Update on the Safety and Efficacy of REP 2139-Ca Monotherapy and subsequent Combination therapy with Pegylated Interferon Alpha-2A in Caucasian Patients with Chronic HBV / HDV Co-Infection

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CONCLUSIONS

• REP 2139-Ca is able to simultaneously reduce HBsAg and HDV RNA in patients with chronic HBV / HDV co-infection.

• Pharmacologic effect of NAPs on serum HBsAg observed in Asian patients in previous trials is confirmed in Caucasian patients.

• NAPs may have distinct antiviral mechanisms against HDV and HDV/HEV.

• Increased anti-HBs production and/or liver flares correlated with the start of peg-INF exposure may be related to the extent of clearance of serum HBsAg.

• Longer combination treatment with immunotherapy will likely result in a higher proportion of patients with a full HBsAg response (>1 IU/ml).

• NAP-based antiviral therapy may become an important new treatment option for patients with HBV / HDV co-infection.

REFERENCES

1. Barrow et al., 2016 J. Hepatol. 65: 682–689
2. Schwabe et al., 2015 PLoS ONE 10: e0126599
3. McDonald et al., 2017 J. Hepatol. 67: 275–280
4. Kazemi et al., 2016 J. Hepatol. 65: 6–12

BACKGROUND

• 15-20 million patients are affected by HBV / HDV co-infection.

• Most aggressive form of viral hepatitis with the fastest progression to cirrhosis.

• No approved therapy: Interferon-based treatment can intermittently achieve functional cures with long-term exposure.

• HDV is a critical component of the HDV life cycle:
  - HBsAg not produced by HDV but is required for its assembly
  - HDV infection only occurs with HBV infection
  - HDV assembly may be linked to the assembly of HBV subviral particles (SVPs)
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• NAPs have the ability to reduce HBsAg concentration in the serum

OBJECTIVES

• Demonstrate the safety and efficacy of REP 2139 monotherapy and combination with pegylated interferon alpha-2A in HBV/HDV chronic carriers.

MATERIAL & METHODS

• Caucasian patients treated in Chisinau, Moldova
• All patients received peg-IFN co-treatment with REP 2139-Ca
• Clinicaltrials.org # NCT02233075

RESULTS

• Serum HBsAg titers
• Serum HBV DNA titers

24 weeks of follow-up is planned at the end of peg-IFN therapy

Hypothesis

NAPs have the ability to reduce HBsAg concentration in the serum

• Anti-HDAg (+), HDV RNA validated at two external test sites (data not shown).

Diasorin (anti-HDAg)
Abbott PCR (HBV DNA)

• HBsAg is a critical component of the HDV life cycle:
  - HDV assembly may also block HBsAg synthesis

Viremia monitored at University of Duisburg-Essen, Germany:

• Anti-HBsAg
• Serum HBsAg > 1 IU/ml prior to peg-IFN addition

Compensated liver disease, mild to moderate fibrosis, non-cirrhotic.

• 3. 33 weeks peg-IFN (180 μg qW SC)
• 2. 15 weeks REP 2139-Ca 250mg qW IV plus pegylated interferon alpha 2a (peg-INF)

Dosing in three stages:

- Increased anti-HBs production and/or liver flares correlated with the start of peg-INF exposure may be related to the extent of clearance of serum HBsAg.
- Longer combination treatment with immunotherapy will likely result in a higher proportion of patients with a full HBsAg response (>1 IU/ml).
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