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EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Ferrara

università di ferrara
DA SEICENTO ANNI GUARDIAMO AVANTI.

HIV HCV

Epatite da HCV e HIV in reumatologia

Laura Sighinolfi

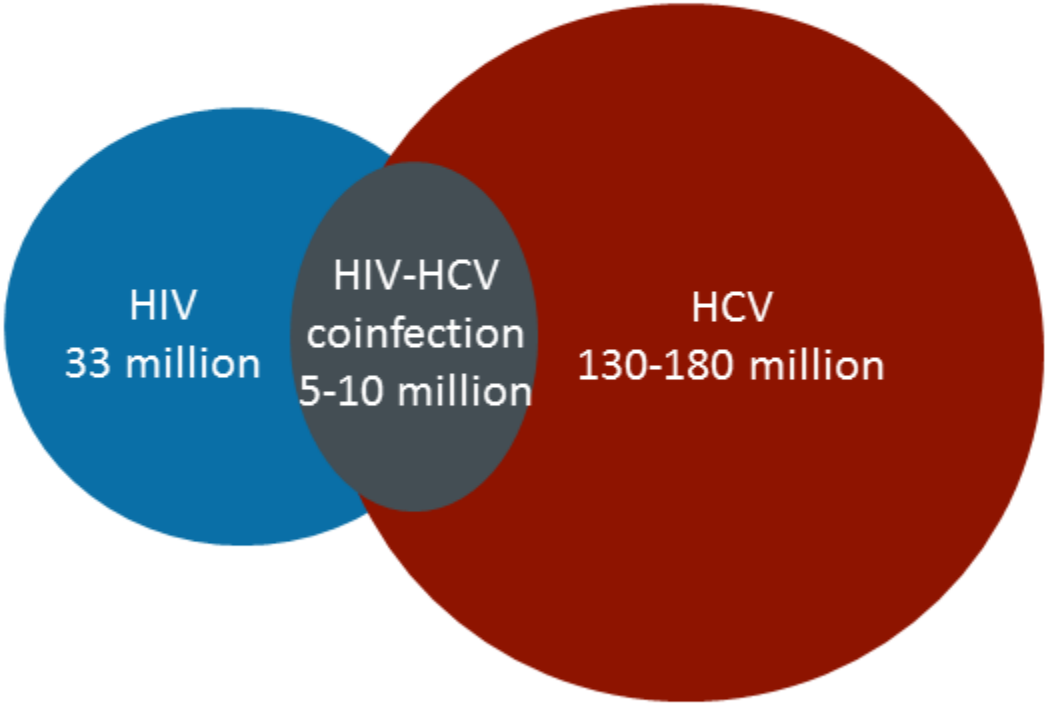
U.O.Malattie Infettive

Azienda Ospedaliero Universitaria - Ferrara

Ferrara, 29 maggio 2017

HCV and HIV Coinfection

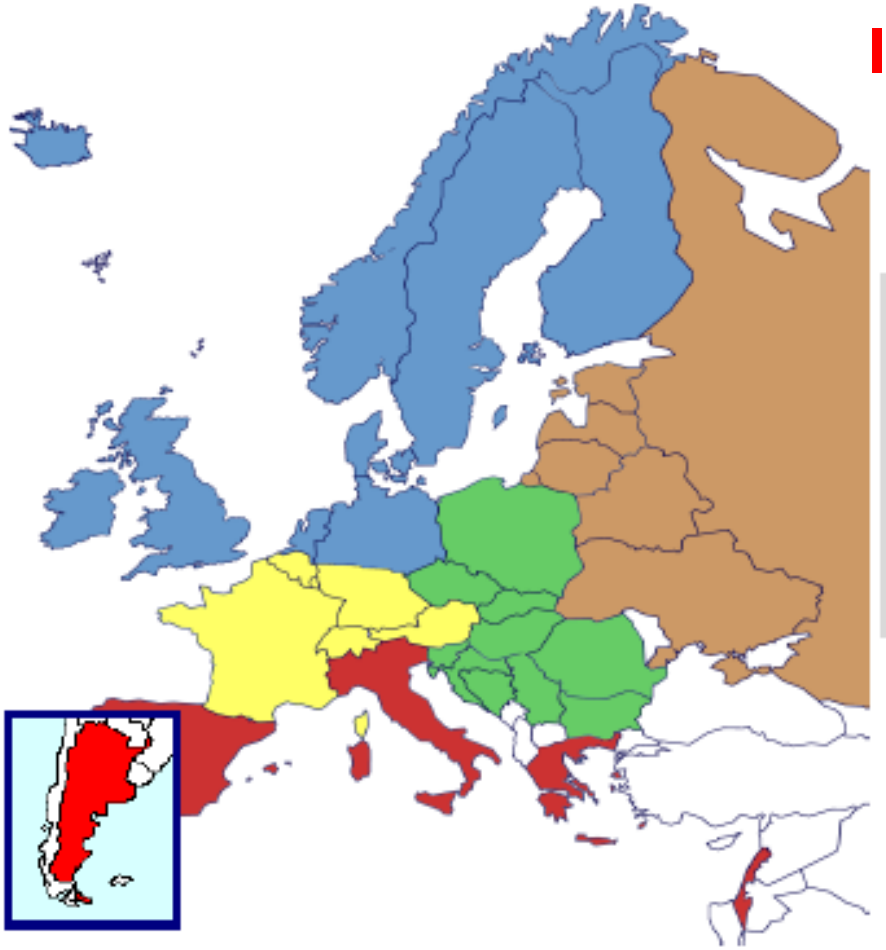
Prevalence Worldwide[a]



- HCV/HIV coinfection treated same as HCV monoinfection[b]

a. Clausen LN, et al. *World J Gastroenterol*. 2014;20:12132-12143.
b. EASL. EASL Recommendations on Treatment of Hepatitis C 2015.

Anti-HCV antibody prevalence in HIV positive individuals from different EuroSIDA regions



Italia 30.000 HIV/HCV

- South: 28.8%
- West: 20.1%
- North: 17.3%
- East Central: 34.0%
- East: 57.7%
- Argentina: 20.6%

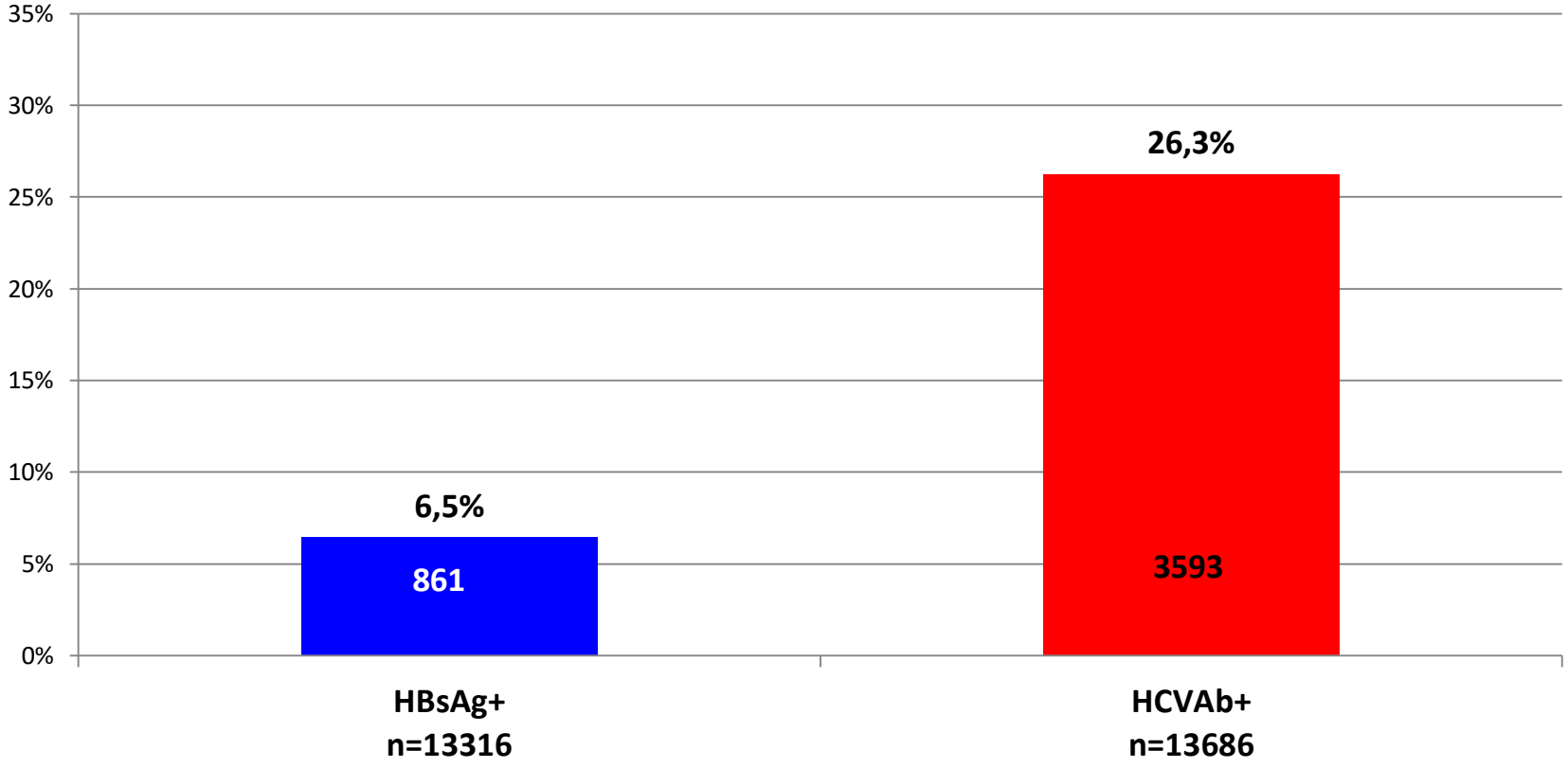
Peters et al, BMC Infect Dis, 2014

HEPAicona Hepatitis Icona Cohort

Fondazione Icona
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Italian Cohort I.C.O.N.A. Naive Antiretrovirals

HBsAg and HCVAb positivity in 13.934 patients enrolled in ICONA



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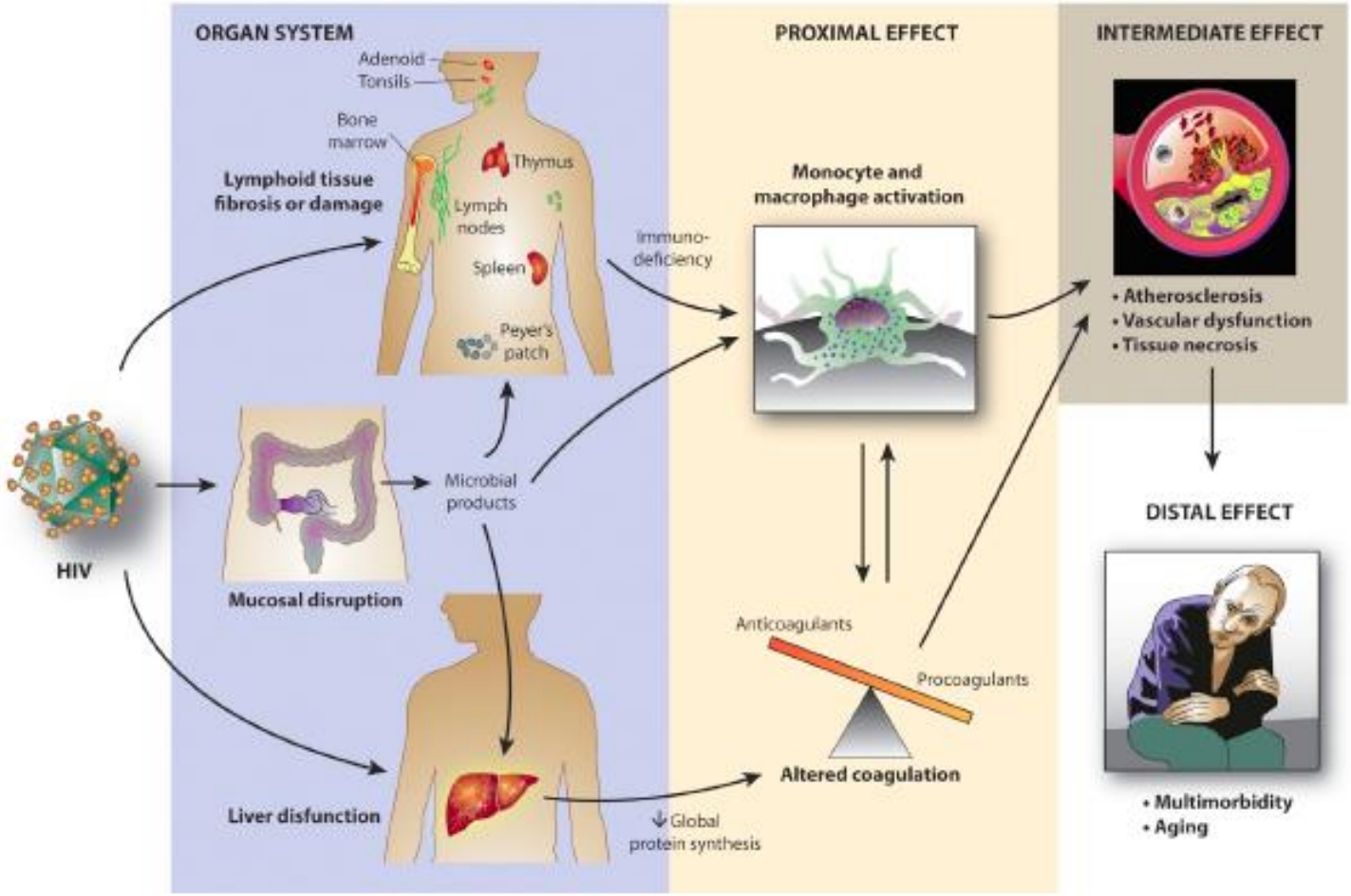
HIV/HCV

- **Fattore di rischio principale: tossicodipendenza**

- **Problema emergente:**

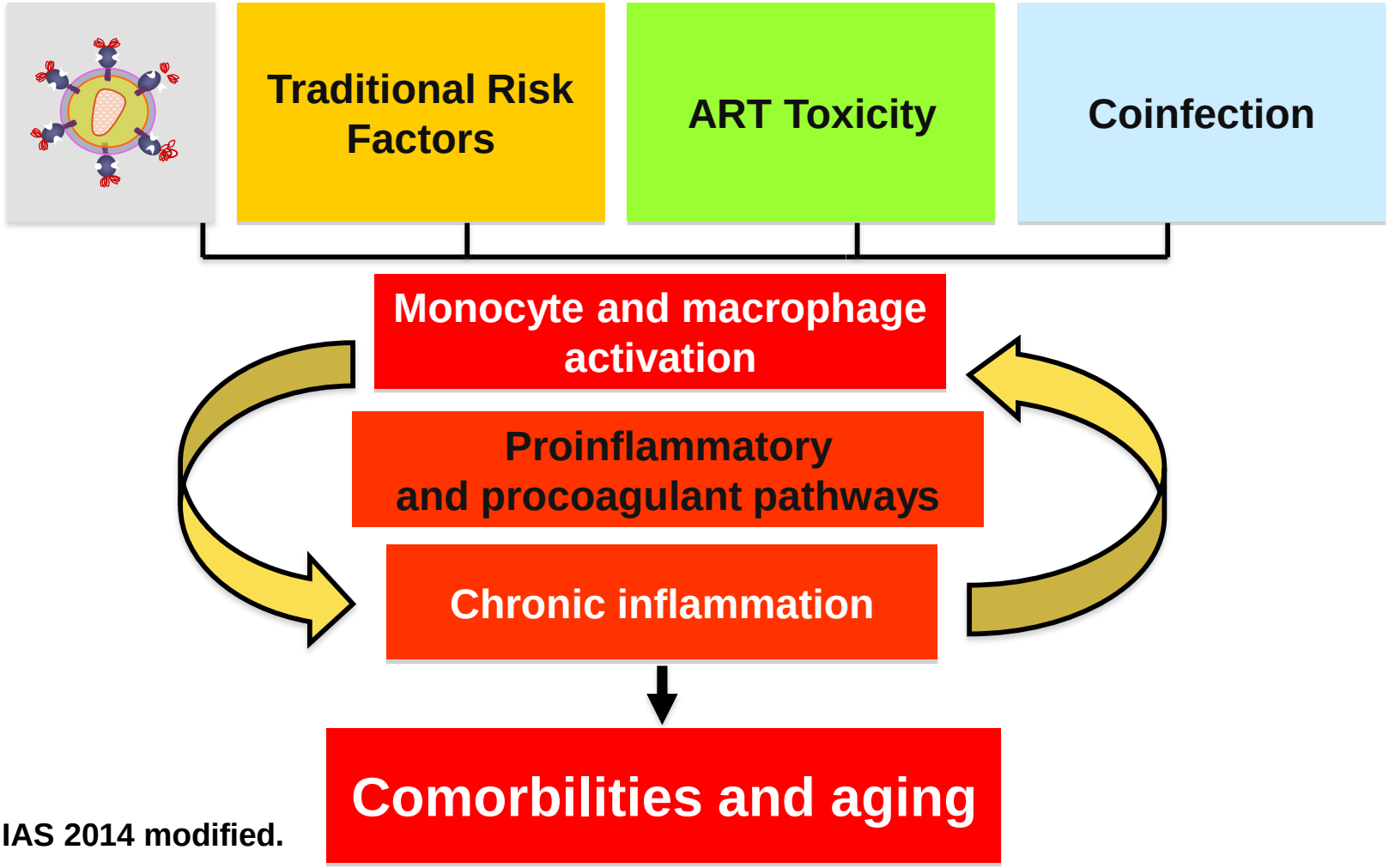
  trasmissione sessuale in MSM

Systemic Effects of Inflammation on Health During Chronic HIV Infection



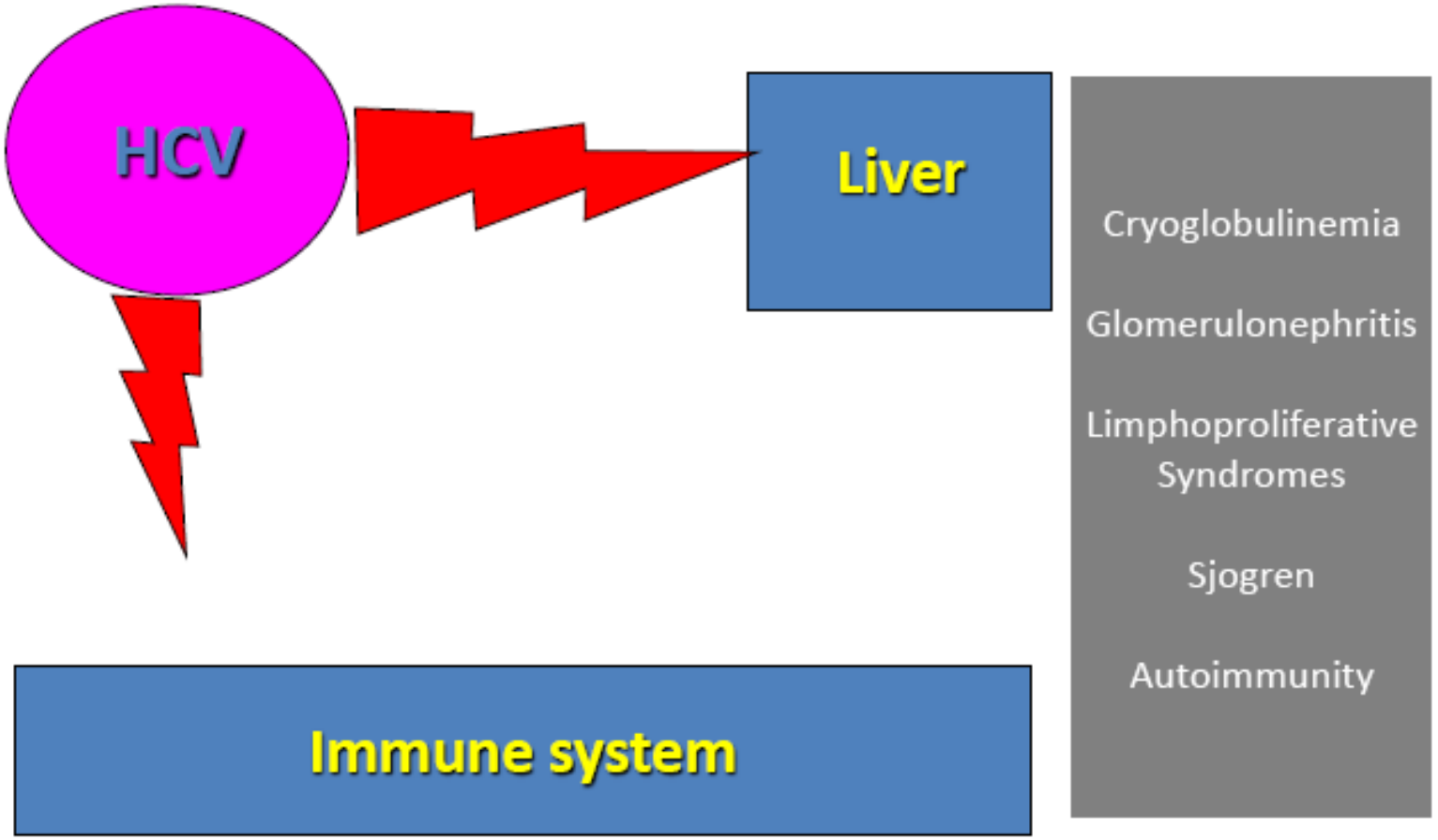
Deeks SG, et al. *Immunity*. 2013;39:633-645.

Factors Contributing to “inflammaging” in HIV-Positive Pts



Crowe S. IAS 2014 modified.

Manifestazioni extraepatiche di HCV



Ganga R. 2015 mod.

Manifestazioni extraepatiche di HCV

Classification according to the strength of the association

A. Significant prevalence, consistent pathogenetic data and "ex-adjuvantibus" criteria
- Mixed cryoglobulinaemia/cryoglobulinaemic vasculitis
- B-cell NHL

B. Higher prevalence than controls
- Type 2 diabetes mellitus type 2
- Insulin resistance
- Glomerulonephritis
- Renal insufficiency
- Fatigue
- Cognitive impairment
- Depression
- Impaired quality of life
- Cardiovascular disorders (i.e. stroke, ischemic heart disease)
- Sicca syndrome
- Arthralgia/myalgia
- Auto-antibody production (i.e. cryoglobulins, rheumatoid factor, and antinuclear, anticardiolipin, anti-thyroid and anti-smooth muscle antibodies)
- Monoclonal gammopathies
- Immune thrombocytopenia
- Porphyria cutanea tarda
- Lichen planus

C. Possible association
- Polyarthritis
- Pruritus
- Fibromyalgia
- Chronic polyradiculoneuropathy
- Lung alveolitis

D. Anecdotal association
- Polymyositis
- Dermatomyositis
- Polyarteritis nodosa
- Psoriasis
- Mooren corneal ulcer
- Erythema nodosum

E. Association with antiviral treatment (interferon alpha)
- Hypo-hyperthyroidism
- Depression
- Fatigue
- Impaired quality of life
- Sarcoidosis
- Lichen
- Skin vasculitis
- Peripheral neuropathy

Cacoub et al, Digestive and Liver Disease 2014

INTERNATIONAL JOURNAL OF STD & AIDS
International Journal of STD & AIDS
2017, Vol. 28(2) 110–119

Table 2. HIV virological and immunological profiles of individual patients at time of initiation of biologic therapy displayed by clinical indication.

Diagnosis (number of patients)	Age (years)[a]	Male	ART at time of biologic agent	Viral suppression at time of biologic agent	Baseline CD4 cell count prior to biologic[b]
Dermatology					
Pemphigus vulgaris (1)	54	1/1	1/1	1/1	444
Psoriasis (4)	44	4/4	2/4	2/4	432
Gastroenterology					
Crohn disease (2)	39	0/2	2/2	2/2	603
Ulcerative colitis (1)	69	1/1	1/1	1/1	357
Rheumatology					
Psoriatic arthropathy (8)	45	7/8	5/8	4/8	324 (50–750)
Rheumatoid arthritis (4)	45	3/4	3/4	4/4	666 (530–974)
Reactive arthritis (2)	36	2/2	2/2	2/2	752
Ankylosing spondylitis (1)	34	1/1	1/1	1/1	634
Undifferentiated spondyloarthopathy (1)	50	0/1	1/1	1/1	779
ANCA-associated vasculitis (1)	51	0/1	1/1	1/1	400

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STD & AIDS
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Table 3. Summary of biologic agent use according to clinical indication.

Diagnosis (total number of patients)	Treatment episodes	Biologics (number of treatment episodes[a])	Median duration of treatment (weeks; range if total patients>2)	Clinical response
Dermatology				
Pemphigus vulgaris (1)	1	R	24	Good
Psoriasis (4)	8	E (4), A, Al, I, U	30 (12–72)	Good 1/8; partial 2/8; transient 2/8; unknown 2/8; unresponsive 1/8
Gastroenterology				
Crohn disease (2)	2	I	18	Good 2/2
Ulcerative colitis (1)	1	I	20	Partial
Rheumatology				
Psoriatic arthropathy (8)	13	I (6), E (5), A (2)	96 (90–162)	Good 8/13; partial 3/13; transient 1/13; unresponsive 1/13
Rheumatoid arthritis (4)	5	E (4), I	18 (8–200)	Good 5/5
Reactive arthritis (2)	2	E, I	44	Good 2/2
Ankylosing spondylitis (1)	1	E	12	Transient
Undifferentiated spondyloarthopathy (1)	3	A, E, I	Unknown	Partial 3/3
ANCA-associated vasculitis (1)	1	R	One dose	Good

3. Conditions where failure to diagnose HIV infection may have severe consequences for person's health

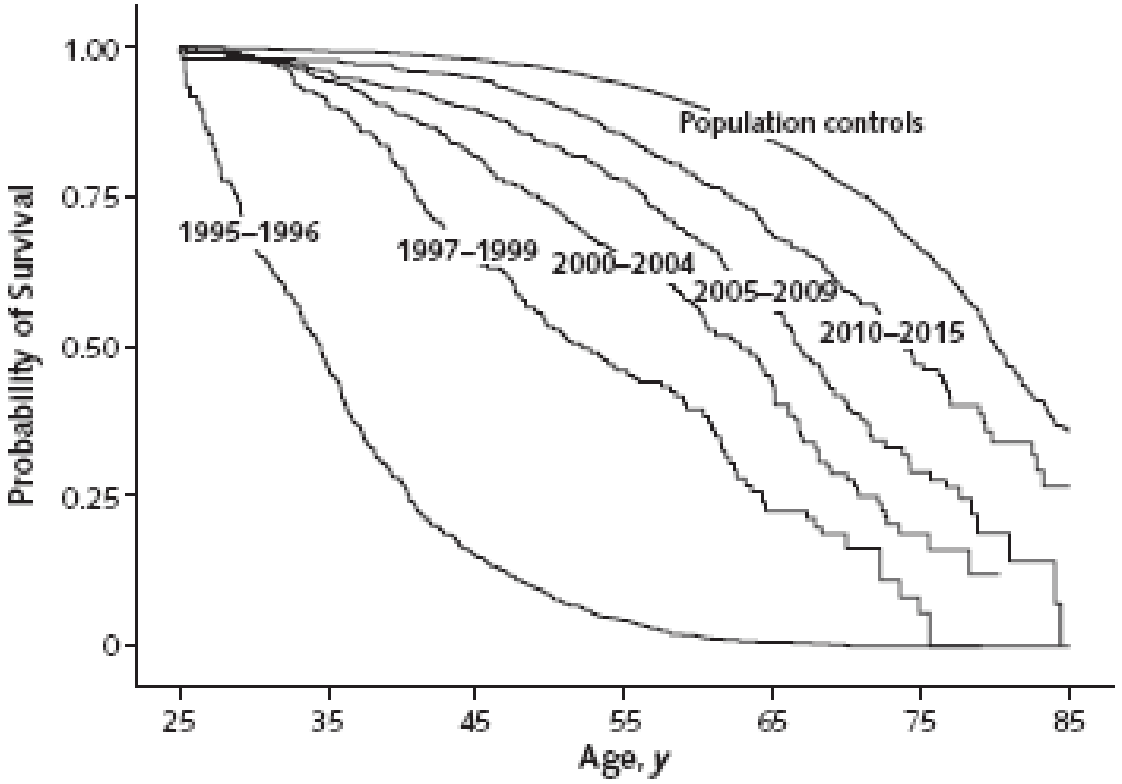
- Prior to initiating aggressive immuno-suppressive therapy
  - Malignancy
  - Transplantation
  - Auto-immune disease
- Primary space occupying lesion of the brain

Rheumatology	Autoimmune disease treated with aggressive immunosuppressive therapy[3]
Ophthalmology	Cytomegalovirus retinitis[1]
Otorhinolaryngology	Candidiasis tracheal/oesophageal[1]
	Mononucleosis-like illness[2]
Nephrology	Unexplained chronic renal impairment[2]
General practice	Symptomatology fitting any of the listed conditions
Emergency medicine	Symptomatology fitting any of the listed conditions
Dentistry	Oral hairy leukoplakia[2]
	Candidiasis, oral and oesophageal[1]
	Kaposi's sarcoma[1]

Update of Survival for Persons With HIV Infection in Denmark

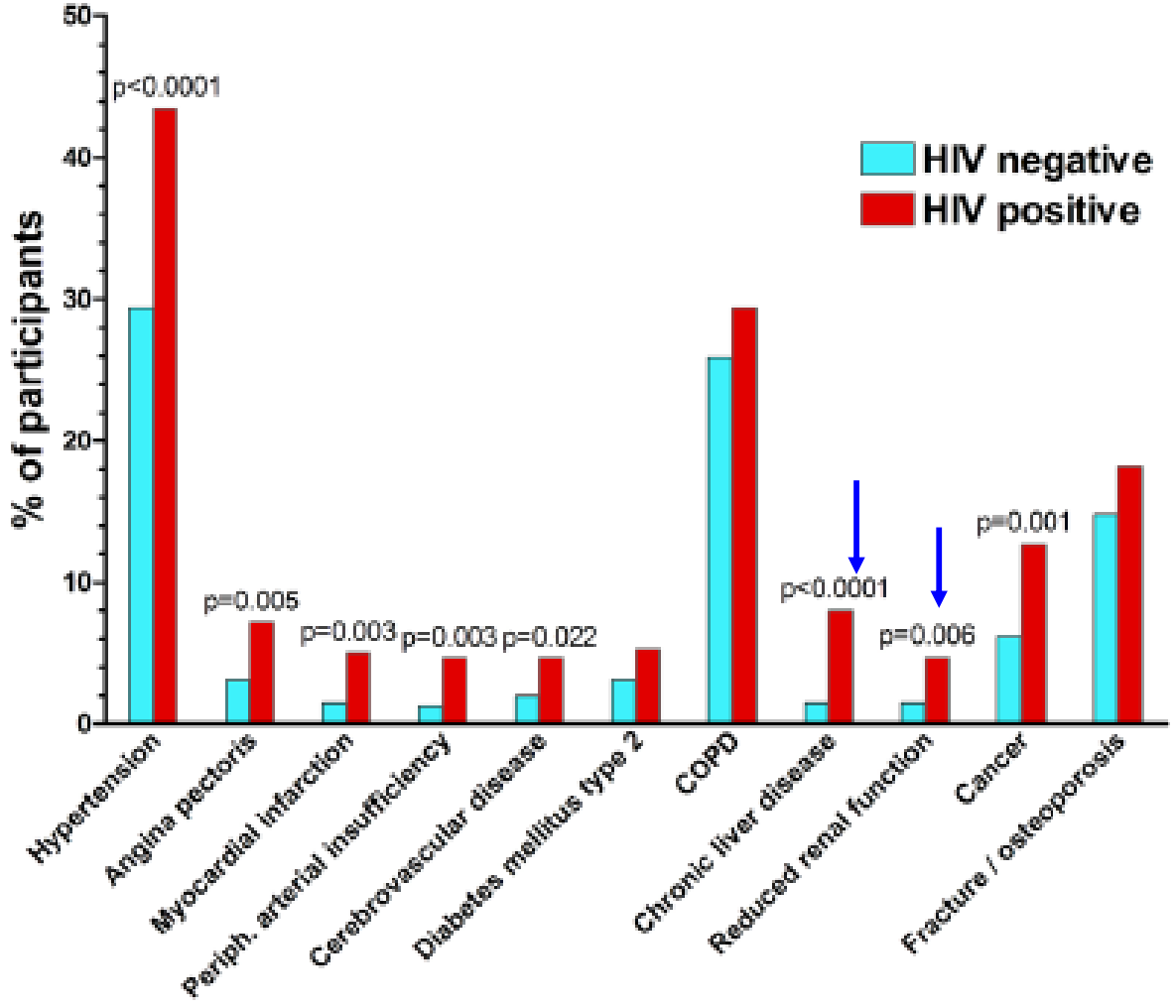
***Lohse et al* .**

Data 1995-2015



Comorbidity distribution

CROI 2016



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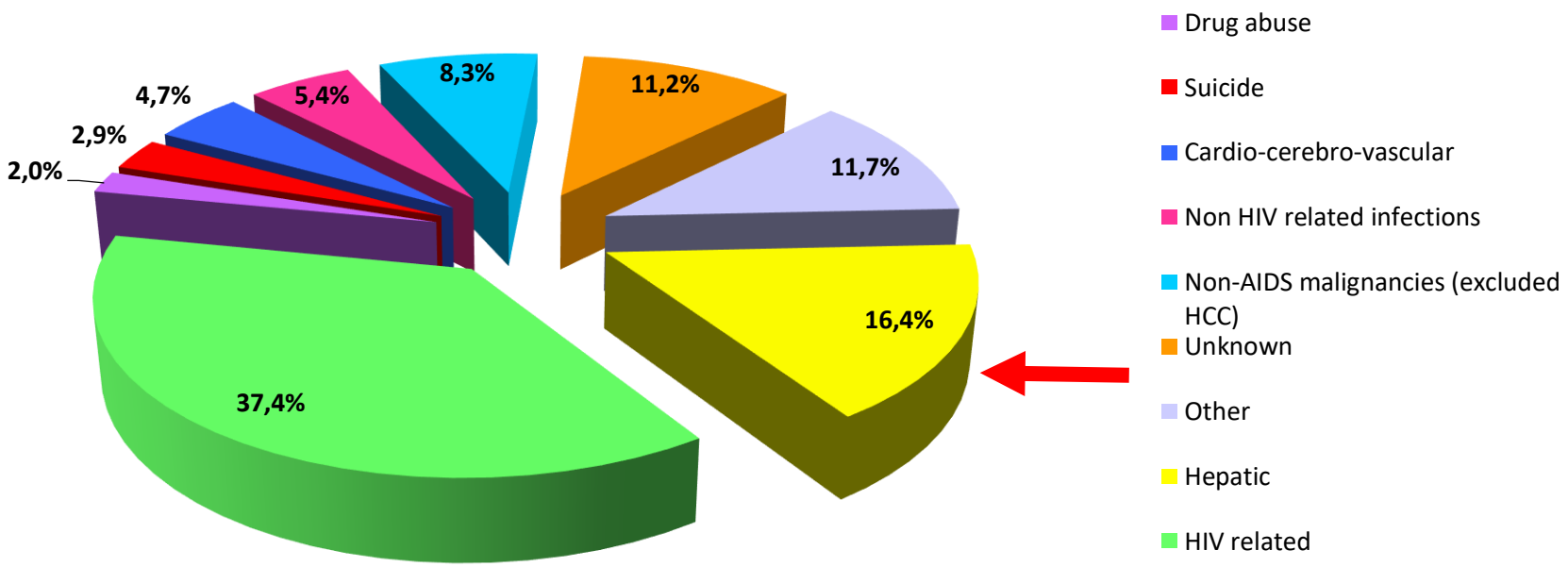
Italian Cohort I. C. O. N. A. Naive Antiretrovirals

Cause of death, n= 848



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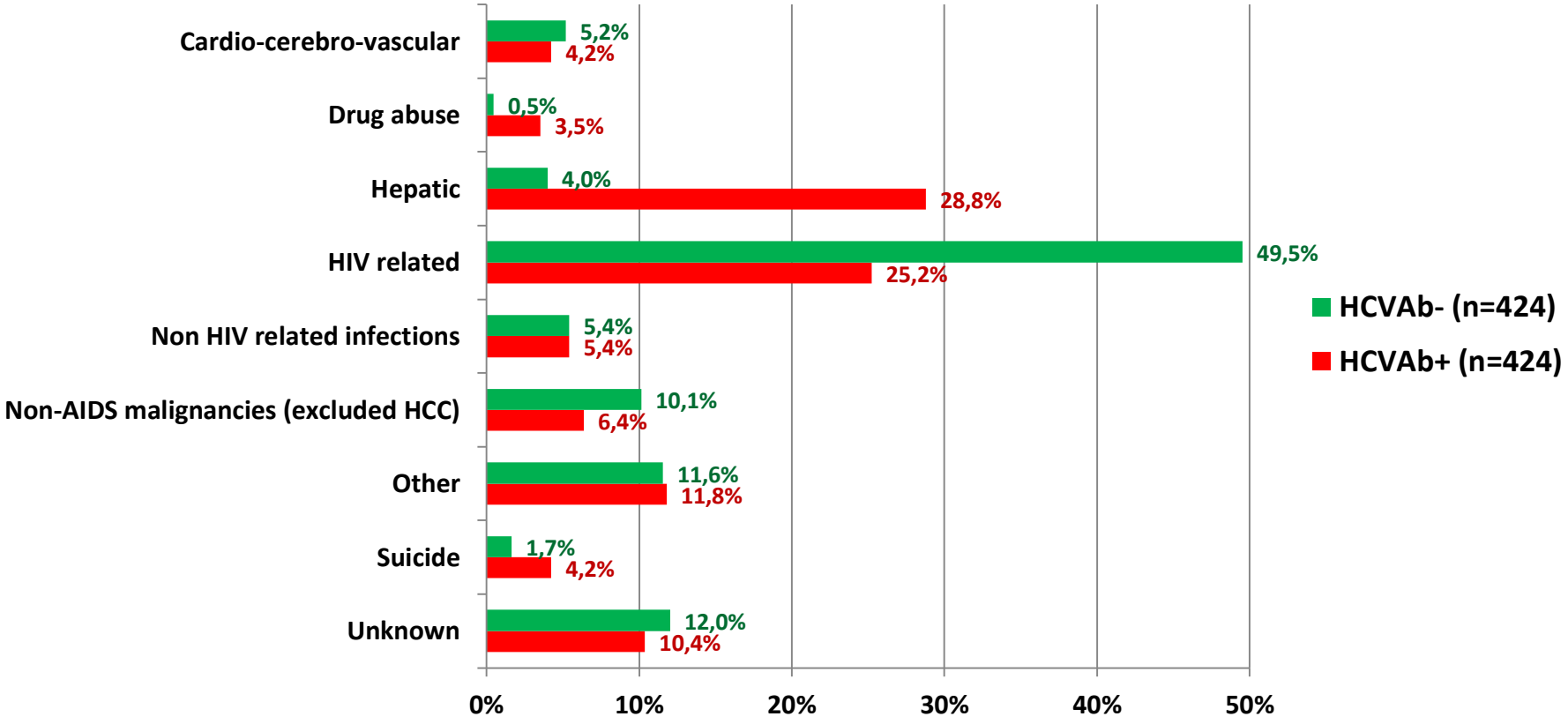
ITALIAN COHORT NAIVE ANTIRETROVIRALS

Italian Cohort I.C.O.N.A. Naive Antiretrovirals

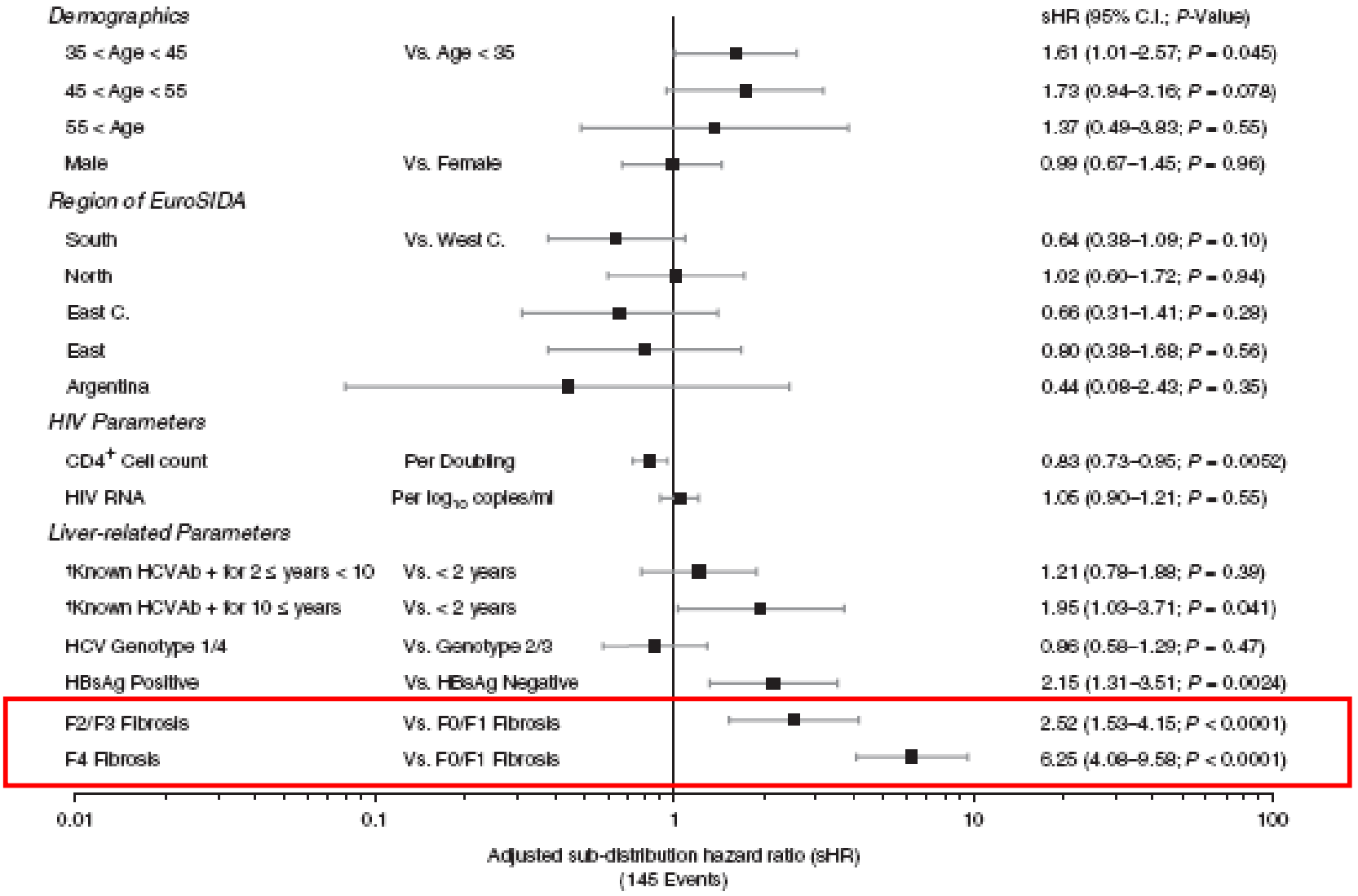
Cause of death according to HCVAb status



Jan 2017 Report

Fattori correlati alla mortalità per cause epatiche: dati EUROSIDA

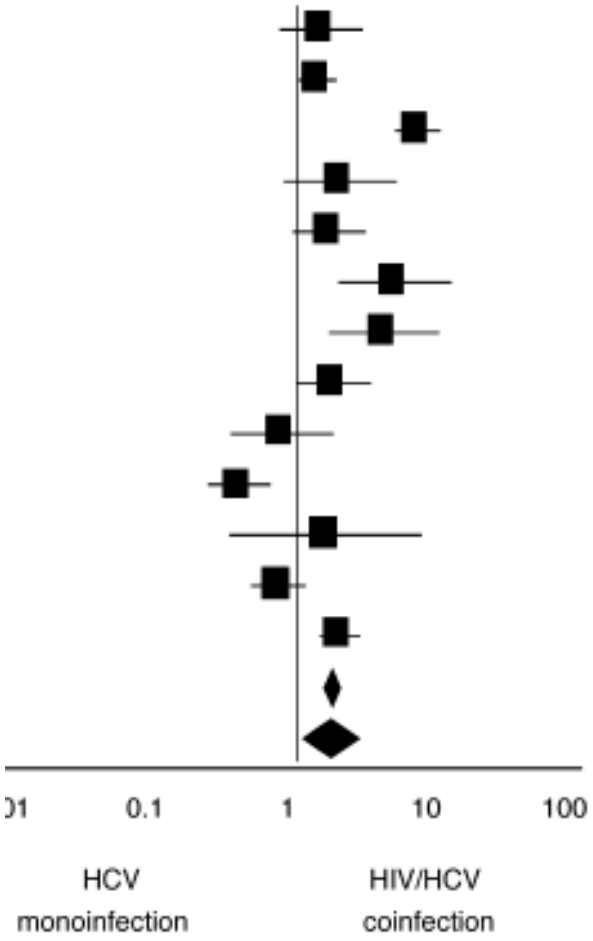
(Grint. D AIDS 2015)



HIV/HCV

- HIV accelera la progressione di HCV
- Rischio di evoluzione in cirrosi maggiore HIV/HCV

- Cirrosi a 10-15 anni:
  15-25% HIV/HCV
  2.6-6.5% HCV



•***(Thein H AIDS 2008 al.)***

Risk of End-Stage Liver Disease in HIV-Viral Hepatitis Coinfected Persons in North America From the Early to Modern Antiretroviral Therapy Eras

CID • Klein et al

2016

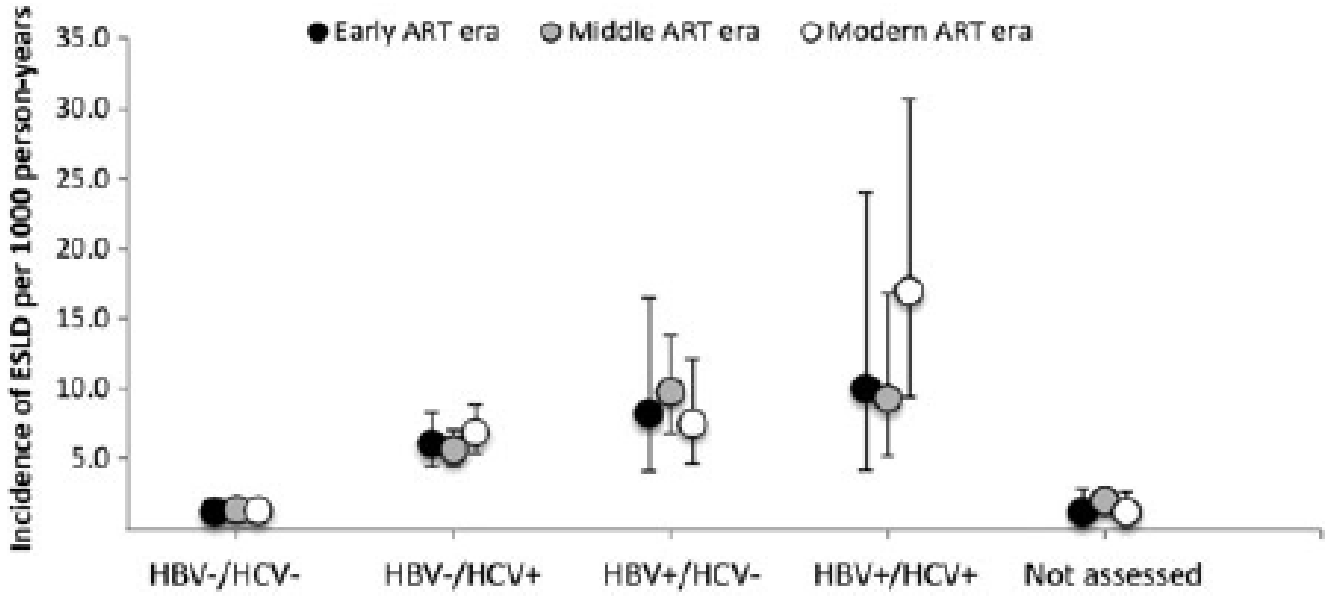


Figure 1. End-stage liver disease (ESLD) incidence rates and 95% confidence intervals by viral hepatitis coinfection status and antiretroviral therapy (ART) era, North American AIDS Cohort Collaboration on Research and Design, January

HIV/HCV
Terapia DAAs

- **% risposta uguale ai monoinfetti**
- **risposta non condizionata dal valore CD4**
- **Scarsi effetti collaterali**

La coinfezione HIV/HCV

L'efficacia dei DAAs è equivalente negli HCV monoinfetti e HIV/HCV coinfetti

Study	HCV direct-acting antiviral regimen	Study size (*n*)	SVR 12 weeks proportion (95% confidence interval)
C-EDGE CO-INFECTION (12)	Grazoprevir/ Elbasvir	218	96% (93–98)
TURQUISE-I (10)	Ombitasvir/ Paritaprevir/ ritonavir + Dasabuvir + Ribavirin	31	94% (79–98)
ION-4 (9)	Ledipasvir/ Sofosbuvir	335	96% (93–98)
ALLY-2 (11)	Daclatasvir + Sofosbuvir	127	96.4% (90–99)

HCV-HIV co-infected patients: no longer a 'special' population?

Mark S. Sulkowski Liver Int. 2016; 36 (Suppl. S1): 43–46

EASL HCV recommendations

Hepatology 2015

- Indications for HCV treatment in HCV/HIV coinfected persons are identical to those in patients with HCV-monoinfection **(A1)**

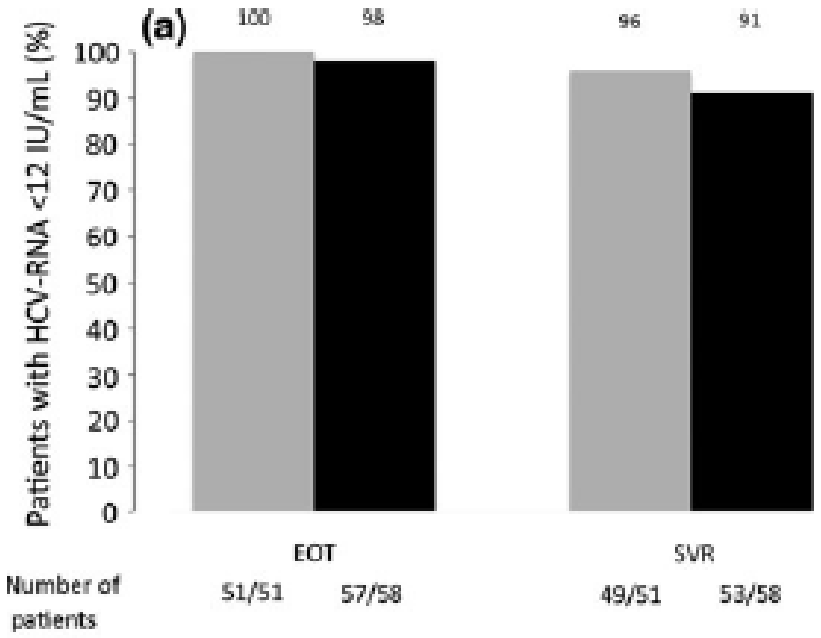
- Notwithstanding the respective costs of these options, IFN-free regimens are the best options when available in HCV-monoinfected and in HIV-coinfected patients without cirrhosis or with compensated (Child-Pugh A) or decompensated (Child-Pugh B or C) cirrhosis, because of their virological efficacy, ease of use and tolerability **(A1)**

- The same IFN-free treatment regimens can be used in HIV-coinfected patients as in patients without HIV infection, as the virological results of therapy are identical **(A1)**

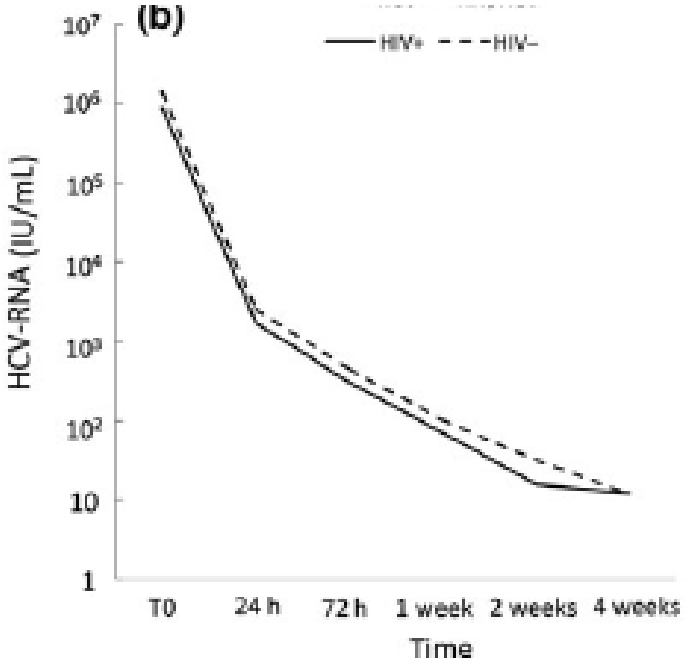
Direct-acting antivirals in hepatitis C virus (HCV)-infected and HCV/HIV-coinfected patients: real-life safety and efficacy

HIV Medicine (2016)

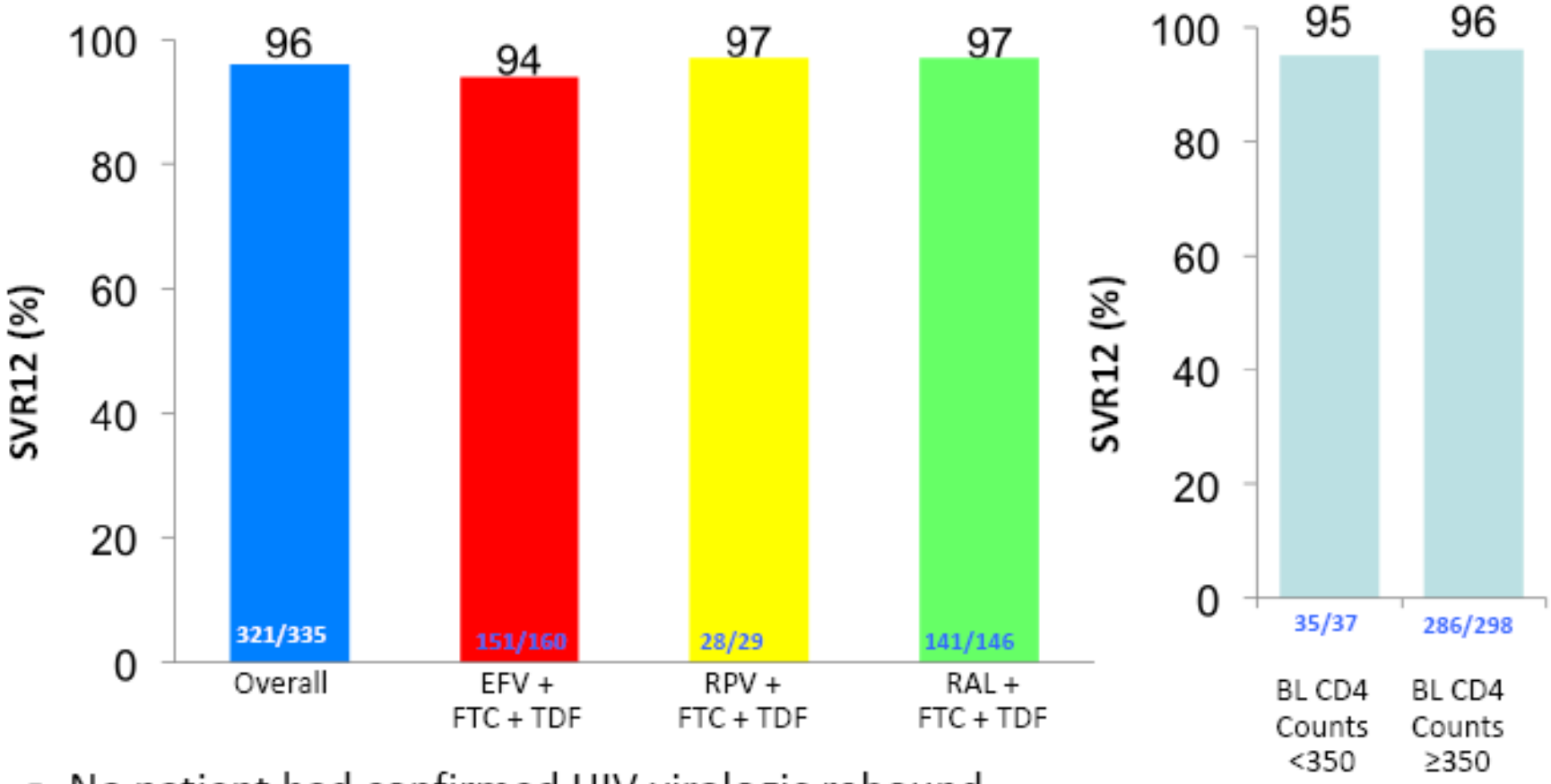
L. Milazzo,[1,*] A. Lai,[1] E. Calvi,[1] P. Ronzi,[1] V. Micheli,[2] F. Binda,[1] A.L. Ridolfo,[1] C. Gervasoni,[1] M. Galli,[1] S. Antinori[1] and S. Sollima[1]



Cirrosi 60%



SVR12 by HIV ARV Regimen and BL CD4 Count



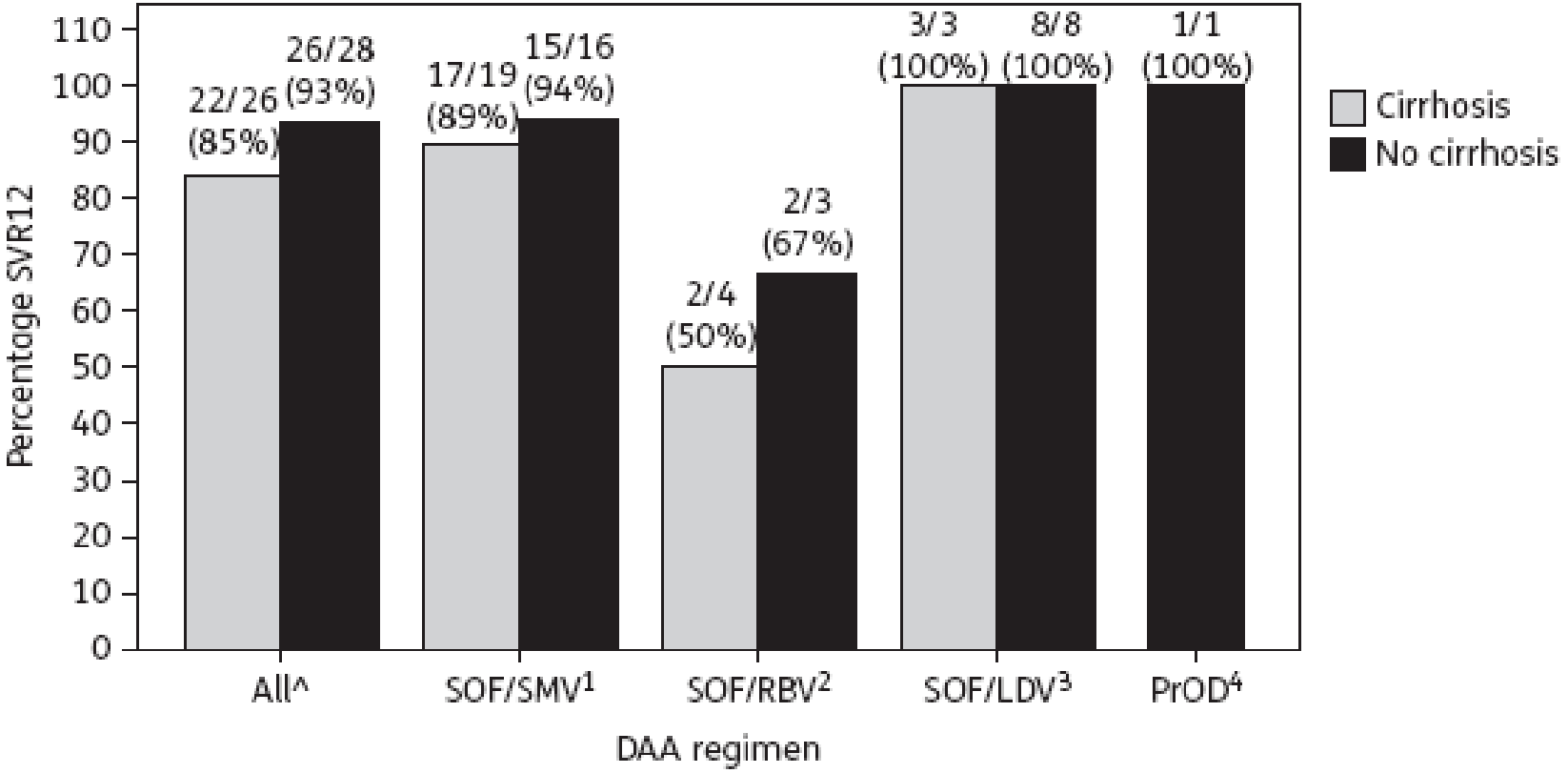
- No patient had confirmed HIV virologic rebound
- Stable CD4 counts through treatment and follow-up phase

Cooper C, et al. EASL 2015. Abstract P1353.

High rates of hepatitis C virus (HCV) cure using direct-acting antivirals in HIV/HCV-coinfected patients: a real-world perspective

Claudia Hawkins[1]*, Jennifer Grant[1], Lauren Rose Ammerman[2], Frank Palella[1], Milena Mclaughlin[3,4], Richard Green[5], Donna Mcgregor[1] and Valentina Stosor[1]

J Antimicrob Chemother **2016**

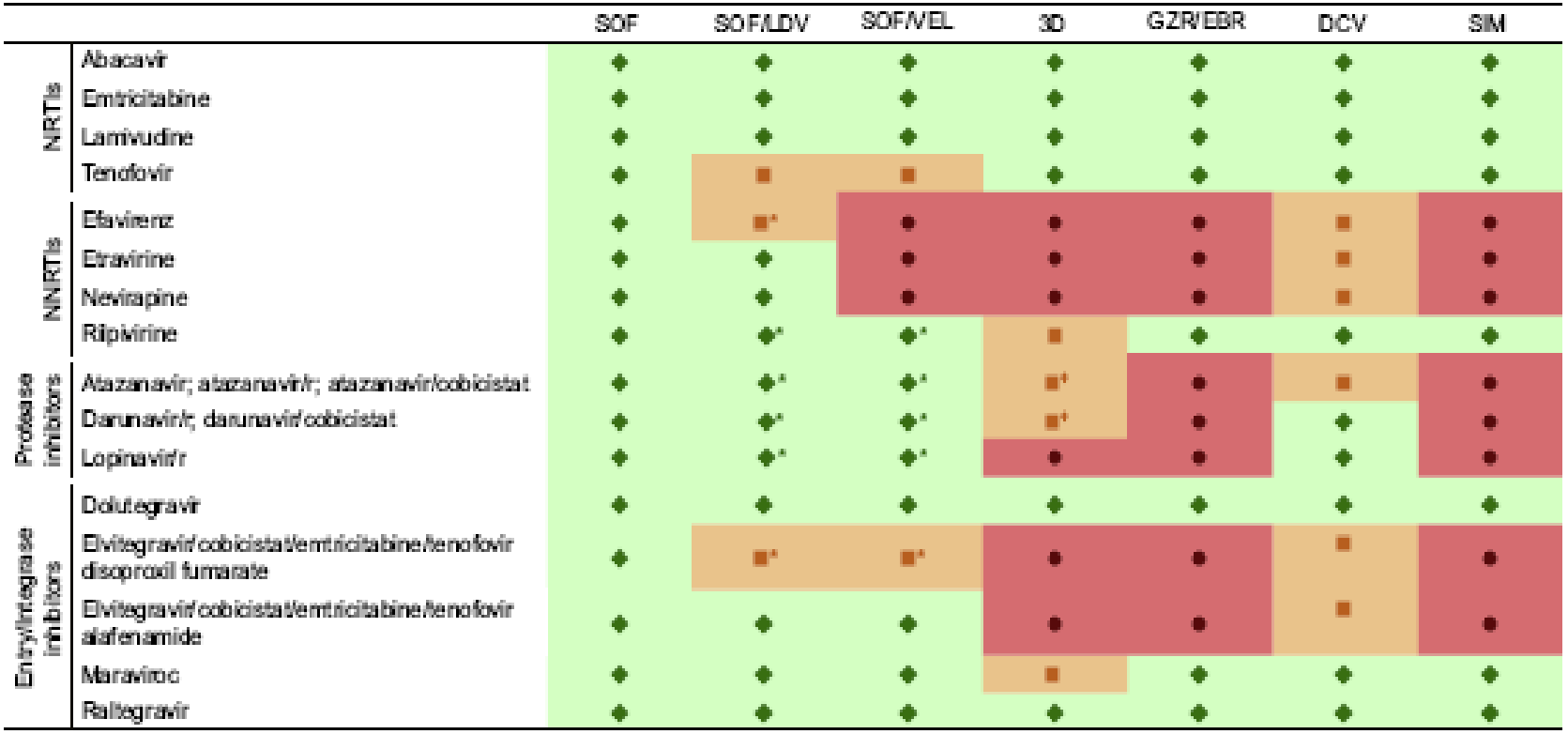


HIV/HCV
terapia DAAs: criticità

- **Interazioni con terapia antiretrovirale**
- **Durata della terapia**

EASL Recommendations on Treatment of Hepatitis C 2016☆

EASL JOURNAL OF HEPATOLOGY



		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	◆	◆	◆	◆	◆	◆	◆

Interazioni DAAs e terapia antiretrovirale

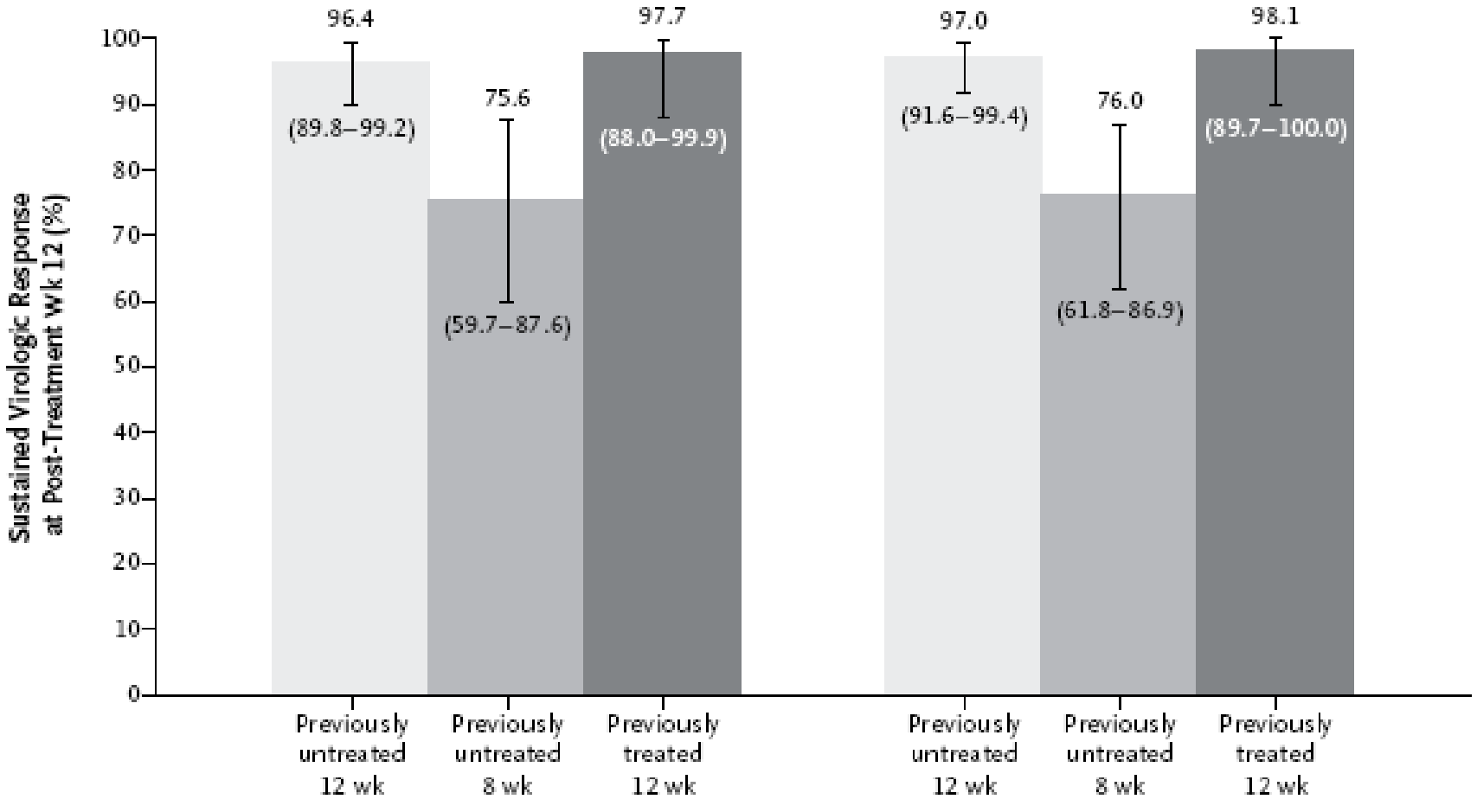
HIV/HCV
terapia DAAs: criticità

- **Interazioni con terapia antiretrovirale**
- **Durata della terapia**

Daclatasvir plus Sofosbuvir for HCV in Patients Coinfected with HIV-1

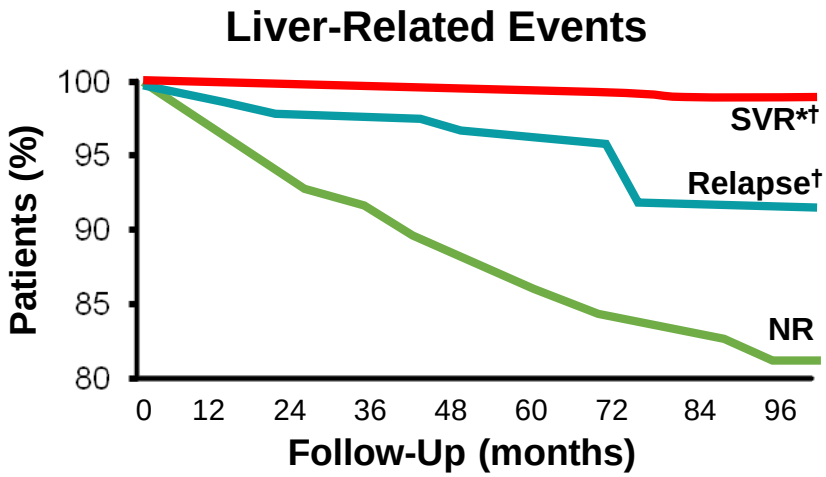
ALLY-2 Investigators*

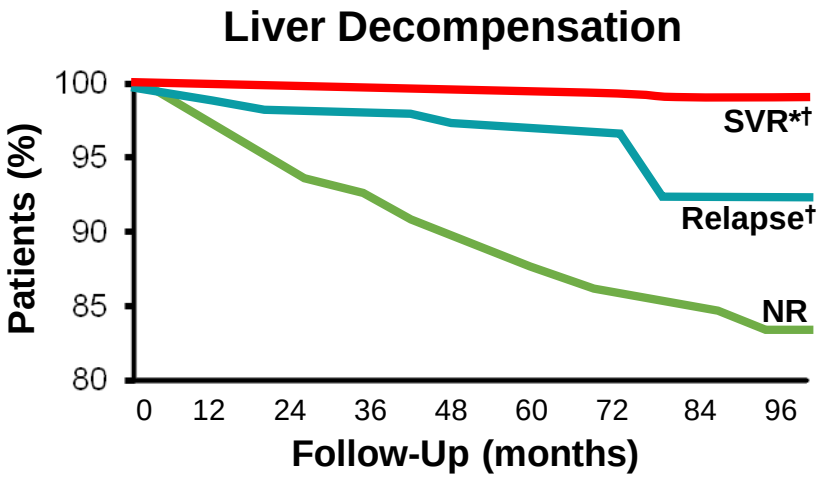
N ENGL J MED 373;8 NEJM.ORG AUGUST 20, 2015

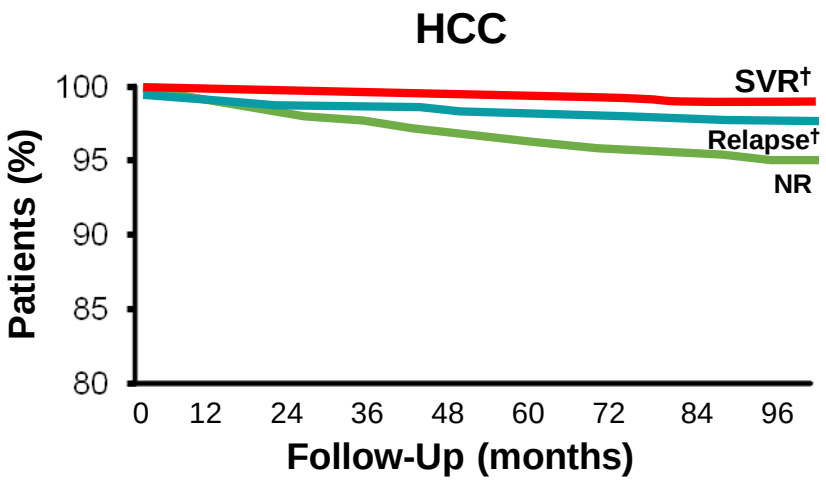


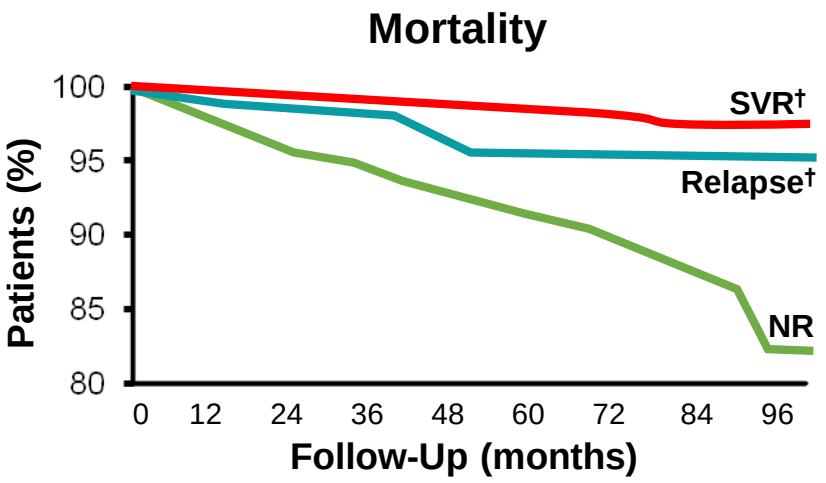
	Genotype 1			Genotypes 1 to 4		
No. of Events	80	31	43	98	38	51
Total No. of Patients	83	41	44	101	50	52

GESIDA HIV/HCV Cohort: HCV Eradication Reduces Liver-Related Outcomes









*P<0.05 versus NR and relapse; †P<0.05 versus NR.

Berenguer J, et al. *J Hepatol*. 2013;58:1104-1112.

Eradication of HCV and non–liver-related non–AIDS-related events in HIV/HCV coinfection

GESIDA HIV/HCV Cohort Study

Hepatology in press

Table 4. Crude and adjusted hazards for events during follow-up for 997 non-responders to interferon plus ribavirin compared with 628 responders

	Univariate analysis[a]		Multivariate analysis[a,b]	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***
Overall deaths	0.35 (0.24 - 0.52)	<.001	0.36 (0.24 - 0.54)	<.001
	sHR (95% CI)	***P***	**sHR (95% CI)**	***P***
Cause-specific deaths				
Liver-related deaths	0.12 (0.05 - 0.28)	<.001	0.13 (0.06 - 0.28)	<.001
Non–liver-related deaths	0.69 (0.43 - 1.1)	.119	0.73 (0.44 - 1.20)	.214
AIDS-related deaths	0.45 (0.09 - 2.22)	.325	0.37 (0.09 - 1.43)	.148
NLR-NAR deaths	0.73 (0.44 - 1.19)	.204	0.79 (0.47 - 1.35)	.388
New AIDS-defining events	0.34 (0.16 - 0.72)	.004	0.37 (0.17 - 0.79)	.010
Liver-related events				
Liver decompensation	0.09 (0.04 - 0.2)	<.001	0.10 (0.05 - 0.21)	<.001
Hepatocellular carcinoma	0.12 (0.03 - 0.5)	.004	0.13 (0.03 - 0.50)	.003
Liver transplantation	0.10 (0.01 - 0.77)	.027	0.12 (0.02 - 0.78)	.027
NLR-NAR events				
Diabetes mellitus *	0.54 (0.34 - 0.87)	.011	0.57 (0.35 - 0.93)	.024
NLR-NAR Cancer	0.91 (0.6 - 1.38)	.650	0.91 (0.58 - 1.45)	.703
Cardiovascular events	1.41 (0.93 - 2.13)	.105	1.57 (0.99 - 2.50)	.056
NAR-Infections	0.55 (0.33 - 0.92)	.024	0.65 (0.37 - 1.14)	.131
Bone events	1.39 (0.82 - 2.35)	.225	1.28 (0.69 - 2.38)	.433
Renal events *	0.41 (0.17 - 0.99)	.049	0.43 (0.17 – 1.09)	.075

DAAs nella terapia della crioglobulinemia mista HCV correlata

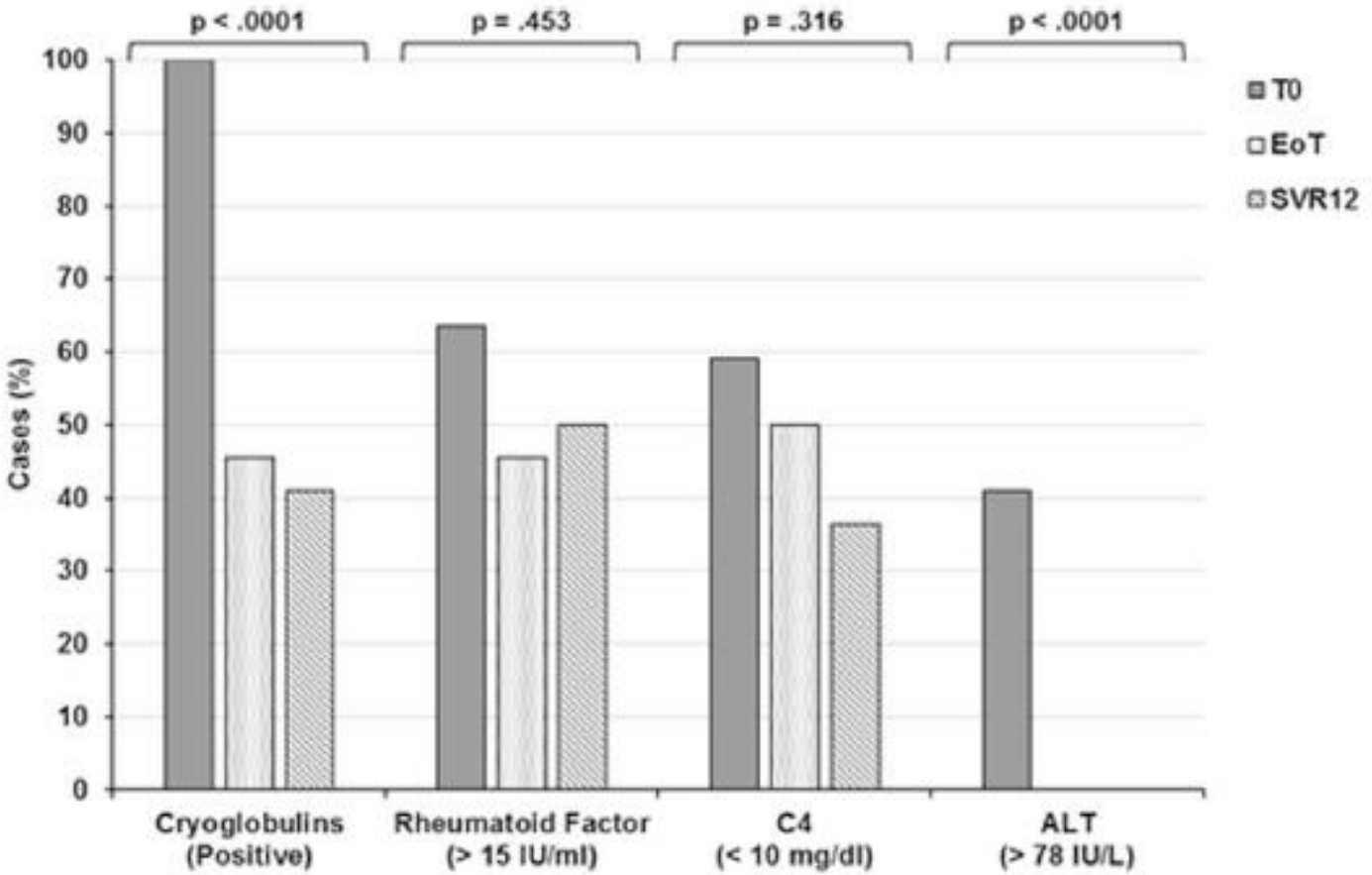


Fig. 3 Cross-tab analysis and χ^2 tests showing modifications of cryocrit, rheumatoid factor (RF), C4 and ALT levels in relation to antiviral therapy. Besides hepatitis C virus RNA, cryocrit and ALT values were significantly influenced by therapy with respect to RF and C4 ($p < 0.0001$ and $p < 0.0001$, respectively). *ALT* Alanine transaminase, *C4* Complement component C4, *EoT* End of treatment, *SVR12* Sustained virological response 12 weeks after therapy completion

Lauletta *et al. Arthritis Research & Therapy* (2017) 19:74

HIV HCV

Grazie per l'attenzione