Presentation #63

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

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Disclosures

Pietro Lampertico 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. **Heiner Wedemeyer** 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. **Maurizia Rossana Brunetto** reports speaker's bureau for AbbVie, EISAI-MSD, and Gilead Sciences, Inc., and advisory/consultancy for AbbVie; Gilead Sciences, Inc.; Janssen; and Roche. **Pavel Bogomolov, Adrian Streinu-Cercel, George Sebastian Gherlan,** and **Tatyana Stepanova** report no conflicts of interest. **Marc Bourlière** reports being a board member and speaker for AbbVie; Gilead Sciences, Inc.; Intercept; and Roche. **Helène Fontaine** reports personal fees and invitations to medical meetings from AbbVie; Bristol Myers Squibb; Gilead Sciences, Inc.; Janssen; and Merck Sharp & Dohme. **Ben L Da, John F Flaherty, Catherine Frenette, Anu Osinusi, Grace M Chee, Dmitry Manuilov, Qi An, Renee-Claude Mercier,** and **Audrey H Lau** are employees of Gilead Sciences, Inc., and may own stock in Gilead Sciences, Inc. **Stefan Zeuzem** 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. **Markus Cornberg** received honoraria from AbbVie; Falk; Gilead Sciences, Inc.; GSK; Janssen-Cilag; Merck Sharp & Dohme; Novartis; Roche; Spring Bank Pharmaceuticals; and Swedish Orphan Biovitrum. **Dominique Roulot** is a speaking and teaching associate of Gilead Sciences, Inc. **Fabien Zoulim** received consulting fees from Aligos; Antios; Assembly Biosciences; Gilead Sciences, Inc.; and GSK; and research funding to INSERM from Assembly Biosciences, Beam, and Janssen. **Soo Aleman** 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. **Tarik Asselah** acted as a speaker and investigator for AbbVie; Eiger Biopharmaceuticals; Gilead Sciences, Inc.; Janssen; Merck; MYR Pharmaceutical; and Roche.

Introduction

- BLV, a novel entry inhibitor of HDV, is approved in the EU at 2 mg/day for the treatment of CHD in patients with compensated liver disease (full approval received in July 2023)[1]
- 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[2,3]
- In the Phase 3 Study MYR301, treatment with BLV 2 mg/day monotherapy results in virologic response rates of 73% and 76% at 1 and 2 years, respectively[3,4]
- 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 response among patients who have early suboptimal virologic response at W24**

BLV, bulevirtide; CHD, chronic hepatitis delta; HDV, hepatitis delta virus; EU, European Union.

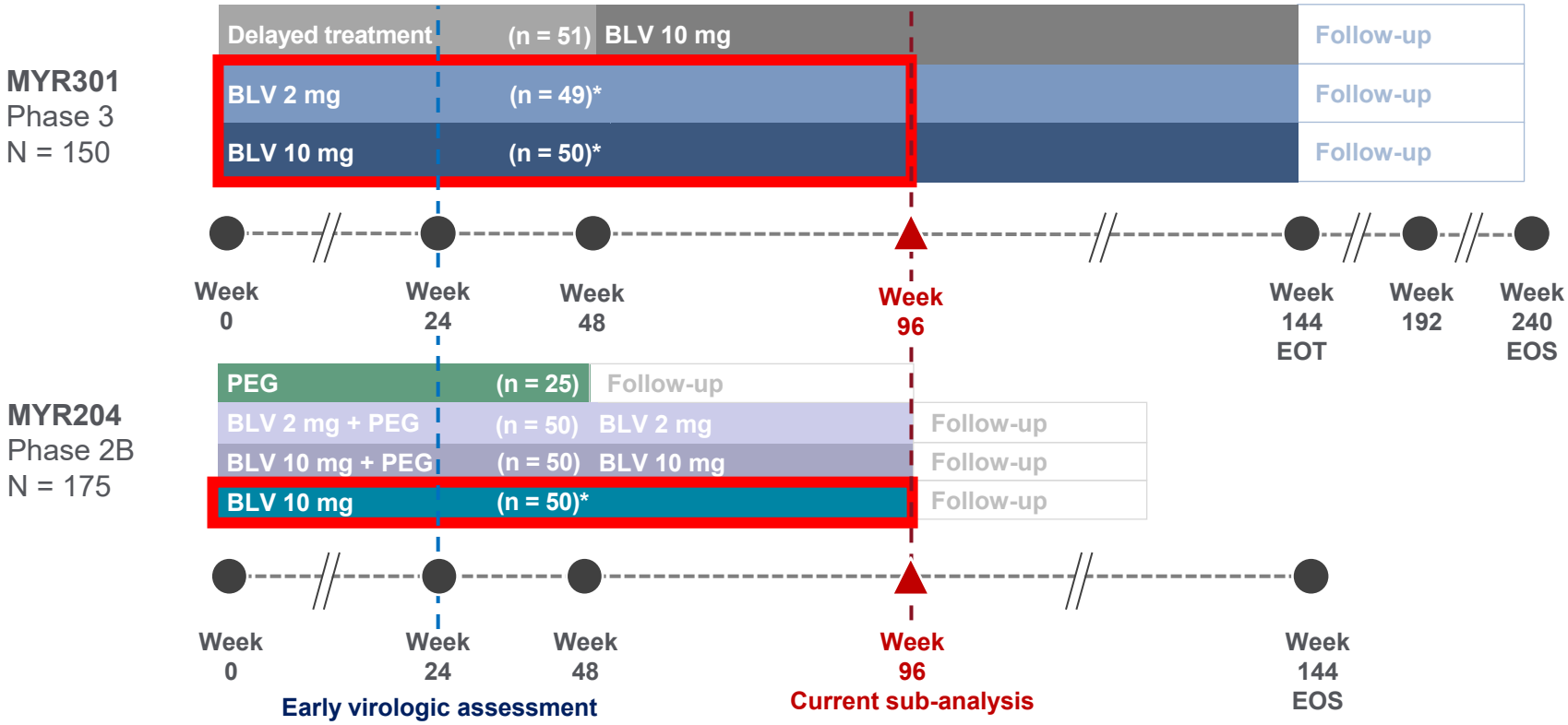
1. Hepcludex SmPC. 2. Sandmann L, et al. *Liver International* 2022;00:1-11. 3. Wedemeyer H, et al. *NEJM* 2023;389:22-32. 4. Wedemeyer H, et al. EASL 2023. Oral #OS-068.

Study Design

- **Sub-analysis 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 (CPT score ≤6 or ≤7 in MYR204 and MYR301, respectively)
  - ALT >1 × to <10 × ULN
  - Platelets ≥90,000 cells/mm^3 (MYR204) or platelets ≥60,000 cells/mm^3 (MYR301)
- **Viral response groups were defined as:**
  - Non-responder (NR): HDV RNA decrease <1 log_{10} IU/mL from 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
- **Early suboptimal VRs were defined as being a NR or PR at W24**

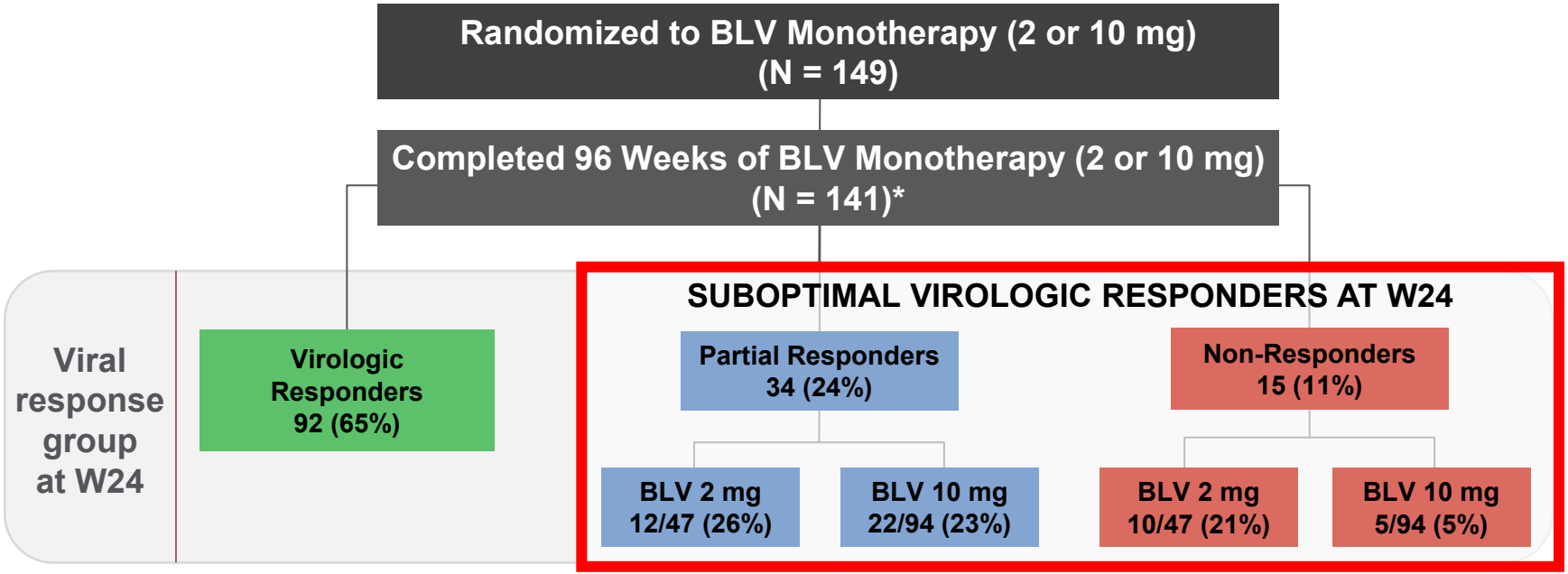
HDV RNA levels determined by RT-qPCR using RoboGene® HDV RNA Quantification Kit 2.0 (lower limit of quantification 50 IU/mL, lower limit of detection 6 IU/mL).
ALT ULN: ≤31 U/L for females and ≤41 U/L for males (Russian sites) and ≤34 U/L for females and ≤49 U/L for males (all other sites).
ALT, alanine aminotransferase; BL, baseline; BLV, bulevirtide; CHD, chronic hepatitis D; CPT, Child-Pugh-Turcotte; HDV, hepatitis delta virus; RT-qPCR, reverse transcription- quantitative polymerase chain reaction; ULN, upper limit of normal; W, week.

MYR301 and MYR204 Study Designs



*3 patients from MYR204 Arm D (BLV 10 mg) and 5 patients from 301 Arms B (BLV 2 mg) and C (BLV 10 mg) 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 α.

Early Viral Response at W24



35% (49/141) were suboptimal virologic responders at W24

*8 patients discontinued the study by W96 and were not included: 4 were VR at W24, 1 patient receiving BLV 10mg 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.

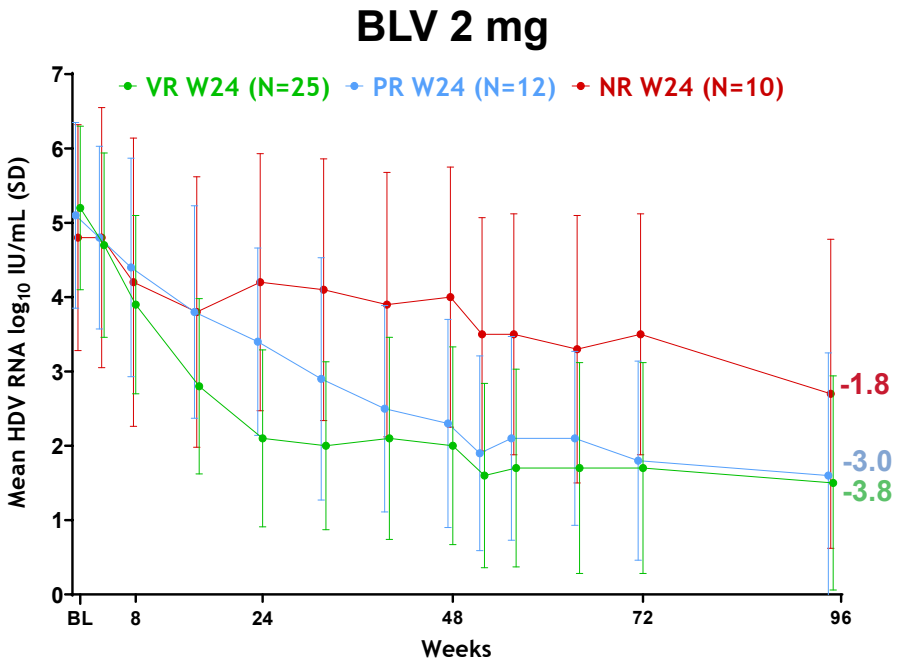
Baseline Characteristics by W24 Viral Response Group (BLV 2 + 10 mg)

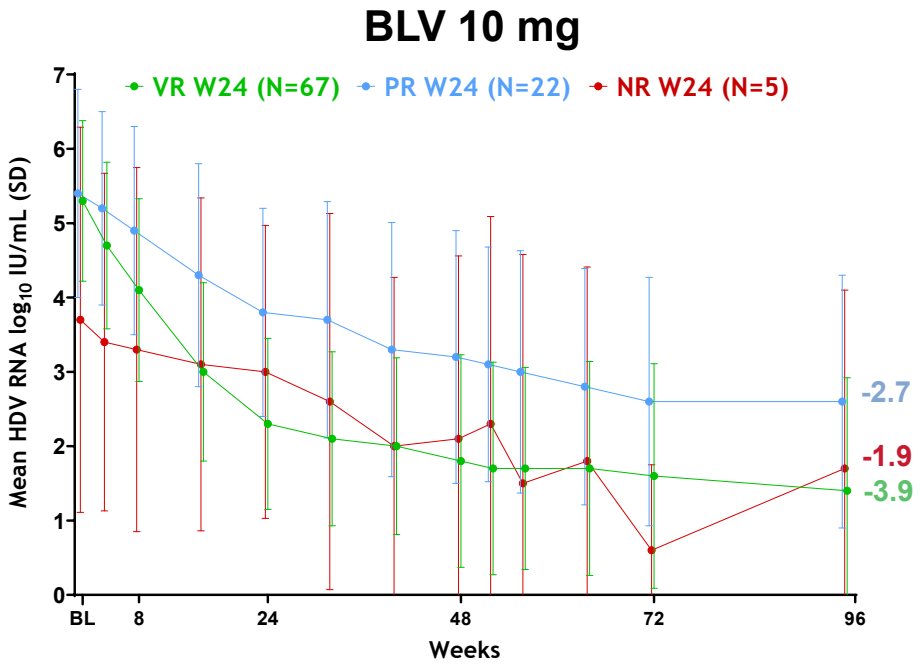
		VR n = 92	PR n = 34	NR n = 15
Mean age, years (SD)		41 (9)	41 (7)	44 (12)
Male sex, n (%)		62 (67)	21 (62)	11 (73)
Race, n (%)	White	81 (88)	33 (97)	8 (53)
	Asian	9 (10)	1 (3)	7 (47)
	Black	2 (2)	0 (0)	0 (0)
Cirrhosis, n (%)		44 (48)	13 (38)	4 (27)
Mean platelets, $\times 10^3$ cells/mm^3 (SD)		162 (49)	170 (49)	157 (59)
Mean liver stiffness, kPa (SD)		14.6 (8.9)	13.0 (6.6)	11.8 (7.1)
Median ALT, U/L (Q1, Q3)		95 (71,139)	93 (60,125)	101 (52,146)
Mean HDV RNA, $\log_{10}$ IU/mL (SD)		5.3 (1.1)	5.3 (1.3)	4.4 (1.9)
HDV genotype 1, n (%)*		89 (97)	34 (100)	15 (100)
Mean HBsAg, $\log_{10}$ IU/mL (SD)		3.7 (0.5)	3.6 (0.8)	3.5 (0.7)
Mean HBV DNA, $\log_{10}$ IU/mL (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 NUC therapy, n (%)		52 (57)	18 (53)	9 (60)

Baseline characteristics were evenly balanced among W24 viral response groups

*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; NR, non-responder; NUC, nucleos(t)ide; PR, partial responder; Q, quartile; SD, standard deviation; VR, virologic responder; W, week.

Mean HDV RNA Over Time by Dose

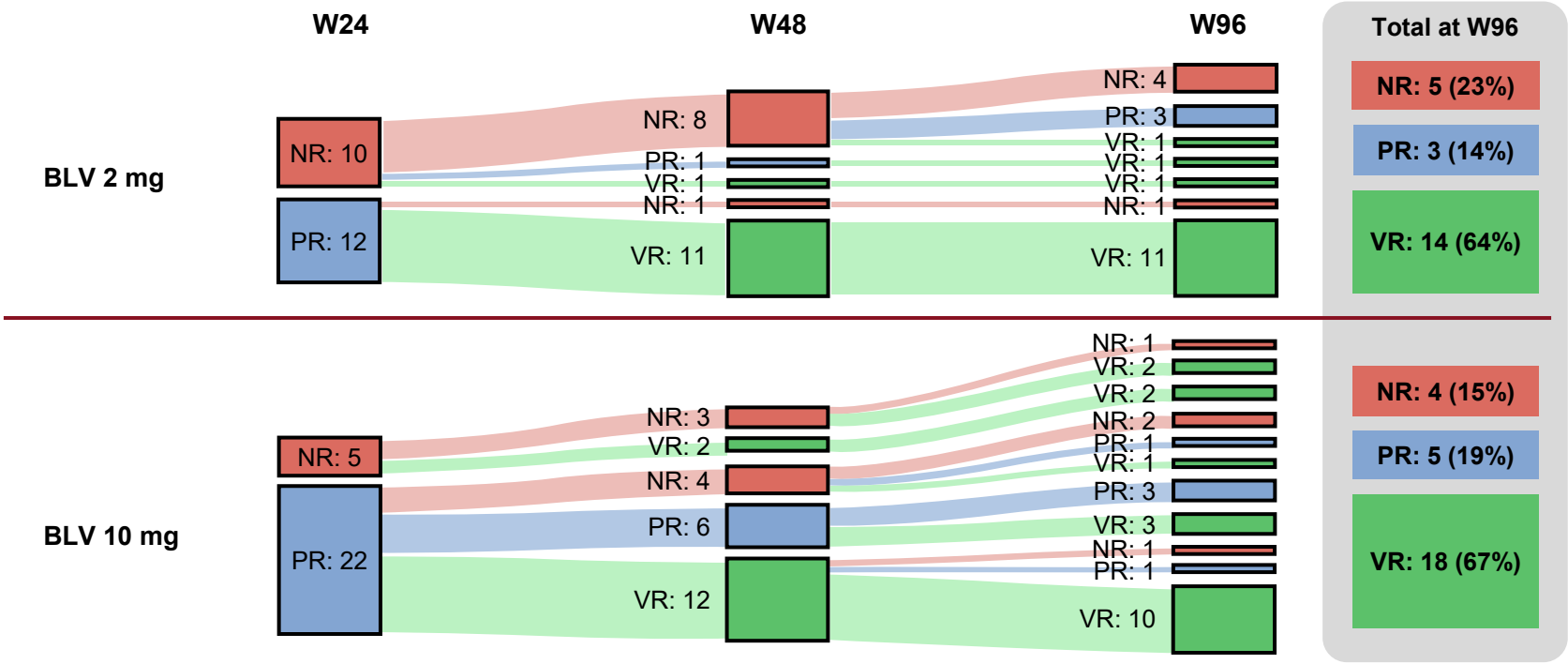




Mean HDV RNA levels declined over time in all W24 viral response groups

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

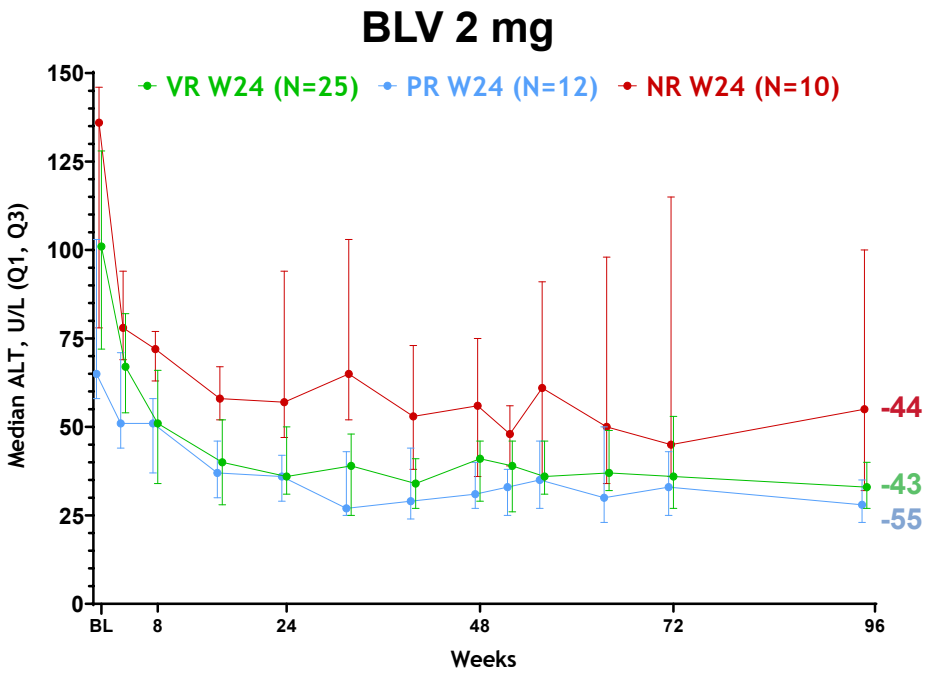
Progression of Responses in W24 Suboptimal Virologic Responders

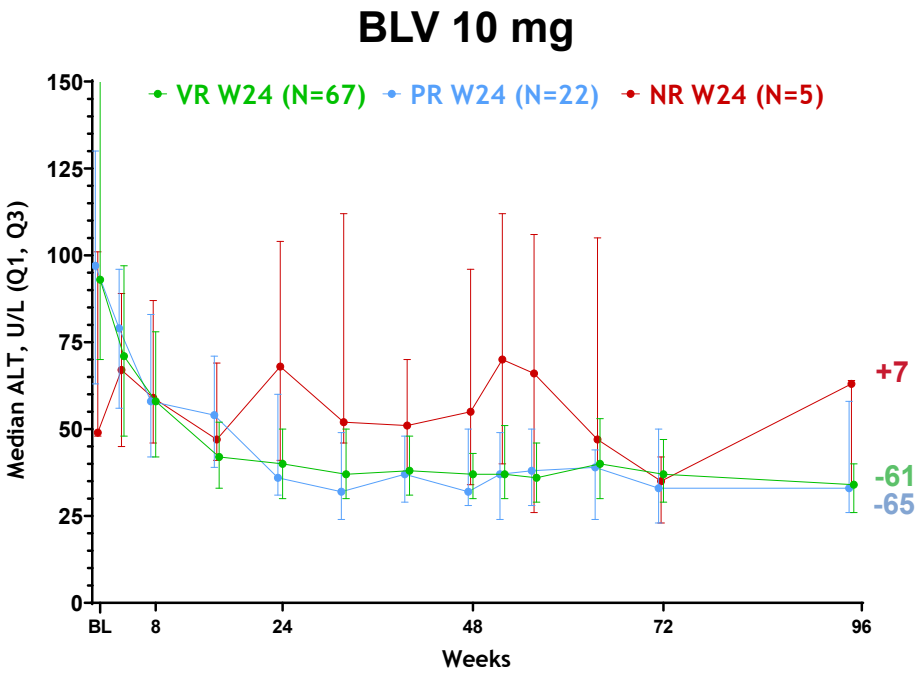


Treatment responses improved over time in W24 suboptimal virologic responders

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

Change in ALT Levels Over Time

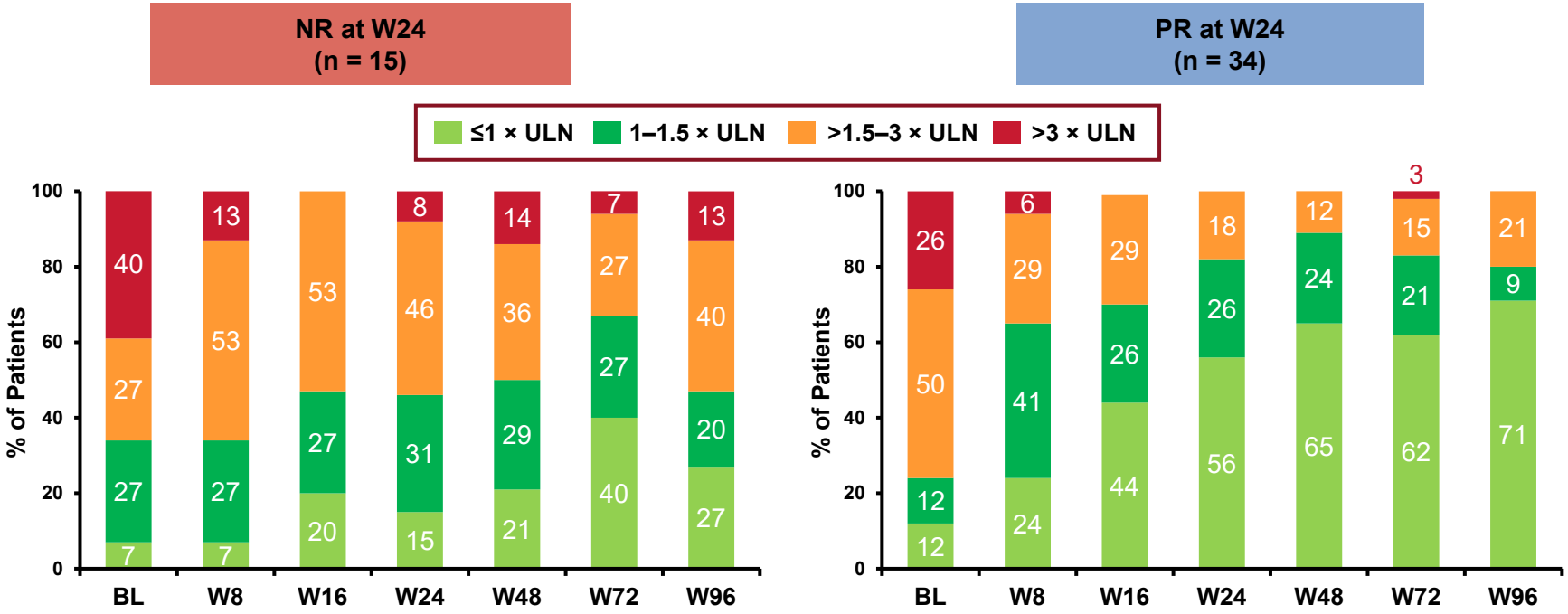




Improvements in ALT levels were observed in most W24 suboptimal virologic responders over time

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

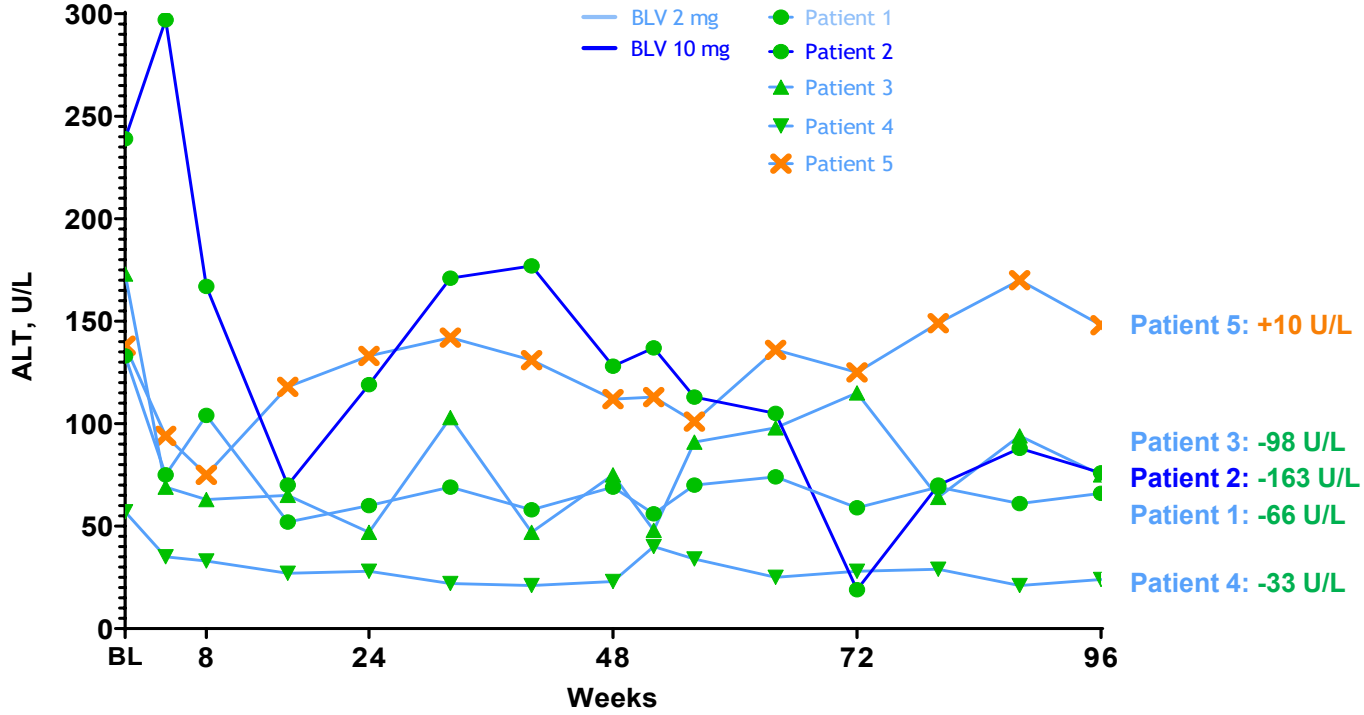
ALT Categorical Shifts Over Time in W24 Suboptimal Virologic Responders (BLV 2 + 10 mg)



ALT categories improved over time in W24 suboptimal virologic responders

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, non-responder; PR, partial responder; ULN, upper limit of normal; VR, virologic responder; W, week.

ALT Change in the 5 Patients Who Remained a NR From W24 to W96



ALT improved by greater than 50% from BL in 4 of the 5 Patients at W96

ALT, alanine aminotransferase; BL, baseline; BLV, bulevirtide; NR, non-responder; W, week.

Summary and Conclusion

- At W24, 35% of patients treated with BLV 2 or 10 mg monotherapy had suboptimal virologic response including 11% NR and 24% PR
- After 96 weeks of BLV 2 or 10 mg monotherapy:
  - W24 PR: 74% VR, 23% PR, 3% NR
  - W24 NR: 47% VR, 20% PR, 33% NR
- Biochemical responses were observed in the majority of W24 PR and a subset of W24 NR, primarily occurring in the first 24 weeks
- Virological and biochemical responses at W96 were similar between BLV 2 and 10 mg in early suboptimal virologic responders (NR or PR at W24)
- **Continued BLV monotherapy through 96 weeks benefits the majority of early suboptimal virologic responders**

ALT, alanine aminotransferase; BLV, bulevirtide; NR, non-responder; PR, partial responder; VR, virologic responder; W, week.

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