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Strategies for the cure of chronic and acute hepatitis C infection in HIV coinfected subjects. And after the cure?

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HIV WORKSHOP
COMPREHENSIVE MANAGEMENT OF AGING IN HIV-INFECTED SUBJECTS

Conflict of Interest

- Honoraria for lectures and/or consultancies from Abbott, AbbVie, Bionor, BMS, Cipla, Gilead, Janssen, Merck, Roche, ViiV.
- Research grants from Dt. Leberstiftung, DZIF, NEAT ID.

Deutsche Leberstiftung

DZIF

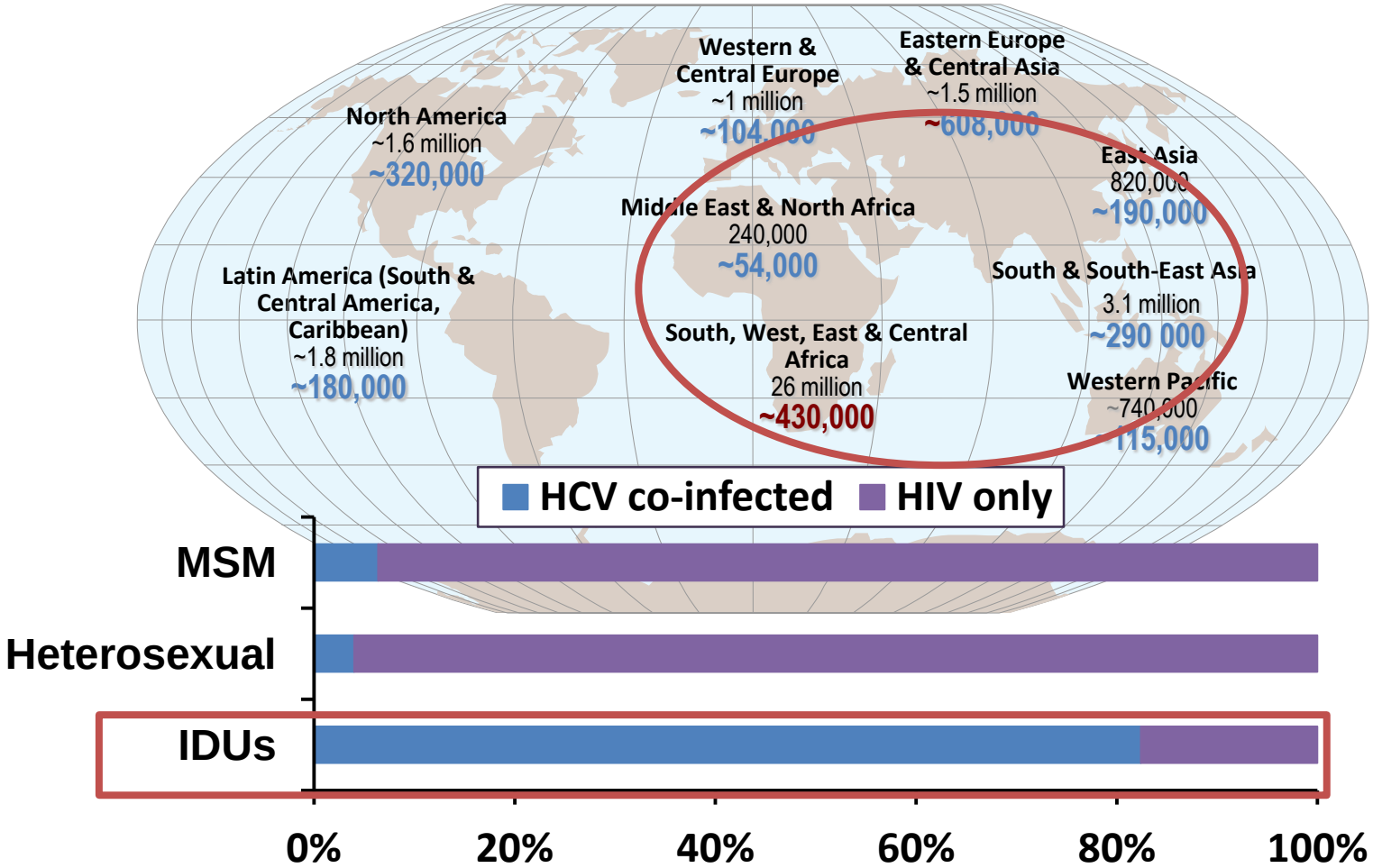
neatid

Strategies for the cure of chronic HCV in HIV-coinfection

Burden of HIV/HCV co-infection

37 million HIV infected

2.3 million co-infected with HCV

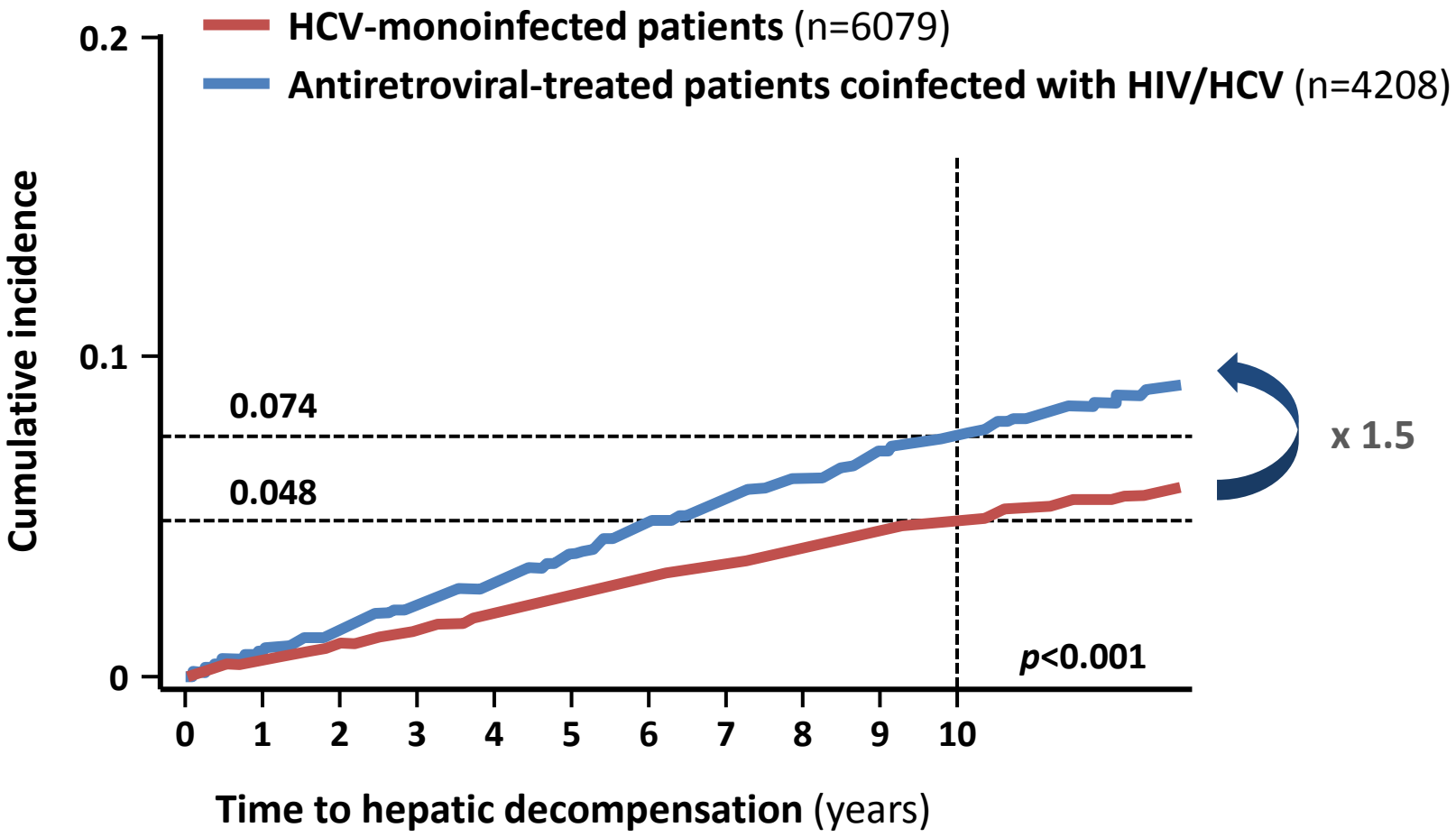


- IDU: injecting drug user; MSM: men who have sex with men

Platt L, et al. Lancet Infect Dis 2016; doi: 10.1016/S1473-3099(15)00485-5

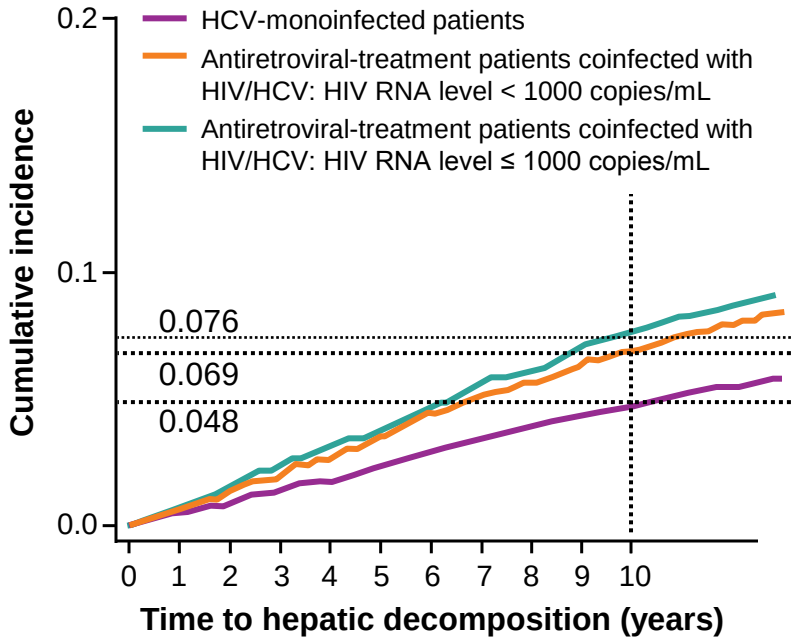
How is the natural history of HCV different in HIV coinfection?

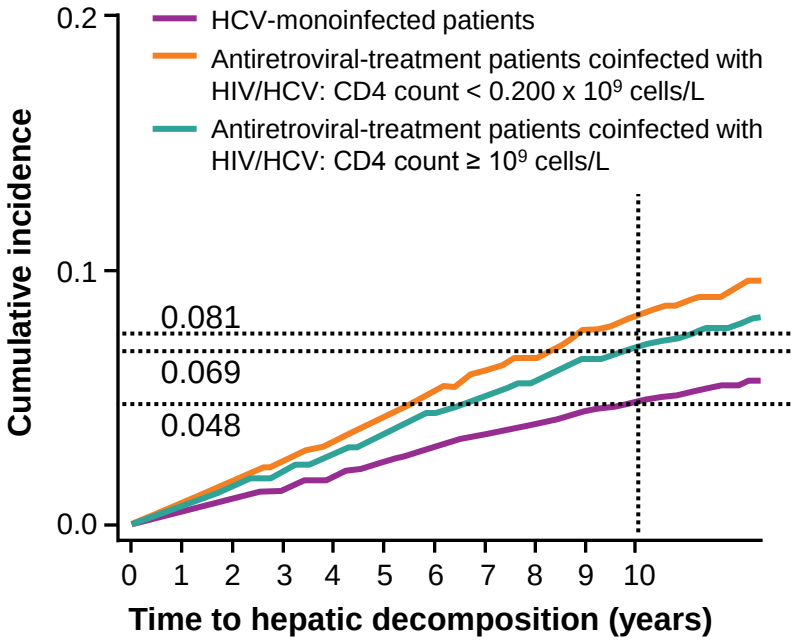
HCV Disease Progression Remains Faster in Coinfected Patients, Despite Effective ART



Adapted from: Lo Re 3rd V, et al. Ann Intern Med 2014;160:369–79.

HCV Disease Progression Remains Faster in Coinfected Patients, Despite Effective ART





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

Adapted from: Lo Re 3rd V, et al. Ann Intern Med 2014;160:369–79.

Are HIV/HCV coinfected patients still a special patient population?

Treatment of chronic hepatitis C, including patients without cirrhosis and patients with compensated (Child-Pugh A) cirrhosis

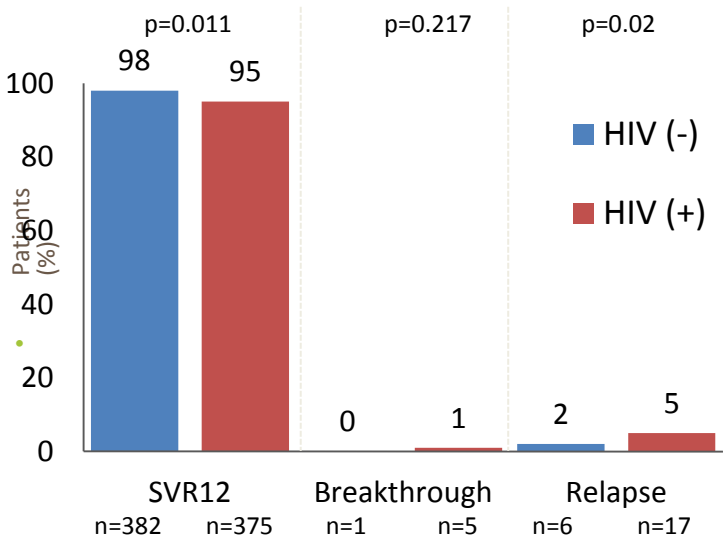
- Indications for HCV treatment in HCV/HIV coinfected persons are identical to those in patients with HCV monoinfection (**A1**).
- IFN-free regimens are the best options in HCV-monoinfected and in HIV-coinfected patients without cirrhosis or with compensated (Child-Pugh A) cirrhosis, because of their virological efficacy, ease of use and tolerability (**A1**).
- The same IFN-free treatment regimens can be used in HIV-co-in-fected patients as in patients without HIV infection, as the virologi-cal results of therapy are identical. Treatment alterations or dose adjustments may be needed in case of interactions with antiretroviral drugs (**A1**).

EASL 2016 Guidelines, Sept.22,2016

Does HIV coinfection impair the response to DAA-based HCV therapy?

- Prospective multicohort Spanish study
- **Aim**: Evaluate impact of HIV coinfection on the efficacy of DAA-based treatment in clinical practice
- **Treatment groups:**
  - *IFN-free therapy (n=827)*: SOF plus either SMV, DCV or LDV ± RBV, or 3D/2D ± RBV
  - *IFN-based therapy (n=449)*: BOC, TVR, SMV or SOF + pegIFN and weight-adjusted oral RBV

Treatment outcome (on-treatment analysis): IFN-free therapy



Parameter	HIV(-) n=404	HIV (+) n=423	p
Median age	54	51	<0.001
Male, n (%)	269 (67)	347 (82)	<0.001
HCV RNA >6x10^6 IU/mL, n (%)	59 (15)	70 (17)	0.441
Prior injecting drug users, n (%)	118 (29)	353 (84)	<0.001
HCV genotype, %			<0.001
1a/1b/1 (other)	29/50/3.5	42/19/5.7	
3/4	6.7/10	12/21	
Prior response to HCV therapy, n (%)			0.529
Naive	191 (47)	186 (44)	
Null response	81 (20)	105 (25)	
Partial response	28 (6.9)	24 (5.7)	
Relapse	49 (12)	49 (12)	
Other	55 (14)	59 (14)	
Cirrhosis, n (%)	208 (52)	272 (64)	<0.001

- Response rates lower in HIV coinfected patients
- Caution to be applied to findings given baseline differences in coinfected vs monoinfected patient groups

Neukam K, et al. EASL 2016. Barcelona #LBP513.

GreenShoots
FOUNDATION

GreenShoots
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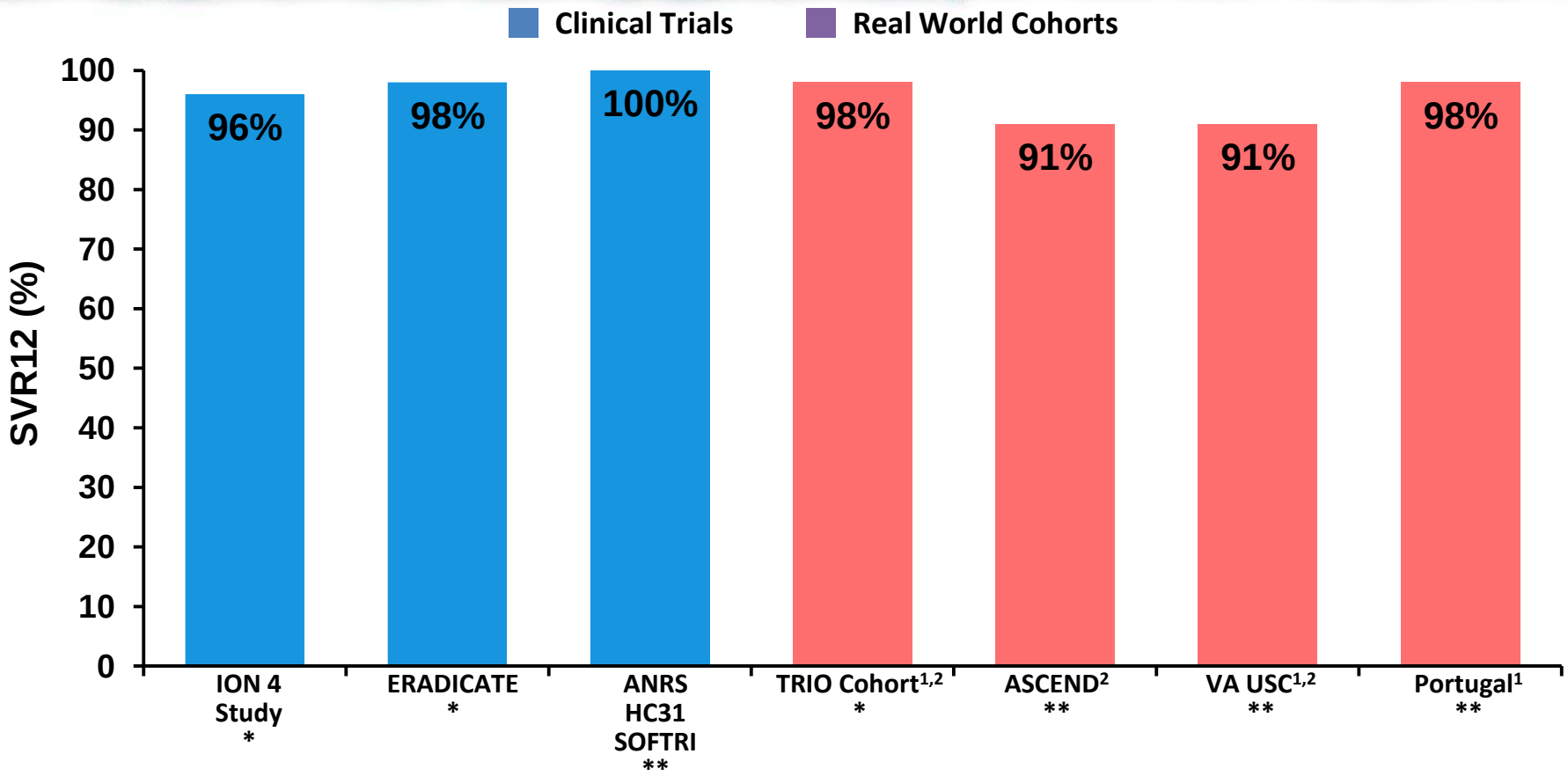
SVR12 in GT 1 HIV/HCV Coinfected Patients Treated with LDV/SOF for 12-24 Weeks: Clinical Trials Compared to Real-World Cohorts



†ITT analysis in GT1 patients; *ITT analysis; ** Per Protocol; [1] ±RBV; [2] small number of patients may have received 8 weeks of LDV/SOF

Naggie S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 892.

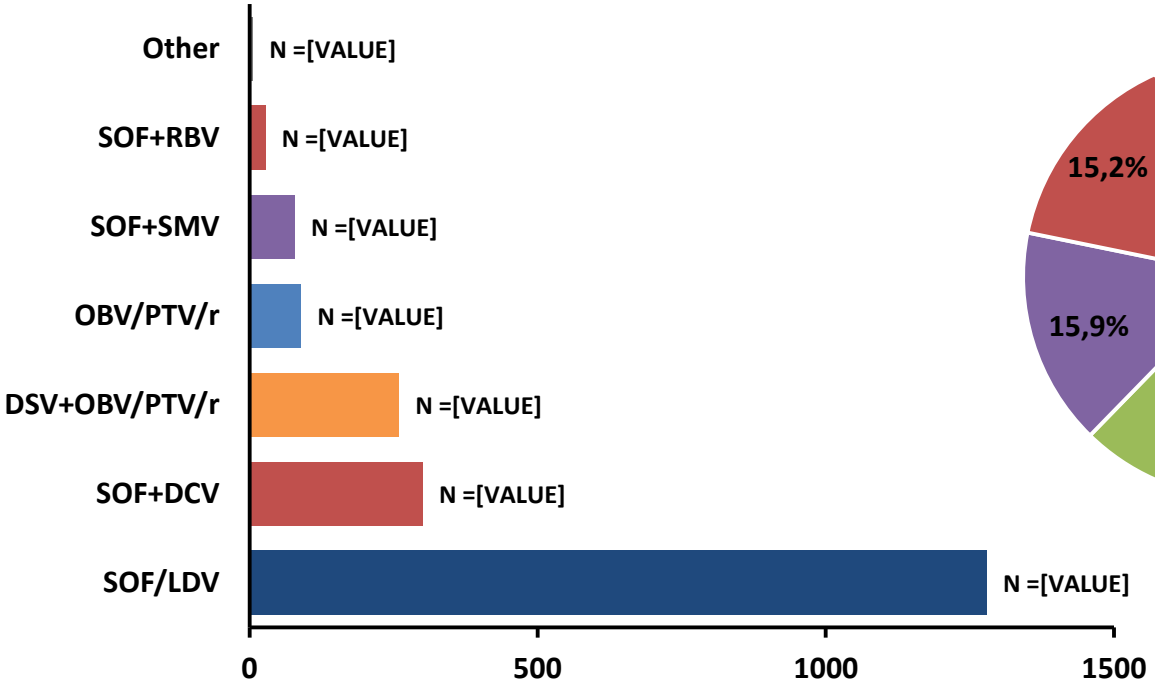
Madrid-CoRe (Madrid Coinfection Registry): Baseline Characteristics

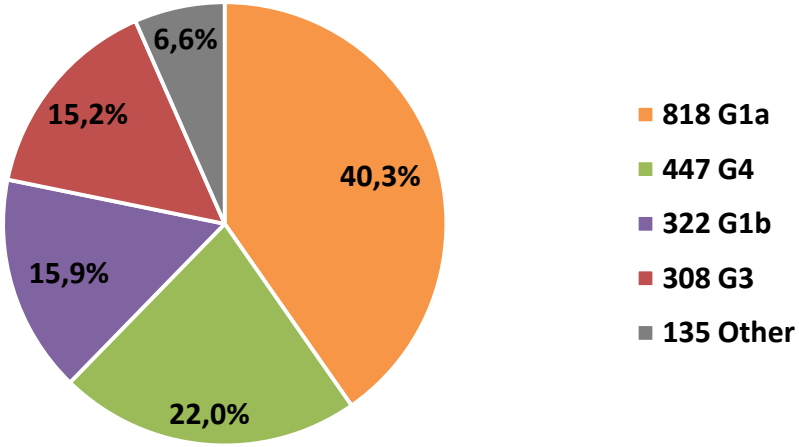
Variable	N = 2030
Age years – median (IQR)	50 (47 – 54)
Male – n (%)	1591 (78.4)
CD4+ T cells/µL – median (IQR)	570 (356 – 785)
cART – n (%)	1930 (95.1)
Liver disease severity	
No cirrhosis – n (%)	1125 (55.4)
Compensated cirrhosis – n (%)	754 (37.1)
Decompensated cirrhosis – n (%)	146 (7.2)
Unknown – n (%)	5 (0.3)
History of hepatocellular carcinoma – n (%)	15 (0.7)
Liver transplantation – n (%)	17 (0.8)
Liver transplantation waiting list – n (%)	7 (0.3)
Severe extrahepatic manifestations – n (%)	143 (7.0)
Anti-HCV – naïve – n (%)	1256 (61.9)
Liver stiffness kPa – median (IQR)	11.4 (8.1 – 20.2)

Berenguer J, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 78.

HCV Genotypes and DAA Combinations

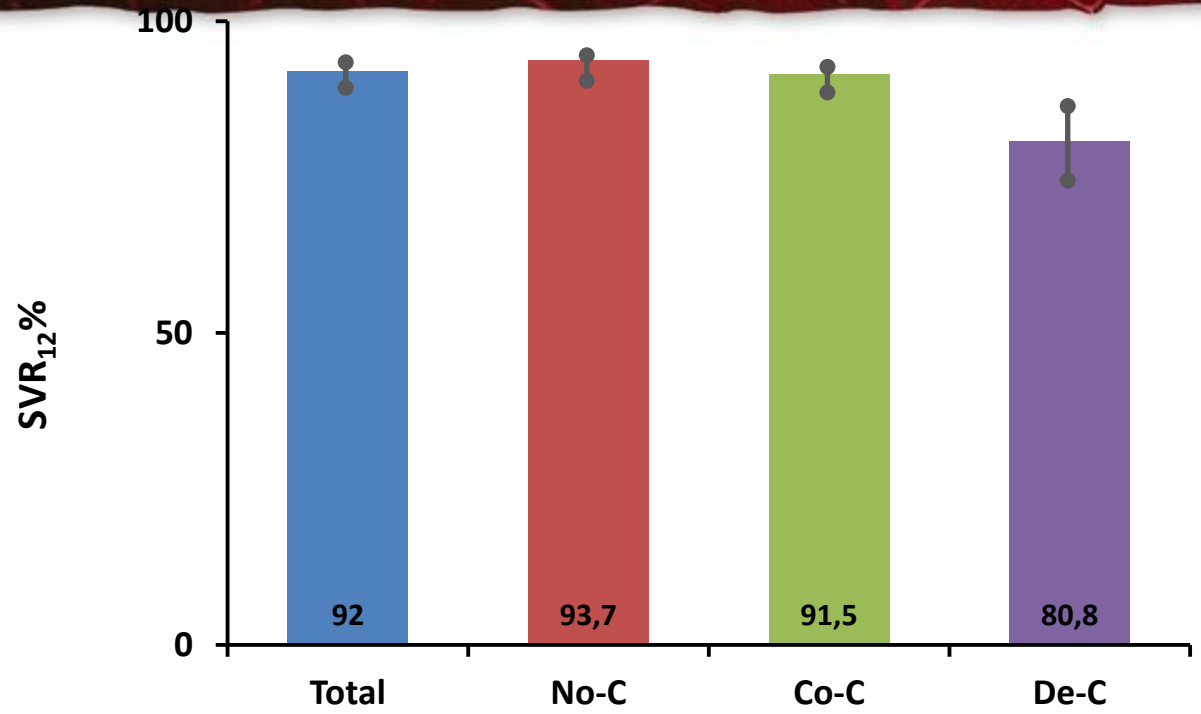
Ribavirin	No. (%)	Log_{10} HCV-RNA
Yes	627 (30.9)	Median = 6.3
No	1403 (69.1)	IQR = 5.8 – 6.7





Berenguer J, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 78.

Treatment Outcomes by Severity of Liver-Disease



	Total	No-C	Co-C	De-C
No.	2030	1125	754	146
SVRITT	1867 (92.0)	1054 (93.7)	690 (91.5)	118 (80.8)
SVR (95% CI)	(90.7 – 93.1)	(92.1 – 95.0)	(89.3 – 93.4)	(73.5 – 86.9)
Relapse	89 (4.4)	36 (3.2)	36 (4.8)	17 (11.6)
Breakthrough	5 (0.2)	3 (0.3)	1 (0.1)	1 (0.7)
DC Due to AE	14 (0.7)	7 (0.6)	5 (0.7)	2 (1.4)
DC Other	36 (1.8)	23 (2.0)	10 (1.3)	3 (2.0)
Death	19 (0.9)	2 (0.2)	12 (1.6)	5 (3.4)

* Severity of liver disease was not evaluated in 5 patients

No-C = no cirrhosis
Co-C = compensated cirrhosis
De-C = decompensated cirrhosis

Decompensated cirrhosis, and therapy with SOF+SMV, SOF+RBV, and SMV+DCV were independently associated with treatment failure

Berenguer J, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 78.

Check for DDIs between HCV and HIV drugs!

- **Drug interactions**
  - http://www.drugs.com/drug_interactions.html
  - http://www.medscape.com/druginfo/druginterchecker
  - http://www.drugstore.com/pharmacy/drugchecker/
  - http://drugchecker.aol.com
  - http://hcvdruginfo.ca
- **List of CYP substrates, inhibitors, inducers**
  - http://medicine.iupui.edu/clinpharm/ddIs
- **HIV drug interactions**
  - http://www.hiv-druginteractions.org
  - http://www.hep-druginteractions.org

Khoo S. 15th International Workshop on Clinical Pharmacology of HIV & Hepatitis Therapy, May 2014 [oral presentation].

CYP, cytochrome

Low potential for drug–drug interactions with some HCV DAA and HIV antiretrovirals

		SOF	SOF/LDV	SOF/VEL	3D	GZR/EBR	DCV	SIM
NRTIs	Abacavir	◆	◆	◆	◆	◆	◆	◆
	Emtricitabine	◆	◆	◆	◆	◆	◆	◆
	Lamivudine	◆	◆	◆	◆	◆	◆	◆
	Tenofovir	◆	■	■	◆	◆	◆	◆
NNRTIs	Efavirenz	◆	■*	●	●	●	■	●
	Etravirine	◆	◆	●	●	●	■	●
	Nevirapine	◆	◆	●	●	●	■	●
	Rilpivirine	◆	◆*	◆*	■	◆	◆	◆
Protease inhibitors	Atazanavir; atazanavir/r; atazanavir/cobicistat	◆	◆*	◆*	■‡	●	■	●
	Darunavir/r; darunavir/cobicistat	◆	◆*	◆*	■‡	●	◆	●
	Lopinavir/r	◆	◆*	◆*	●	●	◆	●
Entry/Integrase inhibitors	Dolutegravir	◆	◆	◆	◆	◆	◆	◆
	Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate	◆	■*	■*	●	●	■	●
	Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide	◆	◆	◆	●	●	■	●
	Maraviroc	◆	◆	◆	■	◆	◆	◆
	Raltegravir	◆	◆	◆	◆	◆	◆	◆

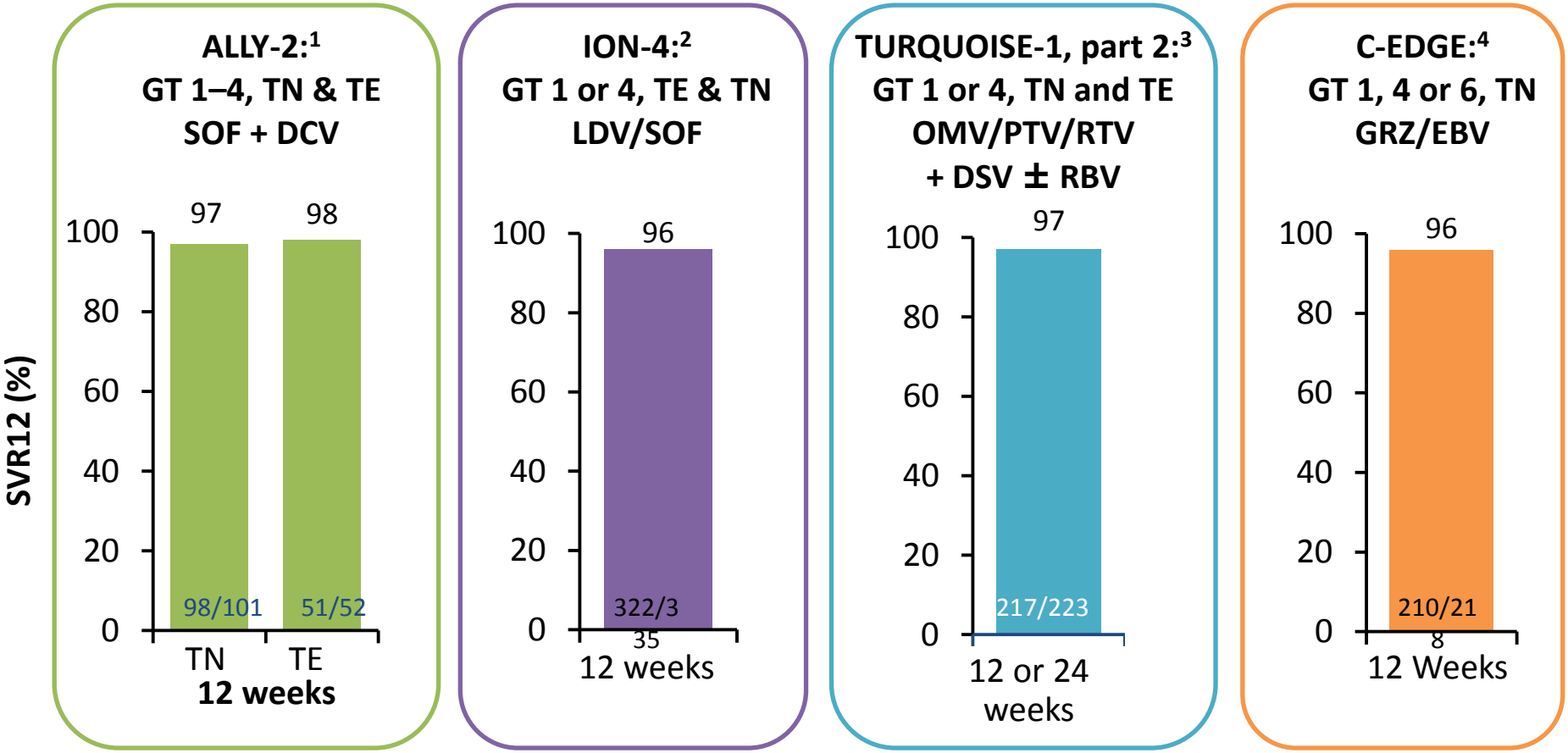
◆ No clinically significant interaction expected.
■ Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring.
● These drugs should not be co-administered.

Regularly updated Information on DDIs can be found at: http://www.hep-druginteractions.org

EASL Recommendations on treatment of hepatitis C. Available at: http://www.easl.eu/medias/cpg/HCV2016/English-report.pdf (accessed September 2016)

DDI: drug–drug interaction; NNRTI: non-nucleoside reverse transcriptase inhibitor;
NRTI: nucleoside reverse transcriptase inhibitor

High SVR in adult patients with HIV/HCV co-infection treated with DAAs

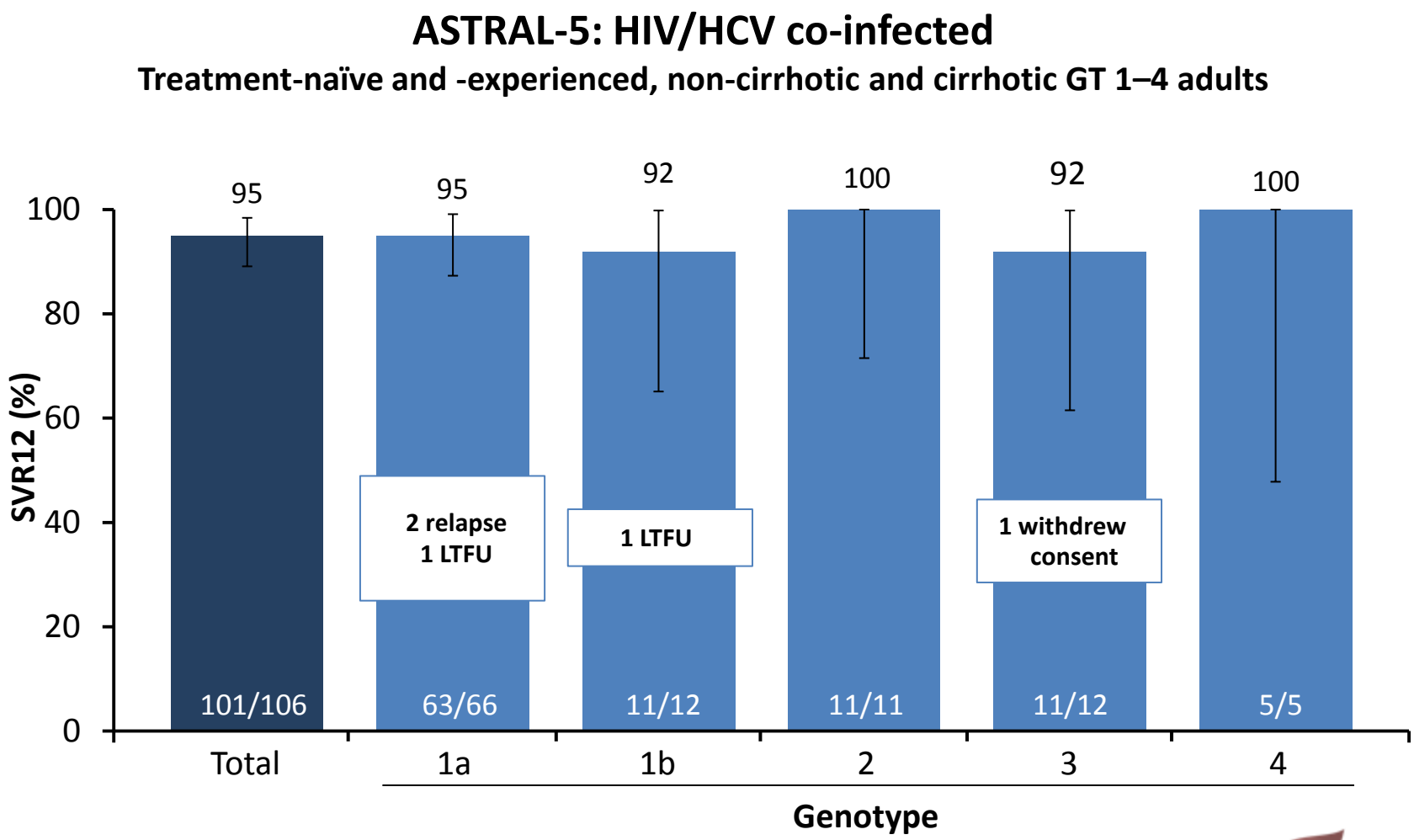


1. Wyles D, et al. N Engl J Med 2015;373:714–25;
2. Naggie S, et al. N Engl J Med 2015;373:705–13;
3. Rockstroh JK, et al. IAS 2016; Abstract # 10333;
4. Rockstroh JK, et al. Lancet HIV 2015;2:e319–27

NOT HEAD-TO-HEAD COMPARISONS

- Studies included non-cirrhotic and cirrhotic patients.
- TE: treatment-experienced

ASTRAL-5: high SVR across genotypes 1–4 in adult HIV/HCV co-infected patients treated with 12 weeks' SOF/VEL



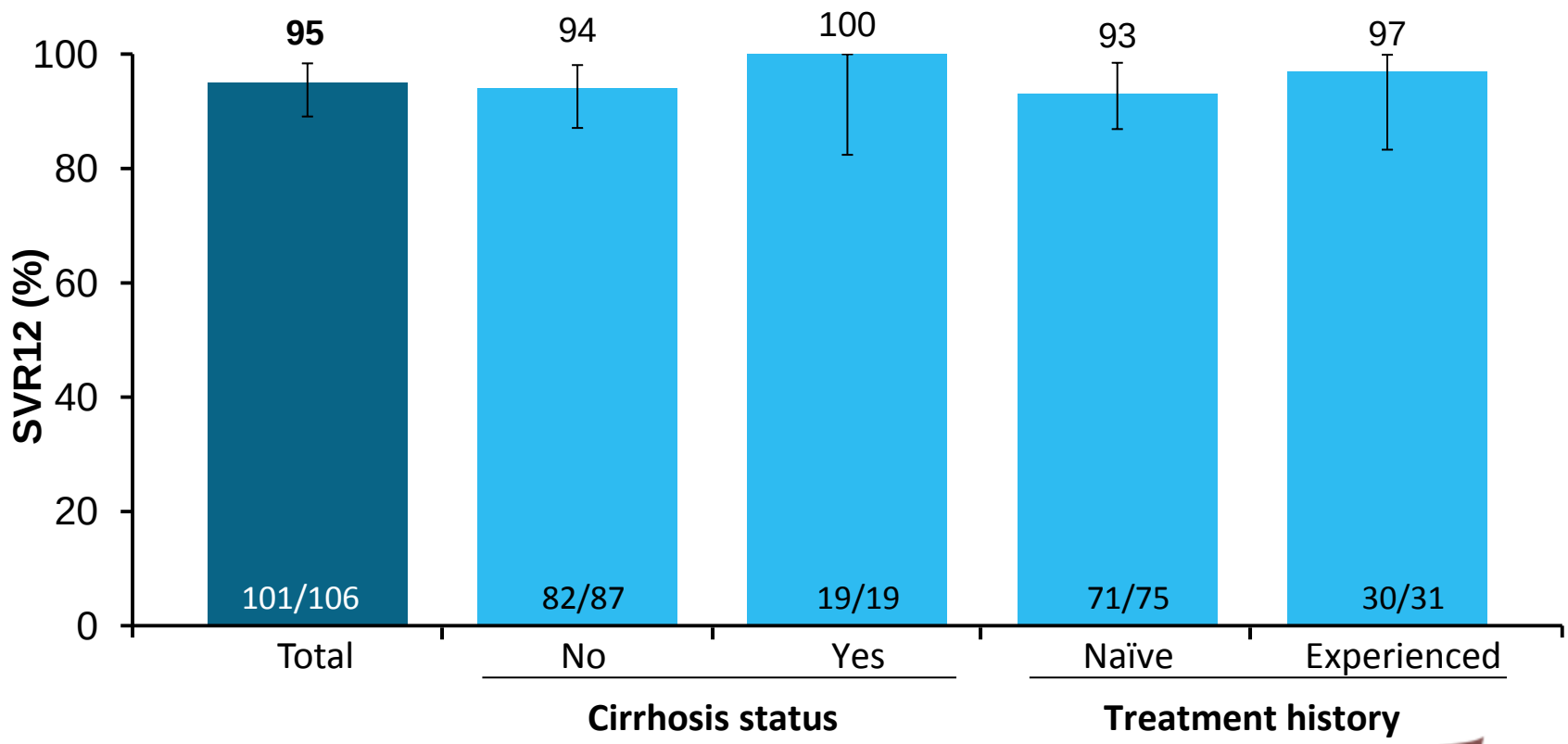
- Error bars represent 95% confidence intervals.
- LTFU: lost to follow-up

Brau N, et al. IAS 2016; Abstract #708

ASTRAL-5: high SVR across all patient types in adult HIV/HCV co-infected patients treated with 12 weeks' SOF/VEL

ASTRAL-5: HIV/HCV co-infected

Treatment-naïve and -experienced, non-cirrhotic and cirrhotic GT 1–4 adults



Error bars represent 95% confidence intervals

Brau N, et al. IAS 2016; Abstract #708

DAAs were well-tolerated in clinical trials of HIV/HCV co-infected patients

Adverse events common across all DAA regimens in HIV/HCV co-infection trials

	ALLY-2	ION-4	TURQUOISE-I Part 2	C-EDGE CO-INFECTION	ASTRAL-5
	DCV + SOF N=203	LDV/SOF N=335	OMV/PTV/RTV + DSV ± RBV N=228	GRZ/EBV N=218	SOF/VEL N=106
Fatigue	17%	21%	23%	13%	25%
Headache	11%	25%	14%	12%	13%
Diarrhoea	7%	11%	14%	7%	8%
Nausea	13%	10%	20%	9%	7%
D/C due to AE	0	0	0	0	2 (2%)

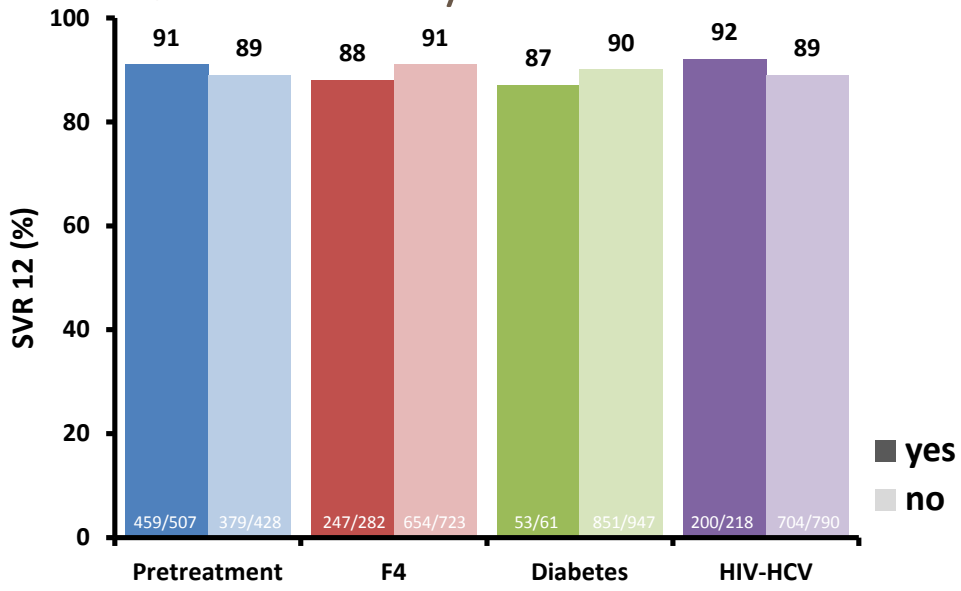
Wyles D, et al. N Engl J Med 2015;373:714–25;
Rockstroh JK, et al. IAS 2016; Abstract # 10333;
Naggie S, et al. N Engl J Med 2015;373:705–13;
Rockstroh JK, et al. Lancet HIV 2015;2:e319–27;
Brau N, et al. IAS 2016; Abstract #708

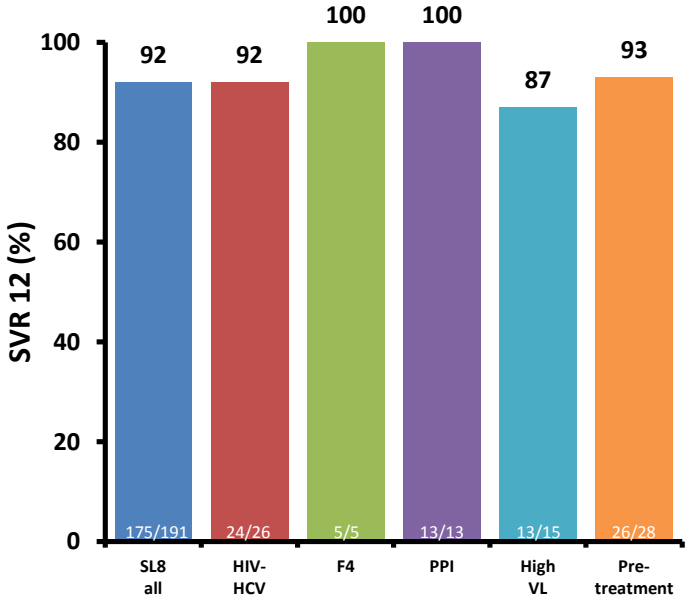
NOT HEAD-TO-HEAD COMPARISONS
This table illustrate adverse events obtained between different regimens from different studies and are therefore not directly comparable as study populations are NOT matched

Real world experience

Real Life DAA Data from Germany: GECCO Cohort

- 1346 patients from 9 centres: 21% HIV/HCV co-infected, 29% F4 fibrosis/cirrhosis

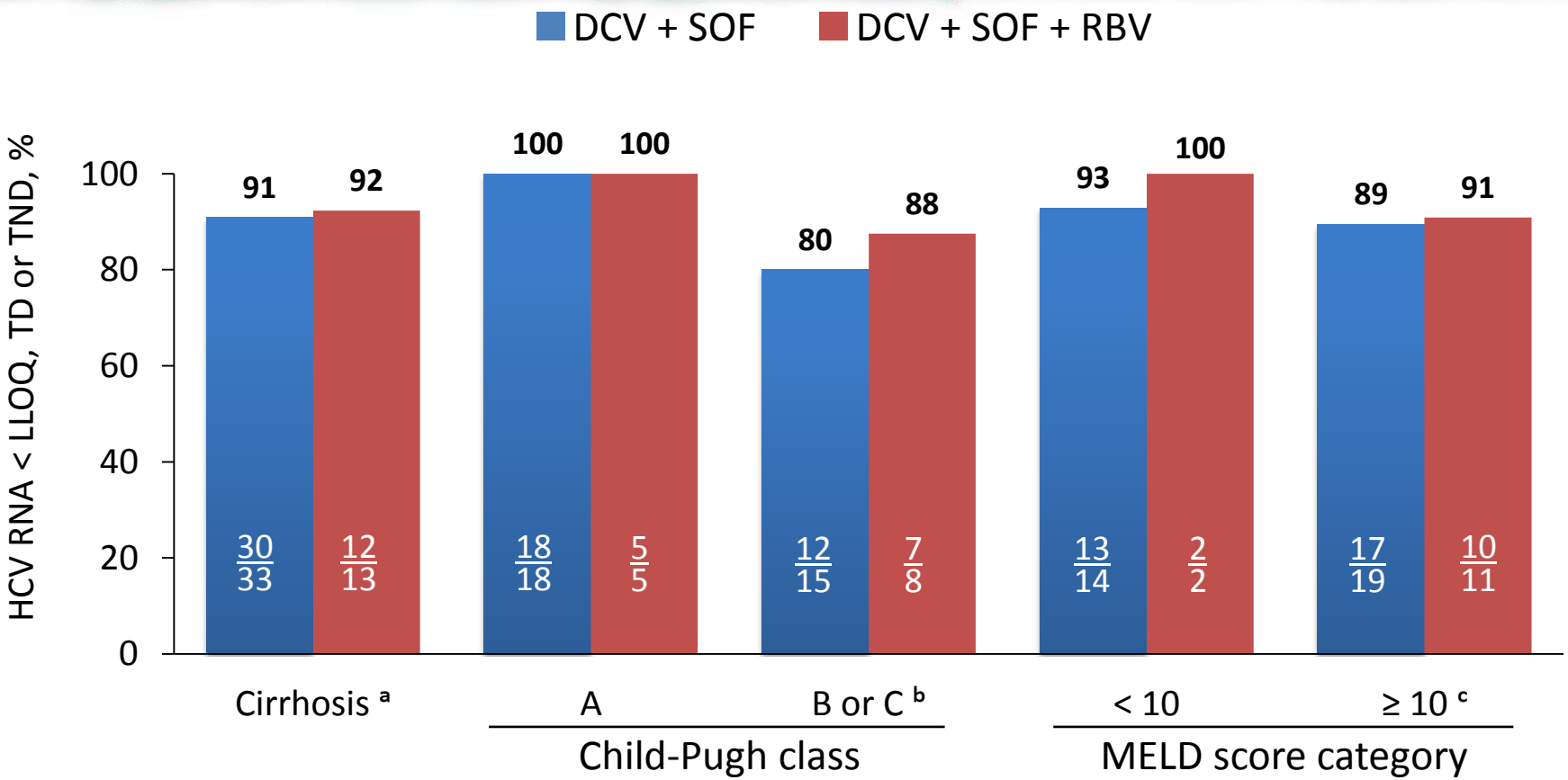




- Good response rates also in Tx experienced, F4, diabetics, co-infected
- 8 weeks of SOF/LDV very effective – even in "problematic" patients

Christensen S, et al. 23rd CROI; Boston, MA; February 22-25, 2016. Abst. 584.

SVR12 (mITT) by Liver Disease Status
Real-life experience from the EAP



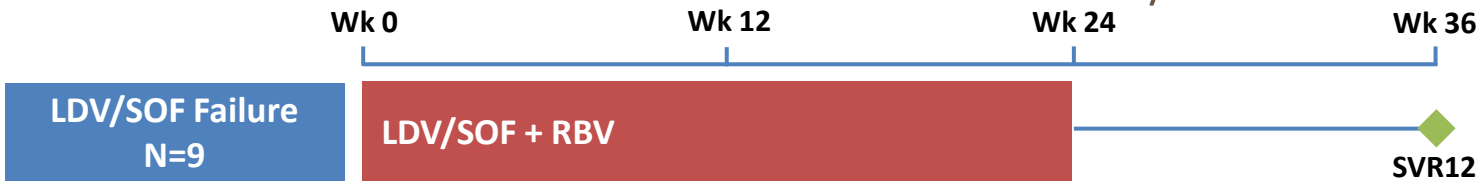
[a] Excludes 3 patients with indeterminate cirrhosis status; all achieved SVR12. No patients without cirrhosis were enrolled.
[b] 3 patients had Child-Pugh class C; 1 of 3 (DCV + SOF) achieved SVR12; 2 died for reasons unrelated to program therapy (non-SVR12).
[c] 4 patients had MELD scores 16–20 (2 of 4 achieved SVR12); 1 patient had a MELD score >25 (non-SVR12 due to death).

Rockstroh *et al*., AASLD 2015; Poster 1058.

How to treat after DAA failure?

Re-treatment after failure to LDV/SOF

9 patients without SVR in ION-4 after 12 weeks of LDV/SOF



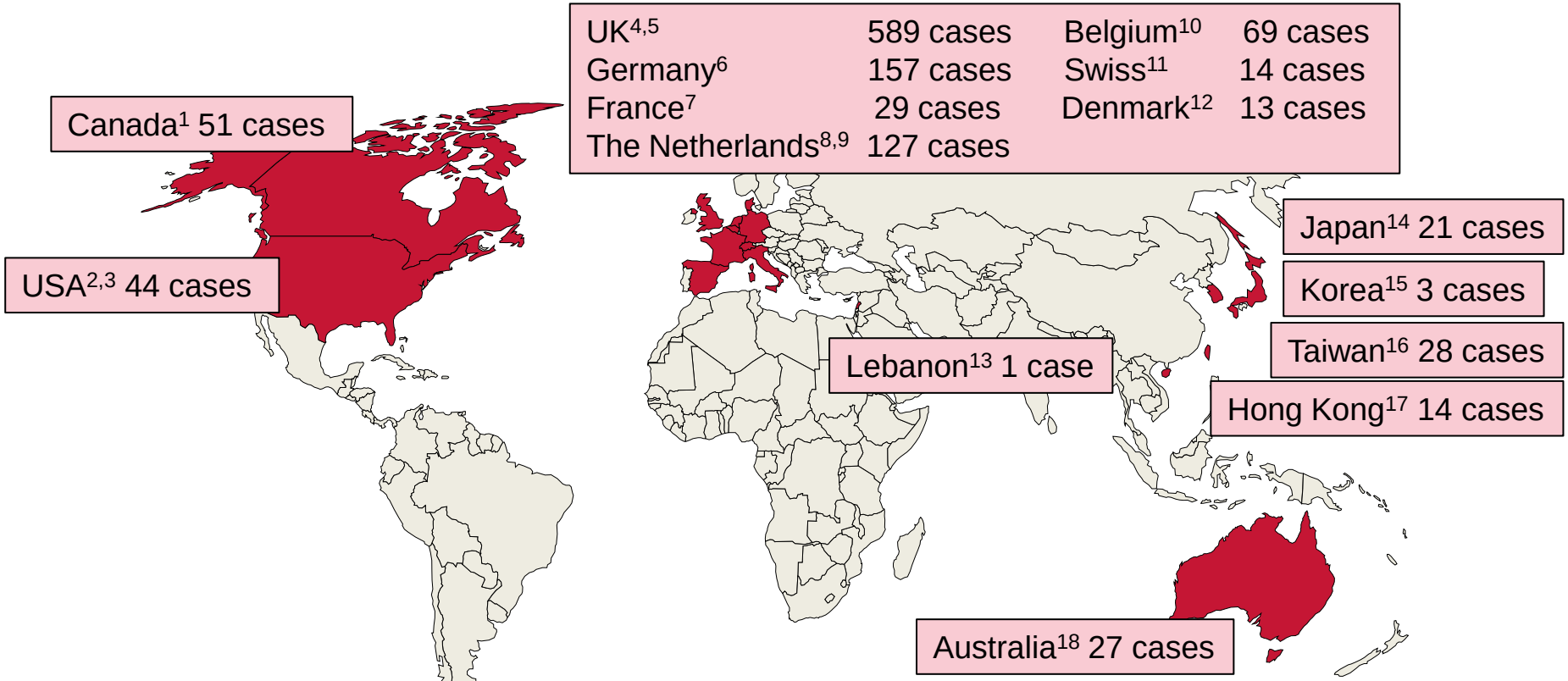
GT	NS5A RAVs Before Primary Study (%)	NS5A RAVs at Virologic Rlapse After Primary Study (5)	SRV12
1a	None	None	Yes
1a	None	None	Yes
1a	L31M (>99), H58D (92)	L31M (>99), H58D (92)	Yes
1a	Y93F (1), Y93N (10)	Y93N (<99)	Yes
1a	L31M (>99), Y93N (<25)	L31M (>99), Y93N (>99)	Yes
1a*	None	Y93N (>99)	Yes
1b	Y93H (>99)	L31I (11), Y93H (>99)	Yes
1b	None	L31V (>99)	Yes
1a	None	L31M (>99)	No

- SVR in 8/9
- 1 relapse 4 weeks after EOT: GT1a, no cirrhosis

Cooper C, et al. 23rd CROI; Boston, MA; February 22-25, 2016. Abst. 573.

Strategies for the cure of acute HCV in HIV-coinfection

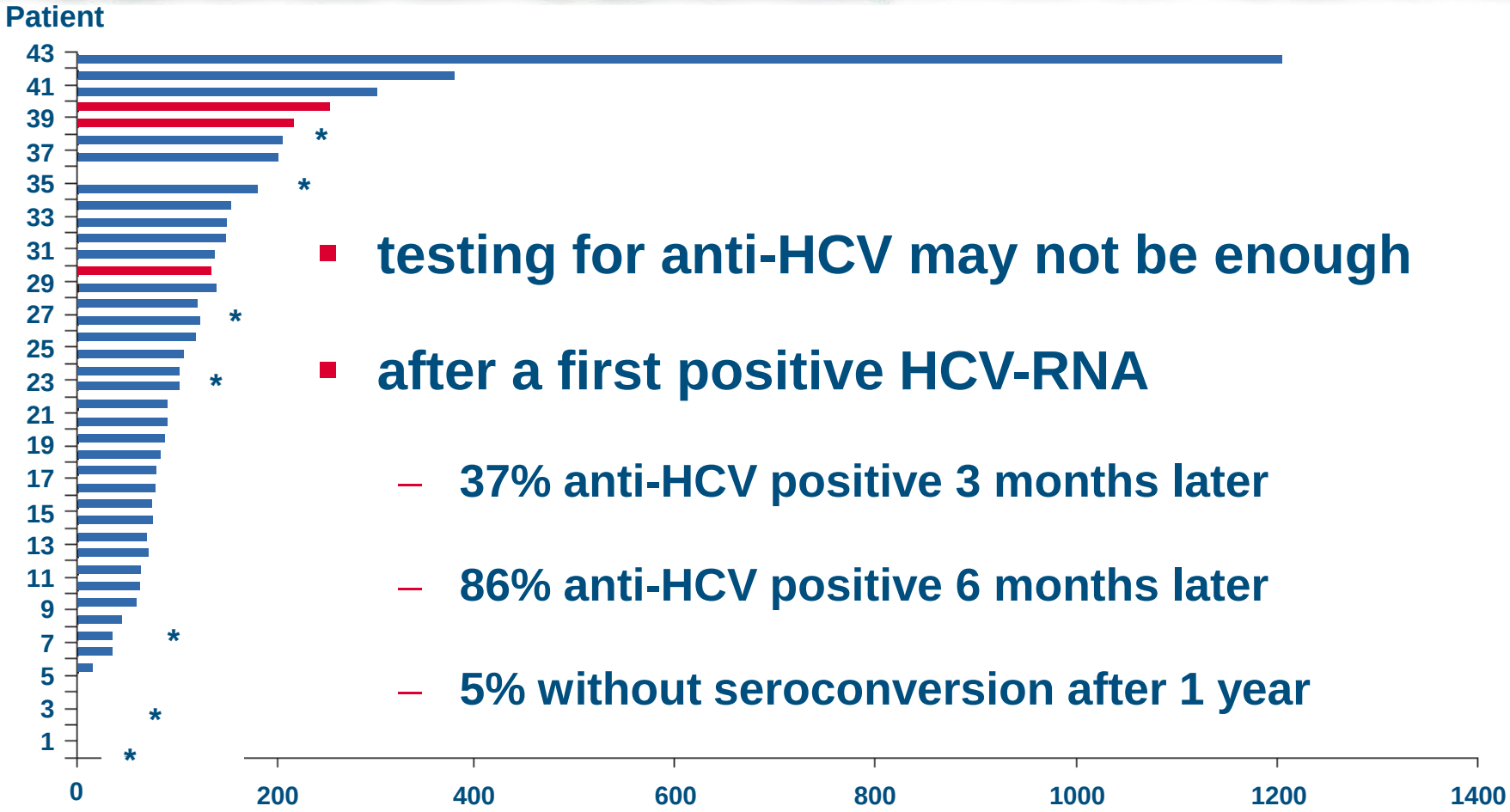
Acute outbreaks of HCV have been reported in HIV+ MSM across the world



Total number of cases reported in the literature from these countries

1. Burchell AN, et al. Can J Infect Dis Med Microbiol 2015;26:17–22; 2. Luetkemeyer A, et al. J Acquir Immune Defic Syndr 2006;41:31–6; 3. Cox A, et al. Gastroenterology 2009;136:26–31; 4. Giraudon I, et al. Sex Transm Infect 2008;84:111–5; 5. Ruf M, et al. Euro Surveill 2008;13:1–3; 6. Vogel M, et al. Clin Infect Dis 2009;49:317–8; 7. Gambotti L, et al. Euro Surveill 2005;10:115–7; 8. Urbanus A, et al. AIDS 2009;23:F1–F7; 9. Arends JE, et al. Neth J Med 2011;69:43–9; 10. Bottieau E, et al. Euro Surveill 2010;15:1–8; 11. Rauch A, et al. Clin Infect Dis 2005;41:395–402; 12. Barfod TS et al. Scand J Infect Dis. 2011;43:145–8; 13. Dionne-Odom J, et al. Lancet Infect Dis 2009;9:775–83; 14. Nishijima T, et al. J Acquir Immune Defic Sundr 2014;65:213–7; 15. Lee S, et al. Korean J Intern Med 2016; doi: 10.3904/kjim.2015.353; 16. Sun YH, et al. J Clin Microbiol 2012;50:781–7; 17. Lin AWC, et al. J Int AIDS Soc 2014;17:19663; 18. Matthews GV, et al. Clin Infect Dis 2009;48:650–8

HCV seroconversion

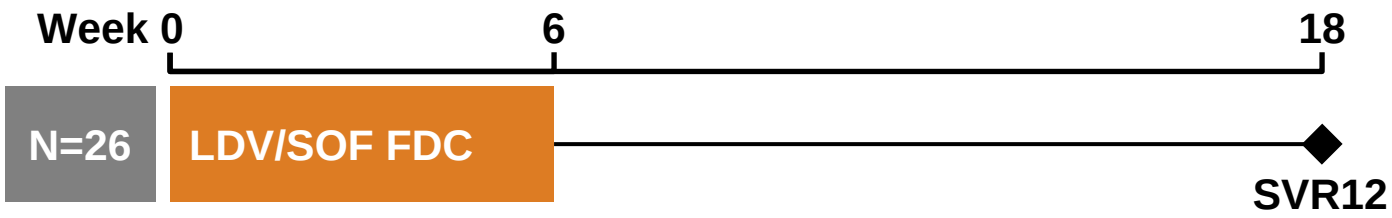


- testing for anti-HCV may not be enough
- after a first positive HCV-RNA
  - 37% anti-HCV positive 3 months later
  - 86% anti-HCV positive 6 months later
  - 5% without seroconversion after 1 year

Thomson et al. AIDS 2009, 23:89–93

Acute HCV: Ledipasvir/Sofosbuvir for 6 weeks in Treatment of acute HCV in HIV coinfection

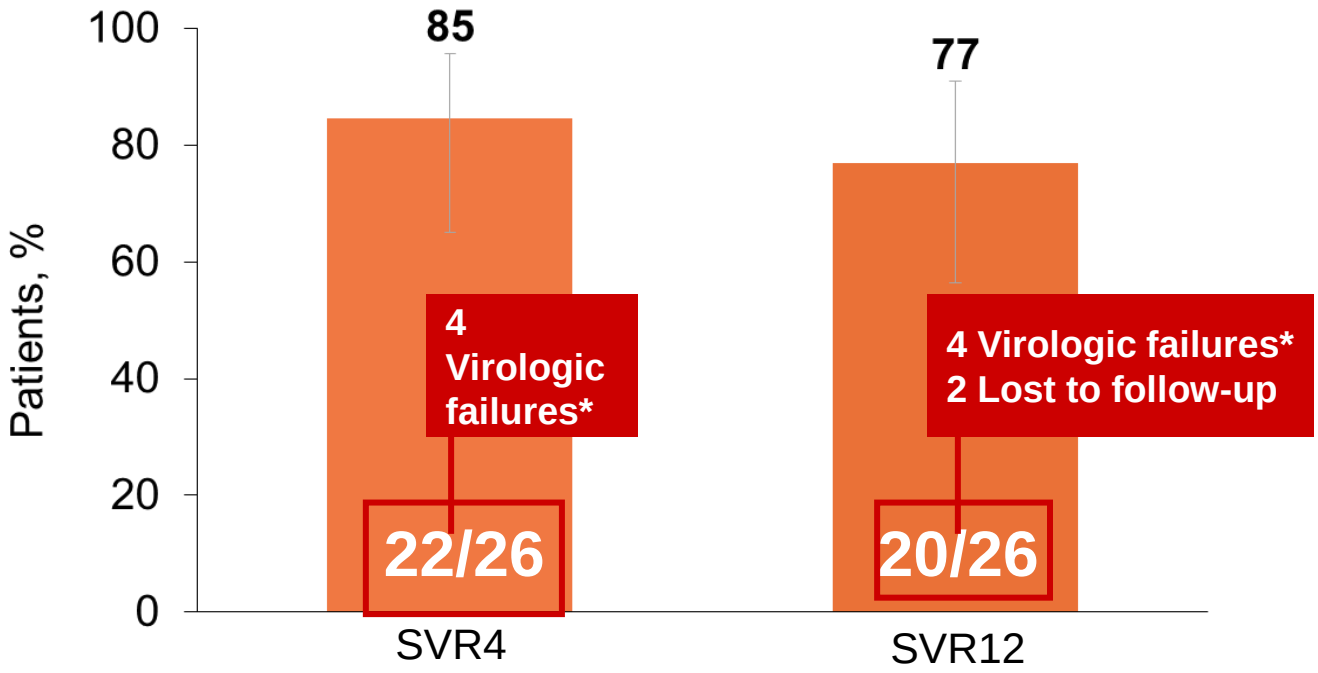
- 26 HIV patients with acute HCV GT 1 or 4
- HCV Ab/PCR negative in previous 6 months



	LDV/SOF N=26
Mean age, y (range)	41 (25-58)
Men, n (%)	26 (100)
White, n (%)	24 (92)
Mean BMI, kg/m2 (range)	24 (20-35)
IL28B CC, n (%)	12 (46)
GT, n (%)	
1a	18 (69)
4	8 (31)
Mean HCV RNA, log10 IU/mL (range)	5.4 (<LLOQ-7.3)
Mean CD4 count, cells/uL (range)	675 (275-1291)

Rockstroh J, et al. 23rd CROI; Boston, MA; February 22-25, 2016. Abst. 154LB.

SVR4 and SVR12

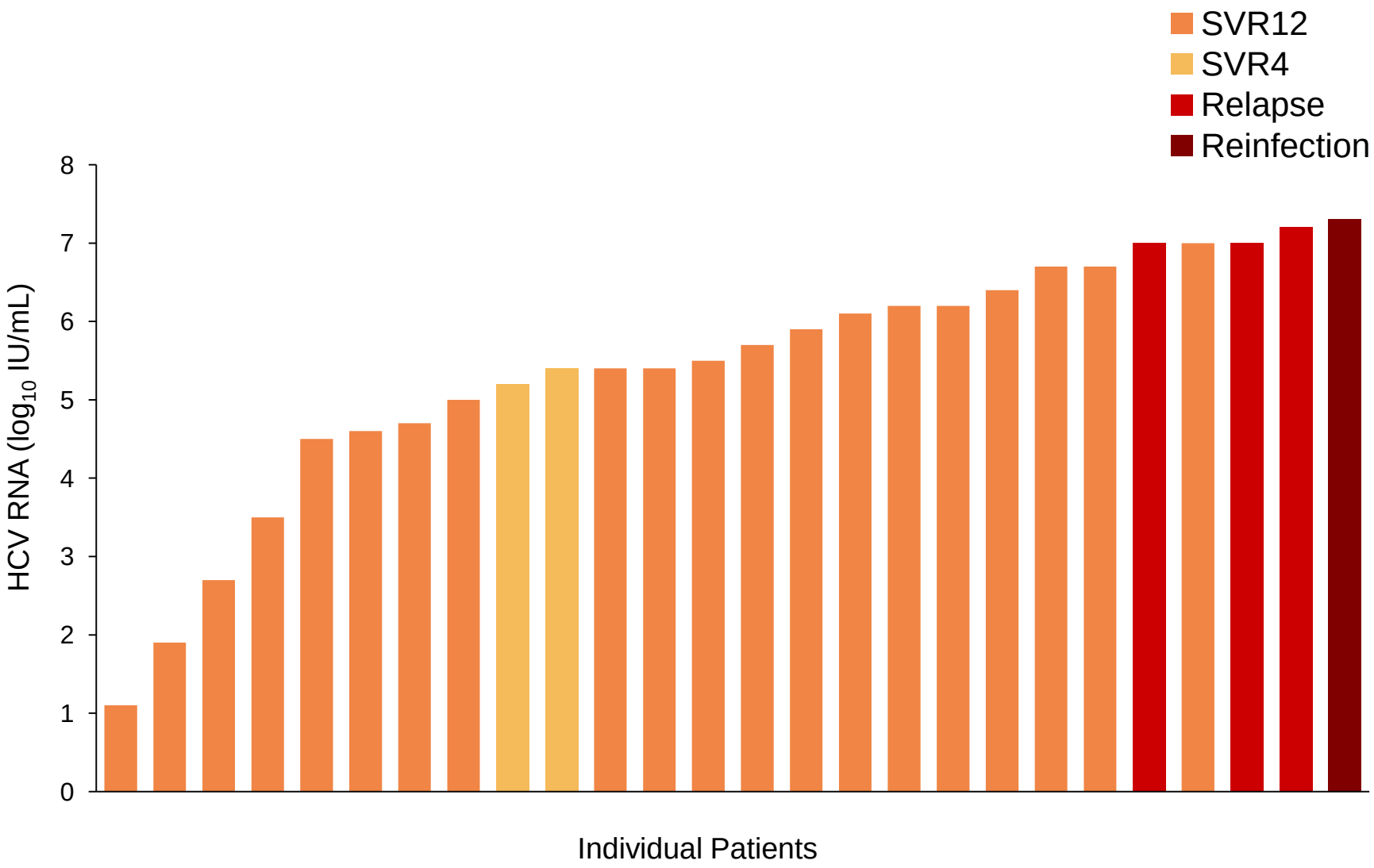


GT (LiPA)	Baseline HCV RNA, log_{10} IU/mL	IL28B	BMI, kg/m^2	Duration of Infection, weeks
4	7.1	CT	24	24.5
1a	7.0	CT	22	N/A
1a	7.2	CT	21	22.5

*3 patients relapsed, 1 was reinfected (GT 1a at baseline, 4d in post-treatment).
Error bars represent 95% confidence intervals.

Rockstroh, J et al. CROI 2016; Boston #154LB

Acute HCV LDV/SOF study: Baseline HCV RNA and Treatment Outcome (SVR)



Rockstroh J, et al. 23rd CROI; Boston, MA; February 22-25, 2016. Abst. 154LB.

Recent data for shortened duration therapy in acute/early HCV in HIV+

Study	Genotype	Number	Regimen	Duration	SVR12 (%)
DAHHS[1]	1a	57	BOC + PegIFN/RBV	12 weeks	86
NYC[2]	1	19	TVR + PegIFN/RBV	12 weeks	84
CHAT[3]	1	9	TVR + PegIFN/RBV	12 weeks	56
SWIFT-C[4]	1/4	17	SOF/RBV	12 weeks	59
DARE-C II[5]	1/3	14	SOF/RBV	6 weeks	21
NYC II[6]	1	12	SOF/RBV	12 weeks	92
SLAM-C Arm 1[7]	1	15	SOF/LDV	4 weeks	100
SLAM-C Arm 2[7]	1	15	SOF/SMV	8 weeks	86

1. Hullegie, J Hepatol 2015; doi 10.1016/jhep.2015.12.004. [Epub ahead of print]. 2. Fierer, Clin Infect Dis; 2014; 58: 873-9. 3. Boesecke, unpublished (personal communication). 4. Naggi, A1094, AASLD 2015, San Francisco CA. 5. Martinello, A1083, AASLD 2015, San Francisco CA. 6. Fierer, A1090, AASLD 2015, San Francisco CA. 7. Basu, A1074, AASLD 2015, San Francisco, CA

EASL guidelines 2016

- Patients with acute hepatitis C should be treated with a combination of sofosbuvir and ledipasvir (genotypes 1, 4, 5 and 6), a combination of sofosbuvir and velpatasvir (all genotypes), or a combination of sofosbuvir and daclatasvir (all genotypes) for 8 weeks without ribavirin (**B1**).
- Patients with acute hepatitis C and HIV coinfection and/or a baseline HCV RNA level >1 million IU/ml (6.0 log IU/ml) may need to be treated for 12 weeks with the same combination regimens (**B2**).
- SVR should be assessed at 12 and 24 weeks post-treatment, because late relapses have been reported (**B2**).
- There is no indication for antiviral therapy as post-exposure prophylaxis in the absence of documented HCV transmission (**B1**).

And after the cure?

HBV Reactivation Associated with DAA Therapy for HCV: A Review of US FDA Spontaneous Post-Marketing Cases

Age in years (n=29)	Mean (60.7) Median (58) Range (36-85)
Sex	Male (n=13) Female (n=16)
Country of Report	USA (n=5) Japan (n=19) Other (n=5)
Days to Event (n=28)	Mean (53) Median (46) Range (14-196)
Treatment Delay	Yes (n=7) Possible (n=7) No delay (n=2) No treatment given or treatment not stated (n=13)
HCV Genotype	Genotype 1 (n=16) Other genotype (n=2) Not reported (n=11)
Baseline HBV Viral Parameters	HBsAg (+) n=13 HBsAg (-) n=4 HBsAg Not reported n=12 HBcAb (+) n=6 HBcAb Not reported n=23 HBsAb (-) n=3 HBsAb Not reported n=26 HBV DNA undetectable n=16 HBV DNA detectable n=9 HBV DNA baseline either not reported or detectability status unclear n=4
Outcome	Death (n=2); Transplant (n=1); Hospitalization (n=6); Other (n=20)
DAA Therapy	Discontinued (n=10); Completed (n=13); Not Reported (n=6)
Treatment for HBV	Entecavir (n=9); Tenofovir (n=6), Tenofovir/Emtricitabine (n=1); Not Reported (n=6); No Treatment (n=7)

Bersoff-Matcha S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. LB-17.

A Review of US FDA Spontaneous Post-Marketing Cases: Baseline HCV/HBV Virological Characteristics & DAA Used

Case #	HBsAg	HBsAb	HBcAb	HBeAg	HBeAb	HBV DNA in IU	Direct Acting Antiviral (DAA)
1				NEG	POS	2700 (elevated)	OBV/PTV/r + DSV/RBV
2	POS		POS	NEG	POS	2.5 log (elevated)	DCV/ASV
3				NEG	POS	Undetectable	DCV/ASV
4	POS			NEG	POS	3.9 log (elevated)	DCV/ASV
5				NEG	POS	2300 (elevated)	SIM/SOF
6	NEG	NEG	POS			Undetectable	SIM/SOF
7	NEG	NEG	POS			Undetectable	SIM/SOF/RBV
8	POS					244 (elevated)	SOF/RBV
9	NEG	NEG	POS	NEG	POS	Undetectable	LDV/SOF
10	POS					Undetectable	LDV/SOF
11			POS			Undetectable	LDV/SOF
12	POS			NEG	POS	Undetectable	SIM/PEG/RBV
13	POS			NEG	POS	Undetectable	SOF/RBV
14	POS					1.3 log (elevated)	LDV/SOF
15	POS			NEG	POS	2.7 log (elevated)	DCV/ASV
16						Undetectable	LDV/SOF
17	POS		POS	NEG	NEG	Undetectable	DCV/SOF/RBV
18				NEG	POS	3.6 log (elevated)	LDV/SOF
19	POS			NEG	POS	<2.1 log	DCV/ASV
20	POS			NEG	POS	Undetectable	DCV/ASV
21				NEG	NEG	Undetectable	DCV/ASV
22						<2.1 log	DCV/ASV
23						Undetectable	LDV/SOF
24				NEG		3.3 log (elevated)	DCV/ASV
25						Undetectable	DCV/ASV
26	POS					<2.1 log	LDV/SOF
27						Undetectable	DCV/ASV
28	NEG					NR	LDV/SOF/RBV
29	POS				POS	Undetectable	LDV/SOF

Blank cell = test result not reported

Bersoff-Matcha S, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. LB-17.

Risk of Incident Liver Cancer Following HCV Treatment with Sofosbuvir-containing Regimens

- Quintiles/IMS PharMetrics Plus™ Claims dataset for ~110M people from 1.1.06 to 9.30.15
- Cohort study of HCV pts 18+ years of age, with ≥ 6 mo of continuous enrollment prior to start of F/U
- SOF-HCV patients (N=9,616)
  - Dispensed ≥ 12 weeks of SOF-containing Rx
  - No subsequent HCV treatment
  - F/U time starting from last SOF dispense
- Untreated HCV patients (N=95,274)
  - F/U time starting ≥ 12 weeks after 12.12.13 (date of first recorded Sovaldi claim in the database)

Characteristics of SOF-treated HCV and untreated HCV cohorts

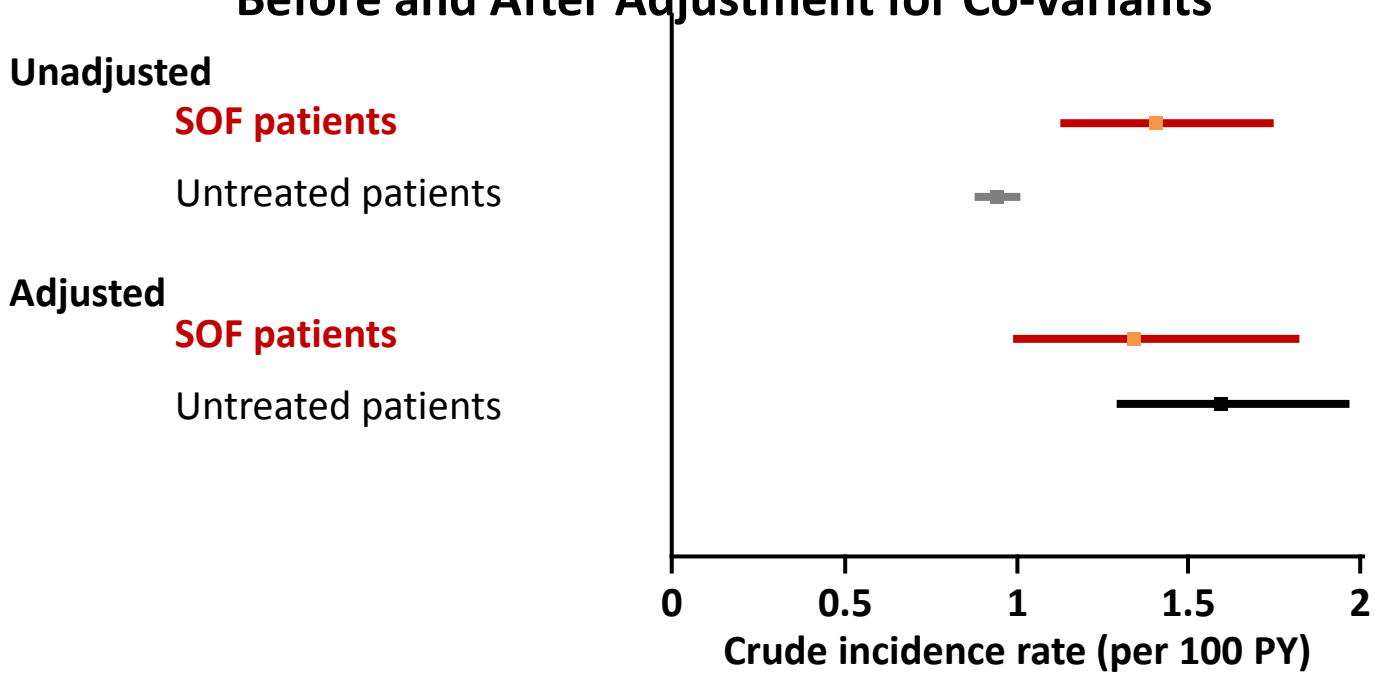
Variable		SOF-treated HCV		Untreated HCV	
		n	(%)	n	(%)
Total		9,616	100.0	95,274	100.0
Age	18–34 y	468	4.9	10,946	11.5
	35–44 y	607	6.3	9,843	10.3
	45–54 y	2,313	24.1	26,017	27.3
	55+ y	6,228	64.8	48,468	50.9
Sex	Female	3,275	34.1	40,284	42.3
	Male	6,341	65.9	54,990	57.7
Prior portal hypertension		1,101	11.4%	2,944	3.1%
Prior cirrhosis		3,517	36.6	10,940	11.5
Prior use of statins		1,090	11.3	17,231	18.1
Prior substance abuse		4,172	43.4	42,416	44.5
Prior use of anti-diabetic meds		1,460	15.2	12,295	12.9
Prior unspecified non-alcoholic liver disease		370	3.8	1,712	1.8
Prior transaminase elevation		3,050	31.7	17,683	18.6
Prior cancer (any)		5,017	52.2	42,550	44.7
Prior hepatic encephalopathy		379	3.9	1,526	1.6
Prior end stage liver disease		342	3.6	1,569	1.6
Follow-up time (days)	Mean (SD)	222	(141)	383	(184)
	Median (min/max)	184	(31–582)	442	(31–574)

Compared to untreated HCV patients, patients completing SOF tended to be older, male, with cirrhosis

Chokkalingam A, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 739.

HCV Treatment with Sofosbuvir-containing Regimens: Cumulative Incidence Rates of HCC

Cumulative Incidence Rates of HCC in Each Cohort, Before and After Adjustment for Co-variants



- Before adjustment for significant covariates, HCC incidence appears higher in SOF-treated patients vs. untreated patients
  - After adjustment for significant covariates, rates in SOF-treated patients are not higher; indeed, they are nominally lower than rates among untreated patients
  - Age, gender, baseline cirrhosis status, and baseline portal hypertension are important covariates that must be considered

Chokkalingam A, et al. 67th AASLD; Boston, MA; November 11-15, 2016; Abst. 739.

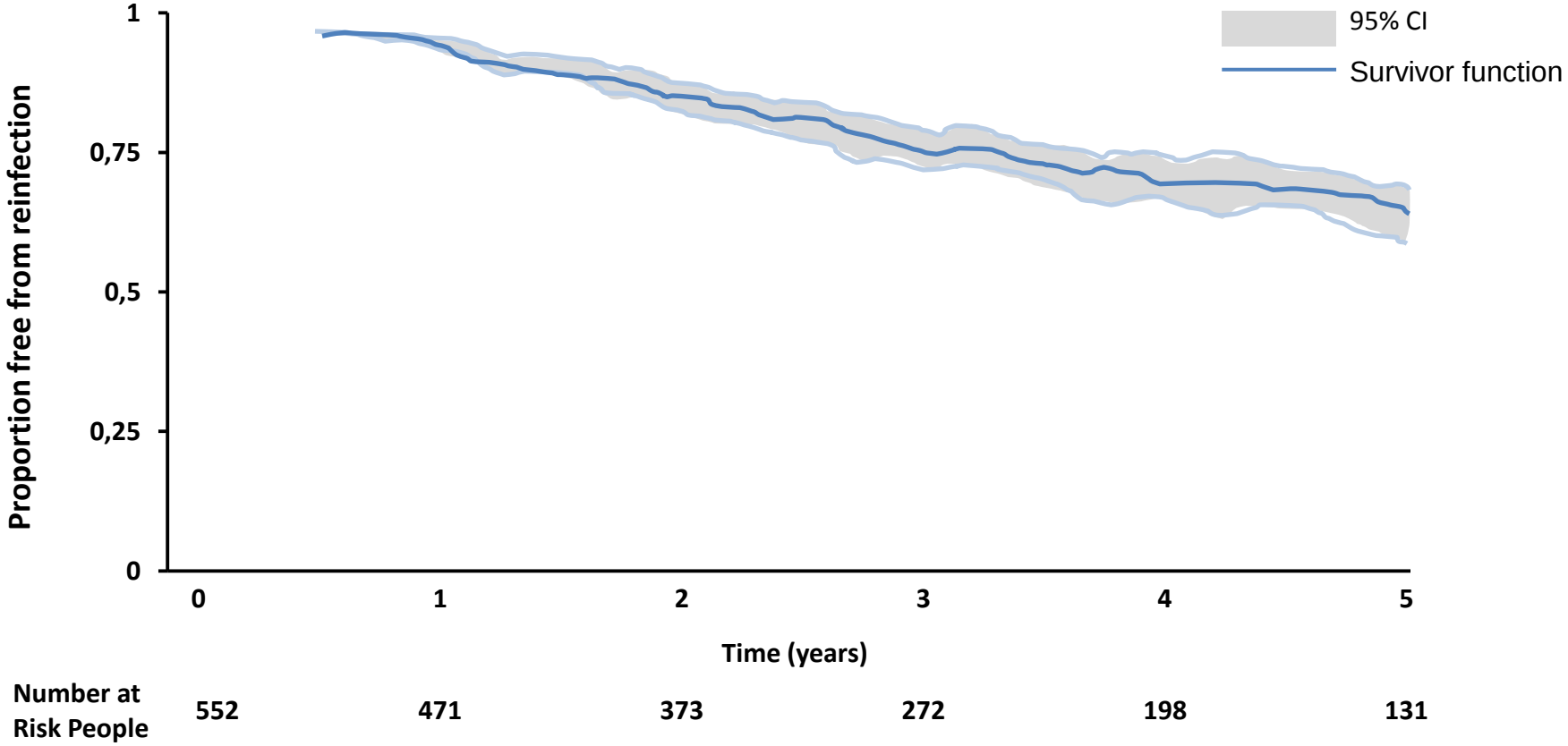
HCV Reinfection Incidence and Outcomes Among HIV-positive MSM in Western Europe

	Incident infection	1st Reinfection
Number included	606	606
Number reinfected (%)	N/A	149 (24.6)
Median time (years) to reinfection (IQR)	N/A	1.8 (1.1-3.2)
Genotypes (%)	G1: 376(70.5) G2: 13(2.4) G3: 46(8.6) G4: 96 (18)	G1: 104(73.2) G2: 1(0.7) G3: 12(8.5) G4: 25(17.6)
Genotype switches (%)	N/A	71/136 (52.2)
Median age at reinfection (IQR)	39 (34-44)	41 (37-45)
Median CD4 at reinfection		553 (412-760)
Proportion with suppressed HIV VL		91/111 (82.0%)
Spontaneously cleared proportion	111/605 (18.3%)	21/135 (15.6%)

113 treated with 87 achieving SVR (78%)

Martin T, et al. 51st EASL; Barcelona, Spain; April 13-17, 2016. Abst. PS006
Ingiliz P et al. J Hepatol 2016.

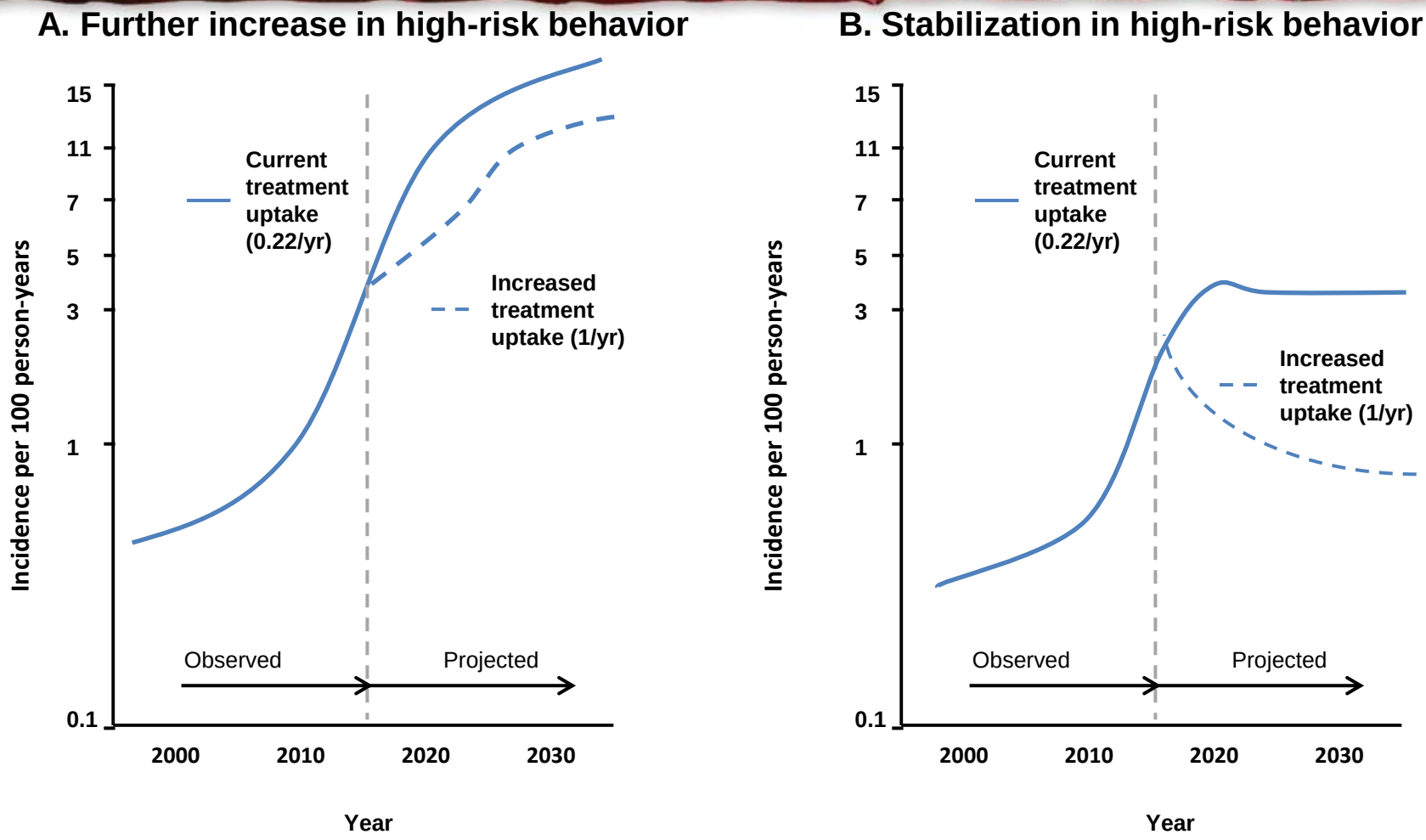
Challenge: HCV Reinfections



24.6% with reinfection Reinfection incidence 7.3/100py

Rauch A, et al. HIV Glasgow; 23-26 October 2016; Glasgow, UK; Abst. O23.
Ingiliz et al, J Hepatology 2016, available online Sept 2016.

Treatment-as-Prevention and Risk Behavior



Rauch A, et al. HIV Glasgow; 23-26 October 2016; Glasgow, UK; Abst. O23.
Salazar et al. Hepatology 2016, in press .

Chronic hepatitis C and HIV: implications for care

- HIV infected individuals with HCV coinfection remain at higher risk for fibrosis progression and hepatic decompensation
- Therefore HCV therapy is prioritized in most guidelines in this patient group
- The short- and mid-term effects of ART on the progression of HCV-related liver disease largely outweigh the potential risks for long-term toxicity.
- HIV therapy needs to consider coadministration with all oral DAA combination therapy and possible drug interactions as well as potential dose modifications with advanced liver disease.
- Strategies beyond administration of DAA therapy are needed to prevent HCV reinfection in HIV-coinfected individuals
- HCV elimination in HIV-coinfected populations appears targetable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