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**Real-world studies confirm effectiveness of bulevirtide to treat chronic hepatitis D**

*Three articles published in the Journal of Hepatology and JHEP Reports demonstrate that bulevirtide is well tolerated and safe for treating chronic hepatitis delta, the most severe form of chronic viral hepatitis*

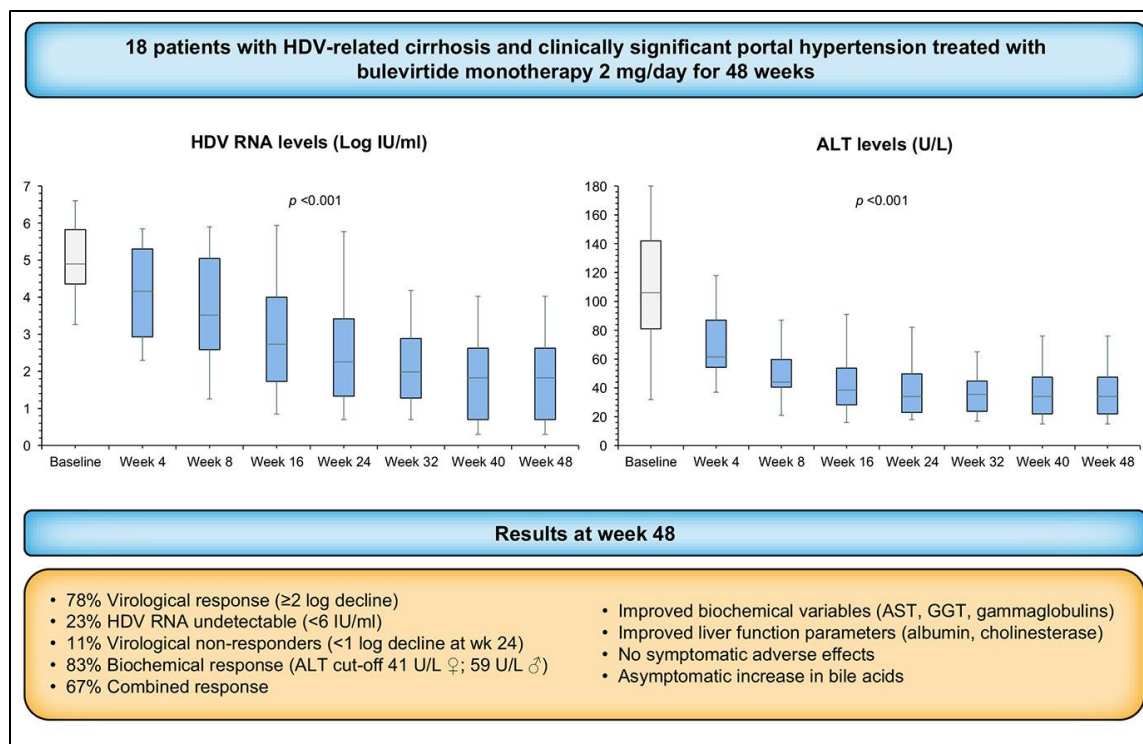
**Amsterdam, March 20, 2023** – In 2020, bulevirtide (BLV) was conditionally approved for treating chronic hepatitis delta (CHD), an inflammation of the liver caused by hepatitis D virus (HDV). Now real-world studies of patients treated outside of clinical trials confirm that long-term suppressive therapy with BLV monotherapy has the potential to reduce viral replication and improve liver tests of these difficult-to-treat patients for the first time in 45 years, report investigators in the [Journal of Hepatology](#) and its companion journal [JHEP Reports](#).

Two of the studies, led by Pietro Lampertico, MD, PhD, Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy, were designed to assess the effectiveness and safety of patients with advanced HDV-related compensated cirrhosis being treated with BLV 2mg monotherapy and the consequences of discontinuing this treatment.

“HDV is the most severe form of chronic viral hepatitis,” explained Dr. Lampertico. “For many years, the only therapeutic option was the off-label administration of pegylated-interferon-alpha (PegIFN $\alpha$ ), an approach characterized by suboptimal efficacy, an unfavorable safety profile and several contraindications.”

In a study of 18 patients with HDV-related advanced cirrhosis treated with BLV 2 mg/day for 48 weeks, Dr. Lampertico and colleagues demonstrated significant virological, biochemical and combined response rates associated with improvement of liver function.

“The efficacy and safety of BLV monotherapy in patients with advanced compensated cirrhosis were unknown before this study. Virological and biochemical responses to BLV monotherapy that we observed in our difficult-to-treat patients with HDV-related compensated cirrhosis were similar to those shown in the phase III registration study,” Dr. Lampertico noted.



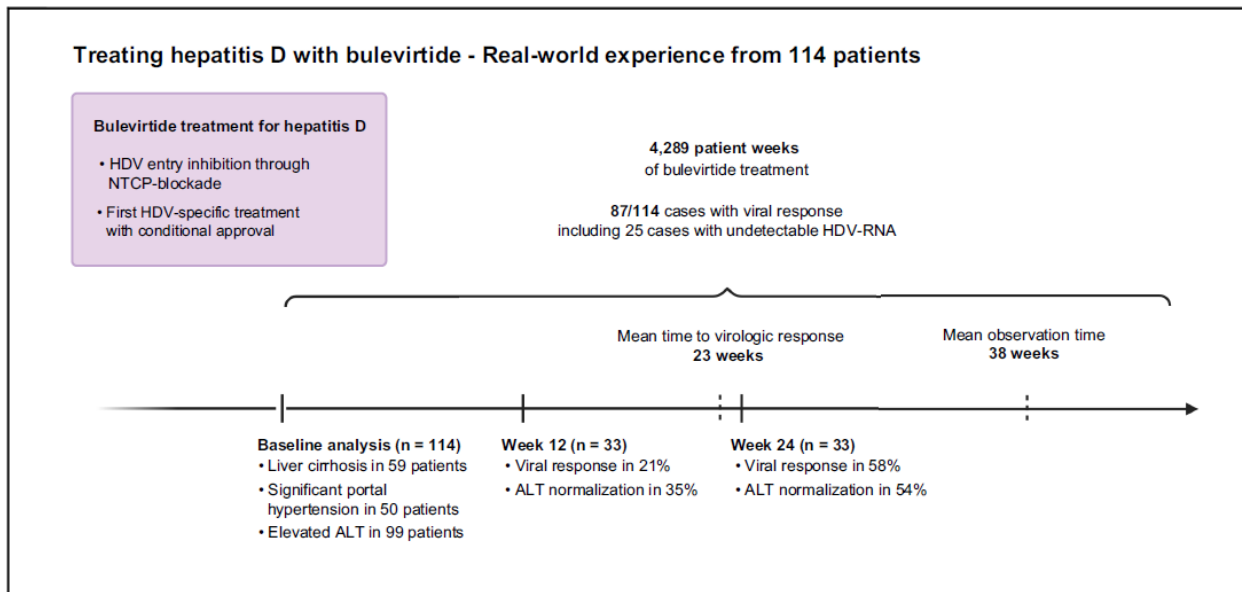
Caption: Effect of bulevirtide (BLV) monotherapy 2 mg/day for 48 weeks on HDV RNA levels and ALT levels in 18 patients with HDV-related cirrhosis and clinically significant portal hypertension (Credit: *Journal of Hepatology*).

In a case report, Dr. Lampertico and co-investigators demonstrated that HDV could be successfully eradicated from both serum and liver following a three-year course of BLV monotherapy, despite the persistence of HBsAg, in a patient with HDV-related compensated cirrhosis and esophageal varices. During the 72-week off-BLV follow-up, liver biopsy, intrahepatic HDV RNA and hepatitis D antigen were undetectable, less than 1% of hepatocytes were HBsAg positive and all were negative for hepatitis B core antigen.

“We were surprised to demonstrate that HDV can be eradicated following a finite course of an entry inhibitor administered as monotherapy such as BLV 2mg/day, despite the persistence of HBsAg positivity,” commented Dr. Lampertico.

In a study in *JHEP Reports* led by PD Dr. med. Katja Deterding, MD, Department. of Gastroenterology, Hepatology and Endocrinology at Hannover Medical School, Hannover, Germany, investigators report the first data from the largest multicenter cohort of patients to date who were treated with BLV under real-world conditions, including 50 patients with signs of significant portal hypertension, elevated pressure in the major vein that leads to the liver.

The retrospective analysis of 114 cases covered 4,289 patient weeks of BLV treatment. Viral response was observed in 87 cases while hepatic inflammation improved, and treatment was well tolerated. More than 50% of patients showed a virologic response with less than 10% of patients not achieving an HDV RNA drop of at least 90% after 24 weeks. An improvement of biochemical hepatitis activity as measured by the liver enzyme alanine transaminase (ALT) values was observed regardless of virologic response. Investigators concluded that treatment was safe and well tolerated and associated with improvements in liver cirrhosis and portal hypertension with prolonged treatment.



Caption: Treating hepatitis D with bulevirtide (BLV). Real-world experience in 114 patients (Credit: *JHEP Reports*).

“In line with other real-world cohorts and clinical trials our real-world study confirms the antiviral activity of BLV,” noted Dr. Deterding. “We were surprised to see an improvement in biochemical hepatitis activity even in cases without viral response. Potential explanations for this phenomenon include anti-inflammatory properties of BLV.”

“This is the first time that patients with HDV-related chronic advanced liver disease can be treated with an antiviral therapy since 1977 when HDV was discovered. Long-term suppressive therapy with BLV 2 mg/day has the potential to improve survival, of these difficult-to-treat patients for the first time in 45 years,” concluded Dr. Lampertico. “We also found that BLV treatment can be successfully discontinued in some HDV patients who achieved long-term viral suppression while on therapy.”

HDV infection occurs when people become infected with both hepatitis B and D virus either simultaneously (co-infection) or acquire the hepatitis D virus after first being infected with hepatitis B (super-infection). According to the World Health Organization, HDV affects nearly 5% of individuals with a chronic infection resulting from hepatitis B virus (HBV). Populations that are more likely to have HBV and HDV co-infection include indigenous populations, recipients of hemodialysis and individuals who inject drugs.

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#### Notes for editors

“Bulevirtide monotherapy for 48 weeks in patients with HDV-related compensated cirrhosis and clinically significant portal hypertension,” by Elisabetta Degaspero, Maria Paola Anolli, Sara Colonia Uceda Renteria, Dana Sambarino, Marta Borghi, Riccardo Perbellini, Caroline Scholtes, Floriana Facchetti, Alessandro Loglio, Sara Monico, Mirella Fraquelli, Andrea Costantino, Ferruccio Ceriotti, Fabien Zoulim, and Pietro Lampertico (<https://doi.org/10.1016/j.jhep.2022.07.016>). It appears in the *Journal of Hepatology*, volume 77, issue 6 (December 2022), published by Elsevier. It is openly available at [https://www.journal-of-hepatology.eu/article/S0168-8278\(22\)02980-4/fulltext](https://www.journal-of-hepatology.eu/article/S0168-8278(22)02980-4/fulltext).

This work was supported in part by a grant from “Ricerca Corrente RC2021/105-01”, Italian Ministry of Health, and by a public grant overseen by the French National Research Agency (ANR) as part of the second “Investissements d’Avenir” program (reference: ANR-17-RHUS-0003).

“A 3-year course of bulevirtide monotherapy may cure HDV infection in patients with cirrhosis,” by Maria Paola Anolli, Elisabetta Degaspero, Lena Allweiss, Angelo Sangiovanni, Marco Maggioni,

Caroline Scholtes, Valerie Oberhardt, Christoph Neumann-Haefelin, Maura Dandri, Fabien Zoulim, and Pietro Lampertico (<https://doi.org/10.1016/j.jhep.2022.12.023>). It appears in the *Journal of Hepatology*, volume 78, issue 4 (April 2023), published by [Elsevier](#).

This study was supported by a public grant overseen by the French National Research Agency (ANR) as part of the second "Investissements d'Avenir" program (reference: ANR-17-RHUS-0003), by the Deutsche Forschungsgemeinschaft (TRR-179; project number 272983813) and in part by an unrestricted grant from Gilead Sciences (IN-IT-589-6246).

"Treating hepatitis D with bulevirtide – Real-world experience from 114 patients," by Christopher Dietz-Fricke, Frank Tacke, Caroline Zöllner, Münevver Demir, Hartmut H. Schmidt, Christoph Schramm, Katharina Willuweit, Christian M. Lange, Sabine Weber, Gerald Denk, Christoph P. Berg, Julia M. Grottenthaler, Uta Merle, Alexander Olkus, Stefan Zeuzem, Kathrin Sprinzl, Thomas Berg, Florian van Bömmel, Johannes Wiegand, Toni Herta, Thomas Seufferlein, Eugen Zizer, Nektarios Dikopoulos, Robert Thimme, Christoph Neumann-Haefelin, Peter R. Galle, Martin Sprinzl, Ansgar W. Lohse, Julian Schulze zur Wiesch, Jan Kempfski, Andreas Geier, Florian P. Reiter, Bernhard Schlevogt, Juliana Gödiker, Wolf Peter Hofmann, Peter Buggisch, Julia Kahlhöfer, Kerstin Port, Benjamin Maasoumy, Markus Cornberg, Heiner Wedemeyer, and Katja Deterding (<https://doi.org/10.1016/j.jhepr.2023.100686>). It appears online ahead of *JHEP Reports*, volume 5, issue 4 (April 2023). It is openly available at [https://www.jhep-reports.eu/article/S2589-5559\(23\)00017-4/fulltext](https://www.jhep-reports.eu/article/S2589-5559(23)00017-4/fulltext).

Full text of these articles is also available to credentialed journalists upon request; contact Freya Weise at +33 (6) 28 51 59 51 or [hmsmedia@elsevier.com](mailto:hmsmedia@elsevier.com). Journalists wishing to interview the authors should contact Pietro Lampertico, MD, PhD, at [pietro.lampertico@unimi.it](mailto:pietro.lampertico@unimi.it) or Dr. med. Christopher Dietz-Fricke at [Dietz-Fricke.Christopher@mh-hannover.de](mailto:Dietz-Fricke.Christopher@mh-hannover.de).

### **About the *Journal of Hepatology***

The [Journal of Hepatology](#), the premier journal devoted to liver diseases, is the official journal of the European Association for the Study of the Liver (EASL). It publishes original papers, reviews, case reports, and letters to the Editor concerned with clinical and basic research in the field of hepatology. The journal has a 2021 Impact Factor of 30.083 (Source: Journal Citation Reports™ from Clarivate, 2022). [www.journal-of-hepatology.eu](http://www.journal-of-hepatology.eu)

### **About *JHEP Reports***

*JHEP Reports* is an open access companion title to the highly respected *Journal of Hepatology*. It publishes original papers, reviews, and letters to the Editor concerned with basic, translation and clinical research in the field of hepatology. *JHEP Reports* is an innovative journal publishing articles on global issues in hepatology, with specific focus on clinical trials, novel diagnostics, precision medicine and therapeutics, cellular and molecular research, metabolism, cancer, microbiome, systems biology, epidemiology, and biotechnology advances and devices. [www.jhep-reports.eu](http://www.jhep-reports.eu)

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