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Poster for you

Treatment of chronic hepatitis D with bulevirtide: 1st year report

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Introduction

In July 2020, the EMA conditionally approved bulevirtide (BLV) for the treatment of adult patients with compensated chronic hepatitis D (CHD); meaning that further evidence on efficacy and safety of BLV was awaited. The most frequently reported adverse reactions with this therapy in registering trials were itching due to increased bile ducts (very common), headache (very common), and injection site reactions (common). From May 2023, we started treating our patients with BLV.

Aim

To report our experience on efficacy and safety of BLV in real practice at 1 year.

Materials and Methods

Data were extracted from the cohort of patients attending the liver clinic of MED1 at AOU Maggiore della Carità of Novara. In the last 10 years, 20 patients have been identified as positive for both HBsAg and anti-HDV. Only 3/20 patients were found to be candidates for therapy with BLV (**Table 1**). All patients received a standard dose of BLV and underwent preliminary, ongoing, and 1-year testing after starting BLV.

Table 1. Patients with hepatitis D attending to our clinic

Patients	Number
Dead	2
Transplanted	3
Lost to follow up	2
Addressed to another Center*	2
Healed spontaneously	1
Serology positive, HDV-RNA negative	6
Positive serology, floating HDV-RNA**	1
Treated	3
Totals	20

* Centers with ongoing trials
** Annual check-up, negative at the time of screening

Results

Of the three patients, two were native Italians and one was from Eastern Europe. All three patients underwent centralized serum HDV-RNA assessment (RoboGene® v2) and HDV genotyping (direct sequencing). The only genotype found was HDV-1. **Table 2** shows data before and after 1 year of therapy. All patients adhered to the therapy regularly. Regarding side effects, no patient developed itching or headache. Two patients developed skin reactions at the injection site (**Figure 1**). One did not require any intervention and experienced spontaneous resolution, while the other required chronic antihistamine therapy to control symptoms. Notably, the latter patient was already being treated with monoclonal antibodies (mepolizumab) due to a history of hyper-eosinophilic asthma. All patients showed an improvement in transaminases and two had a significant reduction in viremia.

Except for one patient, all showed improvement in both liver stiffness and APRI.

Table 2. Baseline and 48 weeks on treatment

Parameters	Patient 1		Patient 2		Patient 3	
Sex	M		F		M	
Age	60		58		46	
Nation of birth	Italy		Italy		Ukraine	
BMI	22,6		27,4		29,3	
Alcohol consumption *	No		No		No	
Important comorbidities	No		Yes		No	
HCC	No		No		No	
HBeAg	Neg		Neg		Neg	
anti-HBeAg	Pos		Pos		Pos	
HBV antiviral therapy	Yes		Yes		Yes	
Time	**T0**	**T12**	**T0**	**T12**	**T0**	**T12**
ALT	35	18	38	24	100	88
Platelets	10000	131000	151000	134000	213000	199000
Albumin	4	4,2	4		4,6	4,4
Total bilirubin	0,74	0,74	0,8	0,32	2,0	1,73
INR	1,08	1,08	1,05	1,08	1,18	1,16
HBcrAg	4,4	nd	4,3	nd	5,9	nd
HBV-DNA	<10	< 10	<10	<10	<10	33
Quanttative HBsAg	16000	24000	7600	12000	3000	3400
HDV Ab	Pos		Pos		Pos	
HDV-RNA°	111000 copie/ml 28311 U/ml TO	27 U/ml	115400 copie/ml 59271 U/ml TO	< 20 U/ml	453000 copie/ml 786 U/ml TO	256 365 U/ml
Genotype HDV	1	--	1	--	1	--
Elastometry	8,7	10,9	11,7	7,7	9,5	7,7
APRI	0.88	0,34	0.63	0,45	1.17	1.11

* >20g/die F; >30g/die M
° copie/ml T0; U/ml T12 (the laboratory has changed its methods)
TO performed at another center

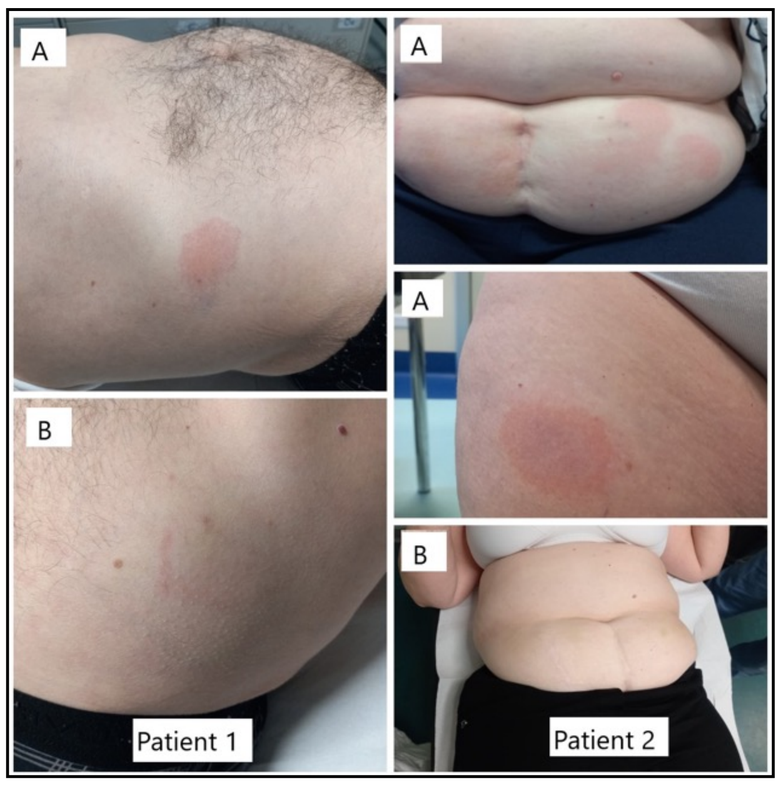

Fig.1

A. Start of therapy
B. Ongoing therapy.
Patient 1 initially only had localized reactions with rapid spontaneous resolution; patient 2 had protracted skin reactions with complete resolution after starting antihistamine. After an attempt to discontinue histamine H1 receptor antagonist, the skin lesions reappeared, so it was decided to leave the antihistamine indefinitely with complet resolution.

Conclusions

BLV treatment was safe and well-tolerated. Adherence to therapy in the patient without virological response is under investigation.