

Hepatitis C

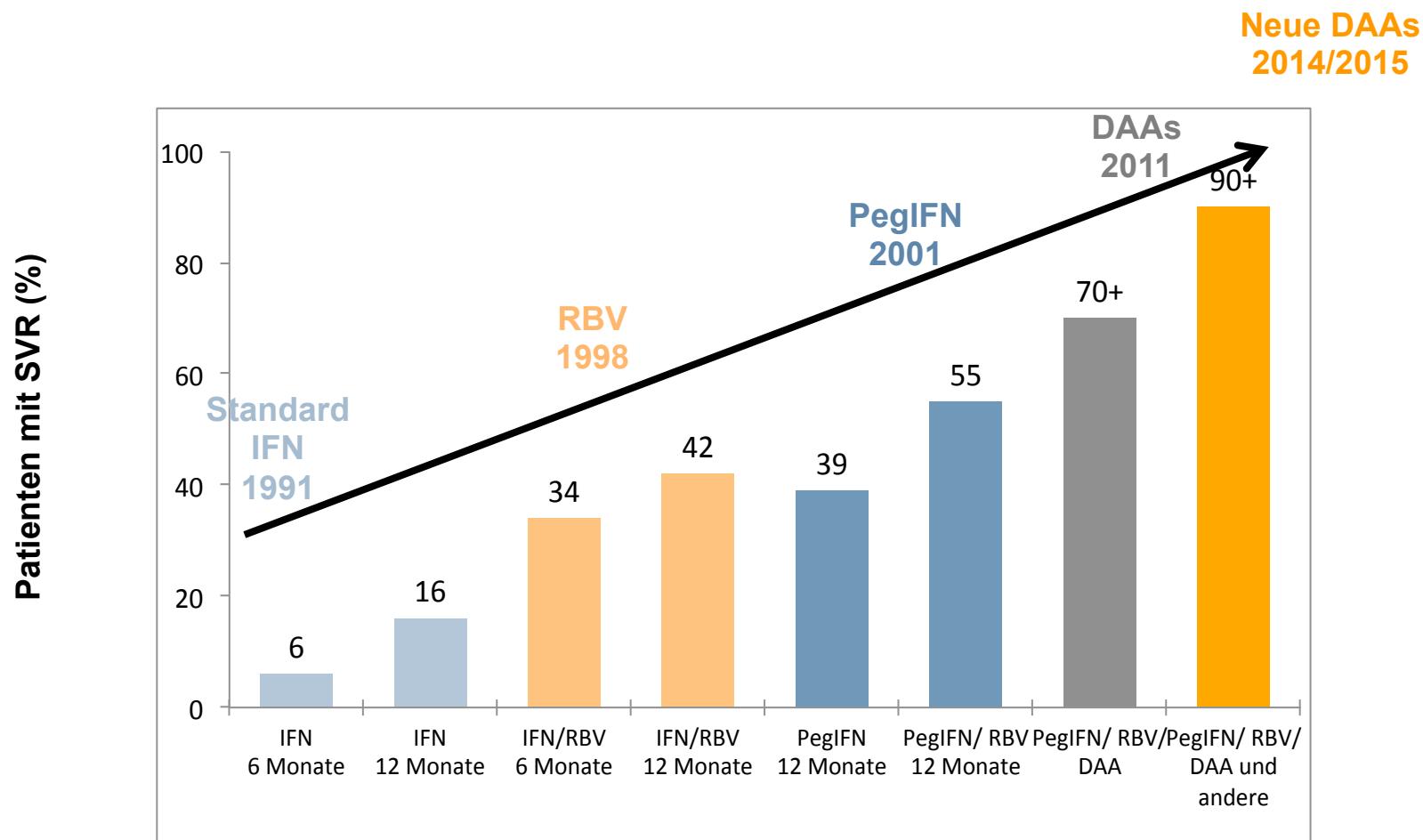
Neuer Therapiestandard 2014

Eckart Schott

Med. Klinik m.S. Hepatologie und Gastroenterologie

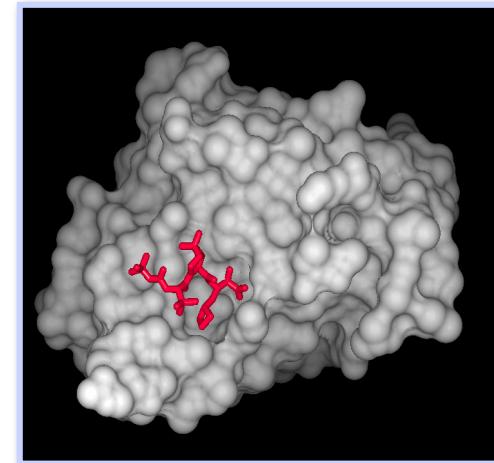
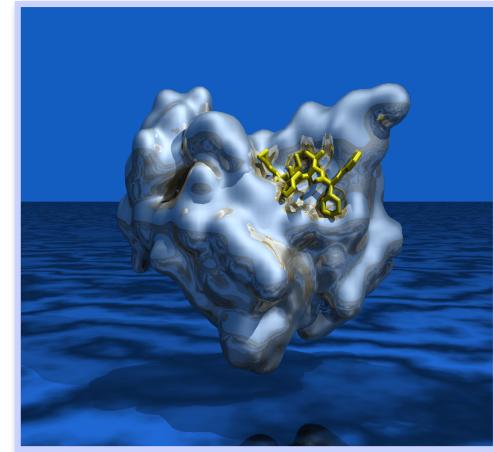
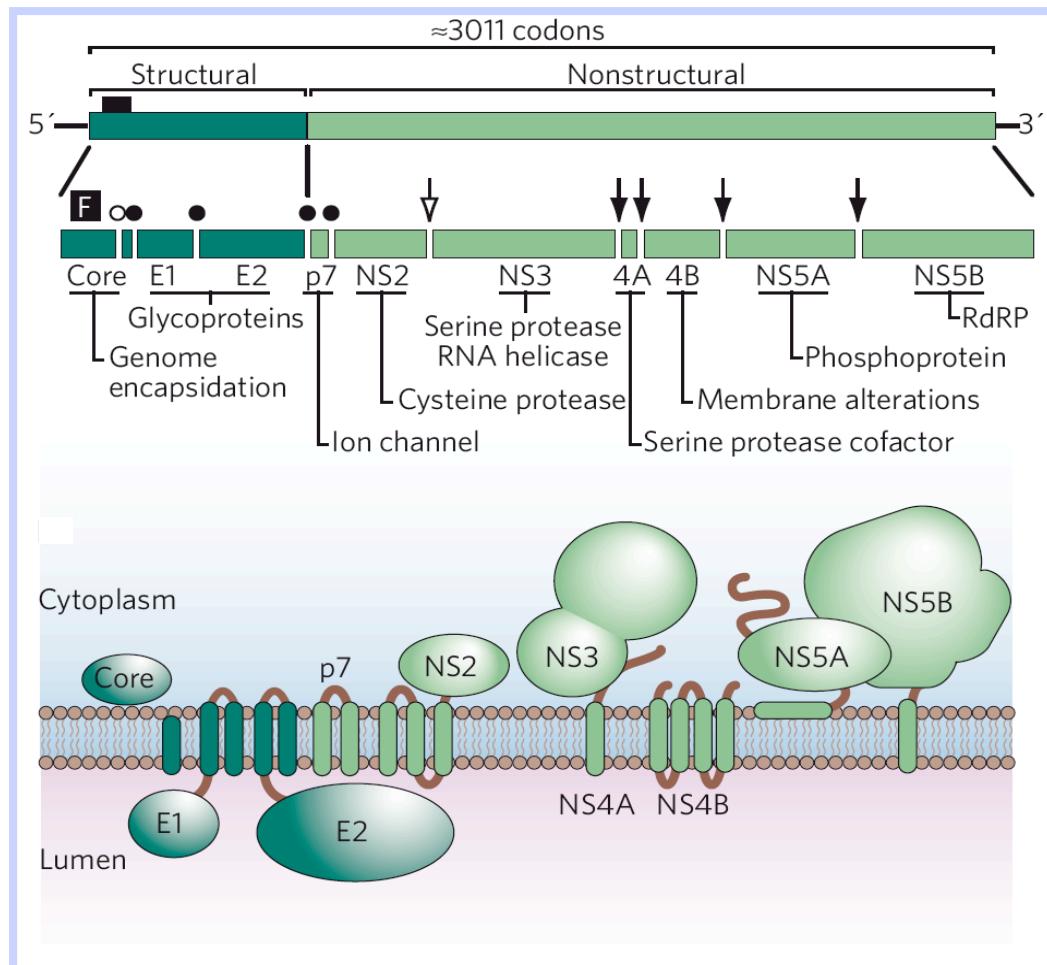


Ansprechraten bei der Therapie der Hepatitis C



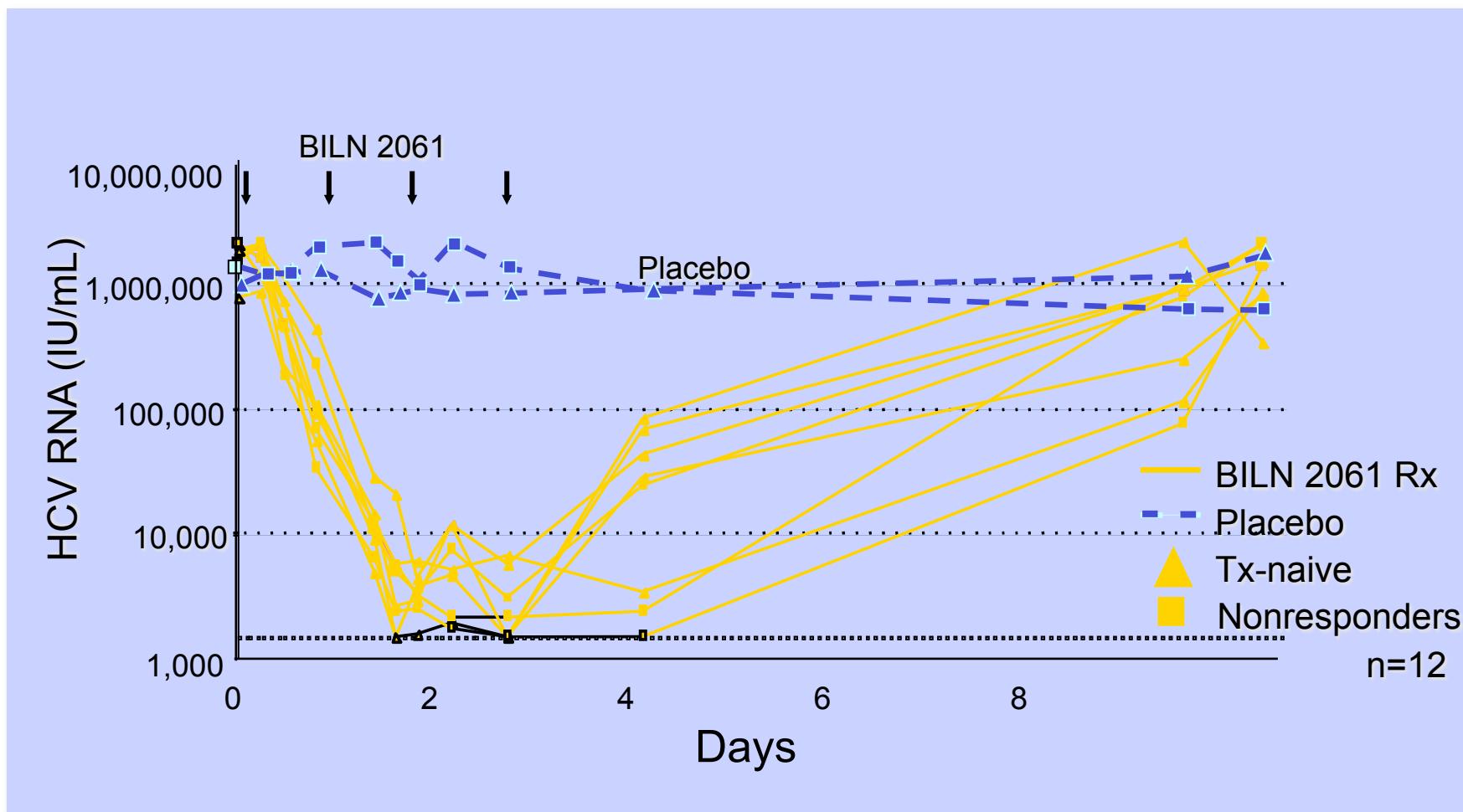
Adaptiert nach: US FDA, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring, MD

NS3/4A Protease-Inhibitoren



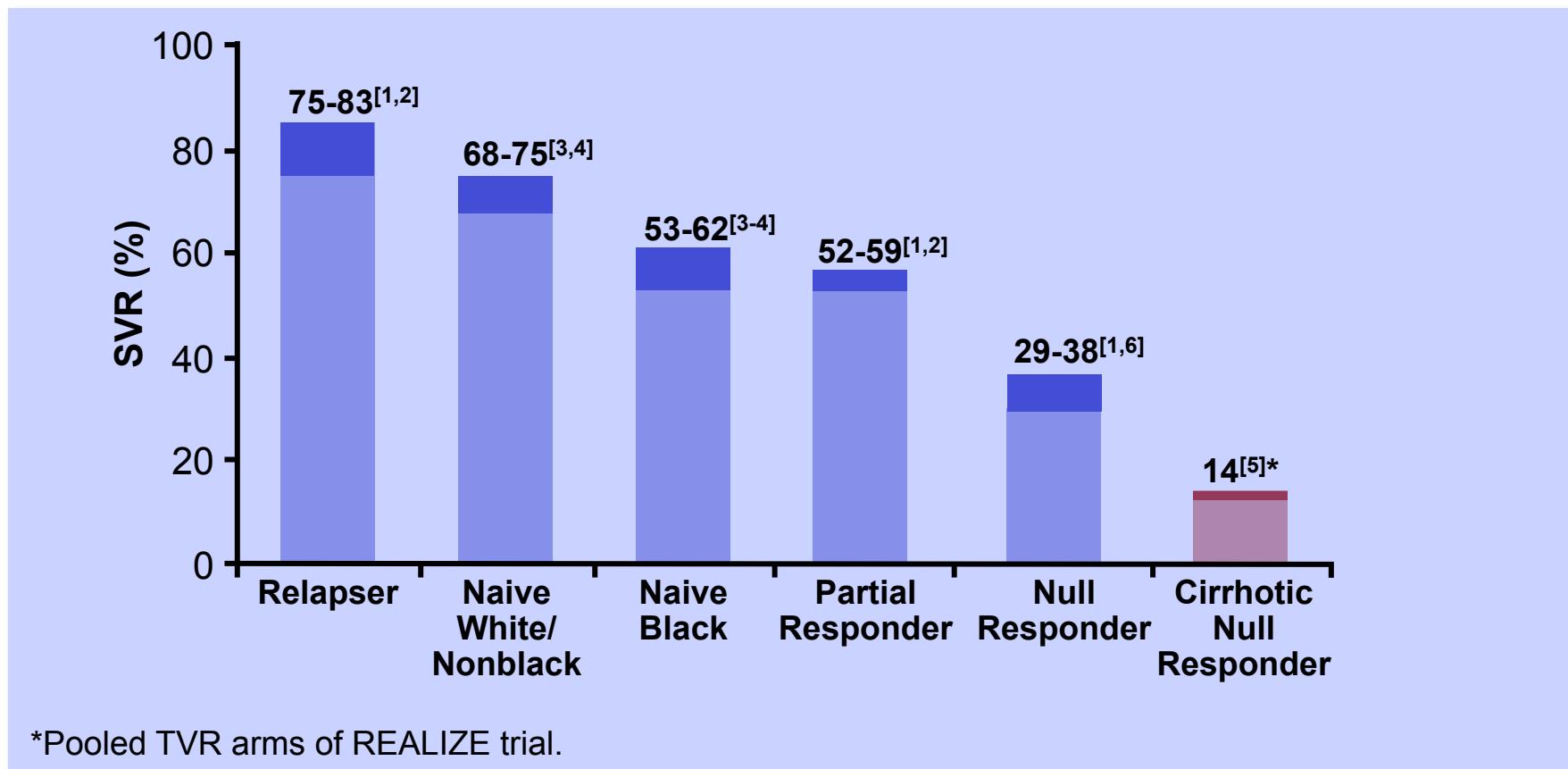
Lindenbach and Rice, Nature 2005

Erste Daten mit einem Proteaseinhibitor (BILN 2061)



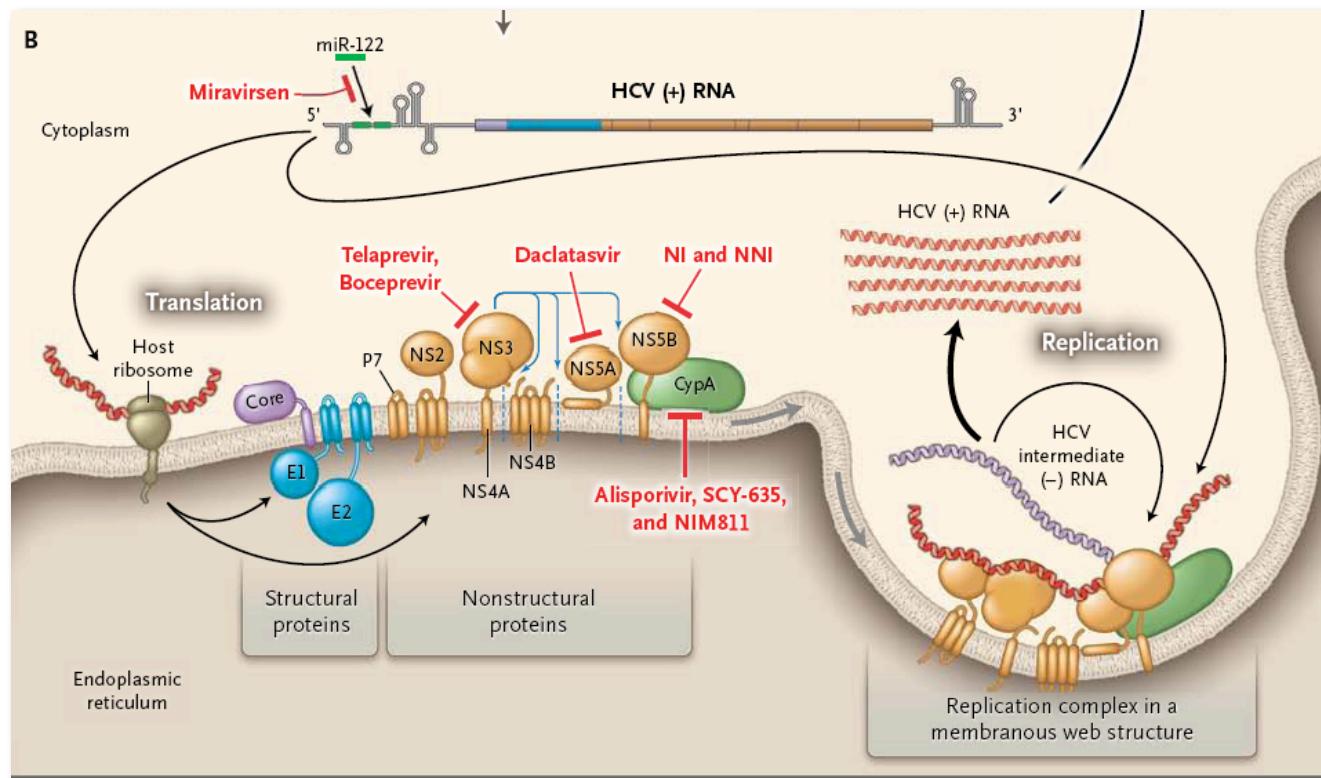
Hinrichsen, Gastroenterology 2004

Der “alte” Standard: Tripel-Therapie



1. Zeuzem S, et al. N Engl J Med. 2011;364:2417-2428. 2. Bacon BR, et al. N Engl J Med. 2011;364:1207-1217.
3. Jacobson IM, et al. N Engl J Med. 2011;364:2405-2416. 4. Poordad F, et al. N Engl J Med. 2011;364:1195-1206.
5. Zeuzem S, et al. EASL 2011. Abstract 5. 6. Vierling JM, et al. AASLD 2011. Abstract 931.

Neue Substanzen



Neue Substanzen

	Protease-inhibitoren	Nucleosidische Polymerase-inhibitoren	Nicht nucleosidische Polymerase-inhibitoren	NS5A Inhibitoren	Cyclophilin-Inhibitoren	miR122 Inhibitor
Wirksamkeit	Hoch	Hoch	Niedrig	Hoch	Mittel	Mittel
Genotyp Abdeckung	Eng	Breit	Eng	Mittel	Breit	Breit
Resistenz-barriere	Niedrig	Hoch	Niedrig	Mittel	Hoch	Hoch
Neben-wirkungen	Viele	Wenige	Unterschiedlich	Wenige	Wenige	?
DDI	Viele	Keine	?	?	?	?

Neue Substanzen

NS3/4A-Inh.

- ABT-450/r
- ACH-1625
- Asunaprevir
- Simeprevir
- Faldaprevir
- Danoprevir/r
- GS-9451
- MK-5172
- Vaniprevir

NS5A-Inh.

- Daclatasvir
- Ledipasvir
- ABT-267
- PPI-668

NS5B-Inh. Nuc

- Sofosbuvir
- Mericitabine
- IDX-184

NS5B-Inh. Non-Nuc

- BI207124
- ABT-333
- ABT-072
- BMS-791325
- Tegobuvir
- Setrobuvir
- VX-222
- Filibuvir

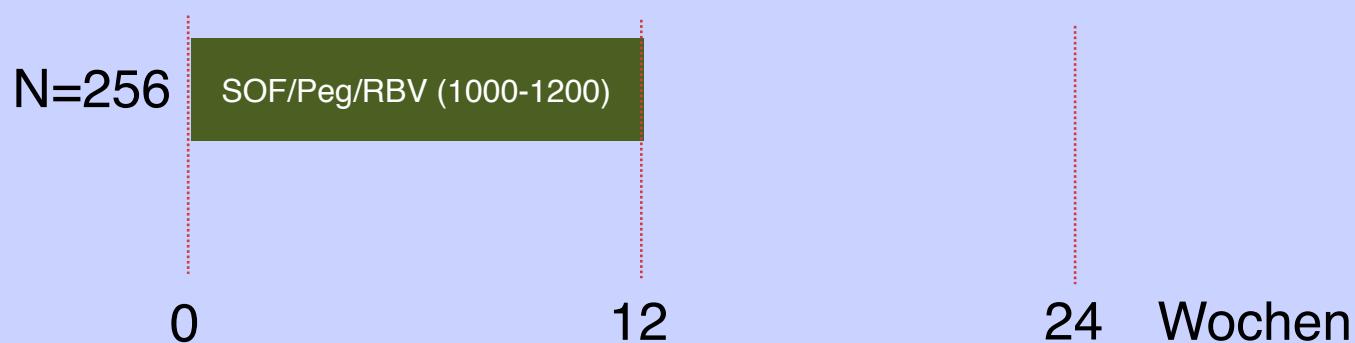
Sofosbuvir (Sovaldi®)

Februar 2014

HCV

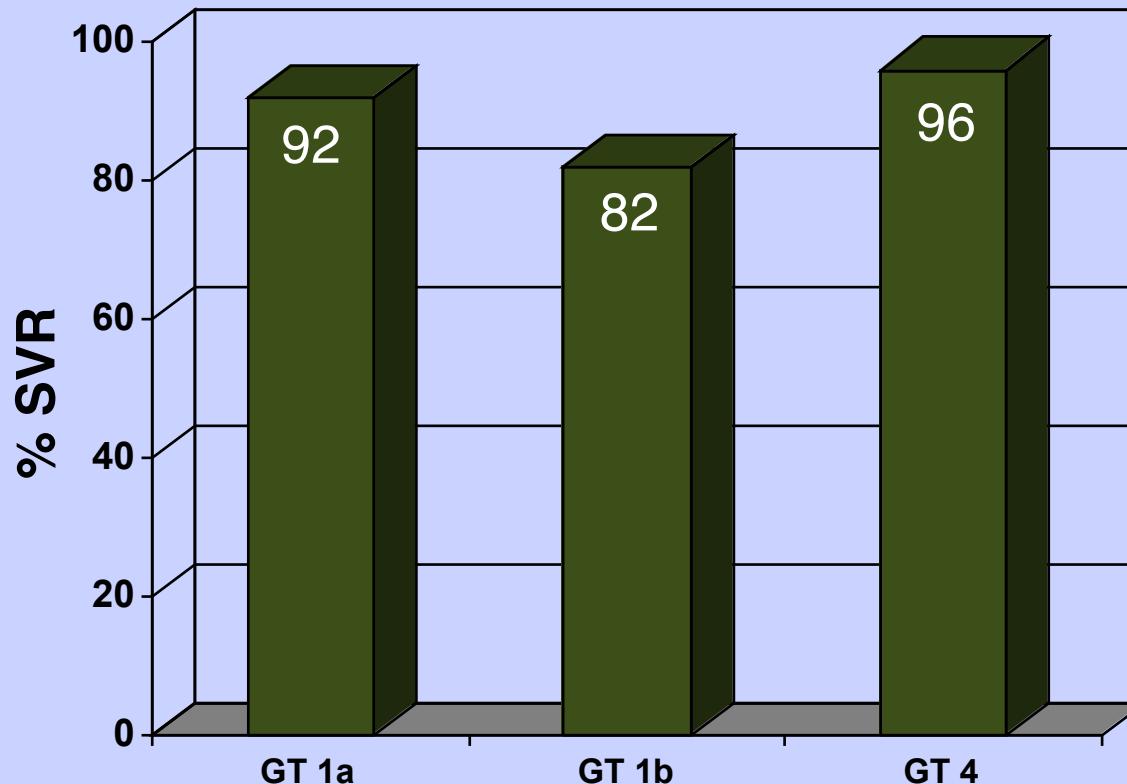
Gilead – SOF/PEG/RBV – GT 1/4/5/6 (Neutrino)

- Genotyp 1, 4, 5, 6
- Therapienaiv
- 20% Zirrhotiker



HCV

Gilead – SOF/PEG/RBV – GT 1/4/5/6 (Neutrino)



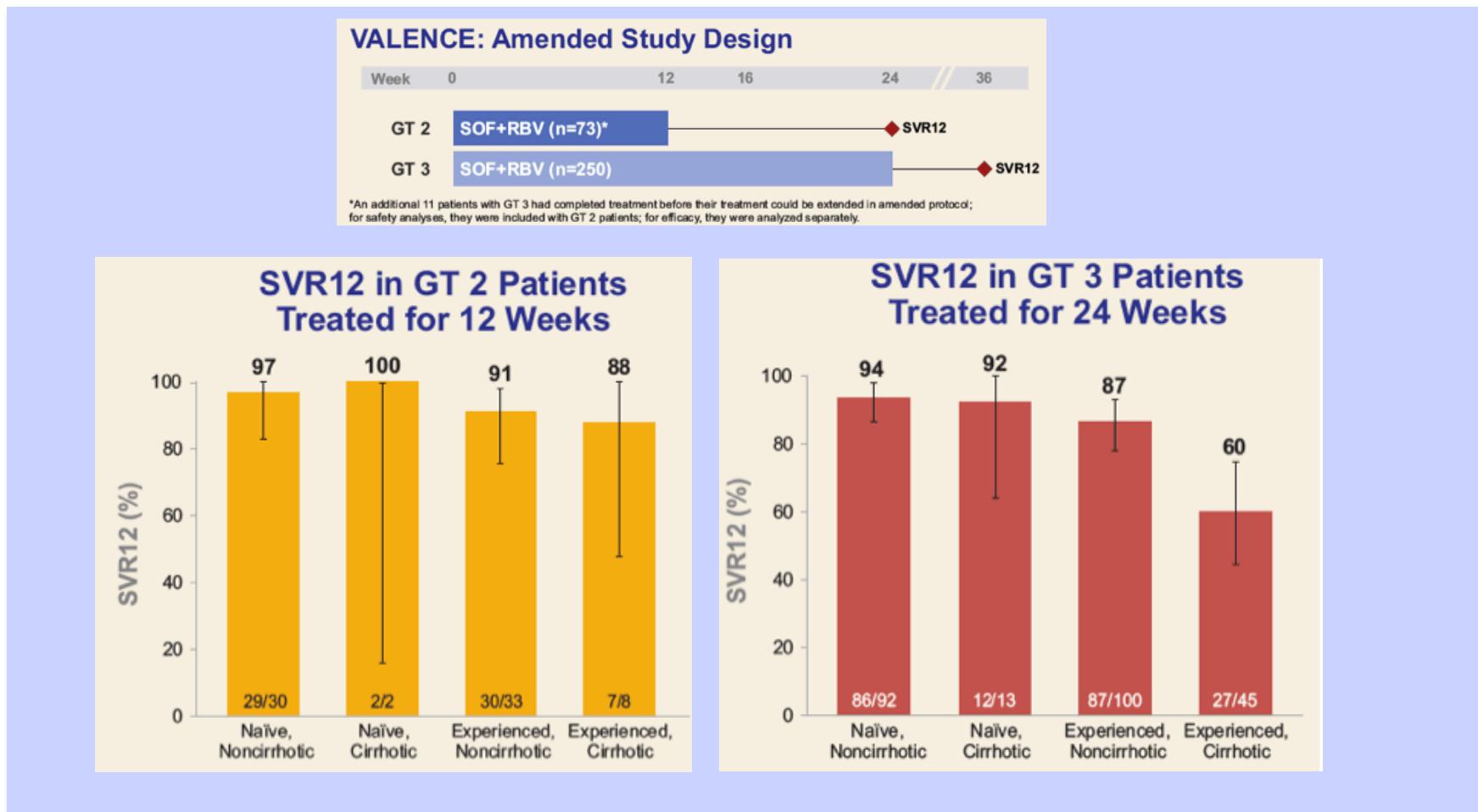
HCV

Gilead – SOF/PR - Genotyp 2/3 (LONESTAR-2)



HCV

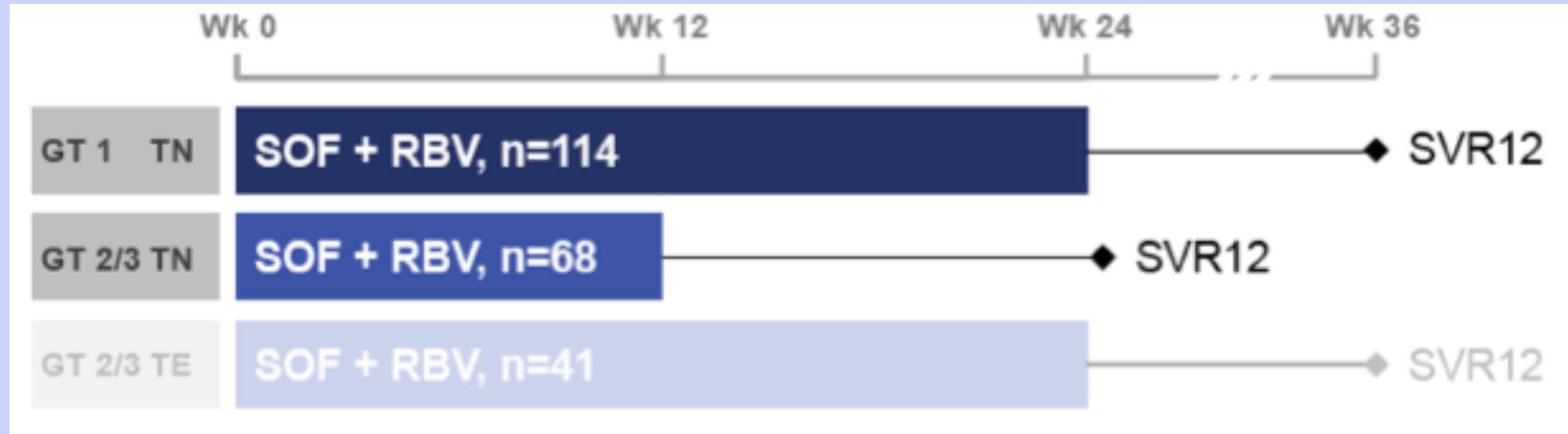
Gilead – SOF/RBV – GT 2/3 (VALENCE)



HCV

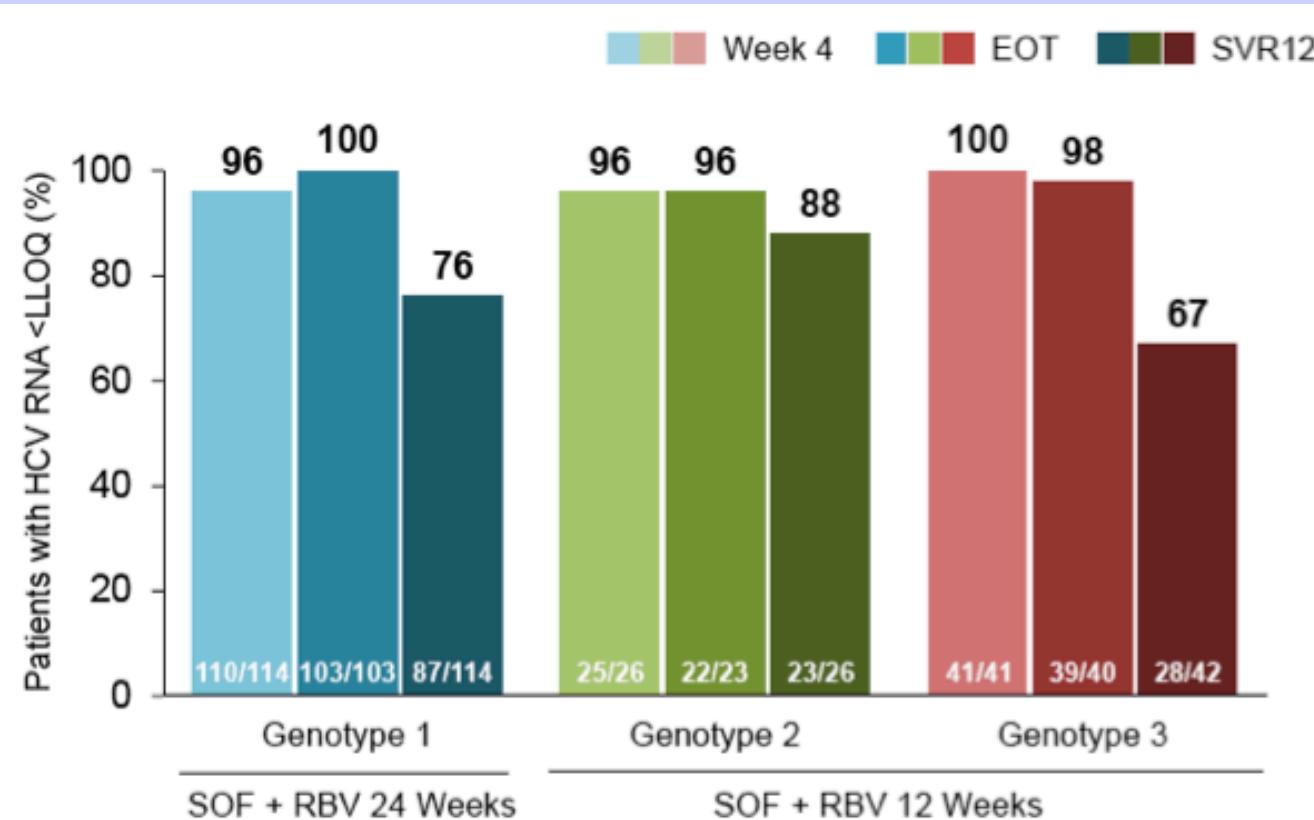
Gilead – SOF/RBV - HIV-Koinfektion (Photon-1)

- Genotyp 1, 2, 3
- HIV-Koinfektion
- Zirrhose erlaubt
- Stabile ART



HCV

PGilead – SOF/RBV - HIV-Koinfektion (Photon-1)



HCV

Gilead – Transplantation

Sofosbuvir 400 mg + Ribavirin 1000-1200 mg

N=61

Therapiedauer 24-48 Wochen

- Patienten mit HCV Zirrhose und HCC
- Except MELD Listung
- Child ≤7
- Tacrolimus, MMF, Prednisolon erlaubt
- Keine Antikörper
- Keine HBV/HIV Koinfektion
- Crea Clearance <60 ml/min.

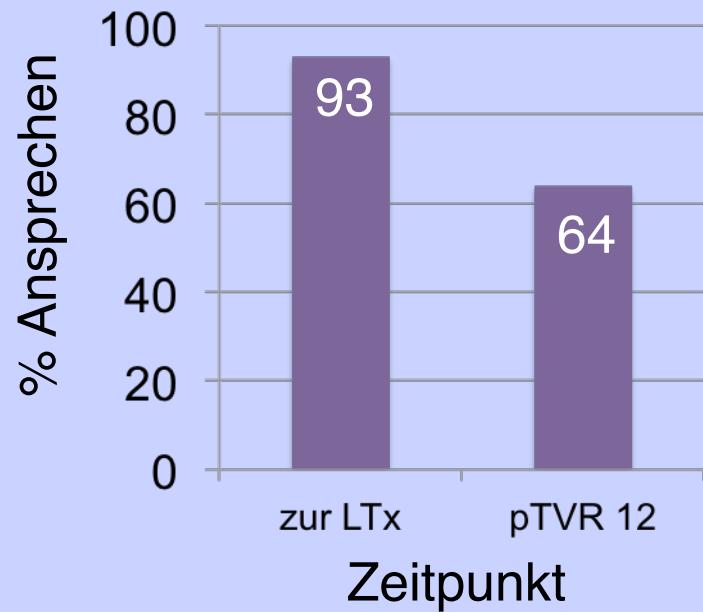
HCV

Gilead – Transplantation

Sofosbuvir 400 mg + Ribavirin 1000-1200 mg

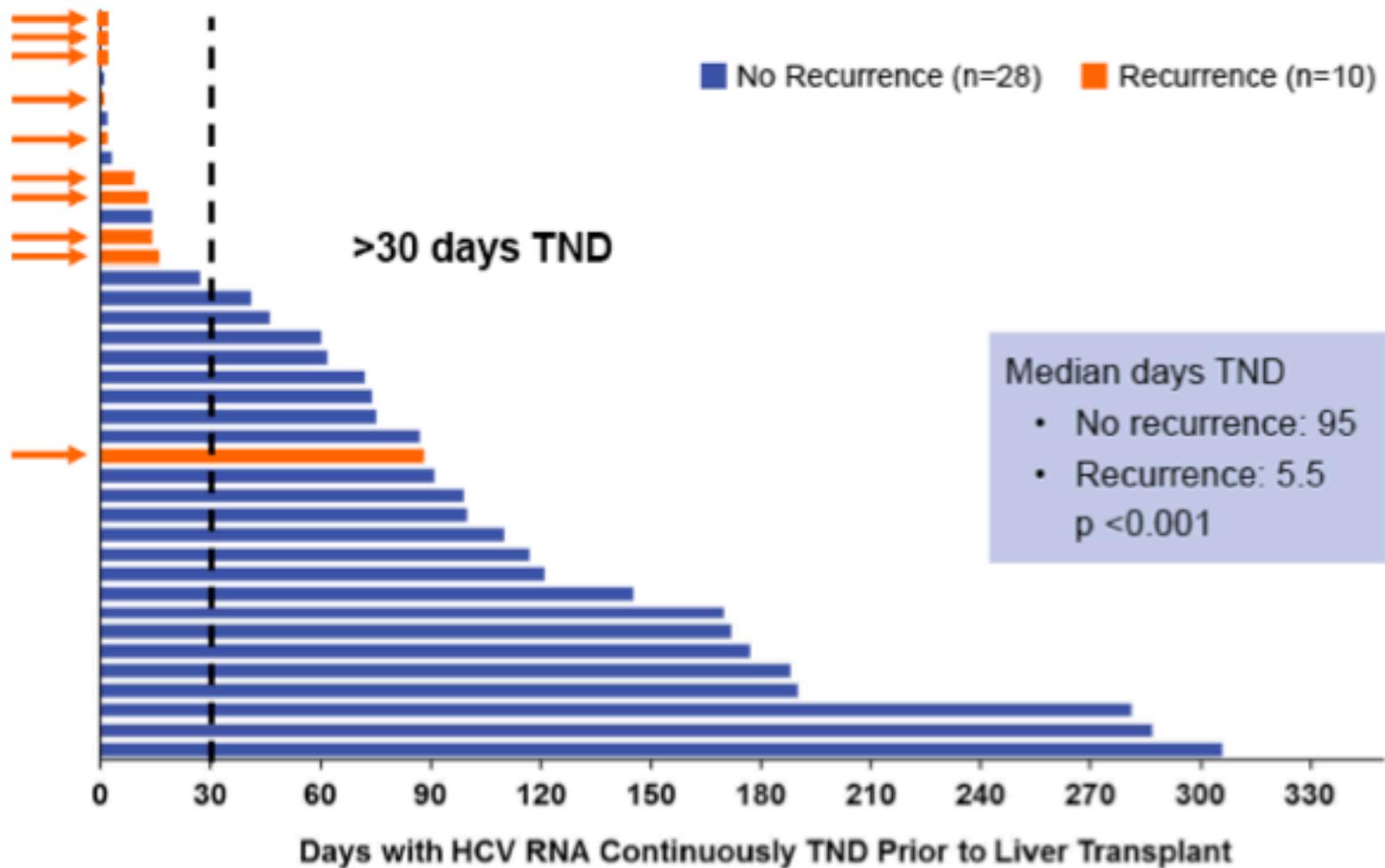
N=61

Therapiedauer 24-48 Wochen



HCV

Gilead – Transplantation



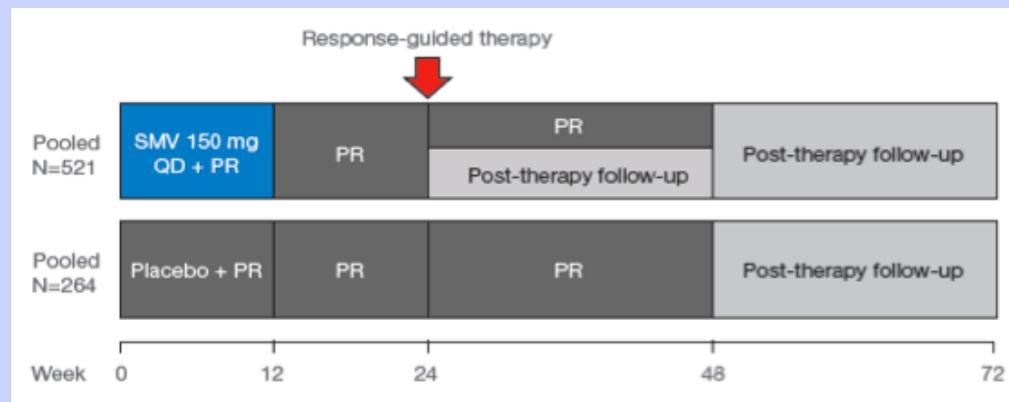
Simeprevir

April 2014

HCV

Pipeline: Janssen – QUEST-1 und -2

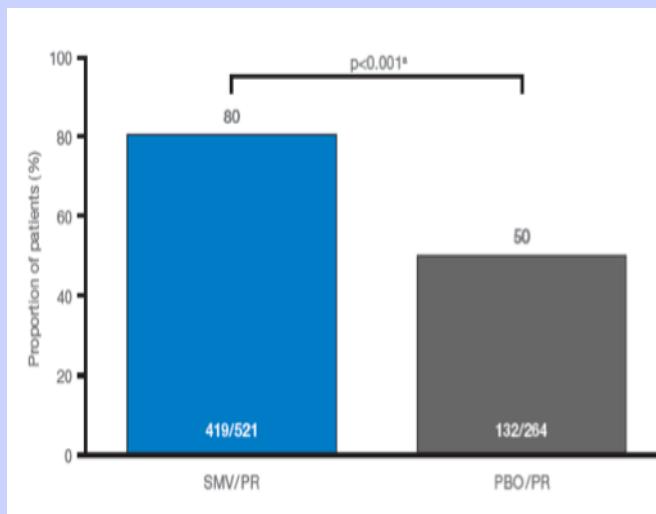
- Therapie-naiv
- QUEST-1: US und Europa, Peg-a2a
- QUEST-2: Europa, Peg-a2a oder Peg-a2b



HCV

Pipeline: Janssen – QUEST-1 und -2

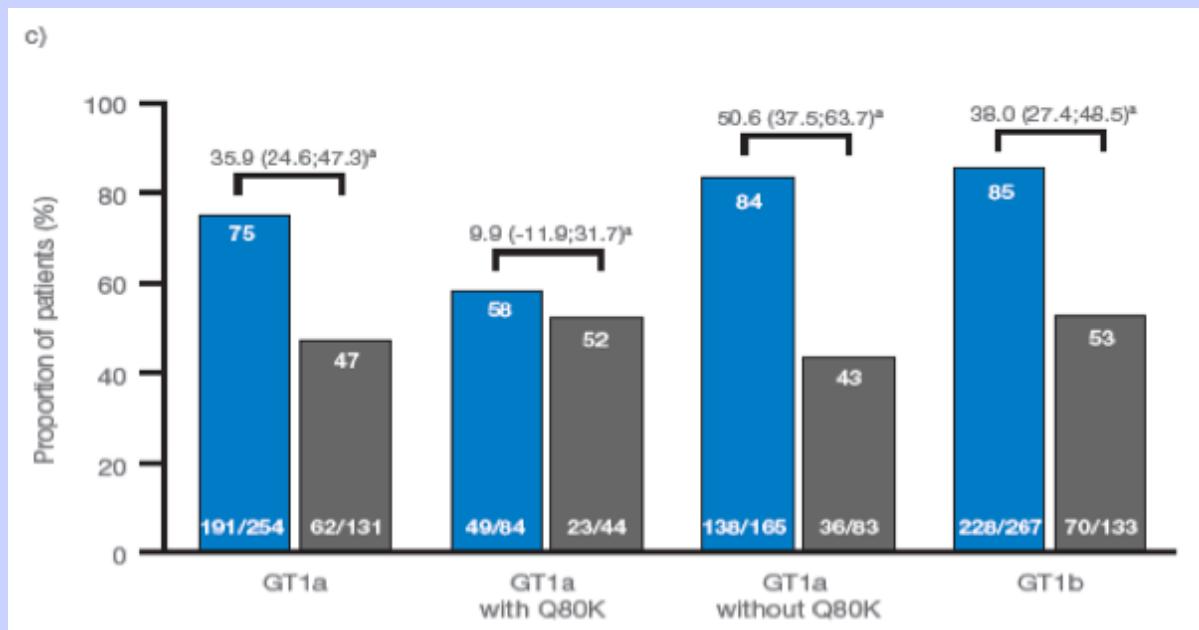
- Therapie-naiv
- QUEST-1: US und Europa, Peg-a2a
- QUEST-2: Europa, Peg-a2a oder Peg-a2b



HCV

Pipeline: Janssen – QUEST-1 und -2

- Therapie-naiv
- QUEST-1: US und Europa, Peg-a2a
- QUEST-2: Europa, Peg-a2a oder Peg-a2b



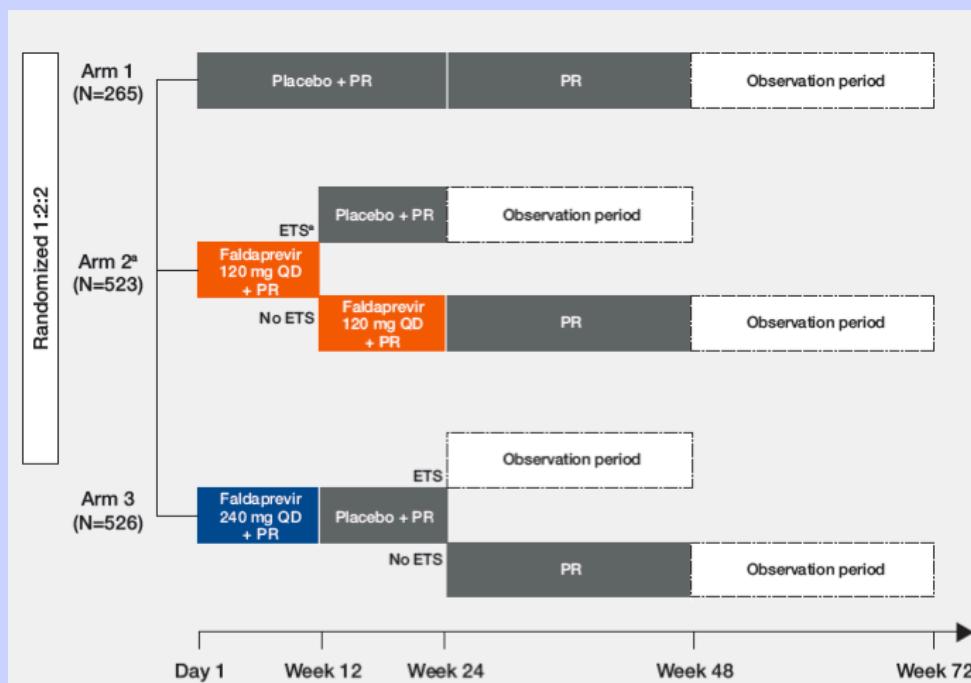
Faldaprevir

Herbst 2014

HCV

Pipeline: Boehringer Ingelheim – STARTVerso1 und 2

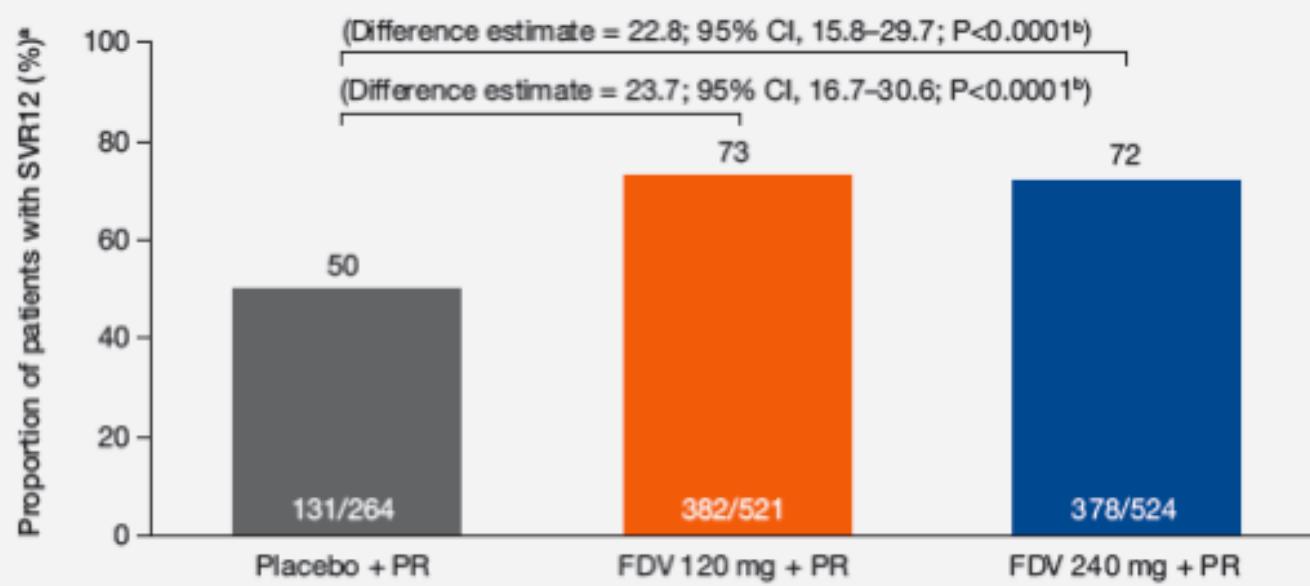
- Therapie-naiv
- Genotyp 1



ETS:
HCV-RNA < 25 U/ml
zur Woche 4 und
TND zur Woche 8

HCV

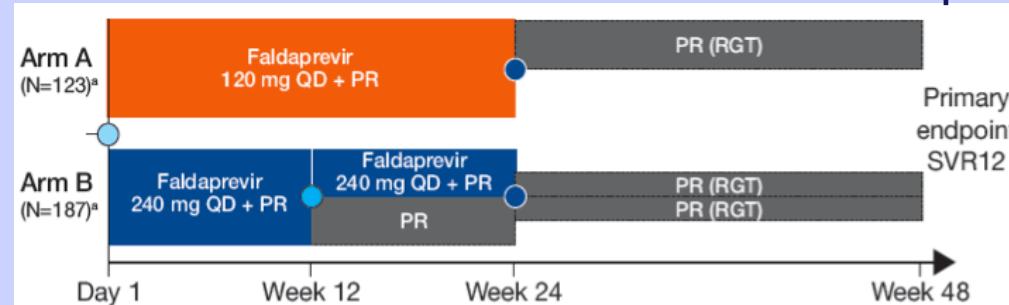
Pipeline: Boehringer Ingelheim – STARTVerso1 und 2



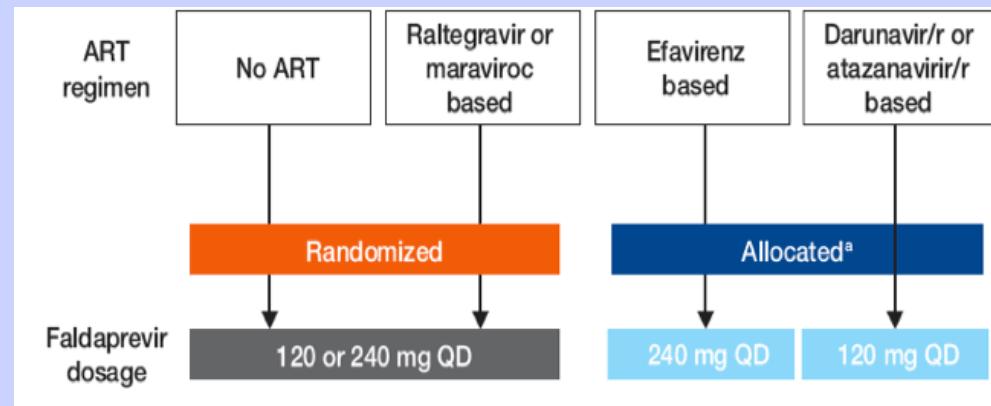
HCV/HIV Co-infektion

Pipeline: Boehringer Ingelheim – STARTVerso4

- Therapie-naiv oder Relapser
- Keine Zirrhose
- ART-naiv oder stabil unter Therapie



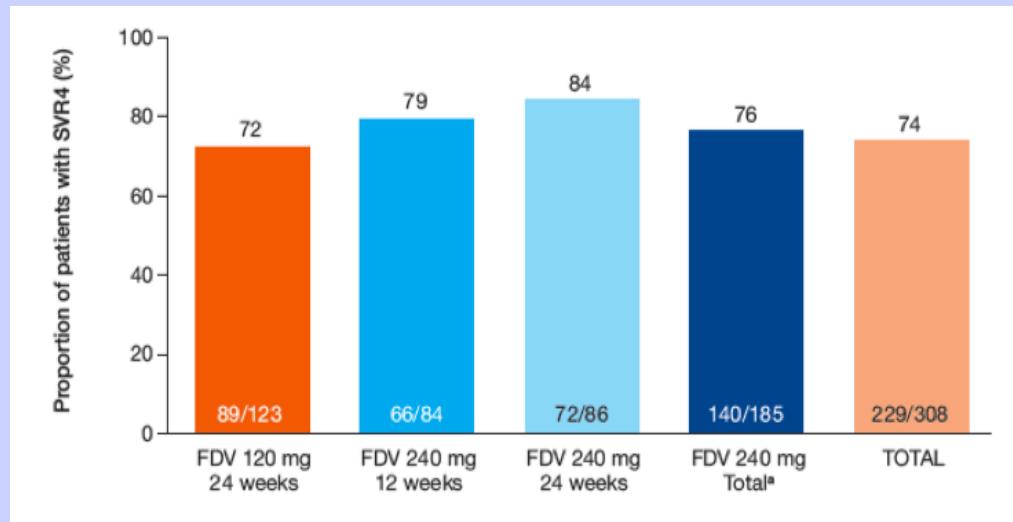
ETS:
HCV-RNA < 25 U/ml
zur Woche 4 und
TND zur Woche 8



HCV/HIV Co-infektion

Pipeline: Boehringer Ingelheim – STARTVerso4

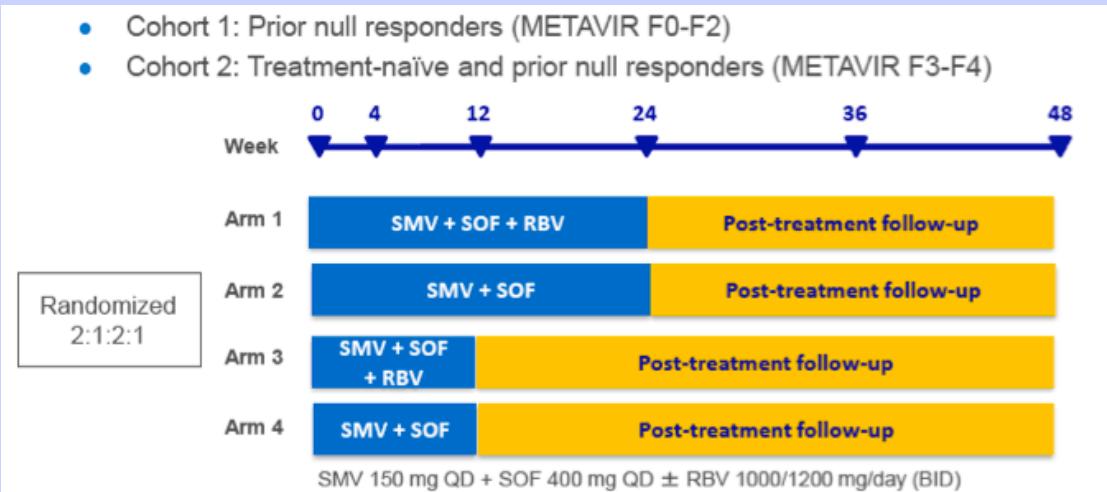
- Therapie-naiv oder Relapser
- Keine Zirrhose
- ART-naiv oder stabil unter Therapie



Interferonfreie Therapien

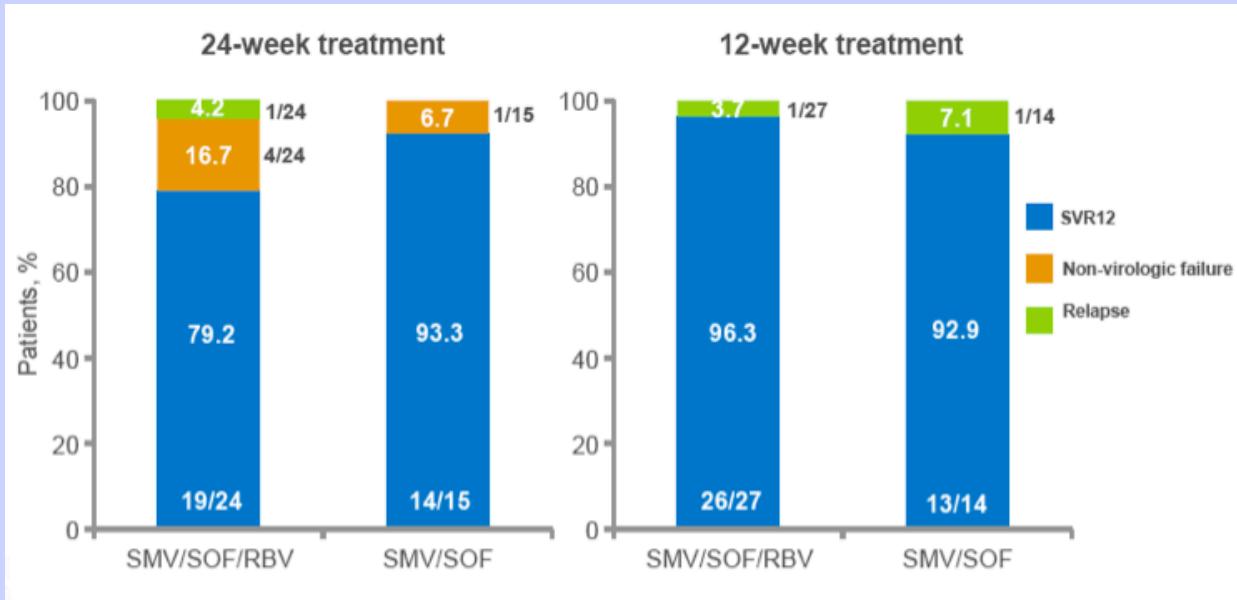
HCV

Sofosbuvir/Simeprevir (COSMOS)



HCV

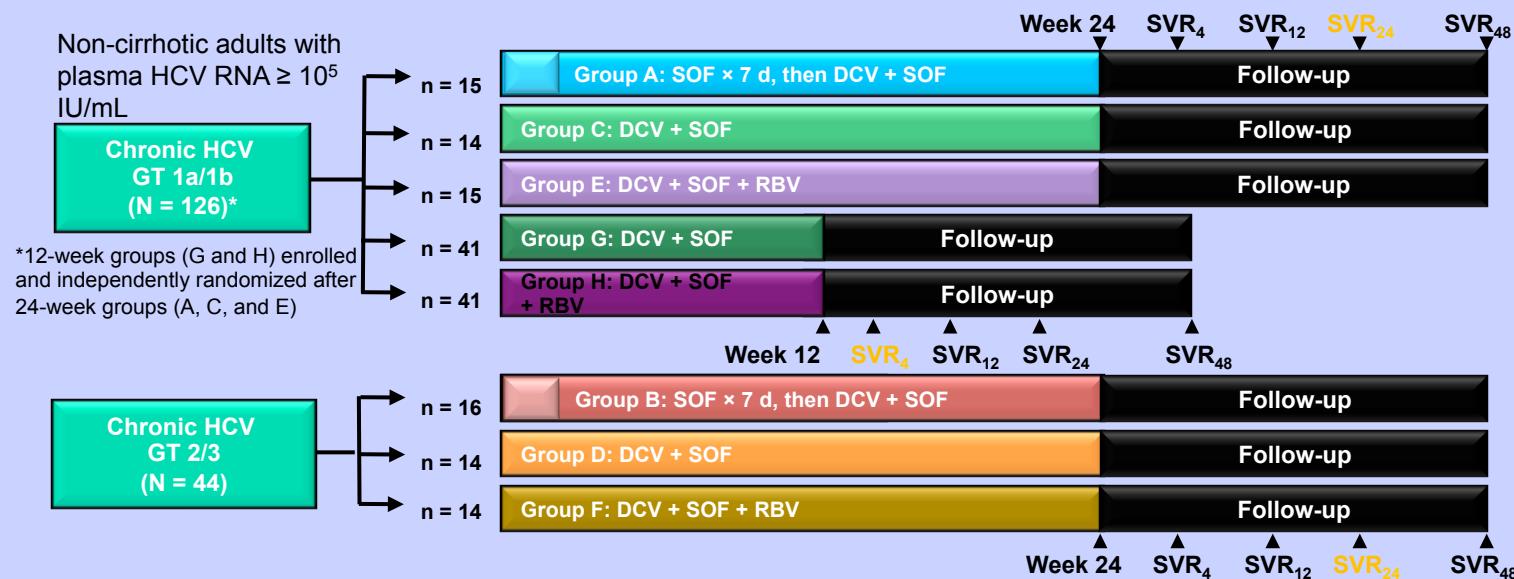
Sofosbuvir/Simeprevir (COSMOS)



HCV

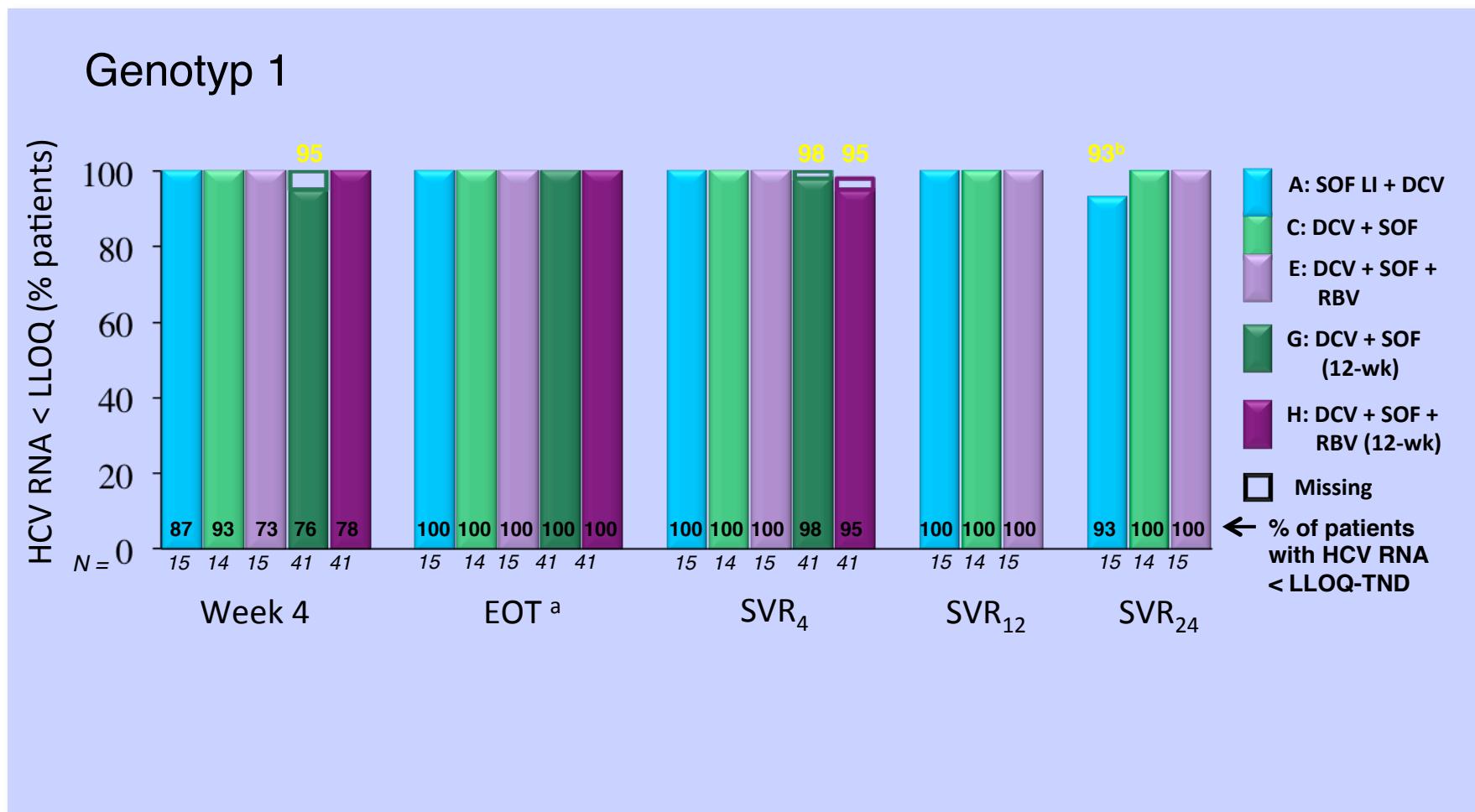
Sofosbuvir/Daclatasvir

- Sofosbuvir (NUC/Gilead) und Daclatasvir (NS5A/BMS)
- Genotyp 1-3
- Therapienaiv



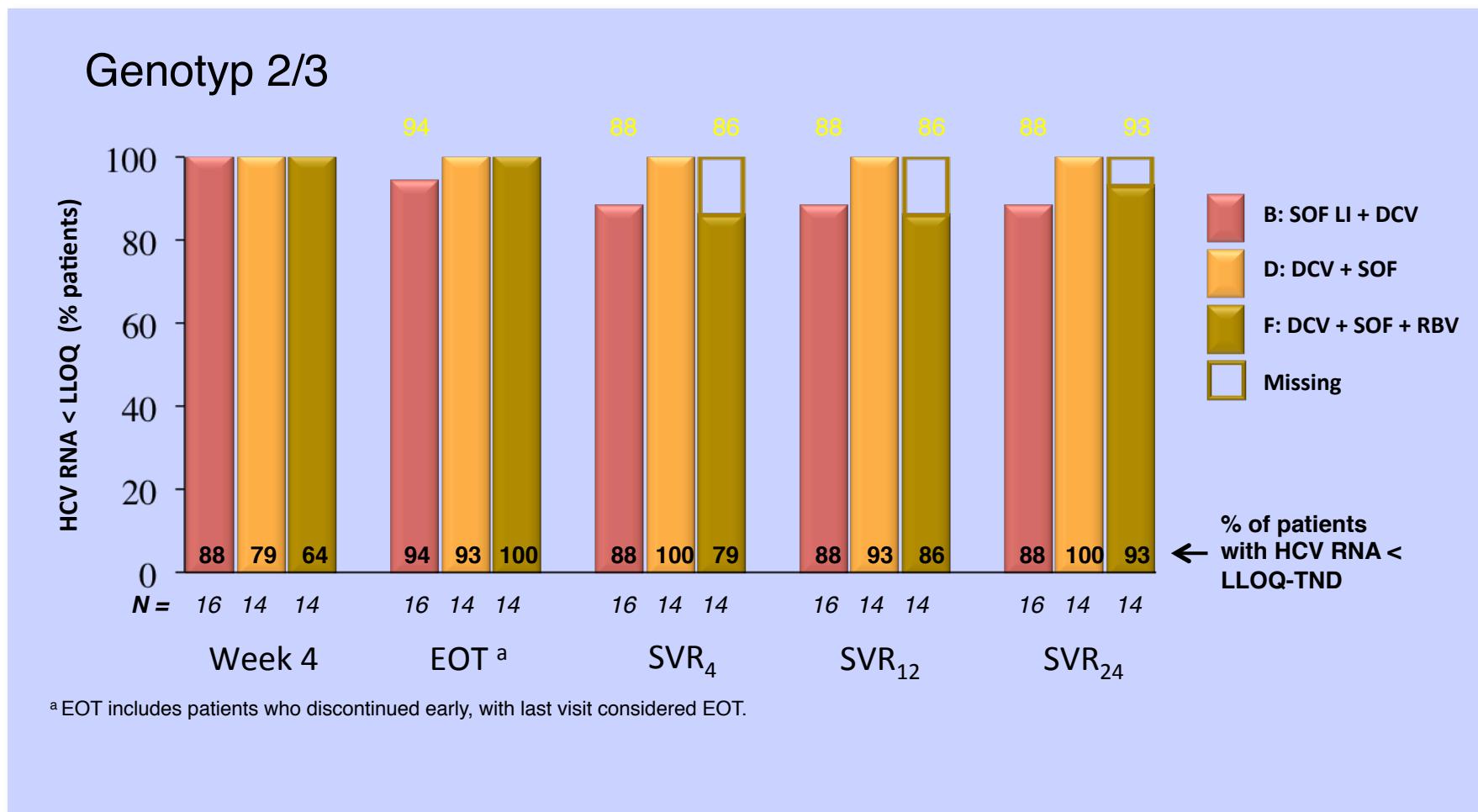
HCV

Sofosbuvir/Daclatasvir

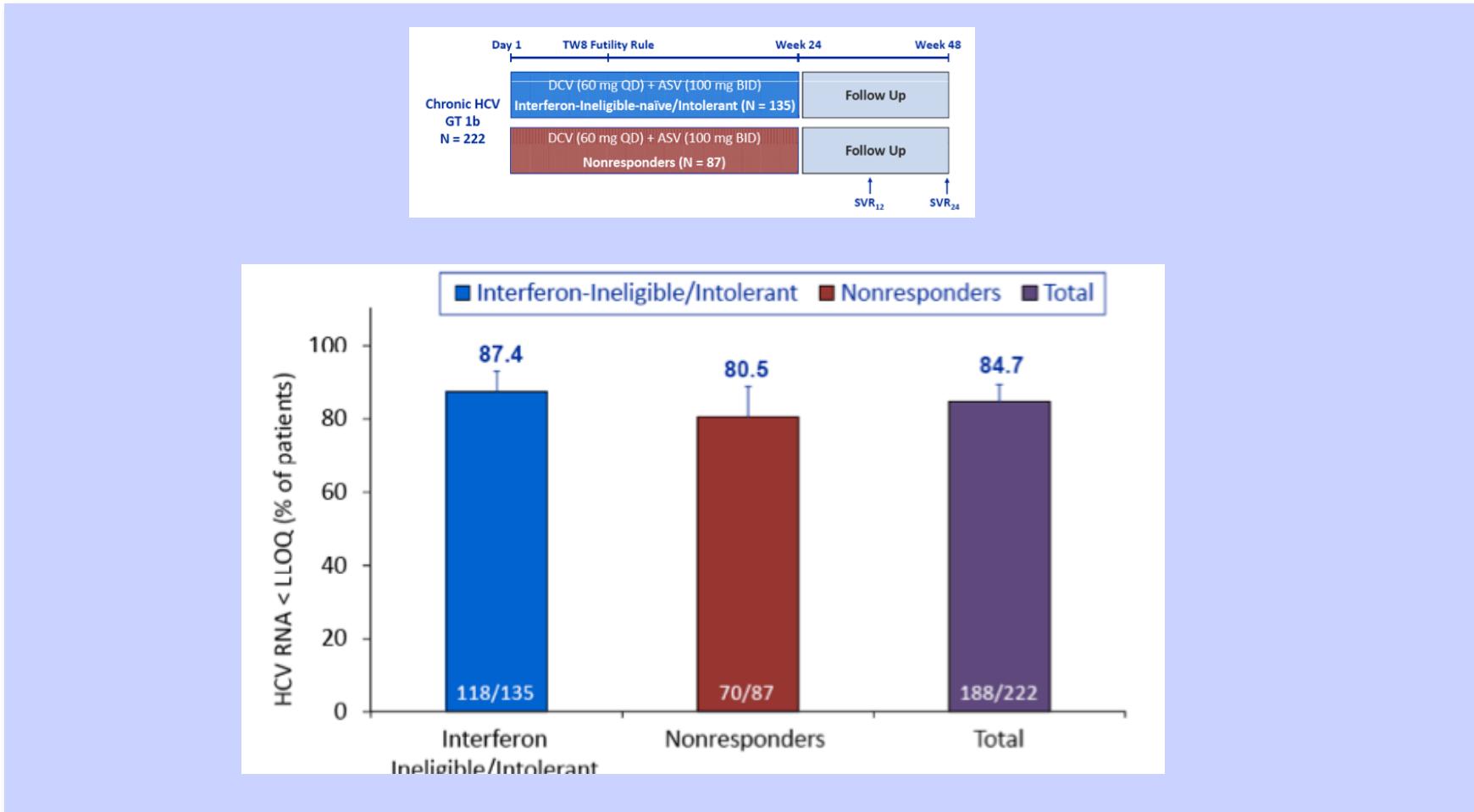


HCV

Sofosbuvir/Daclatasvir



HCV Pipeline: BMS



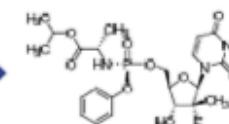
HCV

Pipeline: Gilead – SOF/LDV – GT 1 (LONESTAR)

◆ Sofosbuvir

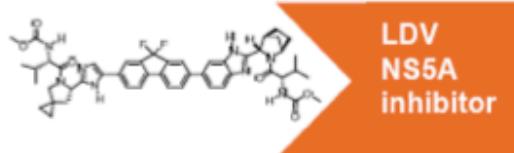
- Potent antiviral activity against HCV GT 1–6
- High barrier to resistance
- Once-daily, oral, 400-mg tablet

SOF
Nucleotide
polymerase
inhibitor



◆ Ledipasvir

- Picomolar potency against HCV GT 1a and 1b¹
- Effective against NS5B RAV S282T²
- Once-daily, oral, 90-mg



LDV
NS5A
inhibitor

◆ Sofosbuvir/Ledipasvir FDC

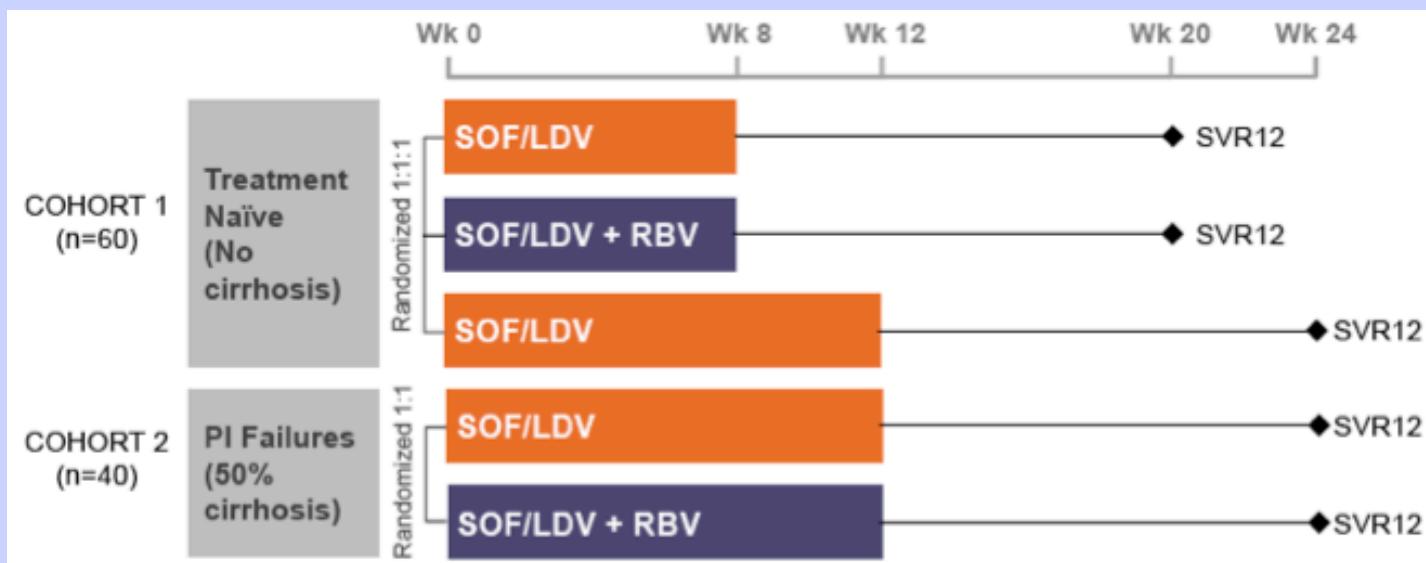
- Once daily, oral fixed-dose (400/90 mg) combination tablet
- No food effect
- >2000 patients treated

SOF
Nucleotide
polymerase
inhibitor

LDV
NS5A
inhibitor

HCV

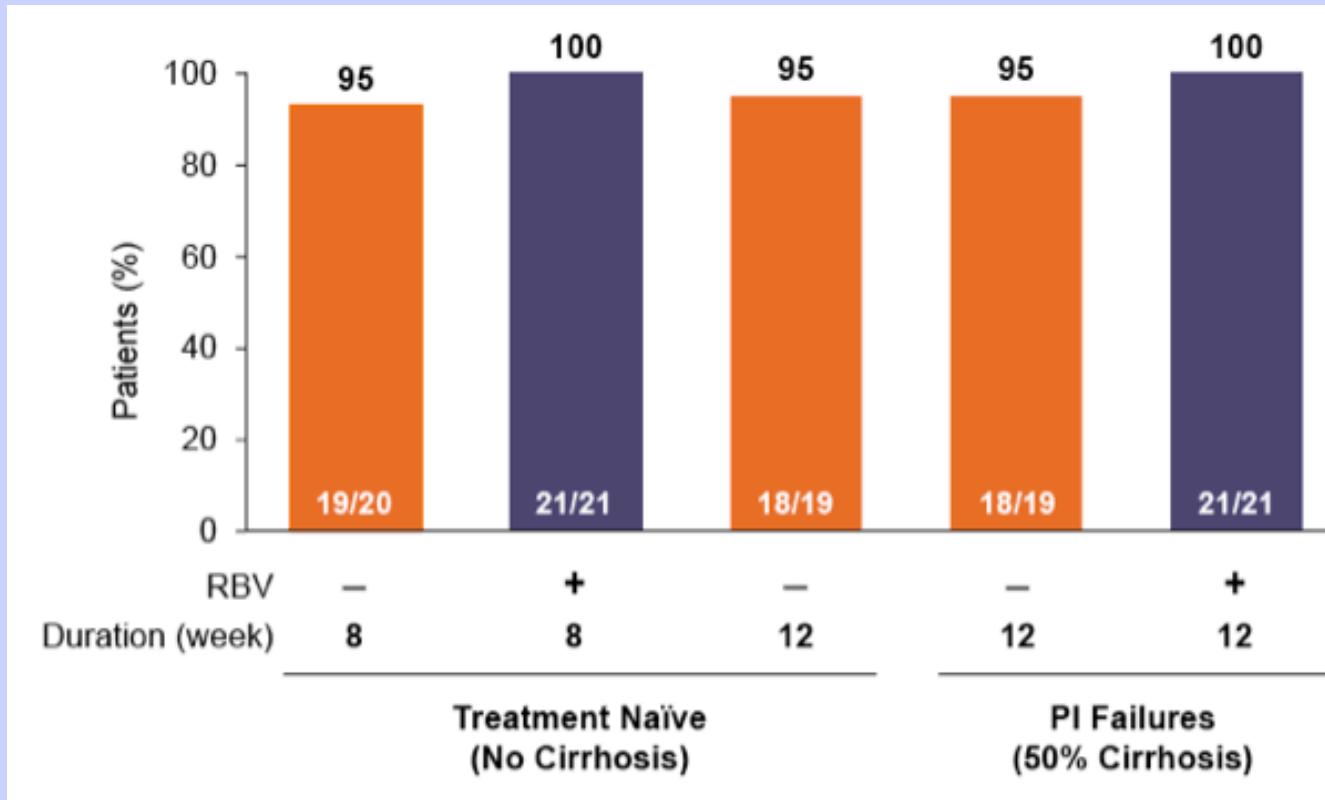
Pipeline: Gilead – SOF/LDV – GT 1 (LONESTAR)



- ◆ Single center study of GT 1 patients
- ◆ Broad inclusion criteria
 - No upper limit to age or BMI
 - Platelets $\geq 50,000/\text{mm}^3$

HCV

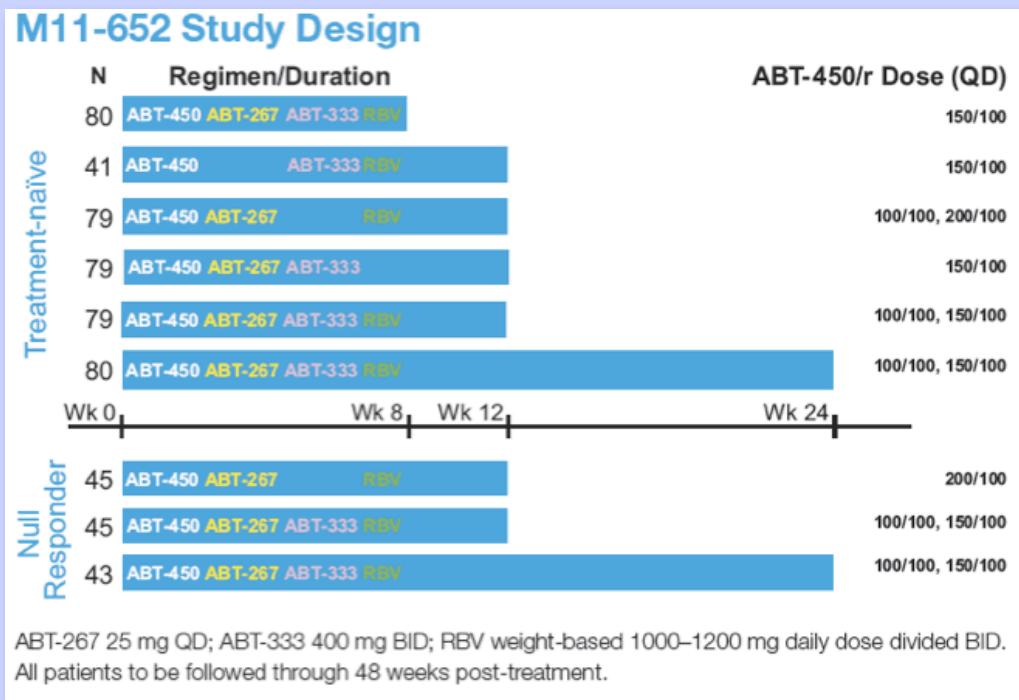
Pipeline: Gilead – SOF/LDV – GT 1 (LONESTAR)



HCV

Pipeline: Abbvie

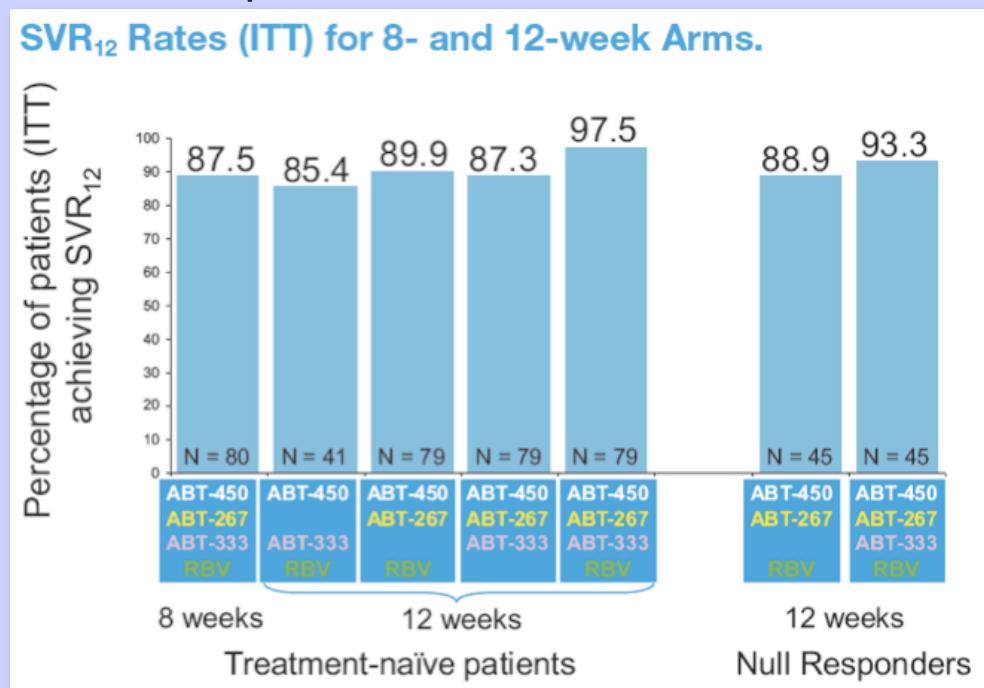
- ABT 450/r (Proteaseinhibitor)
- ABT 267 (NS5A Inhibitor)
- ABT 333 (NN NS5B Inhibitor)
- Therapienaiv oder Nullresponder
- GT1



HCV

Pipeline: Abbvie

- ABT 450/r (Proteaseinhibitor)
- ABT 267 (NS5A Inhibitor)
- ABT 333 (NN NS5B Inhibitor)
- Therapienaiv oder Nullresponder
- GT1



Ausblick

Interferonhaltig

Gilead (GT 1,3,4,5,6)
Sofosbuvir + PR

Nächste Generation PI + PR
▪ Simeprevir (Janssen)
▪ Faldaprevir (BI)

2013

2014

2015

2016

Interferonfrei

Gilead (GT 2)
Sofosbuvir + R

Gilead
Sofosbuvir
+ Ledipasvir

Gilead/Janssen
Sofosbuvir +
Simeprevir

BMS
Daclatasvir + Asunaprevir
GT1b

Gilead/BMS
Sofosbuvir +
Daclatasvir

Abbott
4+1 interferonfrei