

# When to treat HIV/HCV co-infection

Graham R Foster

Professor of Hepatology

QMUL

# When to treat HIV/HCV

## Twist or Stick?

- I have received consultancy fees from:-
- Roche, Gilead, AbbVie, BI, BMS, Idenix, Regulus, Novartis, Chughai, Merck, Janssen

# Twist or Stick?

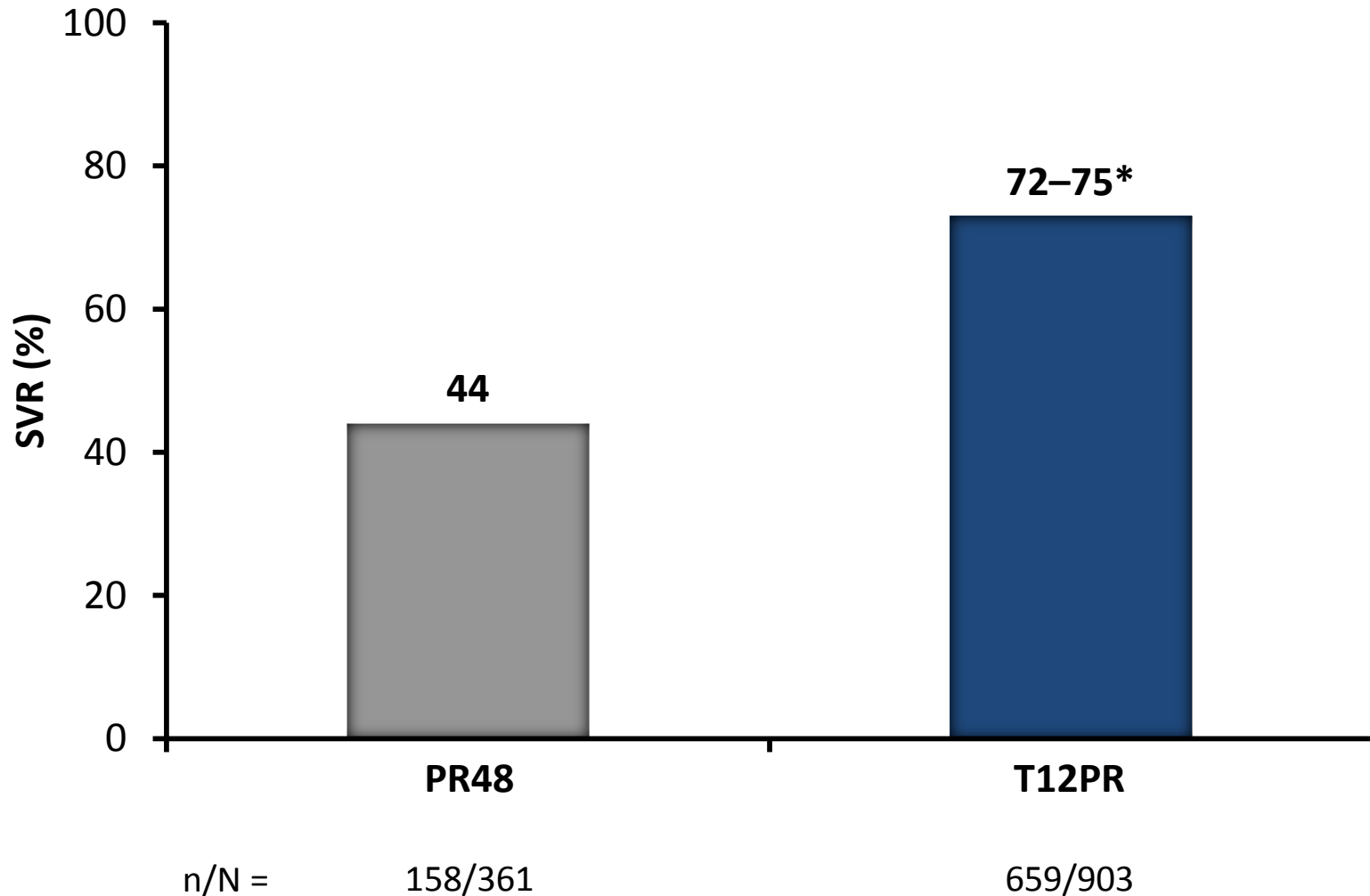
- Today's drugs
- What is emerging
- HIV studies
- My opinion

# Twist or Stick?

- Today's drugs
- What is emerging
- HIV studies
- My opinion

# Genotype 1 – Good Drugs on the market

## PegIFN/Ribavirin and Protease inhibitors



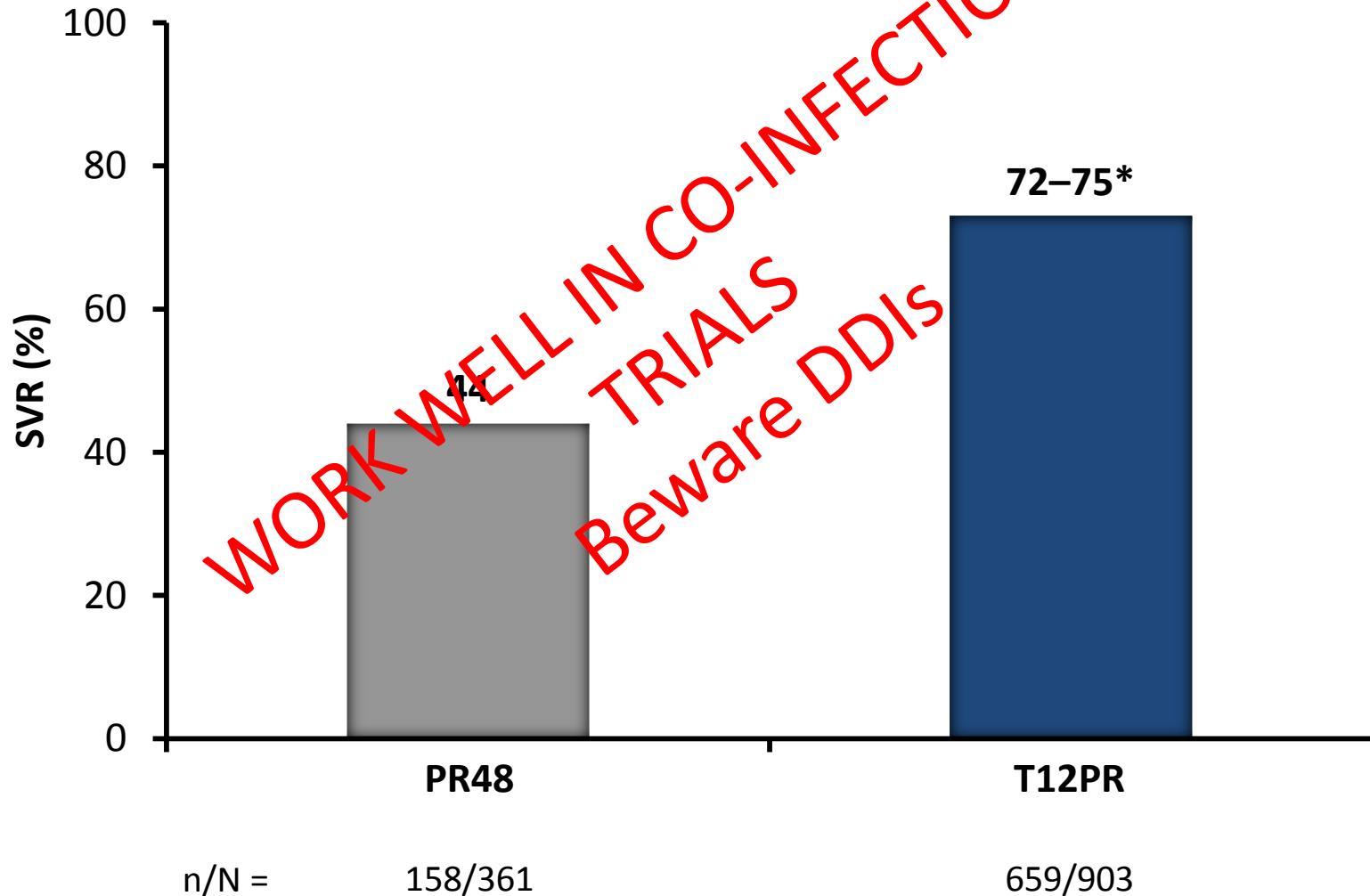
Sherman KE, et al. Hepatology 2010;52(Suppl.):401A

Jacobson IM, et al. N Engl J Med 2011;364:2405-16; Sherman KE, et al. CROI 2011. Abstract 957

\*p<0.001 vs PR48 in ADVANCE (75% versus 44%)

# Genotype 1 – Good Drugs on the market

## PegIFN/Ribavirin and Protease inhibitors

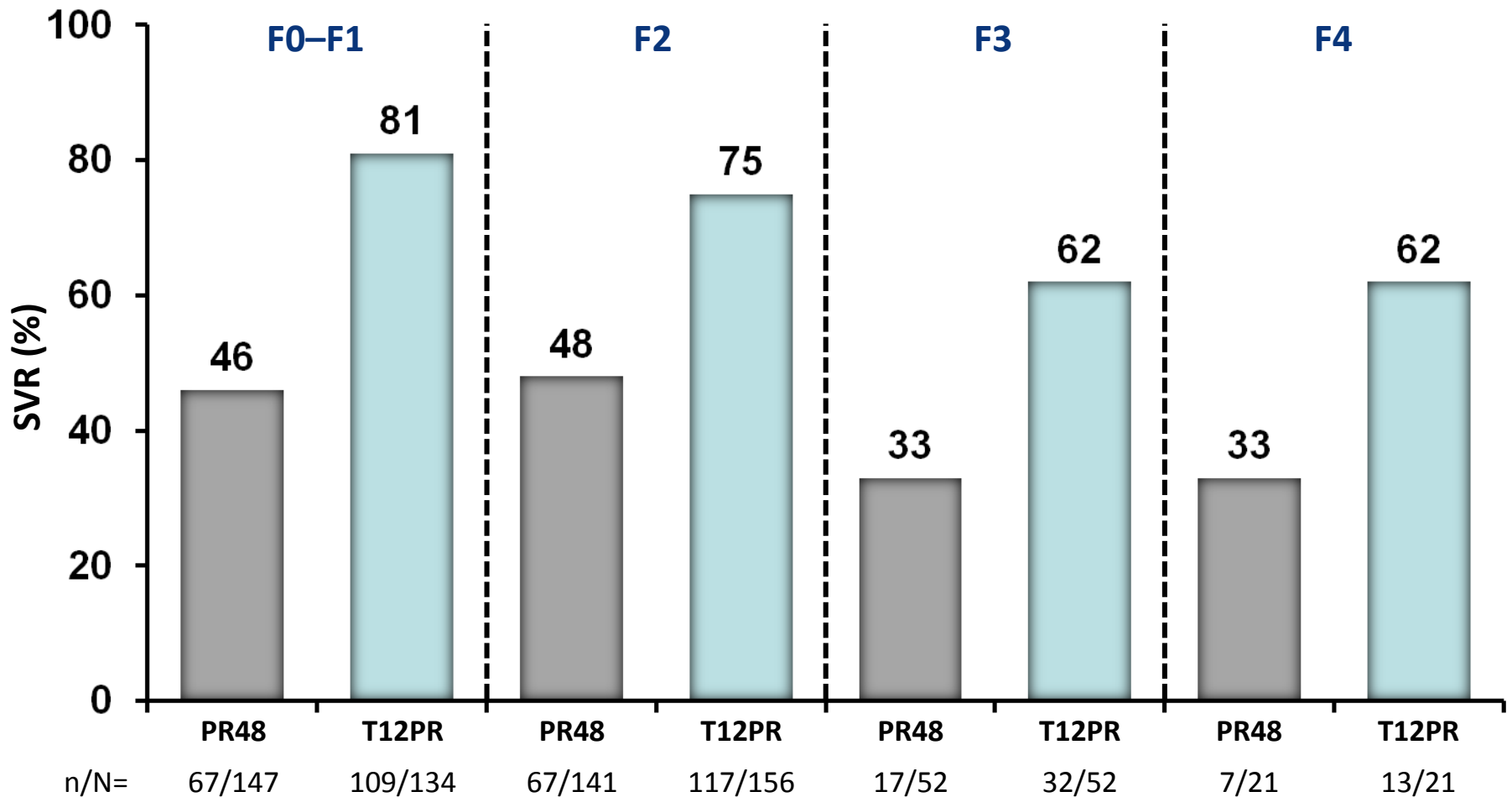


Sherman KE, et al. Hepatology 2010;52(Suppl.):401A

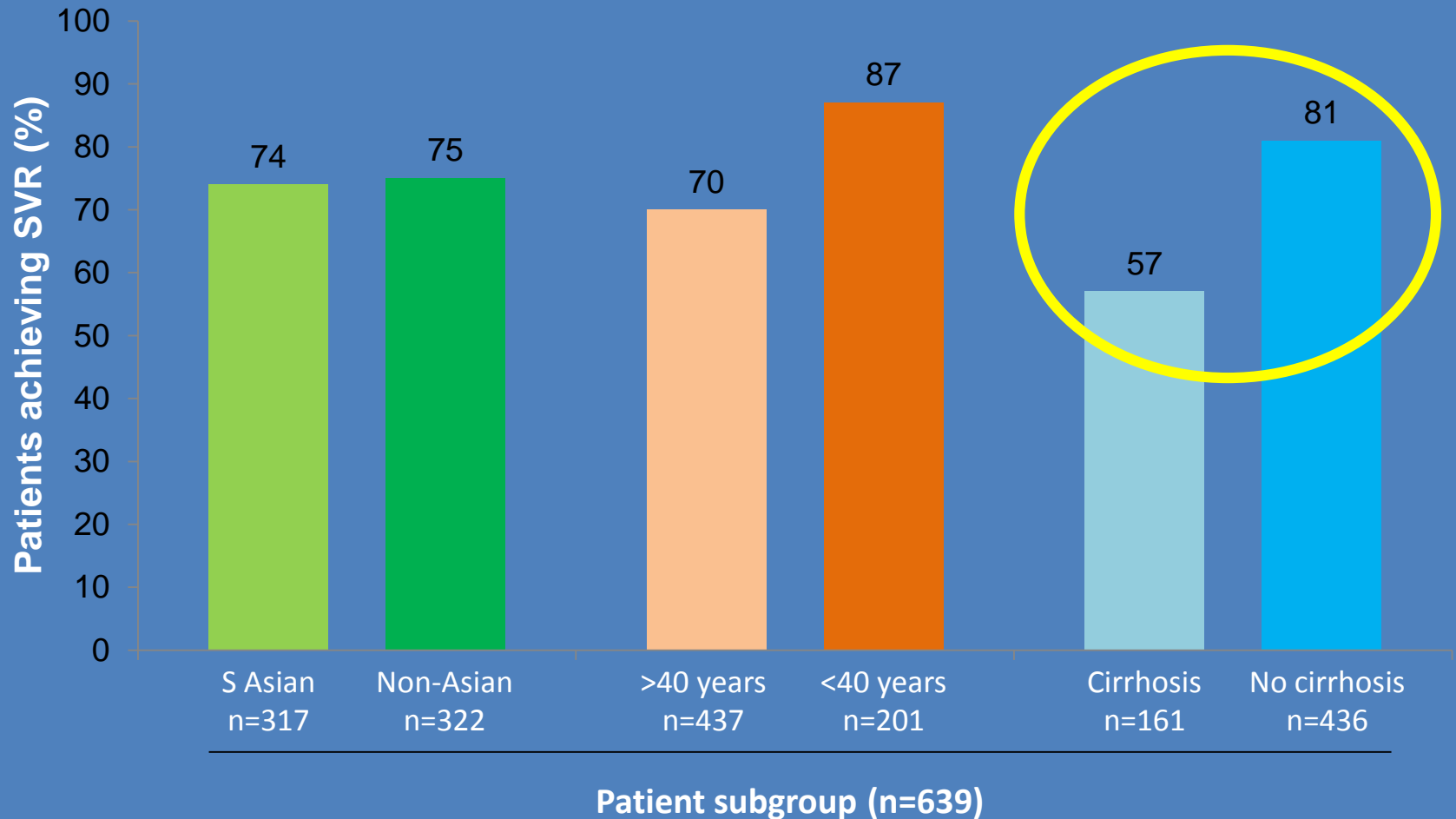
Jacobson IM, et al. N Engl J Med 2011;364:2405-16; Sherman KE, et al. CROI 2011. Abstract 957

\*p<0.001 vs PR48 in ADVANCE (75% versus 44%)

# Telaprevir SVR rates by fibrosis stage in treatment-naïve patients



# Response of HCV G3 patient subgroups to PegIFN/RBV





# Current Drugs - not perfect

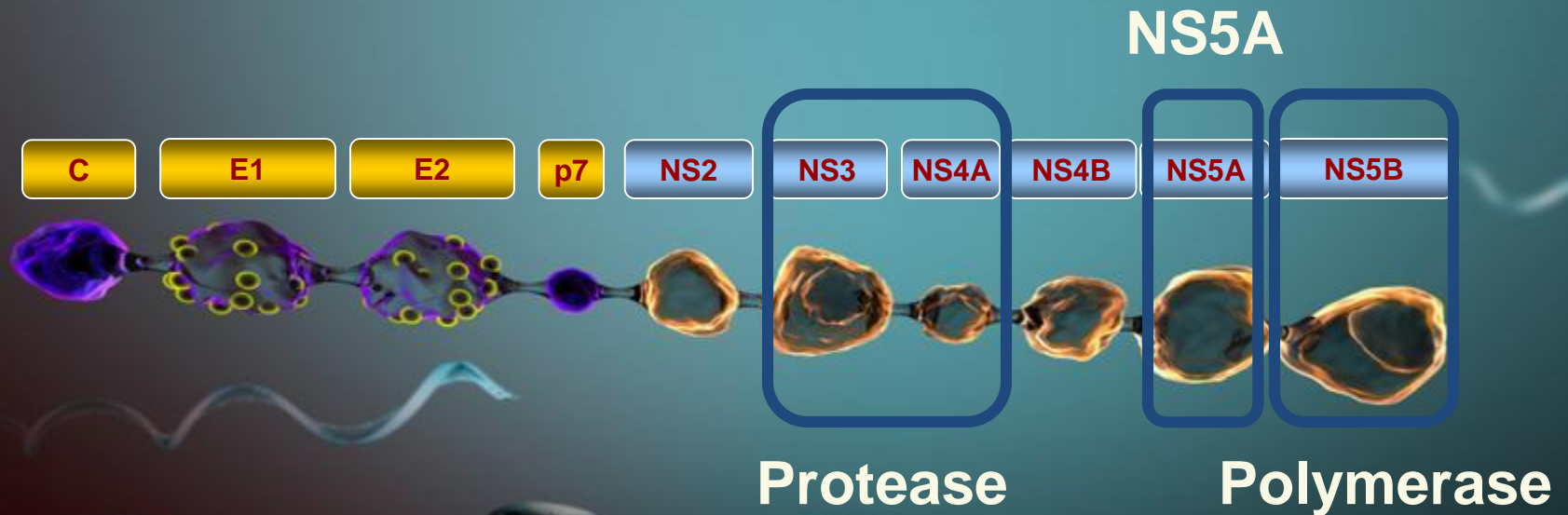
- For G1 – reasonable efficacy, high side effects
- For G2/3 – good efficacy, moderate side effects
- In cirrhosis efficacy falls, side effects rise

**DO NOT LET YOUR PATIENT GET CIRRHOSIS**

# Twist or Stick?

- Today's drugs
- **What is emerging**
- HIV studies
- My opinion

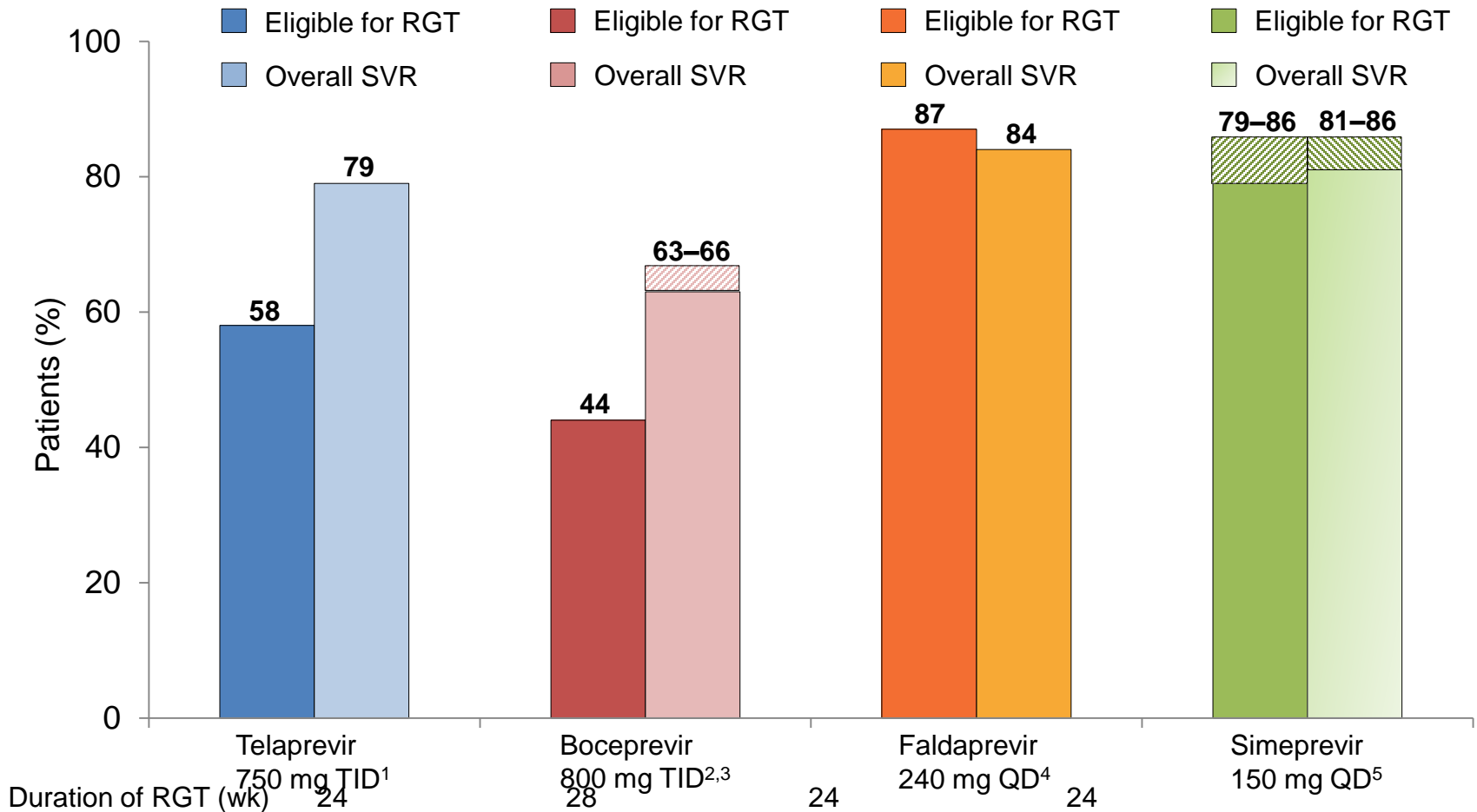
# Specific targets for HCV treatment: protease, polymerase and NS5A inhibition



# New Protease Inhibitors



# New Protease Inhibitors (With Peg + Riba)



Results are for separate trials for each compound, not head-to-head studies, in treatment-naïve patients also receiving PegIFN/RBV

Hatched regions indicate ranges of results

QD, once daily; RGT, response-guided therapy; SVR, sustained virological response;  
TID, three times daily

1. Incivo EU SmPC 2011; 2. Victrelis EU SmPC 2011;
3. Poordad F, et al. N Engl J Med 2011;364:1195-1206;
4. Sulkowski MS, et al. Manuscript in preparation;
5. Fried M, et al. AASLD 2011. Abstract LB-5

# New protease inhibitors



Restricted to the US viral strains

Early data in HIV encouraging

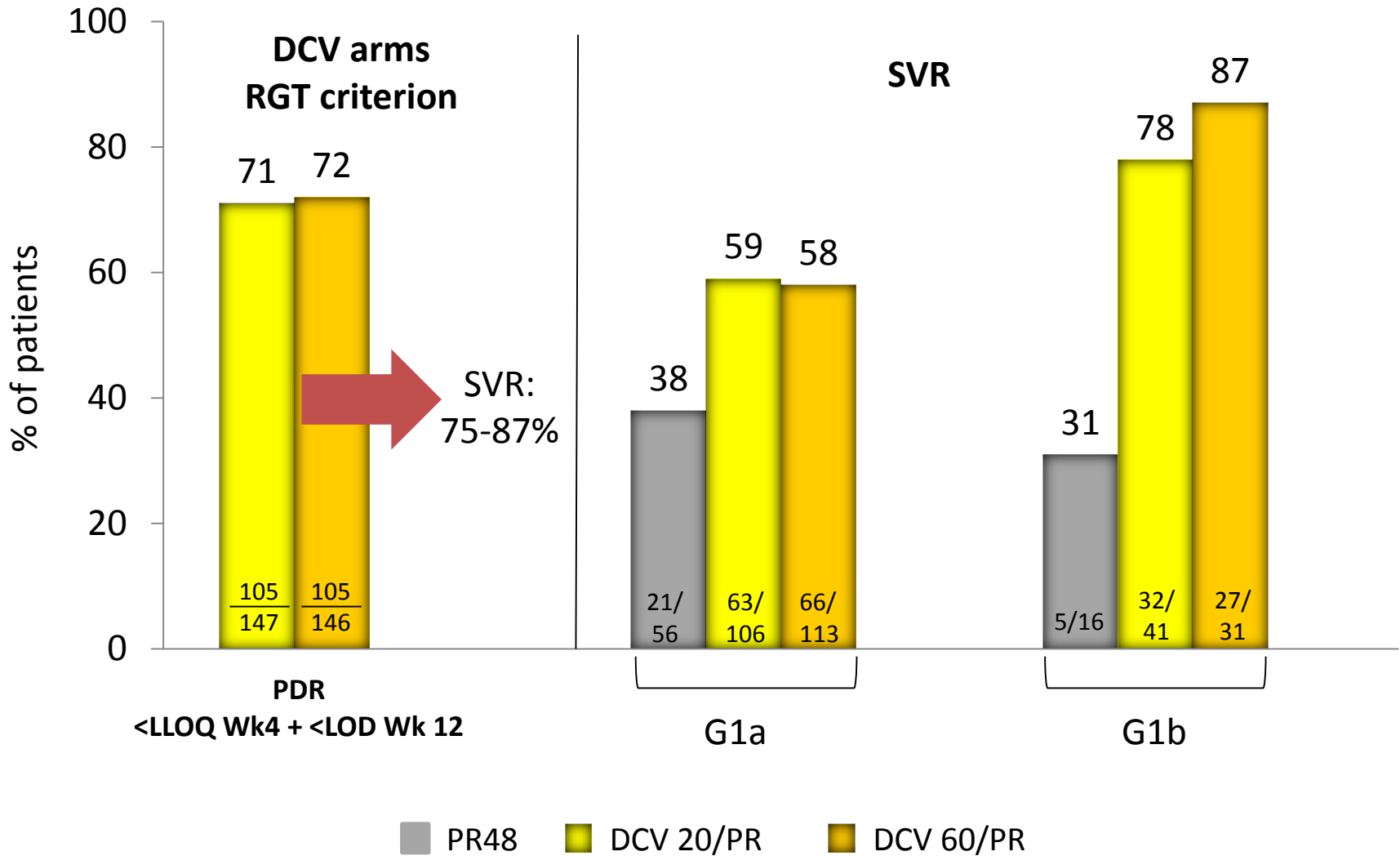
Fewer DDIs

(Not as good as they pretend they are)

# NS5A Inhibitors



# Daclatasvir + PR





# NS5A Inhibitors



Quirky

Large variation in efficacy

Good to work with

# NS5B – Non Nucleotides



# NS5B – Non Nucleotides



Very unpredictable

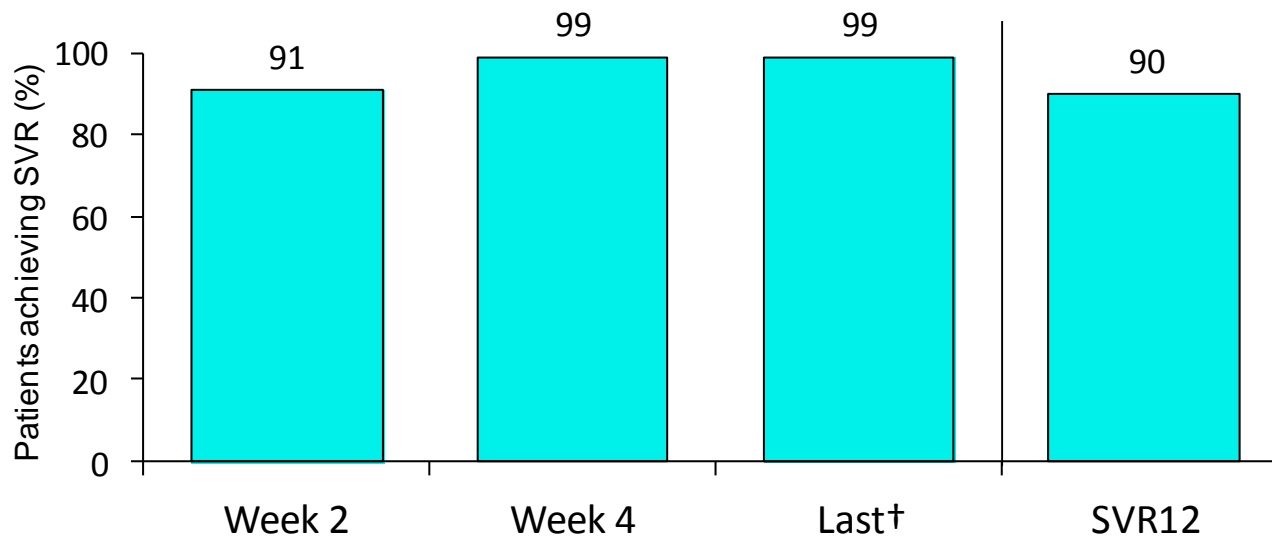
Generally G1 specific

# Nucleotides



# Sofosbuvir with PEG-IFN + RBV

- NEUTRINO Phase III trial
  - Sofosbuvir plus PEG-IFN + RBV\* for 12 weeks
  - Treatment naïve, GT1 (89%), 4, 5 or 6 (N=327)
    - 17% had compensated cirrhosis
  - Primary endpoint: SVR12



\*Dose administered according to body weight

†Last observed measurement

# Nucleotides



Fast  
Effective  
Cures all strains  
Side effect free

(Too good to be true)

# What about interferon free?

- Interferon is horrid - can we go to interferon free?

# Playing Tag (I)



+



BI

+



BMS

Protease Inhibitor + Non – Nuc/NS5A



# PI +

BI 201335 + BI207127 ± R  
(SOUND-C2)

- **Non cirrhotics TN**
- 16-40 week
- SVR12 (with RBV):
  - G1a: 38-47%
  - G1b: 63-83%

SVR12 (with RBV):  
Daclatasvir + Asunaprevir  
(AI-447-017)

- **G1b Null R and IFN ineligible/intolerant**
- **non cirrhotic, japanese**
- 24W
- SVR24:
  - 91% in Null R (N=21)
  - 64% in IFN inel/intol (N=22)

# PI +

## BI 201335 + BI207127 ± R (SOUND-C2)

- **Non cirrhotics TN**
- 16-40 week
- SVR12 (with RBV):
  - G1a: 38-47%
  - **G1b: 63-83%**

## SVR12 (with RBV): Daclatasvir + Asunaprevir (AI-447-017)

- **G1b Null R and IFN ineligible/intolerant**
- **non cirrhotic, japanese**
- 24W
- SVR24:
  - 91% in Null R (N=21)
  - 64% in IFN inel/intol (N=22)

# PI +

## BI 201335 + BI207127 ± R (SOUND-C2)

- **Non cirrhotics TN**
- 16-40 week
- SVR12 (with RBV):
  - G1a: 38-47%
  - G1b: 63-83%

## SVR12 (with RBV): Daclatasvir + Asunaprevir (AI-447-017)

- **G1b Null R and IFN ineligible/intolerant**
- **non cirrhotic, japanese**
- 24W
- SVR24:
  - 91% in Null R (N=21)
  - 64% in IFN inel/intol (N=22)

# Two drugs

- Great for G1b
- Lots of combinations emerging
- May be very cost effective

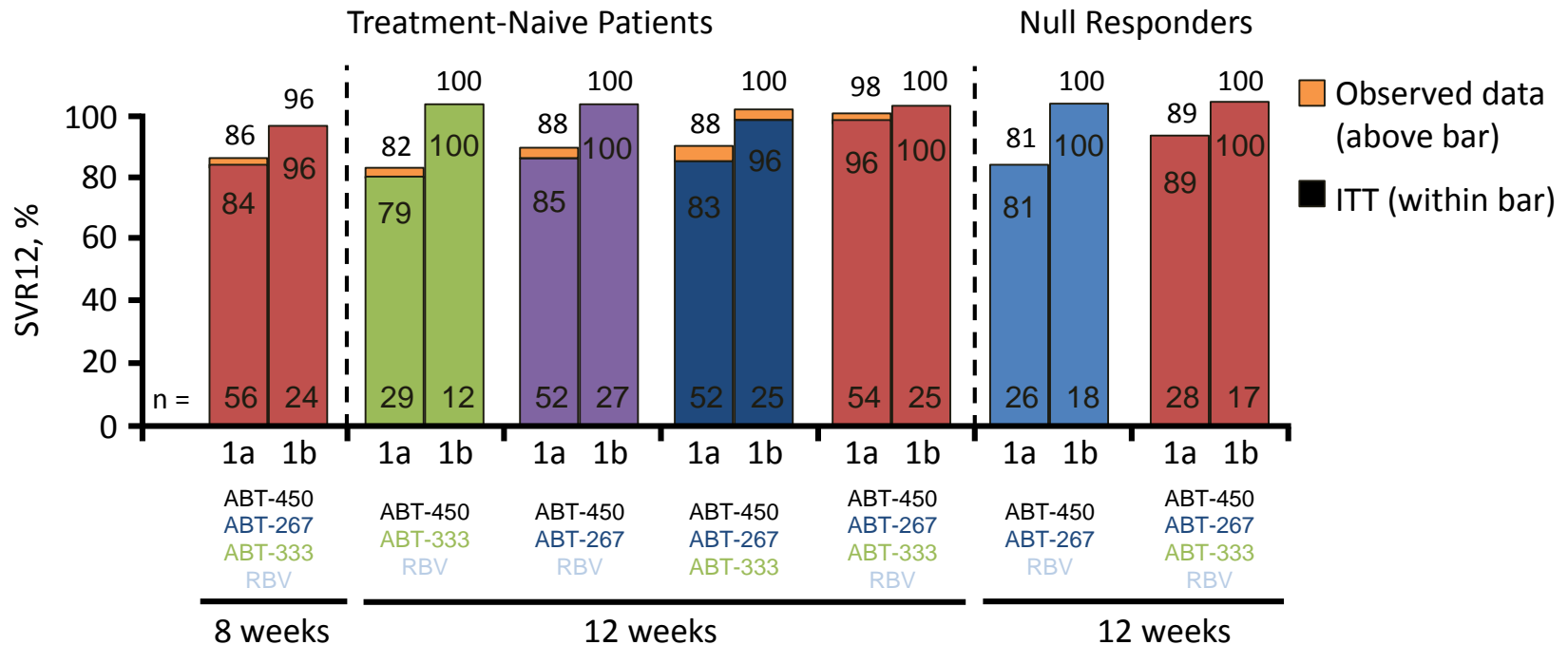
# Two drugs (PI + X) is good

- But not good enough – send in the boys!



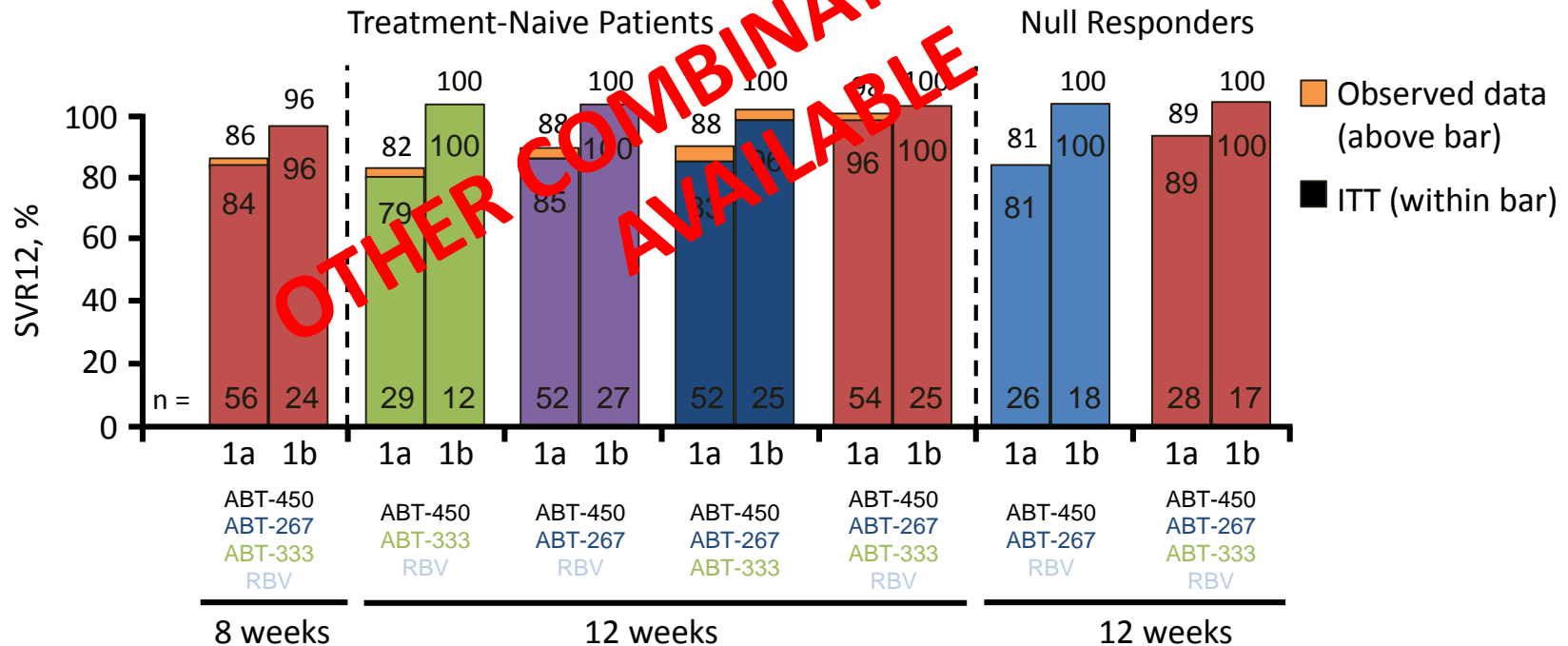
# AVIATOR: SVR12 Rates With ABT-450/RTV, ABT-267, ABT-333, and RBV

- SVR12 rates higher in pts with HCV GT1b, but also high in pts with HCV GT1a
  - 12-wk regimen with all 3 DAAs + RBV produced highest SVR12 rates
- No drug-related SAEs reported; 2 pts discontinued tx due to drug-related AEs



# AVIATOR: SVR12 Rates With ABT-450/RTV, ABT-267, ABT-333, and RBV

- SVR12 rates higher in pts with HCV GT1b, but also high in pts with HCV GT1a
  - 12-wk regimen with all 3 DAAs + RBV produced highest SVR12 rates
- No drug-related SAEs reported; 2 pts discontinued tx due to drug-related AEs



# What about the alternatives?



Sofosbuvir + Ribavirin 24 weeks

Cures 68% of tough patients

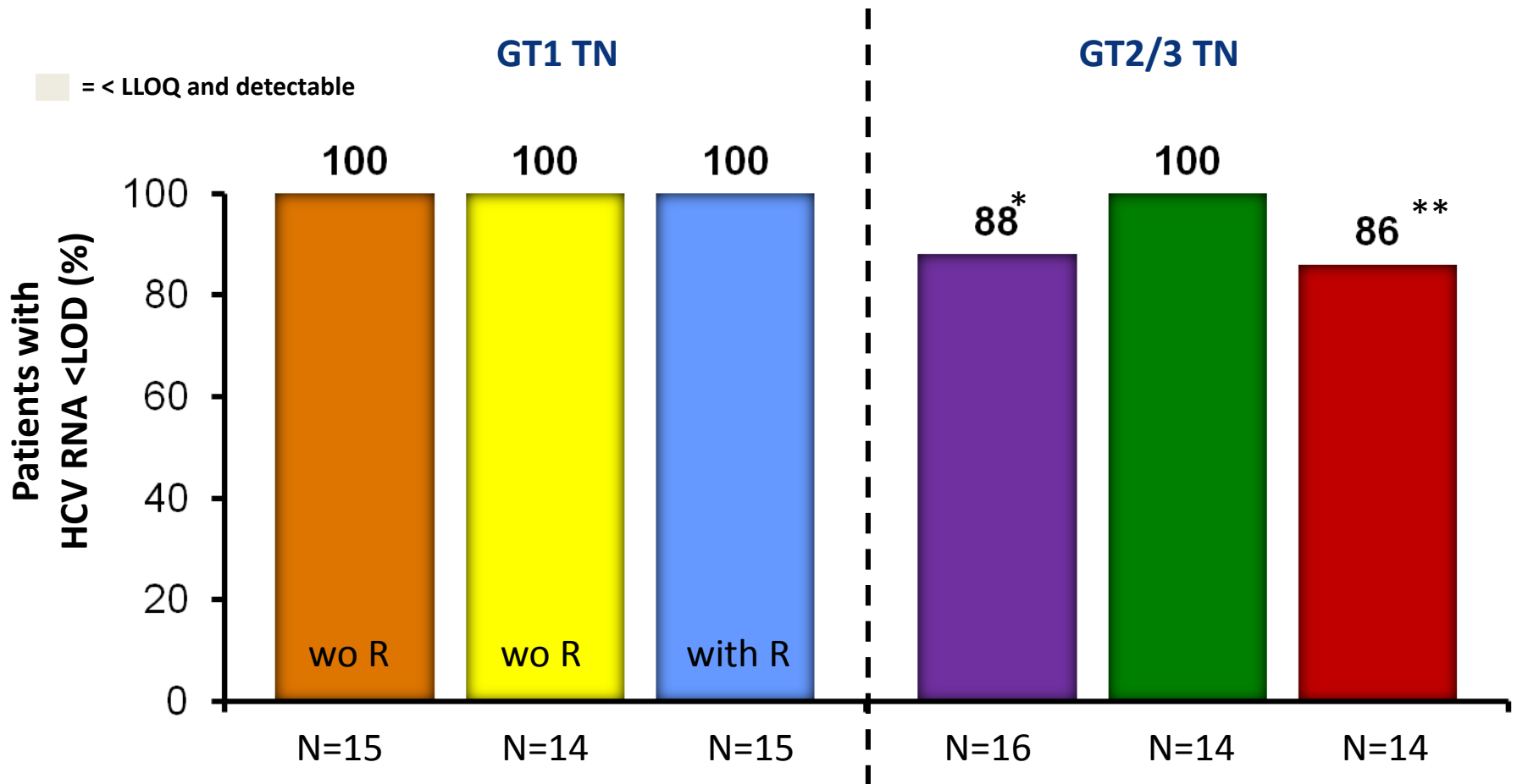
(Kottilil – JAMA 2013)



# Does Superman need a friend



# GS-7977+DCV for 24 weeks)



\*1 patient required addition of peg-IFN/RBV, 1 patient with relapse at Week 4

\*\*2 patients lost to follow-up (following Week 12 and 24 visits)

# Sofosbuvir +

- Sofosbuvir + 'anything potent' looks wonderful
- Sofosbuvir + Ledipasvir (NS5A) = ~100%
- Sofosbuvir + Simeprevir (NS3) = ~100%

# G2

## -Current Therapy

- Interferon therapy for G2 is over
- FISSION trial – SVR >90% for Sofos+Ribavirin  
(Lawitz NEJM 2013)
- PHOTON trial (HIV co-infected) – SVR 81%

# Genotype 3

G3 (NAÏVE) IFN Intolerant		G3 12 WEEKS		G3 16 WEEKS	
Non Cirrhosis	Cirrhosis	Non Cirrhosis	Cirrhosis	Non Cirrhosis	Cirrhosis
68%	21%	37%	19%	63%	61%

# IFN Intolerant and IFN treated G3

G3 (NAÏVE)		G3 12 WEEKS		G3 16 WEEKS	
Non Cirrhosis	Cirrhosis	Non Cirrhosis	Cirrhosis	Non Cirrhosis	Cirrhosis
68%	21%	<b>37%</b>	19%	<b>63%</b>	61%

# IFN Intolerant and IFN treated G2 and G3

G3 (NAÏVE)		G3 12 WEEKS		G3 16 WEEKS	
Non Cirrhosis	Cirrhosis	Non Cirrhosis	Cirrhosis	Non Cirrhosis	Cirrhosis
68%	21%	37%	19%	63%	61%

# Genotype 3

- PHOTON trial (G3 + HIV)
- Sofosbuvir + Ribavirin – SVR = 67% (N=42)
- Breaking news suggests 24 weeks of Sofosbuvir+ Ribavirin may cure G3



# Nucleotide struggles with G3



We are nearly there...

# We are nearly there...

## Genotype 1

- Powerful drugs with Peg+ Riba (PIs, Nucs)
- Multiple PI drug regimes without Peg  
G1b = PI + 1, G1a = PI + 2 (Abbott, Nuc+NS5A)
- Sofosbuvir + AN Other – almost perfect!

# We are nearly there....

## Genotype 2

- Nuc + Ribavirin – Game over

## Genotype 3

- Struggling
- We need a partner for the nuc

# Twist or Stick?

- Today's drugs
- What is emerging
- **HIV studies**
- My opinion

# So What About Co-Infection

- Too little data to know!
- Trials for some combinations are under way but there is inadequate data to comment
- Early data suggests excellent results
- So lets speculate.....

# Co-infection Crystal Ball

## G1

- IFN + regimes will work  
(Drug- drug interactions/side-effects)
- IFN Free regimes will work very well  
(Much better tolerated)

# Co-infection Crystal Ball

G2

- New regimes will be spectacular



# Co-infection Crystal Ball

G2

- New regimes will be spectacular

G3

- New regimes will be pants

# Twist or Stick?

- Today's drugs
- What is emerging
- HIV studies
- **My opinion**

# Co-Infection

## What do I do

- All patients with cirrhosis who are 'edgy' but treatable – offer therapy
- For G1 'peri-transplant' BEG for all oral combo
- For G1 early disease - wait

# Co-Infection

## What do I do

- G2 mild – wait
- G3 – Try current therapy

# Co-Infection

## A word to the wise



# Co-Infection

## A word to the wise

- There is no money (there really isn't)
- The days of protection for HIV are gone
- The new drugs may be available but not funded for early, treatment naive patients

# Co-Infection

## A word to the wise

- There is no money (there really isn't)
- The days of protection for HIV are gone
- The new drugs may be available but not funded for early, treatment naive patients
- I tell my patients you may have to wait 5 years

# New Therapies for HCV/HIV co-infection

- The superheroes are in play
- The optimal combinations are emerging
- The costs remain to be seen



# The Future

- Oral combination therapy for everyone is very close
- It will be here in 5 years

# The Future

- Oral combination therapy for everyone is very close
- It will be here in 5 years
- For NOW
- Sick patients need Peg+Riba+/-PI
- Mild patients should wait