Personalised Treatment with Telaprevir in 2014

Graham R Foster

Professor of Hepatology

Queen Marys University of London

Telaprevir in 2014

Disclaimers

I have received funds from:

BI, BMS, Janssen, Novartis, Merck, Roche, Gilead

Telaprevir in 2014

- Times change!

- SVR rates of ‘only 80%’ are not acceptable

- Interferon is last years drug

Treatment in 2014
Right drug – Right patient

Telaprevir

What role should it play?

- Who needs it?
- Who should be considered for telaprevir?

Telaprevir in 2014
Who needs it?

- People who can not access next generation drugs

- People who can not tolerate next generation drugs (renal impairment, unknown drug interactions)

Telaprevir
Who to consider

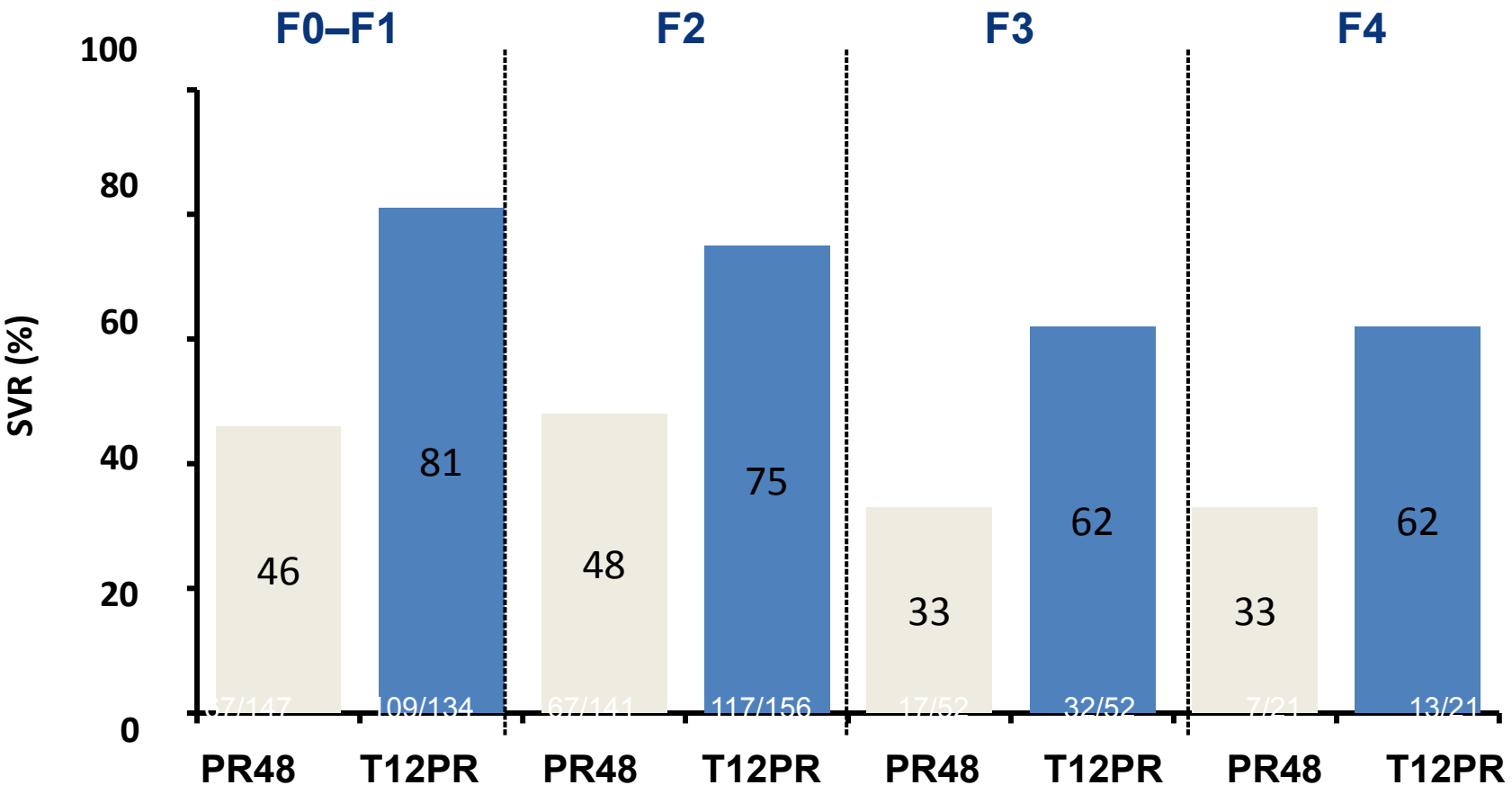
- Patients who can not wait for the new drugs
- Patients who want early treatment
- Patients who are likely to transmit

Telaprevir in 2014

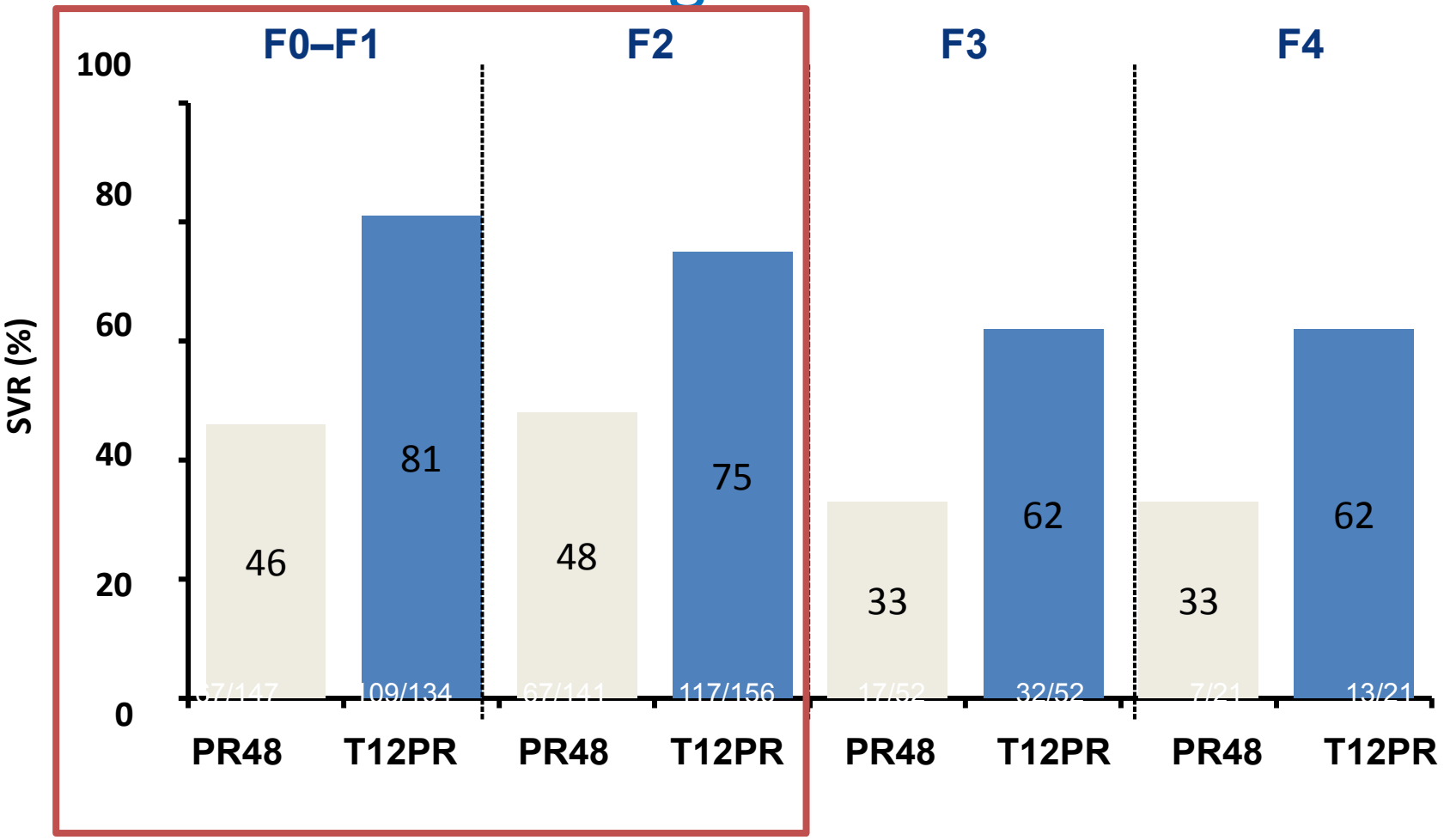
- How good is it?

- (New ‘standard of care’ is >90% SVR)

Telaprevir - Efficacy



Treatment-naïve patients with mild liver disease have a higher chance of cure



Marcellin P, et al. J Hepatol 2011;54(Suppl 1):S183

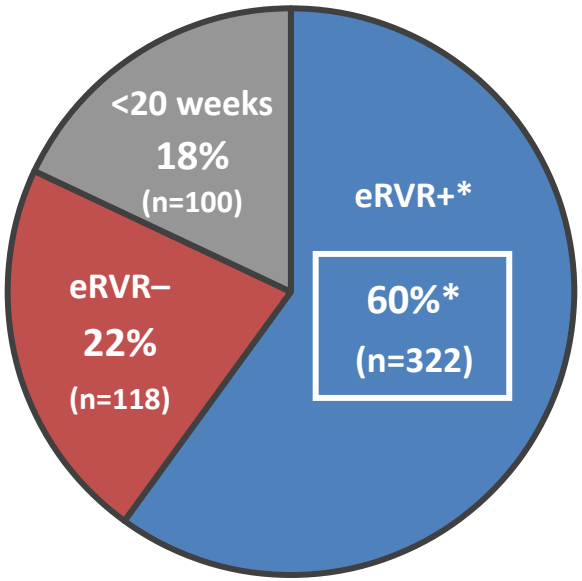
Telaprevir in 2014

- Patients with mild disease often achieve a rapid virological response (eRVR)

- These patients only need 24 weeks therapy

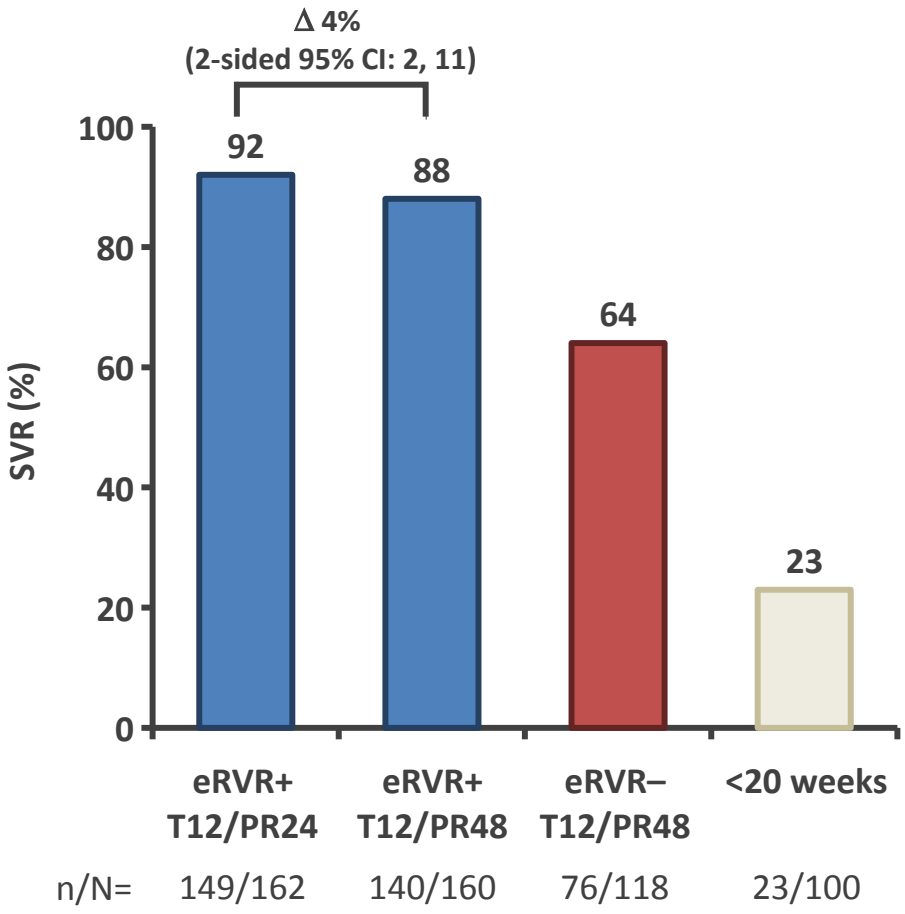
ILLUMINATE (TVR): SVR rates by treatment duration in patients treated with TVR12/PR (N=540)

Treatment duration according to eRVR status



- Eligible for 24 weeks and randomised to 24 or 48 weeks*
- 48 weeks
- <20 weeks (due to premature treatment discontinuation)

SVR rate



*Patients who achieved eRVR (undetectable HCV RNA at Weeks 4 and 12) and completed the Week 20 visit were randomised to receive an additional 4 or 28 weeks of PR alone
65% of patients achieved an eRVR (352/540); 322/352 were randomised and 30/352 patients discontinued before randomisation at Week 20

Sherman KE, et al. N Engl J Med 2011;365:1014–24

TVR Pbo-controlled Phase II and III studies: summary of AEs during TVR/Pbo phase

Patients (%)	T12/PR (750 mg q8h) (N=1346)	Pbo/PR48 (N=764)	Leading to discontinuation of all study drugs* (%)
Skin and subcutaneous tissue disorders			
Pruritus (SSC)	52	26	0.6
Rash (SSC)	55	33	2.6
Gastrointestinal disorders			
Nausea	39	29	<0.5
Diarrhea	26	19	<0.5
Hemorrhoids	12	3	<0.5
Anorectal discomfort	8	2	<0.5
Anal pruritus	6	1	<0.5
Blood and lymphatic system disorders			
Anemia (SSC)	32	15	0.9

*Discontinuation of all study drugs in the T12/PR arms (analysed within SSC for rash and anemia).

• http://www.fda.gov/downloads/AdvisoryCommittees/Committees/MeetingMaterials/Drugs/AntiviralDrugsAdvisoryCommittee/UCM252562.pdf

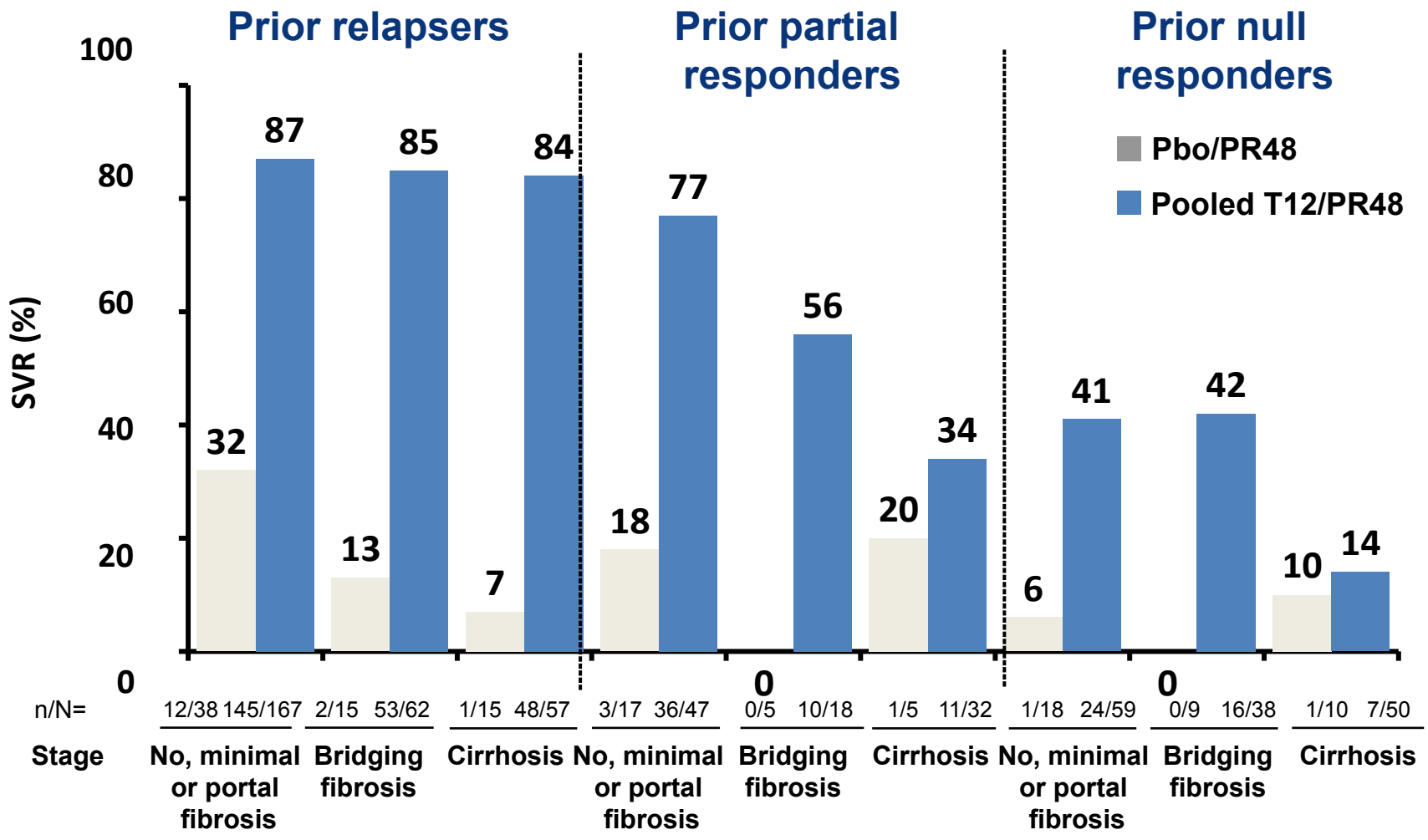
Telaprevir in 2014

- Untreated patients with mild disease do well
- Side effects are manageable

Telaprevir in 2014

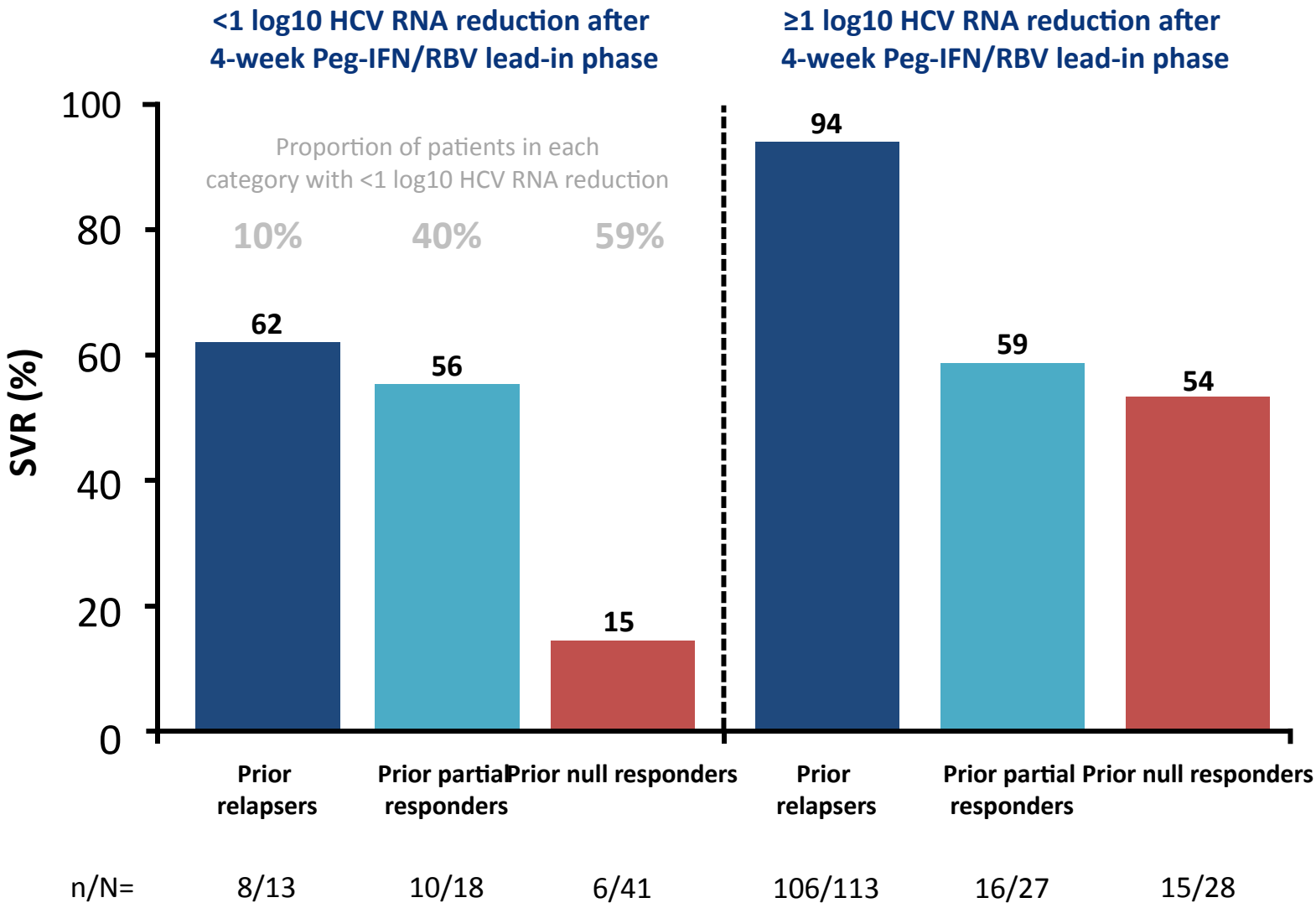
- Untreated patients with mild disease do well
- Side effects are manageable
- What about treatment experienced patients?

Treatment-experienced patients with mild liver disease have a higher chance of cure



Pol S, et al. Hepatology 2011;54(Suppl. S1):374A

REALIZE (telaprevir): SVR by Week 4 response according to prior response category (LI T12PR48 arm)

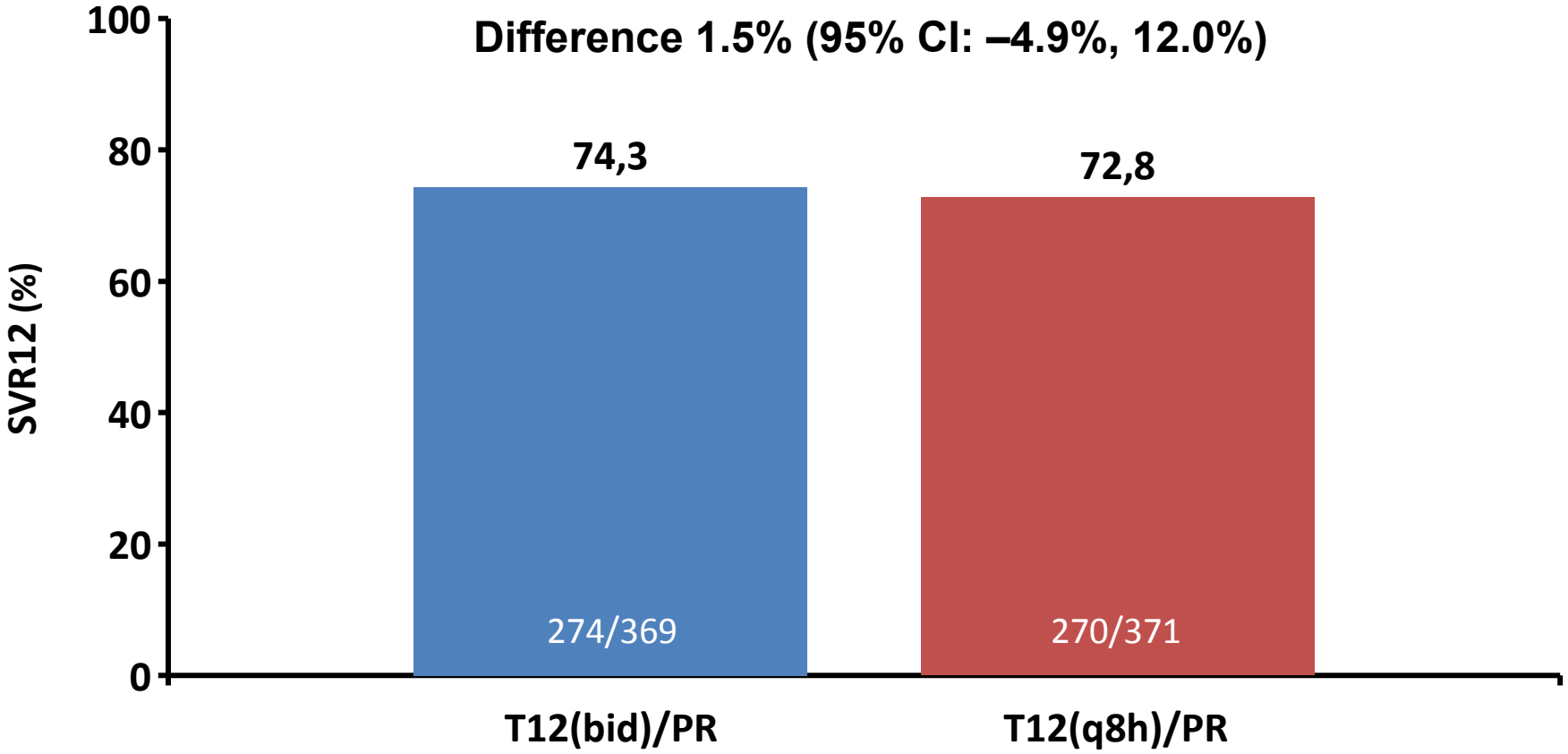


Foster GR, et al. J Hepatol 2011;54(Suppl. 1):S3

Telaprevir in 2014

- We can identify some patients who will do well
- We can use ‘patient friendly’ regimes

OPTIMIZE: telaprevir bid was non-inferior to q8h in terms of SVR



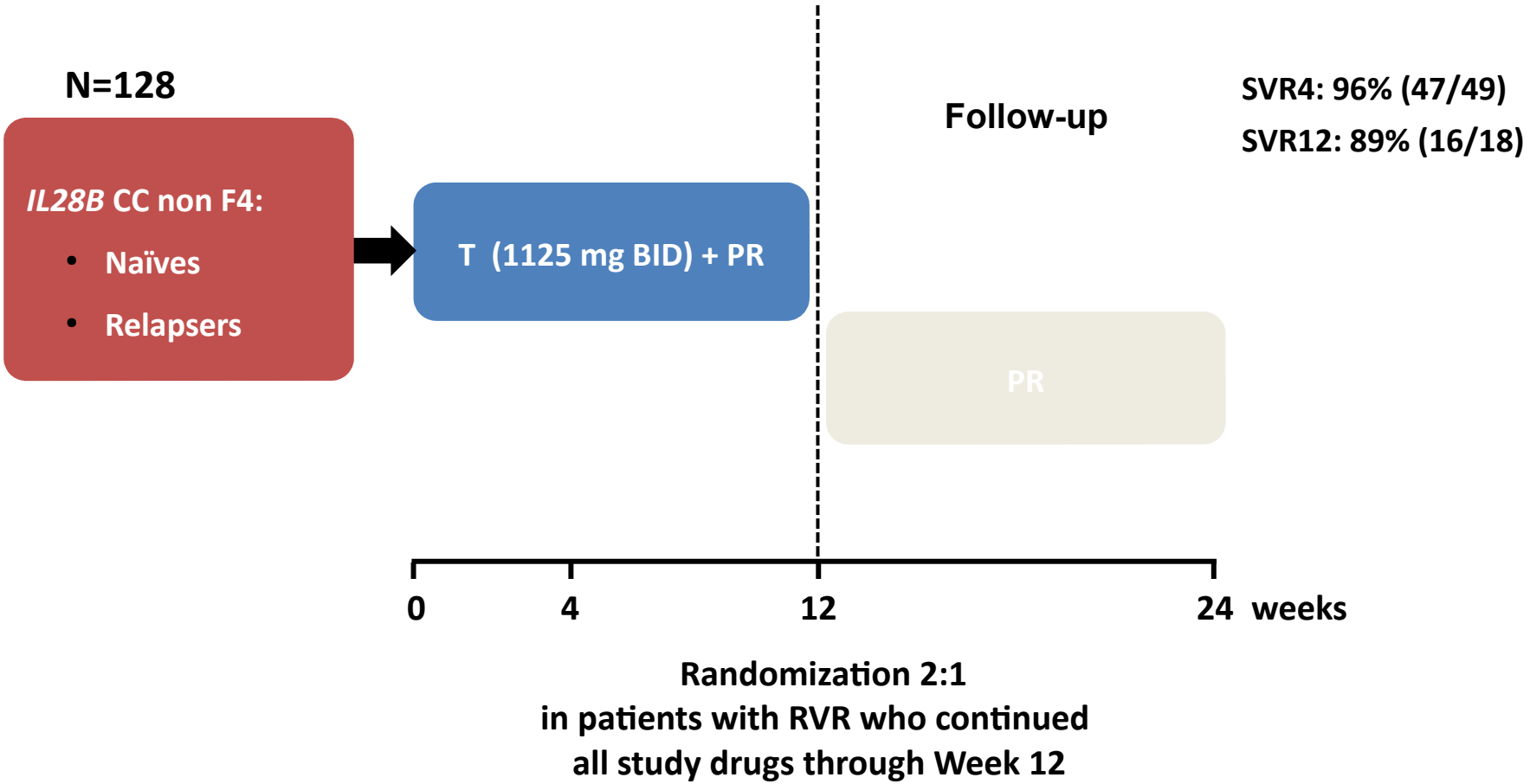
ITT analysis
CI: confidence interval

Buti M, et al. AASLD 2012:LB-8

Telaprevir in 2014

- 24 weeks therapy works quite well
- In ‘easy to cure’ patients is 12 weeks enough?

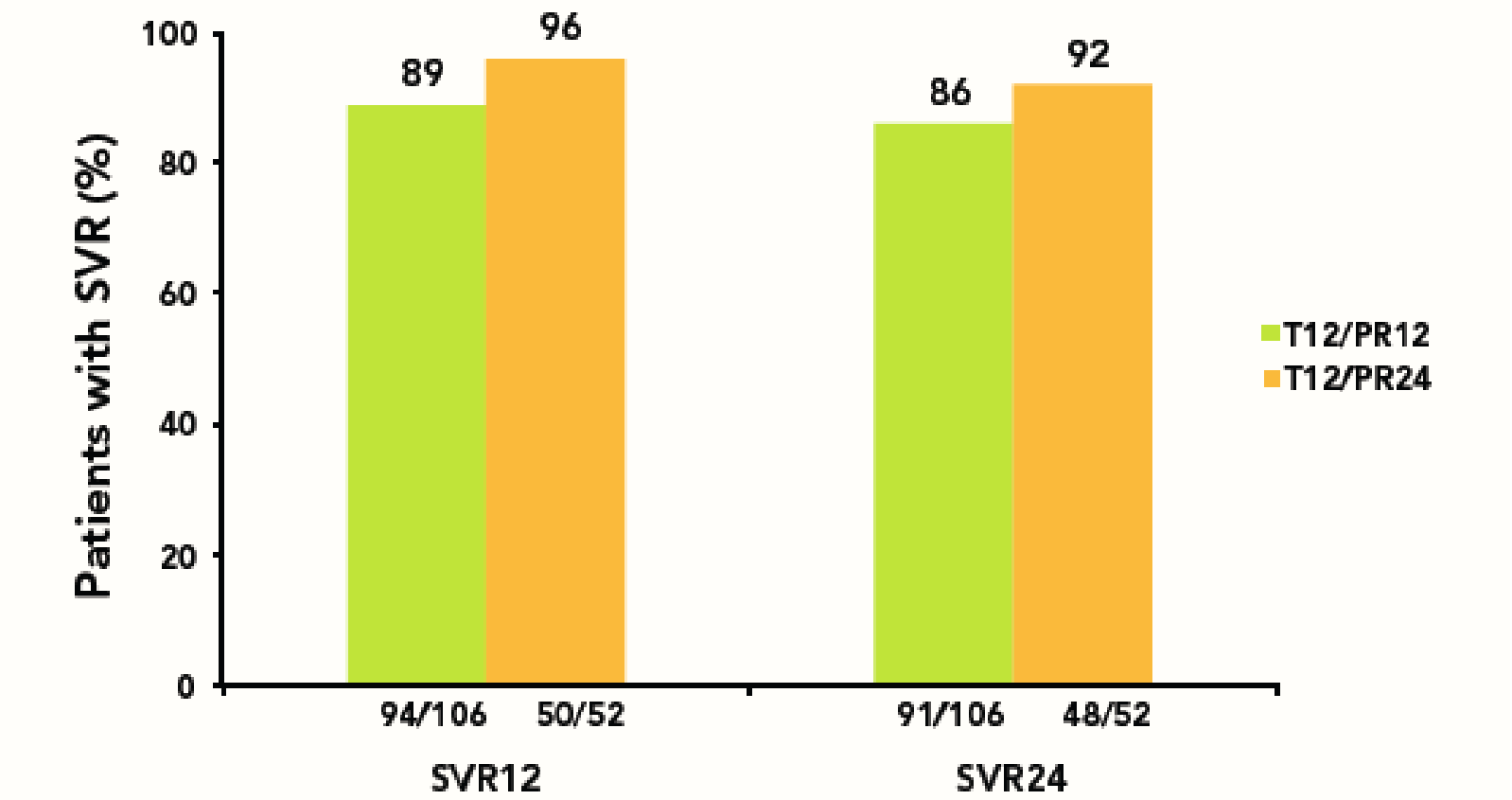
CONCISE study



*128 patients were followed for 16 or more weeks;
66% (N=85) were randomized at Week 12, respectively: 57 in T12PR12 and 28 in T12PR24 arms
RVR: Week 4 HCV RNA< 25 IU/mL, target not detected.
PR: Peg-IFN alfa-2a (180 µg/week) and ribavirin (1000–1200 mg/day)

Nelson DR et al. EASL 2013; Abstract 881

CONCISE study



Telaprevir in Mild HCV

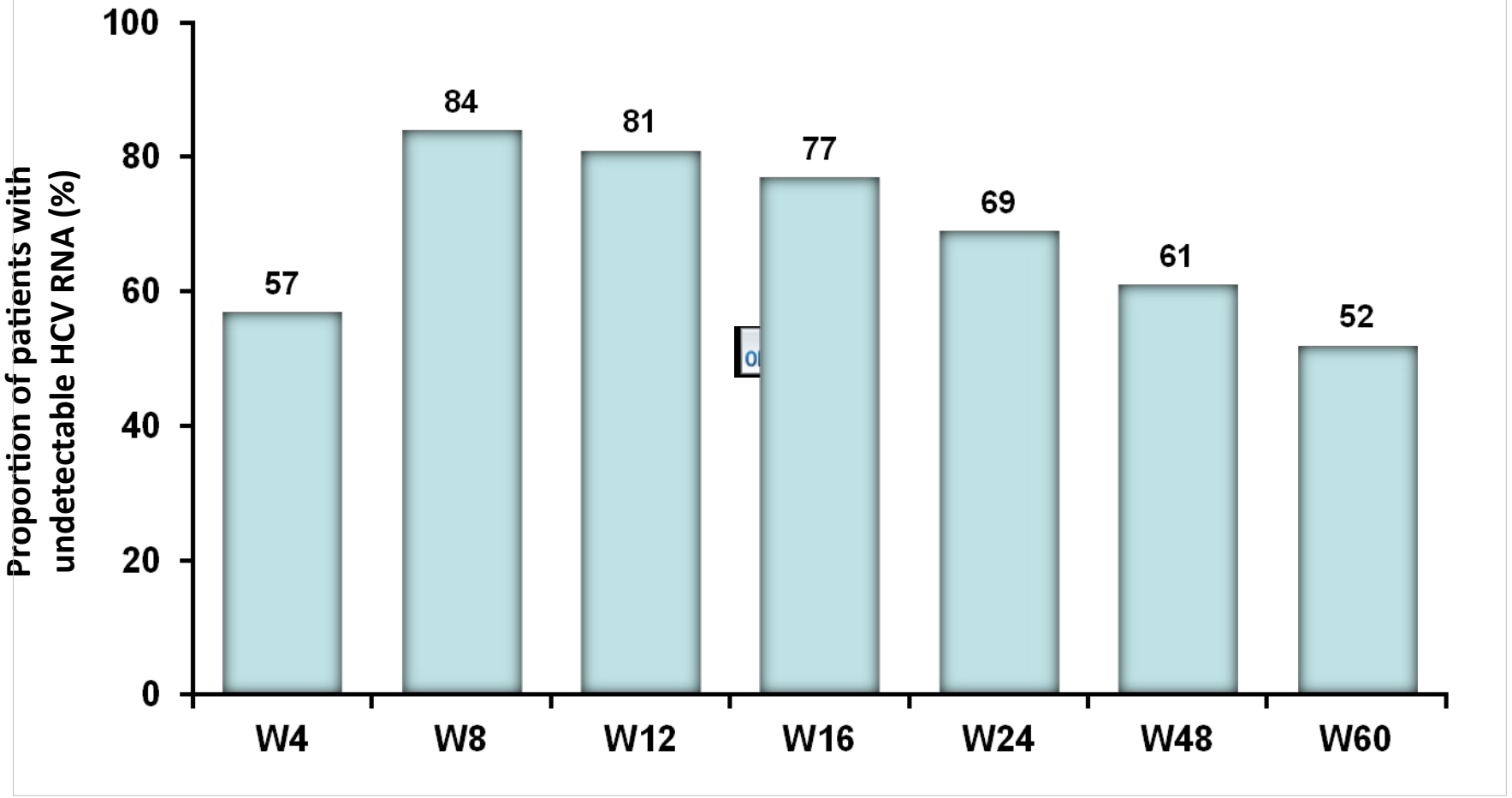
- In ‘easy to cure’ patients short course, twice daily telaprevir is acceptable (and cheap)

Telaprevir in Mild HCV

- In ‘easy to cure’ patients short course, twice daily telaprevir is acceptable (and cheap)

- What about hard to treat patients?

CUPIC: on-treatment efficacy of telaprevir in the intent-to-treat population



Treatment-experienced patients with HCV genotype 1 and compensated cirrhosis

Hézode C, et al. Unpublished data
Updated 26 September 2013

CUPIC Week 60 analysis: safety overview

Outcomes, %	TVR CUPIC N=299	BOC CUPIC N=212
Serious adverse event	53.8	44.3
Premature discontinuations due to serious adverse events	23.8	17.5
Death, n (%)	8 (2.7)	3 (1.4)
Infections (grade 3/4)	9.7	2.4
Hepatic decompensation	4.7	4.2
EPO use	56.5	56.1
Transfusion	17.7	11.8
RBV dose reduction	27.8	23.6

Hézode C, et al. Unpublished data
Updated 26 September 2013

CUPIC Week 60 analysis: safety overview

Outcomes, %	TVR CUPIC N=299	BOC CUPIC N=212
Serious adverse event	53.8	44.3
Premature discontinuations due to serious adverse events	23.8	17.5
Death, n (%)	8 (2.7)	3 (1.4)
Infections (grade 3/4)	9.7	2.4
Hepatic decompensation	4.7	4.2
EPO use	56.5	56.1
Transfusion	17.7	11.8
RBV dose reduction	27.8	23.6

Hézode C, et al. Unpublished data
Updated 26 September 2013

Adverse events in cirrhotic patients with Peg and Riba

26 centres in Spain; 568 treatment-naïve patients with cirrhosis
Treated with PR

Adverse event, n (%)	All patients (N=508)
Ascites / encephalopathy / CPT 2	59 (11.6)
Variceal hemorrhage	19 (3.74)
Development of HCC	31 (6.1)
Any adverse event	89 (17.5)
Liver-related mortality	29 (5.7)

IFN safety in advanced liver disease is poor

CPT: carnitine palmitoyltransferase; IFN: interferon

Fernández-Rodríguez CM, et al. Am J Gastroenterol 2010;105:2164–2172

Telaprevir in 2014

- For patients with mild disease – telaprevir is a highly cost effective choice

- For patients with advanced disease – telaprevir is not ideal

The Telaprevir Dilemma
For Patients with Mild Disease

- From a PUBLIC perspective –

Telaprevir is a good choice

- From a PATIENT perspective –

Telaprevir is a sub-optimal choice

The Telaprevir Dilemma

- ‘For your tomorrows we gave our todays’

The Telaprevir Dilemma

- ‘For your tomorrows we gave our todays’

- In resource limited health care settings will patients with early disease accept adverse events to allow others to access better drugs?

- Should we divert money from other therapies to fund optimal regimes?

Summary

- Telaprevir is an inexpensive drug with good efficacy in patients with mild disease
- Early futility rules and short duration therapy allow personalised, cost-effective therapy
- For patients with more advanced disease drugs with fewer side effects may be preferable