



Paciente con hepatitis B con indicación límite de tratamiento

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CASO CLÍNICO

- Mujer de 29 años de edad.
- Raza caucásica.
- Antecedentes familiares:
 - Madre fallecida joven por AVC, tenía hepatitis.
- Antecedentes personales:
 - Migraña.
 - ERGE.
- Enfermedad actual:
 - Remitida a consulta desde centro de donación de sangre al detectar HBsAg positivo.

CASO CLÍNICO

- Exploración física:
 - Buen estado general.
 - Peso: 75 Kg. Talla 164 cm. IMC 27,9.
 - Sin estigmas de hepatopatía.
- Analítica basal:
 - HBsAg positivo.
 - AntiHBc positivo.
 - ALT 29.

EVALUACIÓN INICIAL DEL PACIENTE CON HEPATITIS B

Natural history and assessment of patients with chronic HBV infection

HBV markers

HBsAg
HBeAg/anti-HBe
HBV DNA

Liver disease

Biochemical parameters: ALT
Fibrosis markers: non-invasive markers of fibrosis (elastography or biomarkers) or liver biopsy in selected cases

Investigar comorbilidades y detección de IgG VHA

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection, 2017

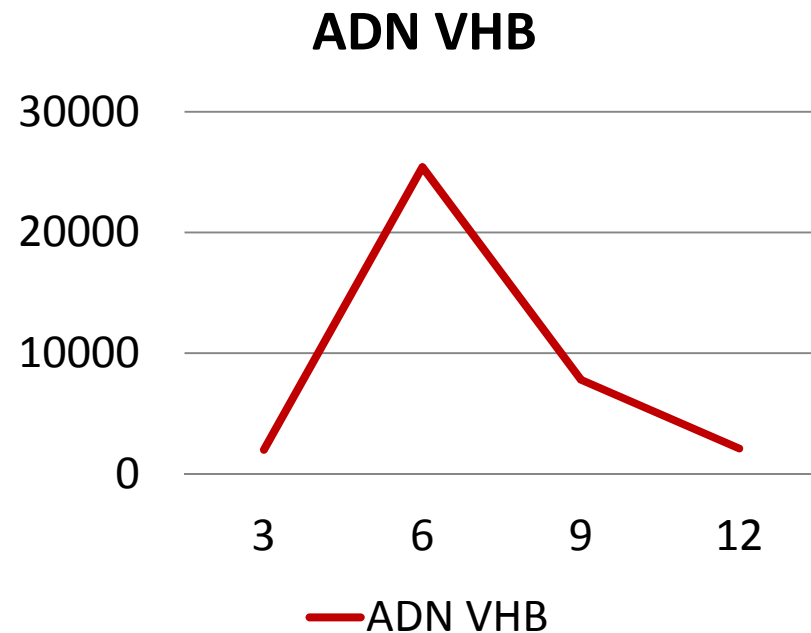
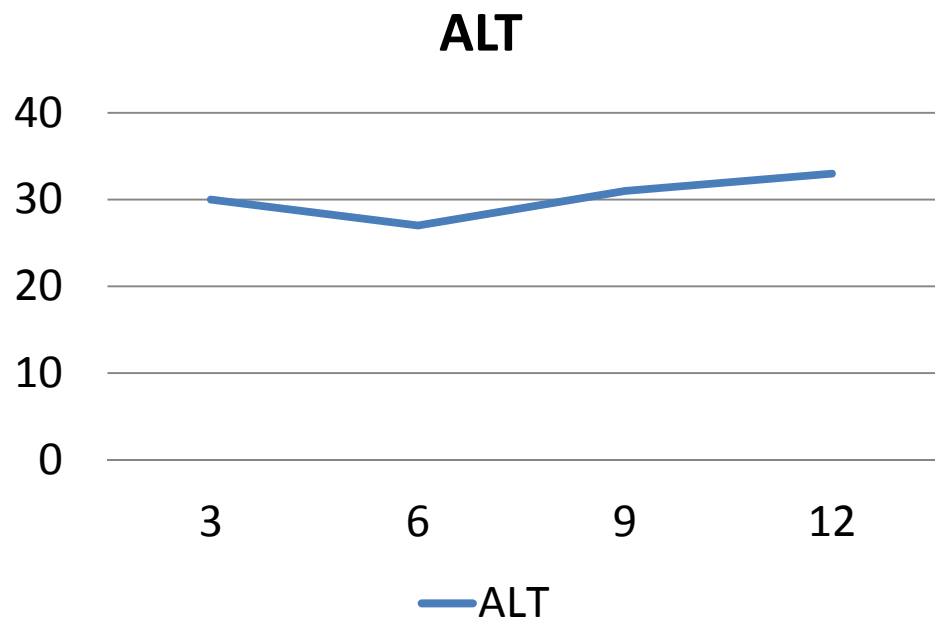
CLASIFICACIÓN DEL PACIENTE CON INFECCIÓN POR VHB

	HBeAg positive		HBeAg negative	
	Chronic infection	Chronic hepatitis	Chronic infection	Chronic hepatitis
HBsAg	High	High/intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10 ⁷ IU/ml	10 ⁴ -10 ⁷ IU/ml	<2,000 IU/ml ⁹⁰	>2,000 IU/ml
ALT	Normal	Elevated	Normal	Elevated*
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe
Old terminology	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis

EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection, 2017

CASO CLÍNICO

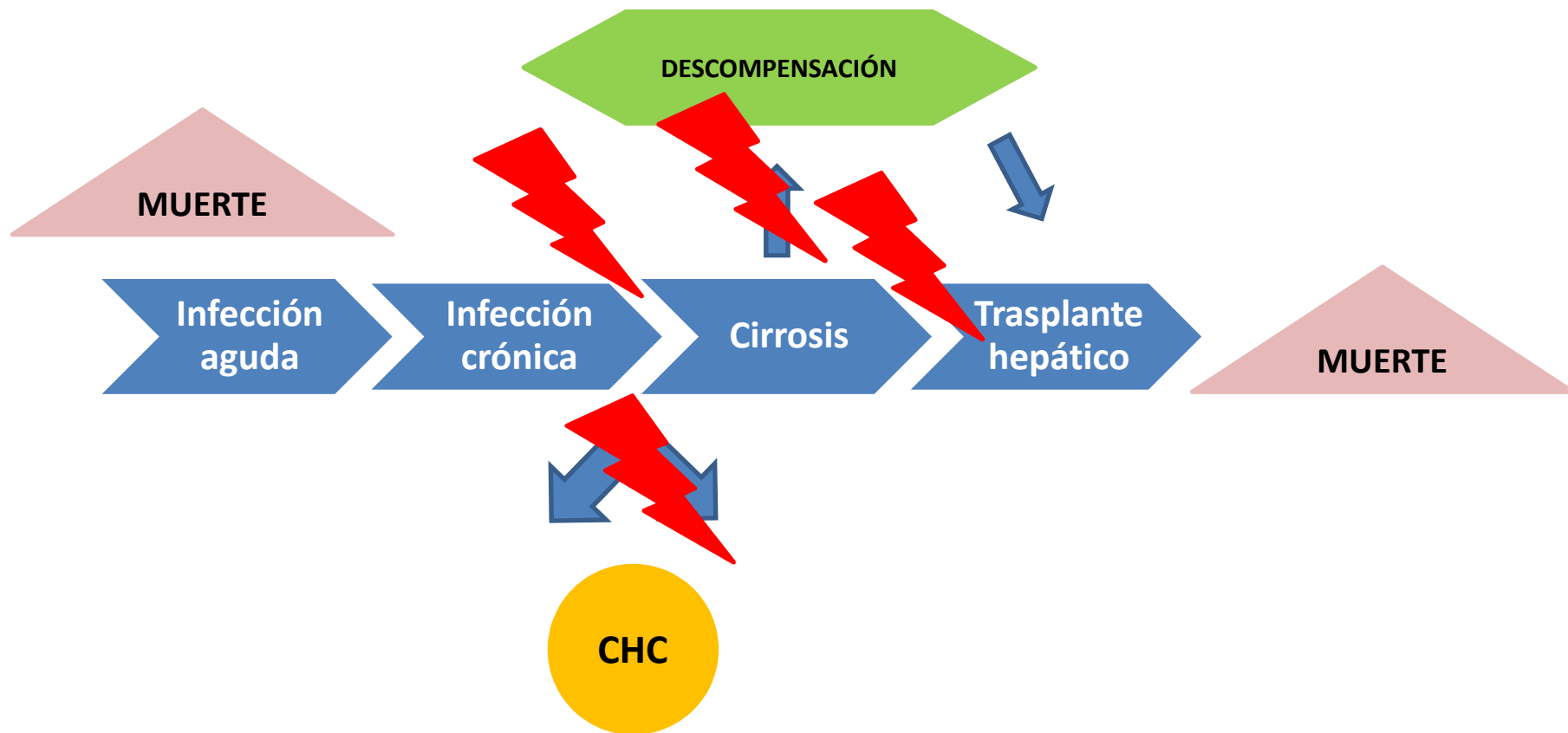
- HBsAg positivo (HBsAgc 15600 UI).
- ADN VHB basal: 2010 UI
- HBeAg negativo/AntiHBe positivo.
- Estudio etiológico negativo



OBJETIVOS DEL TRATAMIENTO

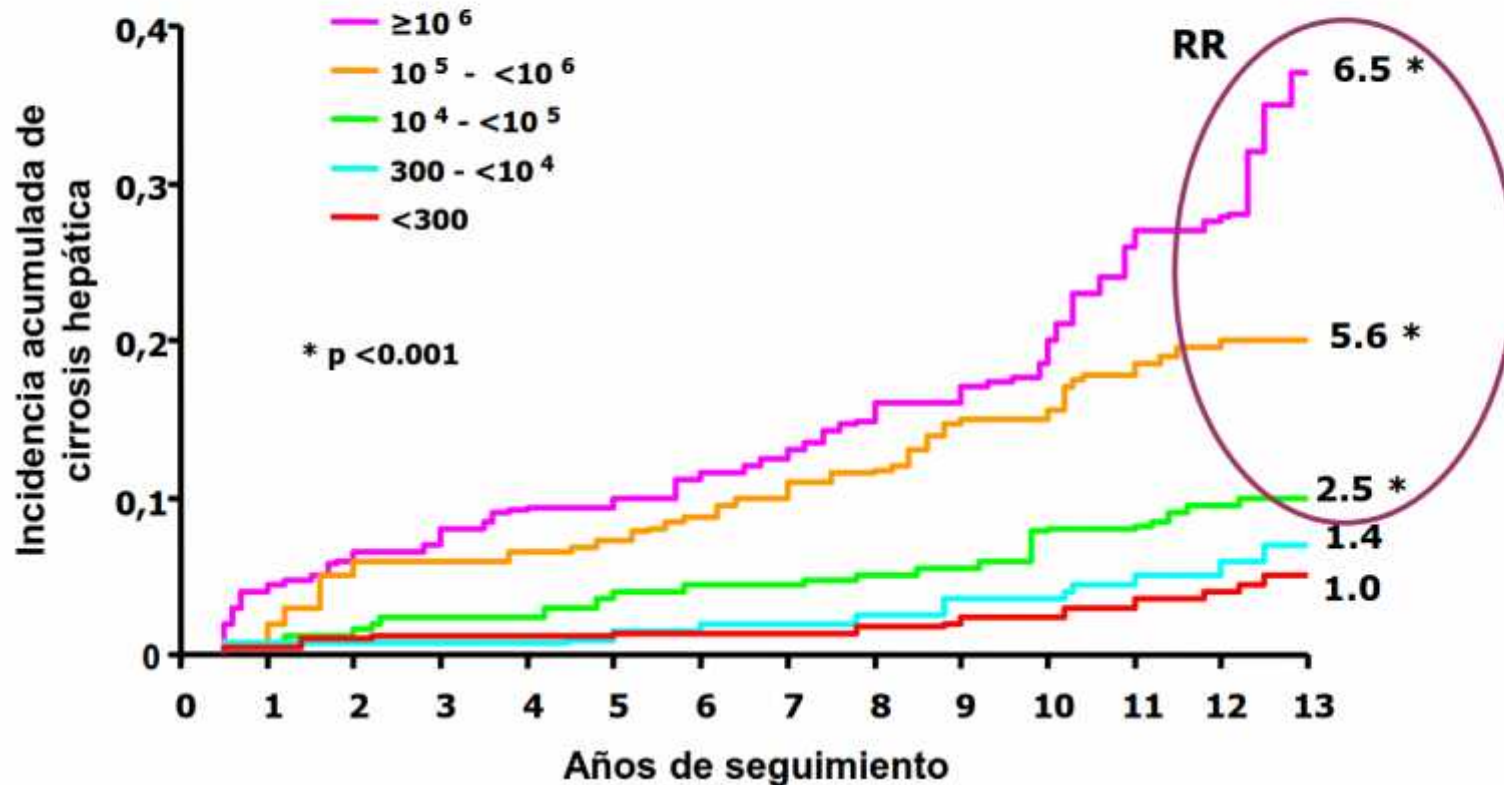
- The induction of long-term suppression of HBV DNA levels represents the main endpoint of all current treatment strategies (Evidence level I, grade of recommendation 1).
- The induction of HBeAg loss, with or without anti-HBe seroconversion, in HBeAg-positive CHB patients is a valuable endpoint, as it often represents a partial immune control of the chronic HBV infection (Evidence level II-1, grade of recommendation 1).
- A biochemical response defined as ALT normalisation should be considered as an additional endpoint, which is achieved in most patients with long-term suppression of HBV replication (Evidence level II-1, grade of recommendation 1).
- HBsAg loss, with or without anti-HBs seroconversion, is an optimal endpoint, as it indicates profound suppression of HBV replication and viral protein expression (Evidence level II-1, grade of recommendation 1).

HISTORIA NATURAL DE LA INFECCIÓN POR VHB

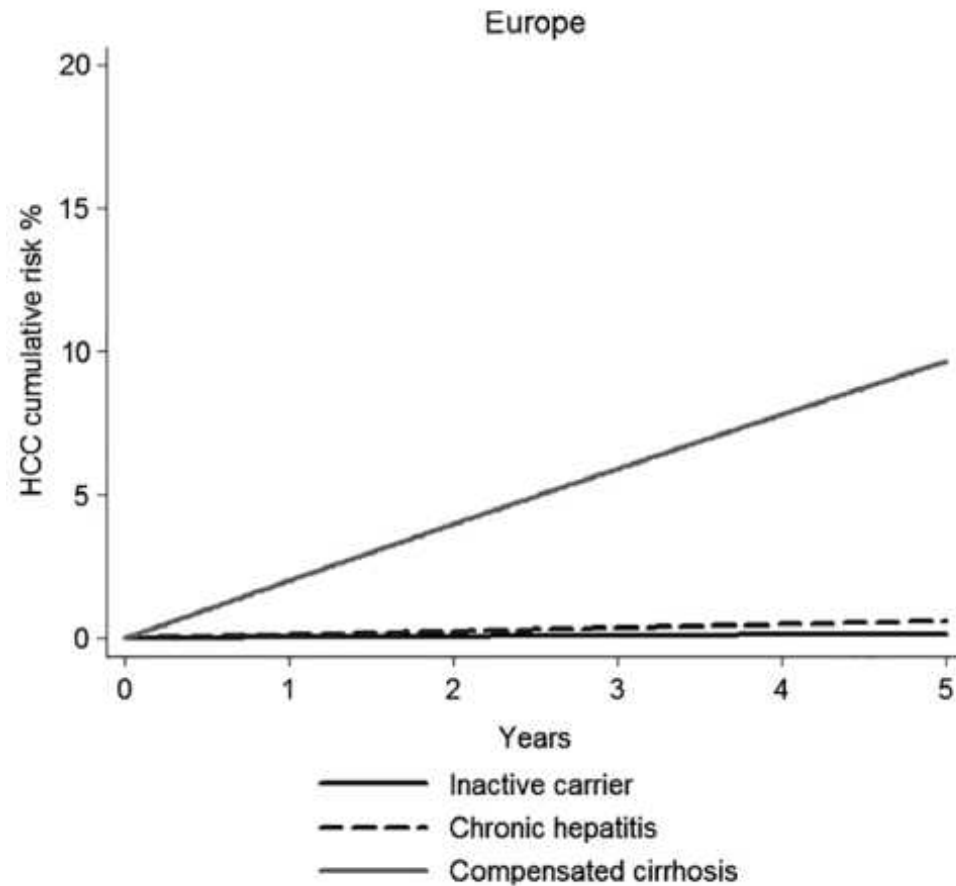


NIVEL DE ADN VHB Y CIRROSIS

Estudio REVEAL: 3.582 sujetos de Taiwan
85% HBeAg negativo 94% ALT normal (<45 U/L)
Seguimiento medio: 11 años sin tratamiento
Diagnóstico ecográfico de **cirrosis**



RIESGO ACUMULADO DE HEPATOCARCINOMA A LOS CINCO AÑOS



INDICACIONES DE TRATAMIENTO

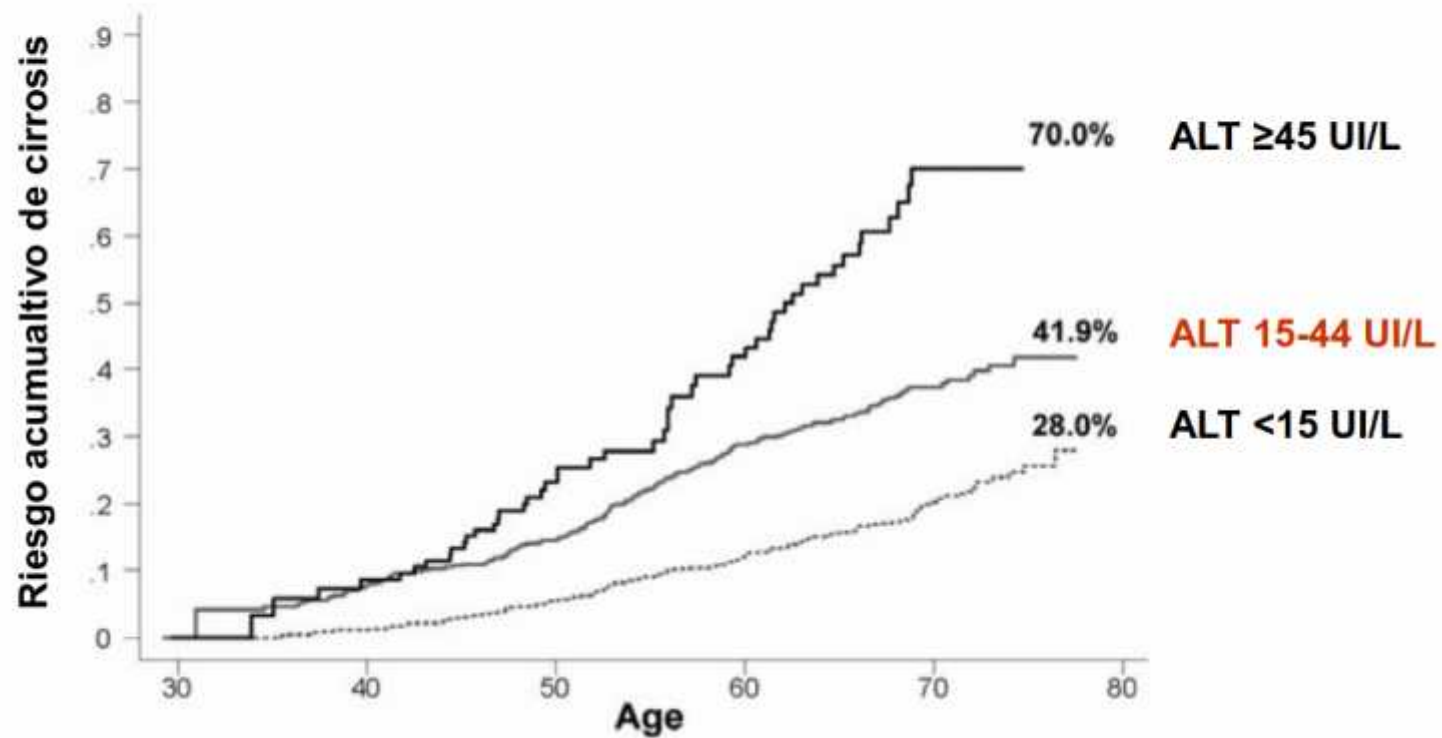
- All patients with HBeAg-positive or -negative chronic hepatitis B, defined by HBV DNA $>2,000$ IU/ml, ALT $>$ ULN and/or at least moderate liver necroinflammation or fibrosis, should be treated (Evidence level I, grade of recommendation 1).
- Patients with compensated or decompensated cirrhosis need treatment, with any detectable HBV DNA level and regardless of ALT levels (Evidence level I, grade of recommendation 1).
- Patients with HBV DNA $>20,000$ IU/ml and ALT >2 xULN should start treatment regardless of the degree of fibrosis (Evidence level II-2, grade of recommendation 1).
- Patients with HBeAg-positive chronic HBV infection, defined by persistently normal ALT and high HBV DNA levels, may be treated if they are older than 30 years regardless of the severity of liver histological lesions (Evidence level III, grade of recommendation 2).
- Patients with HBeAg-positive or HBeAg-negative chronic HBV infection and family history of HCC or cirrhosis and extrahepatic manifestations can be treated even if typical treatment indications are not fulfilled (Evidence level III, grade of recommendation 2).

ALT NORMAL EN VHB

Estudio REVEAL: 3.582 sujetos de Taiwan

85% HBeAg negativo

Seguimiento medio: 11 años sin tratamiento



ALT NORMAL EN VHB

Autor	Año	País	Población sana	ALT normal H (UI/L)	ALT normal M (UI/L)
Prati D	2002	Italia	3927	30	19
Ruhl E	2012	EE UU	3747	29	22
M´Kada H	2011	Francia	7463	31	22
Zheng MH	2012	China	13637	35	23
Park HN	2012	Corea	3337	34	25
Wu WC	2012	Taiwan	2894	21	17

Zheng MH PLOS One, 2012. Wu WC. APT, 2012. Park HN Liver Int, 2012. Ruhl E Hepatology, 2012. Prati D Ann Intern Med , 2002. M´Kada H Reg Toxicol Pharmacol, 2011

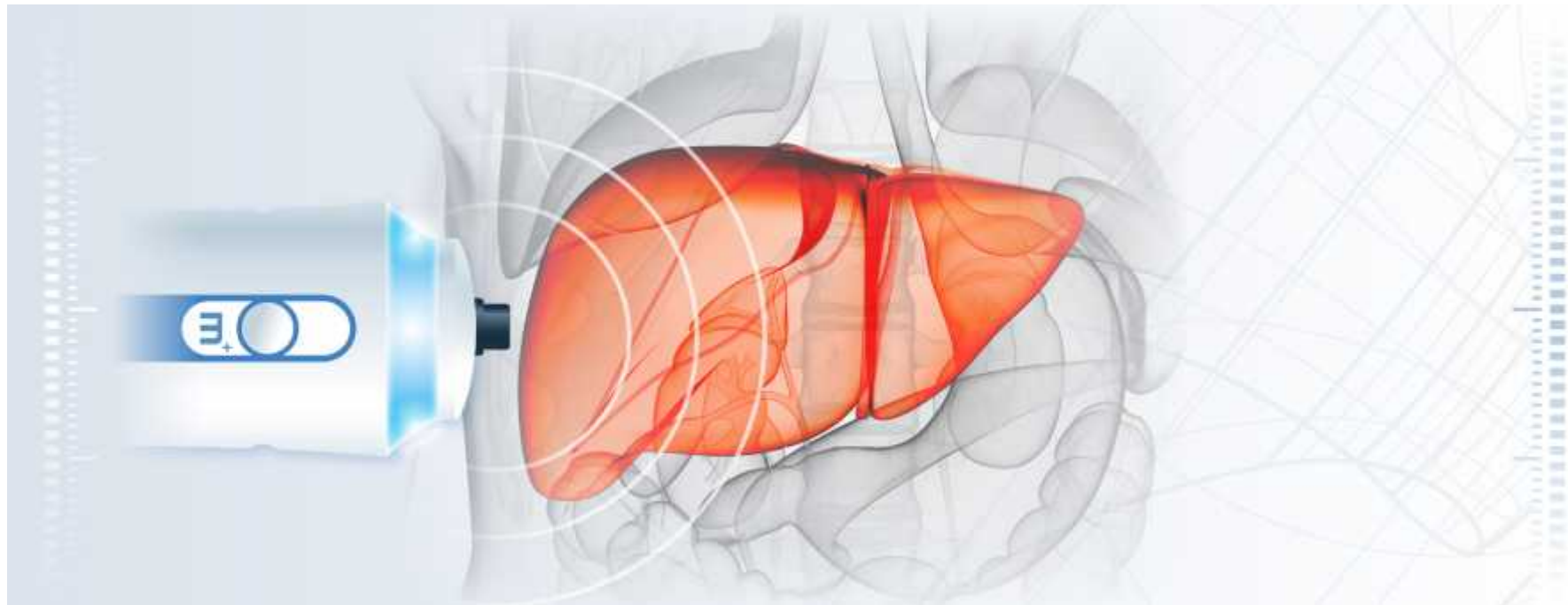
ALT NORMAL EN VHB

ALT NORMAL SEGÚN GUÍAS

- ✓ AEEH: no indica ningún valor
- ✓ AASLD: 30 UI/L (H) y 19 UI/L (M)
 - ✓ EASL: \approx 40 UI/L

CASO CLÍNICO

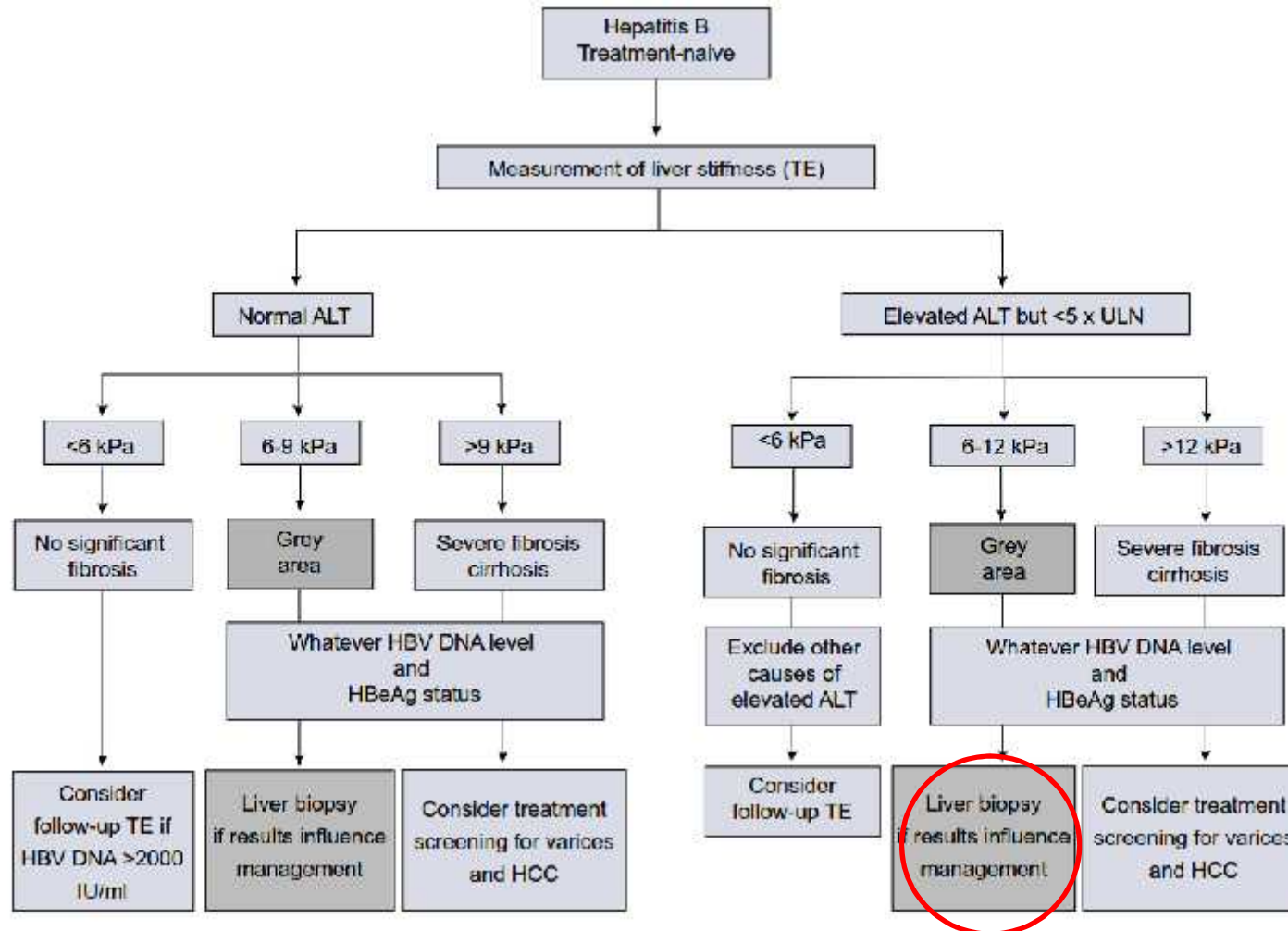
- Elastometría transitoria: 7,2 KPa



ELASTOMETRÍA TRANSITORIA EN VHB

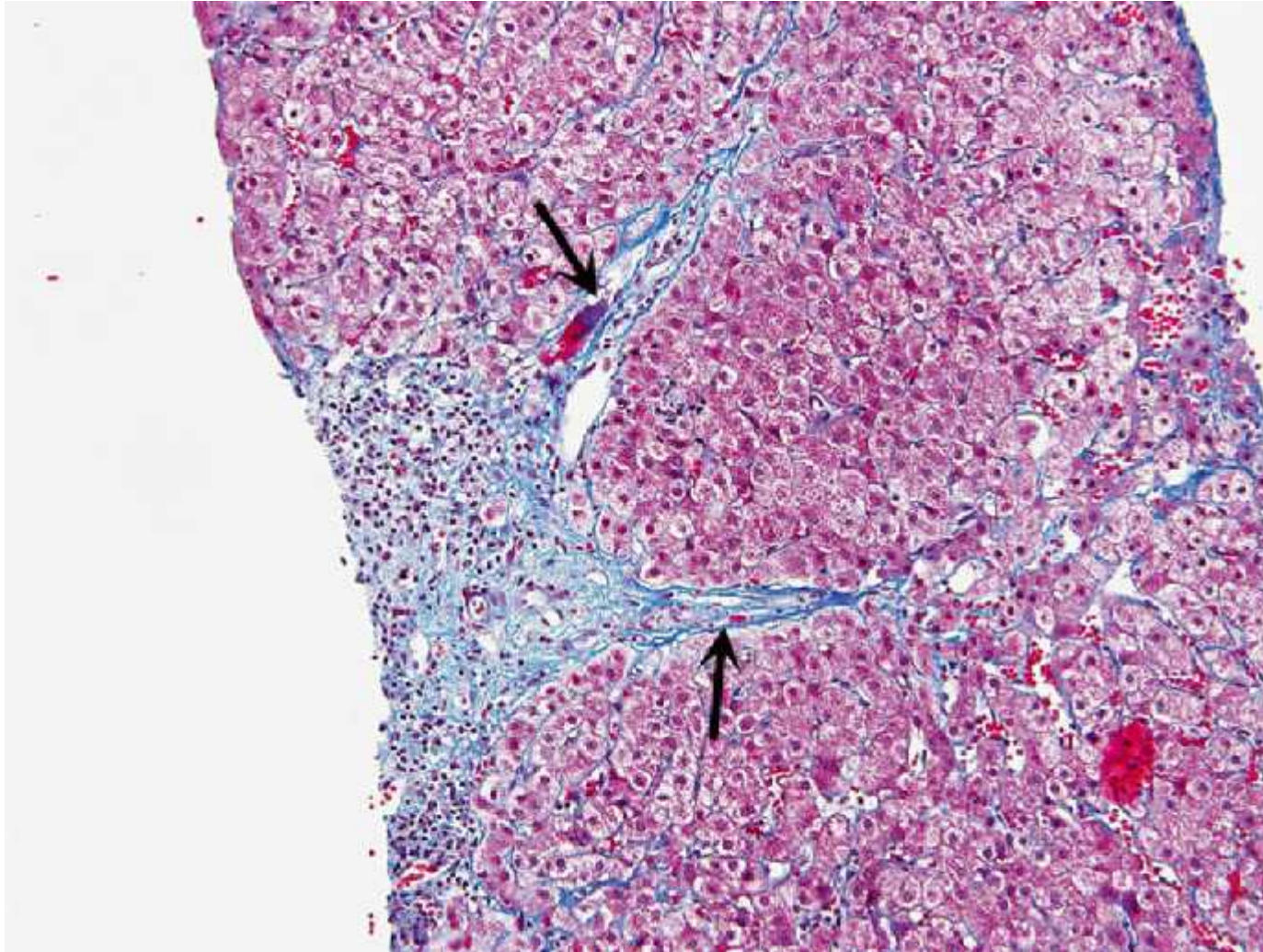
- TE has better prediction for advanced liver fibrosis and cirrhosis than serum biomarkers in chronic hepatitis B **(B1)**
- TE is best used to determine liver fibrosis in hepatitis B patients with active viraemia (HBV DNA >2000 IU/ml) but normal ALT **(A1)**
- TE can be used to exclude severe fibrosis and cirrhosis in inactive carriers (HBeAg-negative, low viral load (HBV DNA <2000 IU/ml) and normal ALT). Liver biopsy should only be considered in doubtful cases after TE **(A1)**
- LS measurement should be interpreted with caution among patients with elevated ALT, and should not be used in patients with very high ALT levels (>10 x ULN) **(A1)**

ELASTOMETRÍA TRANSITORIA EN VHB



EASL- ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis, 2015

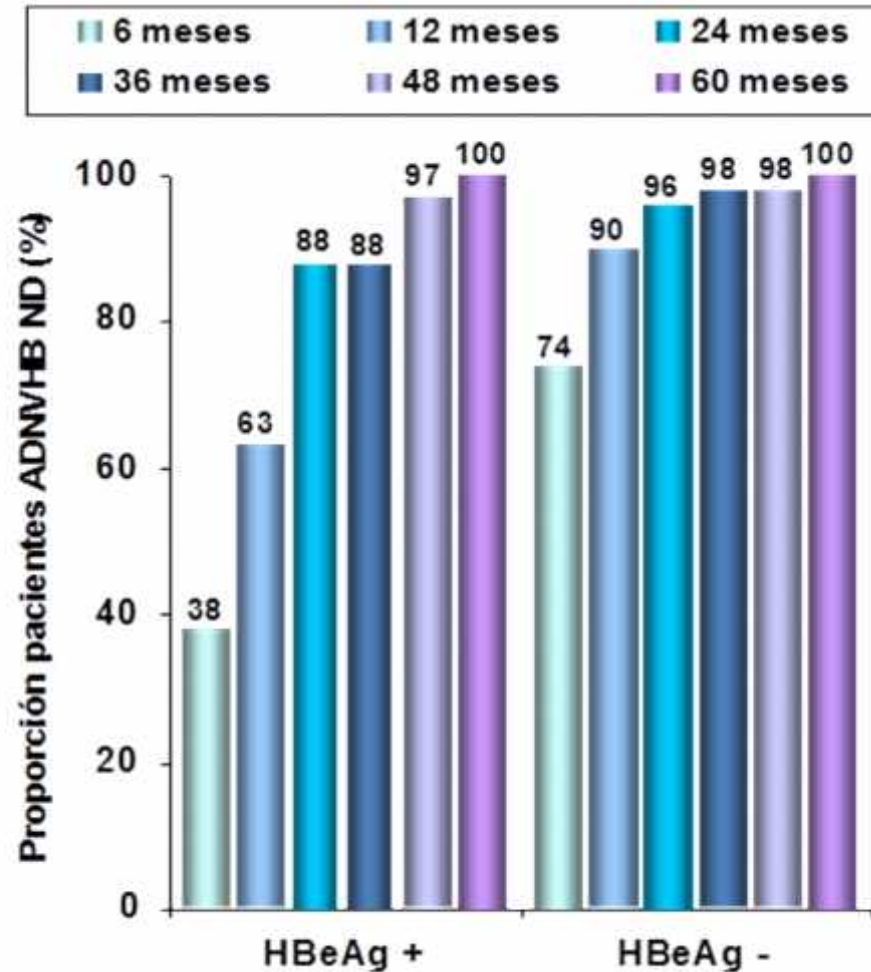
CASO CLÍNICO: BIOPSIA HEPÁTICA



INDICACIONES DE TRATAMIENTO

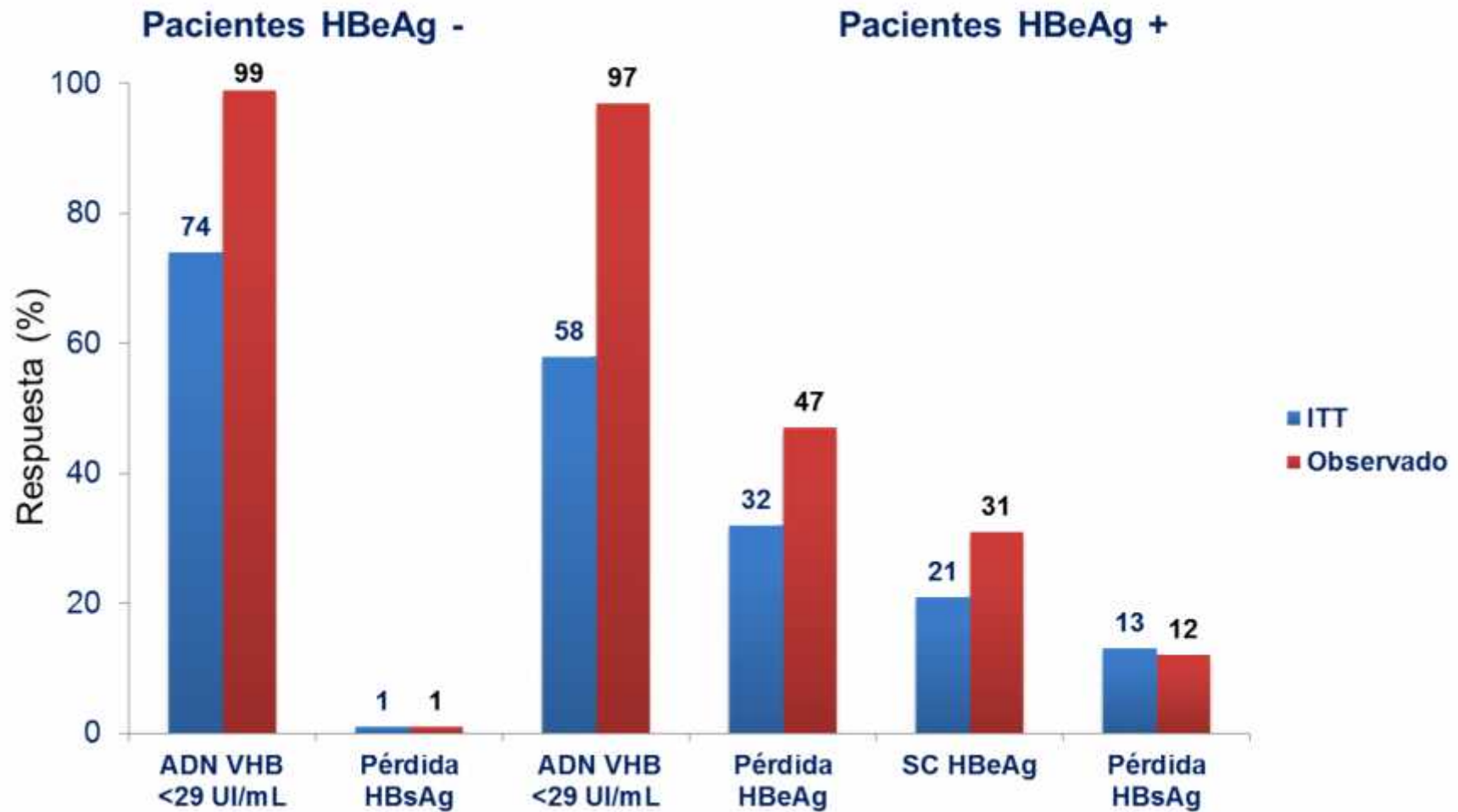
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EFICACIA DE ENTECAVIR (ETV) EN HEPATITIS B



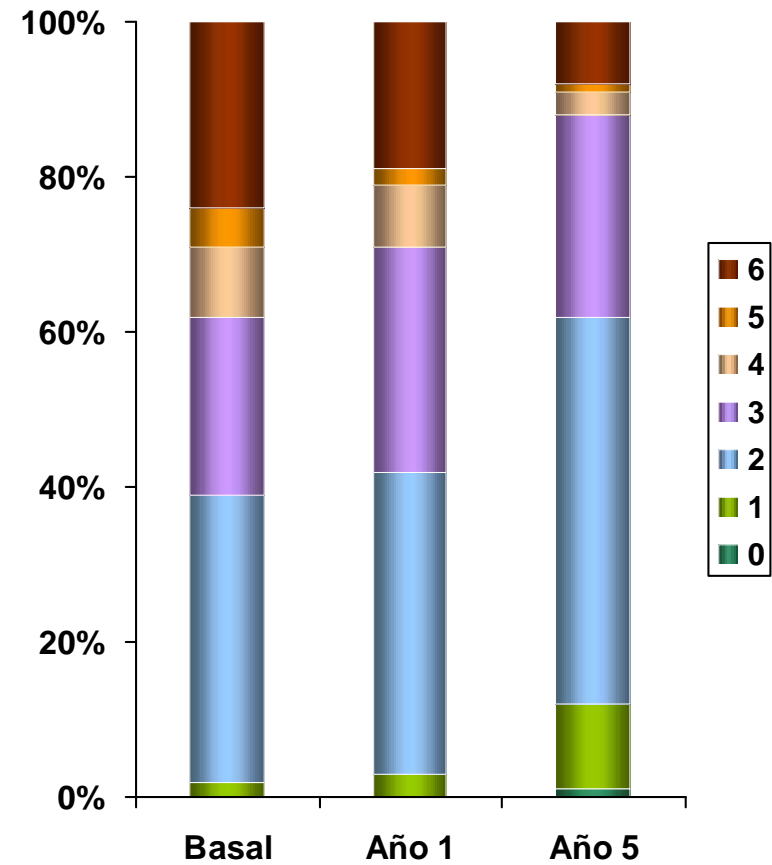
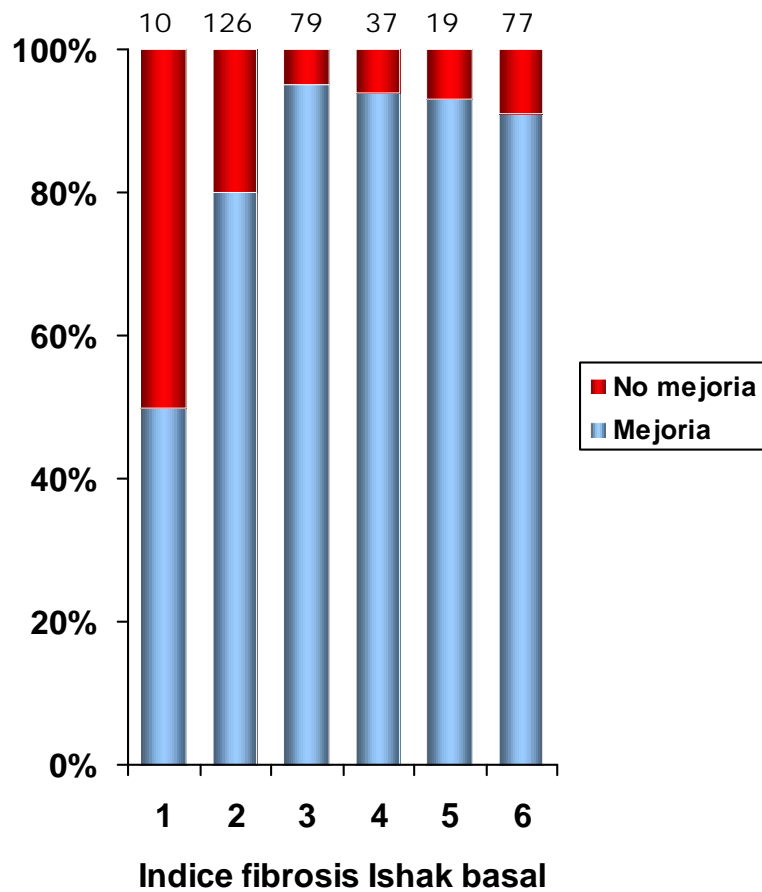
EFICACIA DE TENOFOVIR DF (TDF) EN HEPATITIS B

Seguimiento de **8 años** en dos ensayos randomizados



Marcellin P. Hepatology, 2014 (A)

RESPUESTA HISTOLÓGICA TDF 5 AÑOS



Marcellin P. Lancet, 2013

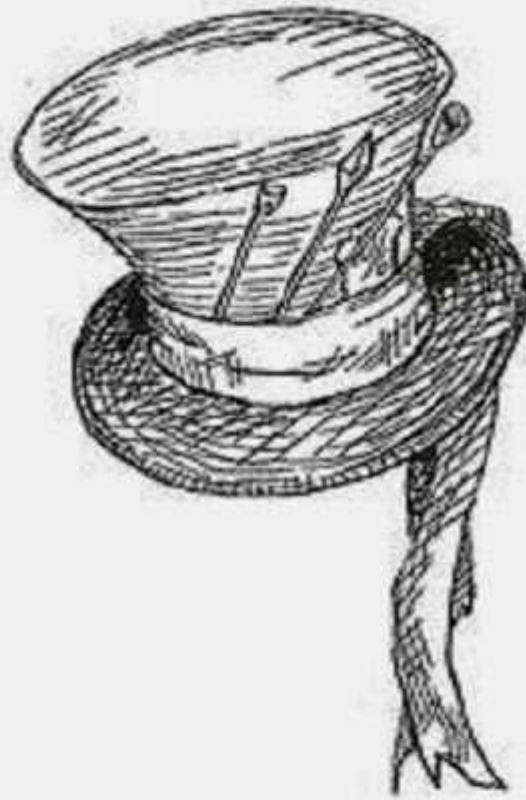
CASO CLÍNICO

- Mujer edad fértil: Tenofovir
- Elastometría a los tres años: 6,5 Kpa.
- No pérdida de HBsAg en esta fecha.



RESUMEN

- Evaluación correcta inicial.
- Importancia de los niveles de ADN VHB.
- Concepto de ALT normal.
- Evaluación no invasiva de la fibrosis.
- Indicaciones de la biopsia hepática.
- Objetivos de tratamiento.
- Respuesta al tratamiento.



"Comienza por el comienzo, y cuando termines de hablar... Te callas."