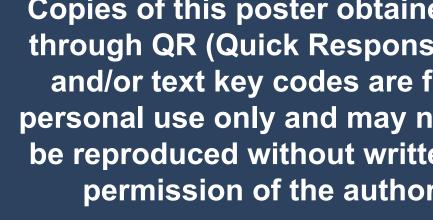
# Hepatitis B Surface Antigen Response in Patients With Chronic Hepatitis Delta Receiving Bulevirtide With or Without Pegylated Interferon Alfa-2a in MYR204

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# Conclusions

- In MYR204, most patients (14 of 17) achieving hepatitis B surface antigen (HBsAg) response through 48 weeks of follow-up were from the bulevirtide (BLV) + pegylated interferon alfa-2a (PegIFNα) arms, suggesting that combination therapy with BLV and PegIFNα improves the chance of HBsAg loss in patients with chronic hepatitis delta (CHD) compared with either monotherapy
- Among patients with HBsAg response, all achieved undetectable hepatitis delta virus (HDV) RNA, 15 of 17 achieved undetectable hepatitis B virus DNA, and 16 of 17 had normalized alanine aminotransferase
- Among patients with HBsAg response, none had cirrhosis at baseline, and only 24% had previously taken interferon
- Lower HBsAg and HDV RNA levels at baseline were predictive of HBsAg response in patients with CHD treated with BLV+PegIFNα

# Plain Language Summary

- People infected with both hepatitis B virus and hepatitis delta virus can develop severe liver disease
- Bulevirtide is a treatment for chronic hepatitis delta infection that is safe and effective
- We evaluated hepatitis B surface antigen (HBsAg) response in patients with chronic hepatitis delta infection receiving bulevirtide with or without interferon
- HBsAg response was most likely in the people who were treated with both bulevirtide and interferon

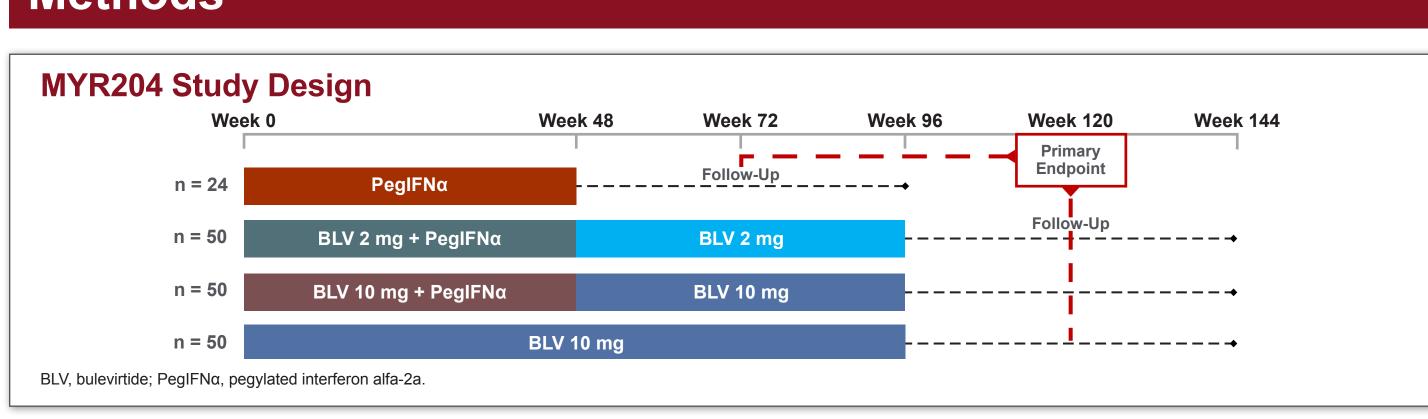
## Introduction

- Bulevirtide (BLV), a 47–amino-acid chemically synthesized lipopeptide, blocks entry of hepatitis delta virus (HDV) into hepatocytes via competitive inhibition of the interaction between the hepatitis B virus (HBV) preS1 domain and the sodium taurocholate cotransporting polypeptide receptor<sup>1,2</sup>
- BLV has been shown to be safe, well tolerated, and efficacious for the treatment of chronic HDV (CHD) infection<sup>3,4</sup>
- BLV 2 mg/day is approved for the treatment of compensated CHD in the European Union, the United Kingdom, Switzerland, the Russian Federation, and Australia<sup>5,6</sup>
- The Phase 2 study MYR204 (NCT03852433) evaluated the efficacy and safety of BLV at 2 and 10 mg/day in combination with pegylated interferon (IFN) alfa-2a (PegIFNα) vs monotherapy with BLV 10 mg/day and monotherapy with PegIFNα in patients with CHD<sup>7</sup>
- IFN therapy is associated with variable rates of hepatitis B surface antigen (HBsAg) loss in different subsets of patients with chronic hepatitis B<sup>8</sup>

# Objectives

- We evaluated HBsAg response in patients with CHD receiving BLV with or without PegIFNα in MYR204
- We also aimed to identify baseline (BL) predictors (host or viral factors) of HBsAg response in this population

## Methods



- HBsAg response was defined as ≥1 log<sub>10</sub> IU/mL decline in HBsAg from BL and HBsAg <100 IU/mL at follow-up week 48 (FU48)
- HBsAg loss was part of HBsAg response
- HBsAg quantification
- Plasma HBsAg levels were measured using the DiaSorin Liaison XL with a lower limit of quantitation (LLOQ) of 0.05 IU/mL
- HDV RNA quantification
- Plasma HDV RNA levels were determined by RT-qPCR using the RoboGene HDV RNA Quantification Kit 2.0. The LLOQ and lower limit of detection were 50 IU/mL and 6 IU/mL, respectively
- Data analysis
- Statistical analysis was performed by Fisher's exact test or t-test

## Results

#### **BL Demographics and Disease Characteristics**

	PeglFNα (n = 24)	BLV 2 mg + PegIFNα (n = 50)	BLV 10 mg + PegIFNα (n = 50)	BLV 10 mg (n = 50)
Age, years, mean (SD)	41 (8.4)	41 (9.3)	41 (8.6)	40 (8.5)
Male sex, n (%)	18 (75)	33 (66)	35 (70)	38 (76)
<b>Race</b> , n (%)				
Caucasian	20 (83)	44 (88)	43 (86)	44 (88)
Asian	4 (17)	3 (6)	4 (8)	4 (8)
Black	0	3 (6)	2 (4)	2 (4)
Cirrhosis, n (%)	8 (33)	17 (34)	17 (34)	17 (34)
<b>Liver stiffness</b> , kPa, median (Q1, Q3)	12.2 (8.6, 18.9)	10.7 (7.8, 16.5)	10.5 (7.8, 14.3)	10.8 (8.5, 14.1)
ALT, U/L, median (Q1, Q3)	91 (64, 152)	81 (56, 143)	82 (55, 117)	90 (63, 127)
<b>HDV RNA</b> , log <sub>10</sub> IU/mL, median (Q1, Q3)	5.2 (4.6, 5.8)	5.6 (4.3, 6.3)	5.5 (4.4, 6.1)	5.6 (4.6, 6.3)
<b>HDV GT 1/5/6</b> , n (%)	24 (100)/0/0	48 (96)/1 (2)/1 (2)	47 (94)/2 (4)/0	49 (98)/1 (2)/0
HBsAg, log <sub>10</sub> IU/mL, mean (SD)	3.6 (0.5)	3.7 (0.6)	3.7 (0.7)	3.7 (0.6)
Prior interferon use, n (%)	12 (50)	25 (50)	26 (52)	21 (42)
Concomitant NA for HBV, n (%)	11 (46)	24 (48)	25 (50)	23 (46)

• The BL demographics and disease characteristics, including HBsAg and HDV RNA levels, were well balanced across the groups

#### HBsAg Response in Patients Through FU48

Response	PeglFNα (n = 24)	BLV 2 mg + PegIFNα (n = 50)	BLV 10 mg + PeglFNα (n = 50)	BLV 10 mg (n = 50)	Total (N = 174)
Total HBsAg response, n (%)	2 (8)	8 (16)	6 (12)	1 (2)	17 (10)
HBsAg loss, n (%)	0 (0)	5 (10)	2 (4)	1 (2)	8 (5)

- 14 of 17 (82%) patients who achieved HBsAg response were from BLV+IFN treatment groups
- 7 of 8 (88%) patients who achieved HBsAg loss were from BLV+IFN treatment groups

# Patients With HBsAg Response Achieved Undetectable HDV RNA and HBV DNA and ALT Normalization at FU48

Response	Total HBsAg Response (n = 17)	HBsAg Loss (n = 8)
Achieved undetectable HDV RNA, n (%)	17 (100)	8 (100)
Achieved undetectable HBV DNA, n (%)	15 (88)	8 (100)
Achieved ALT normalization, n (%)	16 (94)	7 (88)

- All 17 HBsAg responders achieved undetectable HDV RNA
- All 8 patients with HBsAg loss also achieved undetectable HBV DNA
- All achieved alanine aminotransferase (ALT) normalization except 1 patient who had declining ALT but had not reached ALT normalization at FU48

## Results

### BL Characteristics of Patients Achieving HBsAg Response at FU48

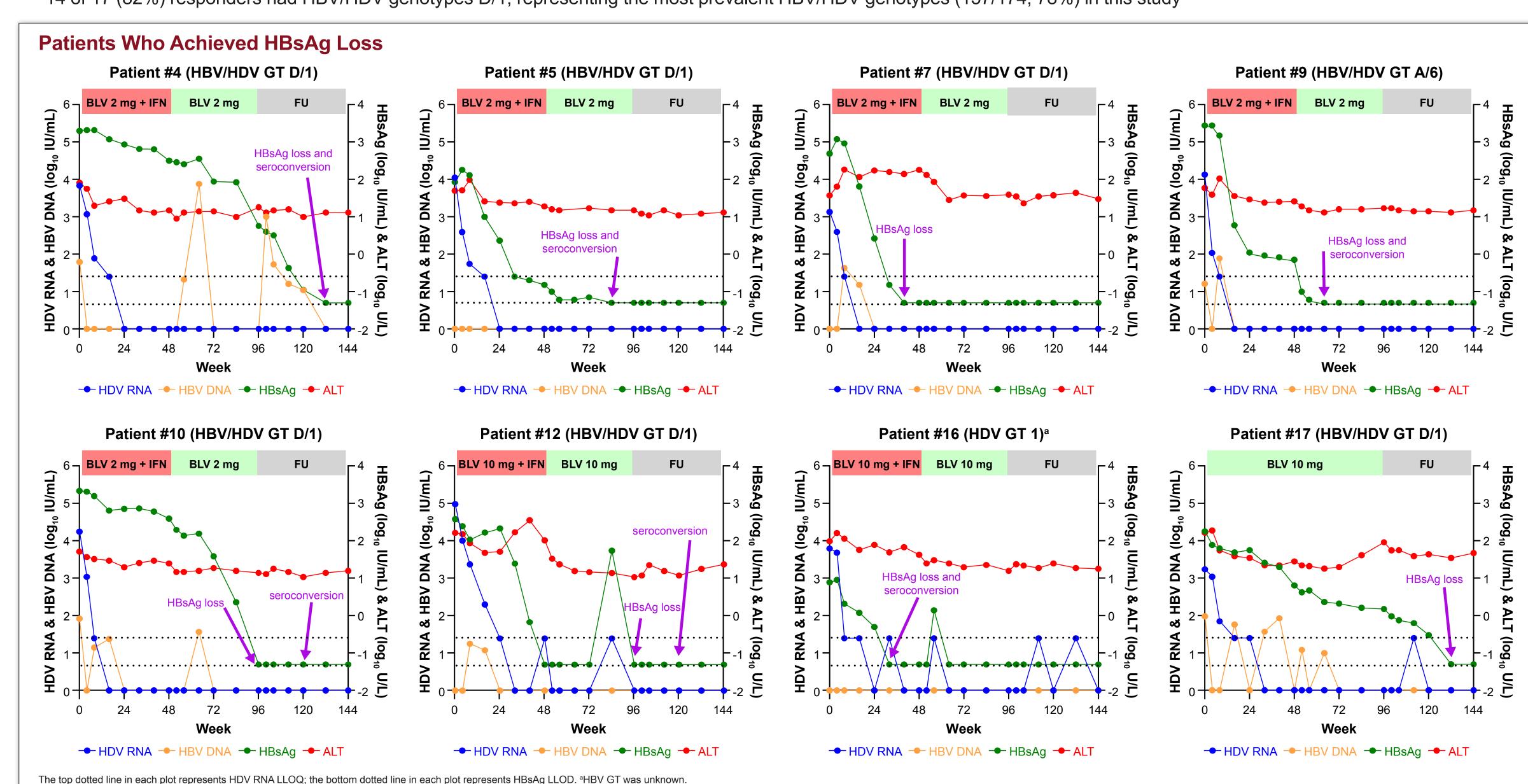
ID	Loss	Group	Genotype	Sex	Race	Age, y	Status	Therapy	Current NA	HBeAg	(U/L)	(IU/mL)	(IU/mL)	(IU/mL)
1	N	IFN	D/1	М	Asian	35	Absent	N	N	Negative	187	1500	65,267	0
2	N	IFN	D/1	М	White	48	Absent	N	Y	Negative	65	590	18,425	0
3	N	BLV 2 mg + IFN	D/1	М	White	46	Absent	N	N	Negative	81	6900	8994	29
4	Y and SC	BLV 2 mg + IFN	D/1	М	White	39	Absent	Υ	N	Negative	82	2000	6938	62
5	Y and SC	BLV 2 mg + IFN	D/1	М	White	50	Absent	N	N	Negative	50	85	11,163	0
6	Ν	BLV 2 mg + IFN	D/1	М	White	53	Absent	Υ	Y	Negative	45	1200	0	0
7	Υ	BLV 2 mg + IFN	D/1	М	White	41	Absent	N	Y	Negative	37	490	1349	0
8	N	BLV 2 mg + IFN	D/1	М	White	39	Absent	N	N	Negative	58	19,000	123,476	24
9	Y and SC	BLV 2 mg + IFN	A/6	F	Black	50	Absent	N	Y	Negative	59	2800	13,560	16
10	Y and SC	BLV 2 mg + IFN	D/1	F	White	61	Absent	Y	N	Negative	52	2200	17,791	84
11	N	BLV 10 mg + IFN	D/1	М	White	47	Absent	N	N	Negative	102	19,000	1759	958
12	Y and SC	BLV 10 mg + IFN	D/1	М	White	38	Absent	N	N	Negative	168	390	98,887	0
13	N	BLV 10 mg + IFN	D/1	М	Asian	39	Absent	N	N	Negative	90	3300	54,813	0
14	N	BLV 10 mg + IFN	D/1	М	White	45	Absent	N	N	Negative	60	900	3730	17
15	N	BLV 10 mg + IFN	No data/5	F	Black	31	Absent	N	Y	Negative	112	17,000	352,017	0
16	Y and SC	BLV 10 mg + IFN	No data/1	F	White	46	Absent	N	N	Negative	99	7.8	6279	0
17	Y	BLV 10 mg	D/1	М	White	40	Absent	Υ	N	Negative	166	180	1729	96

• All responders were HBeAg negative at BL; none had cirrhosis at BL

• 14 of 17 (82%) responders had HBV/HDV genotypes D/1, representing the most prevalent HBV/HDV genotypes (137/174, 78%) in this study

ALT, alanine aminotransferase; BLV, bulevirtide; FU, follow-up; GT, genotype; HBsAg, hepatitis B virus; HDV, hepatitis delta virus; IFN, interferon; LLOD, lower limit of detection; LLOQ, lower limit of quantitation.

ALT, alanine aminotransferase; BL, baseline; BLV, bulevirtide; F, female; FU48, follow-up week 48; HBeAg, hepatitis B virus; HDV, hepatitis delta virus; IFN, interferon; M, male; N, no; NA, nucleos(t)ide analogue; SC, seroconversion; Y, yes.

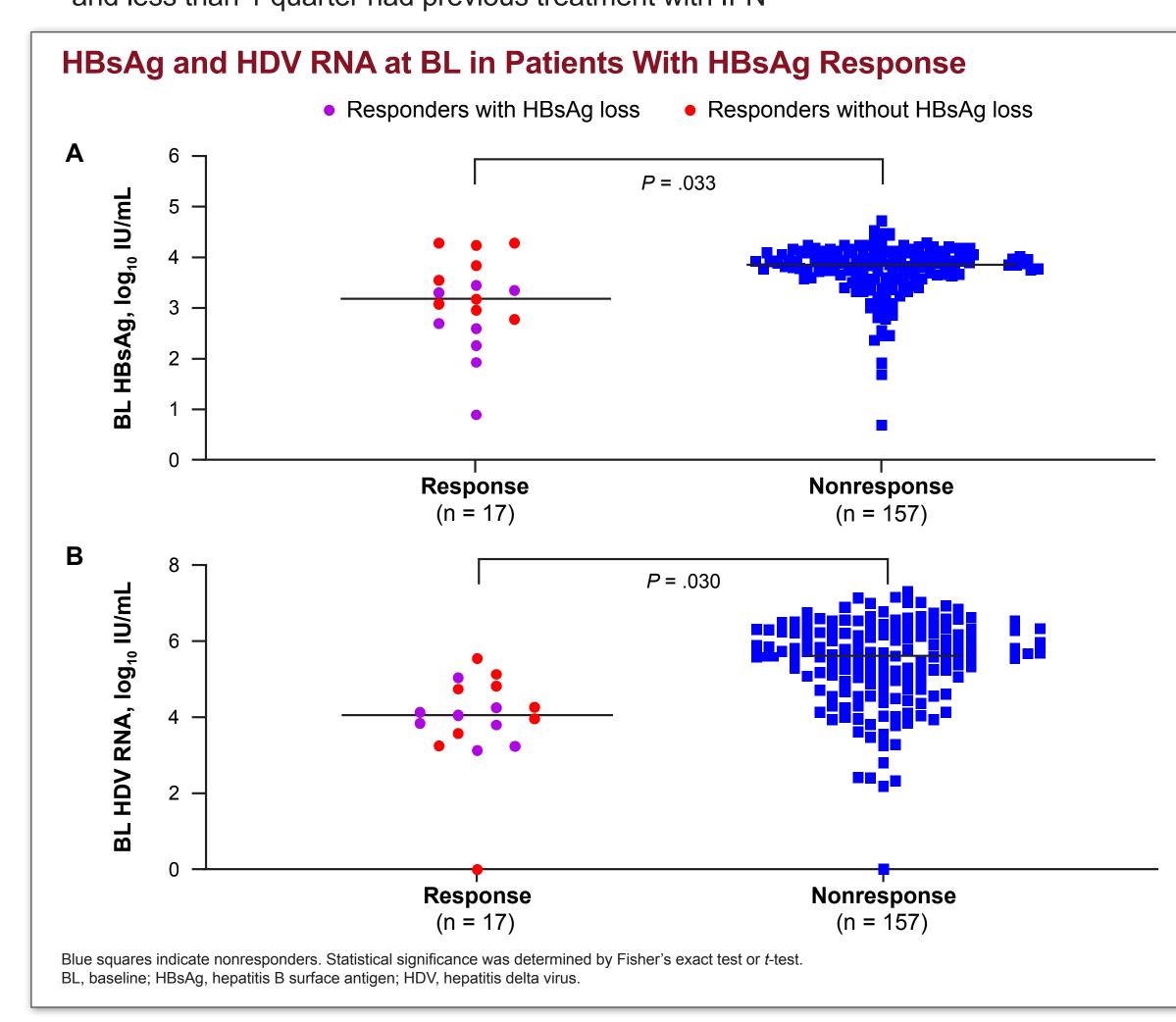


8 patients achieved HBsAg loss and maintained HBsAg loss during the study
6 of these patients also achieved HBsAg seroconversion

#### BL Host/Virologic Factors and HBsAg Response

Host/Virologic Factor	With HBsAg Response (n = 17)	Without HBsAg Response (n = 157)	<i>P</i> -Value <sup>a</sup>
Age, years, median	45	40	.113
Male sex, n (%)	13 (76)	111 (71)	.781
White, n (%)	13 (76)	138 (88)	.248
Cirrhosis absent, n (%)	17 (100)	97 (62)	<.001
Previous IFN treatment, n (%)	4 (24)	80 (51)	.041
Current NA, n (%)	5 (29)	78 (50)	.131
ALT, U/L, median	81	83	.253
HBV/HDV genotype D/1, n (%)	14 (82)	123 (78)	1
HBeAg negative, n (%)	17 (100)	138 (88)	.222
HBV DNA, IU/mL, median	0	32.5	.667
HDV RNA, IU/mL, median	11,163	406,442	.030
HBsAg, IU/mL, median	1500	7000	.033

 While almost 40% of HBsAg nonresponders had cirrhosis and more than half had been treated previously with IFN, none of the 17 patients with HBsAg response had cirrhosis, and less than 1 quarter had previous treatment with IFN



Patients with HBsAg response had significantly lower HBsAg and HDV RNA levels at BL

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