HIV-HCV coinfection

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Disclosures

Principal investigator for research grants

- Funds paid to Johns Hopkins University
  - AbbVie, BMS, Gilead, Janssen, Merck

DSMB member

- Funds paid to Johns Hopkins University
  - Gilead

Scientific advisor/Consultant

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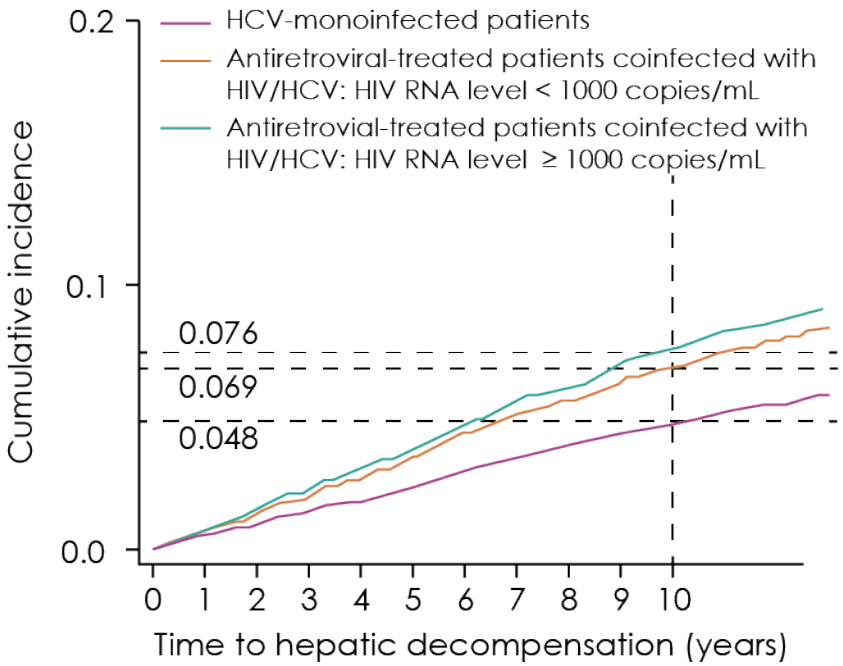
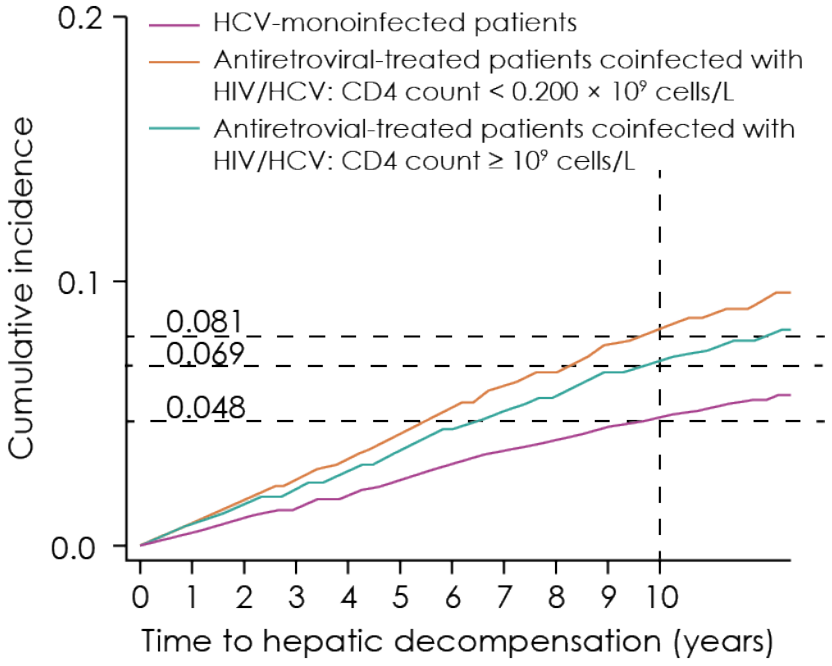
  - Cocrystal Pharma, AbbVie, BMS, Gilead, Janssen, Merck, Trek

HCV disease progression remains faster in HIV infected patients -- despite effective ART



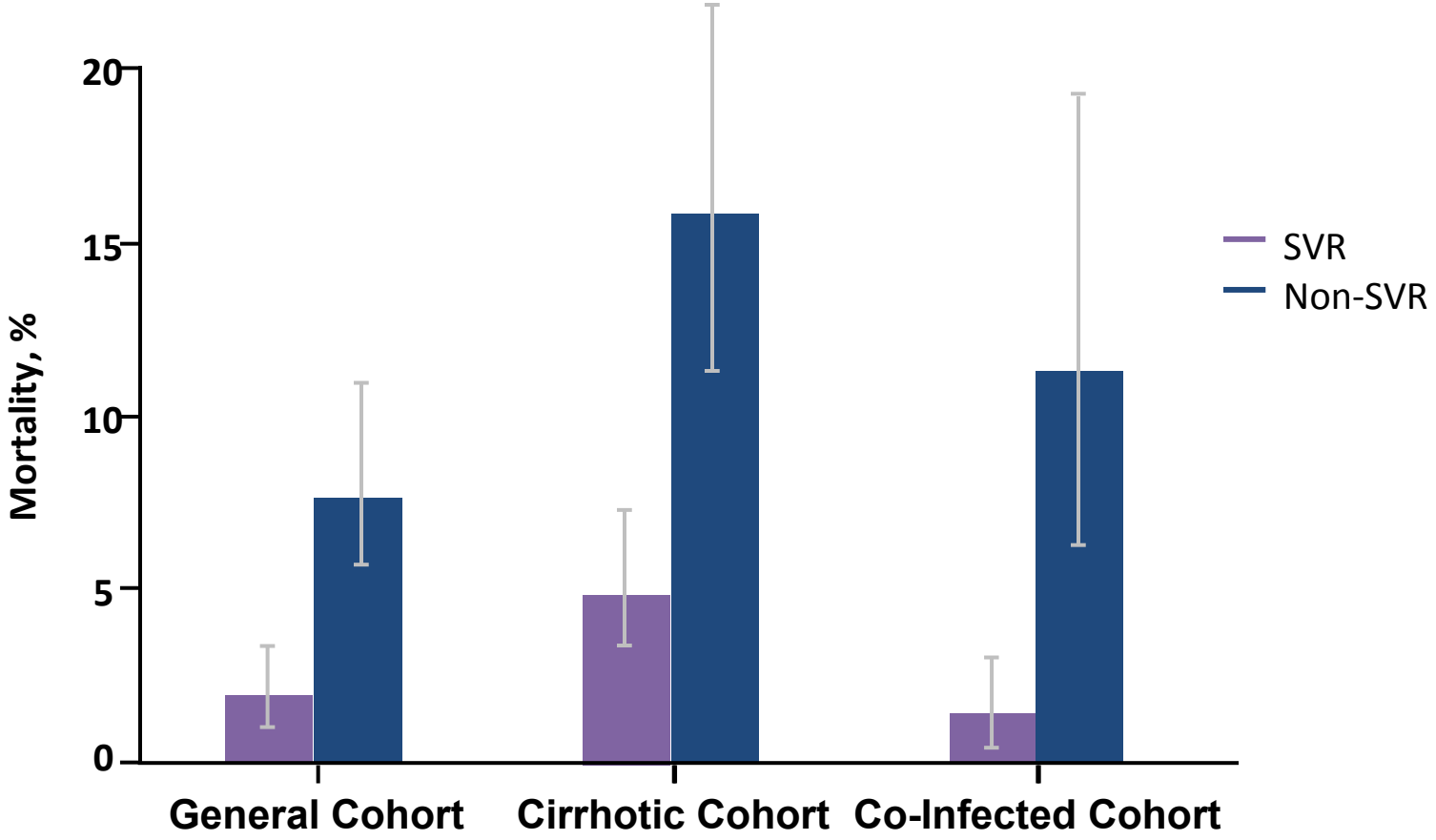
- If HIV RNA **< 1000 copies/mL:** +65% excess risk
- If HIV RNA **> 1000copies/mL:** +82% excess risk



- If CD4 **< 200/mm2:** +203% excess risk
- If CD4 **> 200/mm2:** 56–63% excess risk

ART, antiretroviral therapy; HCV, hepatitis C virus; HIV, human immunodeficiency virus.
Lo Re V 3rd. Ann Intern Med 2014.

Sustained virologic response (SVR) vs non-SVR is associated with a substantial reduction in mortality for the general population, patients with cirrhosis and patients with HIV coinfection



	General Cohort	Cirrhotic Cohort	Co-Infected Cohort
SVR	1.98 (1.00, 3.45)	4.90 (3.45, 7.28)	1.49 (0.50, 2.96)
Non-SVR	7.75 (5.86, 10.98)	15.88 (11.44, 21.80)	11.44 (6.33, 19.31)

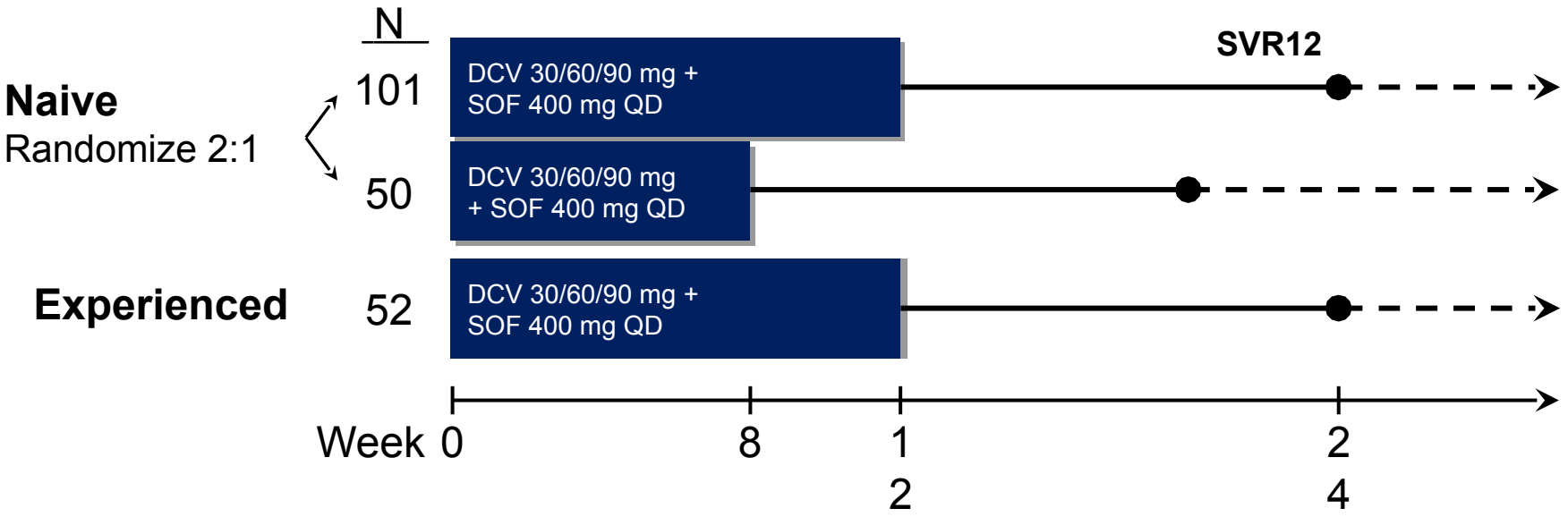
Bryony Simmons et al. Clin Infect Dis. 2015;cid.civ396

Guidelines from EASL and AASLD/IDSA: Prioritize HCV treatment for persons with HIV coinfection

Recommendation
HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications **Rating: Class I, Level B** • Treatment should be prioritized in patients at high risk for liver-related complications which includes patients with HCV/HIV coinfection, regardless of fibrosis stage • Treating patients at high risk for transmitting HCV to others may decrease transmission and HCV disease prevalence which includes MSM with high-risk sexual practices and active injection drug users

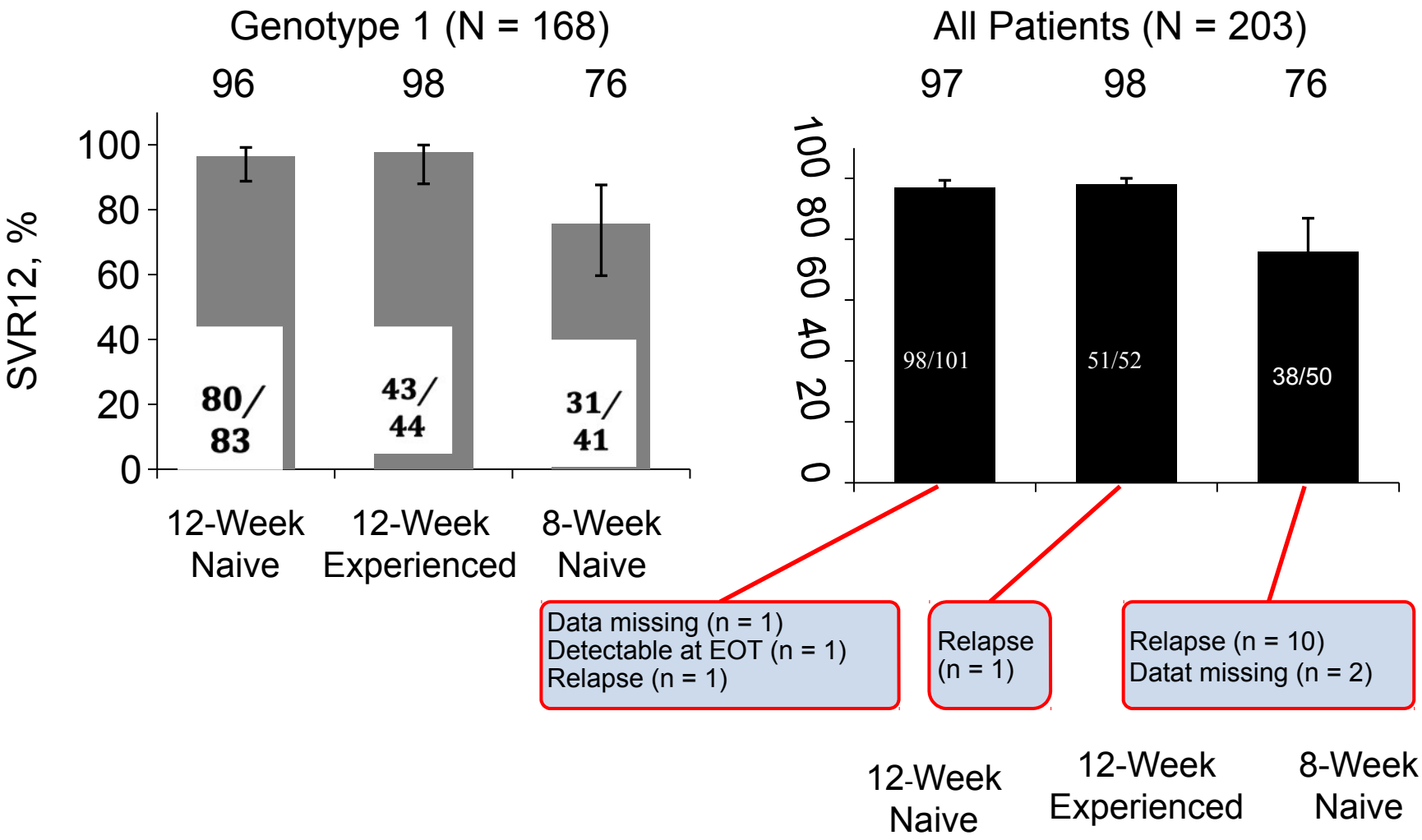
AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org.

ALLY-2: Daclatasvir + Sofosbuvir for patients with HIV coinfection

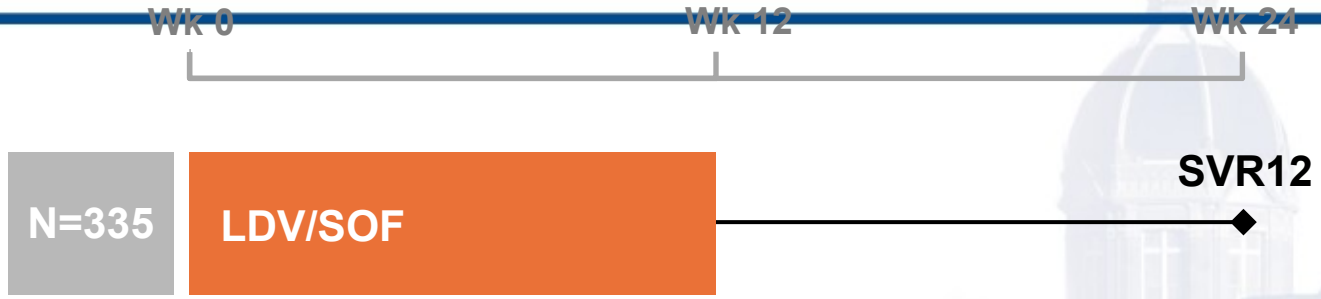


- Phase 3, multicenter, open-label study
- Inclusion criteria
  - HCV Genotype 1, 2, 3, 4 patients
  - HCV treatment-naïve or treatment-experienced
  - Cirrhosis permitted
- ART regimens included HIV-1 protease inhibitors/r (DCV dose = 30 mg), NNRTIs (DCV dose = 90 mg); integrase inhibitors (DCV dose = 60 mg)

ALLY-2: SVR12 by treatment duration and HCV treatment experience



Ledipasvir/Sofosbuvir for patients coinfected with HIV-1



Phase 3, multicenter, open-label study

HCV GT 1 or 4 patients

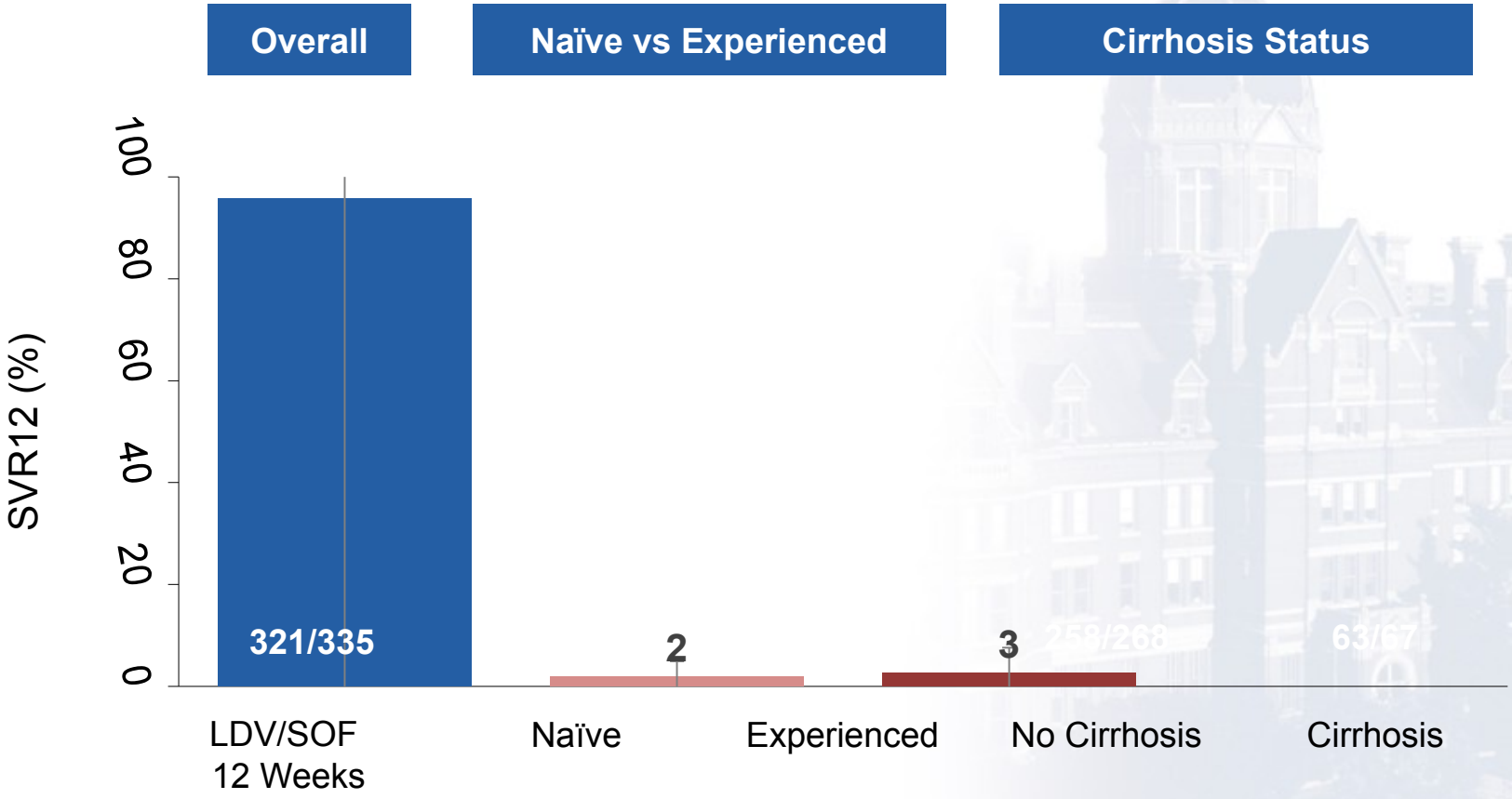
Inclusion criteria

- HCV treatment-naïve or treatment-experienced
- compensated cirrhosis permitted
- Platelets ≥50,000/mm3; hemoglobin ≥10 mg/dL, CrCl ≥60 mL/min
- HIV-1 positive, HIV RNA <50 copies/mL; CD4 cell count >100 cells/mm3

ART regimens included emtricitabine and tenofovir disoproxil fumarate plus efavirenz, raltegravir, or rilpivirine

Naggie et al. N Engl J Med 2015

ION4: SVR12 by Prior Treatment Experience and Cirrhosis Status
LDV/SOF x 12 weeks



Error bars represent 95% confidence intervals.

Naggie et al. N Engl J Med 2015

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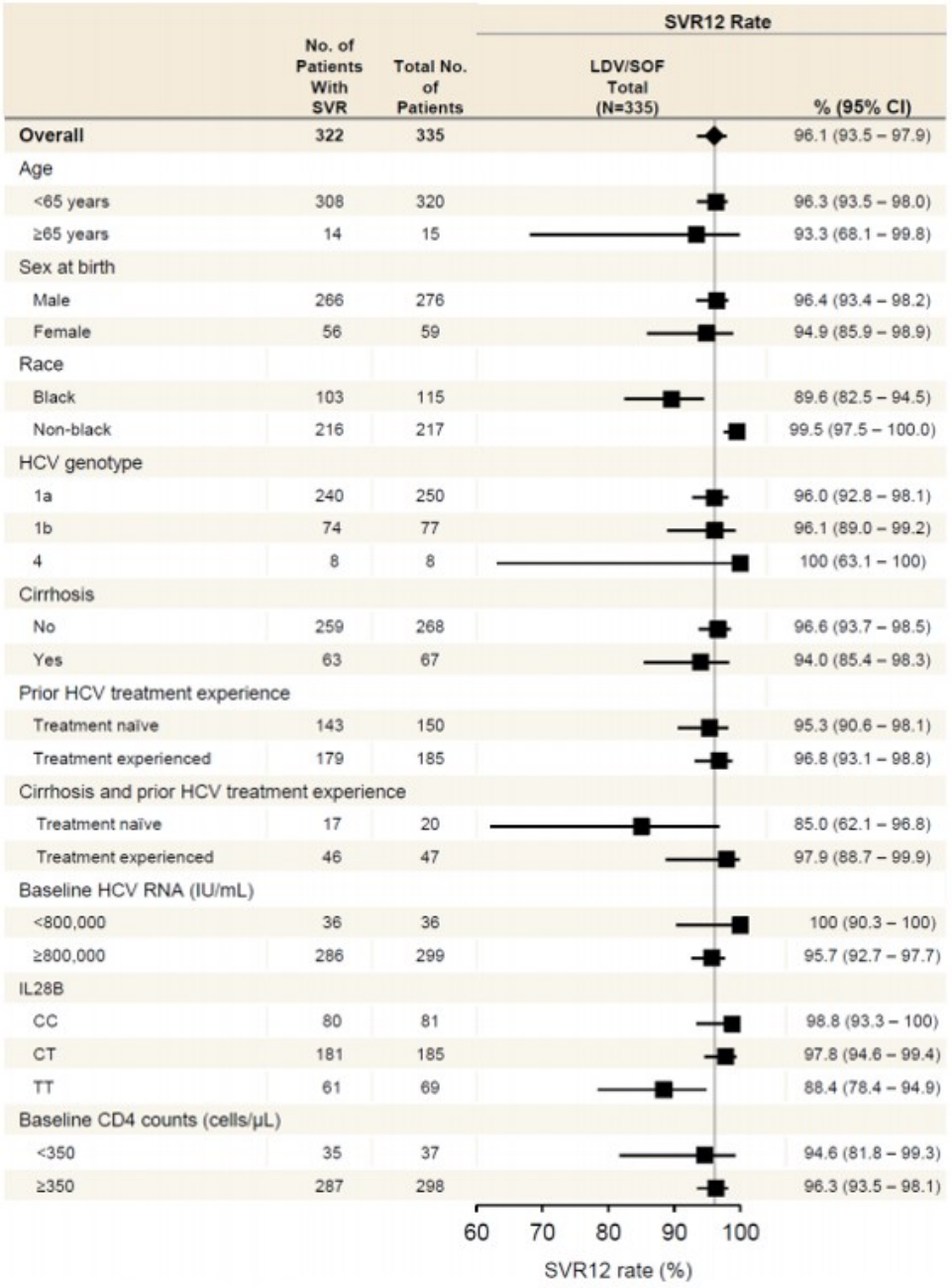
Rates of Sustained Virologic Response by Subgroup and Baseline Factors



	No. of Patients With SVR	Total No. of Patients	SVR12 Rate: LDV/SOF Total (N=335) % (95% CI)
Overall	322	335	96.1 (93.5 – 97.9)
Age			
<65 years	308	320	96.3 (93.5 – 98.0)
≥65 years	14	15	93.3 (68.1 – 99.8)
Sex at birth			
Male	266	276	96.4 (93.4 – 98.2)
Female	56	59	94.9 (85.9 – 98.9)
Race			
Black	103	115	89.6 (82.5 – 94.5)
Non-black	216	217	99.5 (97.5 – 100.0)
HCV genotype			
1a	240	250	96.0 (92.8 – 98.1)
1b	74	77	96.1 (89.0 – 99.2)
4	8	8	100 (63.1 – 100)
Cirrhosis			
No	259	268	96.6 (93.7 – 98.5)
Yes	63	67	94.0 (85.4 – 98.3)
Prior HCV treatment experience			
Treatment naïve	143	150	95.3 (90.6 – 98.1)
Treatment experienced	179	185	96.8 (93.1 – 98.8)
Cirrhosis and prior HCV treatment experience			
Treatment naïve	17	20	85.0 (62.1 – 96.8)
Treatment experienced	46	47	97.9 (88.7 – 99.9)
Baseline HCV RNA (IU/mL)			
<800,000	36	36	100 (90.3 – 100)
≥800,000	286	299	95.7 (92.7 – 97.7)
IL28B			
CC	80	81	98.8 (93.3 – 100)
CT	181	185	97.8 (94.6 – 99.4)
TT	61	69	88.4 (78.4 – 94.9)
Baseline CD4 counts (cells/μL)			
<350	35	37	94.6 (81.8 – 99.3)
≥350	287	298	96.3 (93.5 – 98.1)

60 70 80 90 100

SVR12 rate (%)

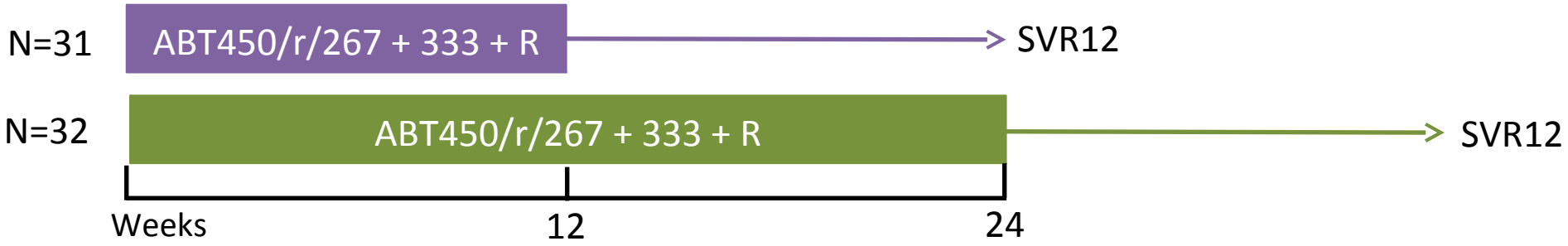
- Ten patients with relapse
  - All Black race
  - All CT or TT (7 with TT)
  - All HCV RNA > 6 log10 IU/mL
  - 8 with HCV genotype 1a
  - 8 received efavirenz
  - 3 with cirrhosis

Multivariate logistic regression association of Relapse with Race, IL28B TT and Efavirenz

	OR	P value
Race	17.73	.0012
IL28B TT	4.27	.07
Efavirenz	3.26	.24

Naggie et al. N Engl J Med 2015

TURQUOISE I: Paritaprevir/r/Ombitasvir + Dasabuvir + RBV

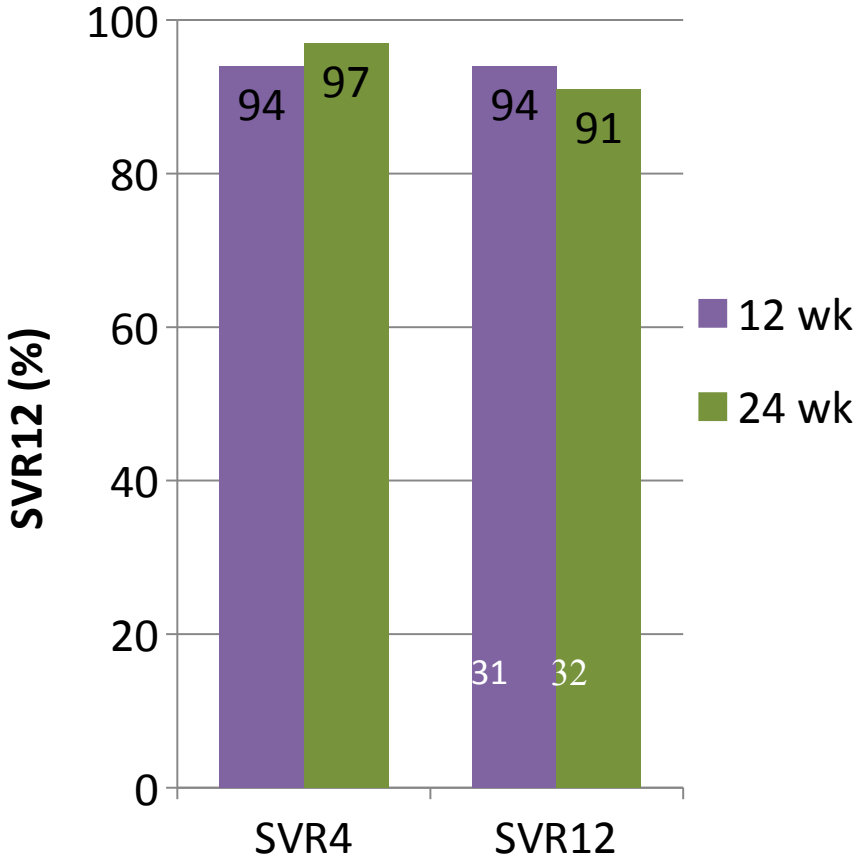


- Stable ART
  - ATV or RAL (part A)
  - HIV RNA <40 copies/mL
  - CD4 >200
- HCV
  - GT1, naïve or experienced
  - Cirrhosis allowed (CPT A)

	12 Week	24 Week
Male	94%	91%
Naïve	65%	69%
Null	16%	16%
1a	87%	91%
F4	19%	19%
CD4	633	625

Sulkowski M. JAMA 2015.

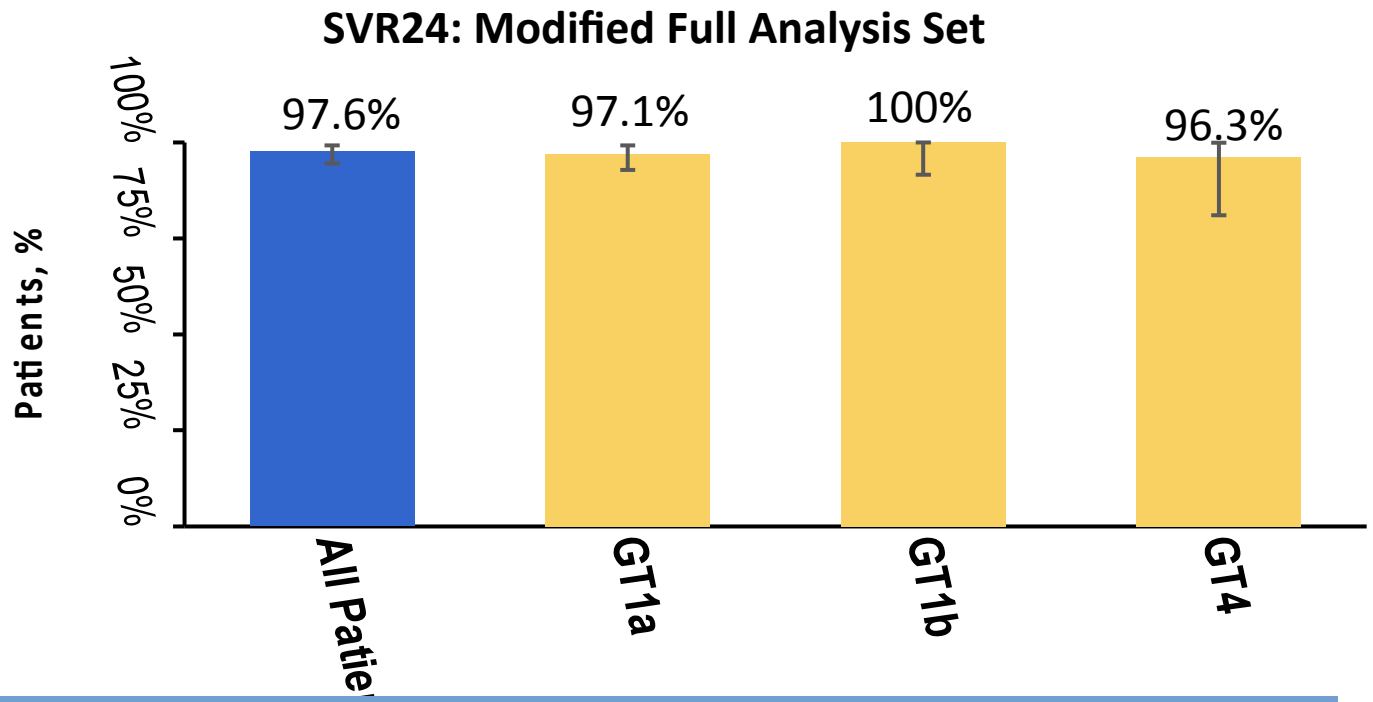
TURQUOISE I: Paritaprevir/r/Ombitasvir + Dasabuvir + RBV



- 2 Virologic failures
  - 1a cirrhotic null responders
    - Relapse in 12-wk arm
    - BT at week 16
- 2 Re-infections
- No discontinuation due to AEs

Sulkowski M. JAMA 2015.

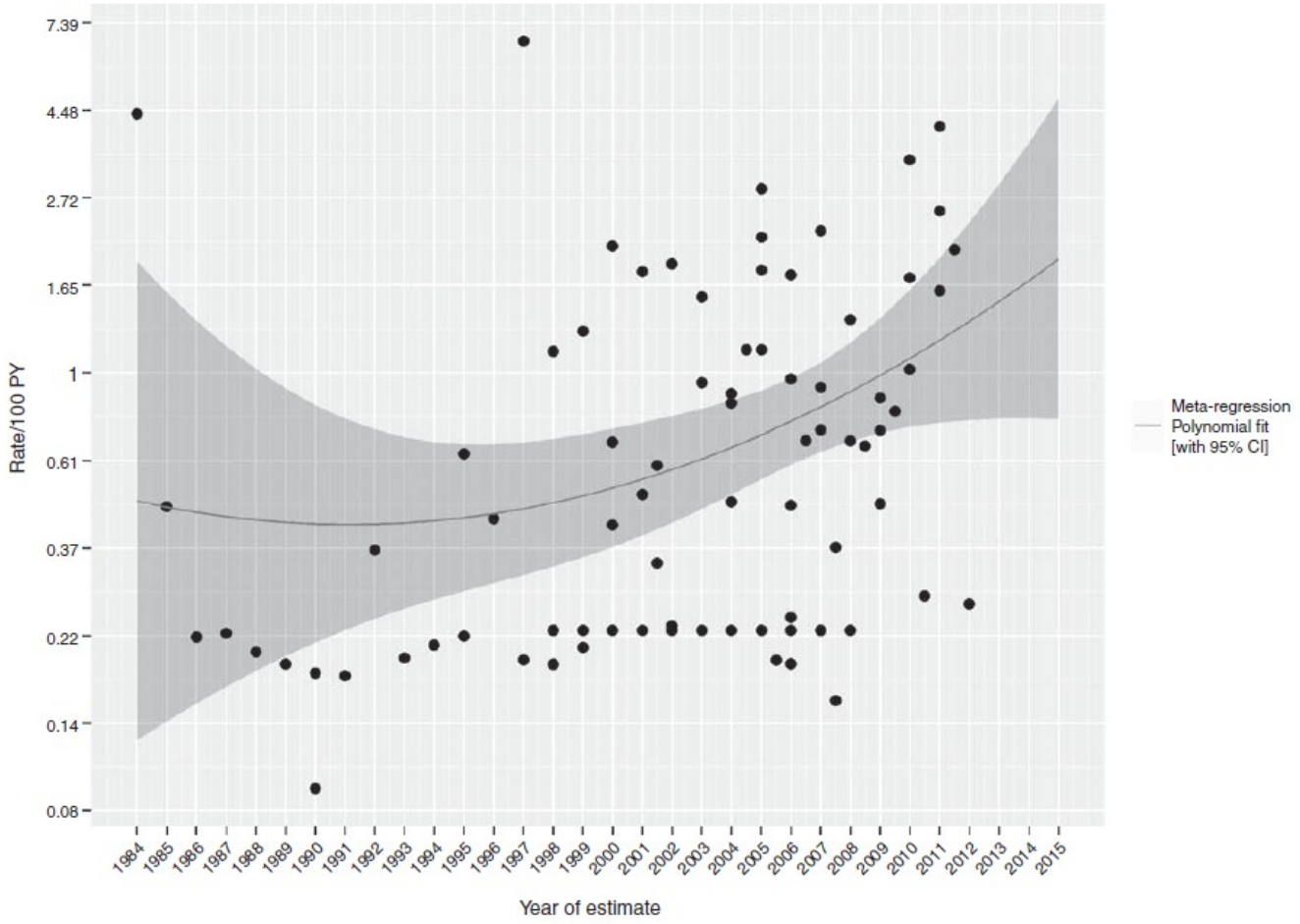
C-EDGE Co-Infected: Phase 3 Study of Elbasvir/Grazoprevir in Patients with HIV/HCV



	All GT	GT1a	GT1b	GT4
	203/208 (97.6%)	135/139 (97.1%)	42/42 (100%)	26/27 (96.3%)
Relapse	5	4	0	1
Excluded				
Reinfection	2	1	1	0
LTFU or discontinued unrelated to VF	8	5	2	1

Rockstroh JK, et al. AASLD 2015. Abstract 210.

Incidence of sexually transmitted hepatitis C virus infection in HIV-positive men who have sex with men: a systematic review and meta-analysis

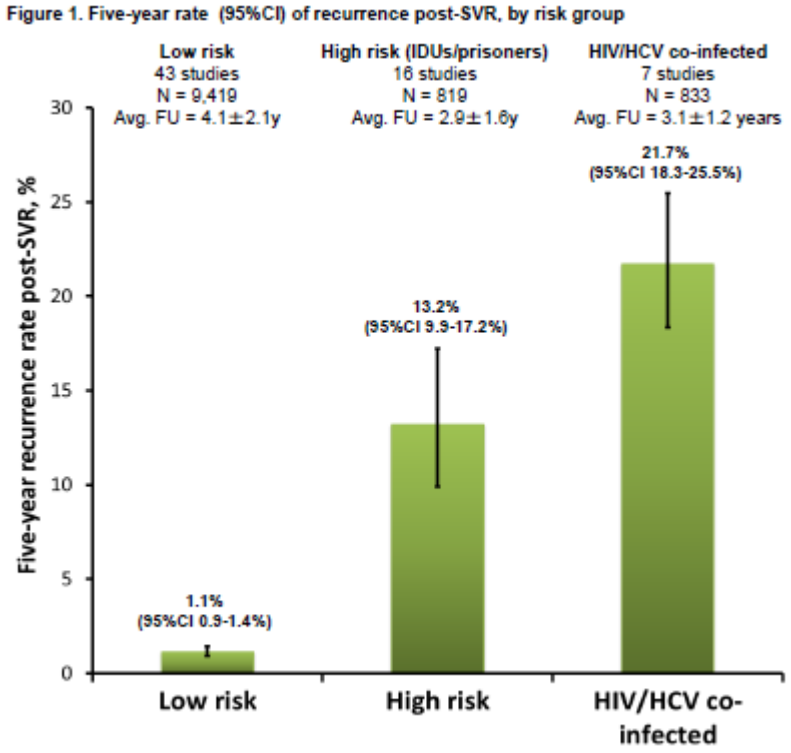


- HCV seroconversion increased from an estimated rate of: 1991: 0.42/100 person-years to 2010: 1.09/100 person-years and 2012: 1.34/100 person-years
- Infections were attributable to high-risk behaviors including traumatic sex and sex while on methamphetamines

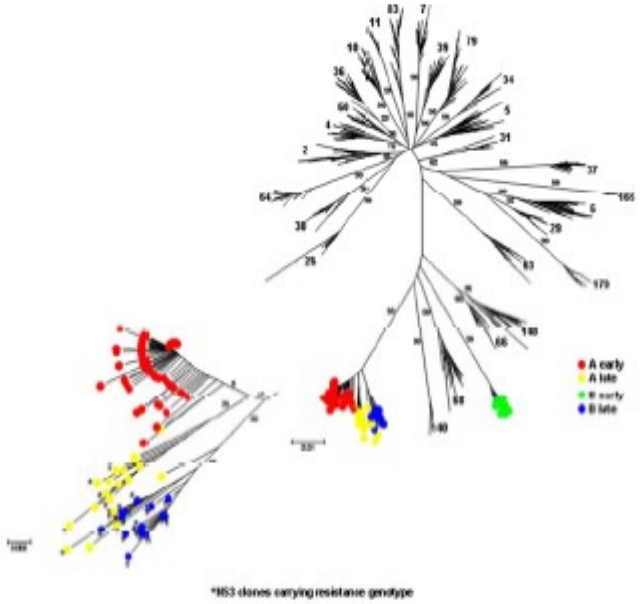
agan H et al. AIDS 2015

Incidence of HCV reinfection after SVR may be higher in persons with HIV infection

Risk of HCV reinfection following SVR: meta-analysis of 66 studies in 11,071 patients



HIV-infected male partners with infection and re-infection with telaprevir resistant HCV (V36M)



Franco et al. Gastroenterology 2014; Hill et al CROI 2015 (#654)

Drug Interactions Between HIV Antiretrovirals and HCV Direct Acting Antivirals

	SMV + SOF	SOF	LDV/SOF	DCV + SOF	OMV/PTV/RTV + DSV
Atazanavir + ritonavir	X	√	≈	≈	≈
Darunavir + ritonavir	X	√	≈	√	X
Lopinavir/ritonavir	X	√	≈	√	X
Tipranavir + ritonavir	X	X	X	X	X
Efavirenz	X	√	≈	≈	X
Rilpivirine	√	√	√	√	X
Etravirine	X	√	√	≈	X
Raltegravir	√	√	√	√	√
Elvitegravir + cobicistat	X	√	X	X	X
Dolutegravir	√	√	√	√	√
Maraviroc	√	√	√	√	≈
Tenofovir DF	√	√	≈ Monitor for nephrotoxicity	√	√
Tenofovir TAF	√	√	√	√	√

No clinically significant interaction expected

Potential interaction may require adjustment to dosage, altered timing of administration, or additional monitoring

Do not coadminister

AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org.

HIV-HCV Co-infected Patients

- Data from phase 3 clinical trials indicate similar SVR rate in persons with and without HIV coinfection *with some caveats*
  - High rate of HCV relapse after 8 weeks of daclatasvir + sofosbuvir
  - High rate of HCV relapse among Black patients treated for 12 weeks with ledipasvir/sofosbuvir
- HCV disease progression is more rapid despite effective HIV treatment
- Incidence of reinfection may be higher after SVR
- Drug interactions must be carefully considered by clinicians with expertise in HIV and/or HCV

Sulkowski M, PHC 2016

FREE Baltimore