Follow Up Results from the REP 301 Trial: Safety and Efficacy of REP 2139 and Pegylated Interferon Alpha-2a in Caucasian Patients with Chronic HBV / HDV Co-infection

Poster# 1848

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INTRODUCTION

HBV / HDV co-infection represents a significant unmet medical need, causes rapid progression of liver disease and has no approved therapy. The nucleic acid polymer (NAP) REP 2139 blocks HBsAg release and can eliminate serum HBsAg in chronic HBV and HBV / HDV co-infection (Vaillant 2016 Antiviral Res. 133: 32-40). In the completed phase II proof-of-concept REP 301 protocol (NCT02233075), the safety and antiviral efficacy of REP 2139 in combination with pegylated interferon alpha 2a (peg-INF) was evaluated in 12 Caucasian patients with HBV / HDV co-infection. Final safety and efficacy data and 6 month follow-up results from this trial are presented.

AIMS

REP 2139 inhibits the release of HBV subviral particles, a mechanism which may also function in the release of HDV virions (Bonino et al., 1986 J. Virol. 58: 945-950, see Figure 1.). The goal of this study was to assess the effect of REP 2139 therapy in HDV infection.

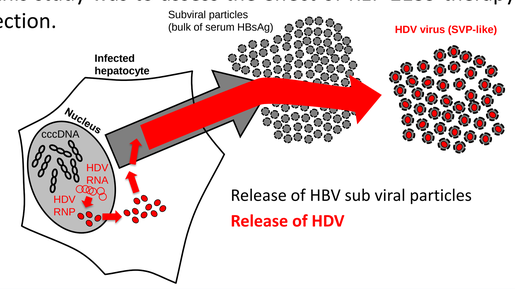

Figure 1. Release of HBV subviral particles and HDV utilize a similar mechanism. RNP = ribonuclear protein complex.

MATERIAL & METHODS

Patients received 500mg REP 2139-Ca (calcium chelate complex) once weekly for 15 weeks by IV infusion, followed by combined therapy for 15 weeks with a reduced dose of 250mg REP 2139-Ca with peg-INF (180ug SC qW) (see Fig. 2). Patients then transitioned to 33 weeks of peg-INF monotherapy. HDV RNA, HBV DNA, HBsAg and anti-HBs are followed every two weeks using standard assays (Robogene RT-PCR [MKI], Abbott RealTime HBV, Abbott Architect). Follow up evaluations were scheduled 4, 12 and 24 weeks following cessation of all treatment.

Figure 2. REP 301 trial design

RESULTS

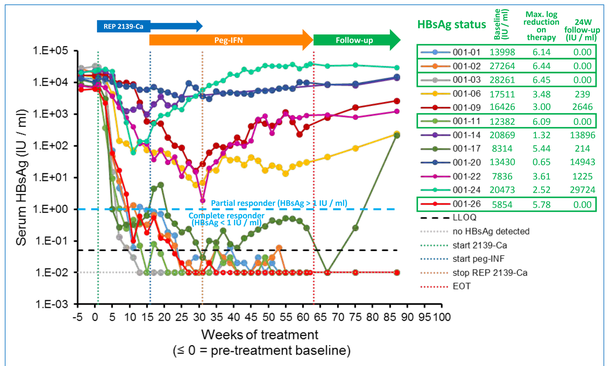

Figure 3. Serum HBsAg levels during treatment and follow-up. HBsAg status is indicated in green in the legend. Boxes highlight patients with no detectable HBsAg at 24 weeks of follow-up. Light blue line indicates threshold for a complete HBsAg response (1 IU / ml)

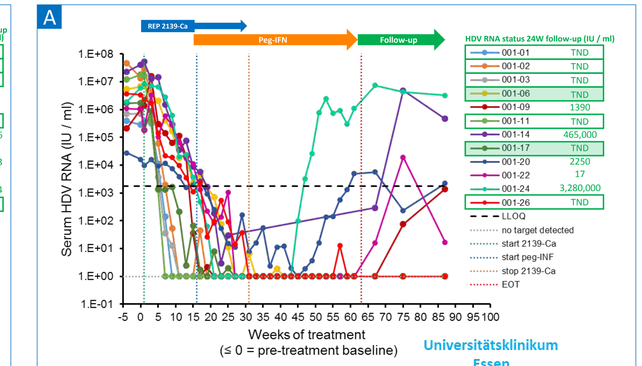

Figure 4. A) Serum HDV RNA levels during treatment and follow-up. HDV RNA status at 24 weeks of follow-up is indicated in green in the legend. Non-highlighted boxes indicate patients with no HBsAg present. Highlighted boxes indicate patients that are HDV RNA negative but HBsAg positive. B). Confirmatory HBV RNA assessments from two independent test labs. TND status is indicated in green in the legend. Highlighted patient (orange in legend) is HDV RNA TND at TUM but HDV RNA positive at ESSEN. TND = target not detected, FW = follow-up week, TW = treatment week.

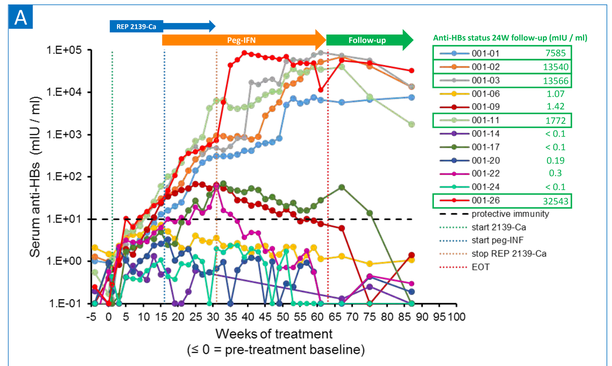

Figure 5. A) Serum anti-HBs levels during treatment and follow-up. Anti-HBs status at 24 weeks of follow-up is indicated in green in the legend. Boxes indicate patients with no HBsAg present. B) Serum anti-HBs levels during treatment and follow-up in HBsAg responders (left) and non-responders (right).

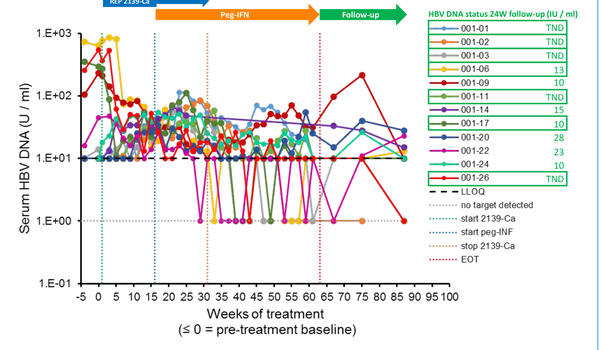

Figure 6. Serum HBV DNA levels during treatment and follow-up. HBV DNA status at 24 weeks of follow-up is indicated in green in the legend. Boxes indicate patients that are HDV RNA negative (TND). TND = target not detected.

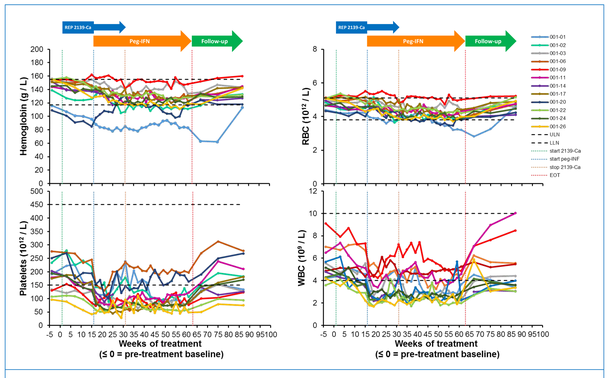

Figure 8. Hematological observations during treatment and follow-up.

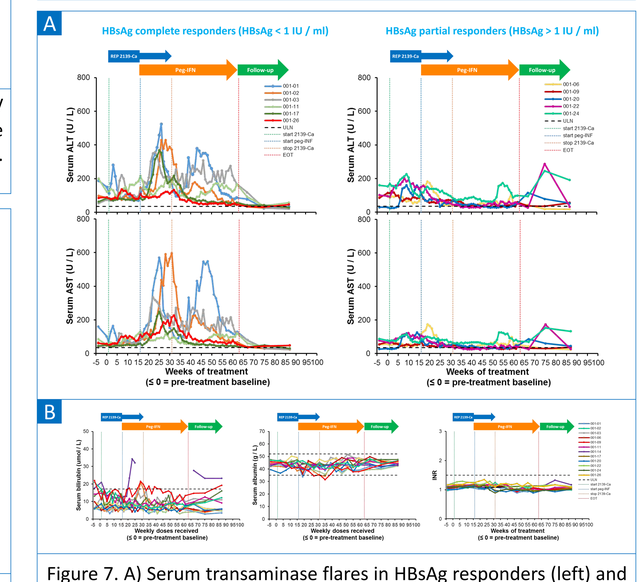

Figure 7. A) Serum transaminase flares in HBsAg responders (left) and partial responders (right). B) Liver function during treatment and follow-up.

CONCLUSIONS

- **REP 2139 simultaneously clears serum HBsAg and HDV RNA.**
- **Universal clearance of HDV RNA during therapy indicates a distinct activity of REP 2139 against HDV upstream of virion secretion.**
- **Improved action of peg-IFN is correlated with HBsAg reduction below 1 IU / ml.**
- **Despite the suboptimal combination regimen used, 5/12 patients maintained HBsAg loss and 7/12 patients maintained undetectable HDV RNA 24 weeks after treatment withdrawal.**
- **Longer concomitant therapy with REP 2139 and peg-IFN is expected to increase the rate of functional control of HBV and HDV infection.**

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Hrvoje Mijočević for his assistance with the confirmatory HDV RNA assays at TUM.

DISCLOSURES

M.Bazinet and A.Vaillant are employees and shareholders in Replicor Inc.
M. Roggendorf is a member of Replicor's SAB.
H. Karimzadeh is a consultant for Replicor.