Establishment of High Rates of Functional Cure of HBeAg Negative Chronic HBV Infection with REP 2139-Mg Based Combination Therapy: Ongoing Follow-up Results from the REP 401 Study

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INTRODUCTION
Establishment of high rates of functional cure of HBV infection and \( \leq 0.89 \) % is synthesized and excreted independently from viral replication as subviral particles (SVP) [1]. REP 2139 blocks the assembly and subsequent release of all HBsAg, allowing the efficient clearance of serum HBsAg [2, 3]. These results are consistent with previous findings (Table 2). The control group was to receive 48 weeks of TDF (300mg PO qD), peg-IFN (180ug SC qW) and REP 2139 in combination with tenofovir disoproxil fumarate (TDF) and pegylated interferon alpha 2a (peg-IFN) in patients with chronic HBV infection, as well as those positive for HBsAg and HBV DNA [3].

METHODS
Twenty four weeks of lead-in TDF (300mg PO qD) was administered to all patients. For the REP 401 study, 20 patients were randomized to receive either REP 2139-Mg or REP 2165-Mg (1:1, 250 mg IV 3 times per week) (Table 2). The control group was to receive 48 weeks of TDF + peg-IFN but all patients were crossed over to 48 weeks of TDF after 24 weeks of peg-IFN (see figure below). Shown is maintained on the Atenolol and all baseline data.

RESULTS
Figure 5. Management of peg-IFN-induced hematological changes

Figure 6. High rates of functional control and normalization of liver function persist after therapy in the REP 411 study.

Table 2. REP 401 Treatment and Follow-up Summary

Table 3. REP 411 Baseline Characteristics

DISCLOSURES
MB and AV are employees and shareholders in Replicor Inc.

CONCLUSIONS
1. Inhibition of subviral particle assembly by REP 2139 leads to intracellular declines of HBsAg, inhibition of release of HBsAg derived from cccDNA and integrated HBV DNA and allows efficient clearance of HBsAg during therapy.

2. When REP 2139-Mg is combined with pegylated interferon over 48 weeks, functional control no longer requiring therapy (inactive chronic HBV or functional cure) is achieved in at least 85% of patients completing therapy.

3. Functional control of HBV infection is accompanied by normalization of liver function and reversal of fibrosis (as measured by Fibroscan).

4. Outcome of therapy may be predicted by HBsAg response after 24 weeks of therapy.

5. Establishment of functional control in the majority (23/28) of patients requires HBsAg clearance to \( \leq 1 \) IU/mL (typically \( \leq 4 \) log10 reduction from baseline).

6. Establishment of functional cure requires elimination of detectable HBsAg from the blood (0.00 IU/mL) during therapy.

7. Transaminase flares appear to be immune mediated and are not associated with any signs of liver toxicity in patients with fibrosis from F1 to F4 (as measured by Fibroscan).

8. "Productive" transaminase flares occur with HBsAg declines > 4 log10, are generally correlated with HBsAches declines > 4 log10 (typically \( < 1 \) IU/mL) and are correlated with the establishment of functional cure.

REFERENCES
1. Blanchet et al., Antiviral Research 2019; in press
5. Blanchet et al., Antiviral Research 2019; in press