

*Hepatitis B, C  
& Δ  
Wat is nieuw in  
2019?*

*Stefan Bourgeois  
ZNA, Antwerpen  
21 juni 2019*

## Disclosures

Spreker en ab board voor Gilead, BMS, AbbVie, MSD en Janssen

*Menu 21 juni 2019*



*Hepatitis C*

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*Hepatitis B*

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*Hepatitis Delta*

**titel**  
ondertitel  
datum

# Menu 21 juni 2019



<b>HBV</b>	<b>HCV</b>	<b>Hep Delta</b>
<b>250.000.000</b>	<b>71.000.000</b>	<b>20.000.000</b>
<b>Bloed-bloed Sexueel</b>	<b>Bloed-bloed</b>	<b>Bloed-bloed Sexueel</b>
<b>Viruscontrole (Functional cure)</b>	<b>Eradicatie</b>	<b>Viruscontrole</b>
<b>Antiviraal (immuun- modulerend)</b>	<b>Antiviraal</b>	<b>Antiviraal (immuun- modulerend)</b>

titel  
ondertitel

datum

# *Hepatitis C*

**titel**

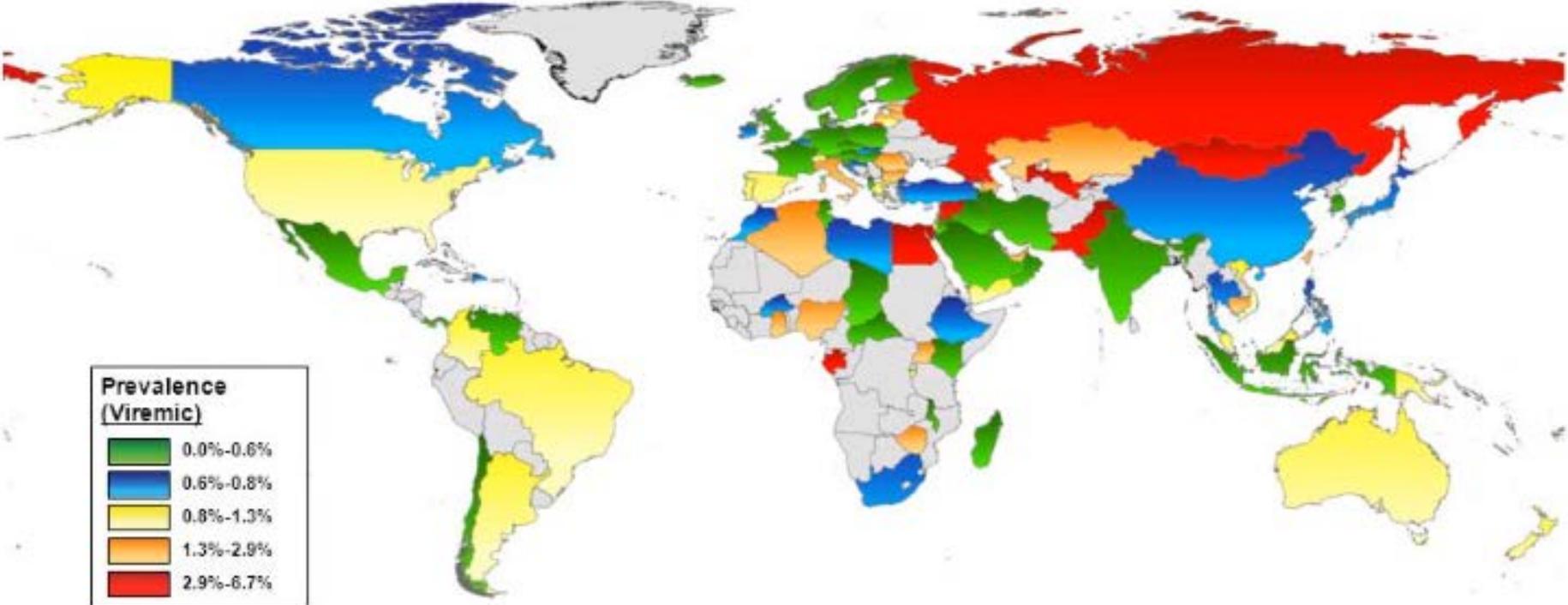
ondertitel

datum

# Global HCV Prevalence



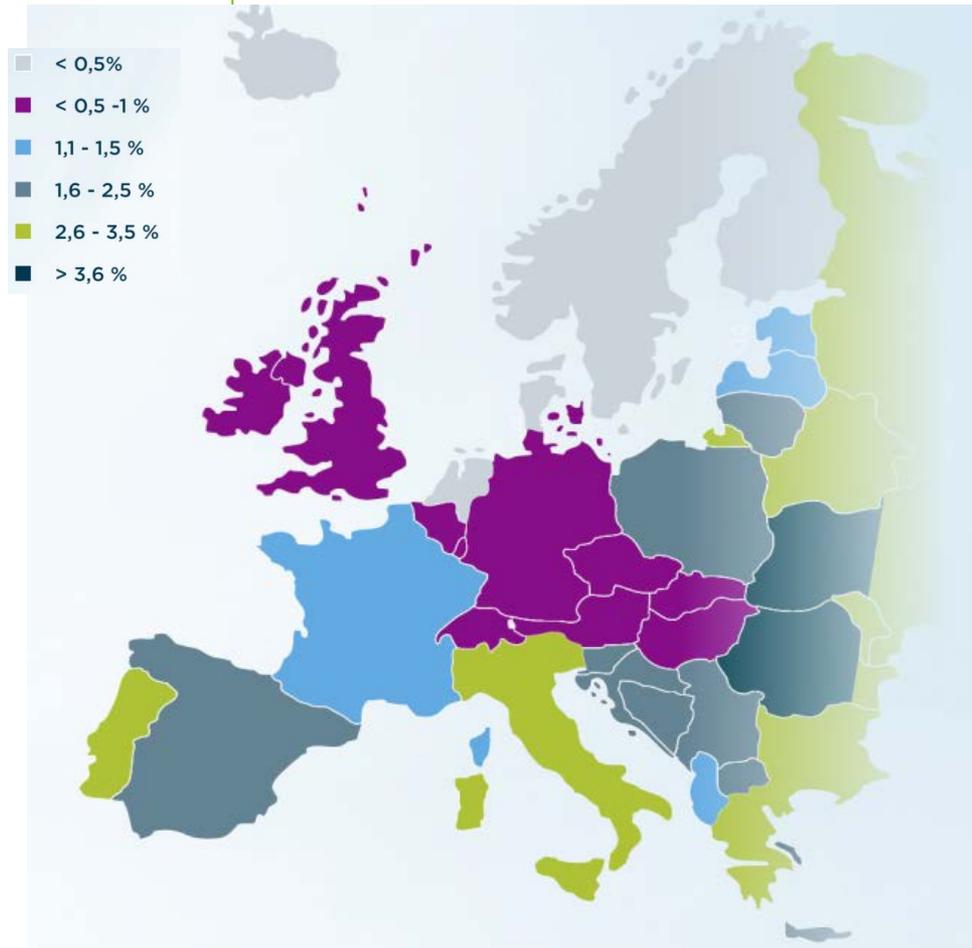
## Countries with HCV Epidemiology Data



~ 71 miljoen mensen  
wereldwijd besmet

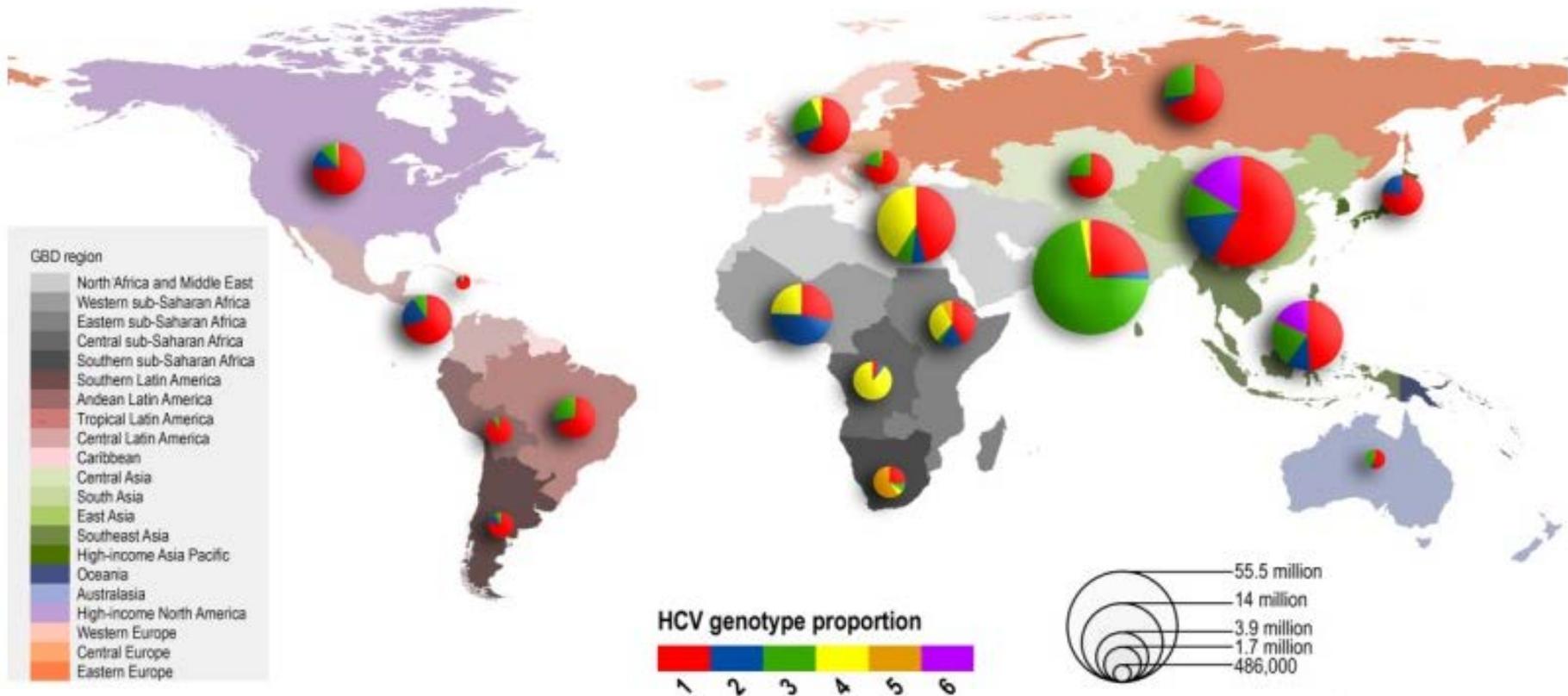
~ 400.000 doden/jaar

# Prevalentie van hepatitis C



- In Europa is de prevalentie van hepatitis C niet homogeen.<sup>1</sup>
- In 2018 was in België naar schatting **0,12%** van de bevolking chronisch besmet met het hepatitis C-virus.<sup>2</sup>

# Genotype distribution: Global Data



HCV: Hepatitis C Virus

Referentie: Messina et al., Hepatology. 2015 Jan;61(1):77-87.

# Transmissie



Blood Transfusions

Sharing of needles & other  
drug taking equipment

Mother to baby transmission

## **Causes of Hepatitis C**

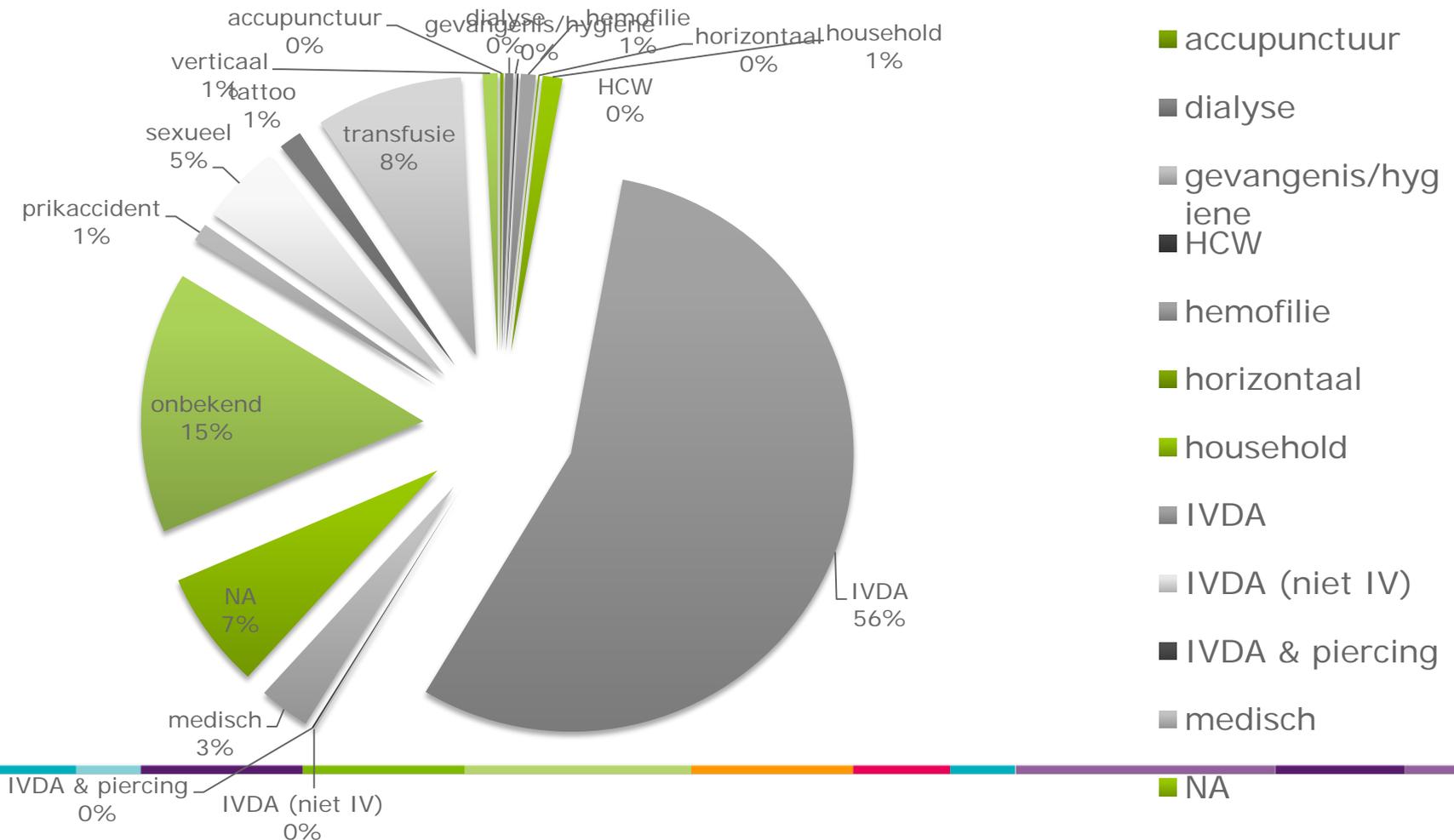


Body piercing

Tattooing

Unprotected sex with multiple  
partners

# Database ZNA Transmissie



# Behandeling

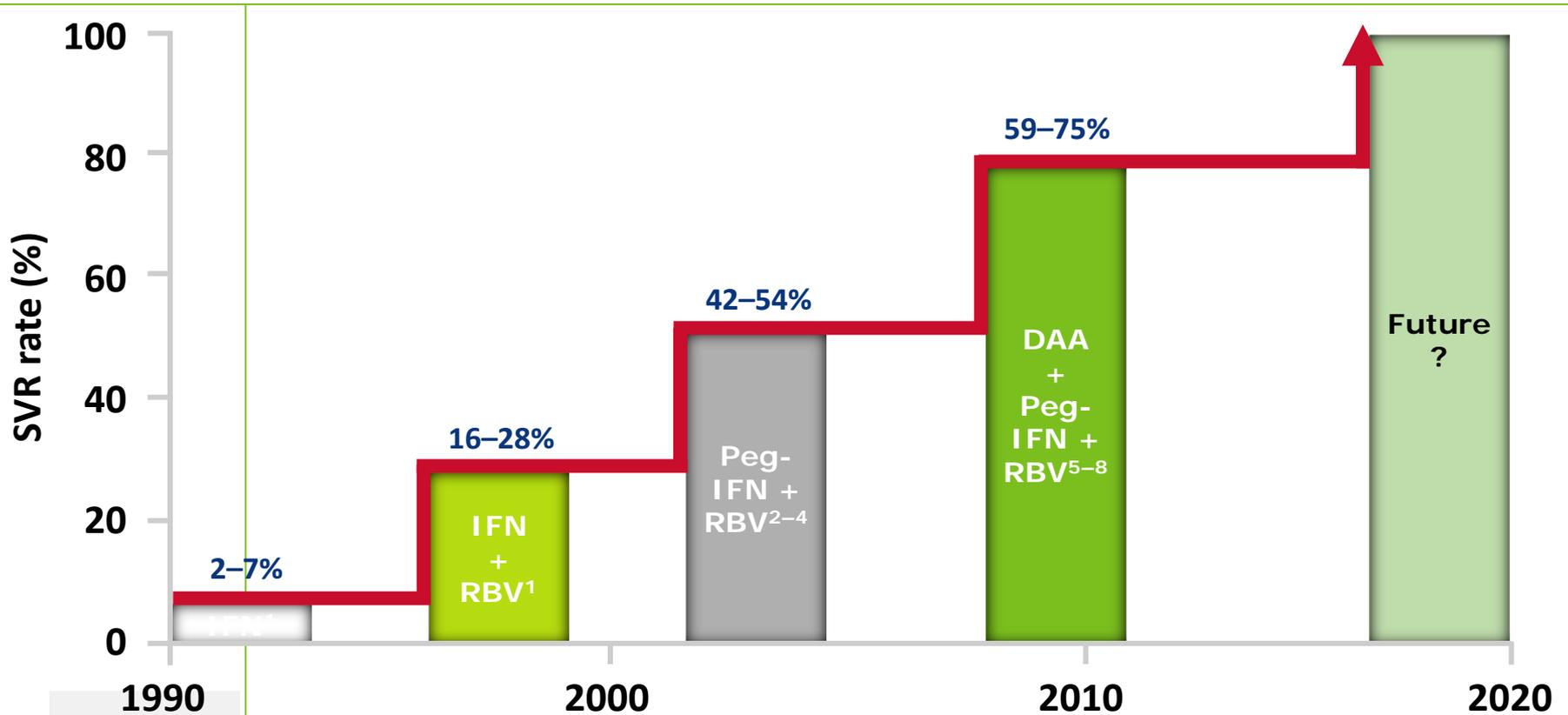


3rd Place

# FIFA Ranking

1	 Belgium	1727	1727	0	⬆️
2	 France	1726	1726	0	⬆️
3	 Brazil	1676	1676	0	⬆️
4	 Croatia	1634	1634	0	⬆️
5	 England	1631	1631	0	⬆️
6	 Portugal	1614	1614	0	⬆️
7	 Uruguay	1609	1609	0	⬆️
8	 Switzerland	1599	1599	0	⬆️
9	 Spain	1591	1591	0	⬆️
10	 Denmark	1589	1589	0	⬆️
11	 Argentina	1582	1582	0	⬆️
12	 Colombia	1575	1575	0	⬆️
13	 Chile	1565	1565	0	⬆️
14	 Sweden	1560	1560	0	⬆️
14	 Netherlands	1560	1560	0	⬆️
16	 Germany	1558	1558	0	⬆️
17	 Mexico	1540	1540	0	⬆️
18	 Italy	1539	1539	0	⬆️

# Evolution of HCV genotype 1 treatment



IFN: interferon; RBV: ribavirin  
Peg-IFN: peginterferon  
DAA: direct-acting antiviral  
SVR: sustained virologic response

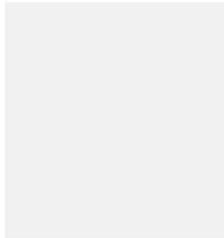
1. McHutchison JG, et al. N Engl J Med 1998;339:1485-92;
2. Fried M, et al. N Engl J Med 2002;347:975-82
3. Manns MP, et al. Lancet 2001;358:958-65;
4. Hadziyannis SJ, et al. Ann Intern Med 2004;140:346-55
5. Jacobson IM, et al. Hepatology 2010;52(Suppl.):427A;
6. Sherman KE, et al. Hepatology 2010;52(Suppl.):401A
7. Poordad F, et al. Hepatology 2010;52(Suppl.):402A;
8. Foster GR, et al. Hepatol Int 2011;5(Suppl.1):14

1 january 2015



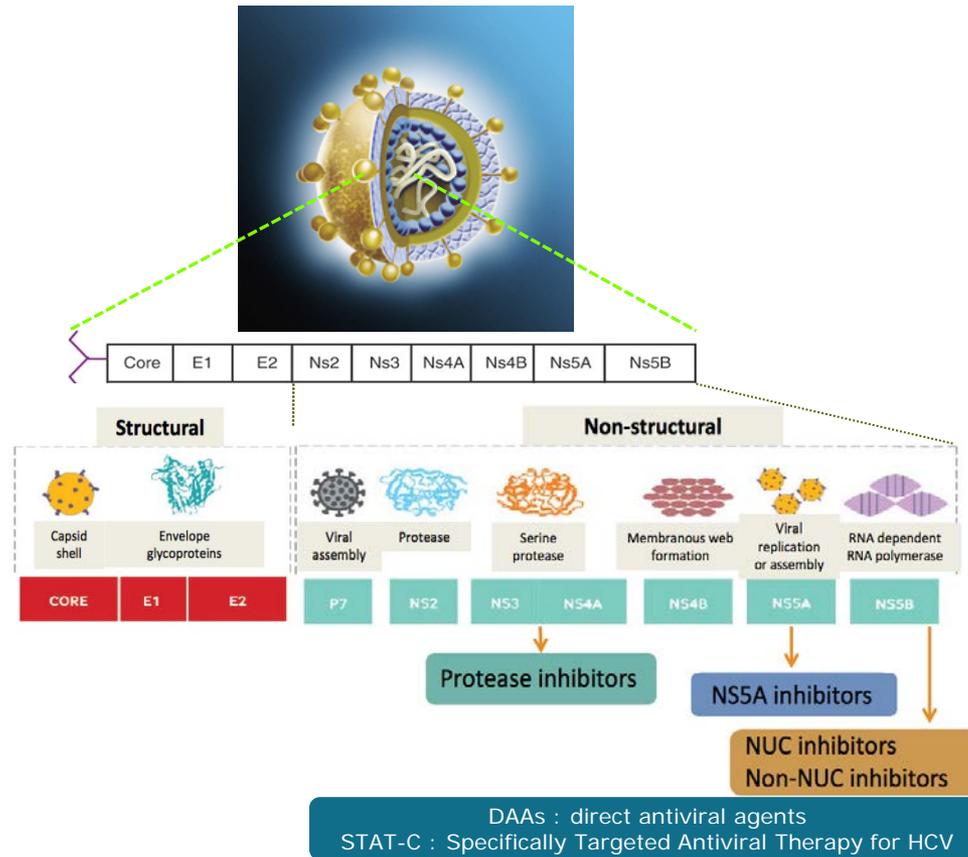
New molecules

New staging techniques



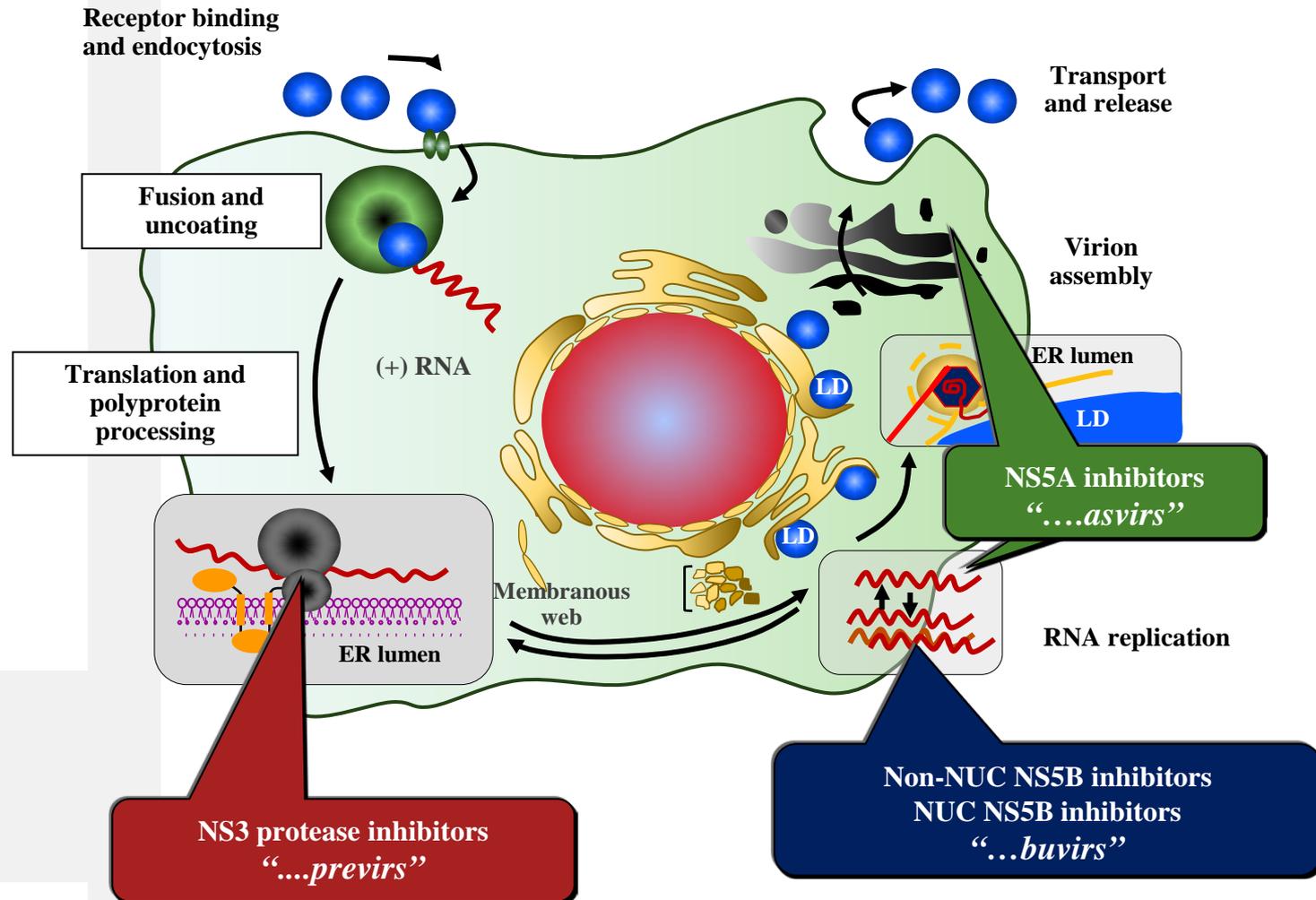
# Hepatitis C

## een ingenieus virus



**titel**  
ondertitel

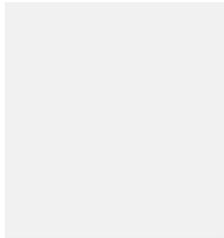
# HCV life cycle and targets for direct-acting antiviral agents (DAAs)

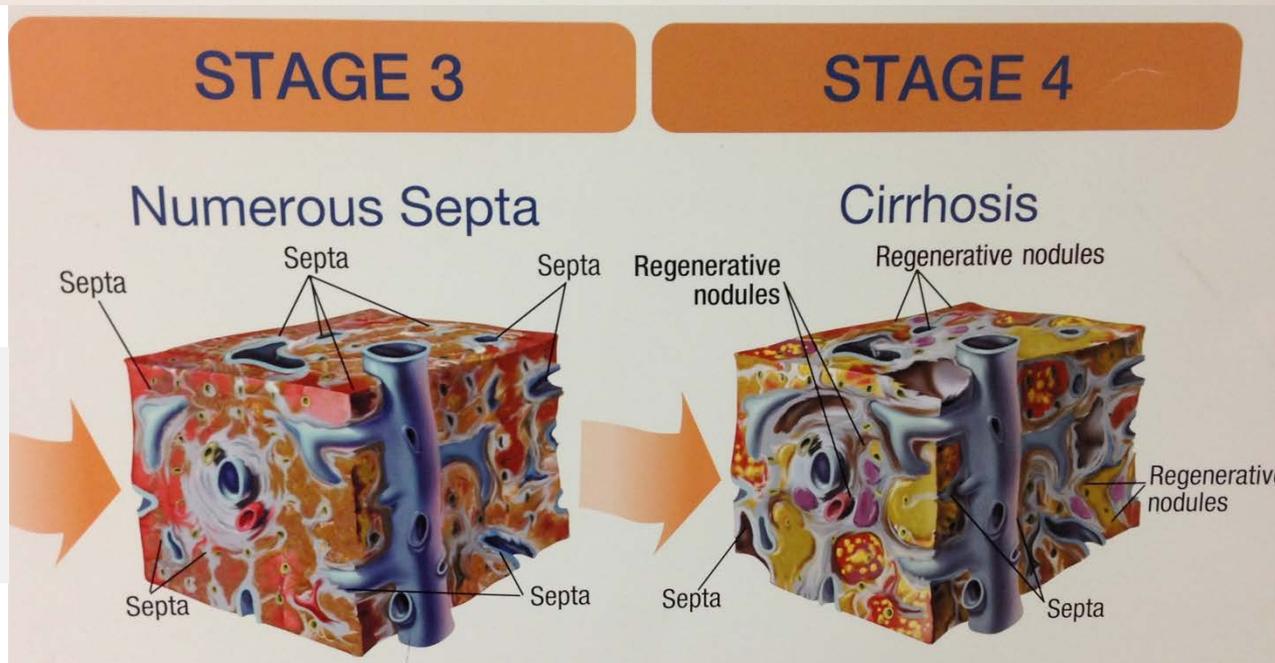
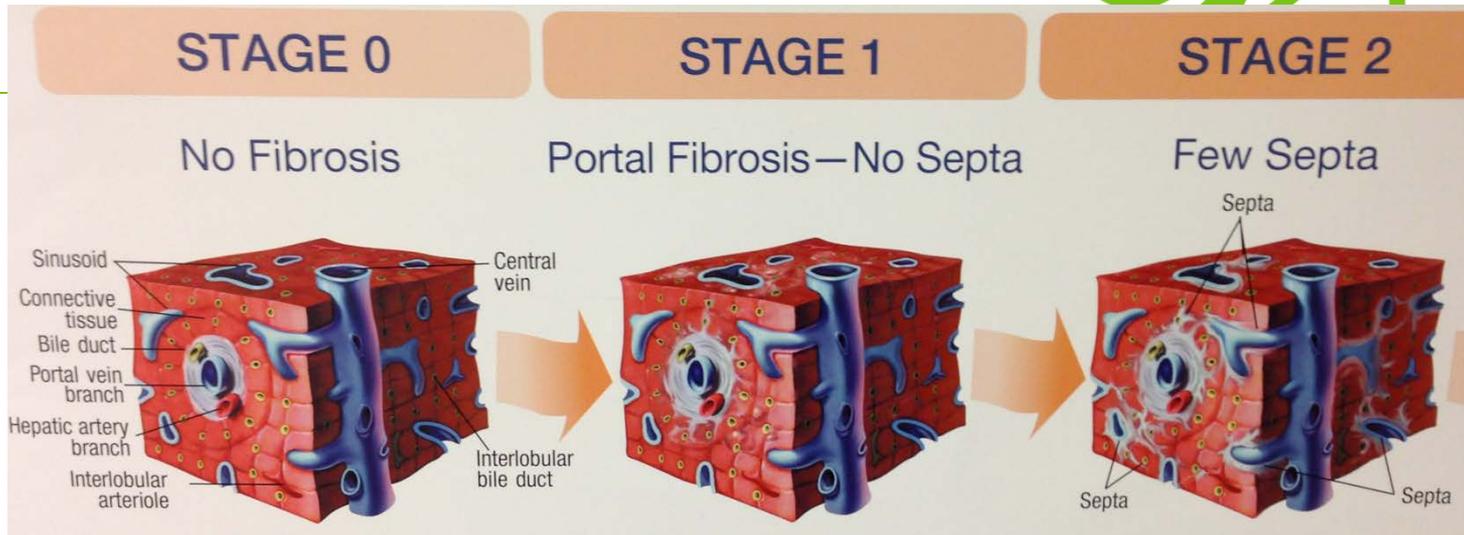


# Treatment

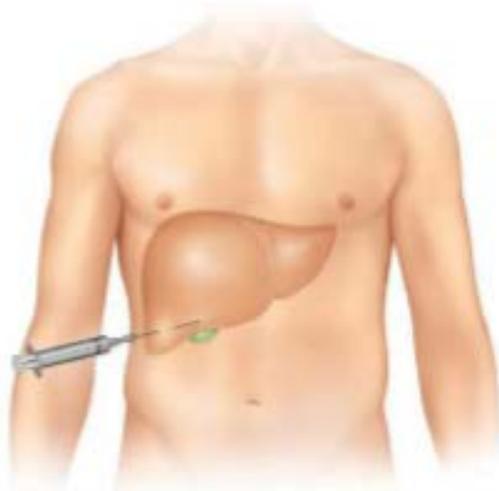


*From 2015*

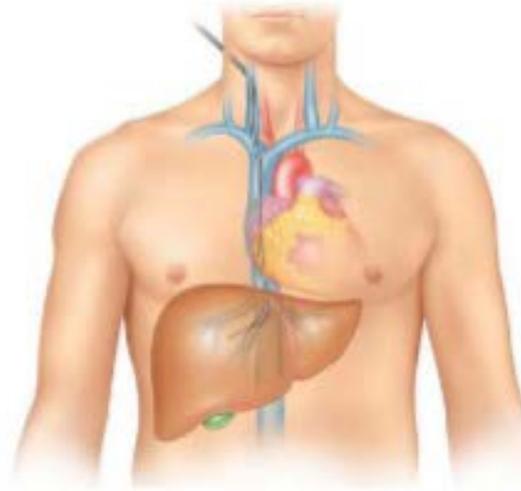




# Leverbiopsie



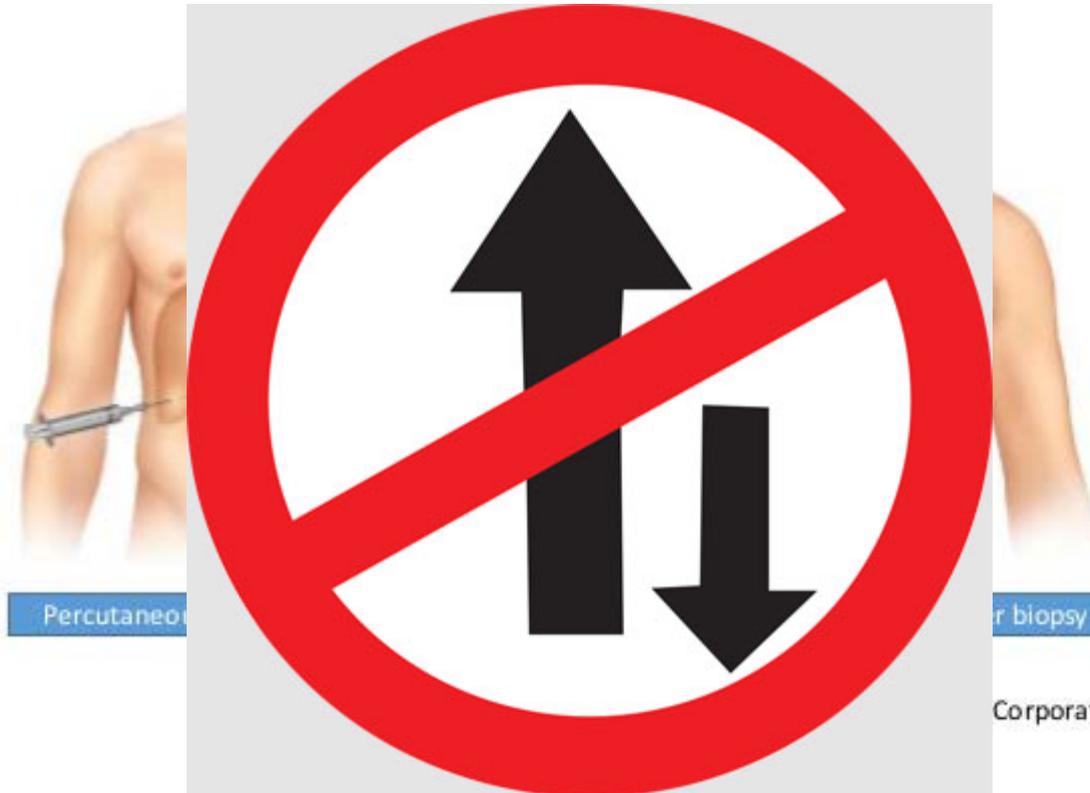
Percutaneous Liver biopsy



Transvenous (transjugular) Liver biopsy

source©2015 Boston Scientific Corporation or its affiliates.

# Leverbiopsie



Percutaneo

r biopsy

Corporation or its affiliates.

cut-offs of ***BIOLOGICAL FIBROSIS-SCORES*** for assessment ***F2-F3-F4***  
***in chronic hepatitis C***  
(agreed at RIZIV-INAMI 01.12.2016)

**1. FIBROTEST (*BIOPREDICTIVE*):**

Elements :  $\alpha$ 2 macroglobulin, haptoglobin, apolipoprotein A1, total bilirubin, GGT

F2 :  $\geq 0.49$

F3: 0.59-0.72

F3-F4: 0.73-0.74

F4:  $\geq 0.75$

**2. APRI (*AST-PLATELET RATIO*)**

In a pure HCV cohort

F2: APRI not to use for detection of F2

F3:  $\geq 1$

F4:  $\geq 1.6$

Reference: Holmberg, Clin Infect Dis 2013

**3. FIB-4 (age, AST,ALT, platelets)**

F2  $\geq 1.45$

F3:  $\geq 2.1$

F3-F4:  $\geq 3.25$

F4:  $\geq 3.85$

# Liver stiffness measurement (Fibroscan)



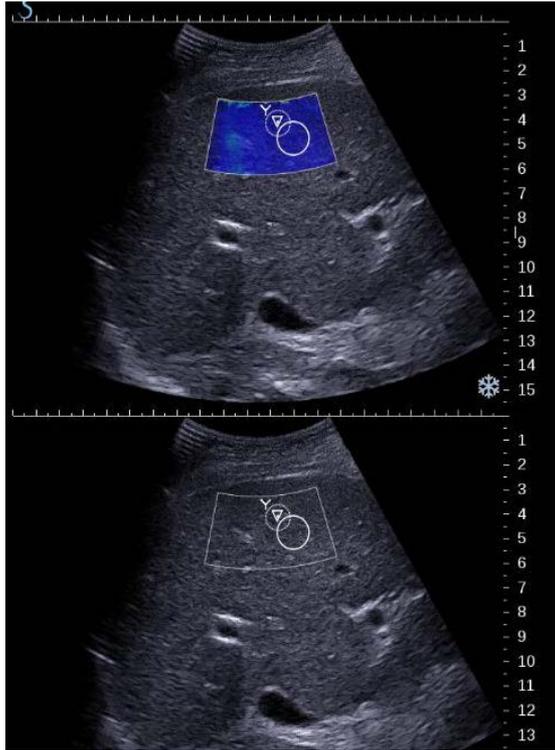
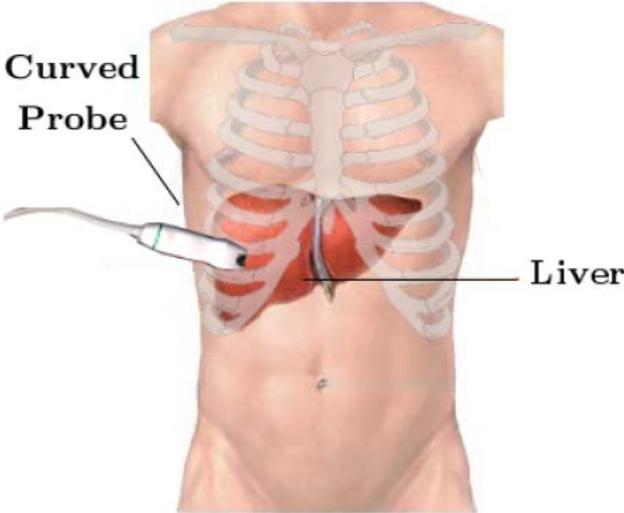
VCTE™

**CAP**  
CONTROLLED ATTENUATION  
PARAMETER

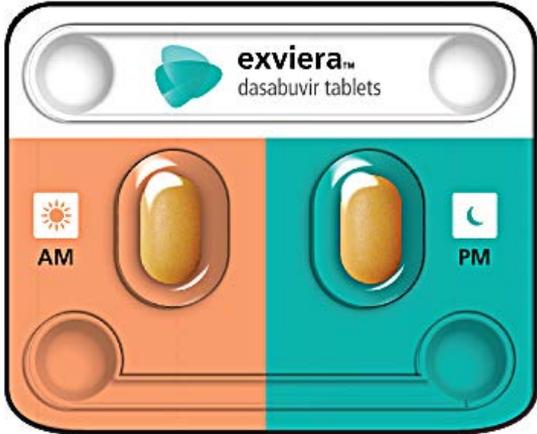
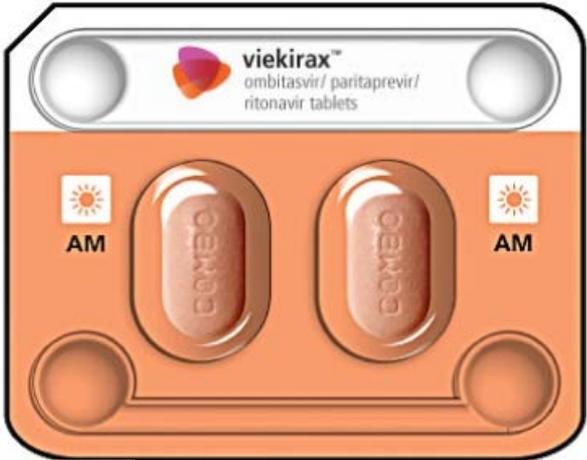
m+ XL+



# Shearwave Elastographie

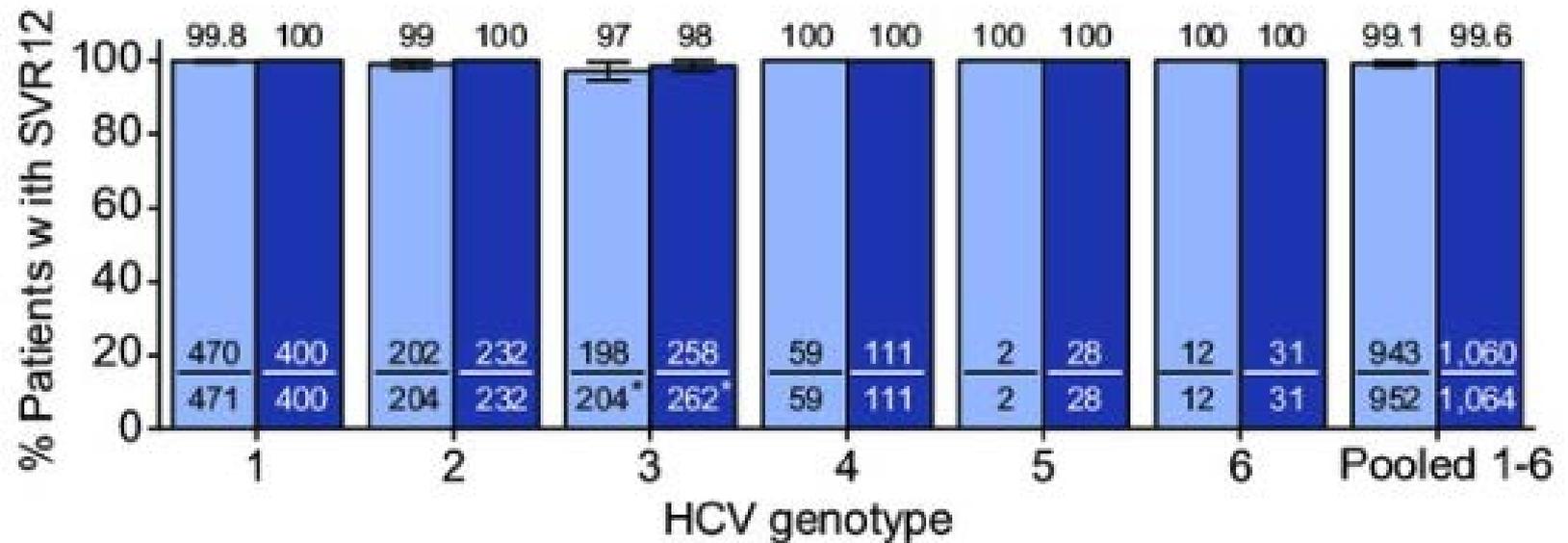




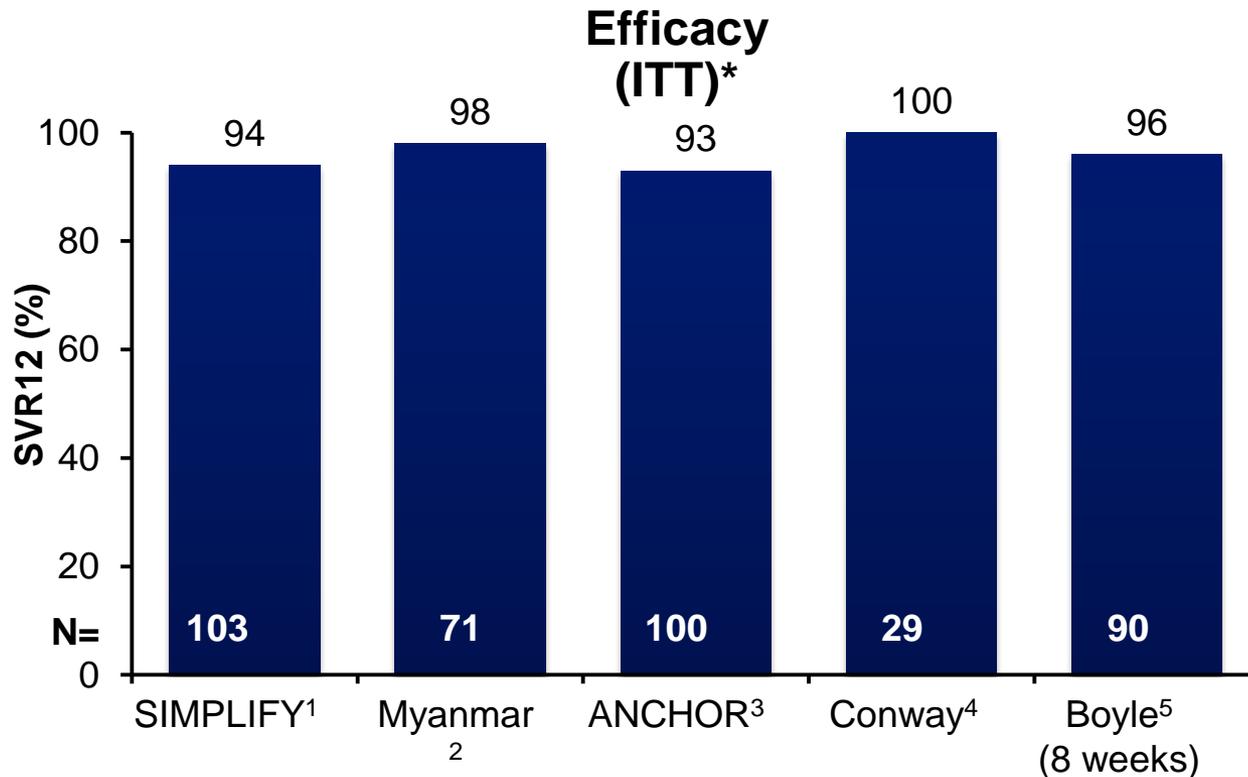




## *SVR resultaten met G/P*



# Cure rates are high in PWID receiving SOF/VEL for 12 weeks: studies presented at INHSU 2018



**NOT HEAD-TO-HEAD COMPARISONS.** These graphics serve to illustrate SVRs obtained between different regimens from different studies and are therefore not directly comparable as study populations are NOT matched

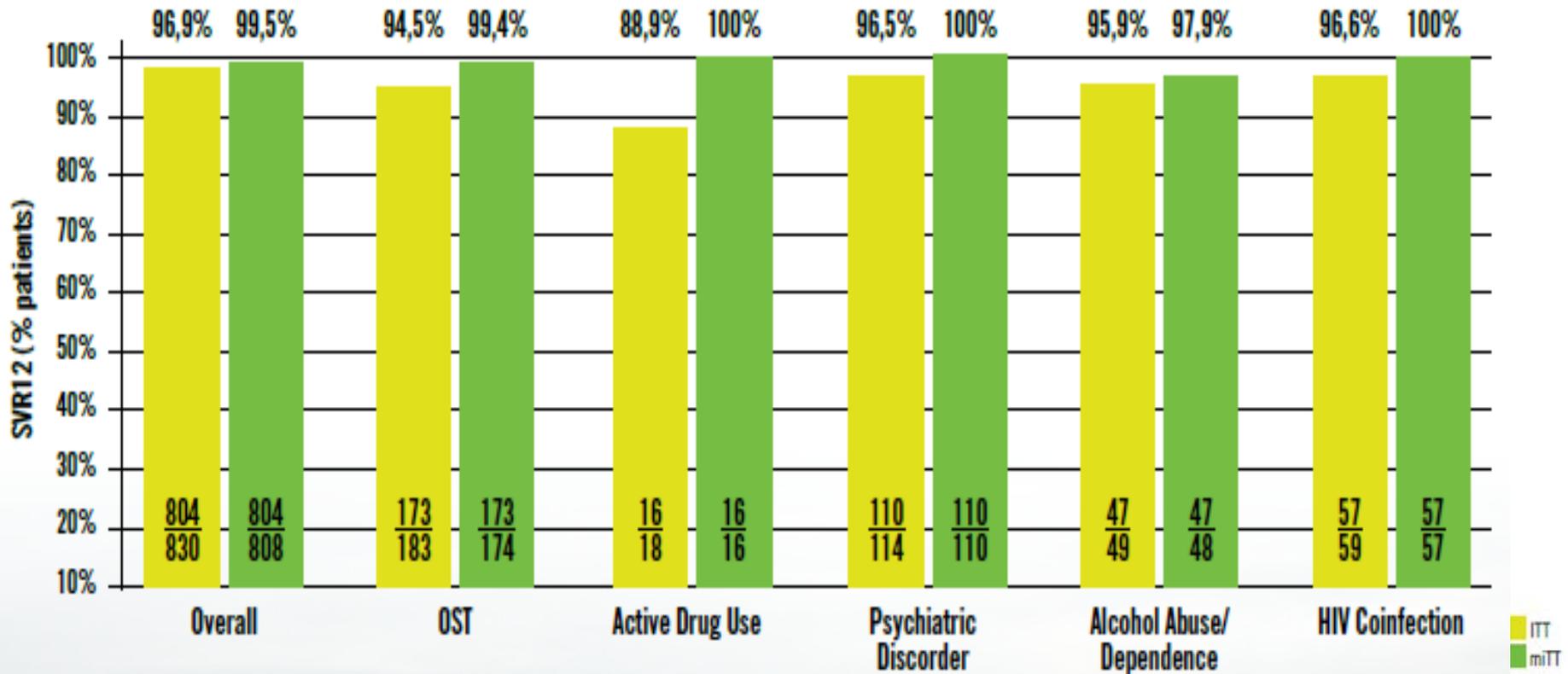
1. Cunningham EI, et al. INHSU 2018; Oral #21Sep 11.30; 2. Thaug YM, et al. INHSU 2018; Oral #20Sep 14.30; 3. Kattakuzhy S, et al. INHSU 2018; Oral #20Sep 14.50; 4. Conway B, et al. INHSU 2018; Poster#9; 5. Boyle A, et al. INHSU 2018; Poster#5

\*Consolidated from different studies.  
ITT: intent-to-treat; PWID: people who inject drugs;  
SOF: sofosbuvir; SVR: sustained virological response; VEL: velpatasvir

# REAL-WORLD DATA: THE GERMAN HEPATITIS C-REGISTRY<sup>1</sup>

⇒ SVR12 Rates in the Effectiveness Population

Received G/P for 8 weeks



Virologic failure	4	4	1	1	0	0	0	0	1	1	0	0
HCV reinfection	3	0	2	0	1	0	1	0	0	0	1	0
Discontinued/LTFU	19	0	7	0	1	0	3	0	1	0	1	0

Patients who discontinued G/P prematurely and achieved SVR12 were counted as virologic responders.

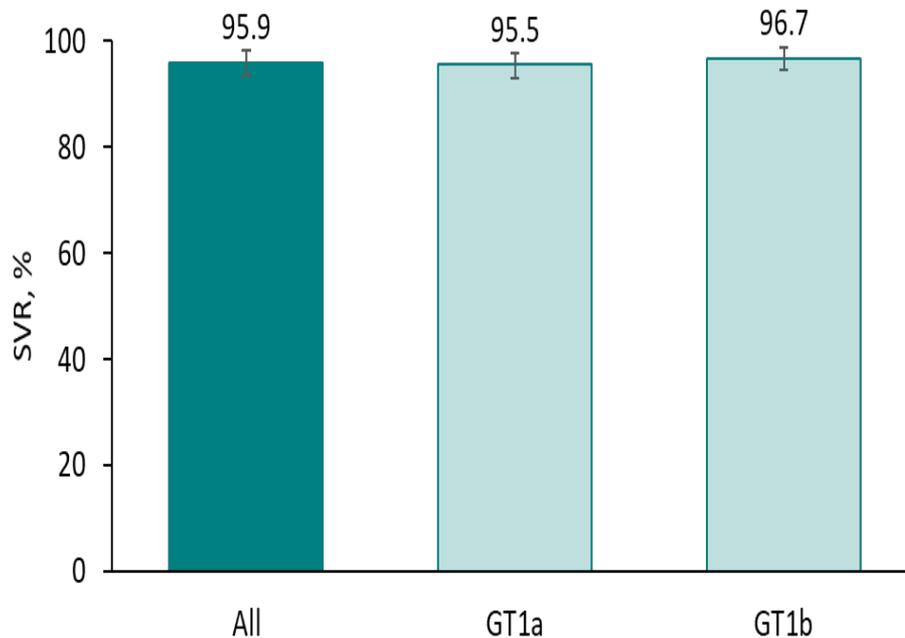
mITT analysis excluded: patients who discontinued G/P prematurely and did not achieve SVR12; patients who were LTFU; patients with HCV reinfection.

G/P: glecaprevir/pibrentasvir; HCV: Hepatitis C Virus; ITT: intention-to-treat; LTFU: lost to follow-up; mITT: modified ITT; SVR12: sustained virologic response at Post-Treatment Week 12.

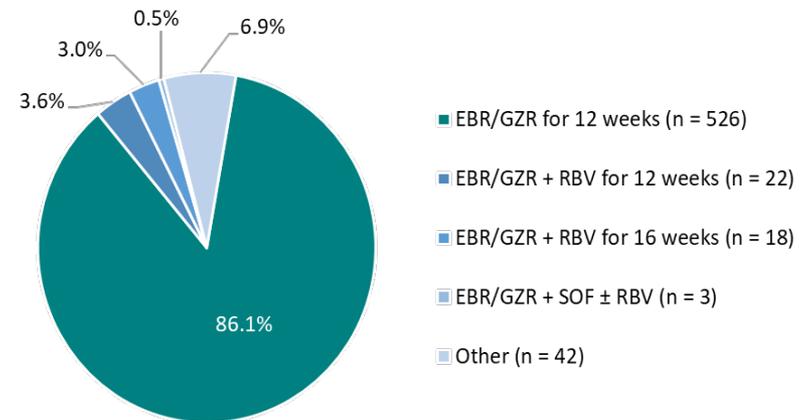
Cornberg M. Et al, Presented at EASL 2019. Vienna, Austria

# Real World Data: Efficacy of ZEPATIER (EBR/GZR) in PWID receiving OAT US Veteran Affairs (VA) population

## Sustained Virologic Response (N=611)



## Utilization of EBR/GZR Regimens



# Behandeling HCV



Kort: 8 à 12 weken

Nevenwerkingen: verwaarloosbaar

Succesratio: 97-99%

Cave DDI's!

# Drug Drug Interactions (DDI) and Direct Acting Antivirals (DAAs)

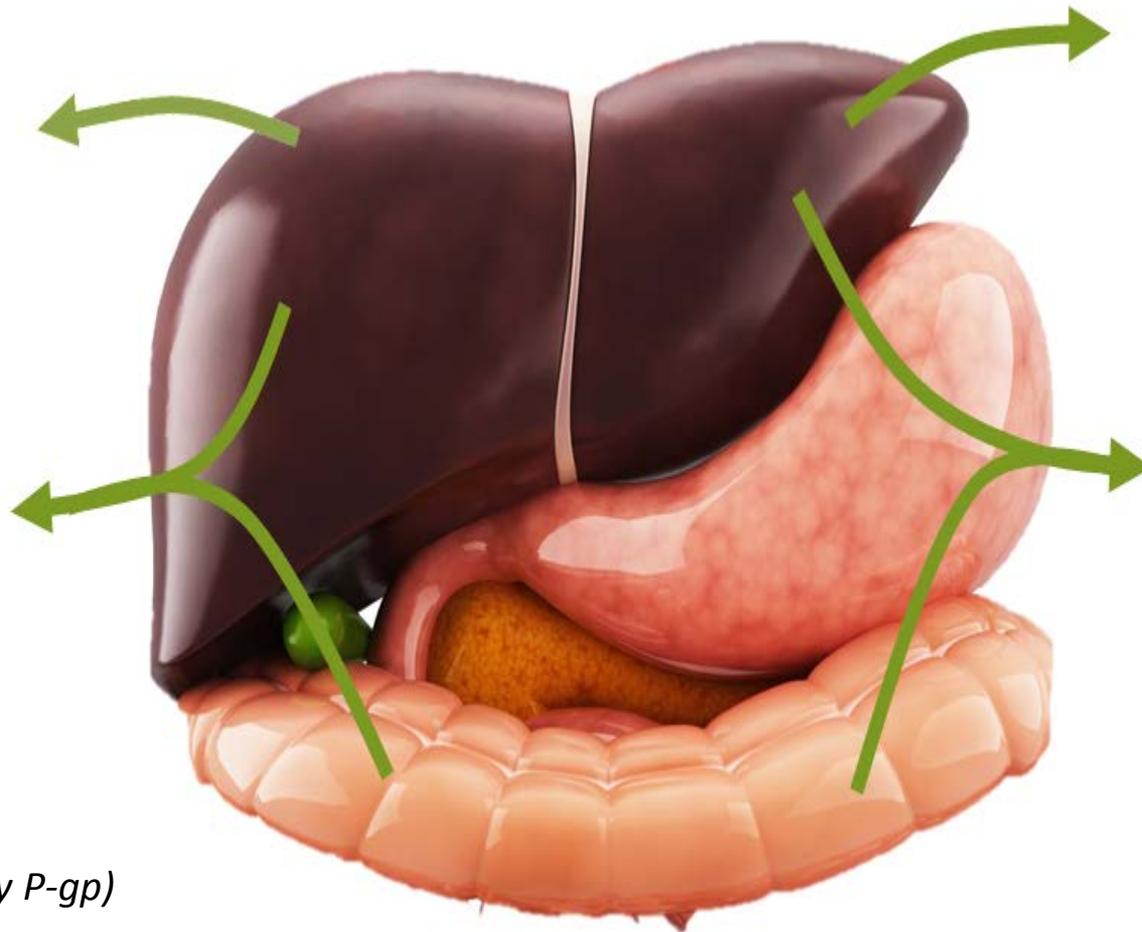
## Metabolic pathways of potential DDI

### OATP1B1/3

Daclatasvir  
Paritaprevir  
Grazoprevir  
Velpatasvir

### P-gp/BCRP

Daclatasvir  
Dasabuvir  
Ledipasvir  
Ombitasvir  
Paritaprevir  
Elbasvir  
Grazoprevir  
Velpatasvir  
Ledipasvir  
Sofosbuvir  
Ritonavir (*only P-gp*)



### CYP2C8

Dasabuvir  
Velpatasvir

### CYP3A

Daclatasvir  
Paritaprevir  
Ledipasvir  
Velpatasvir  
Elbasvir  
Grazoprevir  
Ritonavir

Adapted from: Dick 2016. Hepatology  
63(2); 634–643



HEP iChart app users - please update to the newest version to ensure up-to-date information

# Interaction Checker

Access our free, comprehensive and user-friendly drug interaction charts

## Educational Videos

A series of mini-lectures on topics including pharmacology, hepatitis and drug-drug interactions

## Prescribing Resources

Interaction tables, treatment selectors, clinical prescribing resources, and pharmacokinetic fact sheets

## Twitter

 [@hepinteractions](#)

Follow us on Twitter for interaction news and for the latest additions and changes to the website

## Mobile Apps



## HIV Website



## Cancer Website



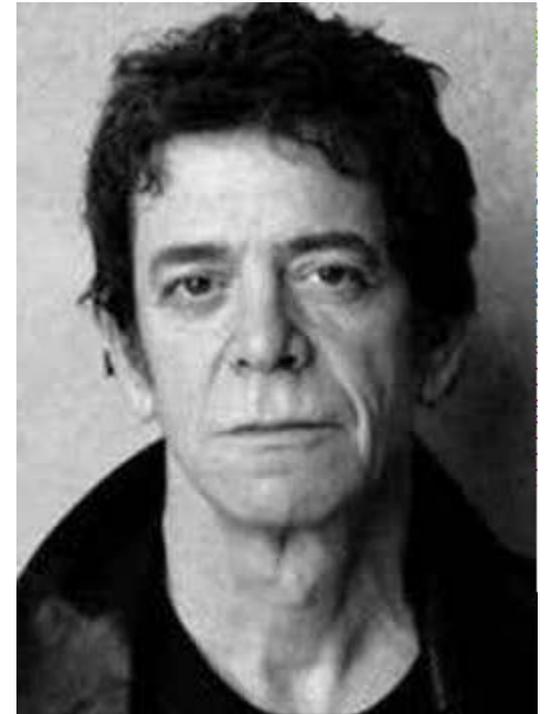
# Challenge 2019



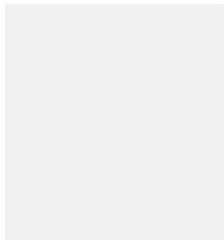
Cure for **all**

Transplantation for **some**

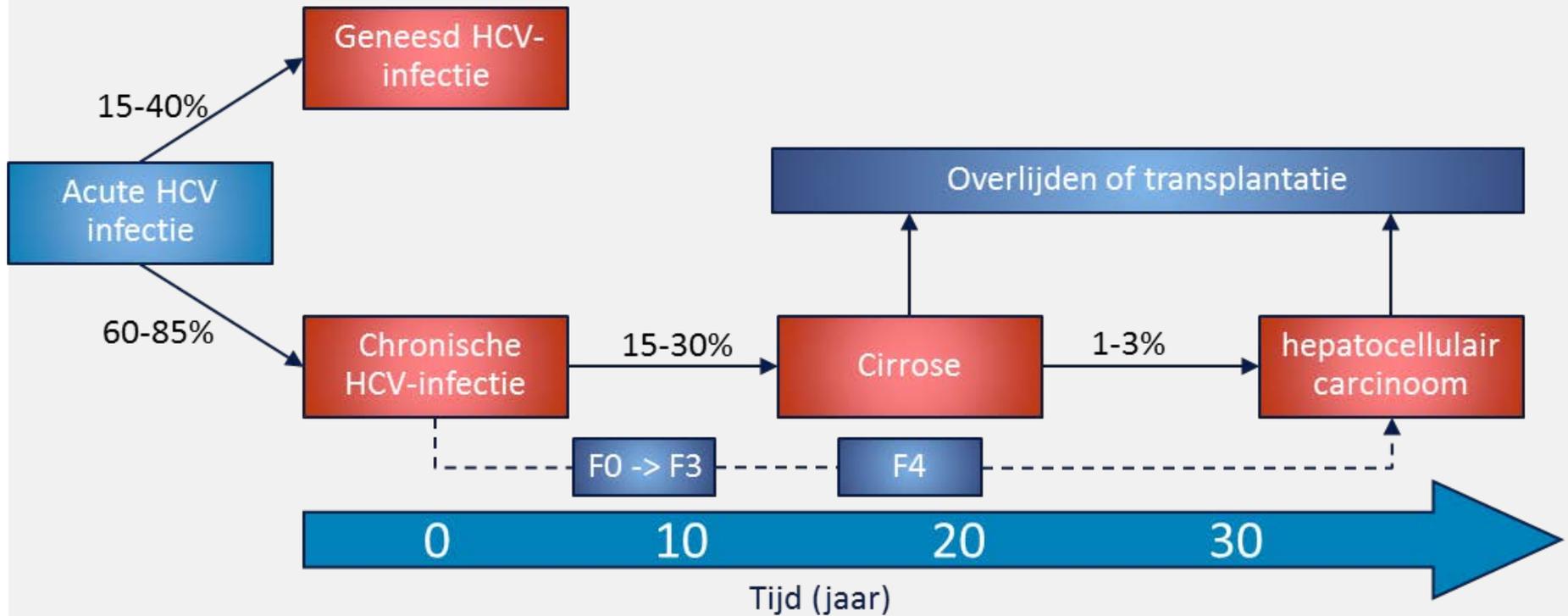
Close FU for **some more**  
screening for HCC  
beware of alcohol



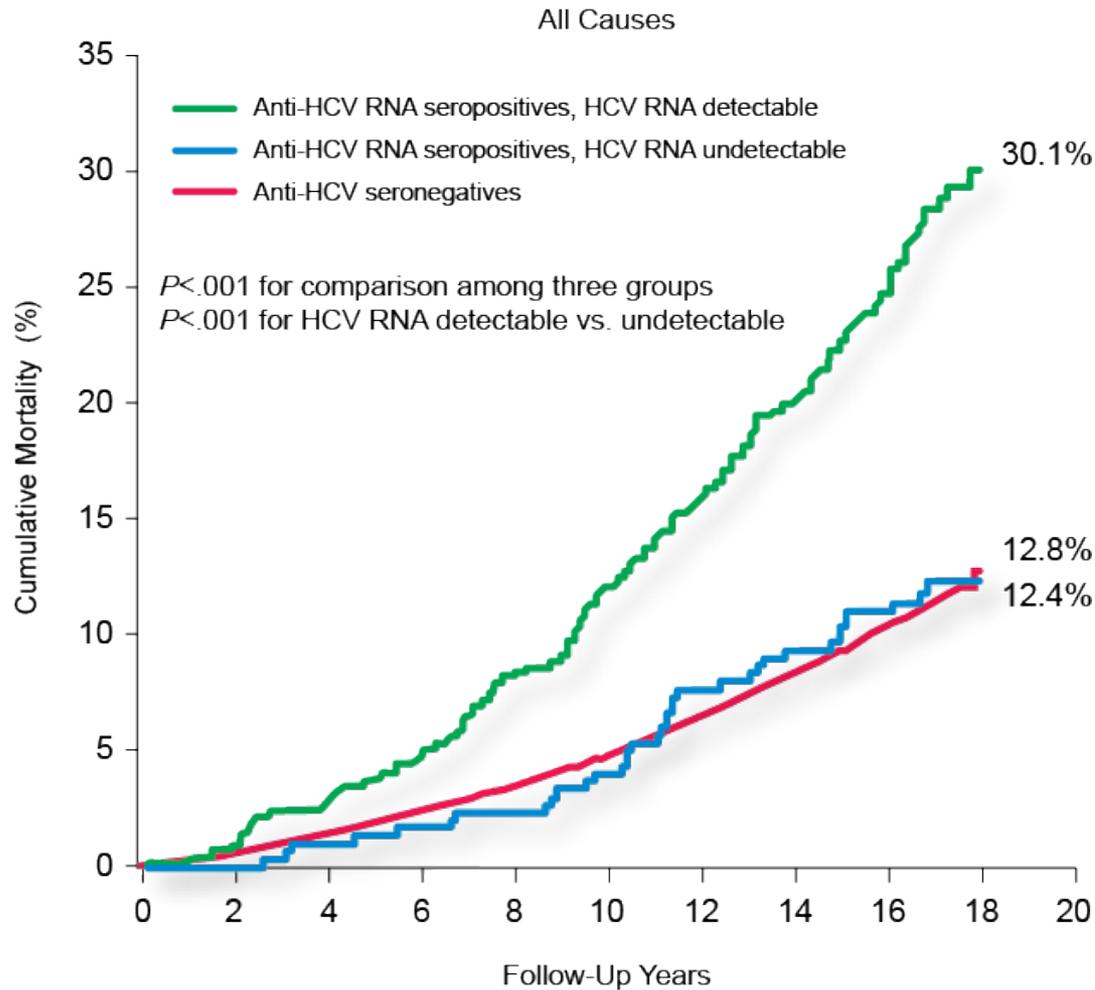
**Why treating  
all hepatitis C  
positive  
patients???**



# Het natuurlijk verloop van Hepatitis C



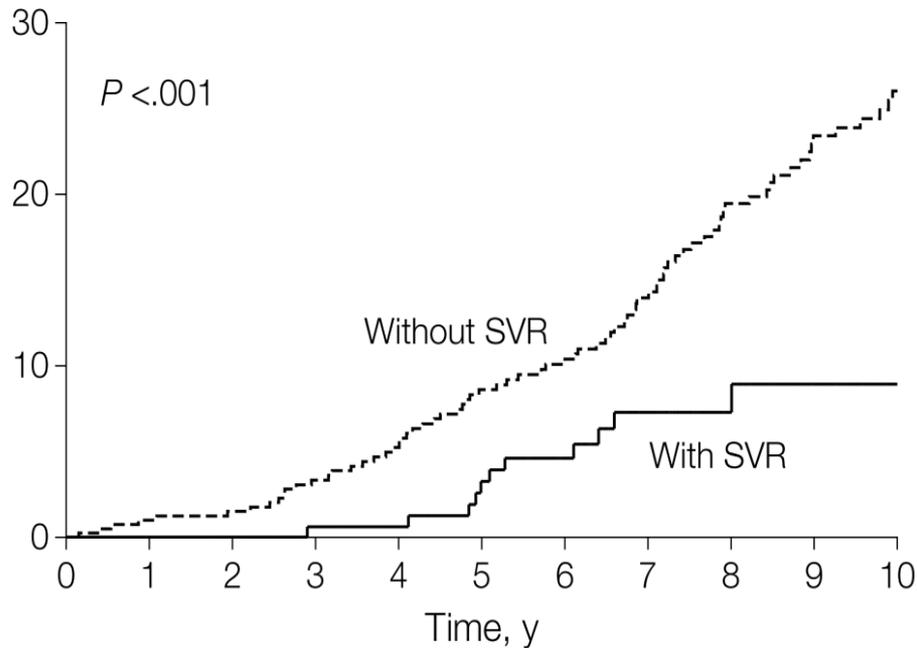
# HCV infection is associated with an increased overall mortality



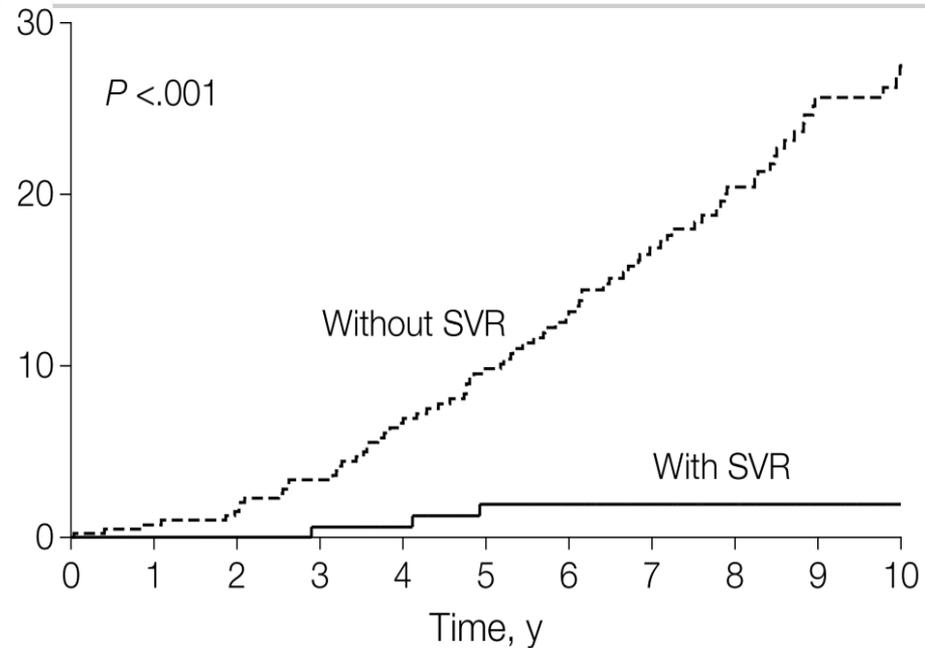
# SVR is associated with reduced mortality



All-cause mortality



LIVER RELATED MORTALITY



SVR: Sustained Virologic Response; y: year

Van der Meer AJ, et al. JAMA 2012

# Patients with SVR have a normal overall survival



Figure 2. Overall survival of patients without SVR compared to the age- and sex-matched Dutch population

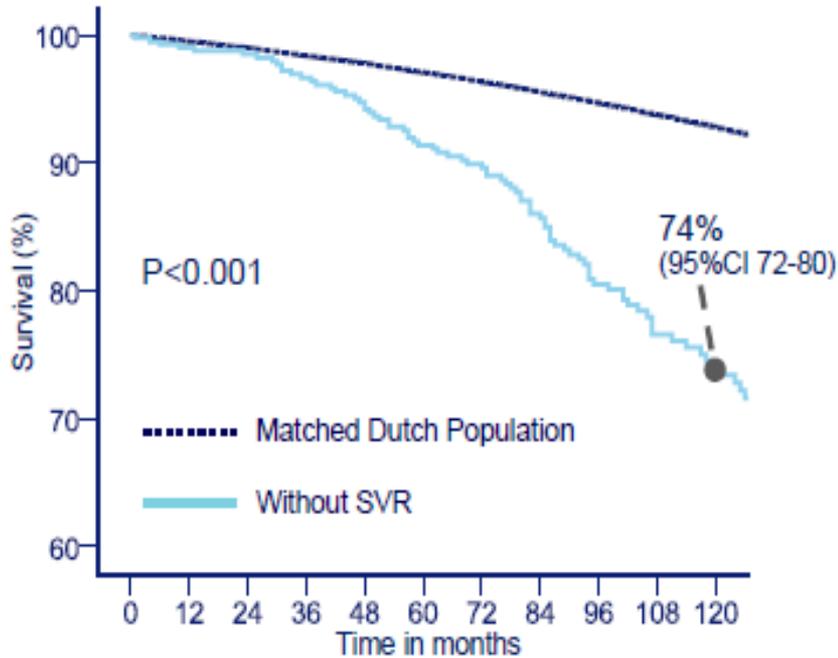
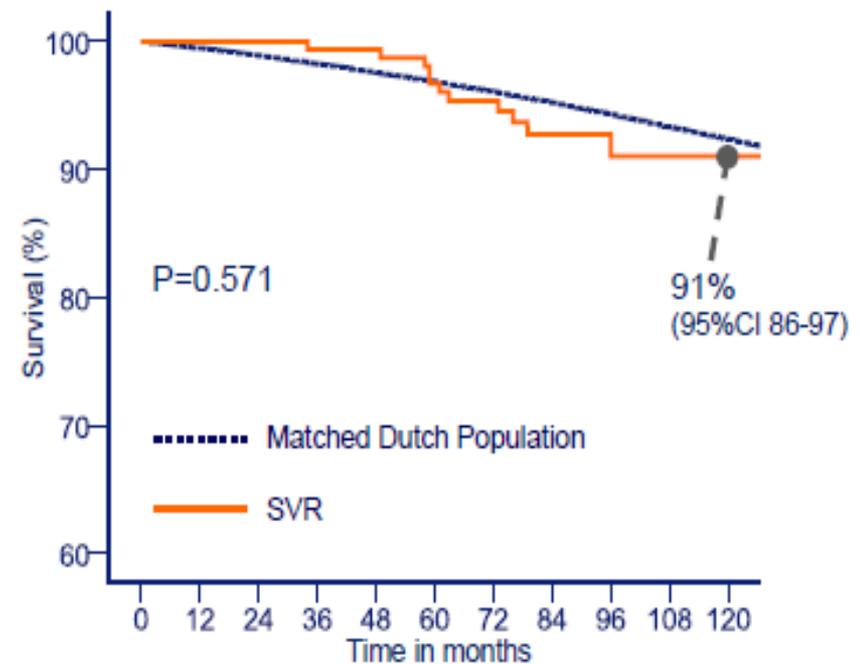
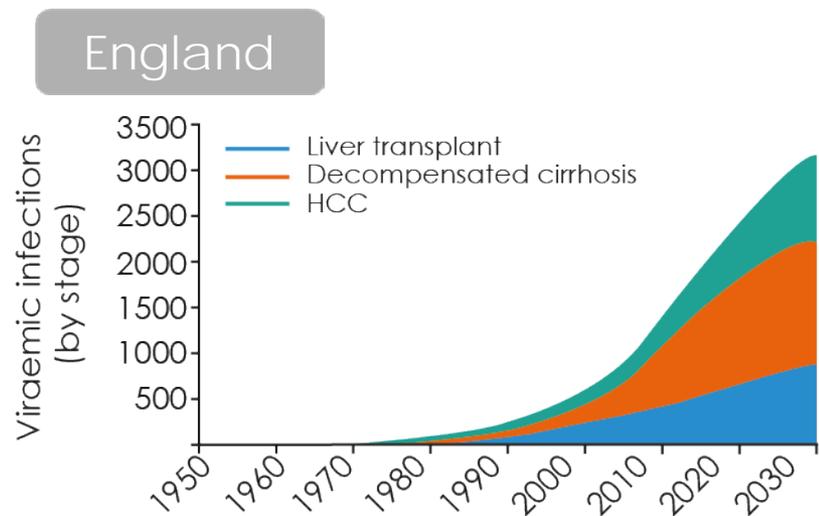
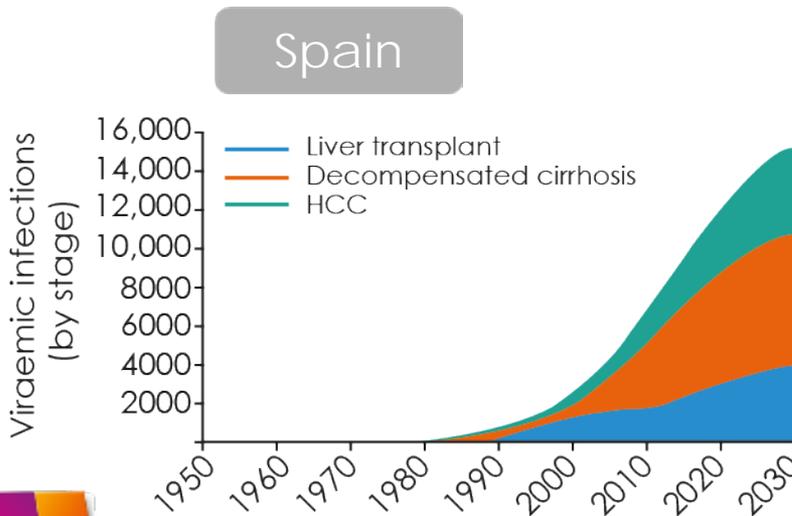
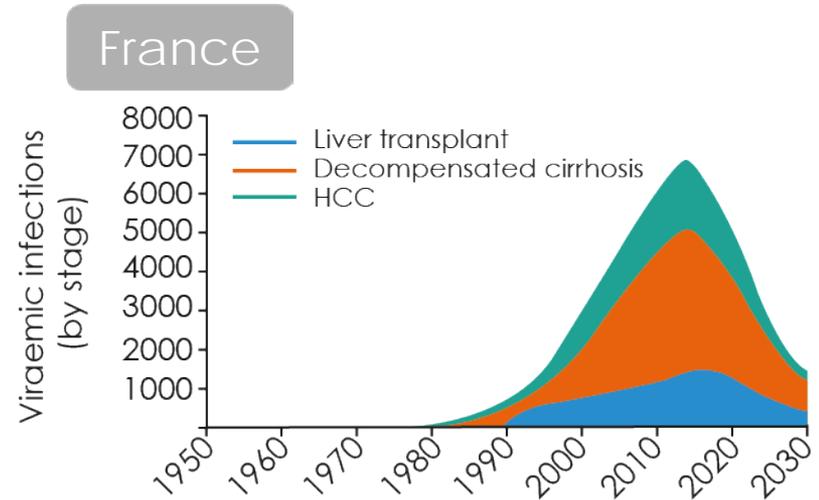
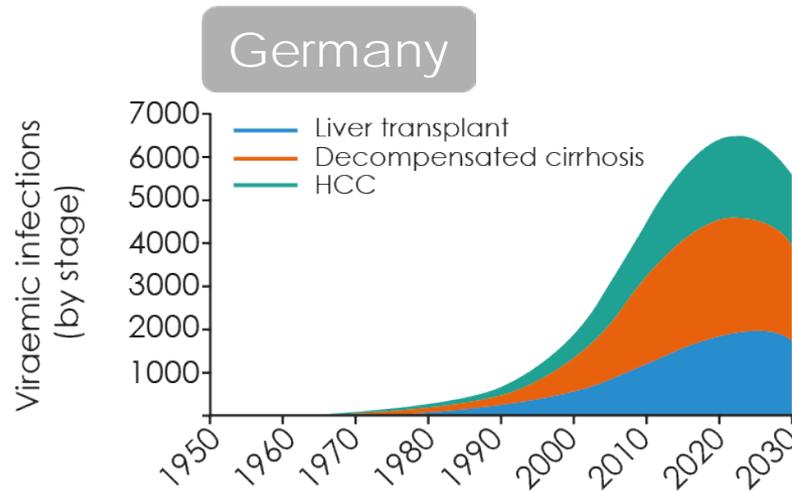


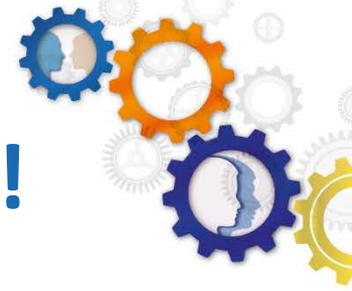
Figure 3. Overall survival of patients with SVR compared to the age- and sex-matched Dutch population



# HCV-associated complications will increase markedly over the next 5–10 years



# Hepatitis C is not only a liver disease!



CNS disorders<sup>1,2</sup>

Endocrine disorders<sup>2</sup>

Dermatologic disorders<sup>1,2</sup>

Cardiovascular diseases<sup>2</sup>

Haematologic disorders<sup>2</sup>

Renal disorders<sup>2</sup>

Rheumatologic disorders<sup>1,2</sup>



Fatigue



Depression



Social/legal consequences



# Hepatitis C is not only a liver disease!

CNS disorders<sup>1,2</sup>

Endocrine disorders<sup>2</sup>

Dermatolog

Cardio

Haematolo

Renal disorders<sup>2</sup>

Rheumatologic disorders<sup>1,2</sup>

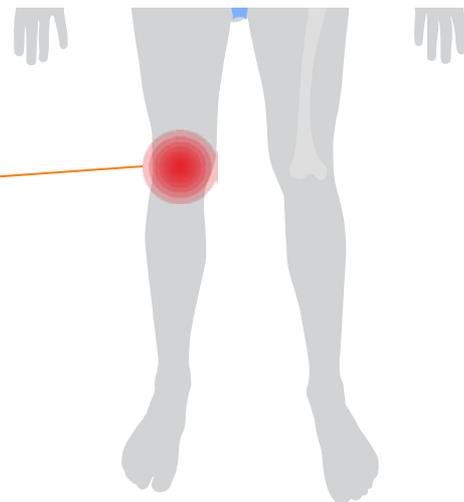
Fatigue



Depression



# Stigma!!



CNS, central nervous system.

1. Cacoub P, et al. Medicine 2000;79:47–56. 2. Mauss S, et al. In: Hepatology – A Clinical Textbook, 2014.

Treating Hep C

Hep C Elimination (WHO)

Downsizing reservoir

Optimal screening

- **Addictiecentra**
- **Gevangenis**
- **MSM**
- **Psychiatrische instelling**
- **Personen uit hoog endemische gebieden**

titel

ondertitel

datum

# *Hepatitis B*

**titel**

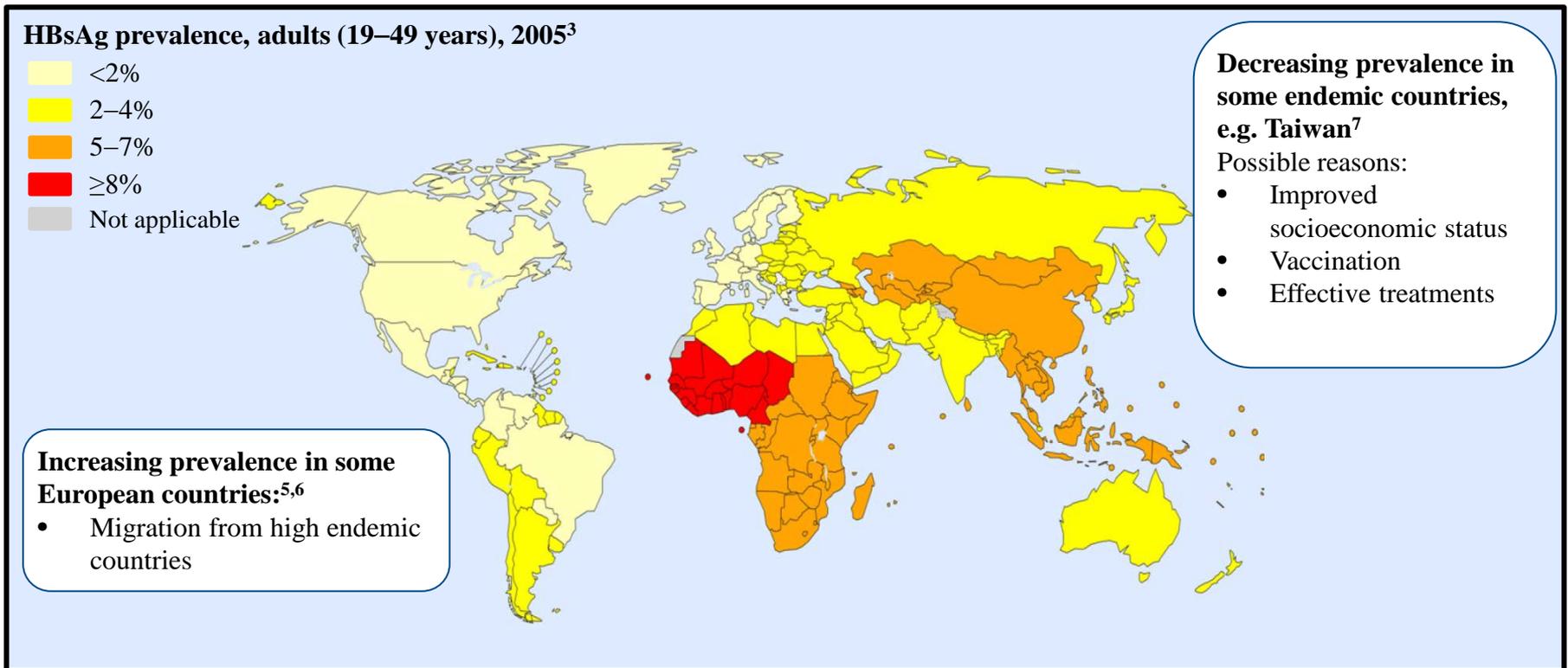
ondertitel

datum

# Epidemiology and public health burden<sup>1</sup>

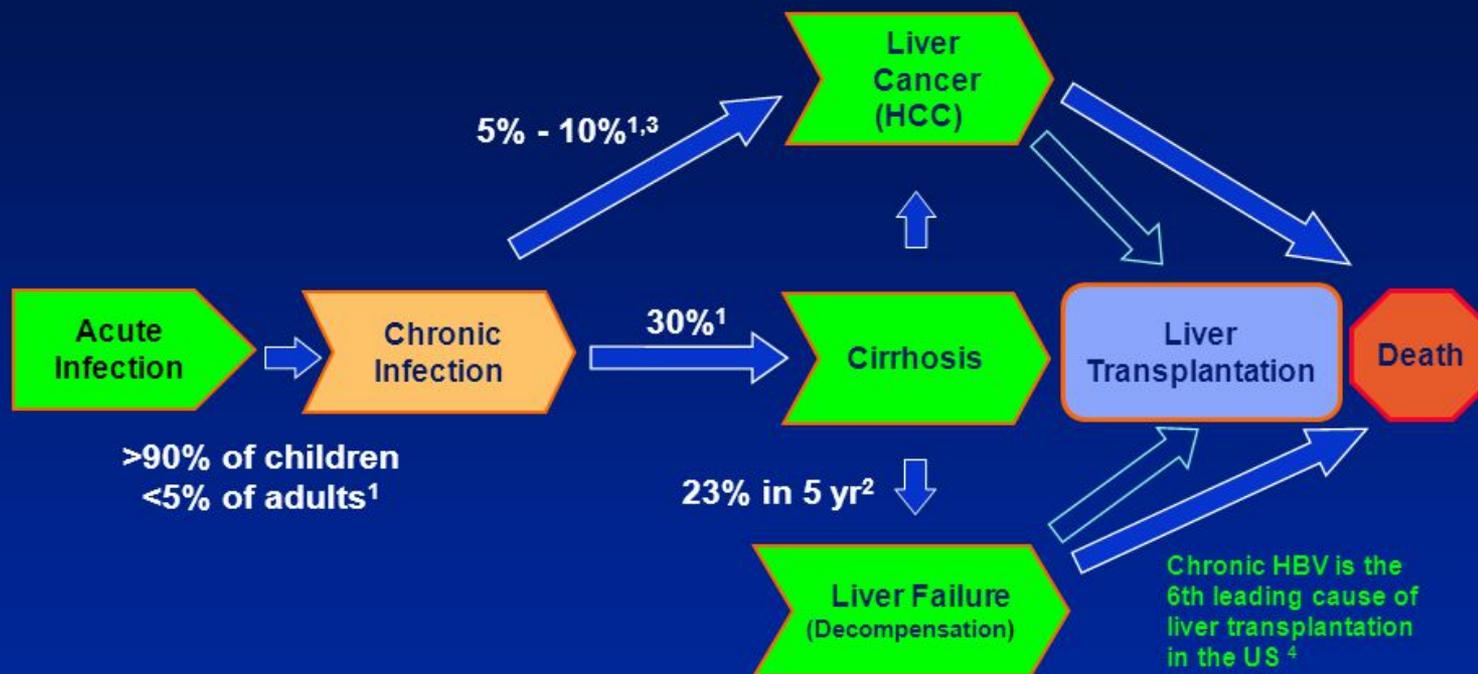


- Worldwide  $\approx$ 250 million chronic HBsAg carriers<sup>2,3</sup>
- 686,000 deaths from HBV-related liver disease and HCC in 2013<sup>4</sup>



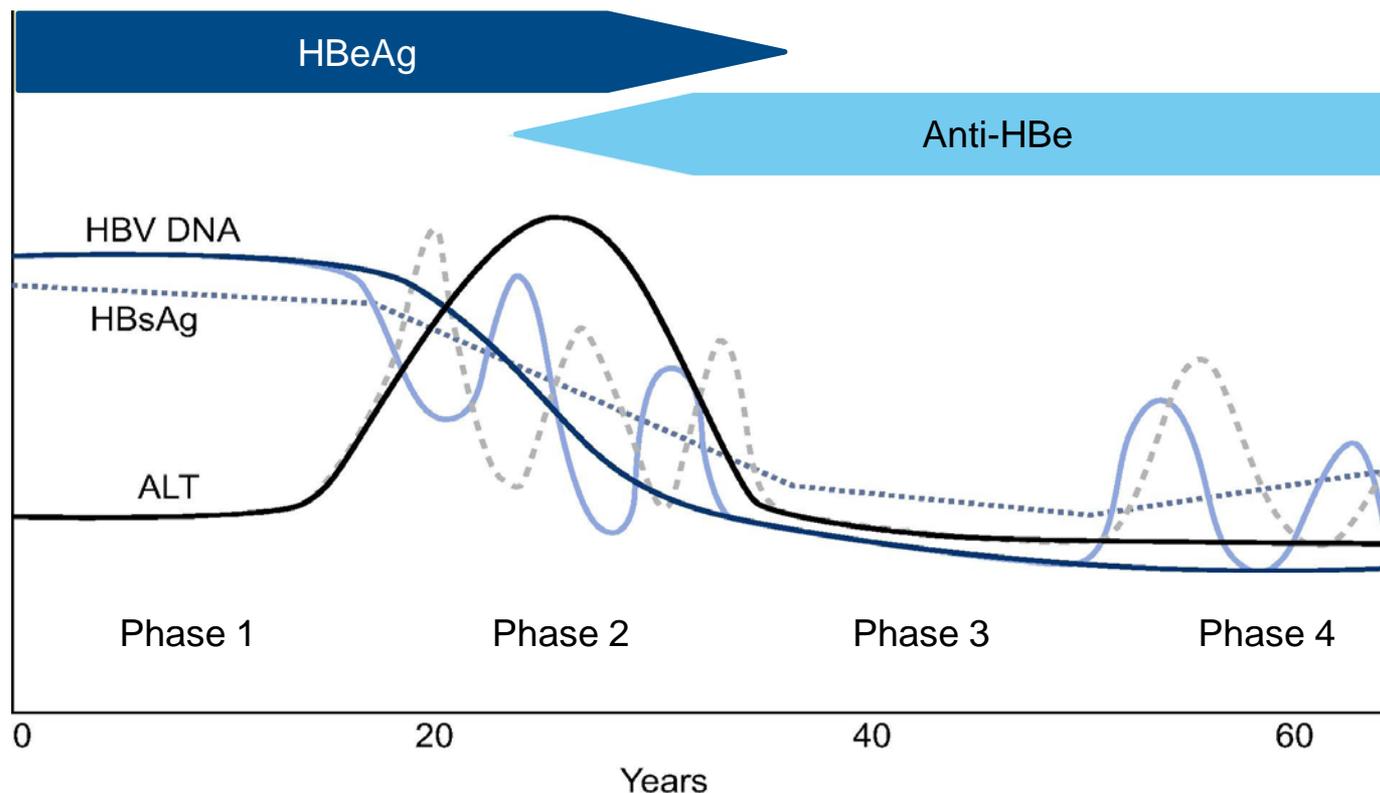
1. EASL CPG HBV. J Hepatol 2017;67:370–98; 2. Schweitzer A, et al. Lancet 2015;386:1546–55;  
3. Ott JJ, et al. Vaccine 2012;30:2212–9; 4. GBD 2013 Mortality and Causes of Death Collaborators. Lancet 2015;385:117–71;  
5. Coppola N, et al. Euro Surveill 2015;20:30009; 6. Hampel A, et al. Bundesgesundheitsblatt Gesundheitsforschung  
Gesundheitsschutz 2016;59:578–83; 7. Chen C-L, et al. J Hepatol 2015;63:354–63.

# HBV Disease Progression



1. Torresi J, et al. *Gastroenterology*. 2000;118 (2 suppl 1):S83-103.
2. Fattovich G, et al. *Hepatology*. 1995;21:77-82.
3. Moyer LA, et al. *Am J Prev Med*. 1994;10:45-55.
4. Perrillo R, et al. *Hepatology*. 2001;33:424-432.

# Phases of chronic HBV infection<sup>1</sup>



## New nomenclature<sup>2</sup>

HBeAg-positive chronic HBV infection

HBeAg-positive chronic hepatitis B

HBeAg-negative

chronic HBV infection

HBeAg-negative chronic hepatitis B

1. Lok A, et al. J Hepatol 2017;67:847–61;  
2. EASL CPG HBV. J Hepatol 2017;67:370–98

# New nomenclature for chronic phases



- The natural history of chronic HBV infection has been schematically divided into five phases

Chronic hepatitis B Chronic HBV infection	HBeAg positive		HBeAg negative		
	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5
	Chronic HBV infection	Chronic hepatitis B	Chronic HBV infection	Chronic hepatitis B	Resolved HBV infection
<b>HBsAg</b>	High	High/intermediate	Low	Intermediate	Negative
<b>HBeAg</b>	Positive	Positive	Negative	Negative	Negative
<b>HBV DNA</b>	>10 <sup>7</sup> IU/mL	10 <sup>4</sup> –10 <sup>7</sup> IU/mL	<2,000 IU/mL*	>2,000 IU/mL	<10 IU/mL <sup>‡</sup>
<b>ALT</b>	Normal	Elevated	Normal	Elevated <sup>†</sup>	Normal
<b>Liver disease</b>	None/minimal	Moderate/severe	None	Moderate/severe	None <sup>§</sup>
<b>Old terminology</b>	Immune tolerant	Immune reactive HBeAg positive	Inactive carrier	HBeAg negative chronic hepatitis	HBsAg negative /anti-HBc positive

\*HBV DNA levels can be between 2,000 and 20,000 IU/mL in some patients without signs of chronic hepatitis;

<sup>†</sup>Persistently or intermittently, based on traditional ULN (~40 IU/L). <sup>‡</sup>cccDNA can frequently be detected in the liver;

<sup>§</sup>Residual HCC risk only if cirrhosis has developed before HBsAg loss.

EASL CPG HBV. J Hepatol 2017;67:370–98

# Terugbetalingscriteria



**Indien 2 x afwijkende GPT  
& PCR VL > 2000 IU/ml**

**Entecavir 0.5 mg/d**

**of**

**Tenofovir disoproxil 245 mg/d**

**of**

**Tenofovir alafenamide 25 mg/d**

**titel**

ondertitel

datum

**Pegasys te overwegen in  
geselecteerde gevallen...**

# Monitoring patients treated with ETV, TDF or TAF



- Periodical monitoring and long-term surveillance is required in patients treated with an NA with a high barrier to resistance

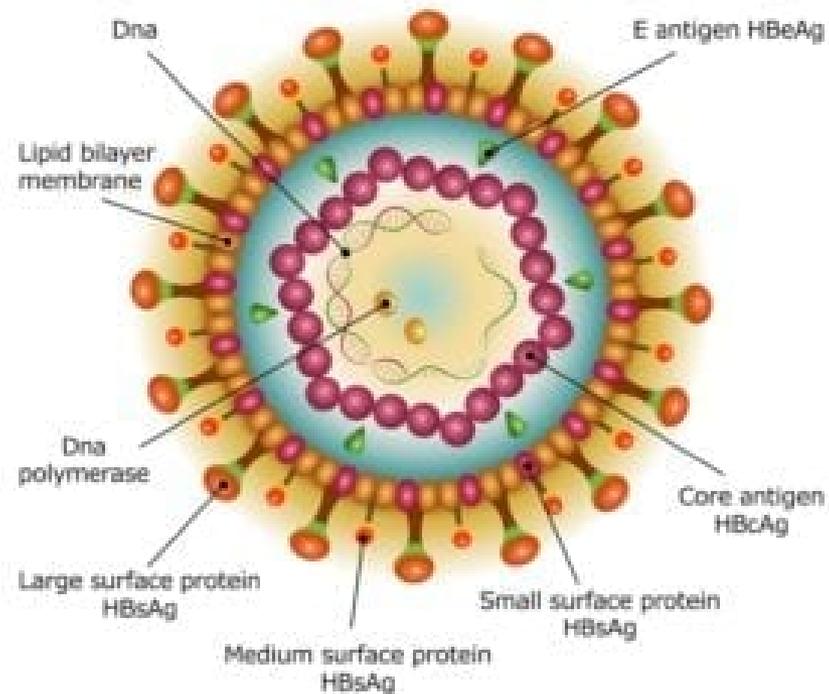
Recommendations (monitoring)	Grade of evidence	Grade of recommendation
<b>ALT and serum HBV DNA*</b> <ul style="list-style-type: none"> <li>All patients treated with NAs</li> </ul>	I	1
<b>Renal monitoring†</b> <ul style="list-style-type: none"> <li>Patients at risk of renal disease treated with any NA</li> <li>All patients treated with TDF, regardless of renal risk</li> </ul>	II-2	1
<b>Switch to ETV or TAF‡</b> <ul style="list-style-type: none"> <li>Should be considered in patients on TDF at risk of development of and/or with underlying renal or bone disease</li> </ul>	II-2/I	1
Recommendations (long-term surveillance)		
<b>HCC surveillance recommended</b> <ul style="list-style-type: none"> <li>All patients under effective long-term NA therapy</li> </ul>	II-2	1
<b>HCC surveillance mandatory</b> <ul style="list-style-type: none"> <li>All patients with cirrhosis or with moderate or high HCC risk scores at the onset of NA therapy</li> </ul>	II-2	1

\*Liver function tests should be performed every 3–4 months during the first year and every 6 months thereafter. Serum HBV DNA should be determined every 3–4 months during the first year and every 6–12 months thereafter; †Including at least eGFR and serum phosphate levels. Frequency of renal monitoring can be every 3 months during the first year and every 6 months thereafter, if no deterioration. Closer renal monitoring is required in patients who develop CrCl <60 ml/min or serum phosphate levels <2 mg/dl; ‡Depending on previous LAM exposure  
 EASL CPG HBV. J Hepatol 2017;67:370–98



# Hepatitis B Virus

Baltimore Group VII (dsDNA-RT)



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- **Nieuwe molecules**
  - > Entry inhibitors
  - > siRNA
  - > Capsid assembly modulators
  - > Nucleic acid polymers
  - > Inarigivir + RIG-I agonist

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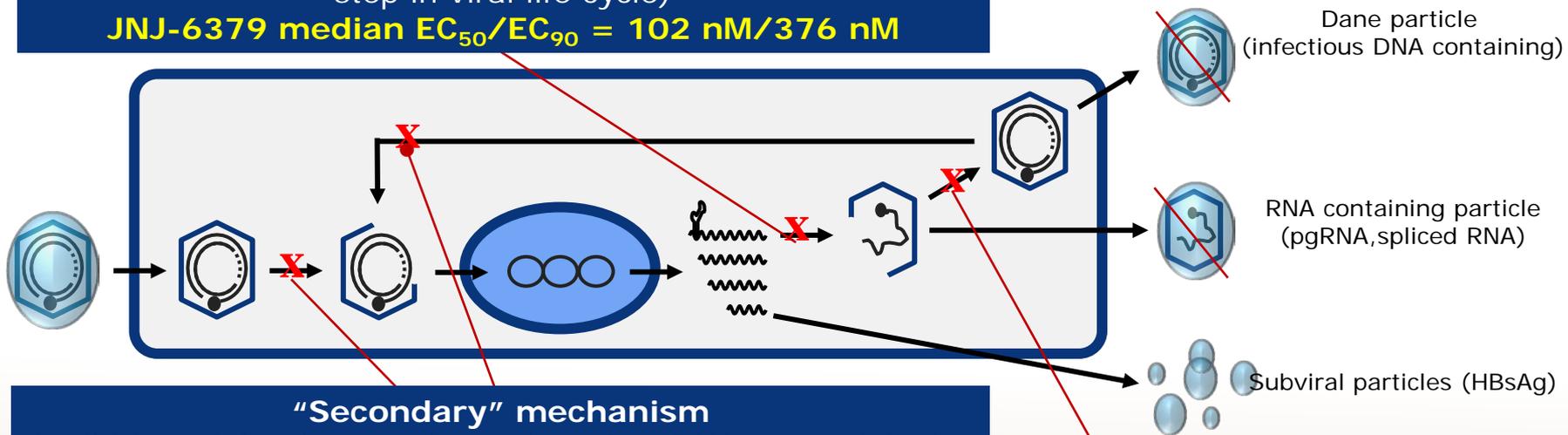
# JNJ-6379 has a dual mechanism of action

JNJ-6379 is a CAM that binds to HBV core protein and disrupts early and late-stage processes in the HBV life cycle.

## “Primary” mechanism (“empty capsid” CAM)

Interference with capsid assembly kinetics, preventing encapsidation of (pg)RNA and blocking HBV replication (late step in viral life cycle)

**JNJ-6379 median  $EC_{50}/EC_{90}$  = 102 nM/376 nM**



## “Secondary” mechanism

Inhibition of the de-novo formation of cccDNA, potentially by interfering with the capsid disassembly process (early step in viral life cycle)

**JNJ-6379 median  $EC_{50}/EC_{90}$  = 876 nM/4019 nM**

NAs block HBV replication but do not inhibit the production of RNA-containing particles

# Safety, PK, and antiviral activity of JNJ-56136379 (JNJ-6379) in patients with chronic hepatitis B

## Objective:

To evaluate the safety, pharmacokinetics, and antiviral activity of multiple doses of the novel hepatitis B virus (HBV) capsid assembly modulator, JNJ-6379, in patients with chronic hepatitis B infection (NCT02662712)

## Methods:

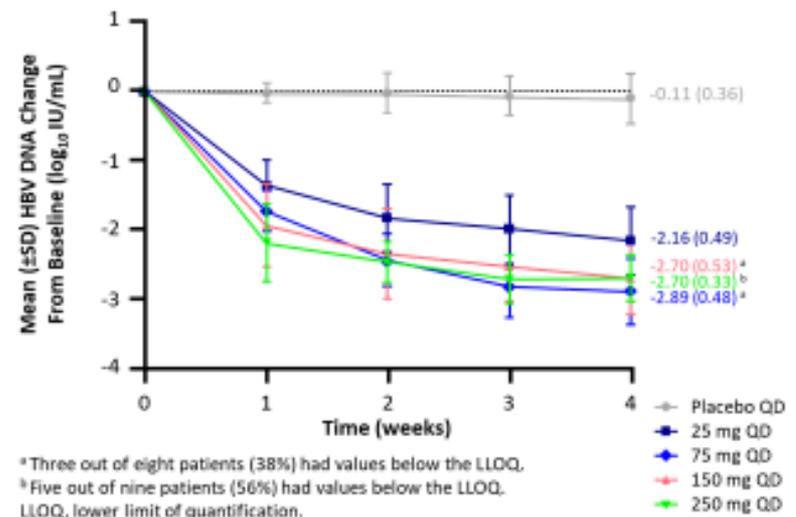
Non-cirrhotic, treatment-naïve, HBeAg-positive or -negative patients were randomized to receive either JNJ-6379 or placebo for 28 days, with 8 weeks follow-up, in one of four 12-patient dose groups: 25 mg QD (after 100 mg loading dose); 75 mg QD; 150 mg QD; and 250 mg QD.

## Conclusions:

All four treatment regimens of JNJ-6379 evaluated were safe and well tolerated; demonstrated dose-dependent PK; and exhibited potent antiviral activity in patients chronically infected with HBV.

Zoulim F, et al., Abstract 74

Mean HBV DNA change during treatment with JNJ-6379



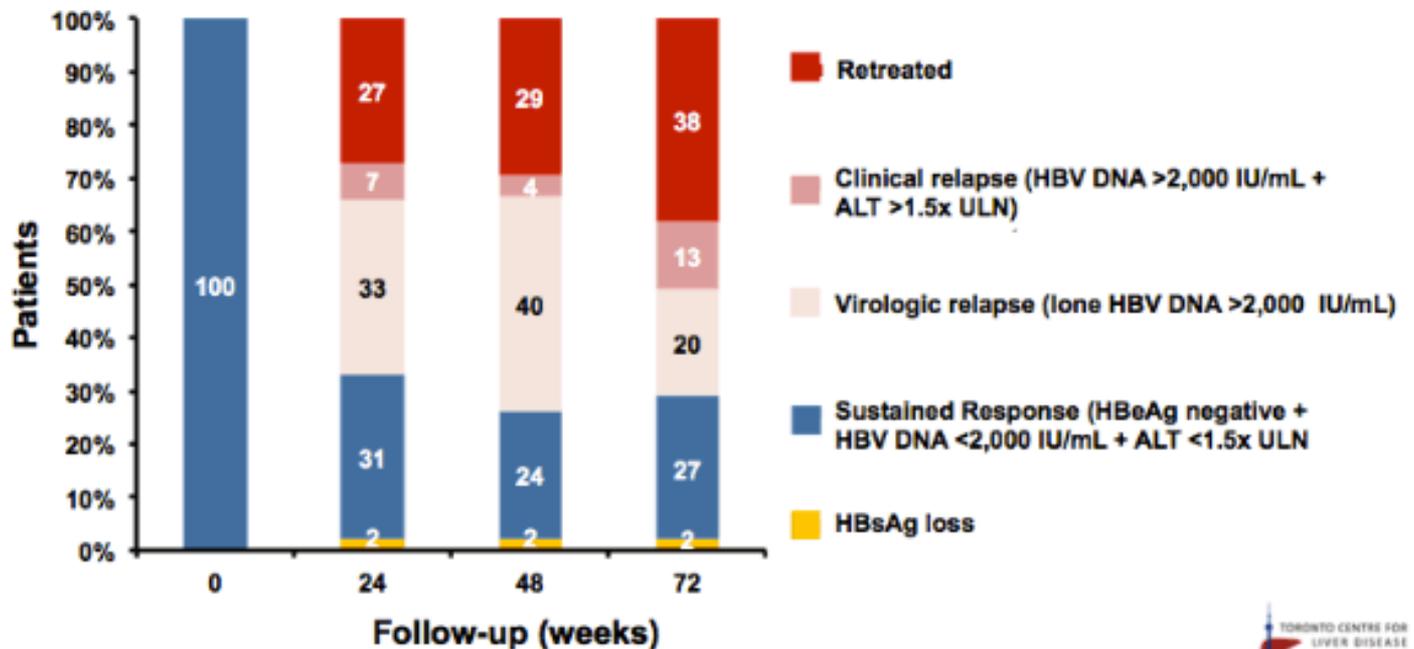
# Discontinuation of NA treatment



- Long-term therapy with NAs is usually required
  - HBV eradication is not usually achieved

Recommendations	Grade of evidence	Grade of recommendation
<b>NAs <u>should</u> be discontinued</b> <ul style="list-style-type: none"><li>• After confirmed HBsAg loss (<math>\pm</math> anti-HBs seroconversion)</li></ul>	II-2	1
<b>NAs <u>can</u> be discontinued</b> <ul style="list-style-type: none"><li>• In HBeAg-positive patients, without cirrhosis, who achieve stable HBeAg seroconversion and undetectable HBV DNA and complete <math>\geq 12</math> months of consolidation therapy</li></ul> <b>Close post-NA monitoring is warranted</b>	II-2	2
<b>NAs <u>may</u> be discontinued</b> <ul style="list-style-type: none"><li>• In selected HBeAg-negative patients, without cirrhosis, who achieve long-term (<math>\geq 3</math> years) virological suppression, <b>if close post-NA monitoring can be guaranteed</b></li></ul>	II-2	2

## Sustained response, retreatment & HBsAg loss in stop arm (n=45)



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- **HBeAg pos**
  - > eAg seroconversie
  - > PCR onder detectielimiet
  - > Normale TA
  - > Laag HBsAg (< 1000)
  - > GEEN cirrose
  - > Perfecte compliance

**titel**

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- **HBeAg neg**
  - > > 3j antivirale therapie
  - > PCR onder detectielimiet
  - > Normale TA
  - > Rol HBsAg-titer minder duidelijk
  - > GEEN cirrose
  - > Perfecte compliance

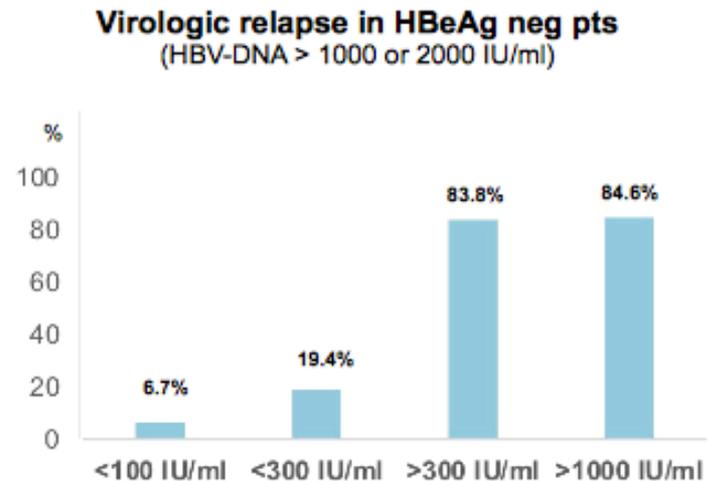
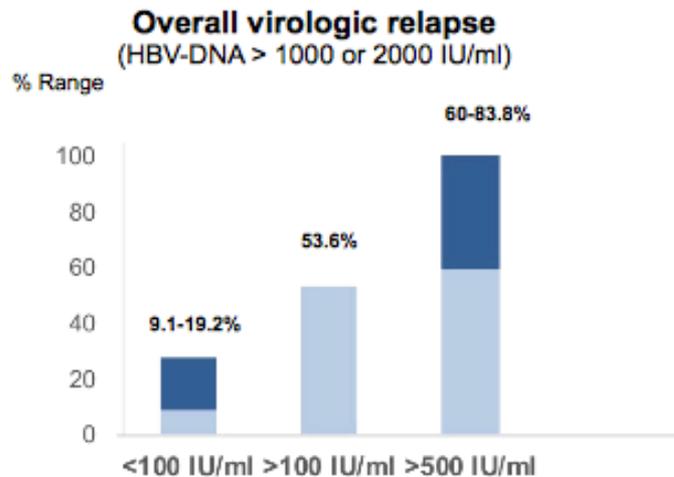
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## The role of HBsAg in NUCs cessation among Asian CHB patients: a systematic review

- 1761 papers were identified on the topics and **11** were included in the review (randomized or observational studies, with at least 10 pts enrolled; NUCs treatment duration of at least 24 months; treatment discontinuation for virological remissions; at least 12 months of post NUCs discontinuation; virological and clinical data available)
- **1716 patients**, median NUCs treatment ranged between 22.3-56.12 months, with a virologic remission before NUCs stop of 12-36.7 months, duration of **post-treatment f.u. 12-157 months**
- **HBsAg loss** ranged **21.1-58.8%** in pts with HBsAg < 100 IU/ml, vs 3.3-7.4% in pts with HBsAg >100 IU/ml



- **Minder goede resultaten in ptn van Aziatische afkomst**
- **Strikte biochemische follow up**
- **Herstart therapie indien TA fors oplopend en/of sterk verhoogde virale lading**
- **HBsAg seroconversie kan zeer laattijdig plaatsvinden!**

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# Hepatitis B



- **Correcte opvolging**
- **Behandeling is doeltreffend en veilig**
- **Nieuwe behandelingen in studie**
- **Proefstop in geselecteerde patienten**

**titel**

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# *Hepatitis Delta*

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‘the facts’



**Ontdekt in 1977 in Italië**

**RNA-virus; kleinste virus**

**Steeds in combinatie met Hep B**

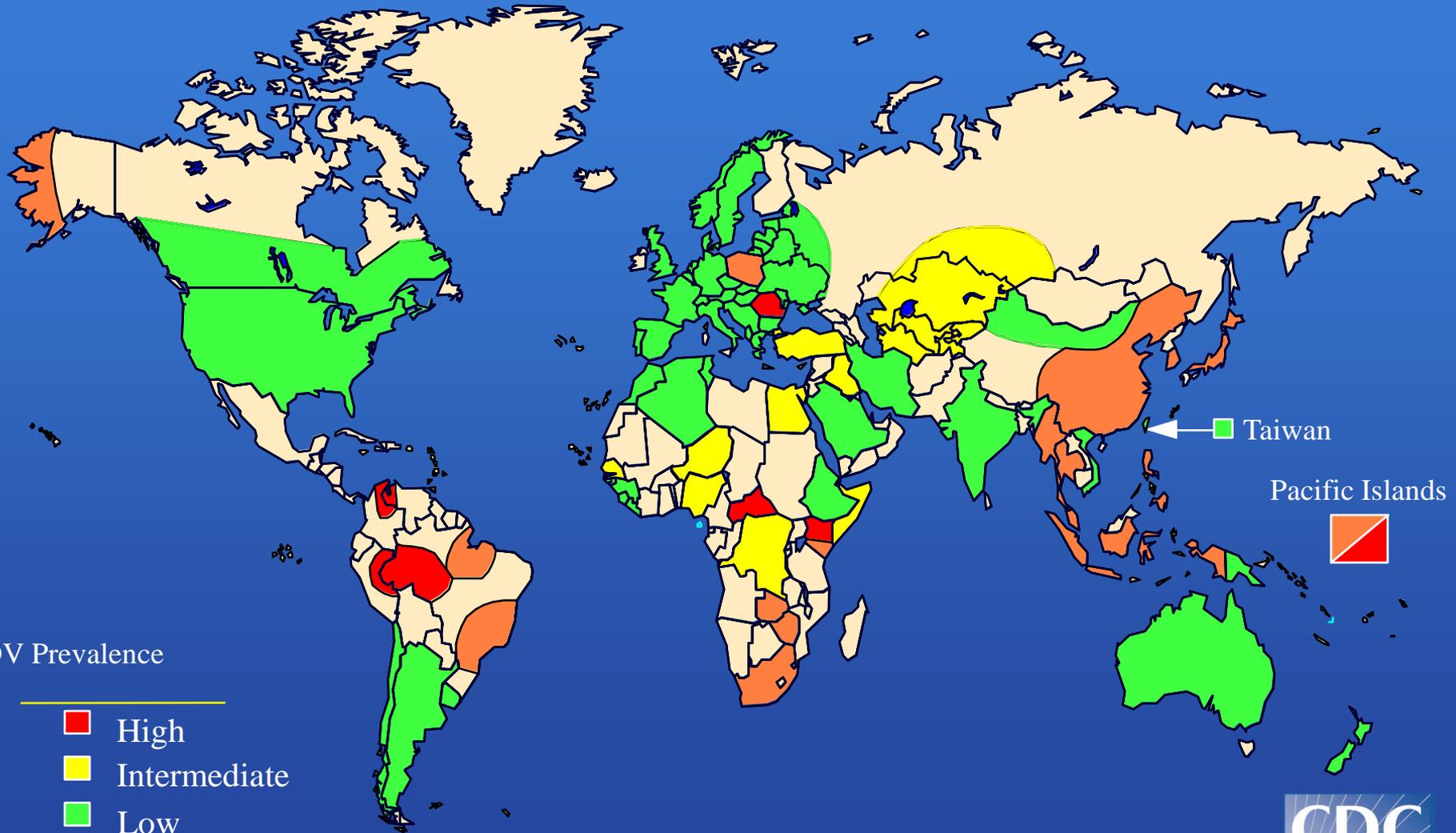
**20 milj mensen wereldwijd besmet**

**Transmissie: bloed-bloed**

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# Geographic Distribution of HDV Infection



Taiwan

Pacific Islands



HDV Prevalence

- High
- Intermediate
- Low
- Very Low
- No Data

- > enkel bij patienten met Hep B
- > aan denken indien TA verhoogd en VL HBV-DNA laag
  
- > Hep Delta As
- > Hep Delta PCR

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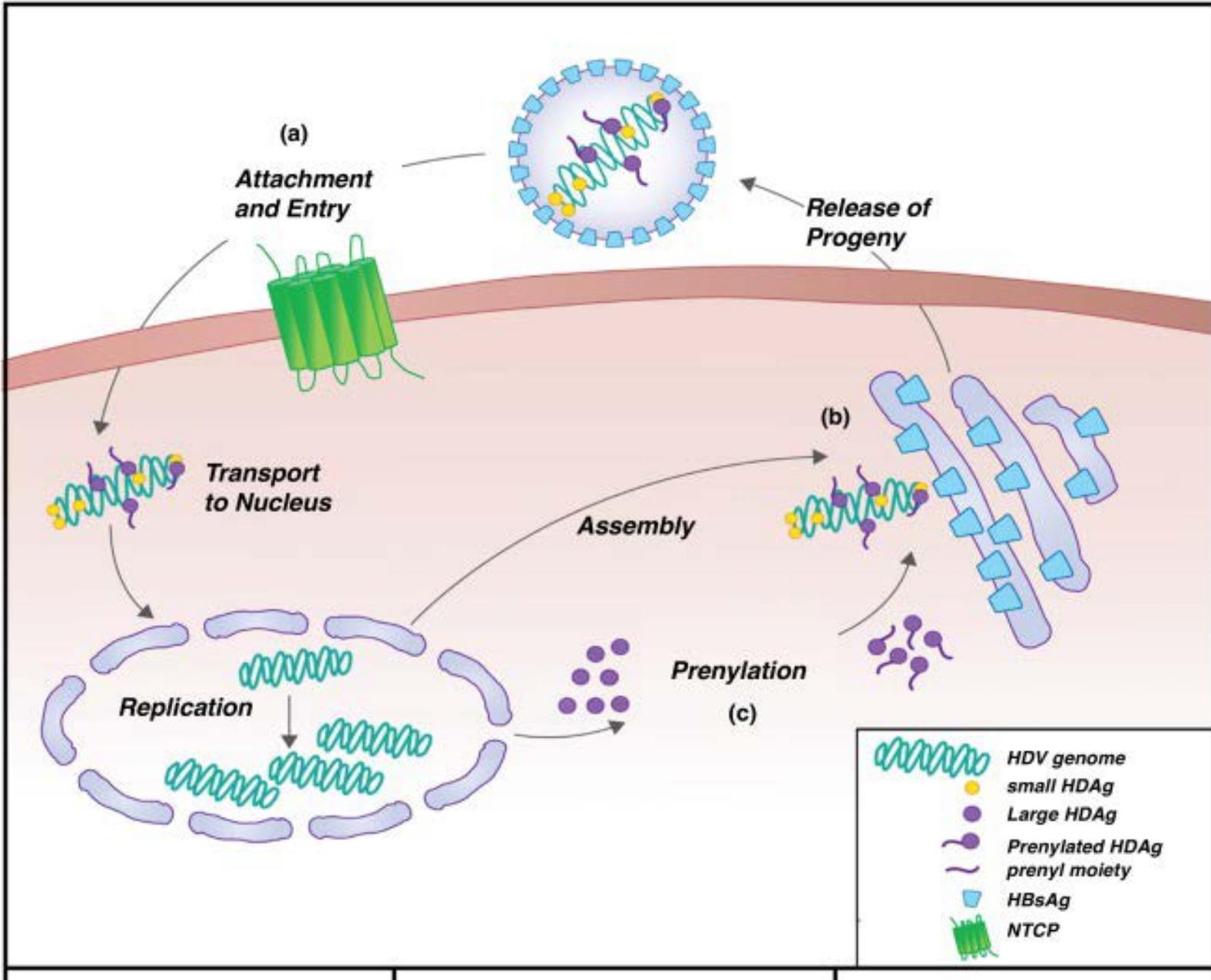
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# Hepatitis D - Clinical Features

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- Coinfection with HBV
  - severe acute disease
  - low risk of chronic infection
- Superinfection on top of chronic HBV
  - usually develop chronic HDV infection
  - high risk of severe chronic liver disease



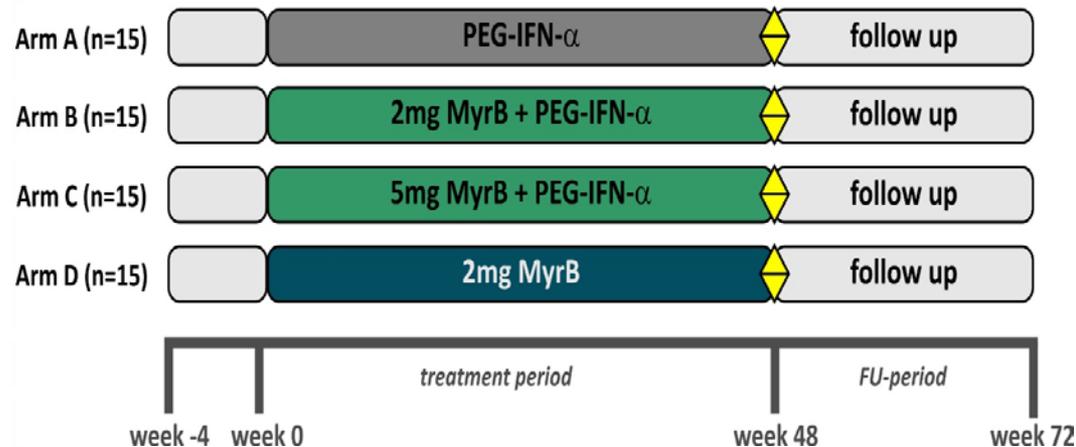
# Myrcludex B with PEG-interferon $\alpha$ 2a: Safety and efficacy in patients with chronic HBV/HDV co-infection in a phase 2 trial (MYR203)



## BACKGROUND & AIMS

- Myrcludex B (MyrB, Bulevirtide) is a first-in-class entry inhibitor for HBV/HDV infection
- In a phase 2 study MYR202, MyrB monotherapy led to HDV RNA decline and improvement of ALT levels
- End-of-treatment data from a MyrB  $\pm$  PegIFN $\alpha$ 2a 48 weeks combination study (MYR203) have been reported<sup>1</sup>
- Here, the 24-week treatment-free follow-up data are presented

## METHODS



- Primary endpoint: undetectable serum HDV RNA at Week 72 (w72)
- Secondary endpoints: ALT normalization, combined treatment response\*, and HBsAg reduction  $>1 \log_{10}$

\* $\geq 2$  log serum HDV RNA decline + normal ALT levels.  
1. Wedemeyer H, et al. Hepatology 2018;68(Suppl):11.  
Wedemeyer H, et al. ILC 2019; GS-13

# Myrcludex B with PEG-interferon $\alpha$ 2a: Safety and efficacy in patients with chronic HBV/HDV co-infection in a phase 2 trial (MYR203)



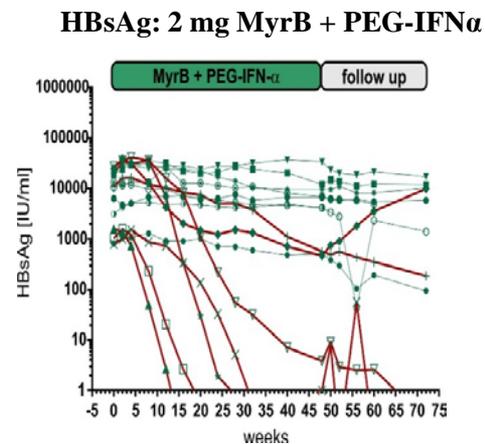
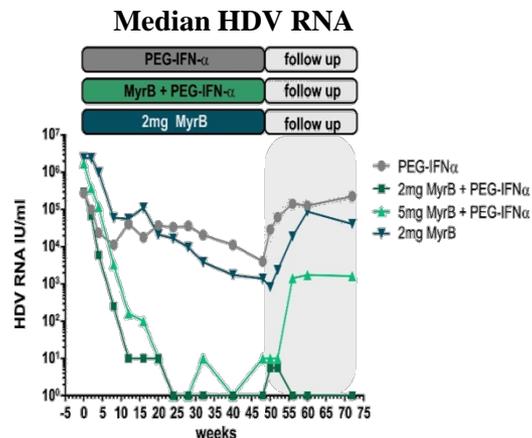
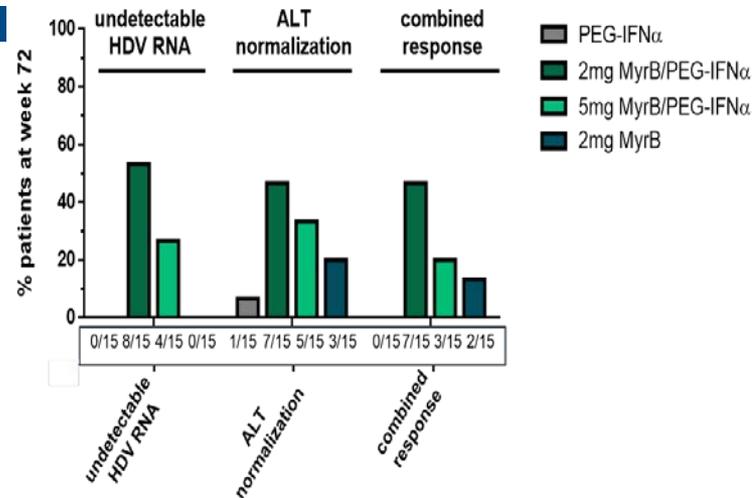
## RESULTS

- Safety:** MyrB was well tolerated, with 155 drug-related AEs up to w72 (mild n=122, moderate n=28, serious n=5), primarily increased total bile salts
  - Most AEs (n=524) related to PegIFN $\alpha$ 2a
  - All cases resolved; bile salts returned to baseline by follow-up Week 50
  - Two SAEs (anal fistula and proctitis) not-related to MyrB occurred in 1 patient of Arm B in follow-up
- Efficacy:** MyrB + PegIFN $\alpha$ 2a induced a significant enhancement of HDV RNA response
  - 40% (12/30) patients had undetectable HDV RNA at Week 72

2 mg MyrB + PegIFN $\alpha$ 2a induces HBsAg response in HBsAg negative patients at Week 72

  - 40% of patients experienced HBsAg response
  - In this group 27% lost HBsAg and 20% seroconverted

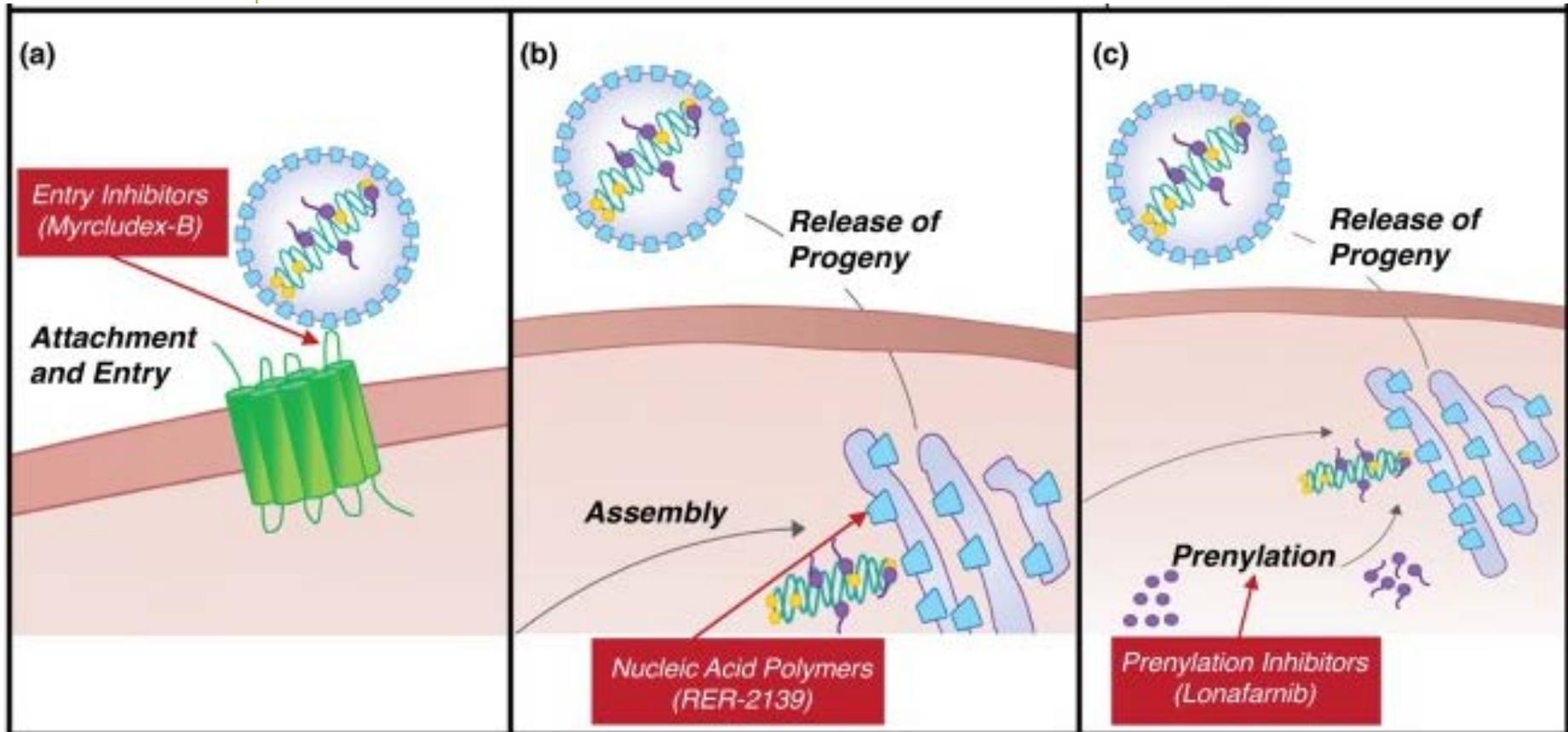
## RESULTS



## CONCLUSIONS

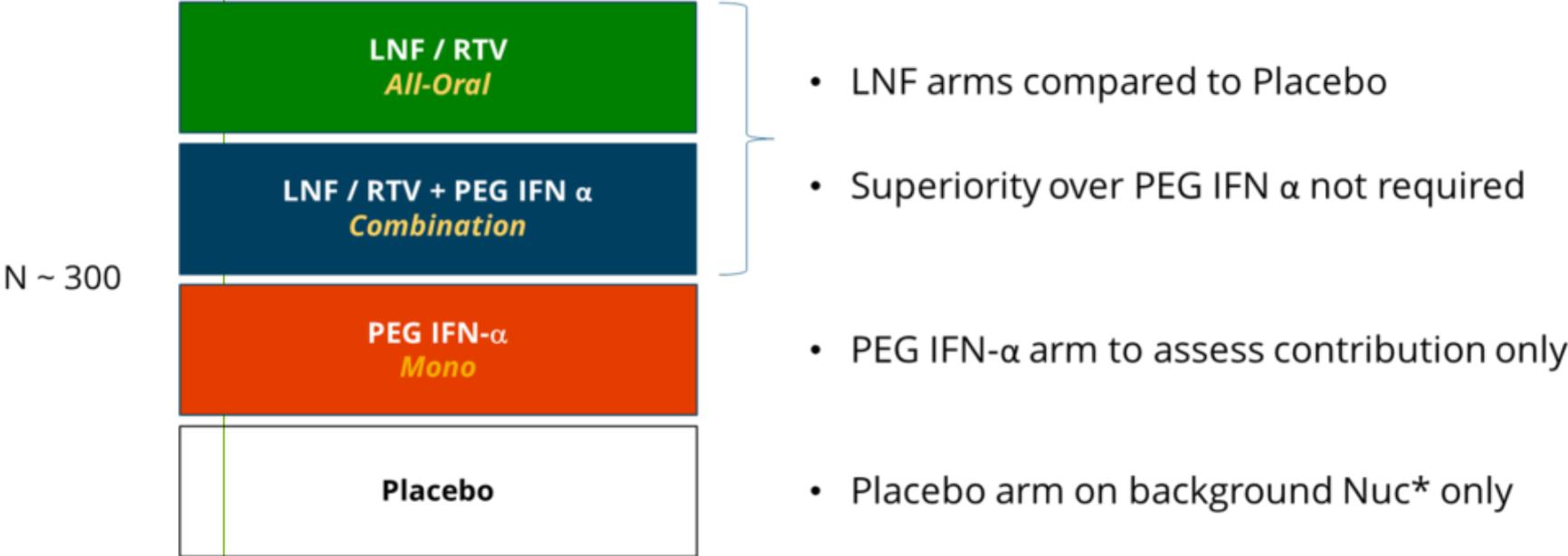
In contrast to PegIFN $\alpha$ 2a monotherapy, MyrB + PegIFN $\alpha$ 2a demonstrated high rates of HDV RNA suppression. HBsAg loss was achieved in 27% of patients, indicating a potential role for MyrB in future HBV cure regimens





# Planned Phase 3 D-LIVR Study

## Delta Liver Improvement and Virologic Response in HDV



\*Nuc = HBV nucleoside or nucleotide Rx. All patients will be on background HBV nuc therapy

**titel**  
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## Casus JL, man, 51 j

- **10/2008**                    **HBsAg pos**
- **7/2009**                    **eerste consult**
- **8/2009**                    **staging**
  - > HBeAg pos
  - > GPT (ALT)    111 & 99 IU/l (nl < 49)
  - > VL: 192.000.000 IU/ml
  - > LeverBx: F1A1
  - > HIV & HCV negatief

**titel**

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## Casus JL, man, 51 j

- **11/2009 start Entecavir 0.5 mg/d**
- **9/2011**
  - > Normale TA
  - > PCR hep B <20 IU/ml
  - > HBeAg neg, HBeAs neg
  - > HCC screening negatief

**titel**

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## Casus JL, man, 51 j

- **6/2018**
  - > HBsAg pos
  - > HBeAg neg, HBeAs neg
  - > TA normaal
  - > PCR hep B: < 15 IU/ml
  - > HBsAg kwant: < 45 IU/ml
  - > HCC screening negatief

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## Casus JL, man, 51 j

- **6/2018**
  - > HBsAg pos
  - > HBeAg neg, HBeAs neg
  - > TA normaal
  - > PCR hep B: < 15 IU/ml
  - > HBsAg kwant: < 45 IU/ml
  - > HCC screening negatief
- **9/2018**
  - > Proefstop Entecavir

**titel**  
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## Casus JL, man, 51 j

- **11/2018**
  - > NI TA
  - > PCR hep B: 60 IU/ml
  - > HBsAg pos
  - > HBeAg pos!
- **1/2019**
  - > NI TA
  - > PCR heb B: 28500 IU/ml
  - > HBeAg pos
  - > HBsAg < 45 IU/ml

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## Casus JL, man, 51 j

- **2/2019**
  - > GPT 176 IU/ml (nl tot 49)
- **3/2019**
  - > Herstart Entecavir 0.5 mg/d
- **3/2019 (4 w na herstart R/)**
  - > GPT 79 IU/ml
  - > HBsAg negatief!
- **6/2019**
  - > NI TA
  - > HBsAg neg, HBsAs neg

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# Case 2: Ms HVW



**Name:** Ms HVW **Age:** 37 years **Sex:** Female

## **Patient notes:**

- Heavy personal history with psychiatric problems ++ (suicidal ideation, domestic violence)

## **Drug use**

- Alcohol+++/cocaine+/benzodiazepine+ (alcohol abuse continued until a fall on 30/11/2017 from 4th floor window; circumstances unclear; severe injuries)

## **Health/social status**

- Homeless; history of severe partner violence (multiple times)
- Borderline personality; various hospitalisations on a psychiatric or addiction unit
- Restored contact with family (daughter living with patient's sister from age 12 years)

## **HCV status**

- GT 3, LVL, F2; infected since 2017; diagnosed 25/10/2017

## **Method of engagement**

- Long hospitalization following the fall was an opportunity to treat HCV
- Education: nurse
- Still living in hospital addiction unit; recovering from injuries, but in good condition and working on a new or different future

# Case 2: Ms HVW



- C-Buddies and Team Leader (HCV nurse) were important in her recovery

Contacted via medical-social support centre (MSOC) and NSP



Diagnosed with HCV infection on admission



After incident C-Buddies are with her daily at ZNA



**Oct 2017**  
First appointment with Dr Bourgeois



## Hep nurse

- Legal advice
- Medical advice
- Contact with social services



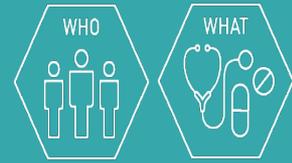
## Peers

- Moral support
- Navigation in hospital,
- Practical support
  - Clothes, meds, food, toiletry supplies
  - Taking her to park and coffee shop

## Treatment started April 2018

- Staging: PCR and ultrasound
- Medication prescribed
- Follow-up

# 2015: Start of the 'not under one roof' HCV management



## Free Clinic

- Pre-counselling (reception, counsellor, GPs, nurses, social workers)
- Screening
- Information
- Referral: passive/active
- Follow-up: medical/social/mental health
- Talking about drug use and risks

## Needle exchange

- Prevention
- Sterile injections
- Safe injecting technique
- Referral
- Screening: swab2know
- Talking about drugs and risks



## Specialist hepatologist

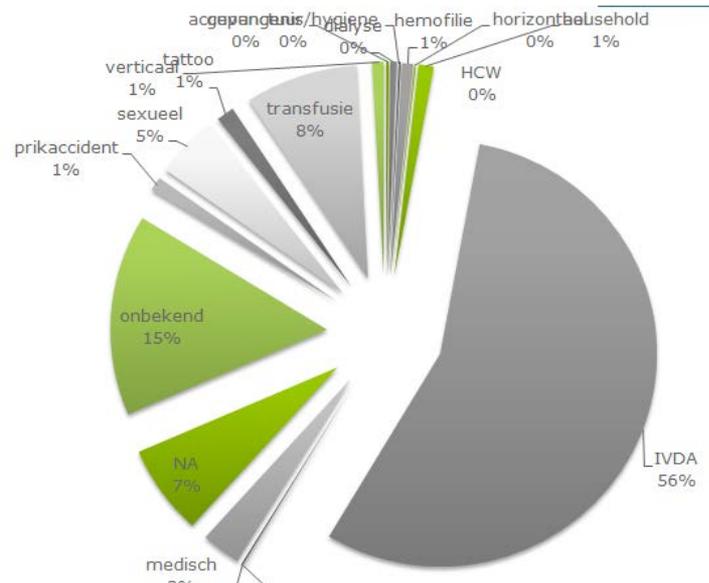
- Staging
- Trials
- Referral for other medical issues (holistic medical approach)
- Medication
- Follow-up
- Talking about drugs
- 'Streetwise' specialist is important

## C-Buddies

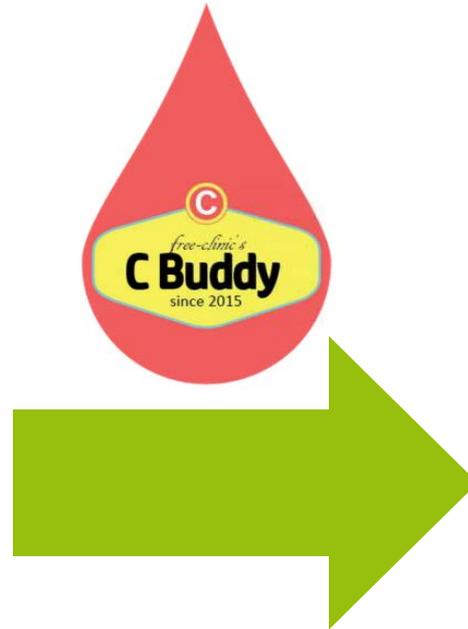
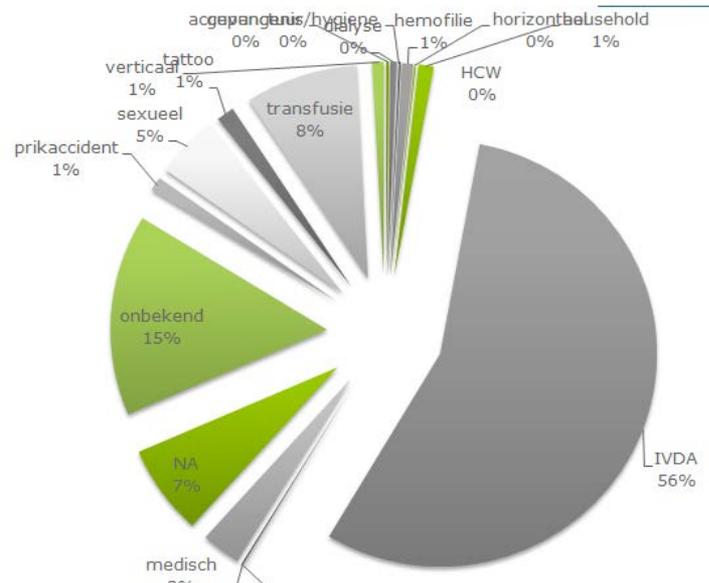
- Meeting people (connecting)
- Dialogue
- Matching
- Start the process together:
  - Appointments
  - Going to the specialist
  - Text & call: appointment reminders
  - Giving advice (food, sleep, healthy living, exercise, medication, appearance)
  - Talking about drug use
  - Translating medical terminology
  - Navigating the hospital system with patients

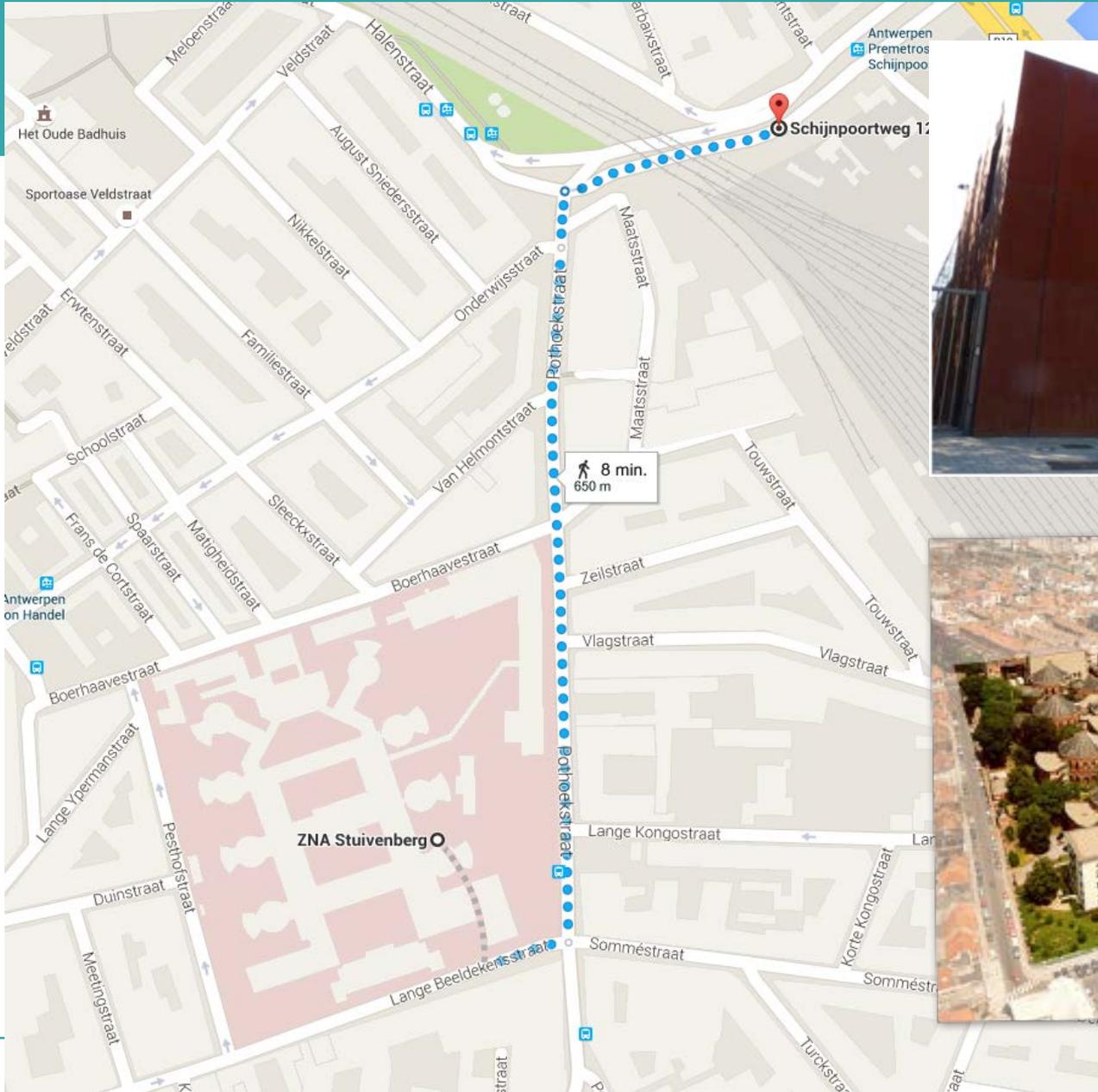


# Hep C in Antwerp



# Hep C in Antwerp







**THE END!**