

First line therapy: interferon or analogues?

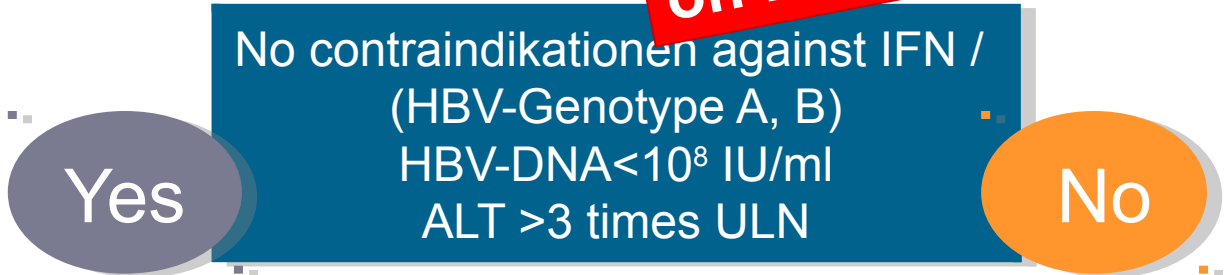
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When IFN?

**reality in Germany 2014:
>90% of tx patients are
on NUCs, <10% PEG-IFN**

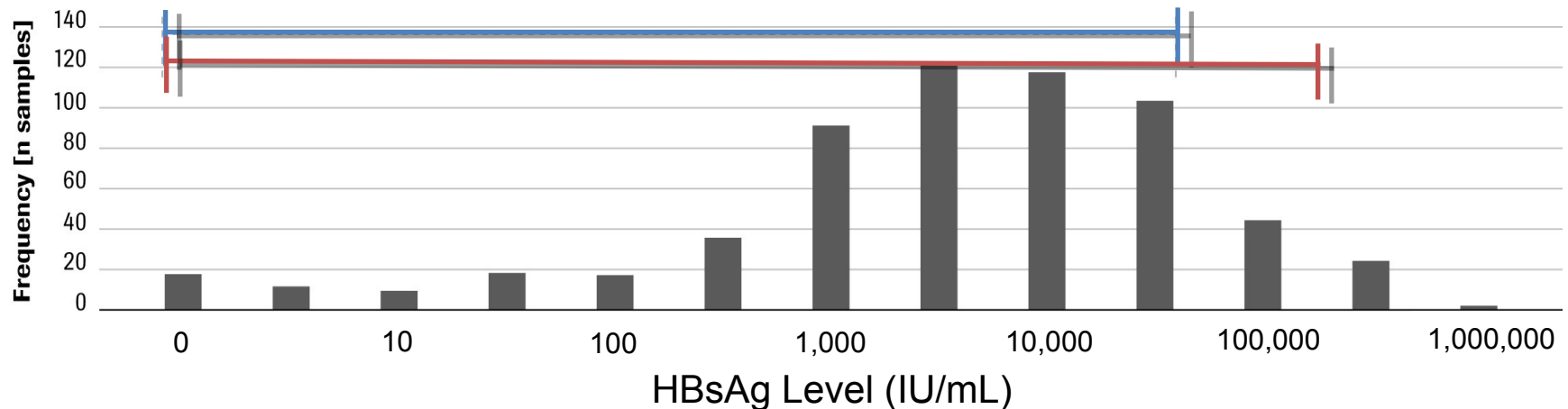


Stopp therapy if
anti-HBs >100 IU/l or SIC (?)

Commercially available quantitative HBsAg tests

Abbott linear range 0.05–125.000 IU/mL

Elecsys linear range 0.05-52.000 IU/ml



Linear Range of tests sufficient for most clinical situations

Where is the demand for an immunomodulatory therapy?

Long-term therapy with NUCs **without** reduction of qHBsAg

PEG-IFN

Long-term therapy with NUCs

Off-label!

PEG-IFN

Off-label?

Long-term therapy with NUCs

Long-term therapy with NUCs

STOPP

When IFN? When NUCs?

Yes

No contraindikationen against IFN /
(HBV-Genotype A, B)
HBV-DNA $< 10^8$

**No dogma to use one or the other – start
thinking on an individual patient basis –
switch might be the right choice for an
individual patient**

Lin

no si
HBs

Useful testing of qHBsAg during therapy

Switch instead of add-on sufficient ?
Add-on off label

Case 4a
32 yo male German patient, teacher

HBV was probably vertically transmitted

2008: HBeAg negative

Genotype D (no routine clinical test)

HBV DNA 34500 IU/ml

ALT 218 IU/ml

Histology 2008: Grading 2, Staging 2 (Metavir)

May 2008: NUC or PEG-IFN ?? (all drugs available)

What would you have suggested in 2008 for this patient?

Case 4a

32 yo male German patient, teacher

HBV was probably vertically transmitted

2008: HBeAg negative,

Genotype D

HBV DNA 34500 IU/ml

ALT 218 IU/ml

Histology 2008: Grading 2, Staging 2 (Metavir)

Tenofovir 245 mg since May 2008, didn't like the idea of PEG-IFN

Since 06/2009 HBV DNA <11 IU/ml, HBsAg stable of about 8000-10.000 IU/ml

Starting discussions about duration of therapy.....becoming intense over time

....adherence over time <100% with reappearance of viremia onn and off

Case 4a

32 yo male German patient, teacher

02/2012: wants to switch to PEG-IFN, didn't like the idea to pause therapy (FINITE study not wanted)

Fibroscan redone: no signs for advanced fibrosis/cirrhosis

2 weeks overlapping tenofovir

Are we within the label for switching and starting PEG-IFN ?

Case - 32a male patient

	ALT U/l	HBV-DNA IU/l	qHBsAg IU/l	
02.2012	19	56	10.487	Start PEG-IFN
03.2012	136	128	9.456	
04.2012	346	218	7.455	
05.2012	198	65	225	
06.2012	68	38	28	
10.2012	33	<11	0,08	
01.2013	28	12	0,13	Stopp PEG-IFN
03.2013	22	<11	0,43	AntiHBs-
06.2013	15	<11	negative	AntiHBs-
12.2013	19	<11	negative	AntiHBs-

Case - 32a male German patient, teacher

12/2013: Is the patient happy ?

No, starts discussing about „missing“ anti HBs,

wants therapeutic vaccination to induce antiHBs, comes in

with a lot of study results from scientific meetings....

Case 4b

25 yo female medical student from Korea

HBV was probably vertically transmitted

HBeAg negative

Genotype B

HBV-DNA 62 298 000 IU/ml

ALT 78 IU/ml

Fibroscan 6,2 kPa

Entecavir 0,5 mg since January 2009

December 2009: HBV DNA <11 IU/ml, HBsAg titer stable of about 7000 IU/ml

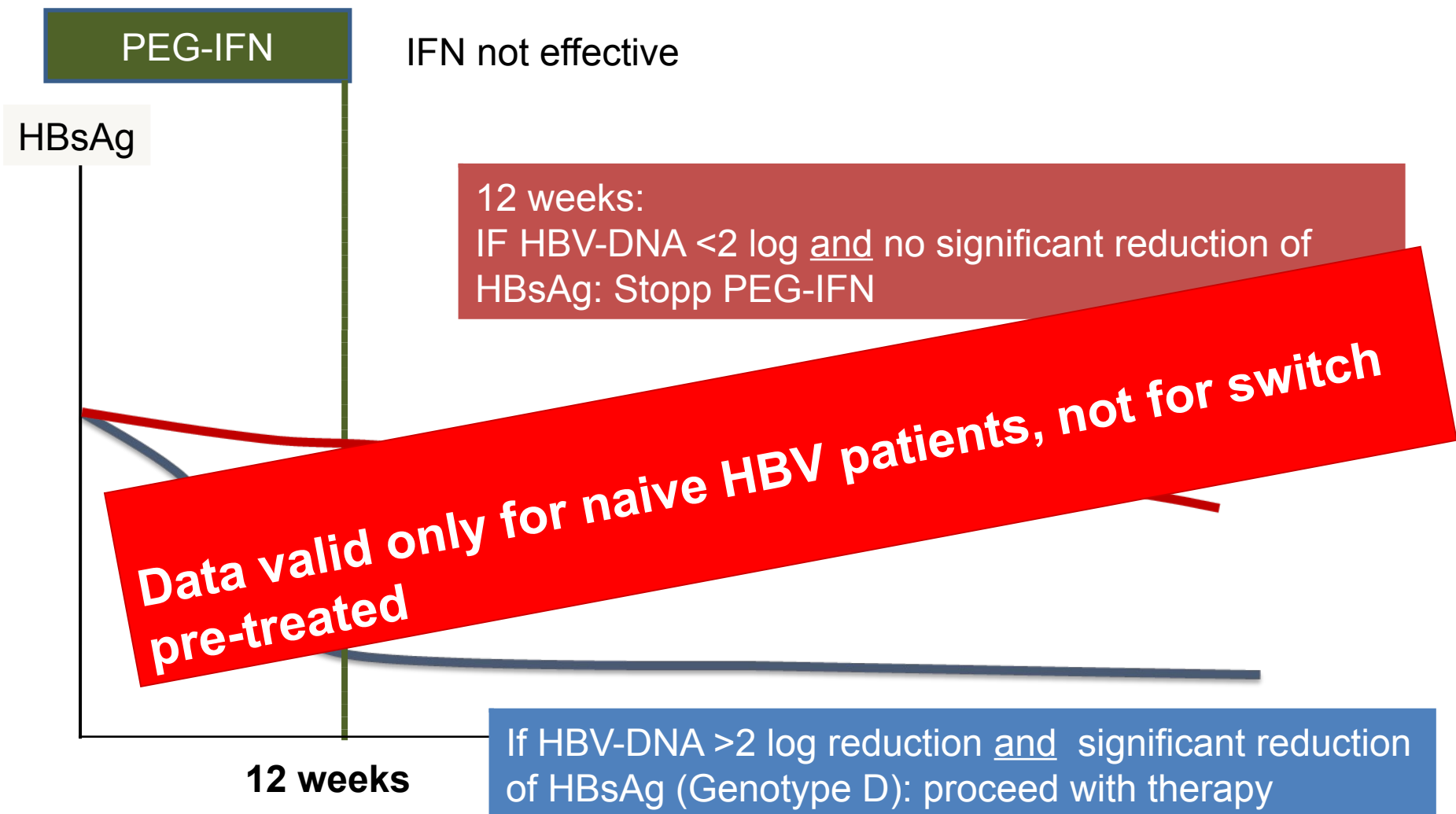
Wishes to be switched to PEG-IFN

Case - 25 female patient

	ALT U/l	HBV-DNA	qHBsAg IU/l	
01.2013	11	<11	7.250	Start PEG-IFN
02.2013	78	36	7.456	
04.2013	141	78	3.455	
07.2013	168	65	2.390	
10.2013	65	<11	1.050	
12.2013	121	<11	850	Stopp PEG-IFN ?

Good tolerability, some hair loss, patient wants extension (Italian data)

Stopping rules for PEG-IFN therapy in HBeAg negative patients



Switch from Entecavir to PEG-IFN (HBeAg+)

HBsAg loss

HBV DNA <10³ copies/ml
qHBeAg <100 PEIU/ml

**ETV 0,5 mg qd
9-36 months**



**Switch to Pegasys 180 µg qw 48W
(n = 97)**

**ETV
0,5 mg qd
8W**

48 W

10,3%

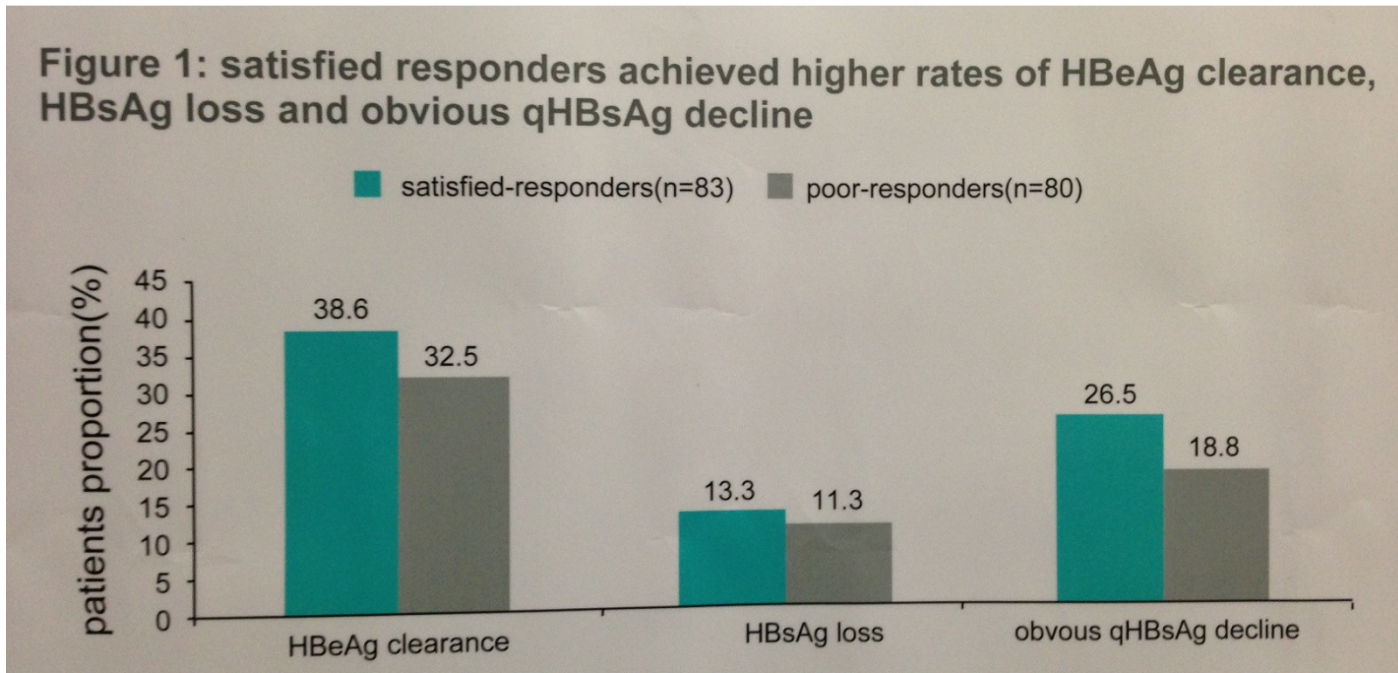
p=0.0014*

**ETV 0,5 mg qd 48W
(n = 100)**

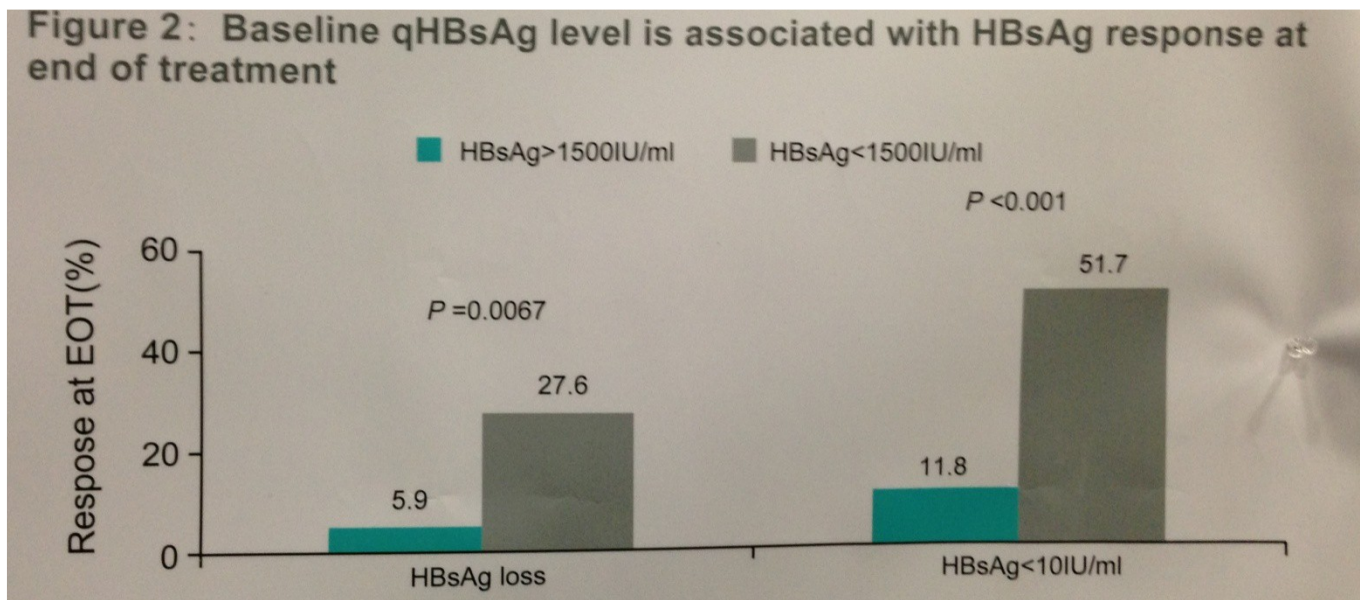
0%

**Baseline HBsAg <3000 IU/ml was
associated with response**

AASLD 2013, Abstract 1006: Higher HBsAg clearance rate achieved in NUC experienced CHB patients treated with pegylated IFN alpha 2a
Yao Xie et al



AASLD 2013, Abstract 1006: Higher HBsAg clearance rate achieved in NUC experienced CHB patients treated with pegylated iFN alpha 2a



AASLD 2013, Abstract 954: Sustained immune control in HBeAg pos. CHB patients who switched from long-term entecavir therapy to PEG IFN alfa 2a: 1 year follow-up pf the OSST study. Meifang Han et al

Stopping of NUCs bevor HBsAg loss – course after stopping in a real life cohort



14/60 patients without relapse (23%) = 77% relapse

Results III: qHBsAg (IU/ml), anti-HBs (IU/ml), viremia and ALT in patients without relapse after stopping NUC therapy

Patient #	Previous therapy / months	qHBsAg at therapy stop	qHBsAg month 12	qHBsAg month 24	qHBsAg month 36	qHBsAg month 48	HBV-DNA (IU) and ALT month 48
1	Lamivudine / 74	930	854	726	788	946	8900 / ALT nl
2	Lamivudine / 62	140	HBsAg-/Anti-HBs-	HBsAg-/Anti-HBs + (19)	HBsAg-/Anti-HBs + (45)	HBsAg-/Anti-HBs + (105)	<20 / ALT nl
3	Lamivudine / 80	453	390	479	486	536	350 / ALT 68 U
4	Lamivudine / 50	0.5	HBsAg-/Anti-HBs-	HBsAg-/Anti-HBs-	HBsAg-/Anti-HBs-	HBsAg-/Anti-HBs-	<20 / ALT nl
5	Lamivudine / 49	1800	2350	1400	1280	1250	20.000 / ALT nl
6	Lamivudine / 62	1250	3400	2500	2050	1460	450 / ALT 64
7	Lamivudine / 47	4270	3890	3580	4300	2350	980 / ALT nl
8	Adefovir / 64	18	qHBsAg 7 / Anti-HBs-	HBsAg <0.05 / Anti-HBs-	HBsAg-/Anti-HBs+ (129)	HBsAg-/Anti-HBs+ (177)	<20 / ALT nl
9	Adefovir / 52	49	19	n.a.	HBsAg-/Anti-HBs-	HBsAg-/Anti-HBs-	<20 / ALT 73U/NASH
10	Adefovir / 49	240	290	380	450	438	<20 / ALT 53
11	Telbivudine / 54	n.a.	379	12	HBsAg-/Anti-HBs-	HBsAg-/Anti-HBs-	<20 / ALT nl
12	Entecavir 0.5 / 37	n.a.	458	357	876	398	<20 / ALT nl
13	Entecavir 0.5 / 42	432	330	HBsAg-/Anti-HBs-	HBsAg-/Anti-HBs-	HBsAg-/Anti-HBs-	<20 / ALT nl
14	Entecavir 1.0 / 48	121	HBsAg-/Anti-HBs-	HBsAg-/Anti-HBs+ (105)	HBsAg-/Anti-HBs + (187)	HBsAg-/Anti-HBs + (78)	<20 / ALT nl

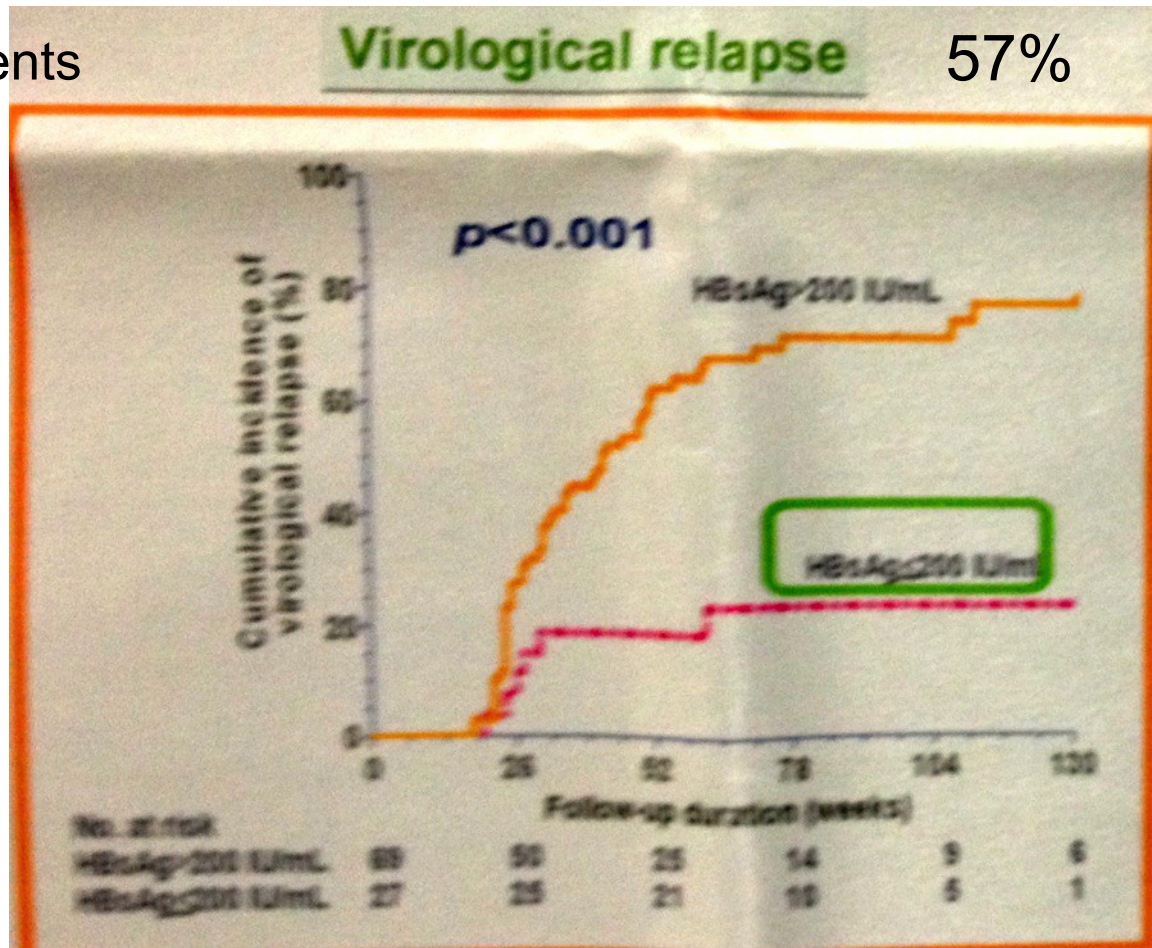
High relapse rates >200 IU/ml HBsAg

AASLD 2013, Abstract #982: Petersen, Hansen, Buggisch, Hinrichsen, Berg, Wedemeyer, Stoehr, Chan, Arends, Wiegand, Brunetto, Cornberg, Janssen

HBV relapse after stopping NUC therapy: Importance of qHBsAg

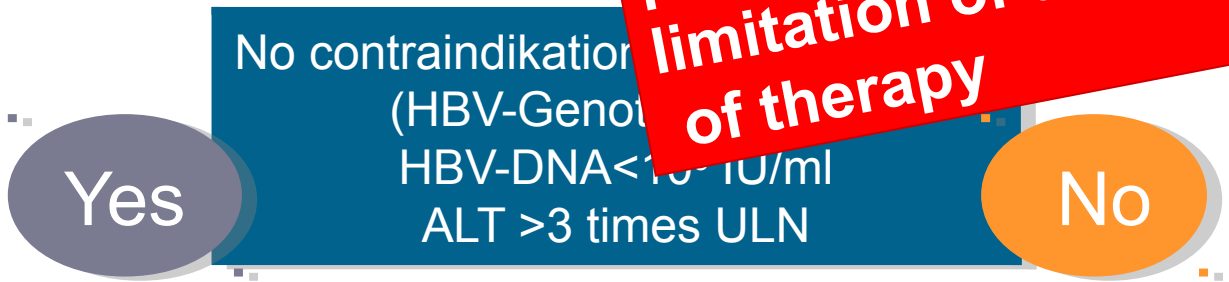
HBeAg negative patients

Virological relapse 57%



When IFN? When NUC?

patient asking for limitation of duration of therapy



Limited duration with PEG-IFN (48 weeks)

Long-term therapy with Nucleosidanaloga (Entecavir or Tenofovir)

qHBSAg after 12 Wochen

HBV-DNA all 3 months

no significant reduction of HBsAg: switch to NUC

qHBsAg ?!

Stopp therapy if anti-HBs >100 IU/l or SIC (?)

Take home messages

- Most HBV treated patients (>90%) receive NUCs in many countries of the EU
- qHBsAg is an important marker to determine the transcriptional activity of HBV replication (for cccDNA)
- Limitation of treatment duration is becoming more important
- There is a need for prospective „switch“ trials
- Stopping rules for qHBsAg need to be evaluated for patients pretreated