

# **Controversy : F1/F2 patients : Treat or Wait ?**

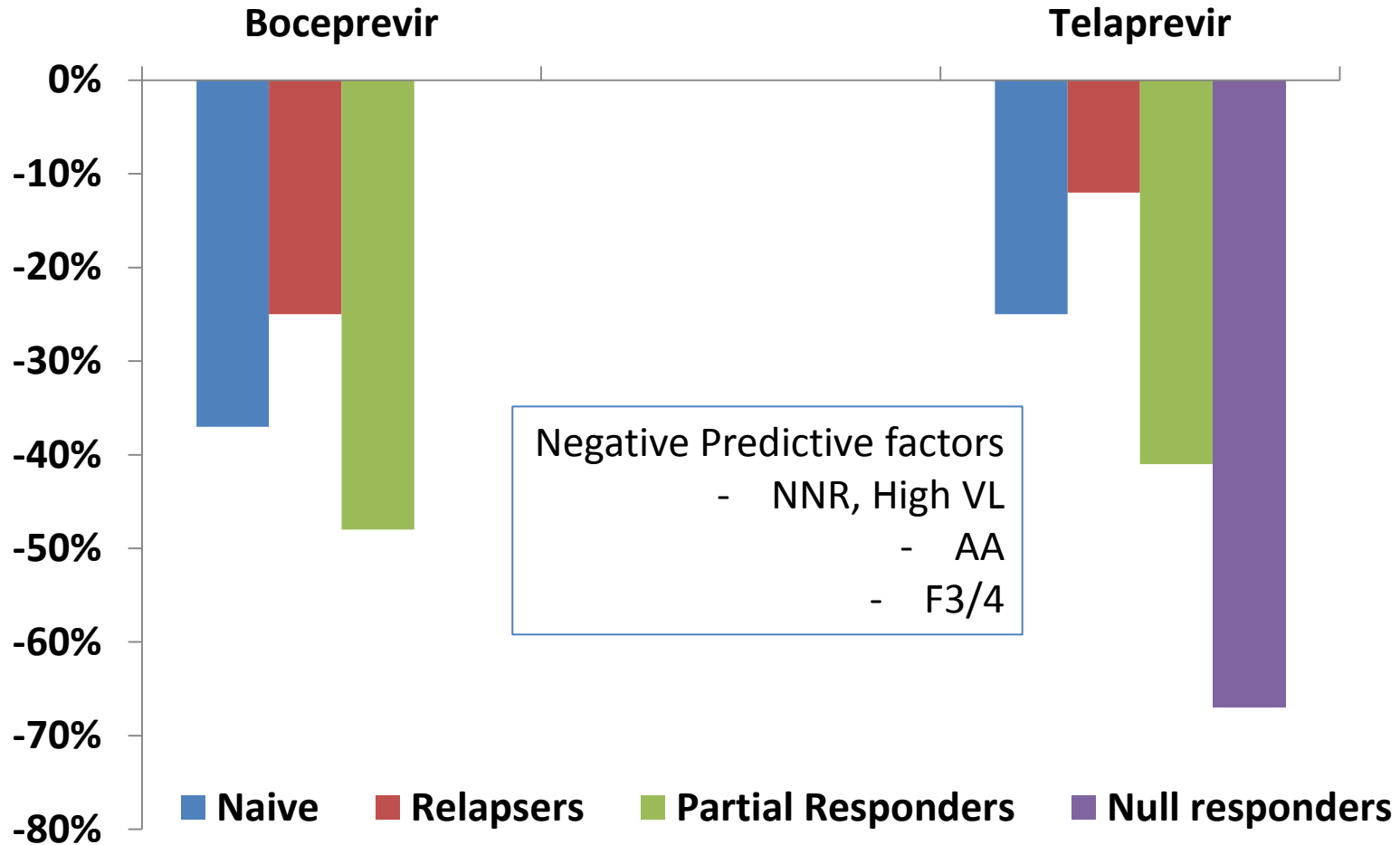
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# Argument to Wait?

## Treatment Failure Still High

Proportion of HCV GT1 Patients with Treatment failure to PR/ Boceprevir and Telaprevir



Poordad F et al. *N Engl J Med* 2011; 364: 1195-1206  
Bacon BR. et al. *N Engl J Med* 2011; 364:1207-1217

Sherman KE et al. *N Engl J Med* 2011; 365: 1014-1024.  
Jacobson IM et al. *N Engl J Med* 2011; 364 : 2405-16.  
Zeuzem S. et al. *N Engl J Med* 2011;364:2417-28

# Argument to Wait

## *Non Optimal Tolerability*

### Boceprevir/Telaprevir: summary of AEs over course of therapy

	<b>BPR</b>	<b>TPR</b>
Serious AEs	11%	7%
Discontinued due to AEs	12%	14%
Anemia	50%	32%
Rash	17%	55%

*Sherman KE et al. N Engl J Med 2011; 365: 1014-1024.*  
*Jacobson IM et al. N Engl J Med 2011; 364 : 2405-16.*  
*Zeuzem S. et al. N Engl J Med 2011;364:2417-28*

*Poordad F et al. N Engl J Med 2011: 364: 1195-1206*  
*Bacon BR. et al. N Engl J Med 2011; 364:1207-1217*

# Argument to Wait

## *Constraining Therapy, Potent Impact on Adherence*

- Drug/Drug interaction
  - Both telaprevir and boceprevir are metabolized by CYP3A4 substantial risk of contraindications and toxicity
- Pill burden: 10 to 18 pills per day
- Dosing: q8h
- Diet recommendation
- May impact adherence and affect SVR

GALAXIE OF HCV DRUGS



SVR

# GALAXIE OF HCV DRUGS

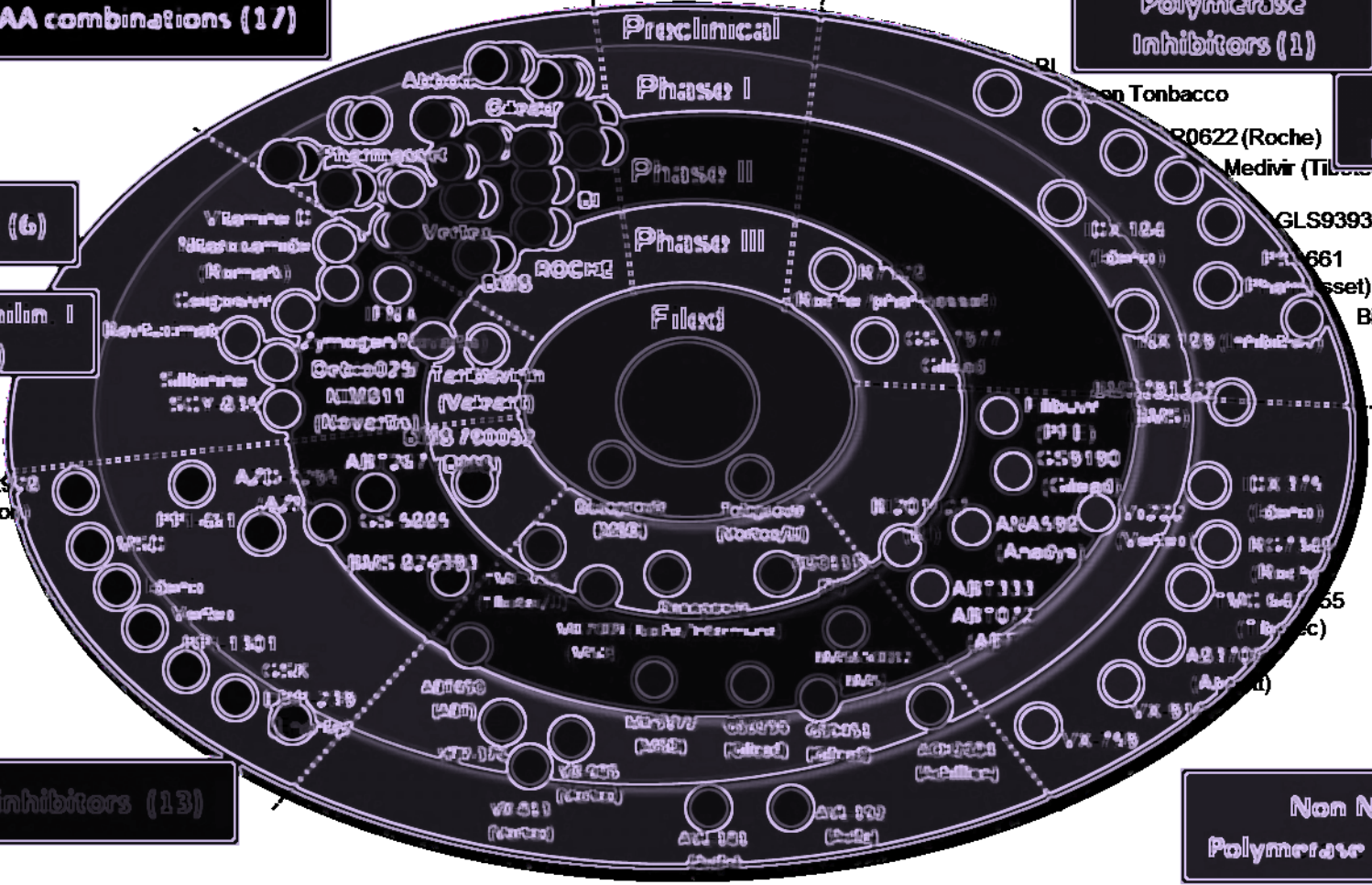
**DAA combinations (17)**

**Nucleotide NSSB  
Polymerase  
Inhibitors (1)**

**Nucleoside  
NSSB  
Polymerase  
Inhibitors (11)**

**(Others (6)**

**(Cyclophilin I  
(2)**



**ACH-2952  
(Acylator)**

**NSSA inhibitors (13)**

**NS3/4A Protease inhibitors  
(19)**

**Non Nuc NSSB  
Polymerase inhibitors (17)**

**Roche  
Toshiba  
Medivir (Tibotec)  
GSK  
Novartis  
Biocryst**

# Argument to Wait

## *SVR with Futur DAA plus PR*

	Simeprevir	Faldaprevir	Danoprevir/r	Sofosbuvir
<b>SVR</b>	<b>GT1a/b Naive: 80% GT1a/b R: 79%</b>	<b>GT1a/b Naive: 83% GT1a/b NNR/PNR: 41%</b>	<b>GT1a/b : Naive 85%</b>	<b>GT1a/b Naive: 90%</b>
<b>Treatment Duration</b>	<b>24W: (eRVR: 85%)</b>	<b>24W: (eRVR: 87%)</b>	<b>24W (eRVR: 59%)</b>	<b>12W – 24W</b>
<b>Treatment discount.</b>	<b>3.5%</b>	<b>5%</b>	<b>6%</b>	<b>5%</b>
<b>SAEs</b>	<b>6.5%</b>	<b>6%</b>	<b>9%</b>	<b>6%</b>
<b>Dosing</b>	<b>qd</b>	<b>qd</b>	<b>bid</b>	<b>qd</b>

*MEDIVIR Press Release December 20, 2012. Fried MW, AASLD 2011, Abstract. LB5. Sulkowski et al. AASLD 2011. Sulkowski et al. EASL 2011. Hassanein T. et al. AASLD 2012. Everson G. et al. AASLD 2012. .*

# Argument to Wait

## *SVR with IFN free Regimens in Patients with GT1*

DAA Combinations				Weeks of Rx	N	SVR
Faldaprevir	BI 207127	RBV		28	30 48	Naive G1a: 43% Naive G1b: 85%
Asunaprevir	Daclatasvir			24	18	NNR G1b: 78%
Danoprevir/R	Mericitabine			24	23 31	PR G1b: 39% NNR G1b: 55%
ABT 450/R	ABT 333	RBV				Naive G1 a/b: 95% NR 1a/b: 47%
ABT 450/R	ABT 267	ABT 333	RBV	12	79 45	Naive G1a/b: 97% NR G1a/b: 93%
Daclatasvir	Sofosbuvir	±RBV		24	15 15	Naive G1a/b: 93% -100%
Asunaprevir	Daclatasvir	BMS791 325		12-24	16	Naive G1a/b: 94%
Sofosbuvir	RBV			24	25	Naive G1a/b: 56%-72%

*Zeuzem S et al. AASLD 2012. Lok A et al. AASLD 2012. Feld J et al. AASLD 2012. Poordad F et al. N Engl J Med. 2013;368:45-53  
Kowdley K et al. AASLD 2012. Everson G et al. AASLD 2012. Sulkowski M et al. AASLD 2012.*

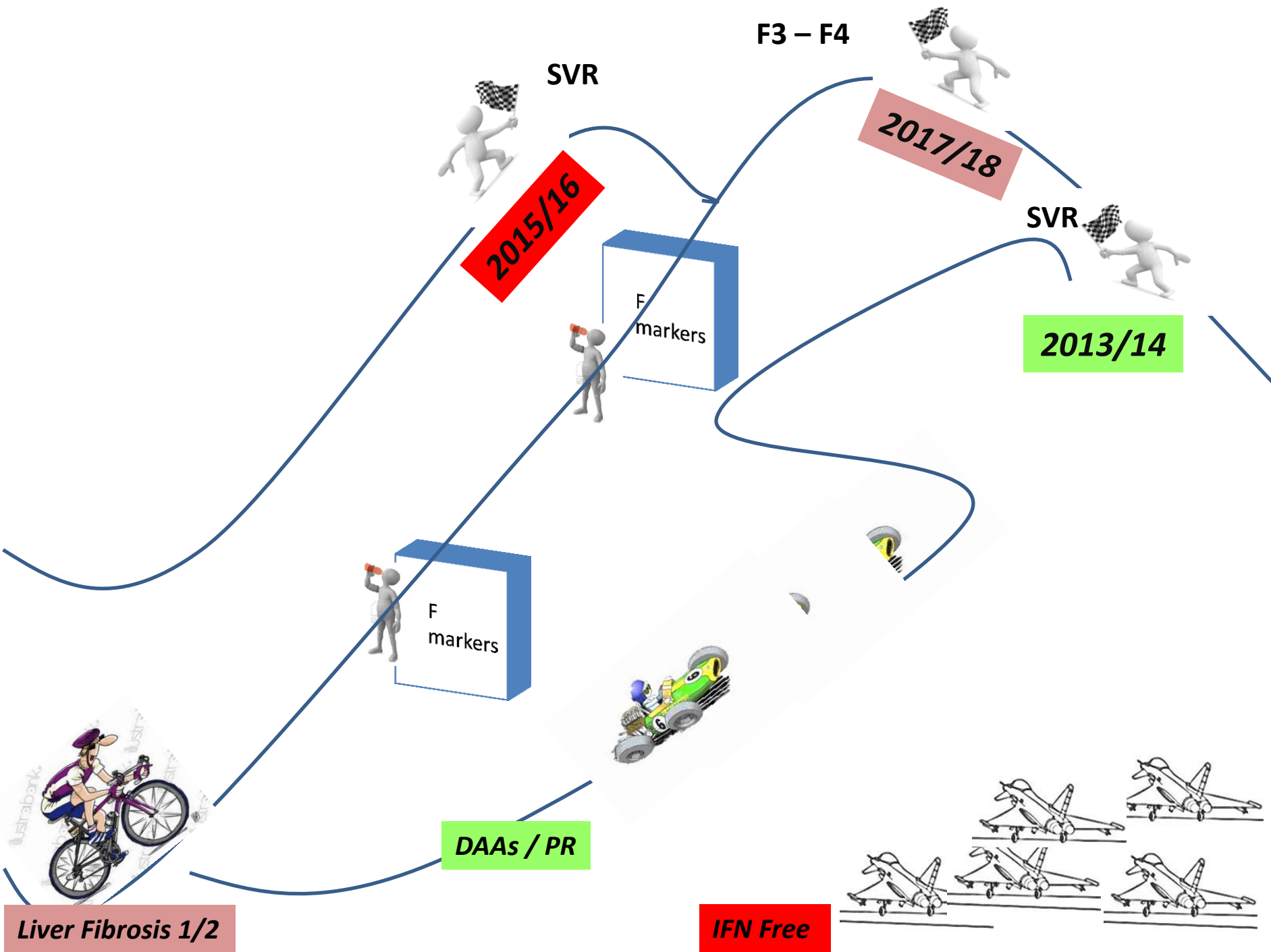


# Arguments to Wait

	BOC/TVR – PR	DAA - PR	IFN Free
<b>SVR</b>			
<b>PR Naive</b>	~ 65%-75%	~ 80%-85%	> 85% ?
<b>PR Failure</b>	~ 30%-50%	~ 40%-75%	> 50%-85% ?
<b>Genotype</b>	1	1 – 2 – 3 – (4?)	1 - 6
<b>Discont.</b>	~ 10%	~ 5 %	~ 2% ?
<b>Treatment Rx</b>	24 W – 48 W	24 W	12 W – 24 W
<b>Dosing</b>	TID	QD	QD

# Wait How Long?

- Decision to treat:
  - Is driven by the liver fibrosis progression
    - Progression of 1 fibrosis stage :  $\sim > 4$  years
  - Balanced by availability of new therapy
    - 1 - 4 years



**Liver Fibrosis 1/2**

**DAAs / PR**

**2015/16**

**F markers**

**F3 - F4**

**2017/18**

**SVR**

**2013/14**

**IFN Free**

**Treat or Wait ?**

# Treat or *Wait* ?

*“Never put off tomorrow what you can do today”*

*...?*

# *Treat* or Wait ?

***“Patience is bitter, but its fruit is sweet”***

*Aristote*

