Lobos XV
Caso Clínico

Laura Blazquez

Hospital Central de Mendoza

Caso Clínico

- Mujer de 70 años
- Antecedentes Patológicos: Hipertiroidismo; Hipertensión Arterial; Anexo histerectomía (20 años)
- Niega consumo de alcohol u otro tóxico
- Antecedente Transfusional dudoso
- Medicación Habitual: Levotiroxina 75 mcg; Enalapril 20 mg/d

Derivada a consultorio de Hepatología por elevación de transaminasas

Caso Clínico

- Lúcida, Sin ictericia
- BMI: 23,2 Kg/m
- Sin hallazgos patológicos en examen físico
- Laboratorio:

Glob. Blancos: 6900 Hto: 42% Plaq: 246000

Glucemia: 0,7 ***Colesterol: 202*** HDL: 37 TAG: 98

Ur: 0,34 Creat: 0,7 ***GOT: 89 (40) GPT: 162 (35)*** FAL: 83

BT: 0,8 BD: 0,12

- Ecografía Abdominal: Hepatomegalia leve; hígado heterogéneo con signos de esteatosis grado1. Bazo, páncreas y riñones ok

Serología

HBsAg : reactivo
Anti HBc: reactivo
Anti HBc IgM: no reactivo

Anti HCV: reactivo

Inmunológico

FAN: negativo
AMA: negativo
PxE : PT: 7,3 Alb: 4,2 GGlob: 1,3

Seguimiento Diagnóstico

Diagnóstico Presuntivo

Seguimiento Diagnóstico

- HIV no reactivo VDRL no reactivo
- AFP 12,2 (Hasta 15)

- **CV HBV 45460 UI/ml**
- HBeAg no reactivo Anti HBe Ag reactivo

- **CV HCV 405564 UI/ml Genotipo 1b**

- **Elastografía:** 8,7 Kpa (F2)

Diagnóstico Presuntivo

Coinfección HCV-HBV

Conducta Terapéutica

Conducta Terapéutica

- Se Inicia Tratamiento Anti hepatitis B con Entecavir 0,5 mg/ d

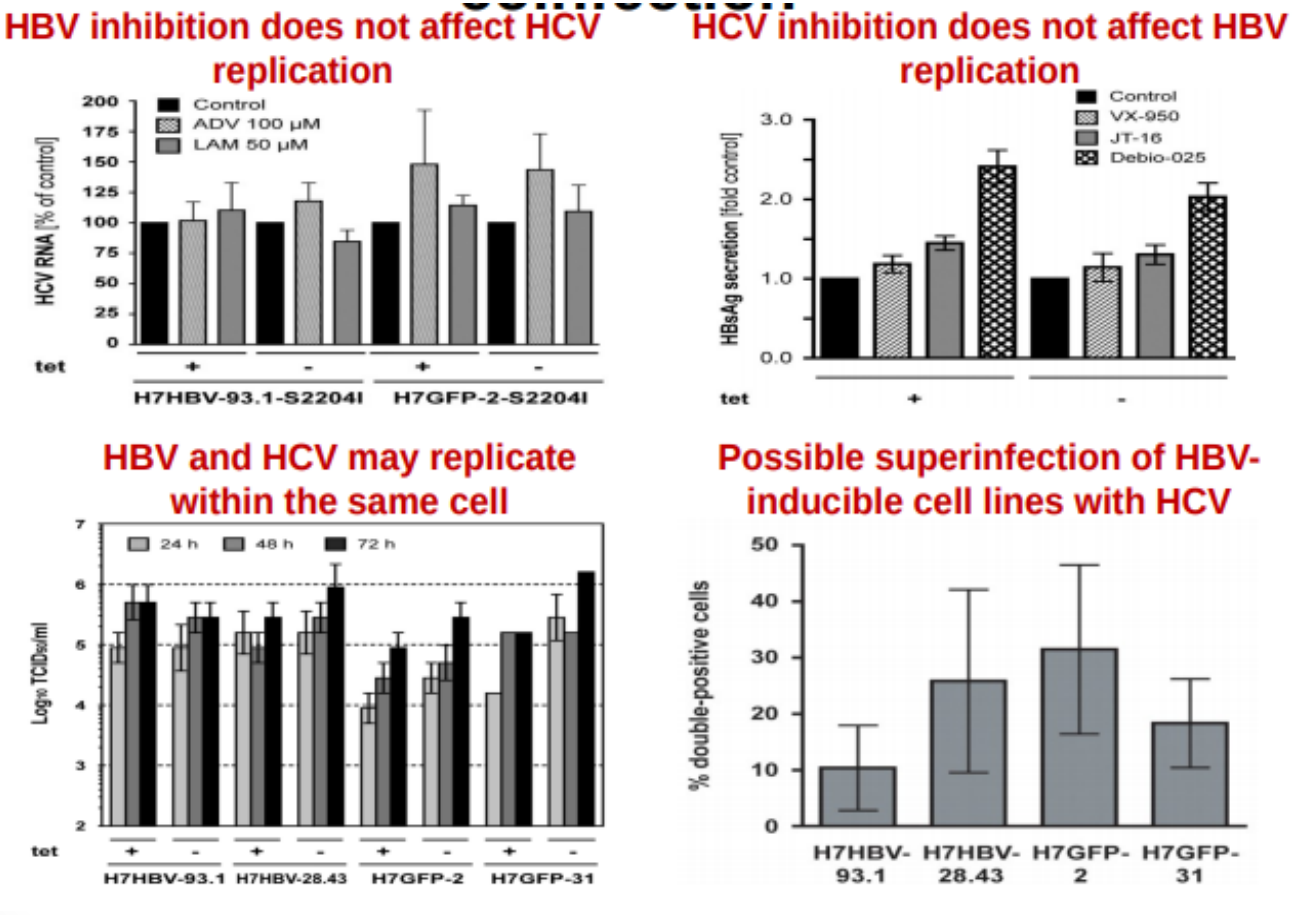
3 meses posteriores: **CV HBV NO detectable**

HBsAg reactivo; Anti HBeAg reactivo

- Luego se agrega Zepatier (Elbasvir/grazoprevir), completando 8 semanas → RVS

- Actualmente continúa con Entecavir mantiene CV indetectable

No hay interferencia Viral directa en Coinfección



Bellecave P et al. Hepatology 2009; 50: 46-55

Cuestiones prácticas para el tratamiento de pacientes coinfectados

- Riesgo de interacción entre antivirales para HCV/HBV
- Posible reactivación de HBV durante o un tiempo después de realizar tratamiento con AAD para HCV

Interacción

	Elbasvir-Grazoprevir	Glecaprevir-Pibrentasvir	Sofosbuvir-Ledipasvir	Sofosbuvir-Velpatasvir	Sofosbuvir-Velpatasvir-Voxilaprevir
Lamivudina	▲	▲	▲	▲	▲
Entecavir	▲	▲	▲	▲	▲
Tenofovir Alafenamida	▲	▲	▲	▲	▲
Tenofovir- DF	▲	▲	▲	▲	▲

▲ Sin Interacciones

▲ Potenciales Interacciones

Reactivación

Table 2. Baseline HBV/HCV Viral Characteristics and DAA Received

Case Number (Reference)	HCV Genotype	HBV Genotype	HBsAg	HBsAb	HBcAb	HBeAg	HBeAb	HBV DNA Level, *copies/mL**	DAA	Country of Report
1	1a	NR	NR	NR	NR	Negative	Positive	2700 (elevated)	Viekira Pak (AbbVie)/RBV	United States
2 (42)	1b	NR	Positive	NR	Positive	Negative	Positive	2.5 $\log_{10}$ (elevated)	DCV/ASV	Japan
3	NR	NR	NR	NR	NR	Negative	Positive	Undetectable	DCV/ASV	Japan
4	1b	NR	Positive	NR	NR	Negative	Positive	3.9 $\log_{10}$ (elevated)	DCV/ASV	Japan
5 (29)	1a	NR	NR	NR	NR	Negative	Positive	2300 (elevated)	SIM/SOF	United States
6 (29)	1a	NR	Negative	Negative	Positive	NR	NR	Undetectable	SIM/SOF	United States
7 (26)	1	NR	Negative	Negative	Positive	NR	NR	Undetectable	SIM/SOF/RBV	United States
8	3a	NR	Positive	NR	NR	NR	NR	244 (elevated)	SOF/RBV	Portugal
9 (38)	4	D	Negative	Negative	Positive	Negative	Positive	Undetectable	LDV/SOF	France
10 (28)	NR	NR	Positive	NR	NR	NR	NR	Undetectable	LDV/SOF	United States
11	NR	NR	NR	NR	Positive	NR	NR	Undetectable	LDV/SOF	Japan
12 (43)	1	B	Positive	NR	NR	Negative	Positive	Undetectable	SIM/PEG/RBV	Japan
13	1	A	Positive	NR	NR	Negative	Positive	Undetectable	SOF/RBV	Japan
14	NR	B	Positive	NR	NR	NR	NR	1.3 $\log_{10}$ (elevated)	LDV/SOF	Japan
15	1b	B	Positive	NR	NR	Negative	Positive	2.7 $\log_{10}$ (elevated)	DCV/ASV	Japan
16	NR	C	Positive	NR	NR	NR	NR	Undetectable	LDV/SOF	Japan
17	1a	NR	Positive	NR	Positive	Negative	Negative	Undetectable	DCV/SOF/RBV	Australia
18	NR	NR	NR	NR	NR	Negative	Positive	3.6 $\log_{10}$ (elevated)	LDV/SOF/RBV	Japan
19	1b	NR	Positive	NR	NR	Negative	Positive	<2.1 $\log_{10}$†	DCV/ASV	Japan
20	1b	NR	Positive	NR	NR	Negative	Positive	Undetectable	DCV/ASV	Japan
21	1	NR	NR	NR	NR	Negative	Negative	Undetectable	DCV/ASV	Japan
22	1	NR	NR	NR	NR	NR	NR	<2.1 $\log_{10}$†	DCV/ASV	Japan
23	NR	NR	NR	NR	NR	NR	NR	Undetectable	DCV/ASV	Japan
24	NR	C	NR	NR	NR	Negative	NR	3.3 $\log_{10}$ (elevated)	DCV/ASV	Japan
25	NR	NR	NR	NR	NR	NR	NR	Undetectable	DCV/ASV	Japan
26	NR	B	NR	NR	NR	NR	NR	<2.1 $\log_{10}$†	LDV/SOF	Japan
27	NR	NR	NR	NR	NR	NR	NR	Undetectable	LDV/SOF	Japan
								NR	LDV/SOF/RBV	France
							sitive	Undetectable	LDV/SOF	China

Solo 6 se testearon para Anti Hbc

AS Ab = hepatitis B core antibody; HBeAb = hepatitis B e antibody; HI epatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C = ribavirin; SIM = simeprevir; SOF = sofosbuvir.
* Food and Drug Administration Adverse Event Reporting System re ecifically stated as undetectable were interpreted as elevated/ detectable.
† Values preceded by "<" were regarded as uninterpretable if not specifically stated as undetectable.

Gastroenterology 2018;154:989–997

Efficacy of Ledipasvir and Sofosbuvir Treatment of HCV Infection in Patients Coinfected With HBV

Chi-Yi Chen,[5] [8] Chohee Yun,[8] [8]

Table 1. Baseline Demographic and Disease Characteristics

Characteristic	HCV genotype 1 (n = 68)	HCV genotype 2 (n = 43)	Total (n = 111)

Table 3. Patients With Concomitant HBV DNA Elevation and ALT > 2 × ULN through Posttreatment Week 12

	Patient 1 Female, 60 years old, with cirrhosis		Patient 2 Male, 61 years old, no cirrhosis		Patient 3 Male, 45 years old, no cirrhosis		Patient 4 Female, 60 years old, no cirrhosis		Patient 5 Male, 47 years old, no cirrhosis	
Visit	ALT U/L	HBV DNA IU/mL	ALT U/L	HBV DNA IU/mL	ALT U/L	HBV DNA IU/mL	ALT U/L	HBV DNA IU/mL	ALT U/L	HBV DNA IU/mL
BL	200	35	228	191	112	453	40	824	167	286,000
Week 1	88	26	104	235	90	300	22	1060	76	310,000
Week 2	47	84	52	338	87	349	19	1540	75	309,000
Week 4	41	406	102	6400	111	808	19	15,900	83	217,000
Week 8	71	6290	74	54,900	124	6140	59	113,000	52	134,000
Week 12	91	<20	47	27,600	109	2240	22	1400	43	134,000
PT week 4	76	<20	115	882,000	118	3380	16	6120	47	61,000
PT week 12	45	<20	32	140	92	2780	87	1,300,000	61	2,150,000
Retest	-	-	-	-	-	-	-	-	212	99,200,000
Retest	-	-	-	-	-	-	-	-	677	38,200,000
PT Week 24	38	<20	23	<20	152	2790	47	1,130,000	576	9,350,000
Retest	-	-	-	-	-	-	-	-	300	7,160,000
Retest	-	-	26	-	-	-	-	-	131	11,700,000
PT week 36	26	<20	37	<20	162	207	44	1,510,000	164	53,700,000
PT week 48	29	<20	28	<20	132	4490	53	2,520,000	34	273

NOTE. Shaded area indicates when the patient began HBV treatment.
ALT, alanine aminotransferase; BL, baseline; PT, post-treatment; ULN, upper limit of normal; -, N/A.

Table 1. Summary of reported virologic outcomes.

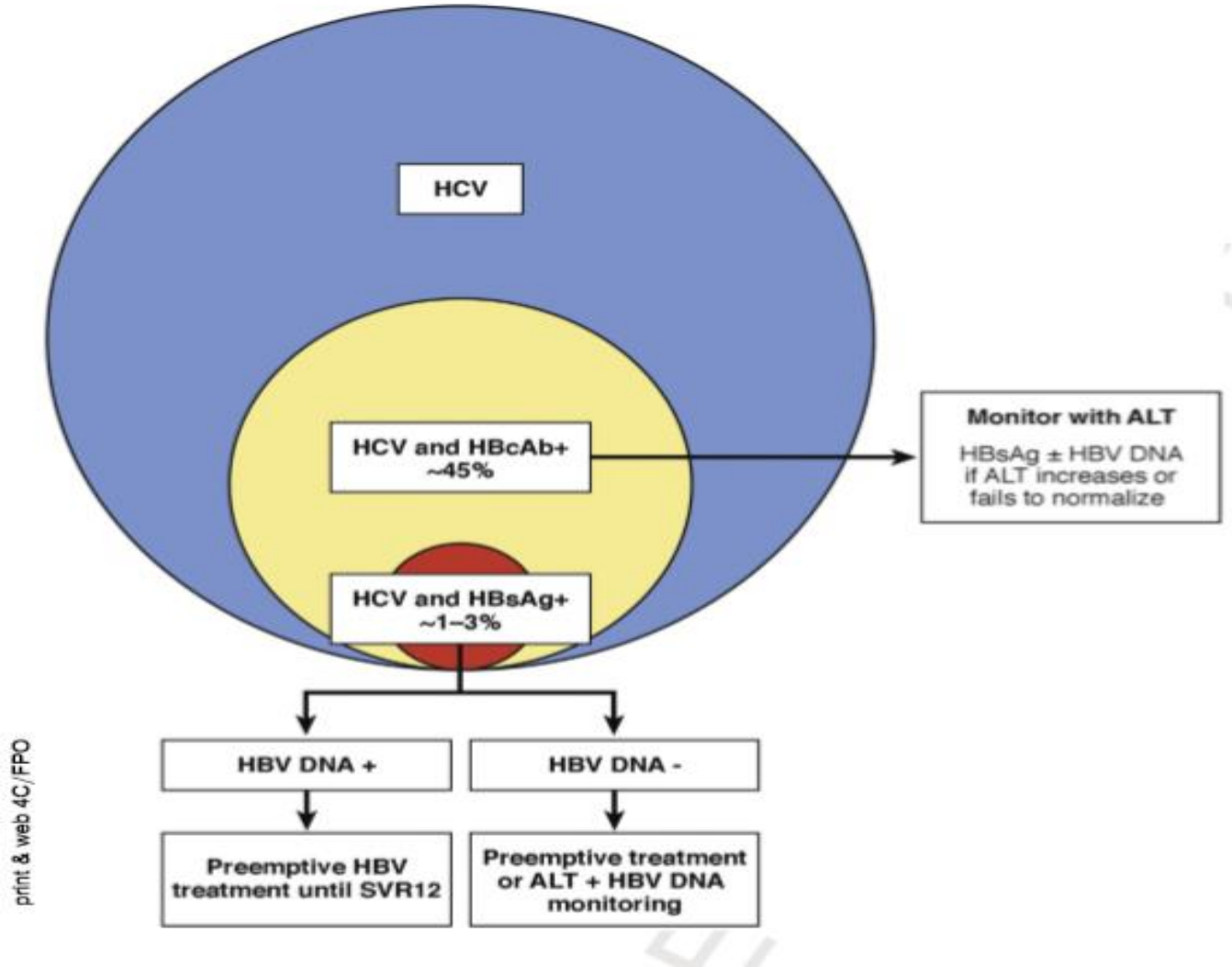
References	Cohort study		Case report			
	Patients, n	- Reactivation(%) - Clinical reactivation (%)	Age	DAAs regimen	- HBV DNAb - HBV DNAr	- Reactivation time - Clinical reactivation
Overt HBV infection (HBsAg positive)						
Collins *et al.*[8]	-	-	55	SOF/SIM	- 3.3 log IU/ml - 7.3 log IU/ml	- 8° week - Yes
Takayama *et al.*[9]	-	-	69	DAC/ASU	- 2.5 logs copies/ml - 7 logs copies/ml	- 2° week - Yes
Wang *et al.*[10]	10	- 3 (30%) - 3/3 (100%)	-	-	-	-
Calvaruso *et al.*[11]	4*	- 3 (75%) - 0%	-	-	-	-
Yeh *et al.*[12]	7	- 4 (57.1%) - 1/4 (25%)	-	-	-	-
Belperio *et al.*[13]	84	- 25 (29.8%) - 6/25 (24%)	-	-	-	-
Patients with occult HBV infection						
Collins *et al.*[8]	-	-	57	SOF/SIM	- <1.3 log IU/ml - 4 log IU/ml	- 4° week - No
Ende *et al.*[17]	-	-	59	SOF/SIM	- Undetectable - 7.4 log IU/ml	- 11° week - Yes
De Monte *et al.*[18]	-	-	53	SOF/LDV	- Undetectable - 8.9 log IU/ml	- 6° week - Yes
Suda *et al.*[5]	-	-	79	DAC/ASU	- Undetectable - 21600 IU/ml	- 21° week of FU - Yes
Wang *et al.*[10]	124	- 0%	-	-	-	-
Calvaruso *et al.*[11]	37	- 0%***	-	-	-	-
Yeh *et al.*[12]	57	- 0%	-	-	-	-
Sulkowski *et al.*[16]	103	- 0%	-	-	-	-
Belperio *et al.*[13]	173	- 4 (2.3%) - 1 (25%)	-	-	-	-
Kawagishi *et al.*[6]	84	- 5 (5.9%) - 1 (20%)	-	-	-	-

ALT, alanine aminotransferase; ASU, asunaprevir; DAA, direct-acting antivirals; DAC, daclatasvir; HbsAg, hepatitis B surface antigen; HBV, hepatitis B virus; LDV, ledipasvir; NUC, nucleos(t)ide analogues; SIM, simeprevir; SOF, sofosbuvir.

* Other 4 HBsAg patients were on NUCs before starting DAAs.

** Clinical reactivation: ALT flares, jaundice.

*** HBV-DNA was detected by highly sensitive PCR in 3 patients (8.1%).



Feld J et al. Gastroenterology 2018 Vol 154, 795–798

Reactivación en Trasplante

HBV status at LT

HBV ADN

Table 1. Patients with detectable HBV DNA during HCV treatment follow-up.

No.	HBV status at LT	HIV status	Liver donor HBcAb status	HBV treatment Pre-DAAs	Baseline fibrosis score*	DAA		HBV status at baseline	HBV DNA (log IU/ml)				ALT (IU/ml)			Clinical event
						Regimen	SVR		Baseline	EOT	FU W12	Post-treatment	Baseline	EOT	FU W12	
0321-048-1	HBcAb+	Neg	Neg	None	F4	24-wks SOF + LDV	Yes	HBsAg+	6.64	5.07	1.72		38	16	13	None
0327-041-1	HBcAb+	Neg	Neg	None	F0-F2	12-wks SOF + DCV	Yes	HBcAb+	2.49	2.09	1.3		26	10	13	None
0304-009-1	HBcAb+	Neg	Neg	None	F4	24-wks SOF + DCV	Yes	HBcAb+	Und. <1	1.52	n.a.	Und. <1 (W48)	72	15	16	None
0327-021-1	HBsAg+	Neg	Neg	None	F4	12-wks SOF + DCV	n.a.	HBcAb+	Und. <1	Und. <1	2.17	n.a.	37	16	30	Death at FU-W38
0902-013-1	HBsAg+	Neg	Neg	TDF + HBIG	F4	24-wks SOF + DCV	Yes	HBsAg+	1.49	3.46	Und. <1		19	n.a.	142	Ascites

DCV, daclatasvir; HBIG, hepatitis B immune globulin; HBV, hepatitis B virus; HCV, hepatitis C virus; n.a., not available; RBV, ribavirin; SOF, sofosbuvir; TDF, tenofovir disoproxil fumarate.
*Metavir score.

Tto HBV previo a DAA

ALT

Fig. 1. HBV markers, HBV prophylaxis and detectable HBV DNA during HCV treatment follow-up. HBV, hepatitis B virus; HCV, hepatitis C virus; HBcAb, HBV core antibody; HBsAg, HBV surface antigen; HIV, human immunodeficiency virus.

Mouna L et al. Journal of Hepatology 2019 Vol 70, 1297–1300

EASL Recommendations on Treatment of Hepatitis C 2018

Journal of Hepatology 2018; 69: 461–511

There is a potential risk of HBV reactivation during or after HCV clearance, but the risk is unpredictable.

Patients commencing DAA-based treatment for hepatitis C should be tested for HBs antigen, anti-HBc antibodies and anti-HBs antibodies.

- Patients with HBV-HCV coinfection should be treated with the same anti-HCV regimens, following the same rules as HCV monoinfected patients (B1).
- Patients coinfected with HCV and HBV fulfilling the standard criteria for HBV treatment should receive nucleoside/ nucleotide analogue treatment according to the EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection (A1).
- Patients who are HBs antigen-positive should receive nucleoside/nucleotide analogue prophylaxis at least until week 12 post anti-HCV therapy and be monitored monthly if HBV treatment is stopped (B1).
- In patients who are HBs antigen-negative but anti-HBc antibody-positive, serum ALT levels should be monitored monthly, HBs antigen and HBV DNA should be tested if ALT levels do not normalise or rise during or after anti-HCV therapy, and nucleoside/nucleotide analogue therapy should be initiated if HBs antigen and/or HBV DNA are present (B1).

Conclusiones

Testear HBsAg en todos los pacientes HCV + candidatos a recibir tratamiento antiviral

En pacientes inmunocomprometidos realizar además Anti HBc

Pacientes con HBsAg + y HBV ADN no detectable, debe ser monitorizadon (ALT)

SI ALT aumentan realizar HBV ADN si este es detectable iniciar NUCs

Si HBV ADN es detectable, se deberia iniciar Nucs al menos 1 mes antes del inicio de tratamiento anti HCV