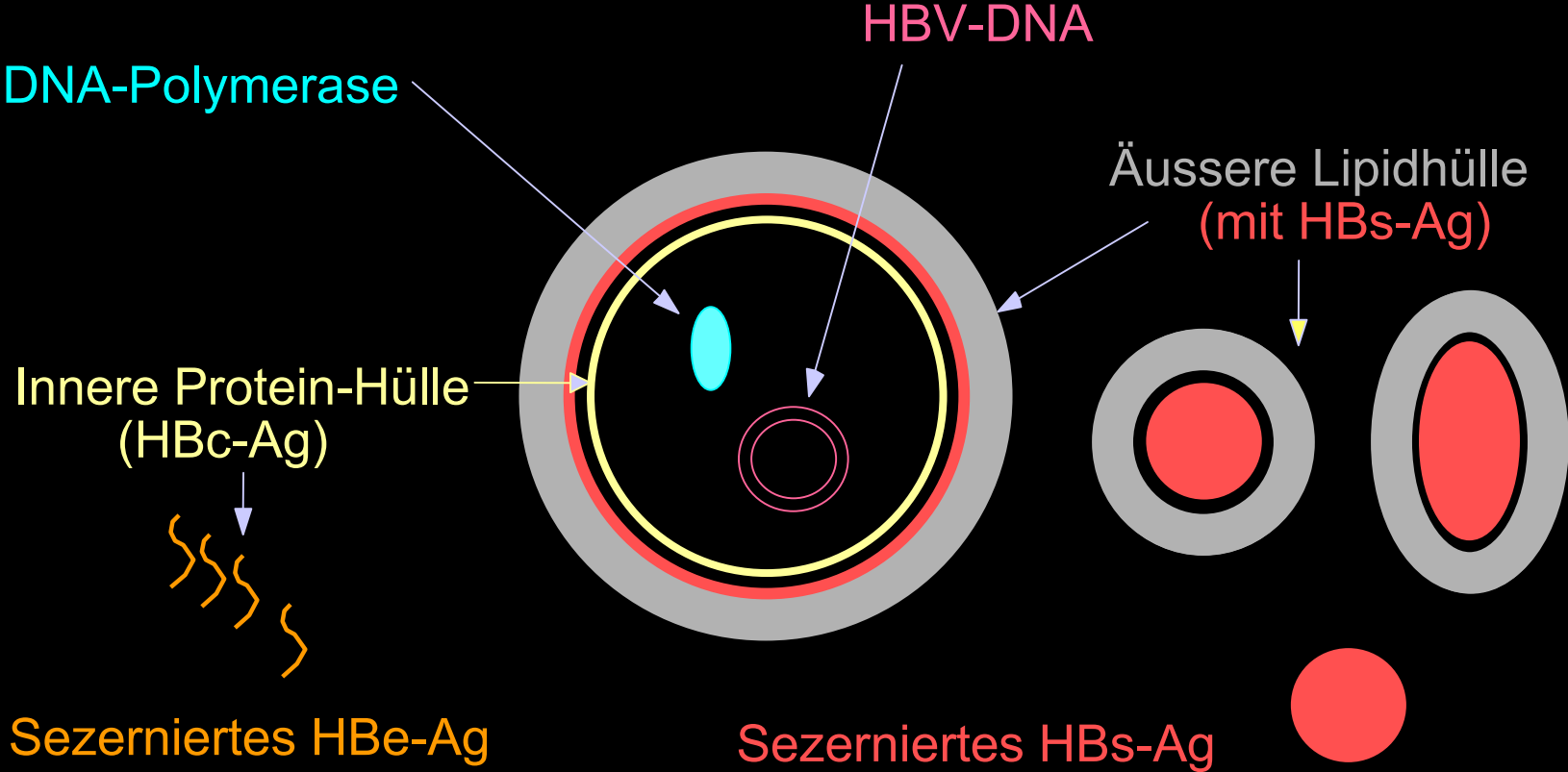


Hepatitis B

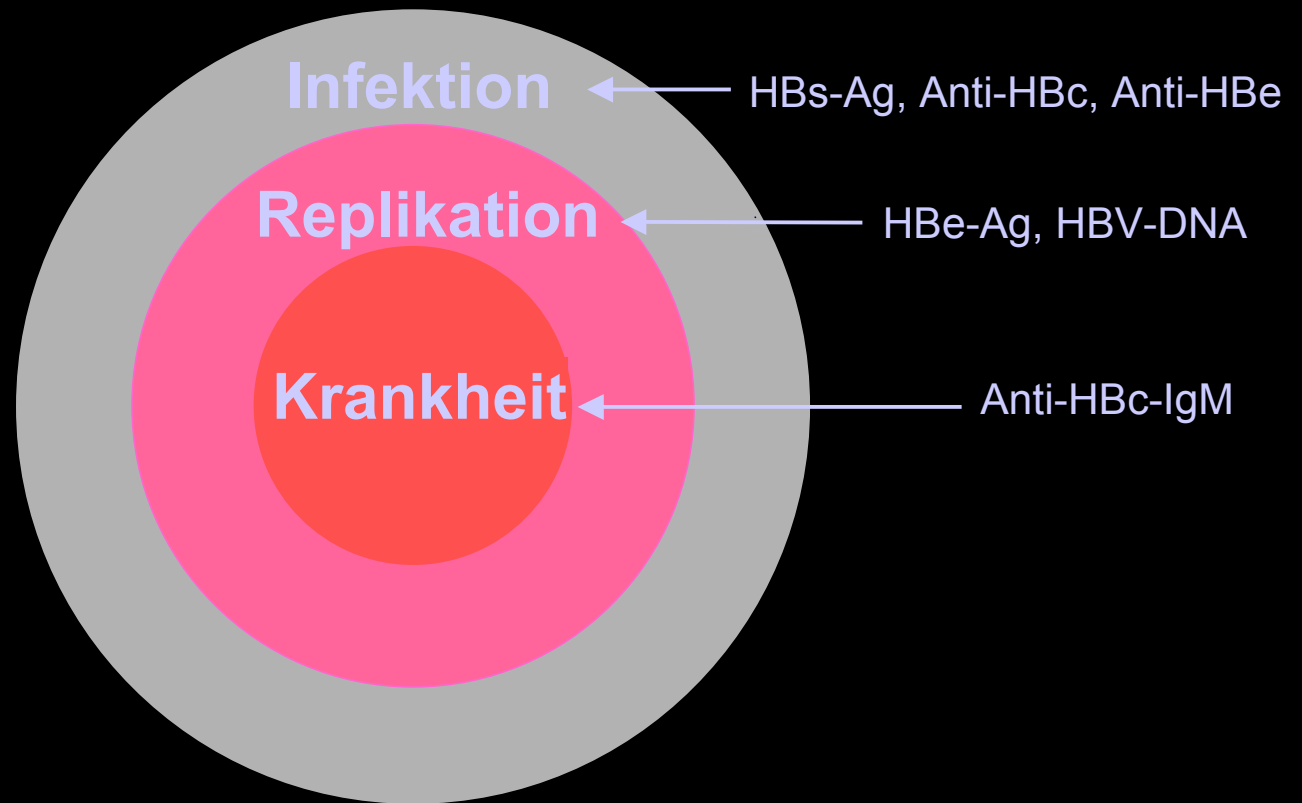
Hepatitis B

HBV - Struktur



Hepatitis B

Serologie



Diagnostische Kriterien

Chronische Hepatitis B

- HBs-Ag positiv > 6 M
- HBV-DNA > 10^5 c/ml
- Transaminasen ↑
konstant /fluktuierend
über >6 M
- Leberbiopsie mit
entzündliche Aktivität*

Inaktiver HBs-Carrier

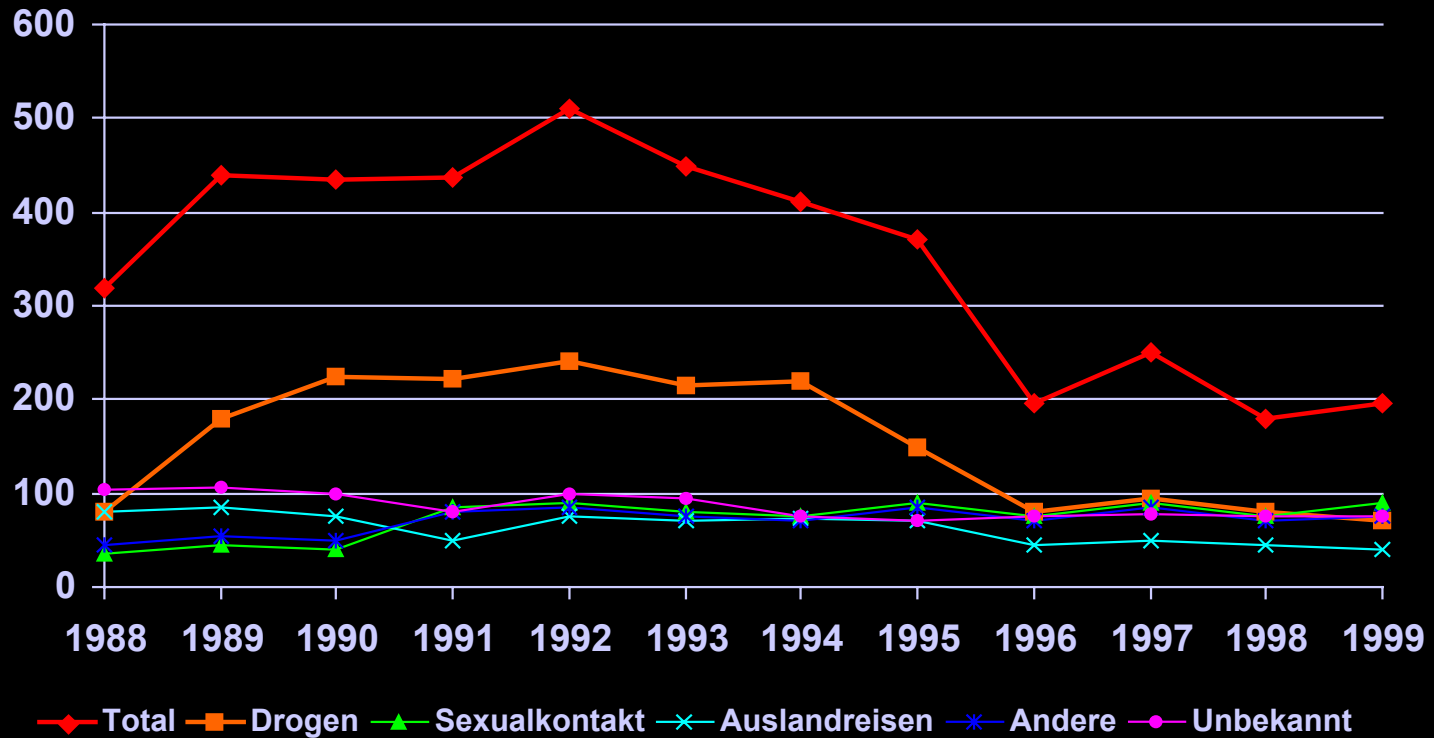
- HBs-Ag positiv > 6 M
- HBe-Ag negativ,
Anti-HBe positiv
- HBV-DNA < 10^5 c/ml
- Normale Transaminasen
- Leberbiopsie ohne
entzündliche Aktivität*

* Optional

Hepatitis B

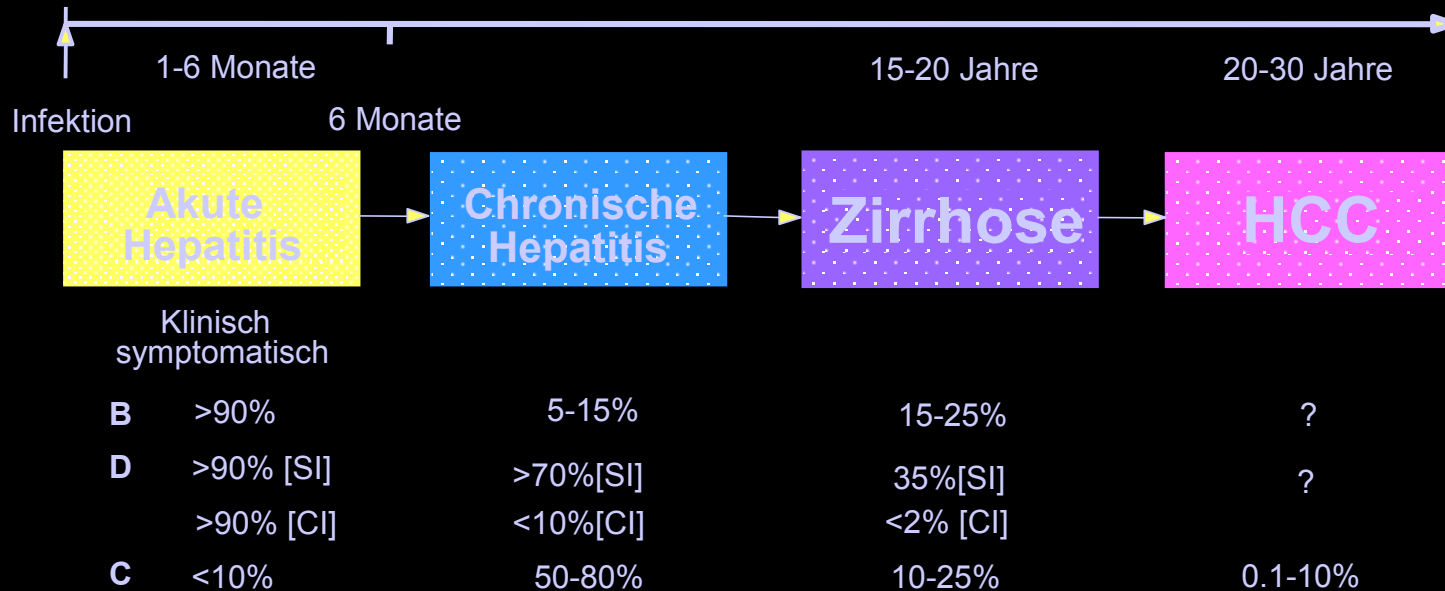
Inzidenz

Jahresinzidenz in der Schweiz
Meldungen von Laboratorien und Ärzten 1988-1999



Chronische Hepatitis B/C/D

Natürlicher Verlauf



[SI] = Superinfektion bei HBV-Carrier ; [CI] = Coinfektion

Interferon - Therapie

- HBe-Anti-HBe-Serokonversion + 20%,
HBs-Elimination + 6%
- Je höher Transaminasen und Viralload, desto höher
Response-Rate
- HBe-Anti-HBe-Serokonversion bewirkt:
 - Komplikationen im Langzeitverlauf ↓
 - HCC-Inzidenz ↓
 - Survival-benefit?

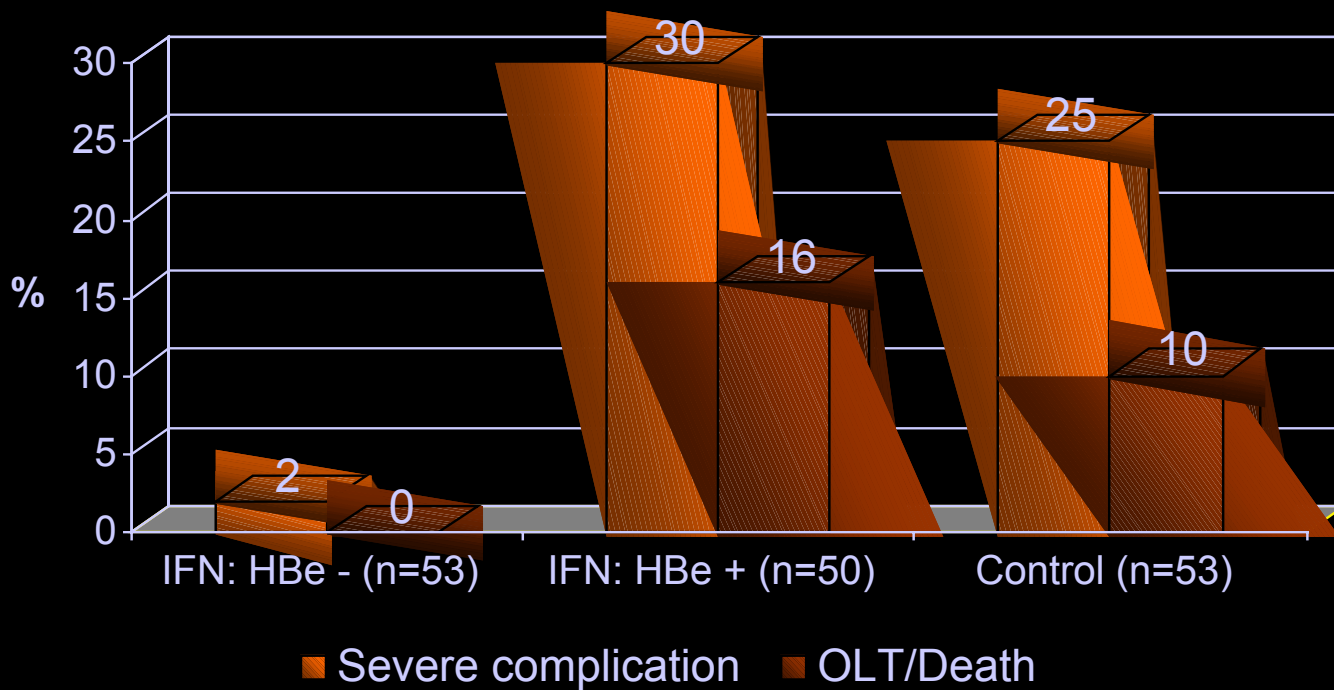
Aber:

- Schlechtere HBe-Anti-HBe-Serokonversions-Rate
(+10%) und hohe Relapse-Rate (50%) bei HBe-Ag-
negativer Hepatitis B auch bei Therapie > 6 Monate

Interferon - Therapie

Long-term follow-up of HBeAg-positive patients treated with interferon alfa for chronic hepatitis B ¹

(IFN:n=103; Control:n=53; Follow-up 50 +/-19.8months)



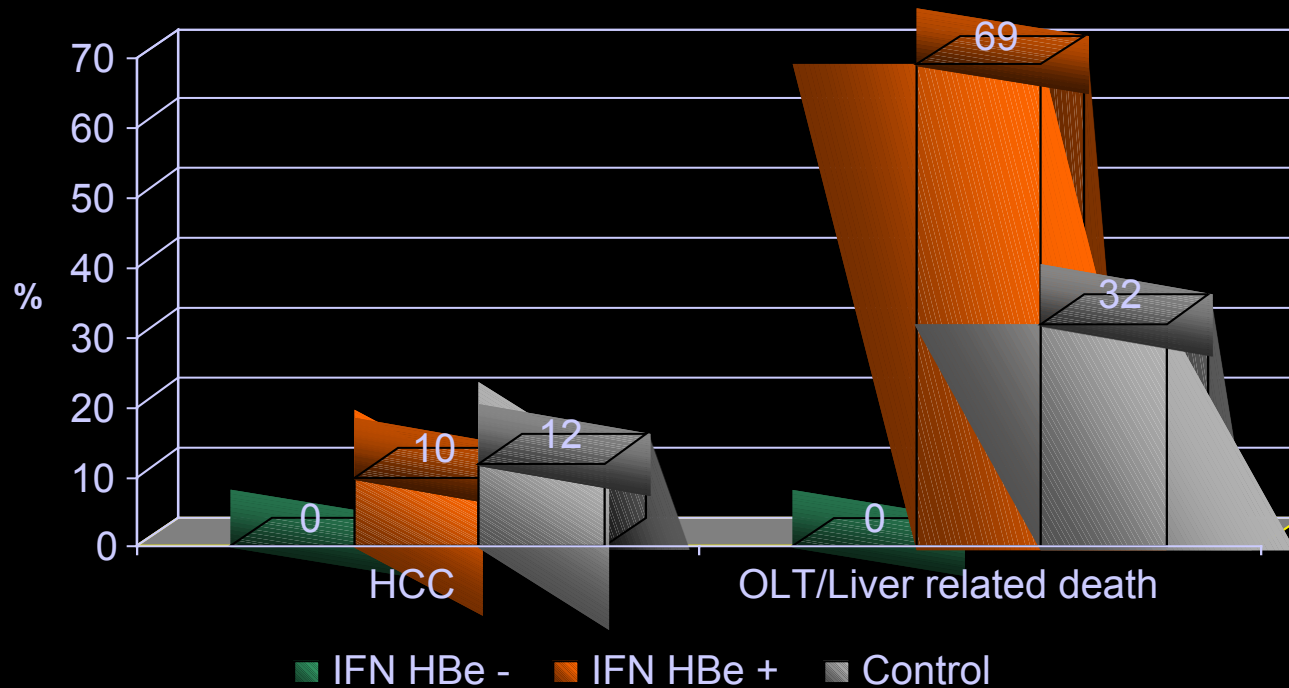
¹ Niederau M.D. et al., NEJM 1996;334:1422-7

Interferon - Therapie

Long-term outcome of HBeAg-positive patients with compensated cirrhosis treated with interferon alfa

(IFN:n=40; Control:n=50; Follow-up 7y)

1



¹ Fattovich G. et al. Hepatology 1997;26:1338-42

Interferon - Therapie¹

Aktuelle Indikation

- Replizierende HBV-Infektion
 - HBV-DNA positiv*
 - HBe-Ag positiv
- Transaminasen $\uparrow > 2 \times N$ über >6 Monate
- Leberbiopsie
 - Entzündliche Aktivität

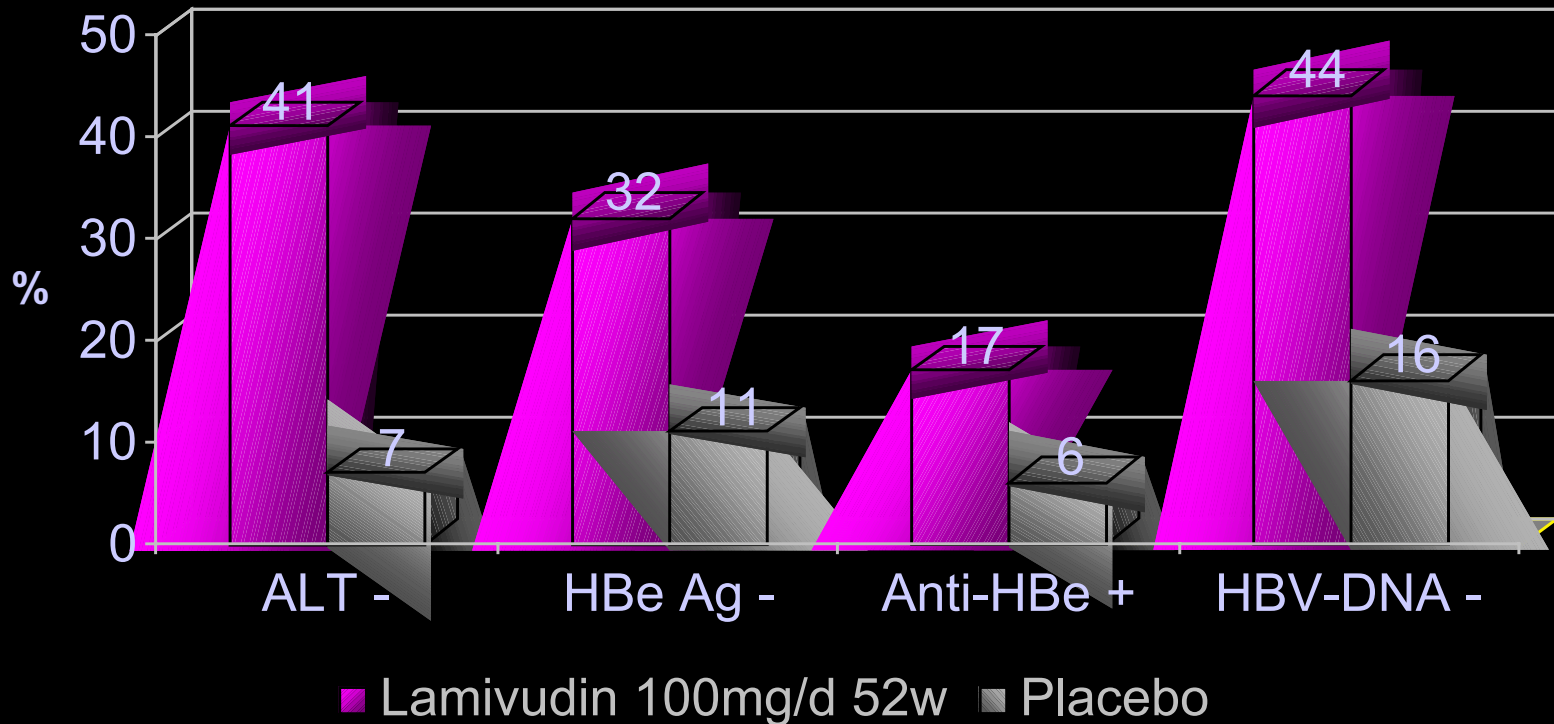
Aktuell keine Indikation

- HBV-DNA negativ (HBs-Carrier)
- Akute HBV-Infektion
- HCV/HIV-Koinfektion
- Precore-Mutante (HBe-Ag negativ)

*Hybridisierungs-Assay mit Detektionsgrenze von 5pg/ml (10^5 - 10^6 c/ml)

Lamivudin - Therapie

Lamivudin as initial treatment for chronic hepatitis B ¹
(SR; N=137; Lamivudin:n=66, Placebo:n=71)

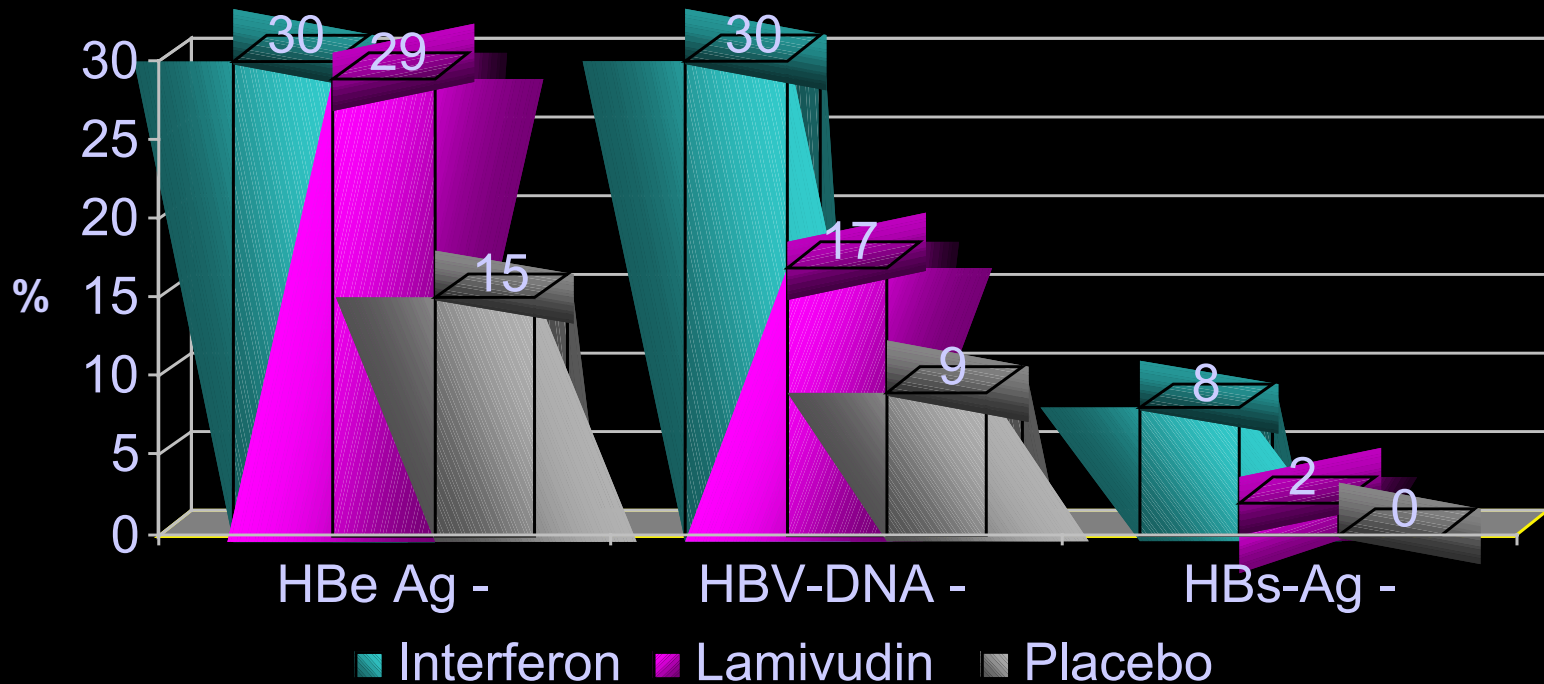


¹ Dienstag J.L. et al., NEJM 1999;341:1256-63

Chronische Hepatitis B

Interferon vs. Lamivudin

Interferon alpha¹ vs. Lamivudin² as initial treatment for chronic hepatitis B
(Sustained response rate at 16-24w follow-up)

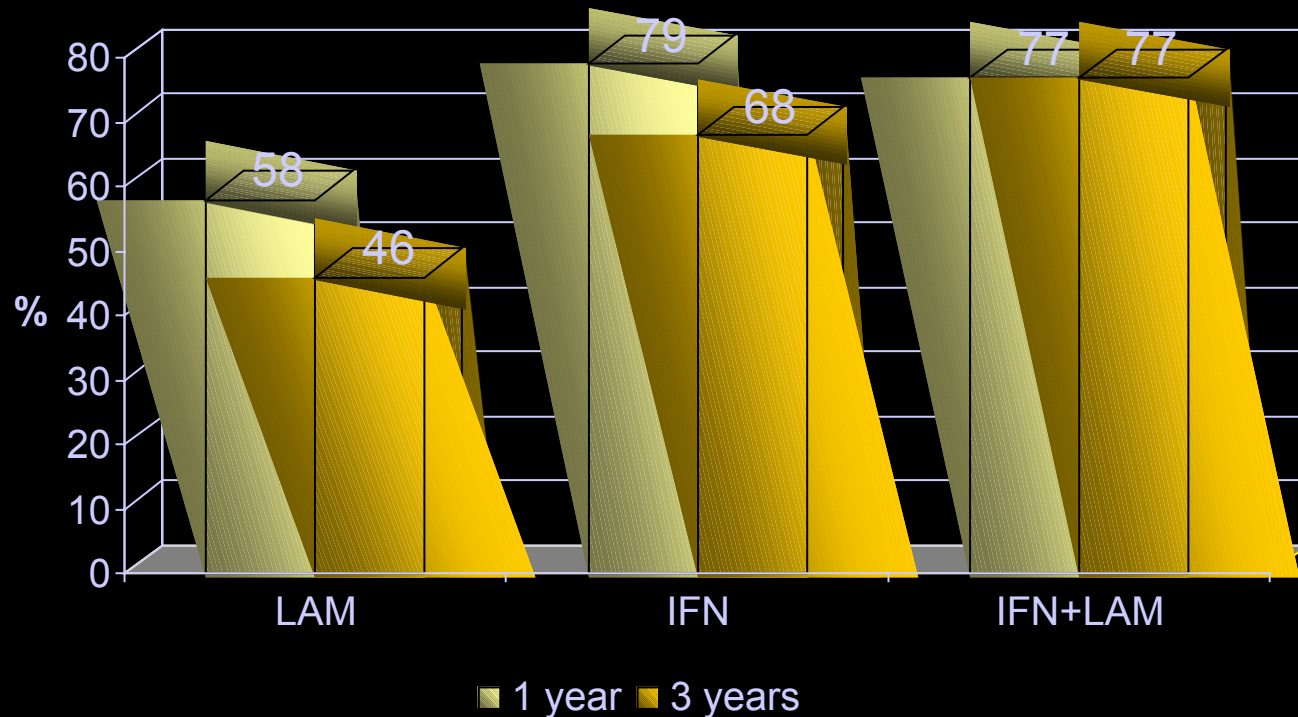


¹ Lau D.T., Gastroenterology 1997;113:1660-67 ²Dienstag J.L. et al., NEJM 1999;341:1256-63

IFN-LAM-Kombinations-Therapie

Durability of HBeAg seroconversion following antiviral therapy for chronic hepatitis B: Cumulative percentag of sustained response rate after mono or combination therapy¹

(LAM:n=59; IFN:n=49; IFN+LAM:=22)



¹ van Nunen AB et al., Gut 2003;52:420-424

Chronische Hepatitis B

Interferon vs. Lamivudin*

ETR-Response	<i>Interferon</i>		<i>Lamivudin</i>	
	<i>12-24 W</i>	<i>Placebo</i>	<i>52 W</i>	<i>Placebo</i>
HBV-DNA-Clearance	37%	17%	44%	16%
- davon sustained response	80-90%		70-80%	
HBe-Clearance	33%	12%	17-32%	6-11%
HBe-Anti-HBe-Serokonversion	+ 18%		+ 12%	
HBs-Clearance	8%	2%	<1%	0%
ALT-Normalisierung	+ 23%		+ 34-48%	
Histologie - 2 Knodell-Punkte			49-56%	23-25%

* HBe-Ag-positive Patienten, first-line-therapy

Aktuelle Therapie¹

“The main role of IFN- α [or LAM] is to reduce the duration of active liver disease by hastening viral clearance“

¹Lok et al., AASLD Practice Guidelines in Chronic Hepatitis B 2001

Aktuelle Therapie¹

- *HBs-Carrier* *Keine Therapie*
-
- Chronische Hepatitis B*
 - ‚Klassisch‘ IFN- α oder LAM
 - Precore-Mutante IFN- α oder LAM longterm
 - Non-Responder LAM+Adefovir (?)
 - Zirrhose Child B/C
 - OLT-Kandidat LAM
 - Kein OLT-Kandidat LAM
-
- *Spezialfälle*
 - *Immunosuppression* LAM
 - *Chemotherapie* LAM

*ALT >2xN