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

Circulating HBsAg levels reduce during treatment of HBV infection with PegIFN-α2a or PegIFN-α2b in nucleos(t)ide analog-naive patients and those relapsing following previous treatment with a nucleos(t)ide analog. Long-term suppression of HBsAg is a critical endpoint facilitating the restoration of functional control of HBV infection by limiting intrahepatic HBV replication. As the main method of HBV replication, that of subviral particles, is insensitive to anti-viral therapy directed against HBV DNA, HBsAg is considered a marker of the serological status of HBV infection and it is crucial for the treatment of chronic HBV infection. The REP 401 study (NCT01547156) is a randomized, controlled trial assessing the safety and efficacy of REP 2165 in combination with nucleoside analog interferon (nIfN) vs nIfN alone for 48 weeks in patients with chronic HBV-negative HBV infection.

RESULTS

Figure 1. Management of pegylated interferon-related side effects during REP 2139-Mg based therapy

Table 1. REP 461 Baseline Characteristics

Table 2. REP 461 Treatment and Follow-up Summary

Table 3. REP 461 Baseline Characteristics

Table 4. REP 461 Treatment and Follow-up Summary

Figure 2. Design of REP 461 study

Figure 3. Circumstances leading to an end of therapy in the REP 401 study

Figure 4. Liver function in the REP 461 study

Figure 5. Liver function in the REP 461 study

Figure 6. High rate of functional control and normalization of liver function persist after therapy in the REP 401 study

DISCLOSURES

All authors are employees and shareholders in Replicor Inc.

REFERENCES

1. Blanchet et al., Arthritis Research 2019; in press

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 < 1 IU/mL (typically > 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 score 4 (as measured by Fibroscan). See poster PO3-07 for additional detail.

8. “Productive” transaminase flares occur with HBsAg declines > 4 log10 from baseline, are generally correlated with HBsAg declines > 4 log10, (typically < 10 IU/mL) and are correlated with the establishment of functional cure.