Real-World Effectiveness of Direct-Acting Antivirals for Hepatitis C among HIV-infected Patients with Genotype 1

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Why Do We Need Data on “Real World Outcomes”?

1. Clinical trials have shown that HIV is not a negative predictor for viral efficacy. However, viral efficacy is one very important component but not the only one to achieve clinical effectiveness

2. Limited external validity of HIV population included in clinical trials. Real world HIV clinical settings are often burdened by population with multiple ongoing barriers to care and advanced liver disease

Study Setting and Methods

- UCSD Owen Hepatitis Co-Infection Clinic. Program co-managed by infectious diseases physicians and clinical pharmacists
- Clinic is funded by The Health Resources and Services Administration through the Ryan White C.A.R.E. Act Part C Early Intervention Services Grant Program
- Retrospective cohort of consecutive HIV-infected patients treated for HCV between 1 January 2014 to 31 December 2015
- Treatment regimens and duration reflect rapid changes in HCV treatment landscape and standards of care

Assessment of Barriers to Care

1. Drug/Alcohol use → Self completion of NIDA-modified ASSIST[1] (drug use) & AUDIT-C[2] (alcohol) instruments. Baseline evaluation by clinic substance use counselor

2. Psychiatric disease → PHQ-9 inventory & baseline formal psychiatric evaluation.

3. Unstable housing → Substance Counselor, Social Worker, and/or clinicians

The NIDA-ASSIST, AUDIT-C and PHQ-9 instruments are administered prior to every HCV clinical encounter.

1.ASSIST = Alcohol, Smoking and Substance Involvement Screening Test
2. AUDIT-C =The Alcohol Use Disorders Identification Test

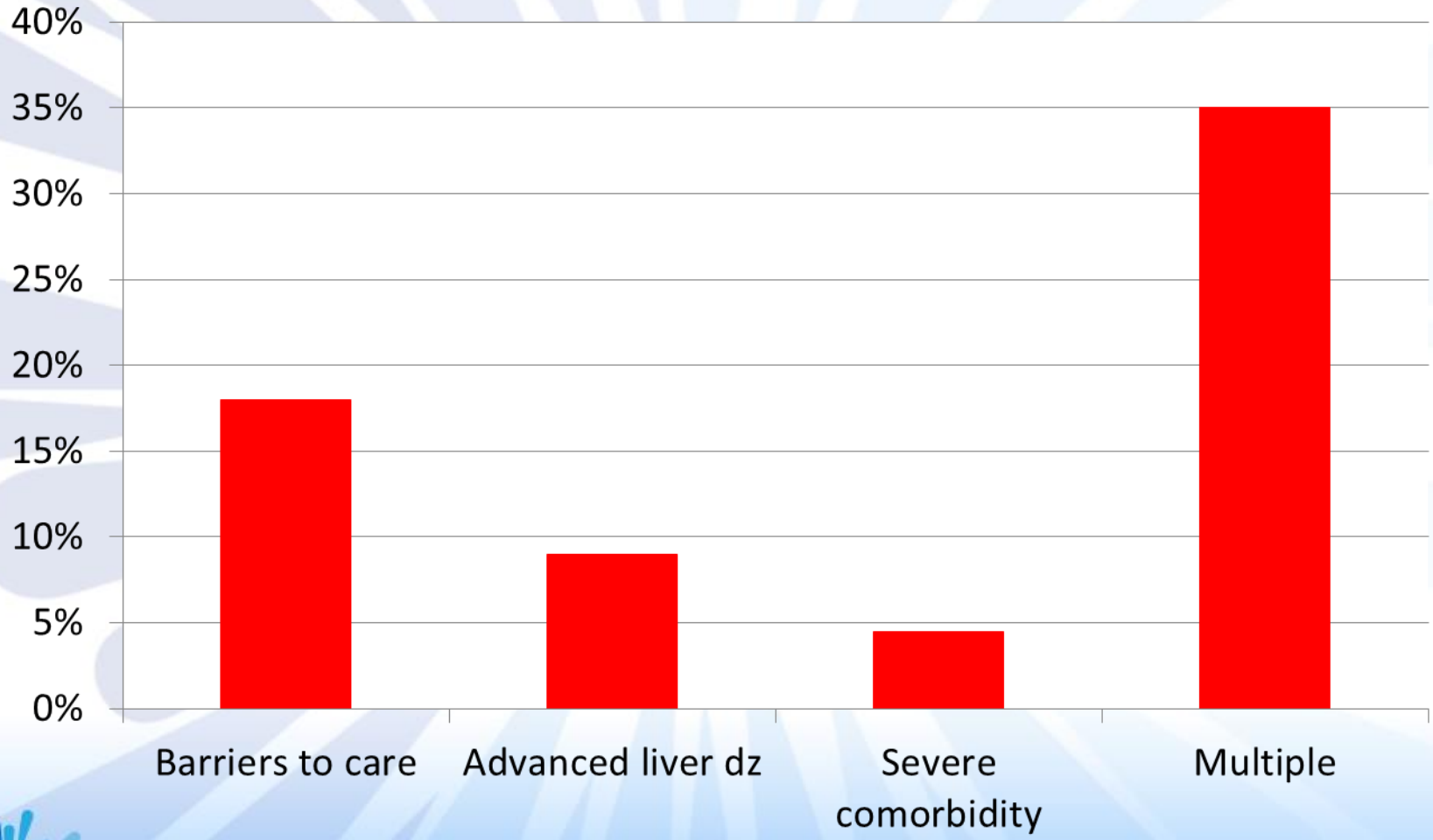
Clinical Features	N=66
Median age – years (range)	54 (26-72)
Biological sex: male (%)	60 (91)
Race: Not-white (%)	19 (29)
Ethnicity: Hispanic (%)	7 (11)
HIV risk factors (%)	
Men who have sex (MSM) with men/bisexual	16 (24)
Heterosexual	1 (2)
Hemophilia	4 (2)
MSM and intravenous drug use	20 (30)
Heterosexual and intravenous drug use	24 (36)
Perinatal acquisition	1 (2)
Median T CD4+ – cells/mm^3 (range)	464 (87-1342)
Detectable HIV viral load (> 40 copy/mL)	3 (5)

HCV Features	N = 66
Genotype	
1a	54
1b	11
unable to sub-type	1
Liver fibrosis	
F0-2	30 (45%)
F3-4	36 (55%)
Prior HCV treatment	29 (44%)
Peg-interferon/RBV (IFN-intolerant: 10; Relapse: 5; null-response: 6)	21
Peg-interferon/RBV/Telaprevir (Intolerant: 1, non-response: 5)	6
DAA Interferon-free (Sofosbuvir/simeprevir:1, Sofosbuvir/ Daclatasvir:1)	2

HIV Patients with Cirrhosis-F4	n=31
Genotype	
1a	29
1b	1
unable to sub-type	1
Median MELD score (range)	13 (8-24)
Patients with prior liver decompensation	13 (42%)
Ascites	11
Spontaneous bacterial peritonitis	1
Hepatic encephalopathy	7
Prior esophageal varices bleeding	4

	DAA HCV combinations	N = 66 (%)
2014	SOF/RBV-24	2 (3%)
	SMV/SOF -12	12 (18.2%)
	SMV/SOF ± RBV -24	5 (7.6%)
2015	LDV/SOF -12	36 (54.5%)
	LDV/SOF ± RBV -24	8 (12.2%)
	PTV-r/ OBV/ DSV± RBV-12	3 (4.5%)

Forty-Four (66.6%) Patients Were Ineligible to Access Any Clinical Trials



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Antiretroviral (ART) Management Prior to HCV Treatment Initiation

- Overall (28 of 66, 42%) required antiretroviral switch prior to initiation.
- ART switch was more frequent among patients treated with SMV/SOF (12 of 15 , 70.6%) than SOF/LDV (15 of 44, 39%), p =0.01

Most common ART combinations used during HCV treatment	N = 66
NRTI + INSTI (%)	52
NRTI + NNRTI (%)	7.5
NRTI + boosted-protease inhibitor (%)	7.5
Other combinations in treatment experienced patients (%)	30
No ART (%)	2

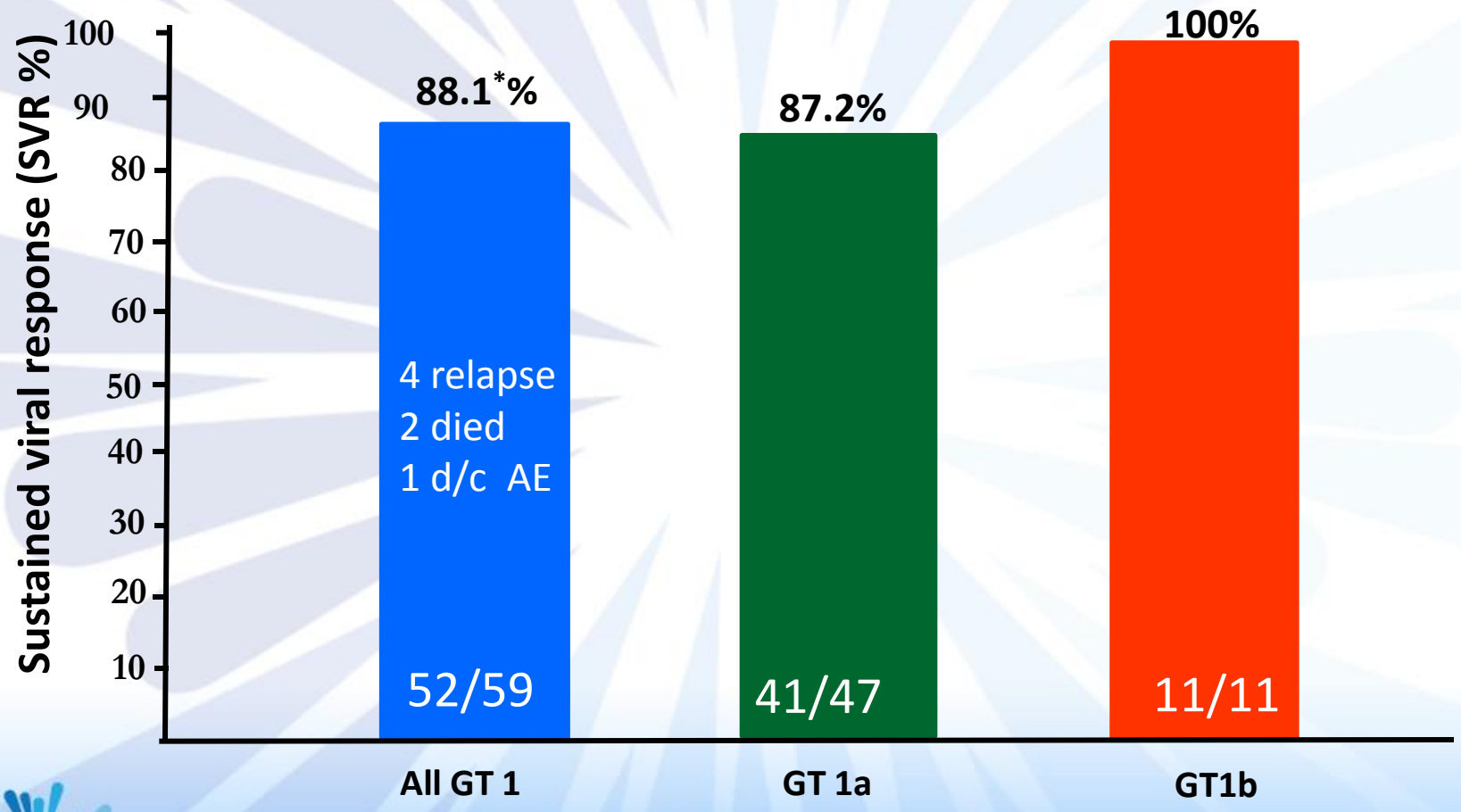
NRTI = nucleoside reverse transcriptase inhibitor

INSTI = Integrase strand transfer inhibitor

NNRTI = non-nucleoside reverse transcriptase inhibitor

SVR-12 Among 59 of 66 HIV-Infected Patients With GT1 who Completed HCV Therapy

* One patient with GT 1 unable to subtype relapsed at week 4.



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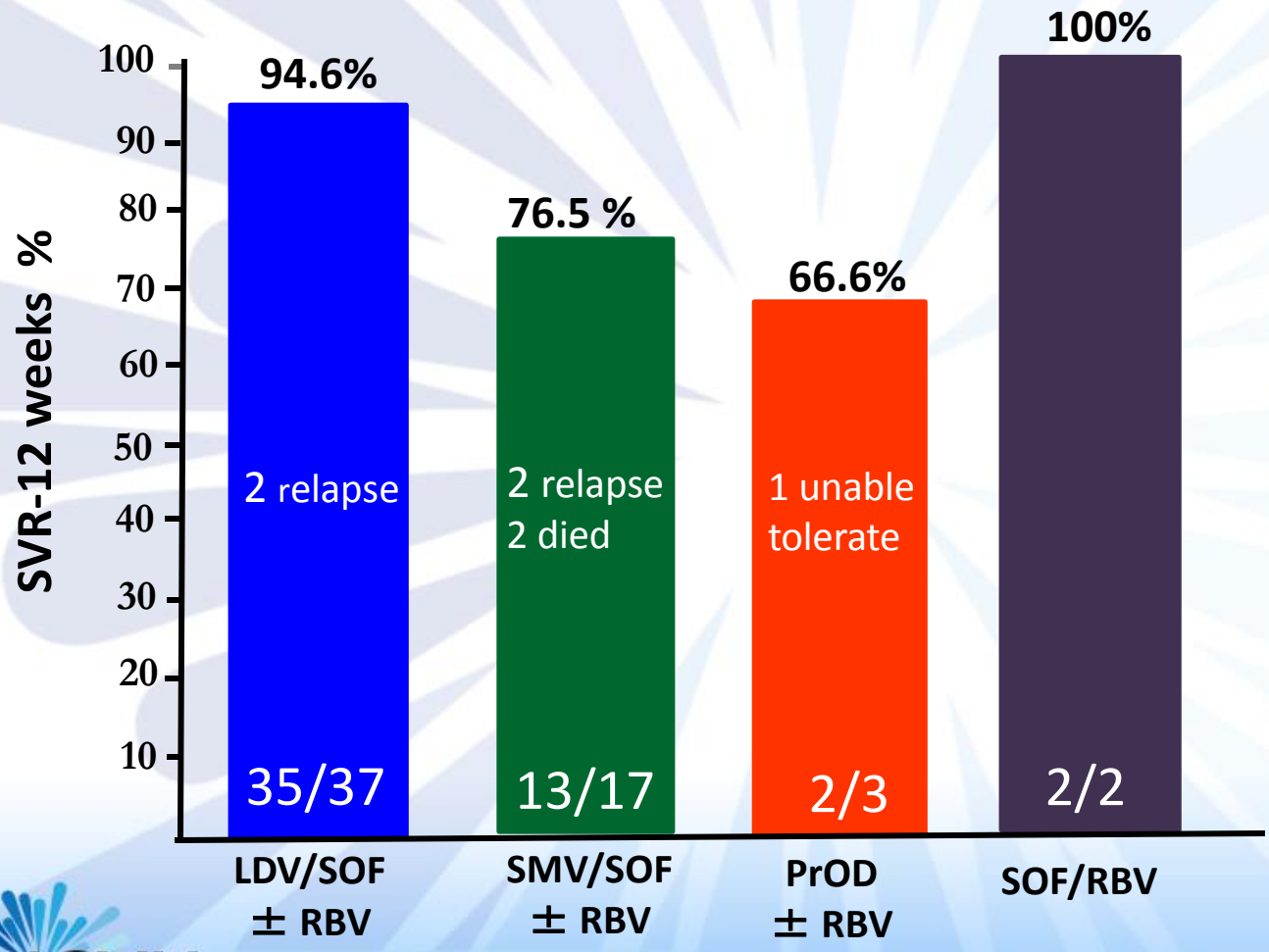
SVR-12 by Regimen (n = 59)



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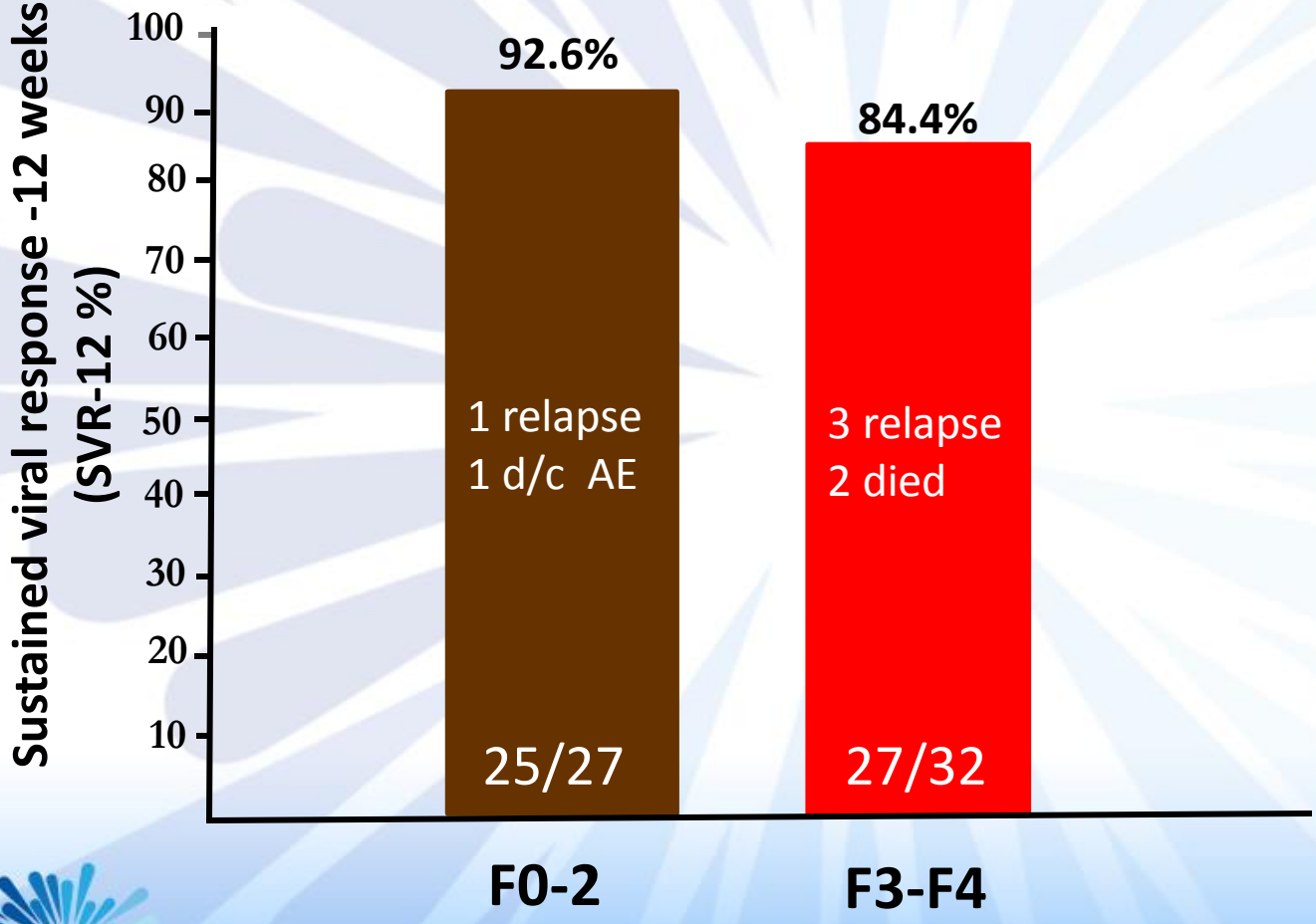
SVR-12 by Fibrosis Stage: All Regimens Included (n = 59)



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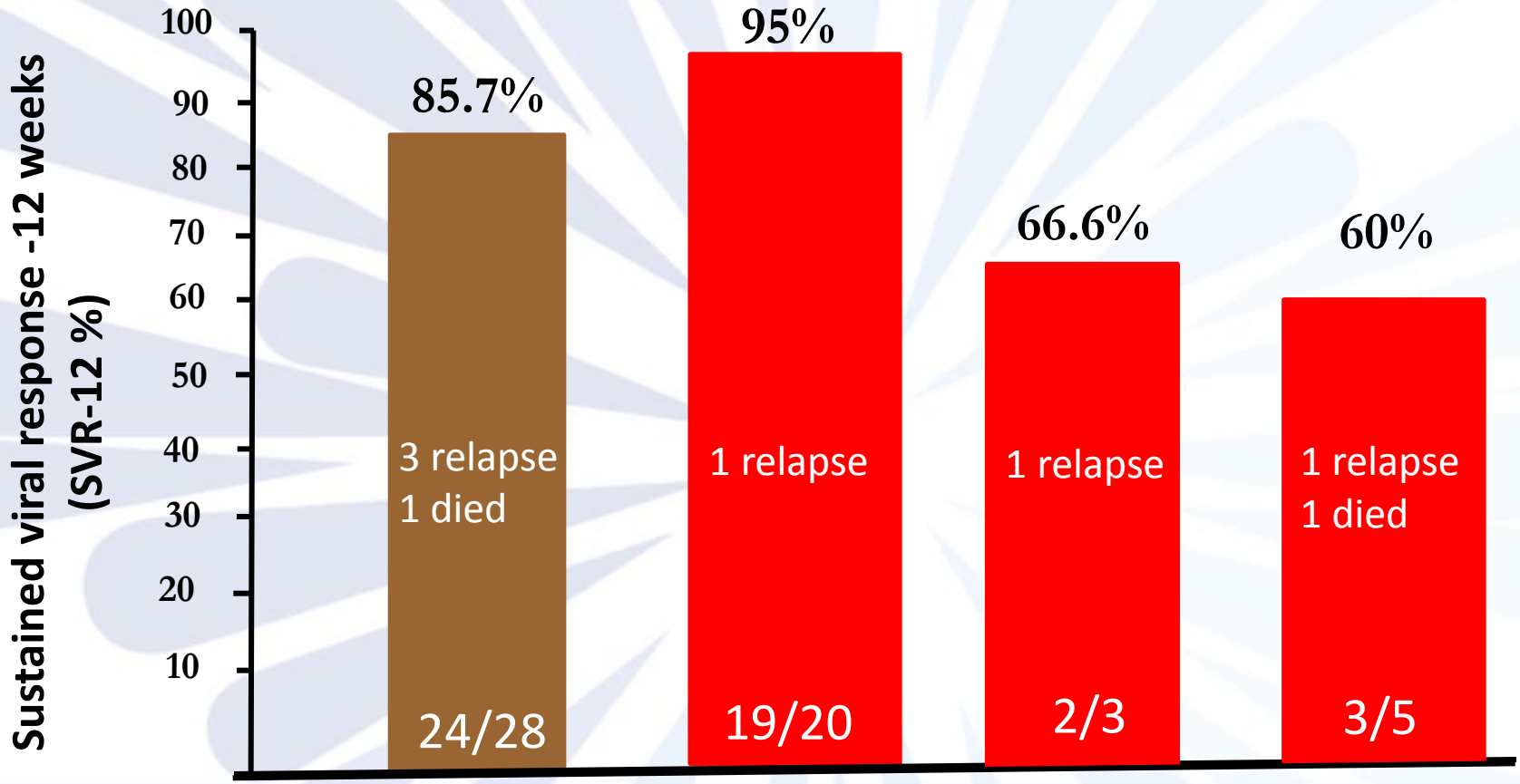
SVR-12 by Cirrhosis-AllRegimens (n=28)



Prior HCV Treatment Failure (n/N):	Overall	Child A	Child B	Child C
	8/27	6/19	2/3	0/5

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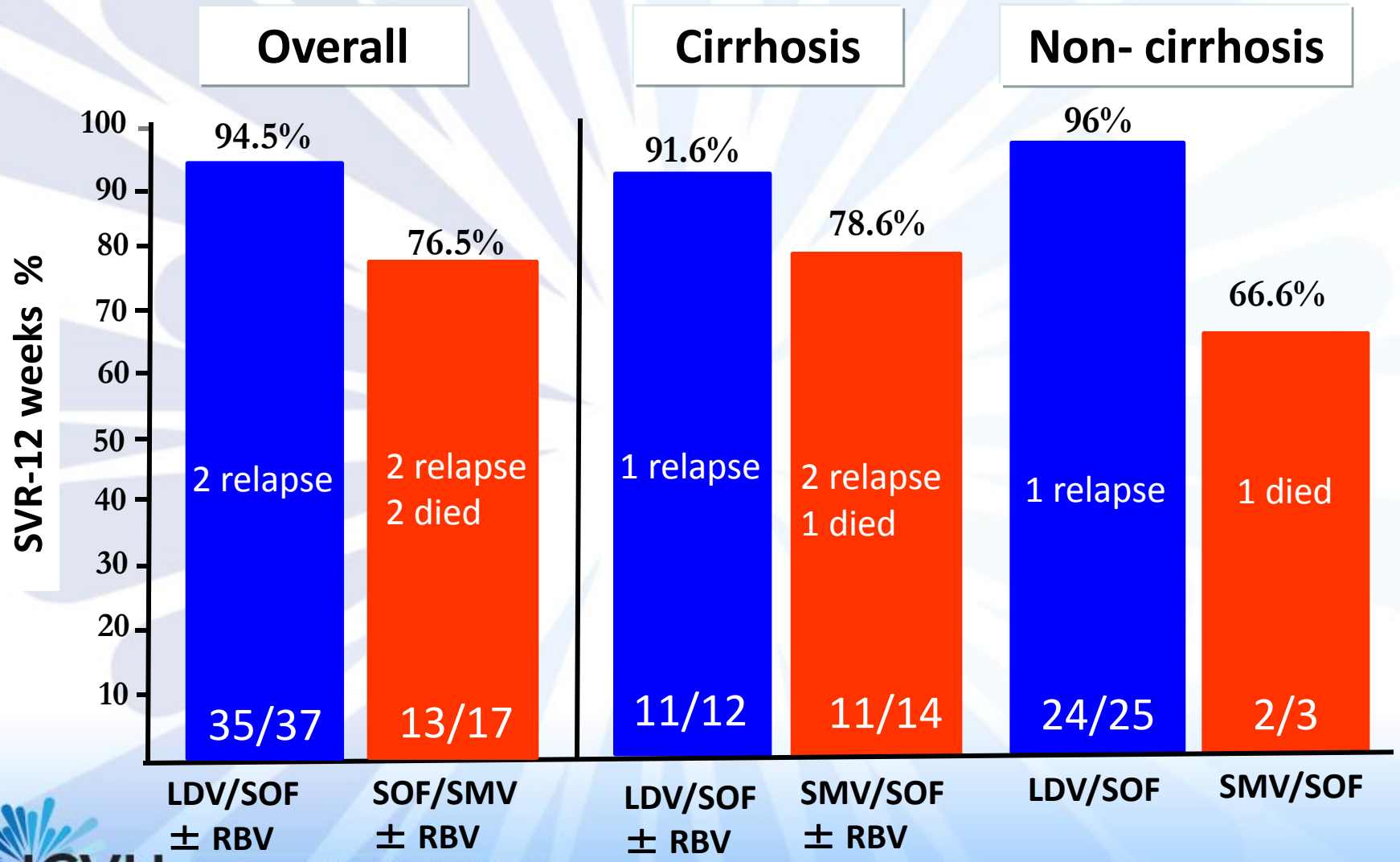
SVR-12: Ledipasvir/Sofosbuvir vs Simeprevir /sofosbuvir



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SVR-12 Bivariate Analysis: LDV/SOF (n=37) vs. SMV/SOF (n =37)

	OR (95% CI)	P-value
LDV/SOF vs SMV/SOF	5.38 (1.01-28.19)	0.0490
GT1a vs 1b	0.28 (0.06-4.35)	0.21
Cirrhosis vs non-cirrhosis	0.51 (0.04-3.61)	0.39
Prior decompensation (yes vs no)	0.17 (0.03-0.90)	0.035
Comorbidity-present (yes vs no)	0.85 (0.18-4.07)	0.85
Barriers to care (yes vs no)	0.60 (0.05-4.26)	0.50

SVR-12 Bivariate Analysis Among Patients with Ongoing Drug/Alcohol Use (n =29)

-- Most patients achieved SVR12: 25 of 29 (86.2%)

	OR (95% CI)	P-value
LDV/SOF vs SMV/SOF	9.5 (1.08-77.5)	0.0406
Cirrhosis vs non-cirrhosis	0.31 (0.04-2.56)	0.32
Prior decompensation (yes vs no)	0.07 (0.00-0.90)	0.018
Comorbidity-present (yes vs no)	0.85 (0.13-5.68)	0.88

Conclusions:

-- Using IFN-free DAA regimens, in a HIV population with high prevalence of ongoing barriers to care and severe concurrent medical comorbidities, 88.1% of patients with GT1 achieved SVR12.

-- A higher proportion of HIV patients with HCV GT1 treated with LDV/SOF (94.5%) achieved SVR 12 in comparison with patients treated with SMV/SOF (76.5%).

-- In this HIV clinic-based cohort, the most important factor associated with lack of HCV treatment response was having a history of prior liver decompensation.

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