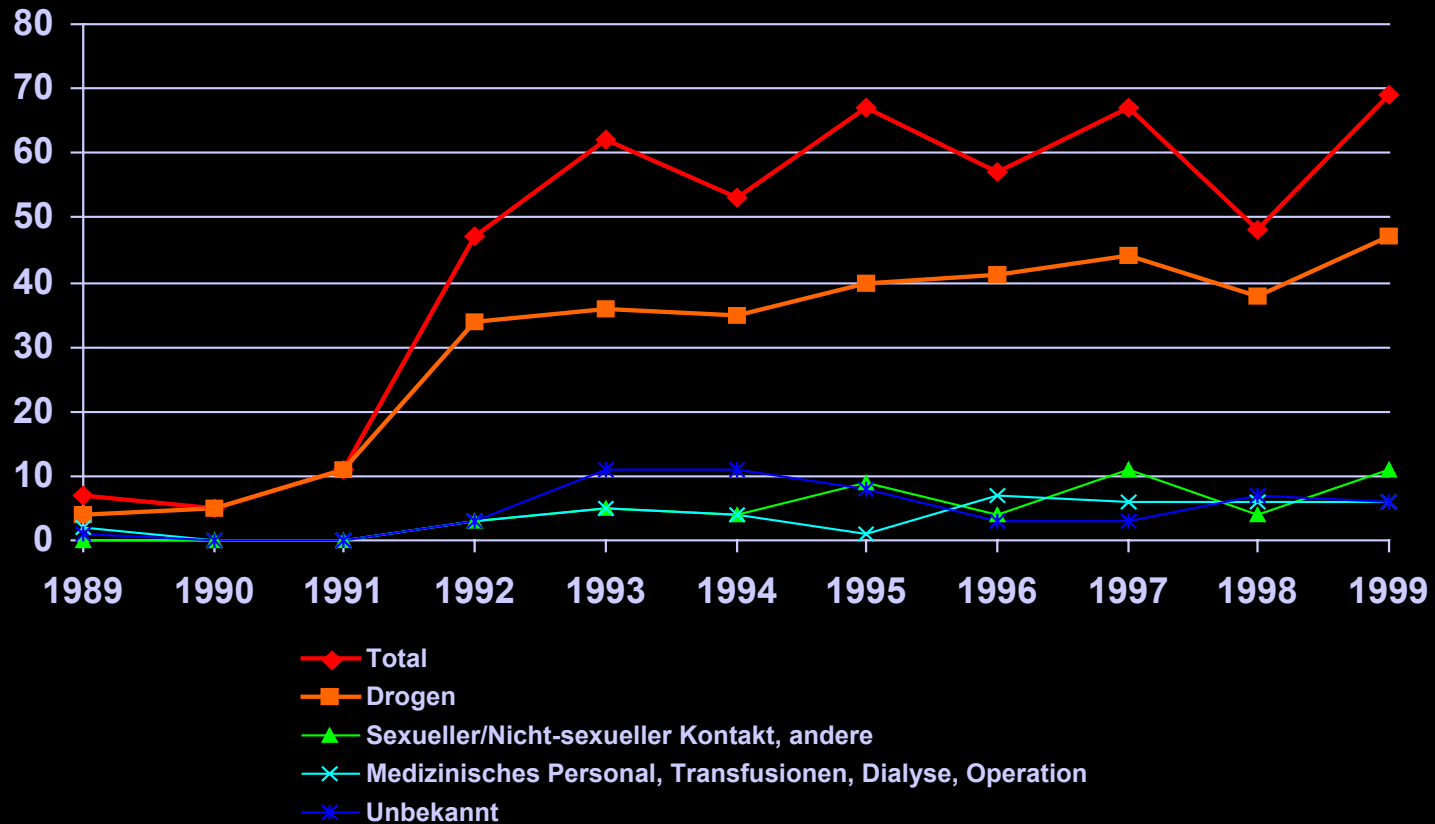


Chronische Hepatitis C

Hepatitis C

Inzidenz

Jahresinzidenz in der Schweiz
Meldungen von Laboratorien und Ärzten 1989-1999



Histologisches Staging

Scoring of Hepatic Fibrosis

Fibrosis	Knodell¹	Ishak²	METAVIR³
No fibrosis	0	0	0
Mild some, septal	1	1	1
Mild most, septal	1	2	1
Moderate occasional bridging	3	3	2
Severe marked bridging	3	4	3
Incomplete cirrhosis	4	5	4
Cirrhosis	4	6	4

¹Knodell et al, Hepatology 1981;1:431-435 ²Ishak K. et al., J Hepatol 1995;22:696-699

³Bedossa et al., Hepatology 1996;24:289-293

Histologisches Grading

Histologic Activity Index (HAI) or necroinflammatory scores

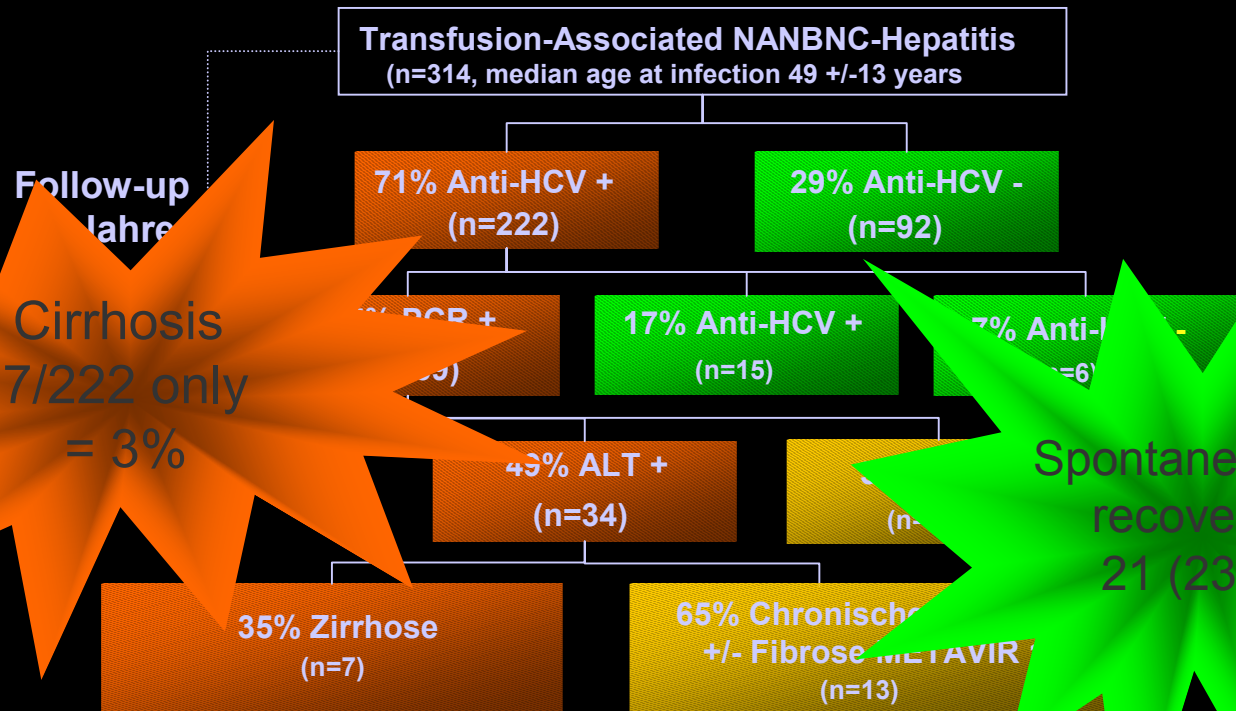
	<i>Knodell</i> ¹	<i>Ishak</i> ²	<i>METAVIR</i> ³
A. Periportal or periseptal interface hepatitis (piecemeal necrosis)	0-10	0- 4	0-3
B. Confluent necrosis	-	0- 6	0 or 1
C. Lobular degeneration or focal lytic necrosis/apoptosis	0- 4	0- 4	0-2
D. Portal inflammation	0- 4	0- 4	0-3
HAI	0-22	0-18	A1 - A3

¹Knodell et al, Hepatology 1981;1:431-435 ²Ishak K. et al., J Hepatol 1995;22:696-699

³ Bedossa et al., Hepatology 1996;24:289-293

Natürlicher Verlauf

Langzeit-Verlauf nach akuter Transfusionshepatitis 1967-80¹



Follow-up
10 Jahre

Cirrhosis
7/222 only
= 3%

Spontaneously
recovered
21 (23%)

¹Seeff et al., Hepatology 2001;33:455-463

Chronische Hepatitis C

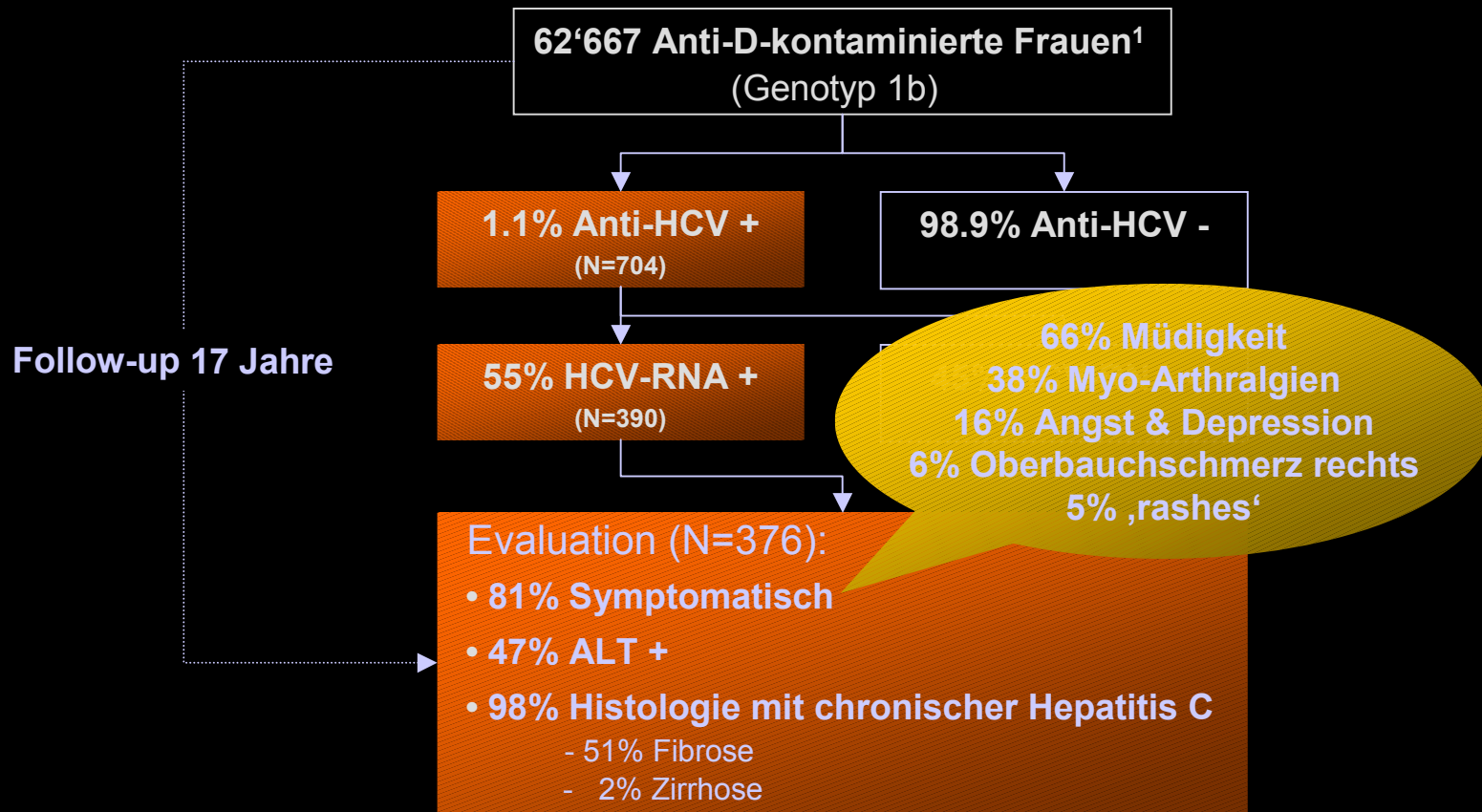
Natürlicher Verlauf

Langzeit-Verlauf nach akuter Transfusionshepatitis 1967-80¹

	Anti-HCV +		Anti-HCV -	
	Cases (n=222)	Controls (n=377)	Cases (n=92)	Controls (n=168)
All deaths	67.1%	65.0%	51.1%	54.8%
Liver related deaths	4.1% (n=9)	p = 0.05 1.3% (n=5)	3.3% (n=3)	p = n.s. 0.6% (n=1)
- HCC	- 3		- 1	
- Decompensated cirrhosis	- 3		- 1	
- ‚Hepatitis‘	- 2		- 1	
- Hepatic failure	- 1			

¹Seeff et al., Hepatology 2001;33:455-463

Natürlicher Verlauf

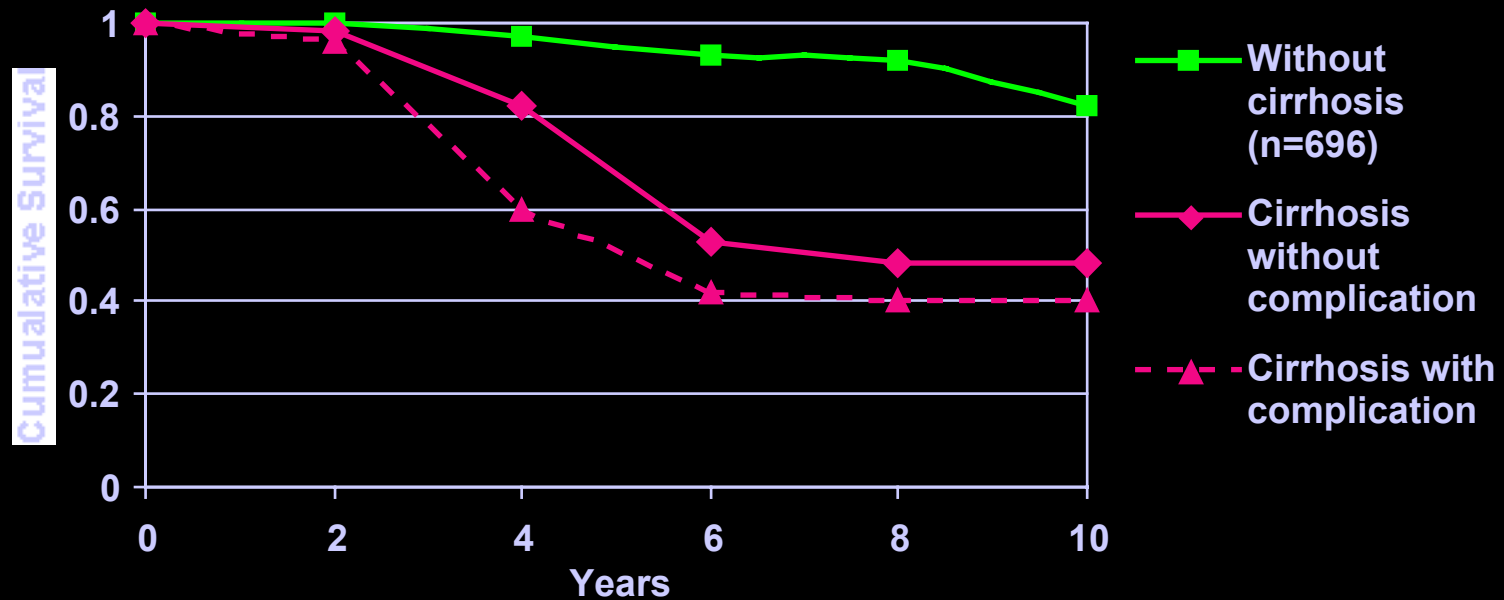


¹Kenny-Walsh E. et al., NEJM 1999;340:1228-33

Chronische Hepatitis C

Natürlicher Verlauf

Prognosis of Chronic Hepatitis C: Results of a Large, Prospective Study¹
(N=838; Follow-up 50±27months)

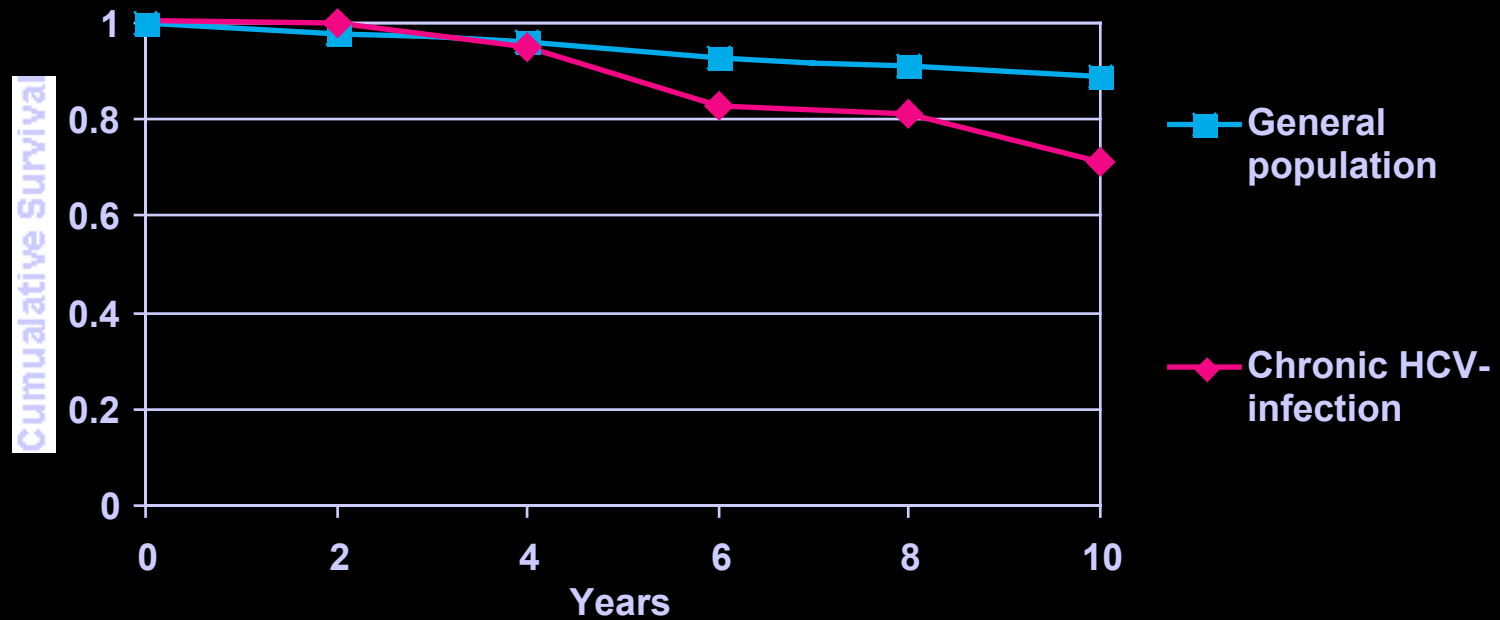


¹ Niederau C. et al., Hepatology 1998;28:1687-5

Chronische Hepatitis C

Natürlicher Verlauf

Prognosis of Chronic Hepatitis C: Results of a Large, Prospective Study¹
(N=838; Follow-up 50±27months)



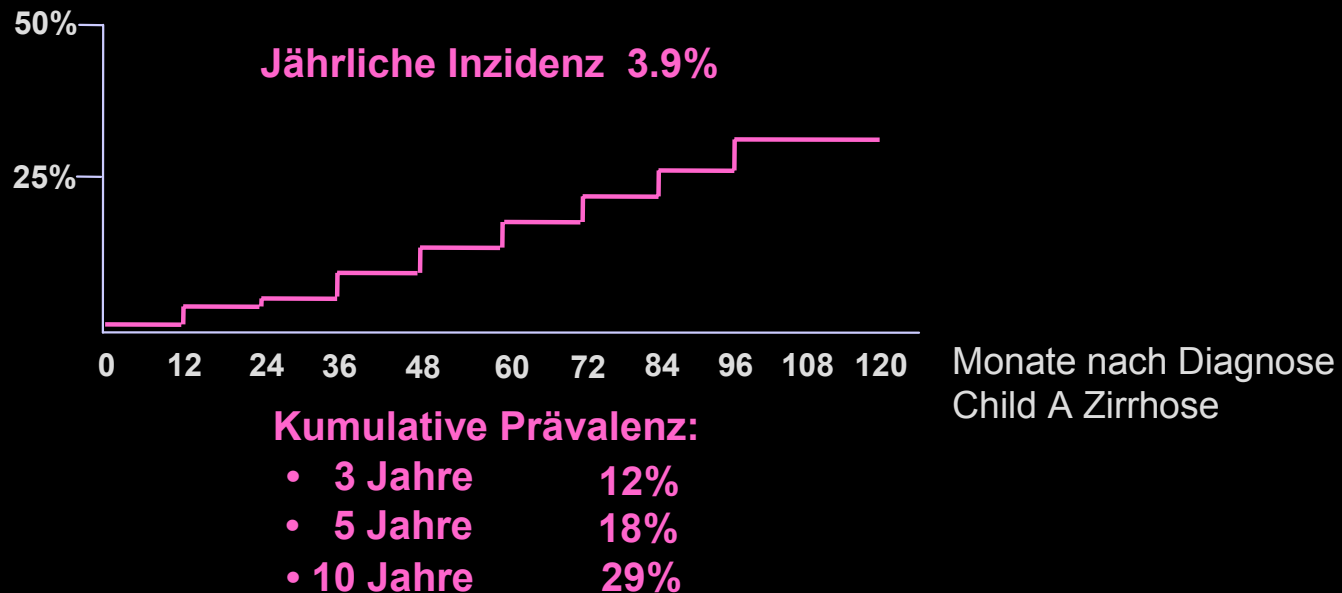
¹ Niederau C. et al., Hepatology 1998;28:1687-5

Chronische Hepatitis C

Natürlicher Verlauf

Typ C Zirrhose - Hepatische Dekompensation¹

Erste Episode mit Aszites, Varizenblutung, Enzephalopathie, Ikterus



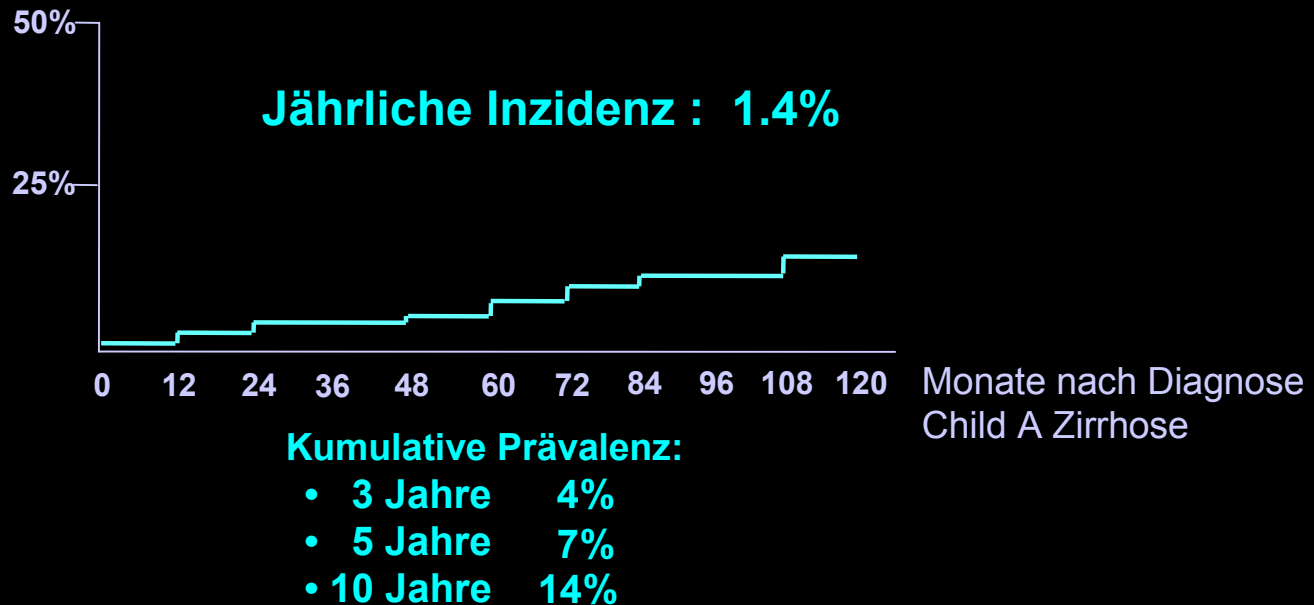
¹ Fattowich et al., Gastroenterology 1997;112:463-472

Chronische Hepatitis C

Natürlicher Verlauf

Typ C Zirrhose - HCC¹

Kompatible Histologie oder AFP >400 + Sonografiebefund



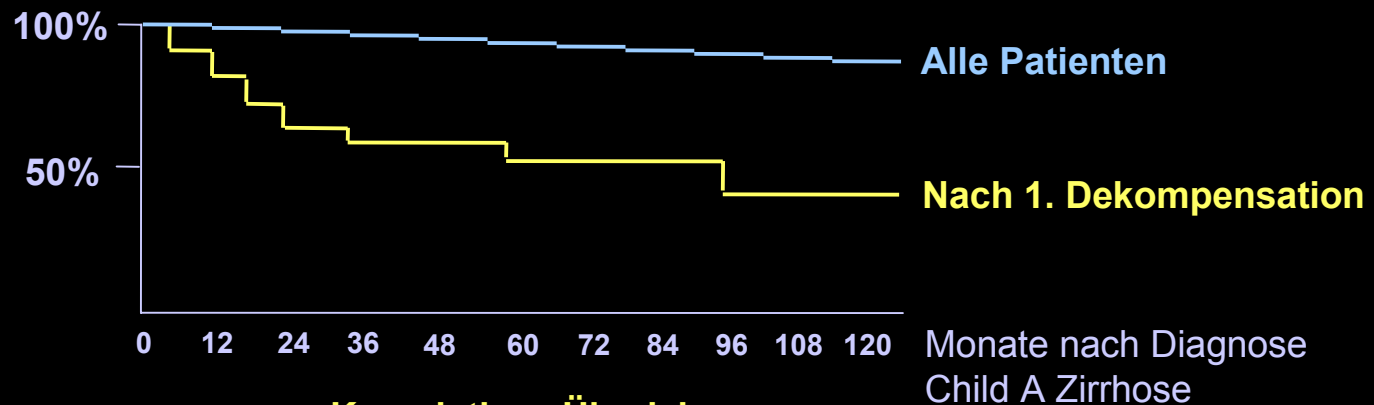
¹ Fattovich et al, Gastroenterology 1997;112:463-472

Chronische Hepatitis C

Natürlicher Verlauf

Typ C Zirrhose - Survival¹

Tod durch Leberversagen, Oesophagusvarizenblutung, HCC



Kumulatives Überleben:

- **5 Jahre 91%**
- **10 Jahre 79%**

Jährliche Letalität : 1.9%

¹ Fattovich et al., Gastroenterology 1997;112:463-472

Interferon - Therapie¹

Aktuelle Indikation

- Replizierende HCV-Infektion
HCV-RNA positiv
- Transaminasen ↑ über >6 Monate
- Leberbiopsie
Entzündliche Aktivität

*Aktuell **keine** Indikation*

- Akute HCV-Infektion
- Normale Transaminasen
- HBV/HIV-Koinfektion

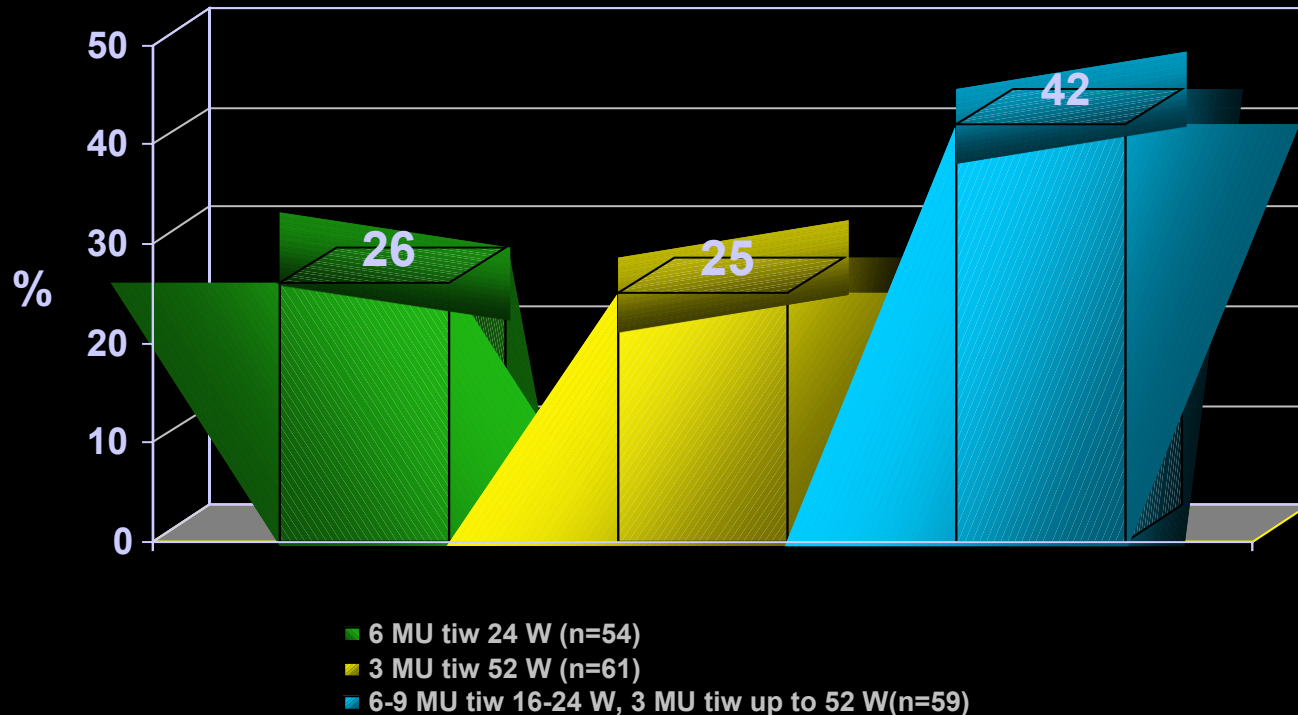
Chronische Hepatitis C

Interferon - Monotherapie

Randomised trial comparing three different regimens of
alpha-2a-Interferon in chronic hepatitis C

(Virological SR after 52 weeks)
Genotyp I 47-54%, II 32-38%, III 13-16%

1

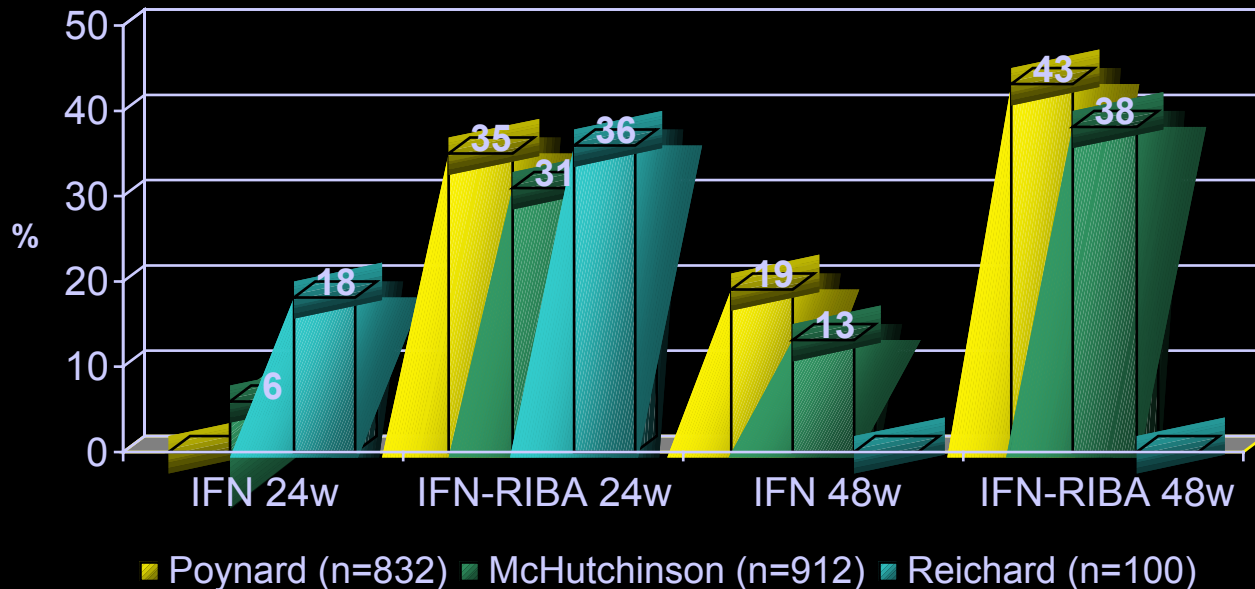


¹Chemello et al., Hepatology 1995;22:700-706

Chronische Hepatitis C

Interferon - Ribavirin

Interferon alpha alone or in combination with ribavirin as initial treatment for chronic hepatitis C¹⁻³
(Virological SR; IFN 3x3 MIU tiw/RIBA 1000-1200mg/d)



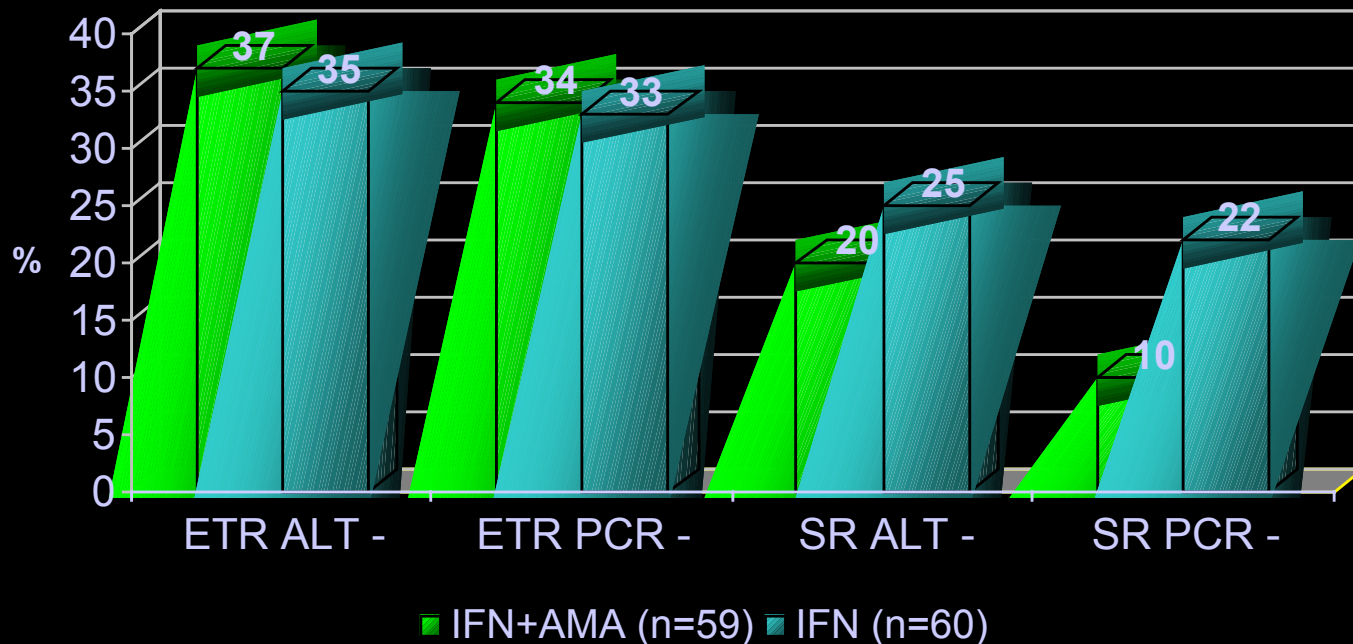
¹ Poynard T. et al. Lancet 1998;352:1426-32. ² McHutchinson J.G. et al. NEJM 1998;339:1485-92.

³ Reichard O. et al. Lancet 1998;351:83-87.

Chronische Hepatitis C

Interferon - Amantadin

Interferon Alfa 2a With and Without Amantadine-Sulphate
as Initial Treatment for Chronic Hepatitis C¹
(Randomized, double-blind, Placebo-Controlled Trial)

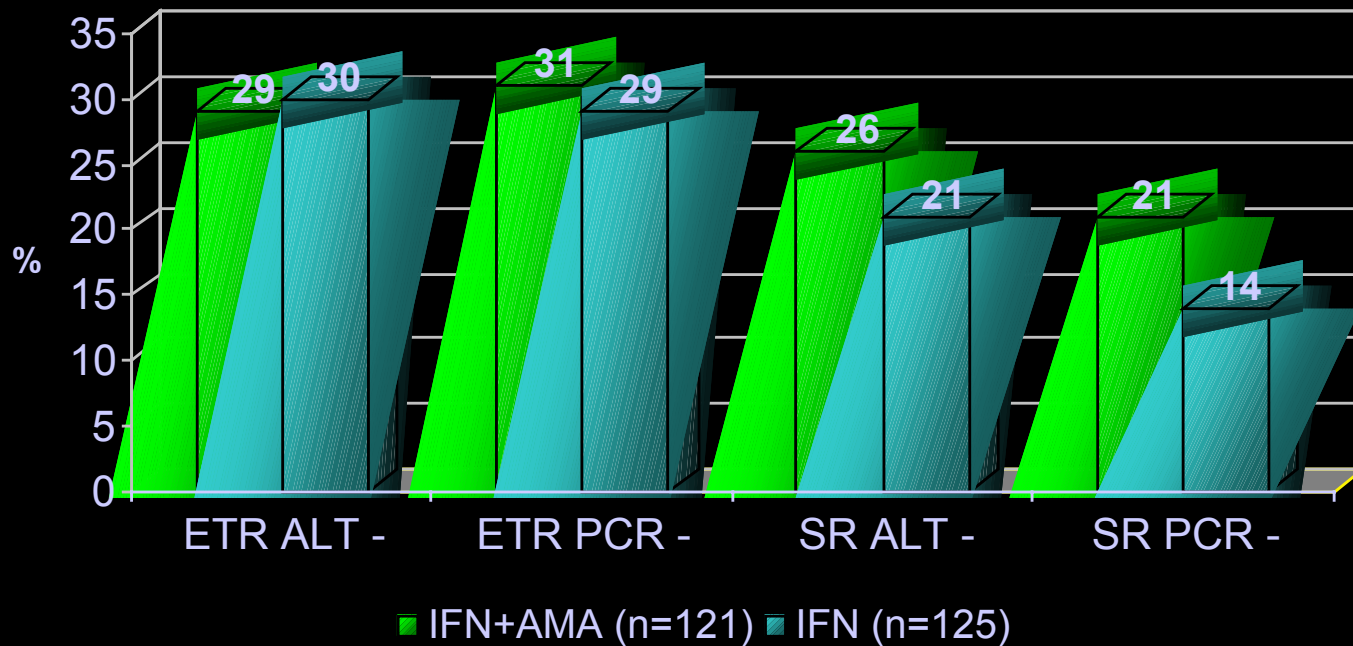


¹ Zeuzem S et al., Hepatology 2000;32:835-841

Chronische Hepatitis C

Interferon - Amantadin

Interferon Alfa 2a With and Without Amantadine-Sulphate
as Initial Treatment for Chronic Hepatitis C¹
(Randomized, double-blind, Placebo-Controlled Trial)

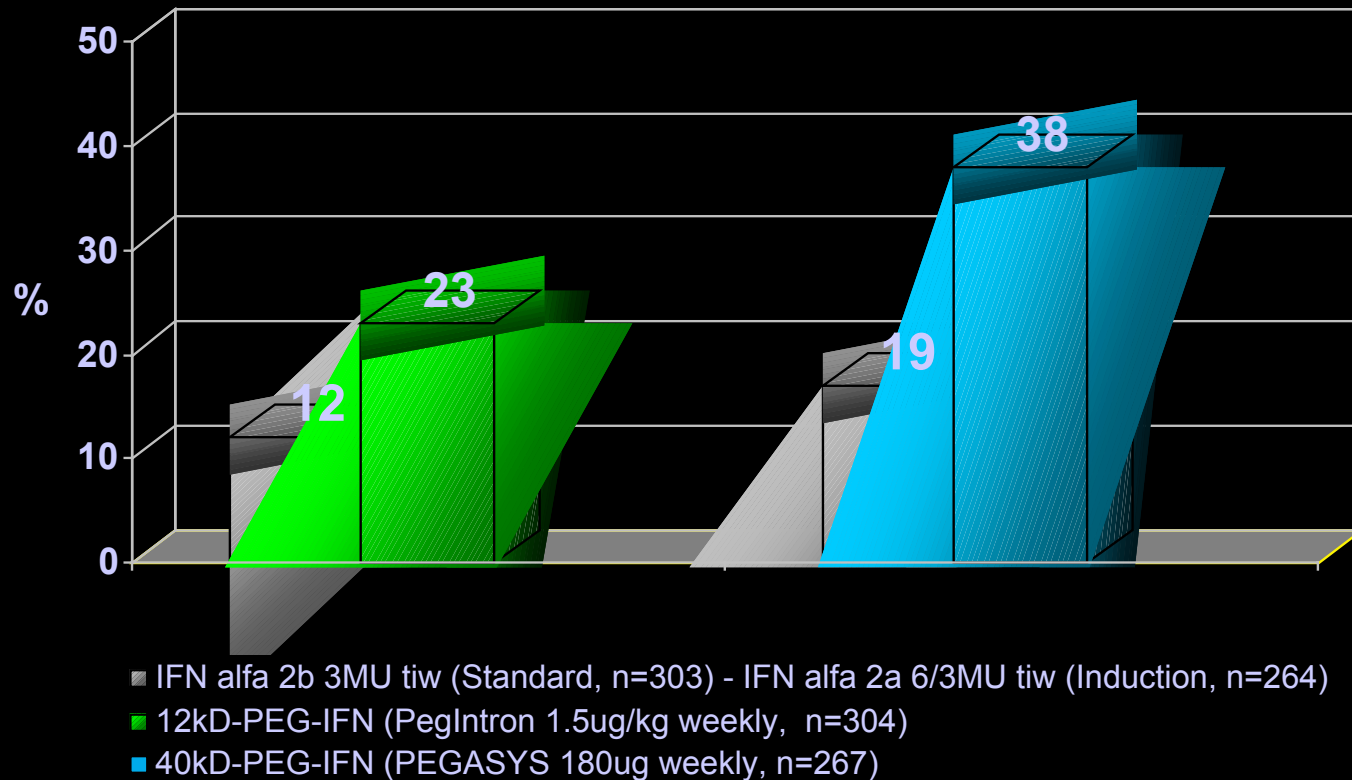


¹ SASL-Study N°10. Hepatology 2002;35:447-454

Chronische Hepatitis C

PEG-Interferone

Interferon alfa alone vs. Pegylated Interferons as initial treatment for chronic hepatitis C ^{1,2}
(Virological SR after 24 weeks)

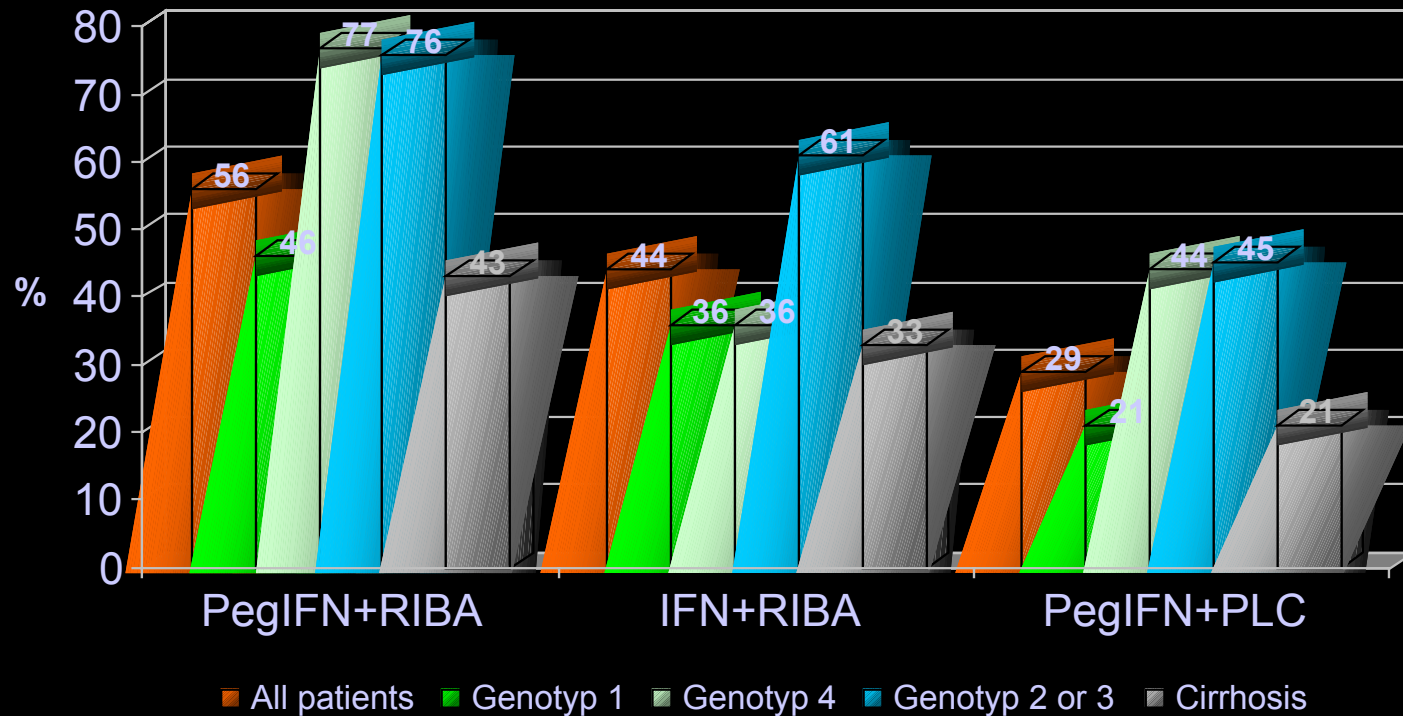


¹ Lindsay et al., Hepatology 2001;34:395-403 ² Zeuzem et al., N Engl J Med 2000;343:1666-72

Chronische Hepatitis C

PegInterferon - Ribavirin

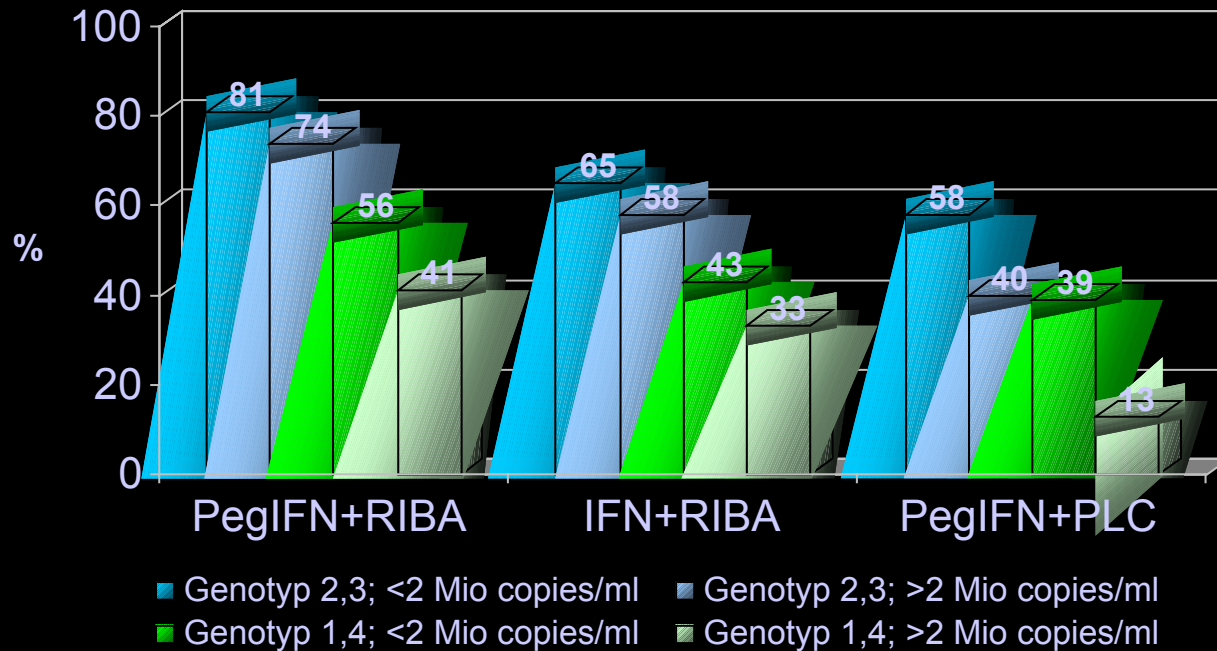
PegInterferon alfa-2a plus ribavirin as initial treatment
(48 weeks) for chronic hepatitis C ¹
(Virological SR depending on genotyp and cirrhosis; n=1121)



¹ Fried M. et al., N Engl J Med 2002;347:975-82.

PegInterferon - Ribavirin

PegInterferon alfa-2a plus ribavirin as initial treatment
(48 weeks) for chronic hepatitis C ¹
(Virological SR depending on genotyp and viral load; n=1121)

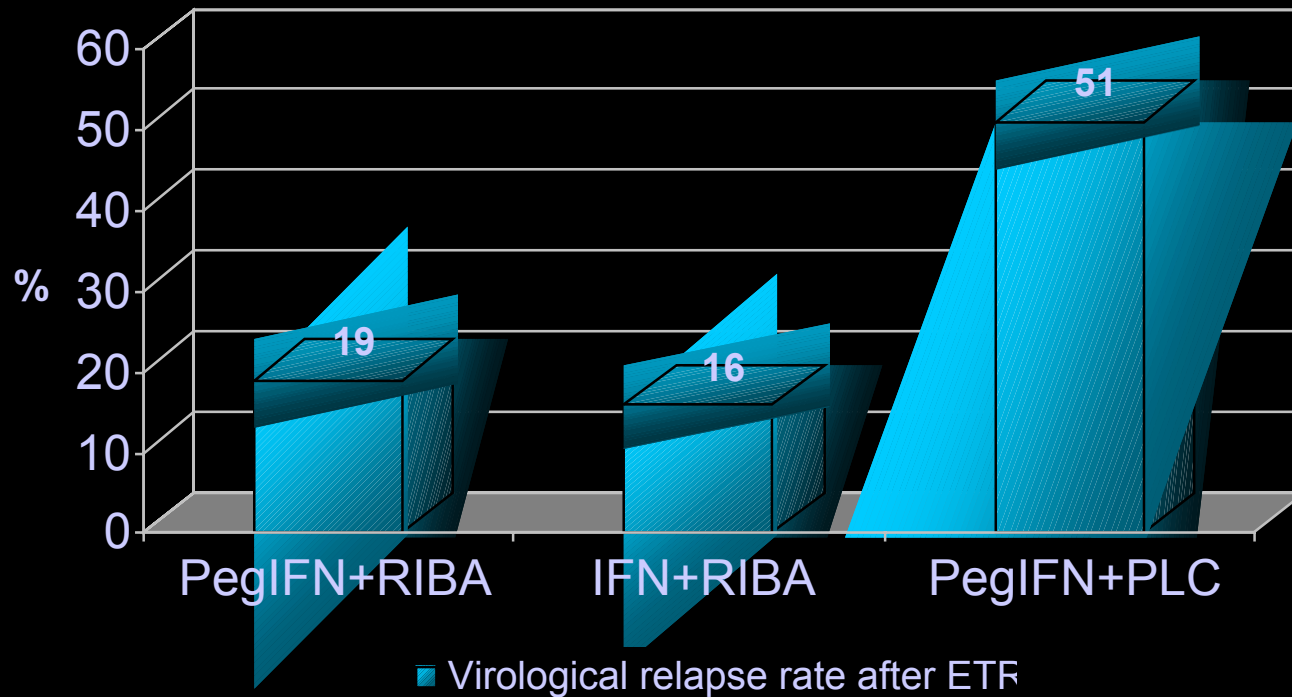


¹ Fried M. et al., N Engl J Med 2002;347:975-82.

Chronische Hepatitis C

PegInterferon - Ribavirin

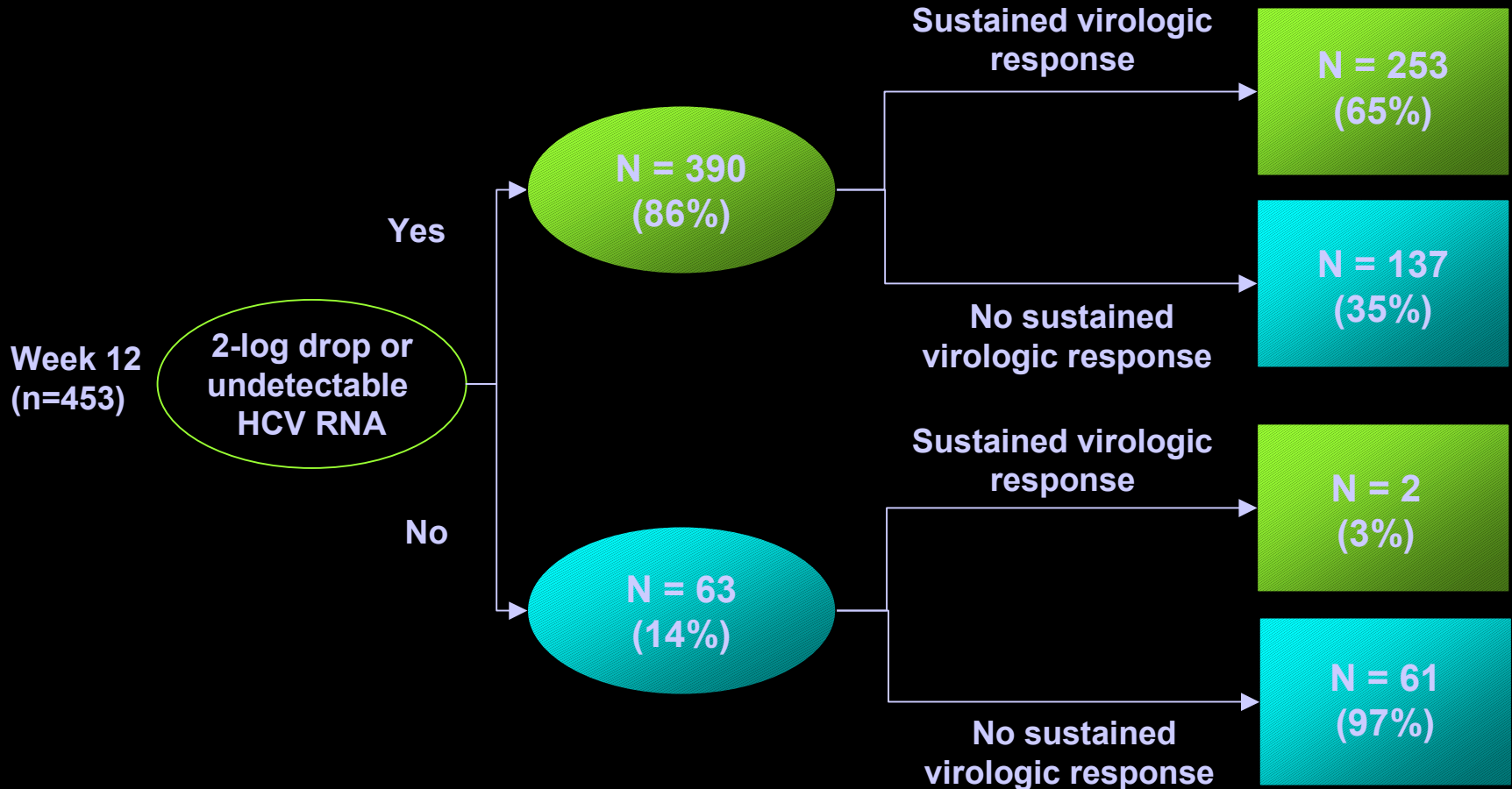
PegInterferon alfa-2a plus ribavirin as initial treatment for chronic hepatitis C
(Virological relapse rate; n=1121)



¹ Fried M. et al., N Engl J Med 2002;347:975-82.

PegInterferon-Therapie

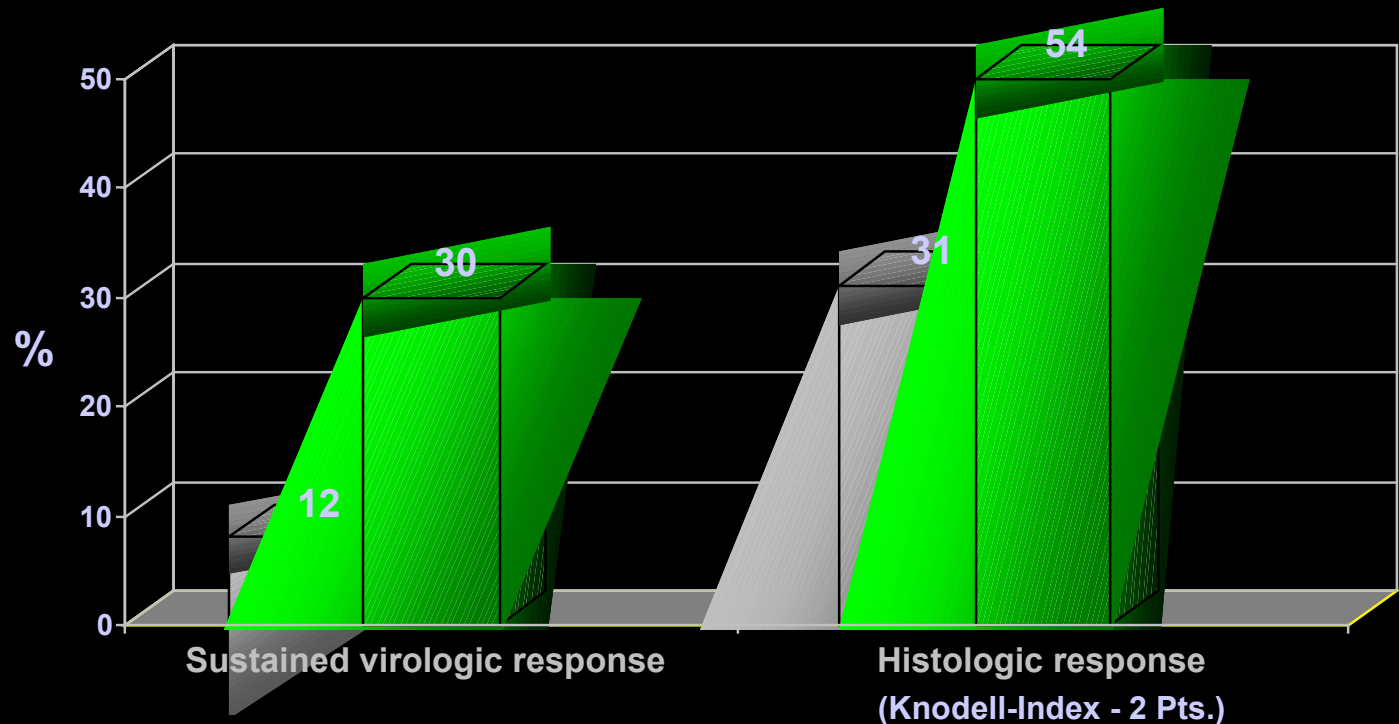
Predictability of sustained virologic response



¹ Fried M. et al., N Engl J Med 2002;347:975-82.

PEG-Interferone

Interferon alfa-2a alone vs. pegylated Interferons as initial treatment for patients with chronic hepatitis C and cirrhosis ¹



■ IFN alfa 2a 3MU tiw (n=88) for 48 W ■ 40kD-PEG-IFN 180ug weekly (N=87) for 48 W

¹ Heathcote J. et al., N Engl J Med 2000;343:1673-80

Aktuelle Therapie

- *Erstbehandlung*

- Genotyp 1 (4)



- PegIFN + 1000-1200mg RIBA
12 Monate

- Genotyp 2,3

- PegIFN + 800mg RIBA
6 Monate

- *Relapse* nach
IFN-Monotherapie

- PegIFN + RIBA analog
Erstbehandlung

- *Non-Responder*

- PegIFN + RIBA+AMA+PHLEBO*