Hépatite C
Comment convertir en vies gagnées les progrès thérapeutiques?

Accès accru au traitement plus important que l'amélioration du taux de RVS

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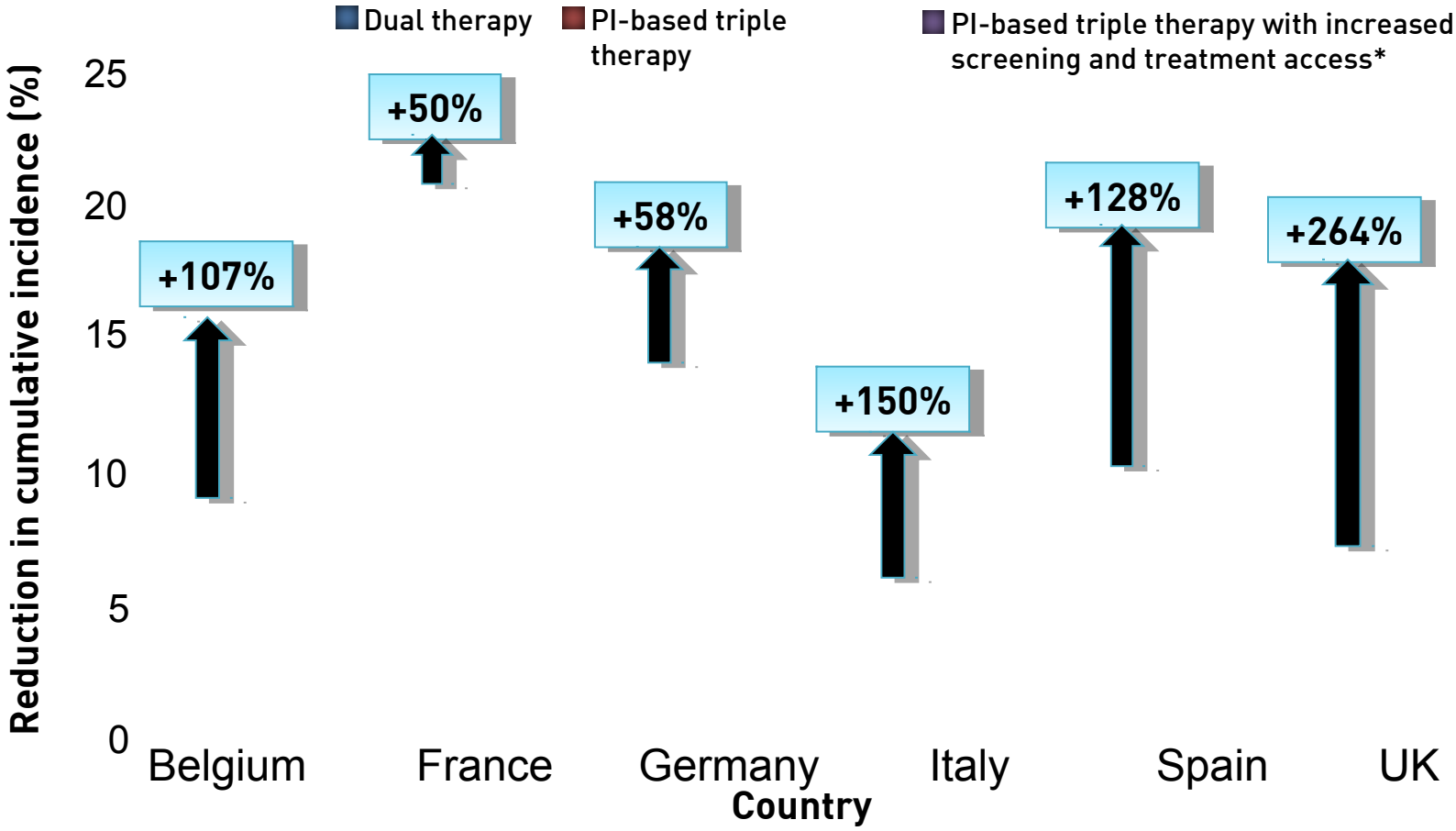
	Belgium	France	Germany	Italy	Spain	UK
HCV Screening, %						
Observed, % (yr)	37 (2000)	57 (2004)	40 (2004)	40 (2005)	33 (2008–9)	30 (2004)
Estimated in 2011, %	50	64	48	46	35	34
HCV Genotype						
G1, %	60	56	60	62	65	44
G2/3, %	27	32	37	34	23	53
Other genotypes %	13	12	3	4	12	3

Accès accru au traitement plus important que l'amélioration du taux de RVS

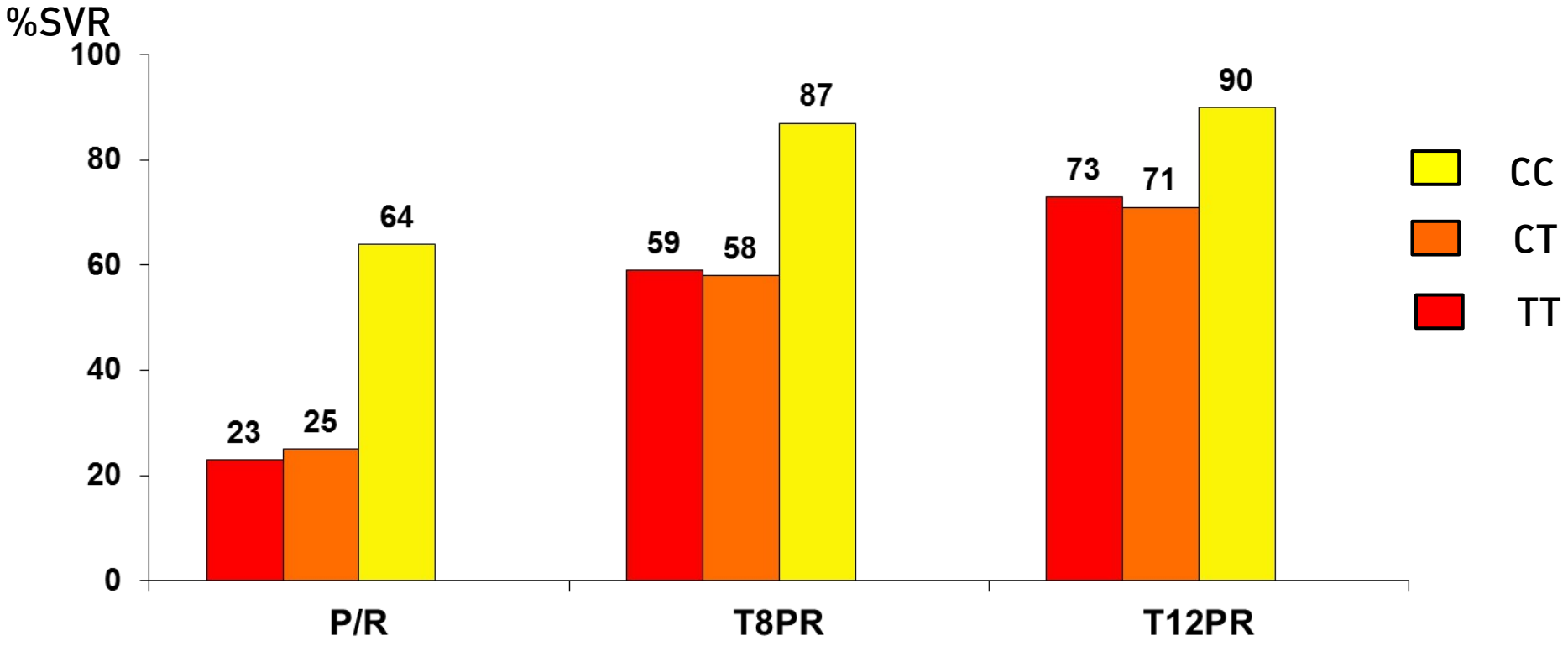


Dramatic reduction in HCV-related deaths with PI-based triple therapy + reinforced screening and treatment access (75% de dépistage et 50% de G1 traités)

Accès accru au traitement plus important que l'amélioration du taux de RVS

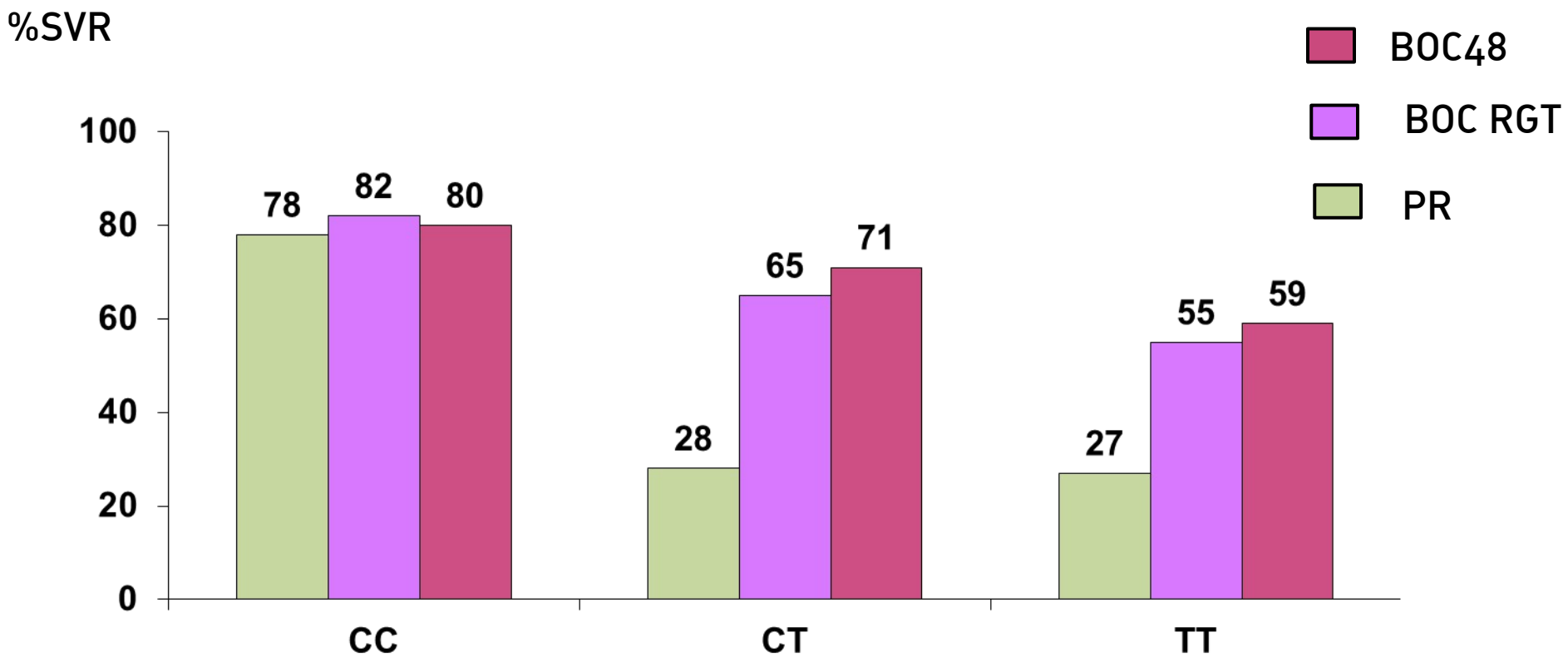
Dans un pays n’ayant pas les nouvelles molécules

PR *vs* TVR: SVR rate according to IL28B in naïve patients *(ADVANCE)*



Jacobson I et al. EASL 2011

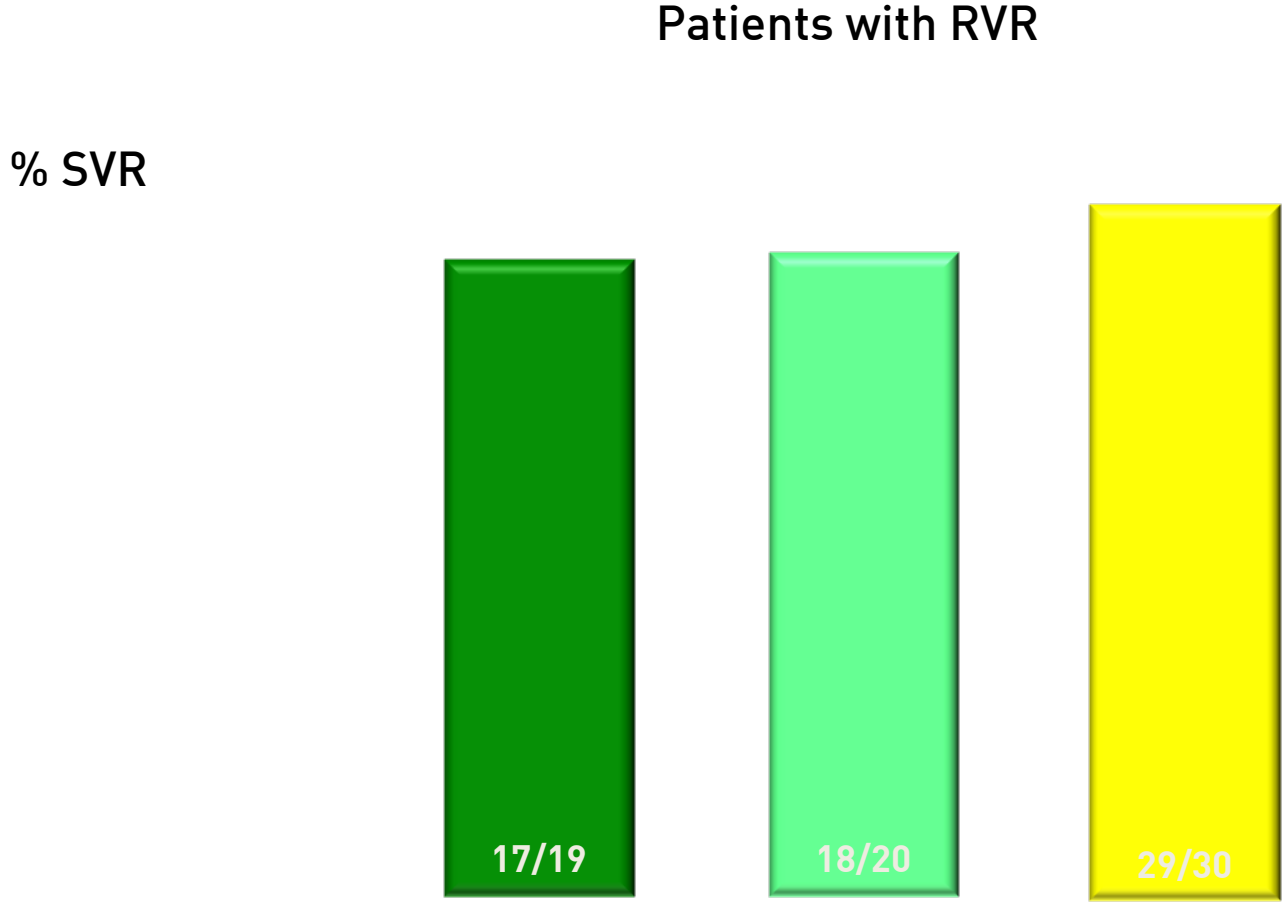
PR *vs* BOC: SVR rate according to IL28B in naïve patients *(SPRINT-2)*



Poordad F et al. Gastroenterology 2012

High rate of SVR in patients with negative HCV RNA at W4 of lead-in

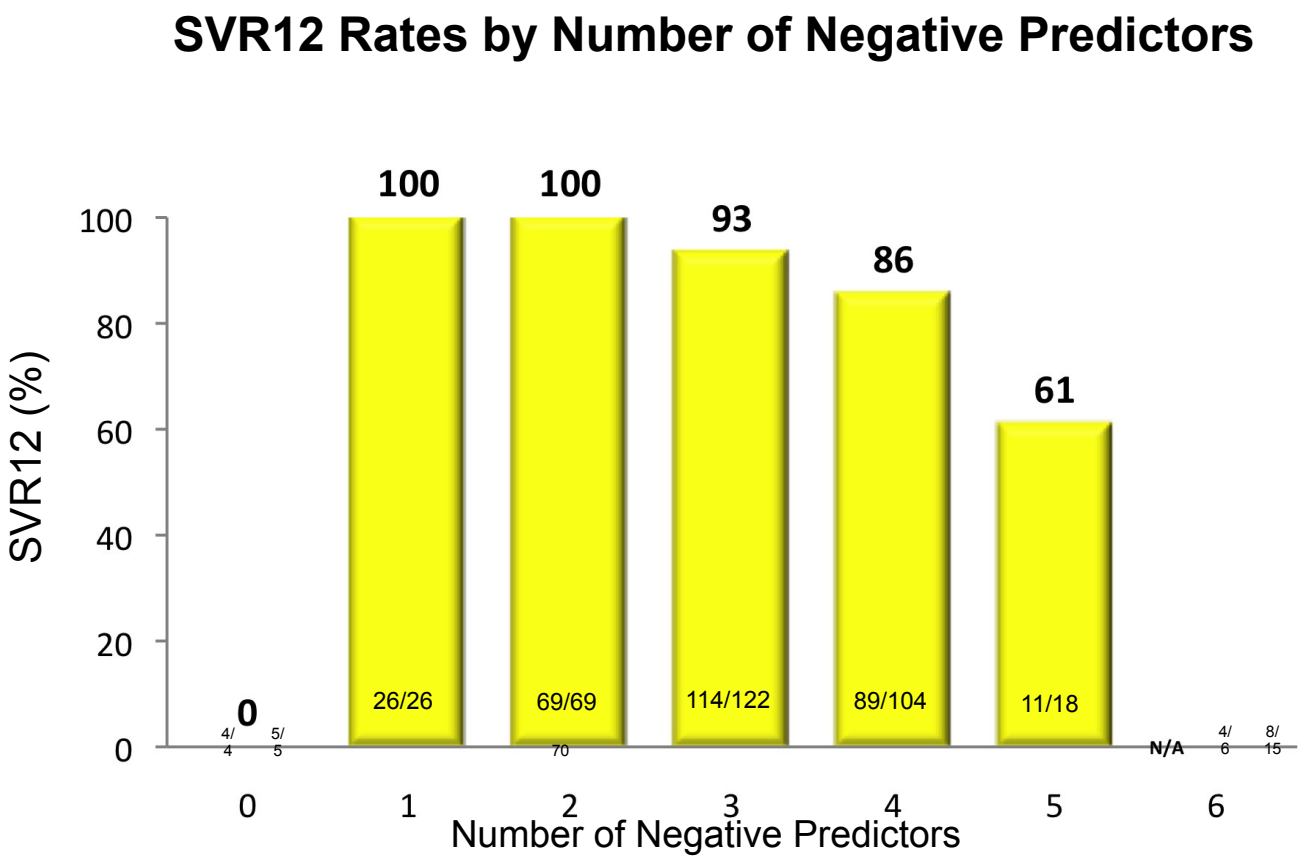
(SPRINT-2)



Vierling JM. et al. J Hepatol 2011: 54: S19

SVR rates of SOF + PR among patients with multiple negative predictive factors (ATOMIC, NEUTRINO)

339 GT1 patients included in SOF-based triple therapy studies
Negative predictors: cirrhosis, *IL28B* non-CC, HCV RNA ≥ 800,000 IU/mL, body weight ≥ 75kg, male gender



Foster G, EASL, 2014

EASL Guidelines 2014

Recommendation

- Patients infected with HCV genotype 1 can be treated with a combination of weekly pegylated IFN-α, daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively), and daily sofosbuvir (400 mg) 12 weeks **(Recommendation A1)**

Recommendations

- Patients infected with HCV genotype 1 can be treated with a combination of weekly pegylated IFN-α, daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively), and daily simeprevir (150 mg) **(Recommendation A1)**
- This combination is not recommended in patients infected with subtype 1a who have a detectable Q80K substitution in the NS3 protease sequence at baseline, as assessed by population sequencing (direct sequence analysis) **(Recommendation A2)**
- Simeprevir should be administered 12 weeks in combination with pegylated IFN-α and ribavirin. Pegylated IFN-α and ribavirin should then be administered alone for an additional 12 weeks (total treatment duration 24 weeks) in treatment-naïve and prior relapser patients, including cirrhotics, and for an additional 36 weeks (total treatment duration 48 weeks) in prior partial and null responders, including cirrhotics **(Recommendation B1)**
- HCV RNA levels should be monitored on treatment. Treatment should be stopped if HCV RNA level is ≥25 IU/ml at treatment week 4, week 12 or week 24 **(Recommendation A2)**

Dans un pays ayant les nouvelles molécules

EASL Guidelines 2014

Recommendations

- Patients infected with HCV genotype 1 can be treated with an interferon-free combination of daily sofosbuvir (400 mg) and daily simeprevir (150 mg) for 12 weeks **(Recommendation B1)**
- Preliminary results do not indicate a major advantage of adding ribavirin to this regimen. However, adding daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively) should be considered in patients with predictors of poor response to anti-HCV therapy, especially prior non-responders and/or patients with cirrhosis **(Recommendation B1)**

Recommendations

- Patients infected with HCV genotype 1 can be treated with an interferon-free combination of daily sofosbuvir (400 mg) and daily daclatasvir (60 mg) 12 weeks in treatment-naïve patients or 24 weeks in treatment-experienced patients, including those who failed on a triple combination of pegylated IFN-α, ribavirin and either telaprevir or boceprevir (pending data with 12 weeks of therapy in treatment-experienced patients) **(Recommendation B1)**
- Preliminary results do not indicate a major advantage to adding ribavirin to this regimen. However, adding daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively) should be considered in patients with predictors of poor response to anti-HCV therapy, especially prior non-responders and/or patients with cirrhosis **(Recommendation B1)**

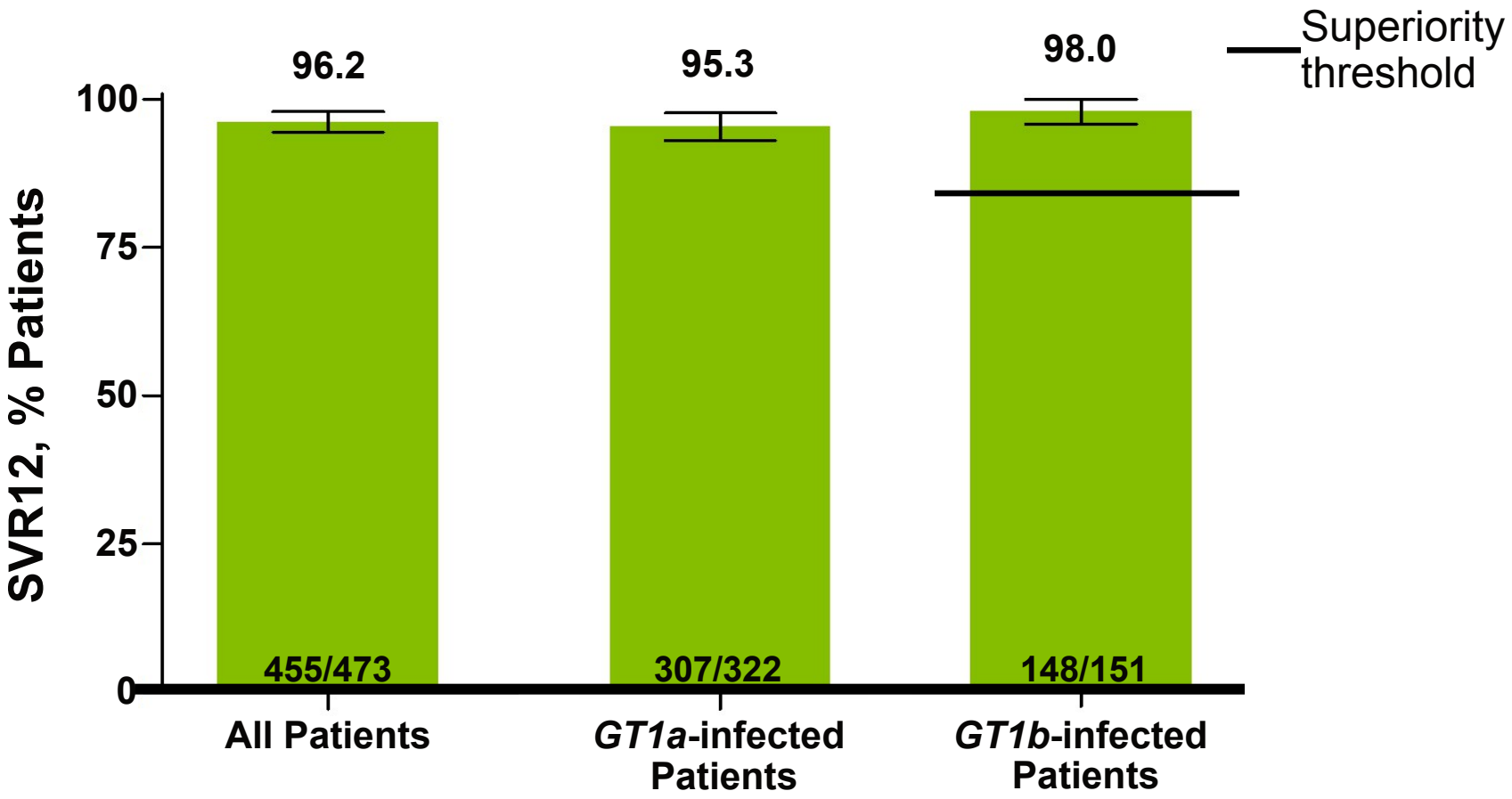
LDV-SOF

Table 2. Response during and after Treatment.

Response	12-Wk Regimen		24-Wk Regimen	
	LDV–SOF (N=214)	LDV–SOF + RBV (N=217)	LDV–SOF (N=217)	LDV–SOF + RBV (N=217)
HCV RNA <25 IU/ml				
During treatment — no./total no. (%)*				
At week 2	174/213 (82)	181/217 (83)	179/216 (83)	180/217 (83)
At week 4	213/213 (100)	215/217 (99)	216/216 (100)	217/217 (100)
At week 12	213/213 (100)	214/214 (100)	213/214 (>99)	216/216 (100)
After end of treatment — no. (%)				
At week 4	211 (99)	213 (98)	215 (99)	215 (99)
At week 12	211 (99)	211 (97)	212 (98)	215 (99)
Virologic failure during treatment — no.	0	0	1	0
Relapse — no.	1	0	1	0
Lost to follow-up — no.	2	4	2	2
Withdrew consent — no.	0	2	1	0

Afdal N, NEJM 2014

SAPPHIRE-I : Treatment Naïve GT1 HCV



3D: Co-formulated ABT-450/r/ombitasvir, 150 mg/100 mg/25 mg QD; dasabuvir, 250 mg BID

RBV: 1000-1200 mg daily according to body weight (<75 kg and ≥75kg, respectively)

The ITT SVR12 rate of 98.0% (95% CI, 95.8-100) in GT1b-infected patients is superior to a calculated historical SVR12 control rate of 80% (95% CI, 75.0-84.0)

Feld et al. *N Engl J Med* 2014

La vérité et les faits sont dépendants du temps

- Une assertion est vraie si elle vérifiée par les faits
- Les faits changent avec le temps, et donc la vérité est relative
- Certaines vérités vont durer plus longtemps que d'autres

Hall JC, Platell C. Lancet 1997;350:1752

Conclusions

- Les avis d'experts devraient prendre en compte les incertitudes de leurs assertions

- Le traitement à large échelle permettra une diminution de la morbidité et de la mortalité

- Les stratégies thérapeutiques devraient être ciblées sur le bénéfice de survie en terme de population générale

- Un développement thérapeutique étourdissant