EARLY CLINICAL AND VIROLOGICAL CHANGES IN HDV PATIENTS WITH ADVANCED CIRRHOSIS TREATED WITH BULEVIRTIDE MONOTHERAPY IN A REAL-LIFE SETTING

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AASLD The Liver Meeting® Nov. 12-15, 2021
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INTRODUCTION AND AIM

Bulevirtide (BLV) has been recently approved for the treatment of HDV-related chronic hepatitis or compensated cirrhosis in Europe, but its effectiveness and safety in patients with compensated cirrhosis and severe portal hypertension are still unknown.

This study aimed to describe the kinetics of biochemical and virological response to BLV in a real-life, single-centre study.

METHODS AND PATIENTS

All consecutive HDV patients with advanced compensated cirrhosis who started BLV 2 mg/day from Dec 2020 were enrolled in this single center study in Milan. All clinical and virologic characteristics were collected at treatment baseline, week 4, 8 and every 8 weeks thereafter.

HDV RNA was quantified by Robogene 2.0 (LOQ 6 IU/mL), HBcrAg by LUMIPULSE® G (LOQ 3 Log U/mL), HBV RNA by cobas® 6800 (LOQ 10 cp/mL) and anti-HBc levels by LG HBcAb-N.

Table 1 – Baseline features of 18 HDV patients included

Baseline variables	n=18	Baseline variables	n=18
Age, years*	48 (29-77)	TDF or ETV treatment°°°	18 (100%)
Males	12 (67%)	Bilirubin, mg/dl*	1.3 (0.5-1.8)
Caucasian	18 (100%)	ALT, U/L*	106 (32-222)
HDV genotype 1	18 (100%)	ALT >ULN	17 (94%)
Compensated cirrhosis	18 (100%)	Albumin, g/dL*	3.9 (2.9-4.4)
Child-Pugh score A6°	4 (28%)	Platelets count, 10^3/mmc*§	70 (37-227)
Esophageal varices°°	14 (78%)	Bile acids, µmol/L*	23 (8-306)
CSPH features**	17 (94%)	HBsAg, Log IU/mL*	3.7 (2.5-4.3)
Spleen size, cm*	17 (10-25)	HBeAg negative	17 (94%)
Fibroscan®, kPa*	16.4 (7.8-57.8)	HBV DNA detectable§§	4 (28%)
CAP, dB/m*	194 (100-271)	HBV RNA detectable	0%
BMI >25 Kg/m^2	8 (44%)	HBcrAg, Log U/mL*	3.8 (2.3-5)
Active HCC	2 (11%)	anti-HBc IgG, COI*	10.8 (1.1-55)
Previous IFN treatment	12 (67%)	HDV RNA, Log IU/mL*	4.9 (3.3-6.6)

* median (range); ** CSPH, clinically significant portal hypertension features: presence of esophageal varices OR plt <100,000/mmc & spleen >12 cm; °mild ascites in 17%; °°50% under primary endoscopic prophylaxis; °°° 10 in TDF; § 33% with plt <60,000/mmc; §§ median HBV DNA 15 (14-22) IU/mL

RESULTS

Table 2 – ALT and HDV RNA responses *vs* baseline during BLV 2 mg/day treatment

Variables	Baseline n=18	Week 4 n=18	Week 8 n=18	Week 16 n=18	Week 24 n=18
ALT normal	1 (6%)	4 (22%)	9 (50%)	14 (78%)	14 (78%)
HDV RNA <6 IU/mL	-	0	0	0	2 (11%)
HDV RNA decline, Log IU/mL*	-	1.1 (0.2-3.0)	1.4 (0.4-3.1)	2.2 (0.4-3.6)	2.6 (0.6-3.9)
HDV RNA decline ≥2 Log IU/mL	-	2 (11%)	2 (11%)	7 (39%)	15 (83%)
Combined Virologic response°	-	2 (11%)	2 (11%)	7 (39%)	15 (83%)
Combined response°°	-	0	0	5 (28%)	12 (67%)

* median (range); ° Combined virologic response: HDV RNA undetectable or ≥2 Log IU/mL decline *vs* baseline;
°° Combined response: normal ALT levels + HDV RNA undetectable or ≥2 Log IU/mL decline *vs* baseline

Table 3 – Time course of virological and biochemical variables during BLV treatment

Variables	Baseline n=18	Week 4 n=18	Week 8 n=18	Week 16 n=18	Week 24 n=18
Bilirubin, mg/dl*	1.3 (0.5-1.8)	1.0 (0.5-2.2)	1 (0.4-2.9)	0.9 (0.5-2.4)	1.0 (0.3-2.5)
AST, U/L*	92 (52-214)	61 (31-130)	52 (26-123)	42 (26-141)	38 (24-134)
ALT, U/L*	106 (32-222)	62 (37-162)	44 (21-114)	39 (16-91)	34 (18-82)
GGT, U/L*	52 (13-262)	46 (14-325)	43 (11-270)	35 (6-229)	30 (6-237)
Albumin, g/dL*	3.9 (2.9-4.4)	4.0 (3.0-4.8)	3.9 (3.1-4.8)	3.9 (3.0-4.4)	3.9 (3.5-4.6)
Platelets count, 10^3/mmc*	70 (37-227)	69 (37-220)	68 (40-210)	67 (35-228)	70 (33-219)
Bile acids, µmol/L*	23 (8-306)	50 (12-552)	60 (11-490)	48 (11-710)	36 (7-748)
AFP, µg/L*°	9 (3-596)	10 (4-773)	9 (3-846)	8 (2-495)	6 (3-14)
IgG, mg/dL*	2,168 (1,047-4,059)	2,287 (1,051-3,480)	2,056 (1,009-3,208)	1,570 (988-2,329)	1,666 (980-2,286)
HBsAg, Log IU/mL*	3.7 (2.5-4.3)	3.8 (2.0-4.3)	3.8 (2.6-4.3)	3.8 (2.6-4.3)	3.8 (2.5-4.3)
HBV DNA detectable	4 (28%)	2 (11%)	0%	0%	0%
HDV RNA, Log IU/mL*	4.9 (3.3-6.6)	3.8 (2.3-5.8)	3.5 (1.2-5.9)	2.7 (0.9-5.9)	2.3 (0.7-5.8)
Fibroscan®, kPa*	16.4 (8-58)	-	21.8 (9-49)	-	17.4 (6-48)

* median (range); ° both patients with HCC, one of them with high AFP levels, underwent successful percutaneous ablation

- Safety profile: no adverse events, no BLV discontinuation, no injection site reactions
- BLV was well tolerated, including in patients with advanced cirrhosis, active HCC and with platelets <60,000/mmc. The increase in bile acids level was fully asymptomatic
- BLV was safe also in the two patients under rivaroxaban and warfarin-based therapies

CONCLUSION

Early changes of virological and clinical parameters confirm the safety and effectiveness of Bulevirtide monotherapy even in difficult-to treat HDV patients with advanced cirrhosis and clinically significant portal hypertension.

REFERENCES

Loglio A, et al. Safety and effectiveness of up to 3 years' bulevirtide monotherapy in patients with HDV-related cirrhosis. J Hepatol 2021; *in press*

Scholtès C, et al. Performance of a novel automated assay for the detection and quantification of HBV pregenomic RNA/circulating RNAs in chronic HBV patients. Hepatology 2020;72:447A

Urban S, et al. Hepatitis D virus in 2021: virology, immunology and new treatment approaches for a difficult-to-treat disease. Gut 2021;70:1782-1794

Kang C, et al. Bulevirtide: First Approval. Drugs. 2020;80:1601-1605

Loglio A, et al. Excellent safety and effectiveness of high-dose Myrcludex-B monotherapy administered for 48 weeks in HDV-related compensated cirrhosis: A case report of 3 patients. J Hepatol. 2019;71:834-839

DISCLOSURES

P. Lampertico: advisor and speaker bureau for BMS, Roche, Gilead Sciences, GSK, MSD, Abbvie, Janssen, Arrowhead, Alnylam, Eiger, Myr Pharma. A. Loglio: travel grant and speaker bureau for Myr Pharma and Gilead Sciences. M. Viganò: consultant/ advisor/ sponsored lecturer for BMS, Gilead and Roche.
The other authors declare that they have no competing interests.

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