CONTINUING MEDICAL EDUCATION INTERNET SYMPOSIUM

ADVANCES IN CHRONIC HEPATITIS C MANAGEMENT AND TREATMENT

Reporting from

THE 63RD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES ANNUAL MEETING

Jointly sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC

Supported by an Unrestricted Educational Grant by Merck & Co.

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Updates on Current Status of HCV Therapy

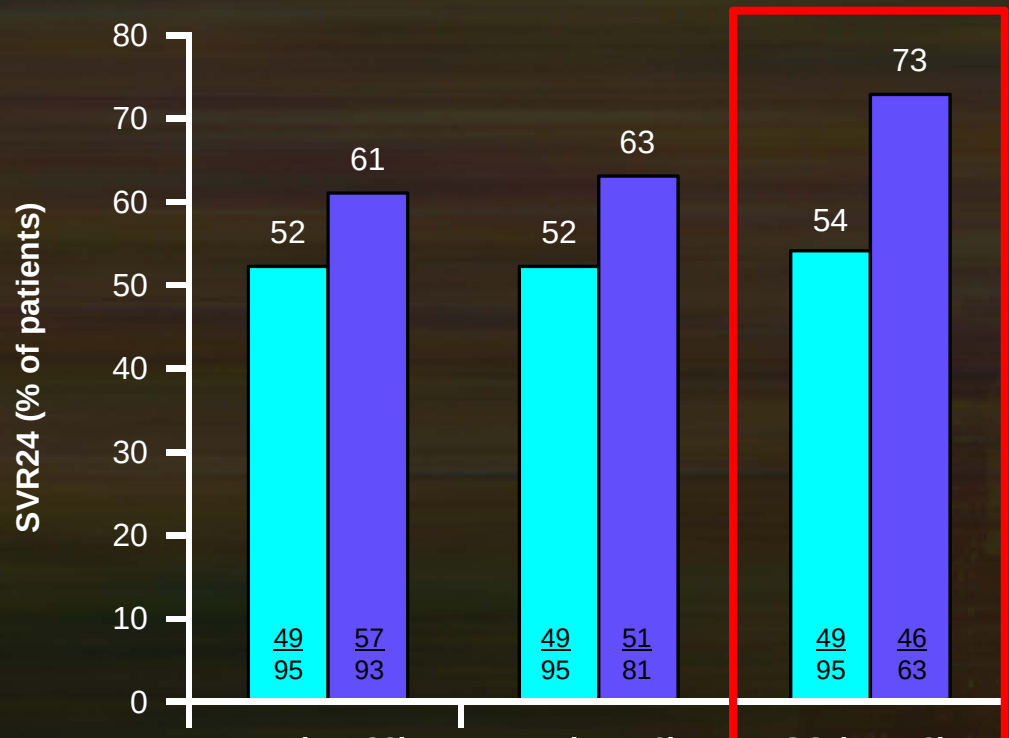
K. Rajender Reddy, MD

Cost-Effectiveness of Screening for Chronic HCV Infection in the US

- Markov Model to simulate natural H/O HCV disease progression
- Base case US population
  - 78 % Caucasian, 13 % African American, 9 % Hispanic, mean age 46 years
- Guideline based treatment (boceprevir or telaprevir as the DAA)
  - Boceprevir costs $ 47,276 per QALY gained
  - Telaprevir costs $ 44,074 per QALY
- Below prevalence of 0.84 %; marginal Cost-Effectiveness Ratio (mCER)
- **Conclusion: Targeted Screening is “cost-effective” when prevalence of HCV exceeds 0.84 %**

Eckman M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 137.

The N-CORE study: Efficacy - SVR24 rates



	ITT (n=188)	PP (n=176)	SC (n=153)
Odds ratio	**0.68**	**0.63**	**0.44**
95% CI	**0.38–1.21**	**0.35–1.16**	**0.22–0.89**
p-value	**0.1934**	**0.1461**	**0.0231**

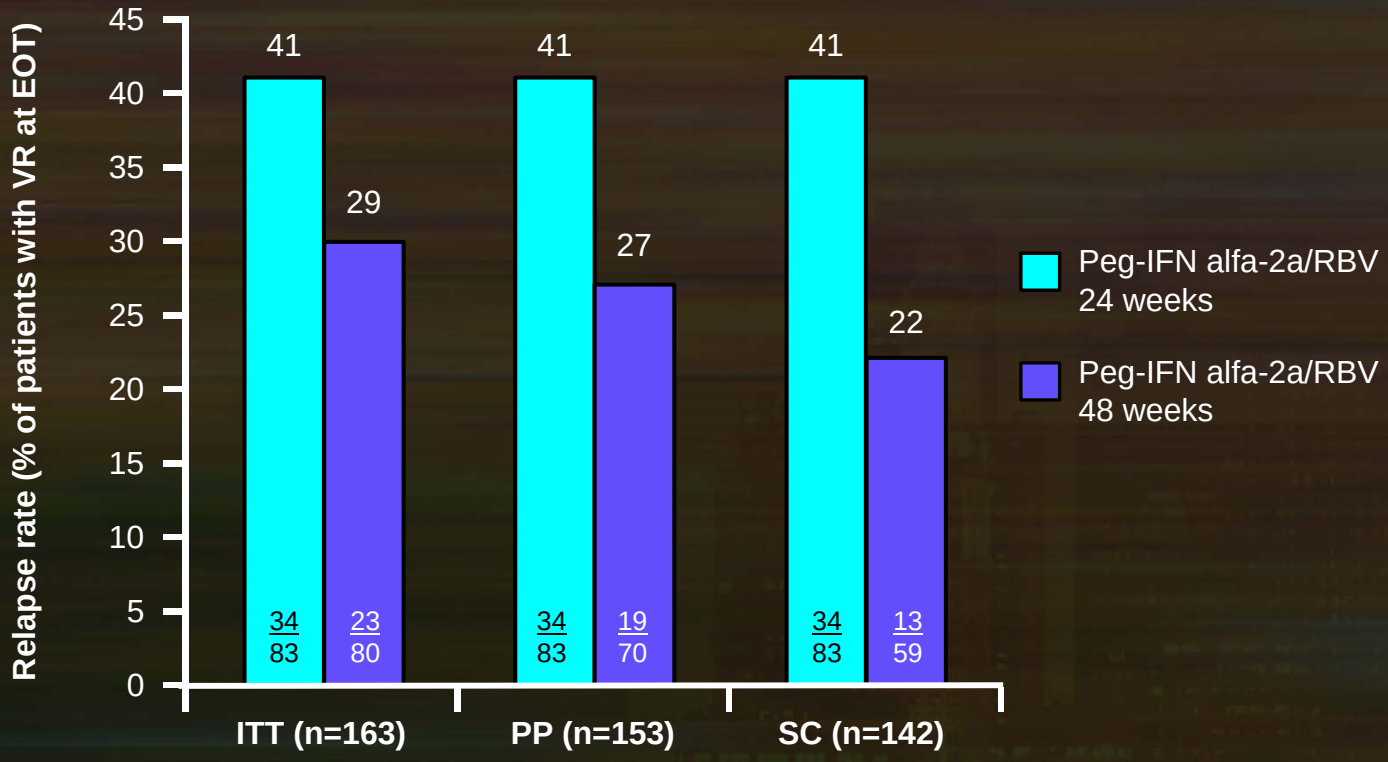
SC population: significantly higher SVR24 rates with 48 weeks vs. 24 weeks of Peg-IFN alfa-2a/RBV

CI = confidence interval; SVR24 = sustained virological response ≥140 days after end of treatment.

Cheinquer H et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 156.

The N-CORE study: Efficacy - relapse rates

- Lowest relapse rates in SC population, 48 weeks



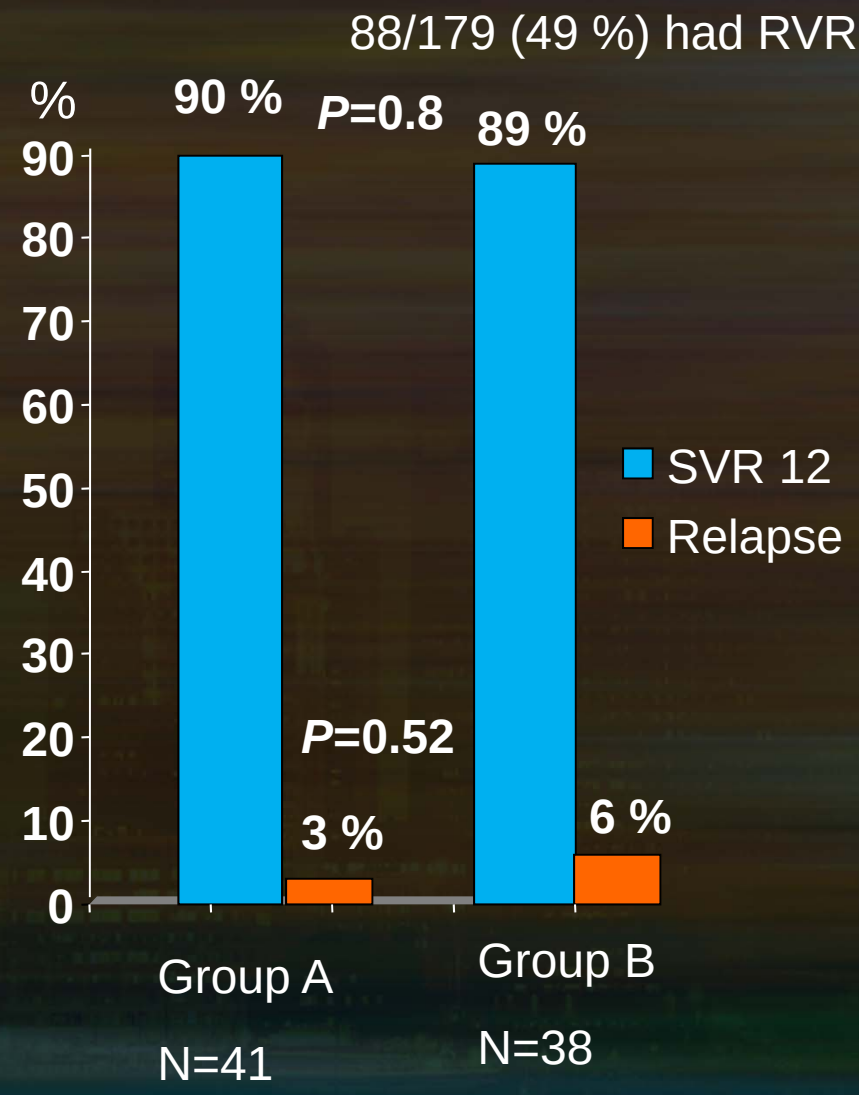
Relapse rates calculated as percentage of patients to relapse from those that achieved a virological response at end of treatment.

No *P*-values are available as the study was underpowered.

Cheinquer H et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 156.

HCV Low Viral Load and RVR: Pegylated Interferon, RBV and Boceprevir Vs. Pegylated Interferon and RBV

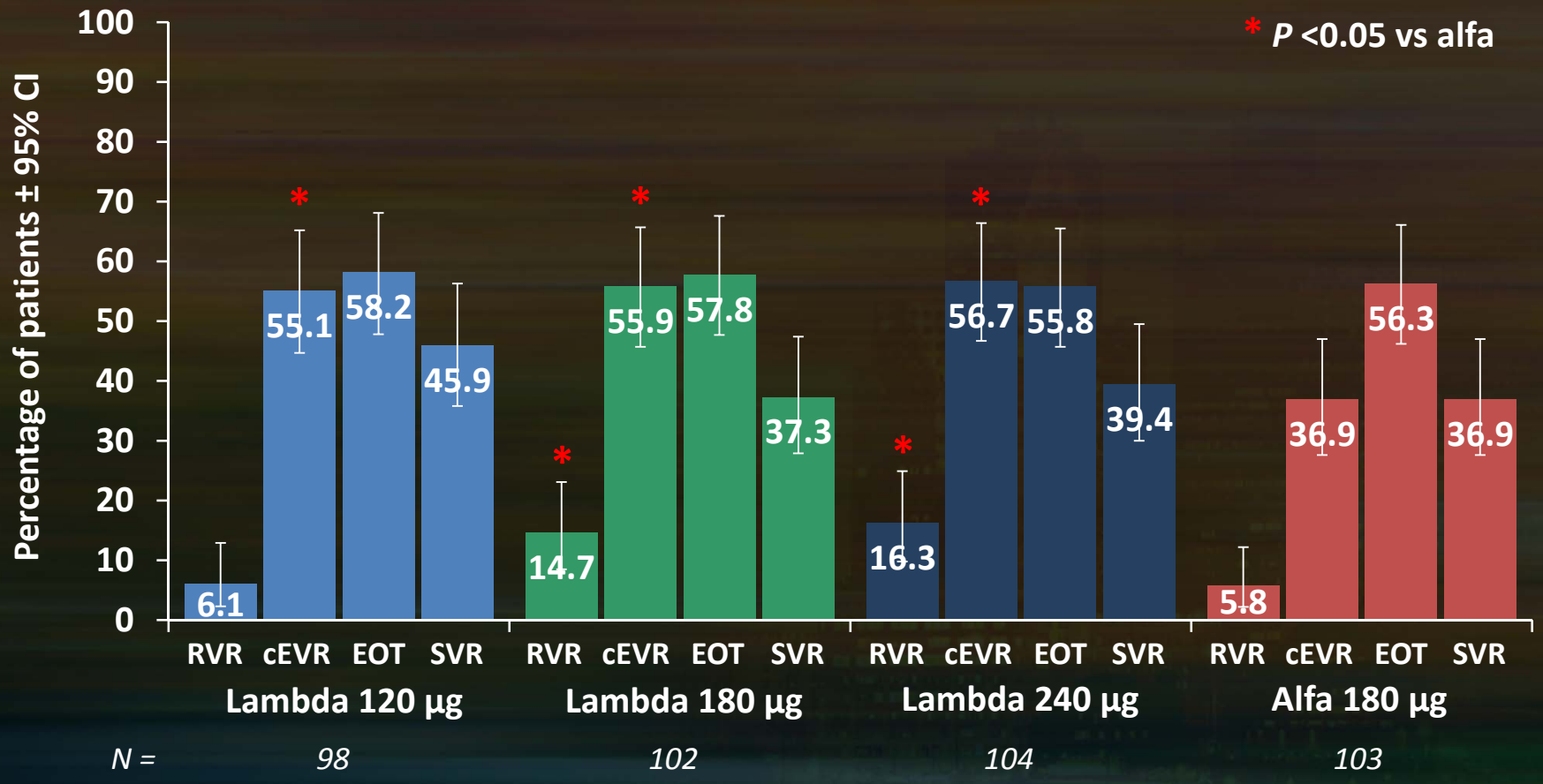
- Randomized Study
- LVL (<600,000IU/mL)
- Treatment naïve
- PEG-IFN alfa 2b plus RBV
- RVR patients randomized to PEG-IFN/RBV/BOC for 28 weeks(Group A) vs. PEG-IFN/RBV for 28 weeks (Group B)



Pearlman B et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 151.

Undetectable HCV RNA at Week 4 (RVR), Week 12 (cEVR), Week 48 (EOT), and Week 72 (SVR_{24})

- The 180 μg dose selected for Phase 3 exhibited more rapid achievement of virologic response, with similar SVR and relapse rates compared with alfa



Muir AJ, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 214.

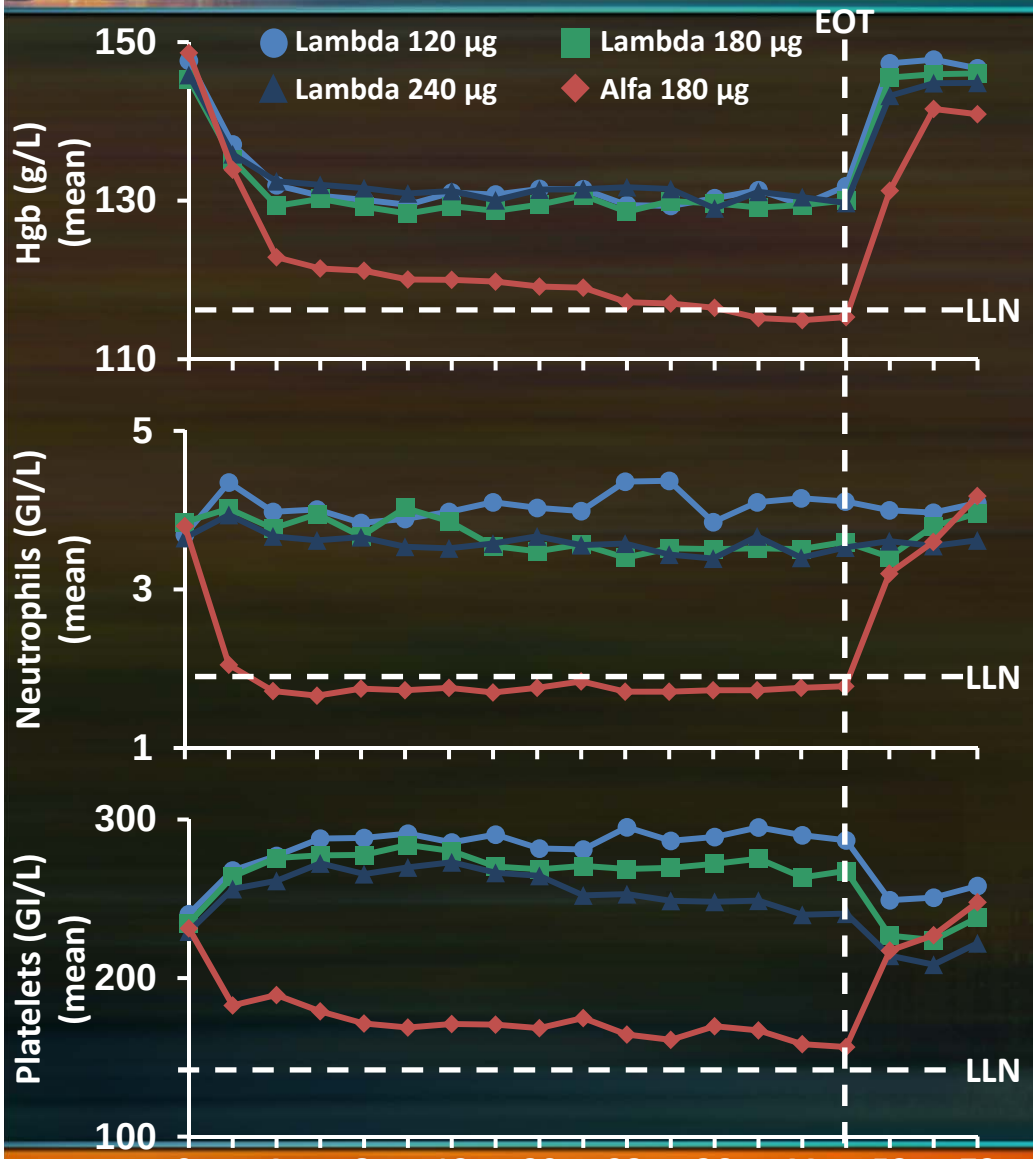
AEs (Any Grade) Occurring in ≥ 20% of Patients in Any Treatment Group

	Lambda			Alfa
Preferred term	**120 µg (N = 98)**	**180 µg (N = 102)**	**240 µg (N = 104)**	**180 µg (N = 103)**
AE (any grade), %	87.8	**88.2**	91.3	**97.1**
Fatigue	37.8	**46.1**	37.5	**42.7**
Headache	26.5	**27.5**	27.9	**41.7**
Myalgia	10.2	**5.9**	12.5	**33.0**
Pyrexia	12.2	**7.8**	4.8	**33.0**
Nausea	25.5	**21.6**	31.7	**30.1**
Pruritus	19.4	**17.6**	27.9	**29.1**
Insomnia	31.6	**17.6**	22.1	**25.2**
Rash	13.3	**14.7**	11.5	**24.3**
Chills	4.1	**3.9**	1.9	**21.4**
Arthralgia	14.3	**5.9**	9.6	**20.4**

> 2-fold difference in frequency, Lambda 180 µg vs alfa 180 µg.

Muir AJ, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 214.

Changes in Hematologic Parameters Over Time and Hematology-Associated Dose Reductions



	Lambda 180 µg (N = 102)	Alfa 180 µg (N = 103)
Hgb low < 9 g/dL *OR* Δ ≥ 4.5 g/dL	**5.9%**	**31.1%**
RBV reduction (Hgb-associated)	**0%**	**23.3%**
Neutrophils low < 750/mm^3	**1.0%**	**20.4%**
Platelets low < 50,000/mm^3	**0%**	**1.9%**
PegIFN reduction (hematologic abnormality)	**0%**	**20.4%**

Muir AJ, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 214.

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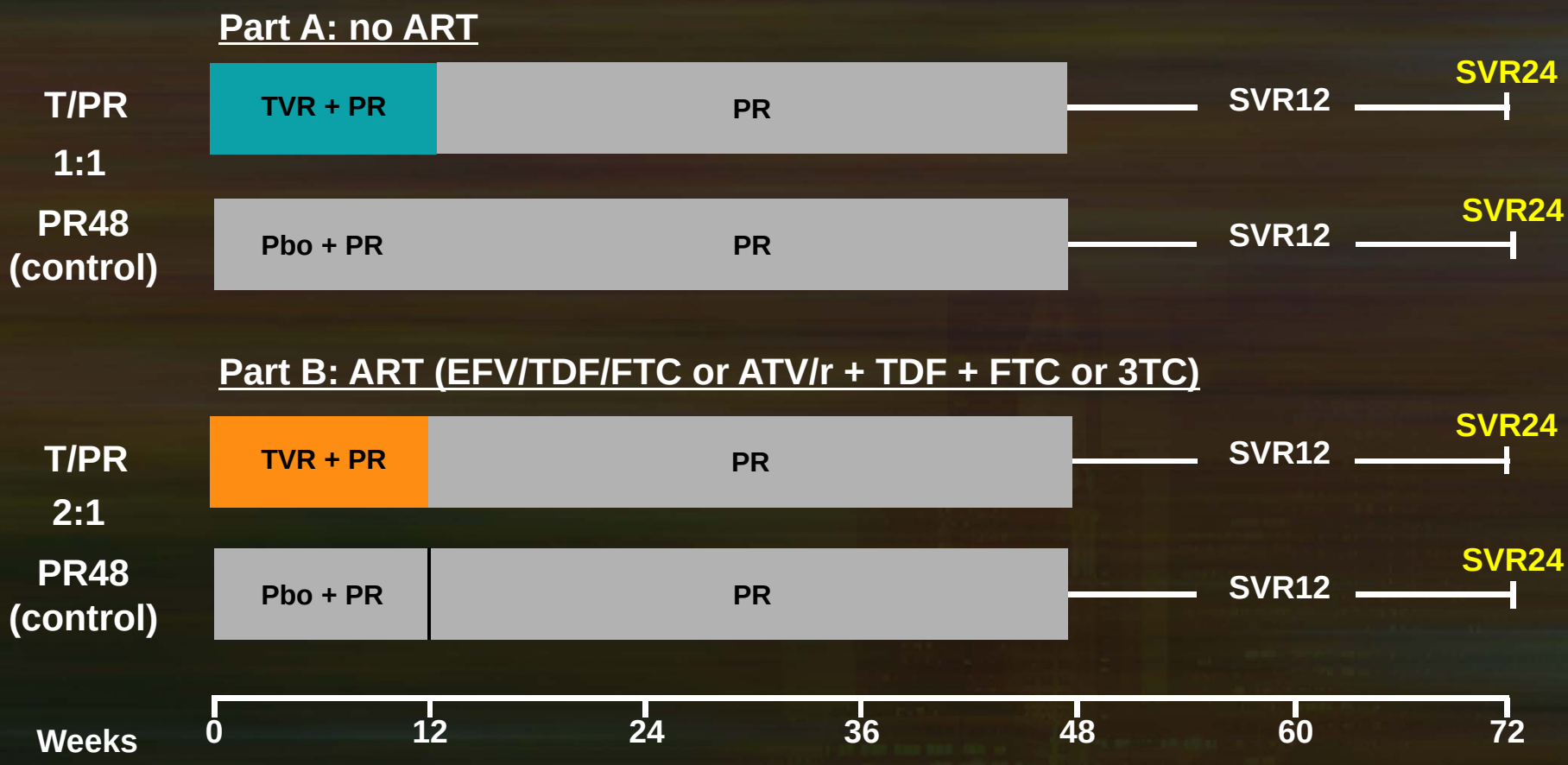
Boceprevir and Telaprevir

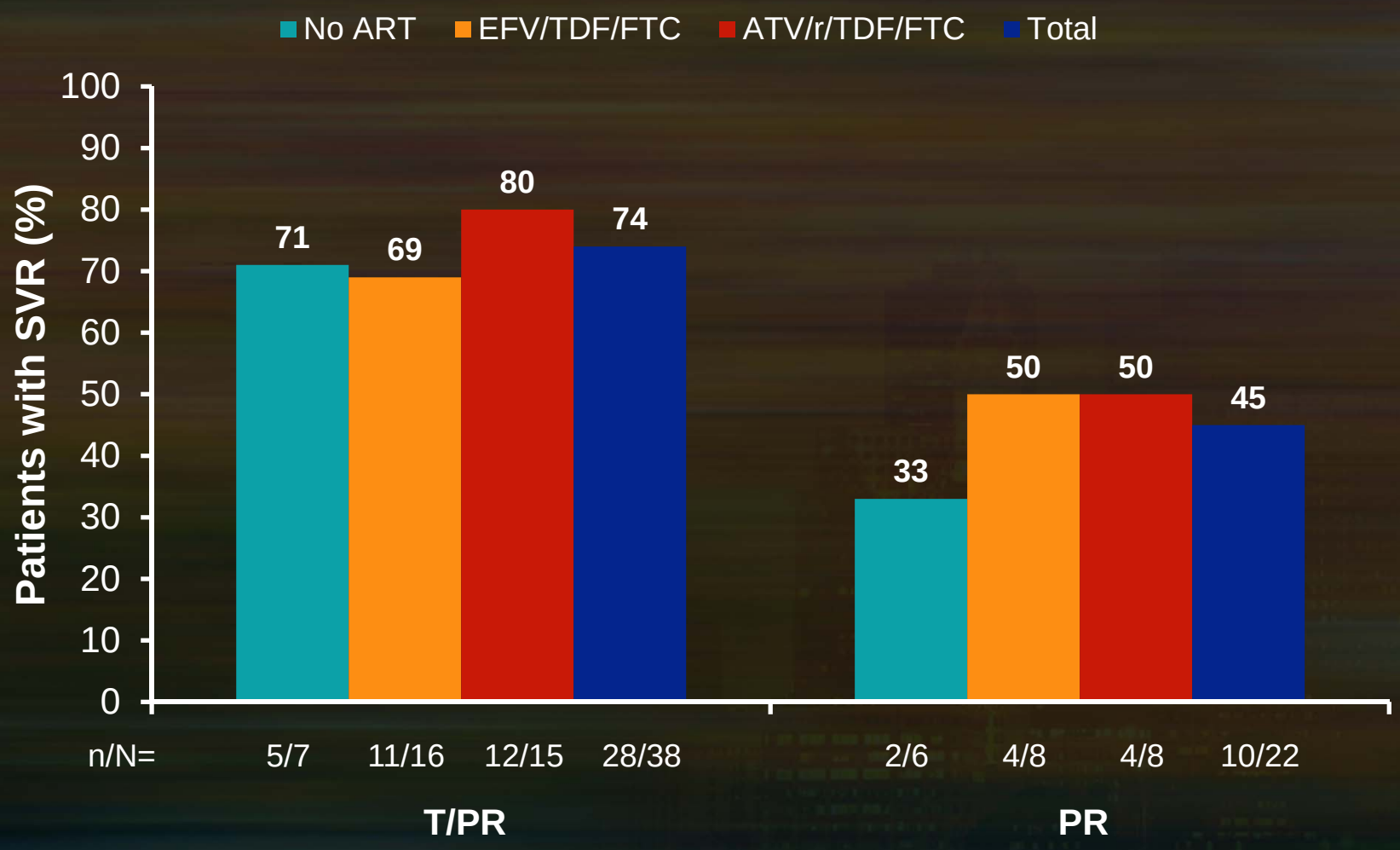
Fred Poordad, MD

Study Design: Randomized, Double-blind, Placebo-controlled Trial



Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 54.

SVR at post-treatment week 24 (SVR_{24})



Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 54.

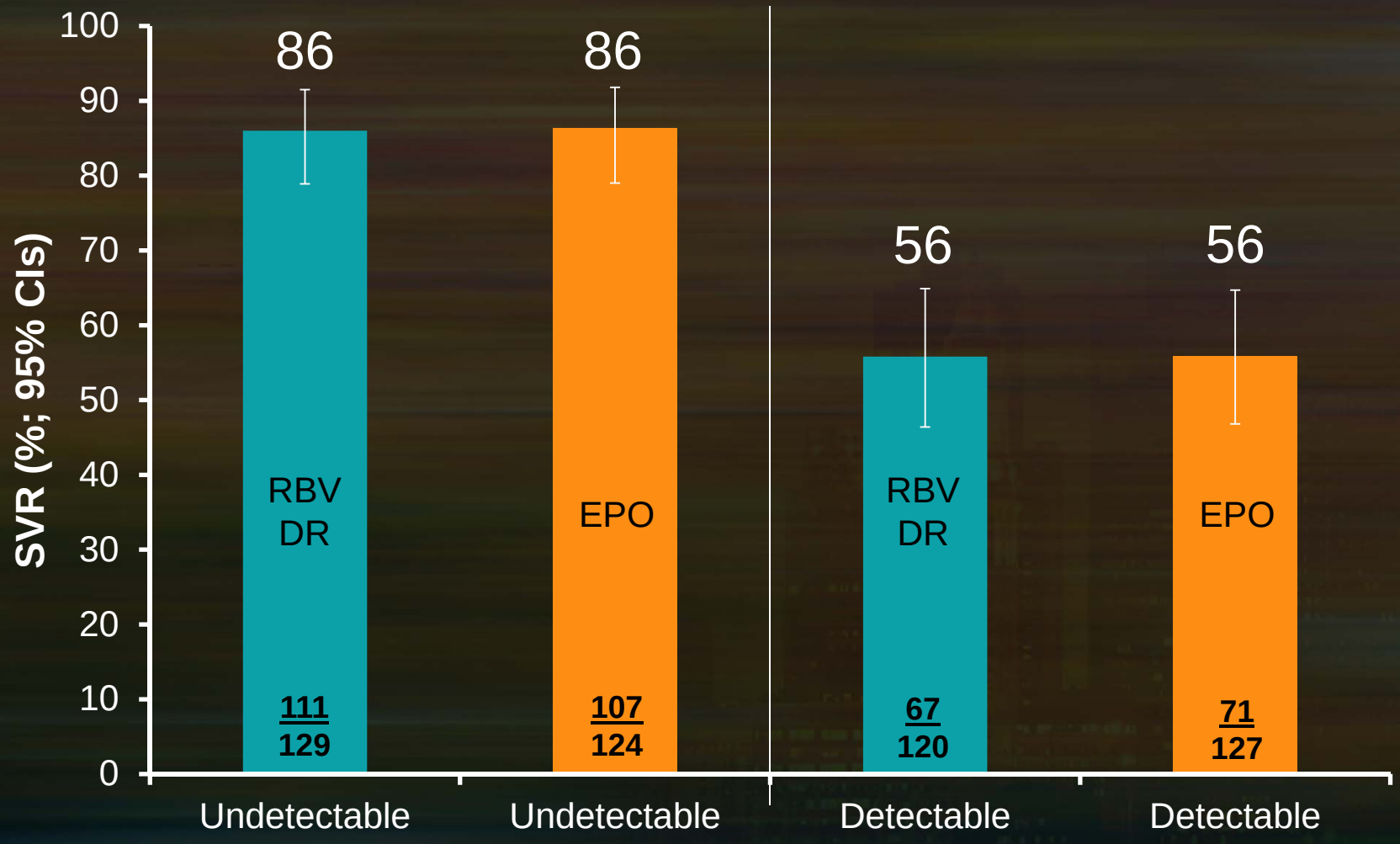
Events of Special Interest: Overall Treatment Phase

n (%)	T/PR N=38	PR N=22
Severe rash	0 (0)	0 (0)
Mild and moderate rash	13 (34)	5 (23)
Any anemia (hemoglobin <10g/dL)	7 (18)	4 (18)
Severe anemia (hemoglobin 7.0-8.9 g/dL or decrease from baseline ≥4.5 g/dL)	11 (29)	5 (23)
Use of erythropoietin stimulating agent	3 (8)	1 (5)
Blood transfusions	4 (11)	1 (5)
Discontinuation due to AE	3 (8)	0 (0)

- No HIV breakthrough; CD4 counts declined in T/PR and PR groups; CD4% unchanged
- 3 T/PR patients discontinued due to adverse event (3 T/PR)

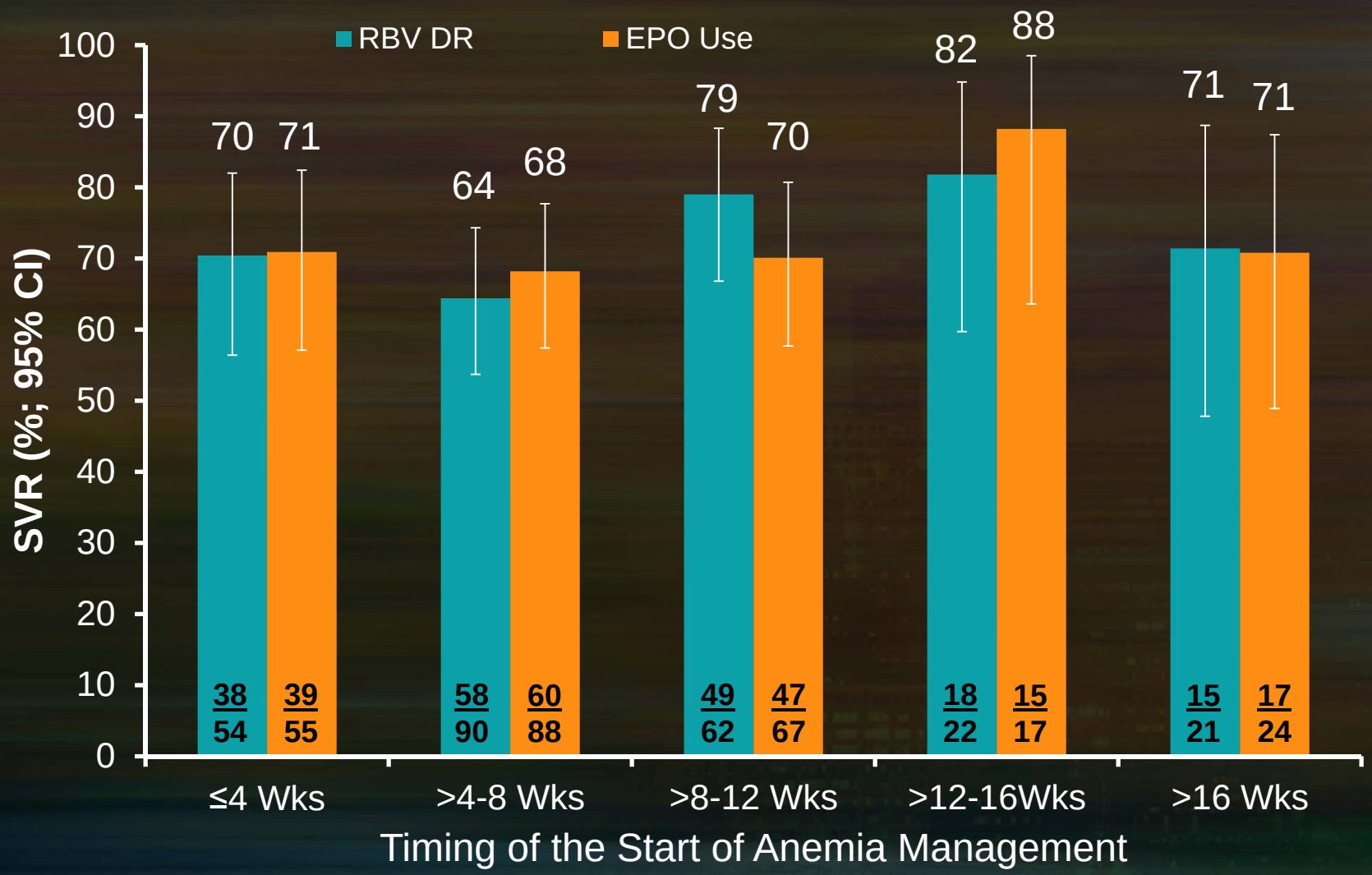
Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 54.

SVRs Were Higher if Undetectable HCV RNA at Start of Primary Anemia Management



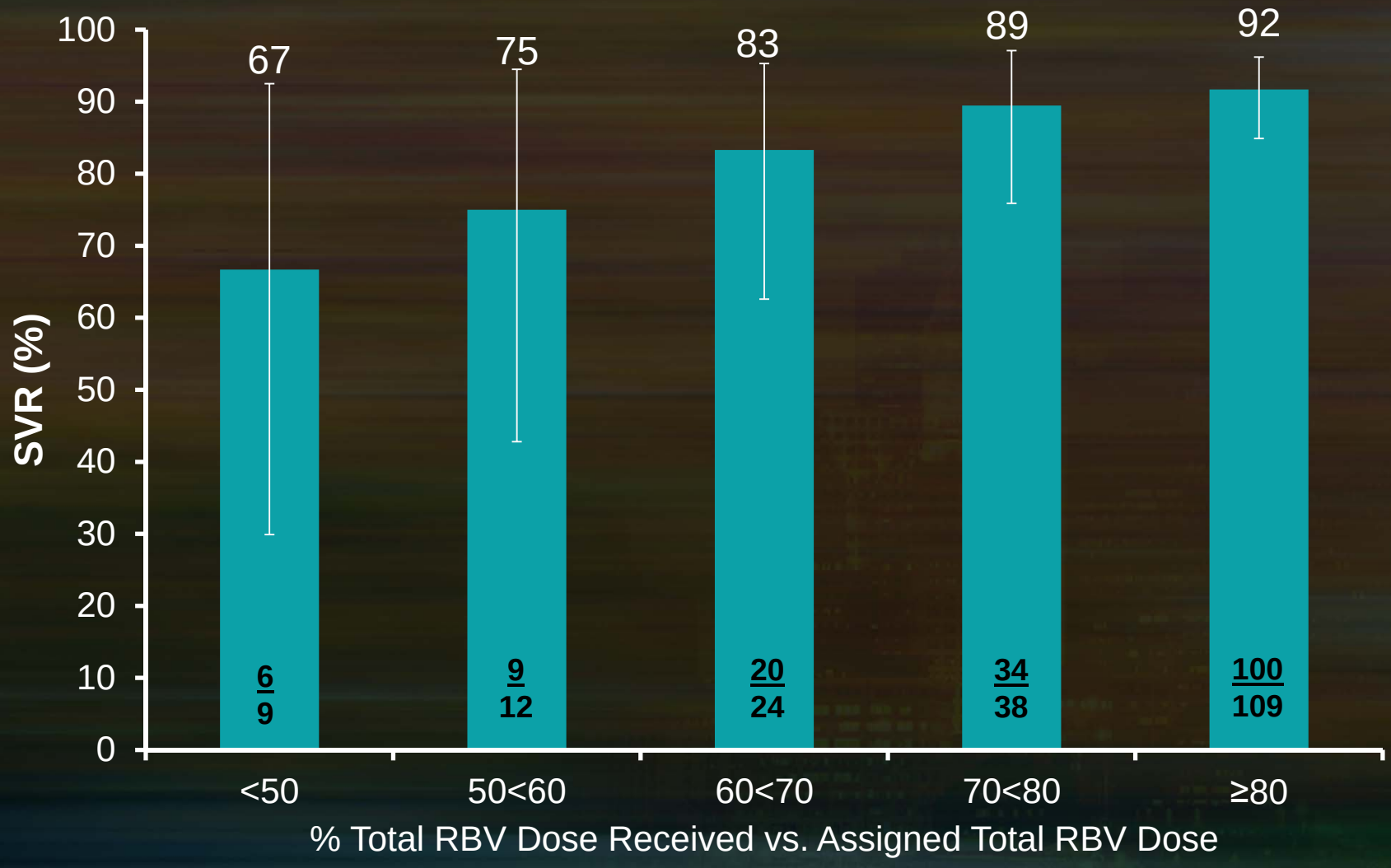
Poordad F, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 154.

SVR Rates Did Not Vary with the Start Time of Anemia Management



Poordad F, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 154.

SVR by Percent Total RBV Dose Received in Patients Who Received ≥80% of Treatment Duration



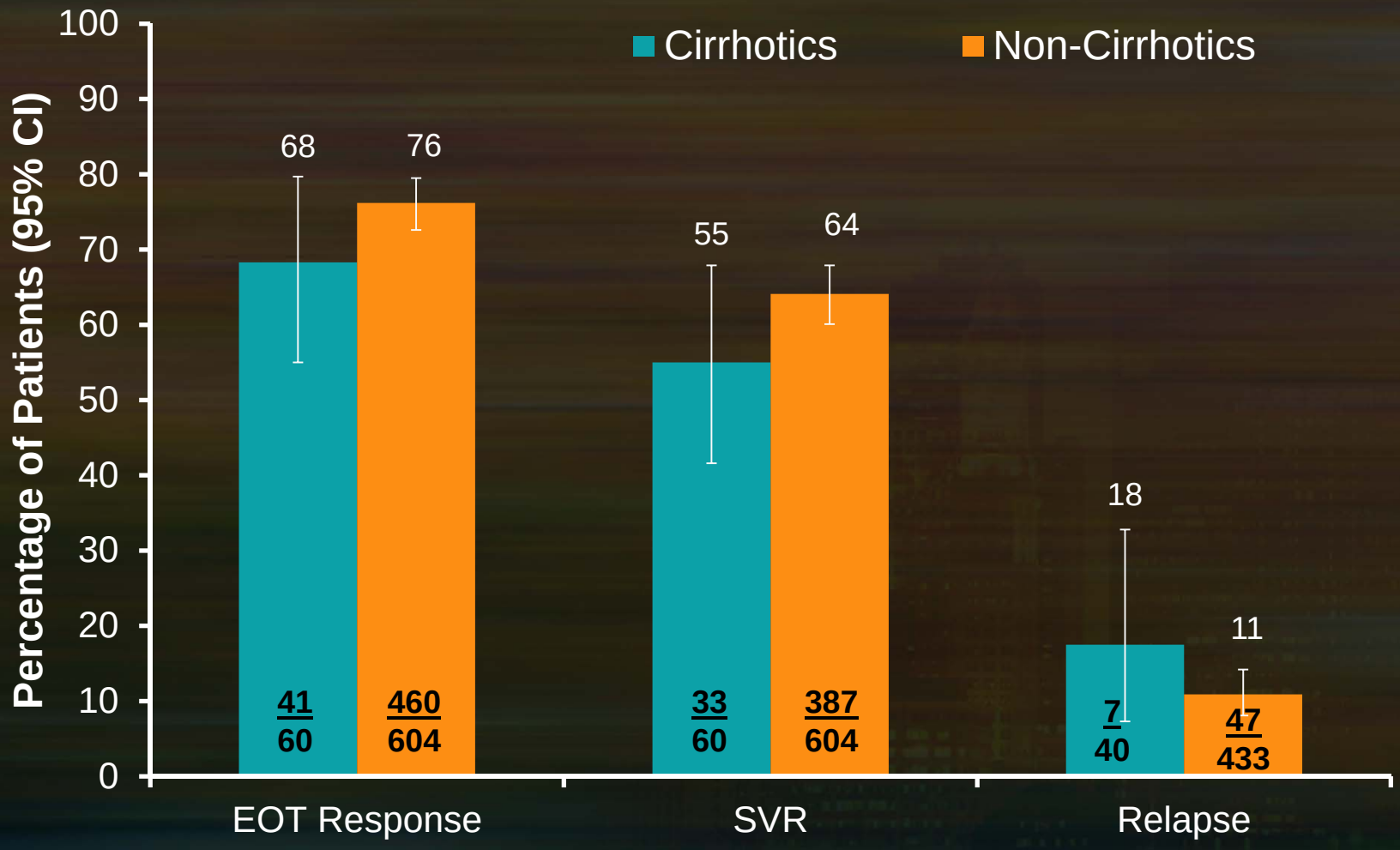
Poordad F, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 154.

Predictors of Anemia by Logistic Regression

Effect	Odds Ratio	95% CI	*P*-value
Baseline Hemoglobin (continuous variable)	0.62	0.49 – 0.79	<0.0001
Normal ITPA Activity†	1.96	1.28 – 3.00	0.0019
Age (>40 vs ≤40)	1.98	1.19 – 3.28	0.0084
Baseline Fibrosis (3/4 vs 0/1/2)	2.02	1.03 – 3.98	0.0421

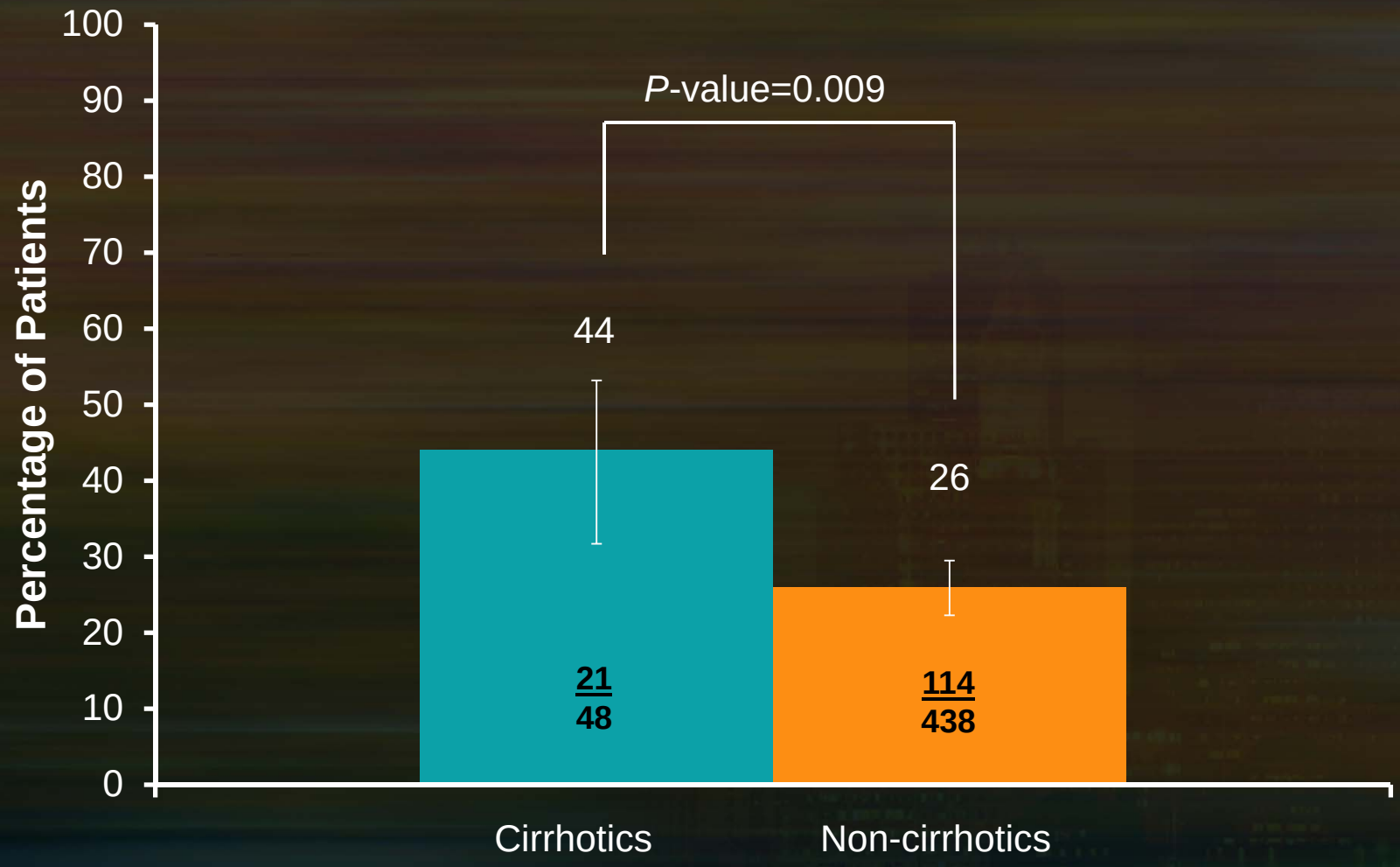
Poordad F, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 154.

Efficacy Results in Cirrhotics and Non-Cirrhotics



Lawitz E, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 50.

A Higher Percentage of Cirrhotics Received Secondary Anemia Intervention Compared to Non-Cirrhotics



Excludes patients who were treated and not randomized to anemia management

Lawitz E, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 50.

Week 24 and EOT Response for DAA Therapy in Veterans with HCV: Results

Demographic and clinical characteristics of entire cohort (n=859)

	BOC	TVR		BOC	TVR
Age (years)	57 ± 6	58 ± 5	Cirrhosis	24%	41%
Sex, male	95%	97%	Diabetes	23%	29%
Race/ethnicity			Naïve	59%	49%
Black	25%	30%	Prior null responder*	10%	19%
Hispanic	6%	6%	Prior partial responder	11%	14%
White	60%	58%	Prior relapser	18%	17%

HCV RNA undetectable rates at week 24 (n=859)

	BOC w24 (n/N)	TVR w24 (n/N)	*P* value
Overall	69%(457/661)	64%(126/198)	0.15
Subgroups of interest:			
Naïve non-cirrhotic	74% (231/314)	60% (36/60)	0.03
All cirrhotic	64% (103/161)	60% (49/81)	0.60
Prior treatment response (including cirrhotic and non-cirrhotic):			
Prior null responder	44% (28/64)	53% (20/38)	0.39
Prior partial responder	69% (50/72)	67% (18/27)	0.79
Prior relapser	76% (91/119)	88% (29/33)	0.15

Backus L, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-30.

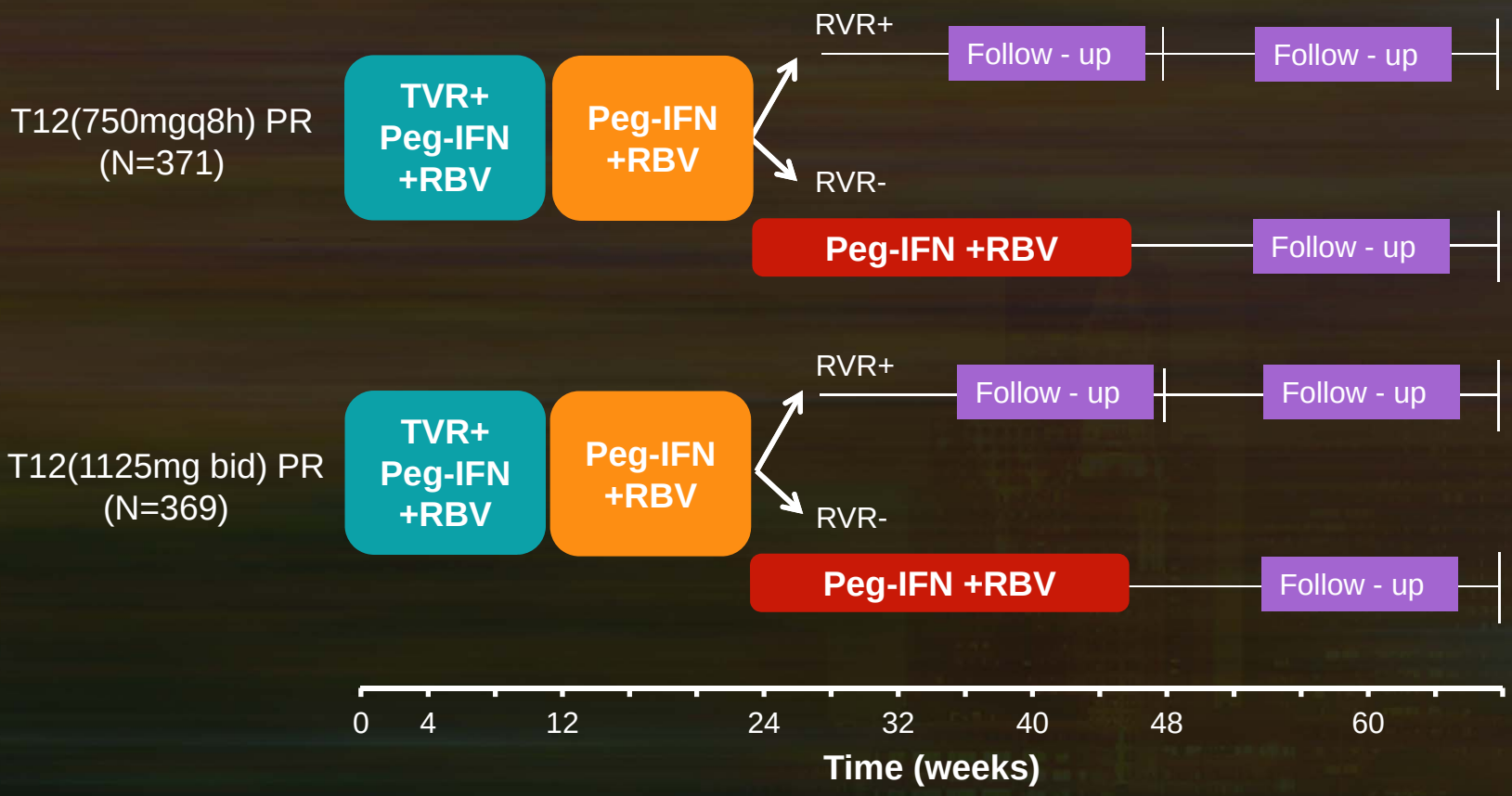
Week 24 and EOT Response for DAA Therapy in Veterans with HCV: Results

HCV RNA undetectable rates at EOT (n=692)

	BOC EOT (n/N)	TVR EOT (n/N)	*P* value
Overall	60%(320/532)	55%(88/160)	0.25
Subgroups of interest:			
Naïve non-cirrhotic	66% (179/270)	60% (31/52)	0.35
All cirrhotic	49% (55/112)	45% (26/58)	0.60
Prior treatment response (including cirrhotic and non-cirrhotic):			
Prior null responder	19% (9/48)	26% (8/31)	0.46
Prior partial responder	59% (32/54)	62% (13/21)	0.83
Prior relapser	67% (64/95)	85% (22/26)	0.08

Backus L, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-30.

OPTIMIZE Study: Study Design

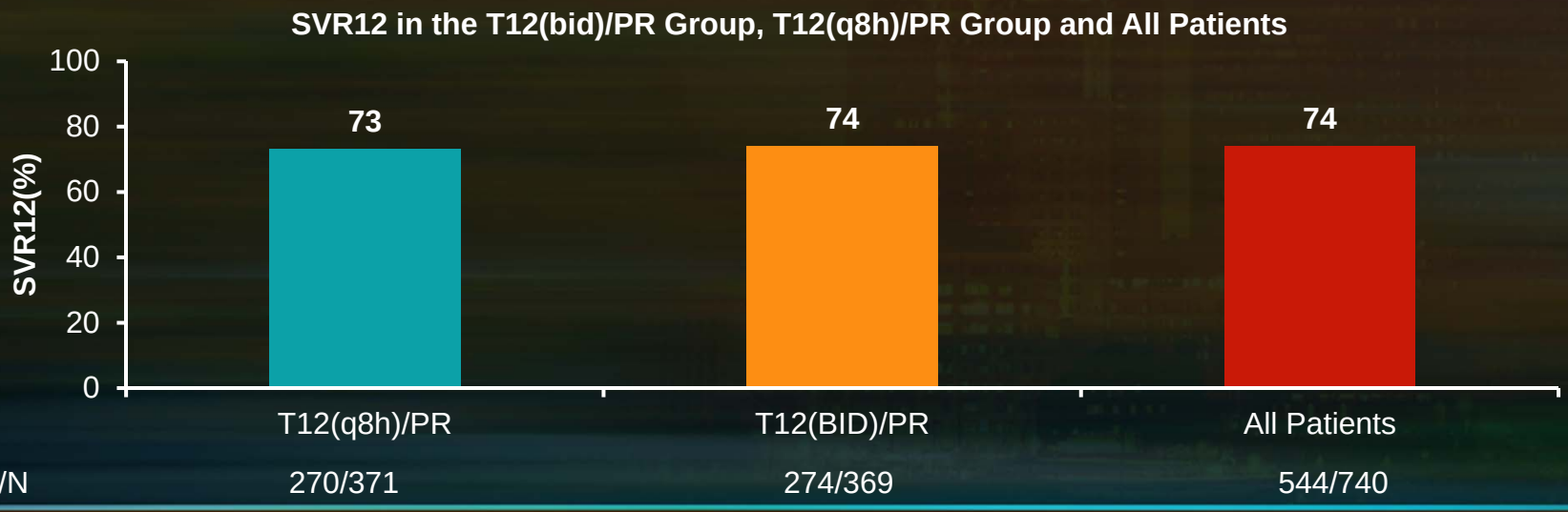


RVR+ = patient achieved HCV RNA <25 IU/mL, target not detected at Week 4 of treatment. All study drugs were stopped if HCV RNA levels were >1000 IU/mL at Week 4 or 25 IU/mL at Weeks 12, 24, 32 or 40.Randomization was stratified by liver fibrosis status (F0–F2; F3–F4) and IL28B subtype (CC, CT, TT).Peg-IFN alfa-2a 180 µg/week; RBV 1000–1200 mg/day; RVR = rapid virologic response.

Buti M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-8.

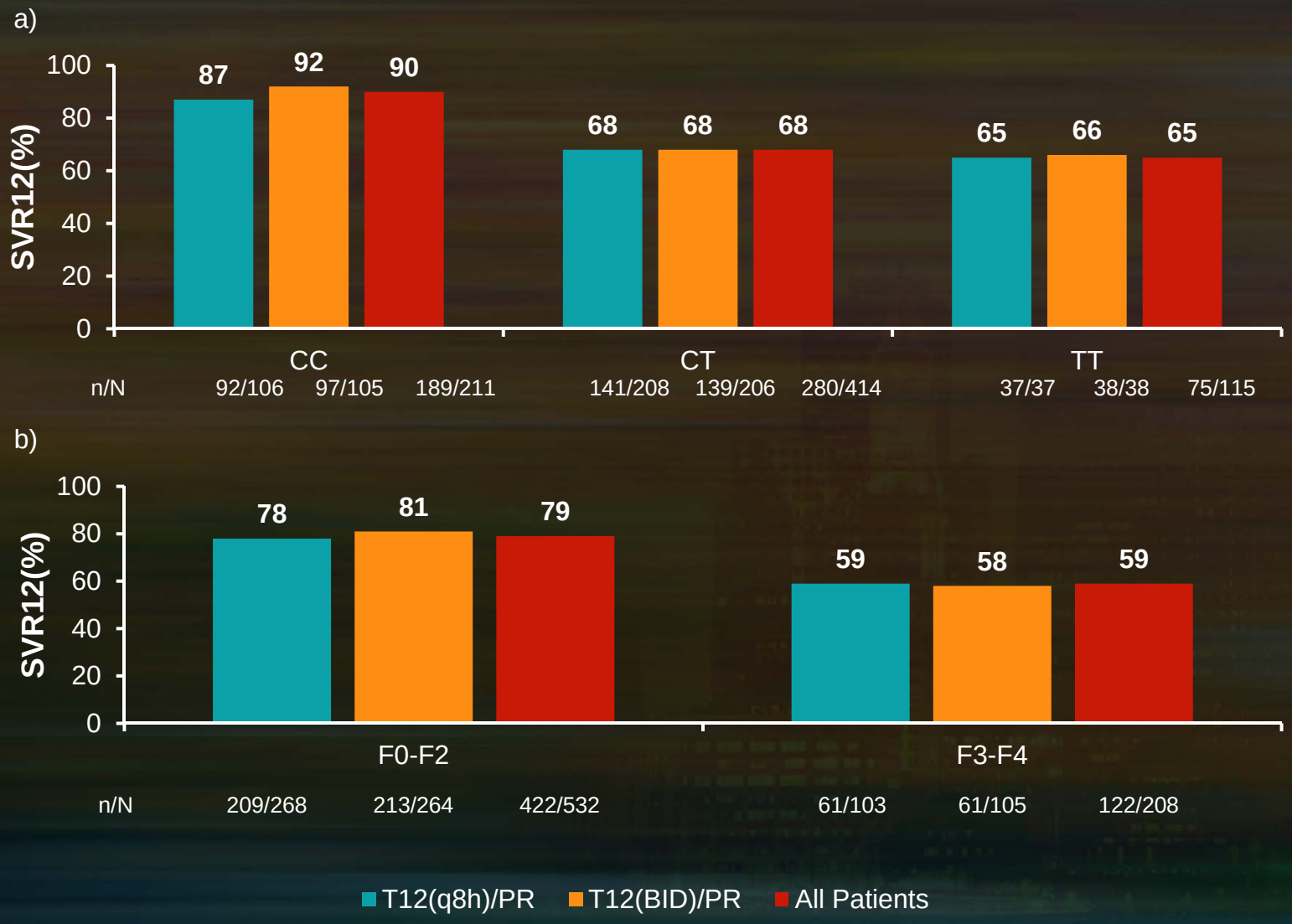
OPTIMIZE Study: Efficacy

- SVR12 was 74% in the T12(bid)/PR group versus 73% in the T12(q8h)/PR group
  - The difference between T12(bid)/PR and T12(q8h)/PR was 1.5% with a 95% CI: –4.9 to 12.0
  - The lower limit of the 95% CI (–4.9%) was well above the predetermined noninferiority margin of –11% and thus establishes the noninferiority of T12(bid)/PR to T12(q8h)/PR. Per-protocol analysis further supported the noninferiority (76% versus 75% in SVR12 for T12(bid)/PR and T12(q8h)/PR, respectively)



Buti M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-8.

OPTIMIZE Study: SVR12 in the T12(bid)/PR Group, T12(q8h)/PR Group and All Patients by a) IL28B Status and b) Liver Disease Status



Buti M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-8.

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Novel Therapies and Strategies with interferon

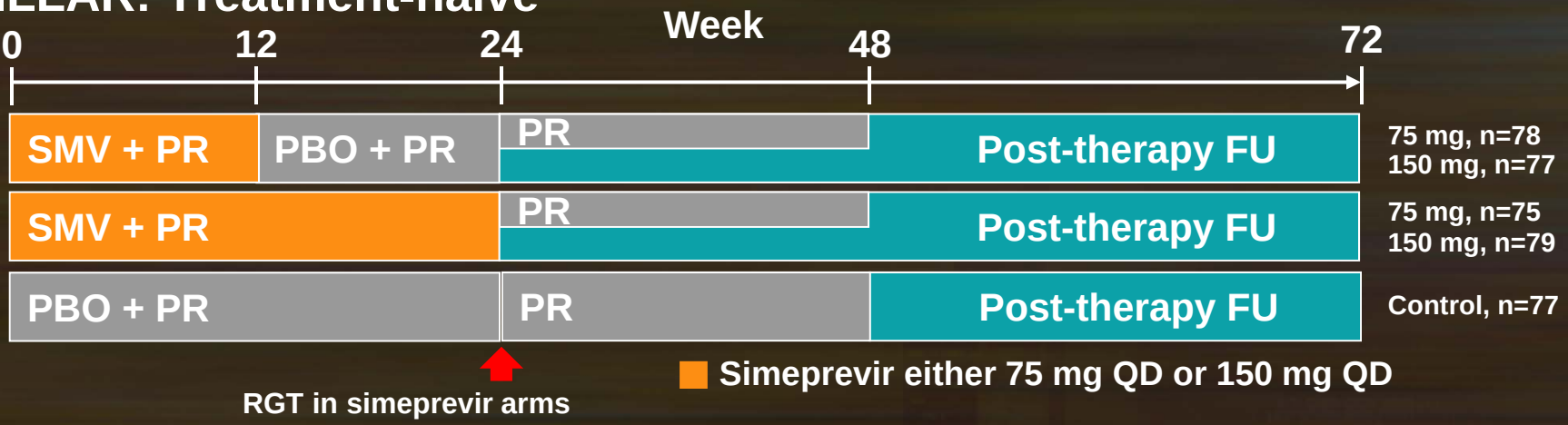
Nezam Afdhal, MD

Interferon Plus Multiple DAAs

- Expectations
  - RVR >80%
  - SVR 70-80%
  - Improved tolerability and side effects
  - RGT strategy
  - 6-12 week therapy for easy-to-treat patients
  - Increased efficacy in null responders

PILLAR and ASPIRE Studies: Study Design

PILLAR: Treatment-naive

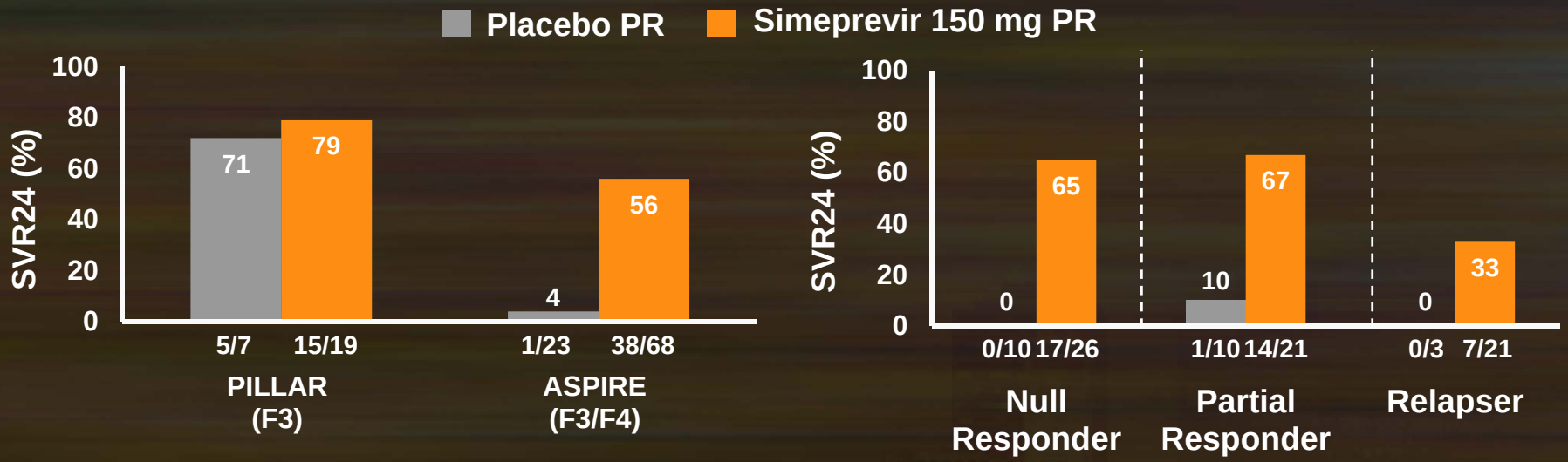


ASPIRE: Treatment-experienced

G1a=49–58%

Poordad F, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 83.

PILLAR and ASPIRE Studies: Results

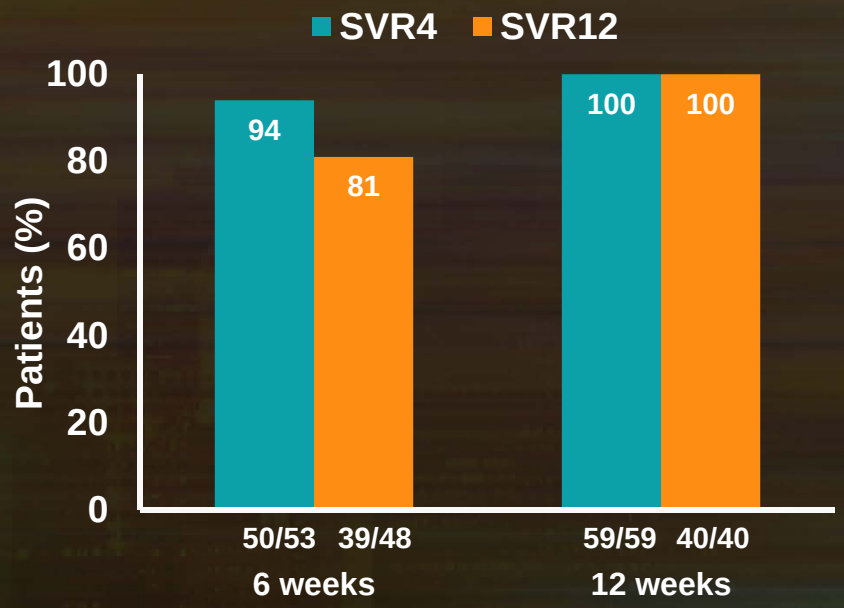


- Short therapy in cirrhotics
  - 16/19 (84%) qualified for 24 weeks
    - 15/16 (94%) achieved SVR24
- Safety profile consistent with PEG-IFN
- Frequency of grade 3/4 bilirubin elevation was higher in cirrhotics
  - Hematologic changes were not exacerbated by simeprevir

Poordad F, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 83.

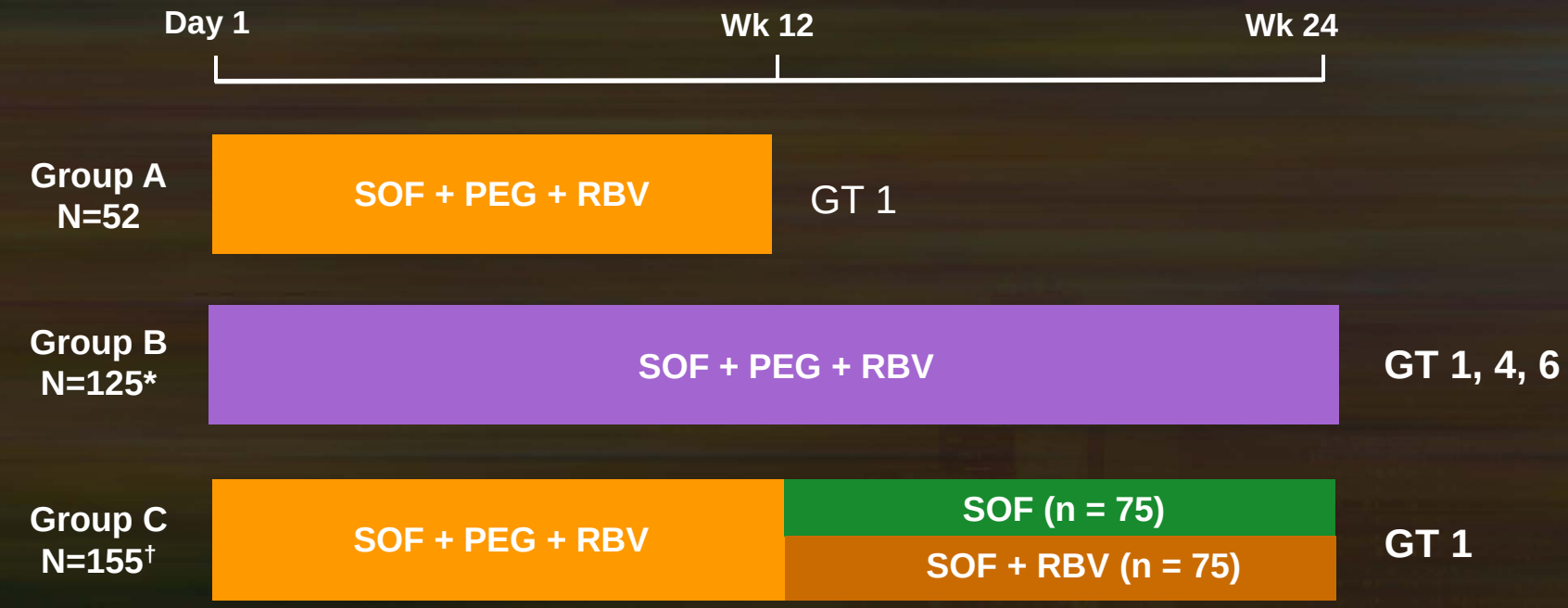
Six Weeks of (GS-5885), (GS-9451) + (PR) Achieves High SVR4 Rates in genotype 1 IL28B CC Treatment Naïve HCV Patients

- Interim Results of a Prospective, Randomized Trial
- PR+GS-5885+GS-9451 (Arm 1) vs PR (Arm 2)
- Arm 1: If HCV RNA <LLQ (vRVR) at Week 2 with Week 4 RVR, re-randomized to receive 6 or 12 weeks
- Arm 2: If HCV RNA<LLQ at Week 4, received 24 weeks of PR
- Quad therapy for 24 weeks for vRVR failures in Arm 1, RVR failures in Arm 2



Thompson AJ, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 759.

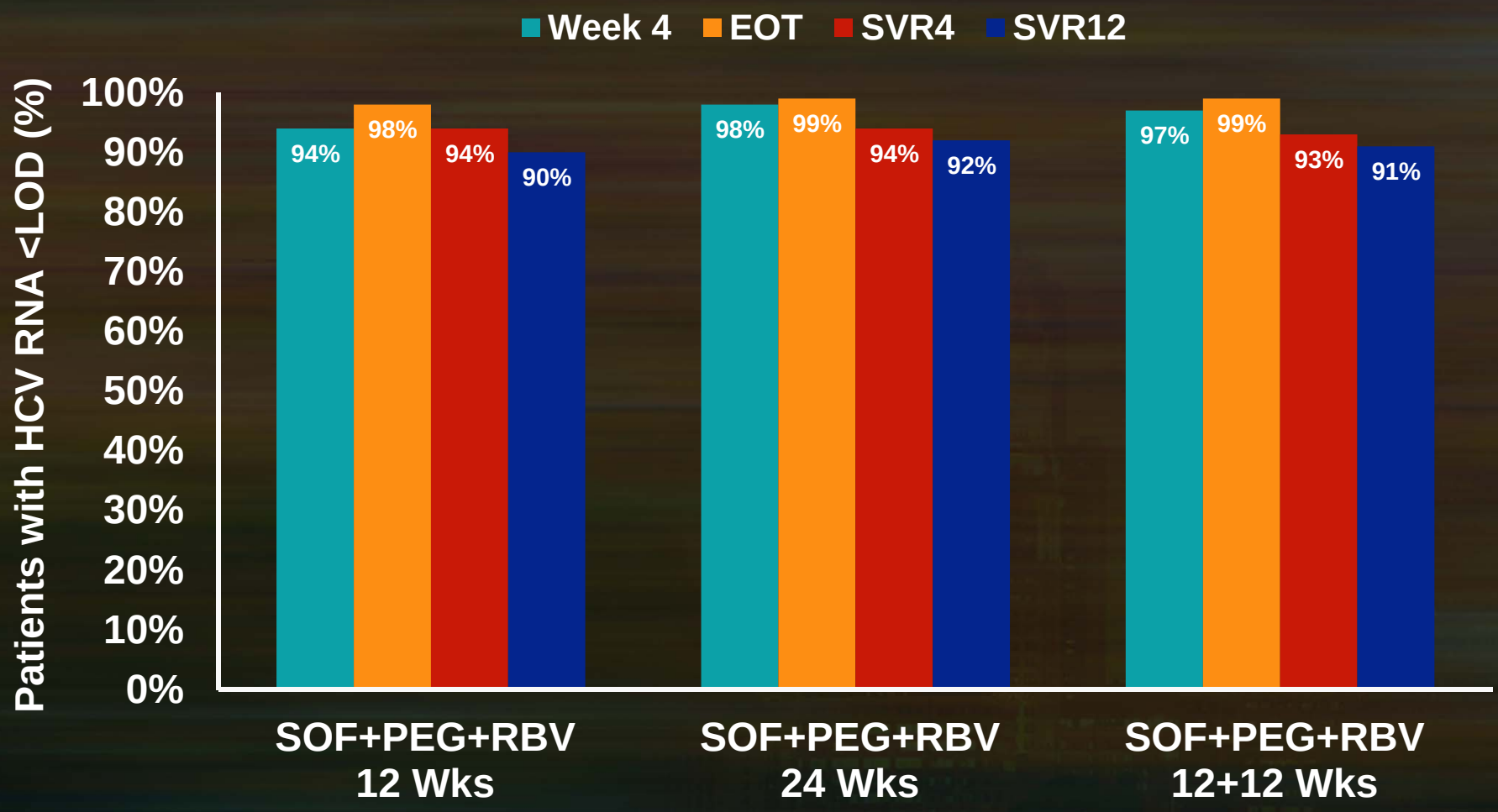
ATOMIC Study Design



- Non-cirrhotic, treatment-naïve patients with HCV genotype 1 were randomized 1:2:3 into open-label arms
- HCV RNA analyzed by TaqMan® HCV Test 2.0 (LOD: 15 IU/mL)

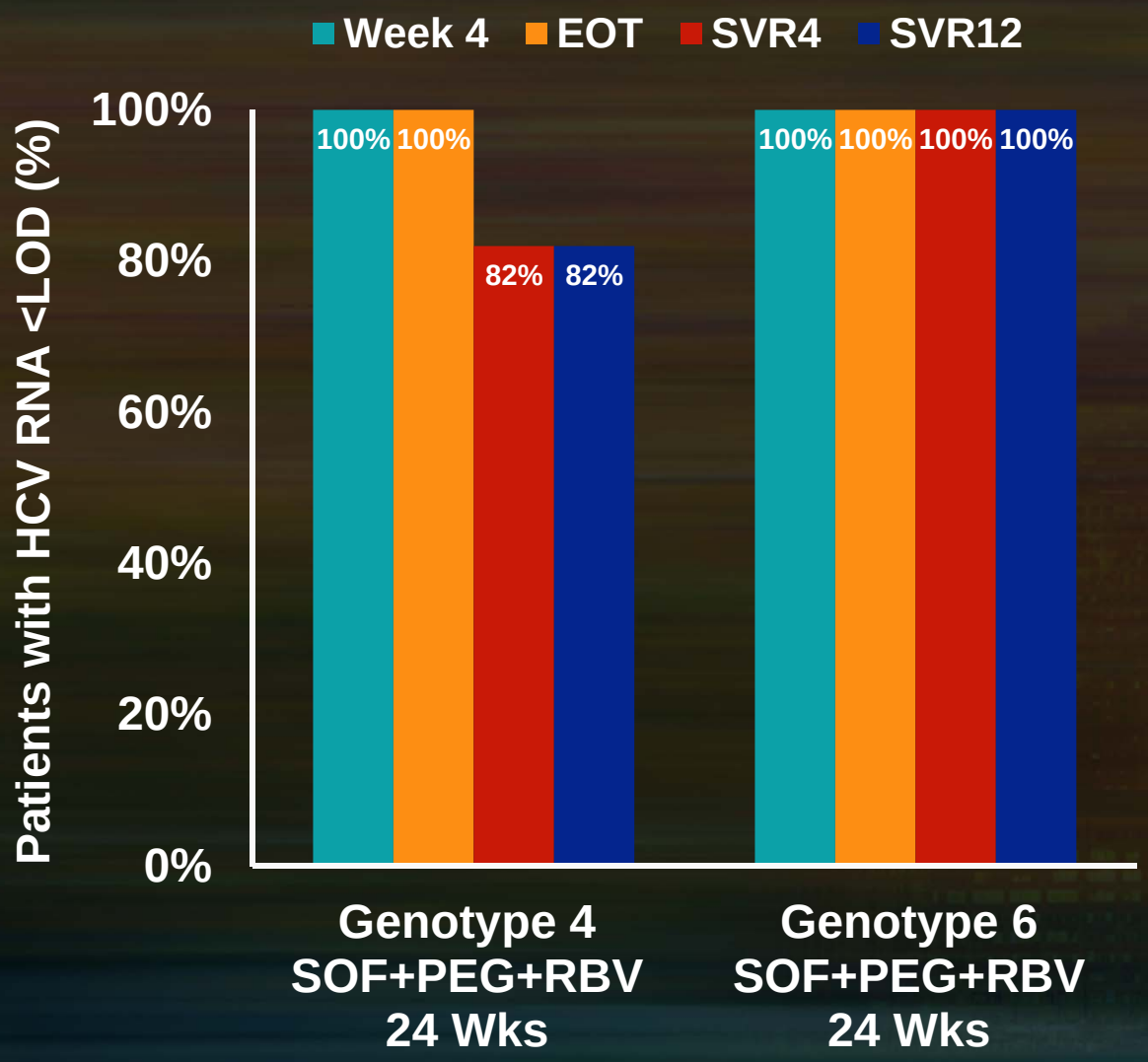
Hassanein T, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 230.

90% of Patients Achieved SVR12: Sofosbuvir + PEG + RBV 12-Week Regimen



Hassanein T, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 230.

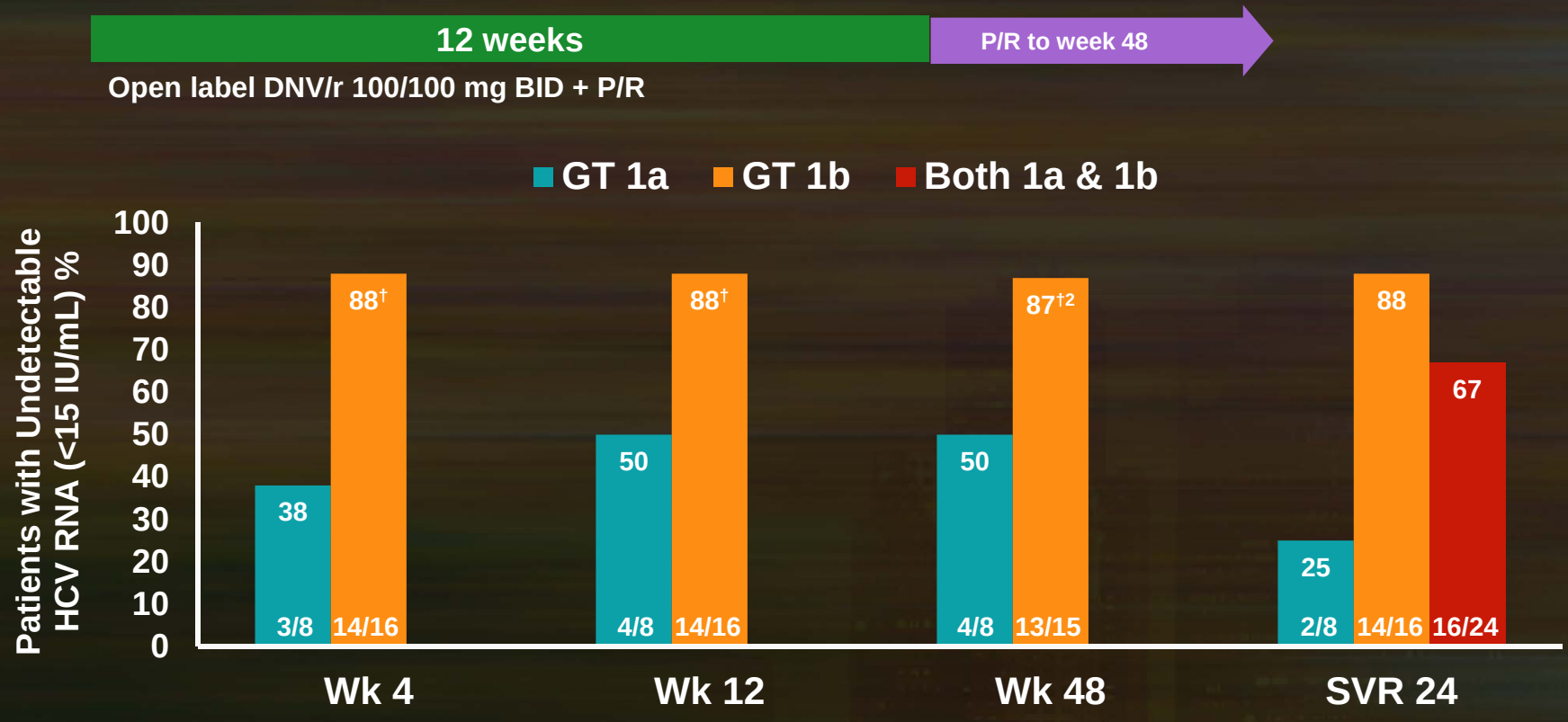
High Efficacy in GT-4 and GT-6



- 11 patients with HCV GT-4 achieved RVR
- None had virologic failure
- Two were LTFU without post-treatment data
- All 5 patients with HCV GT-6 achieved SVR24

Hassanein T, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 230.

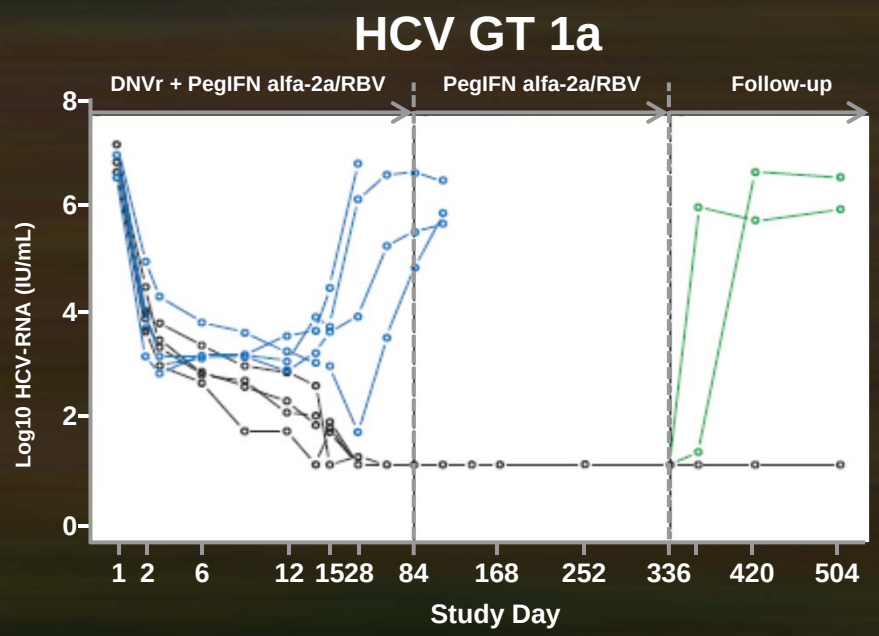
Safety and Efficacy of 12 Weeks RTV-boosted DNV/PR followed by 36 Weeks PR in GT 1 Non-Cirrhotic Prior Null Responders

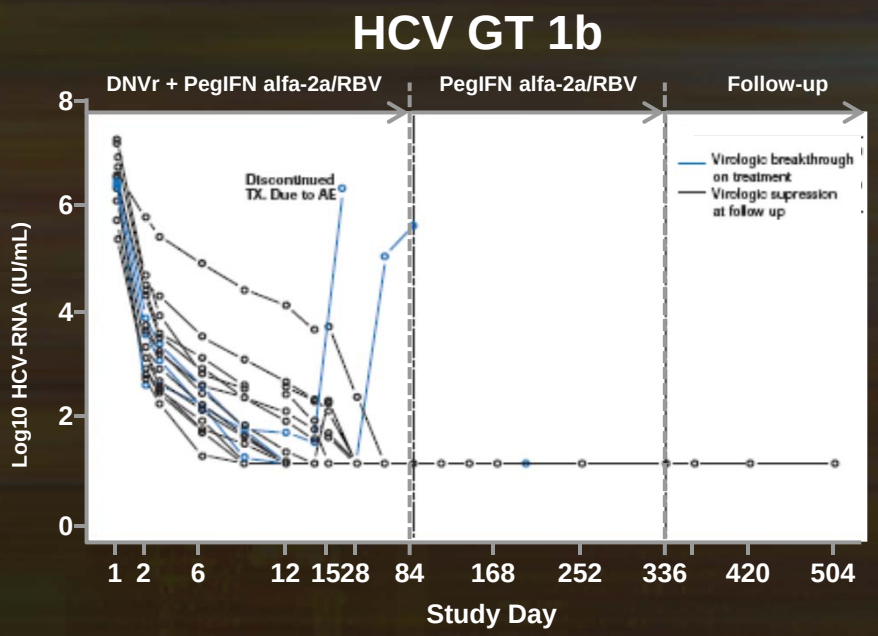


Enrolment of G1a was stopped after first 8 patients due to high breakthrough rate

Gane EJ, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 761.

RTV-boosted DNV/PR Followed by 36 Weeks PR in GT 1 Non-cirrhotic Prior Null Responders





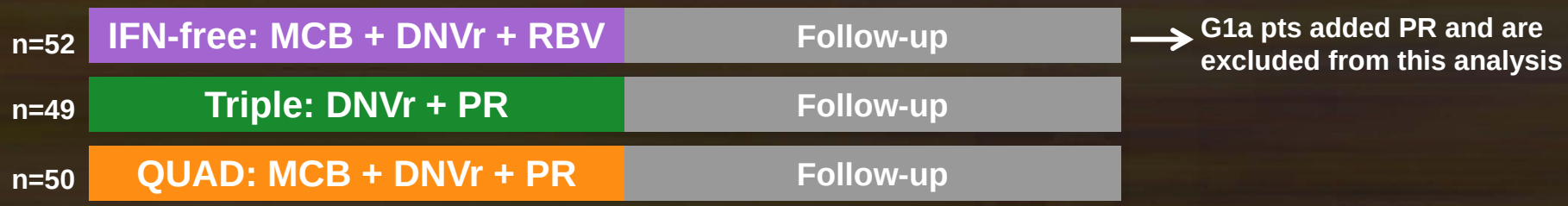
- 7 Treatment failures
- 5 breakthroughs all occurred by Wk 8 (4 1a , 1 1b)
- 2 relapses occurred by Wk 4 f/u (2 1a, no 1b)
- R155K resistance mutation was detected in all 7

Gane EJ, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 761.

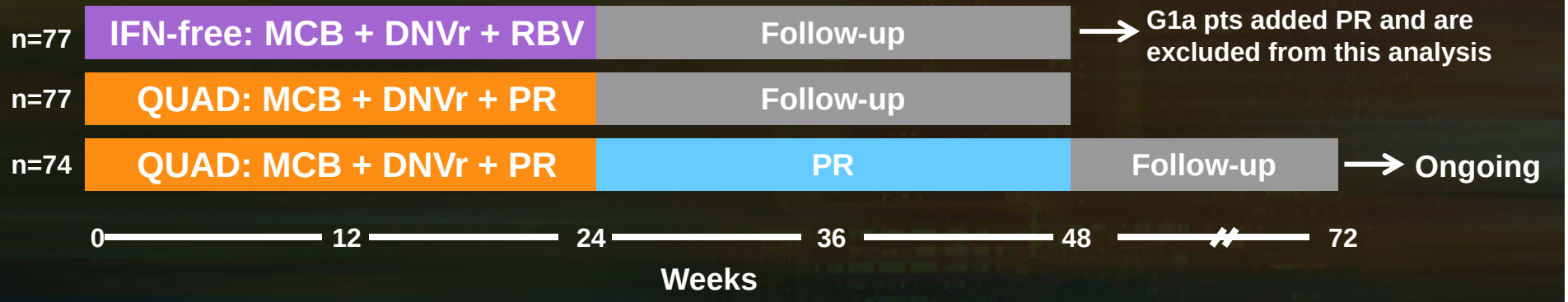
MATTERHORN Study: Phase II Study Design

- Randomized (1:1:1), open-label, multicentre, parallel study of 2 cohorts
- Stratification: G1a/G1b

Cohort A: G1 Prior Partial Responders



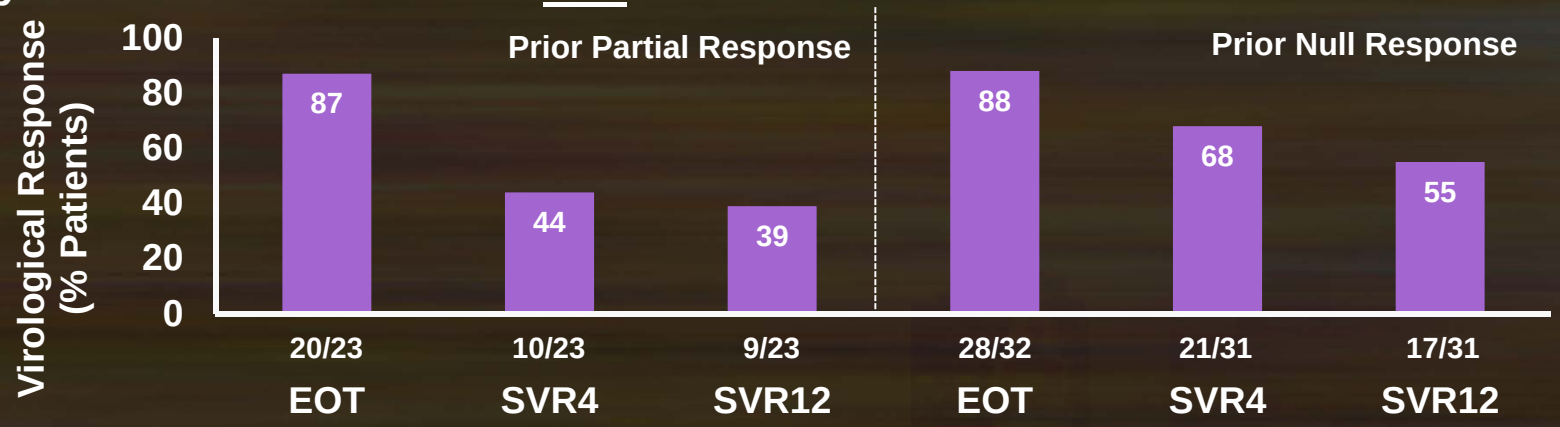
Cohort B: G1 Prior Null Responders



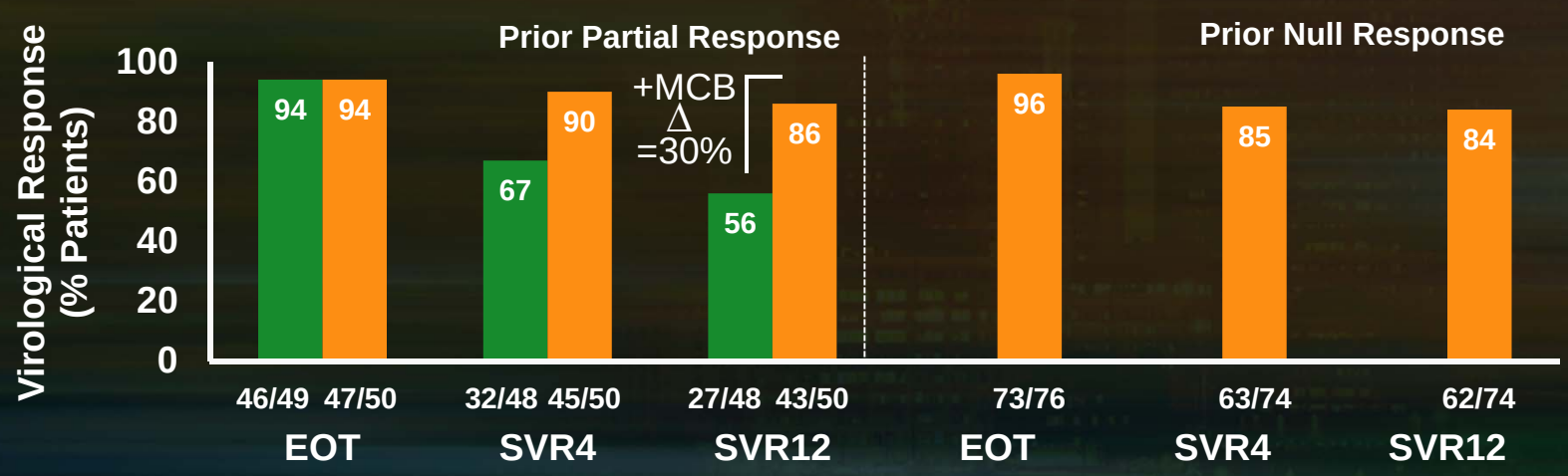
Feld JJ, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 81.
ClinicalTrials.gov Identifier: NCT01331850

MATTERHORN Study: High SVR in Genotype 1 Null responders

Efficacy of IFN-free Treatment for G1b

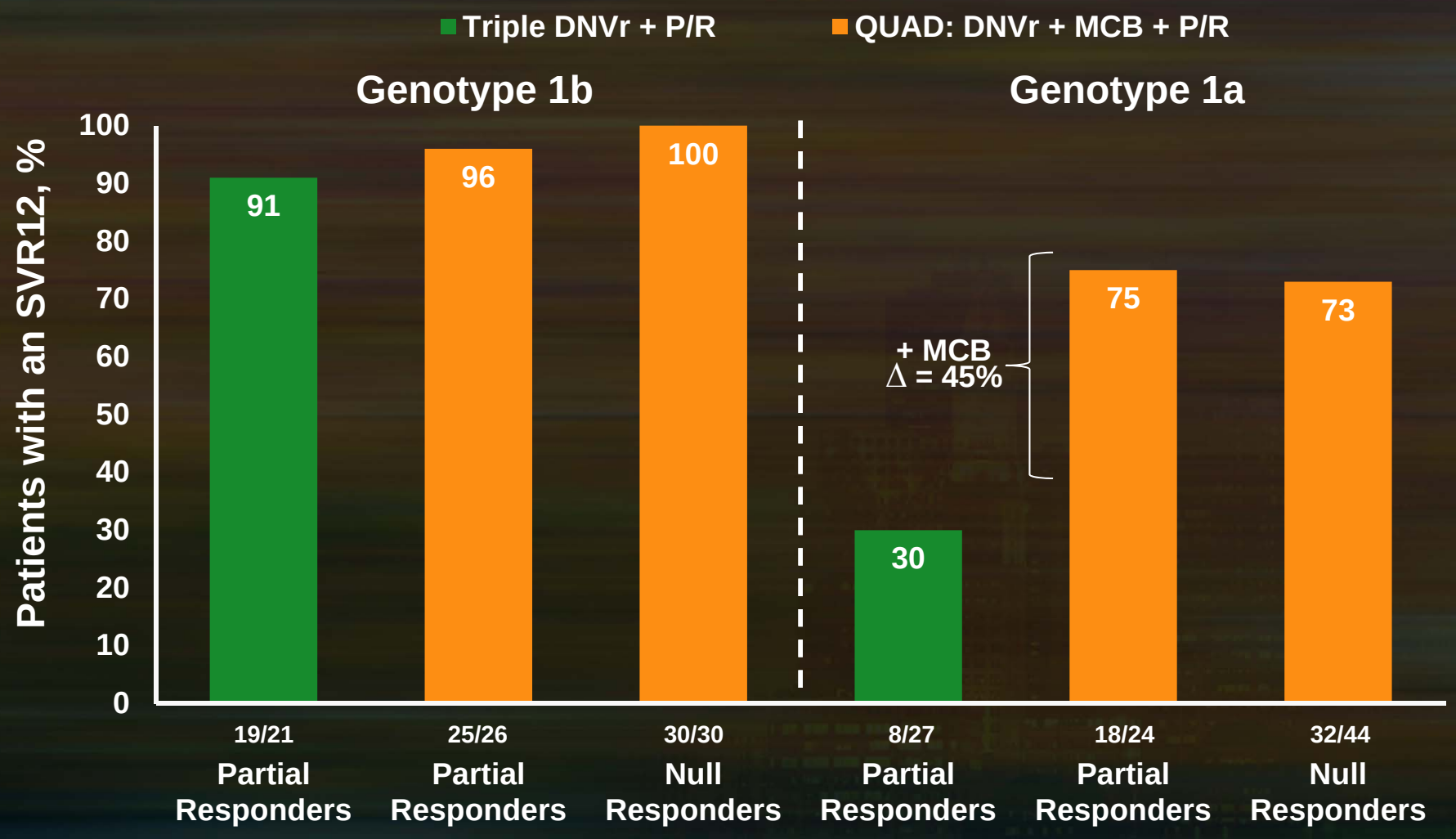


Efficacy of DNVr +PR and QUAD for 24 Weeks



Feld JJ, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 81.

SVR12 by Subtype: Addition of MCB Improves SVR12 in G1a by 45%

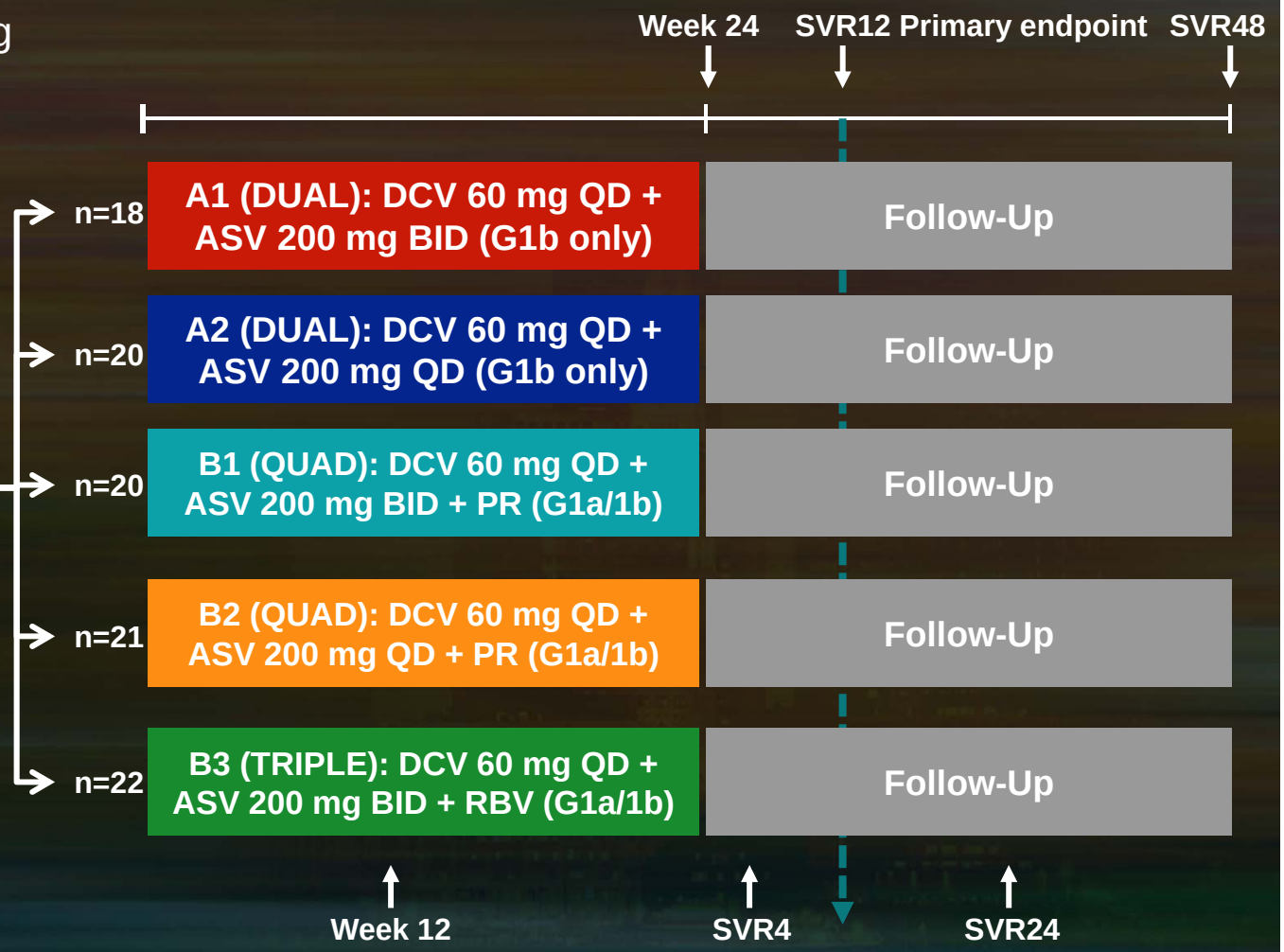


Feld JJ, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 81.

SVR in G1 Null Responders with Combination of DCV (NS5A) and ASV (NS3) ± PR

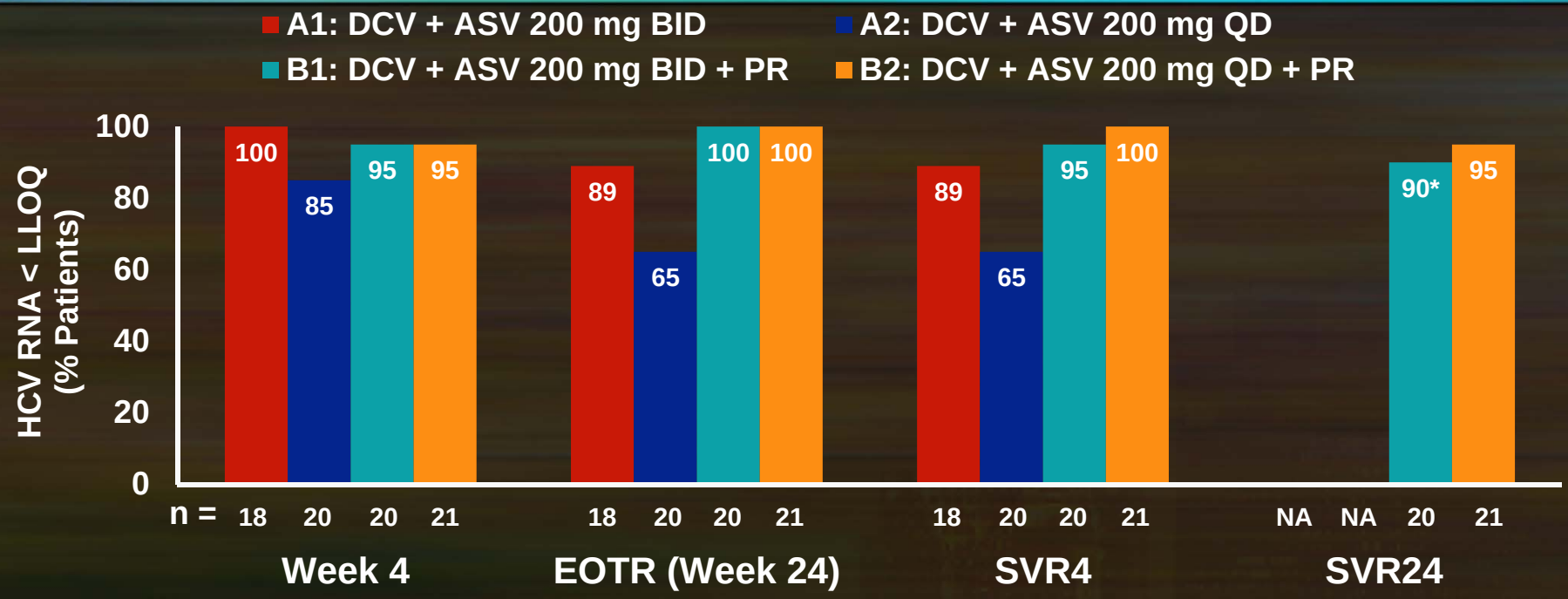
- N=101 null responders
- Mean viral load 6.5 log
- G1b:
  - A1–2: 100%
  - B1–3: 14%
- F3 or higher 15-41%
- One IL28B CC (A1)

Prior null responders to PR



Lok AS, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 79.

DUAL and QUAD Therapy

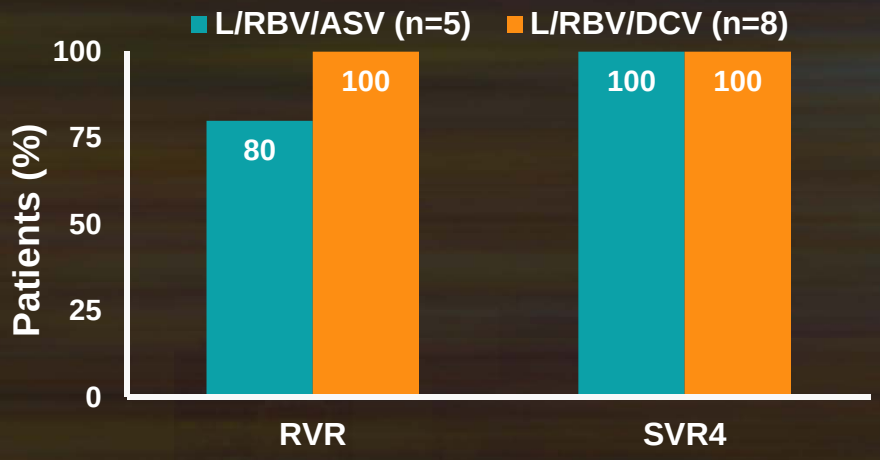


- 2 patients relapsed — 1 at PT Week 4 (B1); 1 at PT Week 12 (B2)
- Safety
  - DUAL: Headache and diarrhea most common AEs
  - QUAD: Addition of IFN AEs
- Resistance: Failure results in dual class (NS5A and NS3) resistance

Lok AS, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 79.

First Report of PEG-IFN Lambda/RBV in Combination with Daclatasvir or Asunaprevir in G1 Japanese Patients: SVR4 Results from the D-LITE Japanese sub-study

- 21 treatment-naive patients
- All HCV G1b
- Assigned to
  - PEG-IFN lambda (L) / RBV / DCV
  - L / RBV / ASV
  - PEG-IFN alfa-2a / R / placebo
- Lambda and alfa dosed at 180 µg QW; DCV 60 mg QD; ASV 200 mg BID; RBV weight-based BID
- Only DAA recipients with PDR had post-treatment data through Week 4
- L/RBV/DCV better tolerated than L/RBV/ASV



PDR+ Subjects, n (%)	L/RBV/ASV (n=5)	L/RBV/DCV (n=8)
SAEs	1 (20)	0
AE-related discontinuations	2 (40)	0
Grade 3-4 AEs	4 (80)	1 (14)
Grade 3-4 hemaglobin	1 (20)	0
Grade 3-4 ALT	3 (60)	0
Grade 3-4 AST	4 (80)	0
Grade 3-4 total bilirubin	1 (20)	0

Izumi N, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 234.

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Interferon-free, oral direct acting antiviral regimens

Mark Sulkowski, MD

Multiple Regimens in Clinical Trials

- Nucleotide analogue polymerase inhibitor alone or plus NS5A inhibitor
  - Sofosbuvir + ribavirin
  - Sofosbuvir + daclatasvir ± ribavirin
  - Sofosbuvir + GS5885 + ribavirin
- Protease inhibitor + NS5A inhibitor ± non-nucleoside polymerase inhibitor ± ribavirin
  - ABT450/r + ABT267 + ABT333 ± ribavirin
  - Asunaprevir + daclatasvir ± BMS-325
  - Faldaprevir + BI7227 + ribavirin

ELECTRON : Sofosbuvir + GS5885 and/or RBV: New Zealand

Treatment	Population	Response
Sofosbuvir + ribavirin 800 mg for 12 weeks	GT 2/3 treatment-naïve	60% (6/10) SVR8
Sofosbuvir + GS5885 + RBV for 12 weeks	GT 1 treatment-naive	100% (25/25) SVR4

Gane E, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 229.

NIAID Study: Sofosbuvir + RBV in Washington DC

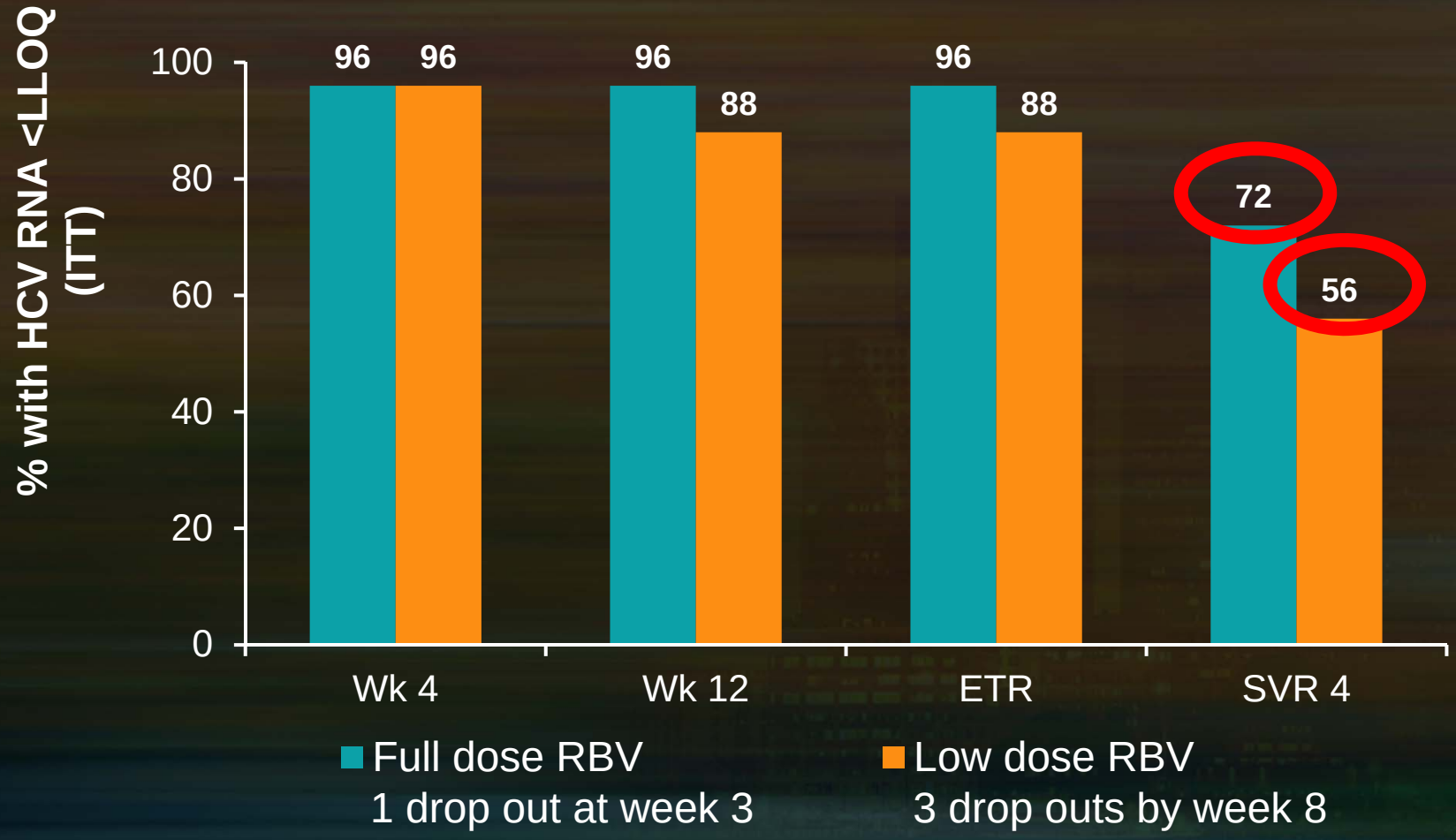
Baseline Demographics

	GS-7977+Full dose RBV N=10	GS-7977+Full dose RBV N=25	GS-7977+Low dose RBV N=25
Median age (range)	54 (30-65)	54 (30-65)	55 (26-78)
Male sex(%)	4 (40%)	20 (80%)	14 (56%)
Genotype 1a(%)	6 (60%)	20 (80%)	16 (64%)
African American (%)	9 (90%)	18 (72%)	23 (92%)
Median BMI (range)	26 (22-43)	18 (72%)	23 (92%)
IL28B CT/TT (%)	6 (67%)	21 (84%)	21 (84%)
Median HCV RNA log (IQR)	6.85 (5.80-7.21)	6.16 (5.37-6.41)	6.05 (5.49-6.36)
Advanced fibrosis (%)	0	6 (24%)	7 (28%)

Osinusi A, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-4.

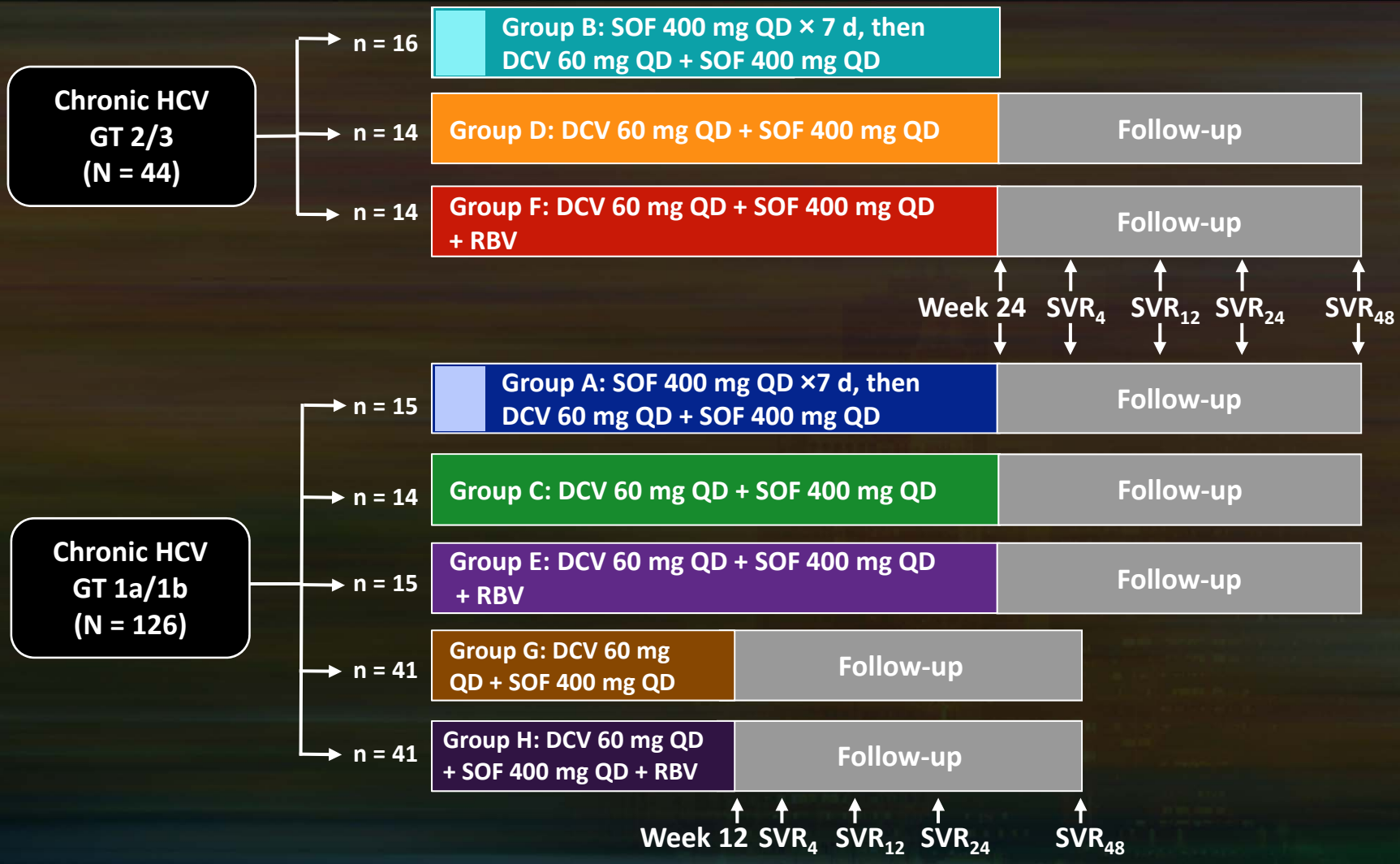
Treatment Response: Part 2

Full dose RBV: 75% SVR4 (*mITT*)
Low dose RBV: 64% SVR4 (*mITT*)



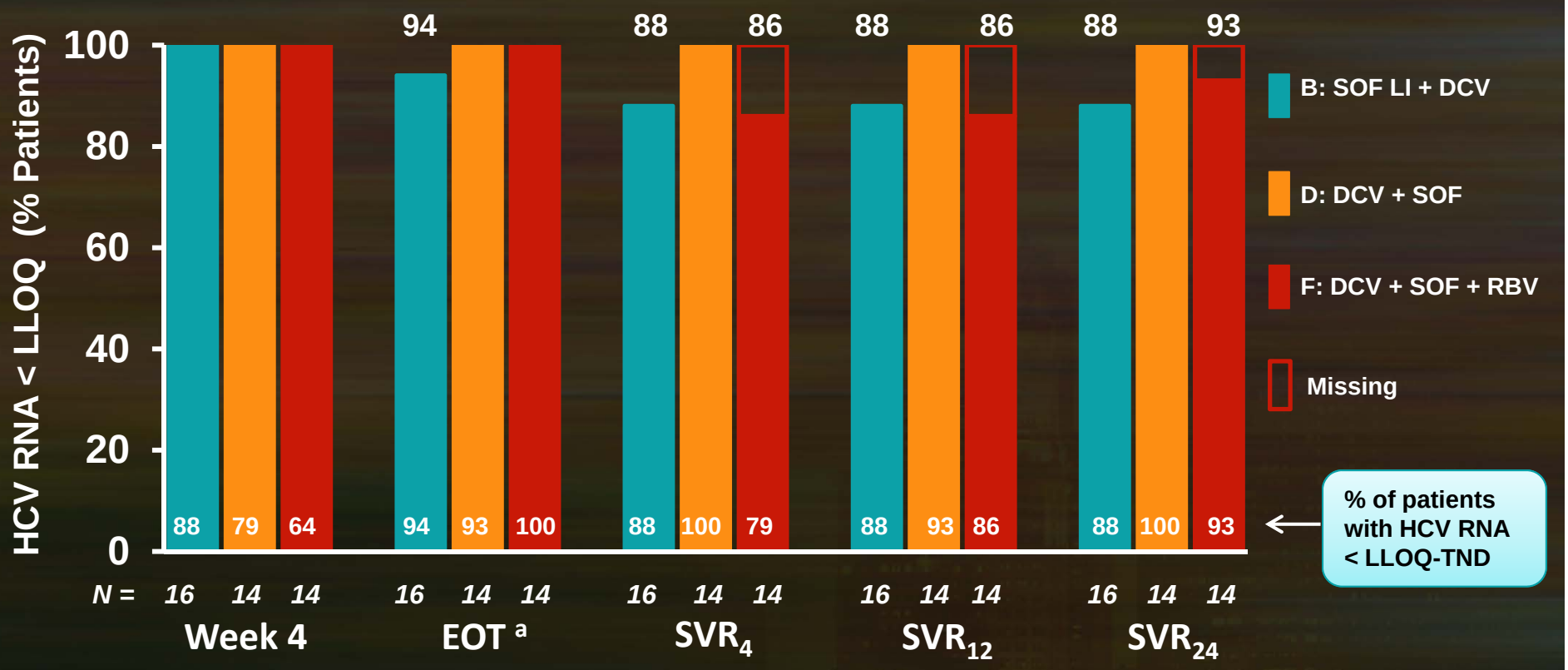
Osinusi A, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-4.

Daclatasvir + Sofosbuvir with or without Ribavirin in HCV genotype 1, 2 or 3



Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-2.

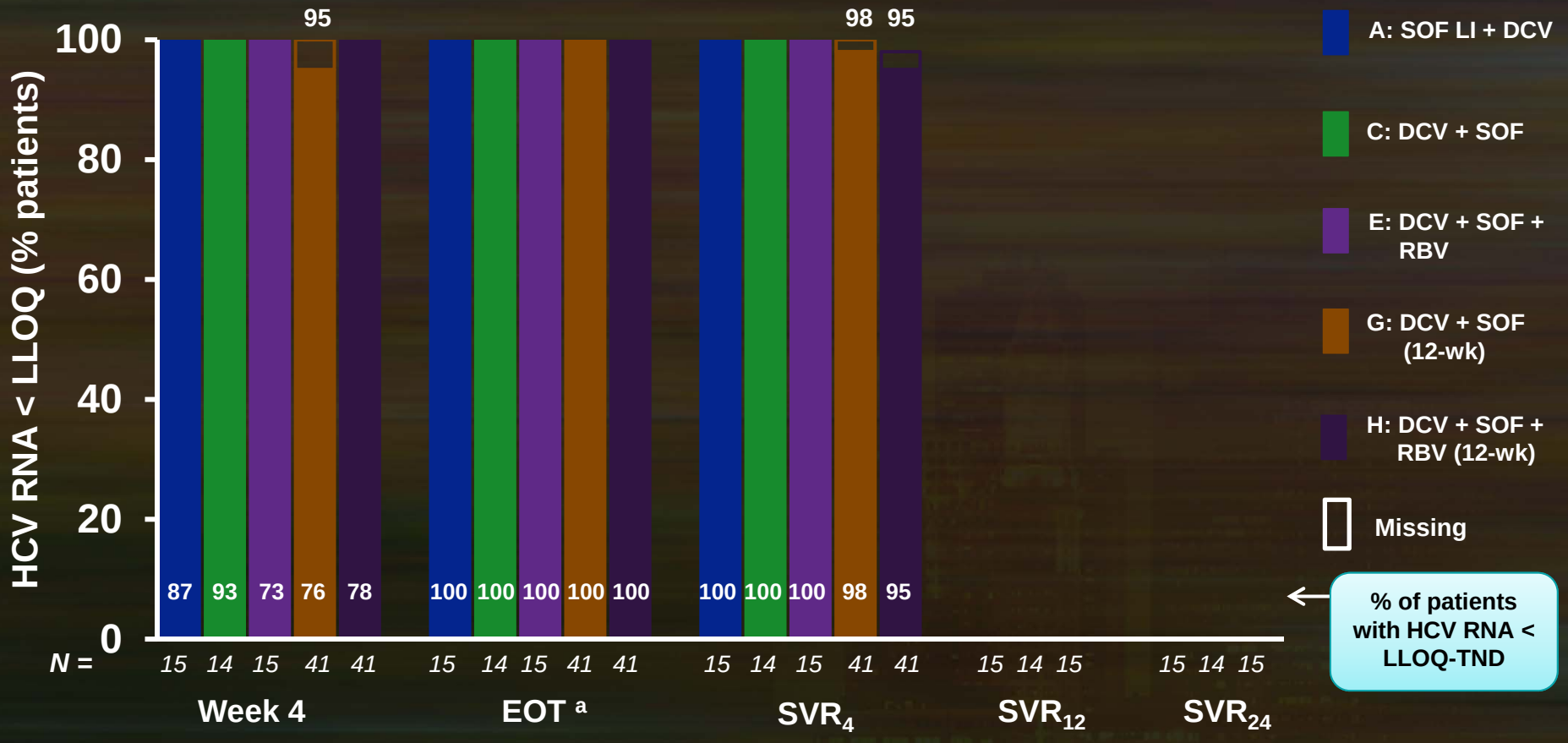
Genotype 2/3: Virologic Response During and After Treatment (mITT)



- **Group B:** 1 patient (GT3) relapsed; NS5A-A30K polymorphism (associated with DCV resistance) detected at baseline and PT Week 4. 1 patient (GT3) met protocol definition of virologic breakthrough; added pegIFN alfa/RBV – achieved SVR_{24}
- **Group F:** 2 lost to follow-up after EOT; 1 returned at PT Week 24 with HCV RNA < LLOQ-TND

Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-2.

Genotype 1: Virologic Response During and After Treatment,12- and 24-Week Groups (mITT)

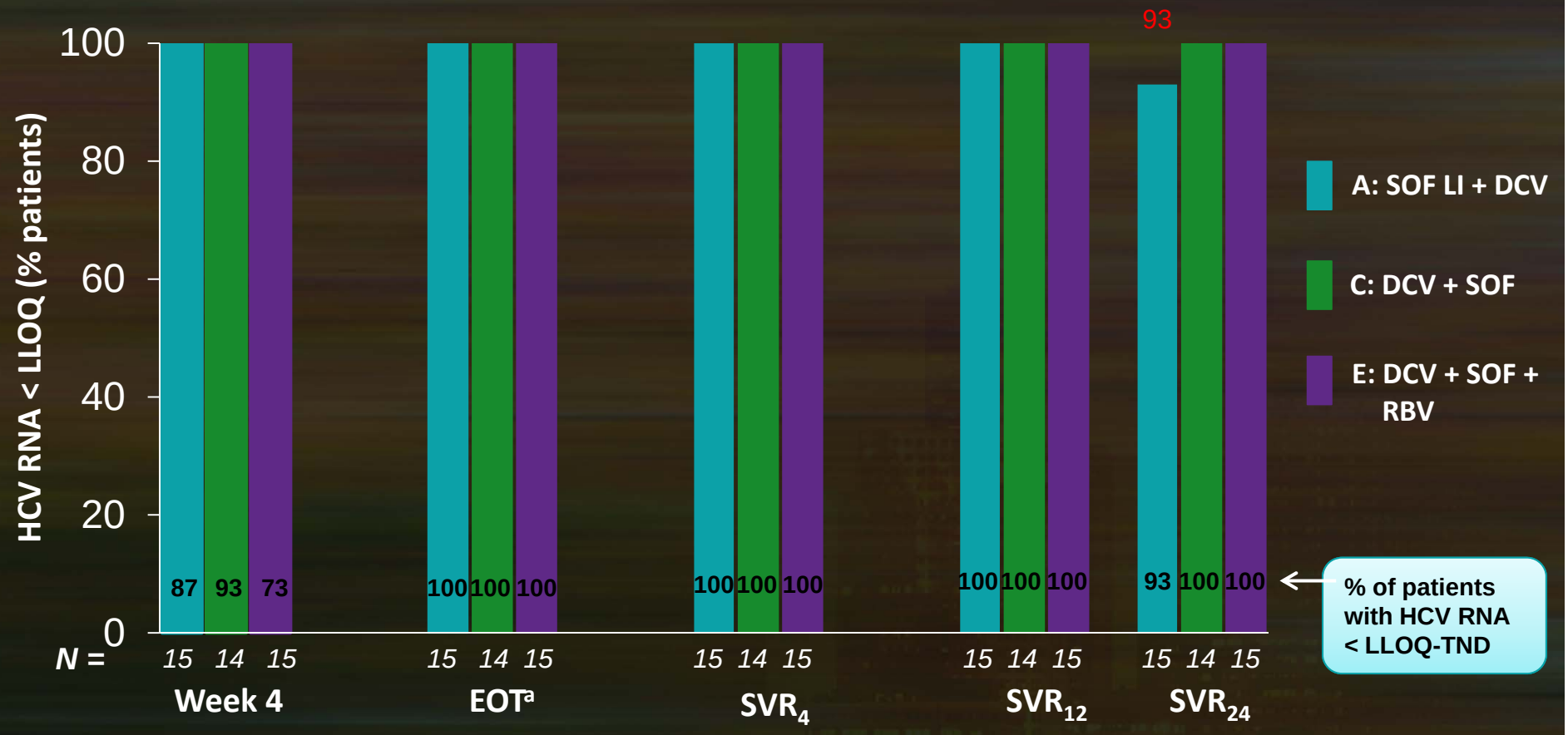


12-week Groups (G and H)

- 2 patients missing at PT Week 4— both achieved SVR_{12}; 1 patient undetectable at PT Week 2
  and with HCV RNA detected at PT Week 4 (not confirmed)—achieved SVR_{12}
- 68 patients have reached PT Week 12—all 68 have achieved SVR_{12}

Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-2.

Genotype 1: Virologic Response During and After Treatment, 24-Week Groups (mITT)



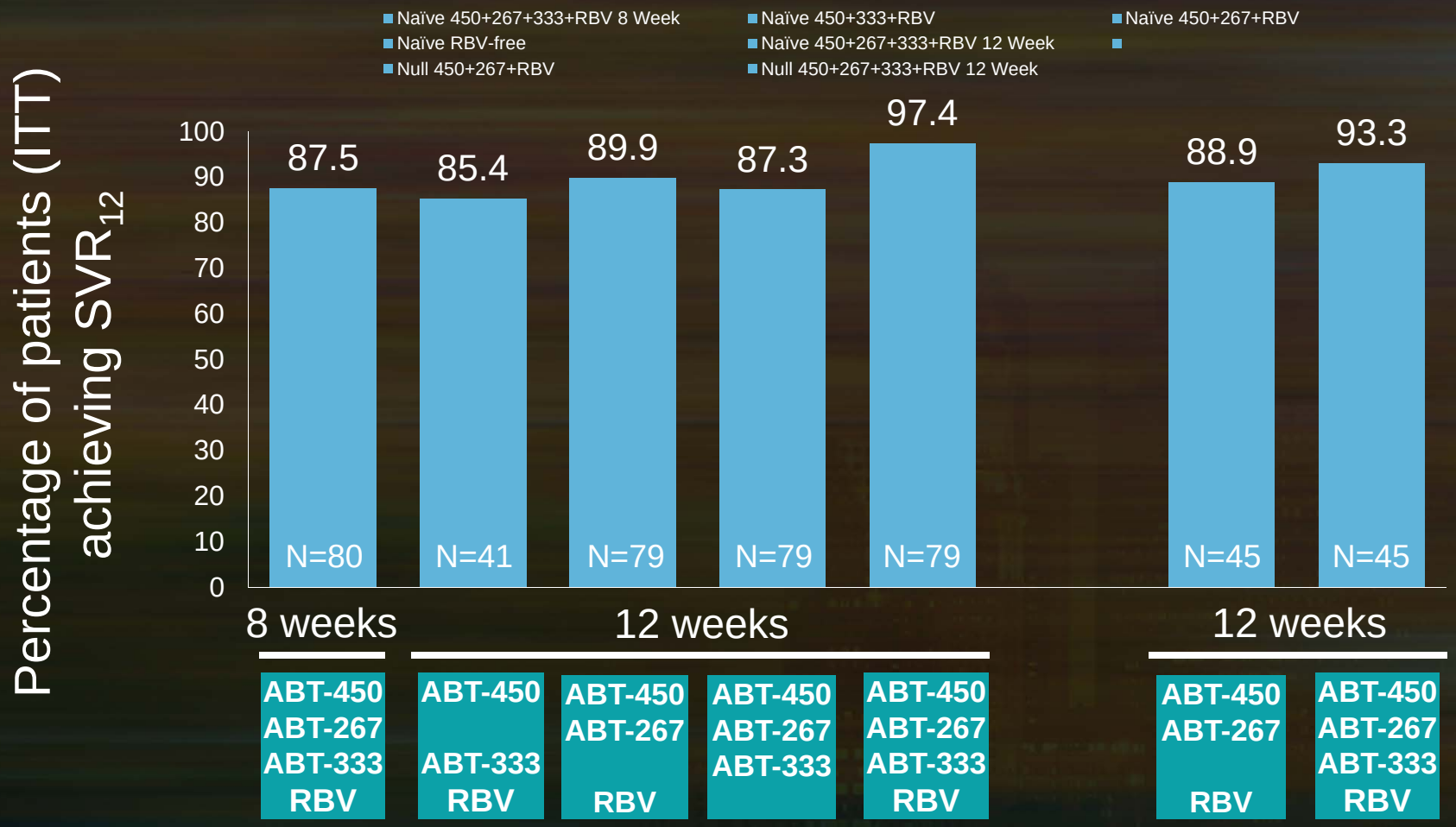
- **Group A**: 1 patient with history of IDU became viremic at PT Week 24: posttreatment viral sequence clearly different from pretreatment virus, consistent with reinfection

Sulkowski M, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-2.

ABT450/r (PI) + ABT267 (NS5A)+/- ABT333 (NNI) +- RBV in Treatment and Prior Null Responders

Kowdley K, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-1.

SVR12 Rates (ITT) for 8- and 12-Week Arms



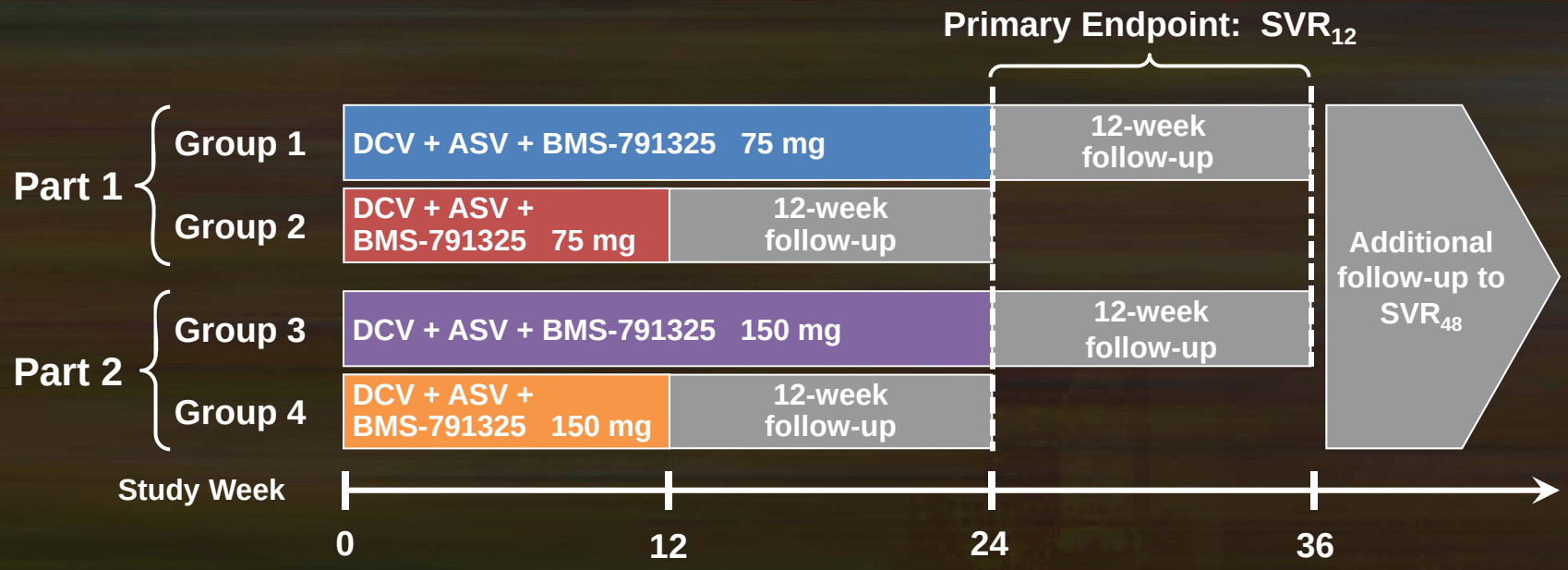
Kowdley K, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-1.

Response Rates

	Treatment-naïve Patients					Null Responders	
Duration	**8 wks**		**12 wks**			**12 wks**	
Regimen	**450/r 267 333 RBV**	**450/r 333 RBV**	**450/r 267 RBV**	**450/r 267 333**	**450/r 267 333 RBV**	**450/r 267 RBV**	**450/r 267 333 RBV**
Number dosed	80	41	79	79	79	45	45
Breakthroughs (N)	0	1	1	1	0	0	3
Relapses (N)	9	4	5	5	1	5	0
Lost to follow-up or withdrawn consent prior to SVR_{12}	1	1	2	4	1	0	0
SVR_{12} rate (ITT), % (n/N)	87.5% (70/80)	85.4% (35/41)	89.9% (71/79)	87.3% (69/79)	97.5% (77/79)	88.9% (40/45)	93.3% (42/45)
SVR_{12} rate (Observed data), % (n/N)	88.6% (70/79)	87.5% (35/40)	92.2% (71/77)	92.0% (69/75)	98.7% (77/78)	88.9% (40/45)	93.3% (42/45)

Kowdley K, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB-1.

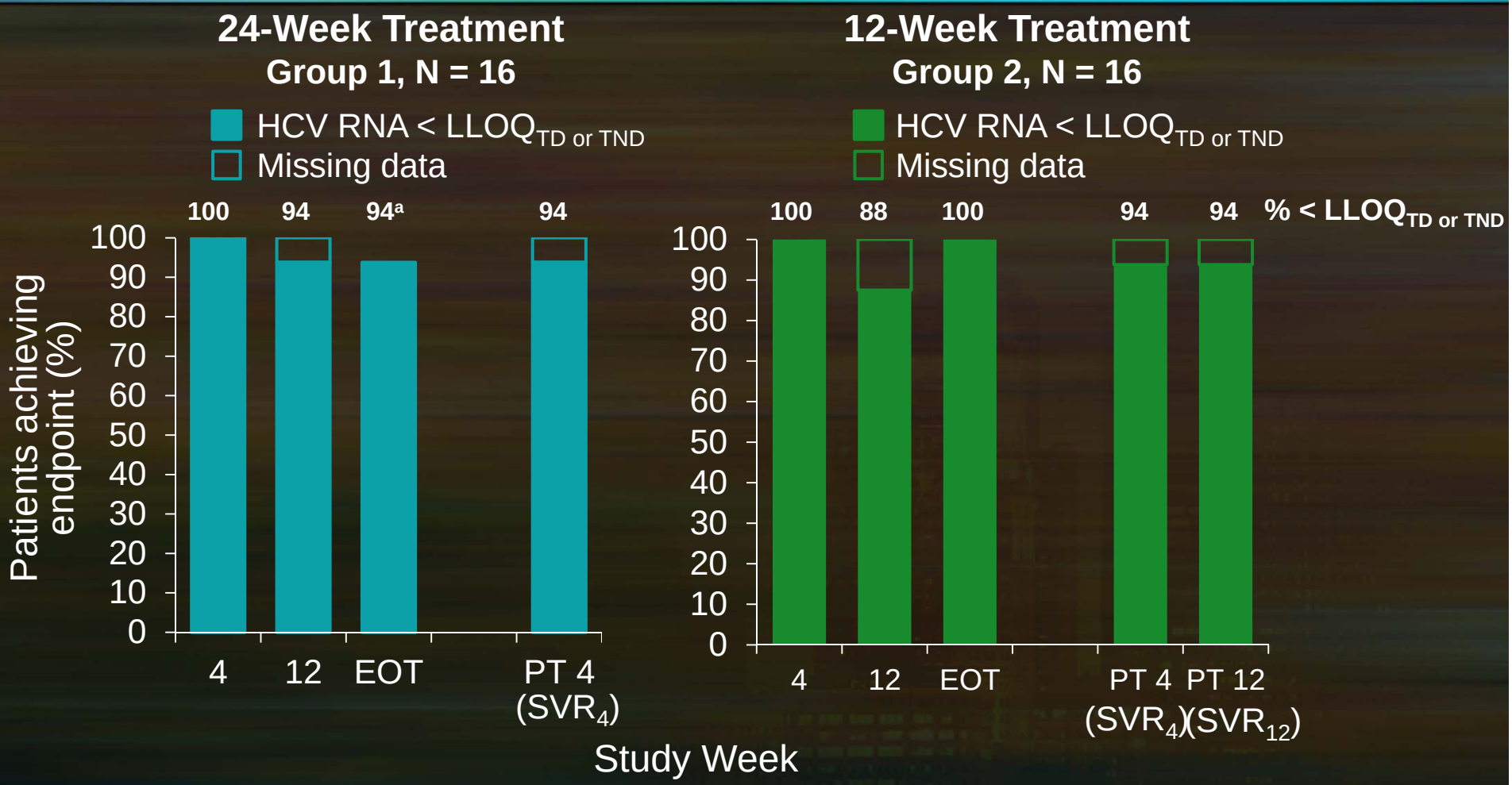
Daclatasvir (NS5A) + Asunaprevir (PI) + Non-nucleoside polymerase inhibitor (no ribavirin)



- Patients: treatment-naïve, non-cirrhotic, HCV GT 1 stratified by subtype 1a/1b
- Treatment: DCV 60 mg QD + ASV 200 mg BID + BMS-791325 either 75 mg BID (Part 1) or 150 mg BID (Part 2)
- HCV RNA endpoints: per FDA guidance, HCV RNA < LLOQTD = target detected but below the assay lower limit of quantitation (LLOQ; 25 IU/mL); LLOQTND = below LLOQ and target not detected (previously referenced as HCV RNA undetectable or < LOD; ≈ 10 IU/mL for this study)
- Primary endpoint: HCV RNA < LLOQ 12 weeks post treatment (SVR12)
  - Modified intent-to-treat analysis: missing, breakthrough, or relapse = failure
- Interim analysis: Part 1 results reported through post treatment week 4 (Group 1; SVR4) or post treatment week 12 (Group 2; SVR12); Part 2 enrolled and ongoing, results not yet available

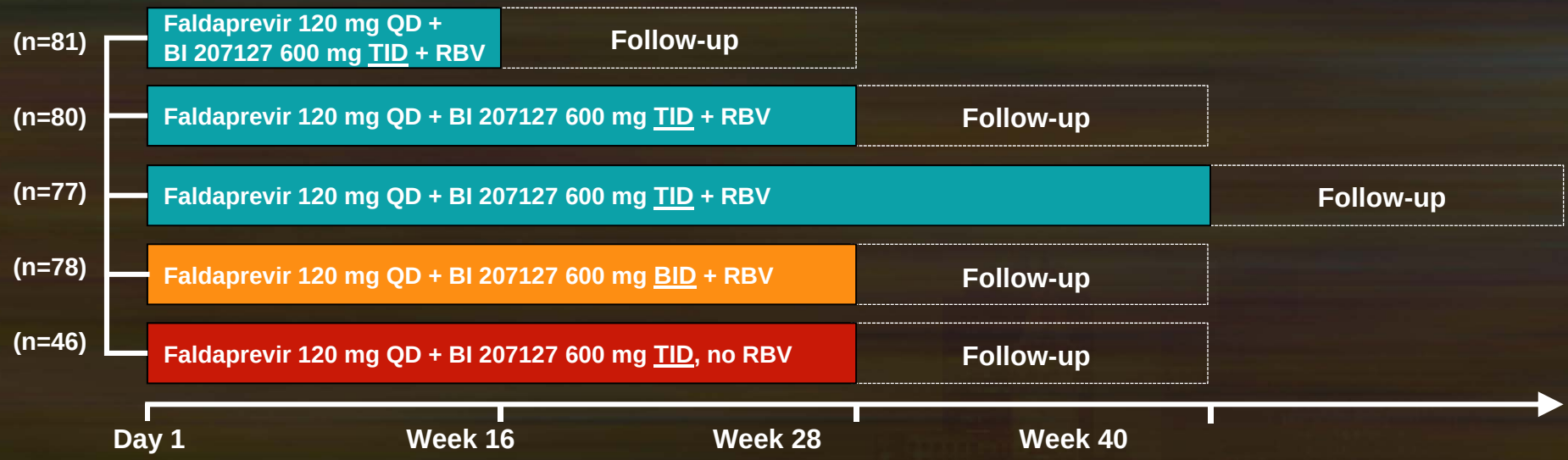
Everson G, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB.-3.

HCV RNA Endpoints: Modified Intention-to-Treat Analysis



Everson G, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. LB.-3.

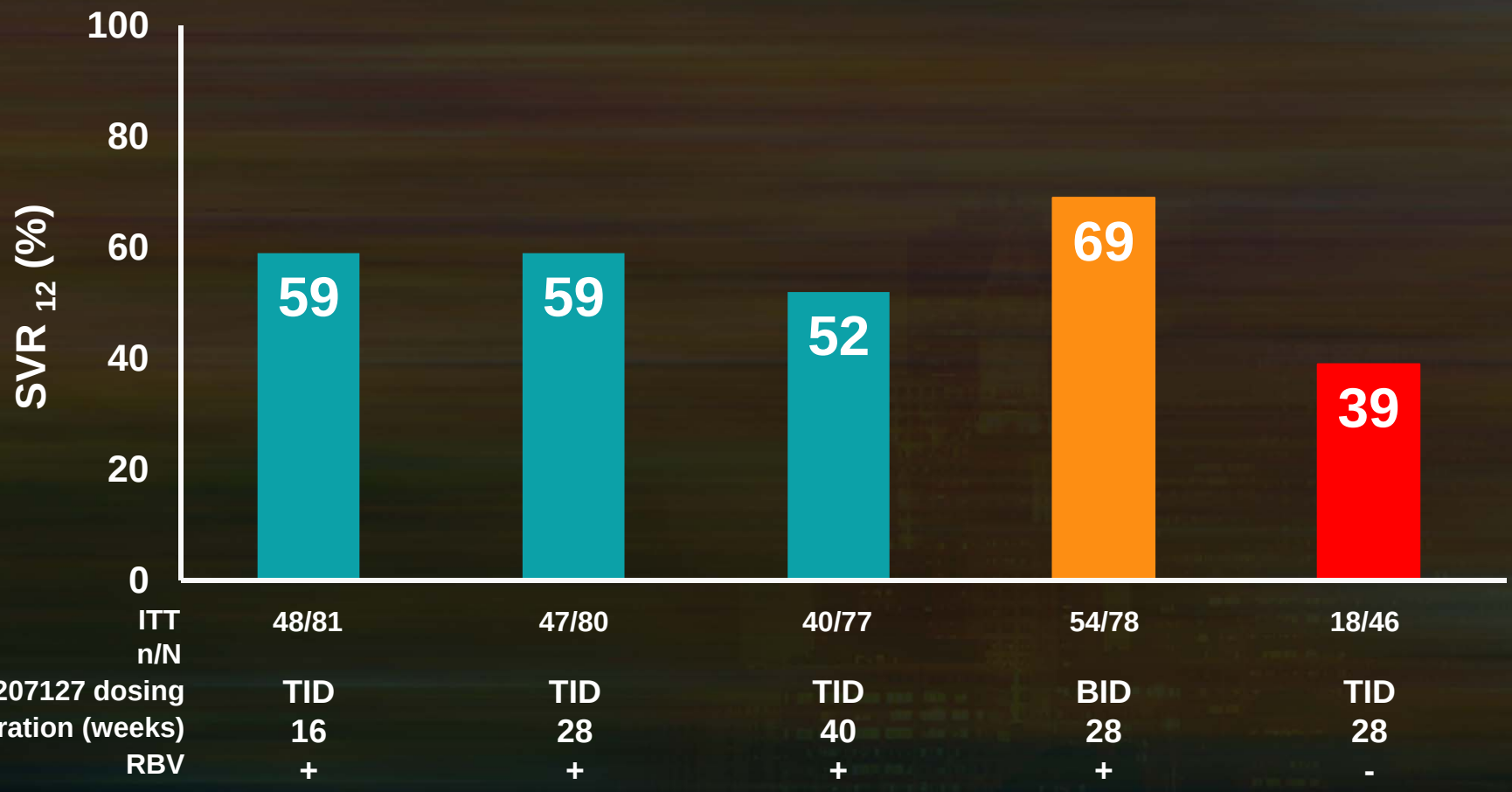
Faldaprevir (PI) + Non-nucloside polymerase inhibitor with or without ribavirin



- Phase IIb, multicenter, open-label, randomized (1:1:1:1:1)a
  - Treatment-naïve patients with chronic HCV GT-1
- Stratified by GT-1 subtype (1a vs 1b) and IL28B (CC vs non-CC)
- Compensated cirrhosis included, 18–75 years of age, HCV RNA >100 000 IU/mL
- Stopping rule: HCV RNA detectable between Weeks 6 and 8
- Primary endpoint: SVR 12 weeks after treatment completion

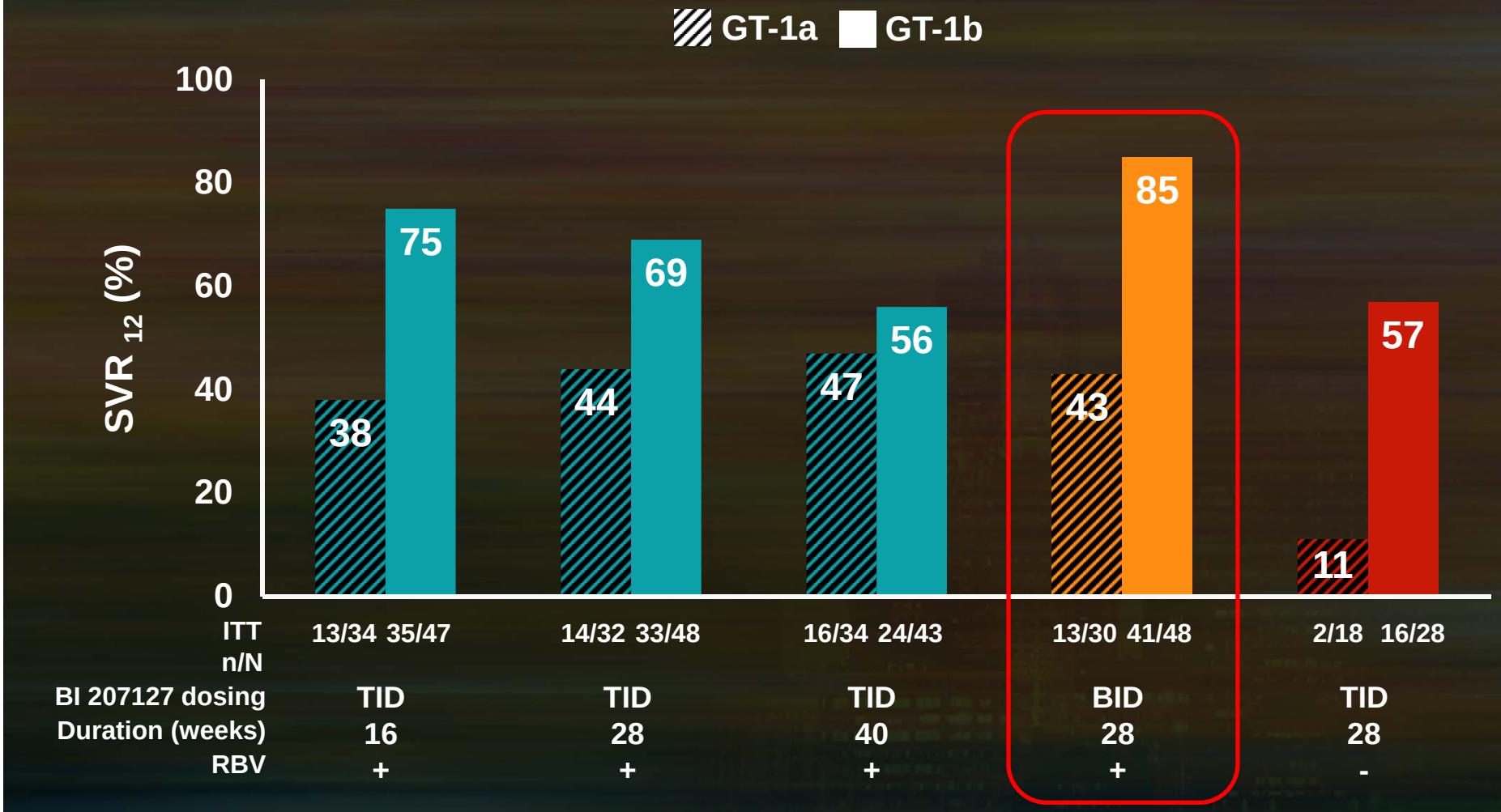
Zeuzem S, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 232.

Primary Endpoint: SVR12 (ITT)



Zeuzem S, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 232.

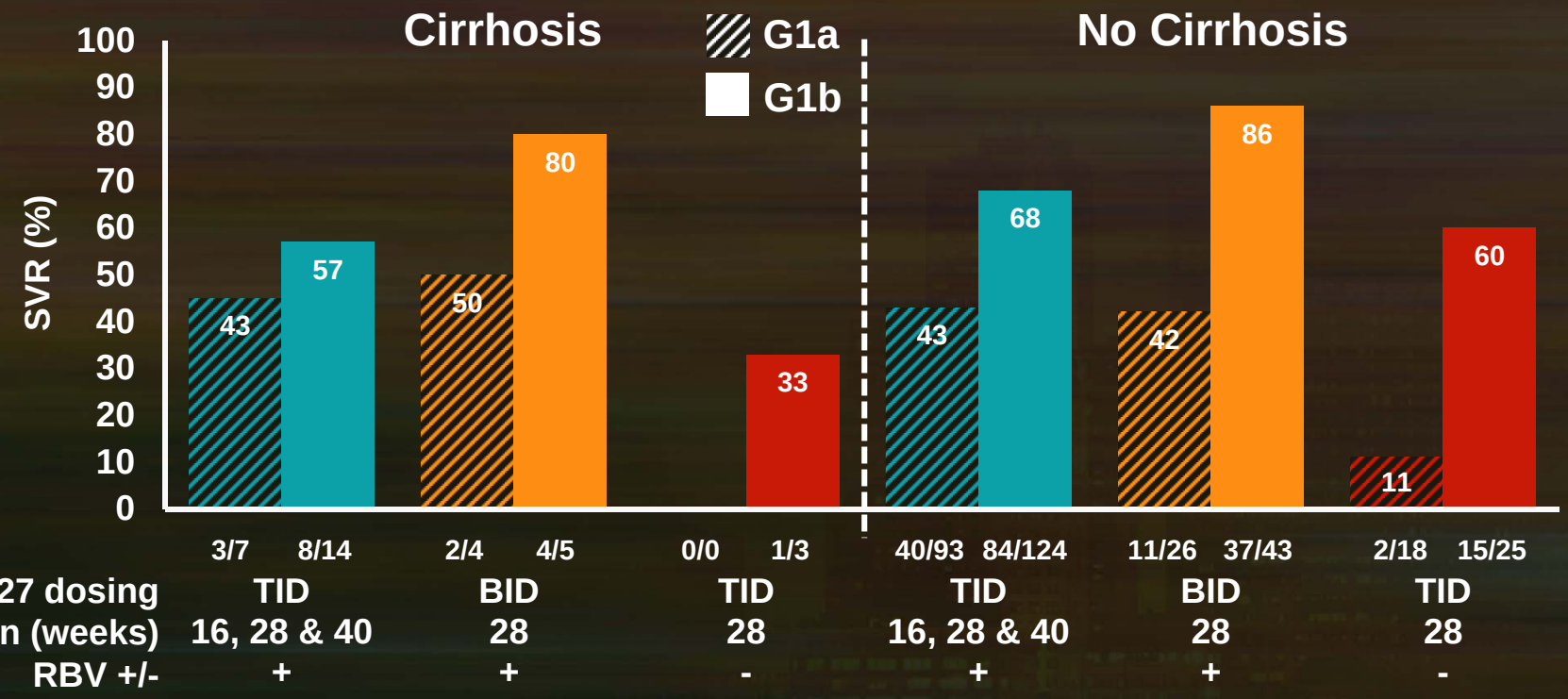
SVR12 According to HCV Subtype (ITT)



Zeuzem S, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 232.

SOUND-C2 Study sub-analysis: Efficacy and Safety of the IFN-free Combination of BI 201335 + BI 207127 ± RBV in Treatment-naive G1 Patients with Compensated Liver Cirrhosis

- SOUND-C2 (N=362); 33 patients (9%) had liver cirrhosis (liver biopsy or Fibroscan)
- Pooled data from pts who received BI 207127 TID + RBV (TID16W, TID28W and TID40W)



- Safety and tolerability profile good – did not differ significantly in cirrhotics vs non-cirrhotics
- Plasma exposure of faldaprevir and BI 207127 higher in cirrhotics (less apparent in BID arm)

Soriano V, et al. 63rd AASLD; Boston, MA; November 9-13, 2012. Abst. 84.

Interferon-free Oral Therapy

- Several regimens have emerged from phase 2 clinical trials with high SVR rates
  - Sofosbuvir + GS5885 (coformulated) QD with and without RBV BID x 12 or 24 weeks
    - in phase 3
  - ABT450/r + ABT267 (Coformulated + ABT333 + RBV BID x 12 weeks)
    - In phase 3
  - Other regimens are also moving ahead
- Encouraging data in cirrhotic patients and null-responders but limited

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