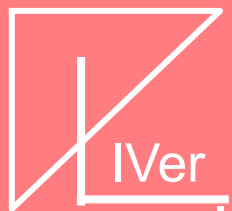
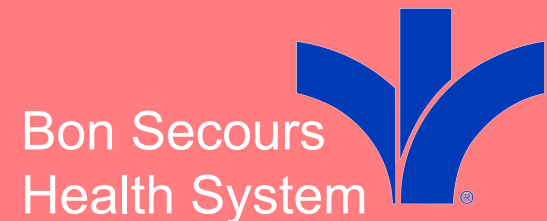


F1-F2 PATIENTS: TREAT OR WAIT CONTINUE TO WAIT!

Mitchell L Shiffman, MD
Liver Institute of Virginia
Bon Secours Health System
Richmond and Newport News, VA, USA



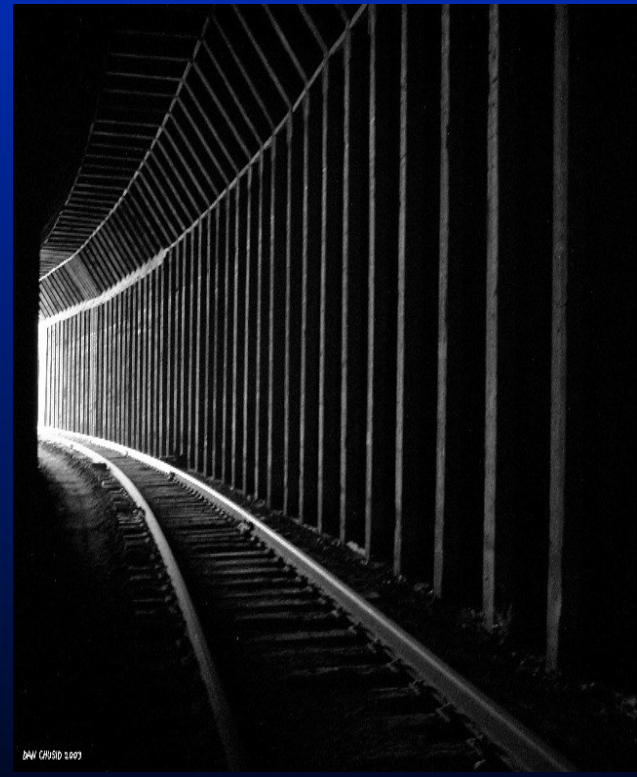
Liver Institute of Virginia
Education, Research and Treatment
for Patients with Liver Disease



PHC 2013

F1-F2 TREAT OR WAIT

- At PHC 2013 there was a light at the end of the tunnel with the promise of new and more potent DAAs for HCV
- In the past year we have moved forward with these agents in the USA
- But in most of the world these drugs are still a light around the corner



HCV AND MILD FIBROSIS

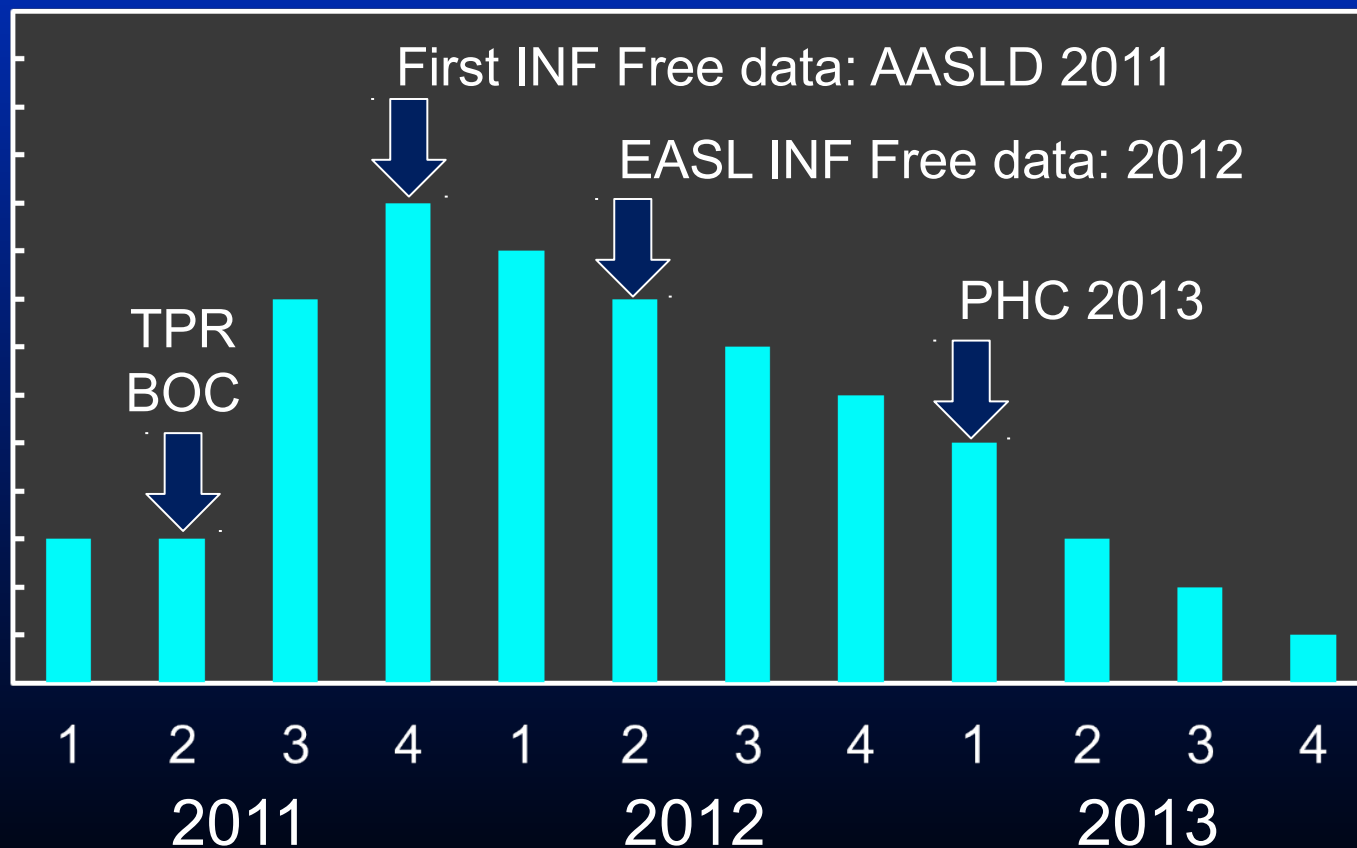
REASONS TO TREAT IN 2013

- Telapreivr or Boceprevir triple therapy achieved pretty good SVR rates or GT1
- Peginterferon and ribavirin achieved pretty good SVR rates for patients with other genotypes
- Mild fibrosis has higher SVR rates regardless of treatment
- IL28B genotype CC and mild fibrosis can be treated for only 12 weeks with PI triple therapy
- Treatment is better tolerated in patients with mild fibrosis
- SIM and SOF, when available, will still require PEGINF for most patients



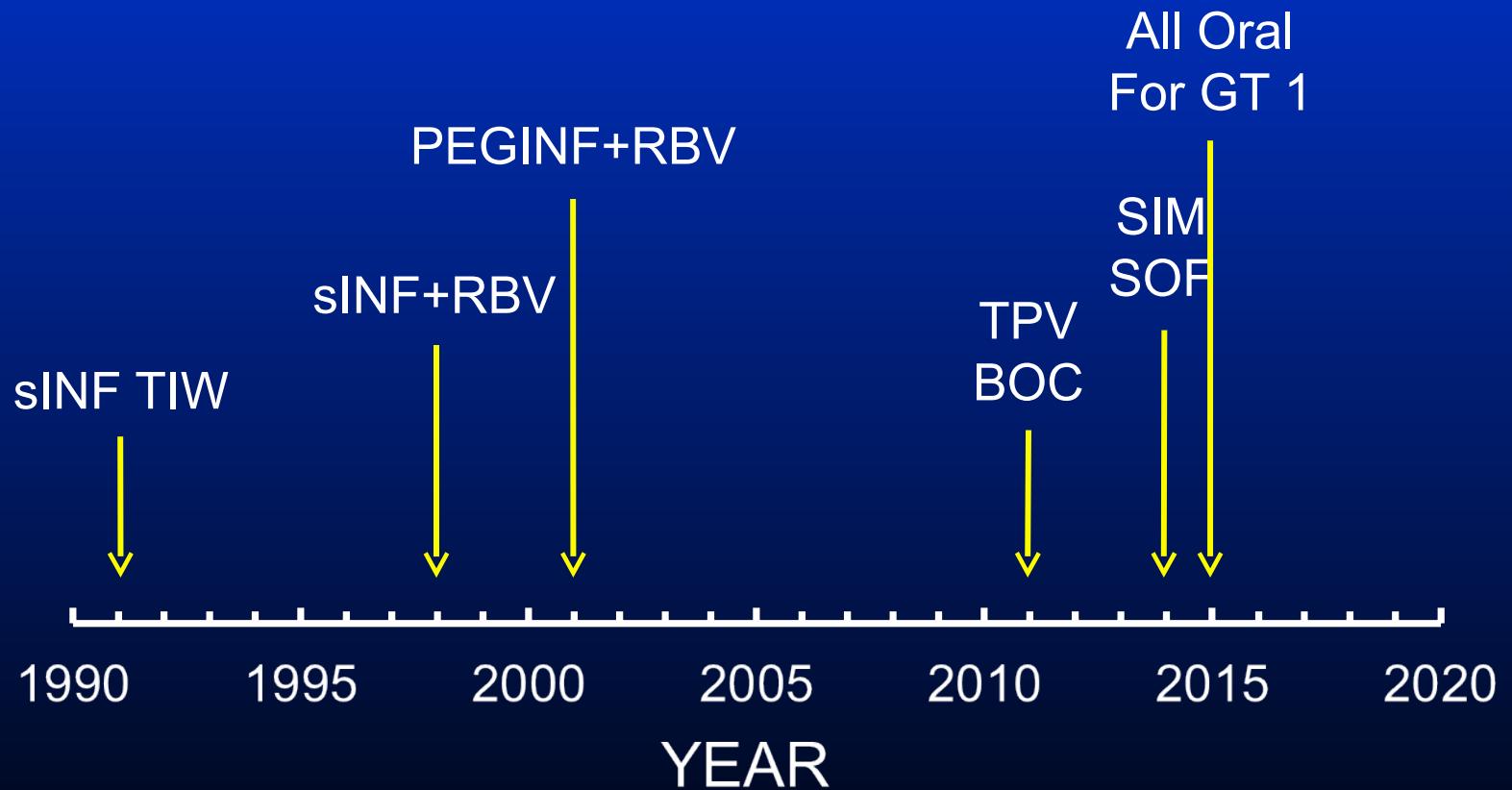
THE PRECEPTION OF INF FREE THERAPY IMPACT ON TREATMENT

PATIENTS RECEIVING
HCV TREATMENT



TREATMENT OF HCV

THE PACE HAS ACCELERATED



TREATMENT OF HCV IN 2014

ANTI-VIRAL AGENTS

Genotype	Agents	Wks of Tx	INF	SVR	Use in USA
1	PEGINF+RBV	48	Yes	40	No
	Telaprevir	24-48 RGT		75	No
	Boceprevir	28-48 RGT		70	No
	Simeprevir	24 or 48 FD		80	Sometimes
	Sofosbuvir	12		90	Preferred
2	PEGINF+RBV	24	No	78	Preferred
	Sofosbuvir	12		95	
3	PEGINF+RBV	24	No	63	Preferred
	Sofosbuvir	24		84	
4,5,6	PEGINF+RBV	48	Yes	66	Preferred
	Sofosbuvir	12		96	

INTERFERON FREE FOR GT1 PHASE 2 STUDY RESULTS

- Phase 3 studies have been initiated or near completion with each of these combinations
- Data to be presented at EASL and AASLD 2014
- Treatment should be available in 2015

	Weeks	SVR
ABT450/r + ABT267 + ABT333 + RBV	12	99%
Sufosbuvir + Ledipasvir \pm RBV	8-12	95-100%
Faldaprovir + Deleobuvir + RBV (GT1B)	28	85%
Daclatasvir + Asunaprevir + BMS-791325	12-24	88-94%

KV Kowdley, et al. AASLD 2013.

E Gane et al. AASLD 2013.

S Zeuzem et al. N Engl J Med 2013; 369:630-639.

GT Everson, et al. AASLD 2013.



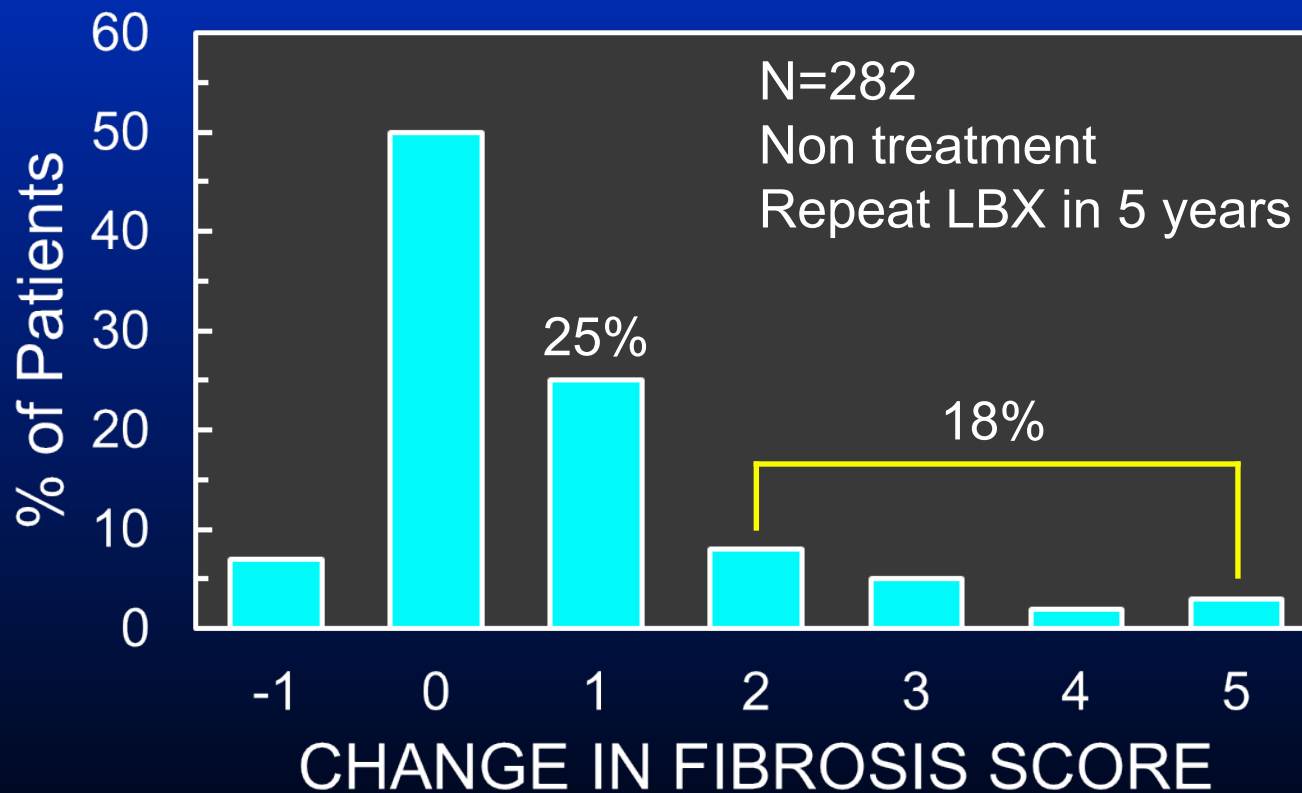
HCV AND MILD FIBROSIS

REASONS NOT TO TREAT IN 2014

- All oral anti-viral therapy is just a year away in the USA and the EU
- It takes many years for fibrosis progression to occur
- SOF and SIM still require peginterferon to optimize SVR for patients with genotype 1
- Peginterferon and ribavirin still cause side effects
- All oral therapies are highly likely to improve SVR even in patients with mild fibrosis
- Prior treatment may reduce the rate of SVR with the newer agents



FIBROSIS PROGRESSION TAKES TIME ALL ORAL IS JUST A YEAR AWAY



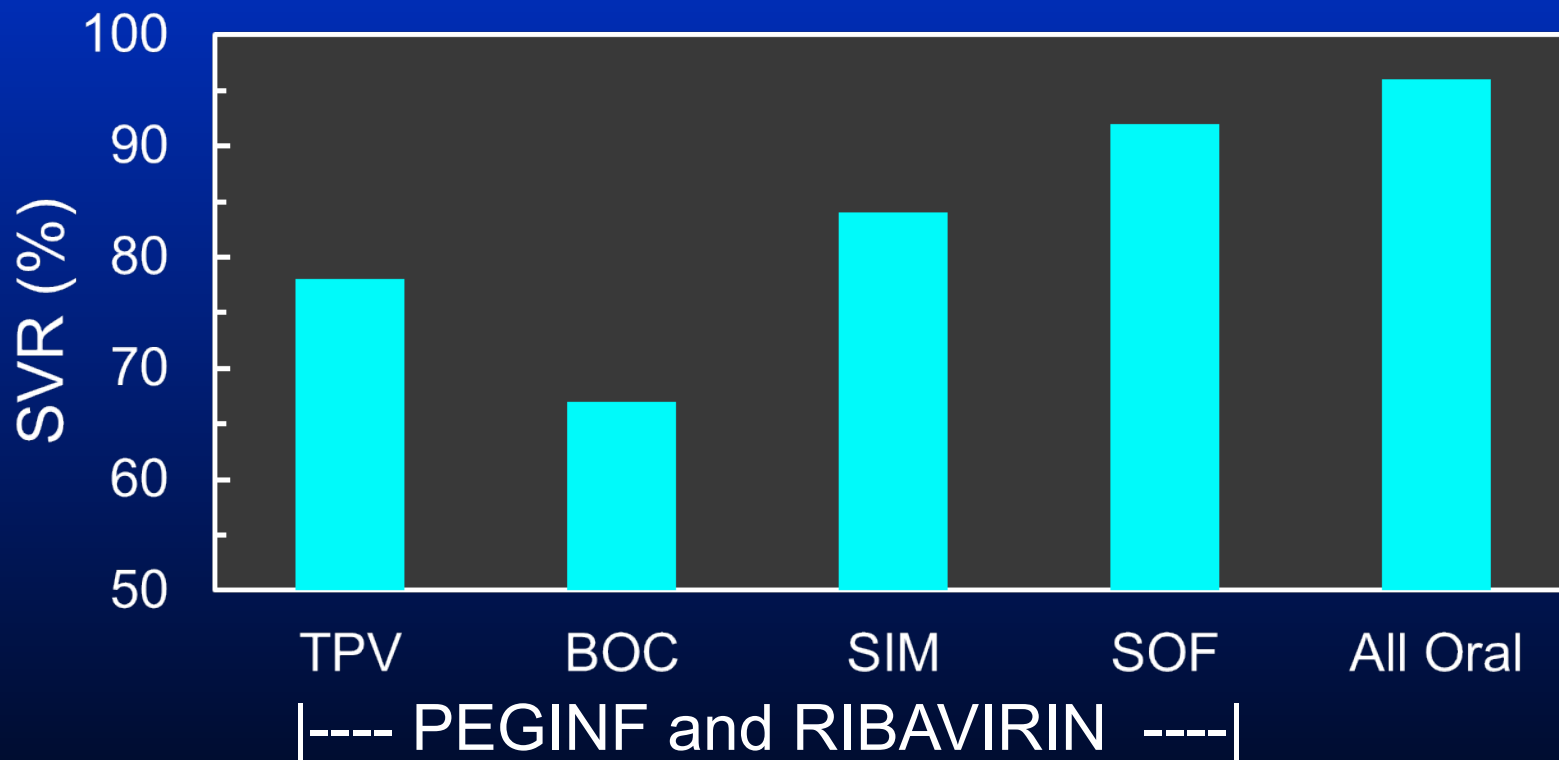
NO INTERFERON SIDE EFFECTS ALL ORAL IS JUST A YEAR AWAY

	Placebo	Sofosbuvir Ribavirin	PEGINF Ribavirin	Sofosbuvir PEGINF Ribavirin
Fatigue	24%	30%	55%	59%
Fevers	0%	4%	14%	18%
Headache	20%	30%	44%	36%
Myalgia	0%	9%	16%	14%
Irritability	1%	10%	16%	13%
Anorexia	10%	6%	12%	21%
Diarrhea	6%	12%	17%	12%
Anemia	0%	6%	12%	21%

IM Jacobson et al. N Engl J Med 2013; 368:1867-77.
E Lawitz et al. N Engl J Med 2013; 368:1878-87.



EVEN BETTER SVR RATES ALL ORAL IS JUST A YEAR AWAY



IM Jacobson et al. N Eng J Med 2011; 364:2405-2416.

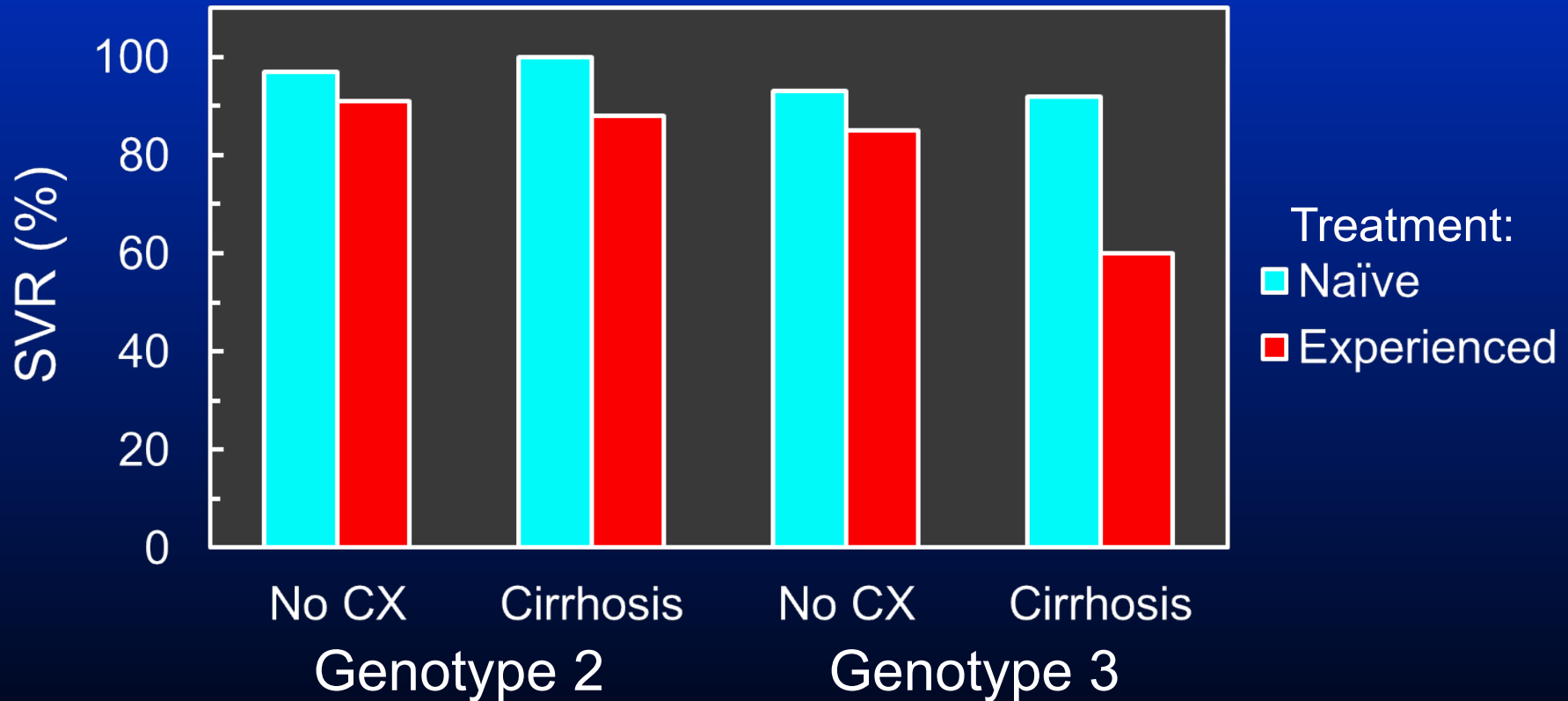
F Poordad et al. N Engl J Med 2011; 364:1195-1206

M Manns et al. EASL 2013.

E Lawitz et al. N Engl J Med 2013; 368:1878-1887



SVR LOWER WITH PRIOR NON-RESPONSE ALL ORAL IS JUST A YEAR AWAY



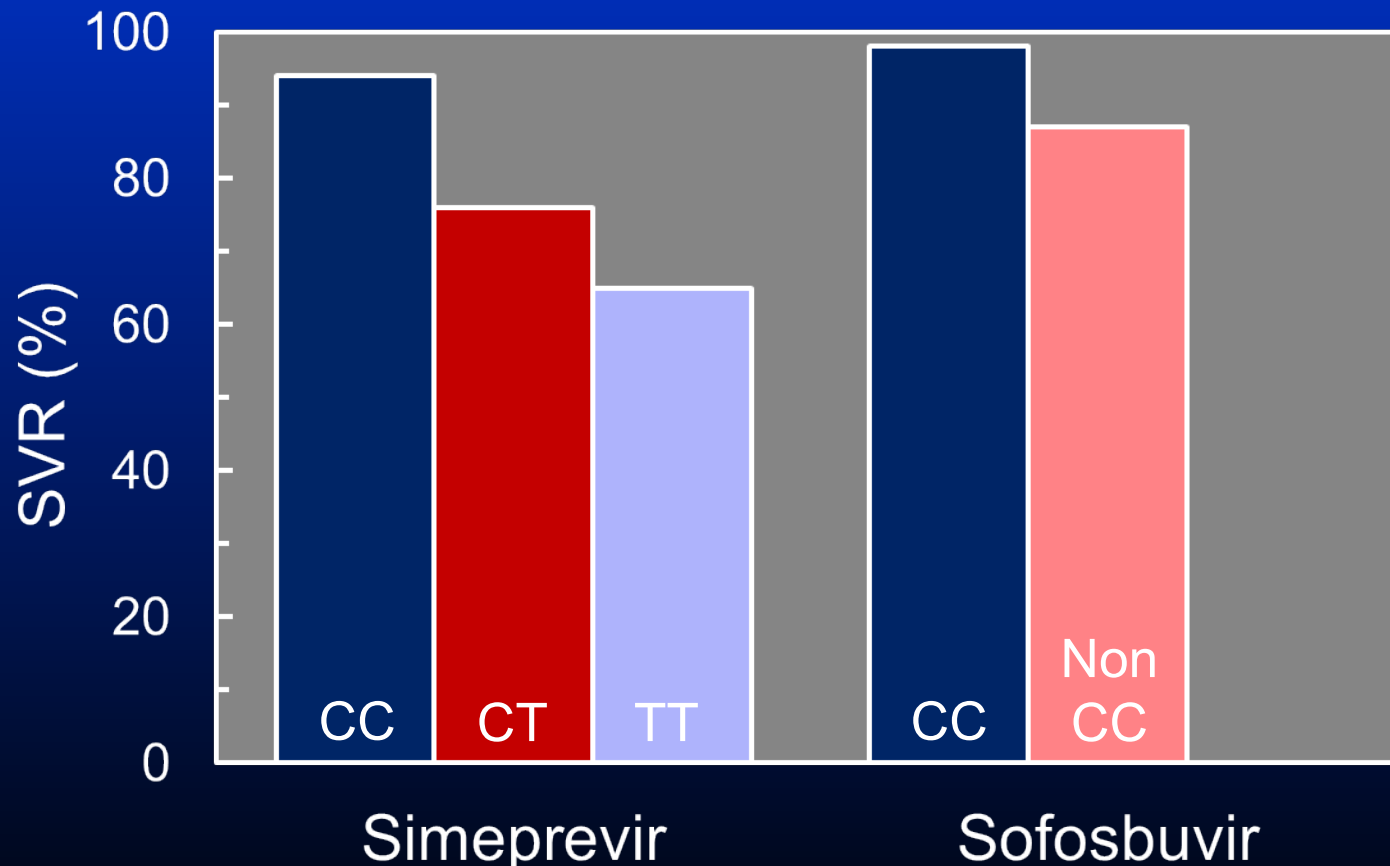
E Lawitz et al. AASLD 2013

S Zeuzem et al. AASLD 2013

IM Jacobson et al. N Engl J Med 2013; 368:1867-77



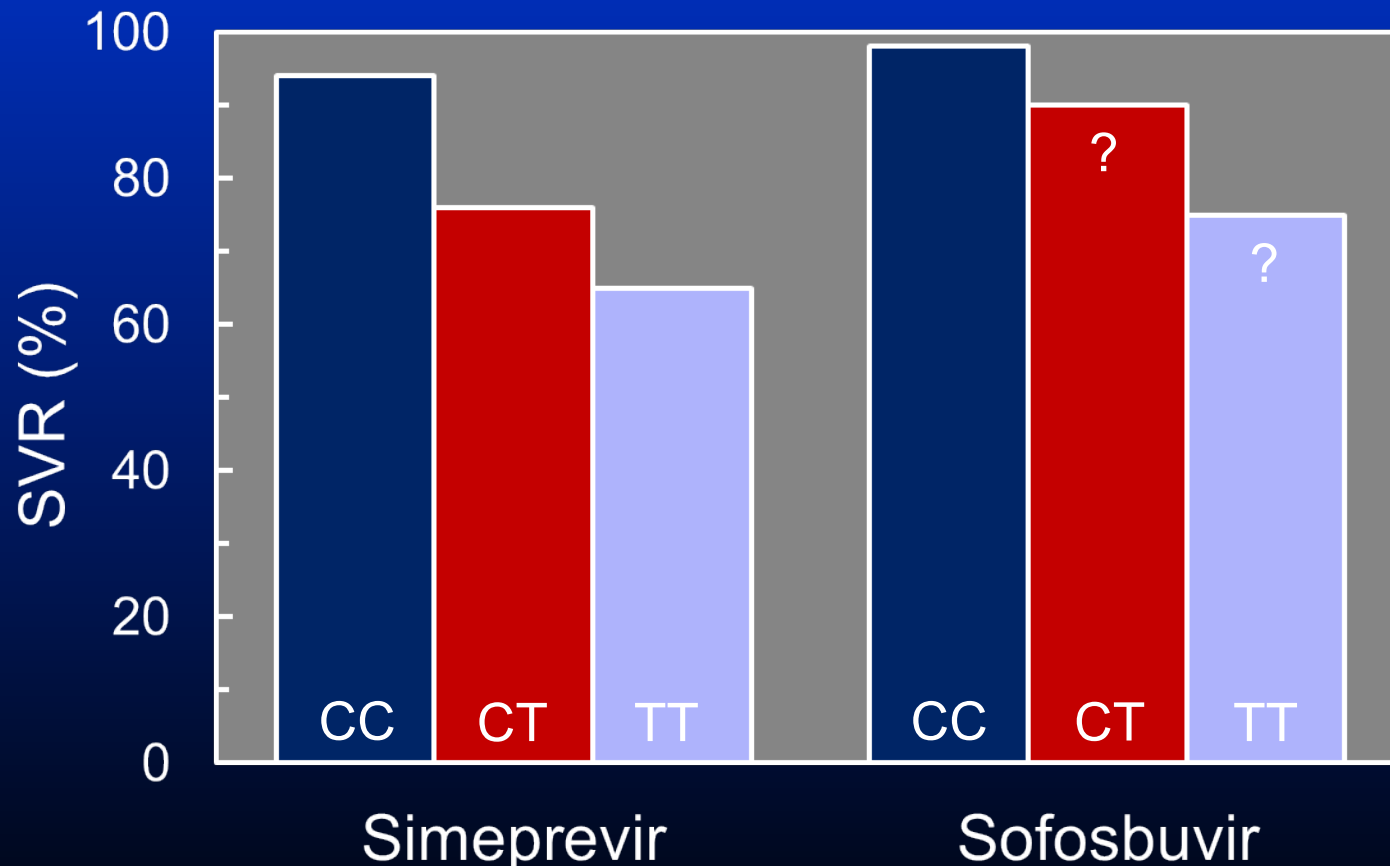
LOWER SVR WITH GT1 AND IL28B TT ALL ORAL IS JUST A YEAR AWAY



M Manns et al. EASL 2013.
E Lawitz et al. N Engl J Med 2013; 368:1878-1887



LOWER SVR WITH GT1 AND IL28B TT ITS JUST A YEAR AWAY



M Manns et al. EASL 2013.
E Lawitz et al. N Engl J Med 2013; 368:1878-1887



F1 AND F2 FIBROSIS

THE BENHAMOU ARGUMENT

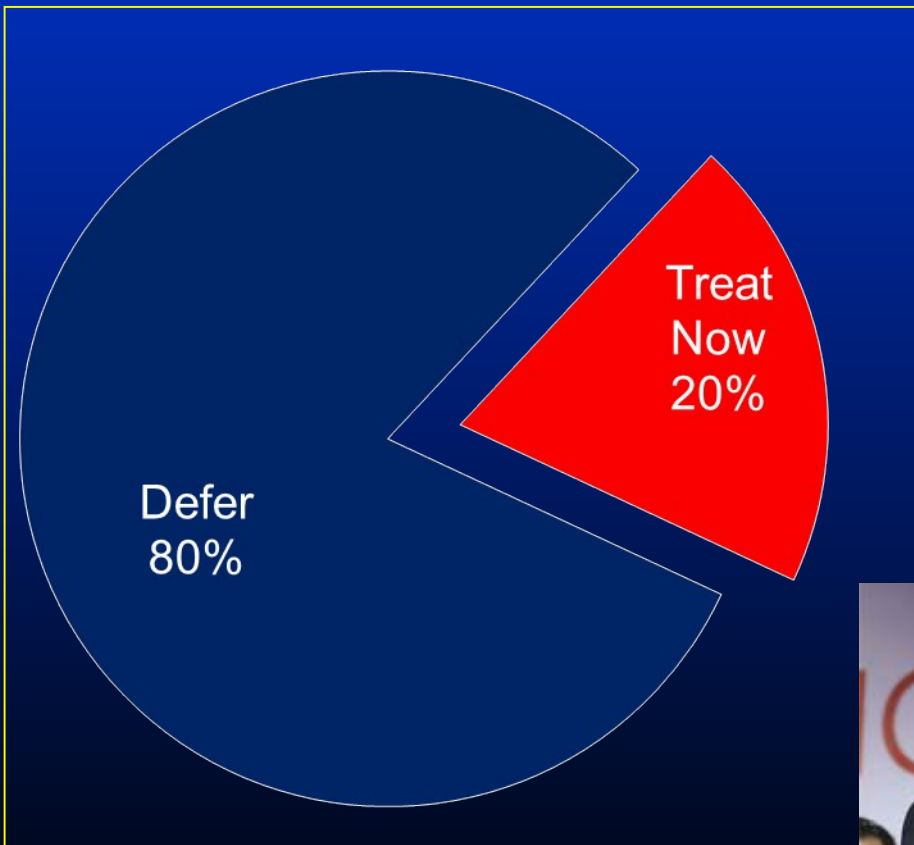
I don't care if better therapy is on the horizon and maybe only a year away. I'm going to treat mild fibrosis with interferon now.

The French are tough, not like those whiney Americans, and can handle the side effects.



HCV AND MILD FIBROSIS

WHAT DO THE PATIENTS THINK



Reasons for wanting to treat now:

- Personal reasons
 - Single and dating
 - Getting married
 - Have time off from work
- Insurance reasons
 - I do not trust that Obamacare




TREATMENT OF HCV (IN THE USA) OKAY TO TREAT NOW (WITH SOF)

- Genotype 2
 - Treatment is already over 90% even with prior non-response
 - Treatment is already all oral.
 - Unlikely to be anything better in the near future
- Genotype 4, 5, 6.
 - Still require interferon.
 - But only 12 weeks with near universal SVR
 - Unlikely to be anything better in the near future



TREATMENT OF HCV

OKAY TO DEFER TREATMENT

- Genotype 1
 - Still requires interferon and ribavirin
 - IL28B TT
 - Prior non-response  SVR unclear but probably sub-optimal ~70-75%
- Genotype 3
 - Requires 24 weeks of treatment
 - Even with this treatment SVR is sub-optimal ~80-85%
 - Although interferon free; the cost is double



PHC 2014: F1-F2 TREAT OR WAIT SUMMARY

There is a figure appearing at the end of the tunnel
It will soon be time for all patients to enter the funnel
And initiate treatment for HCV
With cures as high as they can
possibly be.



PHC 2014: F1-F2 TREAT OR WAIT SUMMARY

But is treatment ready now for those with F1 and F2

Yes it is for genotype 2

Its SOF, Riba and interferon free

With no AE

And an SVR at the top of the tree

For genotypes 4, 5 and 6

SOF is also a good fix

Peginterferon is still in the mix

And with only 12 weeks of needle sticks



PHC 2014: F1-F2 TREAT OR WAIT SUMMARY

I still have an issue with genotype 1

Especially with a prior treatment that was not fun

12 weeks of SOF and interferon may be too much for them

To do it again

So they wait on the side

For an interferon free ride

That may be only 1 year away

And that leaves little time for the virus to play



PHC 2014: F1-F2 TREAT OR WAIT SUMMARY

Genotype 3 is now the worst

And even with SOF the bubble has burst

Extending treatment to 24 weeks

Helps,

But is costly

Still does not cure this beast

And leaves to many with the virus to feast



PHC 2014: F1-F2 TREAT OR WAIT SUMMARY

And so,

There is really little for my friend and I to debate

Whether we treat now or continue to wait

We both agree HCV has a limited fate

For patients with F1, F2 or far more scar

We now (or will soon) have the tools to go very far

If we can only treat as many patients as the sky has star(s)

Will we get the opportunity to not return to the bar

