A case of Hepatitis B+D in transplantation

West Coast Transplant ID Meeting

12/3/2025

Niyati Narsana, MD

UC Davis Medical Center

[redacted] yr old [redacted]

G[redacted]P[redacted] from Afghanistan, 26 weeks pregnant with chronic untreated Hepatitis B + D infection presents with high blood pressure, bilateral lower extremity edema concerning for pre-eclampsia, with worsening renal and liver function tests

- HDV VL 270000 IU/ml (5.4 log)
- HBV VL Less than 20
- AST 121, ALT 74, ALP 116, bilirubin 0.2
- Serum creatinine 2.52 mg/dL (baseline 1.3 mg/dL)

[redacted] yr old [redacted]

- US liver: Liver cirrhosis
- Fibroscan notable for F0-F1 (absent to mild fibrosis, low risk)
- Liver biopsy :chronic hepatitis with periportal fibrosis consistent with HBV/HDV injury
- Renal biopsy: immune complex mediated glomerulonephritis (Hep B pos)

Question

- [redacted] underwent an emergency C section during that admission due to severe pre-eclampsia.

Q: How would you treat the Hep B/D co-infection?

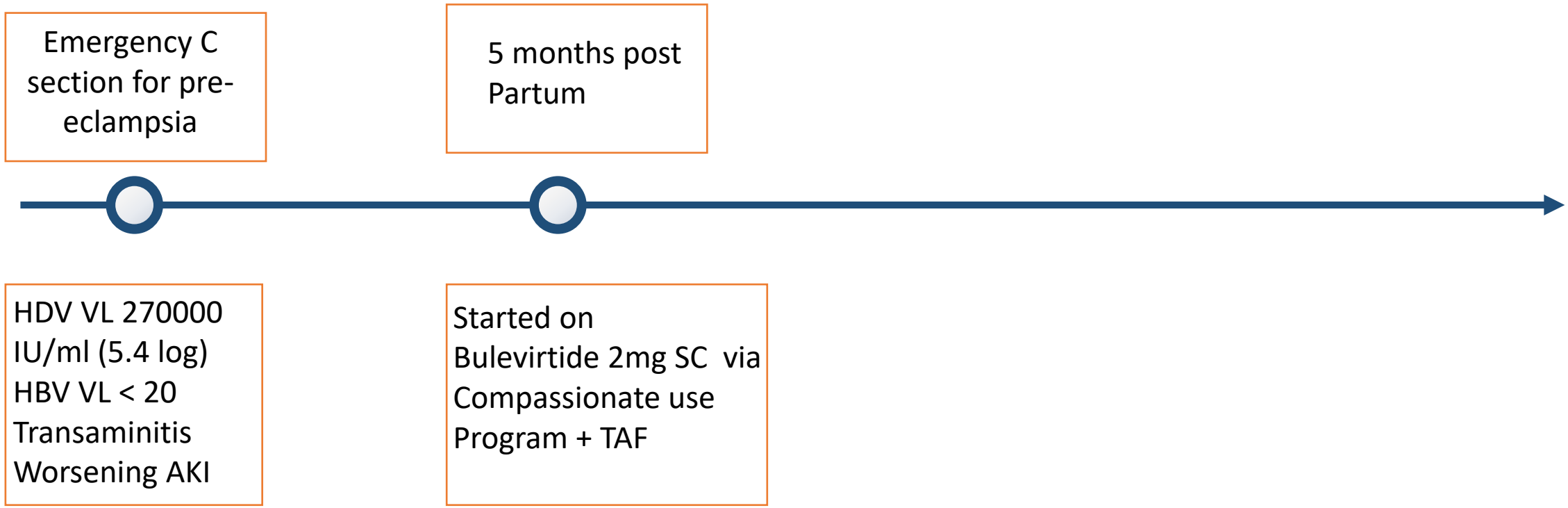
1) TAF/entecavir + Peg interferon alfa 2a

2) TAF/entecavir + Bulevirtide via compassionate use program

3) TAF/entecavir +Bulevirtide +Peg interferon alfa 2a

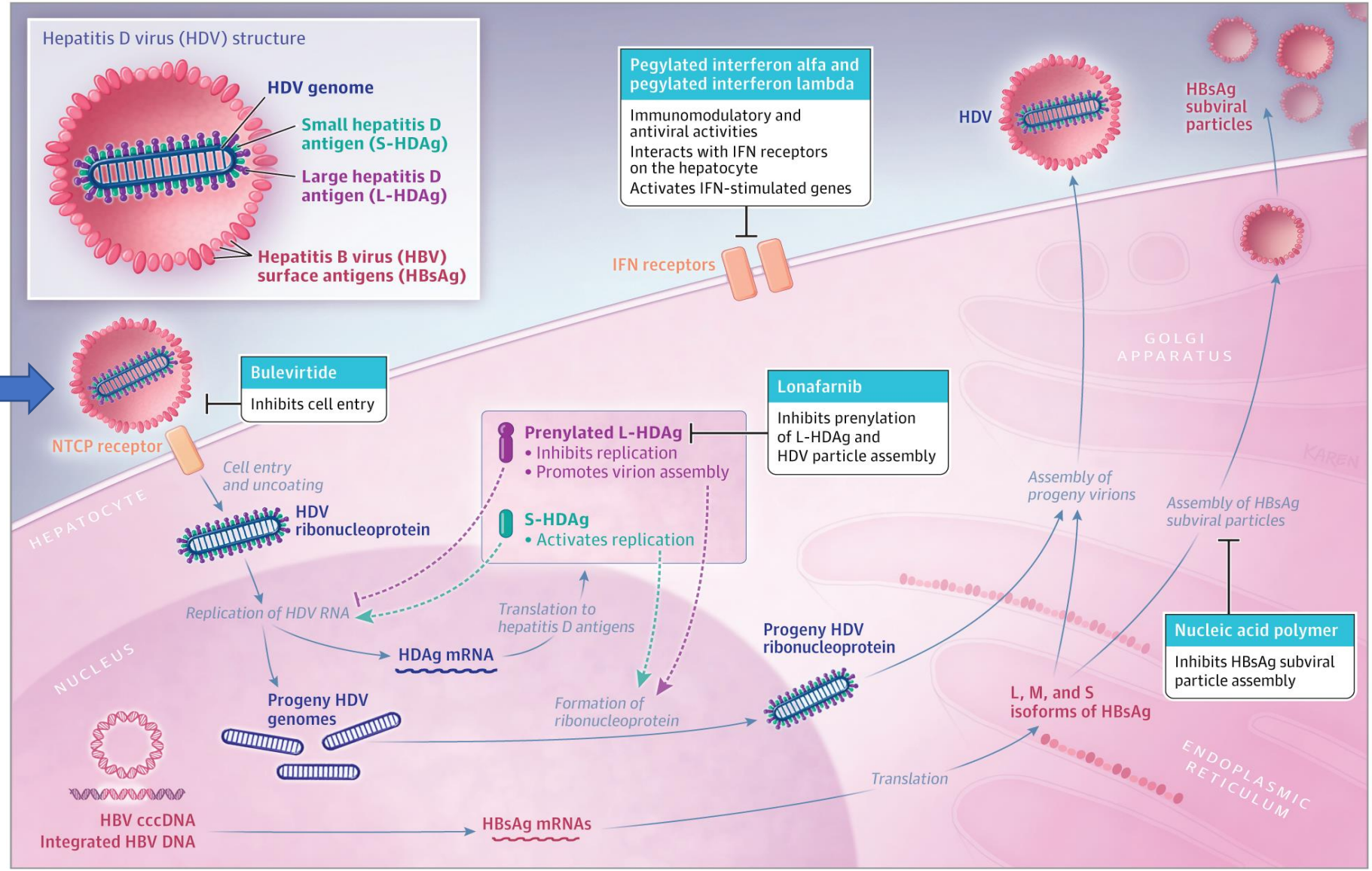
[redacted] yr old [redacted] post partum

- After a multi-disciplinary discussion with nephrology and hepatology, we deferred the use of Peg-interferon alpha for hepatitis D due to concerns for efficacy and hepatic decompensation

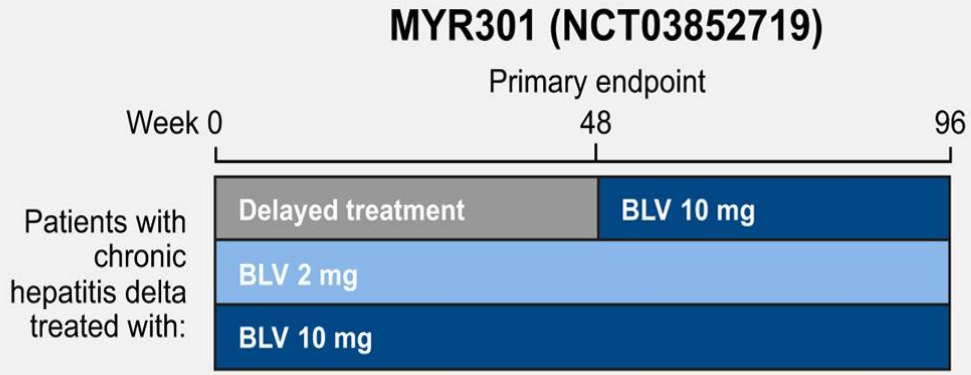


What are treatment options for Hepatitis D?

Approved in Europe in 2023



Phase 3 RCT for Bulevirtide monotherapy in Chronic Hep D (MYR 301)



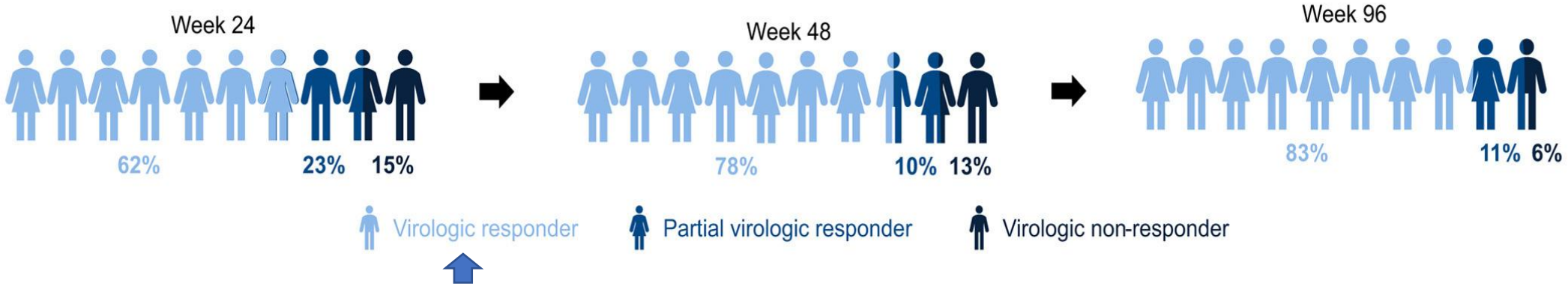
Virologic response rate

	Week 48	Week 96
Delayed treatment → BLV 10 mg	4%	90%
BLV 2 mg	74%	76%
BLV 10 mg	76%	82%

ALT normalization

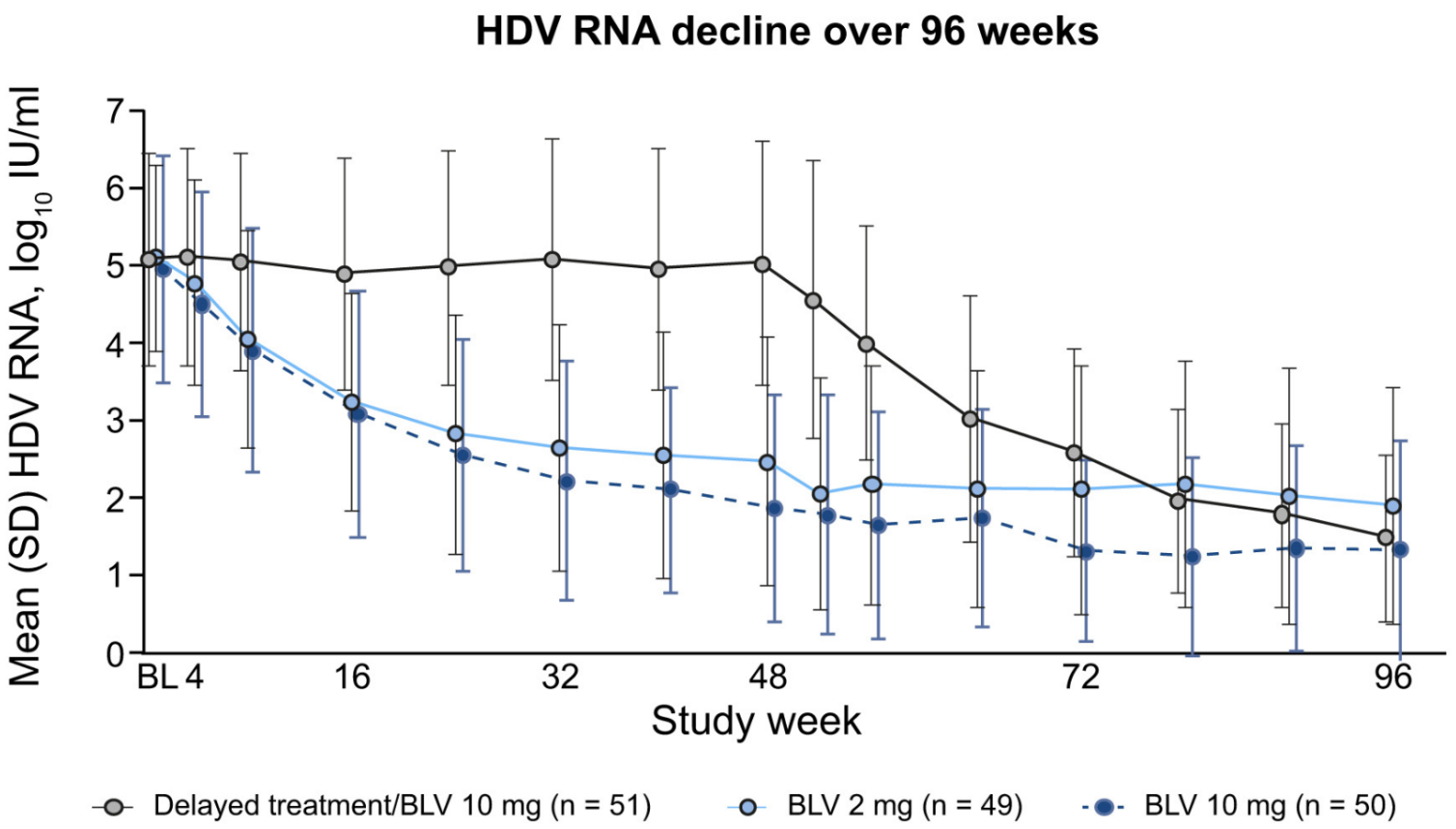
	Week 48	Week 96
Delayed treatment → BLV 10 mg	12%	43%
BLV 2 mg	51%	63%
BLV 10 mg	56%	64%

Proportions of patients receiving BLV 2 and 10 mg with virologic and suboptimal virologic response



J Hepatol. 2024;81(4):621-629.

Bulevirtide RCT



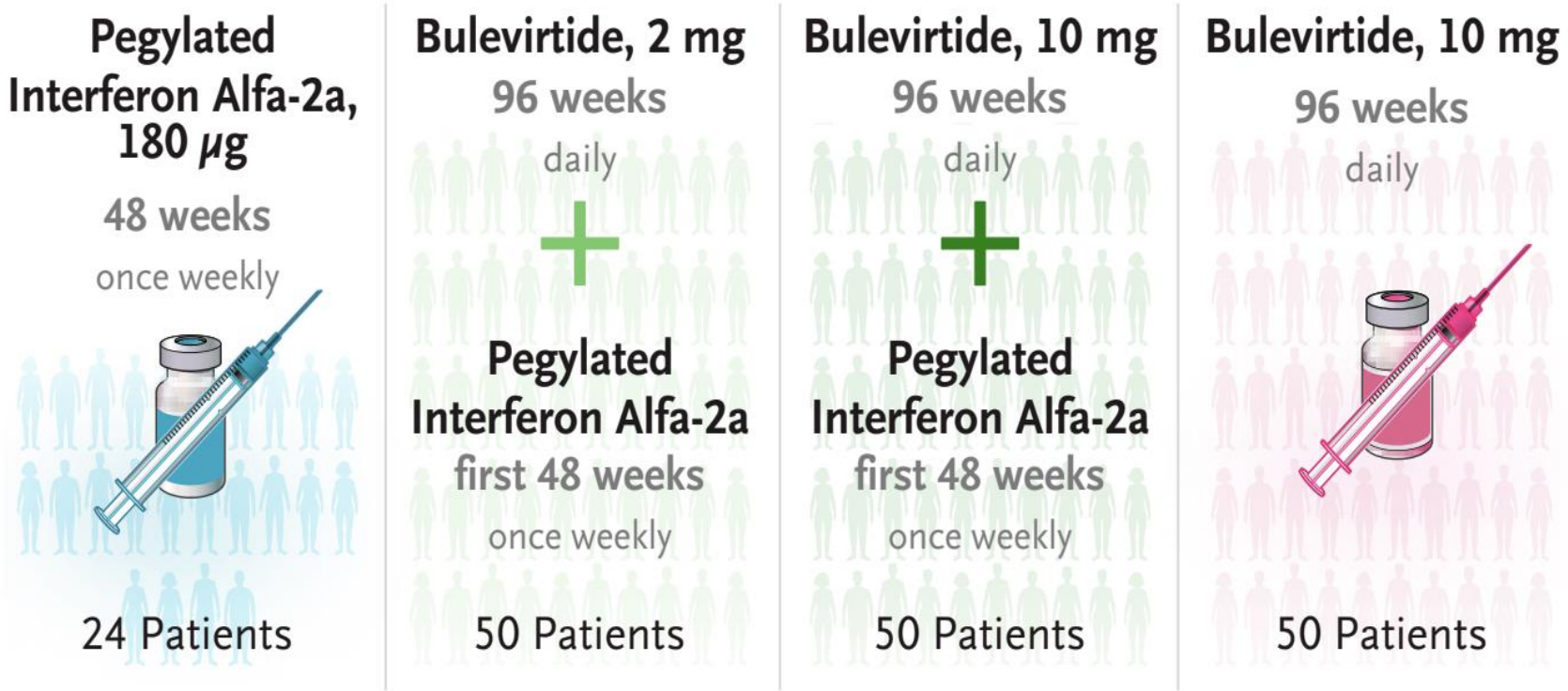
J Hepatol. 2024;81(4):621-629.

Phase 3 RCT for BLV + PEG IFN alpha 2a for CHD

WHO	174 patients 18–65 years of age Men: 71%; Women: 29%
CLINICAL STATUS	Chronic hepatitis D Positive HDV RNA detected by polymerase chain reaction Alanine aminotransferase level above the upper limit of the normal range but less than 10 times above it

TRIAL DESIGN

- PHASE 2B
- MULTICENTER
- OPEN-LABEL
- RANDOMIZED
- CONTROLLED

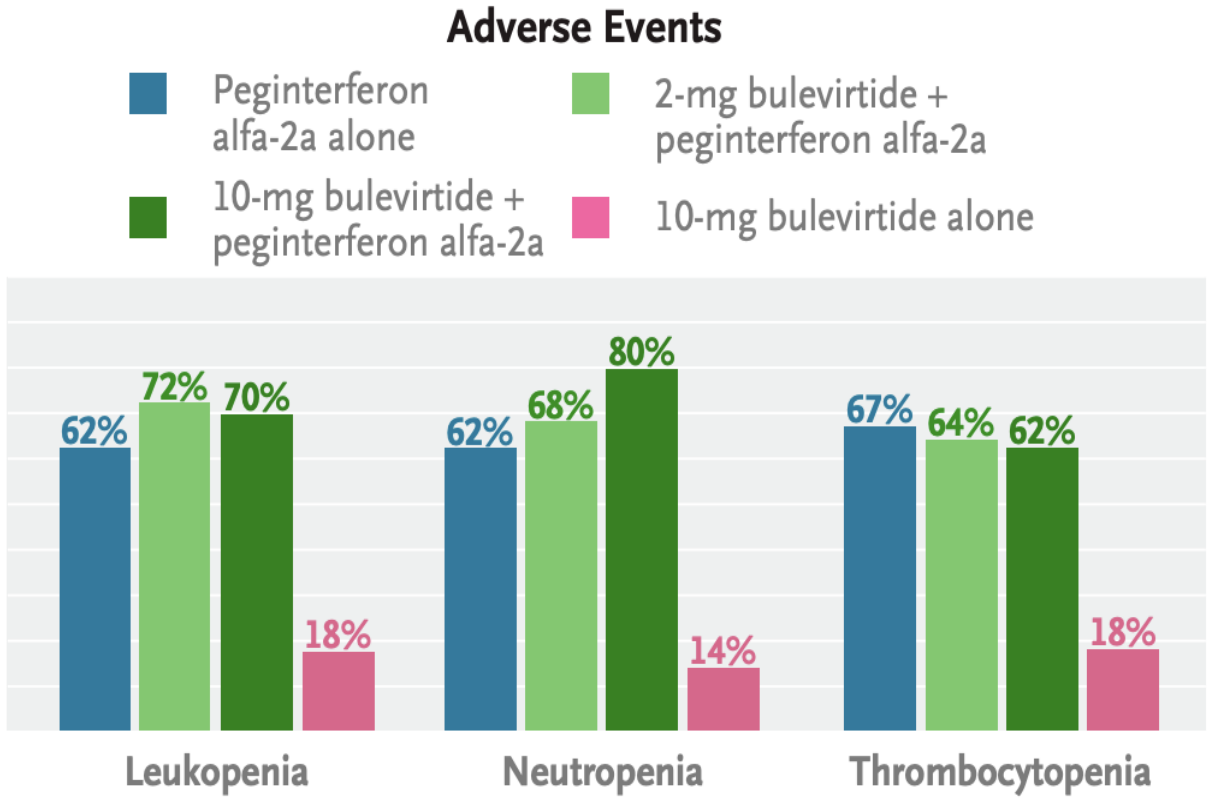


N Engl J Med. 2024;391(2):133-143

Table 2. Efficacy End Points.*

Response	Pegylated Interferon Alfa-2a (N=24)	Bulevirtide, 2 mg + Pegylated Interferon Alfa-2a (N=50)	Bulevirtide, 10 mg + Pegylated Interferon Alfa-2a (N=50)	Bulevirtide, 10 mg (N=50)
Undetectable HDV RNA				
At wk 48				
No. of patients	5	20	30	5
Percentage of patients (95% CI)	21 (7–42)	40 (26–55)	60 (45–74)	10 (3–22)
At wk 96				
No. of patients	NA	22	35	11
Percentage of patients (95% CI)	—	44 (30–59)	70 (55–82)	22 (12–36)
At wk 24 after EOT				
No. of patients	4	16	23	6
Percentage of patients (95% CI)	17 (5–37)	32 (20–47)	46 (32–61)	12 (5–24)
At wk 48 after EOT				
No. of patients	6	13	23	6
Percentage of patients (95% CI)	25 (10–47)	26 (15–40)	46 (32–61)	12 (5–24)
Normalization of ALT level				
At EOT				
No. of patients	5	32	38	30
Percentage of patients (95% CI)	21 (7–42)	64 (49–77)	76 (62–87)	60 (45–74)
At wk 24 after EOT				
No. of patients	6	21	28	15
Percentage of patients (95% CI)	25 (10–47)	42 (28–57)	56 (41–70)	30 (18–45)
At wk 48 after EOT				
No. of patients	10	19	23	11
Percentage of patients (95% CI)	42 (22–63)	38 (25–53)	46 (32–61)	22 (12–36)
HBsAg loss				
At wk 24 after EOT — no. (%)	0	4 (8)	2 (4)	0
At wk 48 after EOT — no. (%)	0	5 (10)	2 (4)	1 (2)

* No multiplicity adjustment was made for any confidence interval. The end of treatment (EOT) was at week 48 in the peginterferon alfa-2a group and at week 96 in all the groups that received bulevirtide. CI denotes confidence interval, and NA not applicable.



N Engl J Med. 2024;391(2):133-143

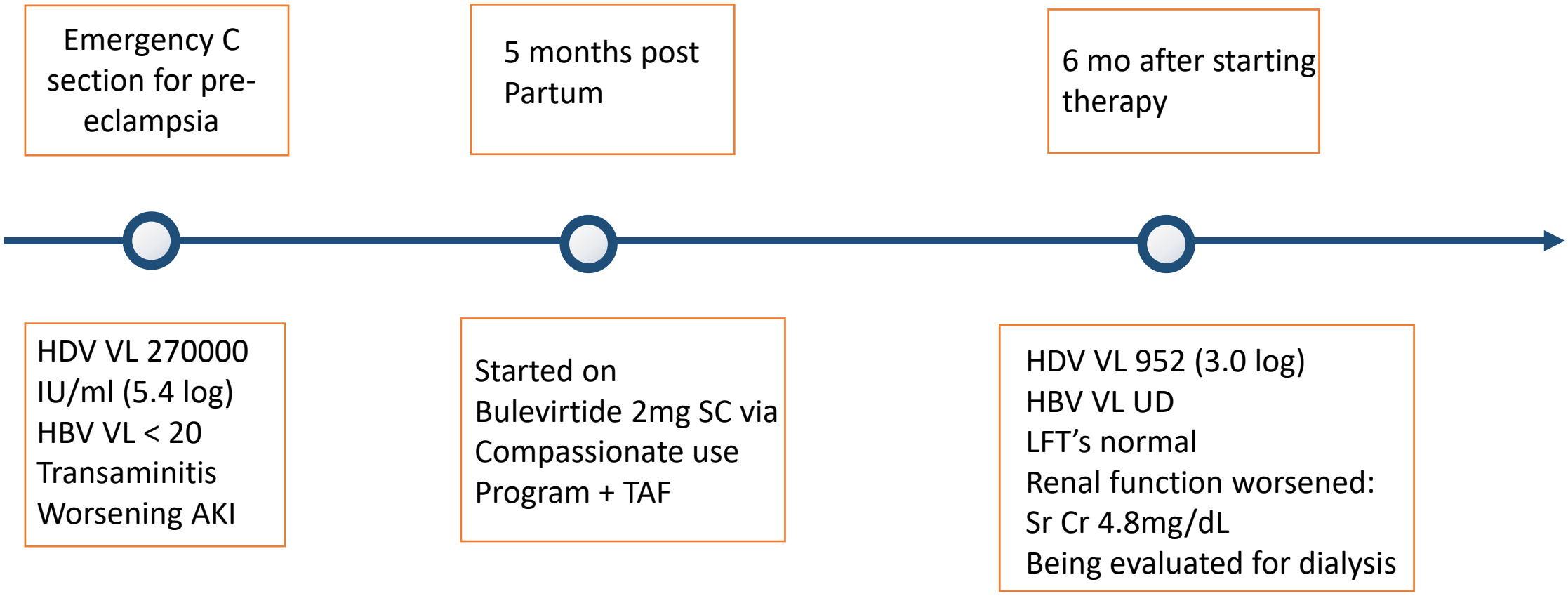
Real World studies of Bulevirtide

Study	No. of patients	Virological response	Biochemical response	Combined response
European SAVE-D 2mg BLV at 96 wks	244	79 %	64%	54%
Italian D-SHEILD 2mg BLV at 32 wks	315	63%	63%	42%
Case series: Off-label use of BLV in patients with decompensated Hep D cirrhosis, Median MELD 12	19	74%	74%	42% 53% with MELD improvement

J Hepatol. 2025;82(6):1012-1022.
https://www.deltacure2024.com/download/poster/P23.pdf
Hepatology. 2024;80(3):664-673.

Back to the patient

[redacted] yr old [redacted] with Hep B+D



Question

If [redacted] is being considered for a renal transplant, would you “clear” [redacted] to proceed ?

1) Yes, [redacted] HBV and HDV are responding appropriately to current treatment and her LFT’s are normal without any hepatic decompensation

2) No, without having full control of the viral infection, there is a risk of reactivation

3)Maybe, for simultaneous liver and kidney transplant evaluation

[redacted] yr old [redacted] with Hep B + D now s/p LDRT

6 mo after starting therapy

HDV VL 952 (3.0 log)
HBV VL UD
AST 38, ALT 22, ALP 128, bilirubin 0.4

-Renal function worsened, Being evaluated for dialysis

Travel to Afghanistan AMA, LDRT from unknown [redacted] yr old [redacted] in Dec 2024

-Stopped Bulevirtide Prior to transplant

-Entecavir
-Cyclosporine
-Prednisone
-Mycophenolate

Feb 2024- Returns to US, Presents with jaundice and abdominal pain

ALT 81, AST 92, ALP 167, bilirubin 3.3

Hepatitis D viral load: 1220000 IU/ml (6.1 log)
HBV : UD

[redacted] yr old [redacted] with Hep B + D now s/p LDRT

Concern for Hep D reactivation
Bulevirtide 2mg SC Daily resumed

LFT's improved over the next month
AST 43, ALT 34,
Alk Phos 221, T. bili 0.7

Course c/b ESBL E.coli Bacteremia from a perinephric abscess requiring drain placement and antibiotics

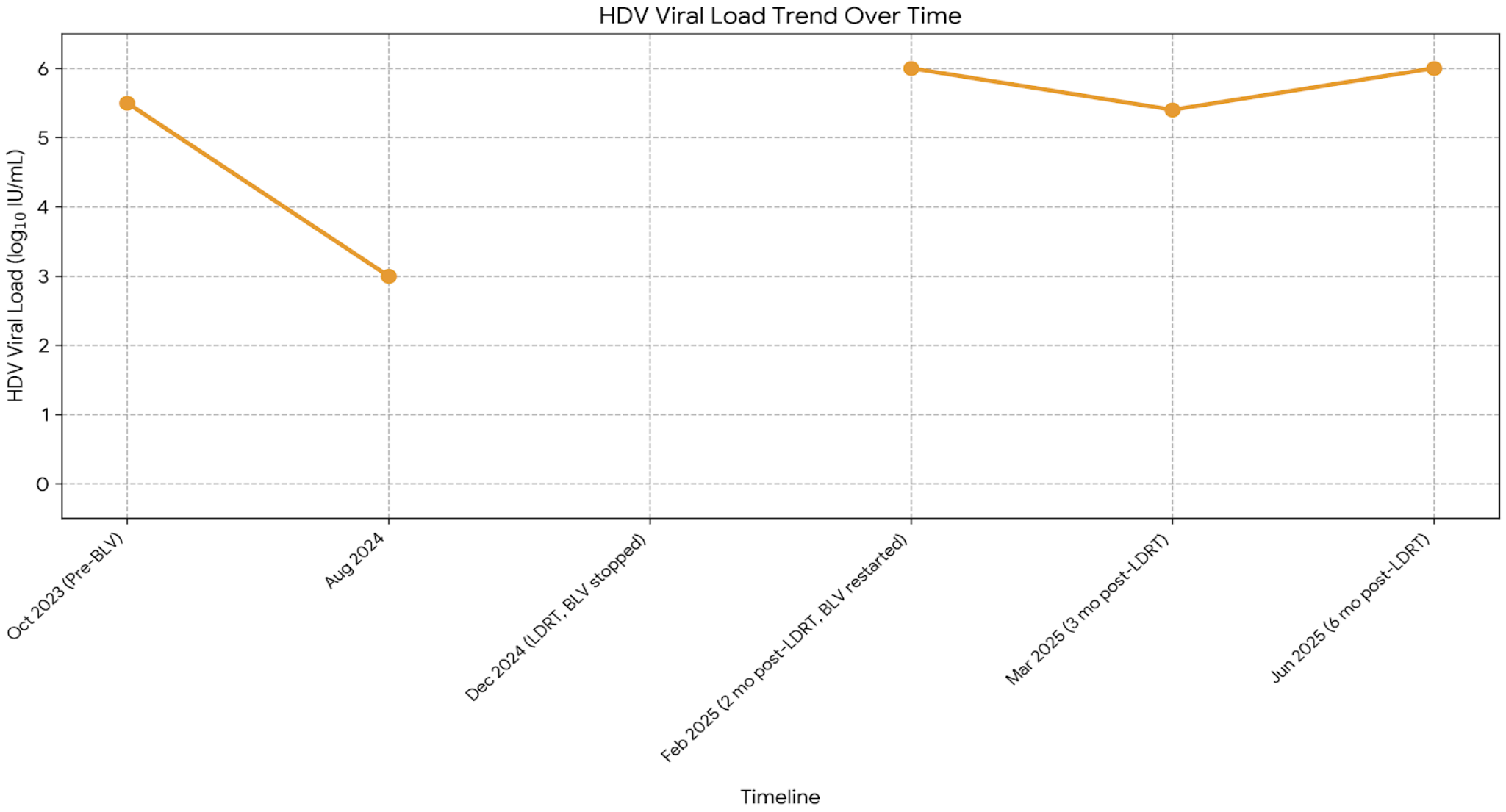
Cyclosporine changed to Tacrolimus due to DDI

HDV VL in 1 month

1220000 IU/ml (6.1 log)
>>
232000 IU/ml (5.4 log)

6 mo post txp: Developed grade 1 ACR due to under Immunosuppression
Treated with 250 mg solumedrol For 3d followed by quick taper

Timeline


HDV Viral Load Trend Over Time
HDV Viral Load (log10 IU/mL)
0
1
2
3
4
5
6
Oct 2023 (Pre-BLV)
Aug 2024
Dec 2024 (LDRT, BLV stopped)
Feb 2025 (2 mo post-LDRT, BLV restarted)
Mar 2025 (3 mo post-LDRT)
Jun 2025 (6 mo post-LDRT)
Timeline

Question

[redacted] HDV VL remains elevated at 1540000 IU/mL (6.2log) 10 months post transplant, despite being on Bulevirtide 2mg SC daily for 8 months. What is the next best step?

1) Check HDV resistance to the drug

2) Stop bulevirtide since the HDV VL is not responding

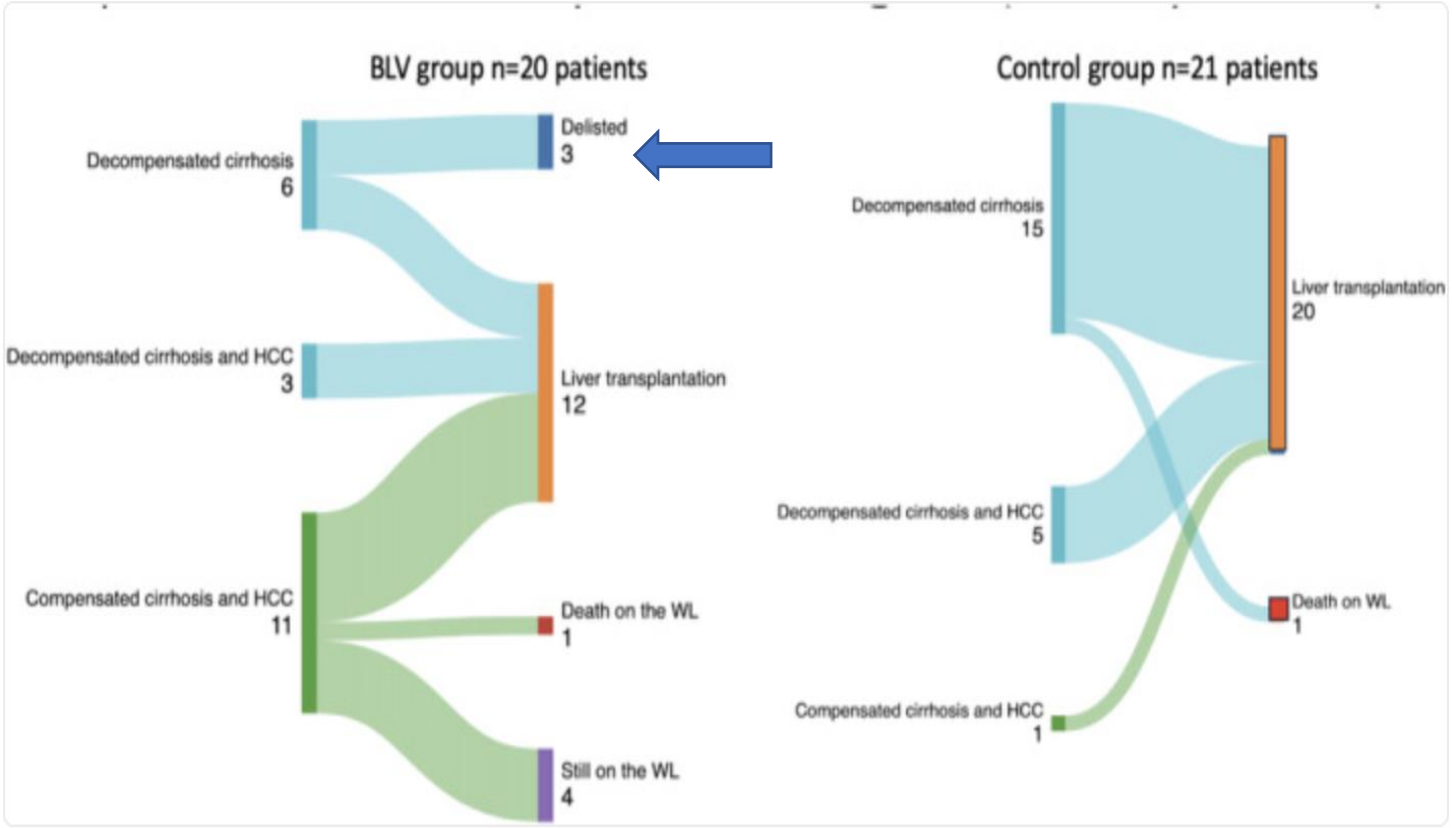
3) Increase the dose of the Bulevirtide to 10mg SC which was used in the studies

4) Refer for liver transplantation

5)All of the above

BLV in patients awaiting Liver transplant

- French, multicenter, retrospective
- 20 pts received BLV 2mg and 21 control pts without any treatment for Hep D
- At wk 48, 73.3% had virological response and 66.6% had biochemical response.



Liver Int. 2025;45(3):e70033.

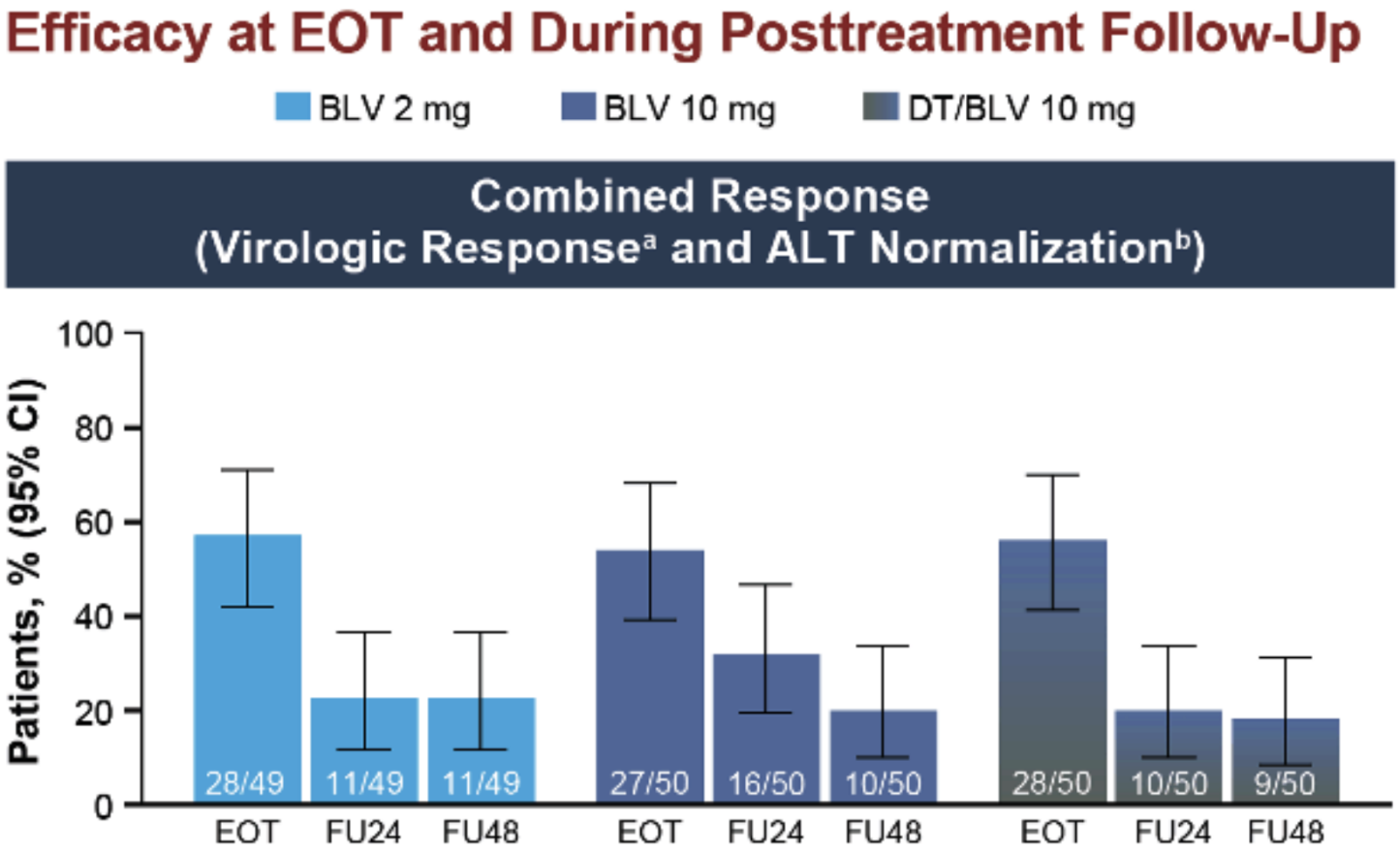
Follow up after LT

- 2 pts died in BLV group after LT: 1 from cholangioCA and other unknown cause
- None in the control group died after LT
- HDV RNA, HBV DNA and Hep B s antigen UD in all patients post LT
- Post-transplant long-term HBIg + NA (Entecavir/TAF/lamivudine)

Liver Int. 2025;45(3):e70033.

Can you stop BLV?

- Post treatment results of MYR 301: Treatment with BLV until 144 weeks



- Most virological relapse in first 24 wks
- Hb s Ag loss in only 2 pts
- Post Tx increase in ALT > HDV rebound
- Severe flares (ALT > 10 ULN) in 9%

https://www.natap.org/2024/AASLD/AASLD_70.htm

Outcomes of Liver transplant for Hep B +D

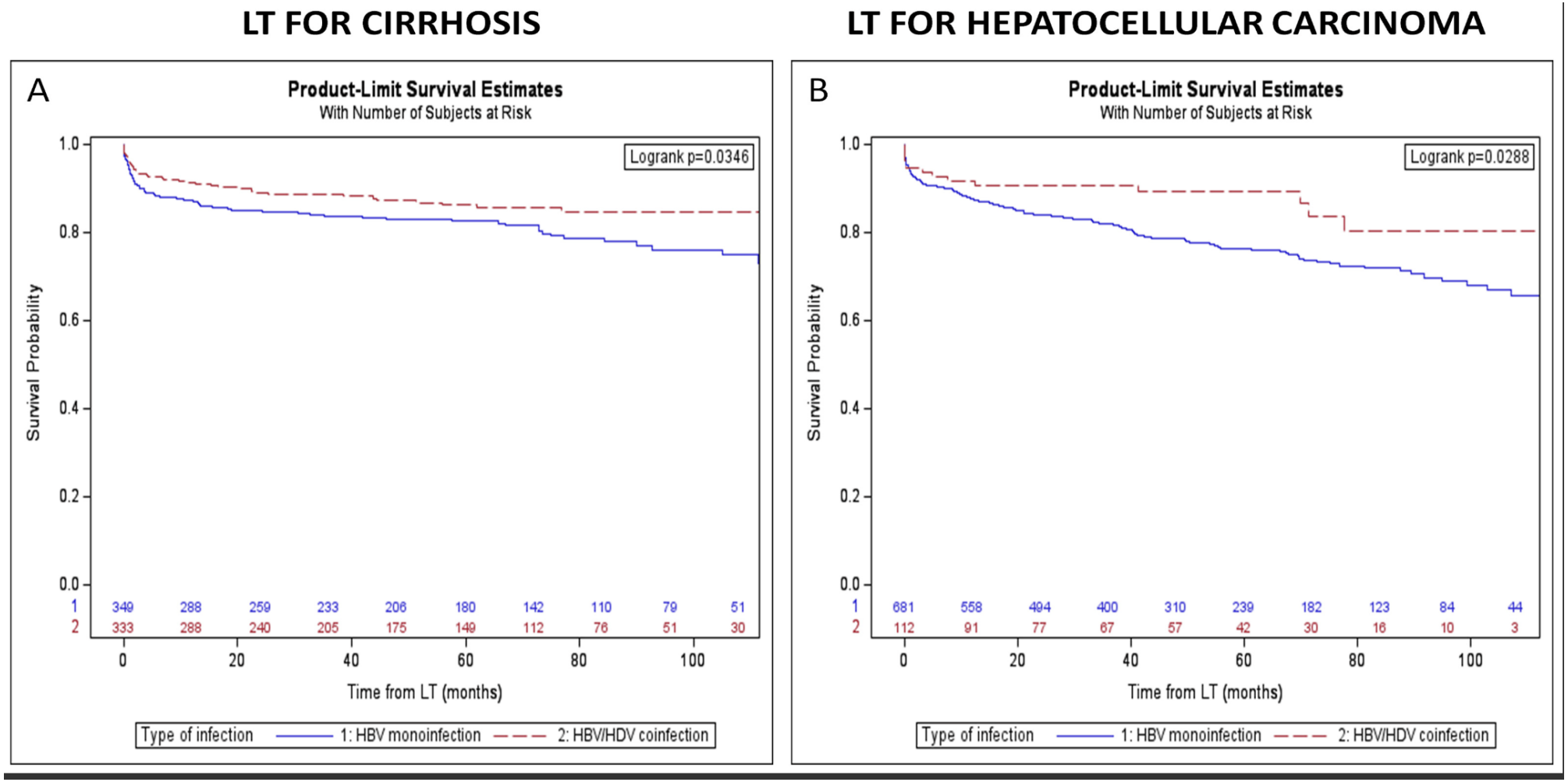
- Italian observational cohort study comparing LT candidates with HDV/HBV coinfection with those with HBV monoinfection who were waitlisted from 2011 to 2020

- 1237 patients (71.5%) presented with HBV monoinfection and 494 patients (28.5%) presented with HDV/HBV coinfection

- HCC lower in HDV/HBV compared to HBV alone (26% vs 65%)

Am J Transplant. 2025;25(7):1502-1514.

Post transplant outcomes



Am J Transplant. 2025;25(7):1502-1514.

Post transplant outcomes

- 38 (8.5%) patients died after LT and 19 (3.8%) were retransplanted within 58 months in HBV/HDV group

- 184 (14.9%) patients died after LT and 45 (3.6%) were retransplanted within 61 months in HBV group

Am J Transplant. 2025;25(7):1502-1514.

Viral recurrence post transplant

Table 4 Antiviral therapy in LT recipients with HDV/HBV coinfection.

Infection prophylaxis	At LT, n (%)	At last follow-up, n (%)
Antiviral therapy		
Nucleos(t)ides analogs (dosage)		
Entecavir (0.5-1 mg/die)	206 (46.82)	250 (60.39)
Tenofovir dipivoxyl (600 mg/die)	115 (26.14)	108 (26.09)
Lamivudine (100 mg/die)	37 (8.40)	52 (12.56)
None	82 (18.64)	4 (0.96)
Missing data	5 (1.4)	31 (7.0)
HBIg		
HBIg administration		
Yes	446 (100.0)	371 (91.83)
No	—	33 (8.17)[a]
Time of HBIg withdrawal after LT (mo)	—	15.4 (1.6-24.3)

- In HBV/HDV cohort, 5 (1.1%) patients developed HBV recurrence
- 2 were donor-derived
- All treated with NA and HBIg
- 1 died after 2 yrs

Am J Transplant. 2025;25(7):1502-151

What is optimal therapy for prevention after liver transplantation for HBV/HDV?

- Combination of NA (Entecavir or TDF/TAF) +HBIg post transplant for HBV recurrence prevention: 10-year survival rates of up to 80%
- AASLD 2018 guidelines: Lifelong NA +HBIg therapy for HBV/HDV infection
- EASL 2025 guidelines: In the absence of data, NA therapy + HBIg for at least first 24 mo post LT or indefinitely

Hepatology. 2018;67(4):1560-1599.
J Hepatol. 2025;83(2):502-583.

Shorter courses of HBIg after transplant

HBIg for 6 months + long term NA therapy	HBIg for 24 months + long term NA therapy
• Cohort of 28 pts : LT for HBV/HDV • 72 mo follow up • 1 pt with appearance of low level Hep B s antigen which resolved with single dose of HBIg	• Cohort of 16 pts: LT for HBV/HDV • No recurrence • 50% with Hep B surface Ab levels > 10 at 74 months

Transplantation 108(9):p e239-e244, September 2024.
Clin Transplant. 2023;37(6):e14971.

Back to my patient

- Clinically stable with normal LFT's on 2mg SC dose, plans to switch to 10mg BLV when available via Expanded Access (in progress)
- Follows with Hepatology team, not a candidate for LT currently due to low MELD
- No HCC on screening
- Stable renal function

Take Home points

- BLV is emerging as first-line HDV therapy.
- Limited but encouraging real-world data in pre-transplant
- Relapse common when BLV stopped
- HBIg duration post-LT still evolving in HBV/HDV co-infection