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P30

Poster for you

Bulevirtide monotherapy in patients with compensated cirrhosis and CSPH: a 96-week interim kinetic analysis

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Introduction

- Bulevirtide (BLV) was recently approved for treatment of HDV in Europe.
- Characterization of long-term (>48 weeks) HDV, HBsAg and ALT kinetics in patients with HDV-related compensated cirrhosis and clinically significant portal hypertension (CSPH) during BLV 2 mg/day is lacking.

Aim

- We aim to extend our recent reports [1,2] to characterize HDV, HBsAg and ALT kinetics under BLV monotherapy in patients with compensated cirrhosis and CSPH during up to 96 weeks of treatment.

Patients and Methods

- We 38 patients with HDV-related compensated cirrhosis and CSPH received BLV 2 mg/day.
- All patients received TDF or ETV for HBV. Blood samples were collected at treatment initiation, weeks 4, 8, 16, 24, 32, 40, 48 and every 12 weeks thereafter.
- 15 (39%) did not complete 96-weeks of therapy; 4 discontined treatment and treatment is ongoing in 11.
- HDV RNA was measured using Robogene 2.0 (lower limit of detection, LLD= 6 IU/mL).
- ALT normalization was defined as 41 U/L and 59 U/L for women and men, respectively.

Results

Baseline

- Mean baseline HDV RNA, HBsAg and ALT levels were 4.9 ± 1.2 log IU/mL, 3.6 ± 0.7 log IU/mL, and 114.4 ± 76.5 U/L respectively (**Table 1**).

Age	50.1±13.1
Male (n)	23
Female (n)	15
BMI	25.8±3.9
HDV RNA (log IU/ml)	4.9±1.2
HBsAg (log IU/ml)	3.6±0.7
HBcrAg (logU/ml)	3.8±0.8
ALT (U/l)	114.4±76.5
AST (U/l)	105.5±66.1
Bile acids (umo l/l)	41.4±54.5

PLT (x10⁹/l)	83.0±40.6
ALP (U/l)	131.5±60.3
Fibroscan (Kpa)	24.5±15.3
Total bilirubin (mg/dl)	1.158±0.53
GGT (U/l)	75.2±68.3
PCHE (U/l)	4951.9±2035.0
Alb (g/dl)	3.8±0.4
AFP (ng/ml)	26.4±96.8
sCr (mg/d l)	0.8±0.1

Table 1. Baseline Characteristics. PCHE: Pseudocholinesterase; HBV DNA was suppressed (<10 IU/ml) in 33/38 patients and <25 IU/ml in the remaining of patients.

HDV Response Patterns

- Five (13%) patients were non-responders (<1.6 log IU/ml decline from baseline throughout treatment).
- All responders (n=33) experienced an initial rapid viral decline (0.19 ± 0.12 log/wk)
- Responders had one of these five patterns:
  - i. Flat partial response (FPR) (n=20, **Fig.1a**),
  - ii. FPR + breakthrough (FPR + B) (n=3, **Fig.1b**),
  - iii. Biphasic (BP) (n=2, **Fig.1d**)
  - iv. BP + B (n=4, **Fig.1e**)
  - v. Triphasic decline (TP) (n=4, **Fig.1c** & **f**).
- A total of 23 (70%) of responder patients had FPR during treatment: 20 patients have sustained their viral plateau thus far. (**Fig. 1a**) and 3 had a viral breakthrough (**Fig. 1b**).
- Only 3 patients (8%) achieved sustained HDV RNA TND (≥24 weeks) at the end of week 96 (**Fig.1 c & f**).
- Baseline characteristics (**Table 1**) were not correlated with HDV response patterns.

ALT and HBsAg Kinetics

- ALT normalization was achieved in 28 (76%) patients at 7.9 ± 6.5 weeks (**Fig.1**).
- HBsAg remained roughly at pre-treatment levels (**Fig.1**).

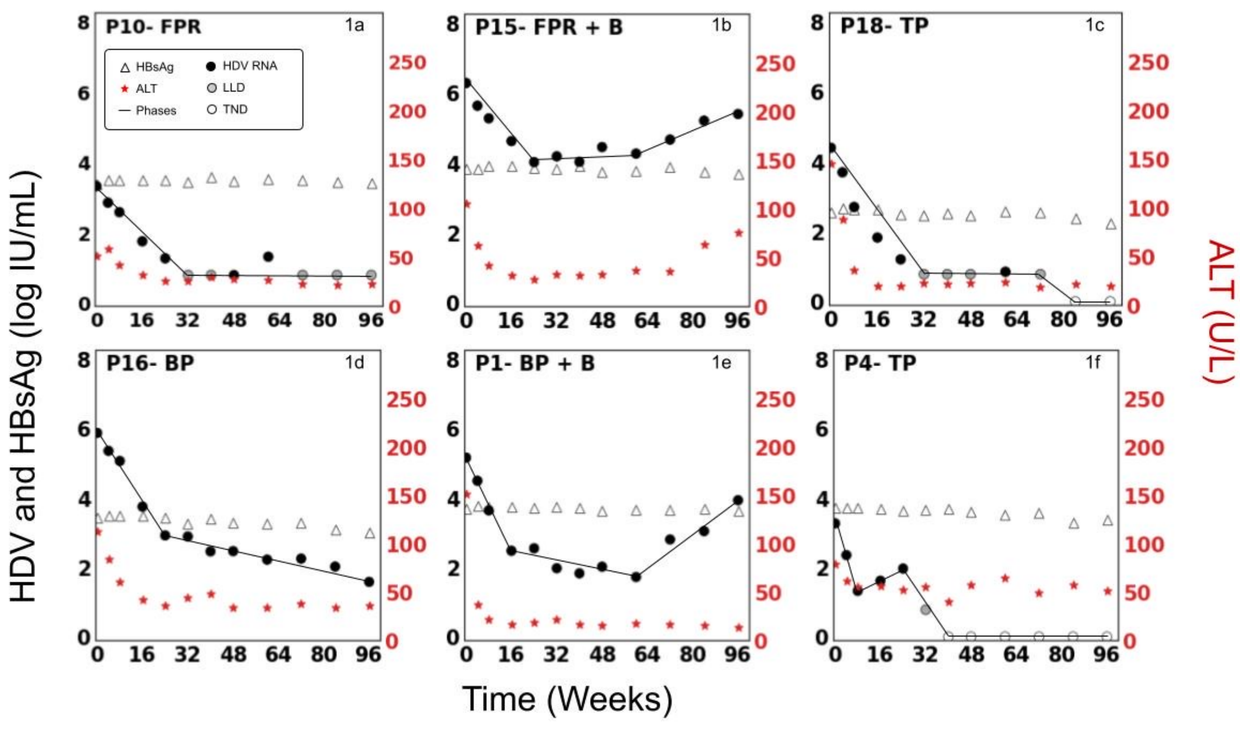

Figure 1. HDV kinetic patterns under BLV monotherapy in patients with compensated cirrhosis and CSPH.
HDV kinetic patterns under BLV monotherapy in patients with compensated cirrhosis and CSPH. FPR, flat-partial response; BP, biphasic; B, viral breakthrough (>1.6 log IU/ml from nadir viral load); TP, triphasic; LLD, lower limit of detection; TND, target not detected. Filled circles, quantifiable HDV RNA. Lines were drawn on each graph to show distinctions in phases.

Conclusions

- Interim analysis finds that 26 patients (79% of responders) reached a low plateau (3.2 ± 1.1 log IU/mL below baseline) that lasted 54 ± 12 weeks (i.e., FPR in **Fig.1 a, b & c**), of whom 3 patients had a further decline (**Fig.1c**).
- Thus far, 7 (18%) responders had viral breakthrough (**Fig.1 b & e**), 2 patients had a sustained 2nd decline phase (**Fig.1d**).
- Only 3 patients (8%) achieved sustained HDV RNA TND (≥24 weeks) at the end of week 96 (**Fig.1 c & f**)
- Understanding how to manage patients experiencing a viral plateau requires further research.

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Reference

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