Interferon-free treatment for Hepatitis C – how and when?

24th ECCMID, Barcelona, Spain, Tuesday, 13th May, 2014

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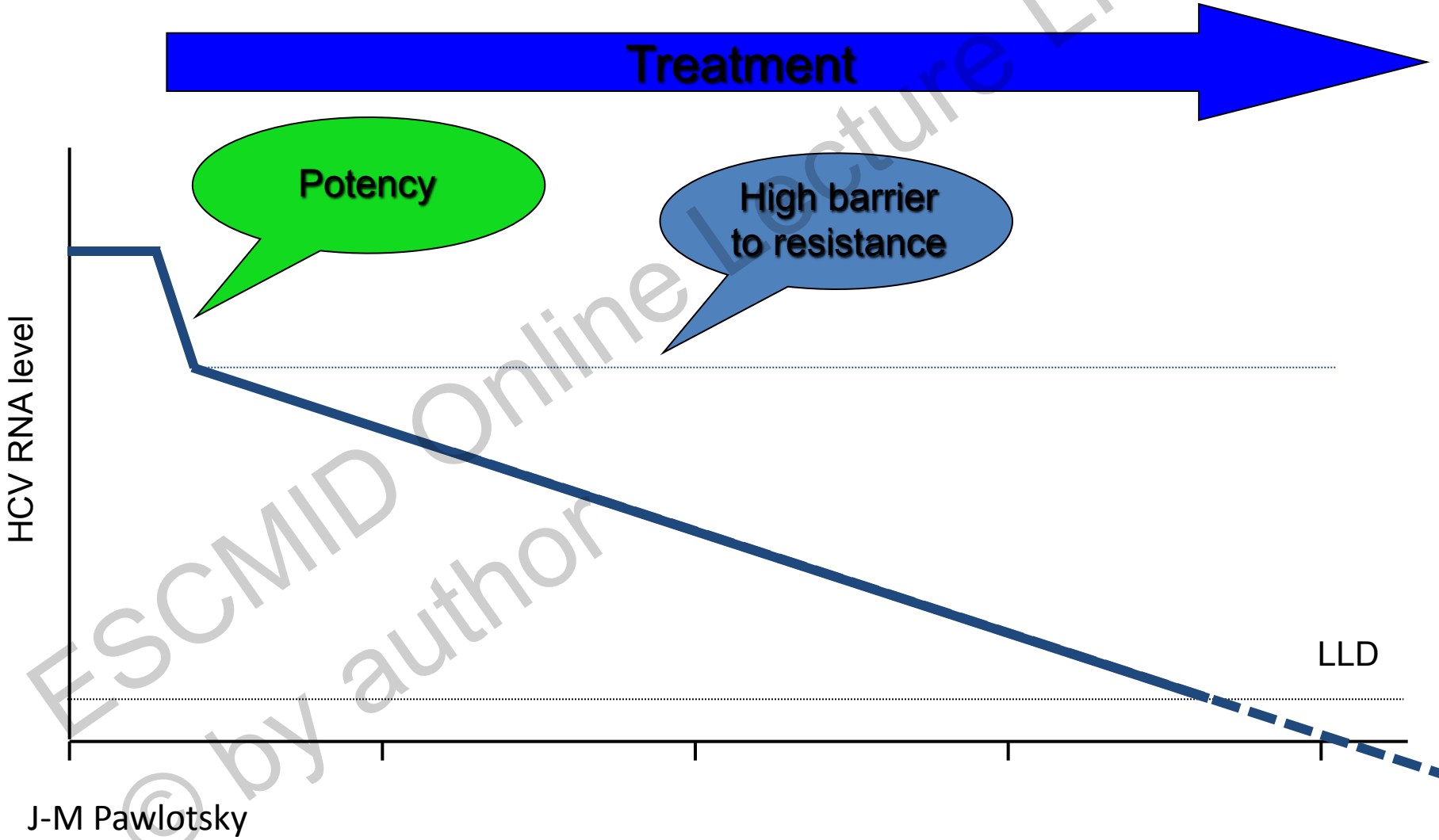
HCV is an easy-to-cure virus

J-M Pawlotsky

Curing HCV Infection



The new DAAs……

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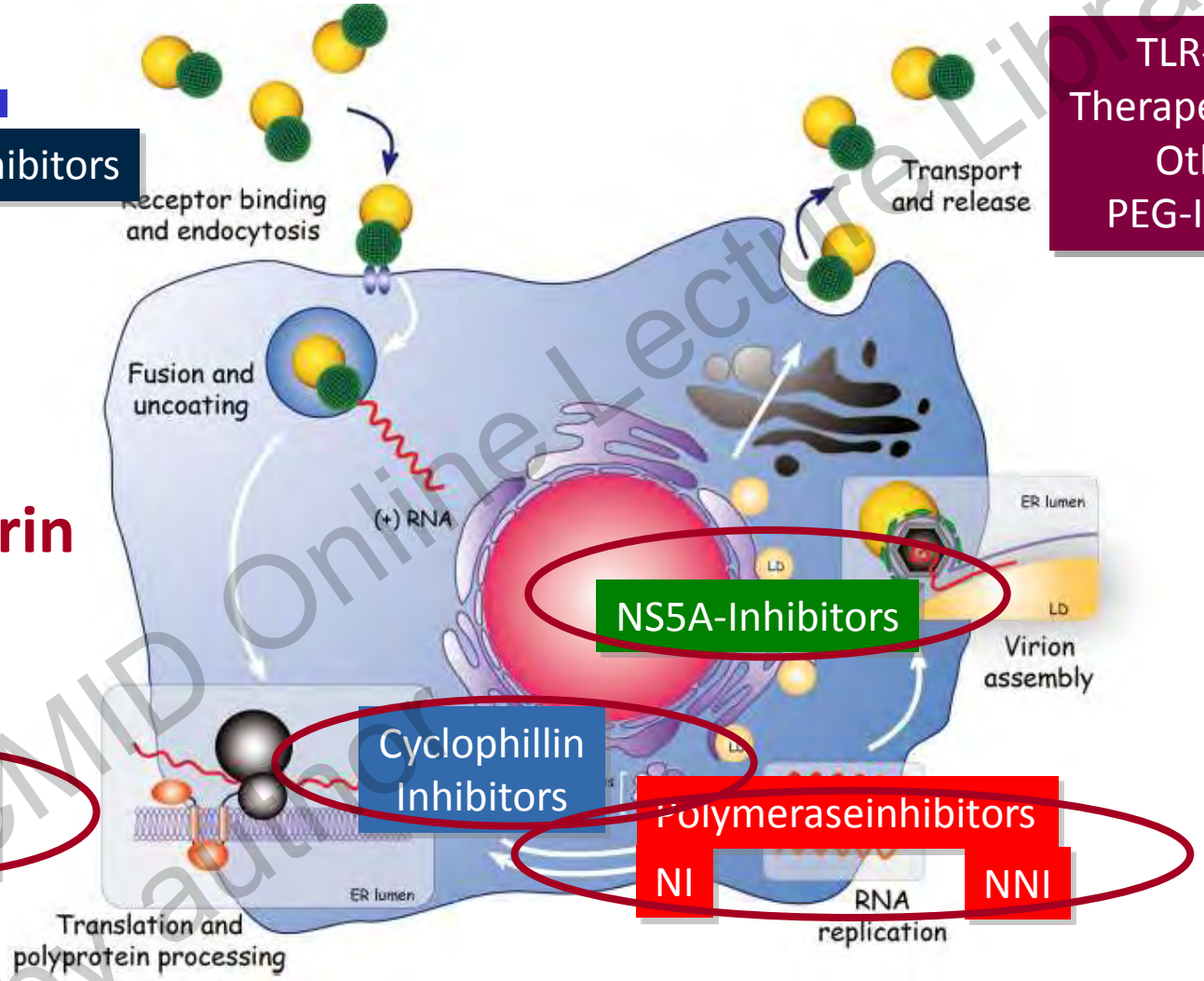
Entry-Inhibitors

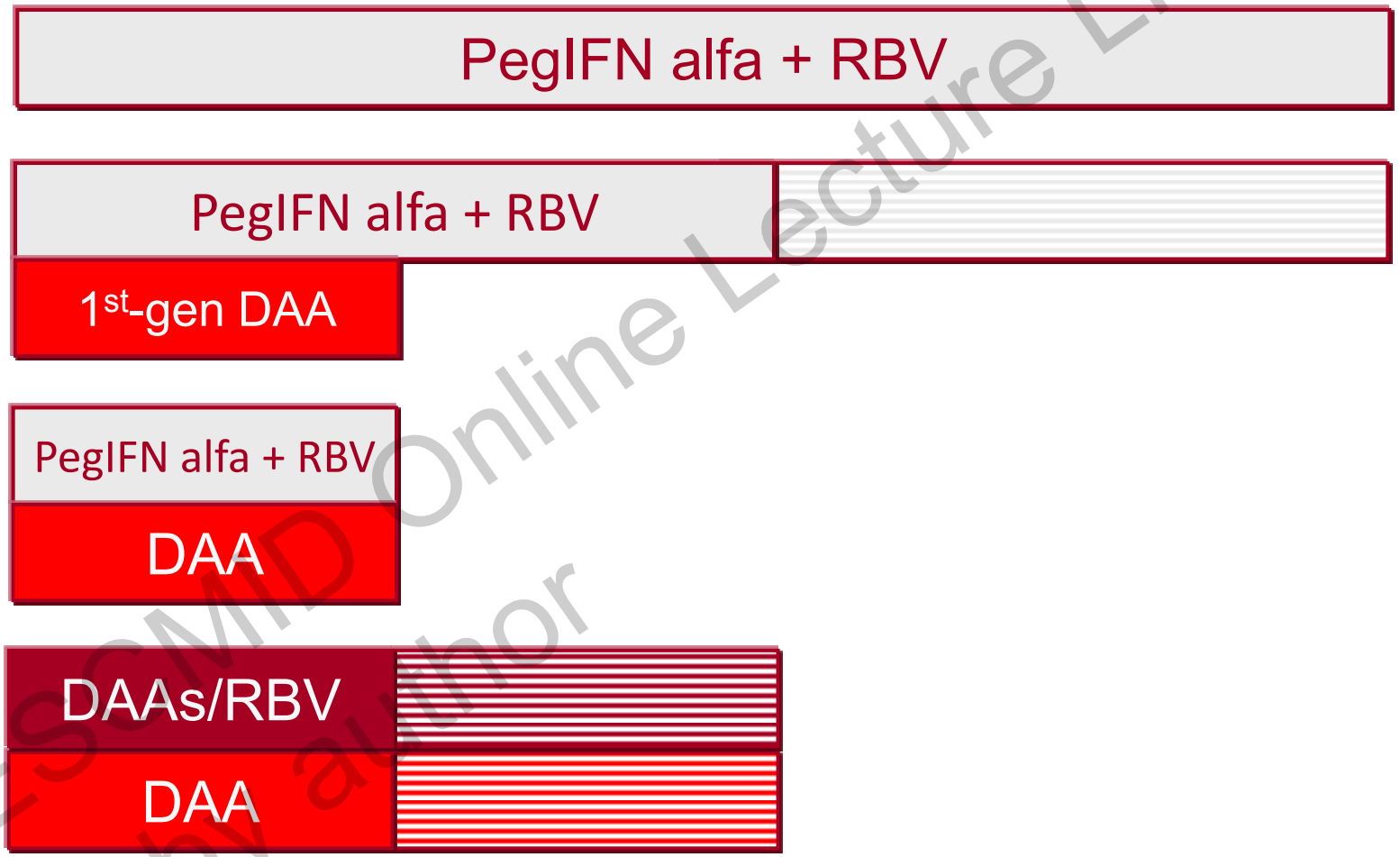
TLR-Agonists
Therapeutic Vaccine
Other IFNs
PEG-IFN lambda



Ribavirin

Popescu C-L & Dubuisson J. *Biol Cell* 2009;102:63-74.

Chronic hepatitis C: treatment concepts 2014/15



New Approved DAAs

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Sofosbuvir

Nucleotide analogue
400 mg qd
All genotypes
High barrier
January 2014

Simeprevir

Protease inhibitor
150 mg qd
Genotypes 1 and 4
Low barrier
May 2014

Daclatasvir

NS5A inhibitor
60 mg qd
All genotypes
Low barrier
September 2014

IFN-free Treatment Options in 2014

Sofosbuvir + ribavirin	**12-24 weeks**
Sofosbuvir + simeprevir (± ribavirin)	**12 weeks**
Sofosbuvir + daclatasvir (± ribavirin)	**12-24 weeks**

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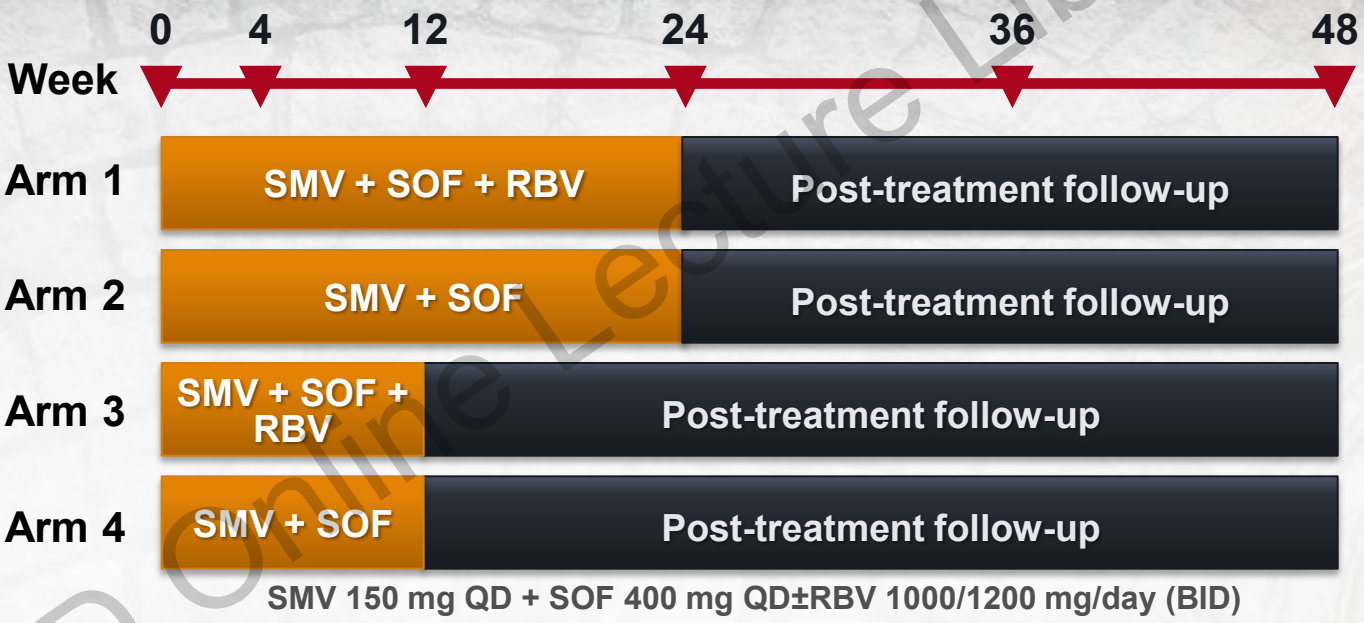
HCV genotype 1

COSMOS Study Design: Randomized, Multicenter, Open-label Trial

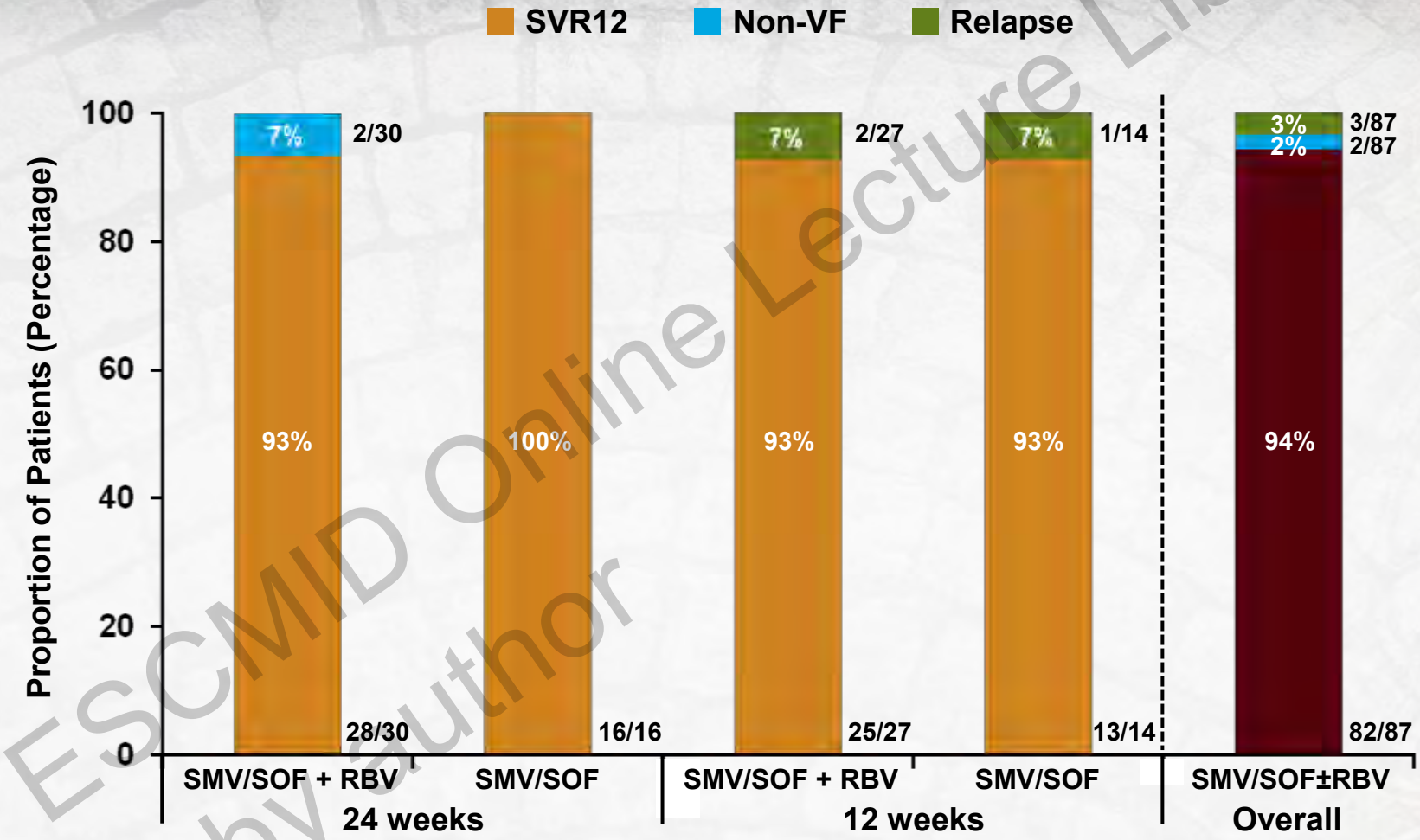


Randomised 2:1:2:1

- Cohort 1: METAVIR F0-F2, prior null responders
- Cohort 2: METAVIR F3-F4, prior null responders or treatment-naïve
  - Stratified by treatment history, HCV GT 1a/1b
- Primary endpoint: SVR12
- Secondary endpoints: RVR, on-treatment failure, relapse rate, safety and tolerability

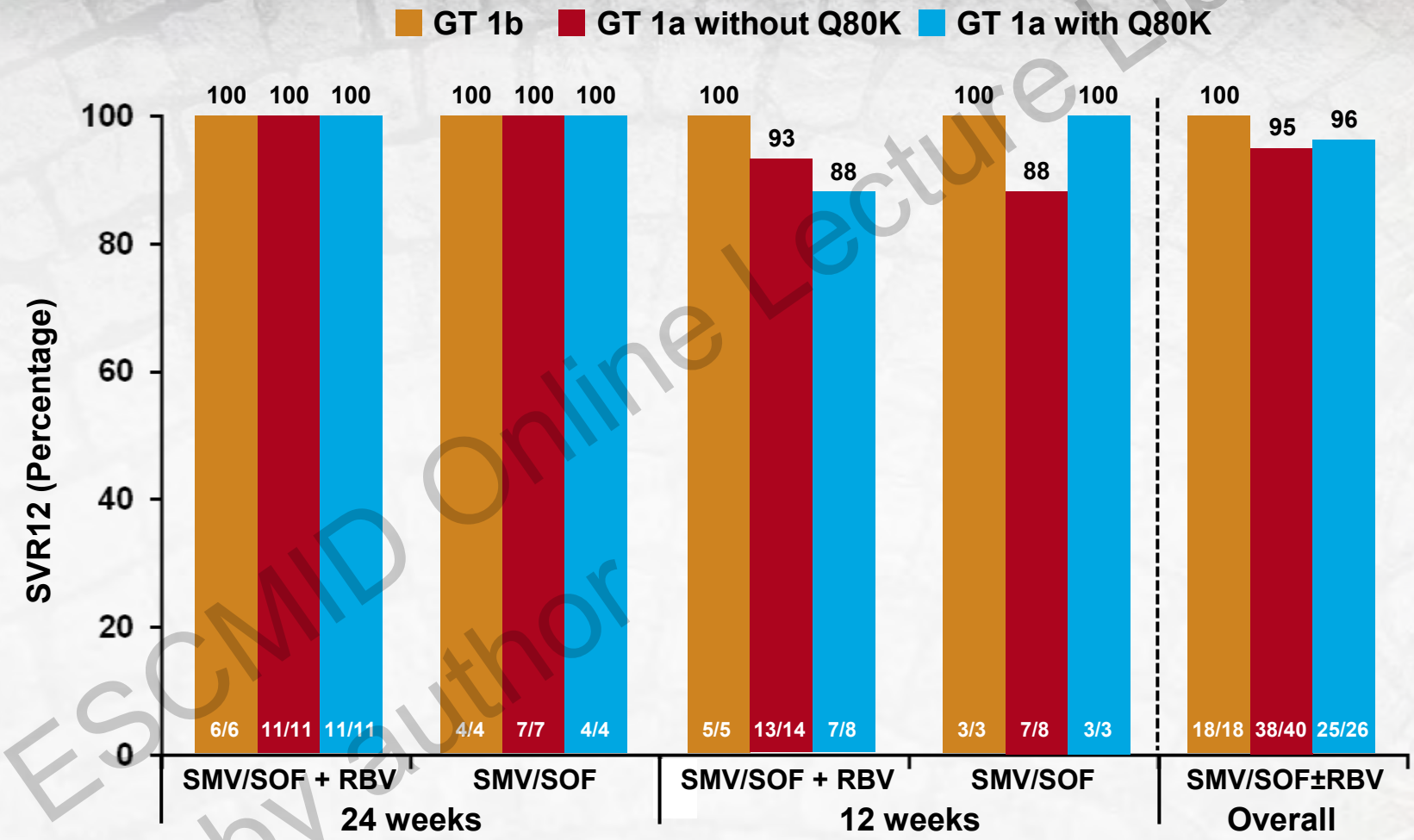
Lawitz E, et al. 49th EASL; London, England; April 9-13, 2014. Abst. O165.

COSMOS Cohort 2: SVR12 – Primary Endpoint (ITT population)



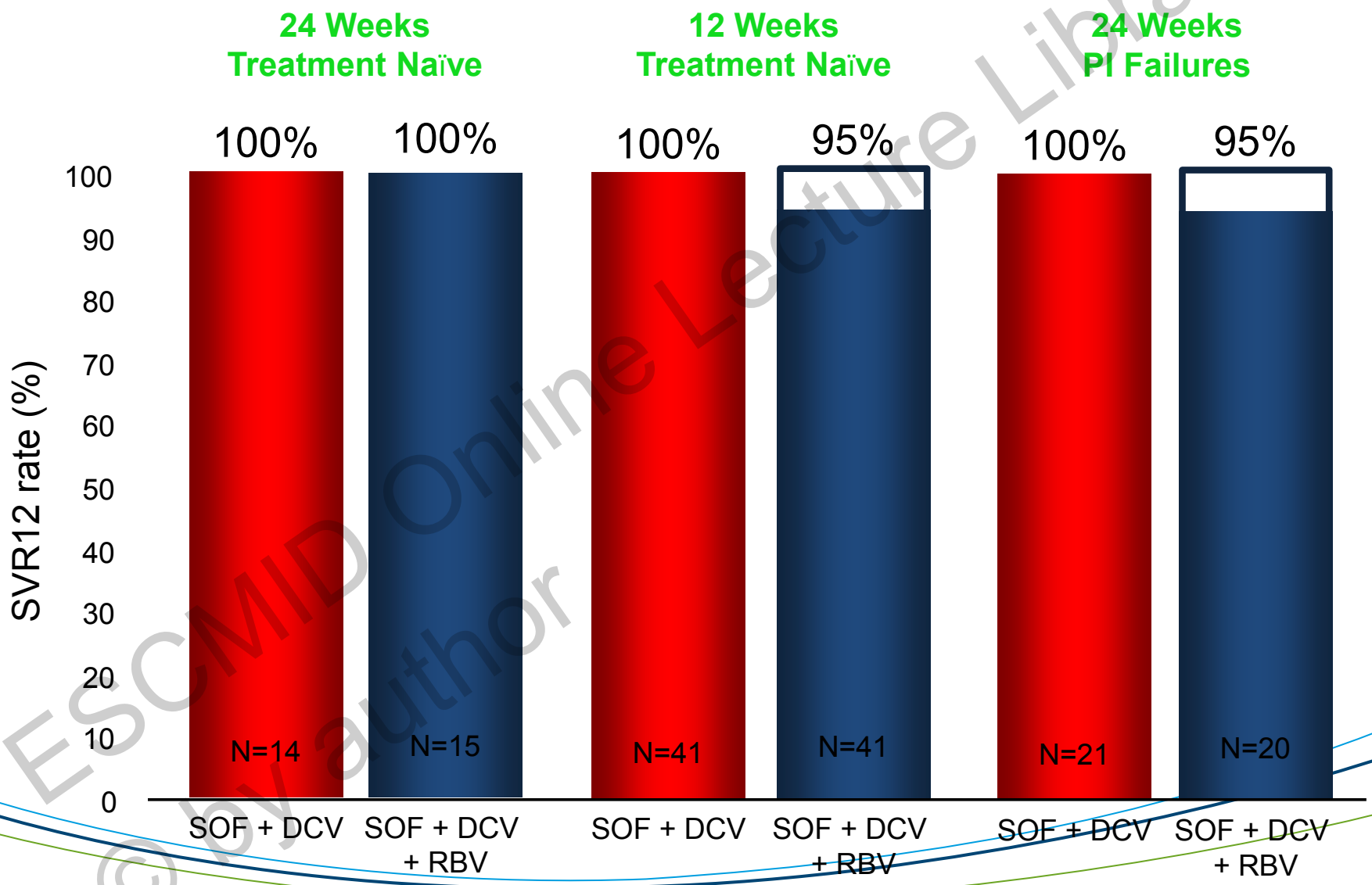
Lawitz E, et al. 49th EASL; London, England; April 9-13, 2014. Abst. O165.

COSMOS Cohort 2: SVR12 by HCV GT 1 Subtype and Baseline NS3 Q80K Polymorphism (excluding non-VF*)



Lawitz E, et al. 49th EASL; London, England; April 9-13, 2014. Abst. O165.

Sofosbuvir + Daclatasvir ± RBV



Sulkowski et al., N Engl J Med 2014;370:211-21

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HCV genotype 2

HCV Genotype 2

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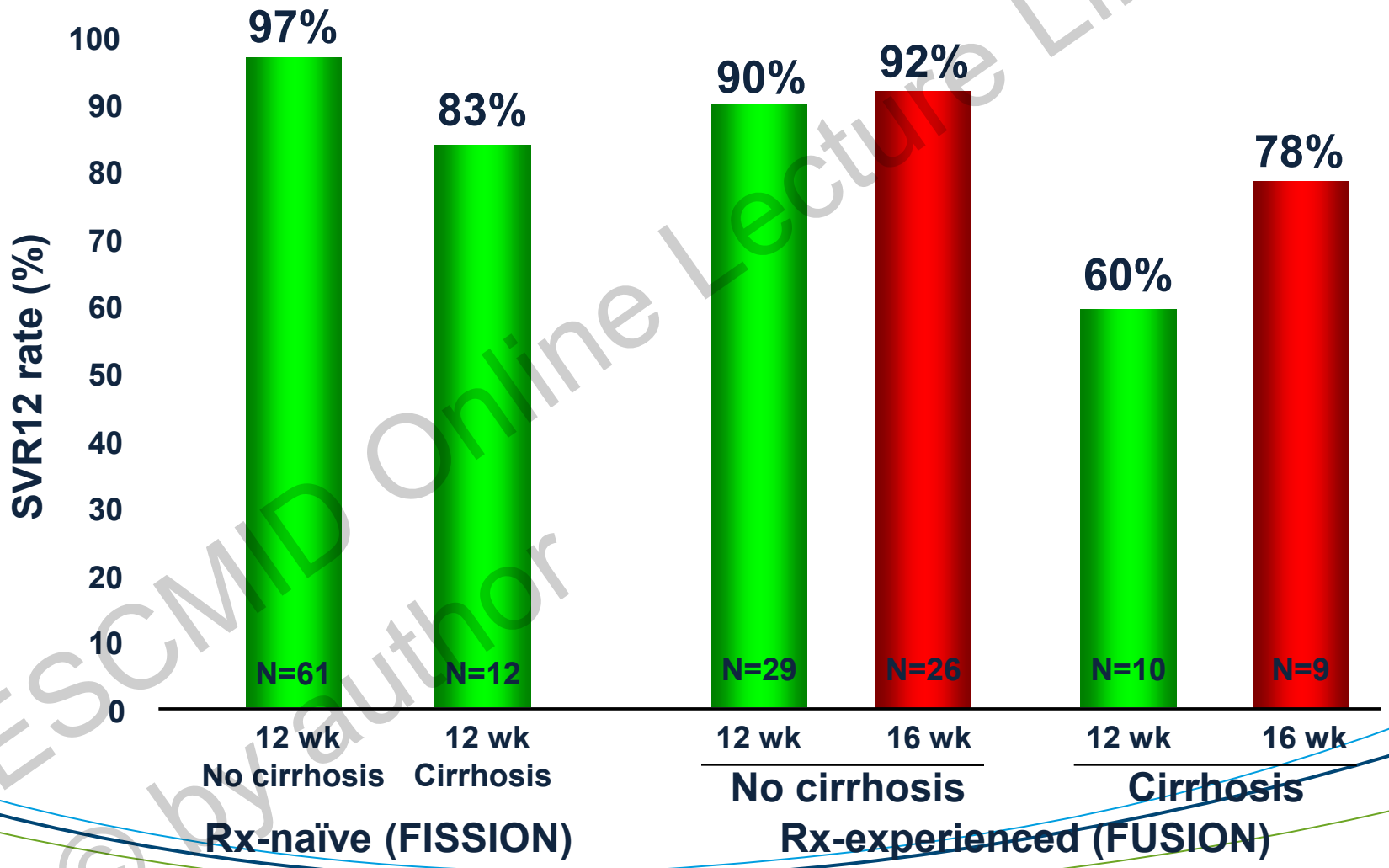
Sofosbuvir + ribavirin

Sofosbuvir + RBV in Gen 2

Phase III, 12/16 weeks, cirrhosis vs no cirrhosis



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

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HCV genotype 3

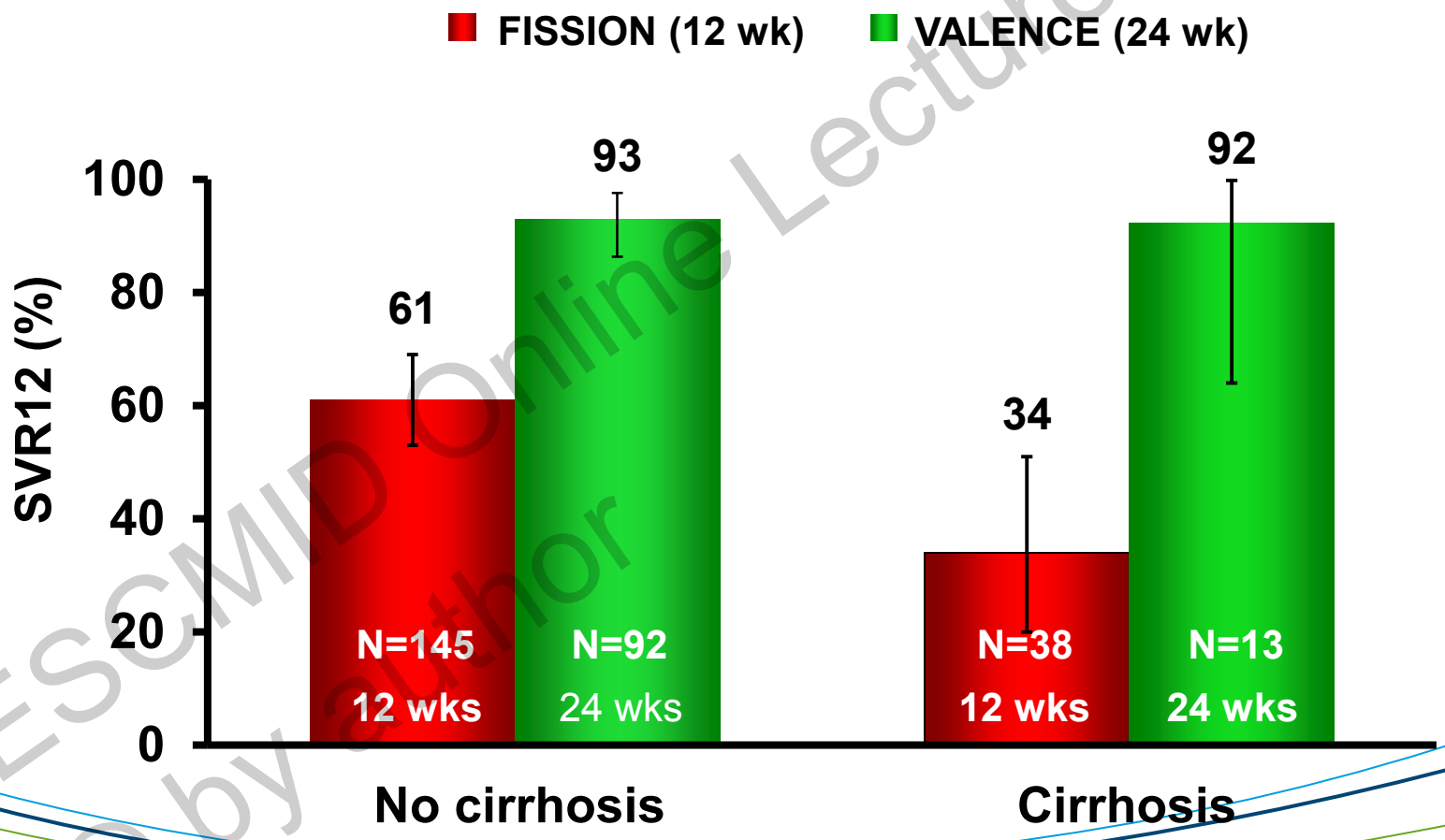
HCV Genotype 3

Sofosbuvir + ribavirin

Sofosbuvir + daclatasvir (± ribavirin)

Sofosbuvir + RBV in GT 3

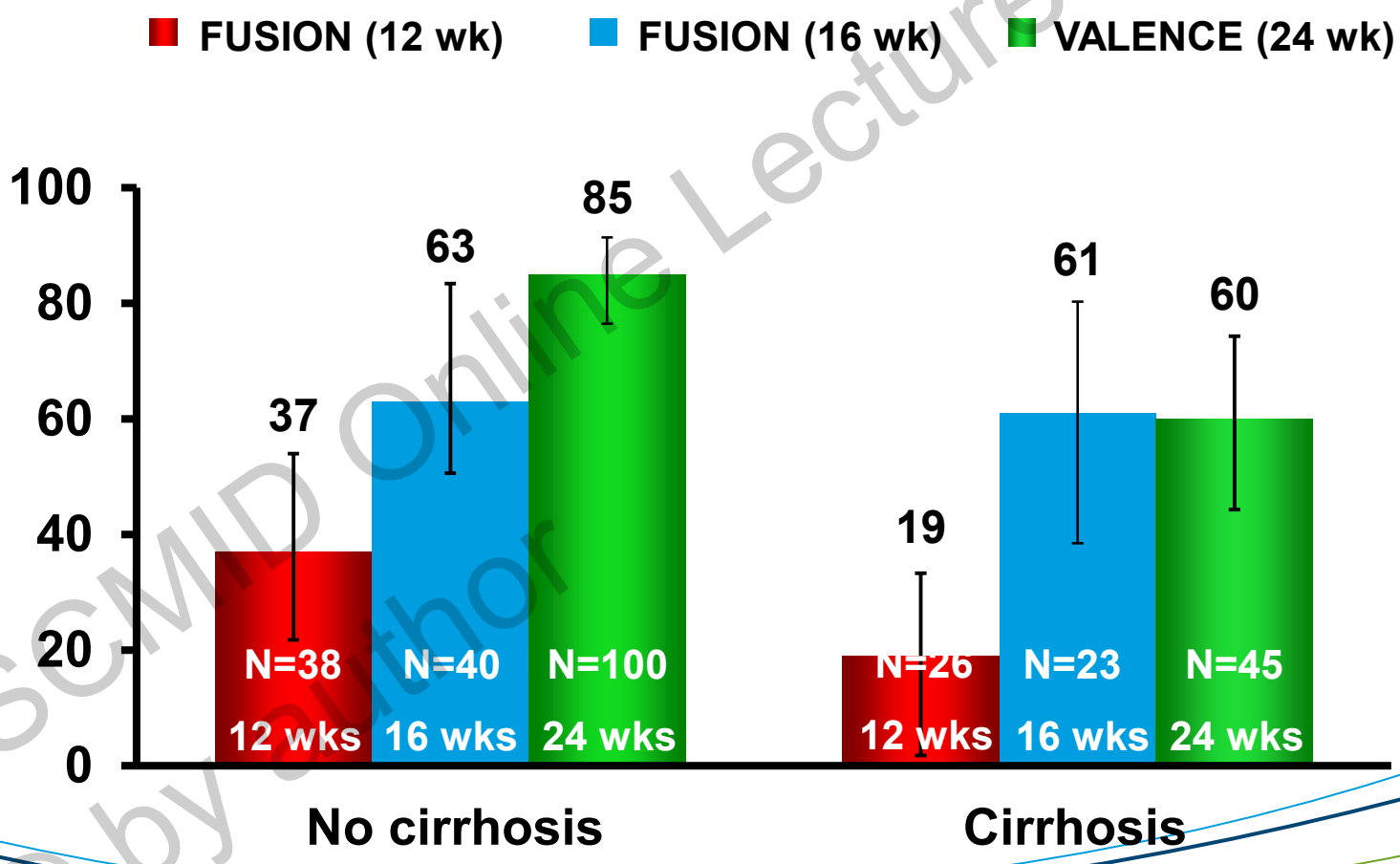
Phase III, Treatment-naive



Lawitz et al., N Engl J Med 2013;368:1878-87; Zeuzem et al., AASLD 2013; FDA hearings, October 25, 2013

Sofosbuvir + RBV in GT 3

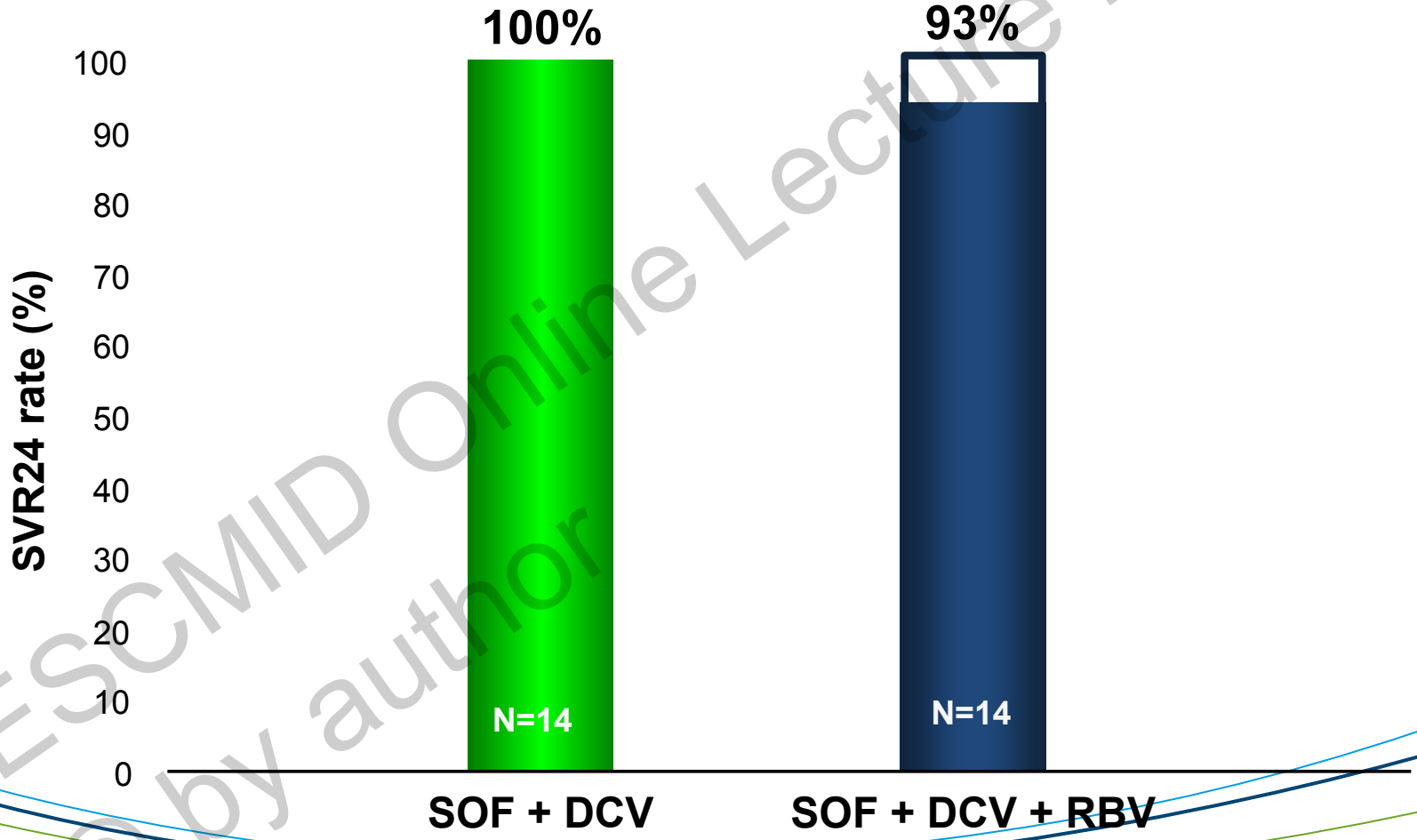
Phase III, Treatment-experienced



Jacobson et al., N Engl J Med 2013;368:1867-77; Zeuzem et al., AASLD 2013; FDA hearings, October 25, 2013

Sofosbuvir + Daclatasvir ± RBV

Treatment-naive, Genotype 2, 3



Sulkowski et al., AASLD 2012

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HCV genotype 4

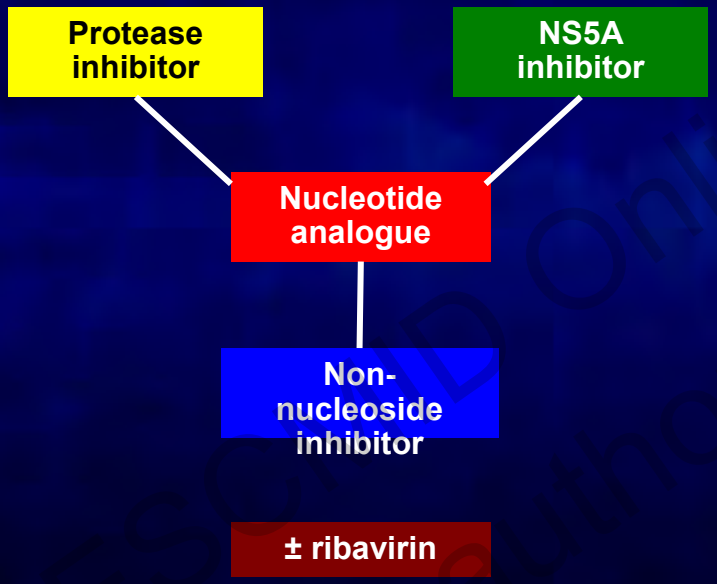
IFN-free Options for Genotype 4

- **No data on the combination of sofosbuvir plus simeprevir**
- **No data on the combination of sofosbuvir plus daclatasvir**

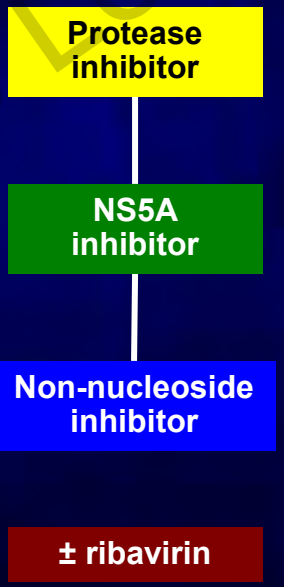
What happens in 2015 and beyond?

IFN-Free Combination Options

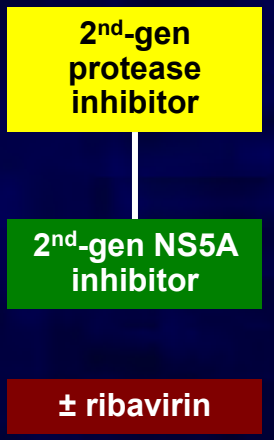
Option 1



Option 2



Option 3



Pawlotsky JM, Gastroenterology 2014; May;146(5):1176-1192

IFN-free Treatment Options beyond 2014

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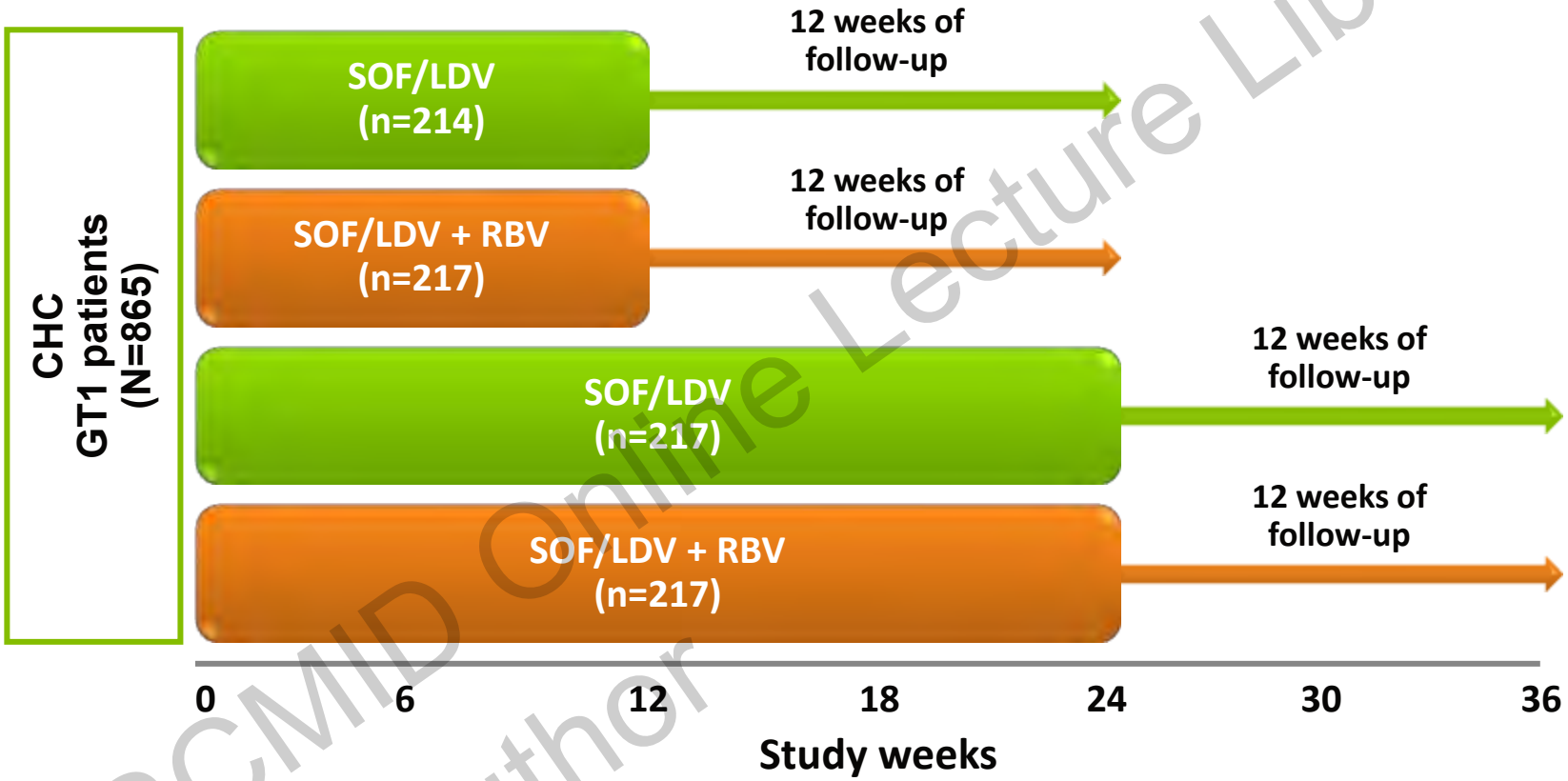
Sofosbuvir + ledipasvir ± GS-9669 or GS-9451	6-12 weeks
ABT-450/r/ombitasvir + dasabuvir (± ribavirin)	8?-12 weeks
MK-5172 + MK-8742 (± ribavirin)	12 weeks
Other DAA combinations	

ION-1: SOF/LDV ± RBV in GT1 treatment-naive patients – study design



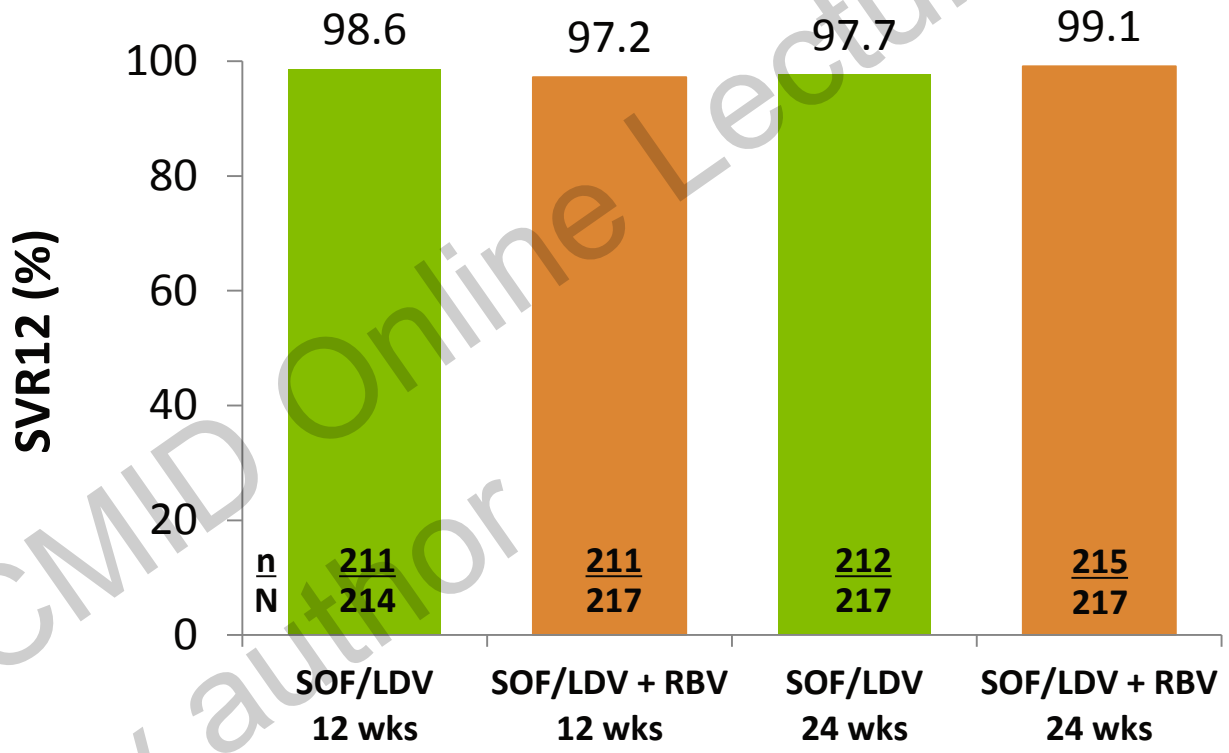
- Including 136 (15.7%) of patients with cirrhosis

SOF = 400 mg/day; LDV = 90 mg/day;
RBV = 1000–1200 mg daily according to body weight.

Afdhal N, *et al. New Engl J Med* 2014; online DOI: 10.1056/NEJMoa1402454.

ION-1: SOF/LDV ± RBV in GT1 treatment-naive patients

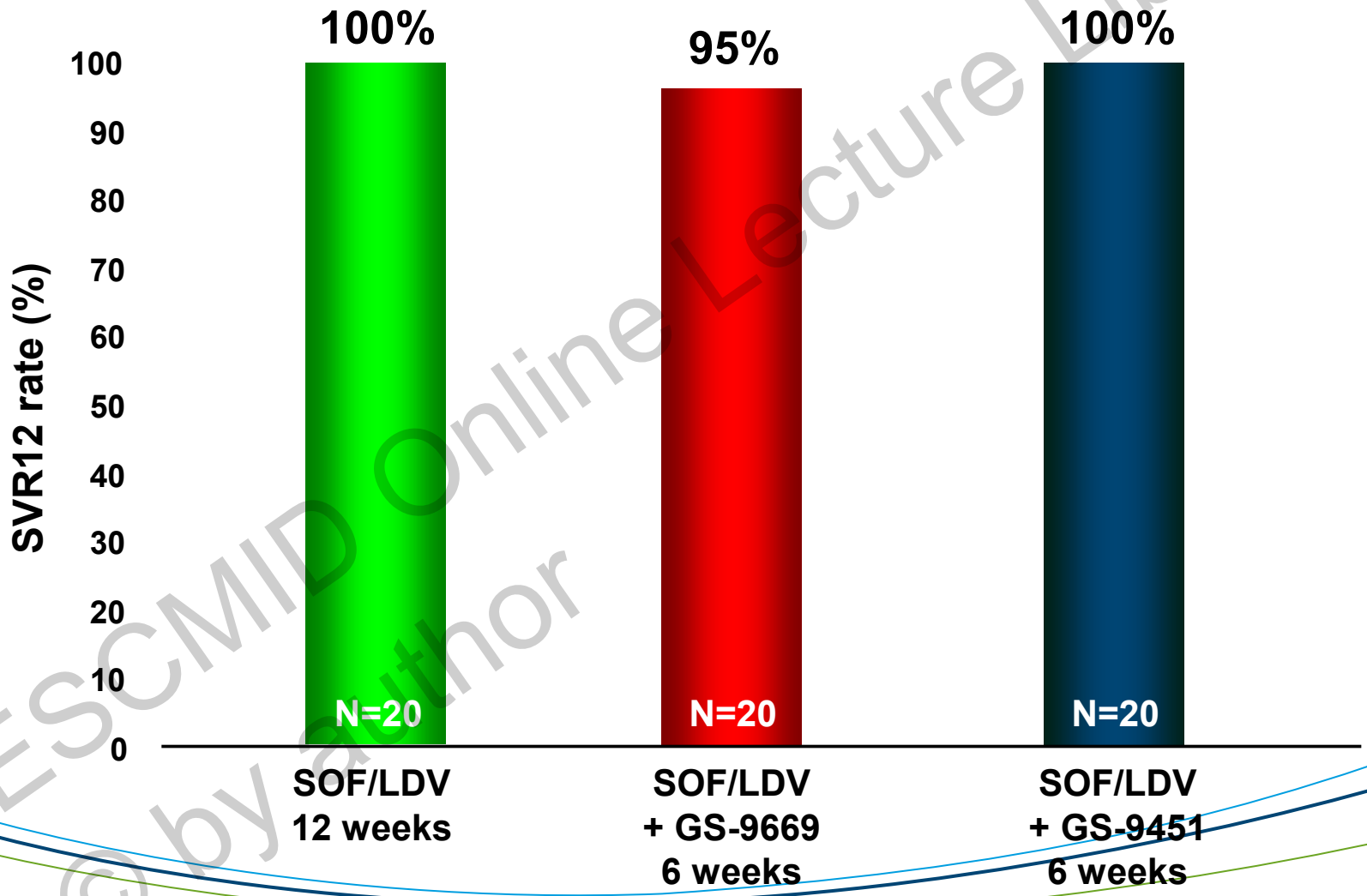
- SVR12 rates in the ITT population (N=875)



Afdhal N, *et al. New Engl J Med* 2014; online DOI: 10.1056/NEJMoa1402454.

SOF/LDV FDC ± GS-9669 or GS-9451

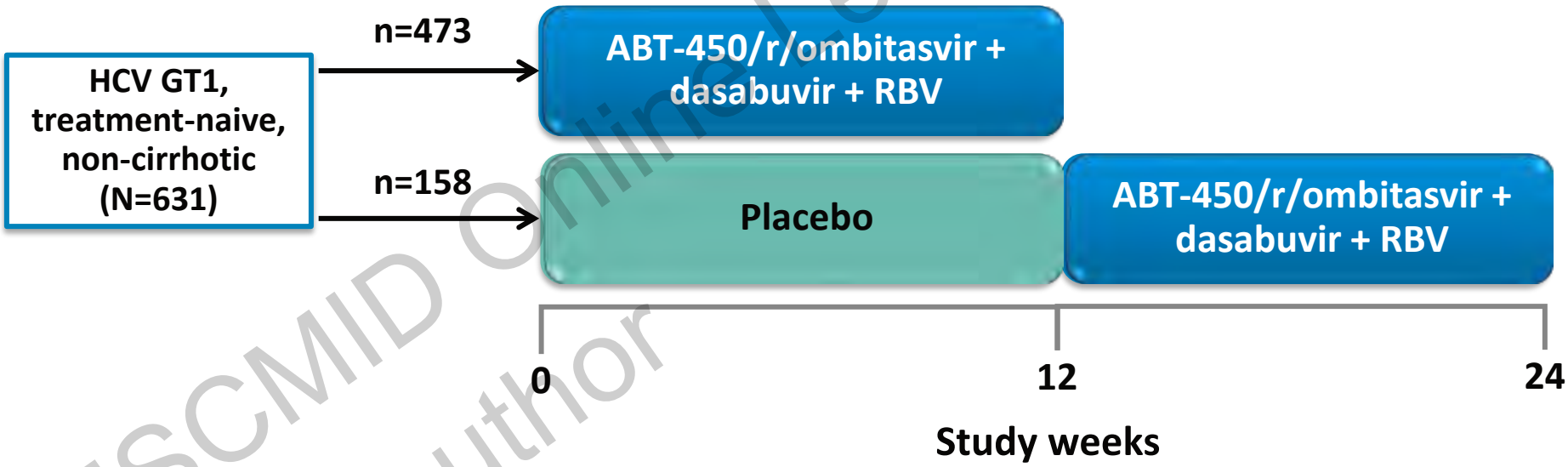
SYNERGY-Phase II, Gen 1, Rx-naïve



Kohli et al., CROI 2014

SAPPHIRE-I: GT1 treatment-naive, non-cirrhotic patients – study design

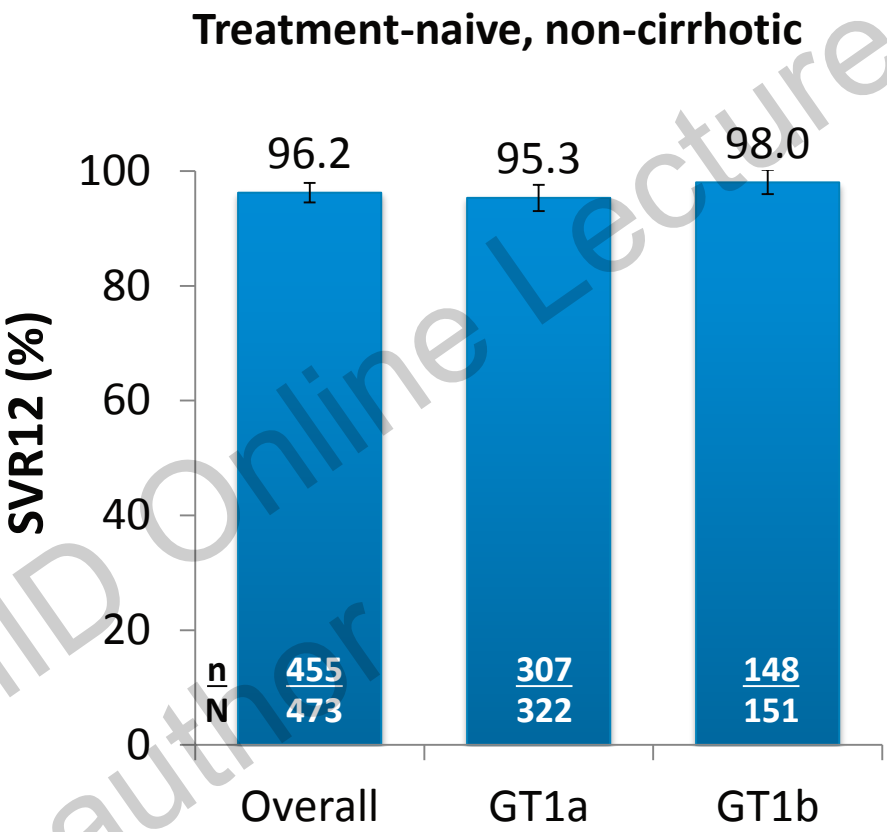
ABT-450/r/ombitasvir + dasabuvir + RBV



ABT-450/r/ombitasvir (ABT-267) = 150/100/25 mg QD co-formulated;
dasabuvir (ABT-333) = 250 mg BID;
RBV = 1000–1200 mg daily according to body weight.

Feld JJ, *et al. New Engl J Med* 2014; online DOI: 10.1056/NEJMoa1315722.

SAPPHIRE-I: GT1 treatment-naive, non-cirrhotic patients – SVR12 rates by HCV GT1 subtype

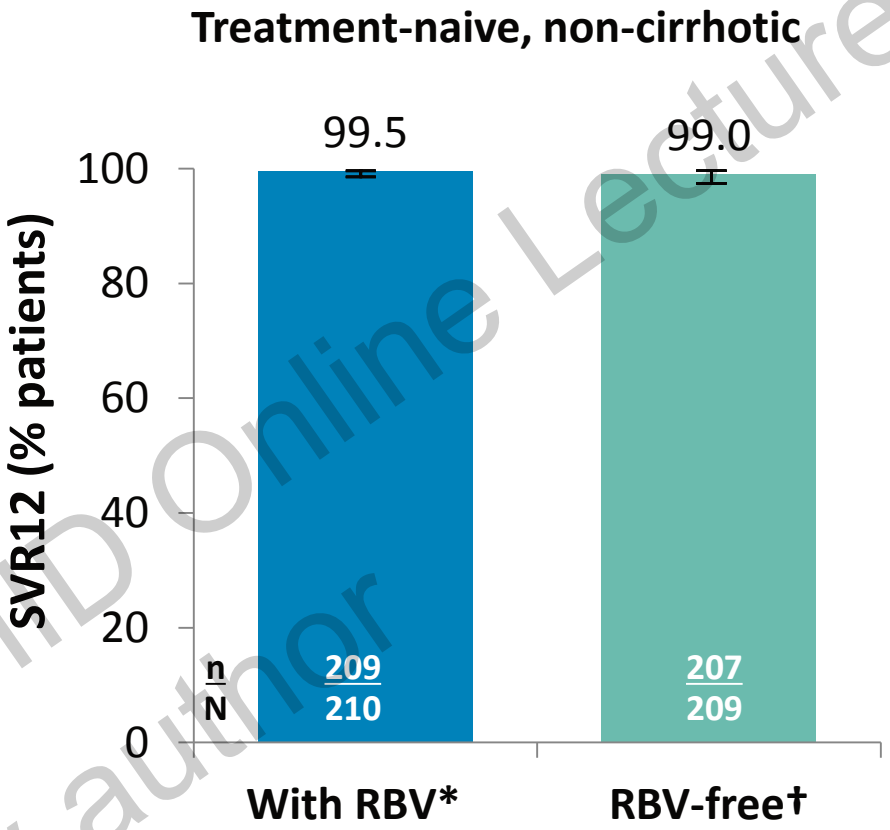


Error bars: 95% CI.

Feld JJ, *et al. New Engl J Med* 2014; online DOI: 10.1056/NEJMoa1315722.

PEARL-III: SVR12 rates with 3D ± RBV in GT1b treatment-naive, non-cirrhotic patients

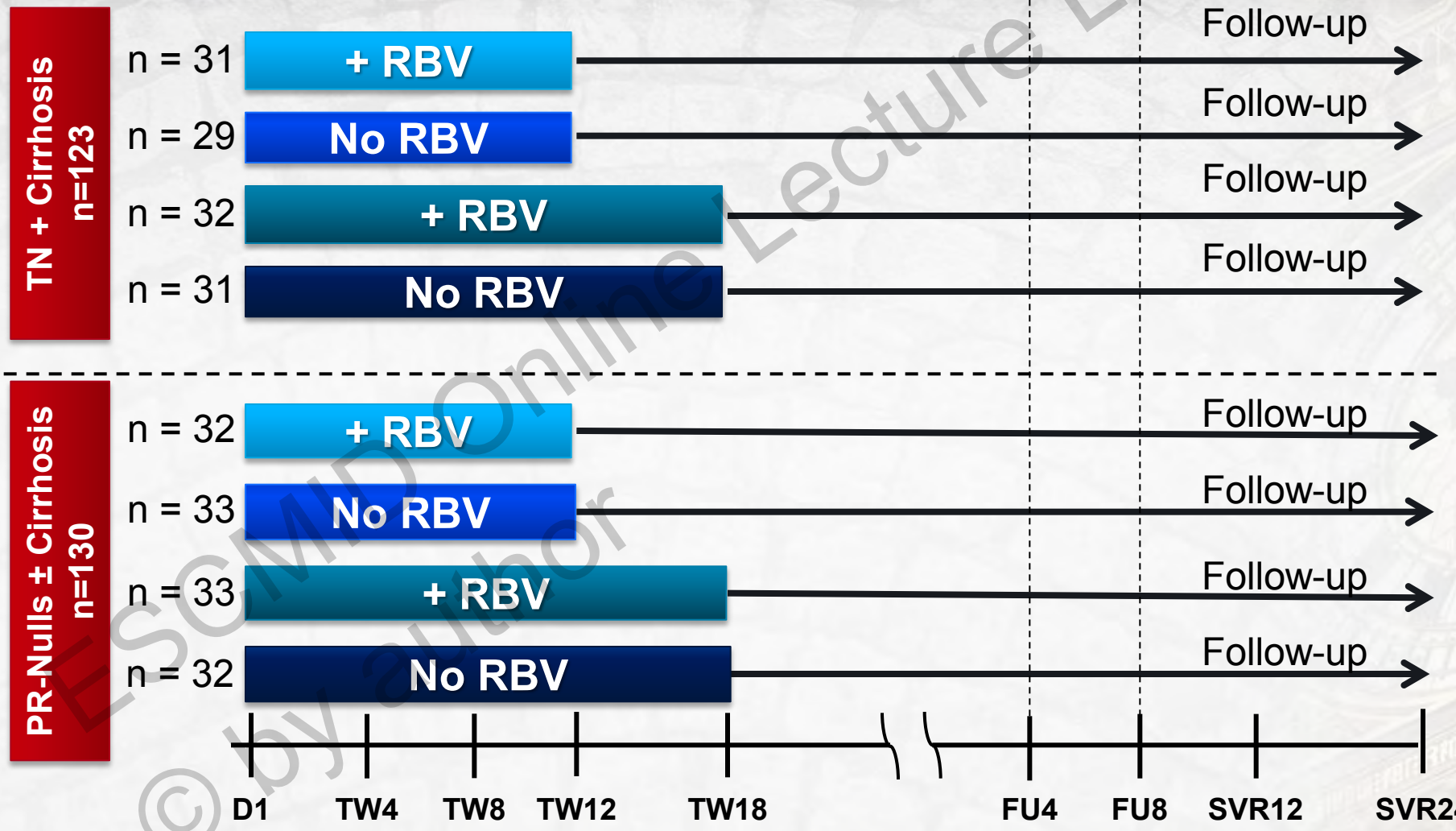
ABT-450/r/ombitasvir + dasabuvir ± RBV



* 1 patient with virologic rebound – emergence of NS5A Y93H;
† 2 patients were lost to follow-up, but subsequently achieved an SVR24; Error bars: 95% CI.

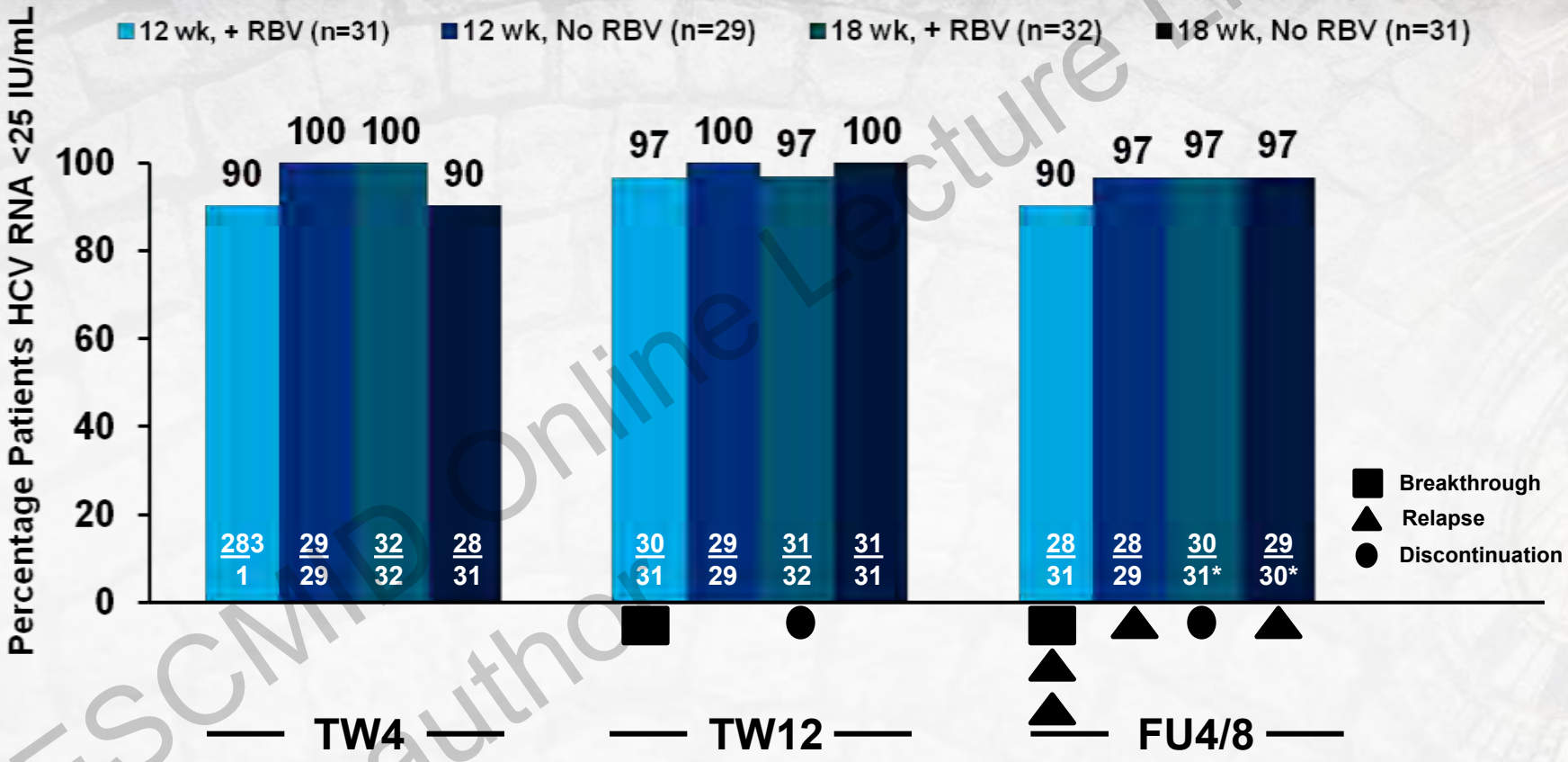
Ferenci P, *et al. EASL* 2014. Abstract 1299 [Latebreaker poster].

Study Design: MK-5172 (100 mg QD) + MK-8742 (50 mg QD) ± RBV in 253 Patients



Lawitz E, et al. 49th EASL; London, England; April 9-13, 2014. Abst. O61.

Efficacy of MK-5172 + MK-8742 ± RBV in Treatment-Naïve Patients with Cirrhosis: 12 vs 18 Weeks



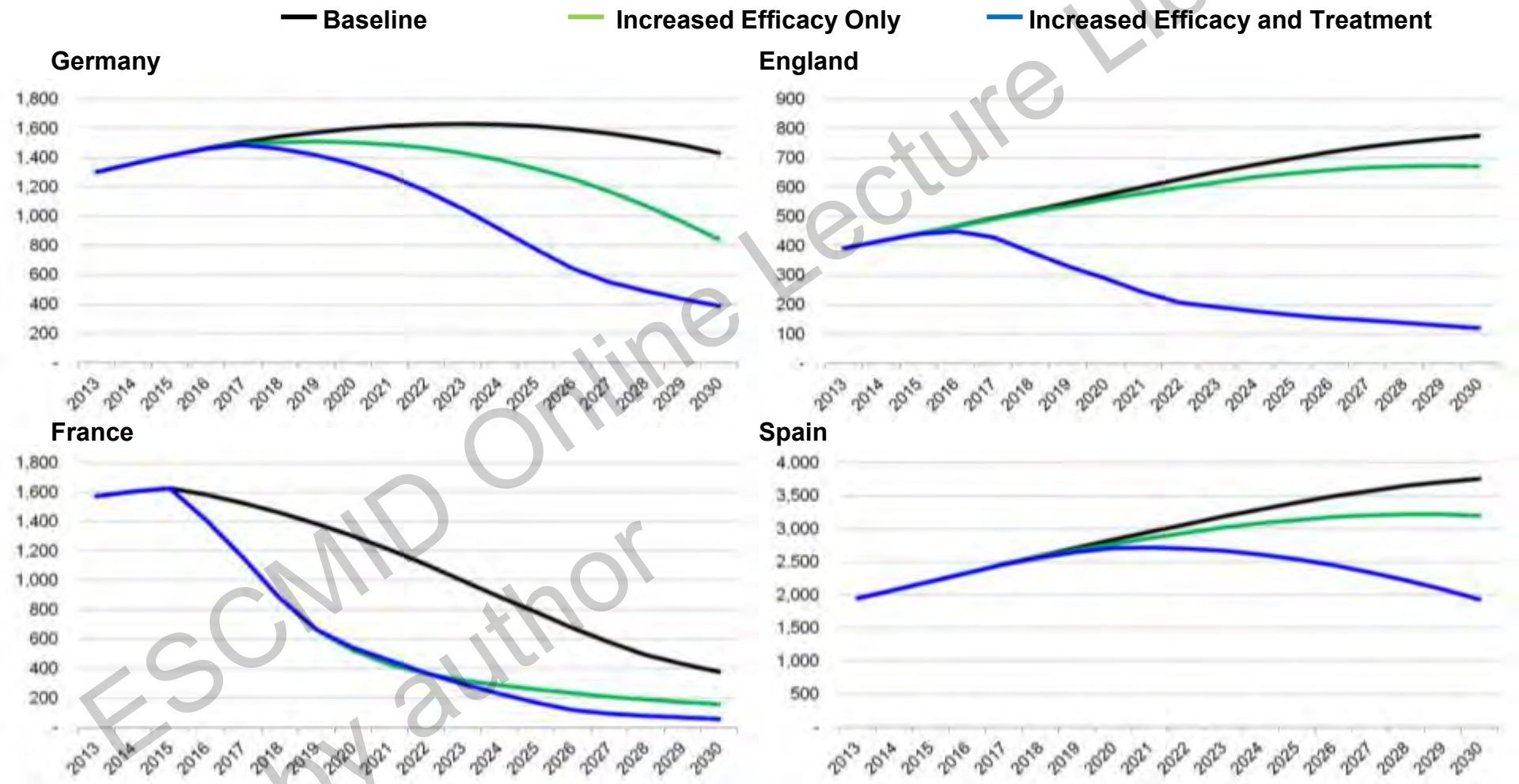
- *Excludes patients who have not yet reached the FU4 time point
- 12 week arms include 97% of FU8 results

Lawitz E, et al. 49th EASL; London, England; April 9-13, 2014. Abst. O61.

Summary of EASL 2014

J-M Pawlotsky

Liver-related deaths, 2013–2030:
Germany, England, France and Spain



Wedemeyer H, *et al. J Viral Hepat* 2014; **21** (suppl. 1):60–89.