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Poster for you

Role of intrahepatic HDV reservoir in potentially modulating response to bulevirtide treatment at 24 weeks.

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Introduction

- Hepatitis Delta Virus (HDV) is a small RNA virus that can cause a severe chronic hepatitis in patients already infected with Hepatitis B virus (HBV). HDV co-infection is a risk factor for cirrhosis and hepatocellular carcinoma (HCC) development.[1]
- For a long time, there was no effective treatment for HDV hepatitis. On January 2023 bulevirtide (BLV) was approved in Italy as the first therapeutic option for HDV infection.[2]
- Despite the observation of a good clinical and laboratory response, the identification of parameters to predict a more rapid and durable response to therapy remains uncertain.

Study Design

- The aim of this study is to analyze which parameters can be predictive of a clinical and laboratory response.

Methods

- We analyzed intrahepatic and peripheral virological parameters, ALT, information on cirrhosis status from five patients of our cohort of HDV patients from Policlinico Tor Vergata of Rome, who received BLV at least for 24 weeks by July 2024. (**Fig.1**)
- Droplet digital PCR was used to quantify intrahepatic HBV and HDV markers. Combined response was defined as HDV-RNA decay >2 log and ALT normalization.

Figure 1

Appearance	Ishak stage: Categorical description	Ishak stage: Categorical assignment	Fibrosis measurement*
	No fibrosis (normal)	0	1.9%
	Fibrous expansion of some portal areas ± short fibrous septa	1	3.0%
	Fibrous expansion of most portal areas ± short fibrous septa	2	3.6%
	Fibrous expansion of most portal areas with occasional portal to portal (P-P) bridging	3	6.5%
	Fibrous expansion of portal areas with marked bridging (portal to portal (P-P) as well as portal to central (P-C))	4	13.7%
	Marked bridging (P-P and/or P-C), with occasional nodules (incomplete cirrhosis)	5	24.3%
	Cirrhosis, probable or definite	6	27.8%

Fig.1 Histopathological chronic liver disease stage "scores" are descriptive categorical assignments which are different from liver fibrosis measurements. **Proportion (%) of area of illustrated section showing Sirius red staining for collagen (collagen proportionate area).*

Results

- Five patients, all virologically suppressed under nucleos(t)ide analogues (NUC), received BLV for 24 weeks.
- Median age was 47 (45-54) years, 1 patient was Italian, 4 from Eastern-Europe. The risk of infection was sexual transmission for 4 patients, and use of injectable drugs for one.
- At baseline, median (IQR) serum HDV-RNA and HBsAg were 7.5 (7.3-7.7) and 4.3 (4.2-4.3) log IU/ml, respectively. Median ALT was 52 (43-116) U/l while Ishak score was 5 for three patients, 4 and 3 for the remaining two (**Tab.1**).
- Intrahepatic median (IQR) HDV-RNA was 2262 (1292-3564) copies/1000cells (**Tab.1**). Two patients received Peg-Interferon-alfa but discontinued after 2 and 4 weeks respectively for adverse effects.
- Combined response was achieved in 3 patients at week 12 and in all patients at week 24 of BLV. At week 24, two patients achieved serum HDV-RNA<2 log IU/ml, while the other three had HDV-RNA>2.5 log IU/ml (**Tab.2**).
- Notably, a lower baseline intrahepatic HDV-RNA tended to correlate with the achievement of serum HDV-RNA<2 log IU/ml after 24 weeks of BLV-treatment (median intrahepatic HDV-RNA: 922 copies/1000cells in 2/5 patients achieving and 3564 copies/1000cells in 3/5 not achieving HDV-RNA<2 log IU/ml).
- Conversely, the intrahepatic HBV markers were comparable between the two groups of patients.

Table 2. Data from patients at 12/24w.

Patient ID	HDV-RNA 12 w.	AST/ALT 12 w.	HDV-RNA 24 w.	AST/ALT 24 w.
HDV_1	564	30/22	127	27/22
HDV_2	235180	28/31	1507	26/27
HDV_3	2041	55/46	61	49/28
HDV_4	4458	37/35	1066	35/26
HDV_5	7598	45/41	660	40/42

HDV-RNA in copies/ml, AST/ALT in U/l

Conclusion

- A limited intrahepatic HDV reservoir at baseline tended to correlate with a higher control of HDV replication after 24 weeks of BLV.
- The virological and clinical monitoring in longer follow-up and larger sample size is ongoing in order to corroborate this result.
- This can also have implication for therapeutic strategies aimed at setting up a finite course of BLV treatment.

Table 1. Data from patients at baseline

Patient ID	Sex	Age	Country of origin	Serum HDV_RNA	AST/ALT	Ishak-Score	Intrahepatic HDV-RNA
HDV_1	43	M	Moldova	9888430	207/357	5	1292
HDV_2	45	F	Moldova	18578800	31/52	5	3564
HDV_3	54	F	Italy	16782	55/38	5	552
HDV_4	62	M	Romania	105059	78/116	3	9331
HDV_5	47	M	Romania	814309	43/43	4	2262

M: male, F: female, ALT/AST: alanine aminotransferase/aspirate aminotransferase; References values: HDV<100 UI/mL; AST: [5-34]; ALT: [0-55]; PLT: [150000-450000];

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Reference

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