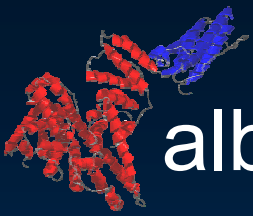


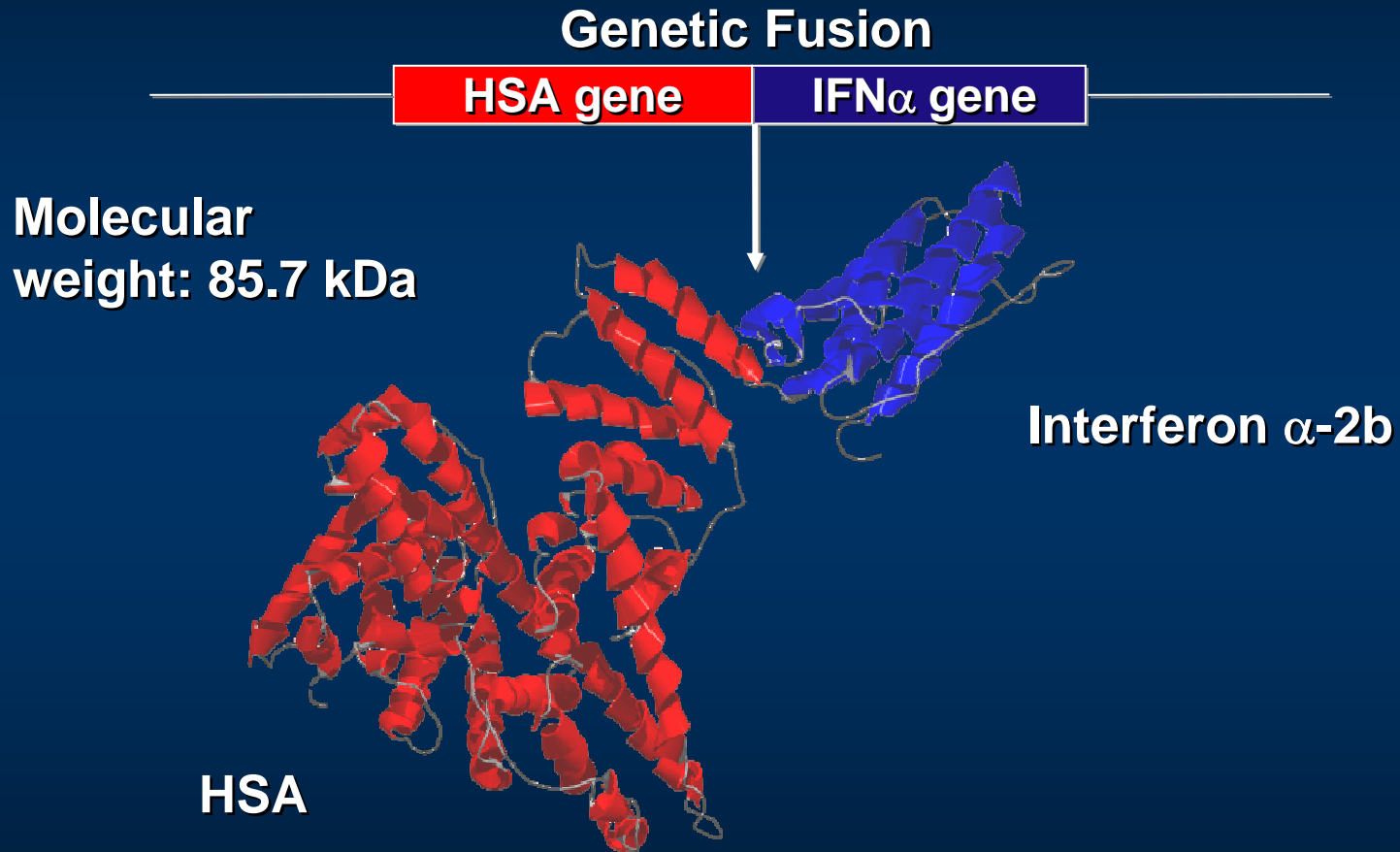
**COMPARABLE ANTIVIRAL RESPONSE  
RATES WITH ALBINTERFERON ALFA-2B  
DOSED AT Q2W OR Q4W INTERVALS IN  
NAIVE SUBJECTS WITH GENOTYPE 2 OR 3  
CHRONIC HEPATITIS C**

**V.G. Bain**, P. Marotta, K. Kaita, E. Yoshida,  
M. Swain, R. Bailey, A. Neumann, P. Cronin,  
J. McHutchison, E. Pulkstenis, M. Subramanian


Study sponsored by Human Genome Sciences, Inc., Rockville, MD, USA



# albinterferon alfa-2b



albinterferon alfa-2b (alb-IFN) is a single polypeptide molecule that combines the therapeutic activity of interferon alpha with the long half-life of human serum albumin



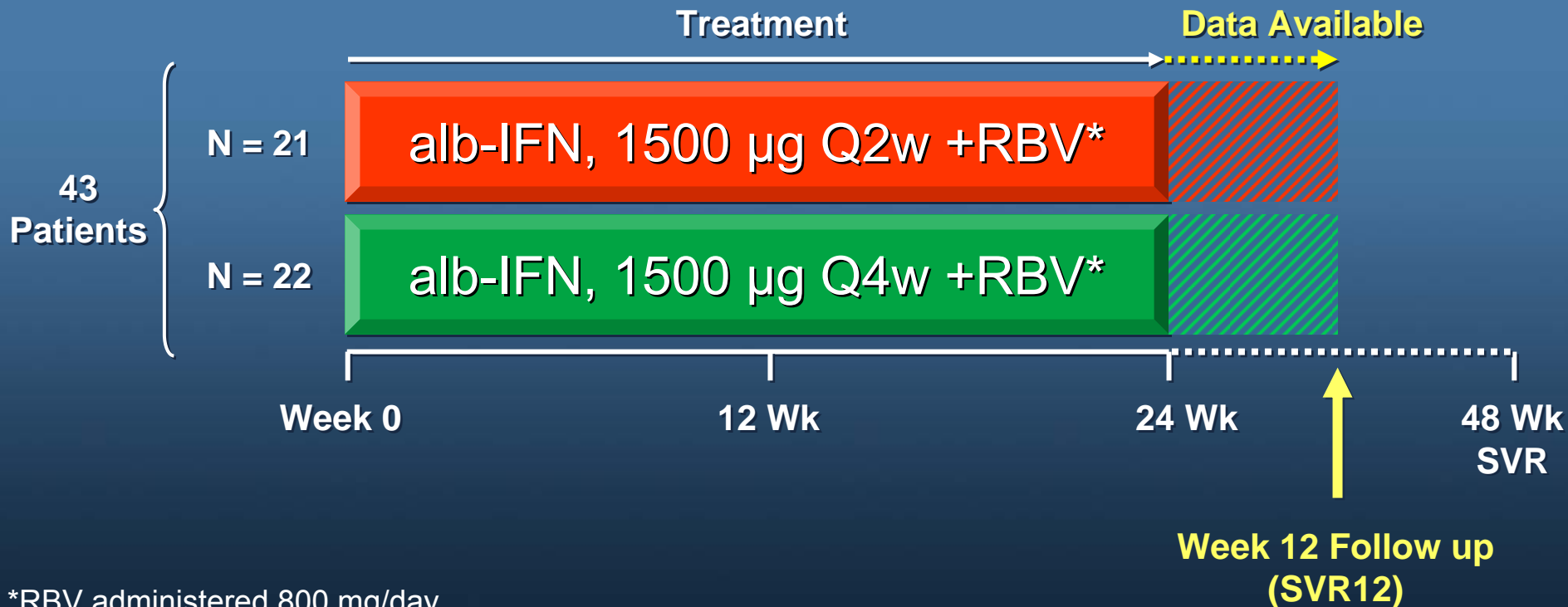
# Study Objectives

- Evaluation of efficacy and safety of albinterferon alfa-2b in genotype 2 and 3
  - Sustained virologic response (SVR) is defined as HCV RNA < 10 IU/mL at 24 weeks after the end of treatment)
- Exploratory analysis of insulin resistance and its effect on SVR
  - Homeostasis Assessment Model Insulin Resistance index (HOMA-IR)



# Study Design

- Randomized, open-label study, 6 sites in Canada
- 43 patients were randomized 1:1 to two study arms
- Stratification:
  - Genotype (2 or 3)
  - HCV RNA ( $< 800,000$  IU/mL or  $\geq 800,000$  IU/mL)



\*RBV administered 800 mg/day



# Endpoints and Methods

- Primary endpoint is SVR (HCV RNA negative at 24 weeks post-treatment)
  - Week 12 follow up (SVR12) is accepted as predictive of SVR<sup>1</sup> and is presented in this analysis
- Methods
  - Analyses are intent to treat (ITT): all subjects randomized and treated
  - HCV RNA was measured using real-time PCR (LOQ = 43 IU/mL, LOD = 10 IU/mL)

<sup>1</sup>Zeuzem, et. al., J Hep 39:106, 2003

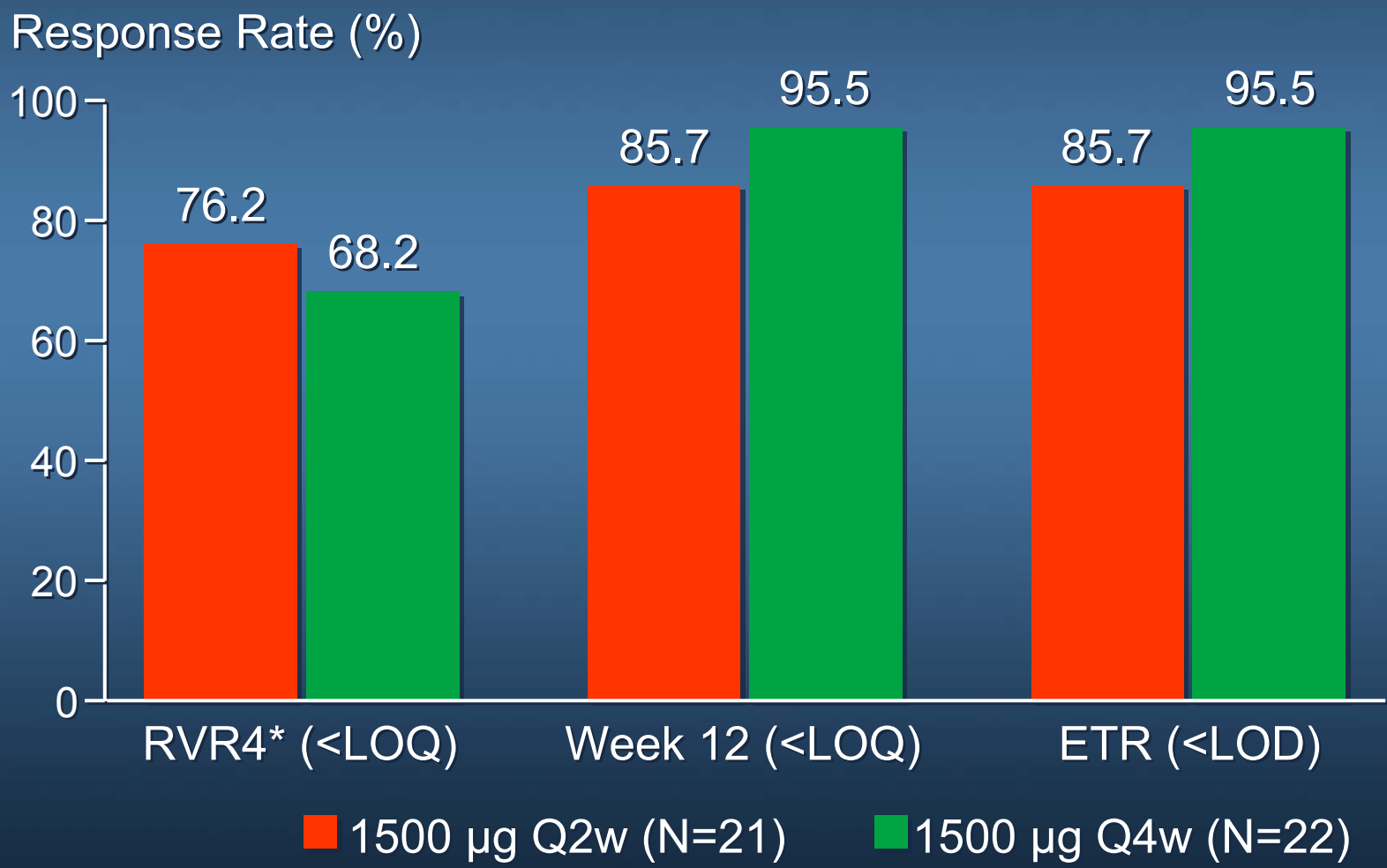


# Baseline Characteristics

albinterferon alfa-2b	1500 µg Q2 N = 21	1500 µg Q4 N = 22
Age (yr) Mean ± SD	44.0 ± 8.8	44.7 ± 9.6
Gender - Male	15 (71.4%)	15 (68.2%)
Ethnicity - White	19 (90.5%)	17 (77.3%)
Genotype 2	10 (47.6%)	10 (45.5%)
Genotype 3	11 (52.4%)	12 (54.5%)
HCV RNA (logIU/mL) Mean ± SD	6.3 ± 0.8	6.0 ± 0.8
≥ 800,000 IU/mL	15 (71.4%)	13 (59.1%)
BMI (kg/m <sup>2</sup> ) Mean ± SD	28.5 ± 5.9	27.8 ± 4.3
HOMA-IR Mean ± SD	2.1 ± 1.1	2.4 ± 1.7
% Insulin Resistant (HOMA-IR>2)	40%	50%



# ITT Analysis of HCV RNA Response

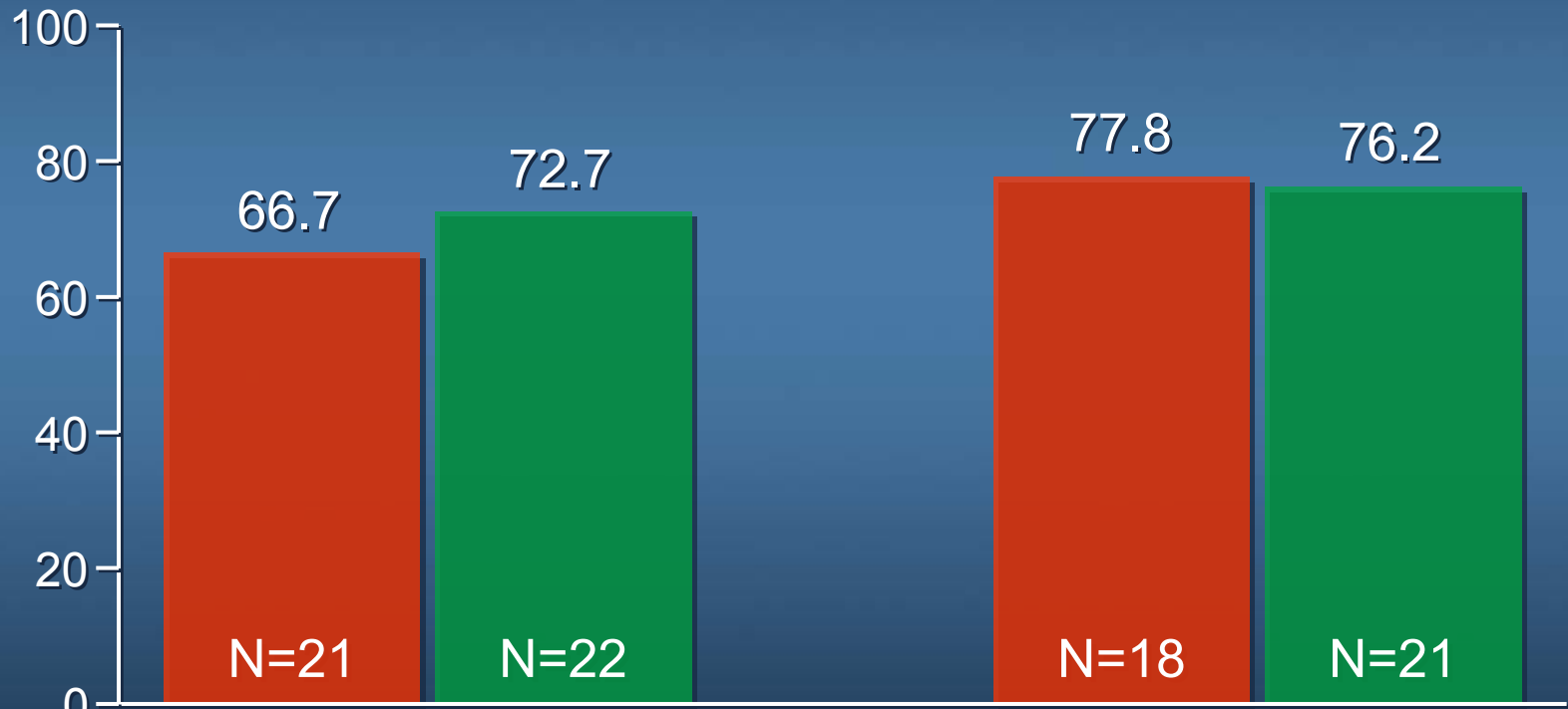


\*Rapid Viral Response at Week 4



# SVR12 Response Rate

SVR12 Response Rate (%)



1500 µg Q2w

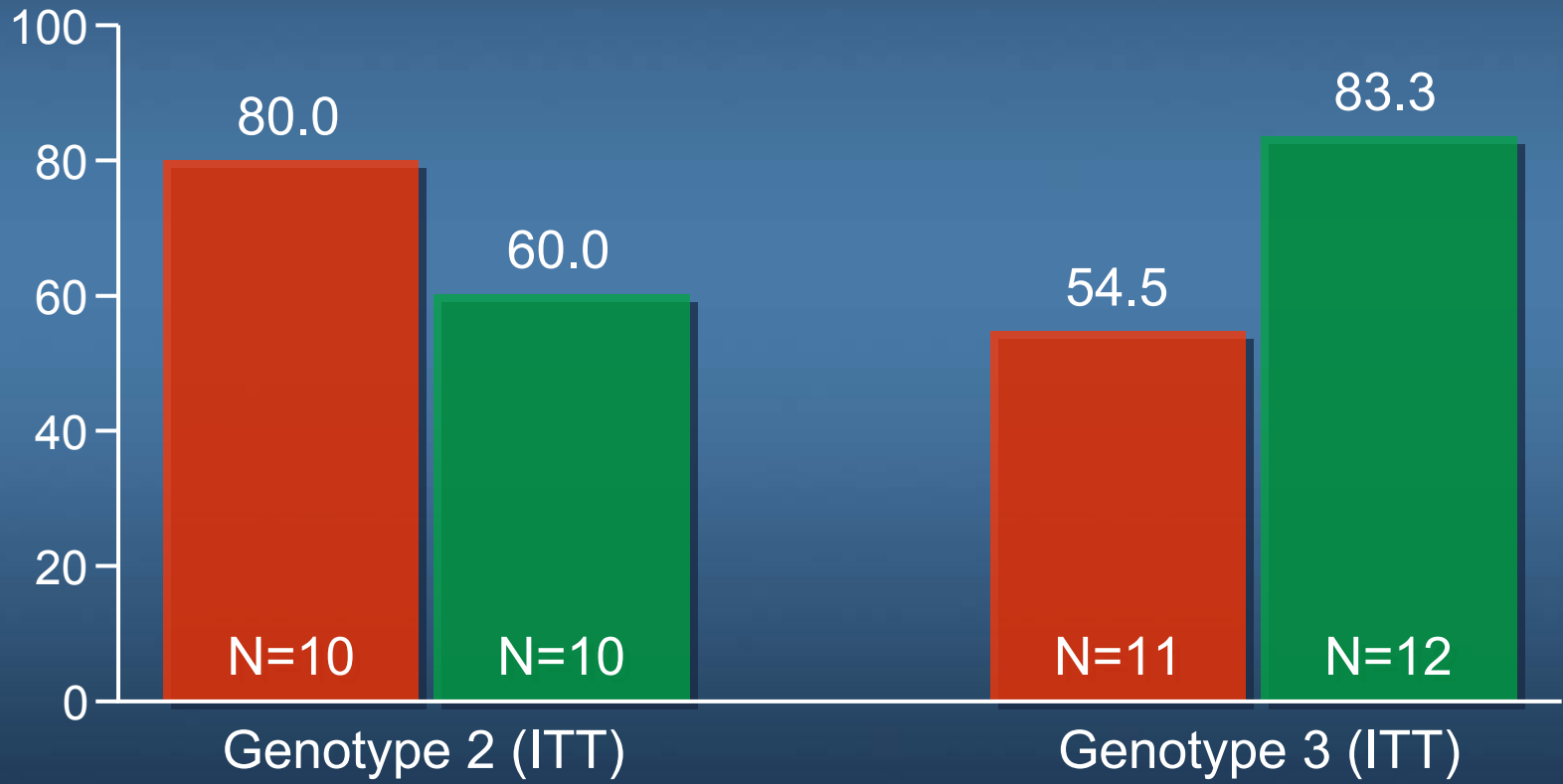
1500 µg Q4w





# SVR12 Response Rate by Genotype

SVR12 Response Rate (%)

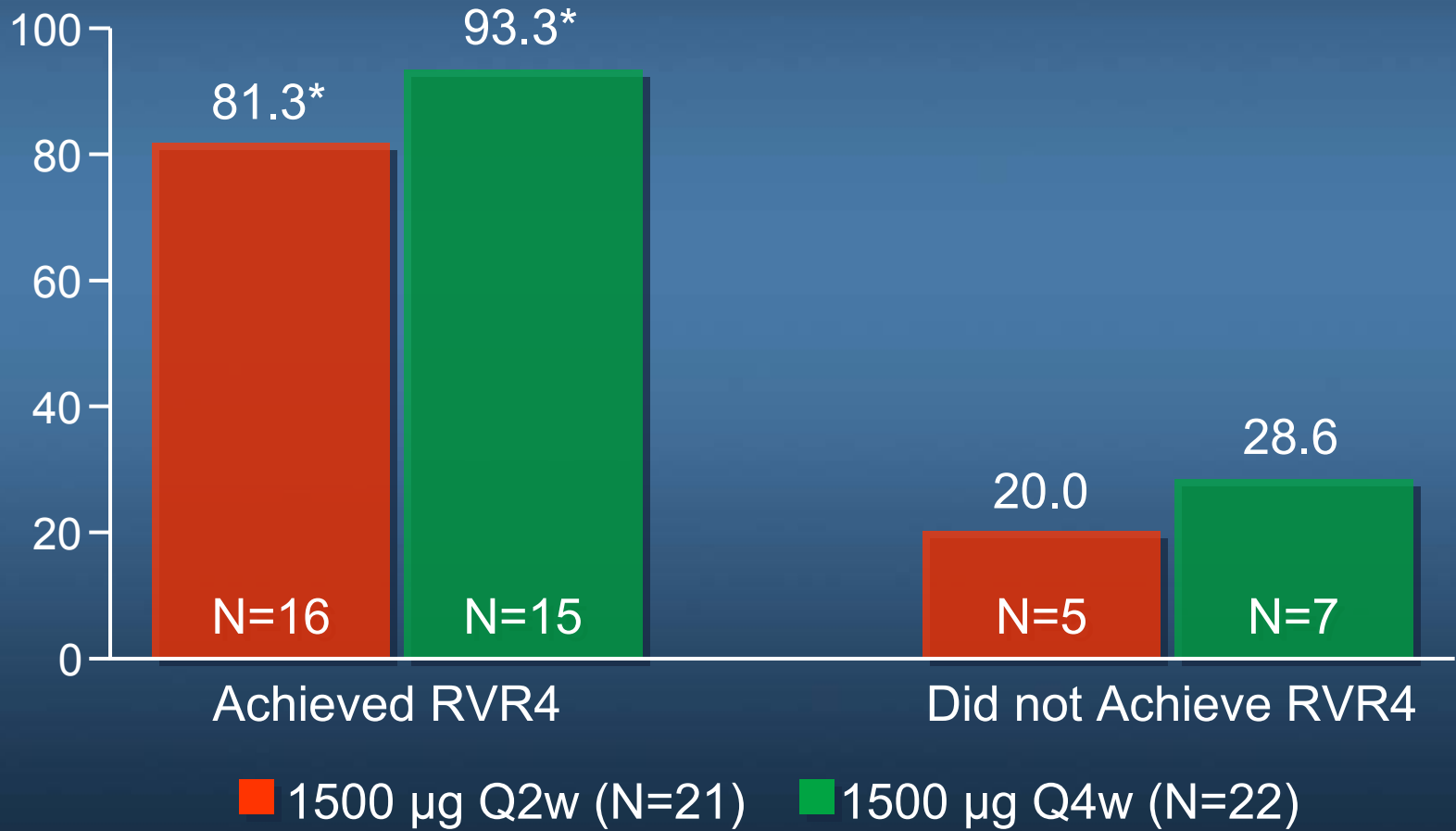


■ 1500 µg Q2w (N=21)    ■ 1500 µg Q4w (N=22)



# Predictive Value of RVR4 for SVR12

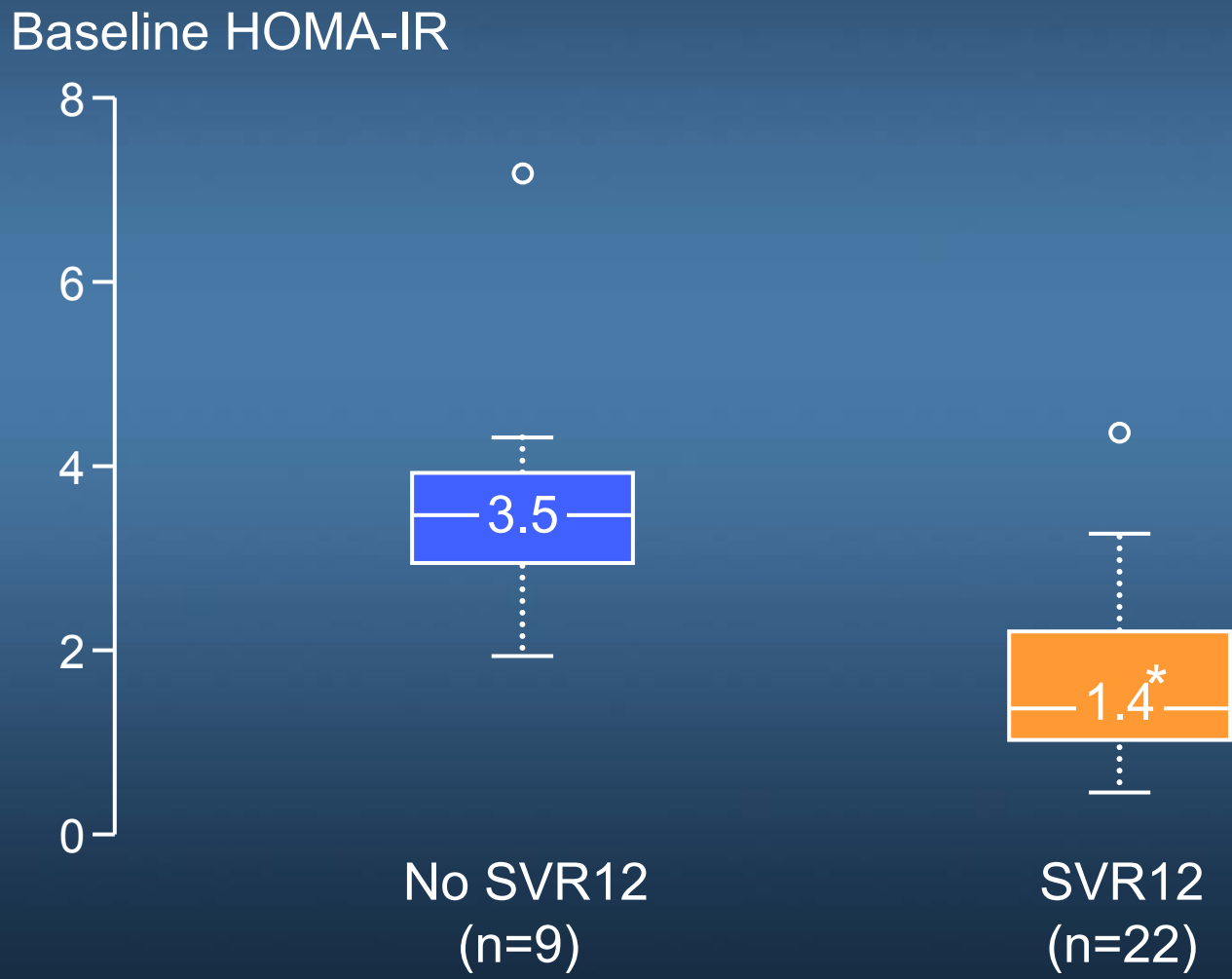
SVR12 Response Rate (%)



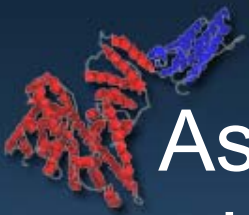
\*P value < 0.05 vs. subjects not achieving RVR4



# Association of Insulin Resistance with SVR12



\* P value = 0.0004



# Association of Insulin Resistance with Viral Response

Insulin Resistance	Insulin Resistant (HOMA-IR > 2) N = 14	Non Insulin Resistant (HOMA-IR ≤ 2) N = 17	P value
BMI (Mean ± SD)	28 ± 3.8	27 ± 5.6	0.2145
Week 4 < LOQ (RVR4)	6 (42.9%)	15 (88.2%)	0.0181
Week 12 < LOQ	11 (78.6%)	17 (100%)	0.0810
SVR12	6 (42.9%)	16 (94.1%)	0.0038*

\*p=0.0105 controlling for baseline weight and BMI via logistic regression modeling.



# Safety and Tolerability

albinterferon alfa-2b	1500 µg Q2w N = 21	1500 µg Q4w N = 22
Severe AE	5 (23.8%)	6 (27.3%)
Discontinued	7 (33.3%)	3 (13.6%)
Discontinued due to AE	3 (14.3%)	1 (4.5%)
IFN Dose Reduction due to AE	2 (9.5%)	0
IFN Dose Reduction due to Labs	3 (14.3%)	0



# Safety and Tolerability

## MOD/SEV AEs by Preferred Term in >15% of Either alb-IFN Group

MedDRA Preferred Term	1500 µg Q2w N = 21	1500 µg Q4w N = 22
Headache	10 (47.6%)	11 (50.0%)
Fatigue	7 (33.3%)	8 (36.4%)
Chills	6 (28.6%)	6 (27.3%)
Myalgia	6 (28.6%)	4 (18.2%)
Nausea	6 (28.6%)	4 (18.2%)
Pyrexia	5 (23.8%)	4 (18.2%)
Weight Decreased	6 (28.6%)	2 (9.1%)
Back Pain	5 (23.8%)	2 (9.1%)
Mood Altered	5 (23.8%)	2 (9.1%)
Arthralgia	4 (19.0%)	2 (9.1%)
Pruritus Generalized	1 (4.8%)	4 (18.2%)
Tremor	4 (19.0%)	1 (4.5%)
Vomiting	4 (19.0%)	1 (4.5%)



# Hematology

albinterferon alfa-2b

1500  $\mu$ g Q2w

1500  $\mu$ g Q4w

N = 21

N = 22

---

## ANC

$\leq 750$  / $\mu$ L

5 (23.8%)

2 (9.1%)

$\leq 500$  / $\mu$ L

2 (9.5%)

0

---

## Hb

< 10 g/dL

2 (9.5%)

0

---

## Platelets

$\leq 50,000$  / $\mu$ L

1 (4.8%)

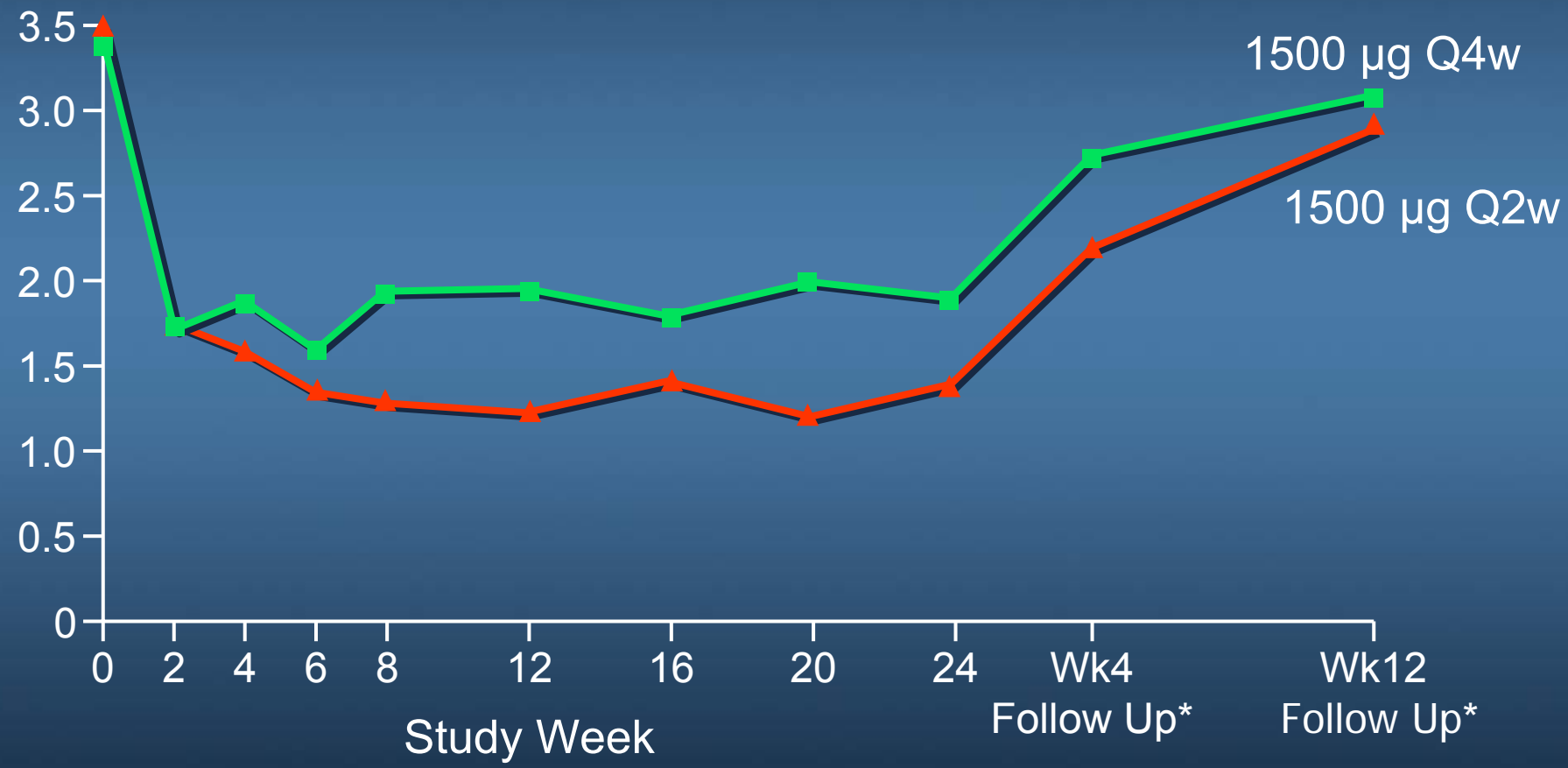
0

---



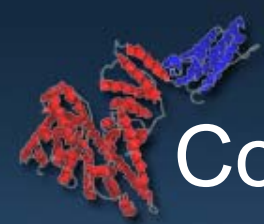
# Absolute Neutrophil Count

Median ANC (X 10<sup>-3</sup>/uL)



\* Includes all data including early discontinuations





# Conclusions

- alb-IFN at 1500  $\mu\text{g}$  Q4w is well tolerated and shows robust antiviral activity in genotypes 2,3
- Hematologic reductions stabilize by Week 8 and recover upon completion of therapy
  - 1500  $\mu\text{g}$  Q4w had less impact on hematology
- Insulin resistance is negatively associated with viral response (RVR4 and SVR12)