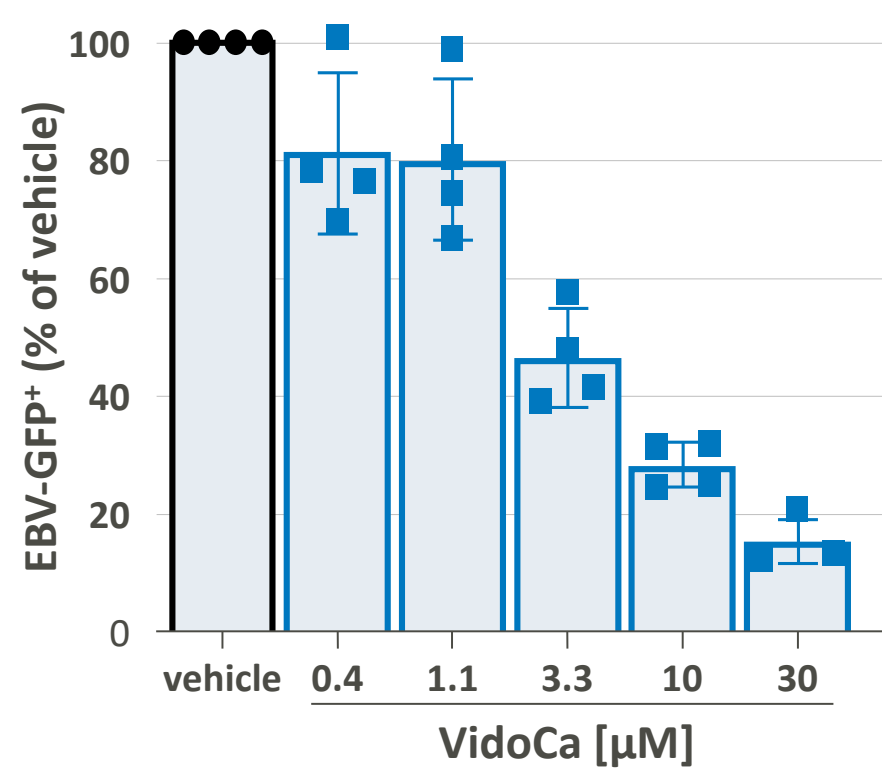
Objectives

Fatigue represents the most common and the most life-limiting symptom in both, multiple sclerosis (MS) and post-COVID syndrome (PCS). So far, no treatment option specifically addresses this severe symptom. Besides lingering inflammation and production of autoantibodies, reactivation of latent viruses like Epstein-Barr virus (EBV) is discussed as trigger for fatigue in both clinical manifestations¹.

- Is VidoCa able to reduce fatigue in MS as it was previously demonstrated for PCS patients^{3,4}?
- Is the inhibition of EBV reactivation responsible for reducing fatigue?

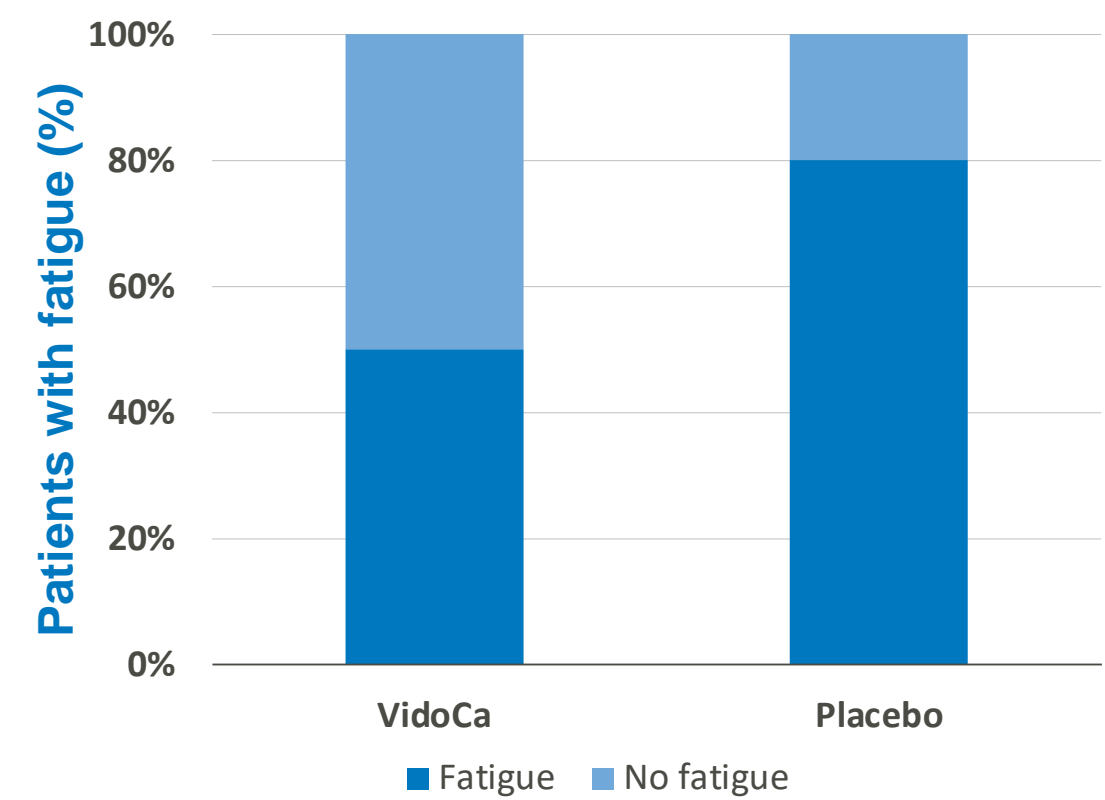


VidoCa dose-dependently inhibits EBV reactivation in Akata-EBV-GFP B cells



VidoCa reduces lytic EBV production from latently infected Akata-BX1-EBV-GFP cells stimulated with human IgG in a concentration-dependent manner. The EC_{50} was calculated as $3.5 \pm 1.2 \mu M$, demonstrating a potent anti-EBV-effect in cell culture. Moreover, VidoCa partially inhibited lytic EBV infection of the epithelial cell line T81-GFP.

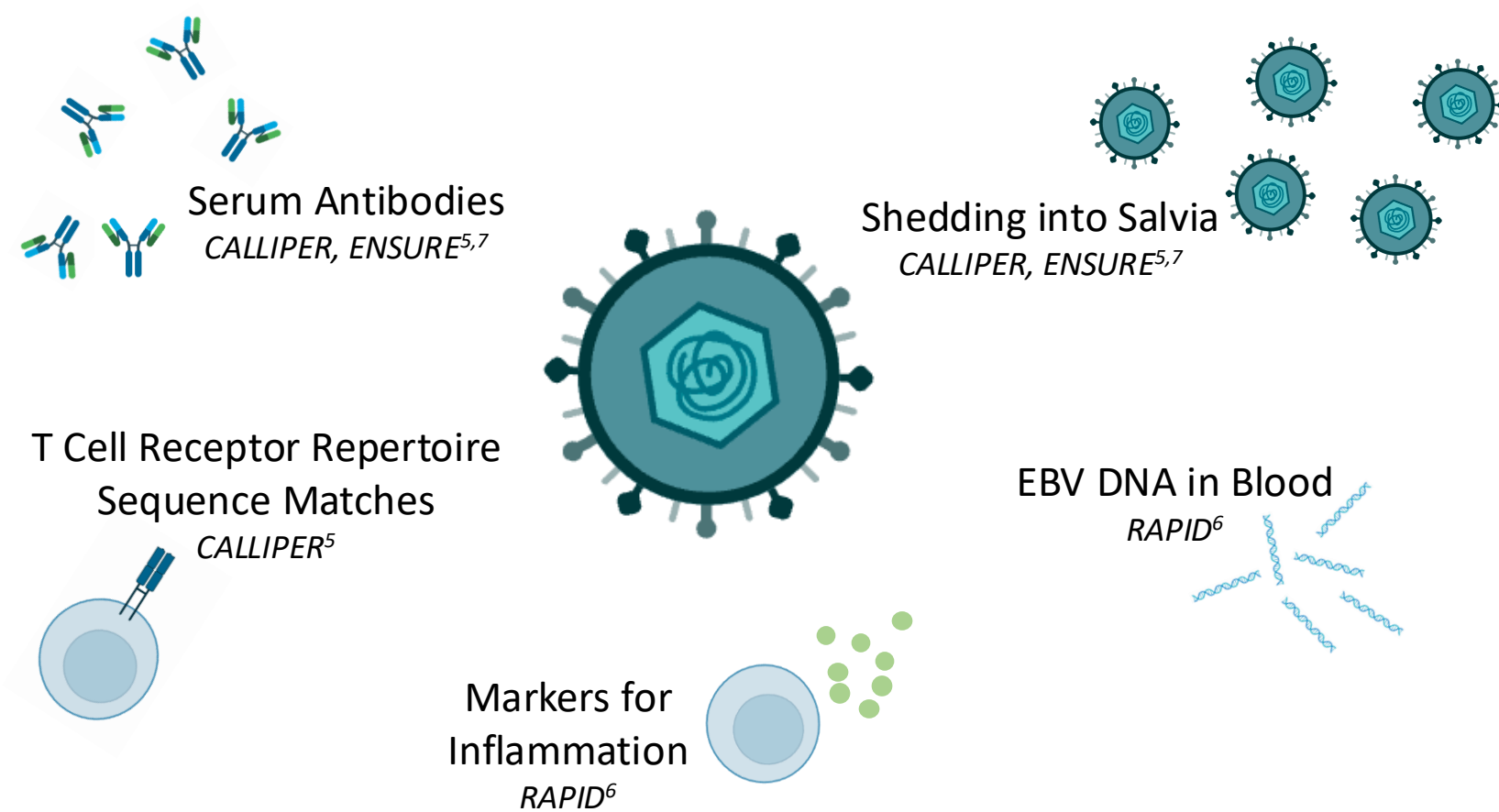
VidoCa reduces long-term fatigue compared to placebo in COVID-19 patients



In the Phase 2 CALVID-1 trial, patients who were tested positive for COVID-19 were randomized to receive placebo or 45 mg VidoCa for 14 days^{3,4}. At the individual study completion, 27 out of 220 patients responded to a post-hoc questionnaire. 80% of patients who received placebo reported fatigue compared to 50% who received VidoCa. Fatigue decreased in both groups within 9-17 weeks to 33% for placebo and 17% for VidoCa.

Analyses of EBV reactivation in MS and PCS patients treated with VidoCa

To elucidate the antiviral effect of VidoCa in patients, changes in serum antibodies and viral shedding into saliva as well as viral DNA will be quantified compared to baseline. Furthermore, the number of EBV T cell receptor repertoire sequence matches and markers for inflammation will be determined.



Assessment of the effect of VidoCa on fatigue in clinical trials for MS and PCS

To further analyze the effect of VidoCa on fatigue, five different questionnaires will be used to assess parameters associated with fatigue in MS and PCS patients.

Modified Fatigue Impact Scale (MFIS)
Effects of fatigue on physical, cognitive, and psychological function (CALLIPER⁵)

SF-36 Survey
General health questionnaire addressing physical, mental, and social well-being (RAPID⁶)

Bell Scale
Determining severity of impairments associated with fatigue (RAPID⁶)



Fatigue Severity Scale
Rating of the level of fatigue (RAPID⁶)

Multidimensional Fatigue Symptom Inventory Form
Assessment of severity, frequency, and daily pattern of fatigue symptoms, and the perceived interference with the quality of life (ENSURE⁷)

Summary and conclusions

- VidoCa inhibits EBV reactivation and primary infection of epithelial cells.
- VidoCa has been shown to prevent PCS fatigue which might be related to EBV reactivation⁸.
- By preventing EBV reactivation, VidoCa may contribute to reducing fatigue in MS patients as well.
- This hypothesis will be verified by analyzing the effects on fatigue and EBV reactivation in currently ongoing clinical trials for MS.

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References

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- Klein et al., 2023; Nature volume 623, pages 139-148
- Data presented as poster presentation at the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis 2021 with the title "IMU-838, a Small Molecule DHODH Inhibitor in Phase 2 Clinical Trial for Multiple Sclerosis, Shows Potent Anti-EBV Activity in Cell Culture-Based Systems: Potential Additional Benefits in Multiple Sclerosis Treatment".
- This analysis was done by sending a post hoc questionnaire to investigators. The participation was voluntary and a selection bias for participation cannot be fully excluded. The questionnaire requested the patient status regarding long-term COVID-19 symptoms.
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