L'AGORA' PENITENZIARIA 2017

XVIII Congresso Nazionale SIMSPe-ONLUS

Salute in Carcere e Lea 2017: Punto di svolta

Roma

5-6 ottobre 2017

Hotel dei Congressi
viale Shakespeare 29, Roma

www.agorapenitenziaria.it

Organizzato da SIMSPE ONLUS Società Italiana di Medicina e Sanità Penitenziaria

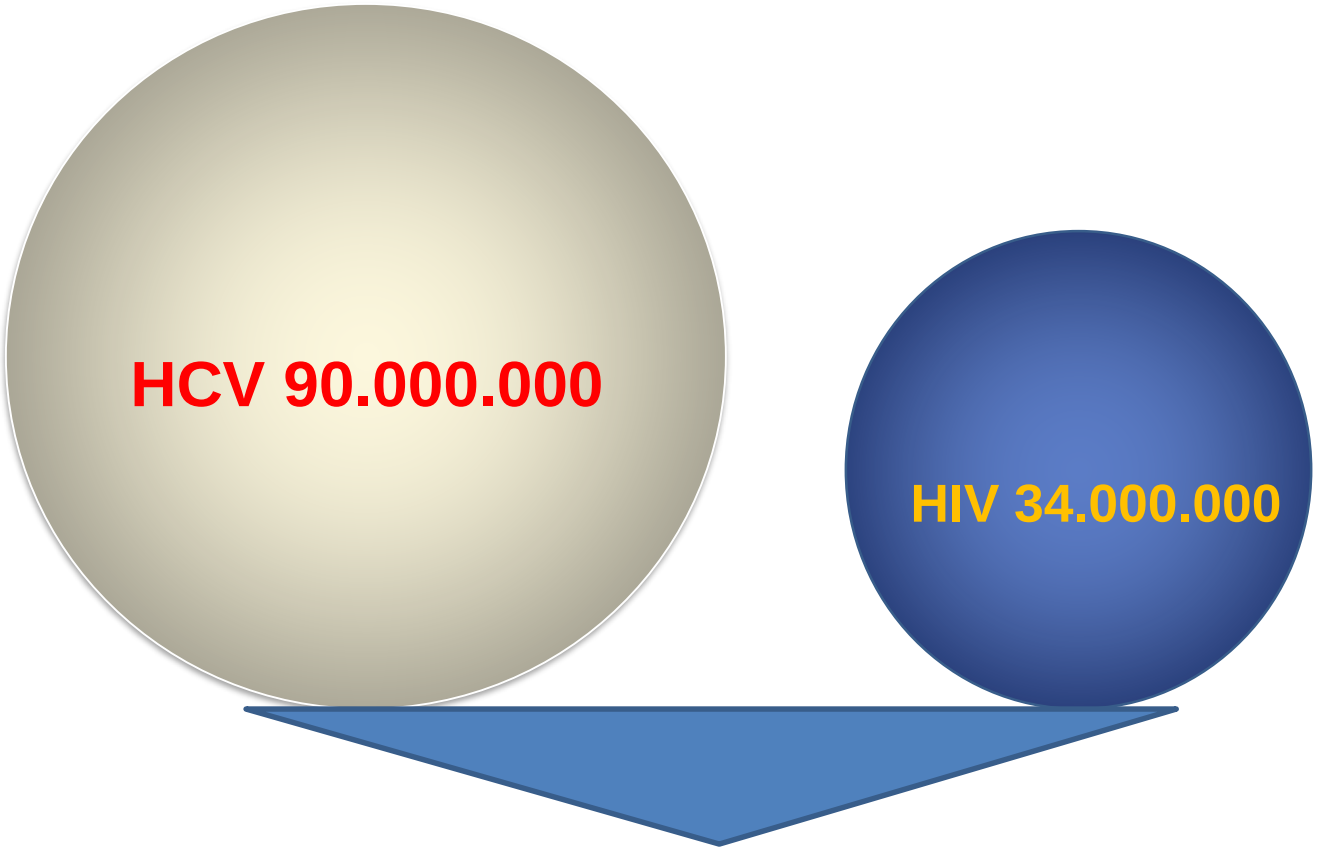
L'ottimizzazione delle terapie antivirali nei pazienti coinfetti HIV-HCV

Gianpiero D'Offizi

Road Map

- *Coinfezione HIV-HCV nel nostro Paese*
- *Prioritizzazione del trattamento in HIV-HCV*
- *Gestione delle comorbidità in HIV-HCV*
- *Gestione della cirrosi in HIV-HCV*
- *Linee guida di trattamento*
- *Accesso alle terapie in HIV-HCV*

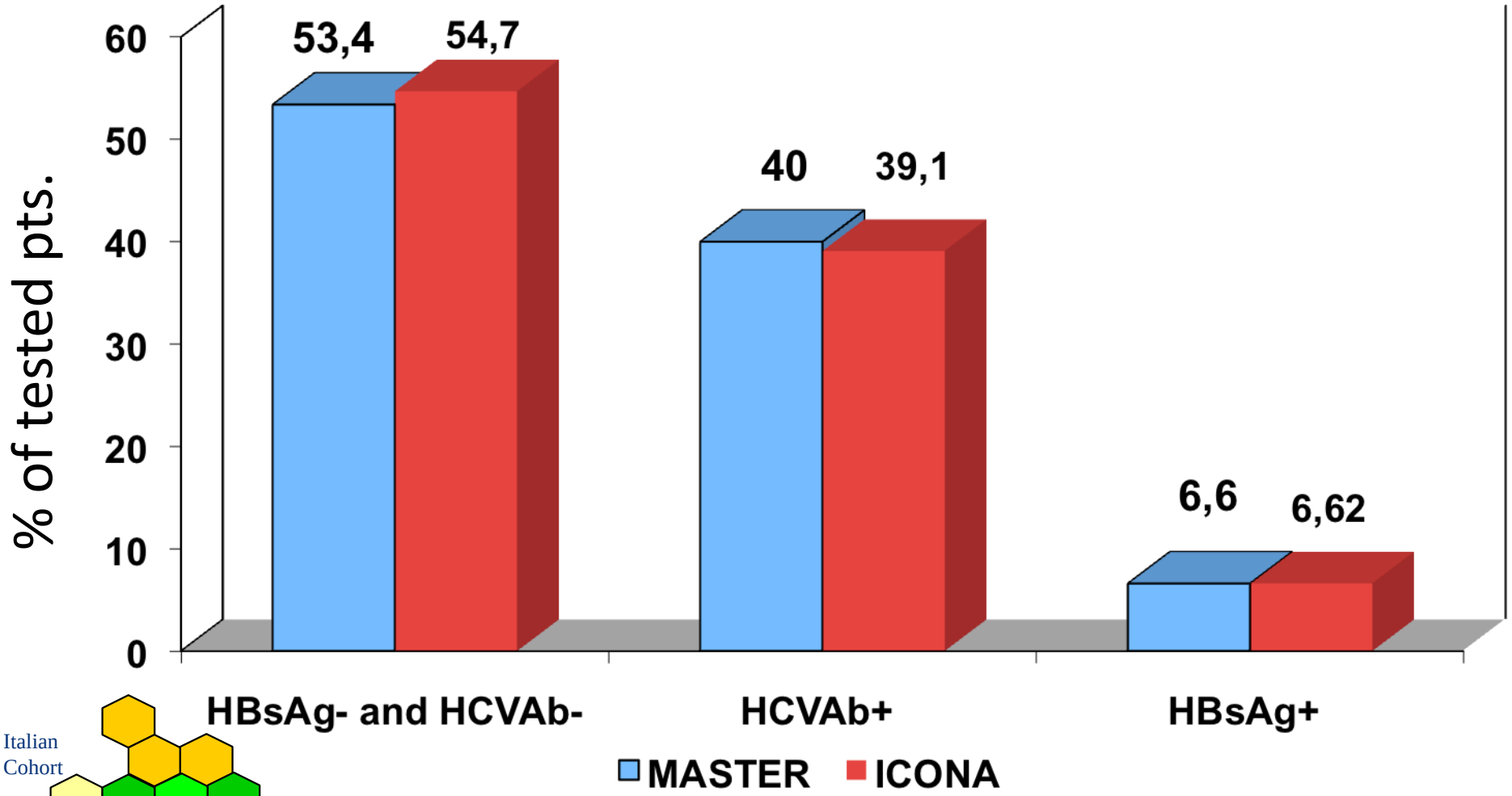
Stima di HIV/HCV nel mondo



HIV/HCV 2.278.000.400
Prevalenza in PLHIV 6.2%

Lancet Infect Dis 2016

Prevalence of hepatitis markers in the MASTER observational database (9098 pts) and in the ICONA cohort (9149)



Italian Cohort

I C O N A

Naive Antiretroviral

THE MASTER PROJECT
Standardized management of antiretroviral therapy

Coinfezione HIV-HCV nel nostro Paese

Incidence and progression to cirrhosis of new hepatitis C virus infections in persons living with human immunodeficiency virus*

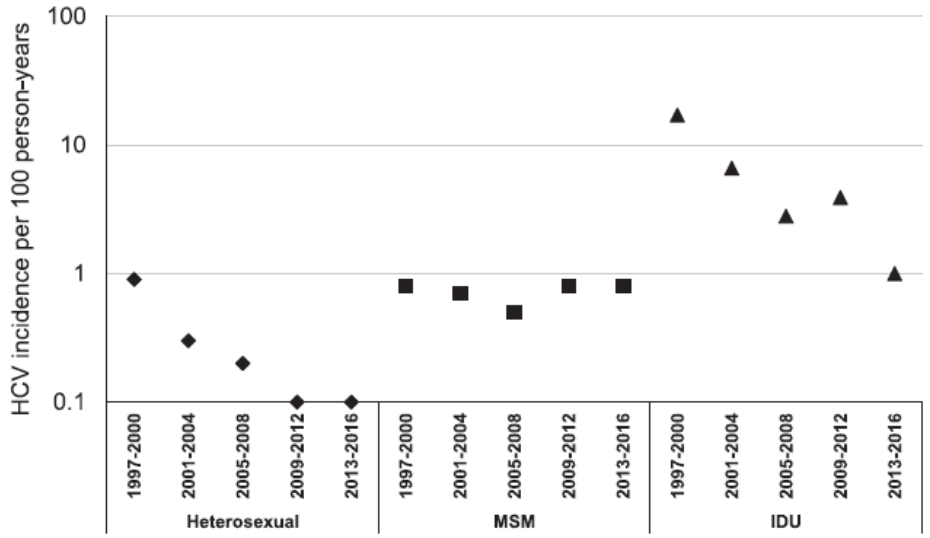


Figure 1. Incidence rates of hepatitis C virus seroconversion by calendar year and human immunodeficiency virus risk facto

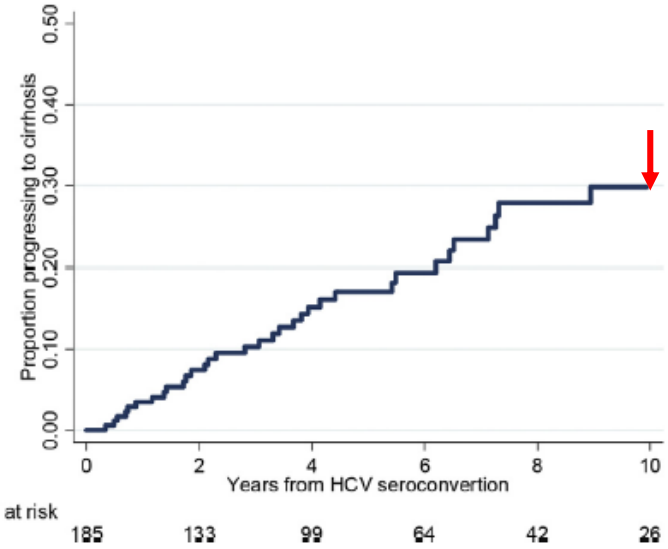
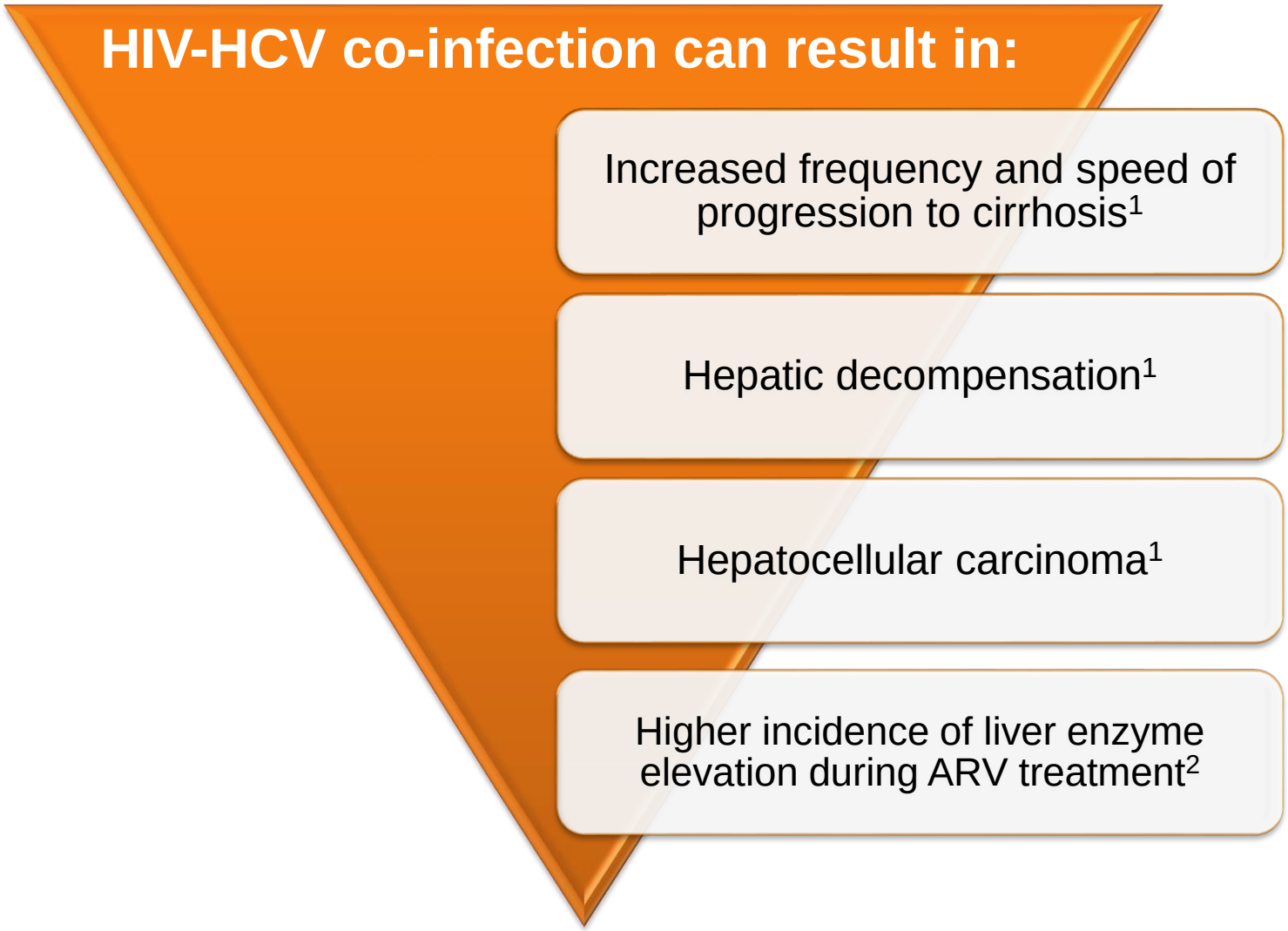


Figure 2. Kaplan–Meier estimate of the probability of progressing to hepatitis C virus-related severe fibrosis/cirrhosis in persons living with human immunodeficiency virus with hepatitis C virus seroconversion in the Icona cohort

Italian Cohort Naive Antiretrovira

M. Puoti et al. / Clinical Microbiology and Infection 23 (2017)

The liver in patients with HIV-HCV co-infection



1. Sánchez-Conde M, et al. Clin Infect Dis 2006;43:640–4; 2. Vispo E, et al. J Antimicrob Chemother 2010;65:543–7

Prioritizzazione del trattamento in HIV-HCV

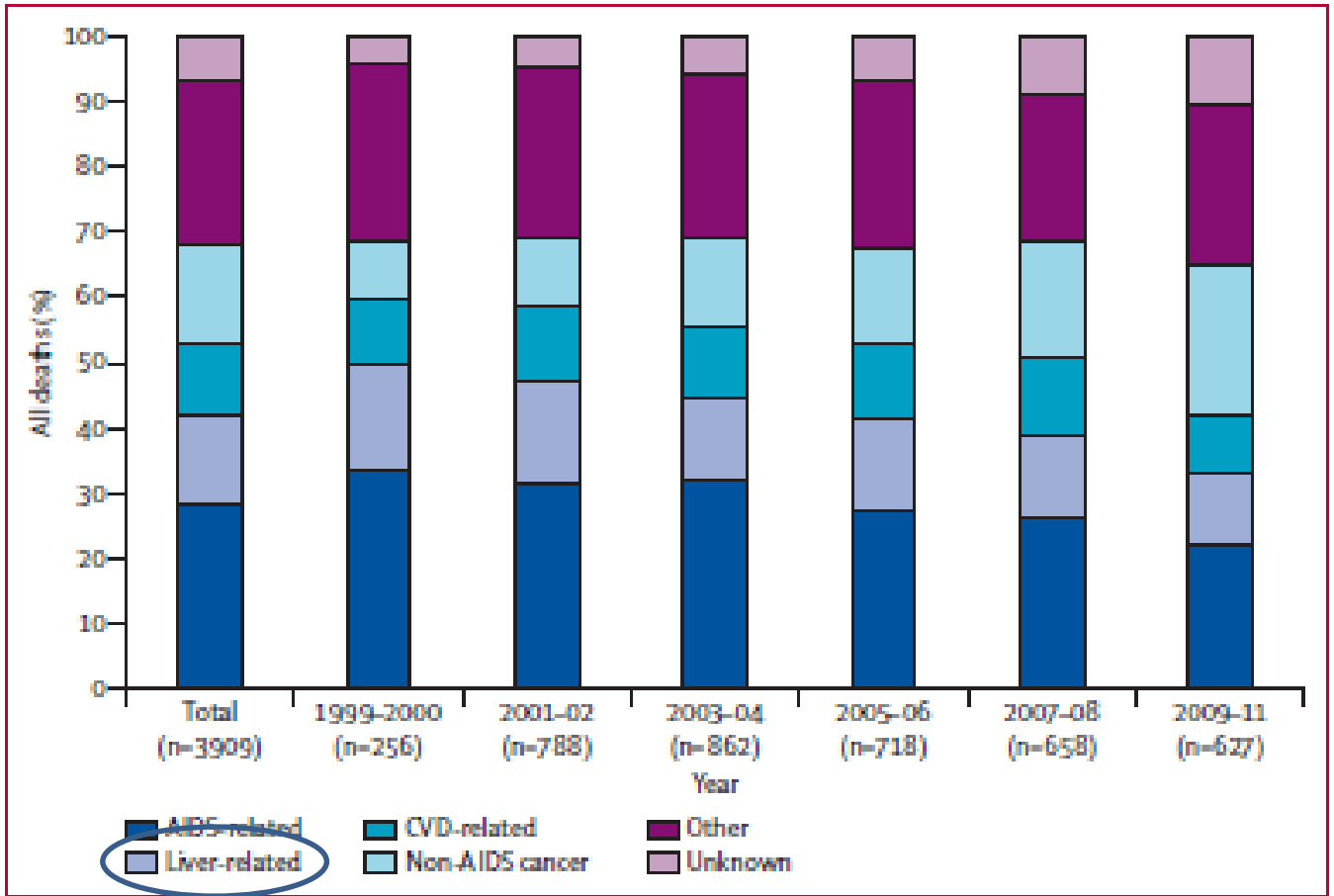
Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration

Lancet 2014

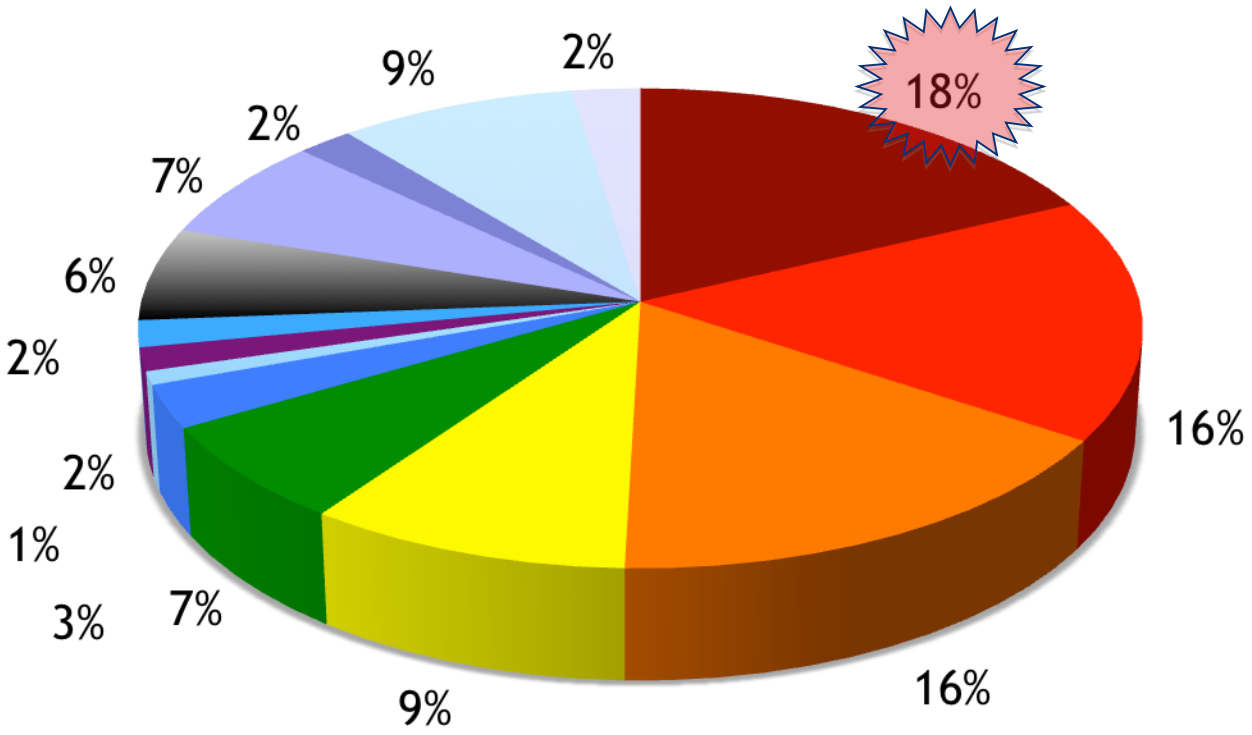
49.371 pts

308.719 p/y

Liver disease Death 13%



Causes of death in the Swiss HIV Cohort study 2005-09

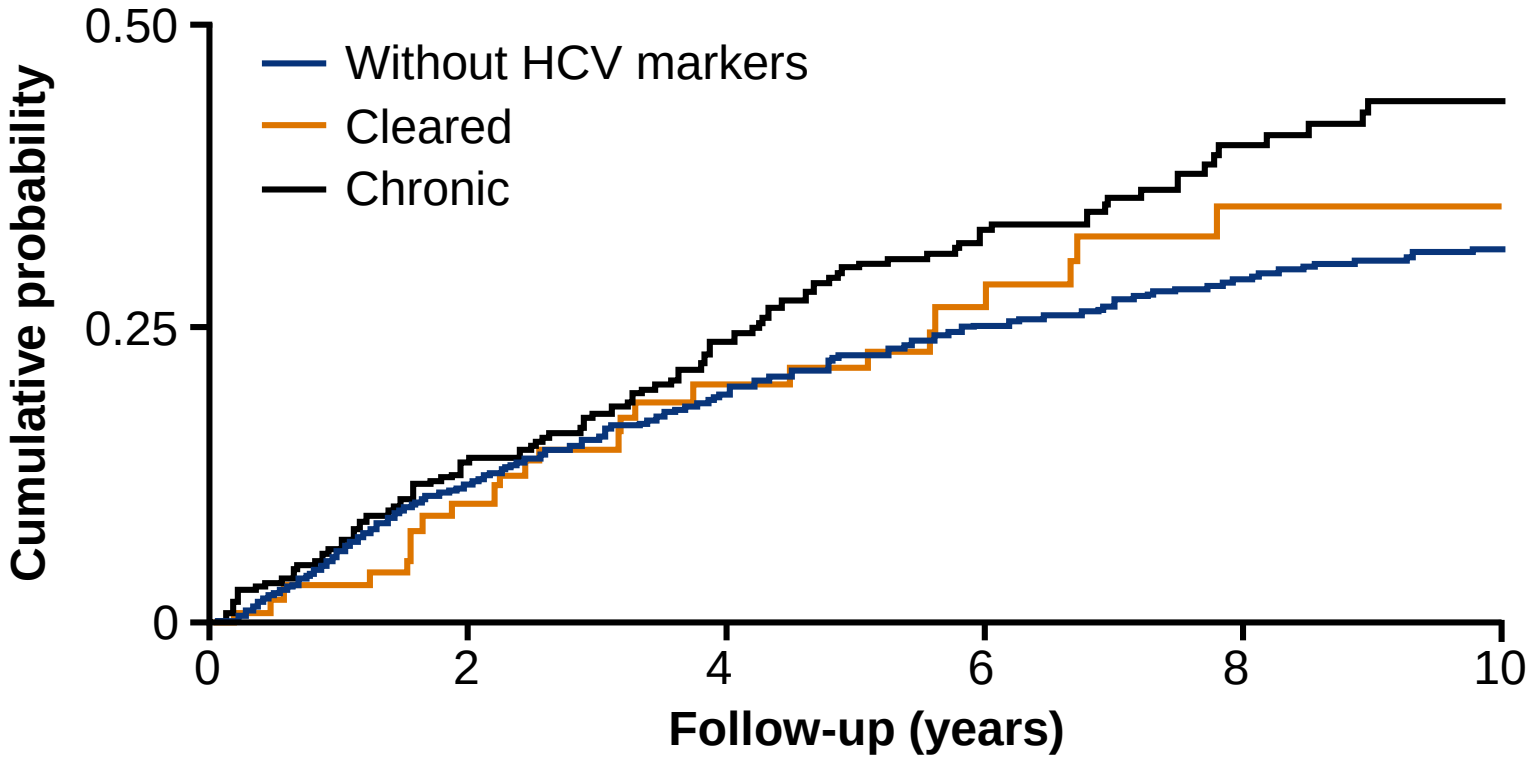


- Liver diseases
- AIDS
- Non AIDS Malignancies
- Non AIDS infections/ sepsis
- Heart diseases
- CNS
- Kidney
- Gastro/pancreas
- Lung
- Suicide or psych.
- Substance use
- Accident or Homicide
- Other or not classified
- Unknown

Ruppik M. et al. Changing patterns of causes of death in the SHCS 2005-2009. CROI 2011.
Poster # 789. Available at: http://www.retroconference.org/2011/PDFs/789.pdf.

Mortality in HCV-infected patients with HIV

- Chronic HCV infection is independently associated with a 50% increase in mortality among patients with a diagnosis of AIDS



Branch A, et al. Clin Infect Dis 2012;55:137–44

Studio COHERE. In pazienti coinfetti HIV-HCV con SVR dopo terapia anti HCV ridotta incidenza di decessi epato-correlati e sopravvivenza migliorata

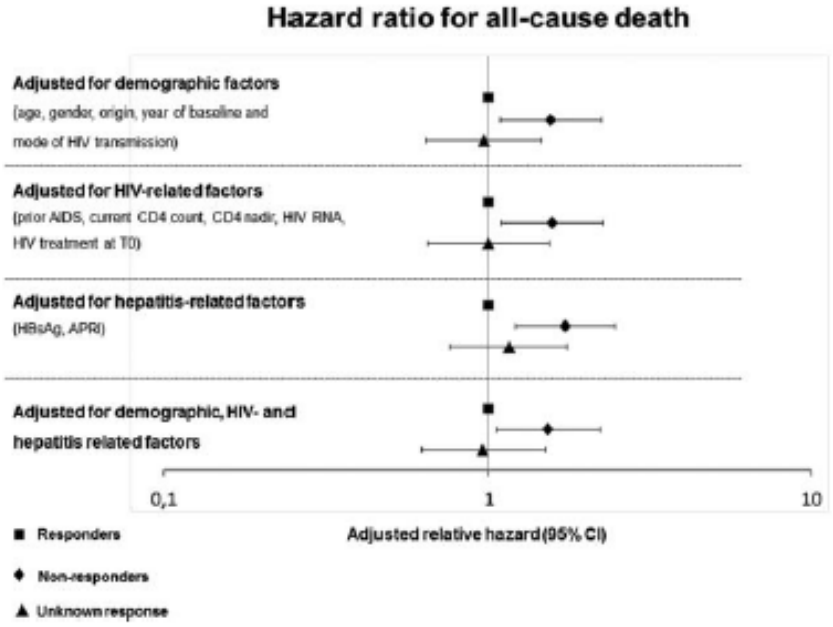


Fig. 3. **Adjusted hazard ratio for all-cause mortality according to hepatitis C virus treatment response.** Adjustments were made for prespecified demographic-related, HIV-related and hepatitis-related factors in three separate Cox regression models as well as for all factors combined.

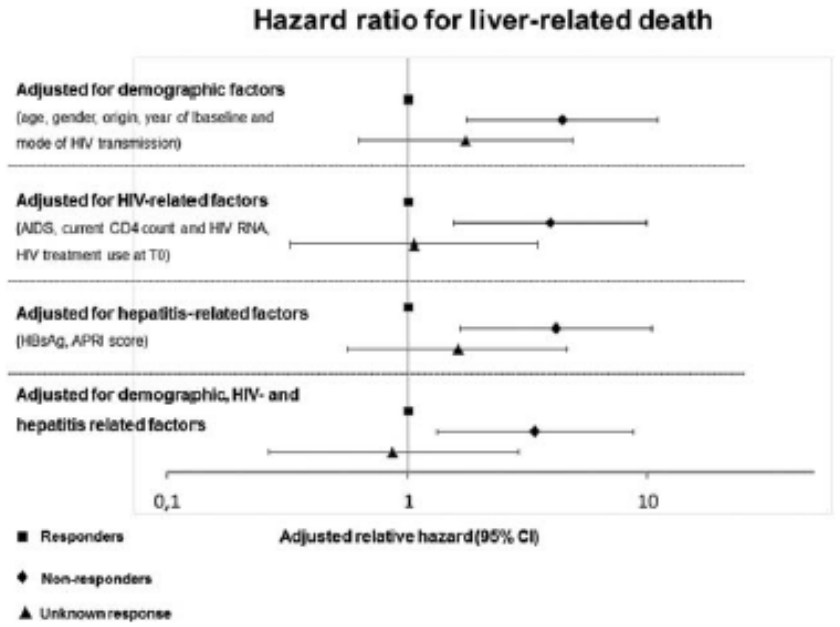


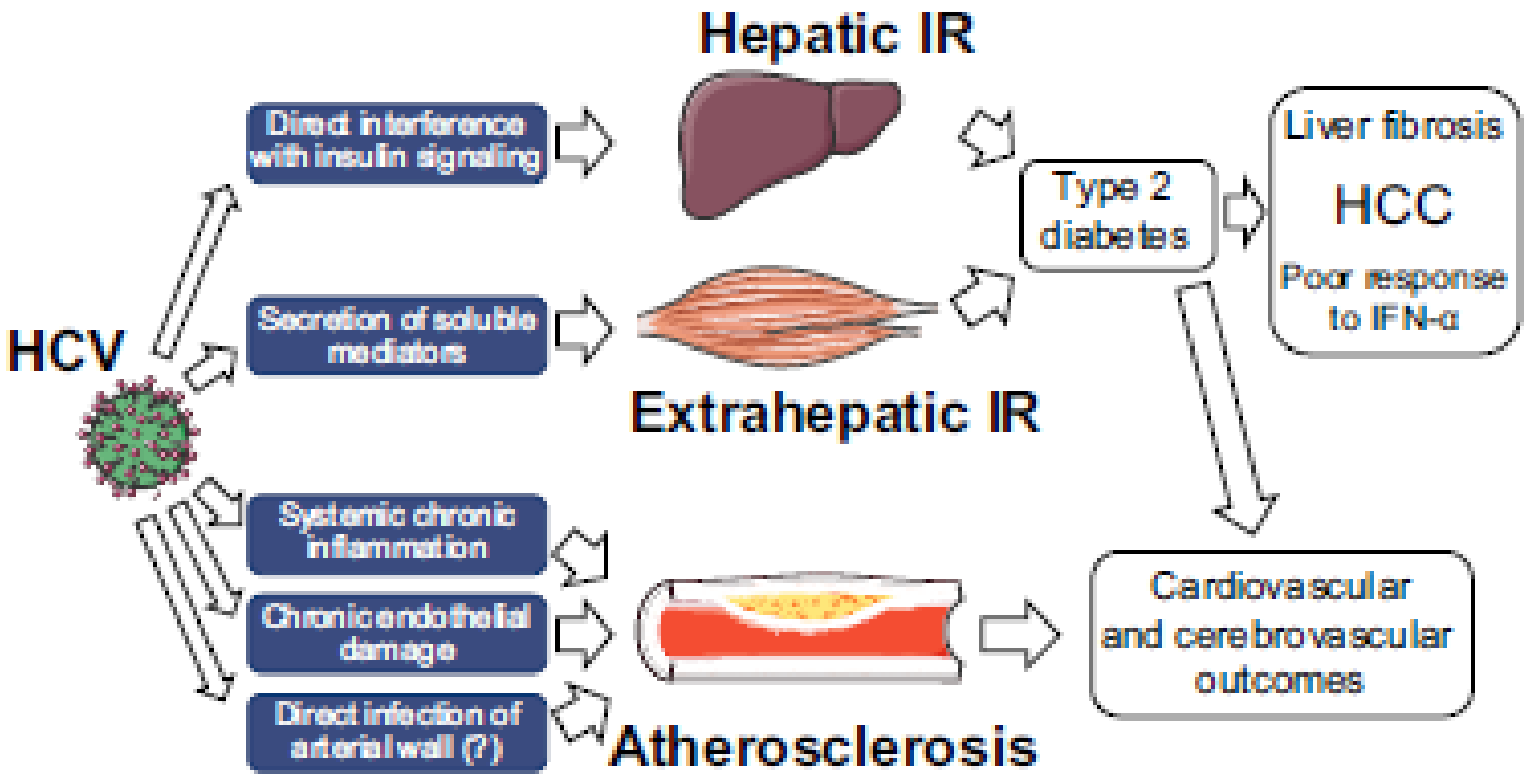
Fig. 5. **The figure shows the adjusted hazard ratio for liver-related death according to hepatitis C virus treatment response.** Adjustments were made for prespecified demographic-related, HIV-related and hepatitis-related factors in three separate Cox regression models as well as for all factors combined.

3755 pts: 27.5 % R; 43.6% NR; 28.9% UR

AIDS 2017

Gestione delle comorbidità in HIV-HCV

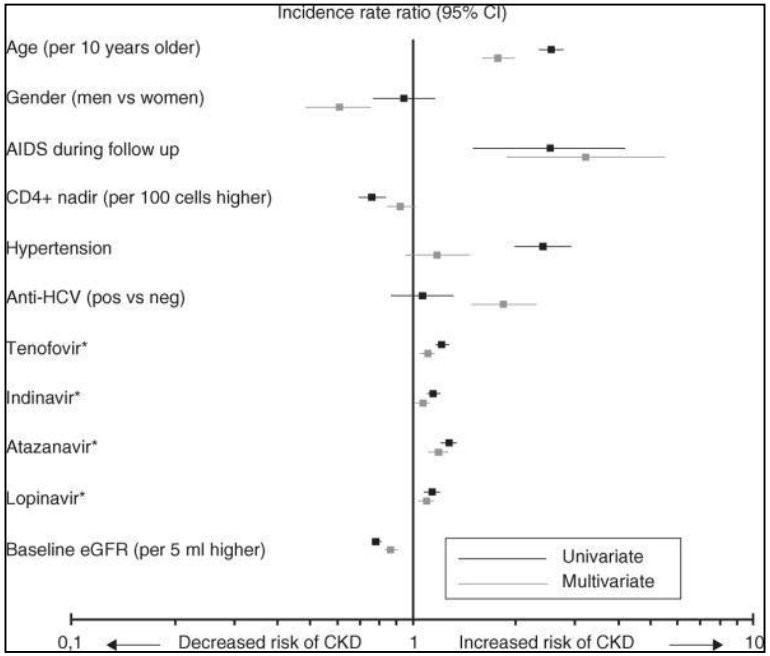
Meccanismi coinvolti nella patogenesi dell'insulina resistenza, del diabete della morbidità cardiovascolare HCV-associati

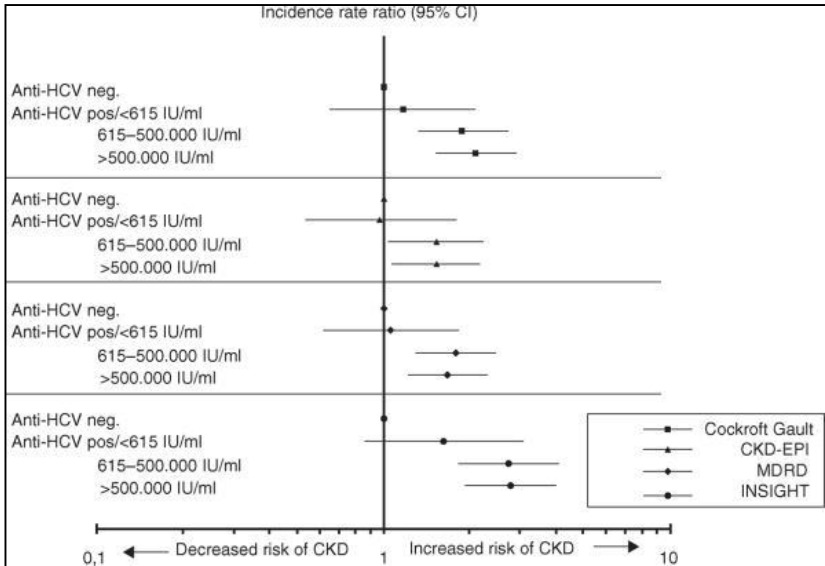


Negro F. 2014

Hepatitis C virus viremia increases the incidence of chronic kidney disease in HIV-infected patients

- 8235 patients → (24.9%) anti-HCV-positive
  - 983 (47.9%) HCV-RNA+,
  - 193 (9.4%) HCV-RNA-
  - 876 (42.7%) unknown HCV-RNA.
- At baseline, the median eGFR was 97.6 (interquartile range 83.8–113.0) ml/min per 1.73 m^2.
- During 36123 person-years of follow-up (PYFU), 495 patients progressed to CKD (6.0%) with an incidence rate of 14.5 per 1000 PYFU (95% CI 12.5–14.9).



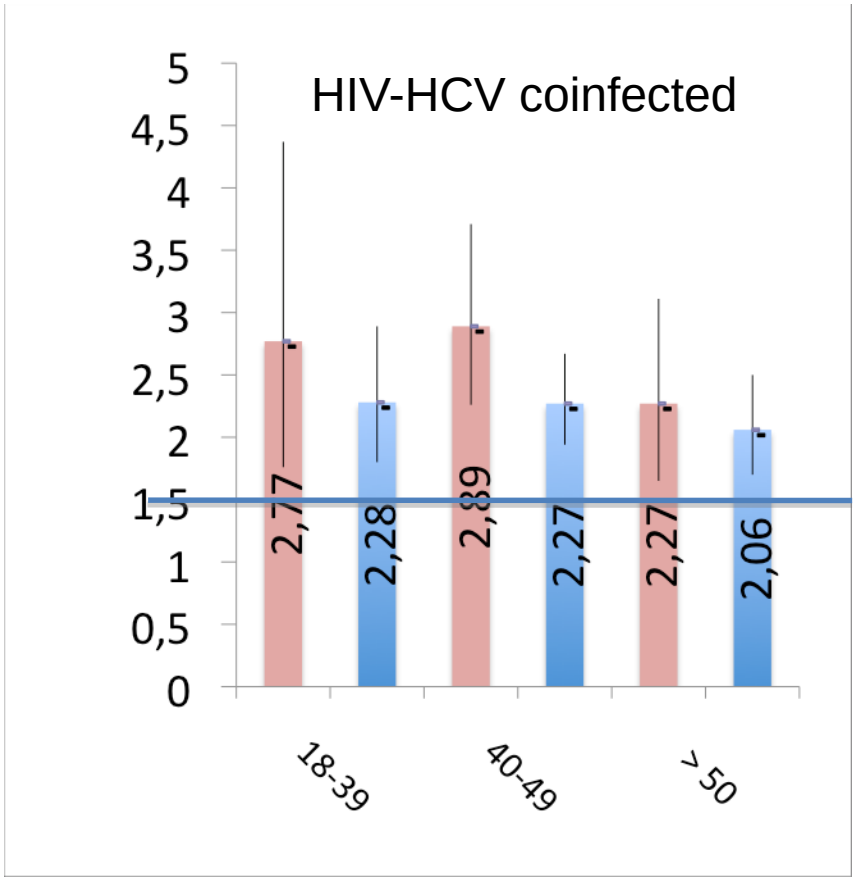


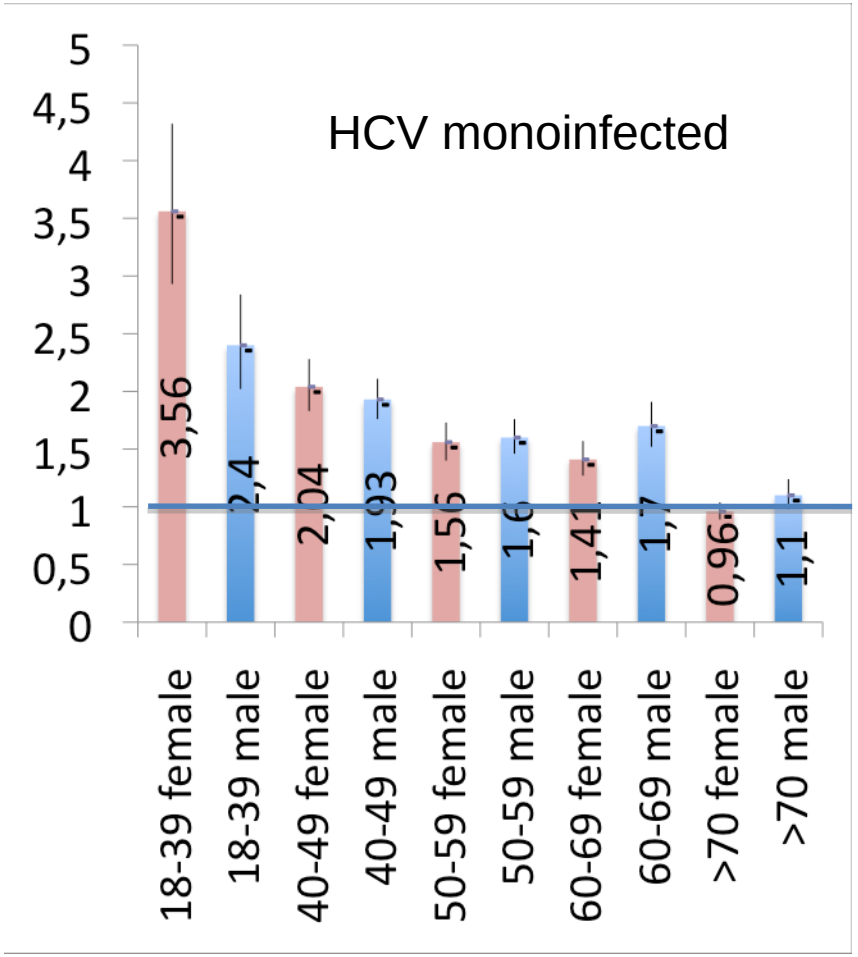
Peters L et al AIDS 2012 26: 1917–1926

HCV/HIV coinfection is associated with increased rates of hip fracture, compared to HCV-monoinfected, HIV-monoinfected, and HCV/HIV-uninfected persons.

Cohort study in 36,950 HCV/HIV-coinfected, 276,901 HCV-monoinfected, 95,827 HIV-monoinfected, and 3,110,904 HCV/HIV-uninfected persons within the U.S. Medicaid

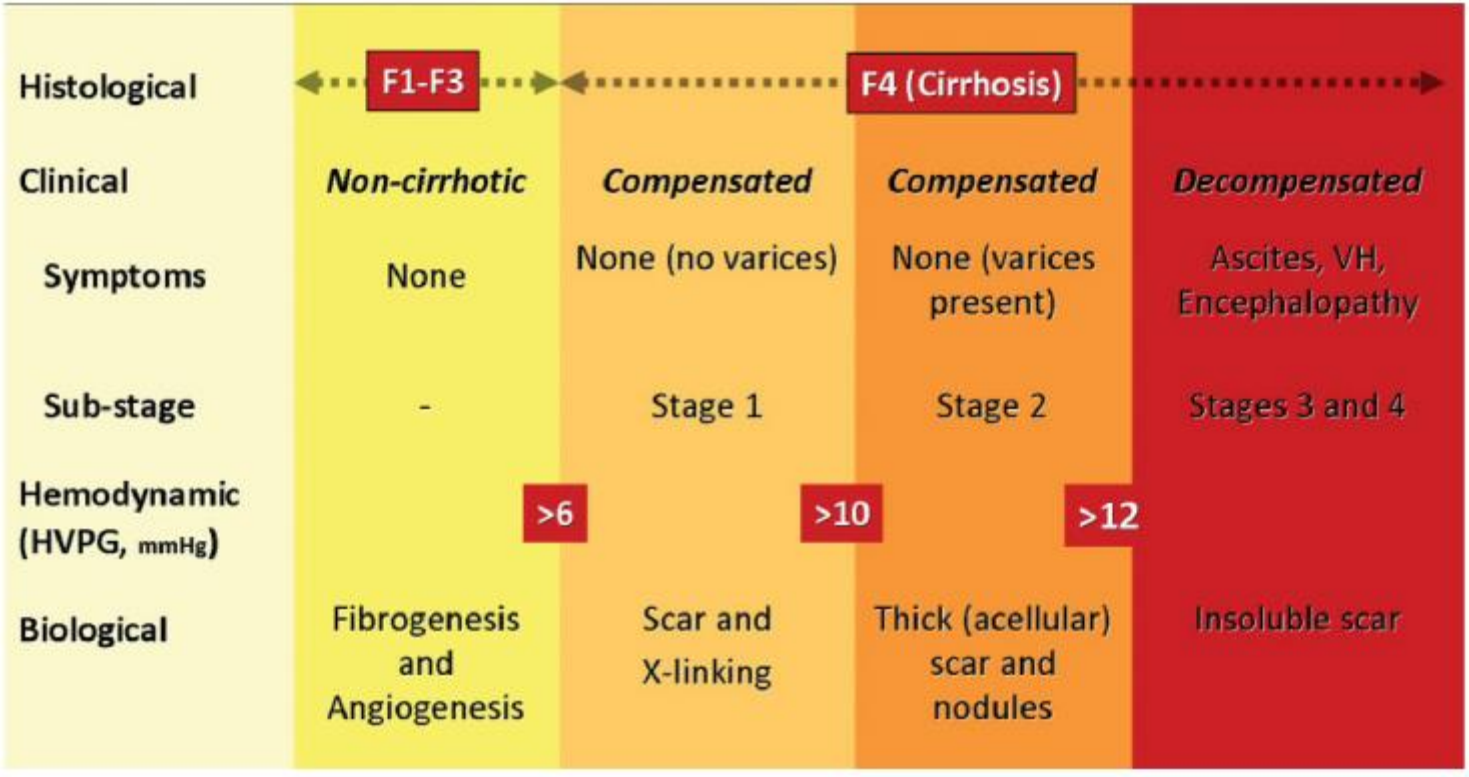
Estimated Relative Hazards of Hip Fracture (With 95% CIs) for HIV-HCV Coinfected and HCV-Monoinfected Patients, Compared to Those Uninfected With Either HIV or HCV Infections, by Sex and Age Group





Lo Re V et al. Hepatology 2012; 2012;56:1688-1698

Gestione della cirrosi in HIV-HCV



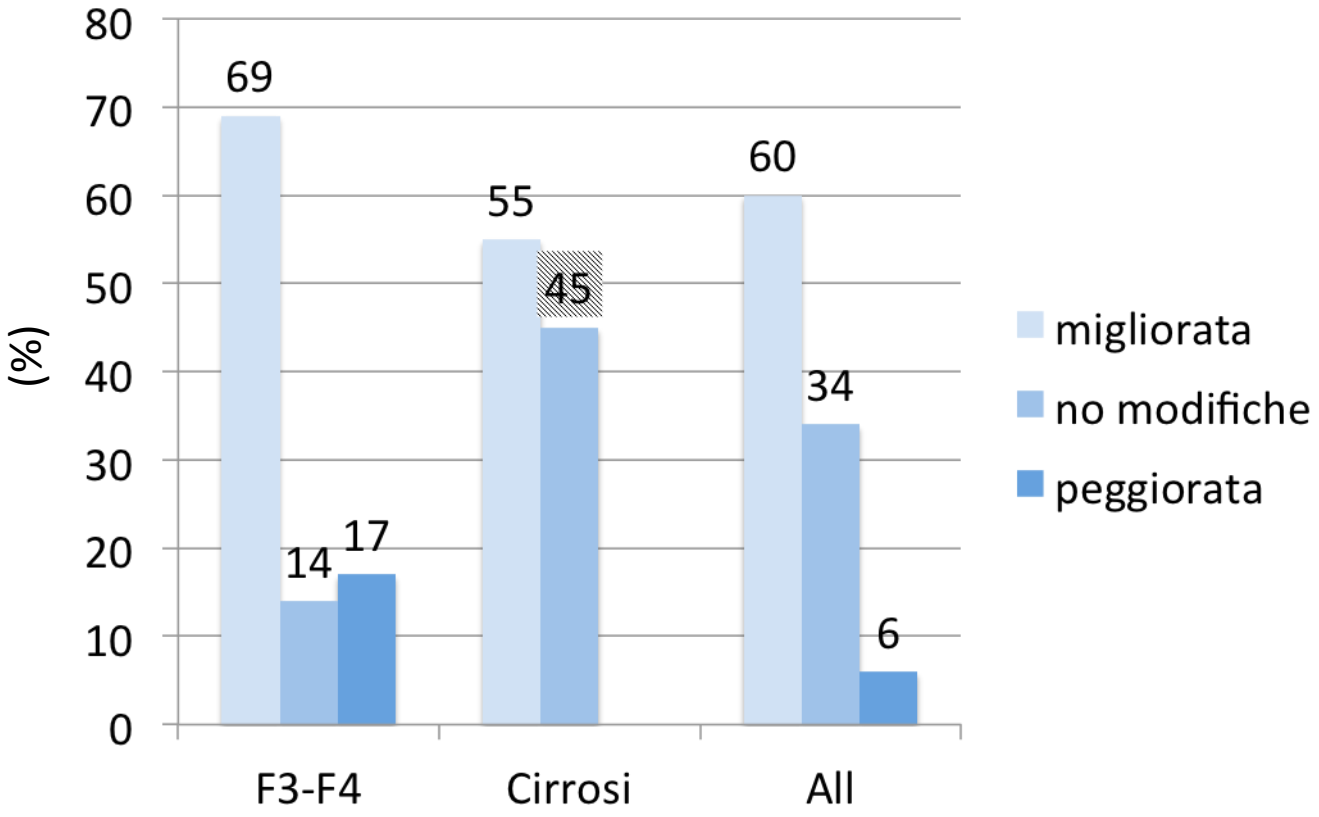
Hepatology 2010

STADI CLINICI DI CIRROSI EPATICA

Le decisioni sul trattamento anti HCV nel cirrotico sono guidate da:

- **Genotipo**
- **Funzione renale**
- **Trattamento Interazioni farmacologiche**
- **Gravità della cirrosi**

La cirrosi puo' persistere nonostante SVR

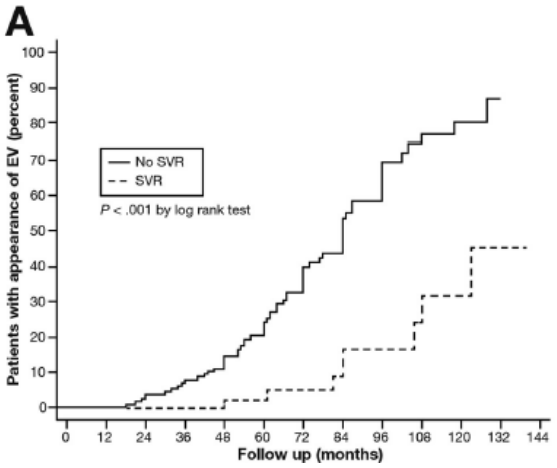


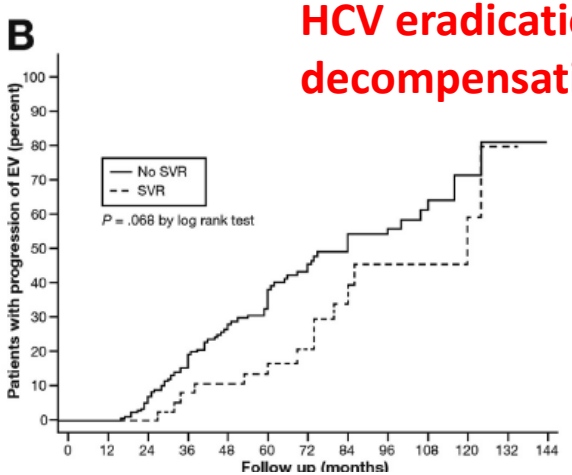
Crissien et al. AASLD 2015

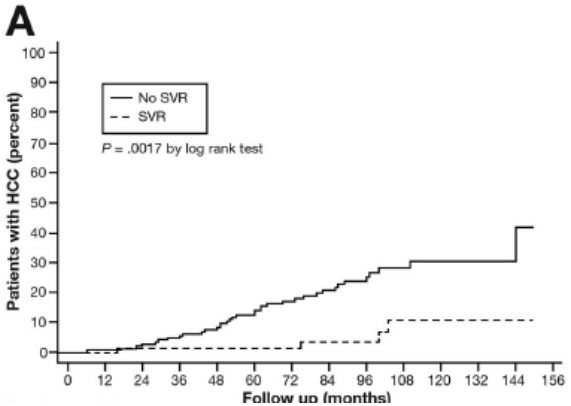
Effects of Eradicating Hepatitis C Virus Infection in Patients With Cirrhosis Differ With Stage of Portal Hypertension

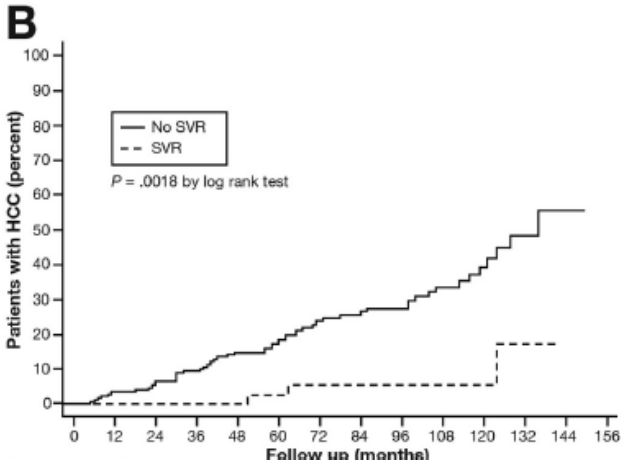
Vito Di Marco et al Gastroenterology 2016

HCV eradication reduced risk for liver decompensation, HCC, and death

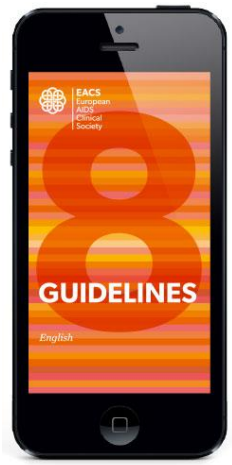








Linee guida di trattamento



SIMIT
Società Italiana di Malattie Infettive e Tropicali

In collaborazione con:

Ministero della Salute

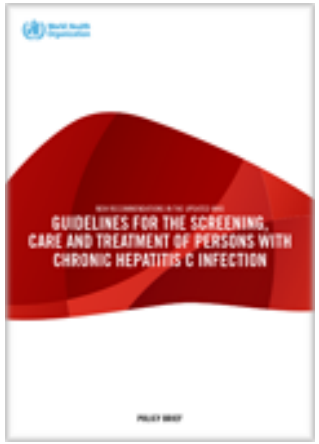
Sezioni L e M del Comitato Tecnico Sanitario

Linee Guida Italiane sull'utilizzo dei farmaci antiretrovirali e sulla gestione diagnostico-clinica delle persone con infezione da HIV-1

22 Novembre 2016

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

IDSA
Infectious Diseases Society of America



A I S F

ASSOCIAZIONE ITALIANA PER LO STUDIO DEL FEGATO

Riconosciuta con D.M. del 7.5.1998, G.U. del 20.6.1998
Iscritta nell'Elenco di cui all'art. 1, comma 353, della Legge 23.12.2005 n. 266, D.P.C.M. 15.4.2011
Iscritta nell'Elenco di cui all'art. 14, comma 1, del D.L. 14.3.2005, n. 35, convertito nella Legge 14.5.2005 n. 80, D.P.C.M. 15.4.2011

PUBLIC AFFAIRS AWARDS
ECCELLENZA 2011
SOCIETA' ASSOCIAZIONI SCIENTIFICHE

Documento di indirizzo

dell'Associazione Italiana per lo Studio del Fegato

per l'uso razionale di antivirali diretti

di seconda generazione nelle categorie di pazienti affetti

da epatite C cronica ammesse alla rimborsabilità

in Italia

Documento pubblicato on line in data 17 Dicembre 2014

Linee guida di trattamento

Factors to be considered in prioritizing treatment

(WHO 2016)

- Increased risk of death:
  - advanced fibrosis and cirrhosis
  - post-liver transplantation
- Risk of accelerated fibrosis:
  - coinfection with either HIV or hepatitis B virus (HBV)
  - metabolic syndrome
- Extrahepatic manifestations and evidence of end-organ damage
  - debilitating fatigue
  - vasculitis and lymphoproliferative disorders
- Significant psychosocial morbidity (due to stigma, discrimination, fear of transmission to others)
- Maximizing reduction in incidence:
  - PWID
  - men who have sex with men (MSM)
  - prisoners
  - sex workers
  - women with childbearing potential
  - health-care workers

Linee guida di trattamento

HCV Treatment Options in HCV/HIV Co-infected Persons

IFN-free HCV Treatment Options				
HCV GT	**Treatment regimen**	**Treatment duration & ribavirin usage**		
		Non-cirrhotic	**Compensated cirrhotic**	**Decompensated cirrhotics CTP class B/C**
1 & 4	SOF + SMP +/- RBV	GT 4 only: 12 weeks with RBV or 24 weeks without RBV[i]		Not recommended
	SOF/LDV +/- RBV	8 weeks without RBV[ii] or 12 weeks +/- RBV[iii]	12 weeks +/- RBV or 24 weeks without RBV[iv]	
	SOF + DCV +/- RBV	12 weeks +/- RBV[iii]	12 weeks +/- RBV or 24 weeks without RBV[iv]	
	SOF + VEL	12 weeks		12 weeks with RBV
	OBV/PTV/r + DSV	8[v]-12 weeks in GT 1b	12 weeks in GT 1b	Not recommended
	OBV/PTV/r + DSV + RBV	12 weeks in GT 1a	24 weeks in GT 1a	Not recommended
	OBV/PTV/r + RBV	12 weeks in GT 4		Not recommended
	EBR + GZR	12 weeks[vi]		Not recommended
2	SOF + DCV	12 weeks		12 weeks with RBV
	SOF + VEL	12 weeks		12 weeks with RBV
3	SOF + DCV +/- RBV	12 weeks +/- RBV[vii] or 24 weeks without RBV	24 weeks with RBV	
	SOF + VEL +/- RBV	12 weeks +/- RBV[vii] or 24 weeks without RBV		24 weeks with RBV
5 & 6	SOF/LDV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV[i]	12 weeks with RBV or 24 weeks without RBV[i]	12 weeks with RBV or 24 weeks without RBV
	SOF + DCV +/- RBV	12 weeks +/- RBV or 24 weeks without RBV[i]	12 weeks with RBV or 24 weeks without RBV[i]	12 weeks with RBV or 24 weeks without RBV
	SOF + VEL	12 weeks		12 weeks with RBV

(EACS 2017)

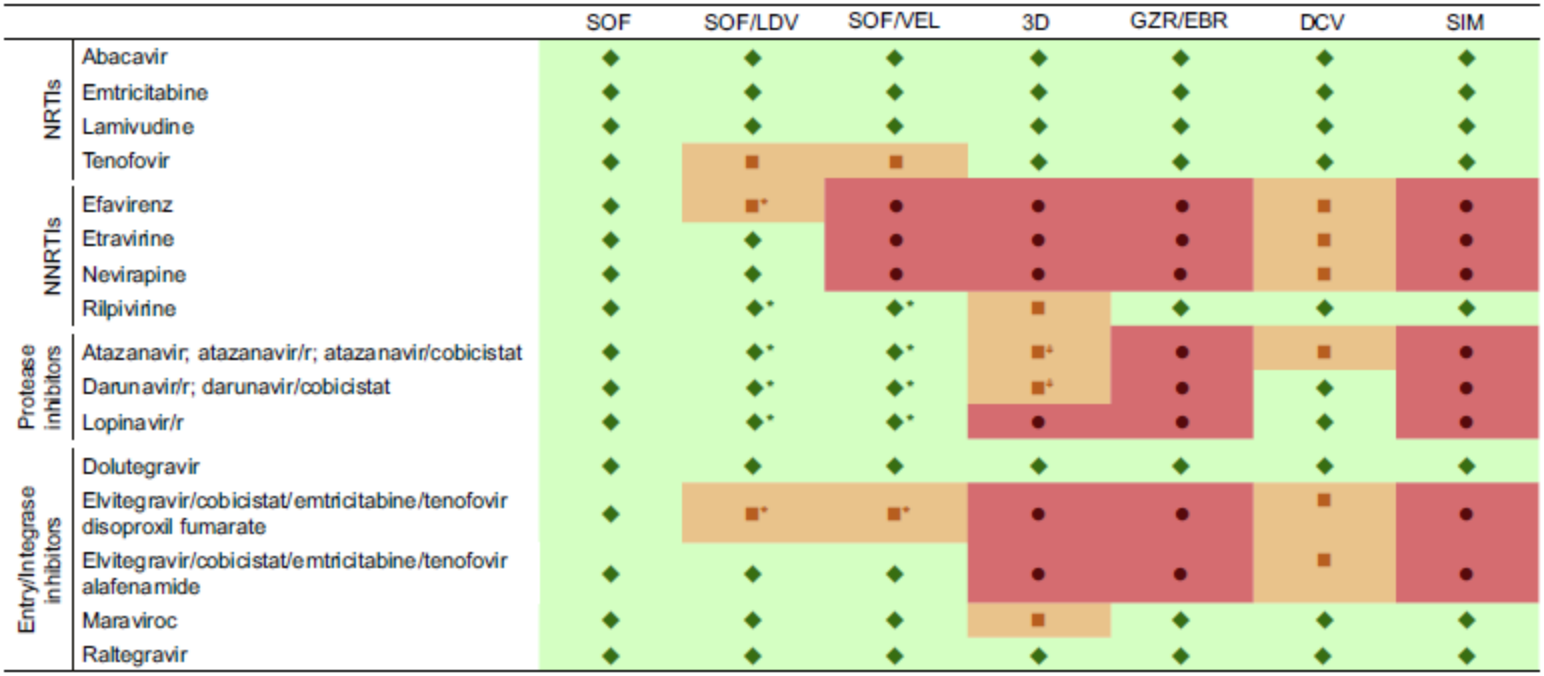
Linee guida di trattamento

Table 7. Treatment recommendations for HCV-monoinfected or HCV/HIV coinfected patients with chronic hepatitis C with compensated (Child-Pugh A) cirrhosis, including treatment-naïve patients and patients who failed on a treatment based on pegylated IFN-α and ribavirin (treatment-experienced, DAA-naïve patients).

Patients	Treatment-naïve or -experienced	Sofosbuvir/ ledipasvir	Sofosbuvir/ velpatasvir	Ombitasvir/ paritaprevir/ ritonavir and dasabuvir	Ombitasvir/ paritaprevir/ ritonavir	Grazoprevir/ elbasvir	Sofosbuvir and daclatasvir	Sofosbuvir and simeprevir
Genotype 1a	Treatment-naïve	12 wk, no ribavirin	12 wk, no ribavirin	24 wk with ribavirin	No	12 wk, no ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml or 16 wk with ribavirin if HCV RNA >800,000 (5.9 log) IU/ml[b]	12 wk, no ribavirin	No
	Treatment-experienced	12 wk with ribavirin[a] or 24 wk, no ribavirin					12 wk with ribavirin[a] or 24 wk, no ribavirin	
Genotype 1b	Treatment-naïve	12 wk, no ribavirin	12 wk, no ribavirin	12 wk, no ribavirin	No	12 wk, no ribavirin	12 wk, no ribavirin	No
	Treatment-experienced							
Genotype 2	Both	No	12 wk, no ribavirin	No	No	No	12 wk, no ribavirin	No
Genotype 3	Treatment-naïve	No	12 wk with ribavirin[c] or 24 wk, no ribavirin	No	No	No	24 wk with ribavirin	No
	Treatment-experienced							
Genotype 4	Treatment-naïve	12 wk, no ribavirin	12 wk, no ribavirin	No	12 wk with ribavirin	12 wk, no ribavirin	12 wk, no ribavirin	12 wk, no ribavirin
	Treatment-experienced	12 wk with ribavirin or 24 wk, no ribavirin				12 wk, no ribavirin if HCV RNA ≤800,000 (5.9 log) IU/ml or 16 wk with ribavirin if HCV RNA >800,000 (5.9 log) IU/ml	12 wk with ribavirin or 24 wk, no ribavirin	12 wk with ribavirin or 24 wk, no ribavirin
Genotype 5 or 6	Treatment-naïve	12 wk, no ribavirin	12 wk, no ribavirin	No	No	No	12 wk, no ribavirin	No
	Treatment-experienced	12 wk with ribavirin or 24 wk, no ribavirin					12 wk with ribavirin or 24 wk, no ribavirin	

EASL 2016

Linee guida di trattamento



SOF, sofosbuvir; SOF/LDV, sofosbuvir plus ledipasvir; SOF/VEL, sofosbuvir plus velpatasvir; 3D, ritonavir-boosted paritaprevir, plus ombitasvir and dasabuvir; GZR/EBR, grazoprevir plus elbasvir; DCV, daclatasvir; SIM, simeprevir; r, ritonavir.

EASL 2016

Lack of clinically important PK interaction between coformulated ledipasvir/sofosbuvir and rilpivirine/emtricitabine /tenofovir alafenamide

Randomized , open label, single center, multiple dose, phase 1 study in 42 healthy subjects

Custodio JM et al
Pharmacol Res Perspect Oct 2017

Linee guida di trattamento

Individuazione del paziente a rischio elevato

PERCORSO DI VALUTAZIONE	RACCOMANDAZIONI/NOTE	RACCOMANDAZIONE (FORZA/EVIDENZA)	RIFERIMENTI BIBLIOGRAFICI
Individuazione dei fattori di rischio	In tutti i pazienti con ipertransaminasemia è indicato uno screening epatologico che comprende lo studio per coinfezioni virali, un'indagine circa l'uso di alcol o di farmaci epatotossici, l'epatosteatosi (NAFLD) o la steatosi associata a HCV (soprattutto genotipo), la steatoepatite (NASH), l'emosiderosi e cause non epatiche di rialzo delle transaminasi (malattia celiaca, miopatia, ipertensione portale, malattie autoimmuni) malattie rare eredometaboliche.	[AII]	[1-3]
	Identificare i pazienti con *Non Alcoholic Fatty Liver Disease* (NAFLD) è importante in quanto tale condizione può assumere un decorso evolutivo progredendo attraverso una fase infiammatoria definita *Non Alcoholic Steato-Hepatitis* (NASH), fino alla fibrosi; la NAFDL può, inoltre, indurre alterazioni metaboliche che favoriscono l'aterosclerosi.	[AII]	[4]
	I pazienti efficacemente trattati per malattia da HCV richiedono un monitoraggio periodico del rischio di sviluppare complicanze associate all'epatopatia cronica.	[AII]	[5]
Stima del rischio	In tutti i pazienti con ipertransaminasemia è indicata una valutazione ecografica e il monitoraggio del FIB-4 score. Nei pazienti con ipertransaminasemia persistente di diagnosi indeterminata, anche dopo gli esami ematici e strumentali, è raccomandata la biopsia epatica per accertare l'eziologia e l'entità del danno epatico.	[BIII] [BIII]	[6,7]
Valutazione individuale di vulnerabilità	Nei pazienti con alterazioni metaboliche (dislipidemia), diabetici o obesi eseguire un'ecografia per valutare la presenza di NAFLD. La Tomografia Computerizzata (TC) e la Risonanza Magnetica Nucleare (RMN) possono essere utilizzate come approfondimento diagnostico in casi selezionati.	[AII]	[8]
	La NAFLD individua i pazienti a rischio aumentato di malattia cardiovascolare e diabete.	[AII]	[9]

Linee guida italiane 2017

La possibilità di generalizzare i risultati ottenuti nei trial clinici all'intera popolazione con co-infezione da HIV/HCV è incerta a causa della scarsa rappresentatività dei pazienti inclusi negli studi

Figure 1. Green figures represent the number of Canadian Coinfection Cohort participants who would be eligible to be screened in NCT01479868 (trial evaluating simeprevir); PHOTON-1: NCT01667731 (trial evaluating sofosbuvir); TURQUOISE-I: NCT01939197 (trial evaluating ombitasvir, paritaprevir/ritonavir/dasabuvir [3D]); ION-4: NCT02073656 (trial evaluating ledipasvir/sofosbuvir); and ALLY-2: NCT02032888 (trial evaluating daclatasvir/sofosbuvir). Gray figures represent participants whose only exclusion was specific antiretroviral (ARV) therapies. Red figures represent participants not eligible regardless of ARV restriction.

Clinical Infectious Diseases

MAJOR ARTICLE

HIV/AIDS

How Generalizable Are the Results From Trials of Direct Antiviral Agents to People Coinfected With HIV/HCV in the Real World?

Sahar Saeed,[1,2] Erin C. Strumpf,[2,3] Sharon L. Walmsley,[4,5] Kathleen Rollet-Kurhajec,[1] Neora Pick,[6] Valerie Martel-Laferrière,[7] Mark Hull,[8] M. John Gill,[9] Joseph Cox,[2,10] Curtis Cooper,[11] and Marina B. Klein[1,5]; for the Canadian Co-Infection Cohort Study

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DAA garantiscono SVR12 >90% nei pazienti HIV/HCV

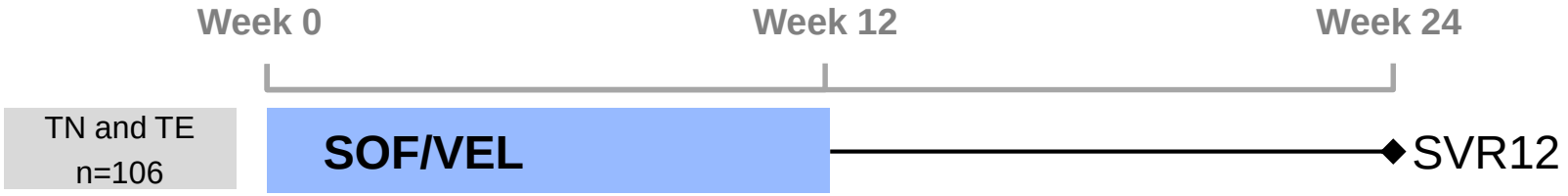
Table 1. Controlled studies on efficacy of interferon-free anti-hepatitis C virus treatments in coinfected patients.

Study	Screened patients	Enrolled patients	Screening failure	Treatment schedule	cART allowed	SVR 12 N /tot % (95% CI)								SAE *n* (%)
						G1	G1 (Cirrhosis)	G2	G2 (Cirrhosis)	G3	G3 (Cirrhosis)	G4	G4 (Cirrhosis)	
PHOTON I + PHOTON II	676	497	177/676 26% (23–29%)	SOF + R 24 weeks SOF + R 12 weeks	TDF/FTC + all	182/226 80% (75–85%)	14/22 64% (54–74%)	67/75 89% (76–100%)	6/6 2/2	110/123 89% (84–94%) 28/42 67% (53–81%)	26/32 81% (68–94%) 4/6	26/31 84% (71–97%)	7/8	29 6%
Turquoise I	113	63	50/113 44% (35–54%)	3D + R 12 weeks 3D + R 24 weeks	ATZ or RAL	29/31 94% (79–98%) 29/32 91% (76–97%)	5/6 5/6							0
ION-4	429	335	94/429 22% (18–26%)	LDV + SOF 12 weeks	EFV or RIL or RAL+ TDF/ FTC	314/327 96% (94–98%)	63/67 94% (85–98%)					8/8		8 2.4%
ALLY-2	238	203	35/238 14% (10–18%)	DAC + SOF + R 12 weeks DAC + SOF + R 8 weeks	All	123/127 97% (94–100%) 31/41 76% (58–94%)	20/22 91% (79–93%) 2/4	13/13	1/1	10/10	1/1 1/1	3/3	-	4 1.6%
C-EDGE	261	218	43/261 16% (11–20%)	GRAZ + ELB	RAL/ DOLU/ RIL + 2 NUC	178/188 95% (92–98%)	35/35 100%					27/28 96% (90–100%)		2 1%

3D, paritaprevir/ritonavir/ombitasvir + dasabuvir; ATZ, atazanavir; cART, combination antiretroviral therapy; DAC, daclatasvir; DOLU, dolutegravir; ELB, elbasvir; FTC, emtricitabina; GRAZ, grazoprecvir; LDV, ledipasvir; NUC, nucleoside analogues; RAL, raltegravir; RIL, rilpivirina; SAE, serious adverse events; SQF, sofosbuvir; SVR, sustained virological response; TDF, tenofovir.

AIDS 2016

SOF/VEL for 12 Weeks in HCV/HIV Co-Infected Patients



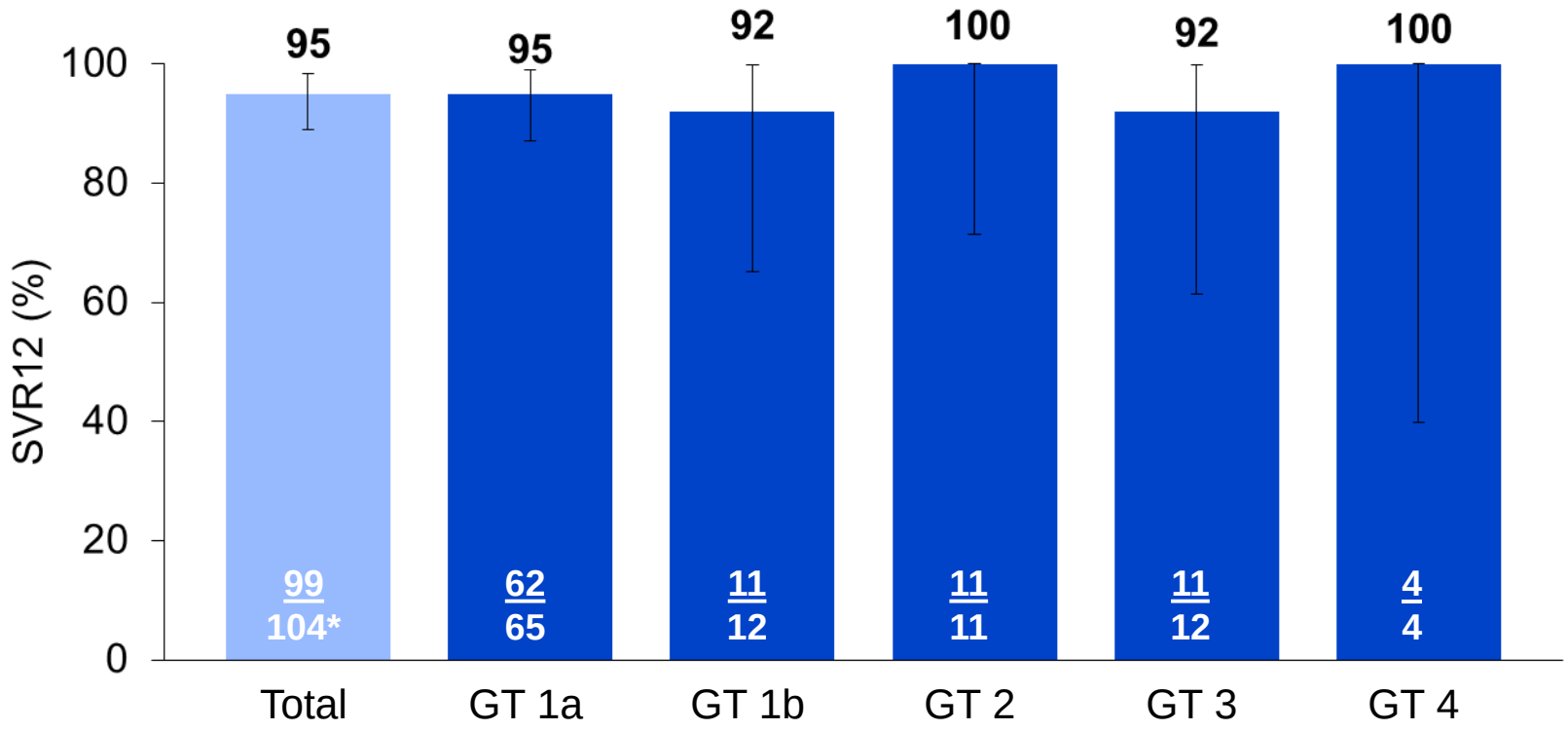
	SOF/VEL N=106
Mean age, y (range)	54 (25–72)
Male, n (%)	91 (86)
Black, n (%)	48 (45)
Mean BMI, kg/m^2 (range)	27 (19–43)
Cirrhosis, n (%)	19 (18)
Treatment experienced,* n (%)	31 (29)
IL28B CC, n (%)	24 (23)
Mean HCV RNA, $\log_{10}$ IU/mL (range)	6.3 (5.0–7.4)
HCV genotype	
1a / 1b	66 (62) / 12 (11)
2	11 (10)
3	12 (11)
4	5 (5)

	SOF/VEL N=106
Mean CD4 count, cells/μL (range)	598 (183–1513)
NRTI backbone	
TDF-based with boosted agent (RTV or COBI)	56 (53)
TDF-based without boosted agent	35 (33)
ABC/3TC-base	15 (14)
ART use at baseline	
PI (DRV, LPV or ATV)	50 (47)
NNRTI (RPV)	13 (12)
Integrase inhibitor (RAL or EVG)	36 (34)
Other (>1 of the above classes)	7 (7)

*Includes PegIFN+RBV failures and PI + PegIFN+RBV failures.

Wyles, EASL 2016, PS104

Results: SVR12 by Genotype



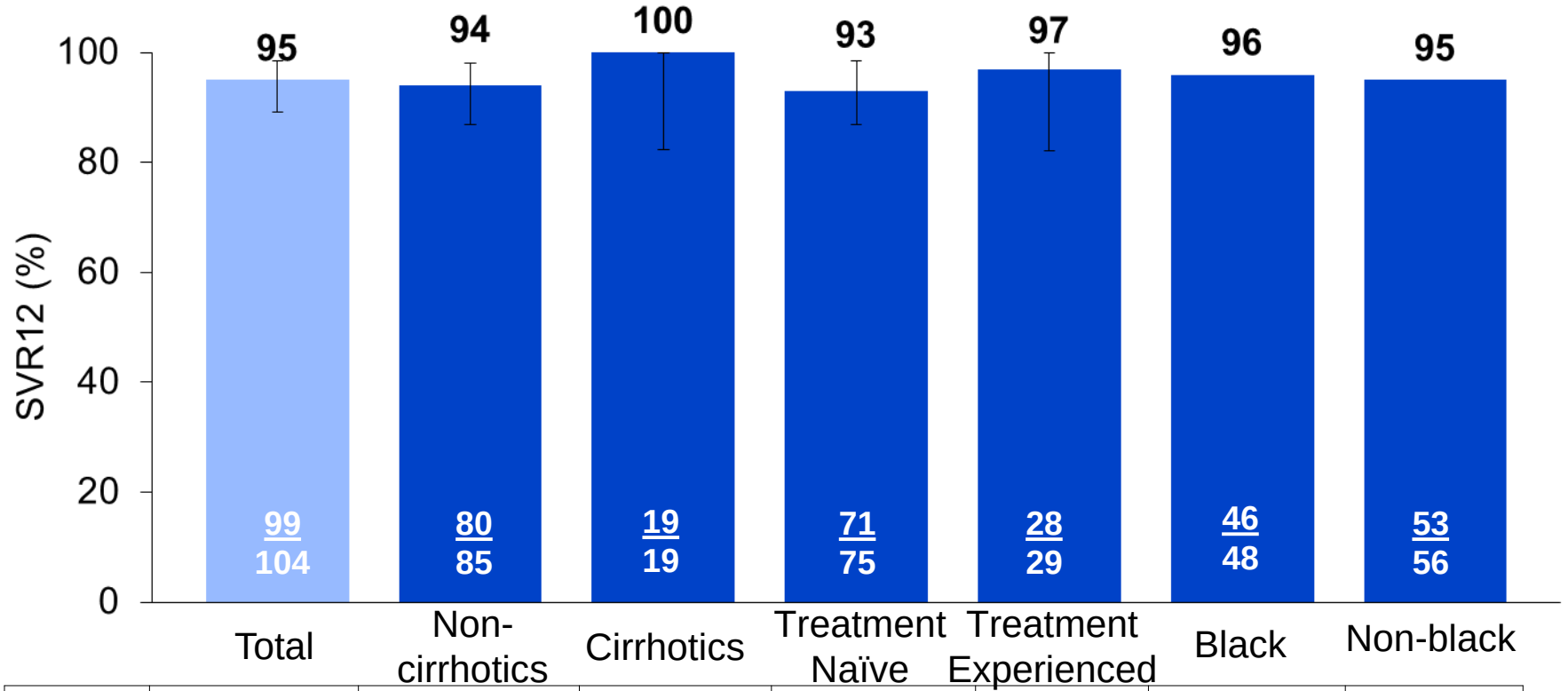
	Total	GT 1a	GT 1b	GT 2	GT 3	GT 4
Relapses	2	2	-	-	-	-
LTFU	2†	1†	1†	-	-	-
W/C	1	-	-	-	1	-

High SVR12 achieved in HIV-coinfected patients regardless of genotype

*Two patients pending results
†Patients LTFU were incarcerated, one patient on Day 1 and one patient on Week 4

LTFU, lost to follow-up. W/C, withdraw consent. Error bars represent 95% confidence intervals.
Wyles, EASL 2016, PS104

Results: SVR12 by Cirrhosis or Prior Treatment



	Total	Non-cirrhotics	Cirrhotics	Treatment Naïve	Treatment Experienced	Black	Non-black
Relapses	2	2	-	1	1	2	0
LTFU	2*	2*	-	2*	-	0	2
W/C	1	1	-	1	-	0	1

High SVR12 achieved in HIV-coinfected patients regardless cirrhosis status and treatment experience

*Patients LTFU were incarcerated, one patient on Day 1 and one patient on Week 4

LTFU, lost to follow-up. W/C, withdraw consent. Error bars represent 95% confidence intervals.

Wyles, EASL 2016, PS104

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6
C-EDGE CO-INFECTION: Study Features

C-EDGE Trial

- **Design**: Prospective, open-label, single-arm study examining the safety and efficacy of a fixed-dose combination of elbasvir-grazoprevir for 12 weeks in treatment-naïve patients with chronic HCV genotype 1, 4, or 6 and HIV coinfection.
- **Entry Criteria**
  - Chronic HCV Genotype 1, 4, or 6
  - 18 years or older
  - HCV RNA ≥10,000 IU/mL
  - No prior treatment
  - Compensated cirrhosis permitted
  - HIV infection
- **Primary End-Point**: SVR12

Source: Rockstroh JK, et al. Lancet HIV. 2015;2:e319-27.

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6
C-EDGE CO-INFECTION: Participants

Baseline Characteristic	**Elbasvir-Grazoprevir** (N=218)
Age, mean	49
Male, n (%)	183 (84%)
Race, n (%) White Black or African-American Other	 167 (77%) 38 (17%) 13 (6%)
HCV genotype, n (%) 1a 1b 4 6	 144 (66%) 44 (20%) 28 (13%) 2 (1%)
Fibrosis stage, n (%) F0-2 F3 F4	 160 (73%) 23 (11%) 35 (16%)
Mean baseline HCV RNA, $\log_{10}$ IU/ml	6.03

Source: Rockstroh JK, et al. Lancet HIV. 2015;2:e319-27.

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6
C-EDGE CO-INFECTION: Participants

HIV Characteristics	**Elbasvir-Grazoprevir** (N=218)
Median CD4 cell count, (IQR)	568 (424-766)
ART Status	
On ART with undetectable HIV RNA	211 (97%)
ART naïve	7 (3%)
ART nucleos(t)ide pair	
Abacavir-containing	47 (22%)
Tenofovir-containing	164 (75%)
None	7 (3%)
ART Third Agent	
Raltegravir	113 (52%)
Dolutegravir	59 (27%)
Rilpivirine	38 (17%)
None	8 (4%)

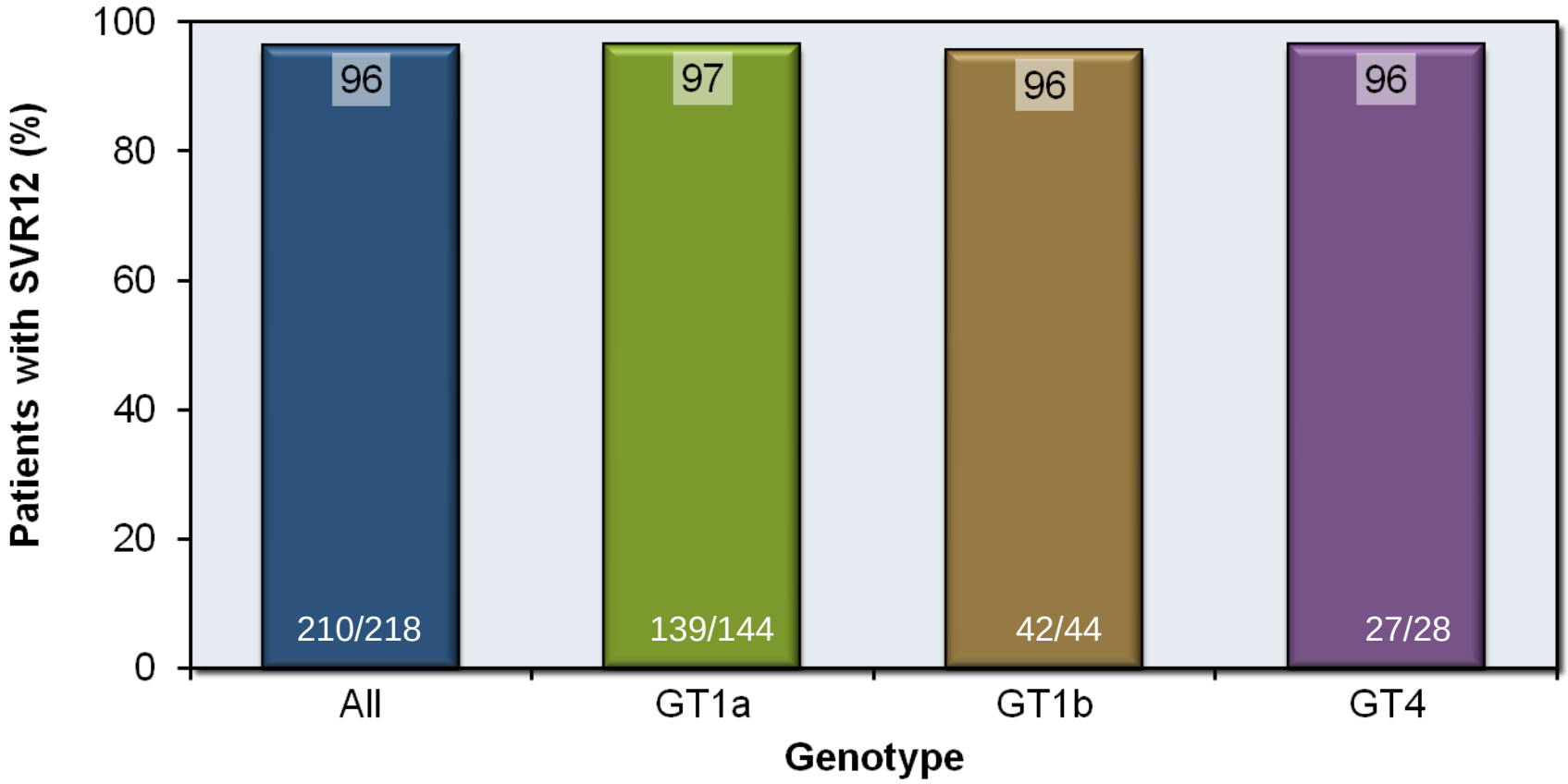
IQR = interquartile range; ART = antiretroviral therapy

Source: Rockstroh JK, et al. Lancet HIV. 2015;2:e319-27.

Hepatitis web study

Elbasvir-Grazoprevir in HCV-HIV Coinfection GT 1, 4 or 6
C-EDGE CO-INFECTION: Results

C-EDGE CO-INFECTION: SVR12 Results by Genotype



Overall SVR12 results includes the 2 patients with GT 6, who both achieved SVR12.

Source: Rockstroh JK, et al. Lancet HIV. 2015;2:e319-27.

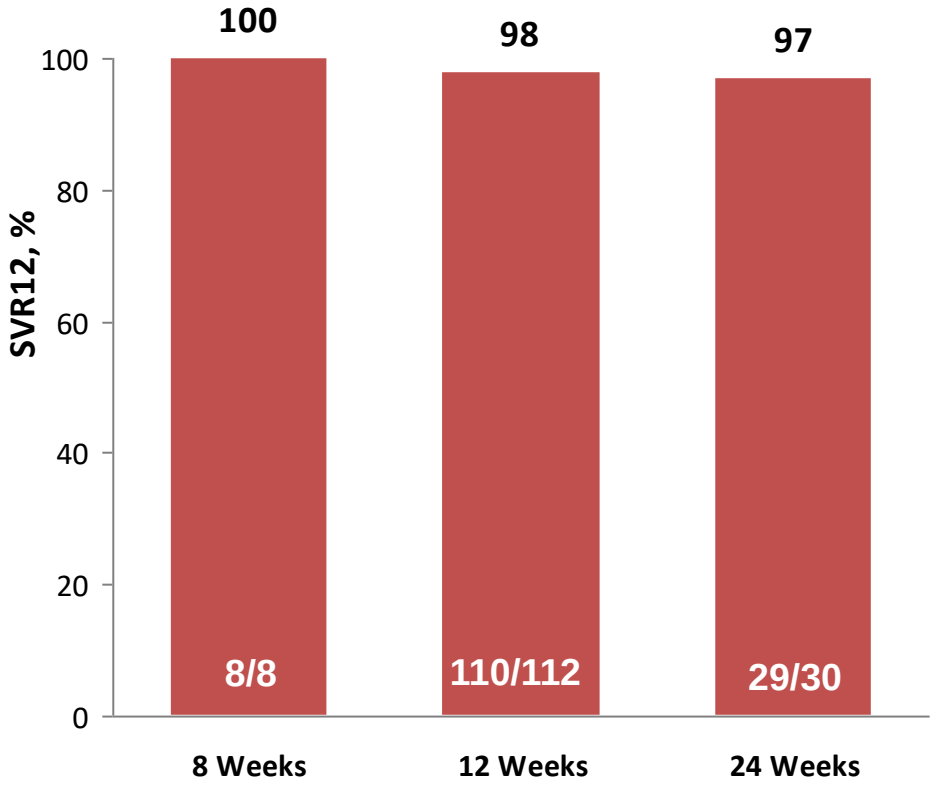
‡

LDV/SOF±RBV in 150 HIV/HCV Co-Infected Patients

Demographics

Patients, n (%)	Total N=150
Age, mean (range)	56 (36–84)
Academic practice	68 (45)
Male	105 (70)
Black	32 (21)
GT1a	120 (80)
Cirrhosis	53 (35)
Platelets <100,000/mL	15 (10)
Baseline RNA >6 MM IU/mL	32 (21)
Prior Treatment, n (%)	29 (19)
Prior Treatment unknown, n (%)	43 (28)
Treatment duration	
8	8 (5)
12	112 (75)
24	30 (20)

SVR12 by Duration (ITT)



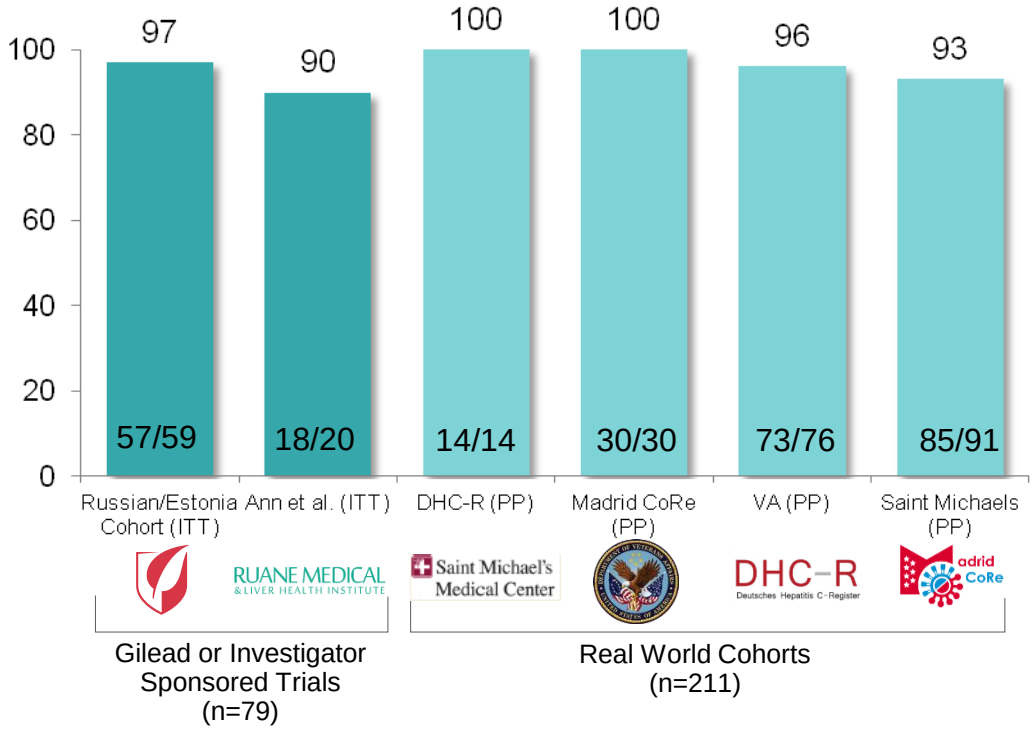
High SVR rates achieved in the Real-World heterogeneous HIV/HCV-coinfected population

Dieterich, EASL 2016, Poster SAT-134

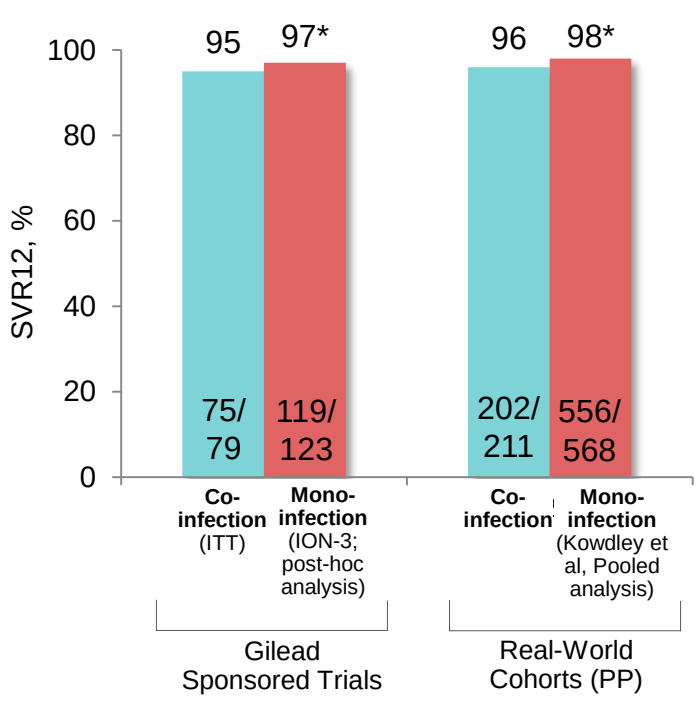
LDV/SOF for 8 Weeks in HIV/HCV Co-Infection

Analysis of LDV/SOF for 8 weeks in HCV GT with HIV/HCV co-infection from 2 prospective studies and 4 retrospective real-world cohorts

SVR12 LDV/SOF 8 weeks



SVR12 Mono vs Coinfected



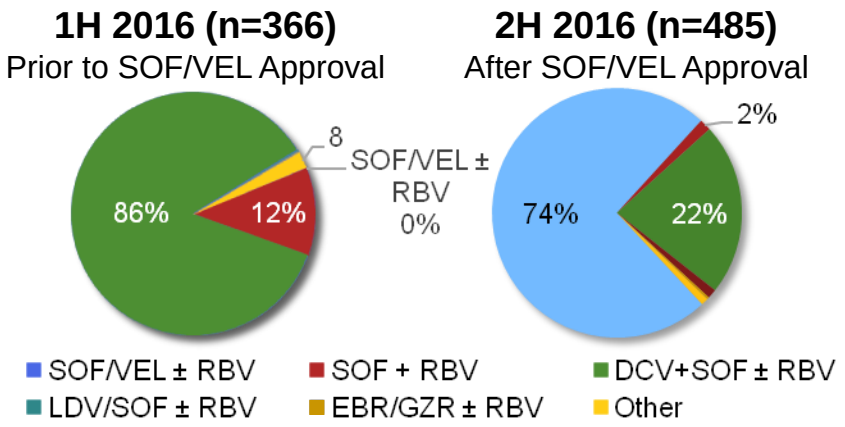
LDV/SOF 8 weeks achieved high SVR rates in HCV/HIV-coinfected patients across multiple cohorts and comparable to monoinfected individuals

Buggisch, EASL 2017, SAT-253

* TN, non-cirrhotic patients with HCV RNA<6 million IU/mL

Real-World Experience of SOF/VEL ± RBV in HCV GT 3

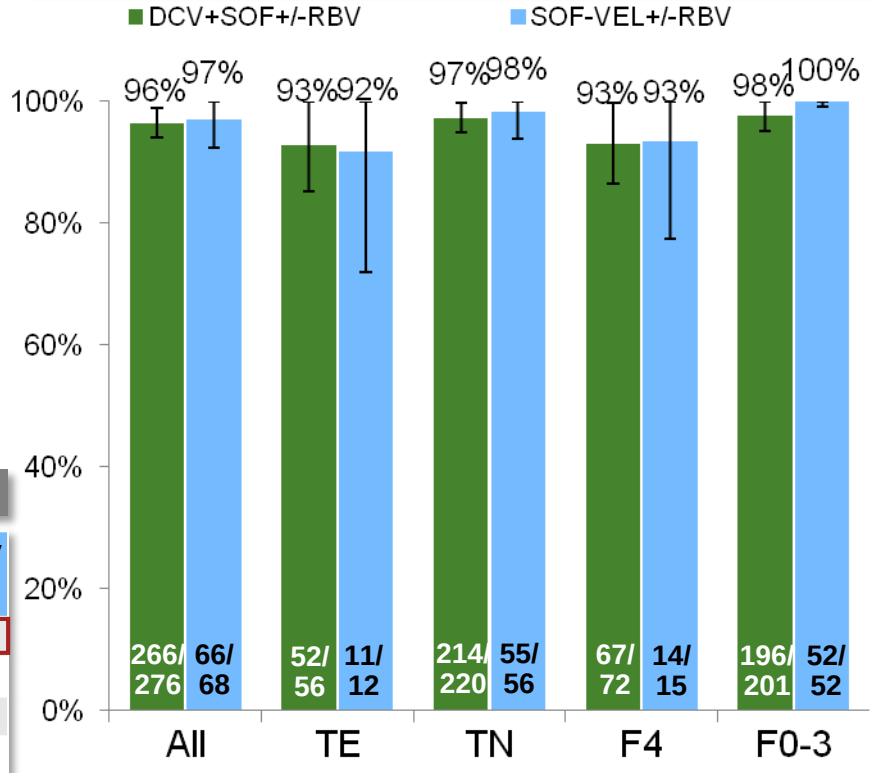
Treatment uptake



Baseline Demographics

	DCV+SOF ± RBV (n=392)	SOF/VEL ± RBV (n=244)
12 week schedule, n (%)	307 (78)	238 (98)
Other schedule, n (%)	82 (21)	6 (2)
+ RBV, n (%)	78 (20)	35 (14)
Age - mean (range)	54 (22-81)	52 (21-83)
Male, n (%)	224 (57)	140 (57)
HIV coinfection, n (%)	7 (2)	5 (4)
TE, n (%)	82 (21)	54 (22)
F4, n (%)	110 (29)	69 (29)
CKD, n (%)	99 (26)	64 (27)
Diabetes, n (%)	46 (13)	33 (14)

SVR12 (PP)



In this RW cohort, high SVR12 was achieved with SOF/VEL in GT3 patients confirm the results observed in ASTRAL-3

Curry, EASL 2017, PS-102

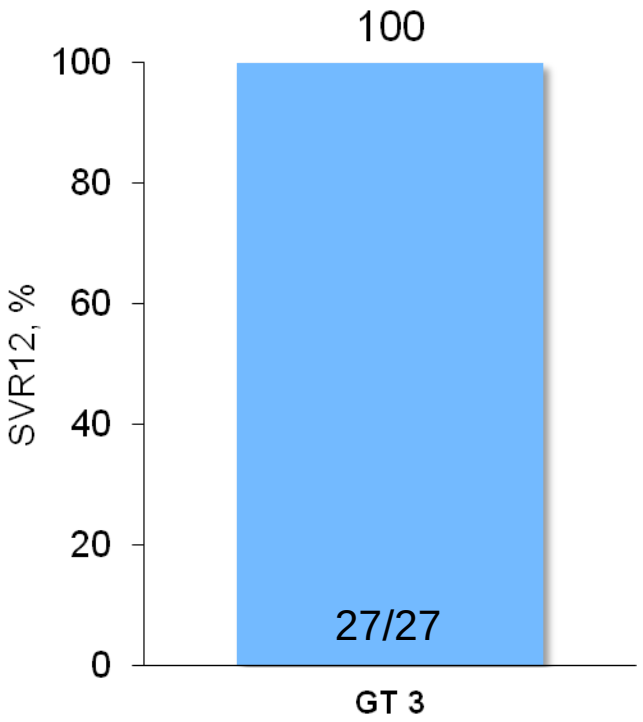
Real-World Effectiveness of SOF/VEL

Characterization, effectiveness, and cost/SVR of population receiving SOF/VEL ± RBV in clinical practice in Germany

Baseline Demographics

	GT 3 N=79	Non-GT 3 N=26
Median age (range), years	48 (26-69)	56 (31-76)
Males, n (%)	61 (77)	14 (54)
White, n (%)	74 (94)	22 (85)
F4 Metavir score, n (%)	39 (49)	9 (35)
Decompensated cirrhosis	5(6)	1(4)
TN, n (%)	65 (82)	21 (81)
TE, n (%)	14 (18)	5 (19)
HIV co-infection , n (%)	3 (4)	2 (8)

SVR4/12 (PP)



1 (1.3%) AEs led to D/C in GT3 patients
In GT 3 patients, RBV was added in 7% in F0-F3, 78% in F4 compensated, 100% in F4 Decompensated

All GT3 patients who completed treatment achieved SVR12

Buggisch, EASL 2017, SAT-254

Real-World Experience of EBR/GZR in the VA Healthcare System

THE INTERNATIONAL LIVER CONGRESS™ 2017
19-23 APRIL, AMSTERDAM, THE NETHERLANDS

Characteristics	EBR/GZR REGIMENS N = 2,436
Age, mean (S.D)	63.5 (5.9)
Male, n (%)	2350 (96.5)
Race/ethnicity, n (%)	
African American	1400 (57.5)
White	824 (33.8)
Hispanic	81 (3.3)
Other	35 (1.4)
Genotype, n (%)	
GT1 (all)**	2324 (95.4)
GT1a	844 (36.3)
GT1b	1428 (61.5)
GT2, GT3	6 (0.3)
GT4	64 (2.6)
BVL >800,000 IU/ml, n (%)*	1560 (67.9)

Characteristics	EBR/GZR REGIMENS N = 2,436
Comorbidities, n (%)	
Cirrhosis	808 (33.2)
CKD (stage 3-5)	800 (32.8)
Depression	1394 (57.2)
Diabetes	1295 (53.2)
History of drug abuse †	1313 (53.9)
History of alcohol abuse†	1473 (60.5)
HIV	74 (3.0)
Prior Treatment, n (%)	
Treatment naïve	1988 (81.6)
Previous treatment	
prior PEG+/- RBV	316 (13.0)
prior BOC/TEL	6 (0.3)
prior SOF/SIM+SOF	9 (0.4)
prior LDV/SOF	82 (3.4)
prior PrOD	35 (1.4)

GT: Genotype; Other = Asian/Pacific Islander/American Indian/Alaska Native; BVL: Baseline viral load; EP: Evaluable population
*Denominator of BVL = 2,326 (missing = 110) ; **missing GT1 subtypes not displayed ;
† Chronic conditions including history of drug abuse or alcohol abuse data were captured through ICD-9 codes at any time prior to HCV treatment

J.R. Kramer et al. Real world experience with elbasvir/grazoprevir in the Veterans Affairs Healthcare System. J.Hepatol PS-095 EASL 2017 Amsterdam

Real-World Experience of EBR/GZR in the VA Healthcare System

THE INTERNATIONAL LIVER CONGRESS™ 2017
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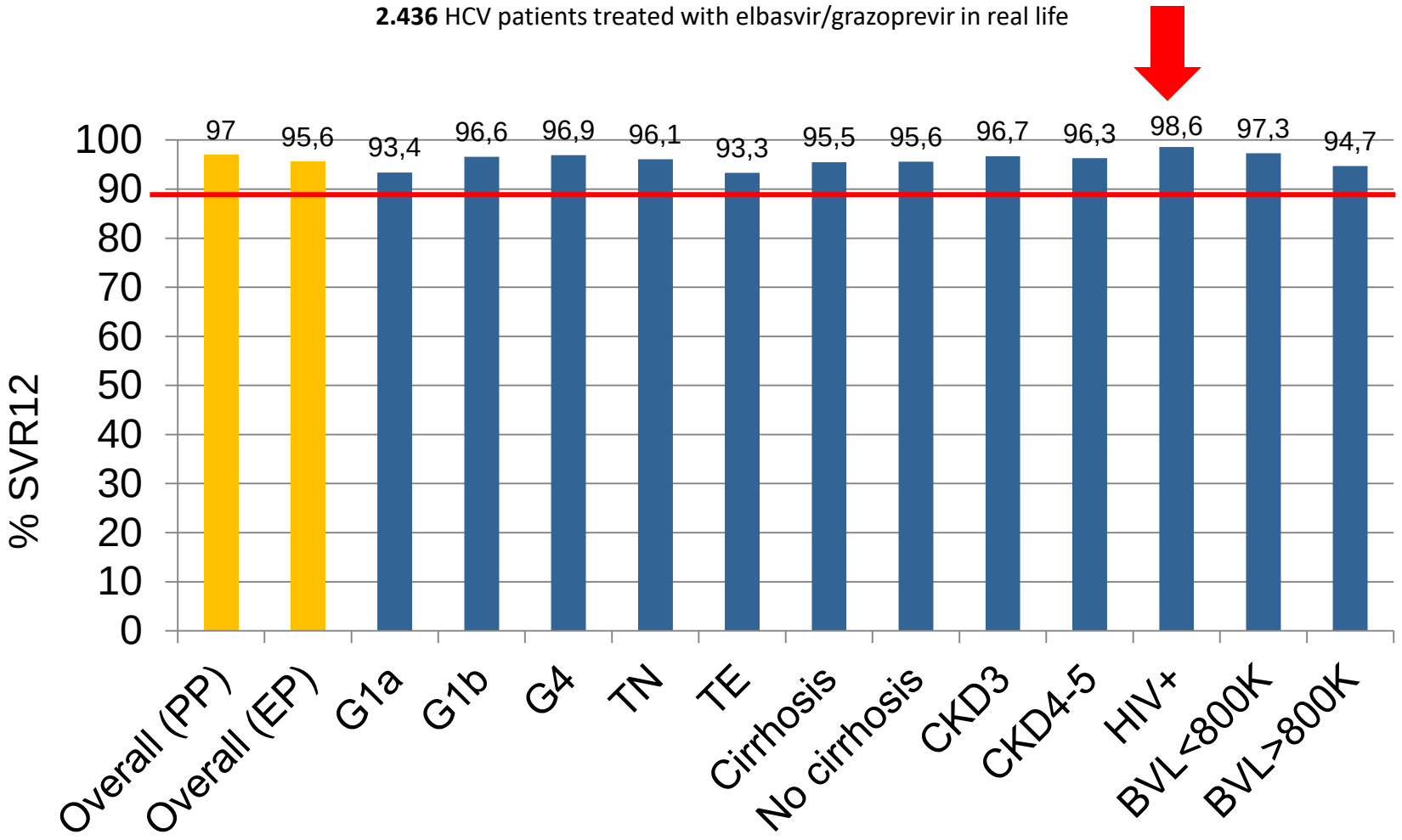
Retrospective analysis from US Department of Veterans Affairs (VA)

2.436 HCV patients treated with elbasvir/grazoprevir in real life



J.R. Kramer et al. Real world experience with elbasvir/grazoprevir in the Veterans Affairs Healthcare System. J.Hepatol PS-095 EASL 2017. Amsterdam.

Hepatitis web study

Efficacy and safety of direct-acting antiviral regimens in HIV/HCV-co-infected patients - French ANRS CO13 HEPAVIH cohort

J Hepatol. 2017

- A total of **323** patients (74% men), 99% of whom were on combination antiretroviral therapy (cART).
- HIV RNA load was <50 copies/ml in 88% of patients; median CD4 cell count was 540/mm3; 60% of patients were cirrhotic;
- cART was protease inhibitor (PI)-based in 23%, non-nucleoside reverse transcriptase inhibitor (NNRTI)-based in 15%, and integrase inhibitor (II)-based in 38%, while 24% of patients received other regimens.
- **The SVR12 rate was 93.5% overall (95% confidence interval [CI]: 90.2-95.9), 93.3% (88.8-96.4) in patients with cirrhosis and 93.8% (88.1-97.3) in patients without cirrhosis**.
- The SVR12 rates were 93.1% (84.5-97.7), 91.8% (80.4-97.7) and 95.8% (90.5-98.6) respectively, in patients receiving PI-based, NNRTI-based and II-based cART. In adjusted analysis, SVR12 was not associated with HIV RNA load, the cART regimen, cirrhosis, prior anti-HCV treatment, the duration of anti-HCV therapy, or ribavirin use.

Next Generation Direct-Acting Antivirals

Glecaprevir
(formerly ABT-493)
pangenotypic NS3/4A protease inhibitor

Coformulated: G/P

Pibrentasvir
(formerly ABT-530)
pangenotypic NS5A inhibitor

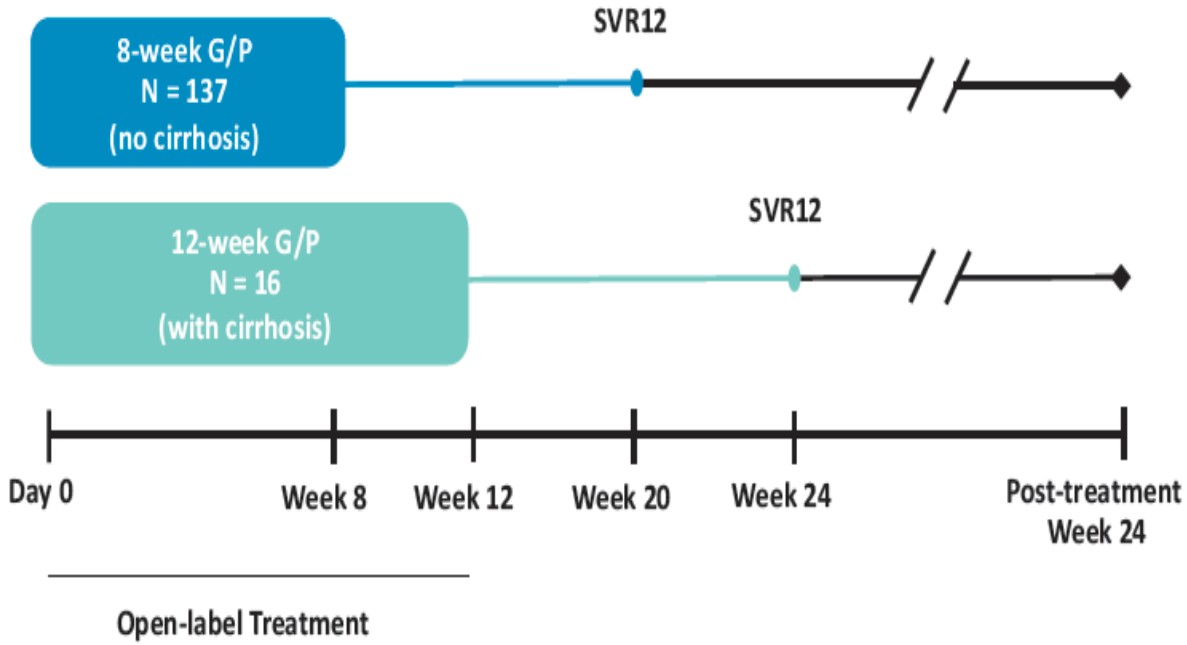
In vitro:[5]
- High barrier to resistance
- Potent against common NS3 polymorphisms (eg, positions 80, 155, and 168) and NS5A polymorphisms (eg, positions 28, 30, 31, and 93)
- Synergistic antiviral activity

Clinical PK & metabolism:
- Once-daily oral dosing
- Minimal metabolism and primary biliary excretion
- Negligible renal excretion (<1%)

G/P is coformulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg.
Glecaprevir was identified by AbbVie and Enanta.

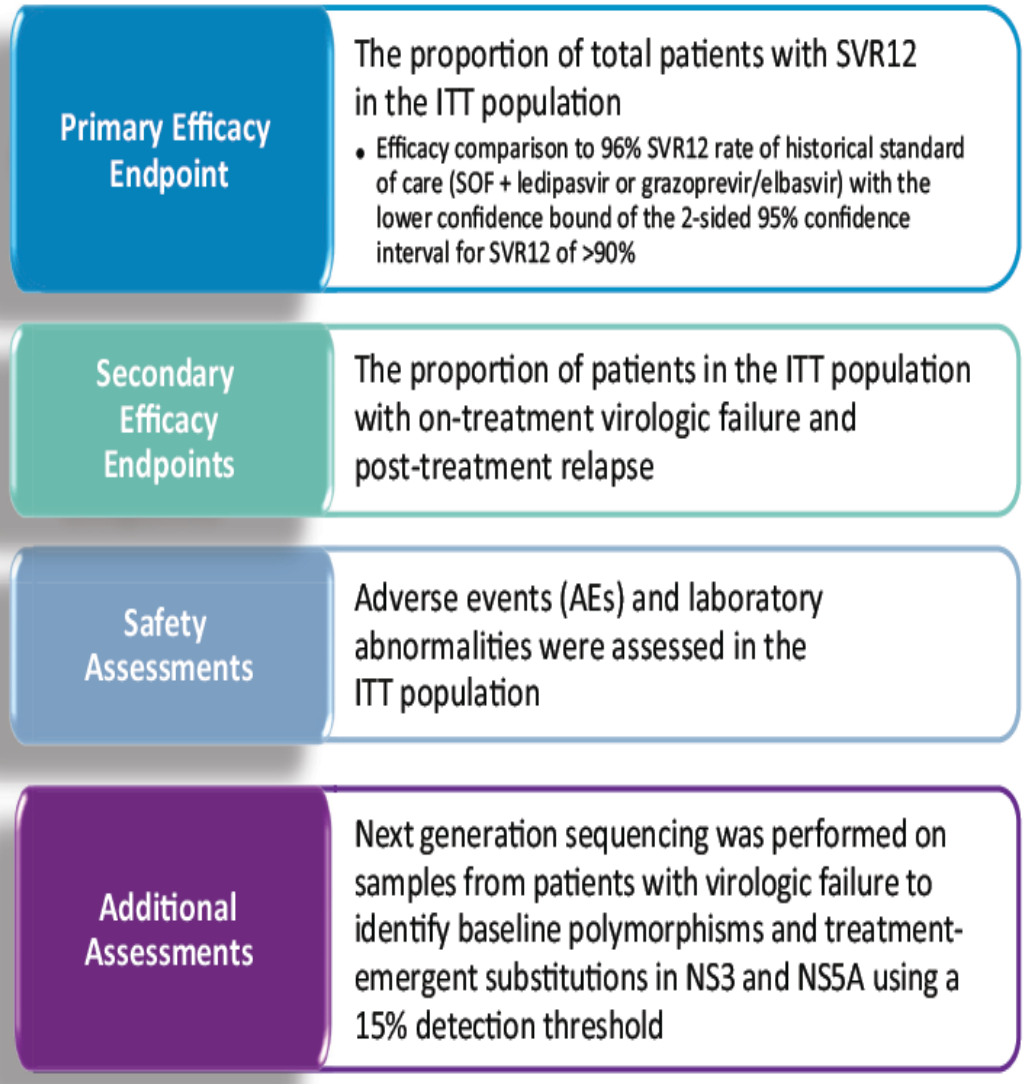
Objective and Study Design

- EXPEDITION-2 is a phase 3, multicenter global study evaluating 8- or 12-week treatment with G/P in HCV/HIV-1 co-infected adults without or with compensated cirrhosis, respectively



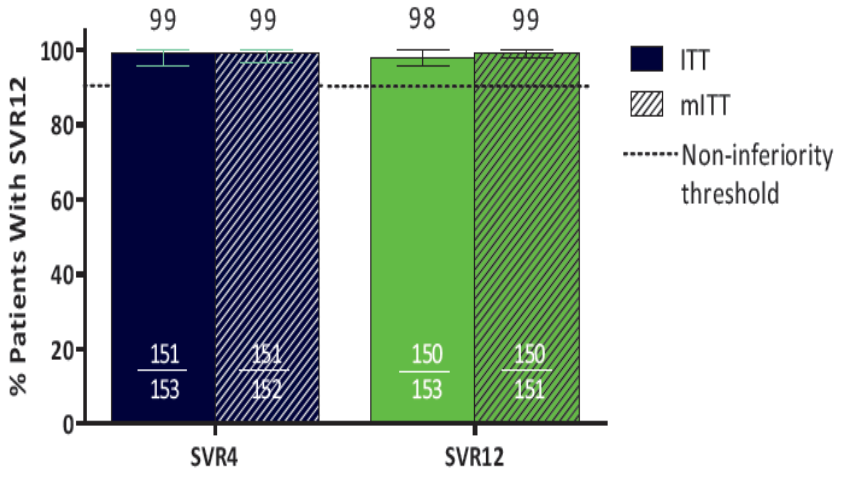
- Patients were enrolled in Australia, Belarus, France, Germany, Poland, Puerto Rico, Russian Federation, United Kingdom and United States

Endpoints and assessments



ITT, intention to treat; includes all patients who received at least 1 dose of study drug.

Results



Breakthrough	1	1
Relapse	0	0
Missing Data	0	1*
Discontinued	1	1

- The SVR12 rate was 100% (136/136) in patients without cirrhosis treated for 8 weeks

- The SVR12 rate in the mITT population of patients with cirrhosis treated for 12 weeks was 93% (14/15)
  - One patient with GT3a infection and cirrhosis had on-treatment virologic failure at treatment Week 8:
    - NS3: no polymorphisms at baseline; Y56H at failure
    - NS5A: A30V at baseline; S24F and M28K (not A30V) at failure

mITT, modified ITT population, which excludes patients with non-virologic failure.
*One patient achieved SVR4 but was lost to follow-up due to homelessness and did not return for PTW12 visit

Conclusion

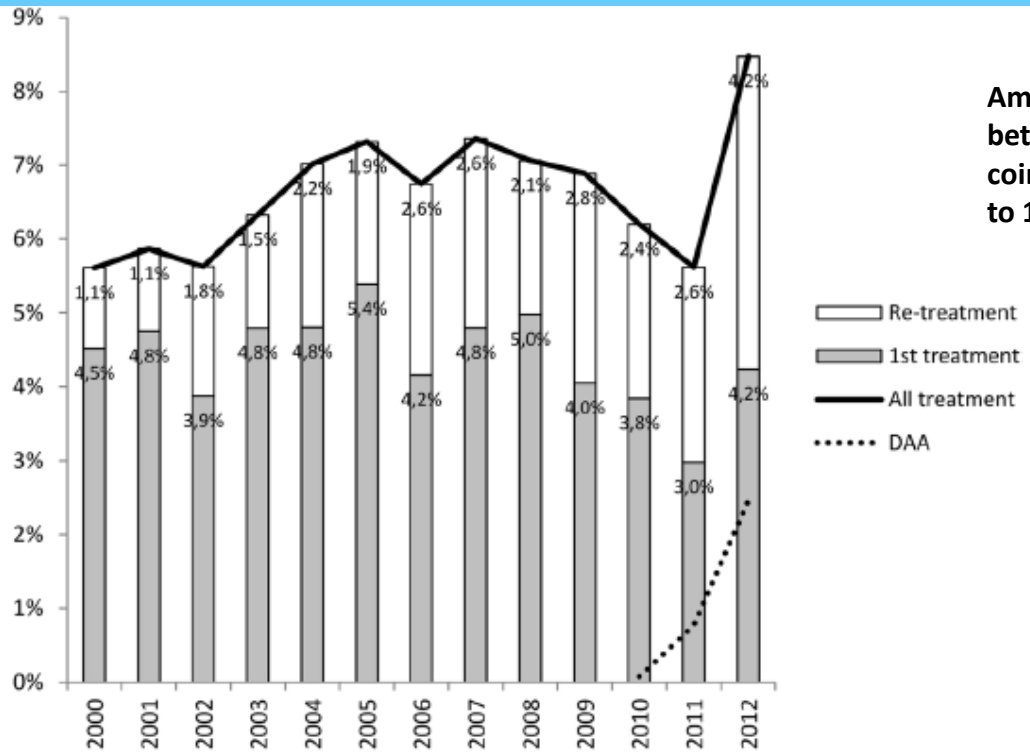
- An overall SVR12 rate of 98% with no relapses was achieved in HCV/HIV-1 co-infected patients without or with cirrhosis following 8 or 12 weeks of G/P, respectively
  - Achievement of SVR12 was not impacted by high baseline viral load, cirrhosis status, or any other baseline factor
  - Non-inferiority to historical standard of care was achieved
- G/P was well tolerated and exhibited a similar safety profile in HCV/HIV-1 co-infected patients with or without cirrhosis; serious adverse events, clinically significant laboratory abnormalities, and treatment discontinuations were rare
- In HCV/HIV-1 co-infected patients without cirrhosis, 8-week G/P yielded a 99.3% SVR12 rate, with no virologic failures
  - These results suggest that the G/P regimen could be the first 8-week pangenotypic treatment option for HCV/HIV-1 co-infected patients without cirrhosis

Accesso alle terapie in HIV-HCV

RESEARCH ARTICLE Open Access

Hepatitis C treatment initiation in HIV-HCV coinfected patients

Few data regarding HCV treatment initiation among HIV/HCV patients



Among 34,308 HIV-infected patients enrolled between 2000 and 2012, 5,562 were HCV coinfected. HCV prevalence declined from 38.4 to 15.1 %.

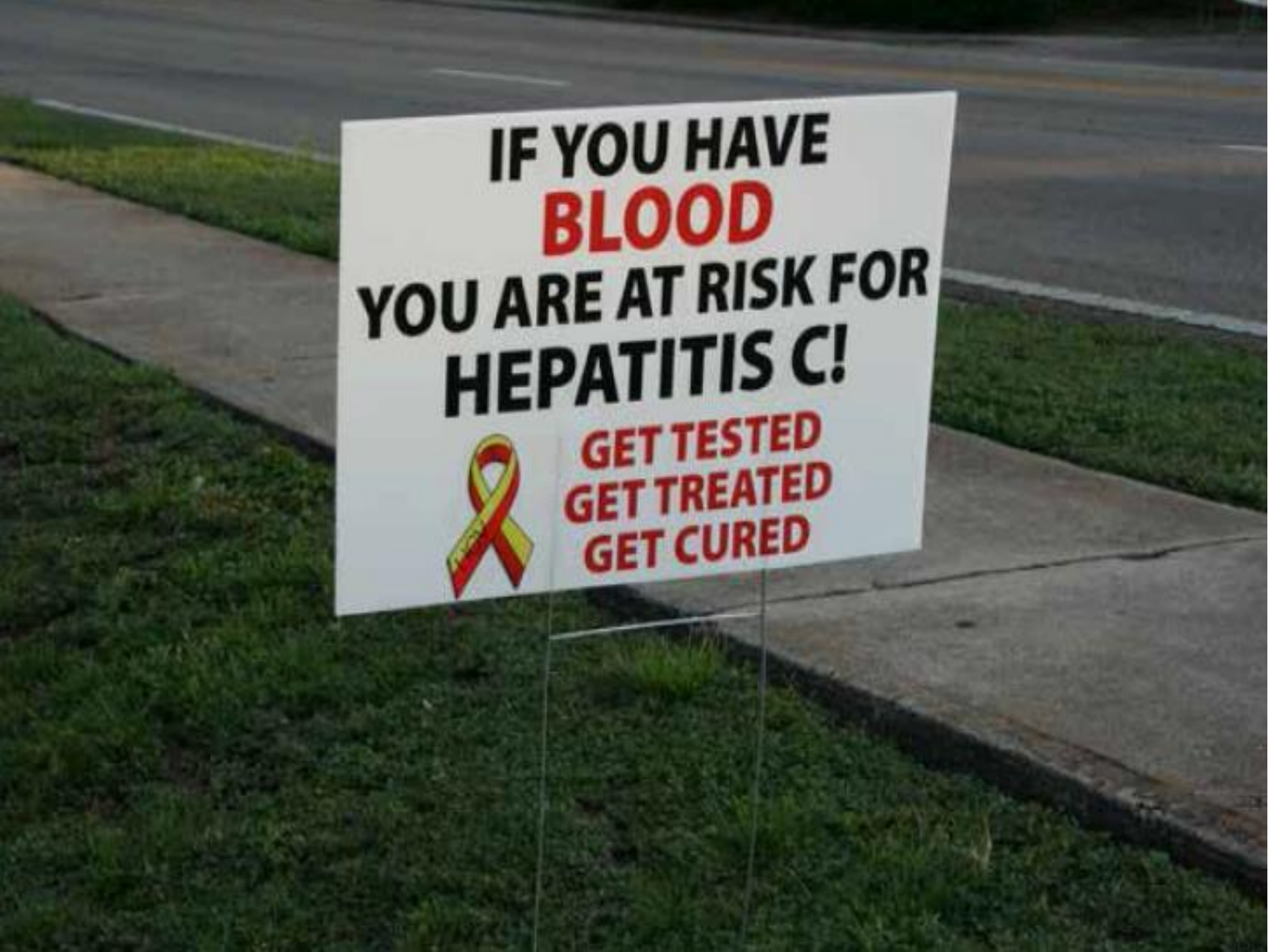
SUPPLEMENT ARTICLE

Breaking Down the Barriers to Hepatitis C Virus (HCV) Treatment Among Individuals With HCV/HIV Coinfection: Action Required at the System, Provider, and Patient Levels

Jason Grebely,[1] Megan Oser,[2] Lynn E. Taylor,[3] and Gregory J. Dore[1]

JID 2013

- **System-level barriers to HCV care**
- **Practitioner-level barriers to HCV care**
- **Patient-level barriers to HCV care**


IF YOU HAVE
BLOOD
YOU ARE AT RISK FOR
HEPATITIS C!
GET TESTED
GET TREATED
GET CURED