Optimising therapy for Genotype 3

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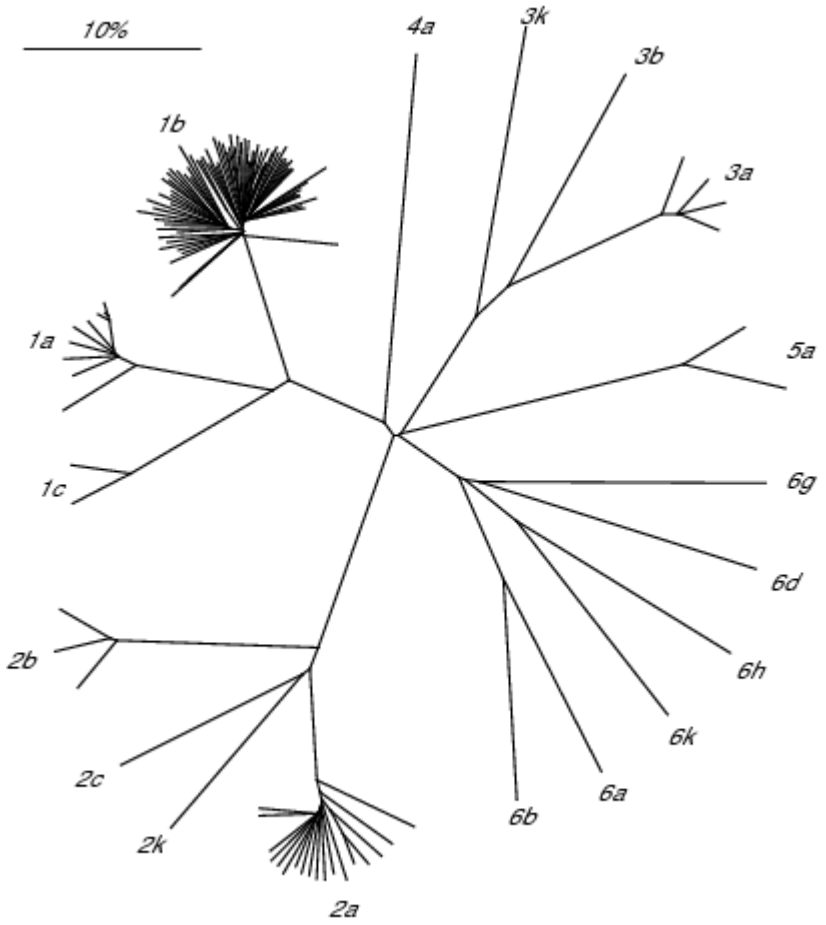
Genotype 3
Extent of the problem



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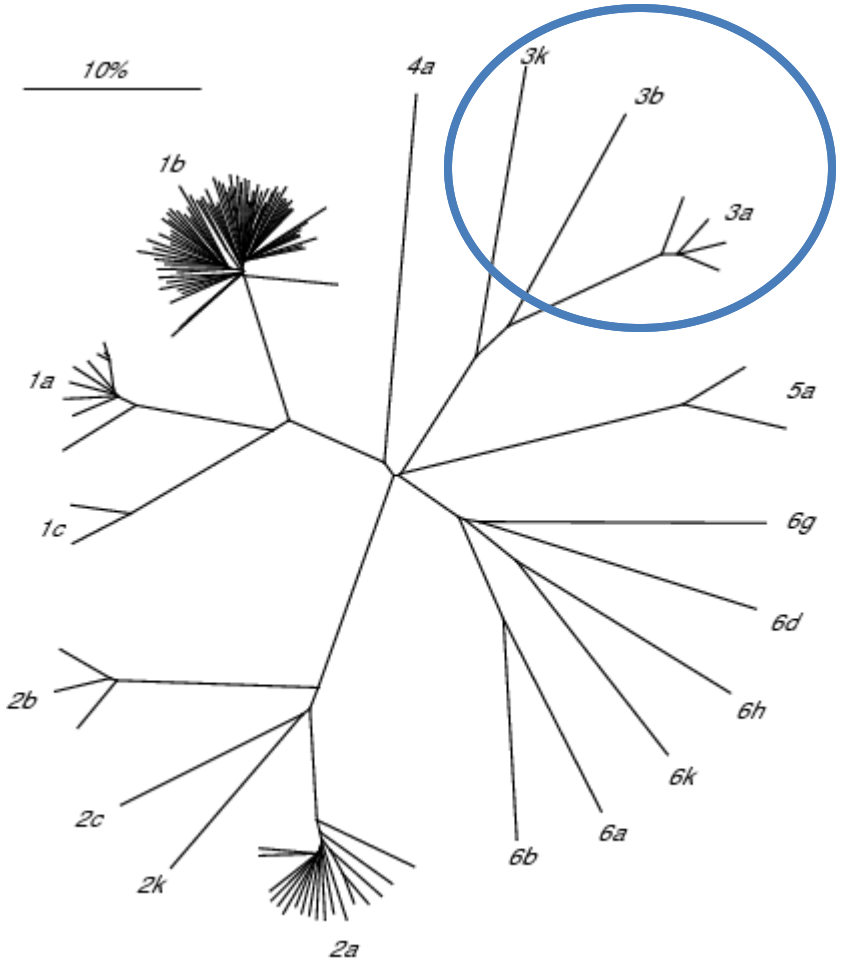
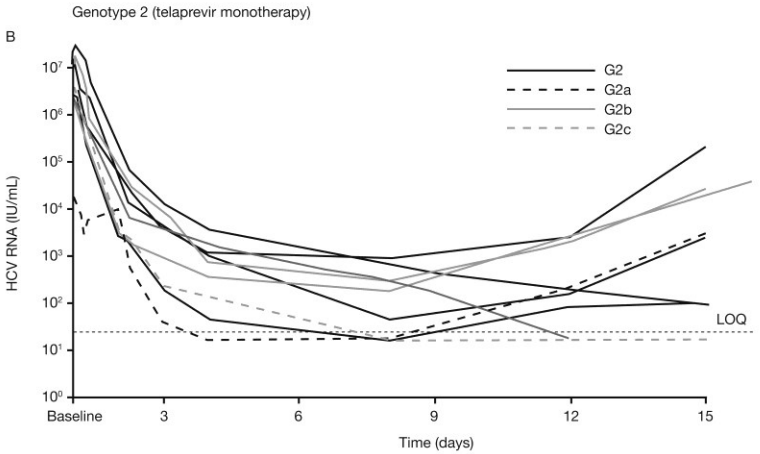
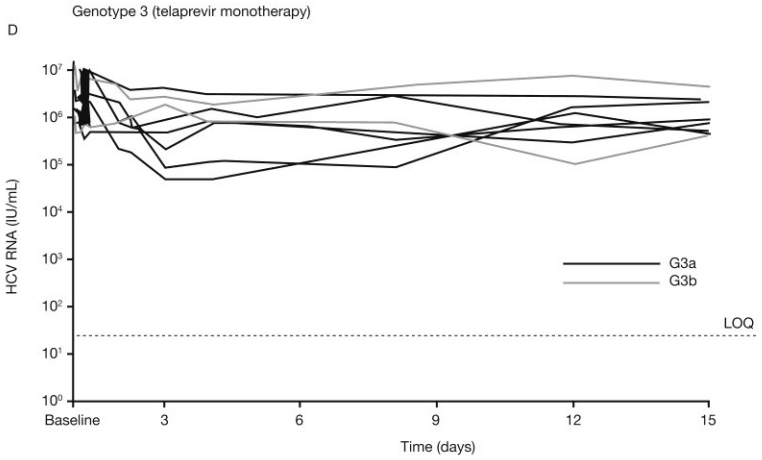


Genotype 3 – a diverse virus
Response to Telaprevir



Genotype 2



Genotype 3

Foster et al Gastroenterology 2011

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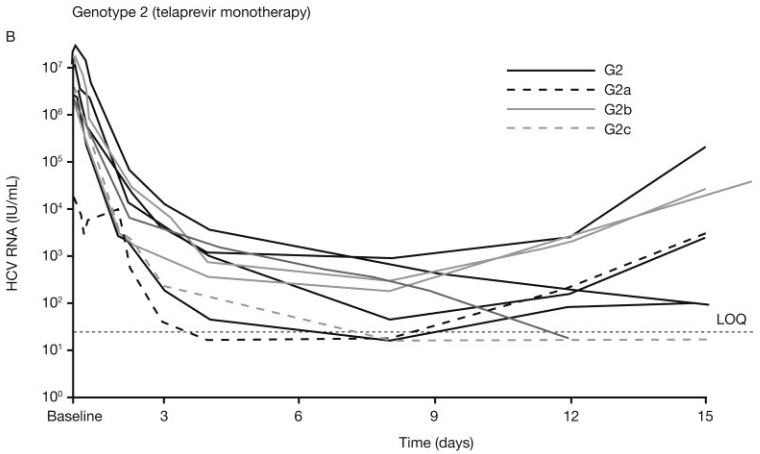

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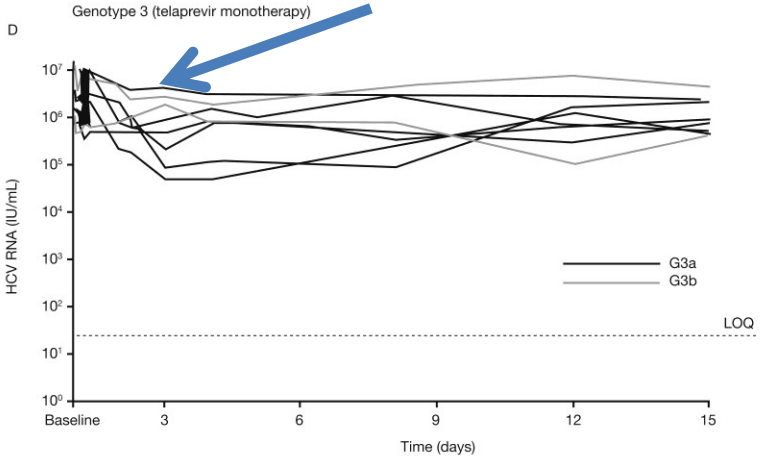

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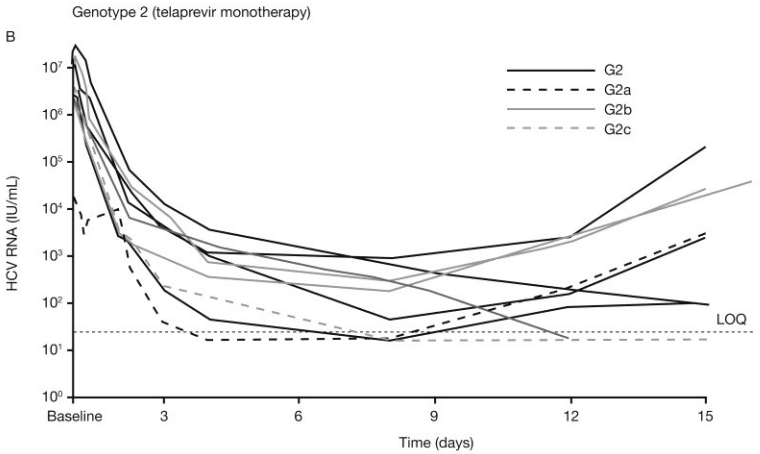

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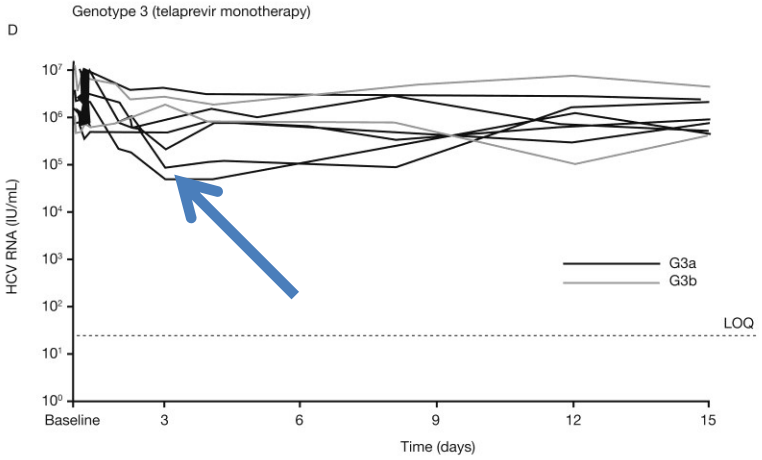
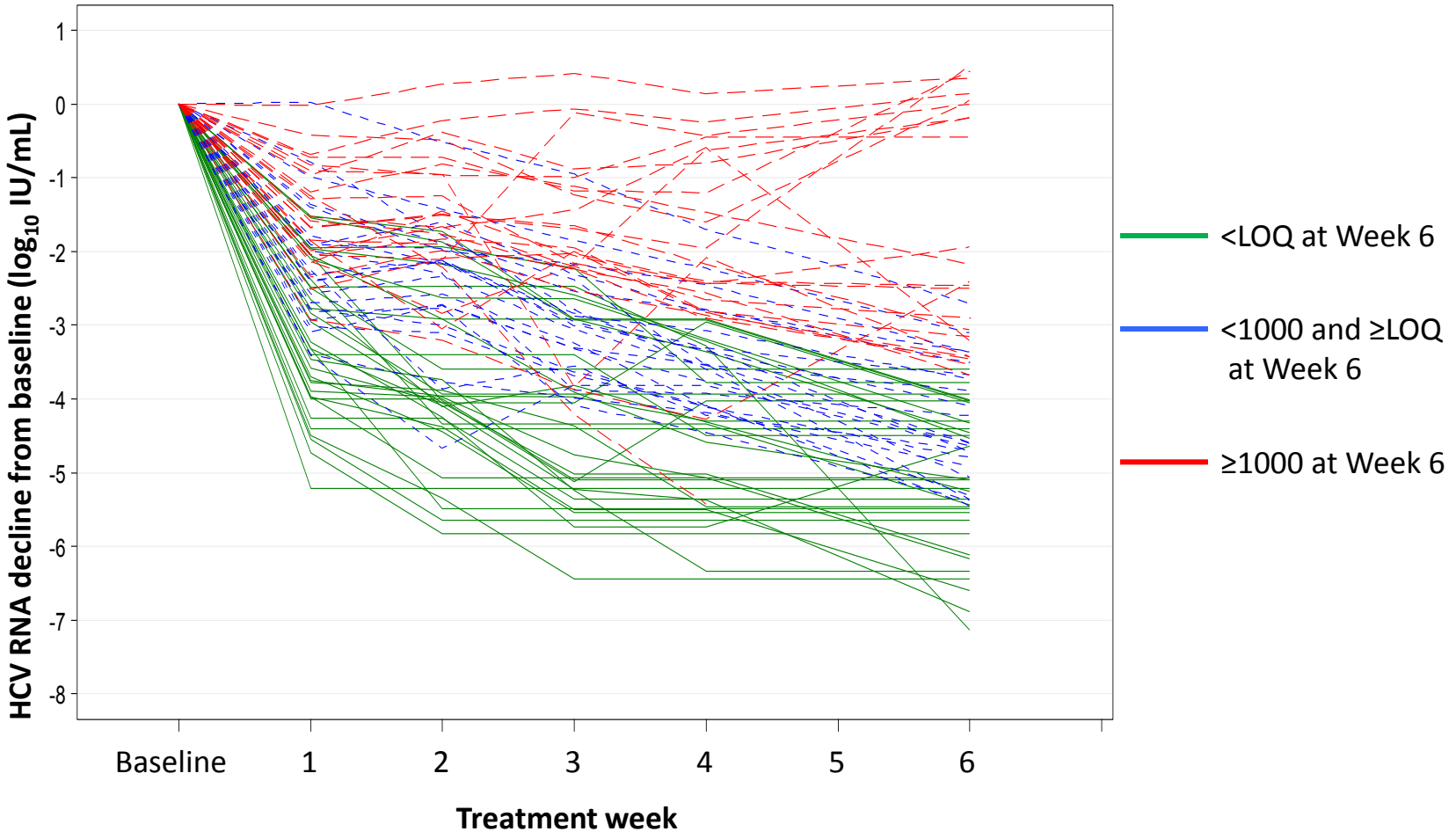


Genotype 3

Foster et al Gastroenterology 2011

Individual plots of HCV RNA decline (Baseline to Week 6) in patients treated with IFN-free alisporivir 800 mg + RBV G2 and 3



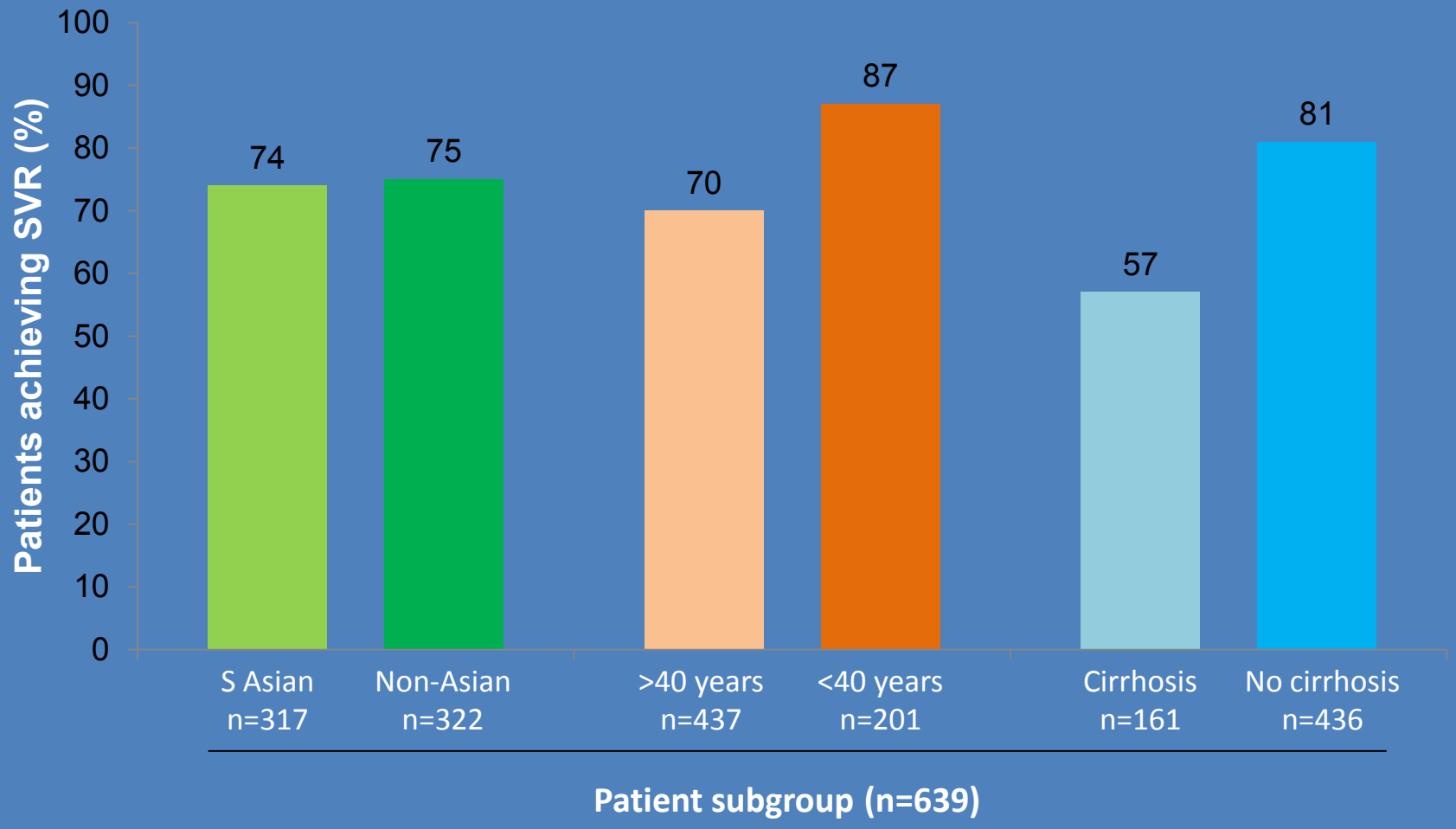
Pawlotsky EASL 2012

Patients from ALV800R group; LOQ=limit of quantification (<25 IU/mL)

Genotype 3 – a diverse virus

- Some patients respond well
- Some patients respond poorly

Response of HCV G3 patient subgroups to PegIFN/RBV



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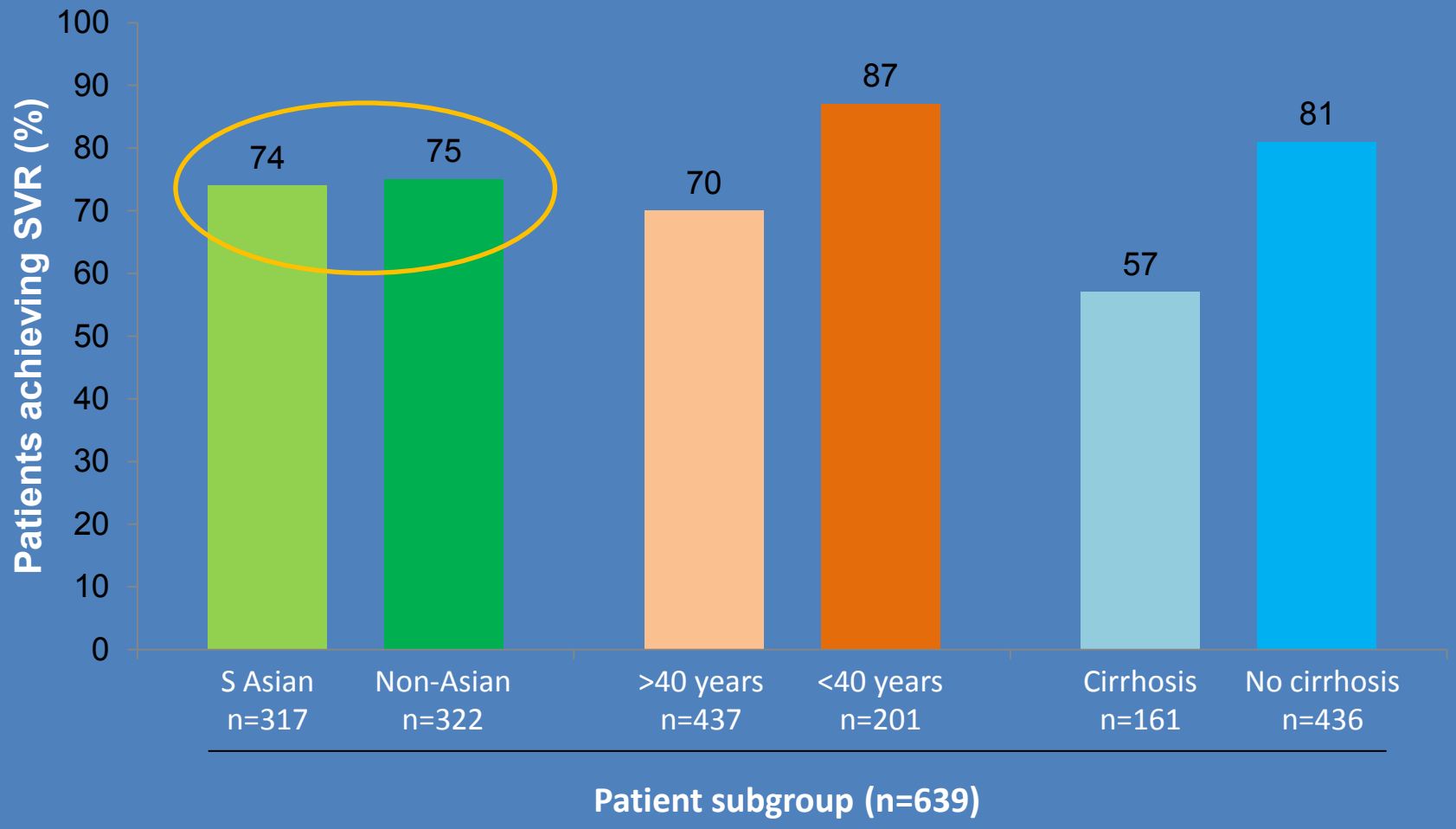

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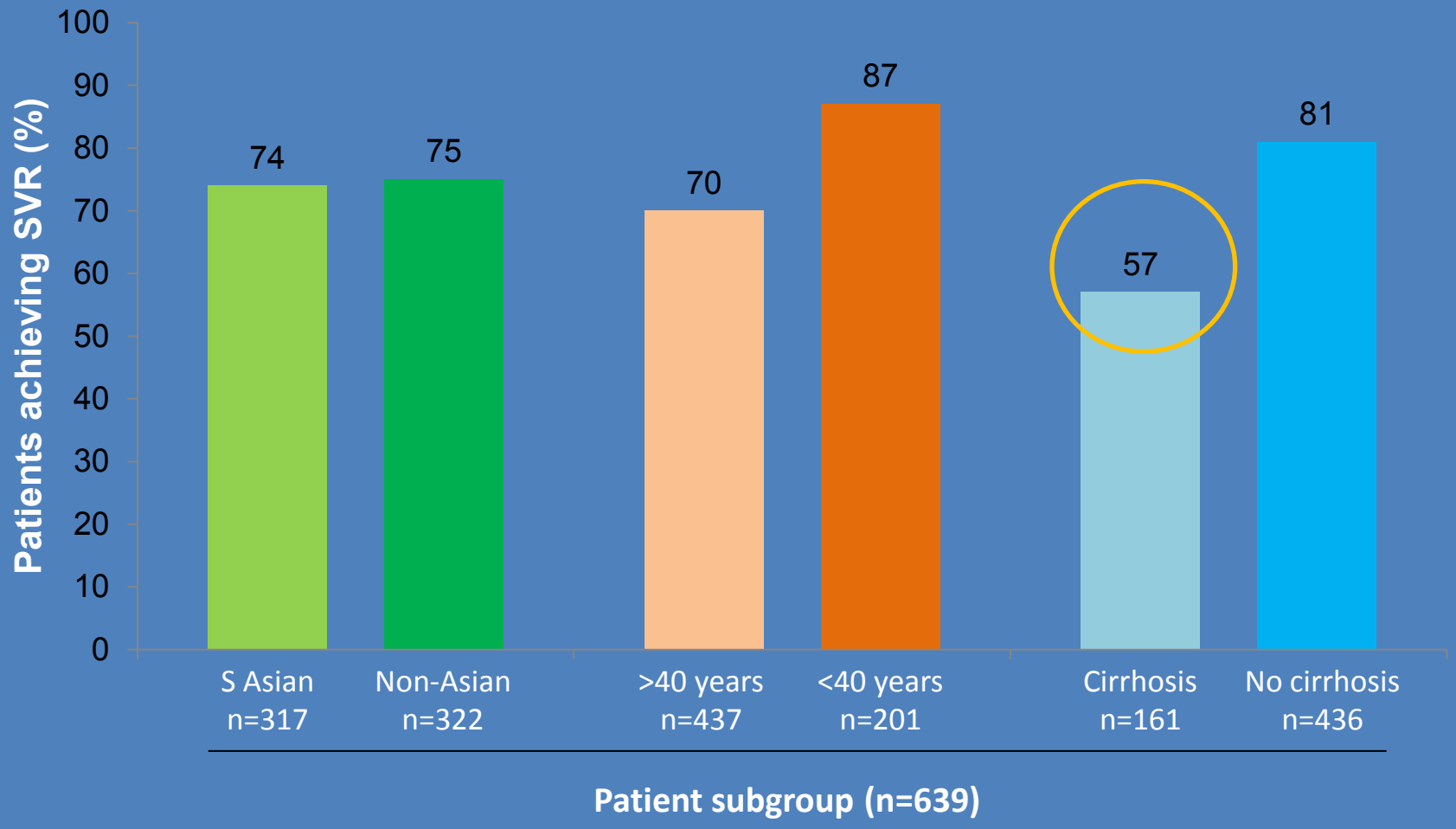

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Optimising therapy for G3

- Easy to treat G3 – short or long?
- Hard to treat – what can we do?

Easy to treat G3

- Several studies examining short duration therapy in G3 HCV
- Many small studies show success with 12 or 16 weeks therapy in patients with an RVR

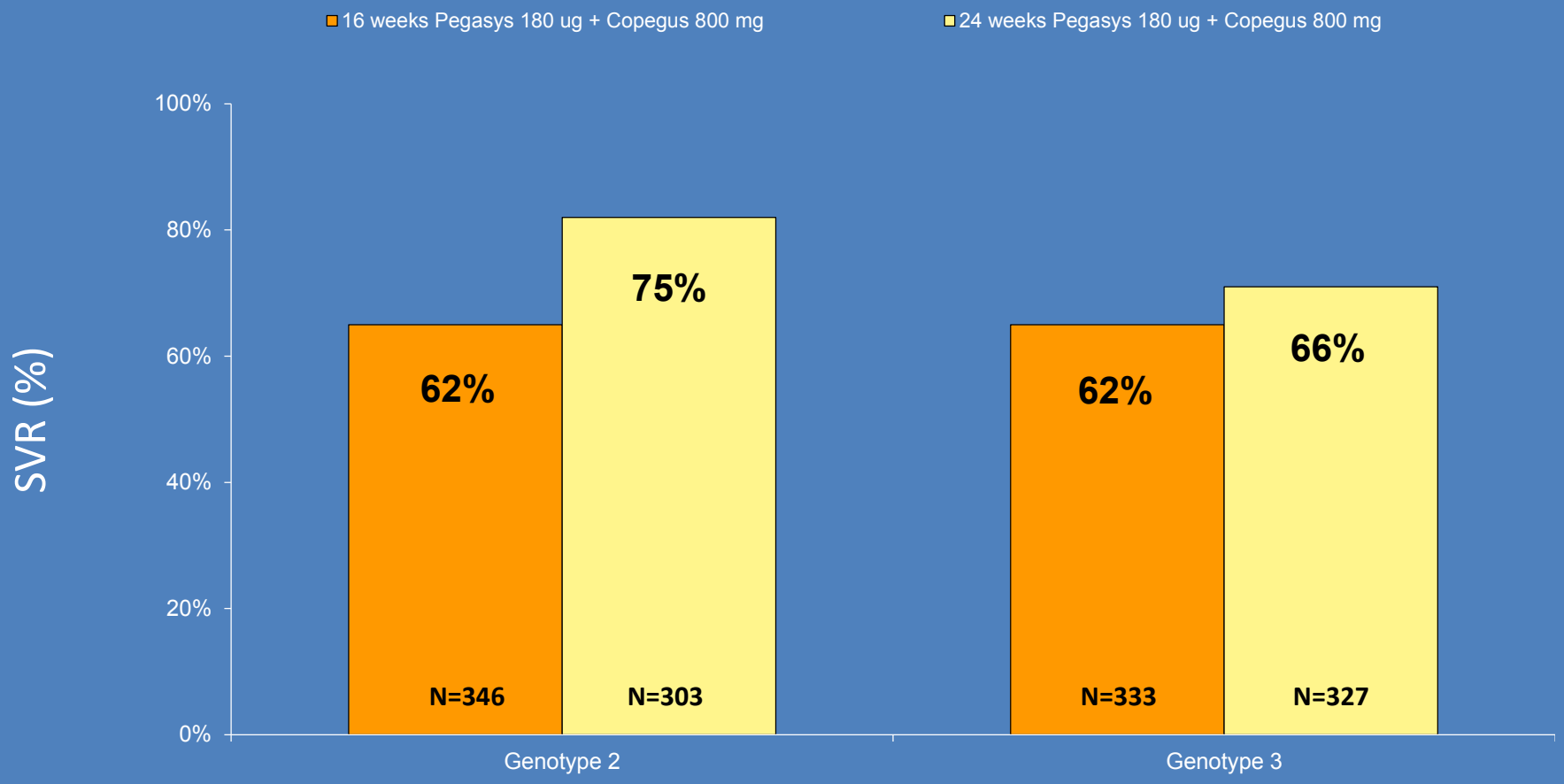
Easy to treat G3

- Several studies examining short duration therapy in G3 HCV
- Many small studies show success with 12 or 16 weeks therapy in patients with an RVR

BUT

- ALL are underpowered studies for G3

The ACCELERATE Study: SVR Rates by Genotype



Standard population; VR = HCV RNA < 50 IU/mL

Shiffman ML et al NEJM 2007 Jul 12;357(2):124-34.

Reducing the duration of therapy in Genotype 3

- For ‘easy to treat’ G3 the evidence that therapy can be shortened is weak

- I treat all my patients for 24 weeks

Tough to treat G3

- Defined by virological response OR histology

Tough to treat G3

- Defined by virological response OR histology

- G3 patients without an RVR randomised to 24 or 48 weeks therapy (N-CORE)
- SVR after 24 weeks = 49/95 (52%)
- SVR after 48 weeks = 57/93 (61%)

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NOT GOOD ENOUGH

Tough to treat G3

- Defined by virological response OR histology
- G3 patients with cirrhosis randomised to 24 or 48 weeks therapy (STEPS)
- Results due at EASL

Tough to treat HCV

- No clear answer
- What about the new drugs?

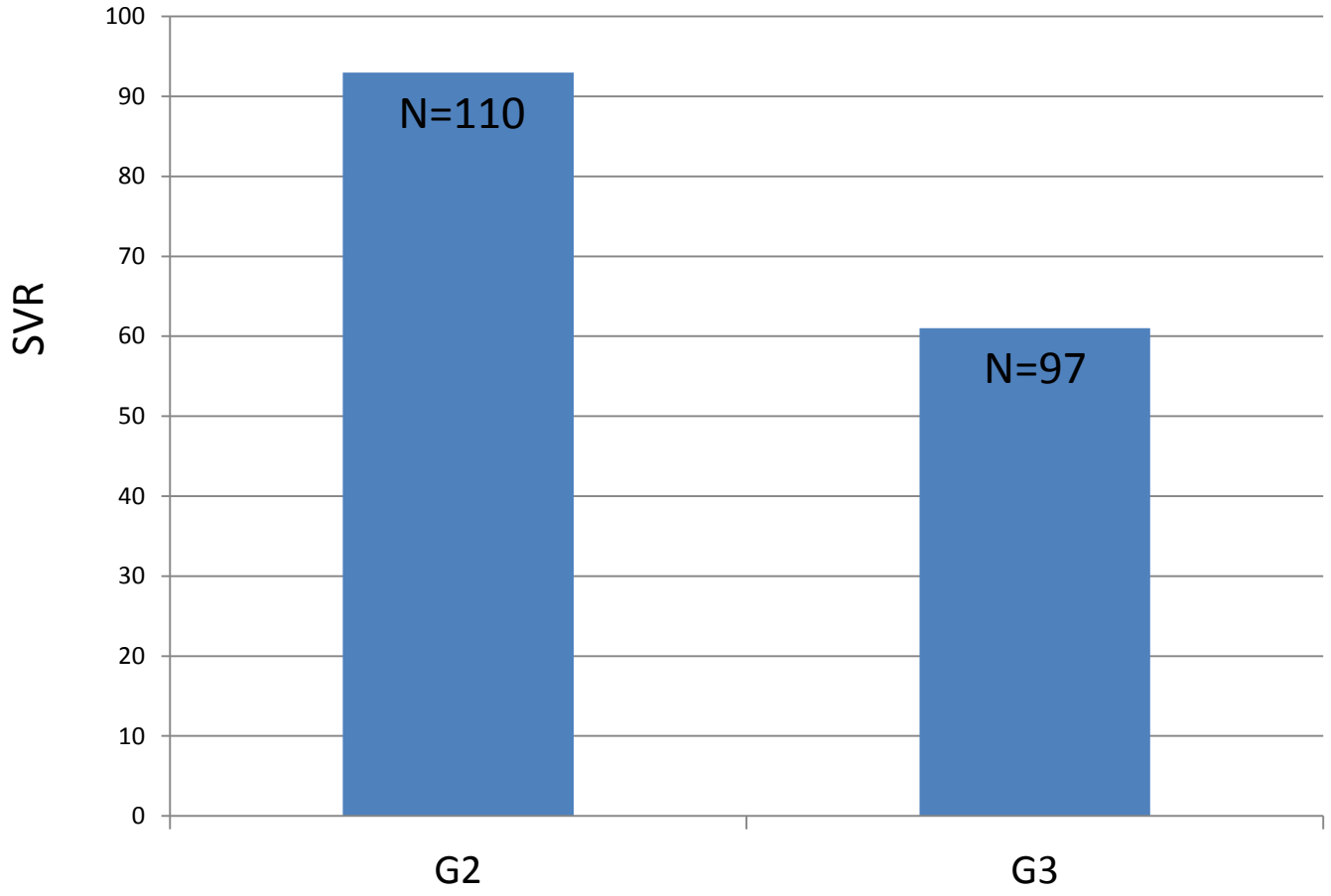
DAAs for G3 HCV

- Proteases - don’t work
- Non-nucs – don’t work
- Nucs?
- NS5A?
- CyA inhibitors?

Nucleotides for G3

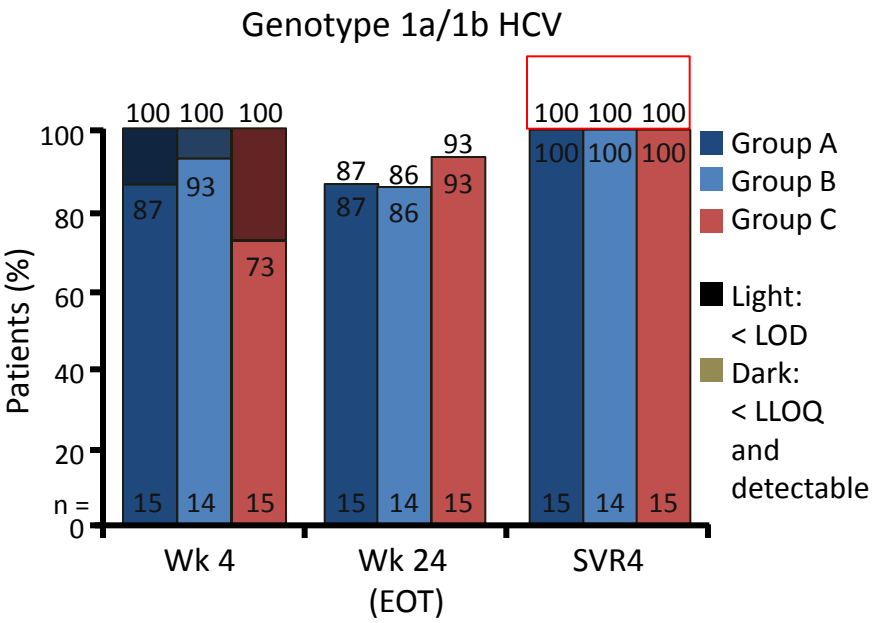
- ELECTRON showed 100% SVR with sofosbuvir + ribavirin

Nucleotides for G3 – sofosbuvir+RBV POSITRON N =207

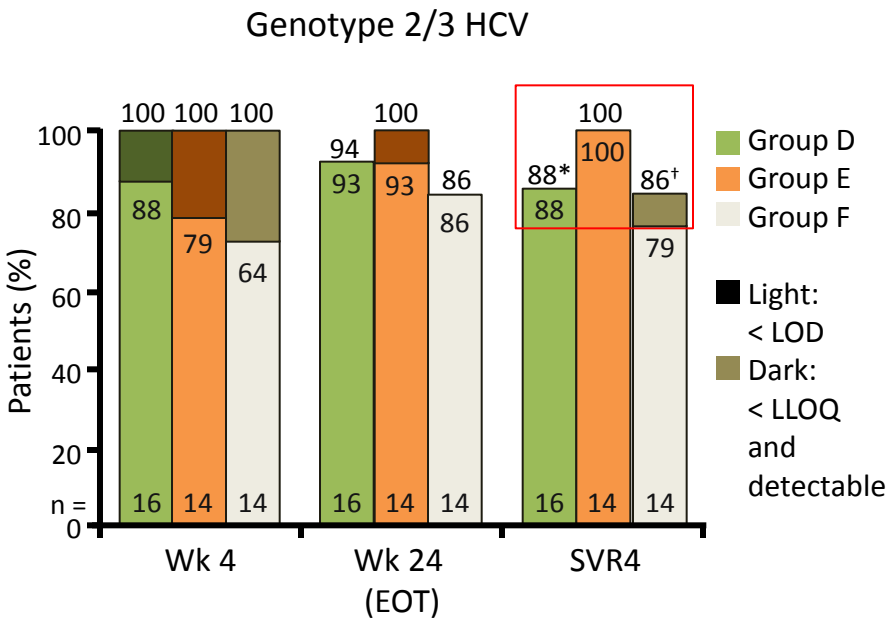


Gilead – Press release 2012

Daclatasvir + GS-7977 ± RBV: Efficacy Analysis According to Genotype



mITT analysis, bars not reaching 100% after Wk 4 reflect missing values.



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*1 patient required addition of pegIFN-alfa/RBV (tx intensification), 1 patient with relapse at posttreatment Wk 4

†2 patients lost to follow-up (following Wk 12 and 24 visits).

Sulkowski M, et al. EASL 2012. Abstract 1422.

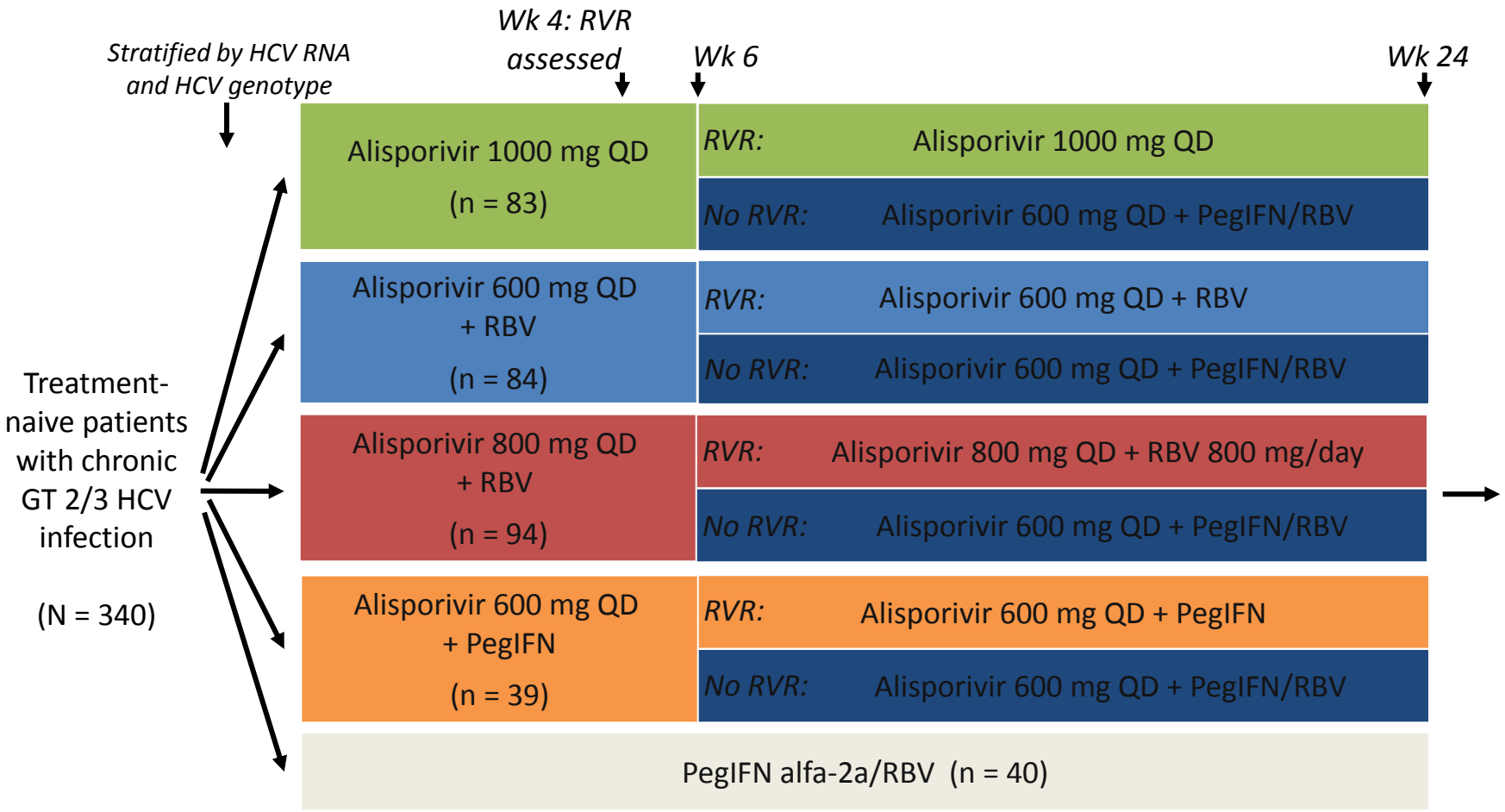
Nucleotides and NS5A inhibitors for G3

- Nucleotides for 12 weeks are not enough
- Nucleotides + NS5A ???
- What will the response rates be in patients with cirrhosis?

Alisporivir G2 and 3

- Alisporivir is a very potent inhibitor of G3 HCV
- Early data suggested monotherapy may be viable!

Alisporivir – G2-3 data



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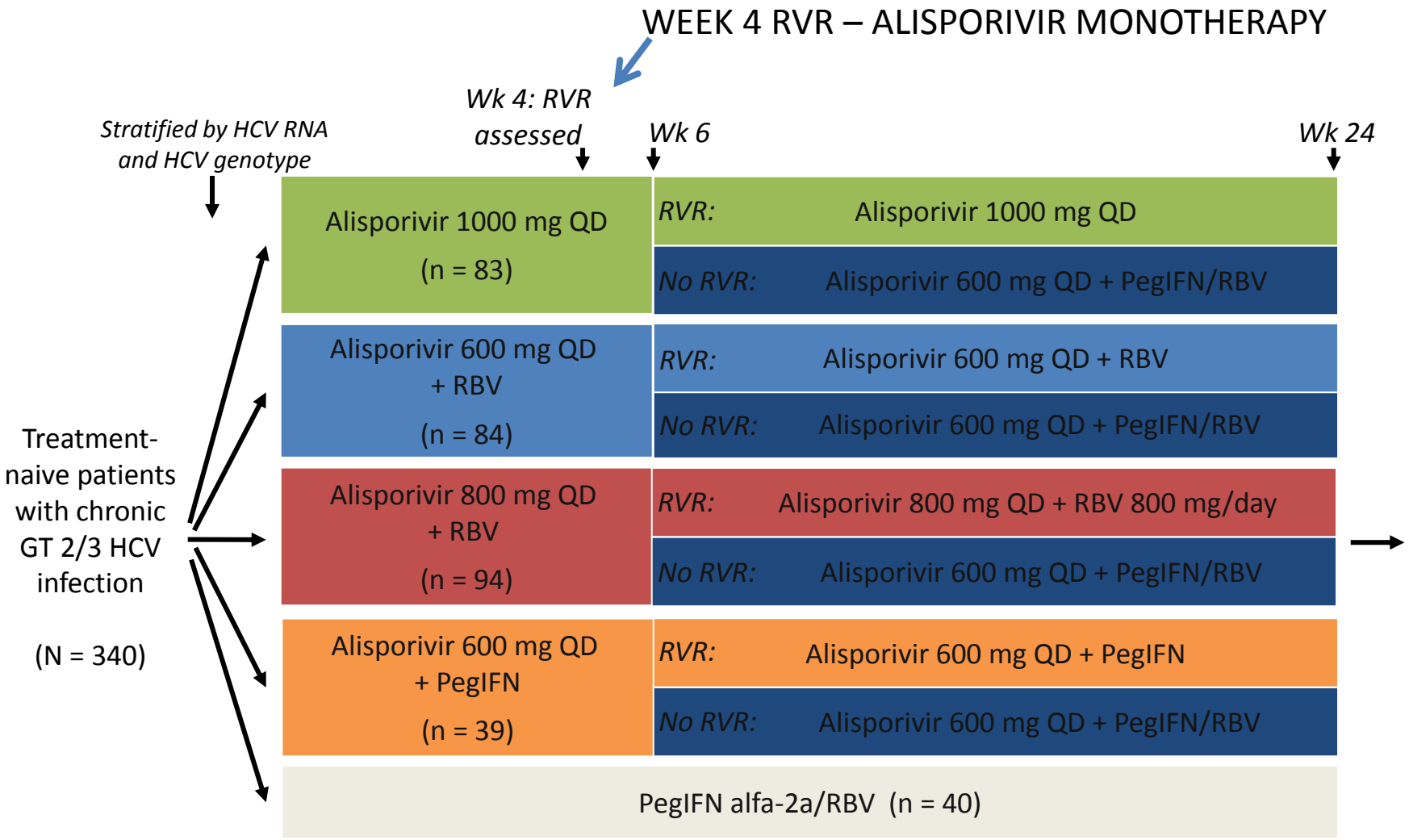
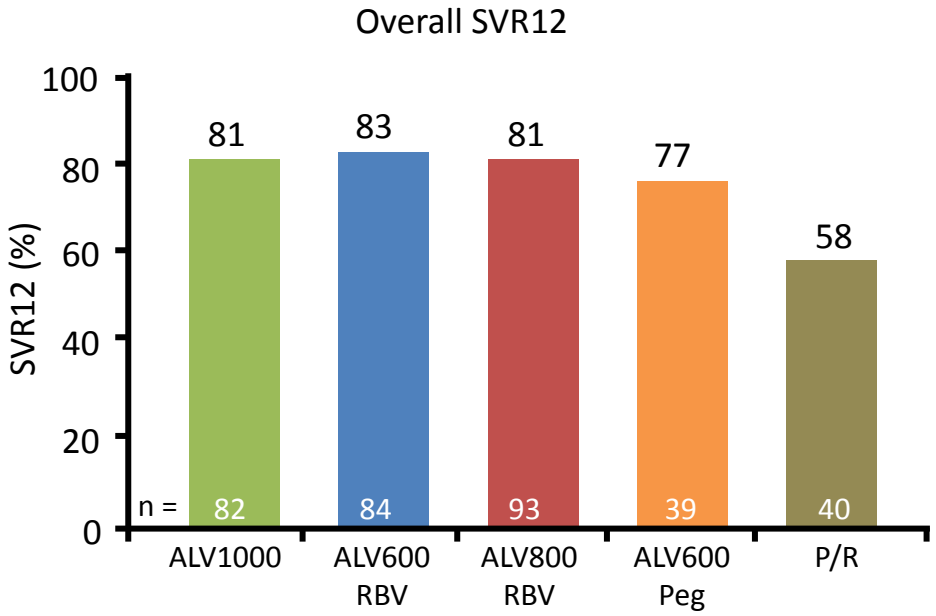
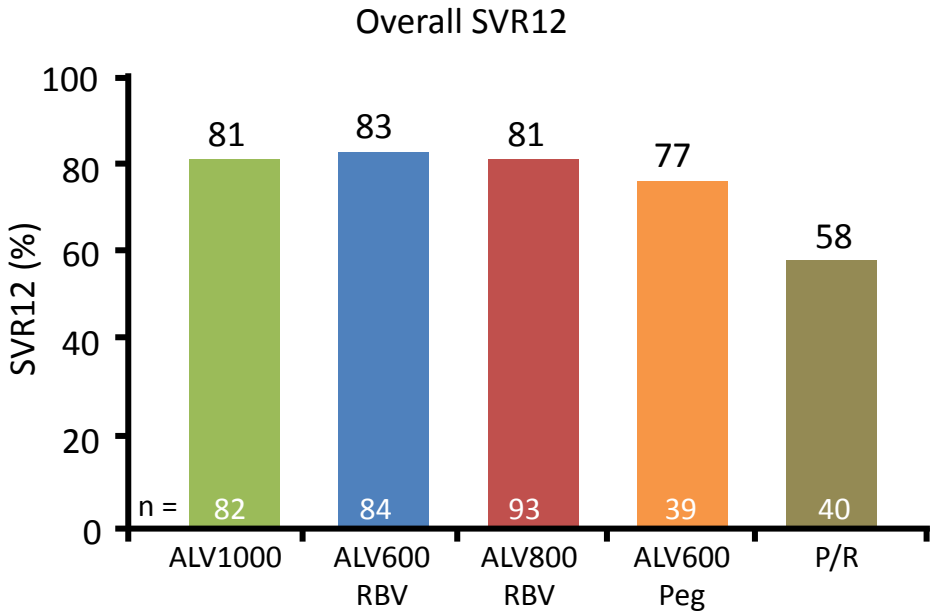


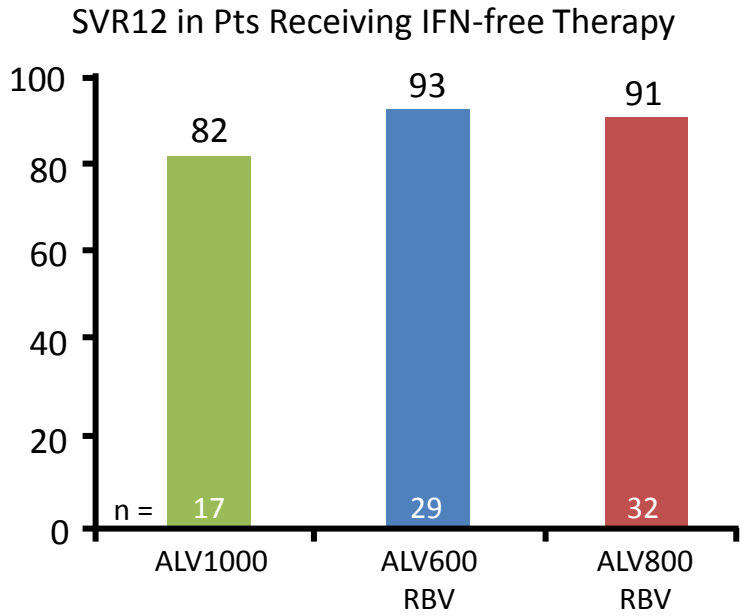
Alisporivir G2-3



Pawlotsky et al EASL 2012

Alisporivir G2-3

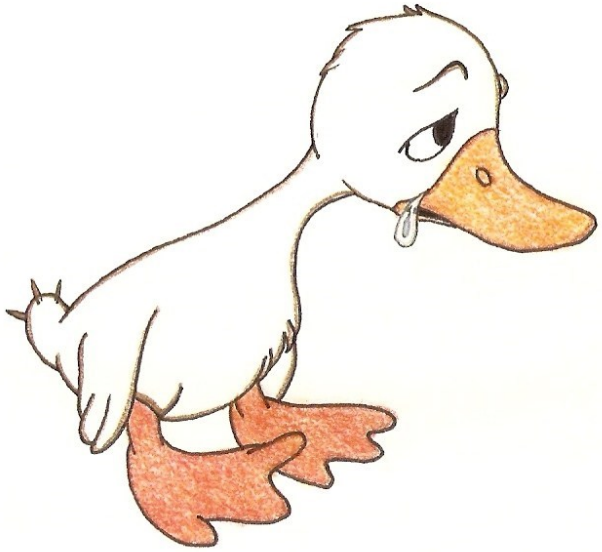




Proportion IFN Free	21%	35%	34%

Pawlotsky et al EASL 2012

Alisporivir – the ugly duckling for G3



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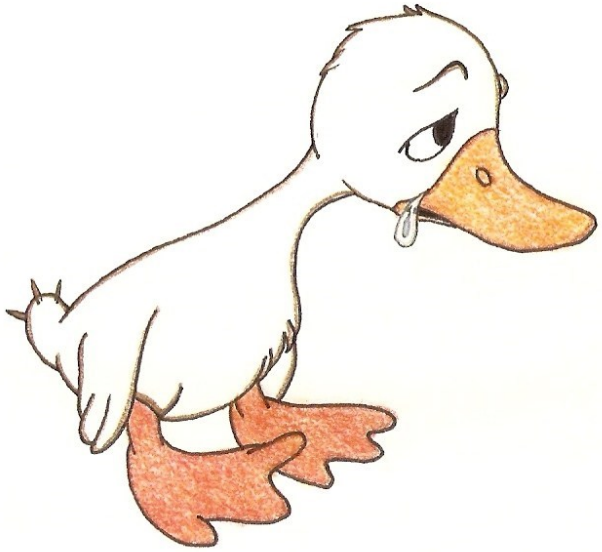

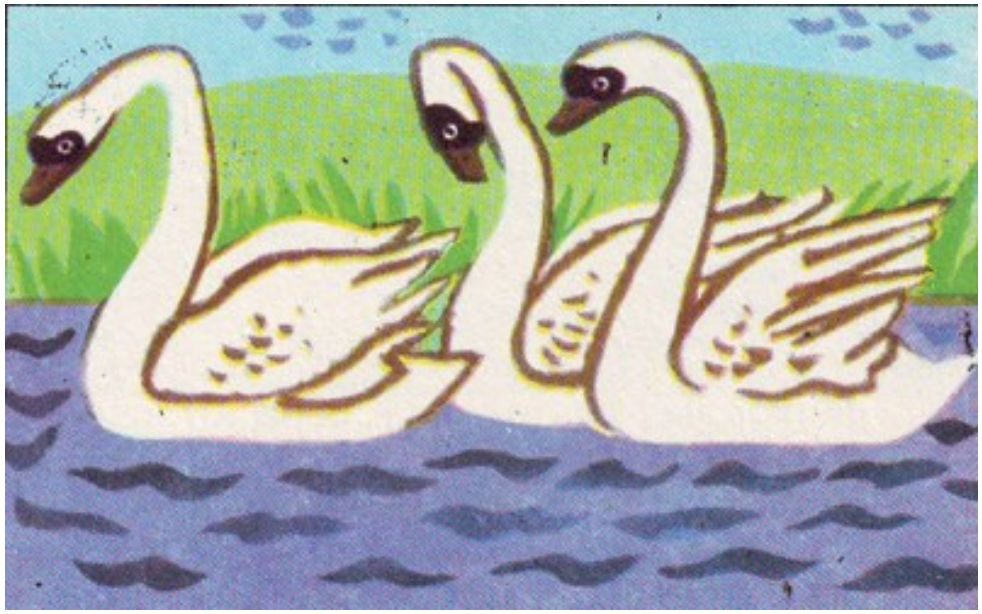

Alisporivir currently on clinical hold with concerns about pancreatitis
Is this a class effect?
Is this an interferon effect?

G3 HCV

- Easy G3 patients respond well to Peg+ Riba

- Tough G3 patients are common
- Tough G3 patients are becoming more common

- Tough G3 patients are the REAL problem area in HCV eradication