

The medical options: viral hepatitis can be cured or controlled in all patients

Thomas Berg

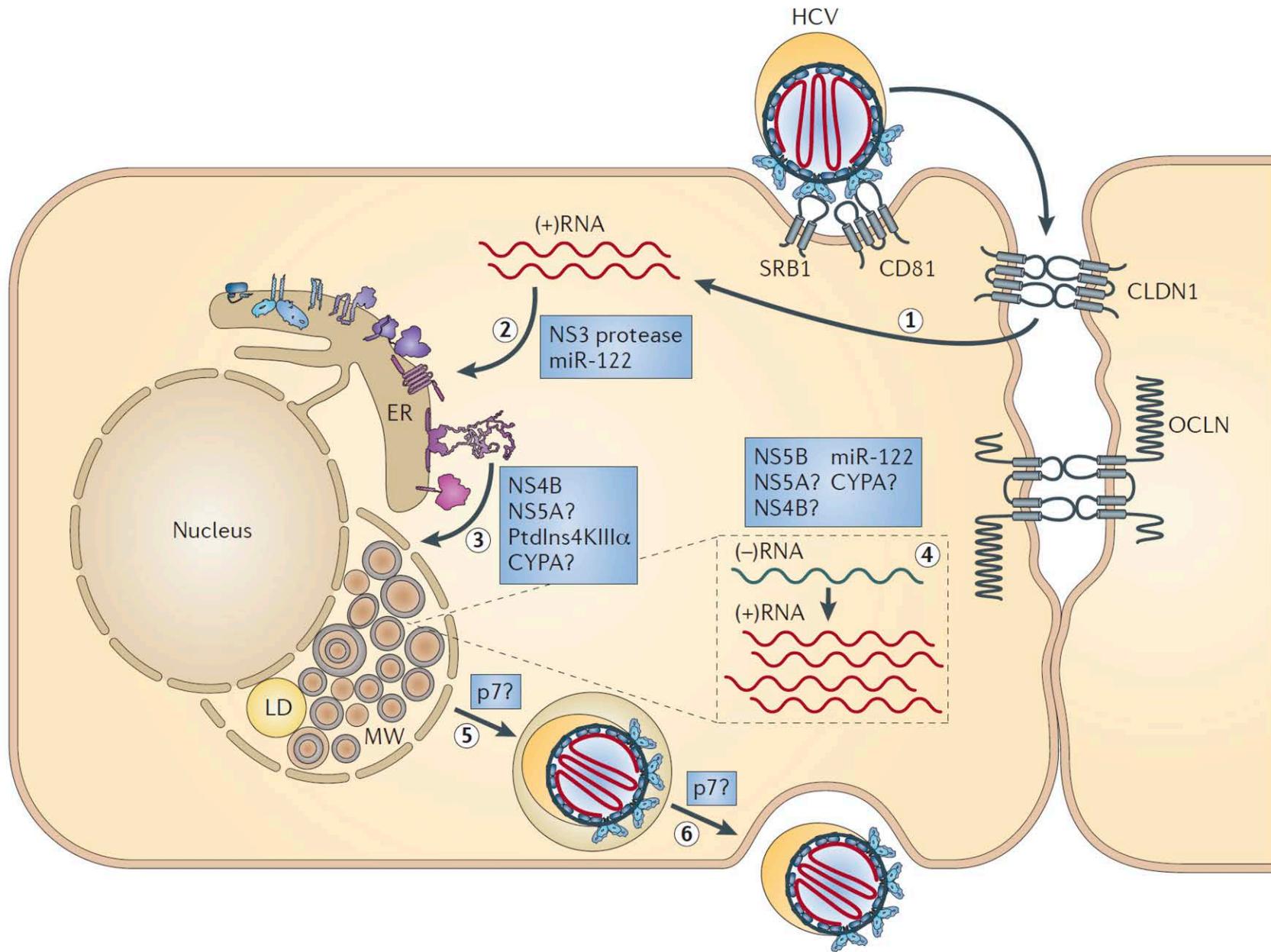
Sektion Hepatologie

Klinik und Poliklinik für Gastroenterologie
und Rheumatologie
Universitätsklinikum Leipzig

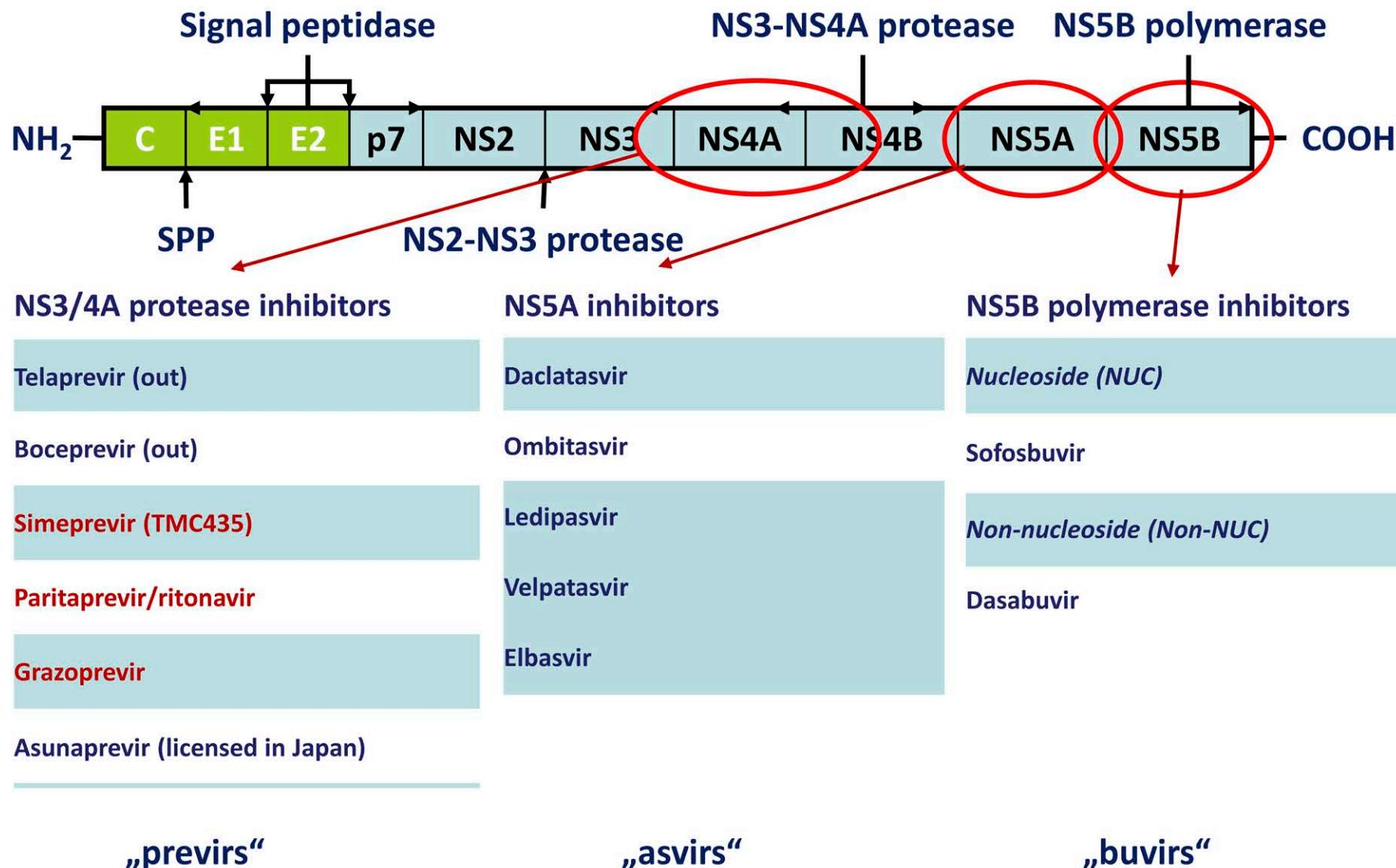
Leber- und Studienzentrum am Checkpoint, Berlin



HCV replication cycle – Targets for direct acting antivirals



Currently available direct-acting antivirals (DAA)



2016 Lasker Award for the development of a system to study the replication of the virus that causes hepatitis C and for use of this system to revolutionize the treatment of this chronic often lethal disease



Charles M. Rice

Ralf Bartenschlager

Michael J. Sofia

Approved direct acting antivirals (DAAs) in the EU

2015

2016

2017

Sofosbuvir (pangenotypic)
(Sovaldi®)

Simeprevir
(Olysio®)

Daclatasvir (pangenotypic)
(Daklinza®)

Fixe regimens:

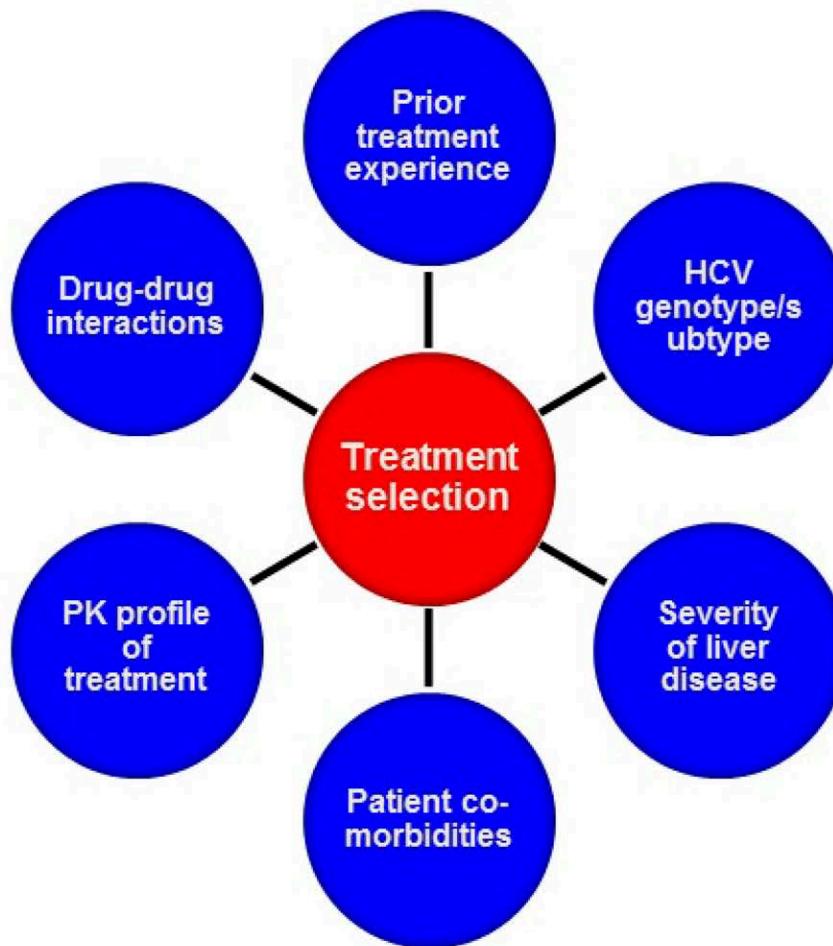
Sofosbuvir + Ledipasvir
(Harvoni®) (HCV 1,2,4-6)

„3D“
Paritaprevir/r
+ Ombitasvir
+ Dasabuvir
(Viekirax® and
Exviera®) (HCV Type 1,4)

Fixe regimens:
Sofosbuvir +
Velpatasvir
(pangenotypic)
(Epclusa®)

Grazoprevir +
Elbasvir
(Zepatier®)
(HCV Type 1+4)

Characteristics that Inform Treatment Option Selection



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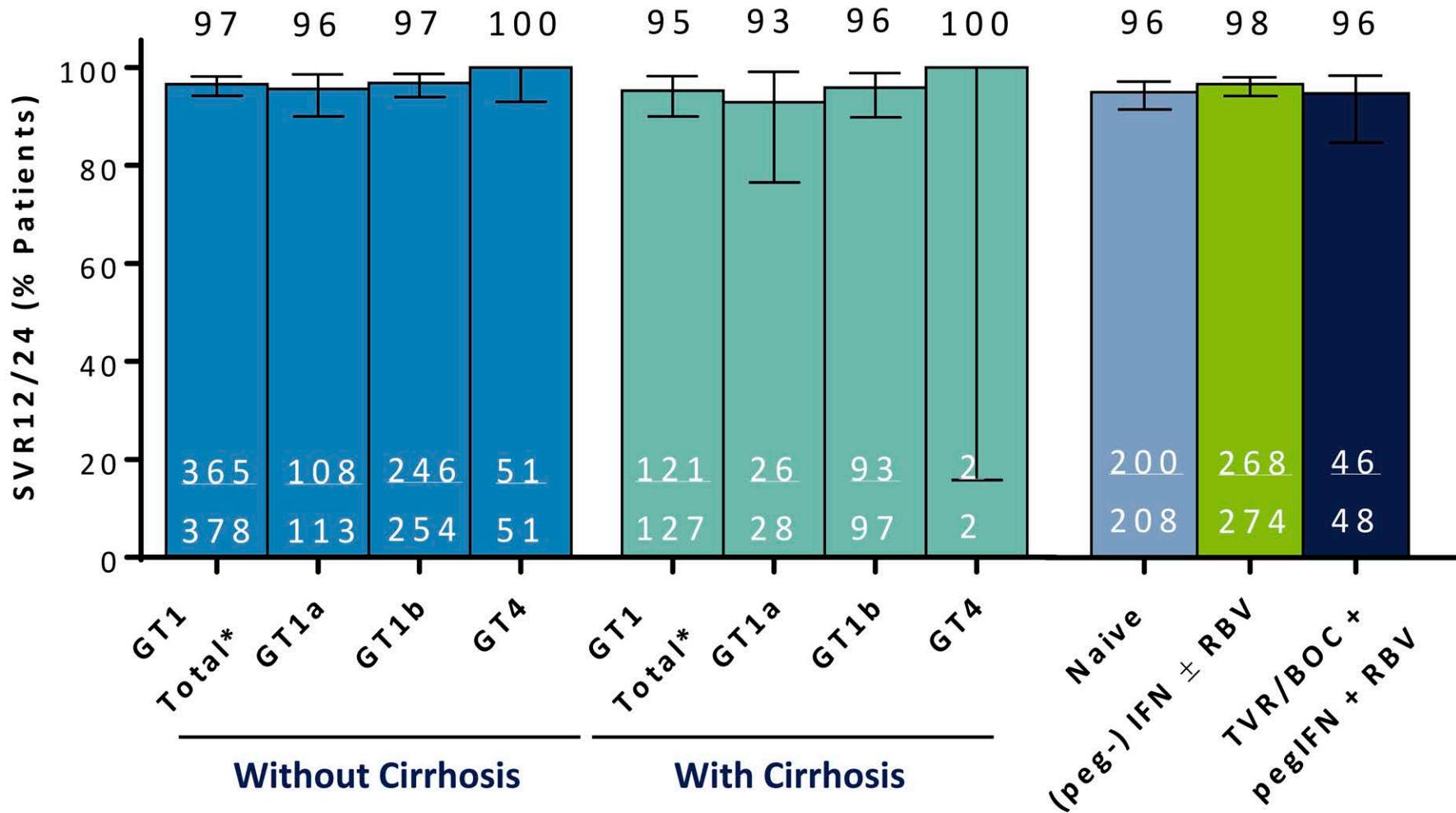
Grazoprevir +
... .

Cure rates in clinical studies ≥ 95%

(Harvoni®) (HCV 1,2,4-6)

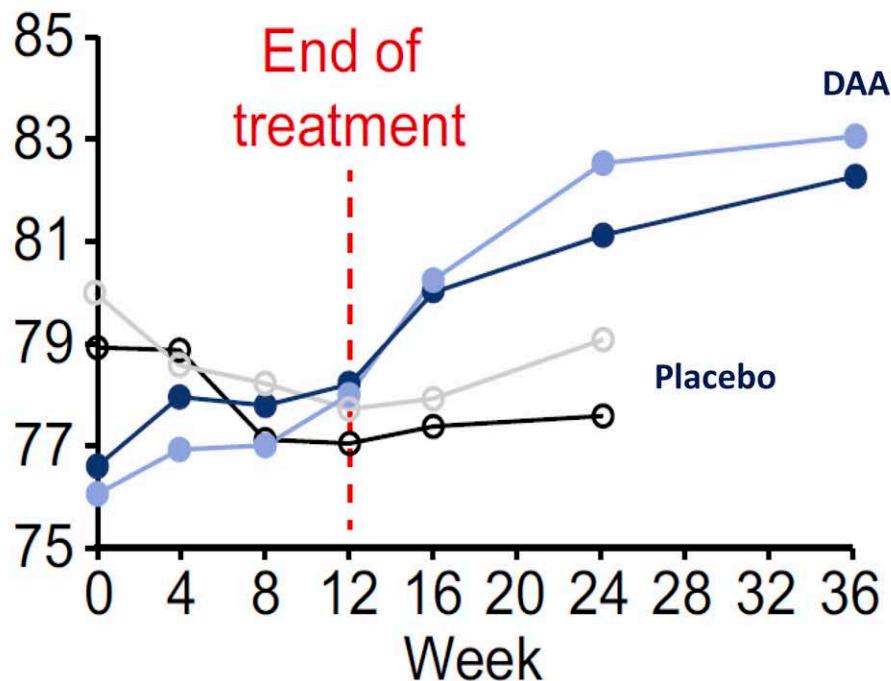
„3D“
Paritaprevir/r
+ Ombitasvir
+ Dasabuvir
(Viekirax® and
Exviera®) (HCV Type 1,4)

Real-World Experience – The German Hepatitis C Registry (HCV type 1+4; 2D/3D Regimen)

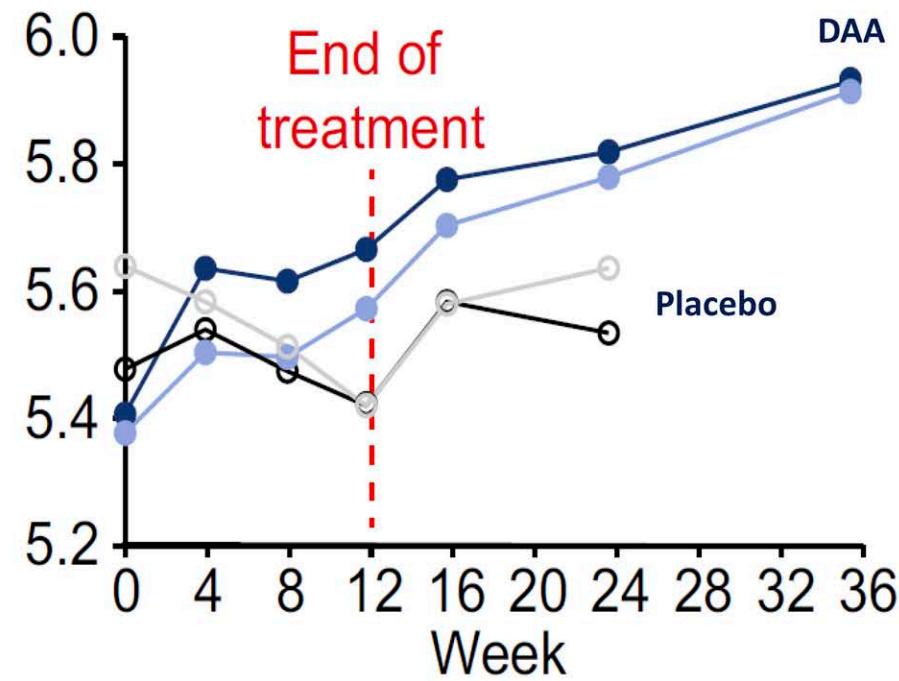


Quality of life - patient-reported outcomes – Placebo-controlled evaluation

“Fatigue”



“Energy”



DAA = direct acting antivirals

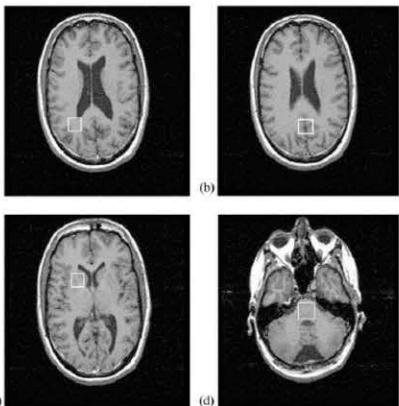
Younossi ZM et al. J Hepatol 2016; 65: 33

Cure for all HCV-infected patients

- **Decompensated cirrhosis**
- **HCV reinfection post liver transplantation**
- **End-stage renal disease (dialysis)**
- **HIV HCV coinfection**
- **Extrahepatic manifestations**

Porphyria cutanea tarda

Neurologic/Psychiatric



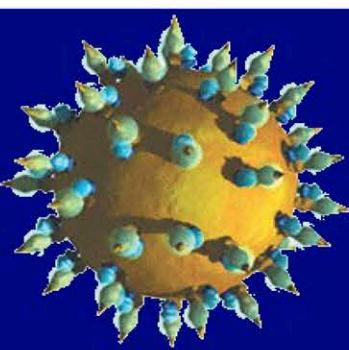
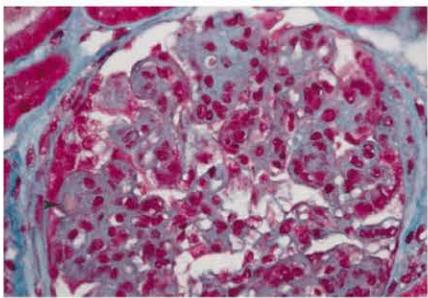
Lichen planus



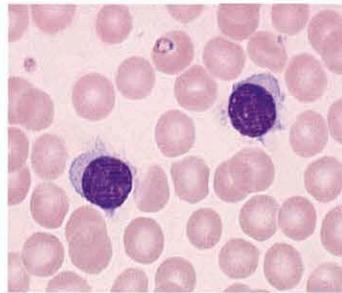
Vasculitis



Glomerulonephritis



Lymphoma



Extrahepatic manifestations of chronic hepatitis C

Before DAA therapy



12 weeks later



Cure for all HCV-infected patients

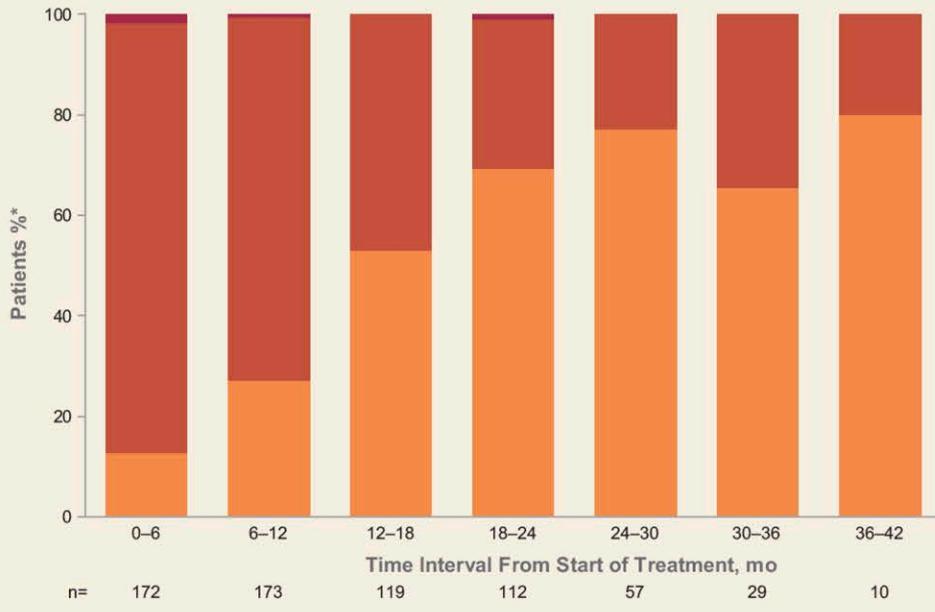
- Decompensated cirrhosis?



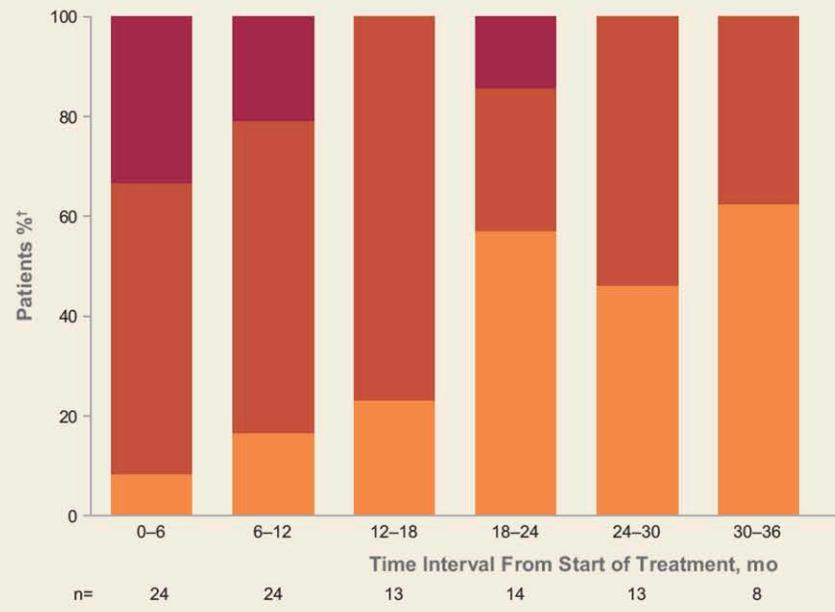
Regression of decompensated cirrhosis following sofosbuvir-based treatment

CPT A CPT B CPT C

CPT B Cirrhosis Pretreatment



CPT C Cirrhosis Pretreatment



What makes the difference?



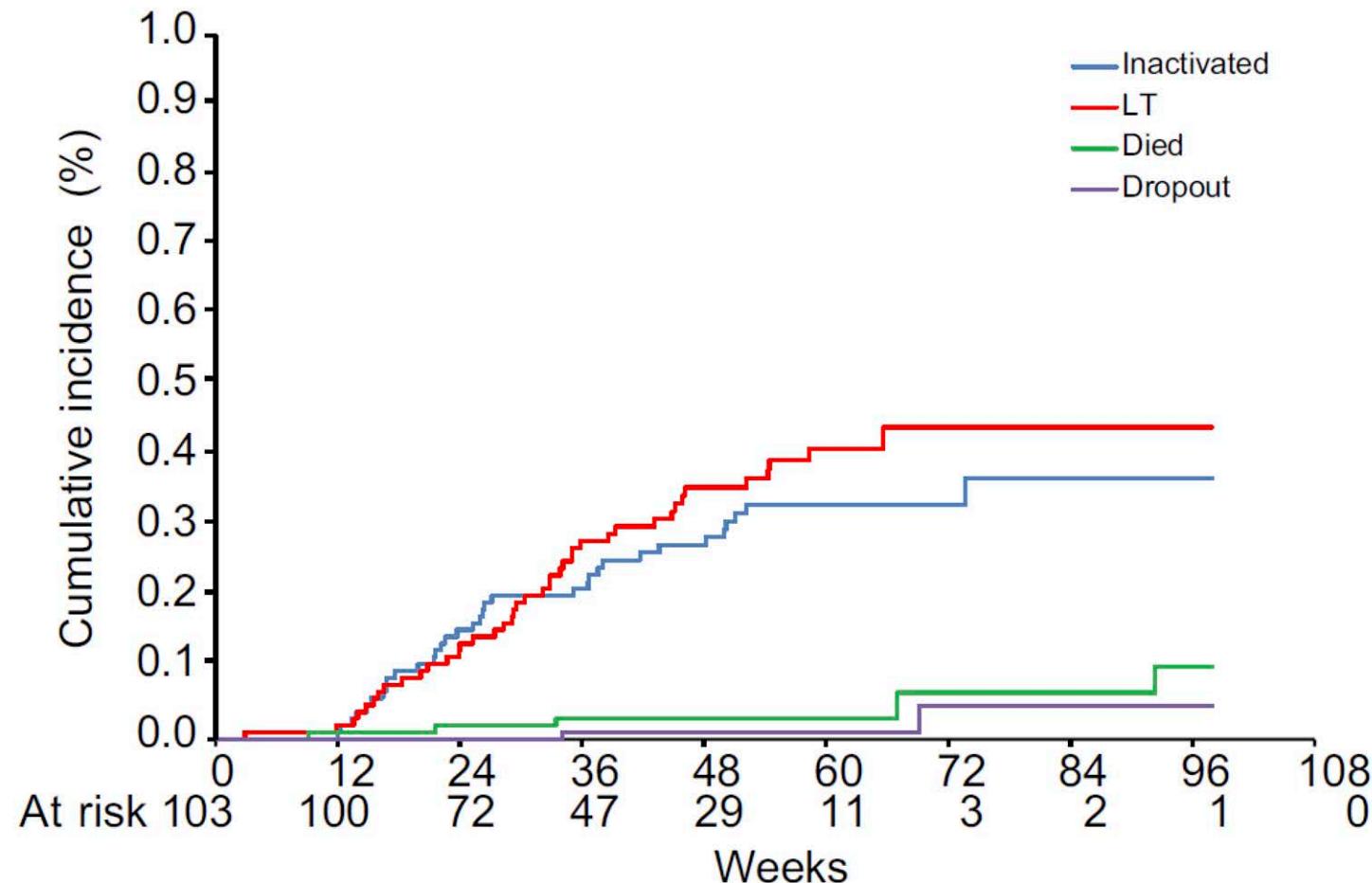
What makes the difference?



SVR = Cure

Treatment of patients on the liver transplant waiting list

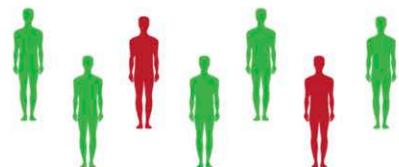
A 30% chance fo delisting



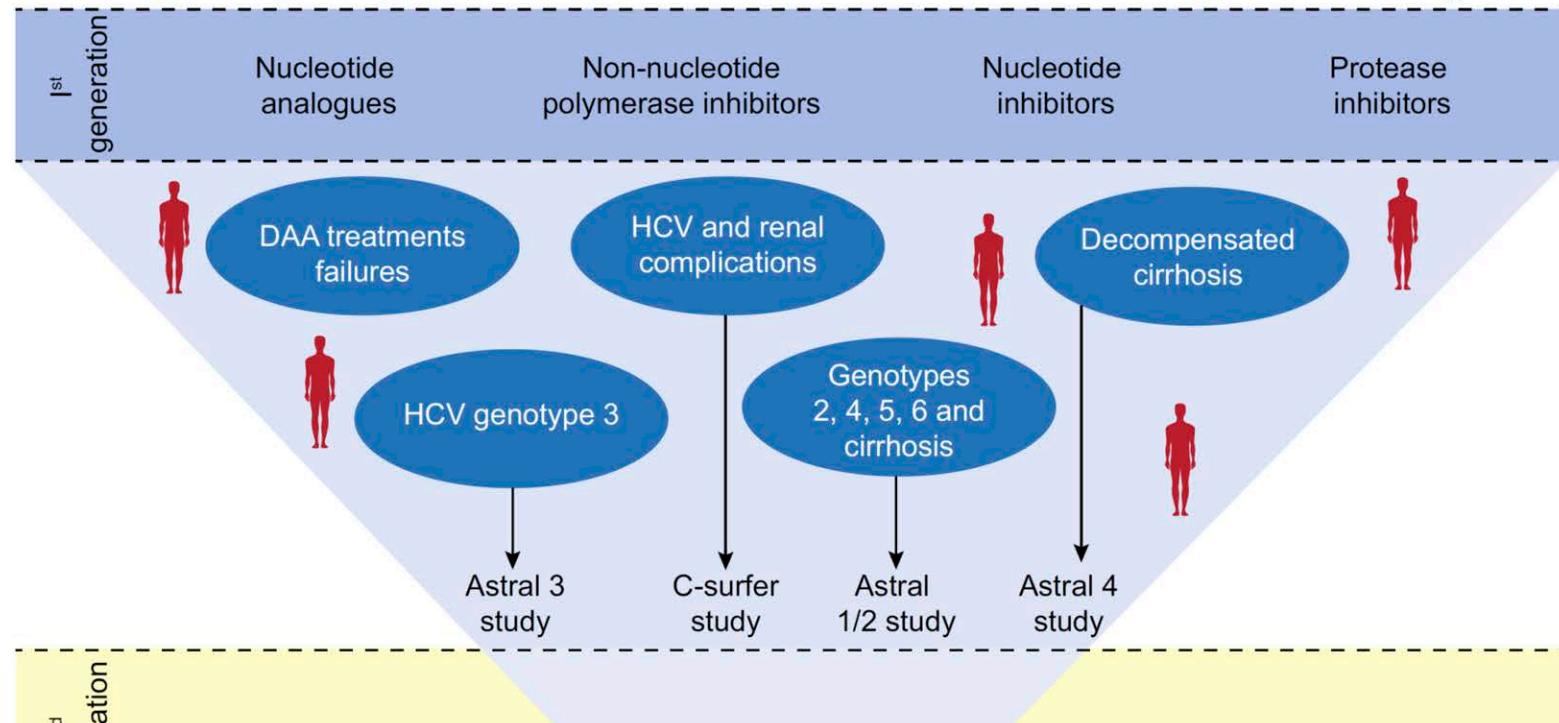
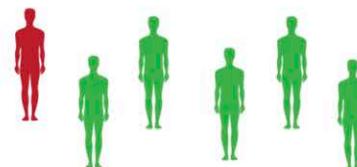
Resistance



The Achilles' heel of DAAs



HCV patient population (130-150 million globally)



Refinement of treatment length and accessibility



HCV ELIMINATION

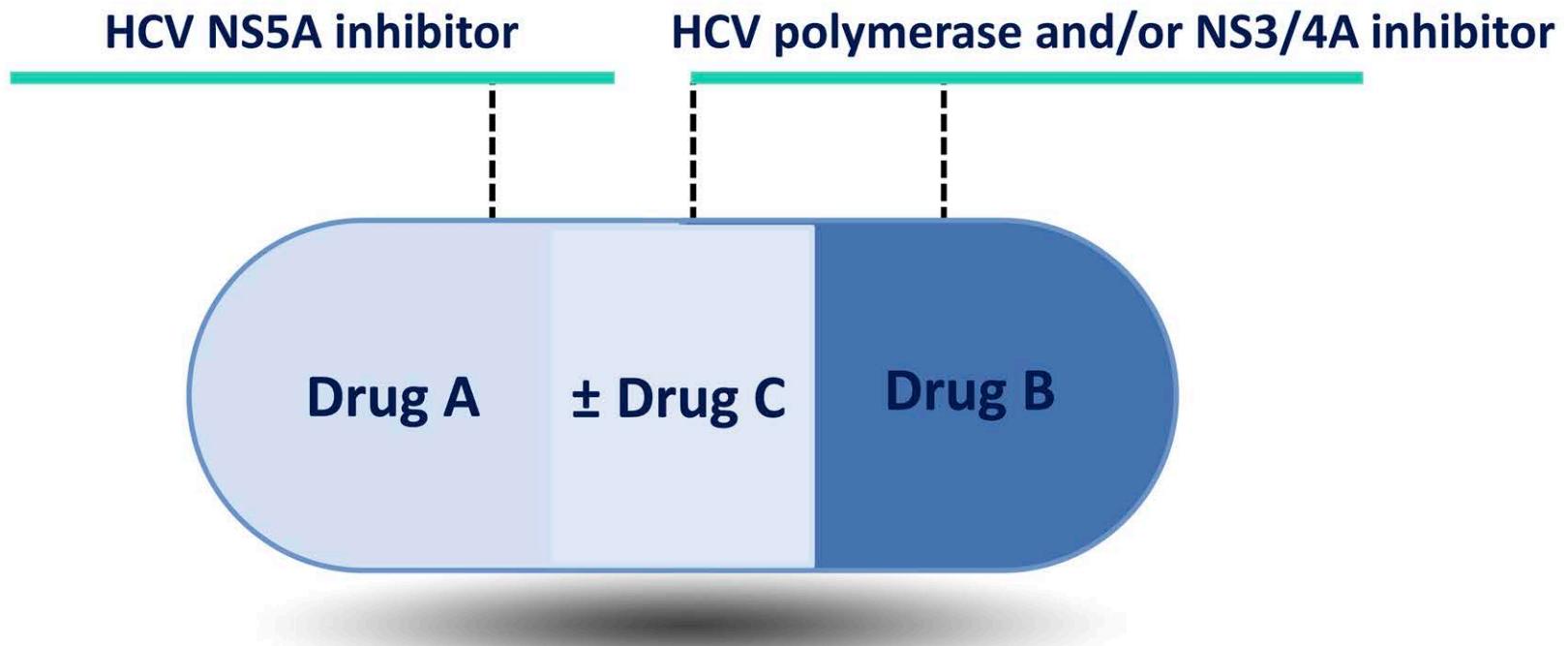


Patients successfully curable with 1st gen. drugs



Patients with treatment complications

FUTURE 2ND GENERATION SINGLE TABLET REGIMENS

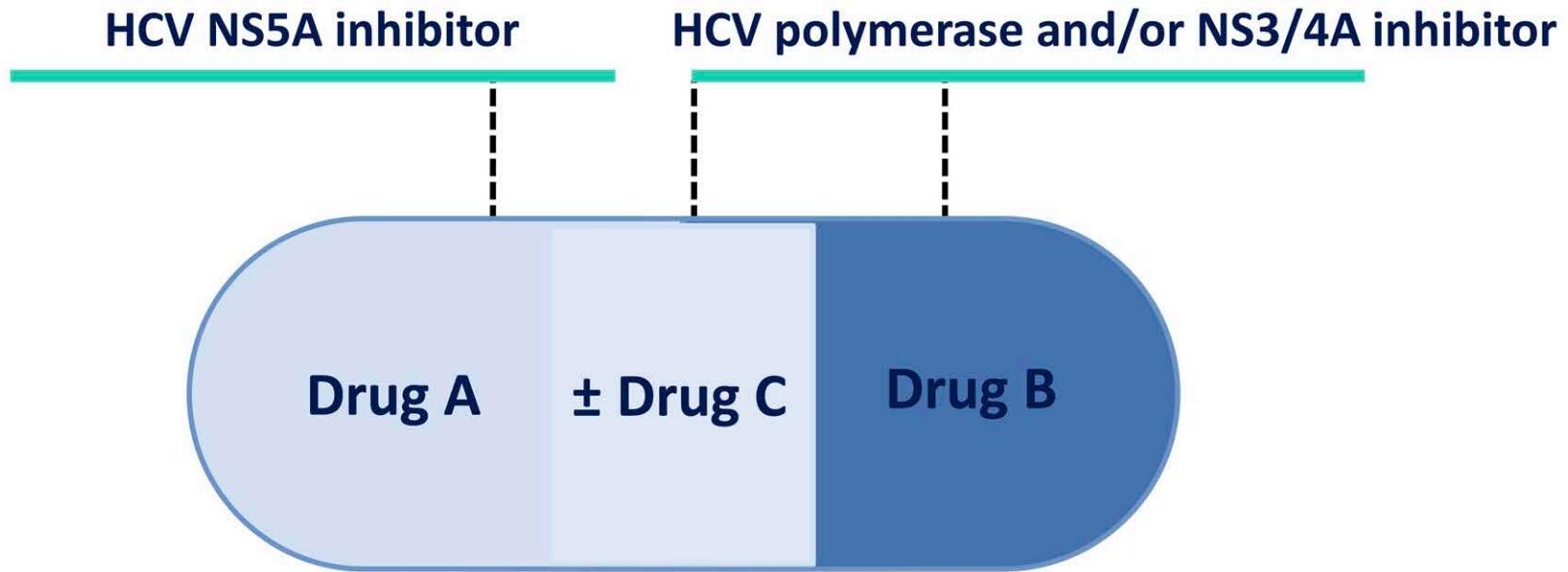


All oral, one table per day

Higher activity against all HCV types as compared to 1. Generation DAA

Active against 1. Generation DAA resistance

FUTURE 2ND GENERATION SINGLE TABLET REGIMENS



Cure rates in clinical studies $\geq 98\%$

All oral, one tablet per day

Higher activity against all HCV types as compared to 1. Generation DAA

Active against 1. Generation DAA resistance

Cure for all HCV-infected patients – a tailored strategy

Treatment duration

6-8 weeks

12 weeks

12-24 weeks + ribavirin

Easy-to-treat

Disease characteristics

No advanced fibrosis,
no co-morbidities, tx-naive

Compensated cirrhosis

HCV type 3

Decompensated cirrhosis,
DAA failure

Cure for all HCV-infected patients – a tailored strategy

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Disease characteristics

No advanced fibrosis,
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Appr. 80% of all HCV-infected patients in Germany

12 weeks

Compensated cirrhosis

HCV type 3

12-24 weeks + ribavirin

Difficult-to-treat

Decompensated cirrhosis,
DAA failure