Poster Abstract P7

Subcutaneous Administration of REP 2139-Mg in the Compassionate Treatment of Cirrhotic HBV / HDV Co-infection

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Background
REP 2139-Mg based combination therapy achieves high rates of HBsAg loss, therapeutic transaminase flares and functional cure of HBV and HDV when administered by weekly IV infusion. Like all phosphorothioate oligonucleotides (antisense oligonucleotides, ASOs), subcutaneous (SC) injection site reactions are common with REP 2139 but, like all NAPs, are significantly stronger because of their increased length. Chelate complex formulation of NAPs (REP 2139-Mg) neutralizes administration reactivity. The safety and efficacy of SC injection of REP 2139-Mg in combination therapy was assessed in a cirrhotic patient with chronic HBV / HDV co-infection.

Methods
The patient (male, Senegalese, 51 years old) had confirmed cirrhosis and chronic HBV / HDV co-infection since 2005 (HDV GT3) and had failed previous therapies with TDF (300mg) + pegIFN (180ug) and later with TDF + pegIFN (180ug) + bulvertide (2mg) and was currently receiving only TDF. Eight months following discontinuation of pegIFN + bulvertide, TDF therapy was supplemented with 90ug pegIFN and 250mg REP 2139-Mg given as two subcutaneous injections of 125mg once each week. Safety assessments included liver, kidney and hematological function. Virologic assessments included HDV RNA (Robogene MK II), HBV DNA (Abbott), HBsAg and anti-HBs (Abbott Architect quantitative).

Results
No evidence of pain or inflammation at the injection sites for REP 2139-Mg was observed for the first 9 weeks. Thereafter, mild to moderate discomfort post injection was transient and not accompanied by inflammation. Mild pruritis after week 6 responded well to supportive therapy. Two mild and superficial indurations were not accompanied by pain or inflammation.
Virologic response was rapid, with HDV RNA becoming undetectable at week 4 and HBsAg becoming < 0.05 IU/mL at week 15 and HBsAg seroconversion evident at week 12 of therapy. A strong host-mediated transaminase flare (ALT, AST and GGT) developed after week 6, with its nadir (ALT 373 U/L) at week 9 and rapid normalization (current ALT is 54 U/L at week 16). Liver and kidney functions have remained normal throughout therapy with stable hematological parameters (RBC, WBC, platelets).

Conclusions
SC REP 2139-Mg was safe, well tolerated and highly effective against HBV and HDV infection in combination with TDF and low dose (90ug) pegIFN in this cirrhotic patient. The therapeutic transaminase flare was not associated with any adverse effects and was correlated with HBsAg loss.