SPRINT-1

High Sustained Virologic Response in Genotype 1 Null Responders to Peginterferon α-2b + Ribavirin When Treated with Boceprevir Combination Therapy

Results From HCV Sprint-1

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Sunday, 01 November 2009
5:00
Hynes Auditorium

Background

- Week 4 HCV-RNA response with Peg/ribavirin is highly predictive of SVR
- IDEAL U.S. based HCV-1 Study*
  - < 1 $\log_{10}$ at week 4 SVR: 4.5%
  - < 1 $\log_{10}$ at week 4 corresponds to approximately < 2 $\log_{10}$ at week 12

*McHutchison et al, NEJM, 361;6,2009

Aim and Methods

- Utilizing the treatment groups from the SPRINT-1 boceprevir study that received Peg/ribavirin as a 4 week lead-in
  - Determine the SVR for various levels of interferon responsiveness (log_{10}) at week 4 of Peg/ribavirin

<0.5	2.0-<3.0
0.5-<1.0	3.0-<4.0
1.0-<1.5	≥4.0
1.5-<2.0	Undetectable

  - Examine the characteristics that may underlie response in these patients, particularly null responders (<1 log_{10} at week 4)

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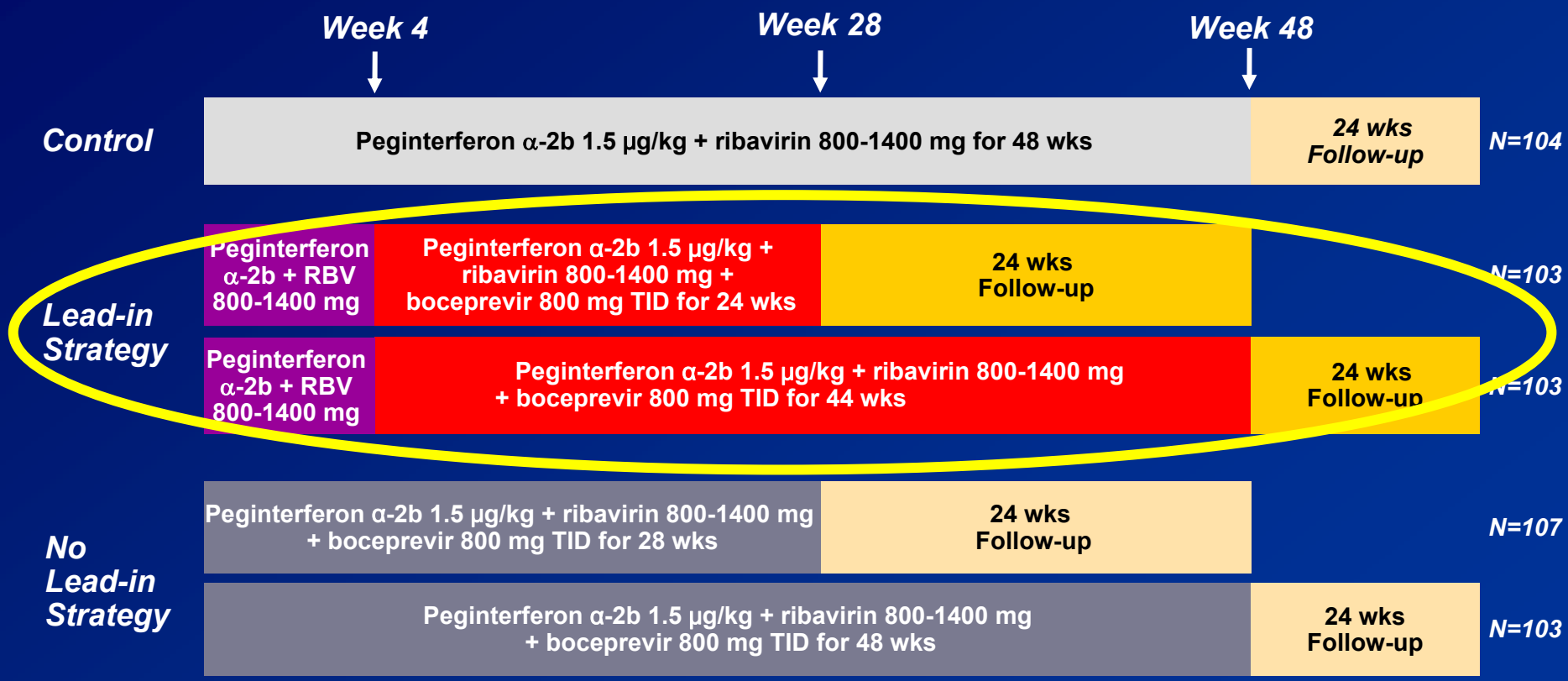
SPRINT-1 Study Design



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Baseline Characteristics

	P/R Control 48 wks N=104	P/R/B 28 wks N=107	P/R 4 wks → P/R/B 24 wks N=103*	P/R/B 48 wks N=103	P/R 4 wks → P/R/B 44 wks N=103*
Gender, % Male	67	59	50	61	56
Race, % Caucasian Black	 80 15	 80 17	 83 15	 84 14	 83 15
Mean age, years	48.3	46.4	47.7	46.7	47.6
Mean weight, kg	83.4	83.4	79.9	80.0	78.4
HCV subtype, % 1a 1b 1 (no sub-type)	 51 40 9	 63 28 9	 51 36 13	 53 35 12	 58 34 8
Mean viral load, log_{10} IU/mL	6.53	6.64	6.53	6.54	6.53
HCV-RNA >600,000 IU/mL, %	90	92	87	91	90
Cirrhosis, %	8	7	7	9	6

*Boceprevir added to treatment regimen after 4 week lead-in of peginterferon alfa-2b + ribavirin.

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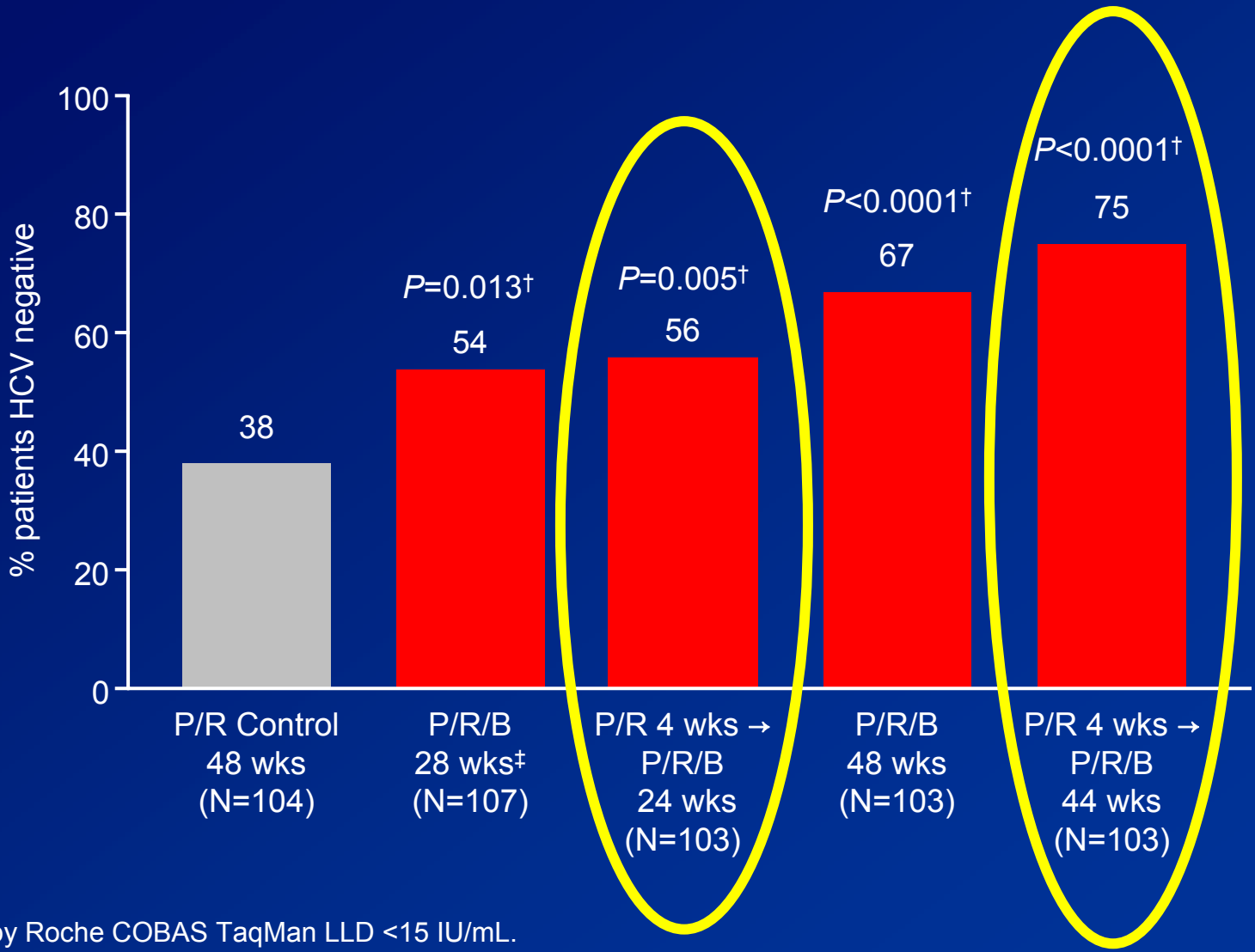
Sustained Virologic Response



*Measured by Roche COBAS TaqMan LLD <15 IU/mL.
†*P* value compared to P/R control.
‡One late relapser after follow-up week 24, not included in SVR.

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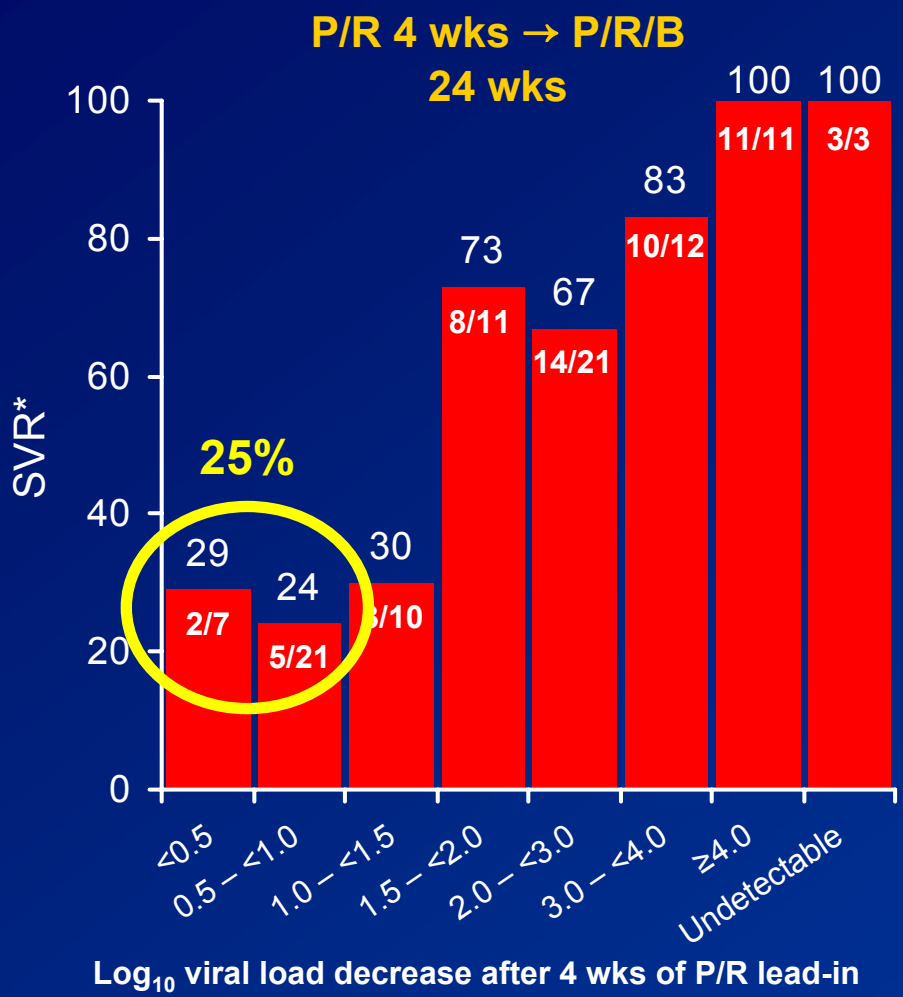
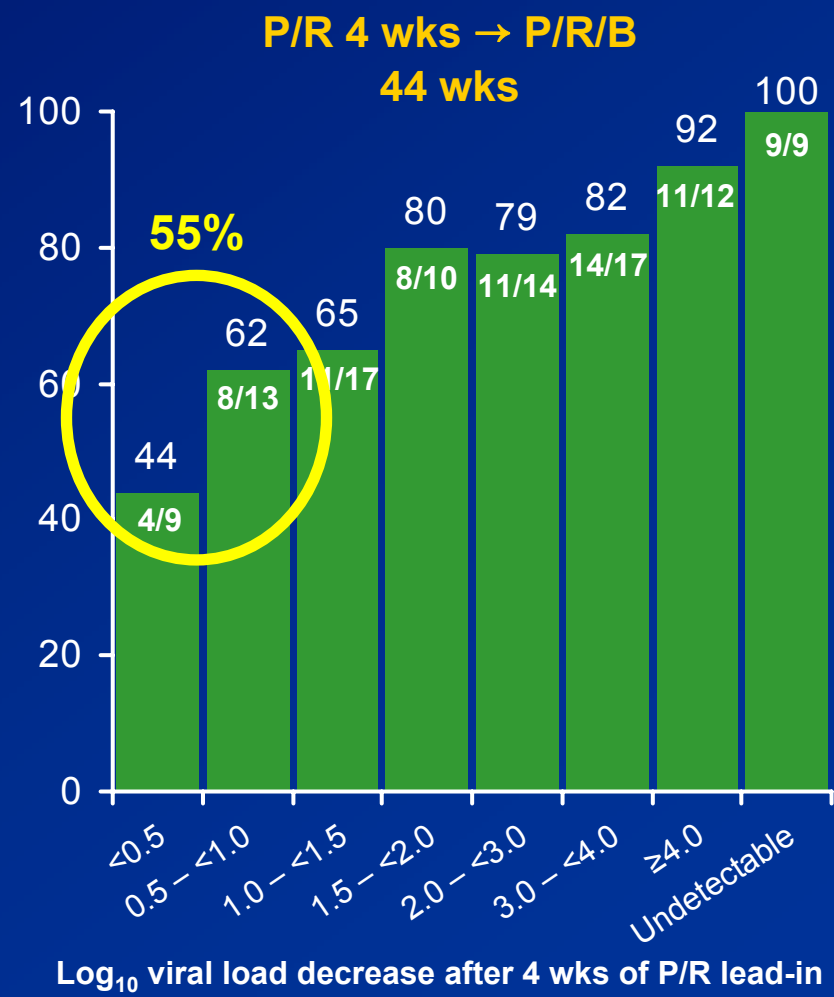
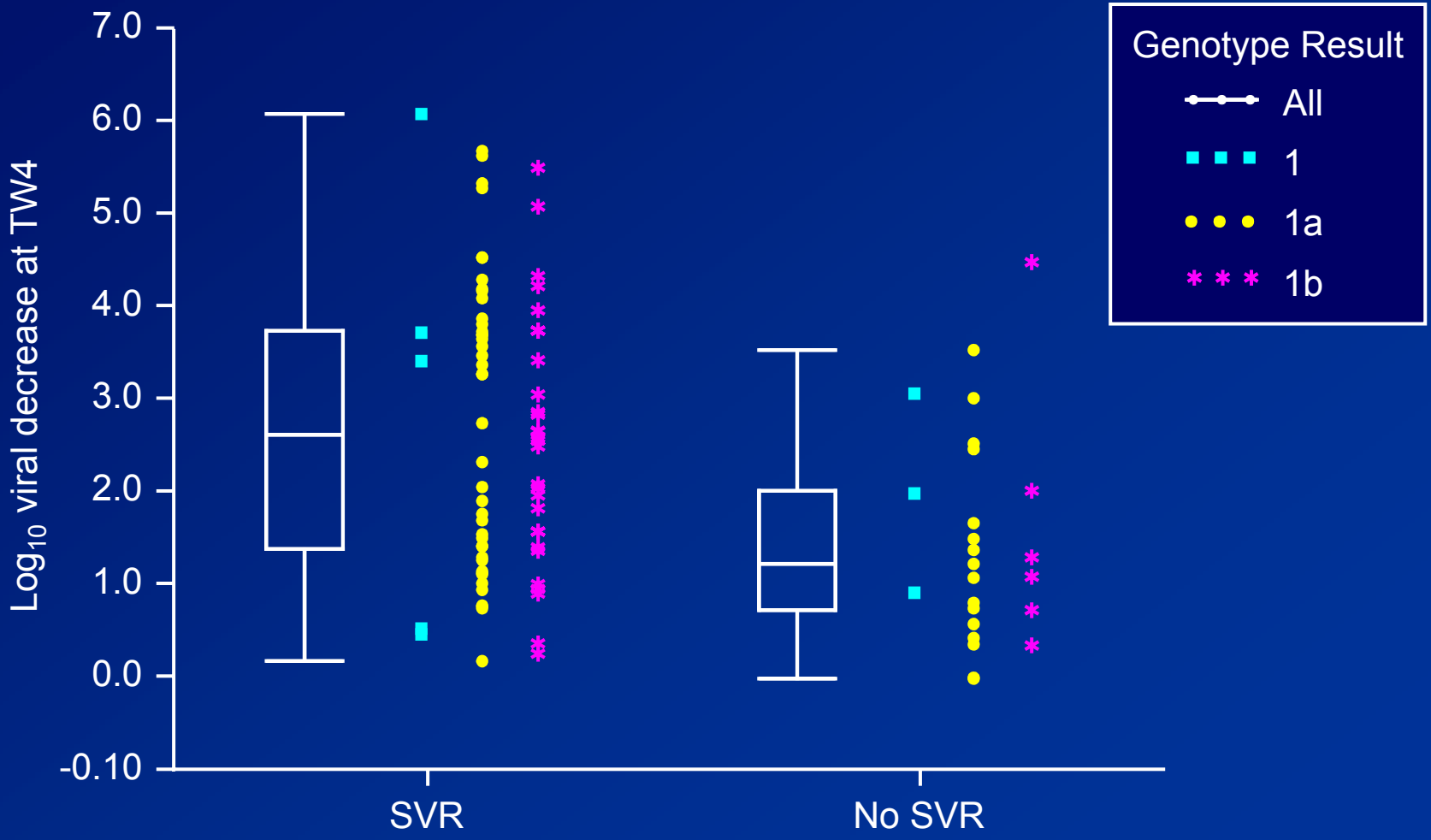
Predictability of SVR Based on Response During 4-Week P/R Lead-in





[a]Undetectable HCV-RNA using Roche COBAS TaqMan with LLD <15 IU/mL; 7 and 2 patients were missing week 4 virology in 28 and 48 wk groups, respectively.

SVR Based on HCV RNA Decrease During 4-Week P/R Lead-In: 48-Week Treatment



Subtyping by Trugene assay.

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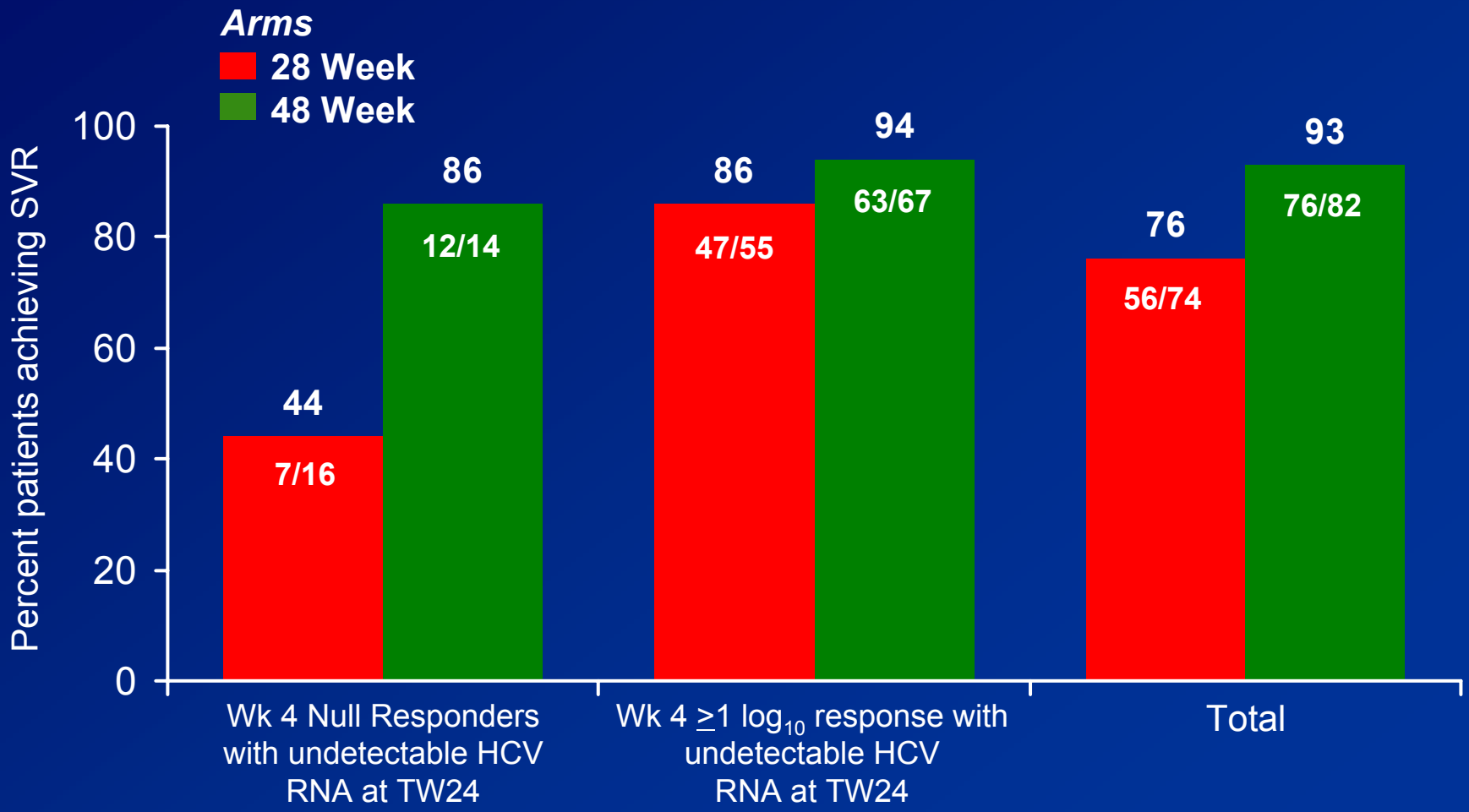
Undetectable HCV RNA at TW 24 as a Predictor of SVR
Null vs ≥1 log_{10} Response at Week 4



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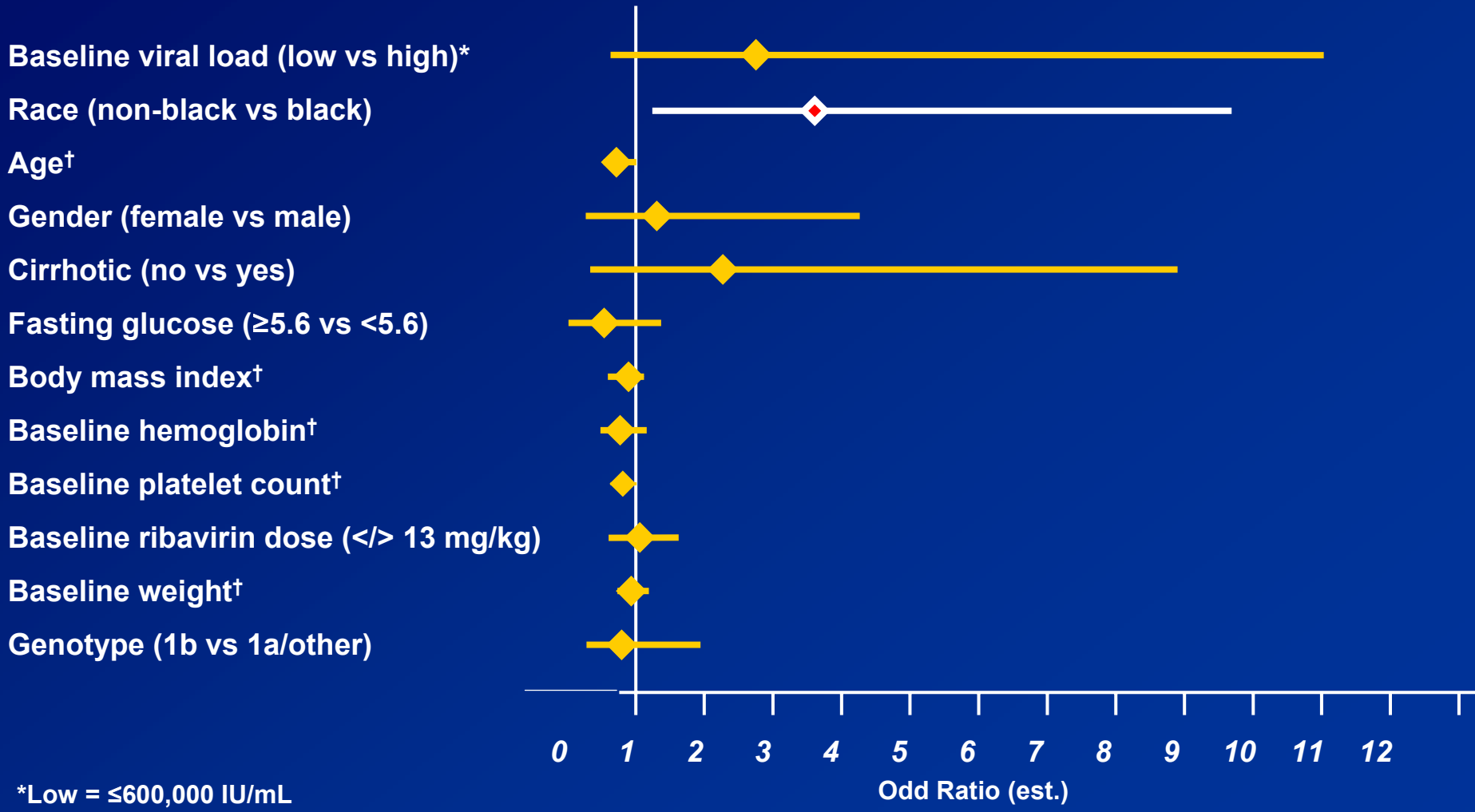
Multivariate Logistic Regression for TW4 Response (Lead-In Arms): Baseline Factors



*Low = ≤600,000 IU/mL
†Continuous variables

Summary

- Boceprevir significantly improves SVR
  - Boceprevir with standard of care for 48 weeks nearly doubles SVR
- Patients with <1 log drop in viral load (null response) after 4 weeks of P/R lead-in went on to achieve SVR:
  - 25% (7/28) of those who received 28 weeks of treatment
  - 55% (12/22) of those who received 48 weeks of treatment
- 77% (113/147) of patients who had a ≥1.0 log drop in viral load (non-null response) after 4 weeks of P/R lead-in went on to achieve SVR
- Race (black) was the only baseline predictor for null response at week 4

Conclusions

- Ongoing boceprevir studies will further define the relationship of Week 4 Peg/RBV (lead-in) response to achievement of SVR
- Despite the small numbers of patients, these results suggest that null responders may achieve an SVR
- Risk of developing protease inhibitor resistance should be weighed against the benefits of treatment

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