New HBV biomarkers: any role in HDV?

Barbara TESTONI, PhD

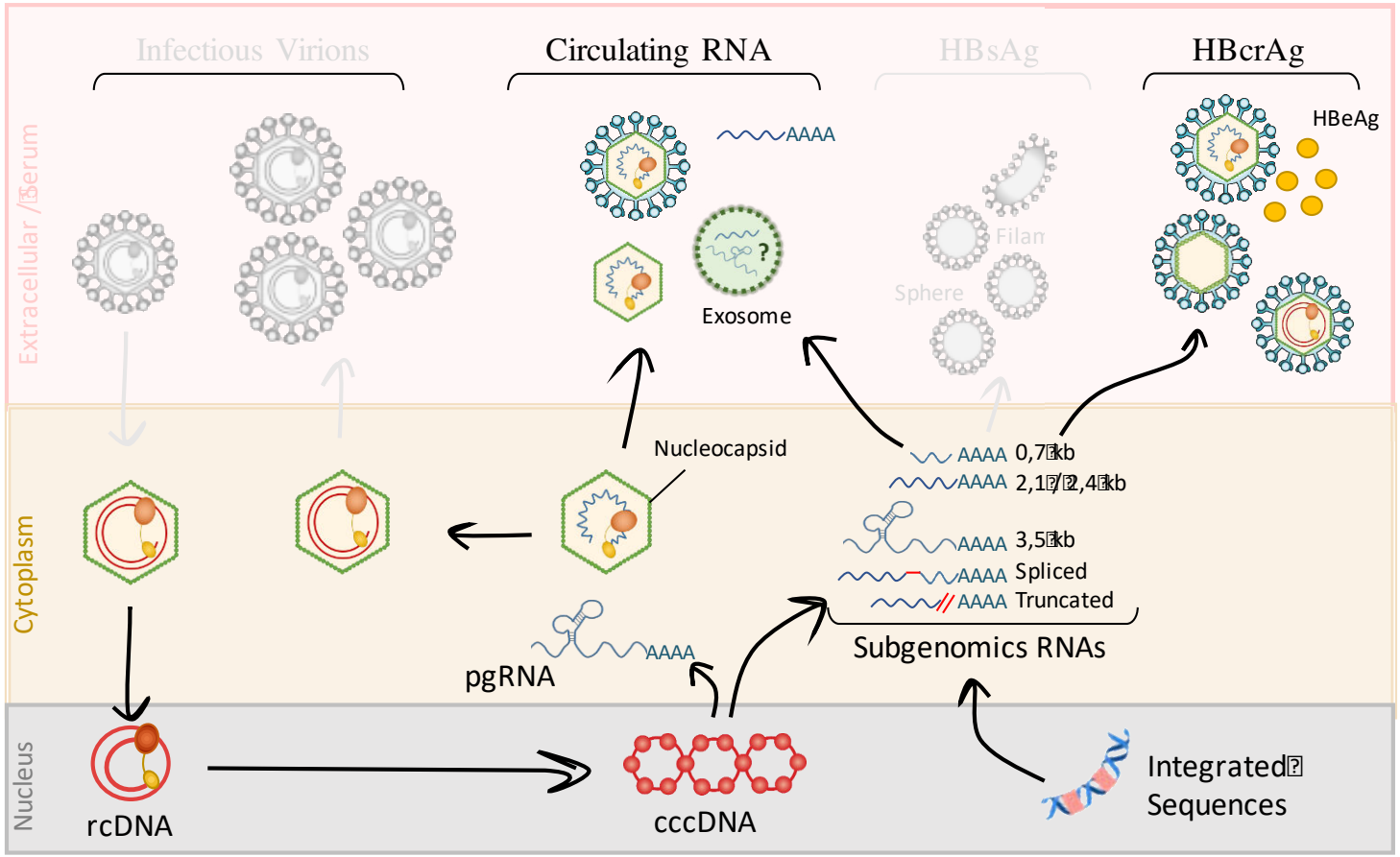
CRCL CENTRE DE RECHERCHE EN CANCÉROLOGIE DE LYON

LYON HEPATOLOGY INSTITUTE
COMPREHENSIVE LIVER CENTER

Disclosures

- Dr. Testoni receives grants from Aligos, Assembly Bio, Beam Therapeutics and BlueJay.

What are the new HBV biomarkers?



Adapted from Testoni, 2017

HBcrAg

Composite marker

Translated from overlength HBV RNA, thus only produced from cccDNA

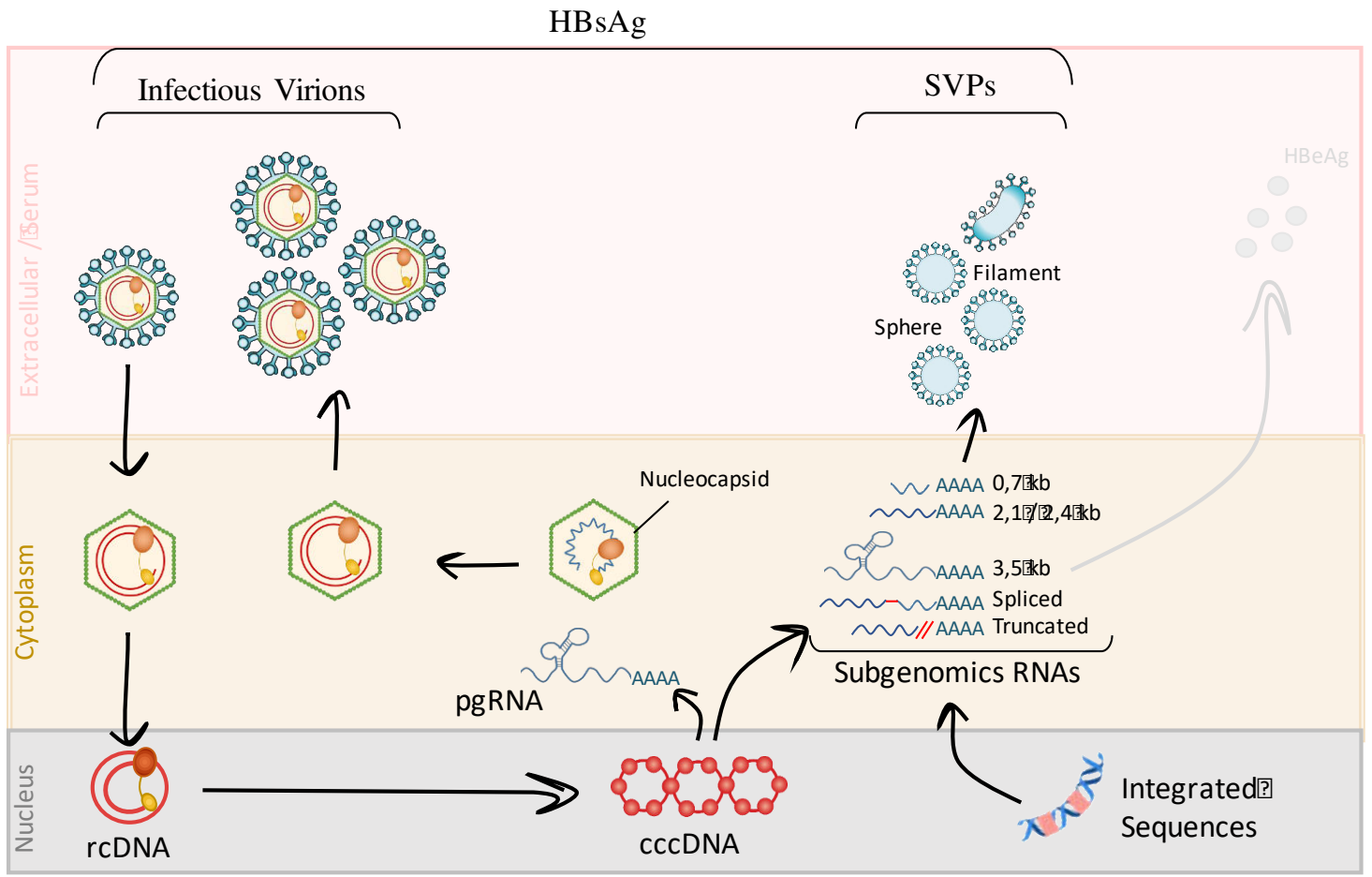
Circulating HBV RNA

pgRNA is transcribed only from cccDNA

Studies in CHB patients correlate serum HBcrAg and HBV RNA to intrahepatic cccDNA levels/activity

Huang, 2017
Wang, 2021
Testoni, Lebossé, 2019
Testoni, Gut 2023

What are the new HBV biomarkers?

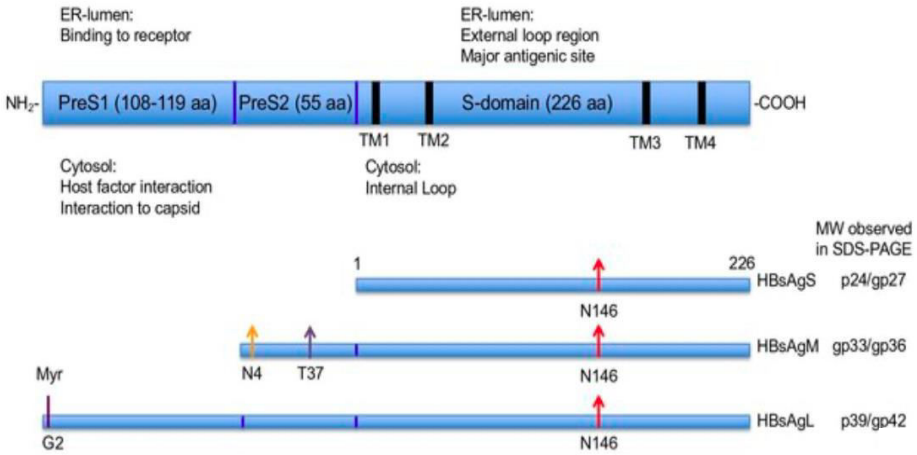


Adapted from Testoni, 2017

Serum HBsAg

qHBsAg can originate from cccDNA AND integrated HBV DNA

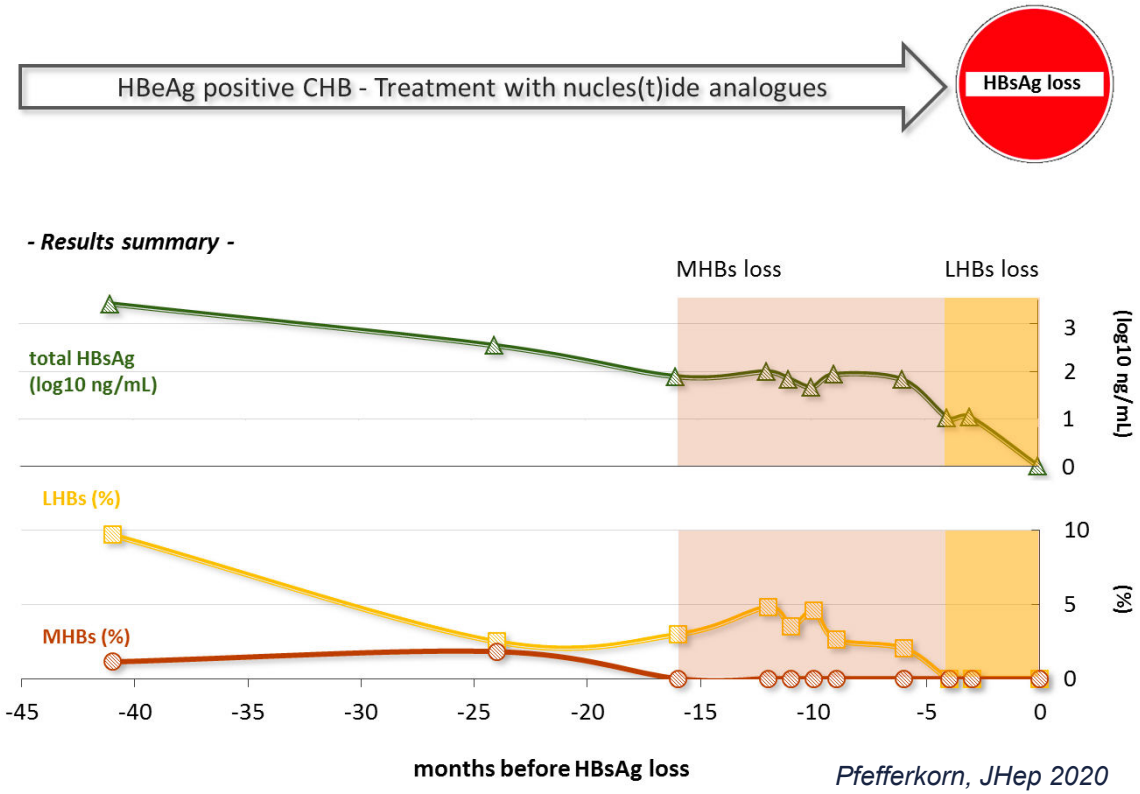
→ **Not specific to cccDNA**



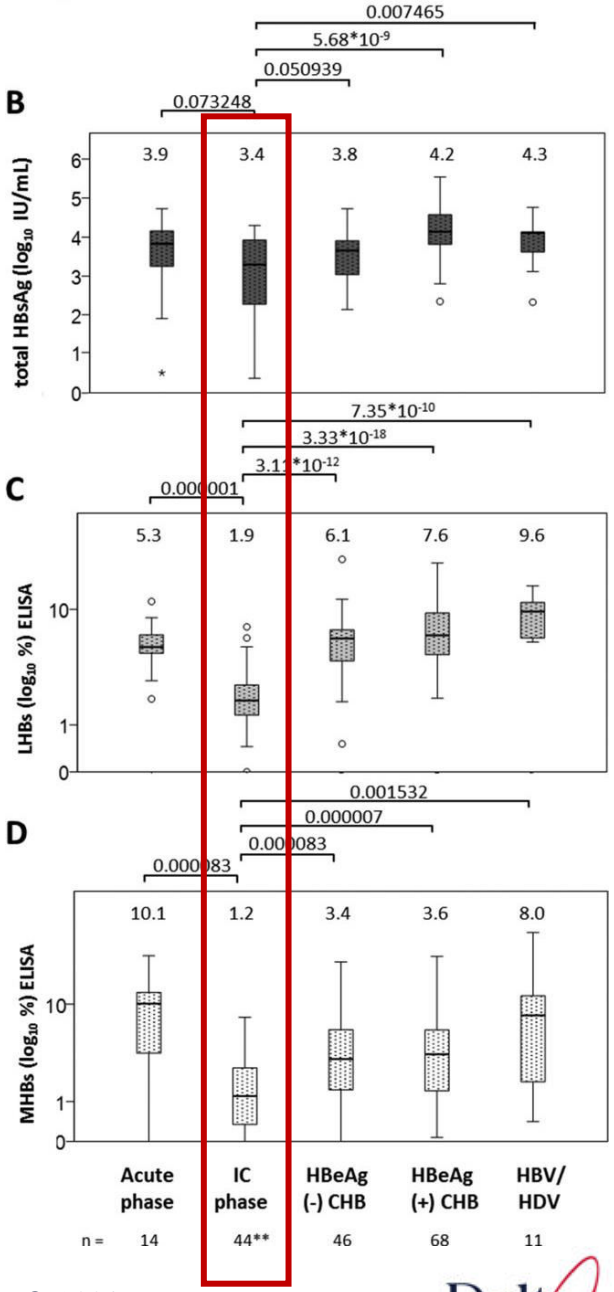
What are the new HBV biomarkers?

HBsAg components better discriminate CHB phase 3 patients (Inactive Carriers)

Different dynamics of HBsAg components under treatment

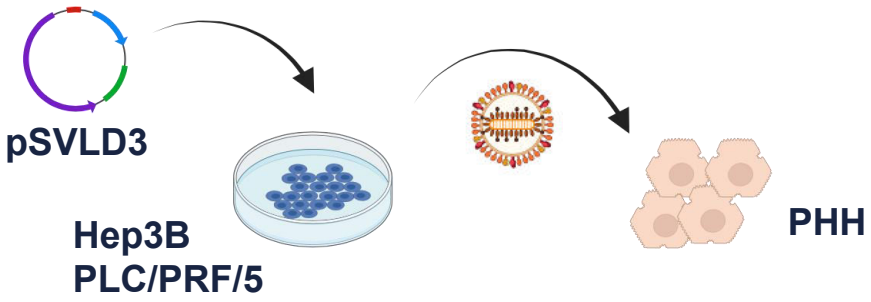


Pfefferkorn, JHep 2020

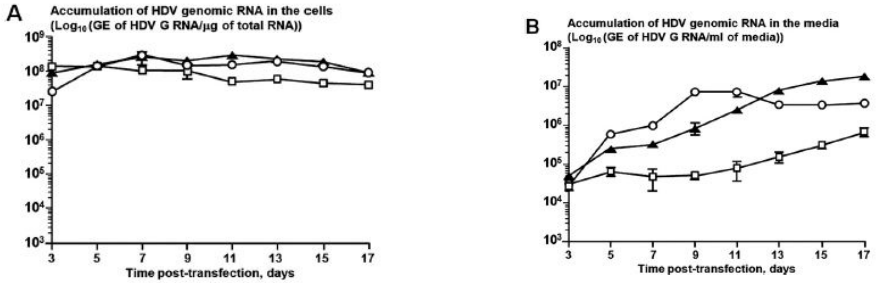


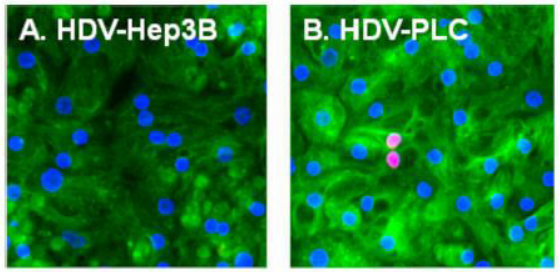
Pfefferkorn, Gut 2017

HBV integration-derived HBsAg sustains HDV replication



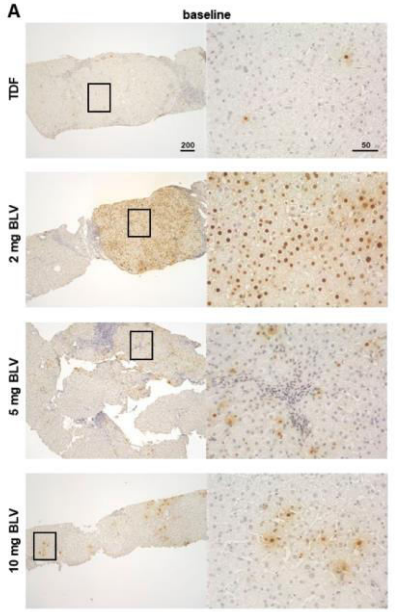
Intracellular HDV RNA Extracellular





Freitas et al. JVirol 2014

HDV staining



Baseline biopsies from MYR-202 study

Diffuse HDAg staining in HBeAg-neg HBsAg+ patients with very low levels of cccDNA and 3.5Kb RNA

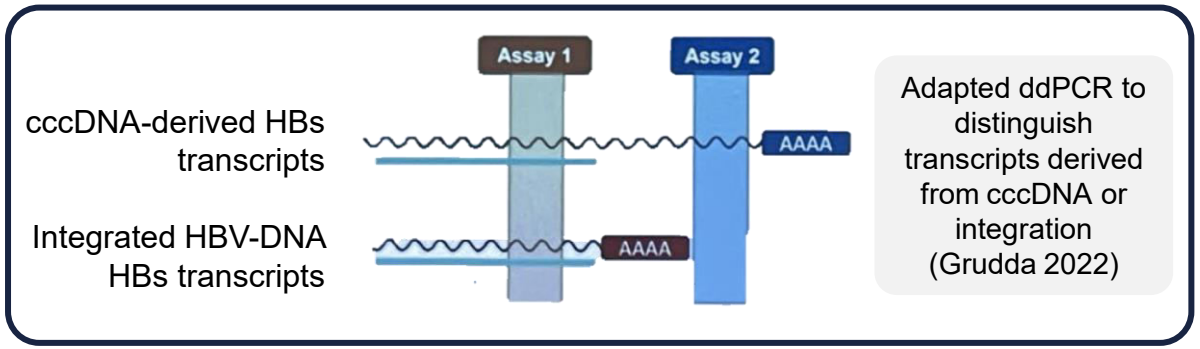
Allweiss, J Hepatol 2024

…L-HBsAg is required for HDV infection!!

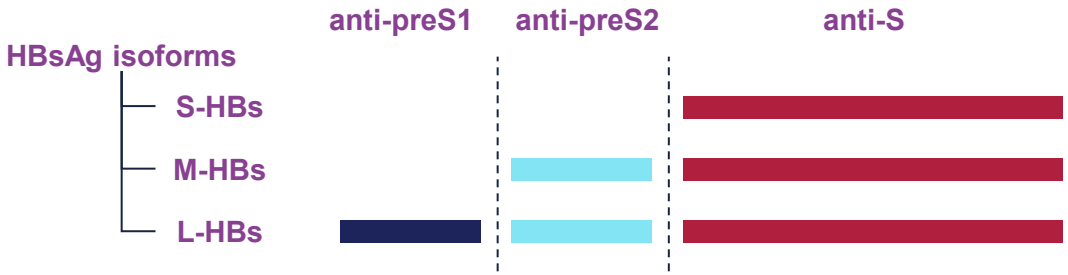
Kumar et al. Poster #48

HBV integration-derived HBsAg sustains HDV replication

35 CHD patients; Liver quantification of cccDNA, 3.5Kb RNA, total HBV DNA and HDV RNA by ddPCR



Serum HBV DNA, HBsAg and HDV RNA quantification[a]



[a]Serum levels off HBsAg isoforms were quantified by ad-hoc ELISA (Brancaccio & Salpini 2021)

HBV/HDV patients stratified by cccDNA levels

Intrahepatic markers	cccDNA <1 copy/ 1000 cells (n=19)	cccDNA >1 copy/ 1000 cells (n=16)	P-value
Total HBV DNA	30 (1–73)	247 (158–406)	<0.001
HBV pgRNA	1.4 (0.4–25)	89 (6–238)	0.005
cccDNA	0.02 (0–0.1)	15 (5–32)	<0.0001
cccDNA-derived HBs transcripts	0.3 (0.1–0.9)	41 (7–179)	0.001
Integrated-derived HBs transcripts	432 (3–7748)	19,312 (5476–42,448)	0.003
HDV RNA	782 (1–5559)	1026 (40–6984)	0.5

Data are median (IQR) copies/1000 cells

- 8/35 patients (23%) had undetectable cccDNA and cccDNA-derived transcripts, but still intensive HDV replication and levels of L-HBsAg comparable to cccDNA(+)

Variables	N=8		
Serum HDV RNA, log IU/mL	6.0 (5.9–7.3)		
Intrahepatic HDV RNA, copies/1000 cells	5495 (976–14,946)		
Integrated HBV DNA-derived transcripts, copies/1000 cells	3 (1–497)		
	cccDNA–	cccDNA+	P-value
Serum HBs, ng/mL			
S-HBs	1116	6183	0.2
M-HBs	368	1637	0.2
L-HBs	1.4	3.2	0.5
Serum HDV RNA, log IU/mL	6.0	6.4	0.3

Data are median or median (IQR)

Salpini R, et al. EASL ILC 2024. OS-094

Untreated CHD patients

Cross-sectional study Italy/Romania

TABLE 3 HBV and HDV markers according disease activity

		ALT > ULN			Multivariate		
		No	Yes				
		n = 26	n = 83	*P*	OR	95% CI	*P*
HBeAg Status	HBeAg+	0 (0.0)	8 (9.6)	.194			
	HBeAg−	26 (100)	75 (90.4)				
HBV-DNA (log_{10} IU/mL)	Median	0.70	1.15	.301			
	Range	0.70-4.03	0.70-5.34				
HBsAg (log_{10} IU/mL)	Median	3.45	3.92	.113			
	Range	−1.00-4.41	1.72-4.48				
Total anti-HBc (IU/mL)	Median	742.66	649.12	.001			
	Range	41.62-8790.81	14.60-20564.87				
HBcrAg (log_{10} U/mL)	Median	3.69	3.95	.001			ns
	Range	2.00-6.29	2.30-6.21				
HDV-RNA (log_{10} cp/mL)	Median	2.70	4.40	<.001	2.366	1.456-3.844	.001
	Range	2.70-5.46	2.70-6.82				
IgM anti-HDV (AU/mL)	Median	12.5	47	<.001			ns
	Range	10-100	10-200				
Total anti-HDV	≤1:100	6 (23.1)	3 (3.6)	.002	10.105	1.671-61.107	.012
	≤1:5000	15 (57.7)	43 (51.8)				
	≤1:50 000	5 (19.2)	37 (44.6)				
Total anti-HBc/ IgM anti-HDV	Median	19.44	9.43	.009			ns
	Range	2.31-699.88	0.10-997.87				

ns, not significant

122 consecutively enrolled CHD patients

Positive correlation between
HDV-RNA and HBV-DNA (P = .005),
HBsAg (P < .001)
HBcrAg (P < .001)

Liver disease progression is associated with active HDV replication which associates with higher levels of HBcrAg

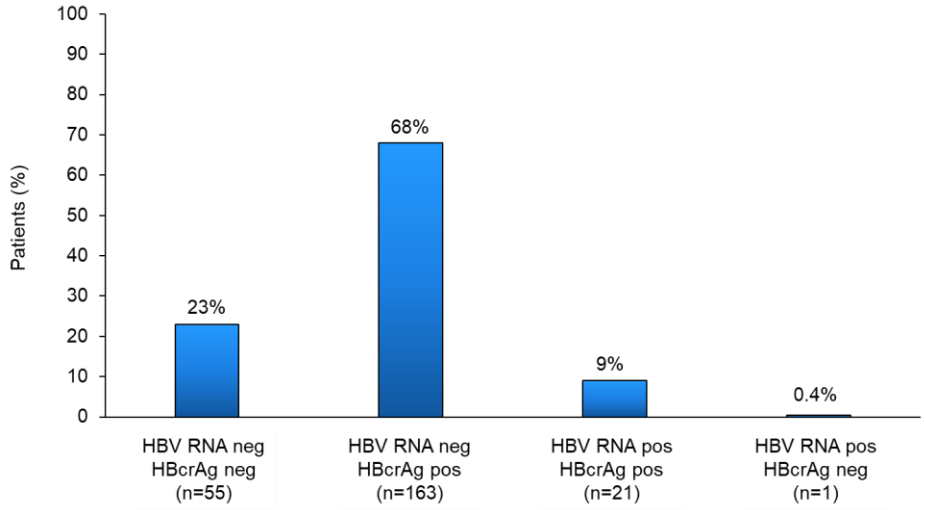
Is active cccDNA transcription required for effective HDV pathogenicity?

(NB: HBcrAg LOD=2logU/ml)

Ricco, JVH 2018

Cross-sectional study Italy/France/Spain

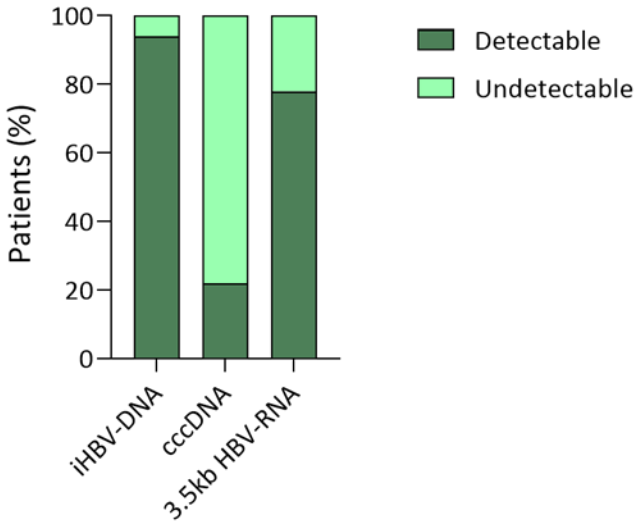
240 untreated CHD Patients Tested for Serum HBV RNA (Roche IA assay) and HBcrAg

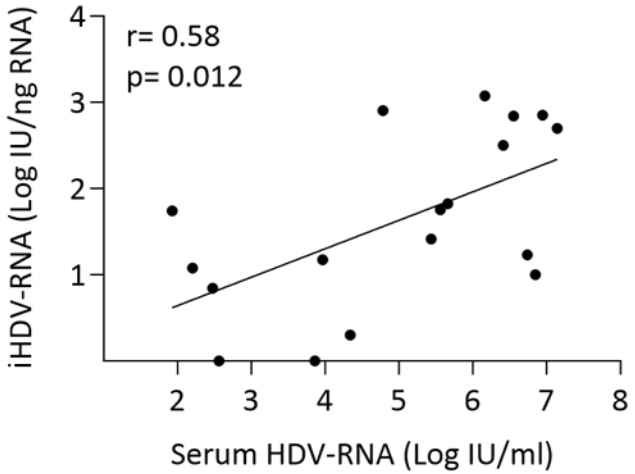


- HBV RNA undetectable and HBcrAg detectable in most patients ("**divergent pattern**").
- Positive HBcrAg associated with higher HBsAg levels.
- Patients positive for both HBV RNA and HBcrAg had higher HBsAg, HDV RNA and HBV DNA levels.

- Intrahepatic HDV RNA and HBV RNA positive in most patients, cccDNA detectable in a minority.
- Intrahepatic HDV RNA correlated with serum HDV RNA levels.

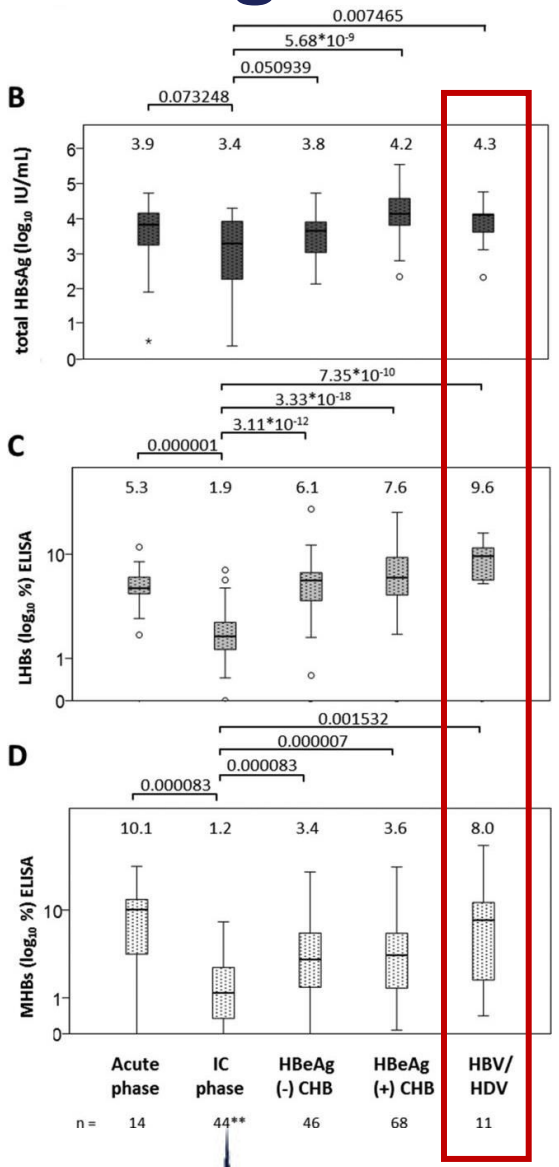
18 Patients with Intrahepatic Analysis





➡ ***De Gasperi et al. Poster #43***

HBsAg isoforms in untreated CHD patients

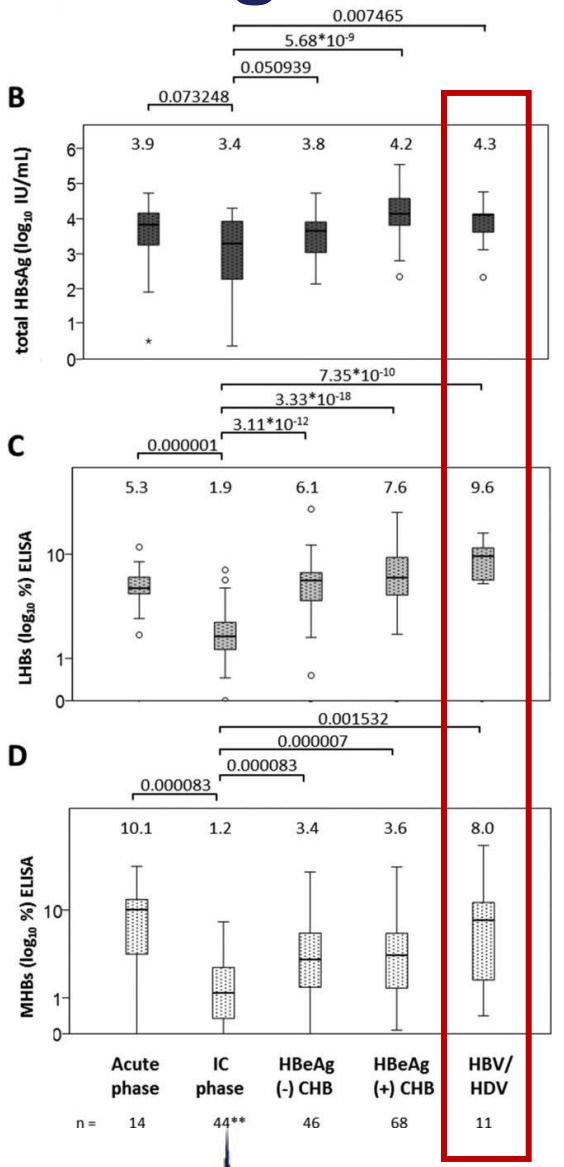


Ratios of LHBs were highest in individuals with HDV/HBV coinfection .
The ratio of MHBs was also higher but the difference was not significant

Semiautomatic in-house sandwich ELISA on a BEP III system using MA18/7 and Q19/10 antibodies and by Western blot

Pfefferkorn, Gut 2017

HBsAg isoforms in untreated CHD patients



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Semiautomatic in-house sandwich ELISA on a BEP III system using MA18/7 and Q19/10 antibodies and by Western blot

Pfefferkorn, Gut 2017

OC-39

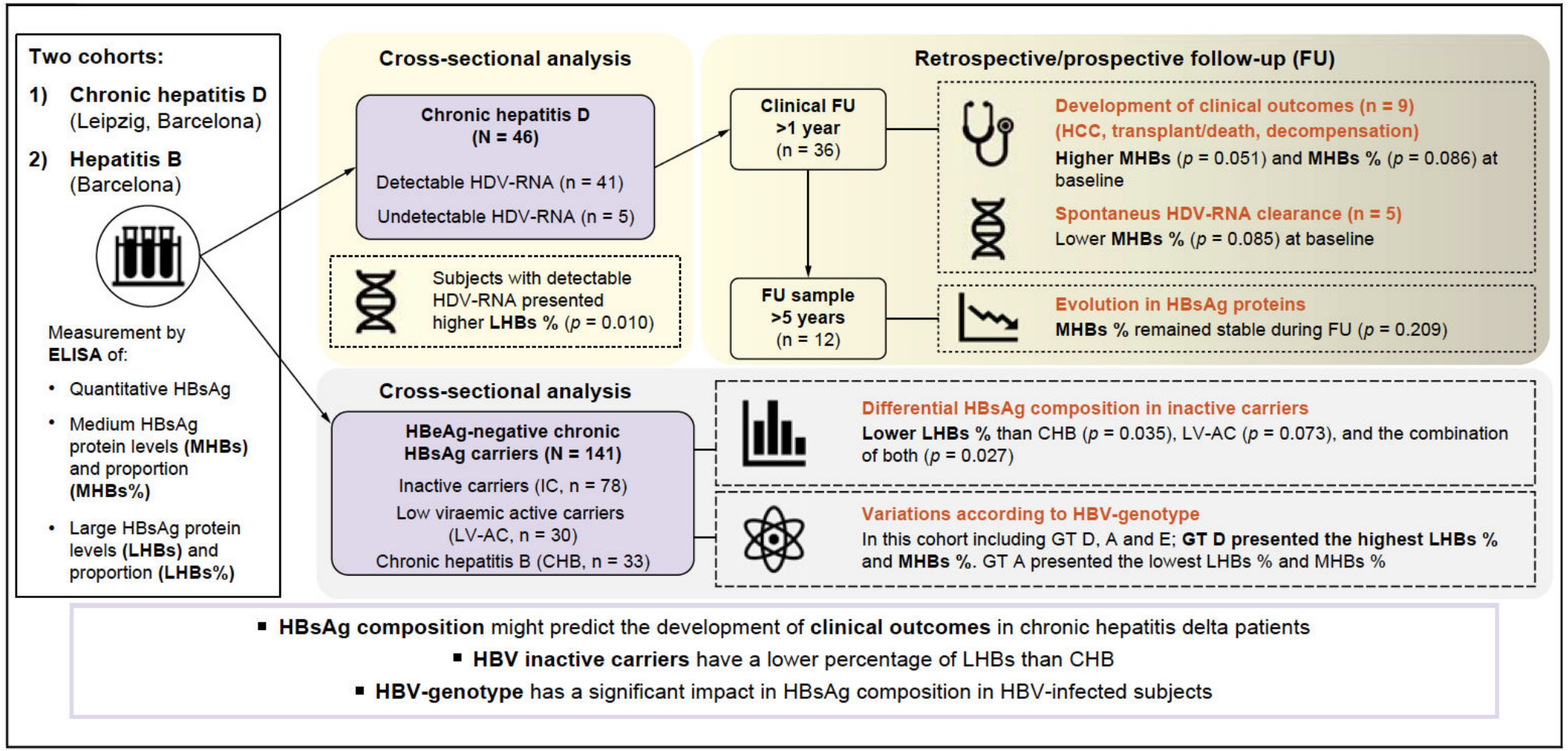
CHRONIC HDV COINFECTION (CHD) IS CHARACTERIZED BY A DIFFERENT HBSAG ISOFORMS COMPOSITION RESPECT TO HBV MONO-INFECTION WITH HIGHER MIDDLE- AND LARGE-HBS LEVELS PARALLELING THE REPLICATIVE AND CYTOLYTIC ACTIVITY OF HDV

[1]A Magnapera, [1]L Piermatteo, [1]S D'Anna, [2]A Olivero, [3]L Duca, [1]G Torre, [1]C Castelli, [4]E Teti, [4]A Di Lorenzo, [4]V Malagnino, [4]M Iannetta, [5]L Baiocchi, [5]S Francioso, [5]I Lenci, [3]F Ceccherini-Silberstein, [6]M Milella, [6]A Saracino, [2]A Ciancio, [4]L Sarmati, [7]P Lampertico, [2]M Rizzetto, [2]GP Caviglia, [1]V Svicher, [1]R Salpini. *[1]Department of Biology, University of Rome Tor Vergata, Rome, Italy; [2]Department of Medical Sciences, University of Turin, Turin, Italy; [3]Department of Experimental Medicine, University of Rome Tor Vergata, Rome, Italy; [4]Department of Systems Medicine, Infectious Disease Clinic, Tor Vergata University, Rome, Italy; [5]Hepatology Unit, Policlinico Tor Vergata, Rome, Italy; [6]Department of Biomedical Sciences and Human Oncology, Clinic of Infectious Diseases, University of Bari 'Aldo Moro', Bari, Italy; [7]Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*

ICAR 2024

Serum levels off HBsAg isoforms were quantified by ad-hoc ELISA (Brancaccio & Salpini 2021)

HBsAg isoforms in untreated CHD patients



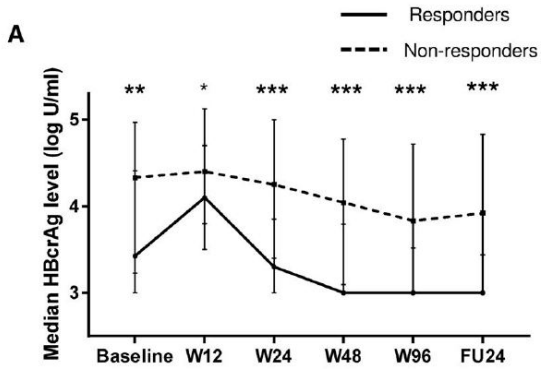
Roade et al. JHEP Reports 2023

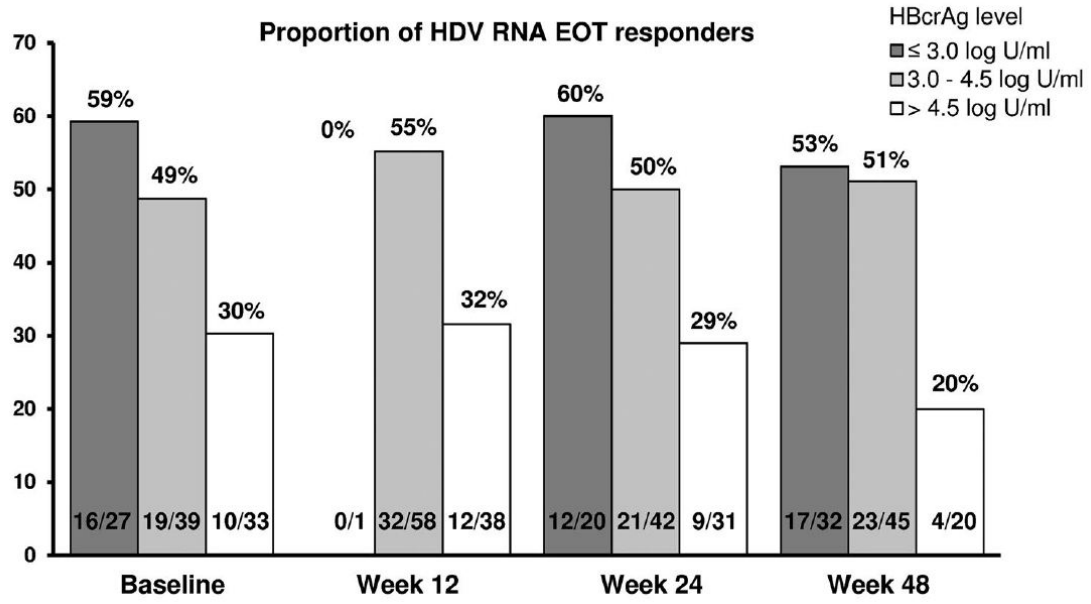
Semiautomatic in-house sandwich ELISA on a BEP III system using MA18/7 and Q19/10 antibodies and by Western blot (Pfefferkorn, 2017)

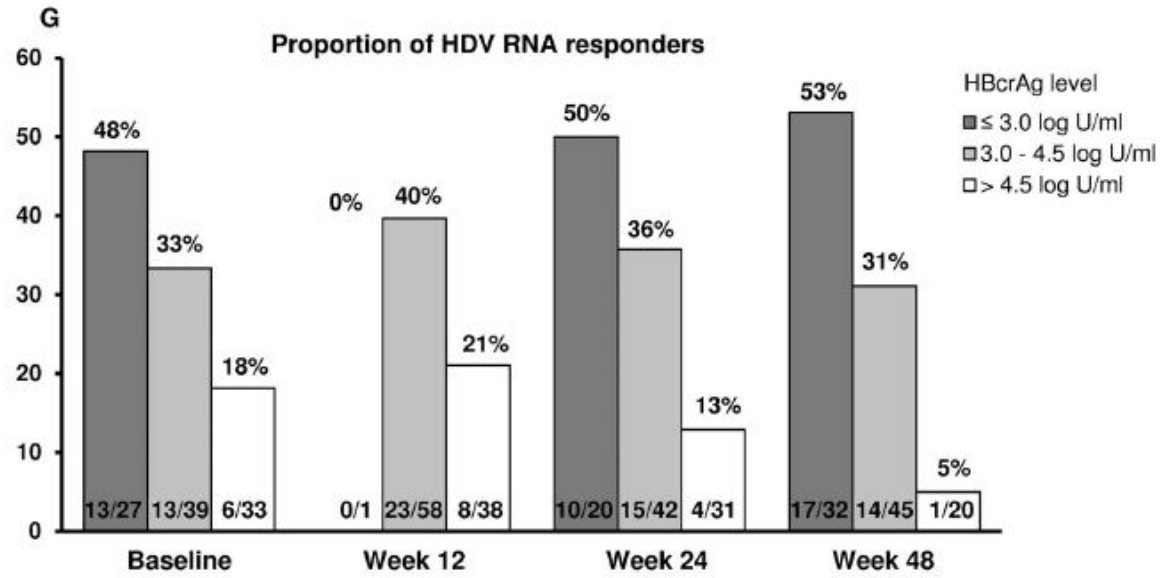
IFN-treated CHD patients

HIDIT-II study

prospective international, multicenter study including 120 CHD patients randomly assigned to either receive peg-IFNα plus tenofovir (TDF) or plus placebo for 96 weeks







Levels of HBcrAg showed high NPVs for achieving undetectable HDV RNA at FU24.
HBcrAg levels at baseline could serve as a helpful marker to better select patients benefiting from antiviral treatment.

Sandmann, Hepatology comm 2022

Serum markers of cccDNA transcriptional activity (HBcrAg and pre-genomic HBV RNA) and large HBsAg (LHBs) protein predict response to pegylated interferon in HDV infection

Ivana Carey[1], Mark Anderson[2], Christiana Moigboi[1], Natalie Bolton[1], Bo Wang[1], Gavin Cloherty[2], Geoff Dusheiko[1], Kosh Agarwal[1]

- 3 years post Peg-IFN therapy, 15 (45%) patients were HDV RNA negative (**responders**), (2 patients with HBsAg loss), whereas 18 patients had persistent HDV RNA (**non-responders**).
- Our analysis showed significant differences at baseline between responders and non-responders (Table 1).

	Responders (n=15)	Non-responders (n=18)	Significance (p=)
Male patients (#, %)	n= **13** (87%)	n= **8** (44%)	p = 0.08
Cirrhosis (#, %)	n= **2** (13%)	n= **10** (56%)	**p = 0.03**
Median age (IQR; range)	**37** years (11; 19 - 61)	**39** years (11; 21 - 53)	p = 0.68
Median therapy baseline HBV DNA (IQR; range)	**28** IU/ml (101; 0 - 2.9E5)	**13** IU/ml (45; 0 – 1.7E8)	p = 0.56
Median therapy baseline HBsAg (IQR; range)	**6801** IU/ml (757; 0.1 - 96231)	**8326** IU/ml (1121; 1238 - 27192)	p = 0.16
Median therapy baseline level of large HBsAg (IQR; range)	**20607** ng/ml (12105; 24 – 88090)	**81106** ng/ml (48251; 20830 – 475000)	**p < 0.001**
Median therapy baseline HDV RNA (IQR; range)	**23300** copies/ml (5937; 648 – 2.5E5)	**671500** copies/ml (1354; 728 – 1.7E7)	**p = 0.016**
Median therapy baseline HBcrAg (IQR; range)	**3.1** $\log_{10}$ U/ml (0.5; 2.6 – 6.8)	**4.25** $\log_{10}$ U/ml (1.3; 3.3 – 6.8)	**p < 0.01**
Median therapy baseline pg HBV RNA(IQR; range)	**1.69** $\log_{10}$ U/ml (1.01; 0 – 4.91)	**2.24** $\log_{10}$ U/ml (0.93; 0 – 5.03)	**p = 0.04**

Table 1. Baseline characteristics according to therapy response after 3 years post stopping therapy

Responders were infected with HDV genotype 5 (93% vs. 27%, p<0.01).

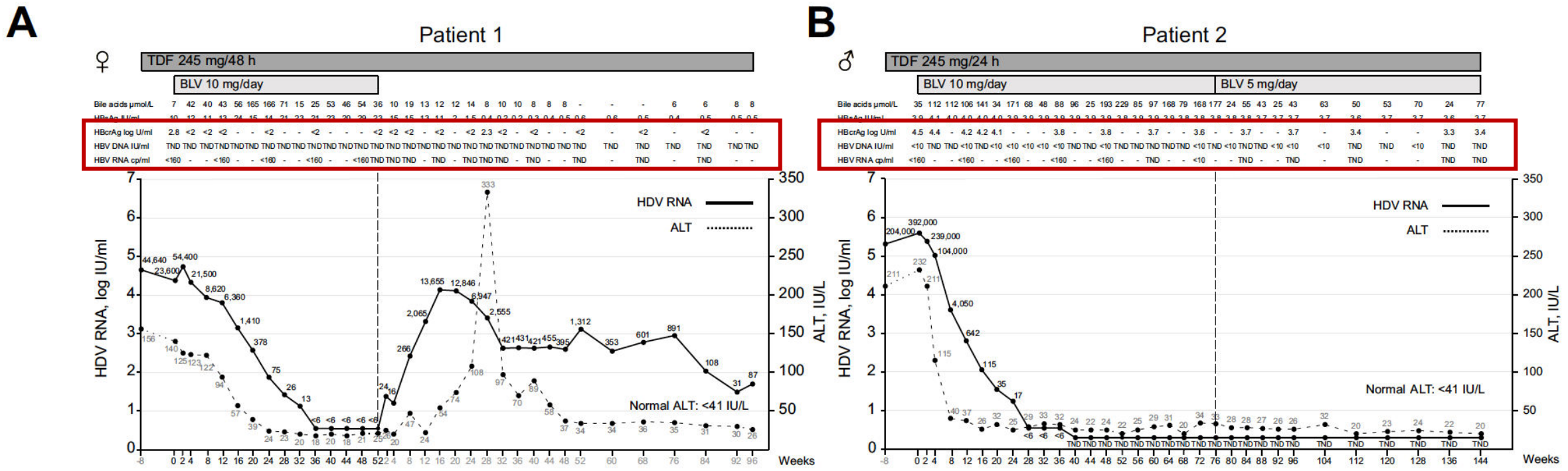
Changes between serum concentrations of HBV DNA, HDV RNA, HBsAg, large HBsAg (LHBs), HBcrAg and pg HBV RNA between start of therapy and after 3 years post stopping treatment are demonstrated in Figures below.

In **non-responders**, although we observed a significant decline in LHBs levels, HBcrAg and pg HBV RNA - these did not reach median baseline levels seen in **responders**.

(Abbott RNA RUO assay; L-HBsAg by in-house ELISA)

BLV-treated CHD patients

BLV monotherapy for up to 3 years



Moderate to high serum levels of HBcrAg were documented while serum HBV RNA was persistently negative

(Roche RNA IA assay)

Loglio, JHepatol 2021

BLV 72 weeks in compensated cirrhotics

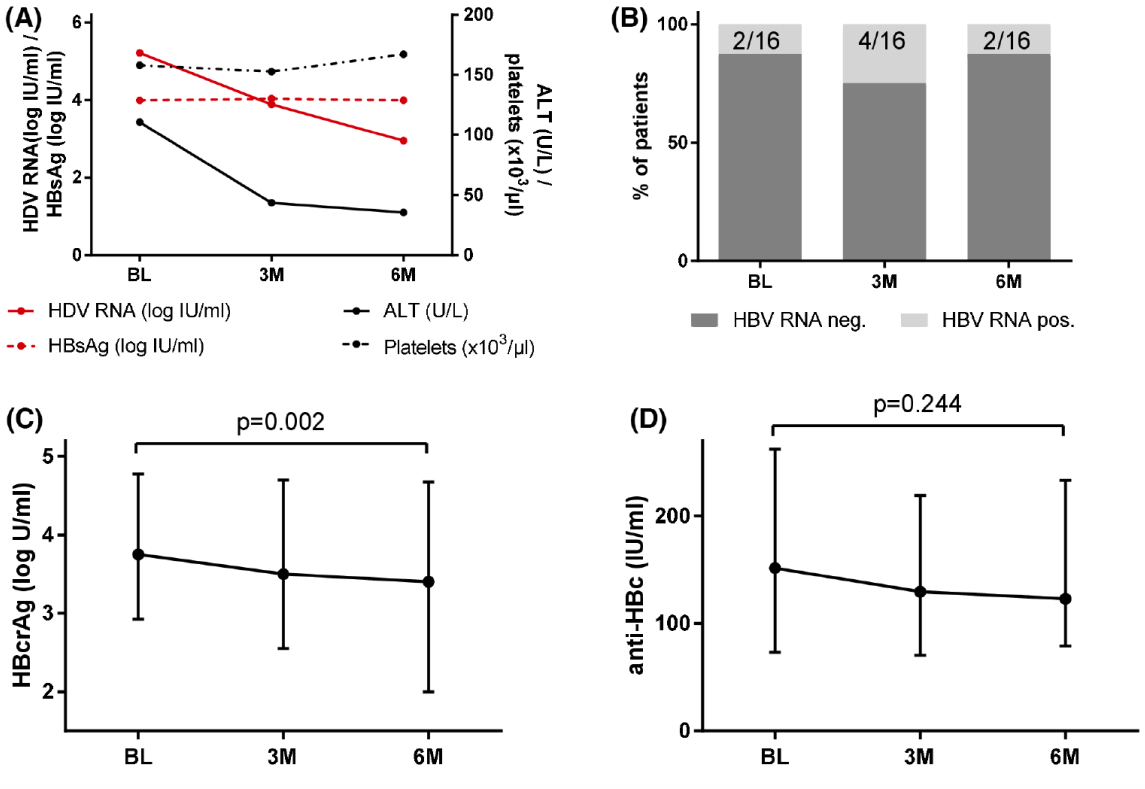
SAT-199

Kinetics of hepatitis B core related antigen in patients with compensated HDV cirrhosis treated with Bulevirtide monotherapy for 72 weeks: a single-center study

Elisabetta Degasperi[1], Maria Paola Anolli[1], Dana Sambarino[1], Floriana Facchetti[1], Caroline Scholtes[2,3,4], Sara Colonia Uceda Renteria[5], Alberto Perego[6], Corinna Orsini[6], Caroline Charre[2,3,4], Marie-Laure Plissonnier[2], Ferruccio Ceriotti[5], Sara Monico[1], Barbara Testoni[2], Massimo Levrero[2,4,7], Fabien Zoulim[2,4,7], Pietro Lampertico[1,8]. *[1]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Division of Gastroenterology and Hepatology, Milan, Italy; [2]ISERM U1052-Cancer Research Center of Lyon (CRCL), Lyon, France; [3]University Claude Bernard Lyon 1 (UCBLI), university of Lyon, Lyon, France; [4]Hospices Civils de Lyoun, Department of Virology, Lyon, France; [5]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Virology Unit, Italy; [6]Fujirebio Italia, Pomezia-Rome, Italy; [7]Hospices Civils of Lyoun, Departmente of Hepatology, Lyon, France; [8]CRC "A.M. and A. Migliavacca" Center for Liver disease, Departments of Pathophysiology and Transplantation, university of Milan, Milan, Italy*

Results: Overall, 49 HDV patients were enrolled: median age 52 (29–77) years, 59% males, platelets 78 (17–217) × 10^3/mm^3, liver stiffness measurement 17.3 (6.4–68.1) kPa, ALT 97 (30–1074) U/L, HBsAg 3.7 (0.8–4.4) LogIU/ml, HDV RNA 5.2 (2.4–6.9) LogIU/ml, HBcrAg 4.1 (3.0–5.2) U/ml. At baseline, HBcrAg was detectable (≥3 U/ml) in 86% of patients and showed a direct correlation with HBsAg levels ($r = 0.33$, $p = 0.03$), while no association with HDV RNA or ALT levels was observed. Following 72 weeks of BLV monotherapy, HDV RNA declined by 2.8 (0.2–5.3) LogIU/ml ($p < 0.001$ vs. baseline), becoming undetectable in 33% of patients. Virological response (undetectable or at least 2 Log HDV RNA decline vs. baseline) was achieved by 78% of patients, a biochemical response (ALT<40 U/L) was observed in 72% and a combined response (biochemical + virological) in 56%. During BLV treatment, patients testing HBcrAg positive declined from 86% to 70%, however the difference was not significant ($p = 0.21$). In HBcrAg positive patients, HBcrAg levels significantly declined from 4.1 (3.0–5.2) U/ml at baseline to 3.9 (3.1–4.7) U/ml at week 72 ($p = 0.03$), while no change in HBsAg levels was observed: from 3.7 (0.8–4.4) to 3.6 (2.5–4.3) LogIU/ml ($p = 0.77$). In HBcrAg positive patients, HBcrAg levels at week 72 were associated with biochemical response (OR 5.2, $p = 0.03$), while week 24 (OR 3.9, $p = 0.04$) and week 48 HBcrAg levels (OR 5.4, $p = 0.01$) were associated with combined response. Conversely, neither baseline nor on-treatment HBcrAg levels correlated with HDV RNA levels or virological response rates.

BLV for 6 months



Study outline

- Retrospective single center study (Germany)
- 16 patients CHD treated with BLV 2 mg/day
- Duration of therapy: 6 months
- 15/16 patients on NUC

Sixteen patients were included in the analysis, and seven (43.8%) had advanced liver disease;

HBcrAg was quantifiable in almost all patients and levels declined significantly during treatment with BLV. In contrast, HBV RNA levels were undetectable in the majority of patients and anti-HBc levels only declined numerically.

(Roche RNA IA assay)

Sandmann, JVH 2023

BLV 48 weeks in compensated cirrhotics with CSPH

Table 2. Time course of virological variables during 48 weeks of BLV treatment (N = 18).

Variables	Baseline	Week 8	Week 16	Week 24	Week 32	Week 40	Week 48	*p* value
HDV RNA, Log IU/ml	4.9 (3.3-6.6)	3.5 (1.2-5.9)	2.7 (0.9-5.9)	2.3 (0.7-5.8)	2.0 (0.7-5.8)	1.8 (0.3-6.0)	2.2 (0.3-6.0)	**<0.001**
HDV RNA decline, Log IU/ml	-	1.4 (0.4-3.1)	2.2 (0.4-3.6)	2.7 (0.6-3.9)	2.8 (0.4-3.9)	3.1 (0.3-4.6)	3.1 (0.2-4.3)	**<0.001**
HDV RNA decline ≥2 Log IU/ml	-	2 (11%)	7 (39%)	15 (83%)	15 (83%)	14 (78%)	14 (78%)	**<0.001**
HDV RNA decline <1 Log/ml	-	2 (11%)	2 (11%)	2 (11%)	2 (11%)	2 (11%)	2 (11%)	0.97
HDV RNA <1,000 IU/ml	0	8 (44%)	10 (56%)	13 (72%)	14 (78%)	14 (78%)	14 (78%)	**<0.001**
HDV RNA <100 IU/ml	0	2 (11%)	7 (39%)	9 (50%)	10 (56%)	10 (56%)	7 (39%)	**<0.001**
HDV RNA <6 IU/ml	0	0	0	2 (11%)	5 (23%)	6 (33%)	5 (23%)	**0.003**
Virologic response°	**-**	**2 (11%)**	**7 (39%)**	**15 (83%)**	**15 (83%)**	**14 (78%)**	**14 (78%)**	**<0.001**
HBsAg, Log IU/ml	3.7 (2.5-4.3)	3.8 (2.6-4.3)	3.8 (2.6-4.3)	3.8 (2.5-4.3)	3.7 (2.5-4.2)	3.7 (2.5-4.3)	3.7 (2.4-4.2)	0.31
HBV DNA detectable**	4 (28%)	0	0	0	2 (11%)	2 (11%)	1 (5%)	0.08
HBV RNA detectable***	1 (6%)	n.a.	n.a.	0	n.a.	n.a.	0	n.a.
HBcrAg, Log U/ml	3.8 (3.0-5.0)	3.7 (3.0-5.1)	3.8 (3.0-5.0)	3.7 (3.0-5.0)	3.7 (3.0-4.9)	3.7 (3.0-4.9)	3.7 (3.0-4.9)	**0.03**
HBcrAg >3 log U/ml	17 (94%)	16 (89%)	16 (89%)	16 (89%)	16 (89%)	16 (89%)	16 (89%)	0.99

Confirms HBcrAg/serum HBV RNA divergent pattern in the pretreatment samples and during BLV monotherapy

Degasperi, JHepatol 2023

BLV 48 weeks in compensated cirrhotics: HBsAg isoforms

WED-399-YI

The composition of HBsAg along with HDV-RNA predicts virological response in chronic hepatitis delta patients treated with bulevirtide for 48 weeks

Stefano D'Anna[1], Romina Salpini[2], Elisabetta Degasperi[3], Leonardo Duca[1], Maria Paola Anolli[3], Lorenzo Piermatteo[2], Dana Sambarino[3], Marta Borghi[3], Floriana Facchetti[3], Francesca Ceccherini Silberstein[1], Riccardo Perbellini[3], Pietro Lampertico[3,4], Valentina Svicher[2]. *[1]Department of Experimental Medicine, University of Rome "Tor Vergata", Rome, Italy; [2]Department of Biology, University of Rome "Tor Vergata", Rome, Italy; [3]Division of Gastroenterology and Hepatology, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [4]CRC "A. M. and A. Migliavacca" Center for Liver Disease, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*

Method: 28 consecutive patients with HDV-related compensated cirrhosis starting BLV 2 mg/day monotherapy were enrolled in this retrospective/longitudinal study, all under effective NUC treatment at entry. L-HBs, M-HBs and S-HBs were quantified by *ad-hoc* ELISAs in baseline and week 48 (W48) samples (Beacle). HDV RNA was quantified by Robogene 2.0. Virological response was defined as HDV RNA undetectable or >2log decline compared to baseline, biochemical response as ALT normalization.

Results: At baseline, median (IQR) age was 53 (40–63) years, liver stiffness 19.4 (15.4–32.9) kPa, ALT 106 (77–147) U/l, serum HDV RNA 5.4 (4.4–6.0) log IU/ml and HBsAg levels 3.7 (3.4–4.9) log IU/ml. Pre-treatment median (IQR) levels of S-HBs, M-HBs and L-HBs were 3999 (1482–7184), 1032 (305–2222) and 6 (2–14) ng/ml, respectively. At W48, serum HDV RNA declined by 3.1 (1.8–3.7) log IU/ml while virological and biochemical responses were observed in 71% and 75% of patients, respectively. A >10% decrease of S-HBs, M-HBs and L-HBs levels was observed in 57%, 54% and 39% of patients with a median (IQR) decline of 1095 (839–2403), 145 (39–350) and 10 (4–15) ng/ml, respectively. Baseline HDV RNA <5 log IU/ml was associated with HDV RNA <100 IU/ml at W48 (75% with vs 25% without, P = 0.02). A similar correlation was observed for baseline L-HBs <9 ng/ml (62.5% with vs 25% without, P = 0.05). The combination of pre-treatment L-HBs <9 ng/ml + HDV RNA <5 log IU/ml was the best predictor for achieving HDV RNA <100 IU/ml (PPV:87.5%, NPV:70%; P = 0.01). This combination showed also the best diagnostic accuracy for predicting HDV RNA <100 IU/ml plus ALT normalization (PPV:75%, NPV:75%; P = 0.03). A different scenario was observed for M-HBs. Patients with baseline M-HBs >500 ng/ml had a significantly greater virological response than those with baseline M-HBs <500 ng/ml (HDV RNA decline of 3.4 [2.5–3.8] vs 1.6 [1.2–3.2] log IU/ml, P = 0.03). Baseline M-HBs >500 ng/ml predicted the achievement of virological response at W48 of BLV (PPV: 88.8%, NPV: 60%; P = 0.01). Superimposable results were observed in a subgroup of 12 patients with serum HDV RNA <5 log IU/ml at baseline (PPV: 100%, NPV: 57%; P = 0.038).

NAPs+IFN-treated CHD patients

REP-310/301-LTF – HBcrAg and serum HBV RNA

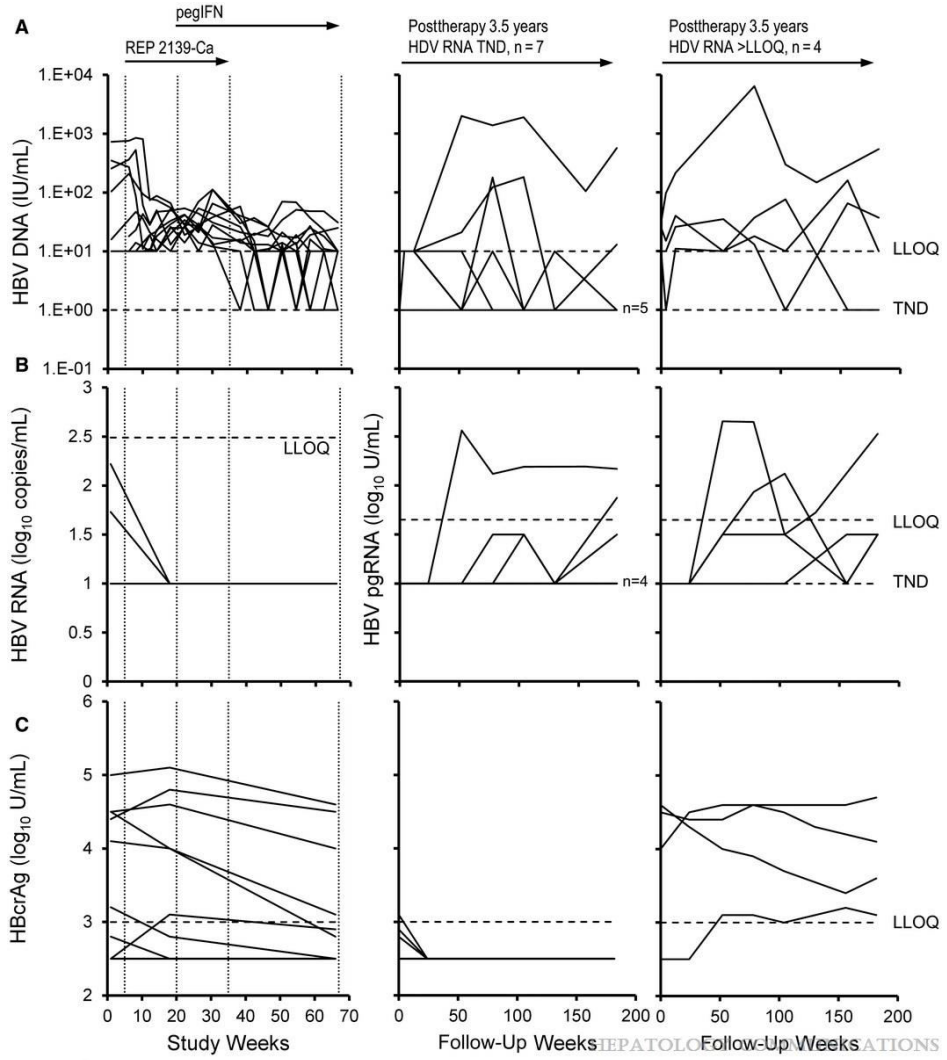


TABLE 4 - Summary of Outcomes in Patients With Functional Cure of HDV*

Follow-Up Completed		Participants at 1 year†	Participants at 3.5 years
Functional cure of HDV during follow-up		7	7
HBV DNA response	≤2,000 IU/mL	7/7 (100%)	7/7 (100%)
	TND	4/7 (57%)	5/7 (71%)
HBV virologic response	VC of HBV‡	3/7 (43%)	3/7 (43%)
	FC of HBV§	4/7 (57%)	4/7 (57%)
	VC + FC: no therapy required low risk of progression, reduced risk of HCC	7/7 (100%)	7/7 (100%)
HBV RNA	<LLOQ (1.65 $\log_{10}$ U/mL)	7/7 (100%)‖	6/7 (86%)¶
	TND	7/7 (100%)‖	4/7 (57%)¶,#
HBcrAg	<LLOQ (3 $\log_{10}$ U/mL)	7/7 (100%)	7/7 (100%)

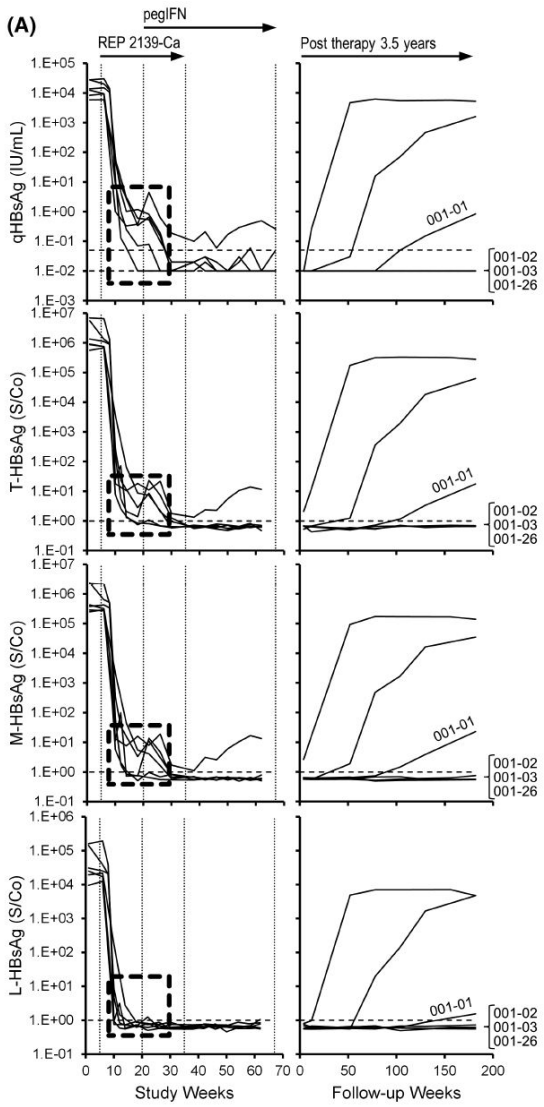
Data show number (percentage) of participants out of total.
*HDV RNA TND with normal ALT.
†Previously published.(19)
‡HBV DNA <2,000 IU/mL with normal ALT.
§HBV DNA TND, HBsAg <0.05 IU/mL with normal ALT.
‖Total HBV RNA (includes pgRNA; LLOQ = 309 copies/mL).
¶HBV pgRNA (estimated LLOQ = 152 copies/mL).
#All with HBsAg <0.005 IU/mL.
Abbreviations: FC, functional cure; HCC, hepatocellular carcinoma; VC, virologic control.

(Abbott RNA RUO assay)

Control of HBV DNA during therapy and follow-up in participants maintaining HDV RNA TND was consistent with declines in and/or absence of detectable HBV RNA and HBcrAg

Bazinet, Hepatology Comm 2021

REP-310/301-LTF – HBsAg isoforms



Abbott RUO assays for HBsAg isoforms (Rogers Hepatology 2019)

No correlation between baseline levels of HBsAg isoforms and HBsAg decline during therapy or therapeutic outcomes during follow-up.

More rapid clearance of SHB than other HBsAg isoforms in patients with strong total HBsAg level declines. (selective clearance of subviral particles consistent with previous NAP studies)

The trace of total HBsAg rebound in some patients consisted primarily of SHB and MHB

Bazinet, Hepatology 2022

Conclusions

Still limited data in CHD patients

Most untreated CHD patients are HBcrAg-positive but serum HBV RNA-negative
Unique pattern respect to HBV mono-infection – confirmed during BLV treatment

In peg-IFN treated patients, high HBcrAg levels at baseline/during treatment may serve as futility rule

In BLV treated patients, relevance of HBcrAg kinetic deserves further investigation

L- and M-HBsAg isoforms are associated with higher HDV replication and development of clinical outcomes
Predictors of response in BLV-treated patients?
→ warning: already multiple in-house assays…