

Aktueller Stand bei der Behandlung der Hepatitis C



- ***individualisiert***

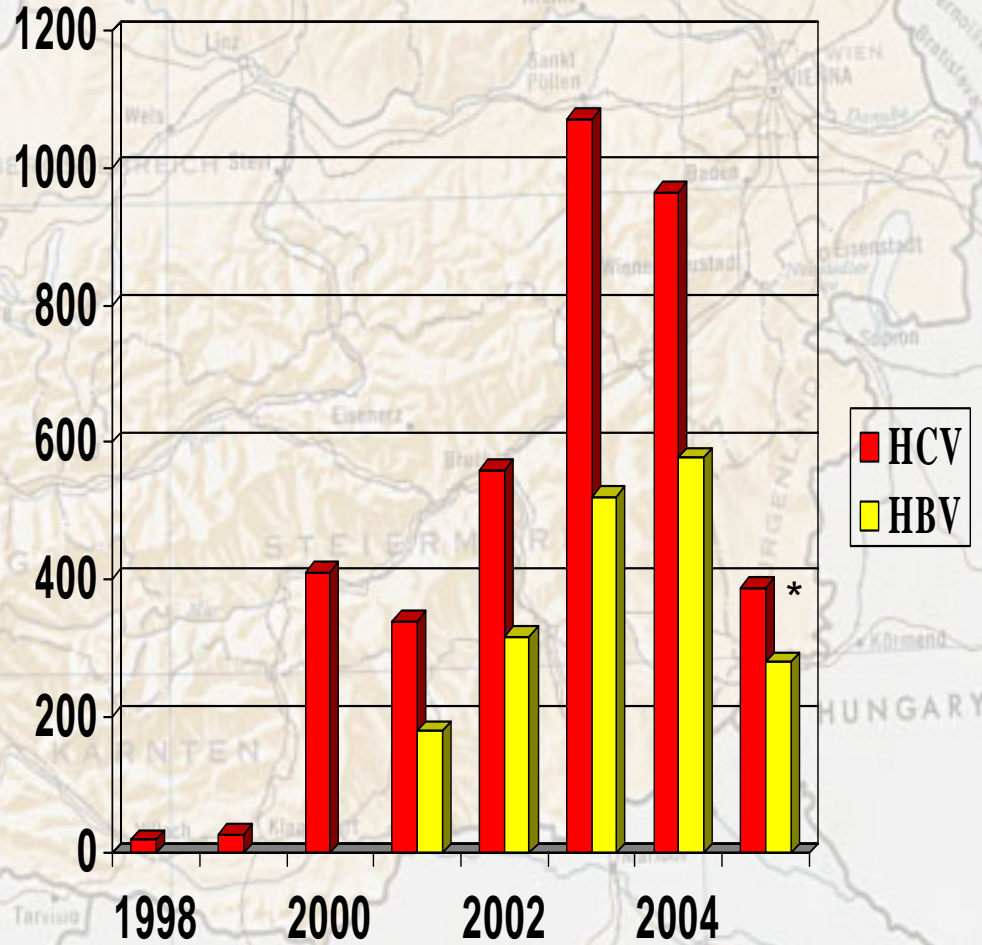
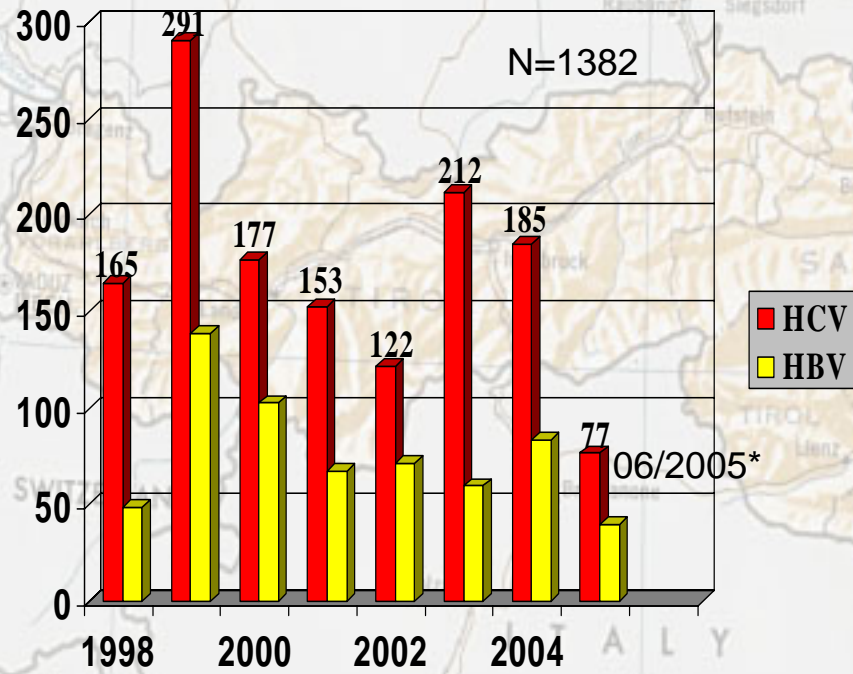
Wolfgang Vogel
Gastroenterologie
Medizin Universität
Innsbruck

Hepatitismeldungen BMFG

Österreich ?

2004		
/100.000	T *	A
B	17	7
C	37	12
Prävalenz 0,5%		?

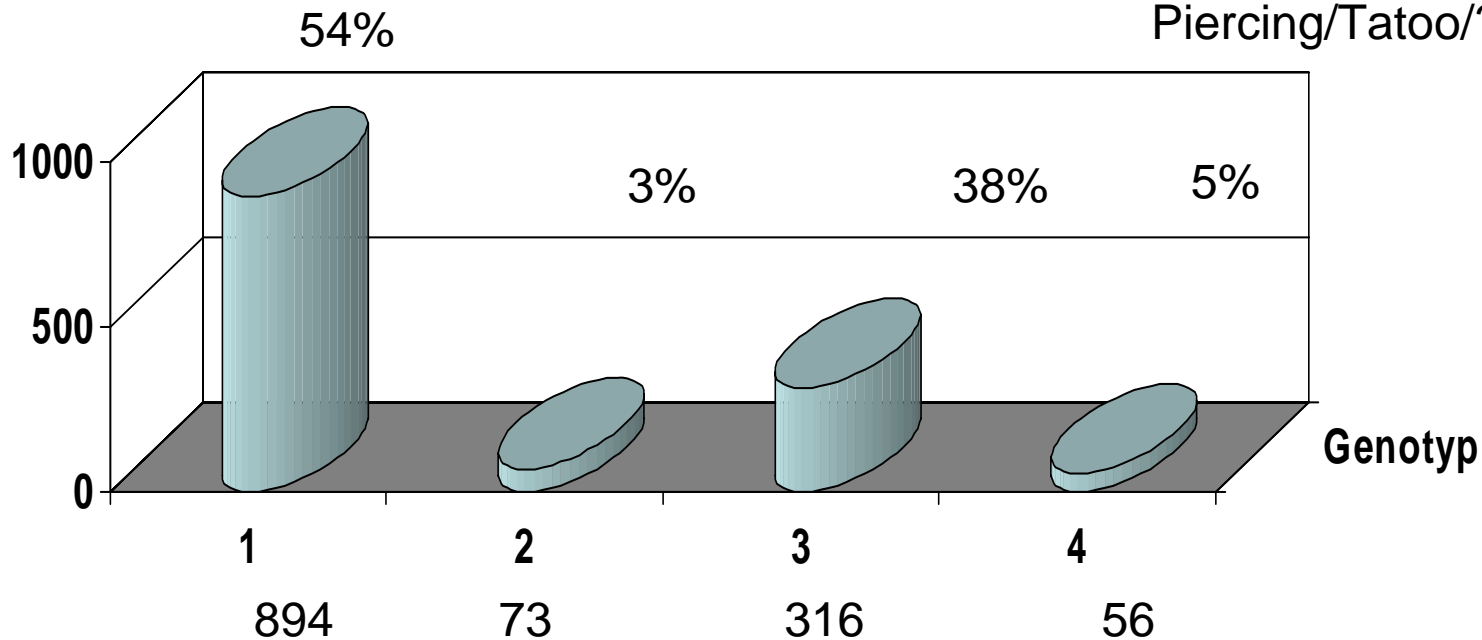
N-Tirol



Epidemiologie

Auswertung 10 2005

N=1341/1709



Alter 47.58 ± 16.26 A
Krankheitsdauer 47.57 ± 10.24 A
Frauen 39%

- Übertragung
 - Transfusion 20% (vor 1992)
 - Unbekannt 30%
 - Drogen 31%
 - Piercing/Tatoo/? 15%

- Andere ? (0 – 5%)
 - Sexuell
 - Perinatal
 - beruflich



Nadelstichverletzungen

Risiko – Prop

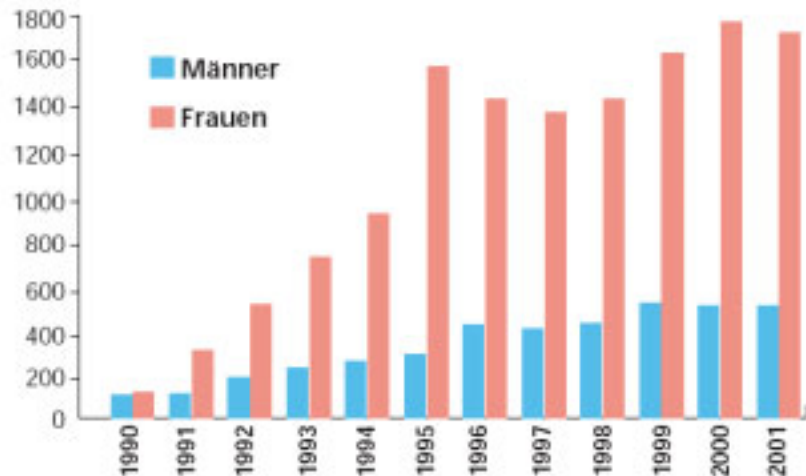
Ausgangsdefinition:

p 4 Wo – RNS

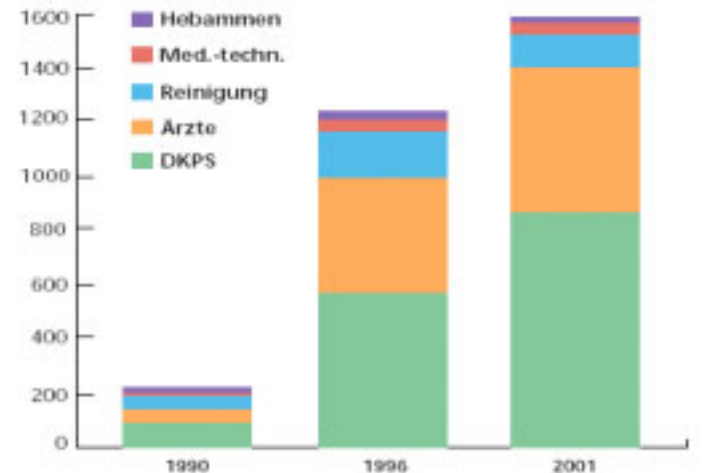
bei ALT(alle 4 Wo) Anstieg

Abschluß nach 6 Monaten

Nadelstichverletzungs-Meldungen
von 1990 bis 2001

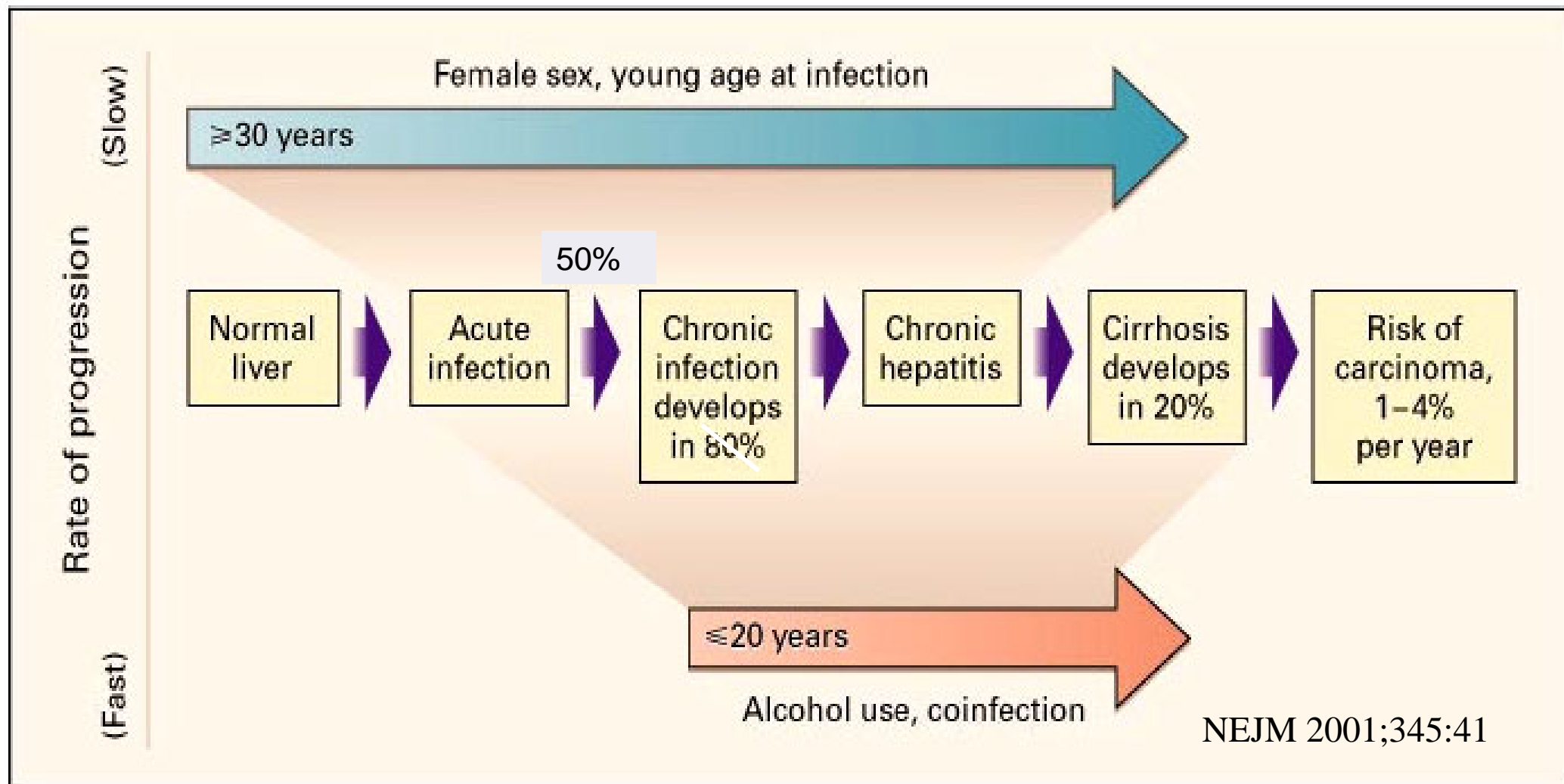


Gemeldete Nadelstichverletzungen
nach Berufen



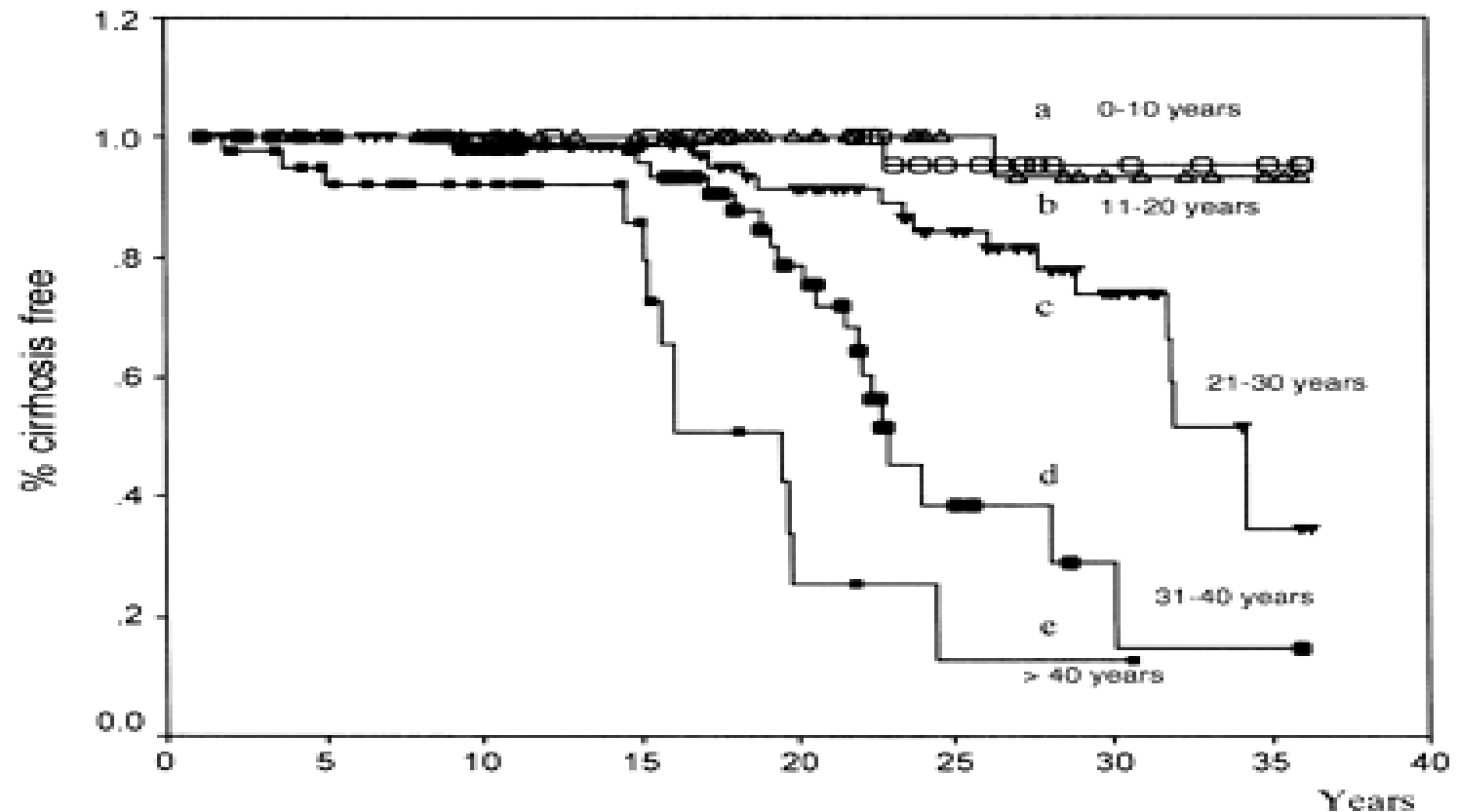
Hepatitis C

Natürlicher Verlauf



Prognosis of transfusion-associated hep C Age at infection

Blood 2002;99:4588

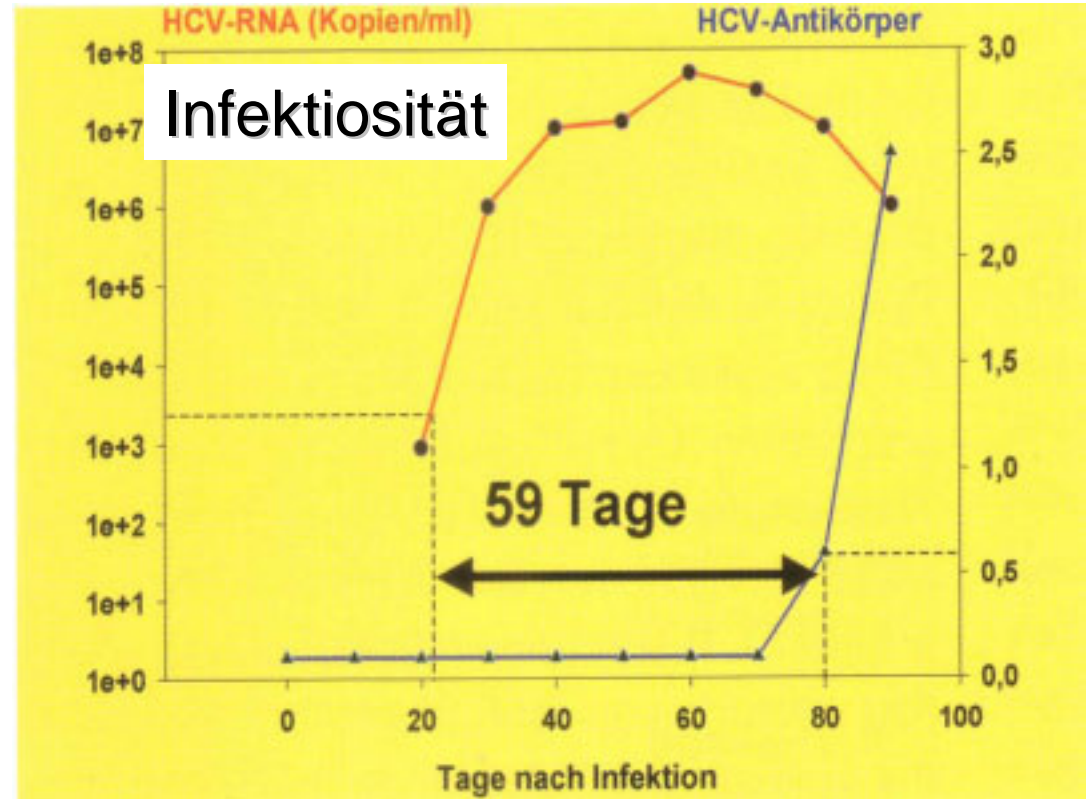
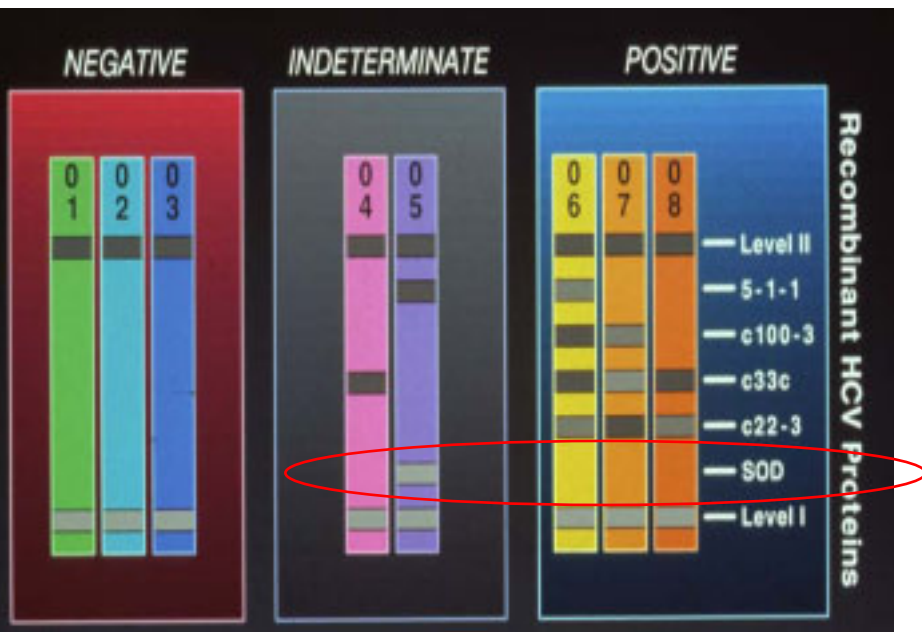


<i>Group</i>					
<i>a</i>	<i>30</i>	<i>30</i>	<i>24 (1)</i>	<i>12</i>	<i>4</i>
<i>b</i>	<i>47</i>	<i>41</i>	<i>25 (1)</i>	<i>10 (1)</i>	<i>3</i>
<i>c</i>	<i>89</i>	<i>76 (5)</i>	<i>46 (6)</i>	<i>16(6)</i>	<i>13</i>
<i>d</i>	<i>59 (1)</i>	<i>48 (8)</i>	<i>25 (10)</i>	<i>2 (2)</i>	<i>-</i>
<i>e</i>	<i>43 (3)</i>	<i>25 (9)</i>	<i>4 (1)</i>	<i>1</i>	<i>1</i>

anti -HCV

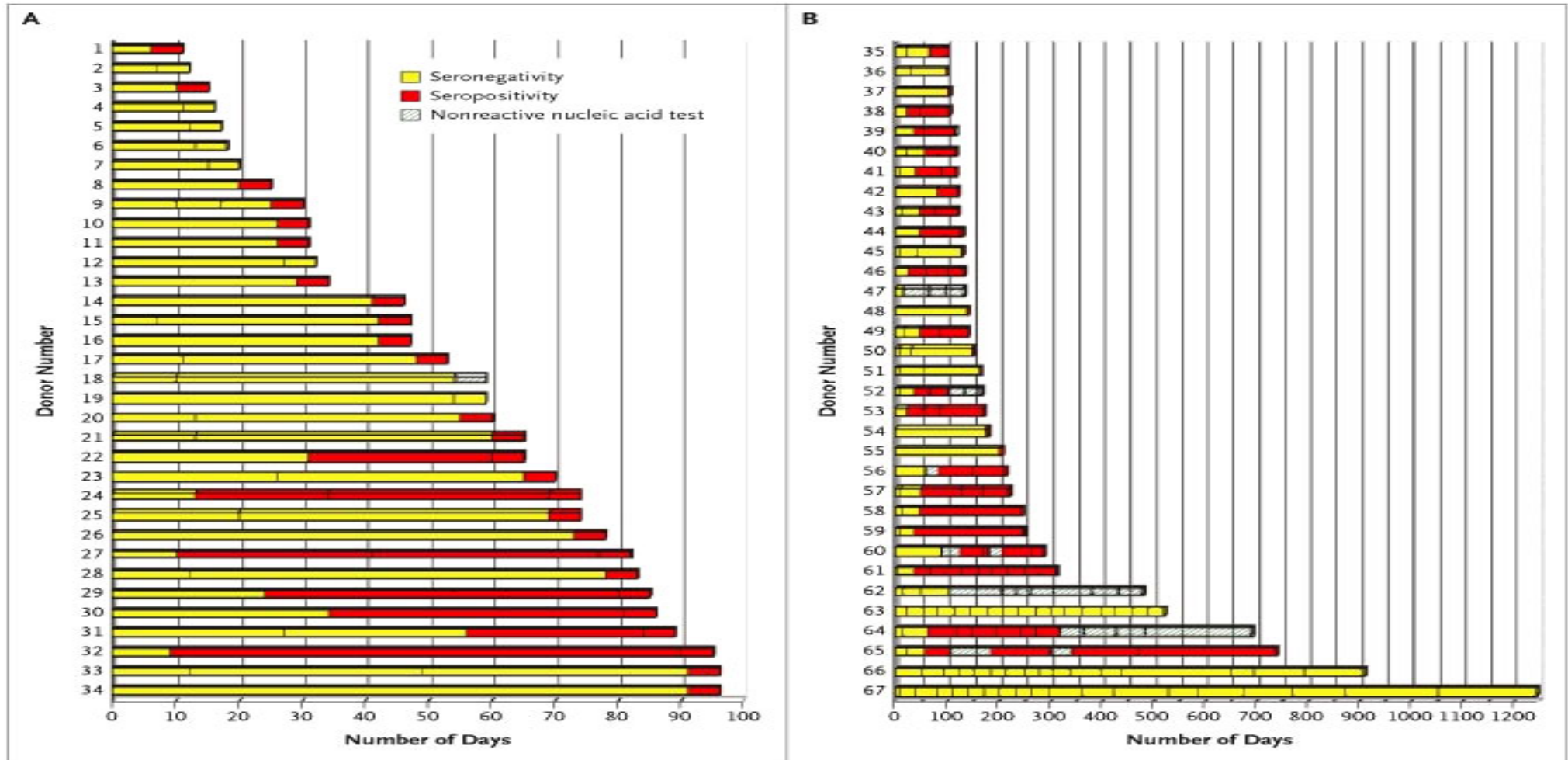
ELISA Gen. 3: Sen./Spez. >90%

RIBA 1,2,3: Bestätigung der Spezifität der AK

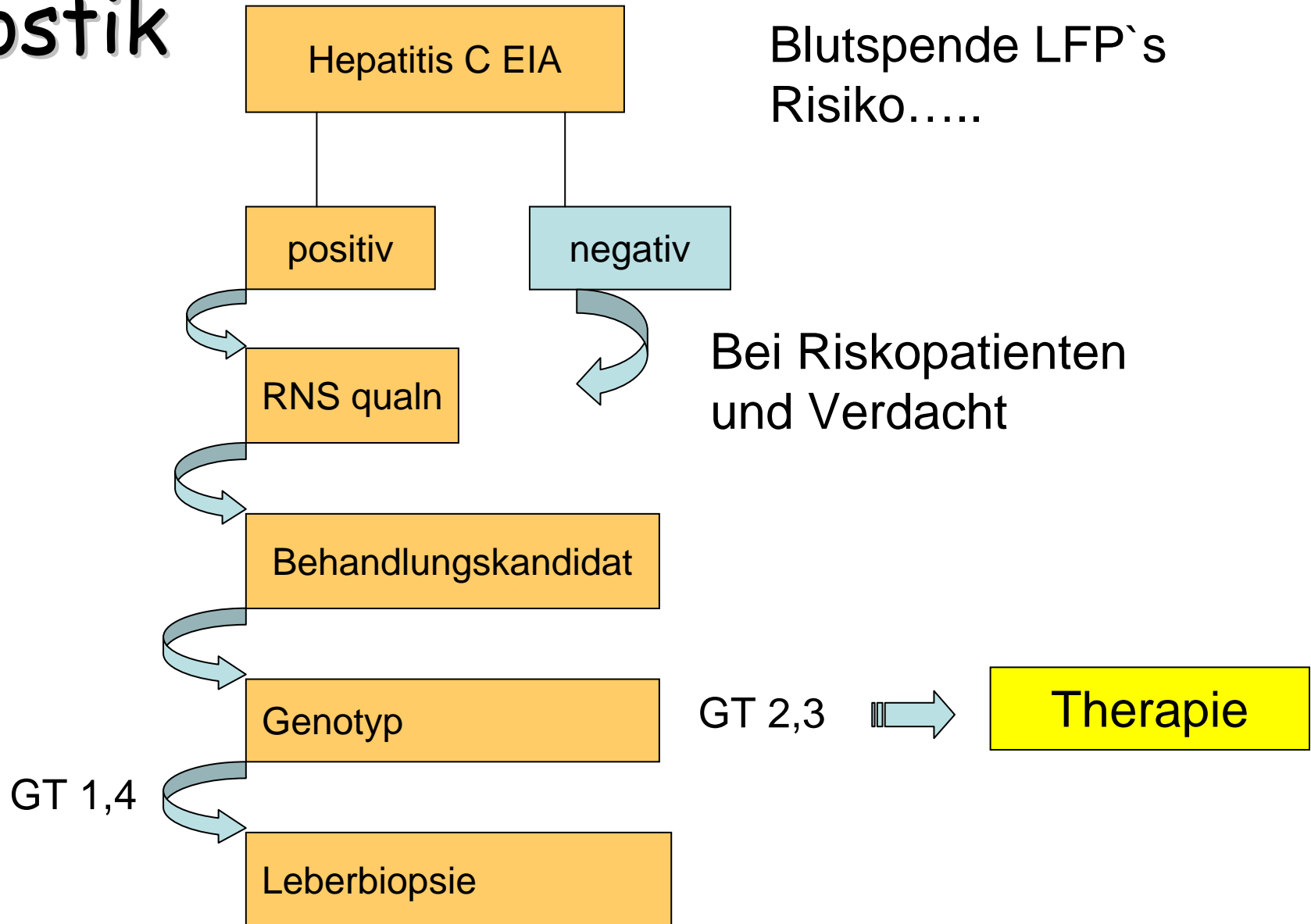


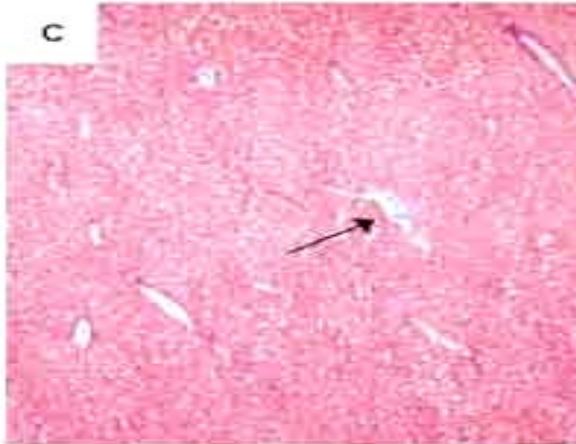
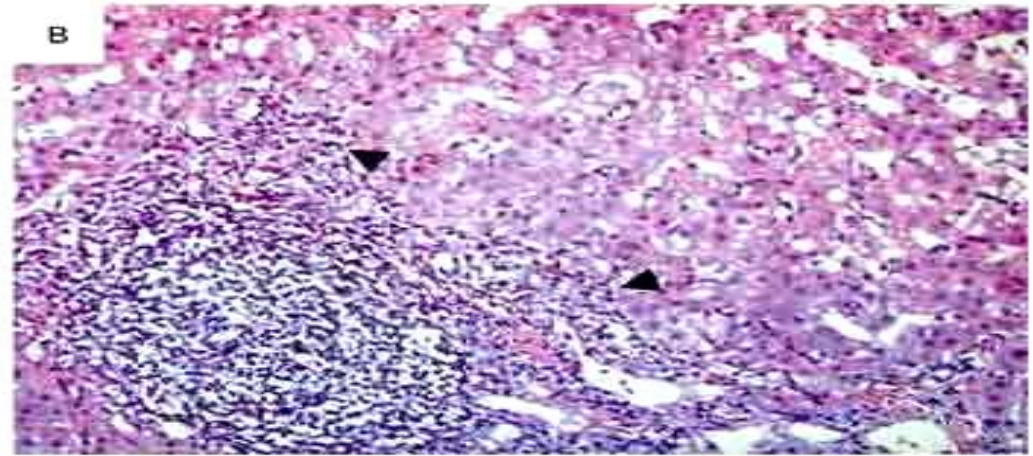
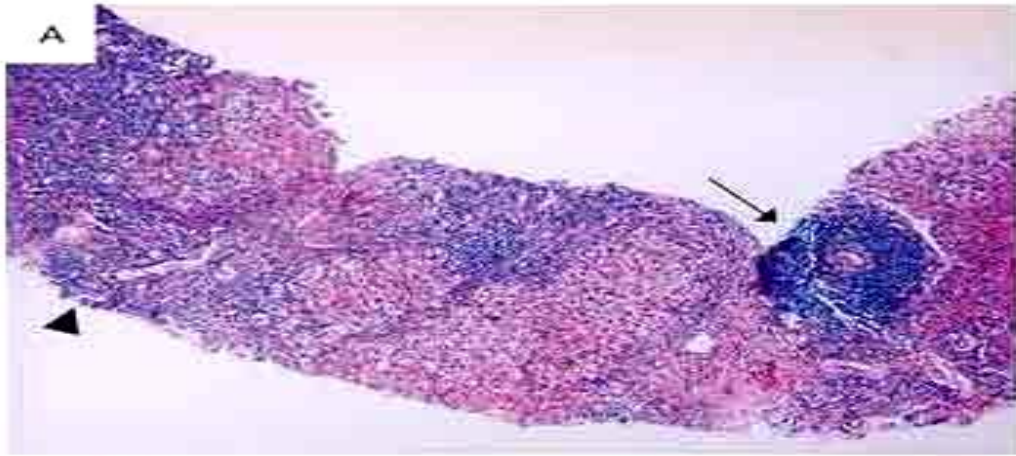
..... nicht zur Bestätigung der Infektiosität

Follow-up Results for 67 HCV RNA-Positive, HCV Antibody-Nonreactive Donors



Diagnostik





Nicht mehr notwendig
Stadium Aktivität Ko-Morbidität
Regredienz

Überraschung 2%

Morbidität 20-30%

Blutung 0,12 -0,24%

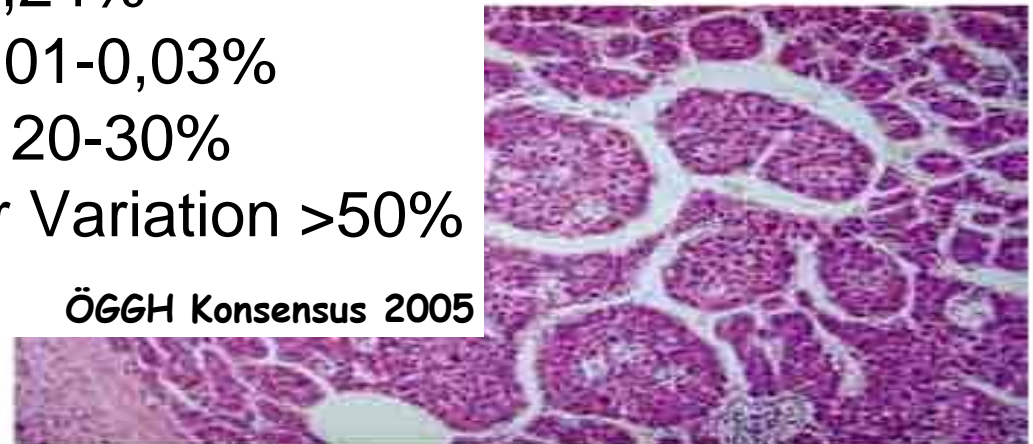
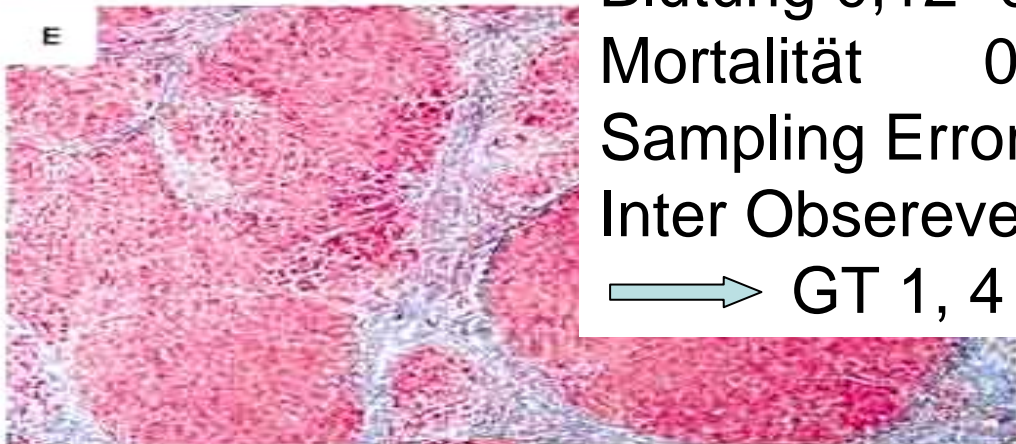
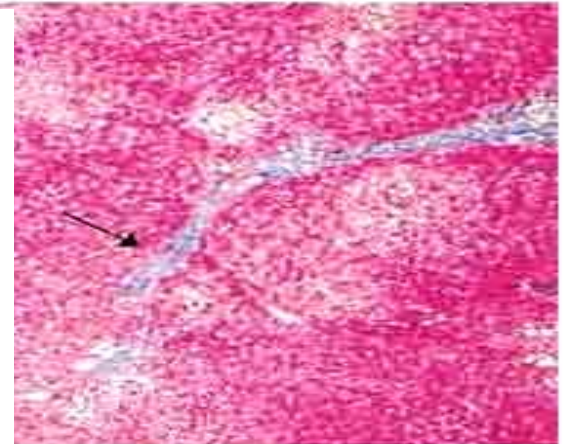
Mortalität 0,01-0,03%

Sampling Error 20-30%

Inter Observer Variation >50%

→ GT 1, 4

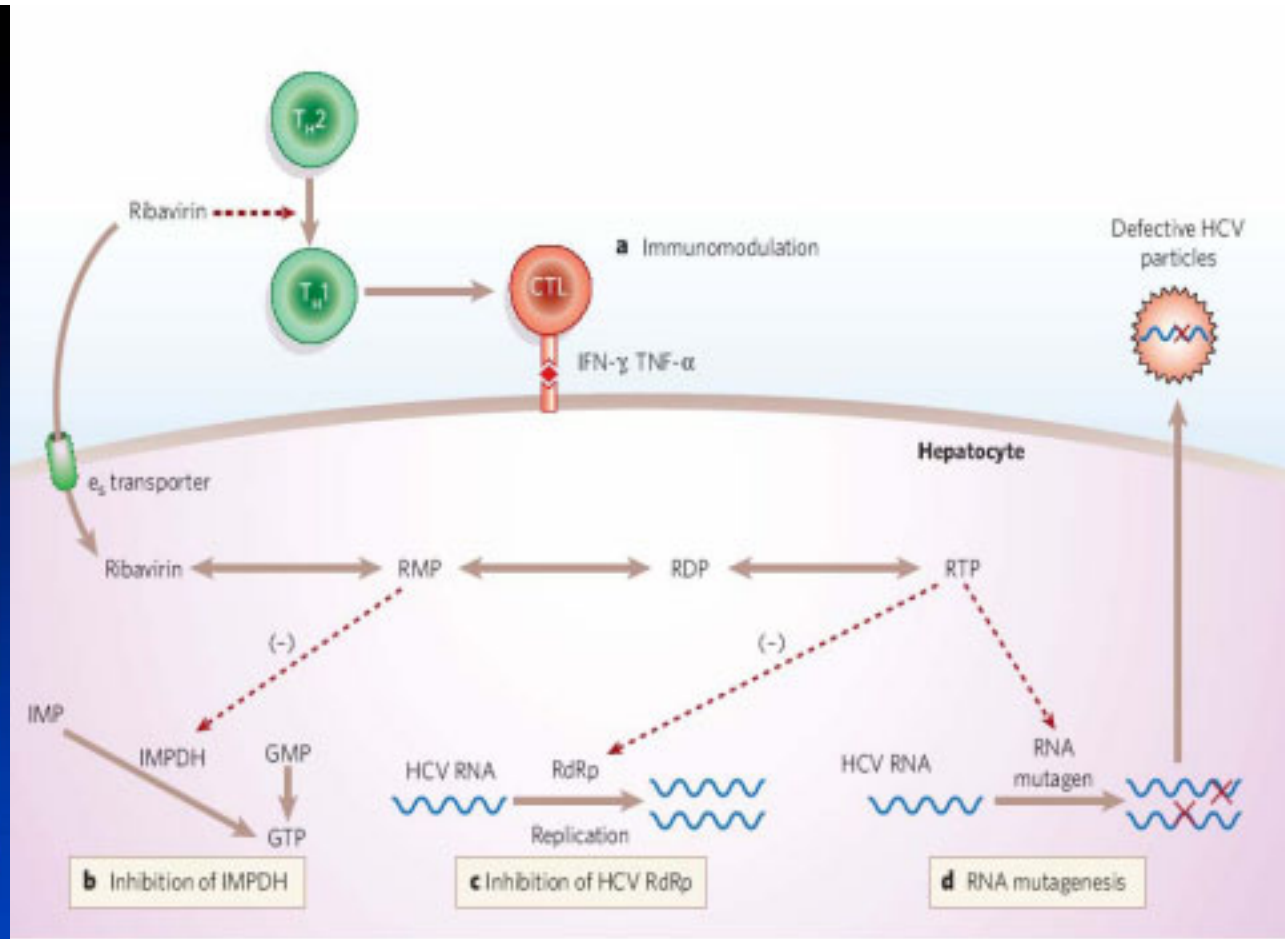
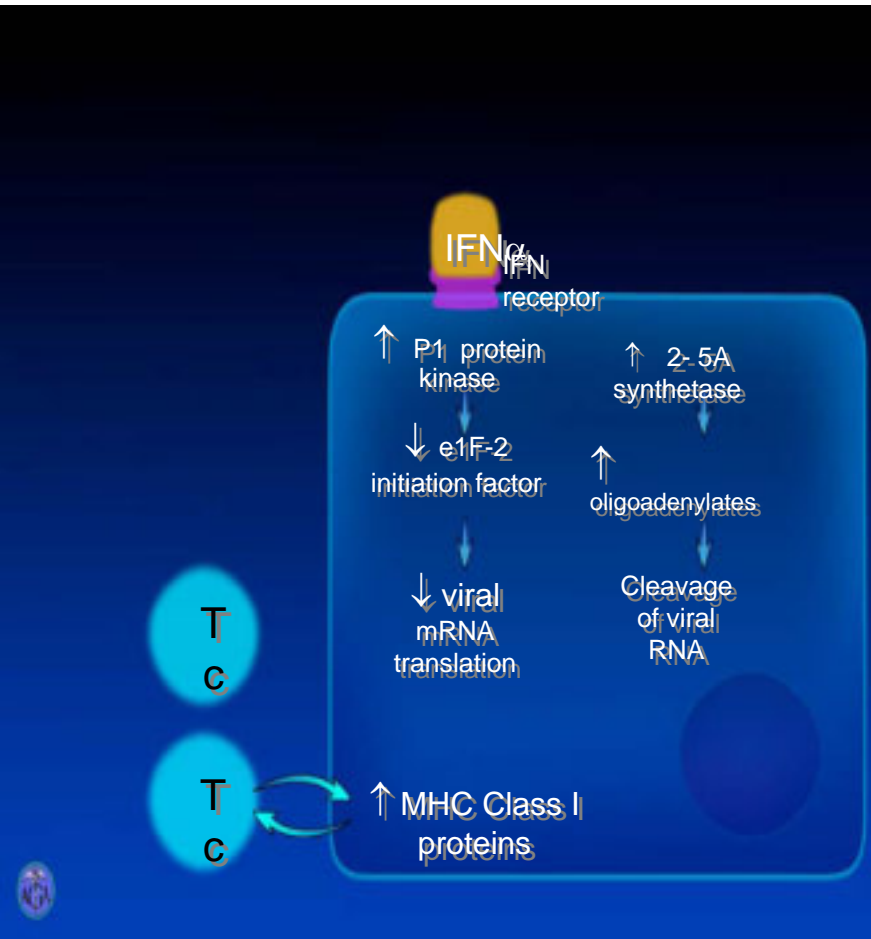
ÖGGH Konsensus 2005



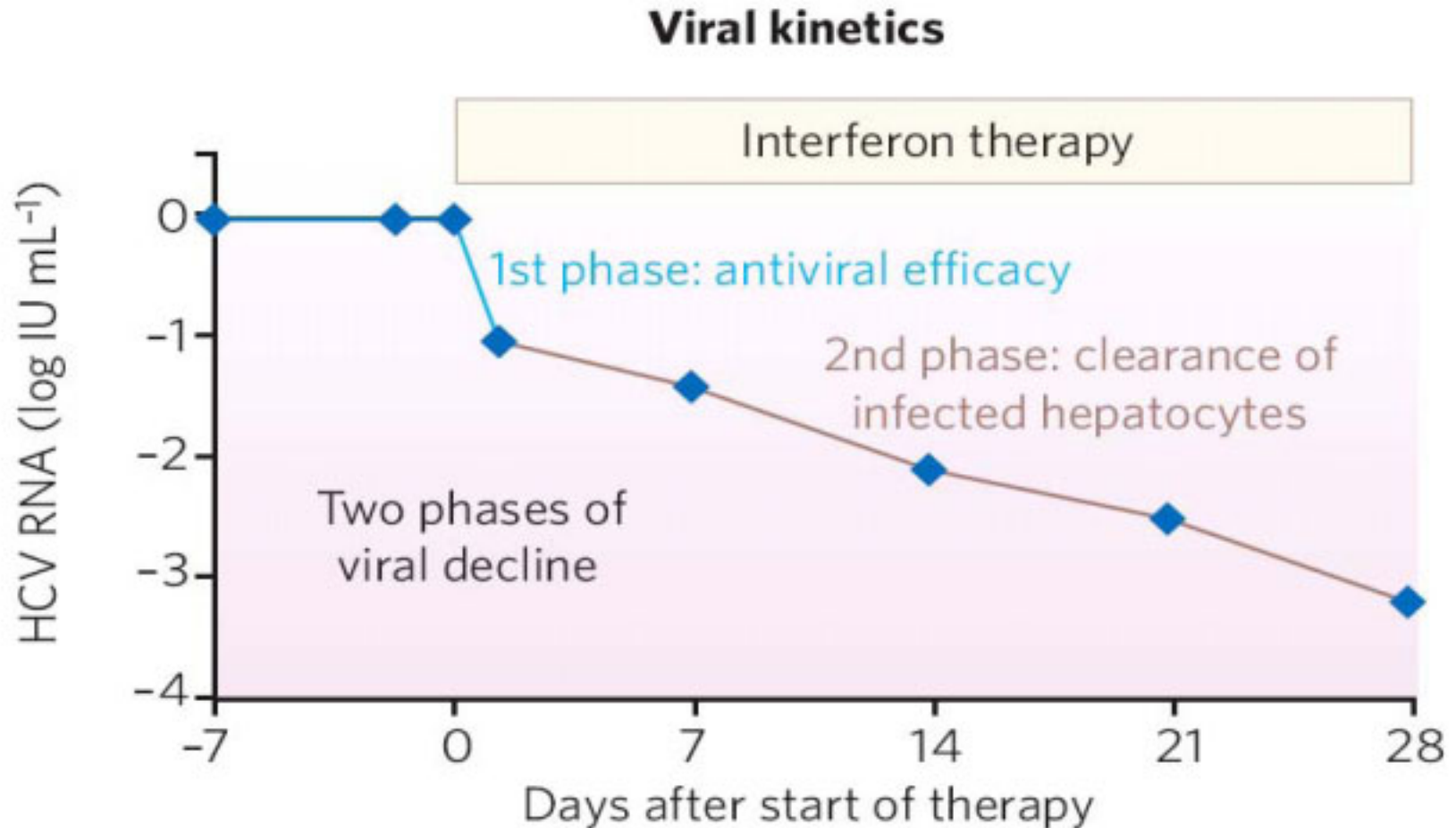
Antiviraler Effekt

Interferon

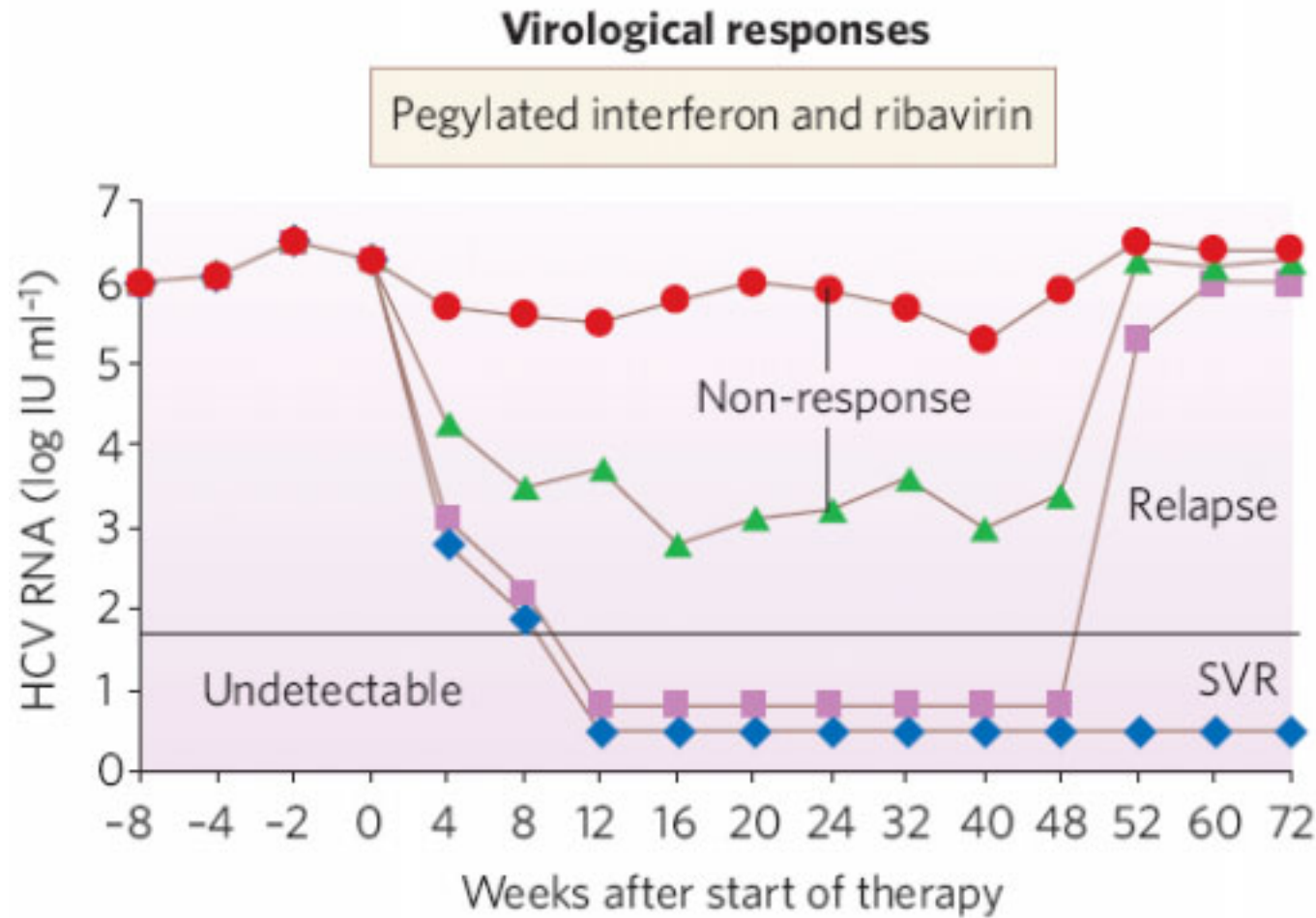
Ribavirin



Viruskinetik unter Therapie



Jordan J. Feld¹ and Jay H. Hoofnagle²



Therapieziel

EVR >2log W4,
W12, W24

ETR DNS negativ

SVR DNS negativ
6 Monate p. Th.

Box 1 | Factors that influence therapy

Factors correlated with a sustained response to combination therapy with pegylated interferon and ribavirin in hepatitis C.

Viral factors

Genotypes 2 and 3 (versus genotype 1)

Lower viral levels

Greater quasispecies diversity

Acute versus chronic infection

Host factors

Female sex

Younger age

Less fibrosis

Lower body weight and body mass index

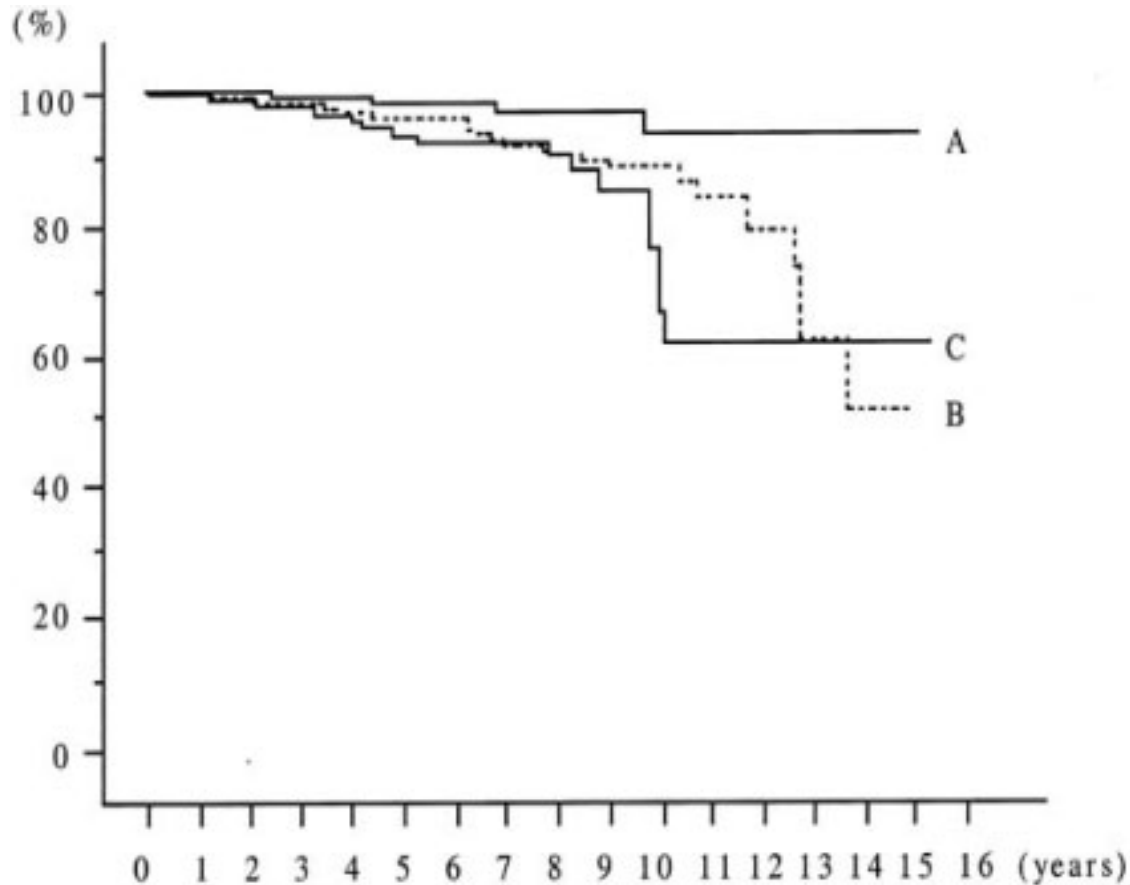
Non-African-American race

Absence of significant co-morbidities

(alcohol abuse, renal disease, HIV infection)

Therapieziel

HCV – Interferon Therapie: kumulative Überlebensraten



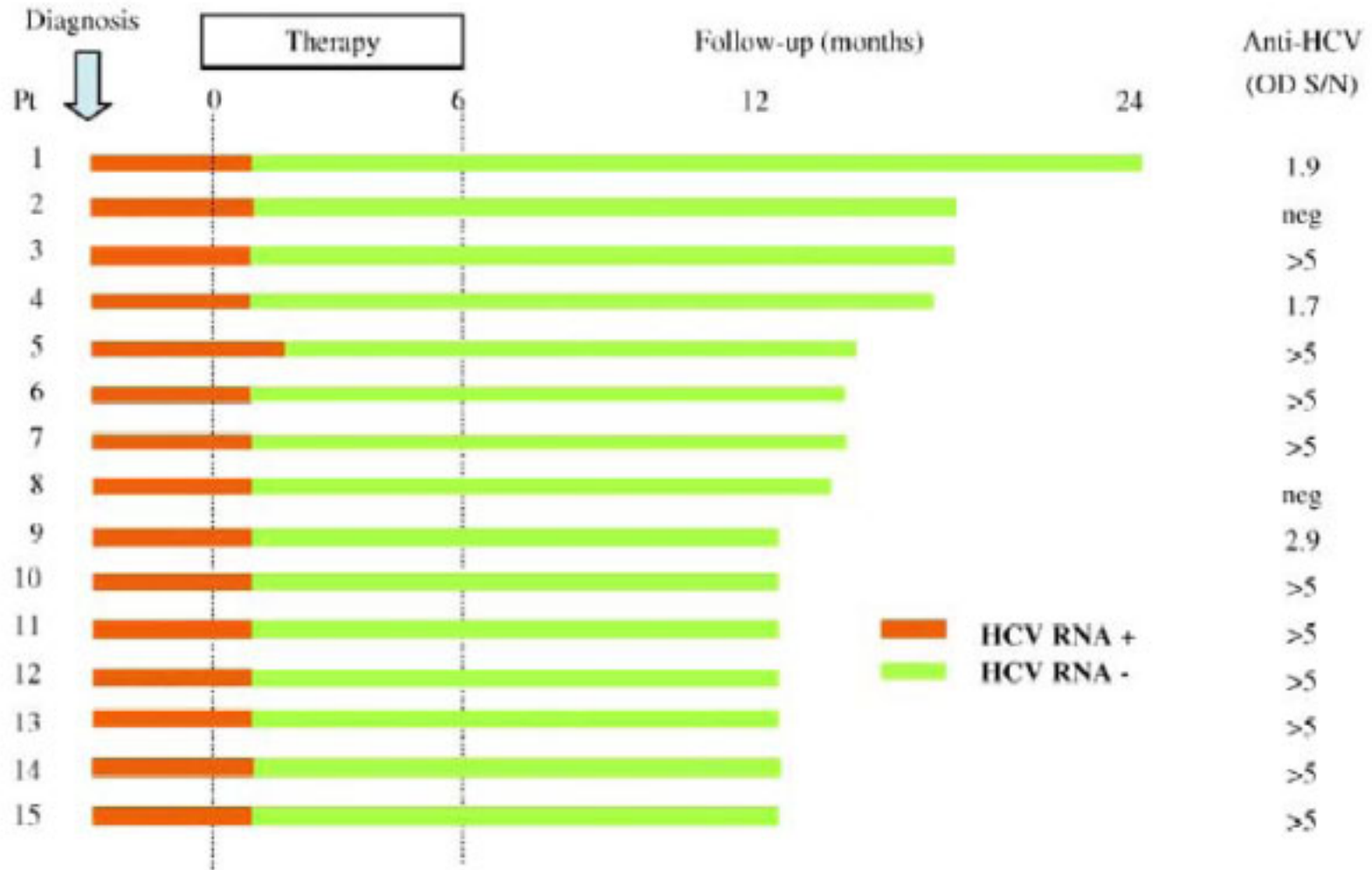
A SVR: 116
B N-Responder: 239
C unbehandelt: 104

*Heilung ist kein Schutz
vor neuerlicher Infektion*

PEG - IFN-2b akute Hepatitis C

Nach 3-monatiger Virämie
1.5 ug/kg x 6 Monate

T. Santantonio et al. / Journal of Hepatology 42 (2005) 329–333



Akute Hepatitis C

Beobachtung !

Therapiedauer ?

asymptomatic patients n= 68 GT 1 + 4

spontaneous clearance n=7

treatment begin at wks 8 (A), 12 (B), 20 (C)

12 wks of treatment

IFN 3 MIU TIW

RBV 10.6 mg/kg

PEG-2b 1.5 ug/kg

	Group A N= 21		Group B N=20		Group C N=20	
	IFN+RBV N=11	PEG N=10	IFN+RBV N=10	PEG N=10	IFN+RBV N=10	PEG N=10
VR W12	7 (63%)	9 (90%)	6 (60%)	10 (100%)	6 (60%)	8 (80%)
VR W24	8 (81%)	10 (100%)	8 (80%)	10 (100%)	7 (70%)	9 (90%)
SVR	7 (63%)	9 (90%)	7 (70%)	9 (90%)	6 (60%)	8 (80%)

HCV Therapie - Dosierungsschema

- GT1,4

PEG-IFN 180ug / 1.5ug/kg

Ribavirin <75 kg KGW: 1g/d
 < 65 0.8g
 < 85 kg 1.0g
 > 85 1.2g

X 48 Wochen

- GT 2,3

PEG-IFN 180ug / 1.5ug/kg

Ribavirin 0.8 g / d

X 12 - 24 Wochen

Bei Zirrhose x 48 Wochen

HCV Therapie Kontraindikationen

Andrew I. Kim, MD,^a Sammy Saab, MD, MPH^b

Table 3 Absolute contraindications to hepatitis C therapy

Active psychiatric illnesses, such as major depression, schizophrenia, or bipolar disorder that is not controlled
Having undergone renal, heart, or lung transplant
Comorbid conditions known to be exacerbated by interferon and ribavirin therapy, such as autoimmune hepatitis
Untreated hyperthyroidism
Severe concurrent disease such as severe hypertension, heart failure, considerable coronary artery disease, poorly controlled diabetes mellitus, severe chronic obstructive pulmonary disease
Known hypersensitivity to drugs used to treat hepatitis C
Pregnancy
Breast feeding
Inability to practice birth control

Data adapted from National Institutes of Health²⁶ and Strader et al.²⁷

The American Journal of Medicine (2005) 118, 808-815

HCV Therapie Nebenwirkungen

Andrew I. Kim, MD,^a Sammy Saab, MD, MPH^b

Selected common adverse effects reported with interferon and ribavirin*

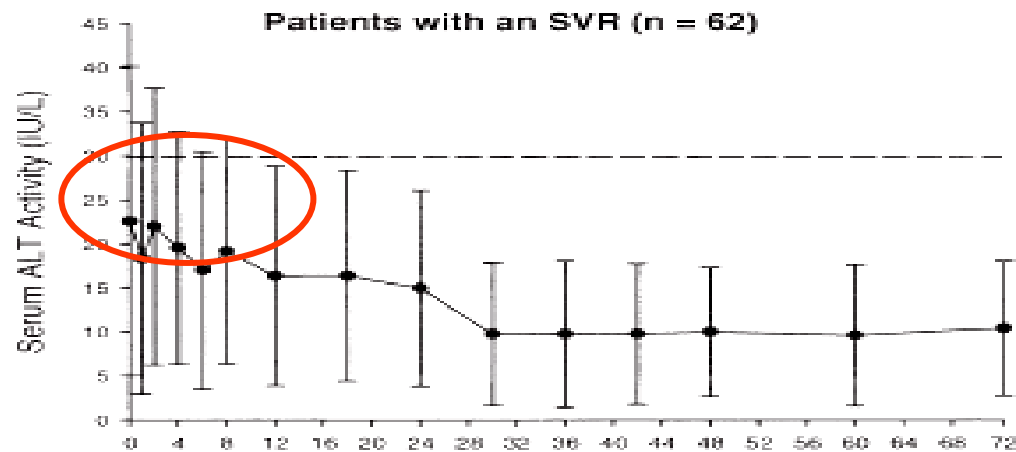
Clinical adverse effect	Frequency of adverse effects (%)	
	Interferon and ribavirin	Peginterferon and ribavirin
Fatigue	55-60	47-64
Fever	33-56	39-46
Headache	52-58	47-62
Myalgia	50	42-56
Arthralgia	28	24-34
Nausea	33	29-43
Cough	13	15-17
Dyspnea	24	23-26
Alopecia	32-34	21-36
Injection site reaction	36	58-59

Adapted from pivotal trials by Manns et al,²⁴ Fried et al,²⁵ and the National Institutes of Health.²⁶

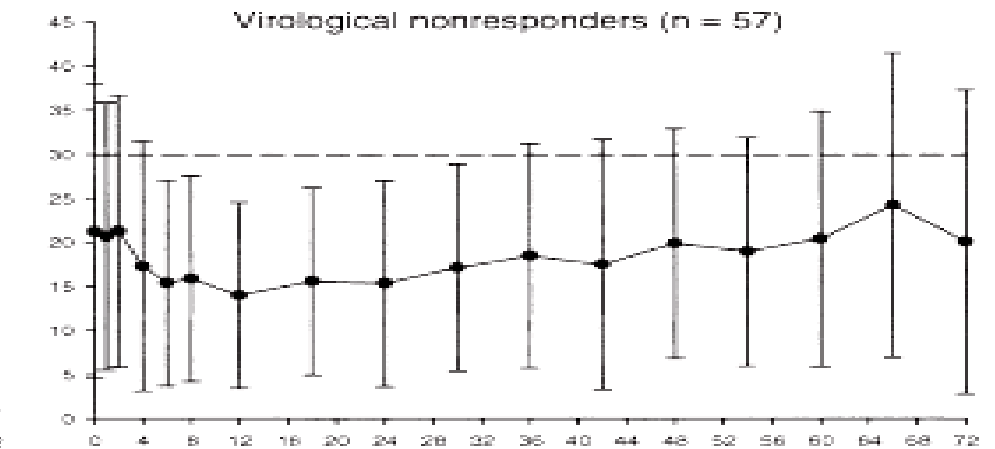
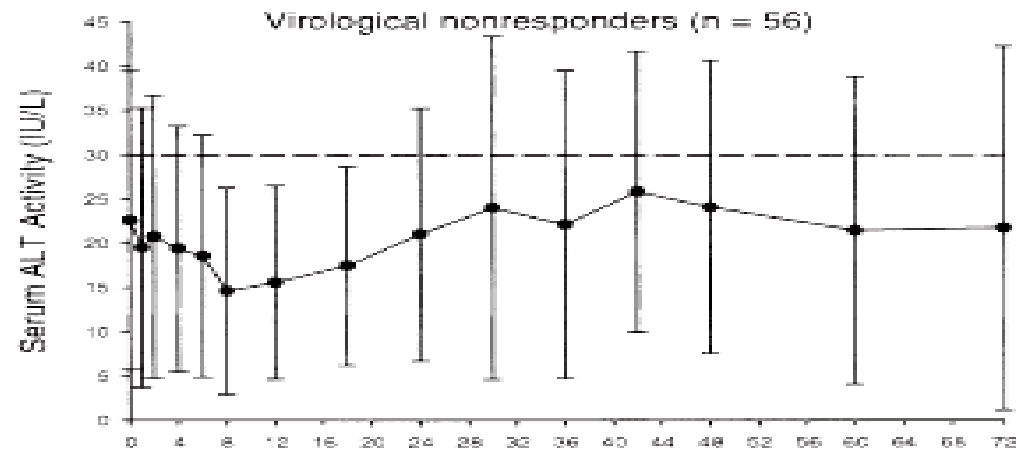
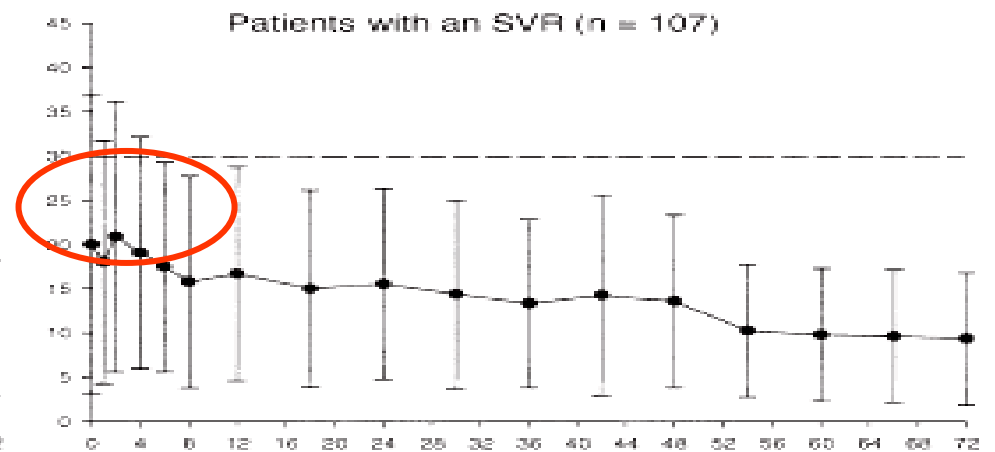
IFN-Therapie bei Patienten mit normalen Transaminasen „Normalisierung“ normaler Transaminasen

Zeuzem St Gastro 2004;127:1724

Group A (24 weeks)



Group B (48 weeks)



HCV -PNALT SVR mit PEG-IFN/ Riba

PEG-IFN α 2a (40 KD) 180 μ g/weekly +
Ribavirin 800 mg/daily

×24 weeks
(212 cases)

×48 weeks
(210 cases)

	×24 weeks (212 cases)	×48 weeks (210 cases)	
All patients	63/212 (30%)	109/210 (52%)	
<i>HCV-1</i>			
All cases	19/144 (13%)	57/141 (40%) ¹	$P = <0.001$
LVL	14/87 (16%)	42/89 (47%)	
HVL	5/55 (9%)	14/51 (27%)	
<i>HCV-2/3</i>			
All cases	42/58 (72%)	46/59 (78%) ²	$P = 0.452$
LVL	24/30 (80%)	25/31 (81%)	
HVL	18/28 (64%)	21/28 (75%)	
<i>HCV-4</i>			
All cases	1/8 (13%)	5/9 (56%)	
LVL	1/6 (17%)	4/6 (67%)	
HVL	0/2 (0%)	1/3 (33%)	

HVL > 800.000 IU/ML

St. Zeuzem et al.
Gastro 2004;127:1724

LVR, low viral load. HVR, high viral load.

EVR - Steuerung der Therapie

Genotyp 1,4

Genotyp 2,3

PEG-IFN + Ribavirin

Nach 12 Wochen 2-log Abfall
oder PCR negativ

Nach 4 Wochen 2-log Abfall
oder PCR negativ

Ja

Nein

12 Monate Therapie

65% - 72%

0% - 3%

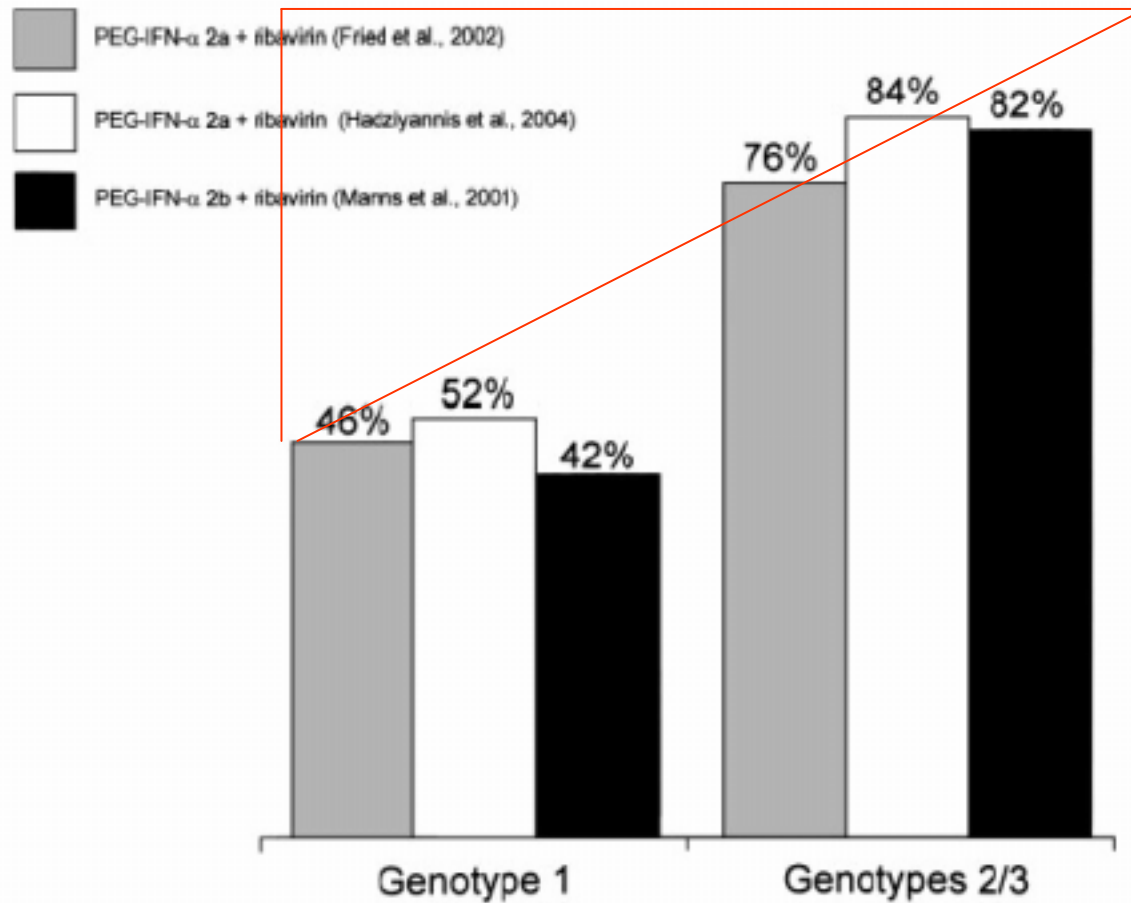
GT 2
GT3 <800.000

3 Monate Tx
93% - 100%

GT3 >800.000

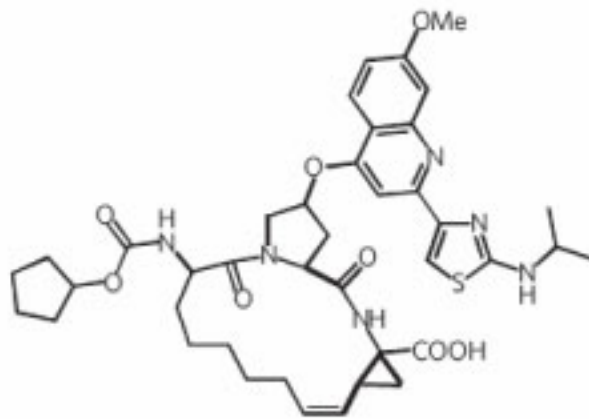
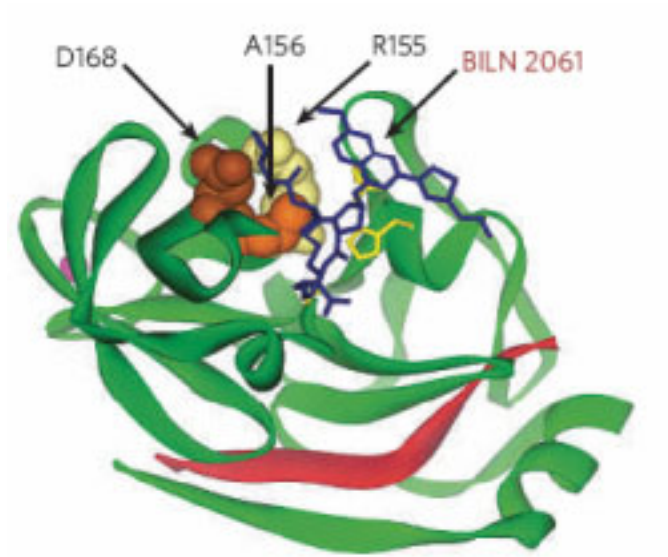
6 Monate Tx
54% - 67%

Non-Responder ?

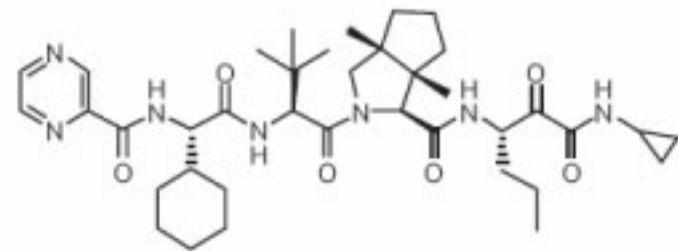


Raffaele De Francesco¹ and Giovanni Migliaccio¹

NS3 Serine Protease



BILN 2061



VX-950

NS3 Protease Inhibitor in patients with chronic hepatitis C

Nature October 26, 2003;

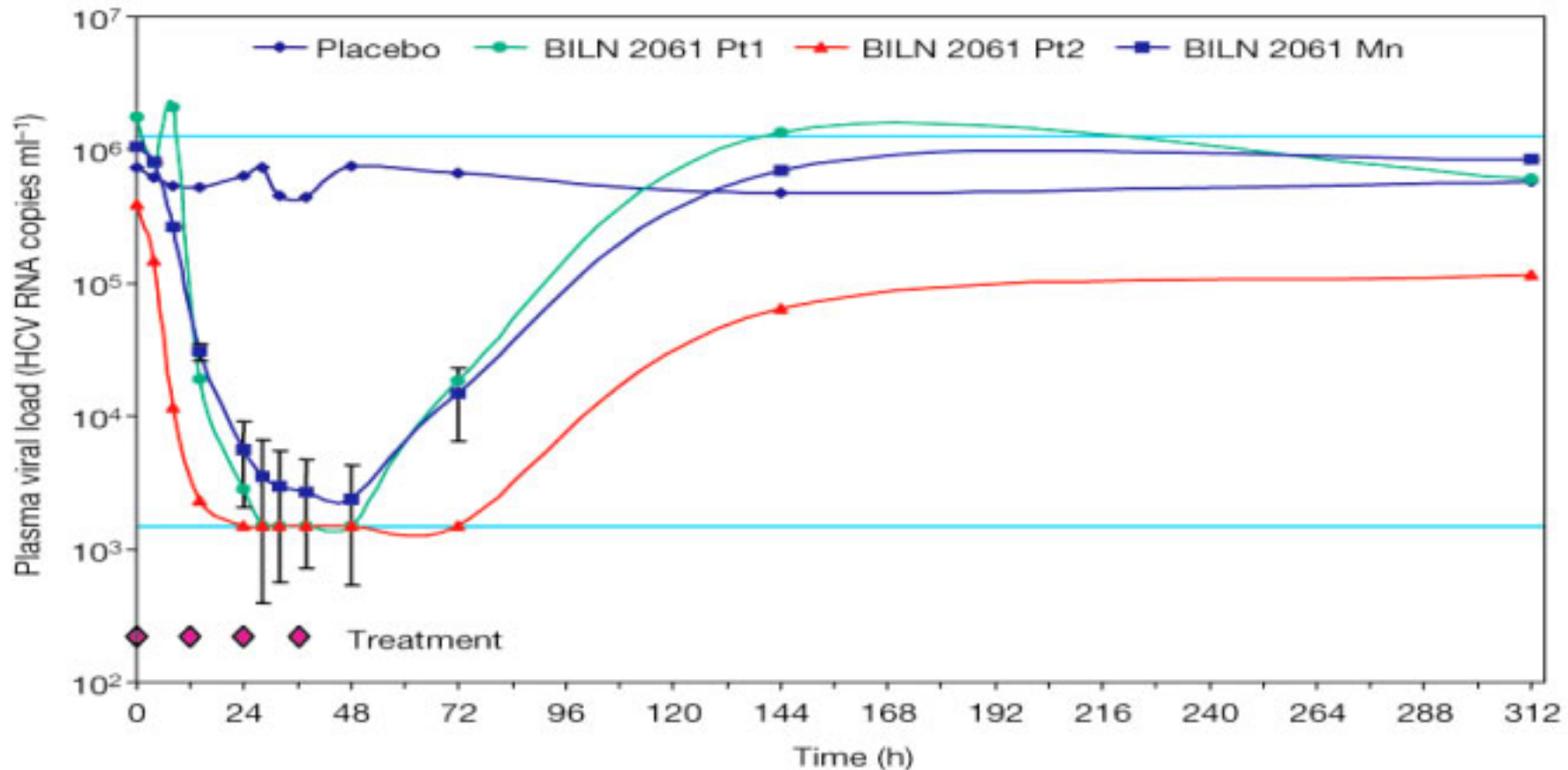
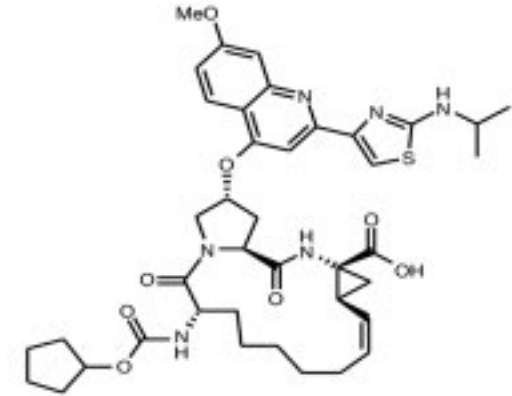




Table 1 | A sample of the drug pipeline for hepatitis C

a HCV-targeted drugs

Compound name(s)	Company	Clinical phase	Target	Mechanism of action
BILN 2061 (Ciluprevir)	Boehringer-Ingelheim	Phase II*	NS3-4A protease	Product-derived serine protease inhibitor
VX-950	Vertex/Mitsubishi	Phase Ib	NS3-4A protease	Serine protease reversible covalent inhibitor
NM283 (Valopicitabine)	Idenix/Novartis	Phase II	NS5B polymerase	Nucleoside analogue (chain terminator)
JTK-103	Japan Tobacco	Phase II	NS5B polymerase	Non-nucleoside allosteric inhibitor
HCV-796	ViroPharma/Wyeth	Phase Ia	NS5B polymerase	Non-nucleoside allosteric inhibitor

*Development halted due to cardiotoxicity in monkeys

b Host targets/immunomodulators

Actilon (CpG-10101)	Coley Pharmaceutical Group	Phase Ib	Toll-like receptor-9	Immunomodulator
ANA245 (Isatoribine)	Anadys Pharmaceuticals	Phase Ib	Toll-like receptor-7	Immunomodulator
ANA975	Anadys Pharmaceuticals	Phase Ia	Toll-like receptor-7	Immunomodulator (prodrug of ANA245)

HEPATITIS C

THE INSIDIOUS
SPREAD OF A
KILLER
VIRUS



TORS HAVE
Saeed Taha
that he has only
weeks to live.
The 48-year-old
electrician is
a Cairo hospital
connected,
every major vein
ago he
hepatitis
fatigue, the
his job and
savings on in-

Hundreds of millions are infected with the stealth virus. Most don't know it.

used, unsterilized needles. Syyeda Hassan Metwally, 54, remembers a nurse injecting her 11 relatives and four neighbors with a single syringe. The campaign ended only when an oral drug came on the market in 1982. Now the government is scrambling to control an epidemic it helped create. This story would be tragic enough even if Egypt were an isolated case, but it's not.