Treating HCV Prior to Liver Transplantation

What Are the Treatment Options?

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Disclosures

Unrestricted Grant Support: Janssen and Abbvie

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Treatment options in HCV-infected patients awaiting LT

Which drug regimens are safe and efficacious?

1. Compensated cirrhosis (HCC)

2. Decompensated cirrhosis

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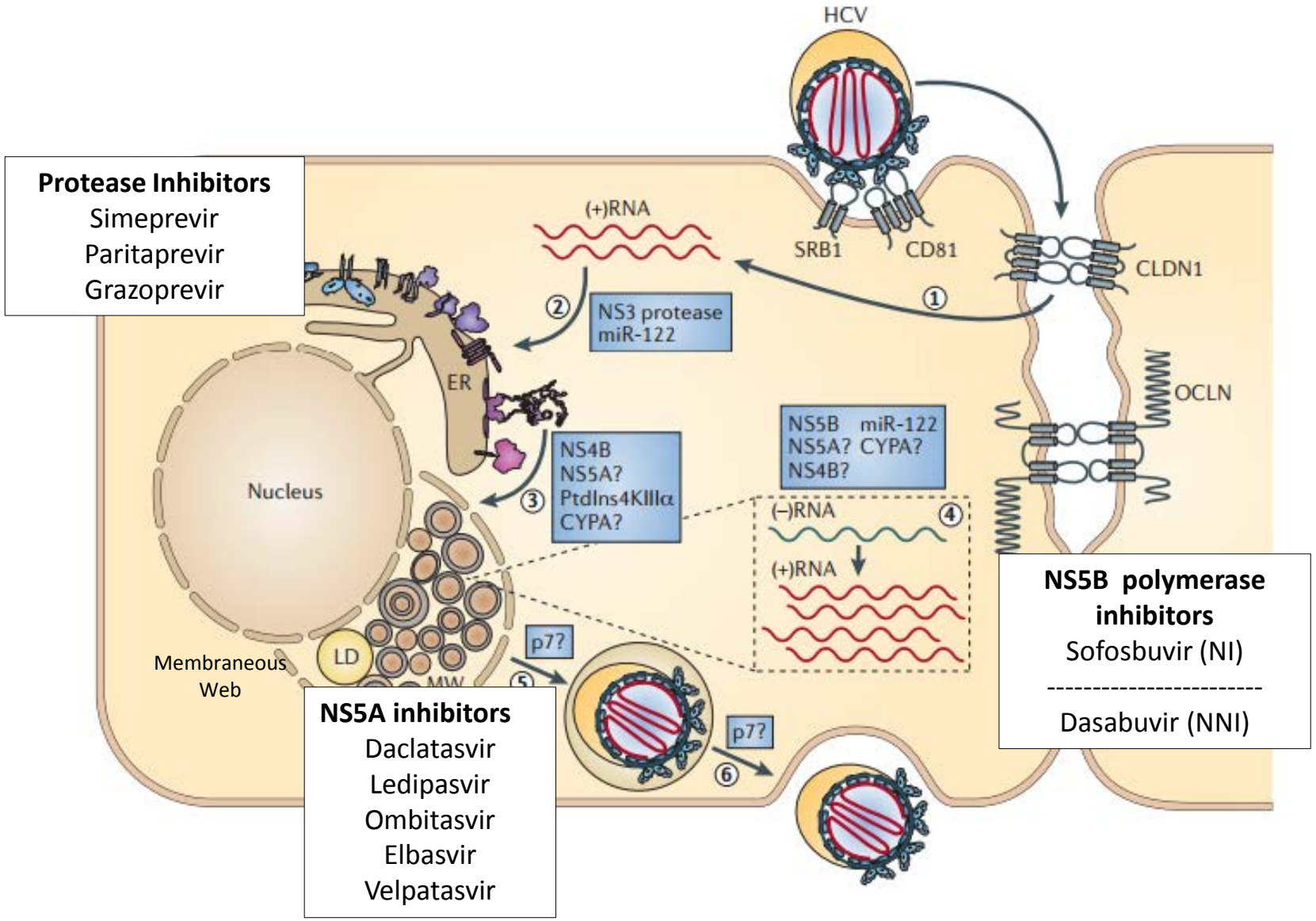
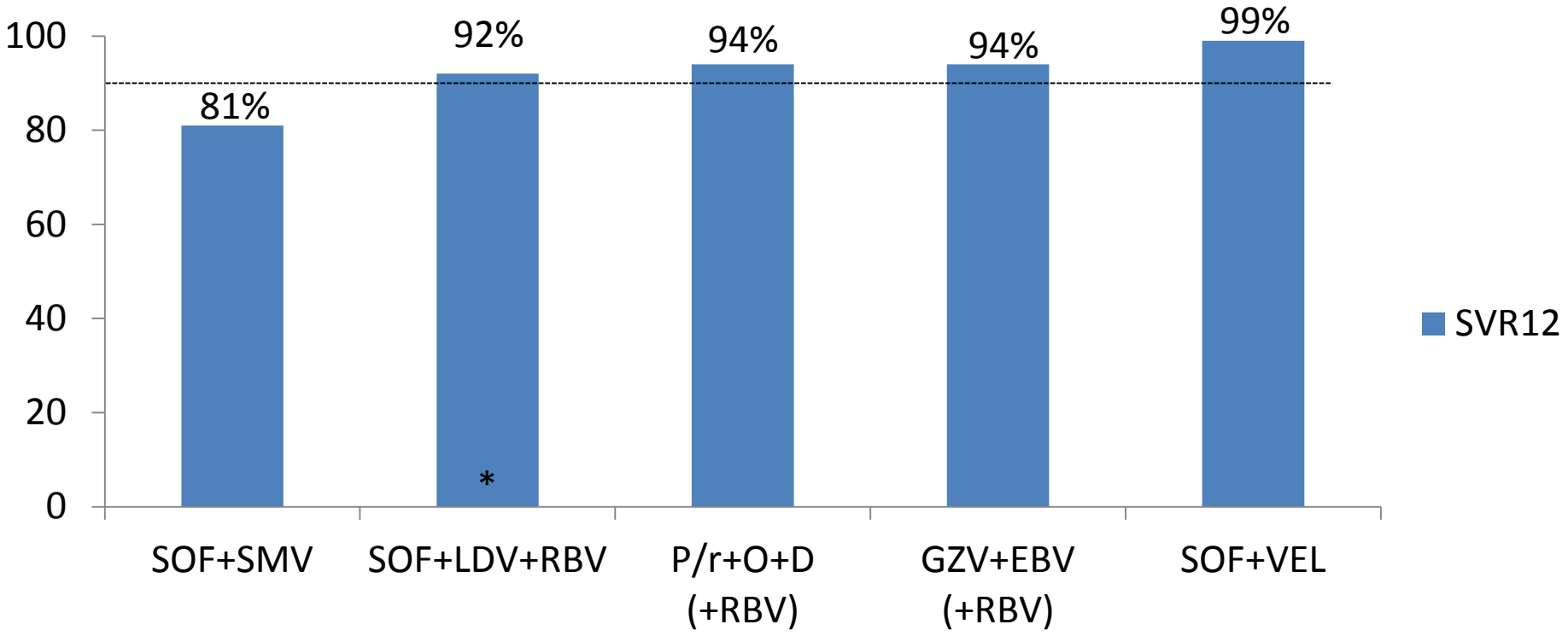
Safety and efficacy of DAA in decompensated cirrhosis



From Bartenschlager et al. Nature Reviews 2013

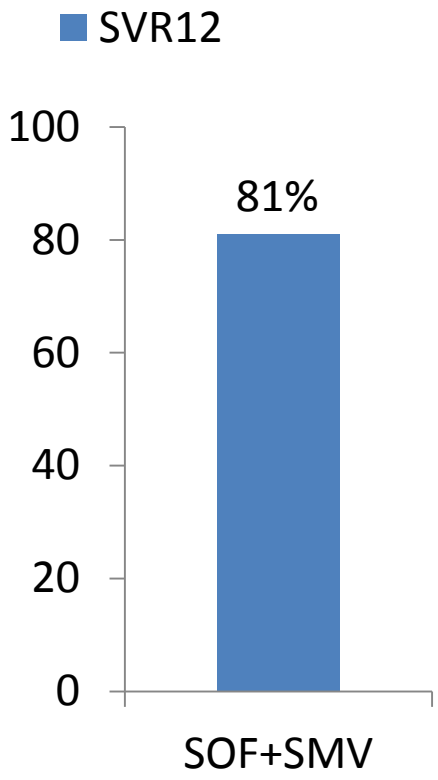
Safety and efficacy of DAA in G1 (4) compensated cirrhosis



* The combination of SOF+DAC+RBV can also be used in G1 (G4) patients with cirrhosis

Sulkowski M *Gastroenterolgy* 2015, Afdhal N *NEJM* 2014, Bourlière M *Lancet Infect Dis* 2015, Poordad F *NEJM* 2014, Jacobson I *AASLD* 2015, Feld J *NEJM* 2015

Safety and efficacy of DAA in G1 (4) compensated cirrhosis

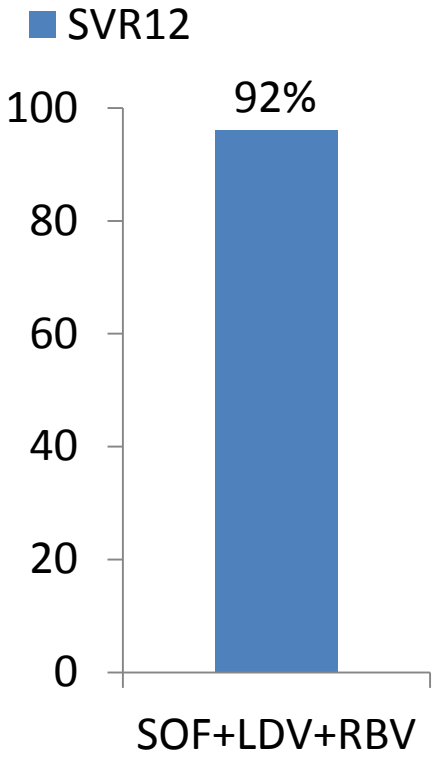


- Real world data
- Large cohort of cirrhotics (n=491)
- Nearly half (45%) history of previous decompensation
- Most patients treated without RBV
- Similar results in OPTIMIST-2 (SOF+SMV no RBV in cirrhosis)

- Real world data (Spanish Cohort)
- Large cohort of cirrhotics (n=946), most G1b
- SVR12: 91%

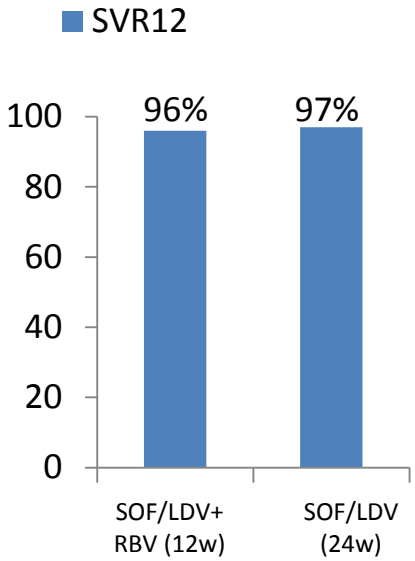
Sulkowski M *Gastroenterology* 2015, Lawitz E *Hepatology* 2015, Mariño Z *EASL* 2016

Safety and efficacy of DAA in G1 (4) compensated cirrhosis



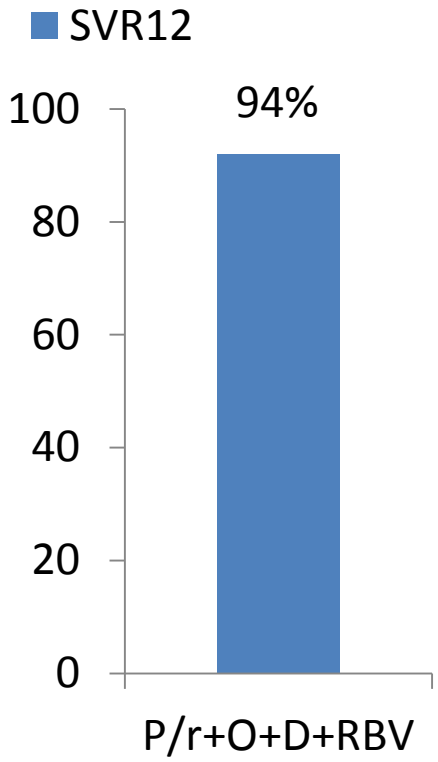
SIRIUS French Study

- Cirrhotics who failed PI-based regimen (n=155)
- Randomized to 12 weeks with RBV vs 24 weeks without RBV



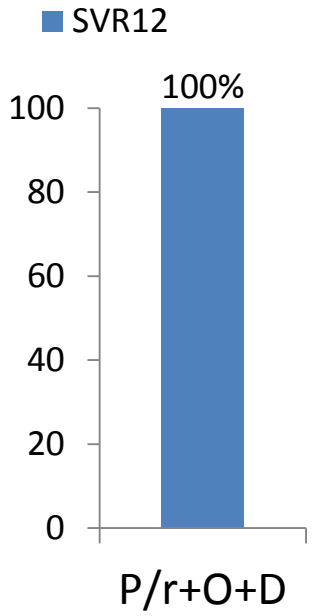
Afdhal N *NEJM* 2014, Bourlière M *Lancet Infect Dis* 2015

Safety and efficacy of DAA in G1 (4) compensated cirrhosis



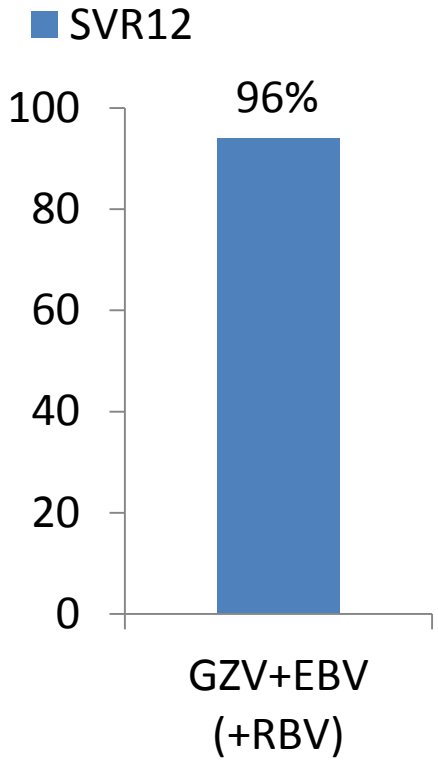
Turquoise III

- 60 cirrhotics
- G1b
- Naive or Experienced
- P/r+O+D



Poordad FJ *NEJM* 2014, Feld J *Hepatol* 2016

Safety and efficacy of DAA in G1 (4) compensated cirrhosis

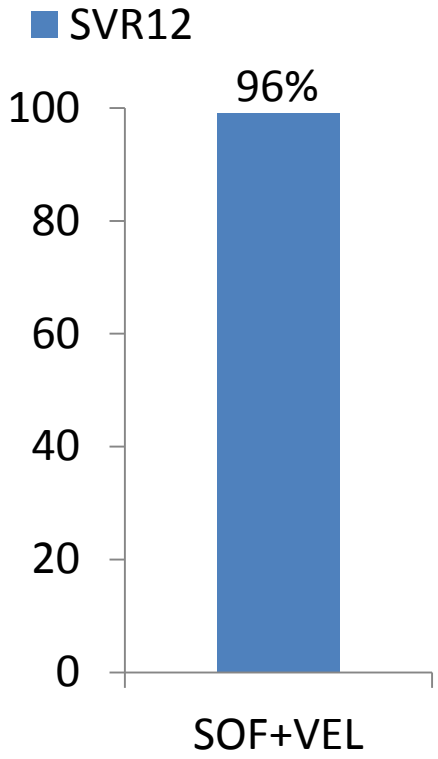


- Lower response rates in G1a with baseline NS5A RAVs:

  Add RBV and extend to 16 weeks

Zeuzem S *Ann Intern Med* 2015, Lawitz E *Lancet* 2015, Jacobson I *AALSD* 2015

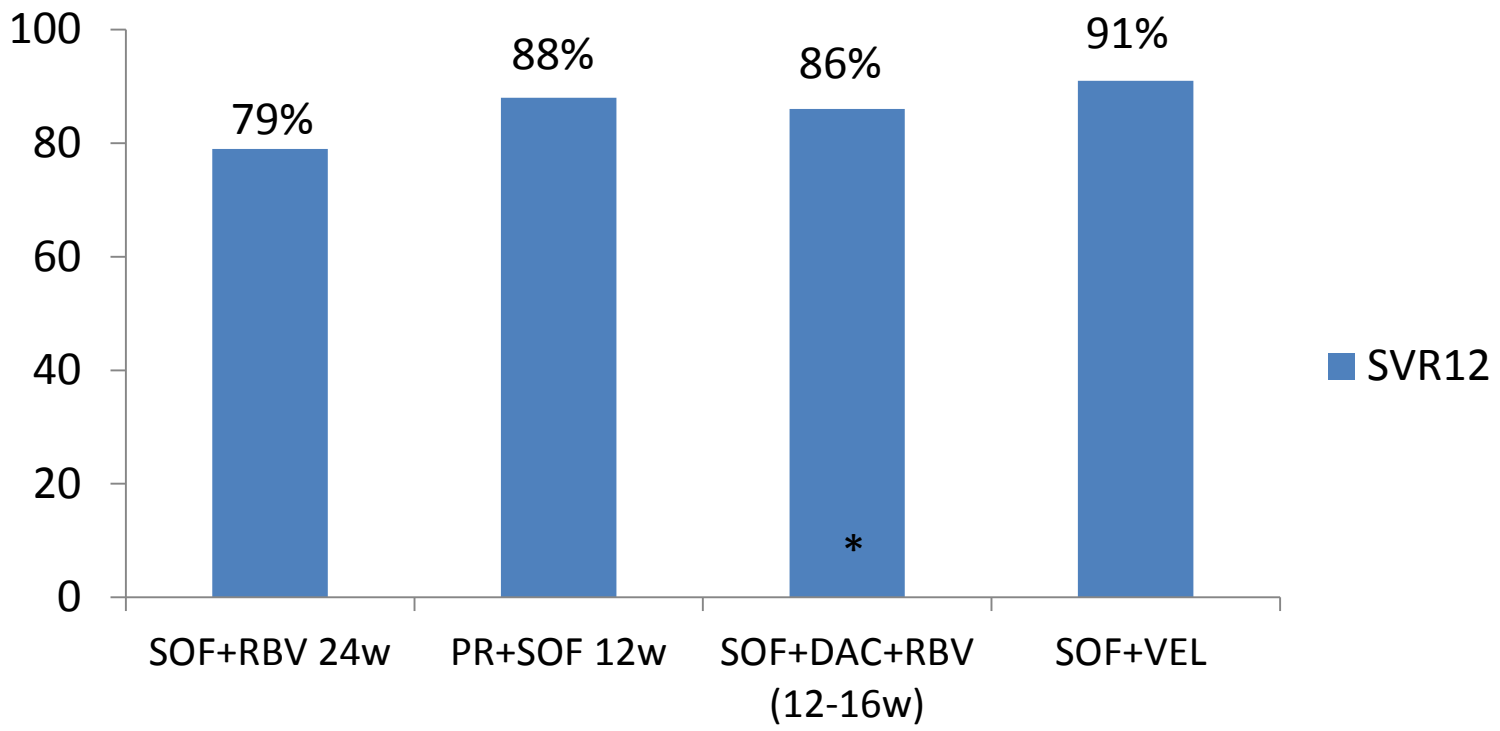
Safety and efficacy of DAA in G1 (4) compensated cirrhosis



- 120 of 121 cirrhotics achieved SVR12
- 72/73 G1 infected cirrhotics achieved SVR12
- The remaining patients were G2, 4, 5 or 6

Feld J *NEJM* 2015

Safety and efficacy of DAA in G3 compensated cirrhosis



* SOF+DAC for 24 w. (no RBV) obtains similar SVR12 rates (French CUP)

Foster GH *Gastroenterology* 2015, Leroy V *Hepatology* 2016, Hezode C *AALSD* 2015, Foster GH *NEJM* 2015

DAA in patients with Hepatocellular carcinoma (HCC)

58 patients with treated HCC (BCLC 0 and A) on complete response, who underwent DAA therapy.

↓

Median time between HCC treatment and DAA initiation: 11 m (P25-75 3-23)

↓

Median time between last radiologic confirmation of complete response and DAA initiation: 1.7 m (P25-75 0.85-3.4)

↓

Tumor recurrence: 16 (27,6%) patients. Median follow-up after DAA therapy 3.5 m (1-8)

Recurrence rate is significantly higher than the expected based on previous studies

Reig M and Mariño Z *J Hepatol* 2016

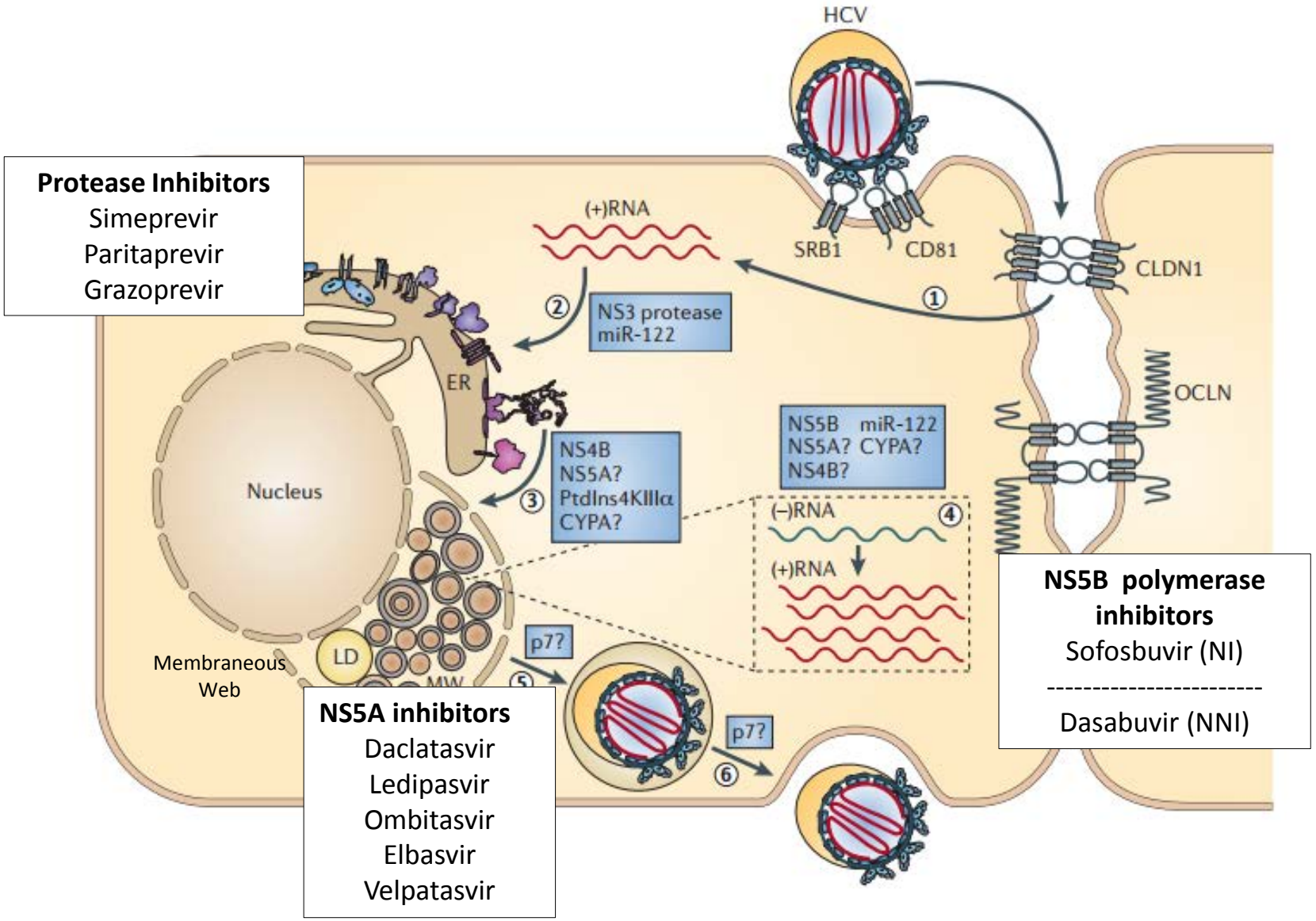
Treatment options in HCV-infected patients awaiting LT

Which drug regimens are safe and efficacious in this group?

1. Compensated cirrhosis (HCC)

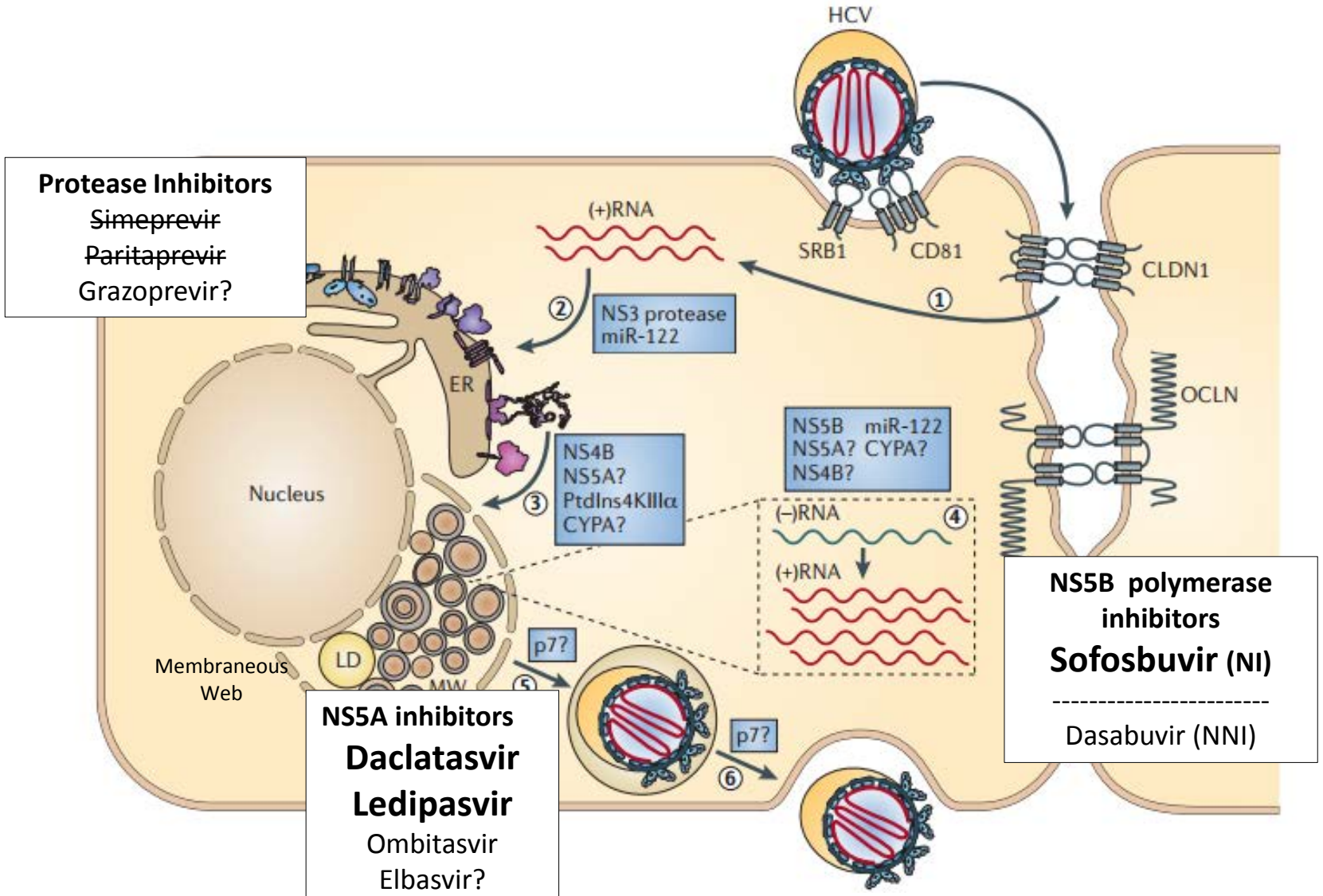
2. Decompensated cirrhosis

Safety and efficacy of DAA in decompensated cirrhosis



Bartenschlager R *Nature Reviews* 2013

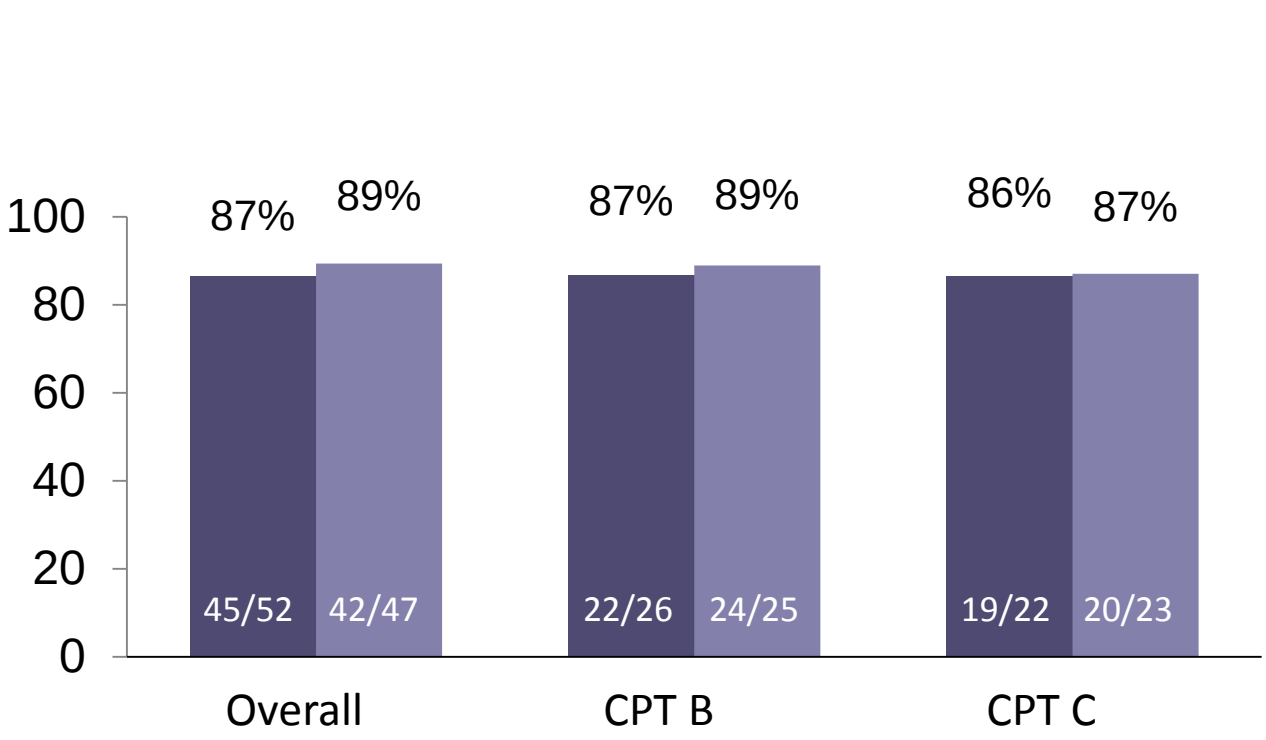
Safety and efficacy of DAA in decompensated cirrhosis



Bartenschlager R *Nature Reviews* 2013

Safety and efficacy of DAA in decompensated cirrhosis

SOF/LDV + RBV in G1 and G4 patients with decompensated cirrhosis



Severe Adverse Events$_*$

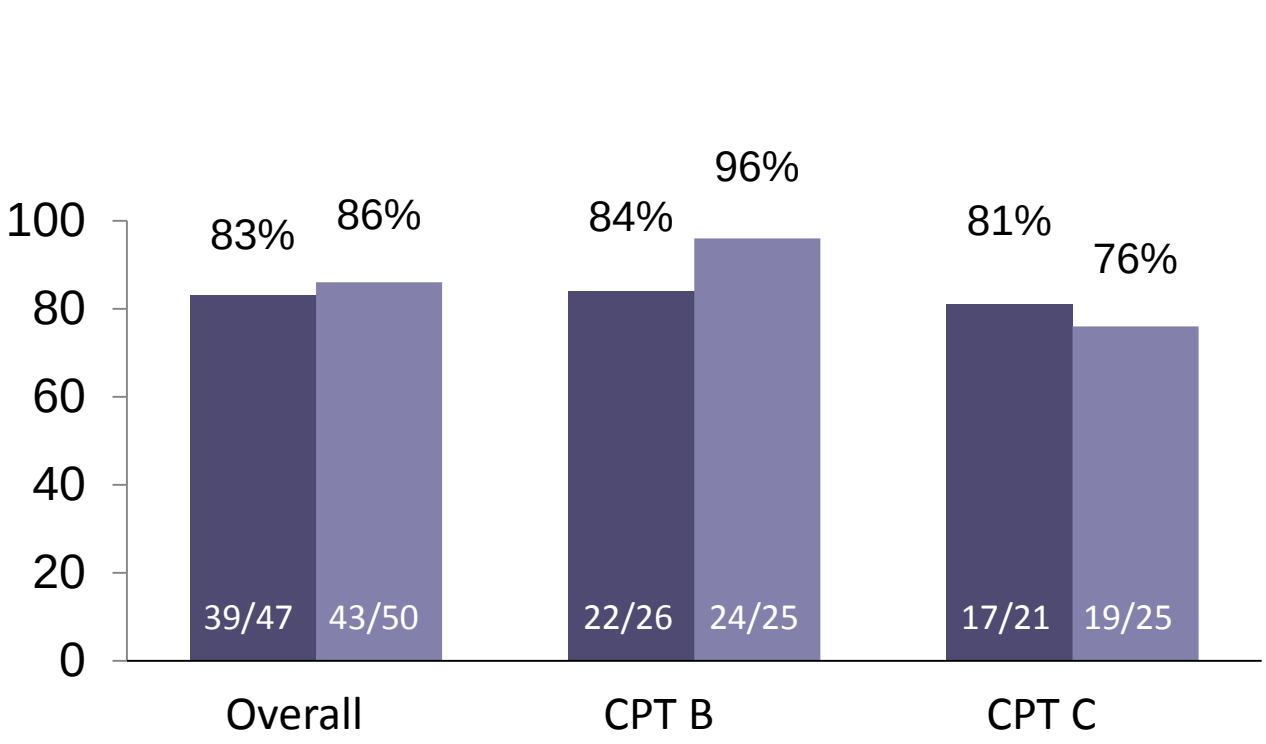
	12w	24w
CP-B	10%	34%
CP-C	26%	42%

Overall safety is good. Cases of severe bradycardia (if combined with amiodarone), a few cases of lactic acidosis and pulmonary hypertension have been reported postmarketing. Few safety data if CP > 12

Charlton M *Gastroenterology* 2015

Safety and efficacy of DAA in decompensated cirrhosis

SOF/LDV + RBV in G1 and G4 patients with decompensated cirrhosis



Severe Adverse Events	12w	24w
CP-B	11%	21%
CP-C	52%	35%

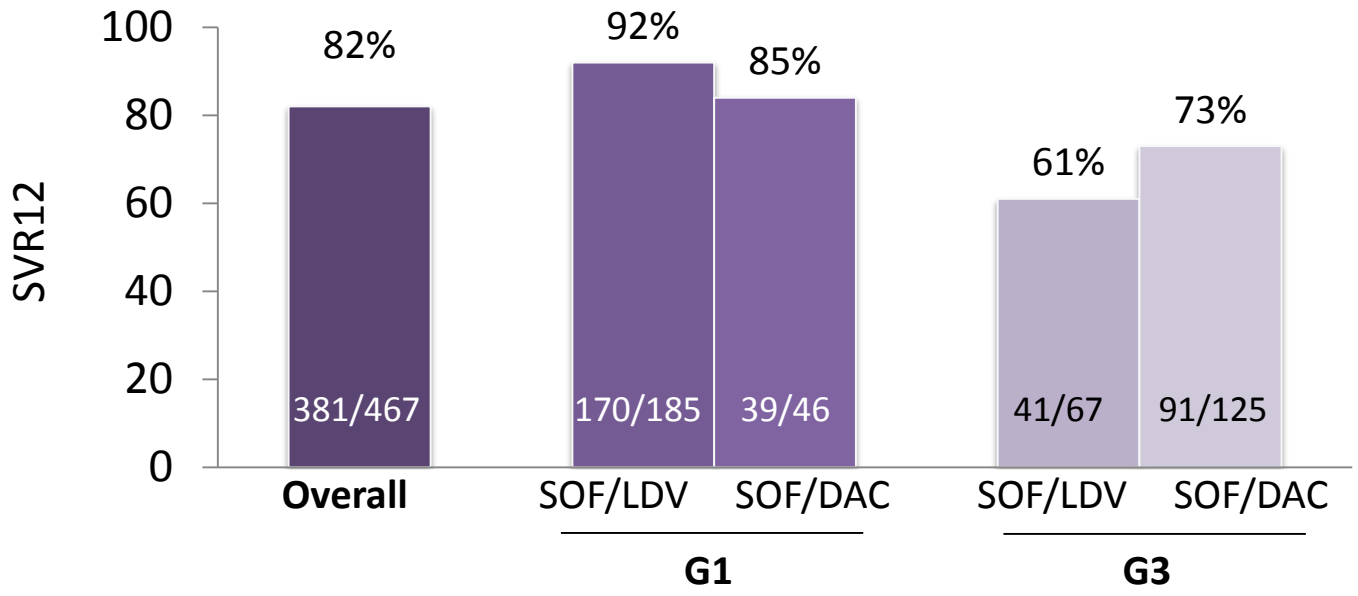
Overall safety is good. Cases of severe bradycardia (if combined with amiodarone), a few cases of lactic acidosis and pulmonary hypertension have been reported postmarketing. Few safety data if CP > 12

Manns M *Lancet Infectious Dis* 2016

Safety and efficacy of DAA in decompensated cirrhosis

Patients with decompensated cirrhosis (CP ≥ 7)
NHS England Expanded Access Program

Treatment duration 12 w; most patients with RBV

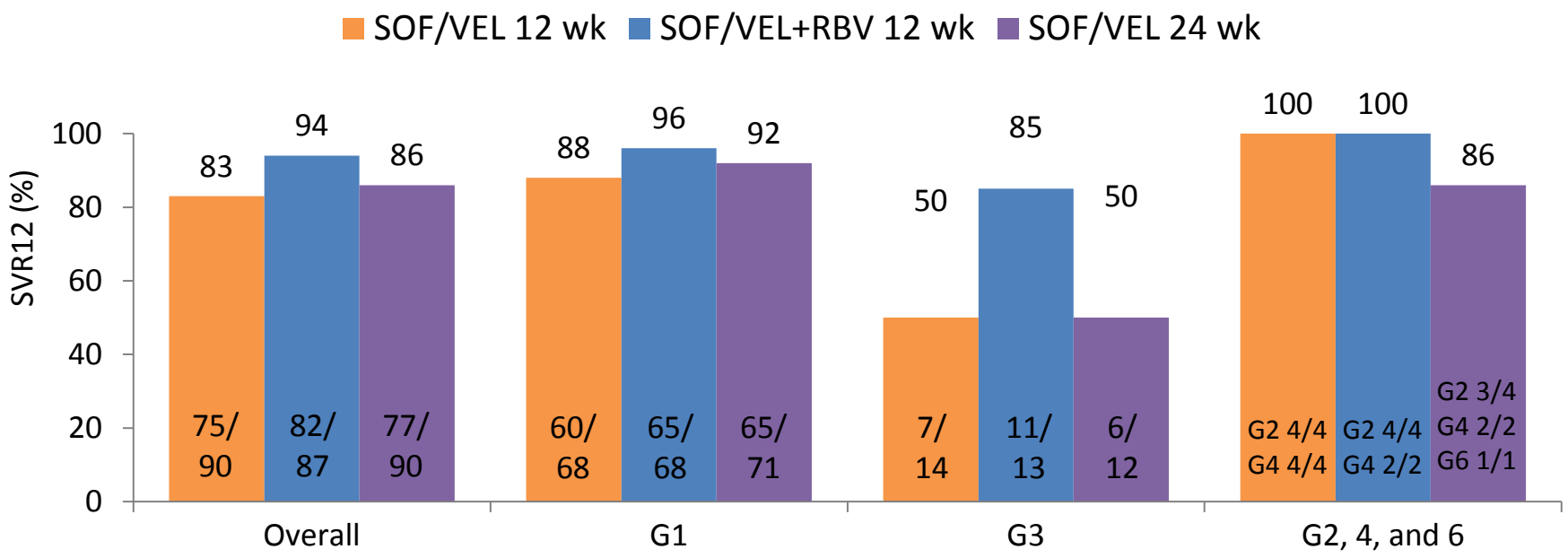


SVR rates similar than in ALLY-1 study in Child B/C (82%)

Foster GH *J Hepatol* 2016, Poordad F *Hepatology* 2016

Safety and efficacy of DAA in decompensated cirrhosis

SOF and Velpatasvir (+/- RBV) in G1-G6 Child B decompensated cirrhosis



Curry MP *NEJM* 2015

Safety and efficacy of DAA in decompensated cirrhosis

SOF and Velpatasvir (+/- RBV) in G1-G6 Child B decompensated cirrhosis

	SOF/VEL (12w)	SOF/VEL+RBV (12 w)	SOF/VEL (24 w)
Discontinuation	1 (1)	4 (5)	4 (4)
Deaths*	3 (3)	3 (3)	3 (3)
SAEs	17 (19)	14 (16)	16 (18)
Hb < 10 g/dL	7 (8)	20 (23)	8 (9)
Hepatic Encephalopathy	2 (2)	2 (2)	1 (1)
Sepsis	1 (1)	3 (3)	1 (1)
GI hemorrhage	3 (3)	0	0

Sepsis and liver failure were the most common causes of death

Curry MP *NEJM* 2015

DDI in HCV-infected liver transplant recipients

Drug	Cefotaxime	Seguril	B-blockers	Ca-antagonist	Amiodarone
Sof/LDV	●	●	●	■	●
Simeprevir	●	●	●	■	■
Daclatasvir	●	●	●	■	●
P/r/O/D	●	■	●	■	●
GZV/EBV	●	●	●	■	■

Drug	Atorvastatin	Acenocumarol	Metformin	Fluconazol	Omeprazol
Sof/LDV	■	●	■	●	■
Simeprevir	■	■	■	●	●
Daclatasvir	■	●	■	●	●
P/r/O/D	●	■	●	●	■
GZV/EBV	■	●	■	●	●

● No interaction ■ Potential interaction ● Drugs should not be coadministered

http://hep-druginteractions.org/interactions.aspx

Treatment regimens in patients awaiting LT

G1 and G4*

- SOF/LDV + RBV 12 w vs SOF/LDV 24 w.
- SOF/DAC+ RBV (12-24 weeks)
- SOF/VEL (12 weeks), consider RBV in decompensated patients

G3

- Sofosbuvir/Daclatasvir+ RBV (12-24 weeks)
- Sofosbuvir/Velpatasvir + RBV (12 weeks)

* 3D or GZV/EBV (G1b) and 3D+RBV or GZV/EBV+RBV (G1a) in compensated cirrhosis awaiting LT for HCC


CENTRE
ESTHER KOPLOWITZ