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Poster for you

BULEVIRTIDE MONOTHERAPY PREVENTS LIVER DECOMPENSATION IN PATIENTS WITH HDV-RELATED CIRRHOSIS: A CASE CONTROL STUDY WITH PROPENSITY SCORE WEIGHTED ANALYSIS

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Introduction/Summary

- Bulevirtide (BLV) monotherapy yields high rates of virological and biochemical response in hepatitis Delta (HDV) cirrhotic patients, however clinical benefits on hard outcomes remain unknown.

Study Design

- Patients with HDV-related cirrhosis treated with BLV monotherapy in a retrospective multicenter European study (SAVE-D) were compared with untreated HDV cirrhotic patients enrolled in a previous cohort study (Romeo, Gastroenterology 2009) [1].

Methods

- The BLV-untreated cohort included patients with compensated HDV-related cirrhosis enrolled between 1978-2006 in a single-center, retrospective, natural history study [1].
- The BLV-treated cohort included patients with compensated HDV-related cirrhosis treated with BLV between 2019-2023 in the multicenter, retrospective, longitudinal European SAVE-D study (37 centers).
- The baseline for study analysis was cirrhosis diagnosis (Untreated) or BLV start (BLV-treated).
- Patients were followed-up from baseline to event, last visit or censoring (24 months – interim analysis).
- Liver-related events [LRE] (HCC, decompensation), death or liver transplantation were recorded.
- Statistical analysis included Kaplan-Meier survival analysis, cox-regression analysis with Inverse Probability of Treatment Weighting (IPTW) and a competing risks regression model.

Results

Table 1. *Baseline features of the study cohorts*

Variables	Untreated (n=140)	BLV-treated (n=176)	p value
Age, years	40 (34-49)	49 (39-59)	**<0.0001**
Males	109 (78%)	104 (59%)	**0.0004**
Caucasians	136 (97%)	161 (91%)	**0.04**
CPT score A - A6	140 (100%) 22 (16%)	176 (100%) 54 (31%)	1.00 **<0.0001**
Previous LRE - HCC - Decompensation	5 (4%) - 5 (4%)	35 (20%) 12 (7%) 23 (13%)	**<0.0001**
Esophageal varices*	64 (46%)	65 (55%)	0.13
IFN-experienced	56 (40%)	103 (59%)	**0.001**
ALT, U/L	102 (57-176)	77 (53-127)	**0.03**
Bilirubin, mg/dL	0.9 (0.7-1.4)	1.0 (0.7-1.4)	0.40
Albumin, g/dL	3.9 (3.6-4.3)	4.0 (3.7-4.4)	0.08
HBsAg, LogIU/mL	pos	3.7 (3.3-4.1)	na
HBeAg negative	132 (94%)	164 (93%)	0.82
HBV DNA ND/low**	109 (78%)	143 (81%)	0.48
HDV RNA, LogIU/mL	pos	5.4 (4.1-6.4)	na

Values are expressed as number (percentage) or median (IQR); *available in 118/176 patients in the BLV-treated cohort; **<2000 copies/mL

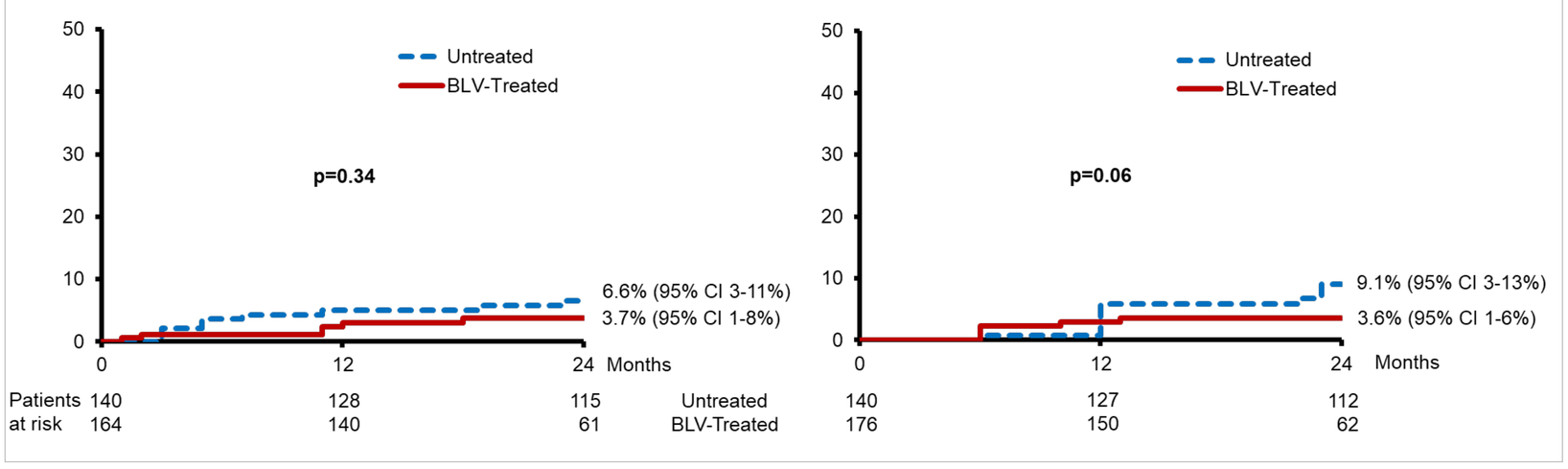
BLV-Treated Cohort: PLT 89 (66-133)x10^3/mm^3, Liver Stiffness Measurement 18.4 (13.0-26.3) kPa; 92% NUC-treated

BLV: Bulevirtide; CPT: Child-Pugh Turcotte; LRE: Liver-related Event; HCC: Hepatocellular Carcinoma; IFN: Interferon; ALT: Alanine Aminotransferase; ND: Not detected; HBV: Hepatitis B Virus; HDV: Hepatitis Delta Virus

Results (Continued)

- BLV monotherapy resulted in 77% virological response, 63% biochemical response and 51% combined response at month 24 (BLV-treated cohort).
- Overall, the 2-year cumulative probabilities of LRE were 7.3% (95% CI 3-13%) in the BLV-treated cohort *vs.* 15.6% (95% CI 9-22%) in untreated patients (p=0.05): 3.7% (95% CI 1-8%) *vs.* 6.6% (95% CI 3-11%) for de-novo HCC (p=0.34) and 3.6% (95% CI 1-6%) *vs.* 9.1% (95% CI 3-13%) for decompensation (p=0.06), respectively (**Figure 1**).
- The 2-year cumulative probability of mortality was 2.7% (95% CI 1-6%) *vs.* 3% (95% CI 1-6%) in BLV-treated *vs.* untreated patients (p=0.34).

Figure 1. *2-Year Cumulative Incidence of De-novo HCC and Decompensation*



- No decompensating events were reported in BLV-treated patients with baseline CPT-A5 (**Table 2**).

Table 2. *Liver-Related Events According to Baseline CPT Score*

Patient Group	Number	Liver-related Events		De-novo HCC		Decompensation		
		n	2-yr Cumulative Incidence (95% CI)	n	2-yr Cumulative Incidence (95% CI)	n	2-yr Cumulative Incidence (95% CI)	
UNTREATED COHORT	**140**	**21**	**15.6% (9-22%)**	**9**	**6.6% (3-11%)**	**12**	**9.1% (3-13%)**	
CPT-A5	118	16	14.2% (7-21%)**	6	5.2% (1-9%)	10	9.2% (4-14%)	
CPT-A6	22	5	23.0% (5-41%)	3	13.9% (1-27%)	2	9.1% (1-22%)	
BLV-TREATED COHORT	**176**	**12**	**7.3% (3-13%)**	**6**	**3.7% (1-8%)**	**6**	**3.6% (1-6%)**	**p=0.003**
CPT-A5	122	4	3.4% (1-8%)**	4	3.4% (1-8%)	0	na	
CPT-A6	54	8	17.0% (7-27%)	2	4.8% (1-12%)	6	12.3% (3-22%)	

**2-year rates of liver-related events in CPT-A5: 14.2% Untreated vs. 3.4% BLV-treated (p=0.01); p=ns for all other comparisons
CPT: Child Purgh Turcotte; CI: Confidence interval

- By inverse probability treatment weighting analysis adjusted for confounding baseline factors and competing mortality risks, the BLV-treated cohort had a significantly decreased risk of all-type liver-related events (HR 0.38; 95% CI 0.23-0.62, p<0.0001), decompensation (HR 0.32; 95% CI 0.16-0.63, p<0.0001) compared to untreated patients. Conversely, the HCC risk was similar in the two cohorts (HR 0.50; 95% CI 0.24-1.06, p=0.07) (**Table 3**).

Table 3. *BLV Treatment Effect on Liver-related Events by IPTW-Adjusted Analysis*

Outcomes	Category	Unadjusted Cox Regression Analysis		IPTW-Adjusted Cox Regression Analysis		IPTW-Adjusted Competing Risks Regression Model	
		HR (95% CI)	p value	HR (95% CI)	p value	SHR (95% CI)	p value
Liver-related Events	Treated vs. Untreated	0.52 (0.25-1.05)	0.07	0.38 (0.23-0.62)	**<0.0001**	0.38 (0.23-0.61)	**<0.0001**
Decompensation	Treated vs. Untreated	0.48 (0.18-1.28)	0.14	0.32 (0.16-0.63)	**0.001**	0.32 (0.17-0.61)	**0.001**
De-novo HCC	Treated vs. Untreated	0.57 (0.20-1.62)	0.29	0.50 (0.24-1.06)	0.07	0.50 (0.24-1.04)	0.06

BLV: Bulevirtide; IPTW: Inverse Probability of Treatment Weighting; HR: Hazard Ratio; SHR: Sub-distribution Hazard Ratio; CI: Confidence Interval; HCC: Hepatocellular Carcinoma; ALT: alanine aminotransferase

Conclusion

- In patients with HDV-related compensated cirrhosis, a 2-year course of BLV monotherapy may reduce risk of liver decompensation, but not HCC, compared to untreated patients.

References

1. Romeo R, Del Ninno E, Rumi M, Russo A, Sangiovanni A, de Franchis R, Ronchi G, Colombo M. A 28-year study of the course of hepatitis Delta infection: a risk factor for cirrhosis and hepatocellular carcinoma. Gastroenterology. 2009 May;136:1629-38