Comparison of two HCV-RNA assays assessing early response to simeprevir+PegIFN/RBV to select patients suitable to shorten therapy to 12 weeks

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Presenting author disclosures

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Study design (HPC3014; NCT 01846832)

Aim:

- Determine if on-treatment response can select patients suitable to shorten overall treatment to 12 weeks of SMV + PR
  - Assess efficacy and safety of this regimen

Population:

- Treatment-naïve adults, infected with HCV GT1 or 4
- METAVIR F0–2
- All *IL28B* genotypes
- In the analysis presented here, only GT1 patients were included

Study design (HPC3014) in Genotype 1

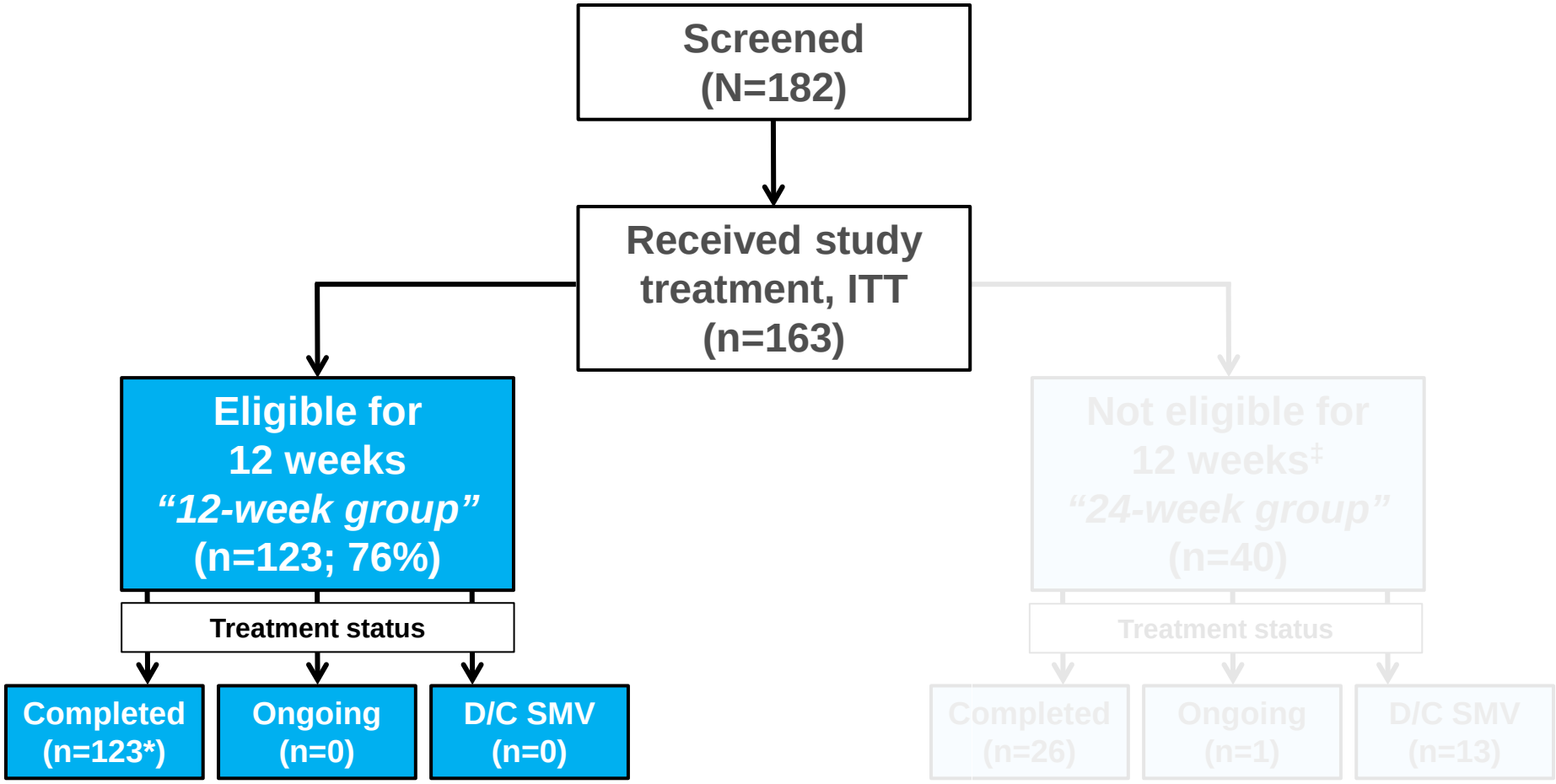
Patients who met the RGT criteria received 12 weeks of therapy:

HCV RNA at Week 2	HCV RNA at Week 4 and 8	Treatment duration
< 25 IU/mL detectable or undetectable	< 25 IU/mL undetectable	12 weeks

If HCV RNA at Week 2, 4 and 8 did not meet the above-outlined criteria, PR was continued up to week 24

*Patients in France had the option to extend treatment to 48 weeks – this option was taken by one patient
Patients stopped all therapy if HCV RNA ≥25 IU/mL at Week 4 or 12 or in case of virological breakthrough at any time point
Assay: Roche High Pure System COBAS® Taqman® LLOQ: 25 IU/mL, LOD: 15 IU/mL.

Genotype 1 patients disposition

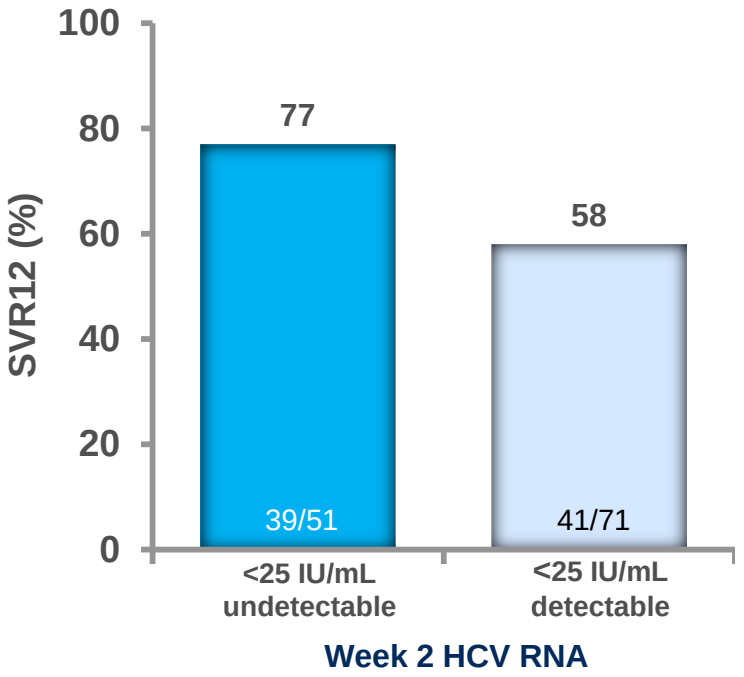


*One patient stopped both SMV and RBV (non-compliant) after RGT was determined (stopped at Week 11). The patient completed PegIFN;
‡Any patient who discontinued early and where eligibility could not be determined (n=2) was automatically included in the 24-week group
ITT: intent-to-treat; RGT: response-guided therapy

HPC3014 Primary analysis: SVR12 in G1 patients treated for 12 weeks

- In the primary analysis, SVR12 rates were suboptimal (66%)
- SVR rates were high in specific subgroups and confirmed as significant predictors by multivariate analysis:
  - *IL28B* CC: 94%
  - METAVIR F0–F1: 74%
  - Baseline viral load ≤800,000 IU/mL: 82%
- SVR12 were notably different according to HCV RNA status at Week 2 (<25 IU/ml undetectable vs detectable) suggesting a more sensitive assay may help better select patients suitable for 12 weeks of therapy

SVR12 in G1 patients treated for 12 weeks according to Week 2 HCV RNA



Asselah T, et al. APASL 2015. Oral Presentation

Post hoc analysis objectives and population

Objective

- Determine if an assay (with LOD/LLOQ: 12IU/mL) could better identify patients with a high chance of SVR on therapy shortened to 12 weeks

Population

- Week 2 and Week 4 samples from 120/123 GT1 patients who qualified for 12 weeks of treatment from the original study were re-analysed with the ART assay

Roche High Pure System / COBAS® Taqman® assay (RCT)

- Lower limit of quantification: 25 IU/mL
- Limit of detection: approx. 15 IU/mL

Abbott Realtime assay (ART)

- Lower limit of quantification: 12 IU/mL
- Limit of detection: approx. 12 IU/mL

Baseline demographics and disease characteristics of G1 patients eligible for 12 weeks of SMV + PR

	12-week group (n=123)
Male, n (%)	65 (53)
Age (years), median	47.0
BMI (kg/m^2), median	25.0
Race,	
White, n/N (%)	98/107* (92)
IL28B genotype, n (%)	
CC	32 (26)
non-CC	91 (74)
HCV RNA (log_{10} IU/mL), median	6.26
≤800,000 IU/mL, n (%)	33 (27)
HCV genotype subtype‡, n (%)	
1b	74 (60)
METAVIR score, n (%)	
F0–F1	93 (76)
F2	29 (24)

120/123 of these patients had samples reanalysed by ART assay

*Data unavailable for 16 patients due to local regulations forbidding collection of this information
‡HCV geno/subtype is based on the NS5B assay, and if not available on the LIPA HCV II or Trugene results

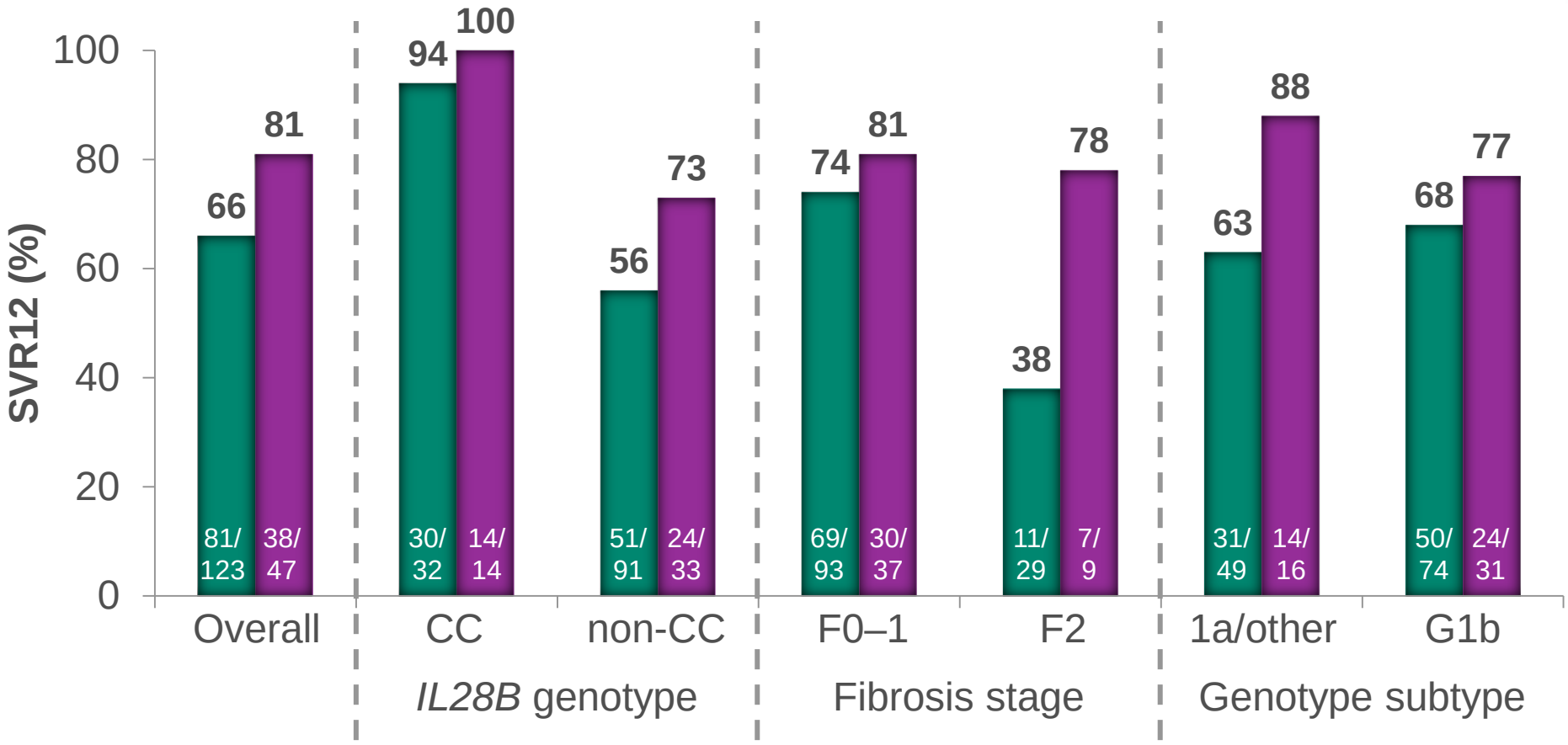
Concordance between RCT and ART in the 12-week group (genotype 1)

Week 2		Abbott RealTime			
		<12 IU/mL undetectable	<12 IU/mL detectable	12–24 IU/mL	≥25 IU/mL
Roche COBAS Taqman	<25 IU/mL undetectable	13/48 (27.1 %)	28/48 (58.3 %)	4/48 (8.3 %)	3/48 (6.3 %)
	<25 IU/mL detectable	7/71 (9.9 %)	12/71 (16.9 %)	19/71 (26.8 %)	33/71 (46.5 %)

Week 4		Abbott RealTime			
		<12 IU/mL undetectable	<12 IU/mL detectable	12–24 IU/mL	≥25 IU/mL
Roche COBAS Taqman	<25 IU/mL undetectable	64/120 (53.3 %)	48/120 (40.0 %)	7/120 (5.8 %)	1/120 (0.8 %)

Samples of patients who received 24 weeks of therapy were not re-analysed, therefore complete concordance cannot be assessed

ART assay reanalysis results I:
Week 2 <12 IU/mL det./und. and Week 4 <12 IU/mL und.

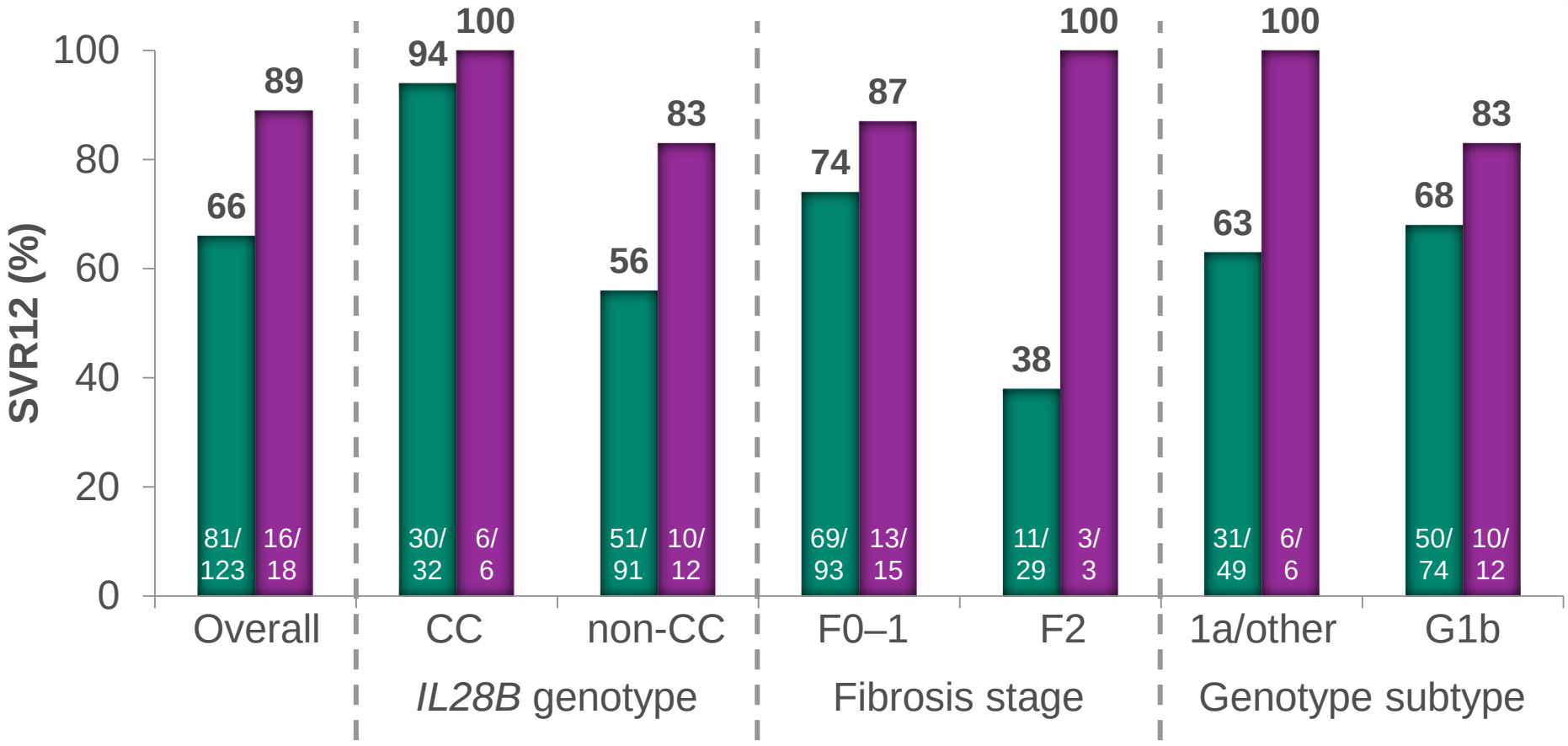


Original RCT criteria*

ART Week 2 HCV RNA <12 IU/mL det./und. and Week 4 <12 IU/mL und.

*Week 2 HCV RNA < 25 IU/ml det./und. and Week 4/8 <25 IU/ml undetectable assessed by RCT

ART assay reanalysis results II: Week 2 and 4 <12 IU/mL und.



Original RCT criteria*

ART Week 2 HCV RNA <12 IU/mL undetectable and Week 4 <12 IU/mL und.

*Week 2 HCV RNA < 25 IU/ml det./und. and Week 4/8 <25 IU/ml undetectable assessed by RCT

Summary and conclusions

- Low concordance was seen between both assays at Week 2
  - Moderate concordance was seen at Week 4

- 123/163 patients qualified for 12 weeks of treatment using the original RCT criteria
  - When re-assessing 120/123 of these patients for RGT with the ART assay, higher SVR12 rates were observed in all subgroups than in the original RCT assay (overall SVR12: ART: 81%; RCT: 66%)
  - However, as samples of patients treated for 24 weeks have not been analysed, it is not yet clear if the ART assay can select patients better than the RCT assay

- Our findings suggest assays with higher sensitivity may improve the ability to select patients with a high chance of SVR with only 12 weeks of simeprevir + PegIFN/RBV therapy

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