DeltaCure 1st International Meeting

n. 27

Poster for you

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

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## Introduction/Summary

- REP 2139 inhibits HDV replication via direct interaction with HDAg and blocks HDV release by inhibiting DNAJB12-mediated envelopment which uses the HBV subviral particle assembly pathway.
- 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 who failed to respond to bulevirtide (BLV).

## Methods

- Following at least one month washout from previous bulevirtide therapy, existing oral TDF therapy was supplemented with 48 weeks of 250mg REP 2139-Mg qW via SC administration.
- Patients with compensated cirrhosis also received 90ug pegIFN. Virologic assessments included HDV RNA (Robogene MK II), HBV DNA (Abbott), HBsAg and anti-HBs (Abbott Architect quantitative).

## Results

- SC administration of REP 2139-Mg was well tolerated in five patients to date. Patient 1 (Senegalese male, 51, GT 5 HDV) completed 48 weeks of therapy without incident. A self-resolving transaminase flare (ALTmax 373 U/L at week 9) was otherwise asymptomatic. HDV RNA became undetectable at week 4 and HBsAg became undetectable with seroconversion at week 12. HDV RNA clearance was verified by pan-genotypic RT-PCR. These virological responses persisted throughout therapy. Anti-HBs titers increased to 509 mIU/mL during therapy. Two months following removal of REP 2139-Mg and pegIFN, HBsAg and HDV RNA has remained undetectable and the anti-HBs titer has increased to 983 mIU/mL.
- In patients 2-5, REP 2139-Mg therapy is still ongoing with HDV RNA and HBsAg responses are evident in all patients (see below). Antiviral responses to SC REP 2139-Mg appear slower in patient 3 which is attributed to a BMI of 30.
- Patient 5 presented as decompensated cirrhosis (Child-Pugh B8) at baseline and was treated with REP 2139-Mg and TDF without pegIFN. At W4, a clear clinical improvement was observed with ascites regression and discontinuation of diuretics with no relapse.

## Conclusion

**SC REP 2139-Mg is safe, well tolerated and effective against HBV and HDV infection in combination with TDF and low dose pegIFN in cirrhotic patients who failed on bulevirtide.**

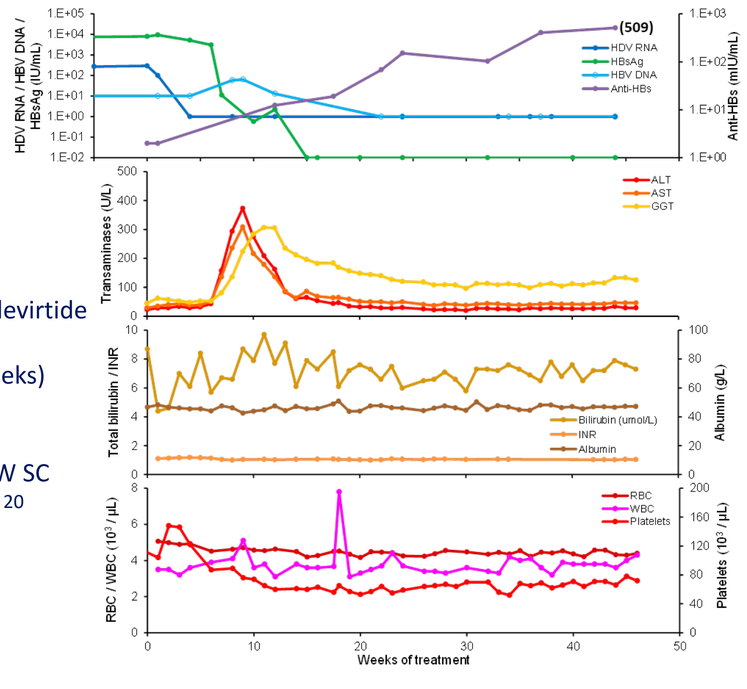
## Patient 1 (Marseille)

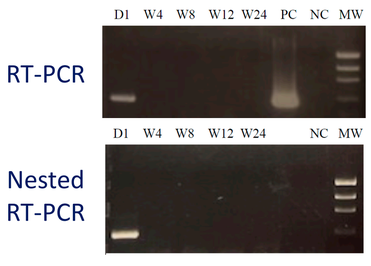
Senegalese male, 51
HBV / HDV (GT5)
Compensated cirrhosis

Previous HDV failure on:
TDF + pegIFN
TDF + pegIFN + 2mg bulevirtide

Combination regimen (48 weeks)
300mg TDF qD PO
90 µg pegIFN qW SC
250mg REP 2139-Mg qW SC
transition to 125mg IV @ week 20

TDF + pegIFN + REP 2139-Mg → Pan-genotypic HDV RT-PCR




**Removal of REP 2139-Mg and pegIFN (2 months)**

**HBsAg not detected (< 0.05 IU/mL)**
**Anti-HBs 983 mIU/mL (509 at EOT)**
**HDV RNA target not detected**
HBV DNA target not detected

ALT 26, AST 35, GGT 84 U/L
T-BIL 6.6 µmol/L, ALB 51 g/L, INR 1.13

Platelets 129x10$^3$ /µL (recovering)

## Patient 2 (Limoges)

Caucasian Male, 47
Chronic HBV/HDV infection (GT1)
Compensated cirrhosis (Child A5, stage 1 esophageal varices)

Previous HDV failure on:
TDF + pegIFN
TDF + pegIFN + bulevirtide 2mg

Combination regimen:
300mg TDF qD PO
90 µg pegIFN qW SC
250mg REP 2139-Mg qW SC

**SC administration of REP 2139-Mg well tolerated**
**14 weeks: no esophageal varices detected**
**9 weeks: HBsAg target not detected (baseline 4650 IU/mL)**
**13 weeks: HBsAg seroconversion anti-HBs 14.3 mIU/mL**
**22 weeks: anti-HBs 342 mIU/mL**
**≤ 4 weeks: HDV RNA target not detected (baseline 607,859 IU/mL)**
Latest LFT: ALT 49 U/L, AST 73, GGT 141 U/L, bilirubin 9.2 µmol/L

## Patient 3 (Clichy)

Asian Male, 54
Chronic HBV / HDV infection (GT1)
Compensated cirrhosis with central obesity

Previous HDV failure on:
TDF + pegIFN
TDF + pegIFN + bulevirtide 2mg
TDF + pegIFN + bulevirtide 10mg

Combination regimen:
300mg TDF qD PO
90 µg pegIFN qW SC
250mg REP 2139-Mg qW SC

**SC administration of REP 2139-Mg well tolerated**
**12 weeks: HBsAg 1890 IU/mL (baseline 10285 IU/mL)**
**HDV RNA decline evident at week 8**
Other efficacy results pending…

## Patient 4 (Limoges)

Caucasian Female, 59
Chronic HBV/HDV infection (GT1)
Compensated cirrhosis

Previous HDV failure on:
TDF + pegIFN (hematological intolerance)
bulevirtide 2mg
bulevirtide 10mg

Combination regimen:
300mg TDF qD PO
90 µg pegIFN qW SC
250mg REP 2139-Mg qW SC

**SC administration of REP 2139-Mg well tolerated**
**PegIFN therapy is now well tolerated**
**16 weeks: HBsAg 135 IU/mL (baseline 44476 IU/mL)**
**12 weeks: HDV RNA < LLOQ (168 IU/mL, baseline 6562 IU/mL)**
Latest LFT: ALT 73 U/L, AST 67 U/L, GGT 147 U/L, bilirubin 5.4 µmol/L

## Patient 5 (Clichy)

Caucasian Female, 54
Chronic HBV / HDV infection (GT1)
**Decompensated cirrhosis (significant ascites)**

Combination regimen:
300mg TDF qD PO
250mg REP 2139-Mg qW SC

**SC administration of REP 2139-Mg well tolerated**
**Week 4: Reversal of ascites (confirmed via ultrasound)**
**Week 10: HBsAg target not detected (baseline 1177 IU/mL)**
**HDV RNA decline evident at week 8**
Other efficacy results pending…