- 45 years-old HCV patient who was contaminated by transfusion after a traffic accident 25 years ago :
- Diagnosis of HCV was performed after investigation of an increase of ALT
- Alcohol consumption was 60 g/day. The patient is completely abstinent since 6 month
- ALT 200 IU/l, GGT 100 UI/l, bilirubin 1.5 mg/dl, INR 1.1, albumin 39 g/l
- White blood cells 8500/mn^3, hemglobin 12.2 g/dl, Platelets 100 000 /mn^3
- Fibrotest® 0.8 (F4); Fibroscan® 16 kPA
- Actitest 0.4 (A1-A2)
- Genotype 3, HCV RNA 720 000 IU/mL (5.86 log)
- BMI 24

- What are the true propositions:

A/ In genotype 2 or 3 patients treated with pegylated bitherapy, 48 weeks is more effective than 24 weeks

B/ weight-based regimen of Ribavirin is superior to a fixed low-dose regimen (800 mg/day)

C/ Extensive fibrosis is not an independent predictive factor of SVR

D/ In patients with genotypes 2 or 3 without extensive fibrosis, shortened therapy (12-24 weeks) is equivalent to standard duration of 48 weeks

E/ Patients

- What are the correct propositions:

A/ In genotype 2 or 3 patients treated with pegylated bitherapy, 48 weeks is more effective than 24 weeks

B/ weight-based regimen of Ribavirin is superior to a fixed low-dose regimen (800 mg/day)

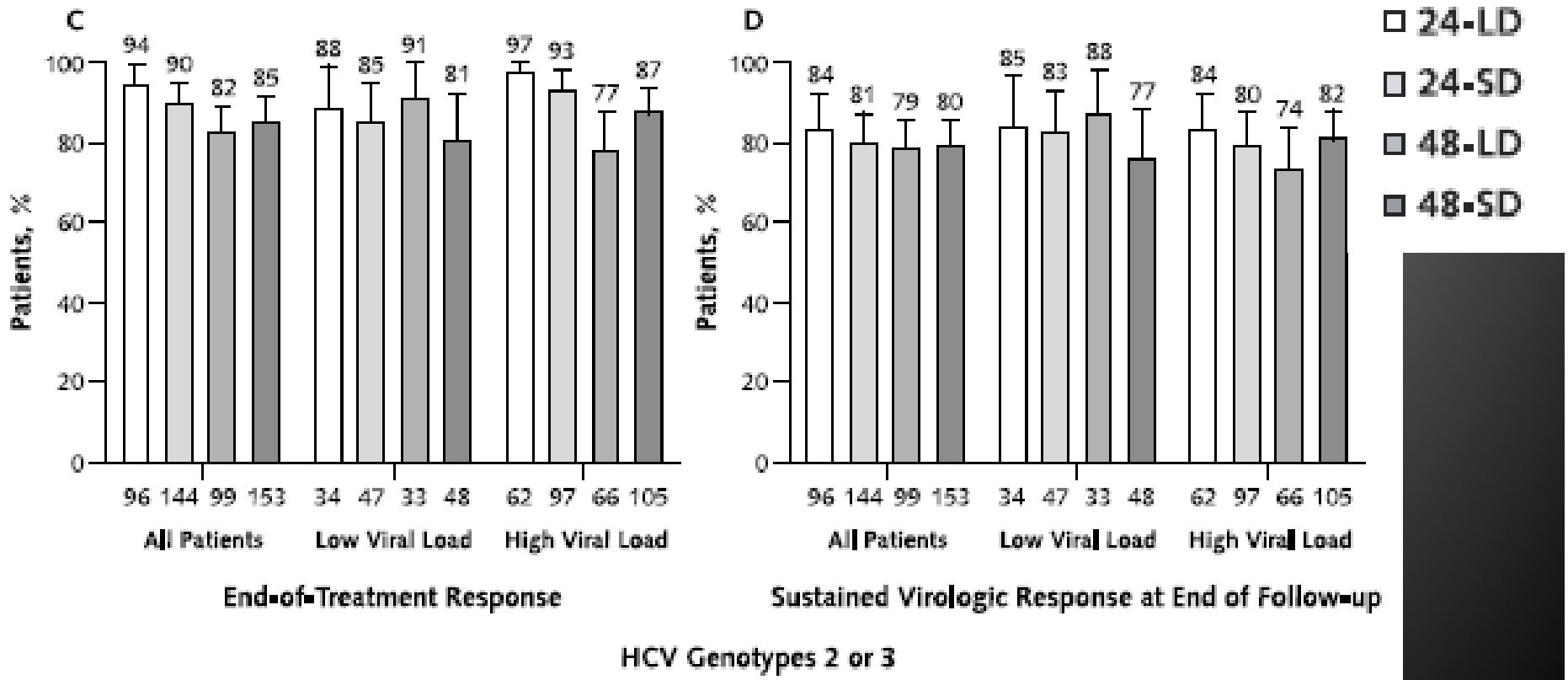
C/ Extensive fibrosis is an independent predictive factor of SVR

D/ In patients with genotypes 2 or 3 without extensive fibrosis, shortened therapy (12-16 weeks) is equivalent to standard duration of 24 weeks

E/ RVR is a good predictive factor of SVR in patients with genotype 3

Extending pegylated biherapy to 48 weeks and weight-based regimen of Ribavirin are not recommended

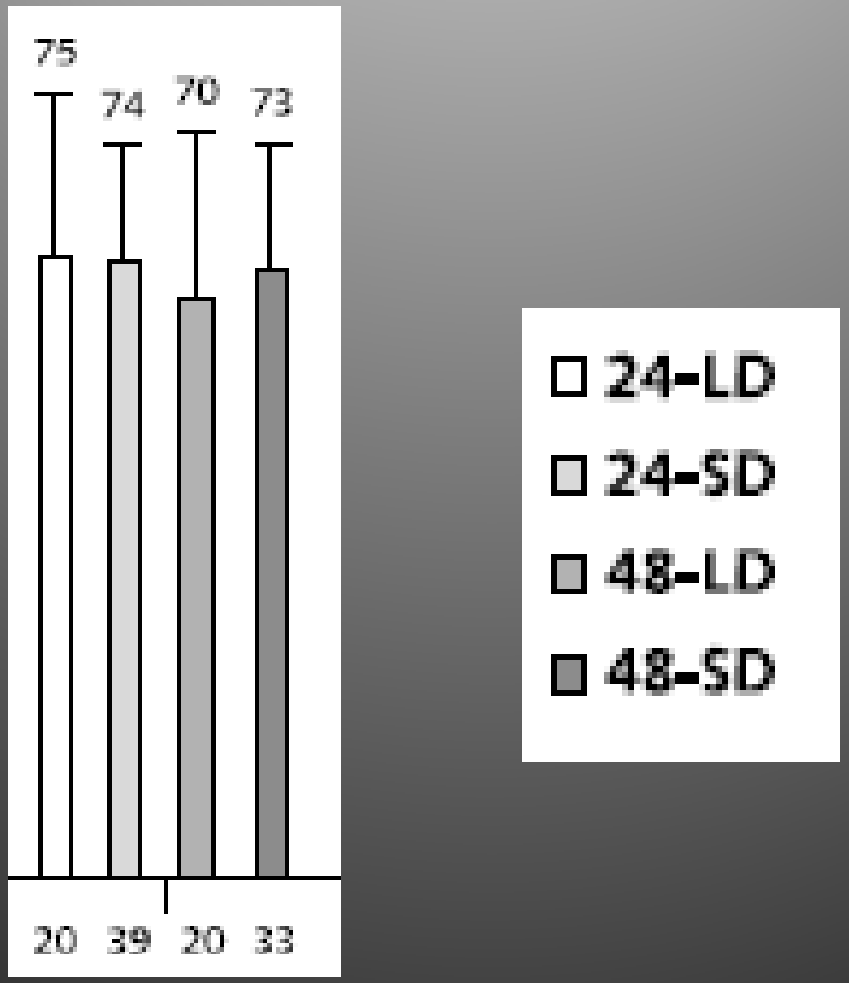
pegIFN-2a 180 g/wk and ribavirin 800 mg/d (LD) or 1000-1200 mg (SD)



Hadziyannis Sj et al., Ann Int Med 2004

Extending therapy to 48 weeks and weight-based regimen of Ribavirin not efficient in patients with extensive fibrosis

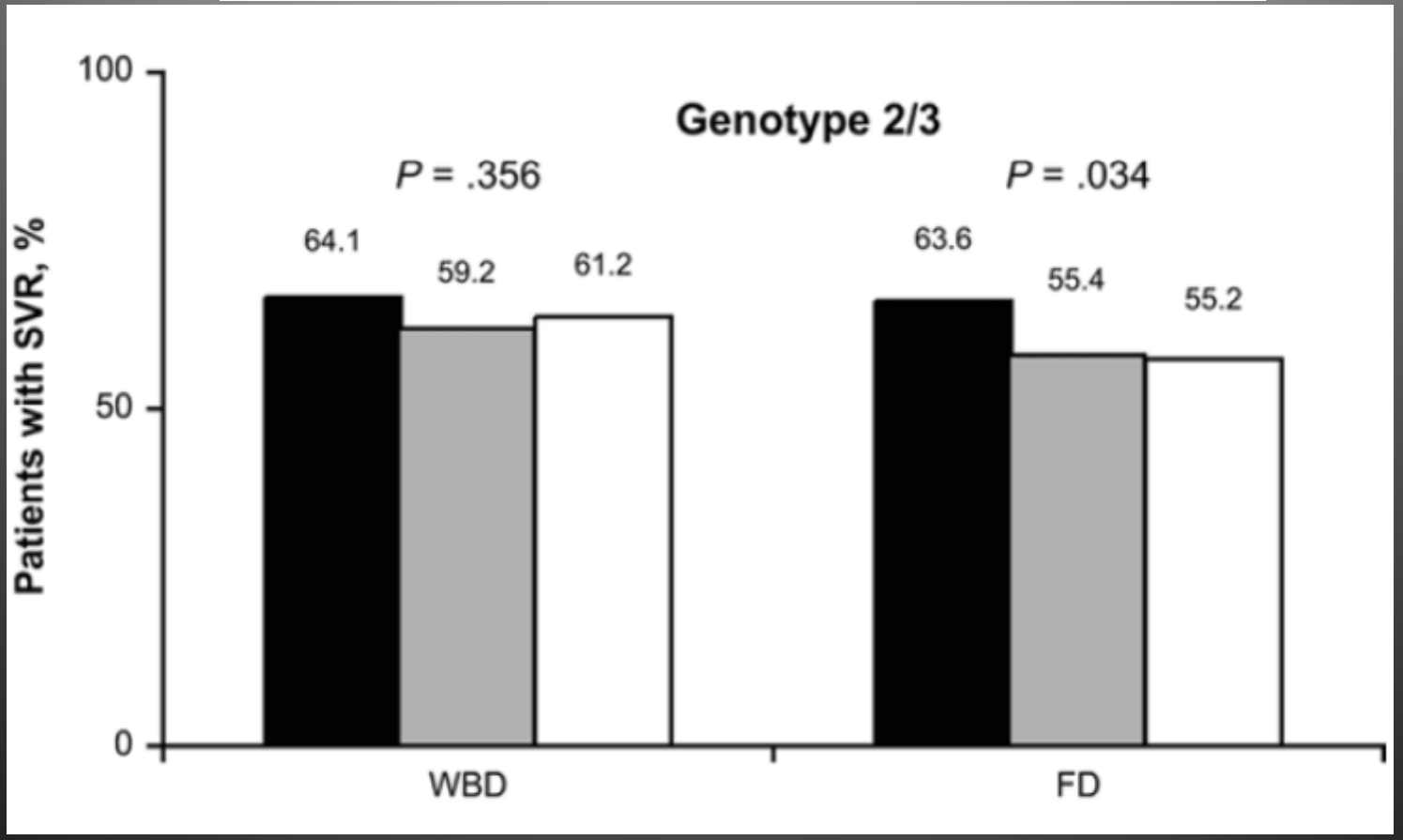
pegIFN-2a 180 g/wk and ribavirin 800 mg/d (LD) or 1000-1200 mg (SD)



Patients with bridging fibrosis or cirrhosis

Hadziyannis SJ et al., Ann Int Med 2004

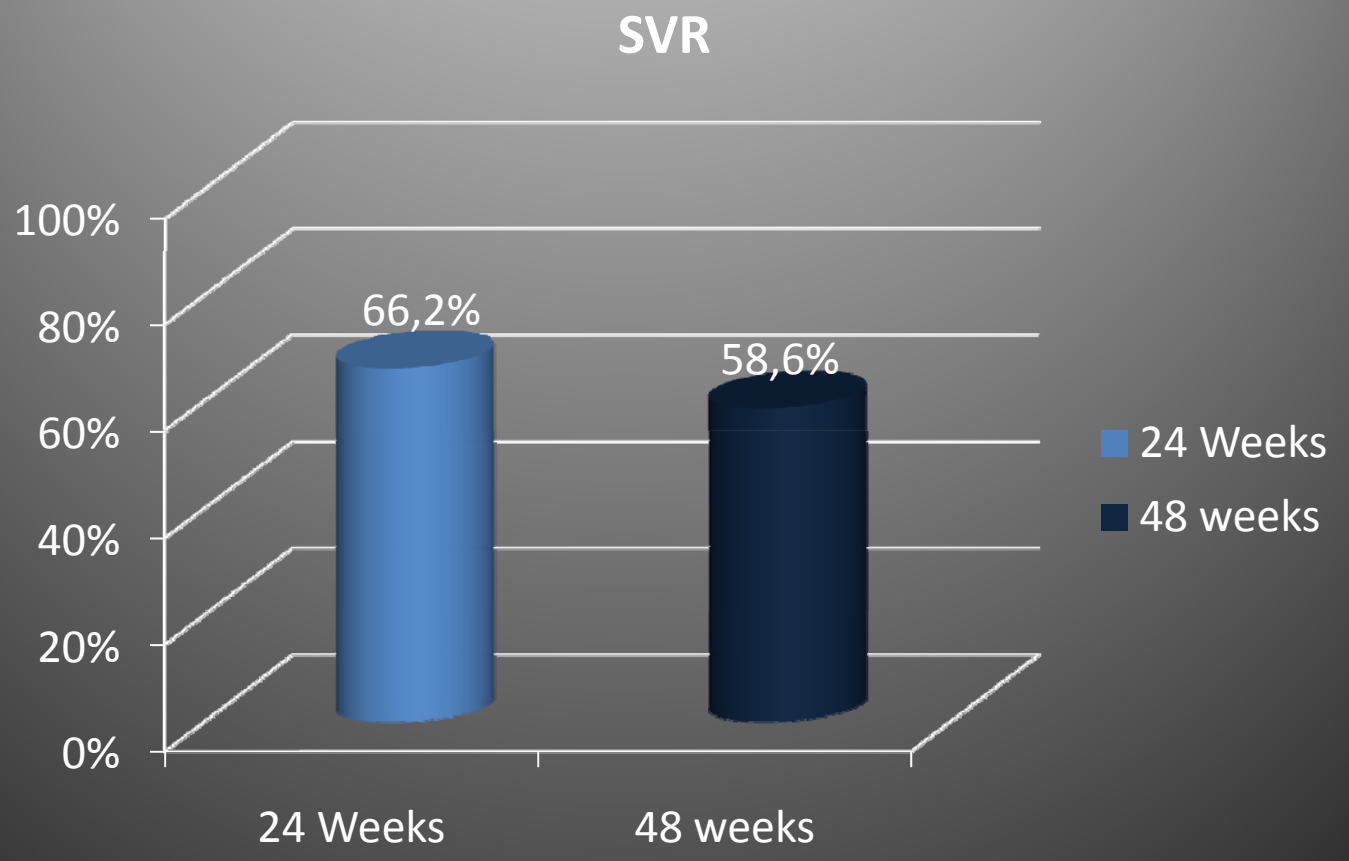
Extending pegylated biherapy to 48 weeks and weight-based regimen of Ribavirin are not recommended



PEG-IFN alfa-2b 1.5 g/kg/week plus flat-dose (800 mg/day) or weight-based (800-1400 mg/day) RBV

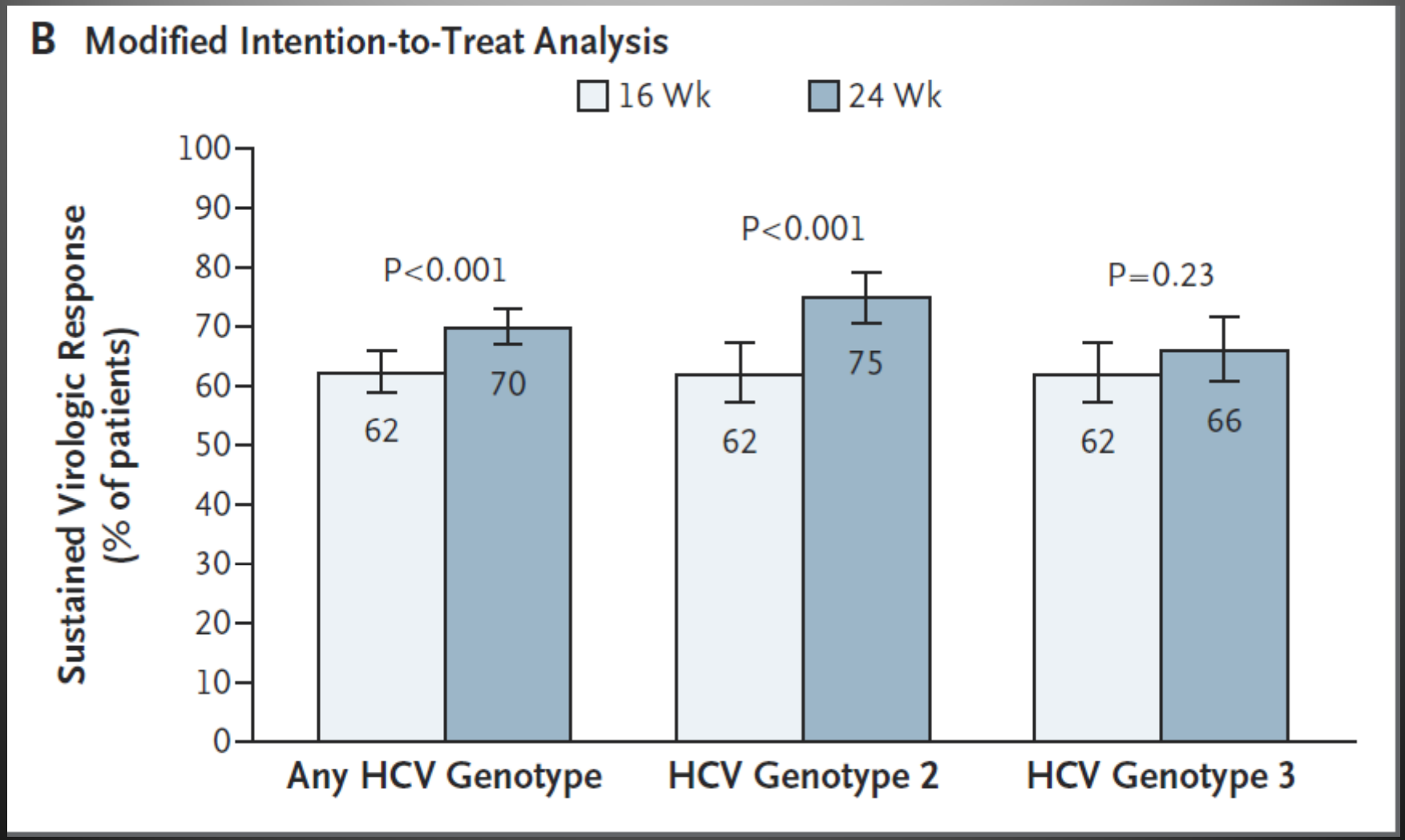
Jacobson IM et al., Hepatology 2007

Extending pegylated biherapy to 48 weeks and weight-based regimen of Ribavirin are not recommended



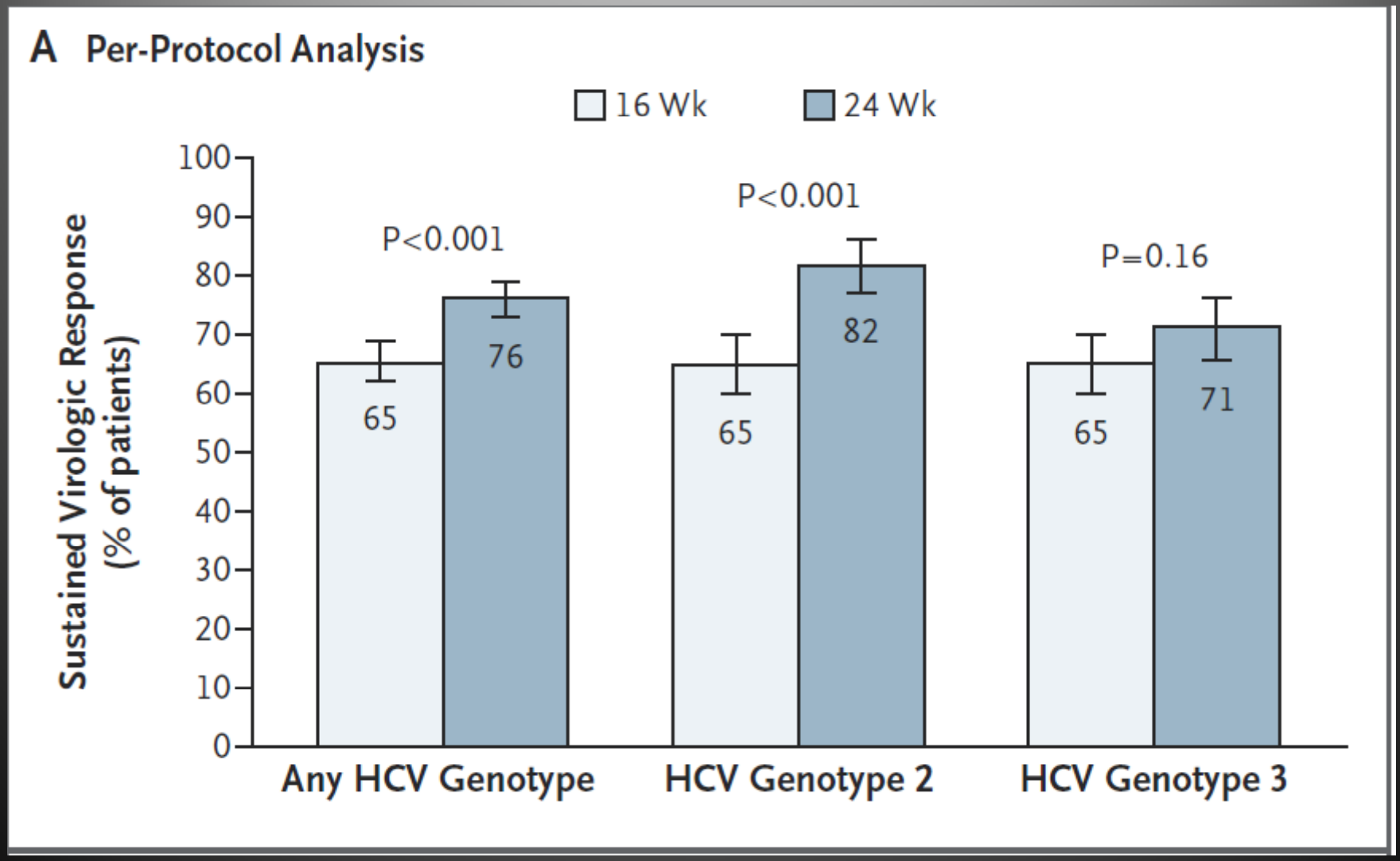
Jacobson IM et al., Hepatology 2007

Duration of 16 weeks is less effective than duration of 24 weeks



Schiffman L et al., New Engl J Med 2007

Duration of 16 weeks is less effective than duration of 24 weeks



Schiffman L et al., New Engl J Med 2007

- What are the true propositions:

A/ SVR rate is lower in genotype 3 patients than in Genotype 2 patients

B/ Younger age and low viral load are predictive factor of SVR

C/ patients who use alcohol and completed the treatment had a response comparable to that of nondrinkers

D/ Eligibility for anti-HCV treatment is reduced in past and recent drinkers.

E/ Recent alcohol use is associated with increased treatment discontinuation and lower SVR

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Independent predictive factors of SVR: lessons from Accelarate study

Parameter	p-value
Genotype Genotype 2 = higher probability of SVR than genotype 3	<0.0001
Log_{10} HCV RNA Lower viral load = higher probability of SVR	<0.0001
Age (years) Younger age = higher probability of SVR	0.029
Weight (kg) Lower weight = higher probability of SVR	<0.0001
Cirrhotic vs non-cirrhotic No cirrhosis = higher probability of SVR	<0.0001
ALT quotient Higher ALT quotient = higher probability of SVR	0.0004

Shiffman N Engl J Med 2007

Alcohol Use and Treatment of Hepatitis C Virus:

Table 4. Alcohol Use and HCV Treatment Candidacy (n = 4061)

Study group	No. screened	Candidate for treatment (%)	*P*
Drinker vs nondrinker			
Nondrinker	721	199 (28)	.01
Drinker	3340	787 (23)	
Amount of alcohol use			
Nondrinker	721	199 (28)	
<6 drinks/day	893	213 (24)	.04[a]
≥6 drinks/day	2447	563 (23)	
CAGE score			
<2	1681	452 (27)	.0003
≥2	2380	523 (22)	
Recent alcohol use			
None	2575	685 (27)	
Within past 12 months	1486	290 (20)	.0001

Anand B et al., Gastroenterology 2006

Alcohol Use and Treatment of Hepatitis C Virus:

Table 3. Effect of Alcohol Use on the ETR, SVR, and Early Discontinuation Rates in Patients With HCV Treated With Interferon and Ribavirin (n = 726)

Study group	No. treated	ETR (%)	SVR (%)	Early discontinuation (%)
Drinker vs non drinker				
Nondrinker	142	45 (32)	29 (20)	38 (27)
Drinker	584	173 (30)	104 (18)	177 (30)
Amount of alcohol use				
Nondrinker	142	45 (32)	29 (20)	38 (27)
<6 drinks/day	178	49 (27)	27 (15)	58 (33)
≥6 drinks/day	406	124 (31)	77 (19)	119 (29)
CAGE score				
<2	339	97 (29)	57 (17)	96 (28)
≥2	387	121 (31)	76 (20)	119 (31)
Recent alcohol use				
None	532	164 (31)	105 (20)	137 (26)
Within past 12 months	194	54 (28)	28 (14)[a]	78 (40)[b]

NOTE. Values in parentheses indicate percentages rounded off to the closest value. There was no significant difference in the response rates in any of the categories of alcohol use.

[a] $\chi^2 = 2.6$; $P = .06$.

[b] $\chi^2 = 14.2$; $P = .0002$.

Anand B et al., Gastroenterology 2006

Alcohol Use and Treatment of Hepatitis C Virus:

Table 5. Treatment Outcomes in Patients With HCV Infection Based on Their Drinking Habits in the Past 12 Months (n = 726)

Treatment response	Nondrinker (n = 532)	≤2 drinks/day (n = 80)	>2 drinks/day (n = 114)	*P*
ETR	164 (31)	28 (35)	26 (23)	NS
SVR	105 (20)	13 (16)	15 (13)	NS
Early treatment discontinuation	137 (26)	38 (48)	50 (44)	.0001

NOTE. Values in parentheses indicate percentages rounded off to the closest value.

Anand Bs, Gastroenterology 2006

- Pegylated alpha 2a 180 Ug/week and Ribavirin 800 mg/day was initiated:
- Planned duration of therapy was 24 weeks
- HCV RNA was detectable at week 4 (250 IU/ml, >2log drop)
- ALT 80 IU/l at week 4 ; Hb is 12 g/dl
- Tolerance is not good (weight-loss of 4 kg, irritability, sorrow)
- No relapse in alcohol consumption
- The patient was asking to shorten therapy when considering his poor tolerance

- What are the true propositions:

A/ RVR is a predictive factor of SVR in genotype 3 patients but not in Genotype 2 patients

B/ Shorten therapy to 16 weeks does not decrease the probability of SVR in genotype 2/3 patients with RVR

C/ The magnitude of differences in term of SVR between 16 weeks and 24 weeks is higher in patients without RVR than in those with RVR patients

D/ IL-28B genotype might be used to guide treatment for genotype 2/3 patients with RVR

E/ IL-28B genotype might be used to guide treatment for genotype 2/3 patients with RVR

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D/ IL-28B genotype might be used to guide treatment for genotype 2/3 patients with RVR

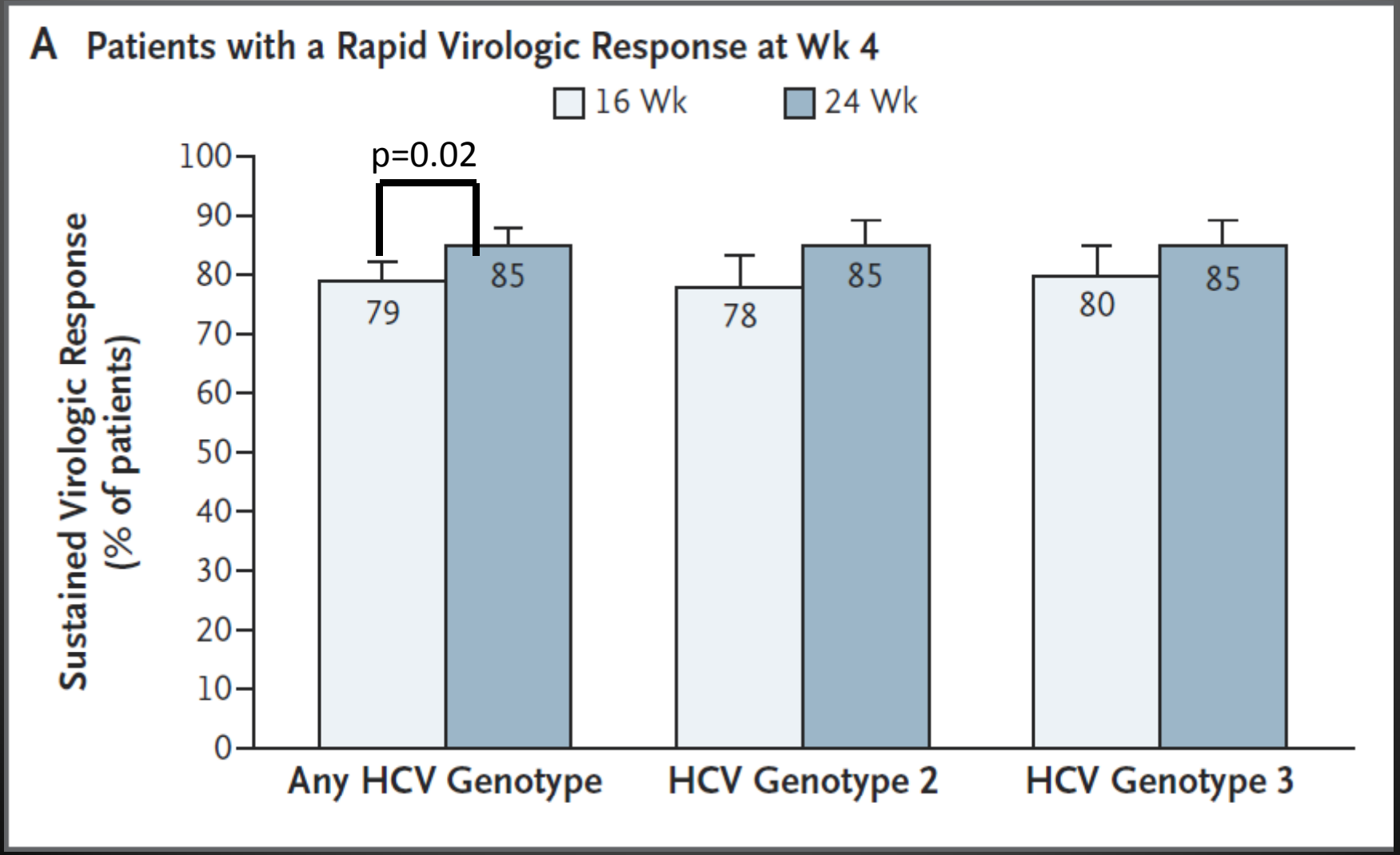
E/ **IL-28B genotype might be used to guide treatment for genotype 2/3 patients without RVR**

Genotypes 2/3 patients with RVR disclose high rates of SVR

Patients and Point in Study	Standard-Duration Regimen (24 Weeks)					
	All Patients		Negative at Week 4 (Early Response)		Positive at Week 4 (No Early Response)	
	no.	% *(95% CI)*	*no.*	% *(95% CI)*	*no.*	% *(95% CI)*
All patients	70		45	64.3	25	35.7
End of treatment	55	79 (68–88)	42	93 (86–100)	13	52 (32–71)
End of follow-up	53	76 (66–86)	41	91 (83–99)	12	48 (28–67)
HCV genotype 2	53		35		18	
End of treatment	42	79 (68–90)	32	91 (82–100)	10	56 (32–78)
End of follow-up	40	76 (64–87)	31	89 (78–99)	9	50 (27–73)
HCV genotype 3	17		10		7	
End of treatment	13	76 (59–97)	10	100	3	43 (6–79)
End of follow-up	13	76 (56–97)	10	100	3	43 (6–79)

Mangia A et al., Engl J Med 2005

24 weeks-duration is superior to 16 weeks-duration regardless of RVR response



Schiffman L et al., New Engl J Med 2007

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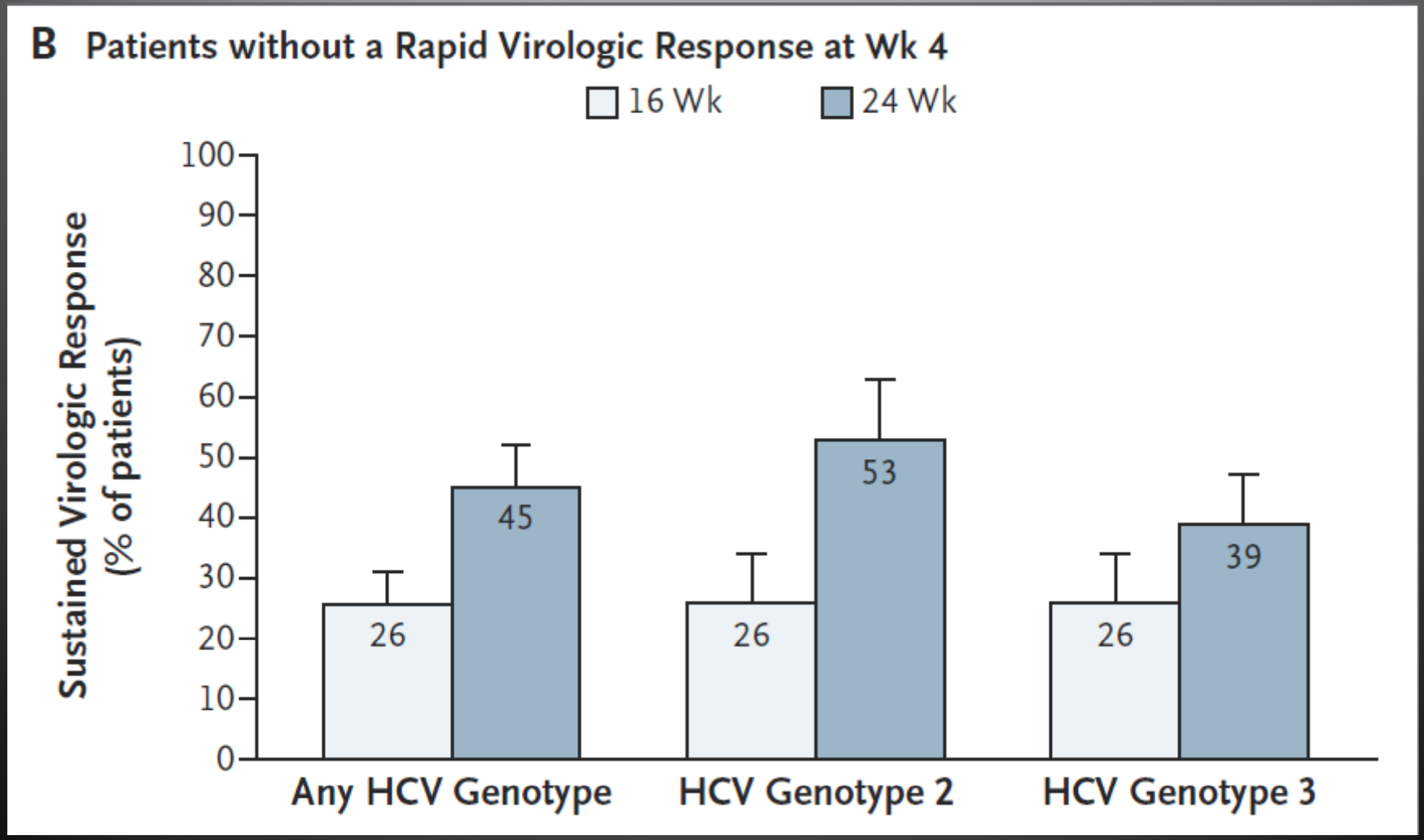
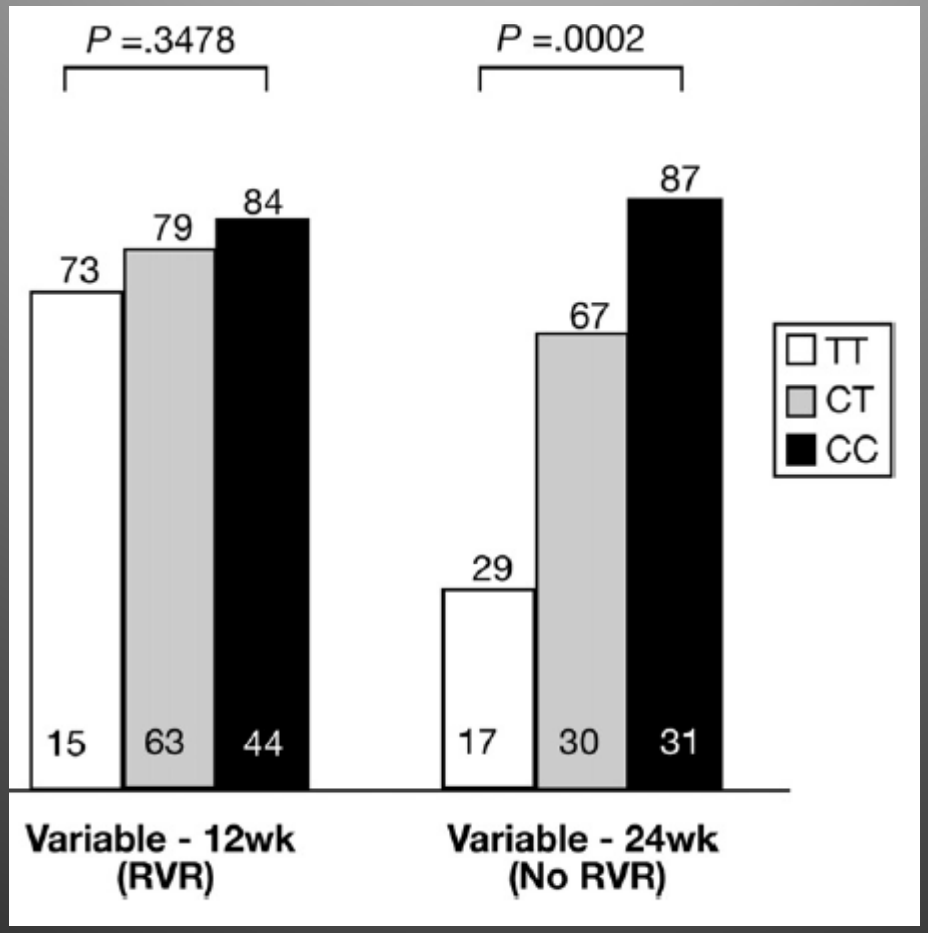


Schiffman L et al., New Engl J Med 2007

An *IL28B Polymorphism Determines SVR respose in* Genotype 2/3 Patients Who Do Not Achieve RVR



Mangia A et al., Gastroenterology2010

- Patient were treated with Prozac® during 36 weeks
- Patient stopped pegylated therapy at weeks 24
- RNA was negative at week 8 and at end of therapy
- RNA was negative 6 months after end of therapy