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Rescue of cirrhotic HBV / HDV infection from bulevirtide failure by subcutaneous REP 2139-Mg

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Introduction

REP 2139 blocks HBV subviral particle assembly and hepatitis delta antigen function, driving HBsAg loss in HBV infection and HBsAg / HDV RNA loss in HBV / HDV co-infection. Compassionate access to REP 2139-Mg is being provided under the Replicor Compassionate Access Program (RCAP, NCT05683548). The safety and efficacy of SC injection of REP 2139-Mg in combination therapy is currently being assessed in cirrhotic patients with chronic HBV / HDV co-infection after failure on bulevirtide (BLV).

Aim

The safety and efficacy of SC injection of REP 2139-Mg in combination therapy is currently being assessed in French cirrhotic patients with chronic HBV / HDV co-infection after failure on bulevirtide (BLV).

Method

Compassionate access to REP 2139-Mg has been approved by the ANSM in 15 patients with compensated cirrhosis having no response or viral escape in HDV RNA during 2 or 10mg BLV. As of May 30, 2023, > 4 weeks of exposure data are available for 13 patients. Existing TDF was supplemented with 48 weeks of QW SC 250mg REP 2139-Mg and 90 µg pegIFN. Weekly safety evaluations were accompanied by virologic assessment every 4 weeks.

Conclusions

SC REP 2139-Mg is well tolerated and safe in compensated cirrhosis

New safety envelope expands REP 2139-Mg use to cirrhotic HBV and HBV / HDV patients

HBsAg and HDV RNA loss observed in previous REP 301 / 401 studies are replicated

Including in bulevirtide failure patients

Lack of ALT / AST flares may reflect altered immunological status in cirrhotic livers

Host mediated ALT/AST flares are frequent with NAPs + pegIFN in non-cirrhotic patients

Functional cure of HBV and HDV is possible in this special patient population

References

Shamur et al., Hepatol. 2017; 66: 504A
Bazinet et al., Lancet Gastroenterol Hepatol 2017; 2: 877-889
Bazinet et al., Hepatology Comm. 2020 5: 189-202
Bazinet et al., Gastroenterol. 2020; 158: 2180-2194
Boulon et al., Hepatol. 2021; 74: 512A
Bazinet et al., J Viral Hep 2021; 28: 817-825
Bazinet et al., Hepatol Comm 2021; 28: 817-825

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Results

Table 1. Baseline characteristics
(in patients with ≥ 4 weeks of therapy completed)

Parameter	Mean (range) where applicable
Number	13
Age	42.75 (21-59)
Sex	5 female, 8 male
Ethnicity	8 Caucasian, 2 African, 1 Asian, 1 Central Asian
Liver status	10 Compensated cirrhosis (CP A5: 7, A6: 3, 1 unknown) 2 Fibrosis (1 F2-F3, 1 F3-F4)
HBeAg status at baseline	11 negative, 2 positive
HDV genotype	6 genotype 1, 1 genotype 5, 6 pending
HDV RNA (IU/mL)	3.36 x10^6 (295-1.68x10^7)
HBsAg (IU/mL)	10760.9 (2100-33559)
HBV DNA (IU/mL) 1=TND	322.8 (1-3440*)
ALT (U/L)	88.1 (20-266)
Bilirubin (µmol/L)	14.6 (4-34)

*TDF therapy started at baseline

Table 2. Virologic response during therapy

Virologic response	Duration of therapy: 1-4 weeks (n=13)	5-8 weeks (n=13)	9-12 weeks (n=12)	13-24 weeks (n=10)	24-48 weeks (n=6)	> 48 weeks (n=2)*	Removal of NAP + pegIFN (n=2)	Removal of TDF (n=1)
HDV RNA decline < 2 $\log_{10}$ from baseline	3	3	4	2	1			
HDV RNA ≥ 2 $\log_{10}$ decline from baseline		3		2	2			
HDV RNA < LLOQ			2			1		
HDV RNA target not detected **	1	1	2	4	3	1	2	1
HBsAg decline < 1 $\log_{10}$ from baseline	2	2	2	2	1			
HBsAg > 1 $\log_{10}$ decline from baseline			1		1			
HBsAg > 2 $\log_{10}$ decline from baseline		1	3	1		1		
HBsAg < 10 IU/mL					1	1		
HBsAg < 0.05 IU/mL				2	2		2	1
Anti-HBs seroconversion			1	2	2	1	2	1
ALT normal	1			3	2		2	1

*treatment extension in two patients (#3 and #4) with currently ongoing
**measured by Eurobioplex assay.

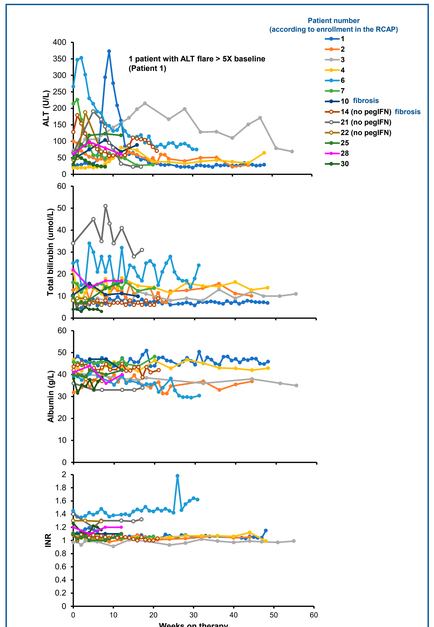

Figure 1. Impact of therapy on liver function. Individual patient tracings for ALT, total bilirubin, albumin and INR are provided. Patients not receiving pegIFN are indicated with hollow markers. Patients with fibrosis at baseline are indicated in the legend.

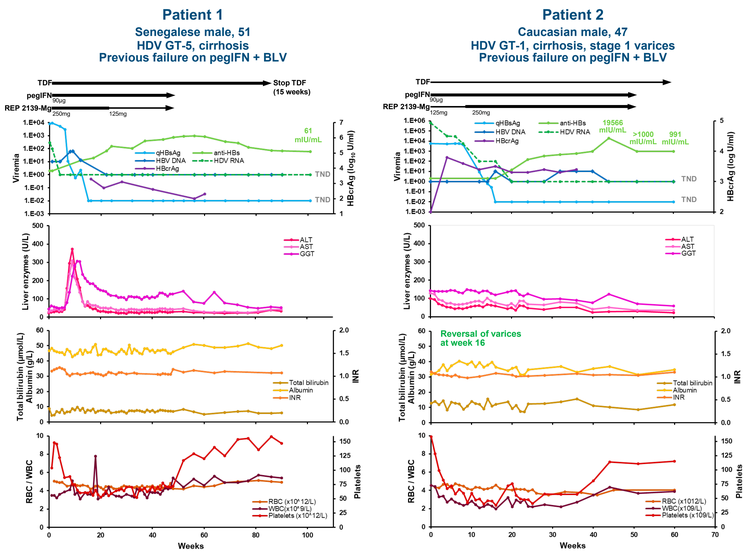

Figure 2. Antiviral control in the two patients completing therapy with REP 2139-Mg and pegIFN.