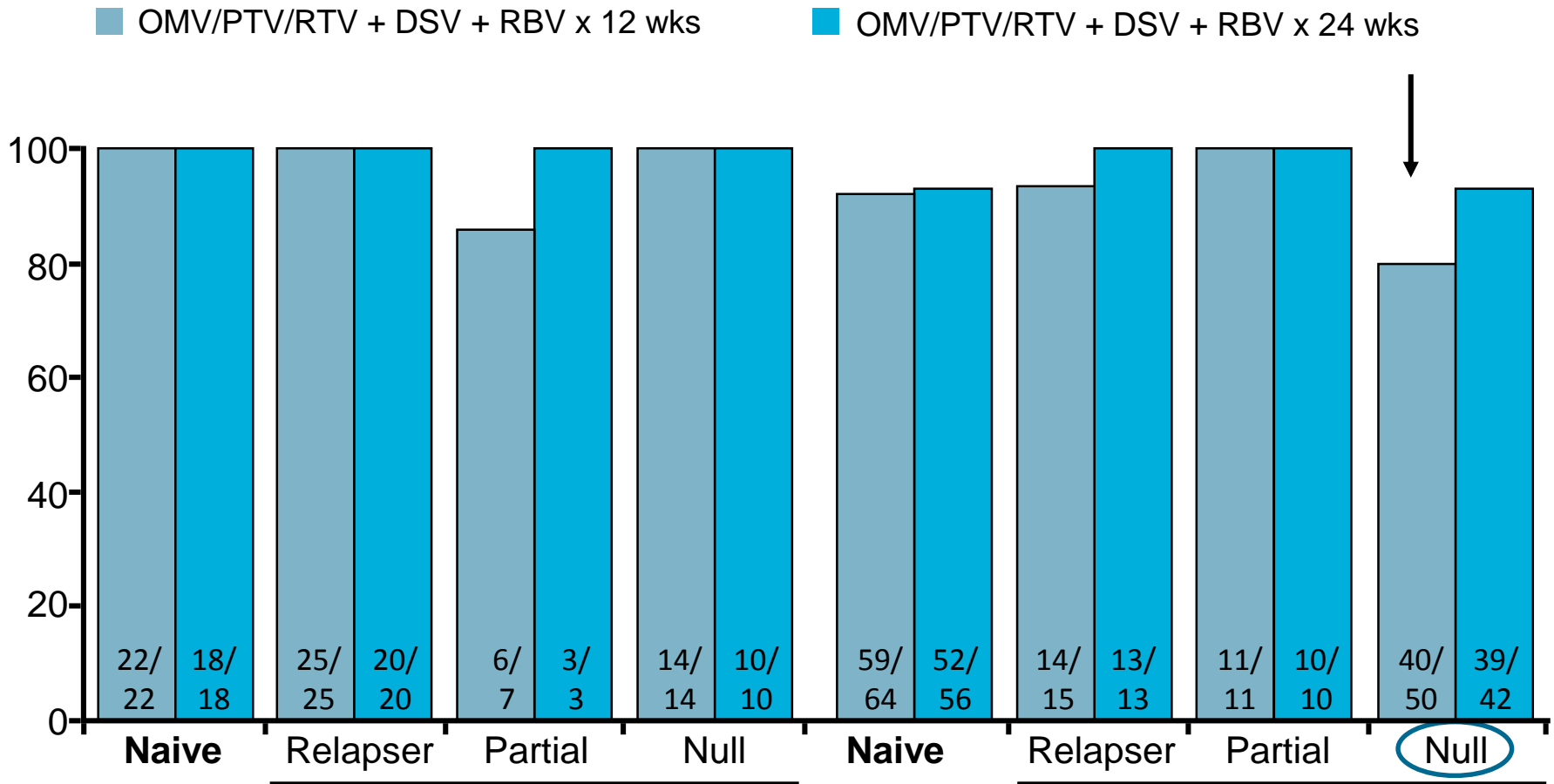


Hepatitis C: Iedereen behandelen en hoe behandelen in 2017 ?

Joost PH Drenth

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HCV presentation



Hepatitis Centra



11 HCV lessons

- 11 lessons
- 1 case
- 2 questions

Lesson 1

- If we start therapy for chronic hepatitis C infection,
- Aim -> Cure

Lesson 2

- Who should be treated?
- Everyone , unless.....
- HCVRichtsnoer
-Derhalve is de richtsnoer commissie van mening dat er een indicatie is voor behandeling voor iedere HCV patiënt in Nederland.....

Lesson 3

- New standard therapies for chronic hepatitis C
- Interferon-free



Lesson 4

- No Monotherapy
- But Combinations

“-previr”

Simeprevir
Paritaprevir
Grazoprevir

“-asvir”

Ledipasvir
Daclatasvir
Ombitasvir

Velpatasvir
Elbasvir

“-buvir”

Sofosbuvir (Nuc)
Dasabuvir (non-Nuc)



NS3-Protease-Inhibitor



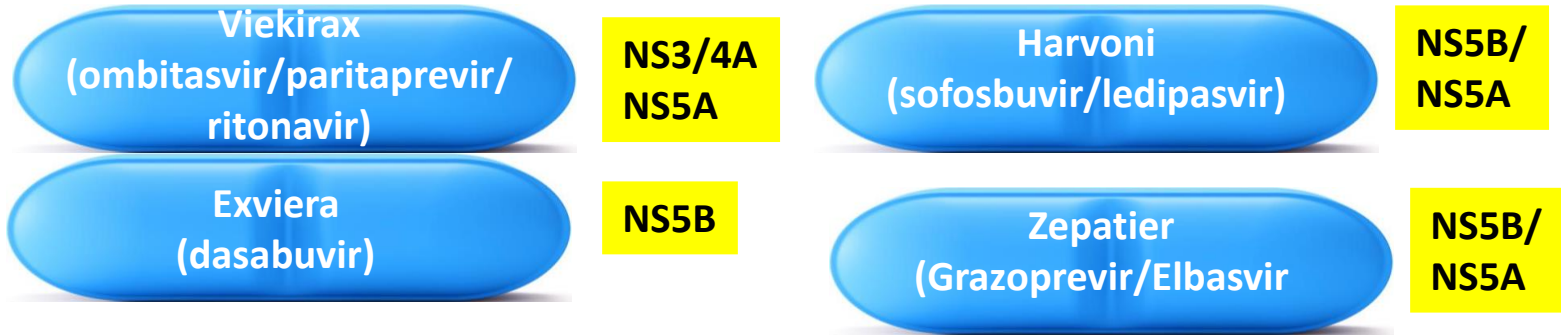
NS5A-Inhibitor



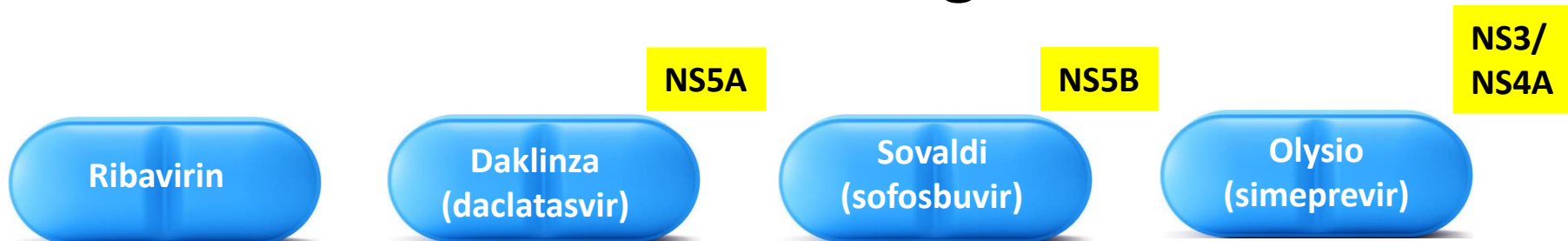
NS5B-Polymerase-Inhibitor

Lesson 4

Fixed combinations



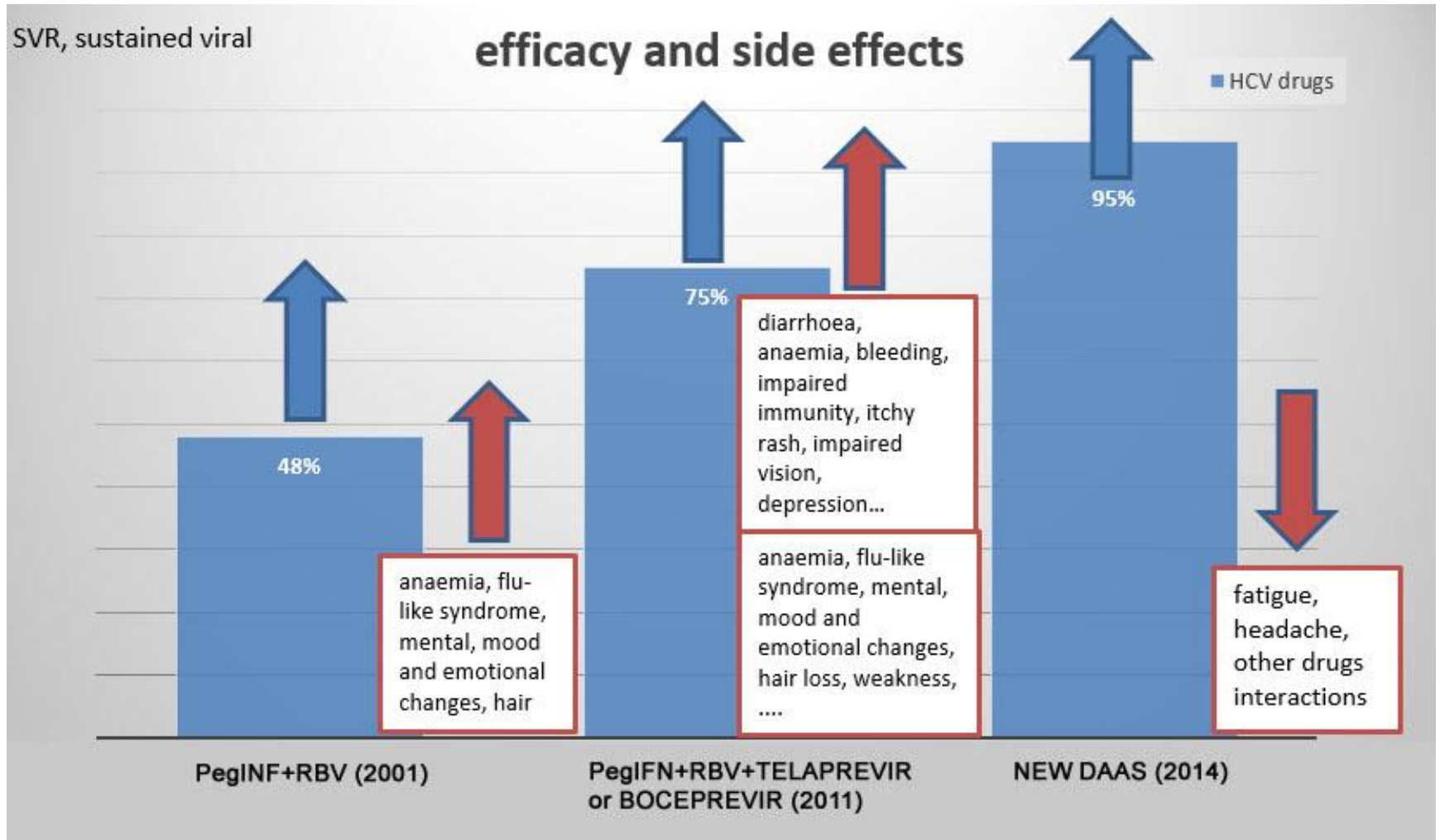
Individual drugs



Lesson 5

- Properties of direct antiviral agents/**combination** therapies
- High sustained virologic response rates > 90%
- Good tolerability
- Simple dosing in the real-life setting

Lesson 5



Lesson 6

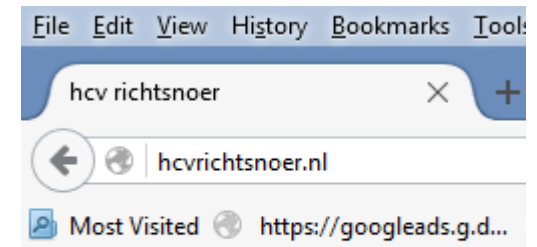
Three important aspects before you start

- **Genotype**
 - 1, 2, 3, 4
- **Fibrosis stage**
 - Cirrhosis or not
- **Treatment history**
 - Naïve / Experienced

Use HCV Richtsnoer

Lesson 7 HCV Dutch guidance

- HCV richtsnoer
 - 11 healthcare professionals
 - NVMDL/NVH/NIV/NVHB/NVZA
 - Updated every 3 months
- Based on other guidelines
 - AASLD/IDSA: Recommendations for Testing, Managing, and Treating Hepatitis C
 - EASL Recommendations on Treatment of Hepatitis C 2015
 - Aktuelle Empfehlung zur Therapie der chronischen Hepatitis C
 - Association Francaise pour l'Etude du Foie (AFEF): Traitement des hépatites virales C, Avis d'experts



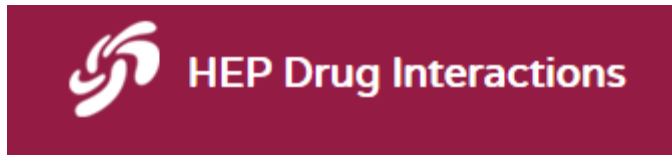
?> **HCV richtsnoer**

Lesson 8: pretreatment

- Screening @ -4 weeks
- **Laboratory**
 - Hematocytometrie, ALT, Creatinin, Bilirubin
 - Hepatitis B & HIV serologie
 - Hepatitis C PCR, C Genotype → if unknown
- **History taking**
 - Manage expectations, side effects, pregnancy, comorbidity
- **Diagnosis**
 - Fibroscan, Ultrasound (HCC, cirrhosis)

Lesson 9

- Interactions



HEP Drugs	Co-medications	Drug Interactions
<input type="text" value="daclatasvir"/>	<input type="text" value="amlodipine"/>	Switch to table view
<input type="radio"/> A-Z <input type="radio"/> Class <input type="radio"/> Trade	<input type="radio"/> A-Z <input type="radio"/> Class	Reset Checker
<input checked="" type="checkbox"/> Daclatasvir ⓘ	<input checked="" type="checkbox"/> Amlodipine ⓘ	Potential Interaction
<input checked="" type="checkbox"/> Daclatasvir ⓘ	<input checked="" type="checkbox"/> Amlodipine ⓘ	Daclatasvir
		Amlodipine

Lesson 10: on-treatment

- On treatment 0-12 weeks
- 4 Visits @ 2, 4, 8, 12 weeks
- Laboratory
 - Hematocytometrie, ALT, Creatinine, Bilirubin
 - Week 12 (EOT) HCV quantitative
- History Taking
 - Side effects, new co-medication?

Lesson 11: post treatment

- After treatment
- 1 Visit @ 24 weeks (12 weeks post treatment)
- Laboratory
 - Hematocytometrie, ALT, Creatinine, Bilirubin
 - Week 24 (SVR) HCV quantitative
- Management
 - Depending on presence of liver cirrhosis

Question 1

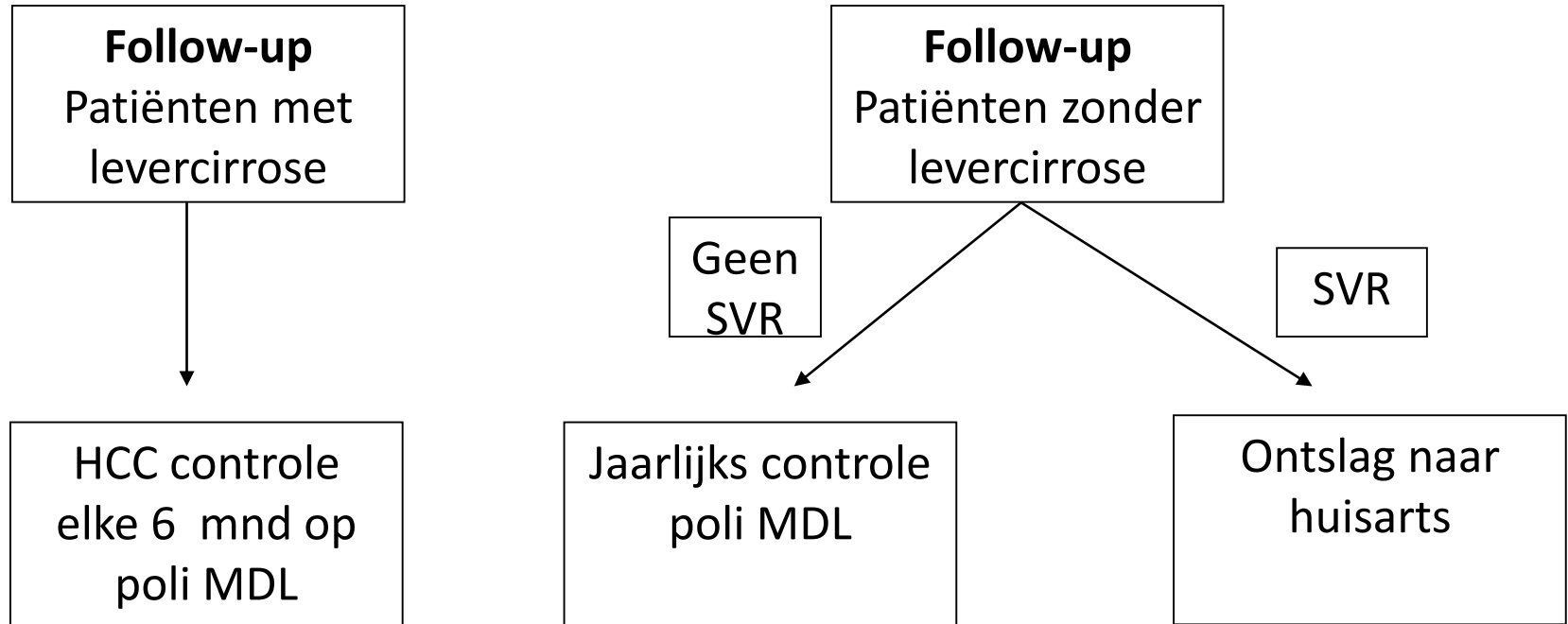
- 57-year-old patient
- Chronic Hepatitis C infection, genotype 1a, transmission route iv drug use, viral load 1 milj IU/ml, ALT 87 IU/L. Fibroscan 3.8 kPa (F0)
- Treatment with Perfectopill (new DAA) & Cure
- Which Follow up?
- Every Year

green

- Discharge

red

Follow-up after treatment



- **Behandelgeschiedenis HCV**
- 32 jarige vrouw
- Chronische hepatitis C genotype 1b. Viral load 6 milj IU/ml , ALAT 83 IU/L
- Leverbiopt: uitgebreide chronische actieve ontsteking bij HCV. Metavir F3-4.

- 2008 PEG-interferon/ribavirine
- PEG Interferon alfa 2A 180 µg /wk & Ribavirine 1000 mg/dg.
 - Week 4 & week 12 positieve PCR HCV
- Null response: na 12 weken behandeling gestaakt

- Behandeling 48 weken: Peginterferon 180 µg per week, Ribavirine 1200 mg per dag
- Eerste 12 weken telaprevir 2250 mg per dag
- Laboratorium
 - HCV t=0 2* milj IU/L, t=4 wk 50 IU/ml, t=12 wk neg
 - Toxiciteit: leukopenie $0.5 \cdot 10^9/l$

Question 2

- Neutropenie is een belangrijke bijwerking van de nieuwe direct antivirale middelen tegen een chronische hepatitis C

Waar

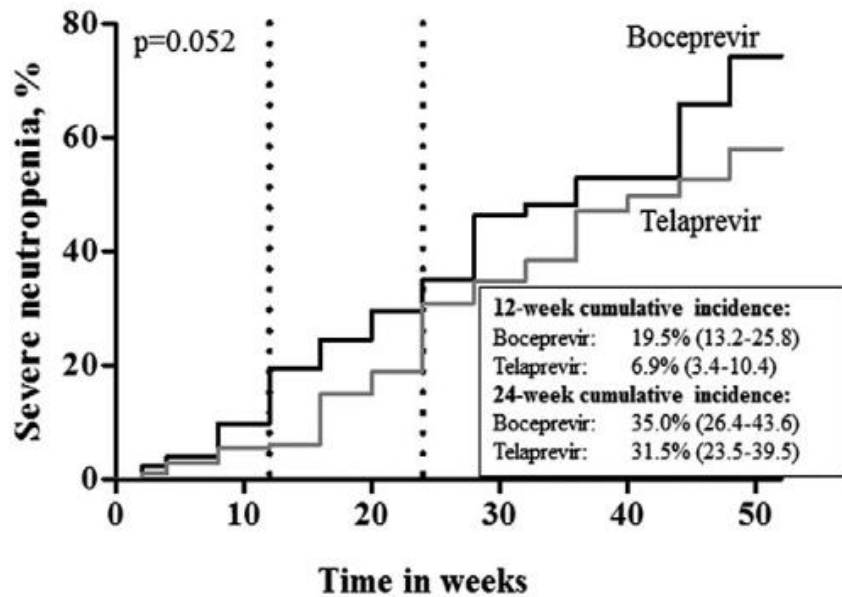
green

Onwaar

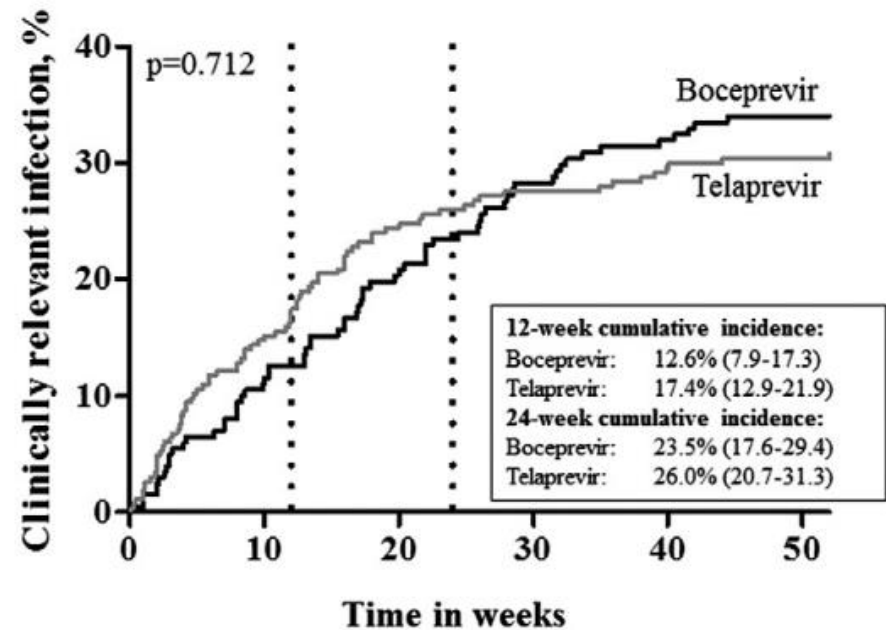
red

Neutropenie en infectie

Neutropenia



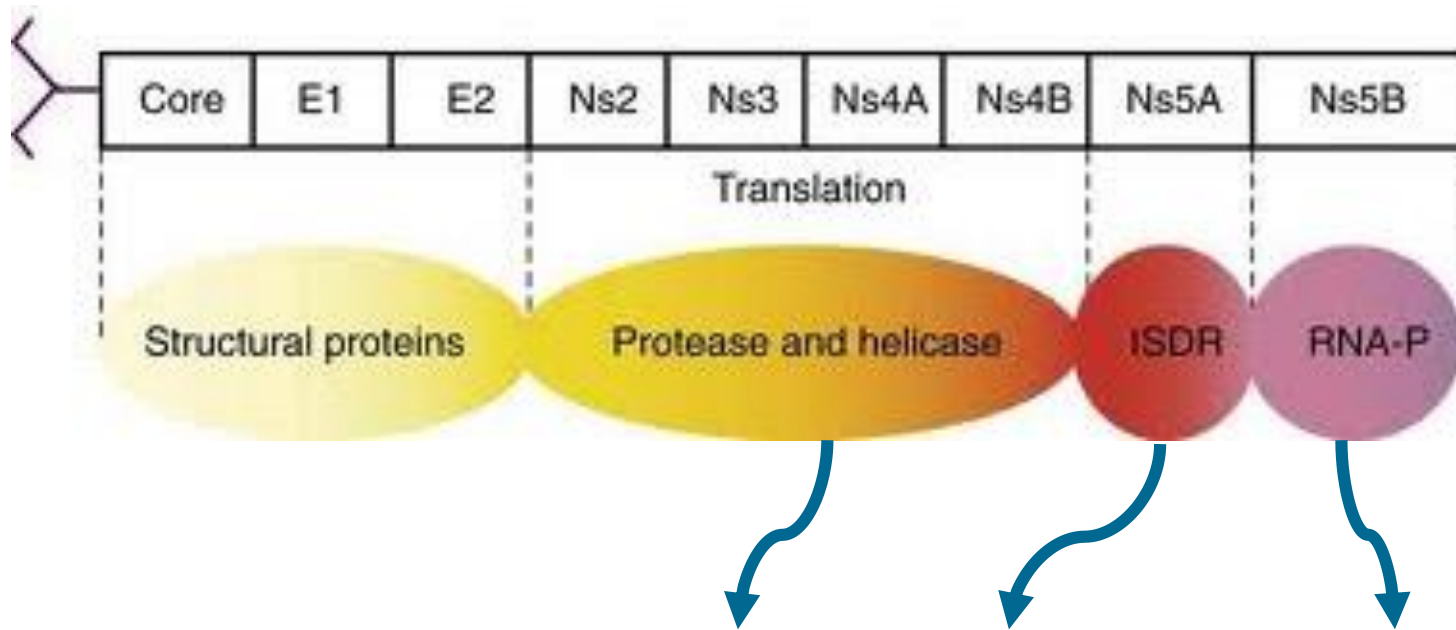
Infections



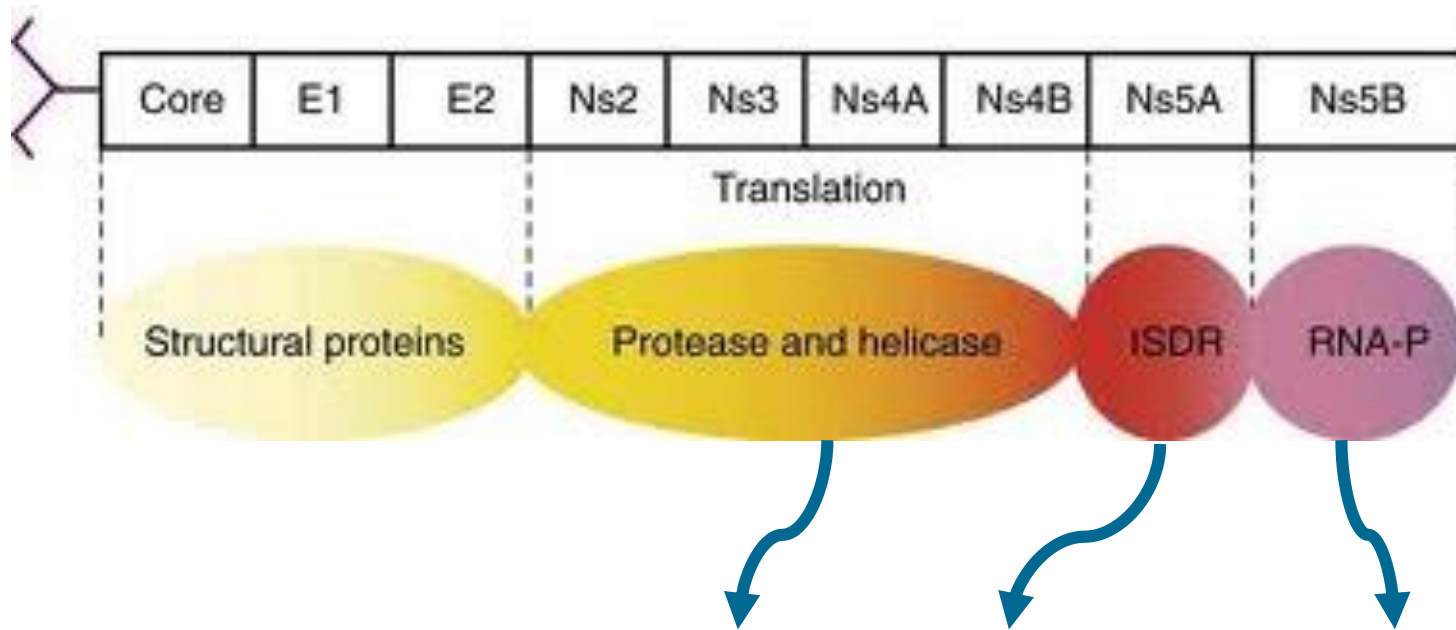
- Na behandeling
 - t= 24 wk : 4000 IU/L ml
- Dus relape
- Geen virale mutaties aantoonbaar (UMCU)

- 36 jarige vrouw
- HCV genotype 1b , hoge virale load, F3-4
- Behandelgeschiedenis
 - Peg / Riba: null response
 - Peg / Riba/ telaprevir: relapse

Welke middelen



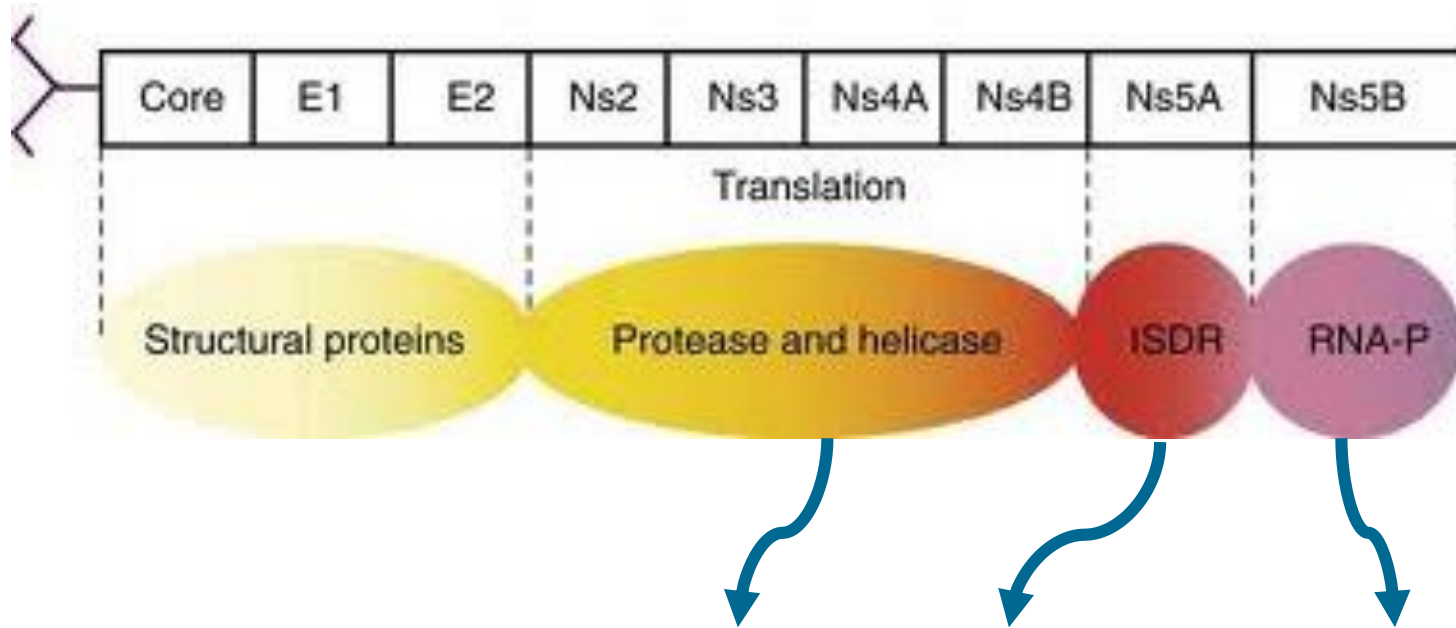
NS3/4a	NS5A	NS5B
Simeprevir	Daclatasvir	Sofosbuvir
Paritaprevir	Ombitasvir	Dasabuvir
	Ledipasvir	Sofosbuvir
Grazoprevir	Elbasvir	
	Valpatasvir	



NS3/4a	NS5A	NS5B
Simeprevir	Daclatasvir	Sofosbuvir
Paritaprevir	Ombitasvir	Dasabuvir
	Ledipasvir	Sofosbuvir
Grazoprevir	Elbasvir	
	Valpatasvir	

- 12 weken sofosbuvir 400 mg/dag en simeprevir 150 mg/dag
- Geen bijwerkingen
- Einde van de behandeling HCV RNA negatief: EOT
- 12 weken na het afronden van behandeling was de PCR HCV positief (6 milj IU/ml): Viral relapse

- 36 jarige vrouw
- HCV genotype 1b , hoge virale load, F3-4
- Behandelgeschiedenis
 - Peg / Riba: null response
 - Peg / Riba/ telaprevir: relapse
 - Sim/Sof: relapse



2016

NS3/4a	NS5A	NS5B
Simeprevir	Daclatasvir	Sofosbuvir
Paritaprevir	Ombitasvir	Dasabuvir
	Ledipasvir	Sofosbuvir
Grazoprevir	Elbasvir	
	Valpatasvir	

- 4^e behandeling
- 24 weken
- Sofosbuvir 400 mg/dag Daclatasvir 60mg/dag , Ribavirine 1000 mg/dag
- Ribavirine spiegel week 8: 2.66 mg/l (nl 2-3mg/L)

- De virale load was aan het eind van de behandeling negatief
- 12 en 24 weken na afronden van de behandeling negatieve virale load
- SVR behaald: genezen

Succes



Summary

- 11 Lessons
- 2 Questions
- 1 Case

- Hepatitis C is a treatable condition
- Eradication is a possibility
- There are a number of principles
- There are resources out there that you can use

Aanbevelen

- Zopf S, Kremer AE, Neurath MF, Siebler J. Advances in hepatitis C therapy: What is the current state - what come's next? World J Hepatol. 2016 Jan 28;8(3):139-47.
doi: 10.4254/wjh.v8.i3.139.
- <http://hcvrichtsnoer.nl/>

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Disclosure belangen spreker

- Als consultant betrokken geweest bij het dossier van indiening van sofosbuvir
- Ad-hoc zitting in adviesraden van Gilead, MSD, BMS, Janssen en Abbvie
- Alle gelden gaan naar de onderzoeksstichting van het Radboudumc