B.S. Female of Italian origin, born in 1956

Family History:

- HBV infection (husband and daughter inactive HBV carriers)

HBV Infection Profile:

1976 Evidence of HBsAg/HBeAg positivity

1992 Spontaneous HBeAg to anti-HBe seroconversion, persistence of active infection with evidence of liver disease

Virological profile

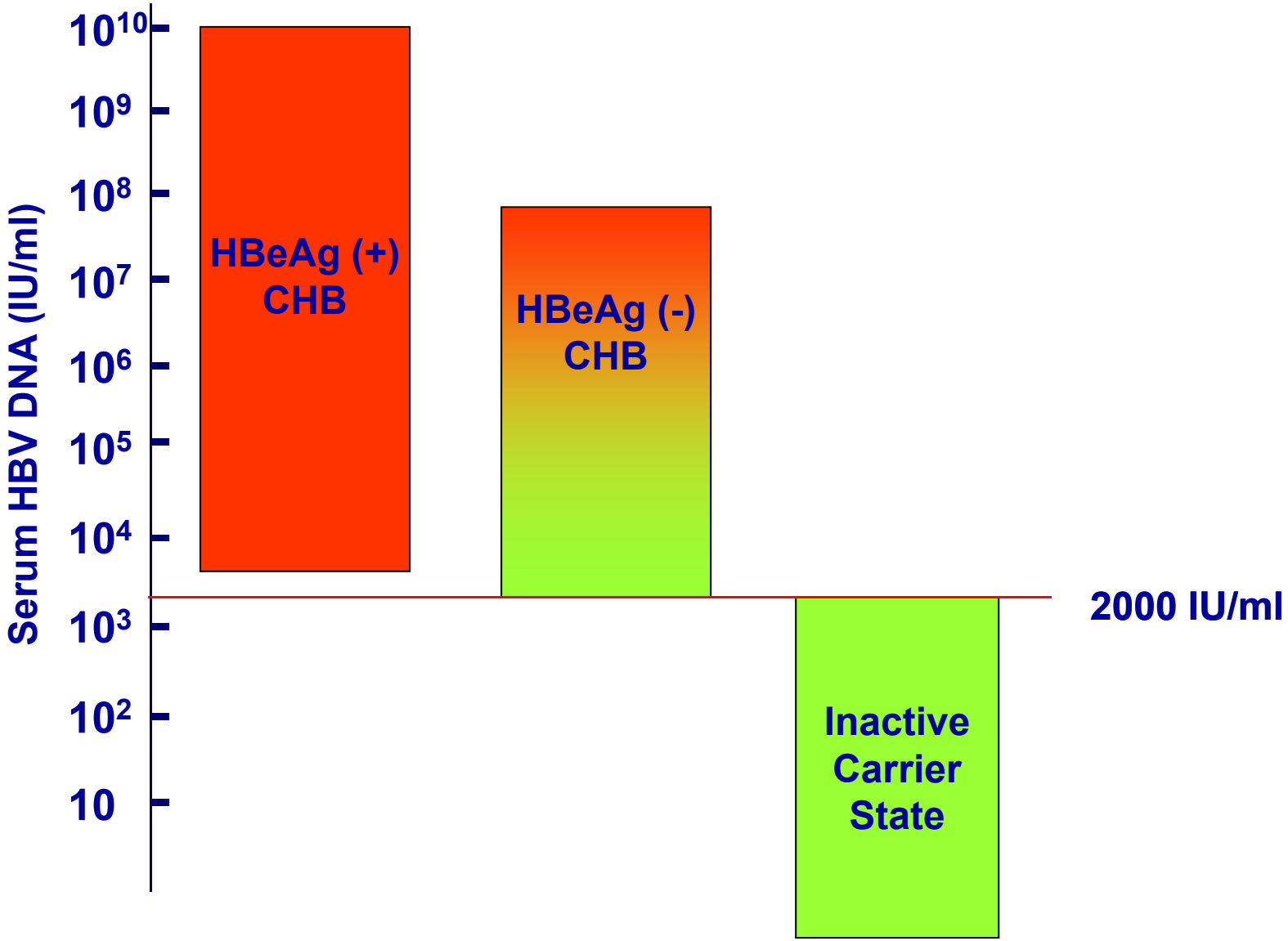
Genotype	D
BCP/pre-core region	A1762 G1764A G1896A G1899A
HBV-DNA	10^5 -10^6 IU/ml (100000-5000000 IU/ml)

IgM anti-HBc	0.16-0.28 IMx Index
HBeAg / anti-HBe	Neg. / Pos.
HBsAg	3157 IU/ml
anti-HDV	Negative
Anti-HCV	Negative

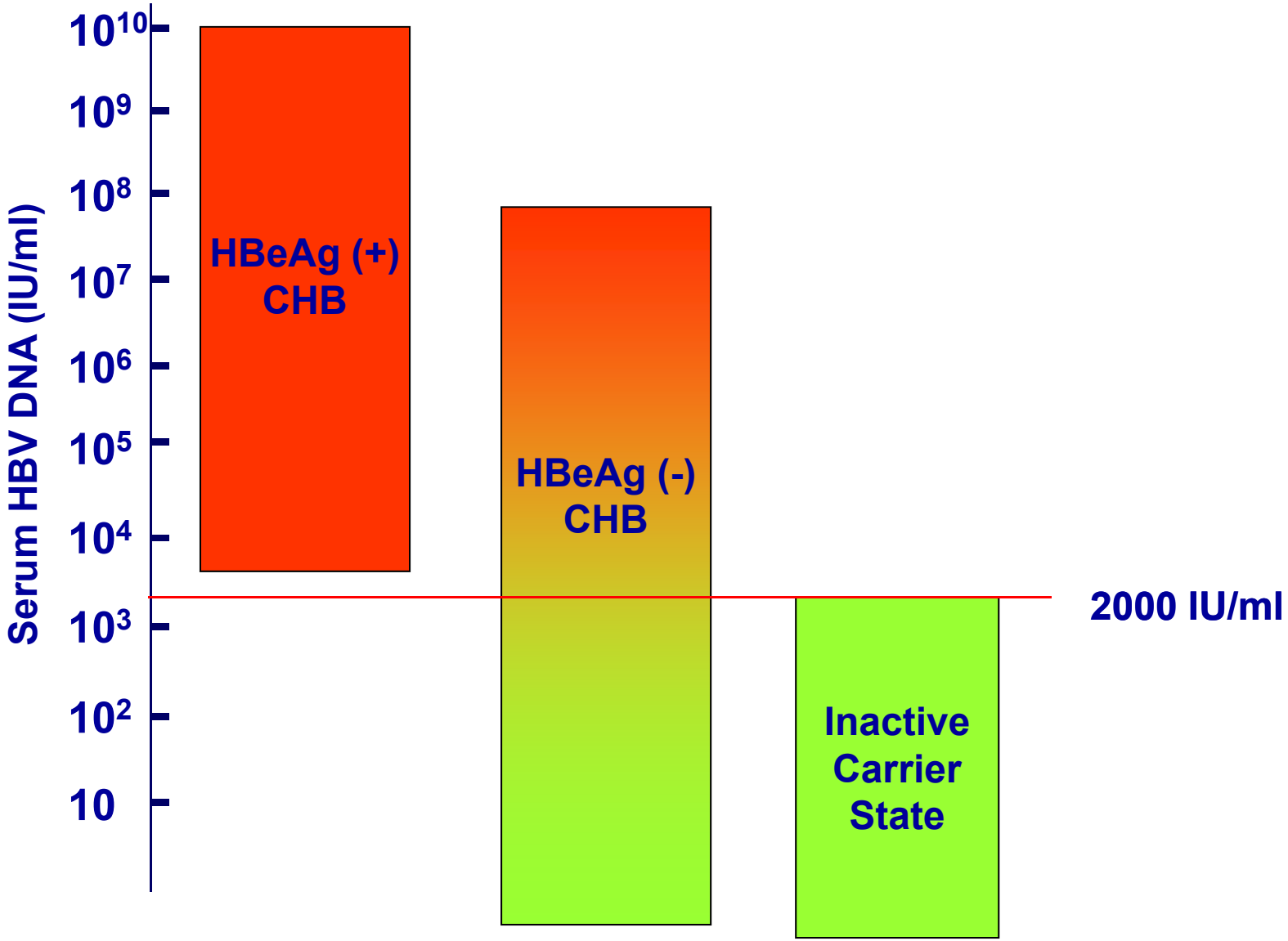
Biochemical profile

ALT persistently elevated (median 83 IU/ml, range 70-200 IU/ml), without flares

Serum HBV DNA levels in HBV carriers



Serum HBV DNA levels in HBV carriers



Identification of the HBsAg\anti-HBe carrier with inactive HBV infection:

Major pitfalls

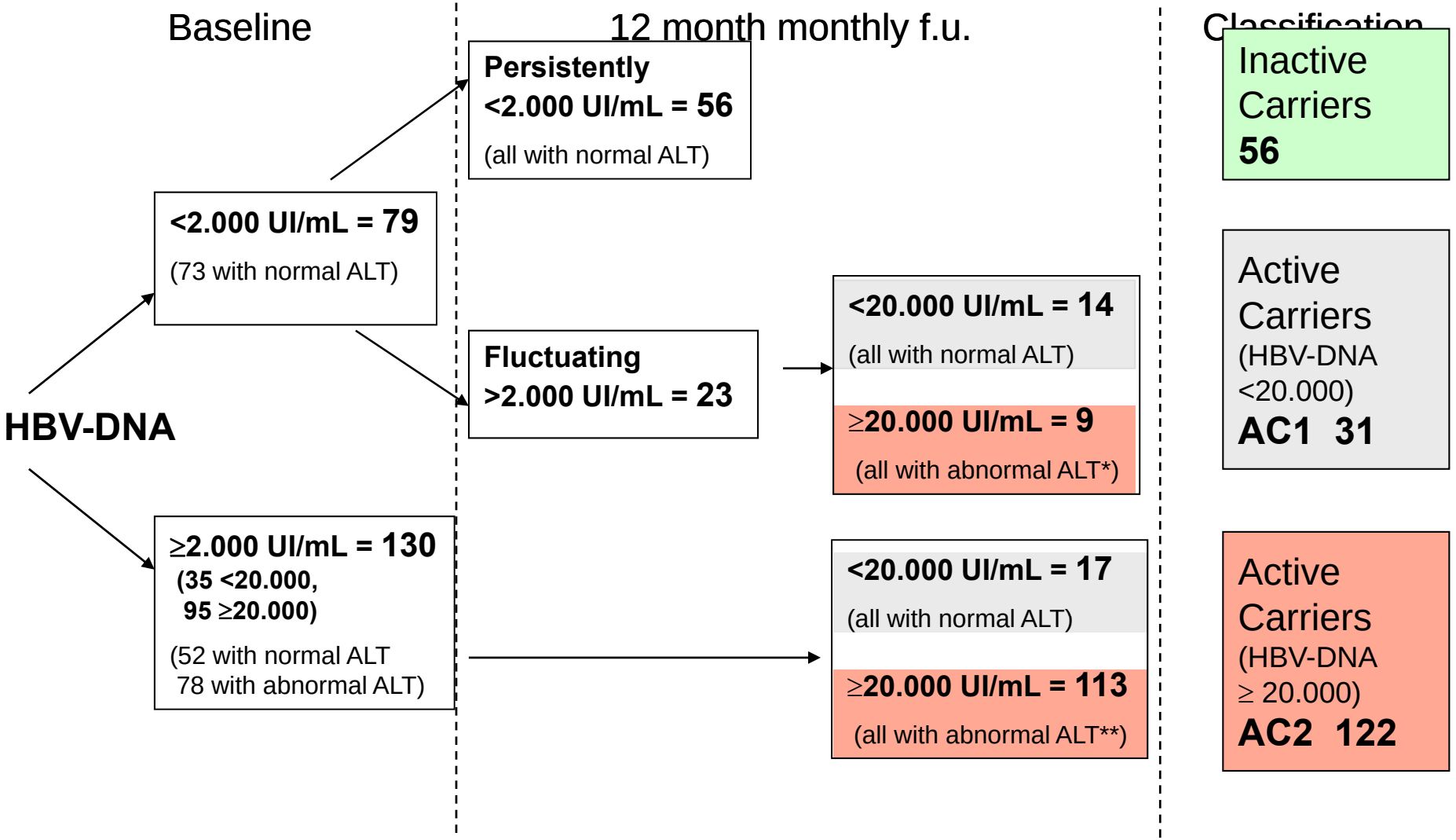
- viral replication and liver disease may have an intermittent pattern

Thus, HBV-DNA levels < 2000 IU/ml and normal ALT at single time point in a HBsAg anti-HBe pos carrier can not exclude the presence of asymptomatic CHB

- liver damage in a HBV carrier may be due to factors different from the virus

Thus, the presence of abnormal ALT in a HBsAg anti-HBe pos carrier with HBV-DNA levels persistently < 2000 IU/ml does not exclude the presence of inactive HBV infection

HBV-DNA and ALT profiles in 209 HBeAg negative/anti-HBe positive genotype D HBV carriers



*Occasionally normal ALT in 3; ** occasionally normal ALT in 17

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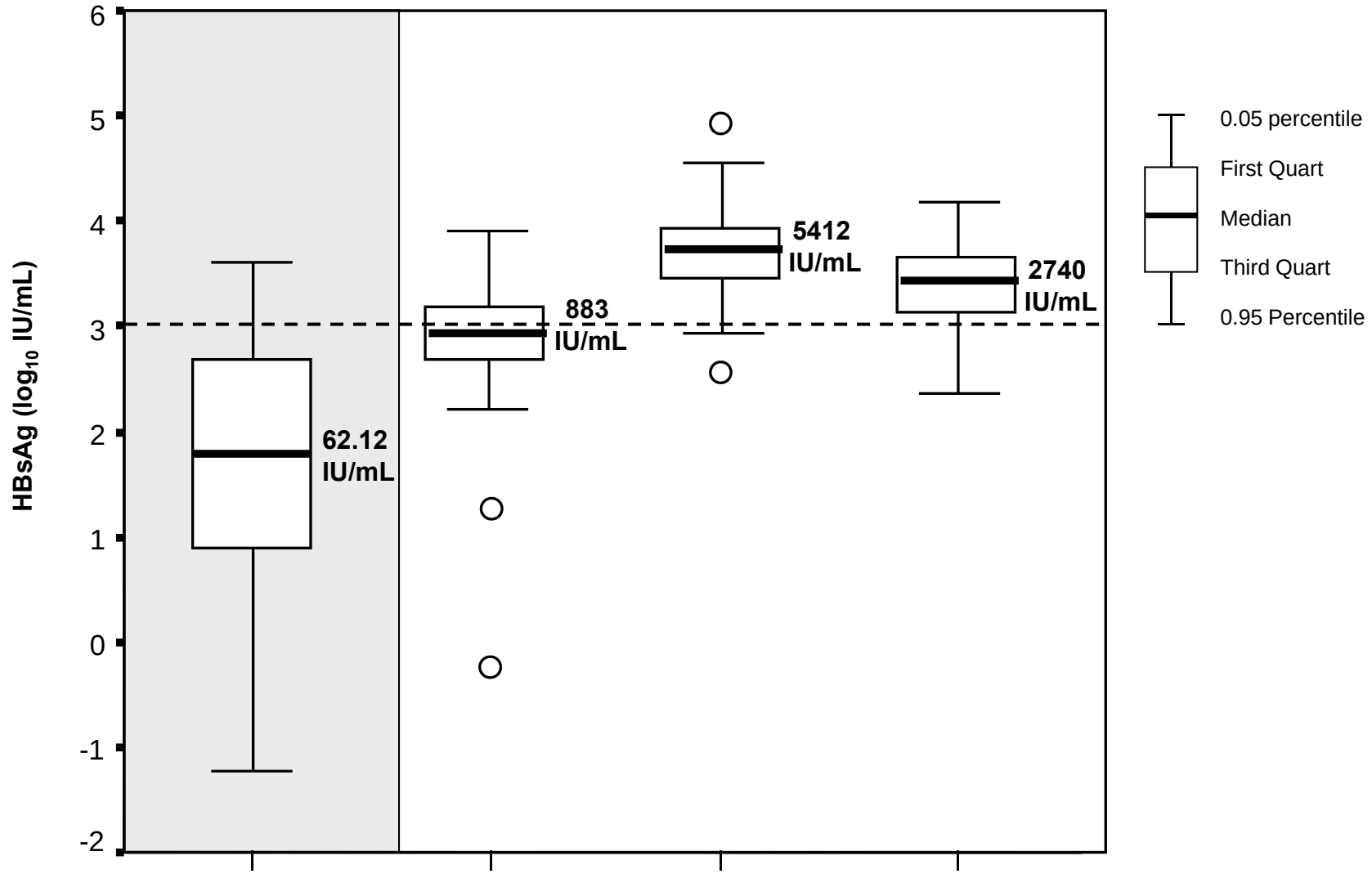

N. of subjects:	**56**	**31**	**84**	**38**
HBV-DNA (IU/mL):	**≤2,000**	**>2,000 & <20,000**	**≥20,000**	**≥20,000**
Liver disease:	**Absent**	**Absent**	**Chr. Hep.**	**Cirrhosis**
Carriers:	**IC**	**AC1**	**AC2**	**AC2**

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Prediction of HBV infection phase by HBsAg and HBV-DNA serum levels

Prediction of:	**Inactive infection**
HBsAg levels ***HBV-DNA levels***	***<1000 UI/mL plus*** ***<2000 IUI/mL***
Population	**209**
Sensitivity	**91.1%**
Specificity	**95.4%**
PPV	**87.9%**
NPV	**96.7%**
Diagnostic Accuracy	**94.5%**

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Histology:

1° liver biopsy (1999): Chronic Active Hepatitis, with minimal fibrosis

2° liver biopsy (2005): Chronic Active Hepatitis
grading 8/18 staging 2/6 (Ishak)

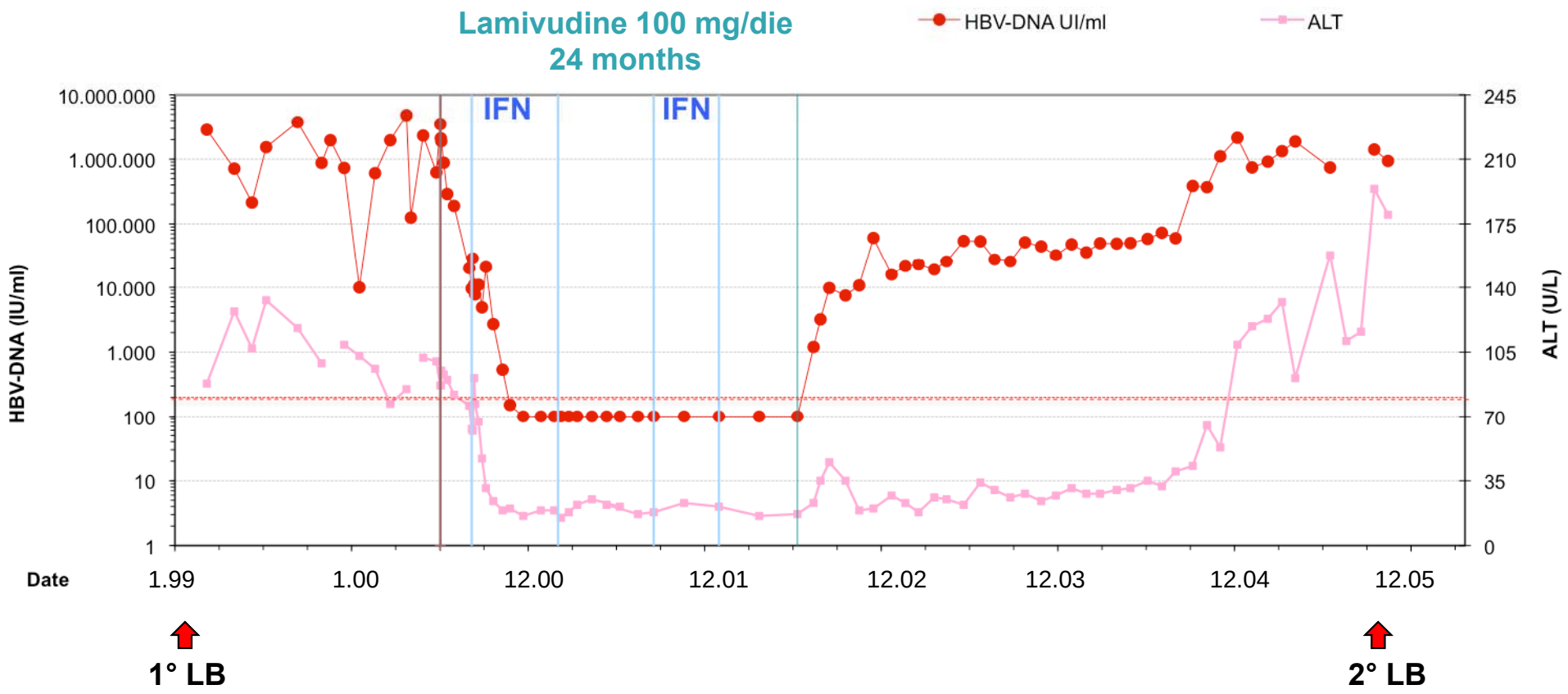
Treatments:

1988	alpha IFN 3 MU thrice w for 6 months *(biochemical response, relapse)*
1997	alpha-IFN 9 MU thrice w for 12 months *(biochemical response, relapse)*
2000	LMV 100 mg/die for 2 months, LMV+ IFN alpha 2a 6 MU every other day for 6 months

III antiviral treatment (2000-2001)

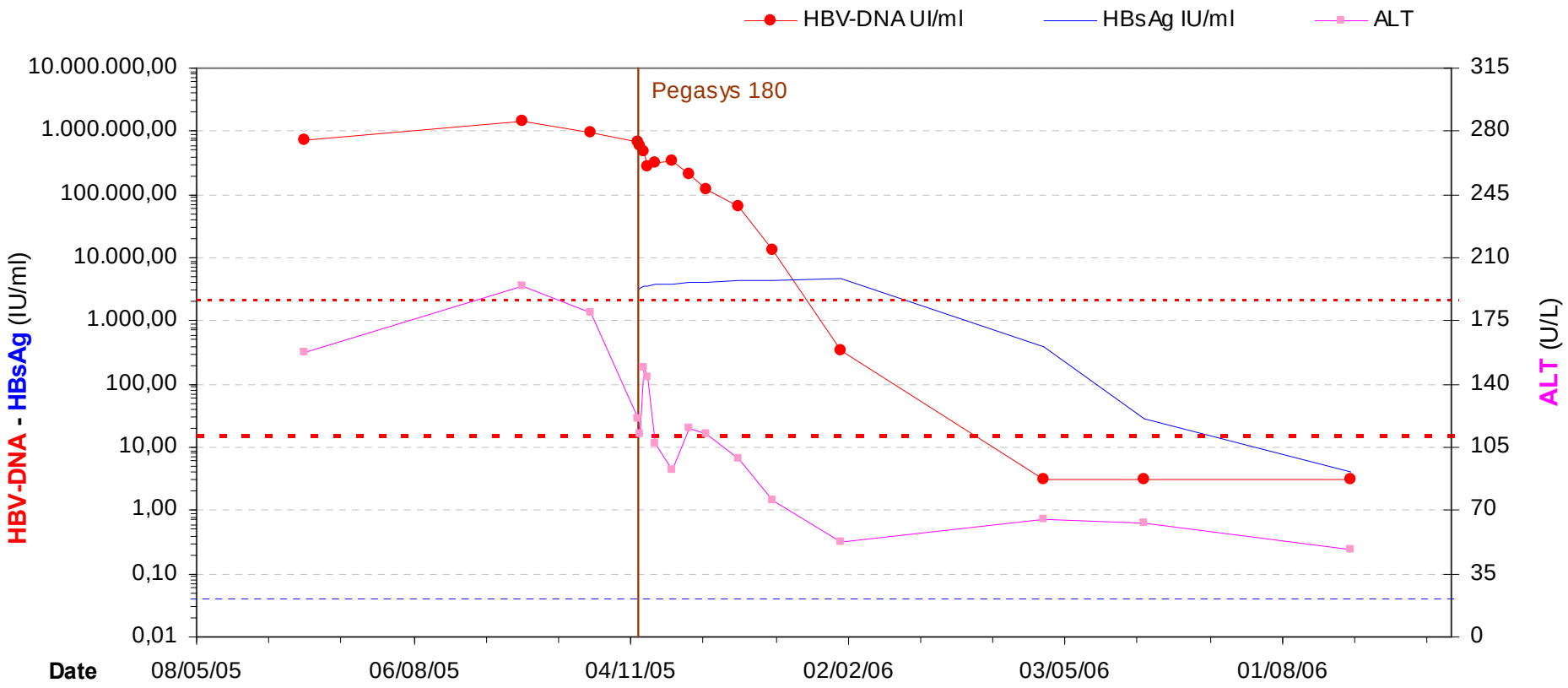
Original treatment schedule: IFN + LMV for 12-18 months

Co-morbidities: major uterine bleedings, that required hysterectomy



IV antiviral treatment (1° year)

Treatment schedule: Peg-IFN 2a 180 ug/w -12 months, Peg-IFN 2a 135 ug/w -12 m.



On treatment kinetics of HBsAg serum levels in HBeAg negative CHB to predict SVR

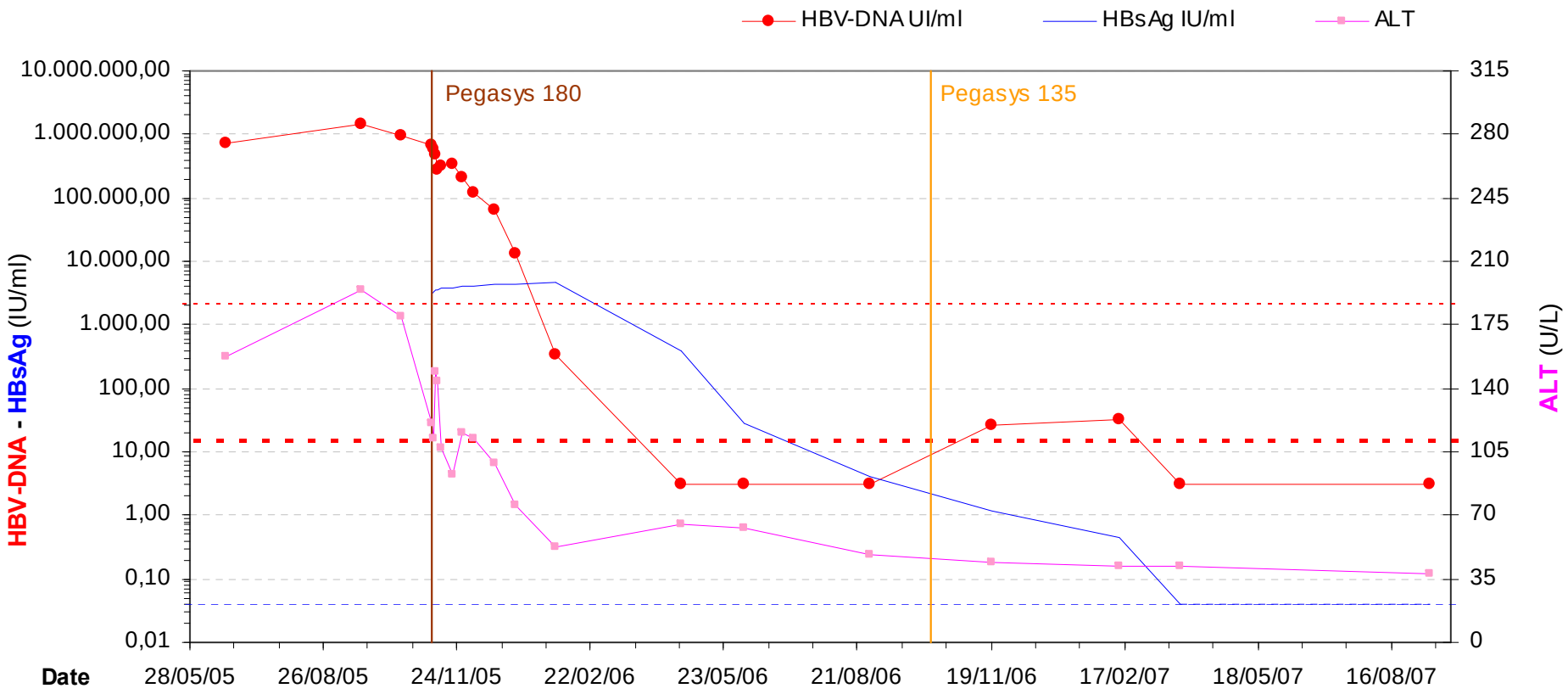
		SVR	PPV
Week 12 ↓ HBsAg ≥ 0.5 Log IU/mL	9 pts	8	89%
Week 24 ↓ HBsAg ≥ 1 Log IU/mL	12 pts	11	92%

		no SVR	NPV
Week 12 ↓ HBsAg < 0.5 Log IU/mL	39 pts	35	90%
Week 24 ↓ HBsAg < 1 Log IU/mL	36 pts	35	97%

Moucari *et al*. Hepatology 2009

IV antiviral treatment (2° year)

Treatment schedule: Peg-IFN 2a 180 ug/w -12 months, Peg-IFN 2a 135 ug/w -12 m.



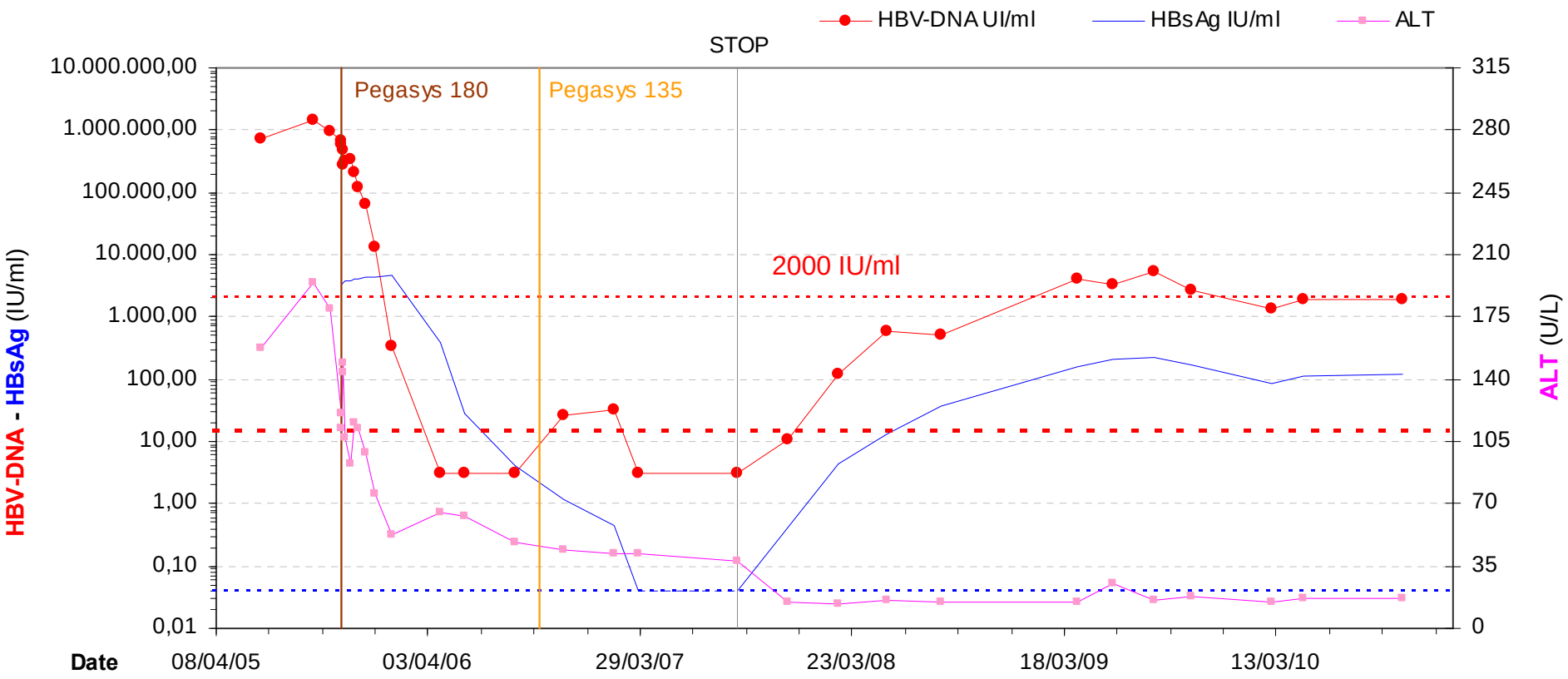
Identification of predictors of HBsAg clearance 3 years post-treatment by logistic regression analysis

	OR*	95% CI value	P value
Age	1.09	0.99–1.20	ns
PEG vs PEG + LAM	0.38	0.06–2.53	ns
BL ALT	1.00	0.99–1.01	ns
BL log HBV DNA	1.10	0.66–1.85	ns
Wk 48 log HBV DNA	1.58	0.37 –6.77	ns
Wk 48 log HBsAg	0.12	0.04–0.37	0.0002
Change in log HBsAg from BL to wk 48	0.22	0.10– 0.50	0.0003

For n=65 (n=64) patients with available data and HBsAg loss at 3 years post-treatment

IV antiviral treatment and post-treatment follow-up

Treatment schedule: Peg-IFN 2a 180 ug/w -12 months, Peg-IFN 2a 135 ug/w -12 m.



End of treatment response:

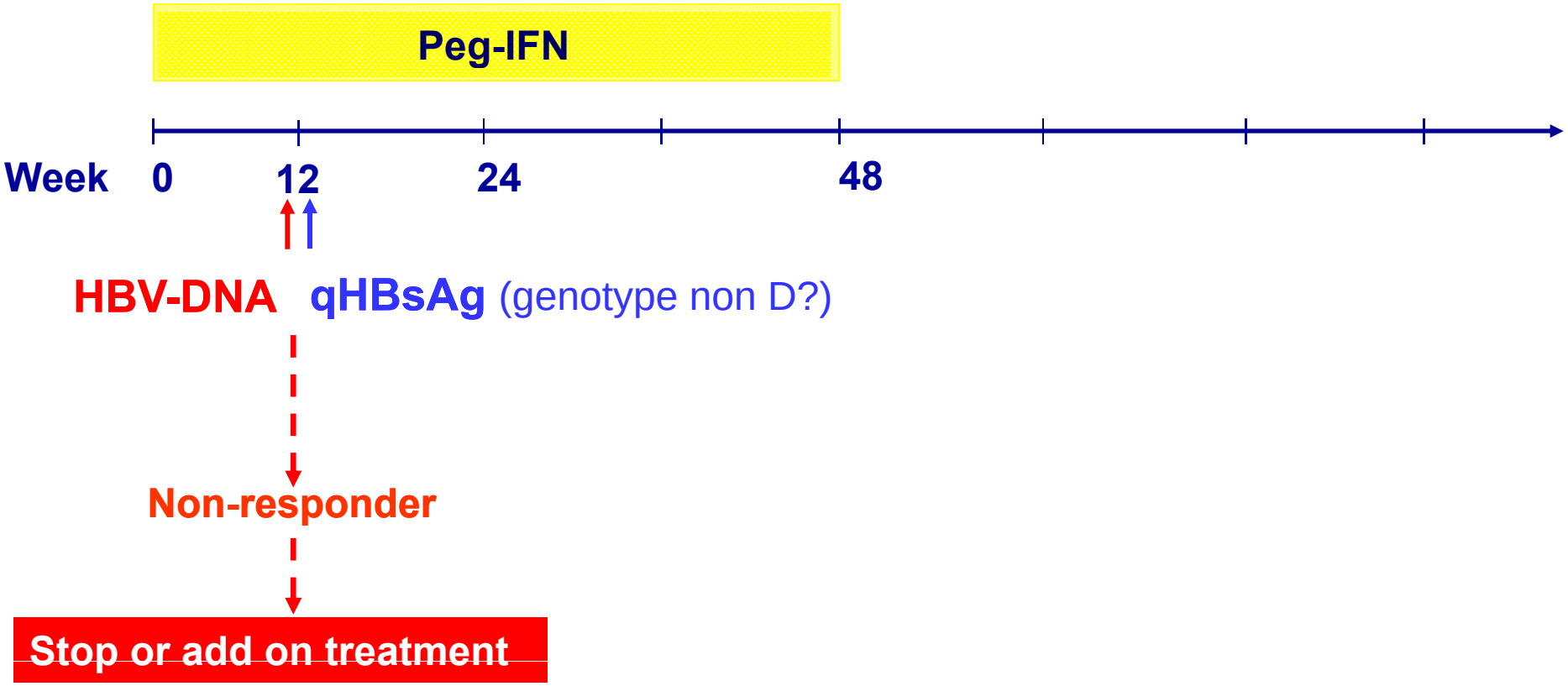
- undetectable HBV-DNA
- HBsAg clearance

Post treatment relapse:

- viremia recurrence, but HBV-DNA levels persistently < 5000 IU/ml
- HBsAg reversion, but levels persistently < 230 IU/ml

In the last 12 months: Inactive Carrier profile
(viremia persistently< 2000 IU/ml, HBsAg persistently < 150 IU/ml)

Future perspective: how to optimise patient management?



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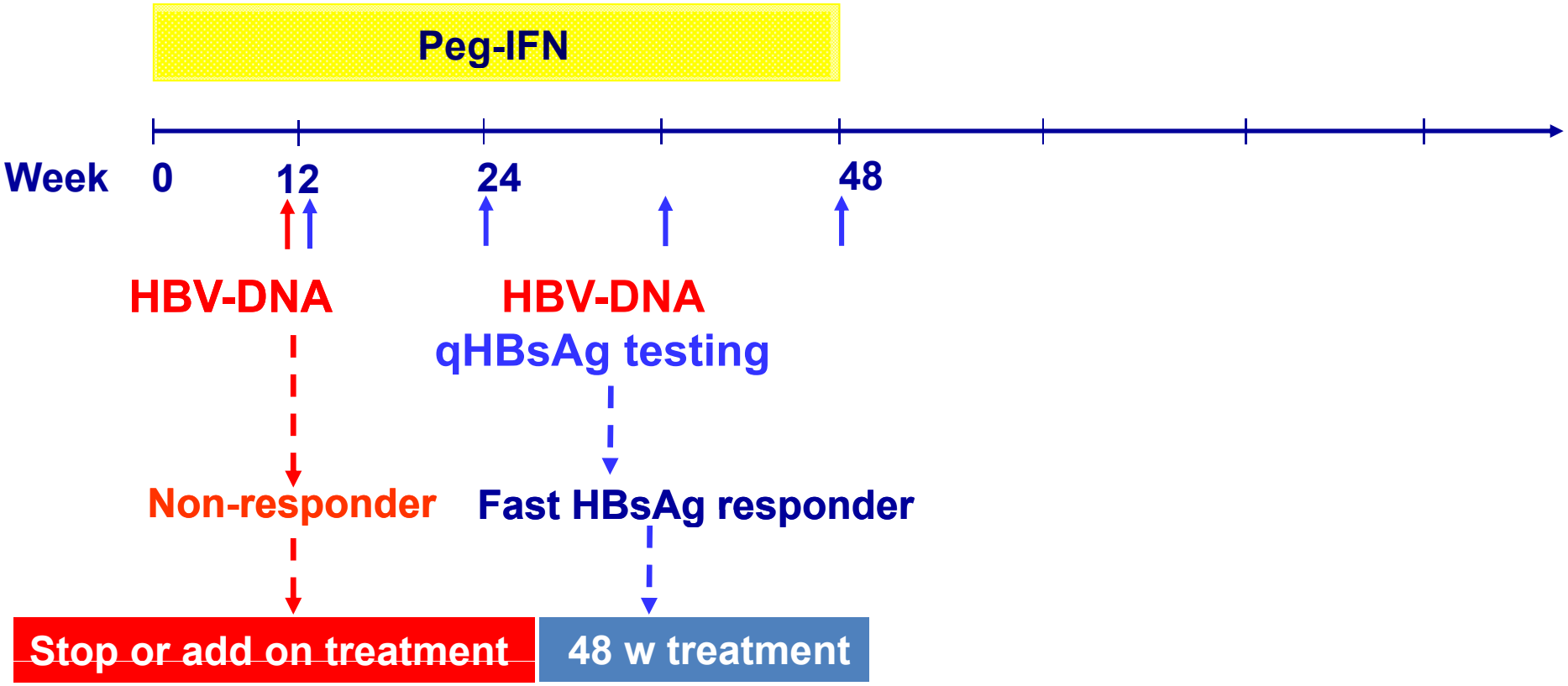
Future perspective: how to optimise patient management?



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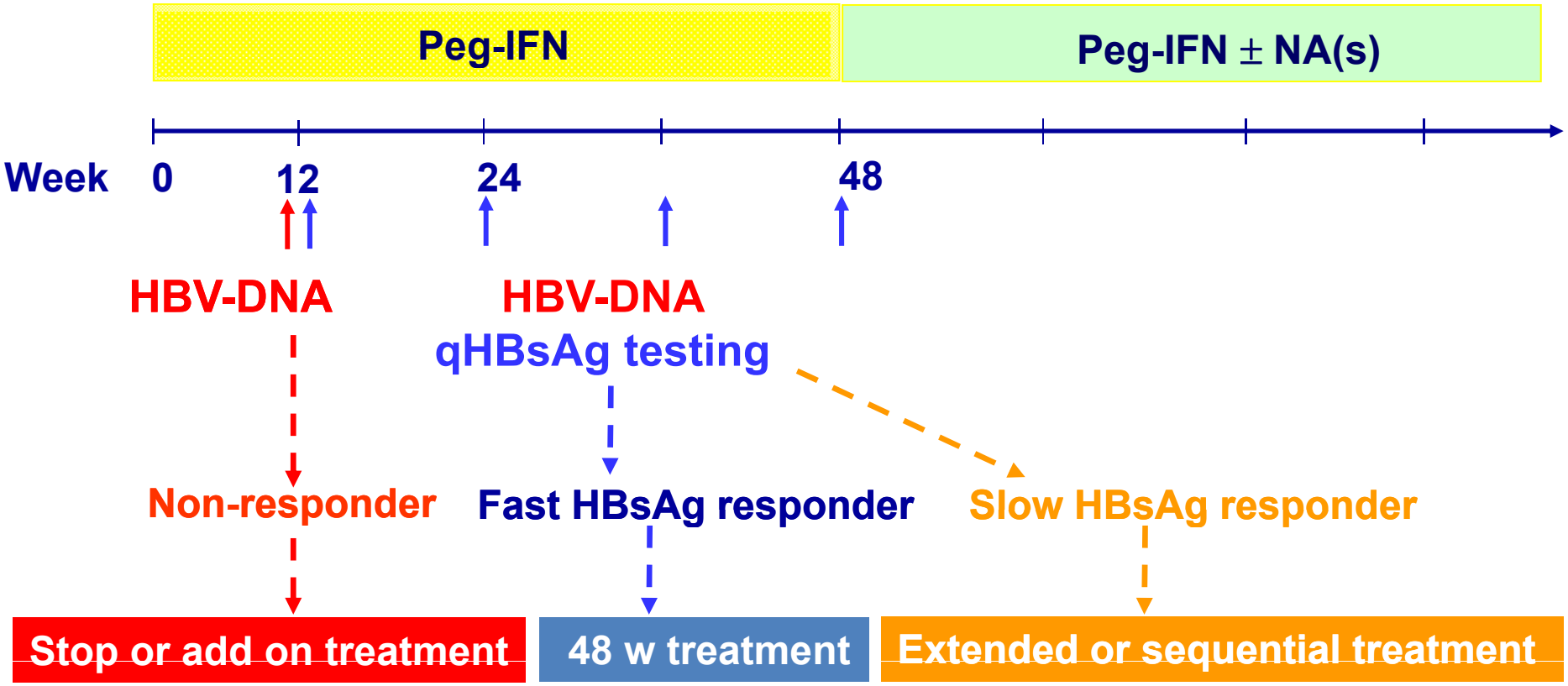
Future perspective: how to optimise patient management?



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