# F1-F2 PATIENTS: TREAT OR WAIT TREAT!

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# TELAPREVIR AND BOCEPREVIR
# EXCELLENT SVR RATES NOW

| | Boceprevir | Telaprevir |
|---|---|---|
| Treatment Naïve: | | |
| eRVR | 96% | 89-92% |
| Delayed response | 66-75% | 64% |
| % with eRVR | 56% | 58-60% |
| Retreatment: | | |
| Relapse | 69-75% | 84-88% |
| Partial response | 40-52% | 56-61% |
| Null response | NA | 31-33% |
| INF sensitive (lead-in) | 73-79% | NA |
| INF insensitive (lead-in) | 33-34% | NA |

ML Shiffman, R Estaban
Liver Intl 2012; 32 (suppl 1):54-60.

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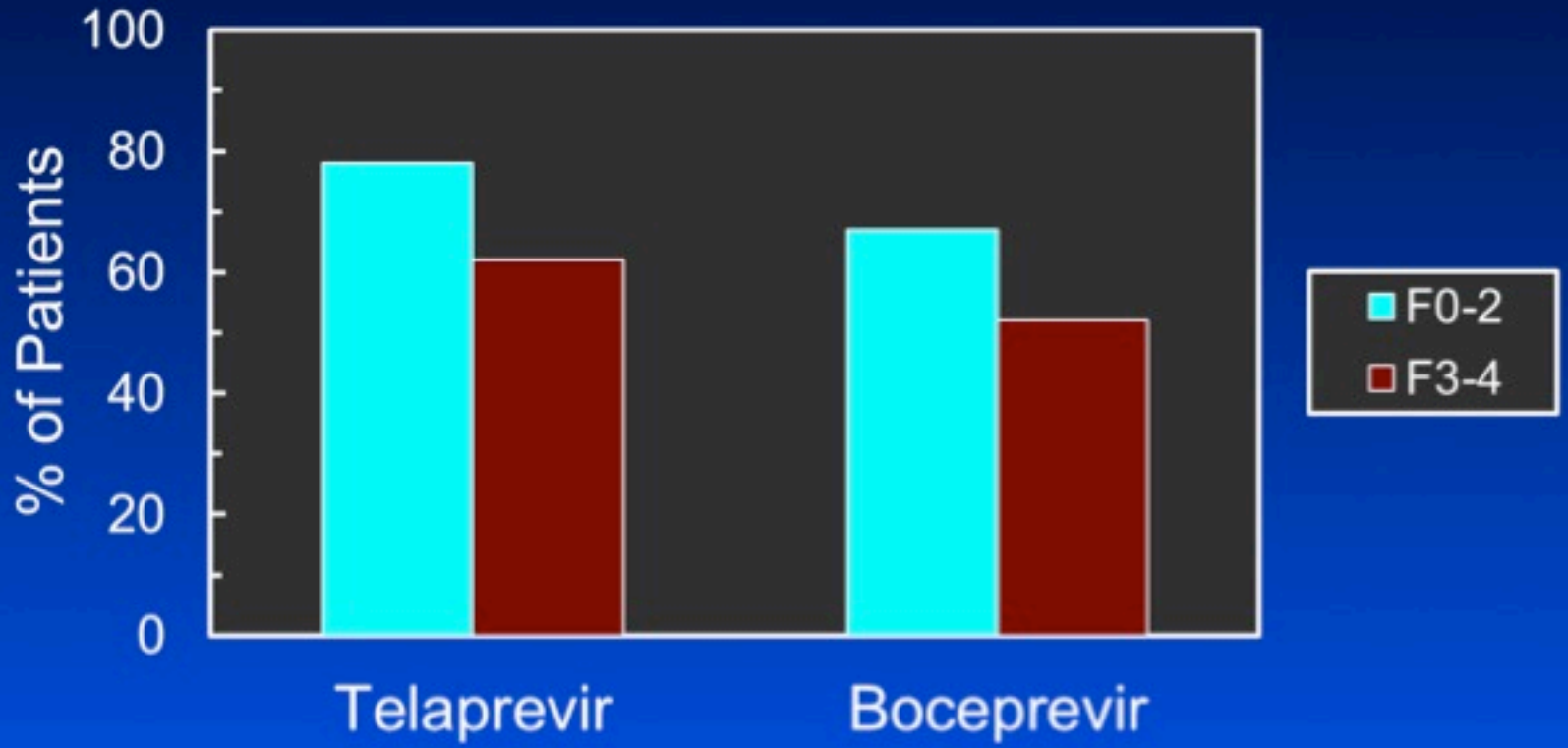
# MILD FIBROSIS
# EVEN BETTER SVR RATES NOW




F Poordad et al. N Engl J Med 2011; 364:1195-1206.
IM Jacobson et al. N Engl J Med 2011; 364:2405-2416.

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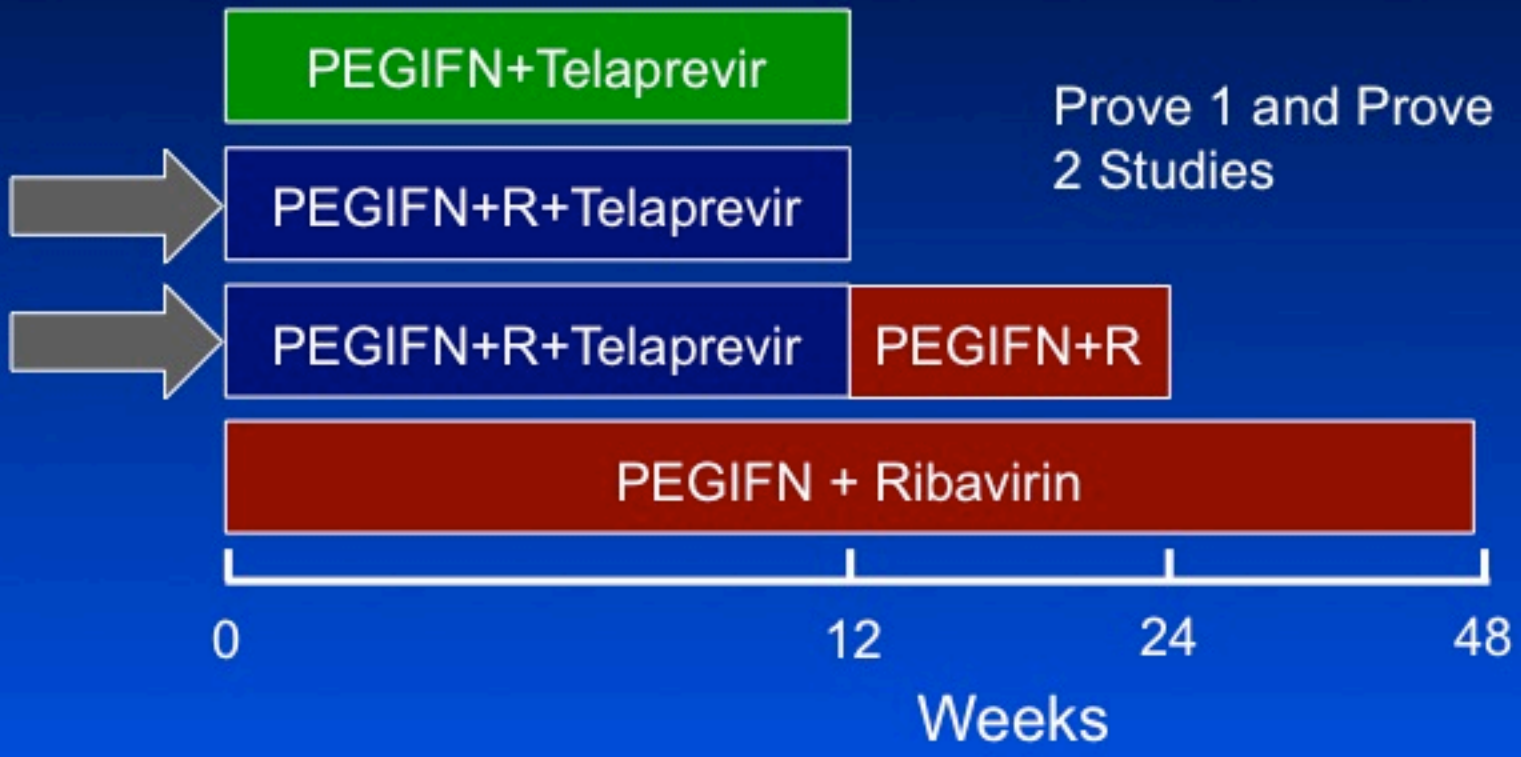
# IL28B GENOTYPE CC
# ONLY 12 WEEKS OF TREATMENT




JM McHutchison et al. N Engl J Med 2009; 360; 1827-1838.
C Hezode et al. N Eng J Med 2009; 360:1839-1850.

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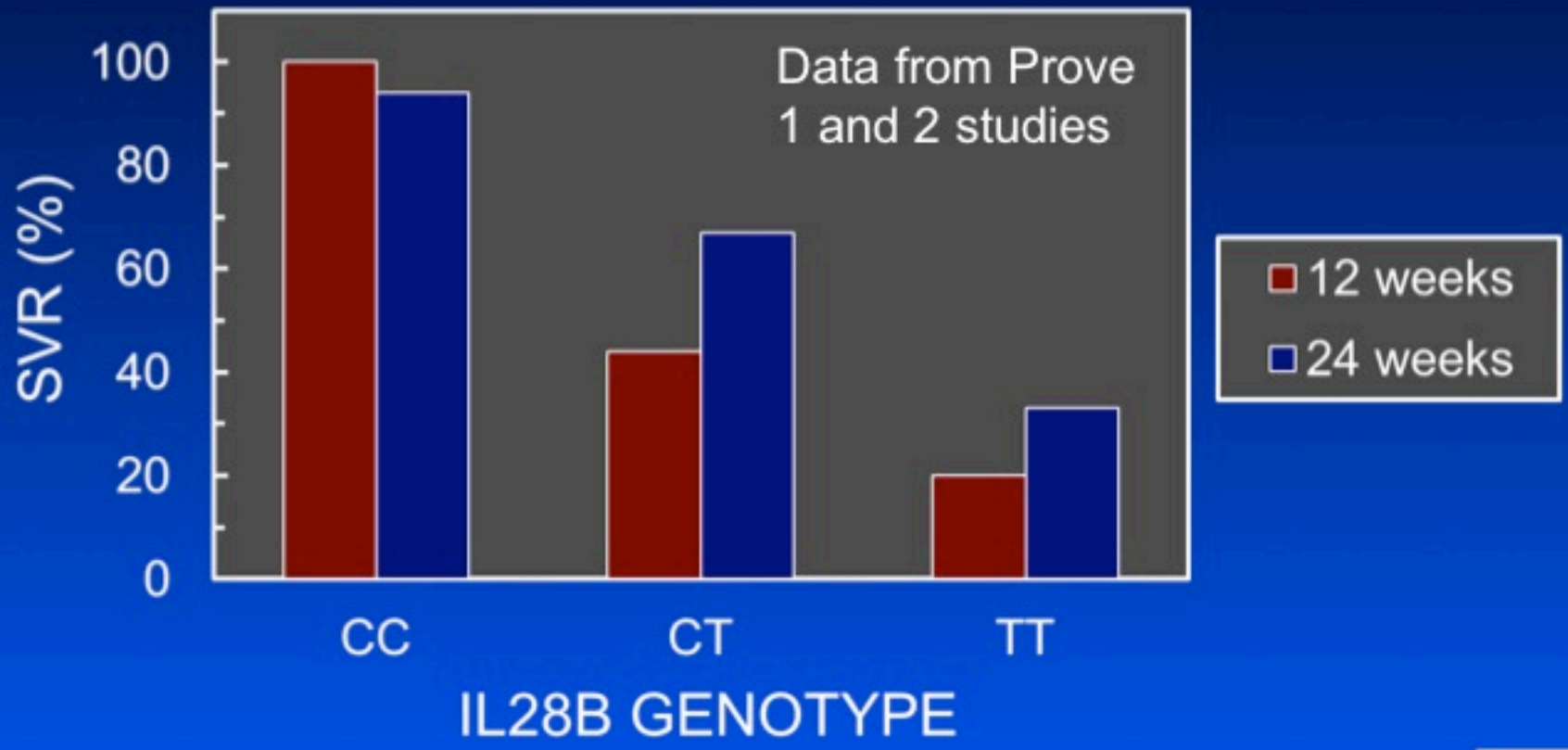
# IL28B GENOTYPE CC
# SUPERIOR SVR NOW




JP Bronowicki et al.
EASL 2012

# LIMITATIONS OF CURRENT TREATMENT
# SIDE EFFECTS

| | Telaprevir | Boceprevir |
|---|---|---|
| Anemia | 19% | 22% |
| Nausea | 41% | 45% |
| Vomiting | 13% | 17% |
| Diarrhea | 30% | 25% |
| Dysgusea | 10% | 39% |
| Pruritus | 47% | NR |
| Rash | 56% | 18% |
| Anorectal Symptoms | 11% | <5% |

F Poordad et al. N Engl J Med 2011; 364:1195-1206.
IM Jacobson et al. N Engl J Med 2011; 364:2405-2416.

# PEGINTERFERON AND RIBAVIRIN SIDE EFFECTS

| Peginterferon | Ribavirin |
| --- | --- |
| Flu-like symptoms | Hemolysis |
| Bone Marrow Suppression | Rash |
| Stimulation of autoimmune diseases | Cough |
| Neurologic injury | Nausea |

- It is the side effects of peginterferon which dictate the side effects of HCV therapy
- That is why we are trying to replace peginterferon

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# PATIENTS WITH ADVANCED FIBROSIS
# EVEN MORE SIDE EFFECTS

| | Telaprevir | Boceprevir |
|---|---|---|
| SAE | 49% | 38% |
| Premature DC | 26% | 24% |
| Infections | 26% | 24% |
| Death | 2% | 1.3% |
| Hepatic decompensation | 4.4% | 4.4% |
| Anemia <8.0 gm/dl | 10% | 10% |
| EPO use | 57% | 66% |

C Herzode et al.
EASL 2012

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# WHY DEFER THERAPY?
# WHO SHOULD DEFER THERAPY?

- The rationale to defer therapy is because better therapy will soon be available
- However:
  - Will therapy really be “better” for patients with HCV genotype 1 or just more convenient
  - How long will we make our patients wait for this “better” therapy
  - Will this “better” therapy be affordable to the majority of patients who are waiting for treatment
  - What are the consequences of doing nothing

# SOON TO BE AVAILABLE: 2013
# "BETTER" OR JUST CONVENIENT

- Genotype 1
  - Simeprevir
  - Faldaprevir
  - Sofosbuvir

  Will likely be available by 2010
  Will be utilized with
  Peginterferon and Ribavirin
  Better, or just more convenient

- Genotypes 2 and 3
  - Sofosbuvir
  - Ribavirin

  → Interferon free
  But will SVR in a large
  homogenous cohort be better
  or just more convenient

# INTERFERON FREE FOR GT1
# "BETTER" OR JUST CONVENIENT

| Company | Drugs | SVR |
|---|---|---|
| Abbott | ABT-245/Ritonovir<br>ABT-267<br>ABT-333<br>± Ribavirin | Better or Similar to the current SOC? |
| BI | Faldaprevir<br>BI202127BI<br>Ribavirin | |
| Gilead | Sofosbuvir<br>GS5855<br>± Ribavirin | |

# INTERFERON FREE THERAPY
# "BETTER" ALWAYS COSTS MORE

Will all patients get convenience, comfort and a speedy treatment.
Who will pay for it?

Or
Given comparable cure rates will patients get what they or the "system" can afford?


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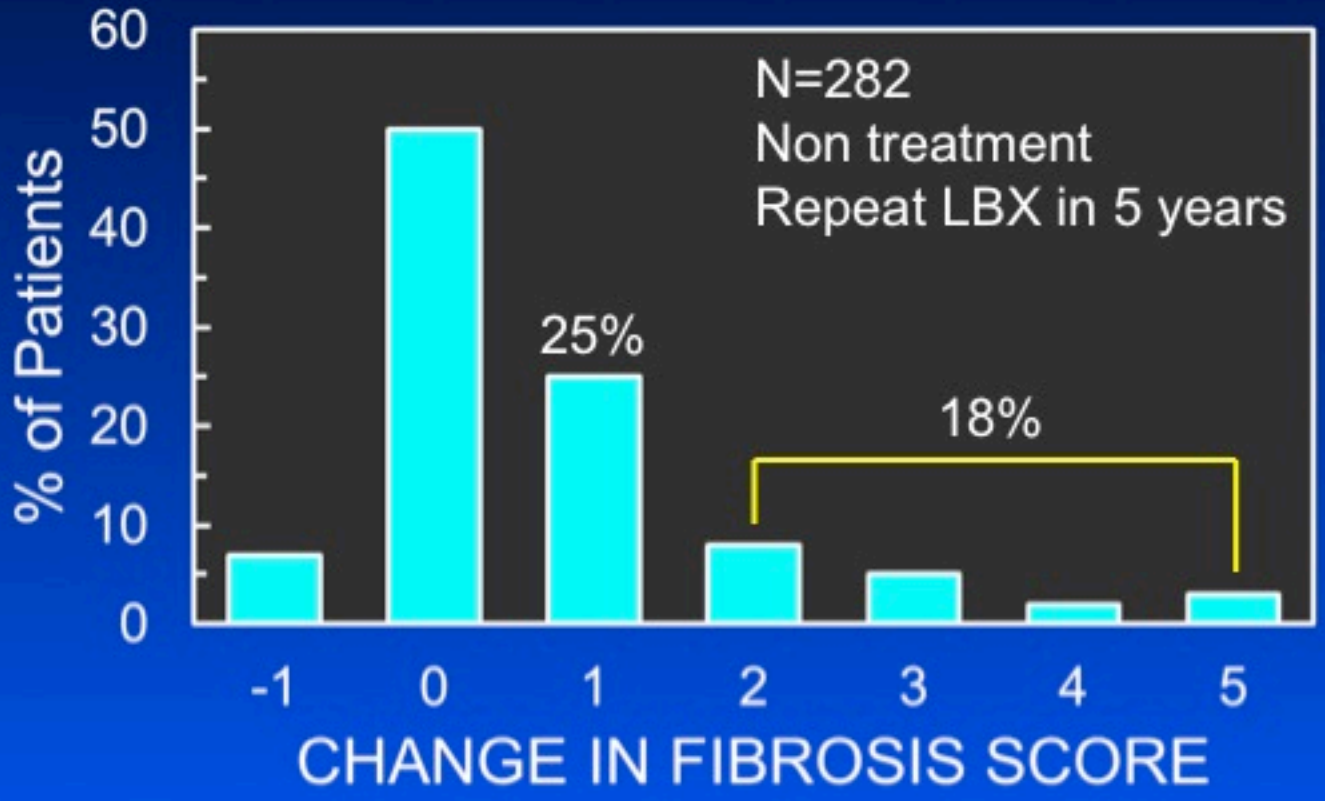
# THE CONSEQUENCES OF WAITING
# FIBROSIS PROGRESSION




MJ Williams and M Lang-Lenton
J Viral Hep 2011; 18:17-22.

# THE CONSEQUENCES OF WAITING
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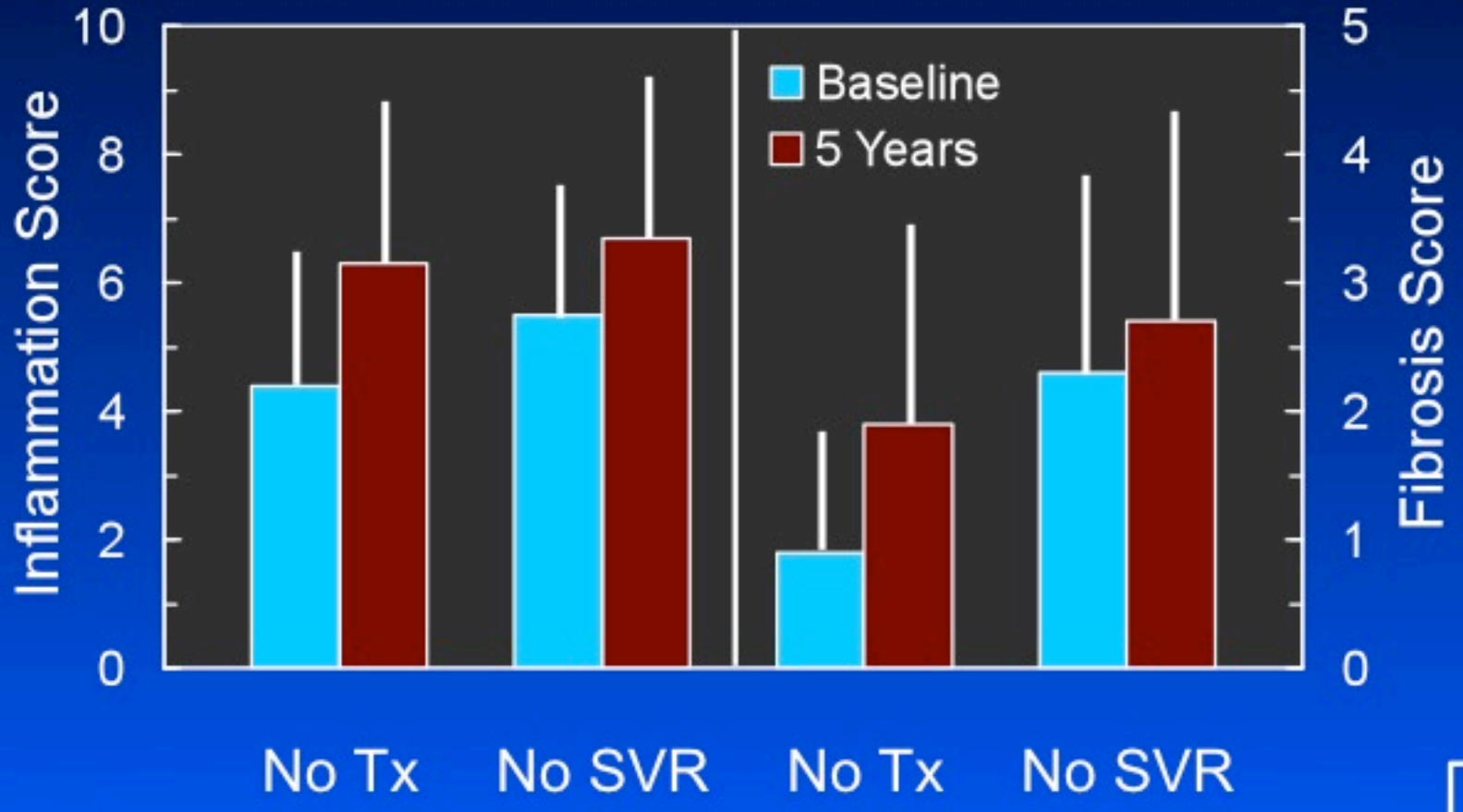


ML Shiffman et al.
EASL 2009

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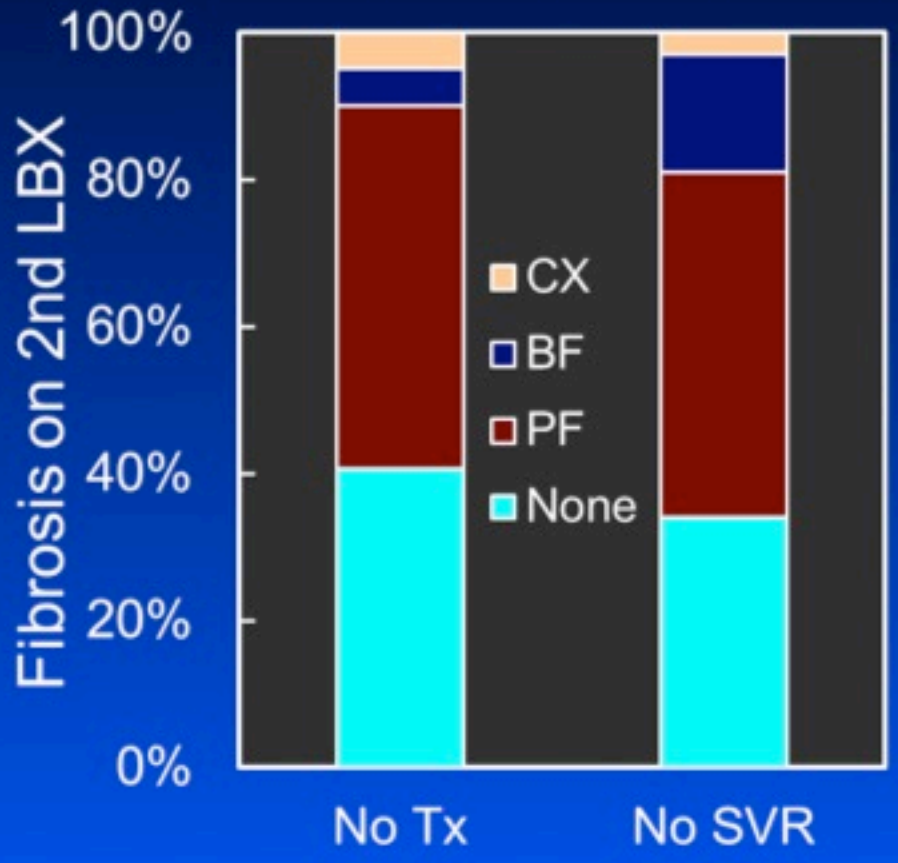
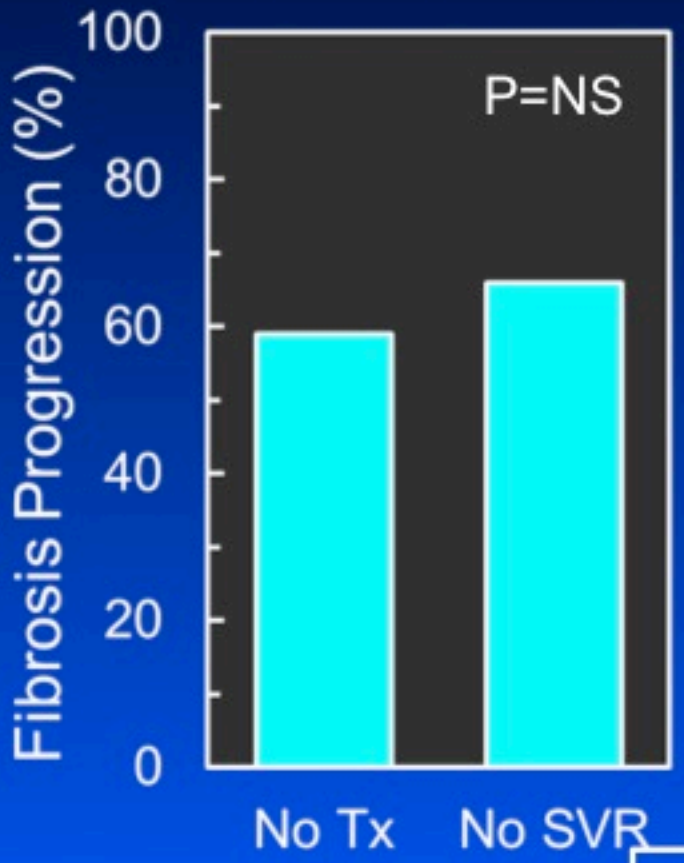
# FIBROSIS PROGRESSION
# NO FIBROSIS AT BASELINE




ML Shiffman et al.
EASL 2009

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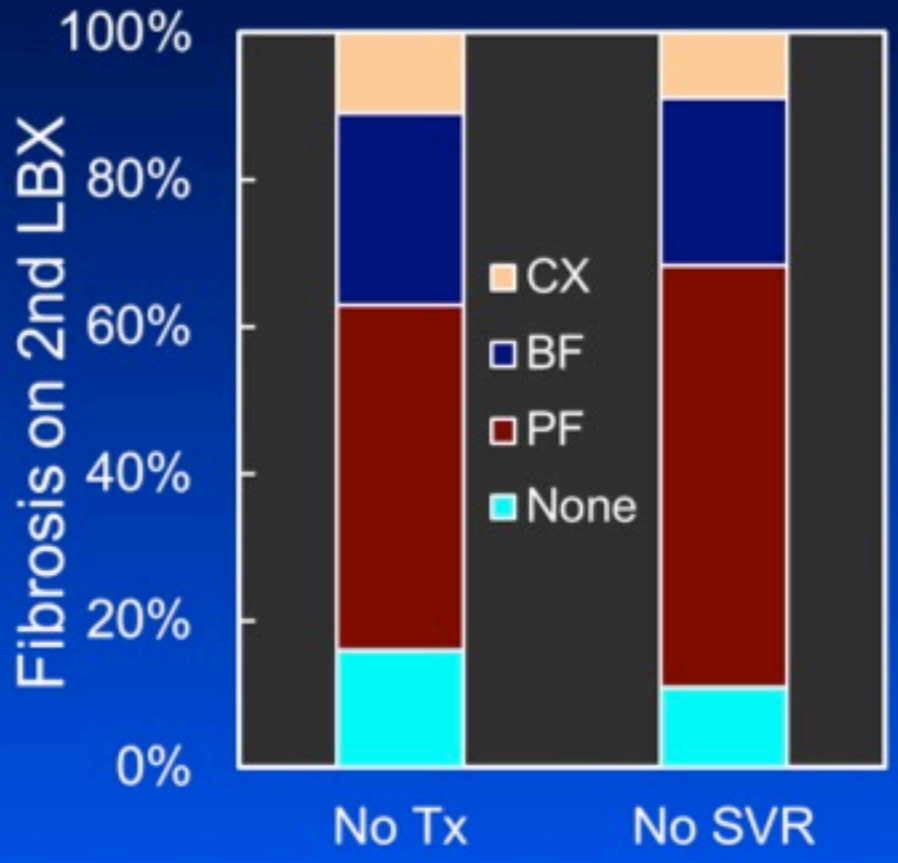
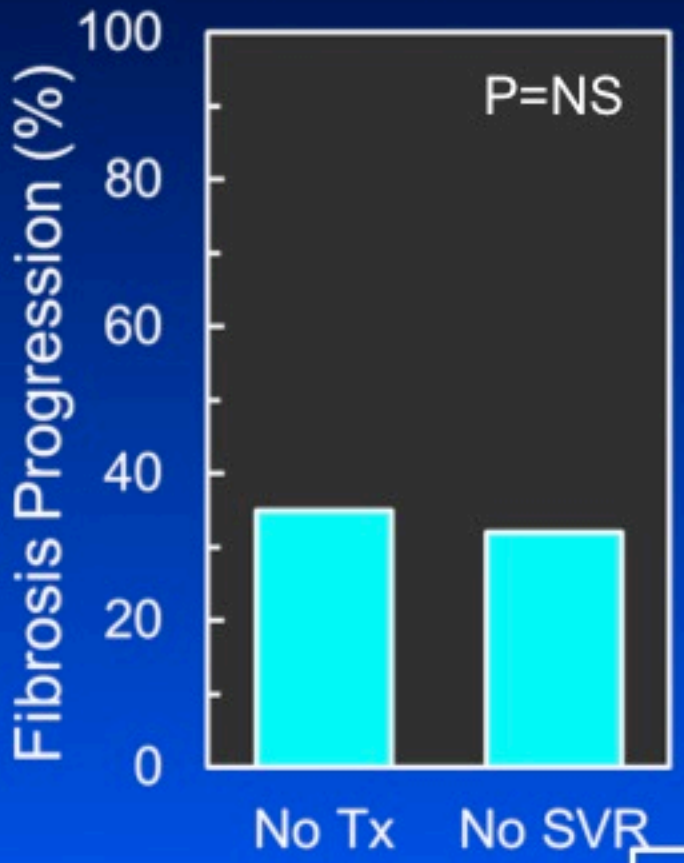
# FIBROSIS PROGRESSION
# PORTAL FIBROSIS AT BASELINE




ML Shiffman et al.
EASL 2009

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# F1 AND F2 FIBROSIS
# THE BENHAMOU APPROACH

I am ignoring my patients with mild fibrosis until they progress have advanced fibrosis and really need HCV treatment.

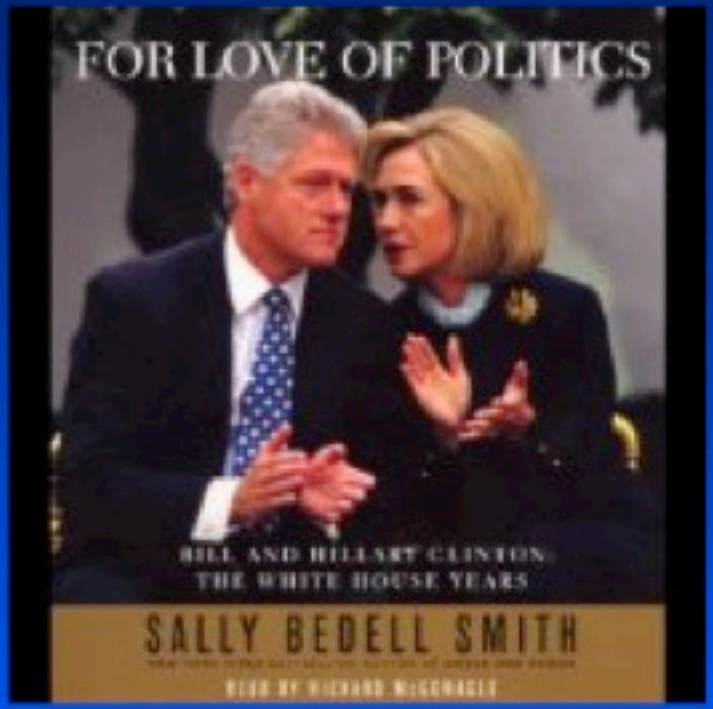
# WHO TO TREAT NOW
# THOSE WE CAN CURE EASILY

- Patients with mild disease (F1-F2)
- IL28B genotype CC
  - These patients are VERY UNLIKELY to have higher cure rates with future therapies
- Patients with extrahepatic manifestations
  - Cryoglobulinemia
  - PCT
  - Lichen Planus
- A patient that is “cured” today is one less patient we need to worry about tomorrow

# TREAT F1 AND F2 NOW
# INTERFERON IS TOLERABLE

- The vast majority of patients with “mild” fibrosis do tolerate interferon based therapy.

- They may want and think there is something better.
- But,
- Most find a way to tolerate what they have.
- Especially if it works for them.



# TREAT F1 AND F2 NOW
# SUMMARY

The treatment of F1 and F2 can be quite a dilemma

The SVR is better than ever

But treatment means symptoms of flu

Anemia, a bad taste and a rash too.

So what do we do.

# TREAT F1 AND F2 NOW
# SUMMARY

New choices for G1 should be available this year
With names like simiprevir, faldaprevir and sofosbuvir
But is this really better
The answer is not clear
For peginterferon will still be hear
And this will still cause our patients to fear

# TREAT F1 AND F2 NOW
# SUMMARY

The future of treatment for HCV

Is multiple agents that are interferon free

For patients with genotypes 2 and 3

This may here as soon as 201 and three

For all the rest it's still just

Wait and see

But what cost will this treatment be

And how will this cost be passed on to you and me

# TREAT F1 AND F2 NOW
# SUMMARY

So my advise to patients with a mild fate
Is to treat now and don't wait
Because I do not want my patients to be left at the gait
One day wondering why it is now too late

My friend has a different approach to F1 and F2
He would rather wait, than do
So when things have progressed
And my patients cry boo hoo
I'll just blame it all on Yves Benhamou