OCTOBER 11-12, 2024 MILAN, ITALY
DeltaCure 3rd International Meeting
P26
Poster for you

Continued Treatment of Early Virologic Nonresponders or Partial Responders With Bulevirtide Monotherapy for Chronic Hepatitis Delta Leads to Improvement in Virologic and Biochemical Responses: Results From an Integrated Analysis at Week 96

Pietro Lampertico[1,2], Heiner Wedemeyer[3], Maurizia Rossana Brunetto[4], Pavel Bogomolov[5], Tatyana Stepanova[6], Mark Bourliere[7], Helène Fontaine[8], Grace M. Chee[9], Dmitry Manuilov[9], Qi An[9], Audrey H. Lau[9], Ben L. Da[9], John F. Flaherty[9], Renee-Claude Mercier[9], Catherine Frenette[9], Anu Osinusi[9], George Sebastian Gherlan[10,11], Adrian Streinu-Cercel[12], Stefan Zeuzem[13], Markus Cornberg[14], Dominique Roulot[15], Fabien Zoulim[16], Soo Aleman[17], Tarik Asselah[18]

[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [2]"A.M. e A. Migliavacca" Centre for the Study of Liver Disease, Università degli Studi di Milano, Milan, Italy; [3]Medizinische Hochschule Hannover, Hannover, Germany; [4]Hepatology Unit, University Hospital of Pisa, Pisa, Italy; [5]Moscow Regional Research Clinical Institute Named After M. F. Vladimirsky, Moscow, Russian Federation; [6]Clinic of Modern Medicine, Moscow, Russian Federation; [7]Hôpital Saint Joseph, Marseille, France; [8]Hôpital Cochin, Paris, France; [9]Gilead Sciences, Inc., Foster City, CA, USA; [10]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [11]Dr. Victor Babes Foundation, Bucharest, Romania; [12]Matei Bals National Institute of Infectious Diseases, Bucharest, Romania; [13]Goethe University Hospital, Frankfurt, Germany; [14]Klinik für Gastroenterologie, Hepatologie und Endokrinologie, Medizinische Hochschule Hannover, Hannover, Germany; [15]Université Sorbonne Paris Nord, Bobigny, France; [16]Hospital Croix Rousee, Lyon, France; [17]Karolinska University Hospital/Karolinska Institutet, Stockholm, Sweden; [18]Hôpital Beaujon, Université de Paris, Clichy, France

Key Findings

- At week (W) 24, 35% of patients treated with bulevirtide (BLV) 2 mg or 10 mg monotherapy had suboptimal early virologic response, including 11% nonresponders (NR) and 24% partial responders (PR)
- After 96 weeks of BLV 2 mg or 10 mg monotherapy:
  - W24 PRs: 74% VRs, 23% PRs
  - W24 NRs: 47% VRs, 20% PRs
- Biochemical responses were observed in the majority of W24 PRs and a subset of NRs, primarily in the first 24 weeks
- Virologic and biochemical responses at W96 were similar between BLV 2 mg and 10 mg in suboptimal early virologic responders (NR or PR at W24)
- 4 of the 5 patients who remained NR from W24 to W96 achieved >50% ALT improvement from BL at W96

Conclusion

- Continued BLV treatment through 96 weeks benefited the majority of suboptimal early virologic responders

Introduction

- Bulevirtide (BLV), a novel entry inhibitor of hepatitis delta virus (HDV), is approved in the EU, Great Britain, Switzerland, Australia, and the Russian Federation for the treatment of chronic hepatitis delta (CHD) in patients with compensated liver disease[1,2,3]
- In HDV clinical studies, on-treatment virologic response has been defined as achieving an undetectable level of HDV RNA or a ≥2 log_{10} IU/mL decline in HDV RNA from baseline[4,5]
- In the Phase 3 Study MYR301, treatment with BLV 2 mg/day monotherapy resulted in virologic response rates of 76% and 82% at 1 and 2 years[5,6]
- The extent of benefit from continued therapy for patients who do not achieve virologic response after 24 weeks of treatment requires further investigation

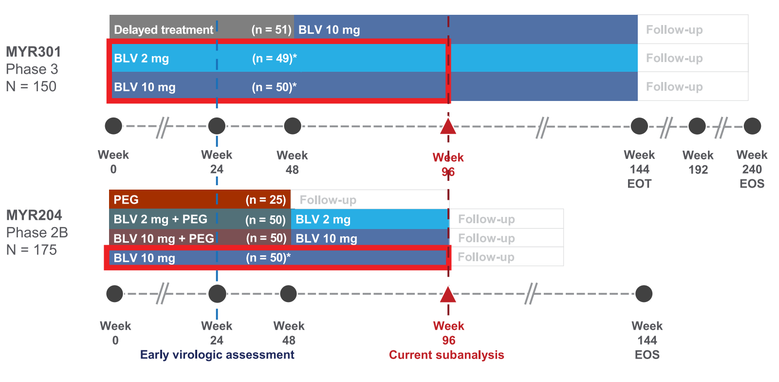
Objective

- Evaluate if continued BLV monotherapy for 96 weeks leads to improvement in virologic and biochemical responses among patients who had suboptimal early virologic response at week (W) 24

Study Design

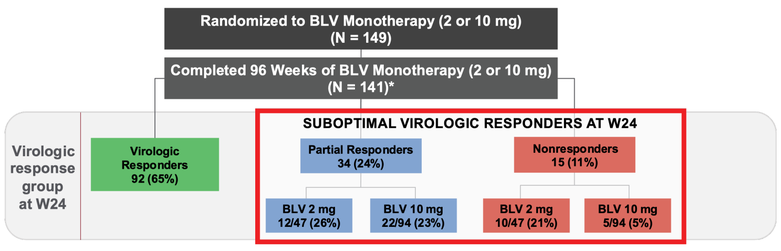
- Subanalysis of interim W96 data from CHD patients receiving BLV monotherapy in studies MYR204 (NCT03852433) and MYR301 (NCT03852719)
- Key inclusion criteria:
  - Participants who completed 96 weeks of treatment with BLV monotherapy (2 or 10 mg) from MYR301 and MYR204
  - CHD with or without cirrhosis (Child-Turcotte-Pugh score ≤6 or ≤7 in MYR204 and MYR301, respectively) Alanine aminotransferase (ALT) >1 × to <10 × upper limit of normal (ULN)
  - Alanine aminotransferase (ALT) >1 × to <10 × upper limit of normal (ULN)
  - Platelets ≥90,000 cells/mm^3 (MYR204) or platelets ≥60,000 cells/mm^3 (MYR301)
- Virologic response groups were defined as:
  - Nonresponder (NR): HDV RNA decrease <1 log_{10} IU/mL from baseline (BL)
  - Partial responder (PR): HDV RNA decrease ≥1 and <2 log_{10} IU/mL from BL
  - Virologic responder (VR): HDV RNA decrease ≥2 log_{10} IU/mL from BL or undetectable HDV RNA
- Suboptimal VRs at W24 were defined as NR or PR

Figure 1 MYR301 and MYR204 Study Designs



*3 patients from MYR204 BLV 10 mg and 5 patients from MYR301 BLV 2 mg and BLV 10 mg groups were not included in this analysis due to not completing 96 weeks of therapy.
BLV, bulevirtide; EOS, end of study; EOT, end of treatment; PEG, pegylated interferon alpha.

Figure 2 Early Virologic Response at W24



*8 patients discontinued the study by W96 and were not included: 4 were VR at W24, 1 patient receiving BLV 10 mg was considered a NR at W24 due to missing data but discontinued the study prior to W96, and the other 3 discontinued the study prior to W24. BLV, bulevirtide; NR, non-responder; VR, virologic responder; W, week.

- At W24, 35% (49/141) were suboptimal VRs

Results

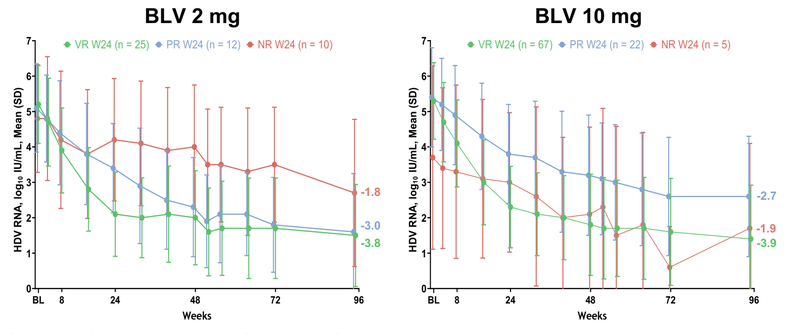
Table 1 Baseline Characteristics by W24 Virologic Response Group (BLV 2 + 10 mg)

	VR n = 92	PR n = 34	NR n = 15
Age, years, mean (SD)	41 (9)	41 (7)	44 (12)
Male sex, n (%)	62 (67)	21 (62)	11 (73)
Race, n (%)			
White	81 (88)	33 (97)	8 (53)
Asian	9 (10)	1 (3)	7 (47)
Black	2 (2)	0 (0)	0 (0)
Cirrhosis, n (%)	44 (48)	13 (38)	4 (27)
Platelets, ×10^3 cells/mm^3, mean (SD)	162 (49)	170 (49)	157 (59)
Liver stiffness, kPa, mean (SD)	14.6 (8.9)	13.0 (6.6)	11.8 (7.1)
ALT, U/L, median (Q1, Q3)	95 (71,139)	93 (60,125)	101 (52,146)
HDV RNA, log_{10} IU/mL, mean (SD)	5.3 (1.1)	5.3 (1.3)	4.4 (1.9)
HDV genotype 1, n (%)*	89 (97)	34 (100)	15 (100)
HBsAg, log_{10} IU/mL, mean (SD)	3.7 (0.5)	3.6 (0.8)	3.5 (0.7)
HBV DNA, log_{10} IU/mL, mean (SD)	1.5 (1.5)	1.3 (1.1)	1.3 (1.7)
HBeAg positive, n (%)	13 (14)	5 (15)	0 (0)
HBV genotype D, n (%)	82 (89)	30 (88)	11 (73)
Previous IFN therapy, n (%)	44 (48)	19 (56)	8 (53)
Concomitant HBV NA therapy, n (%)	52 (57)	18 (53)	9 (60)

*BLV VR group: 2 had HDV GT 5, 1 had missing HDV GT. **BLV VR group: 1 had HBV GT E, 6 had HBV GT A, 3 had missing HBV GT; PR group: 4 had HBV GT A; NR group: 3 had HBV GT A, 1 had missing HBV GT.
ALT, alanine transaminase; GT, genotype; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HDV, hepatitis delta virus; IFN, interferon; IQR, interquartile range; NA, nucleos(t)ide analogue; NR, nonresponder; PR, partial responder; Q, quartile; VR, virologic responder; W, week.

- Baseline characteristics were evenly balanced among W24 virologic response groups.

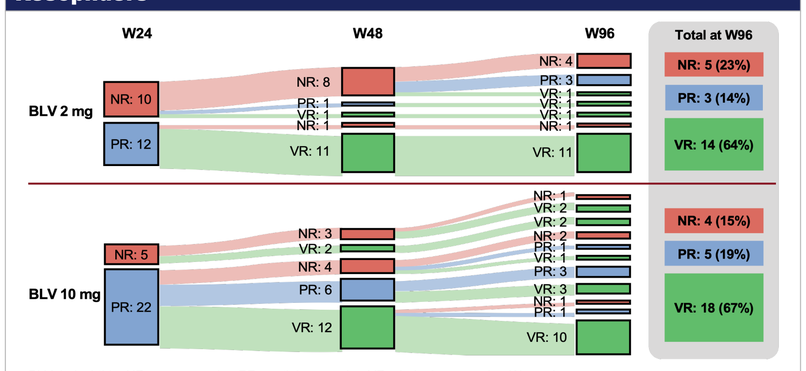
Figure 3 Mean HDV RNA Over Time by Dose



Decline at W96 is expressed as mean (SD) change from BL.
BL, baseline; BLV, bulevirtide; HDV, hepatitis delta virus; NR, nonresponder; PR, partial responder; VR, virologic responder; W, week.

- Mean HDV RNA improved over time in all W24 virologic response groups

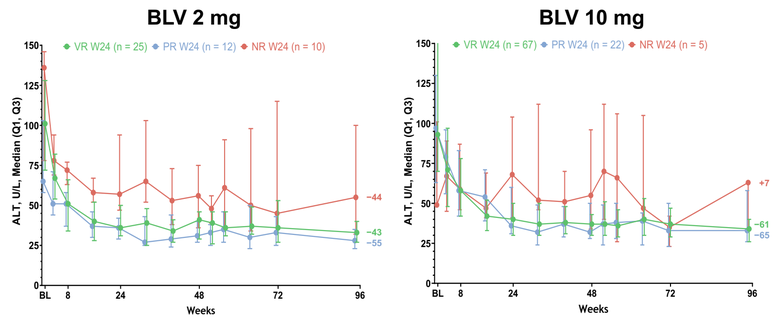
Figure 4 Progression of Responses in W24 Suboptimal Virologic Resopnders



BLV, bulevirtide; NR, nonresponder; PR, partial responder; VR, virologic responder; W, week.

- Treatment responses improved over time in W24 suboptimal virologic responders

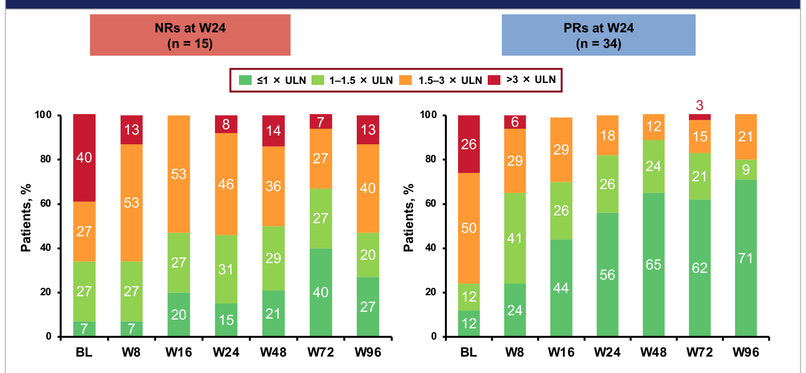
Figure 5 Changes in ALT Levels Over Time



Decline at W96 is expressed as median (Q1, Q3) change from BL.
ALT, alanine aminotransferase; BL, baseline; BLV, bulevirtide; HDV, hepatitis delta virus; NR, nonresponder; PR, partial responder; Q, quartile; VR, virologic responder; W, week.

- Improvements in ALT levels were observed in most W24 suboptimal virologic responders over time

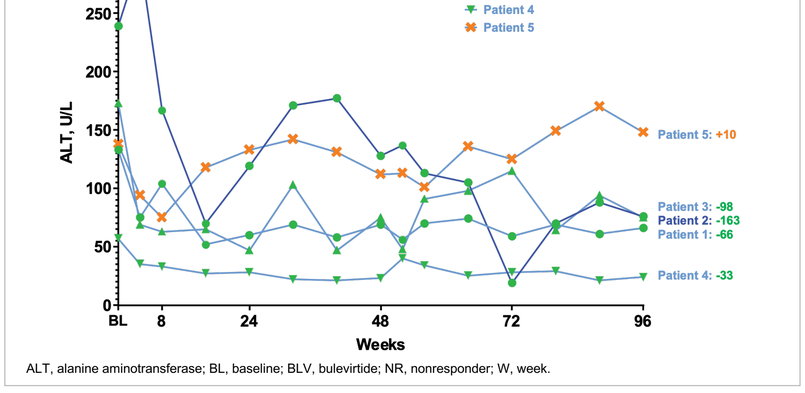
Figure 6 ALT Categorical Shifts Over Time in W24 Suboptimal Virologic Responders (BLV 2 + 10 mg)



2 VRs were missing ALT data at W24 and W72; 1 VR was missing ALT data at W16. 2 NRs were missing ALT data at W24, and 1 NR was missing ALT data at W48.
ALT, alanine aminotransferase; BL, baseline; BLV, bulevirtide; NR, nonresponder; PR, partial responder; ULN, upper limit of normal; VR, virologic responder; W, week.

- ALT categories improved over time in W24 suboptimal virologic responders

Figure 7 ALT Change in the Five Patients Who Remained NR From W24 to W96



ALT, alanine aminotransferase; BL, baseline; BLV, bulevirtide; NR, nonresponder; W, week.

- ALT improved by greater than 50% from BL in Patients 1, 2, 3, and 4 at W96

References: **1.** Hepcludex. European Medicines Agency SmPC. Gilead Sciences, Inc.; 2023. **2.** European Association for the Study of the Liver. *J Hepatol*. 2023;79:433-60. **3.** Hepcludex. Australian Register of Therapeutic Goods. Gilead Sciences, Inc. 2024. **4.** Sandmann L, et al. *Liver Int*. 2022;00:1-11. **5.** Wedemeyer H, et al. *N Engl J Med*. 2023;389:22-32. **6.** Wedemeyer H, et al. EASL 2023. **Acknowledgments:** We extend our thanks to the patients, their families, and all participating investigators. This study was funded by Gilead Sciences. Editing and production assistance were provided by Danielle Shepherd, PhD, of Red Nucleus, funded by Gilead Sciences, Inc. **Disclosures:** **PL** reports speaking and teaching fees from and participation in advisory committees or review panels for AbbVie; Aligos; Alnylam; Antios; Arrowhead; Bristol Myers Squibb; Eiger Biopharmaceuticals; Gilead Sciences, Inc.; GSK; Janssen; Merck Sharp & Dohme; MYR GmbH; Roche; and Spring Bank Pharmaceuticals. **HW** reports honoraria for speaking or consulting from Abbott; AbbVie; Boehringer Ingelheim; Bristol Myers Squibb; Eiger Biopharmaceuticals; Gilead Sciences, Inc.; Janssen; Merck Sharp & Dohme; MYR GmbH; Novartis; Novira; Roche; Roche Diagnostics; Siemens; and Transgene; and research support from Abbott; Bristol Myers Squibb; Gilead Sciences, Inc.; Novartis; Roche; and Roche Diagnostics. **MRB** reports speaker's bureau for AbbVie, EISAI-MSD, and Gilead Sciences, Inc., and advisory/consultancy for AbbVie; Gilead Sciences, Inc.; Janssen; and Roche. **PB, ASC, GSG, and TS** report no conflicts of interest. MB reports being a board member and speaker for AbbVie; Gilead Sciences, Inc.; Intercept; and Roche. **HF** reports personal fees and invitations to medical meetings from AbbVie; Bristol Myers Squibb; Gilead Sciences, Inc.; Janssen; and Merck Sharp & Dohme. **BLD, JFF, CF, AO, GMC, DM, QA, RCM, and AHL** are employees of Gilead Sciences, Inc., and may own stock in Gilead Sciences, Inc. **SZ** reports speaker's bureau and/or consultancy for AbbVie; Allergan; BioMarin; Gilead Sciences, Inc.; Intercept; Janssen; Merck Sharp & Dohme; Novo Nordisk; Swedish Orphan Biovitrum; and Theratechnologies. **MC** received honoraria from AbbVie; Falk; Gilead Sciences, Inc.; GSK; Janssen-Cilag; Merck Sharp & Dohme; Novartis; Roche; Spring Bank Pharmaceuticals; and Swedish Orphan Biovitrum. DR is a speaking and teaching associate of Gilead Sciences, Inc. **FZ** received consulting fees from Aligos; Antios; Assembly Biosciences; Gilead Sciences, Inc.; and GSK; and research funding to INSERM from Assembly Biosciences, Beam, and Janssen. SA received honoraria for lectures and educational events from AbbVie; Biogen; Gilead Sciences, Inc.; and Merck Sharp & Dohme; and reports grants from AbbVie and Gilead Sciences, Inc. **TA** acted as a speaker and investigator for AbbVie; Eiger Biopharmaceuticals; Gilead Sciences, Inc.; Janssen; Merck; MYR Pharmaceutical; and Roche.