Treatment strategy in patients with HIV-HCV co-infection

Should we treat HCV/HIV coinfected as a „special" population?

Robert Flisiak

Department of Infectious Diseases and Hepatology
Medical University of Białystok, Poland

11th PHC
Paris, 15-16 January 2018

MERCK
Be well

Disclosures

Advisor and/or speaker for:

AbbVie, Bristol-MyersSquibb, Gilead, Janssen, Merck, Novartis, Roche

EASL JOURNAL OF HEPATOLOGY

EASL Recommendations on Treatment of Hepatitis C 2016☆

?

Table 6. Treatment recommendations for HCV-monoinfected or HCV/HIV coinfected patients with chronic hepatitis C without cirrhosis, including treatment-naïve patients and patients who failed on a treatment [illegible] 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	8-12 wk, no ribavirin	12 wk, no ribavirin	12 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* or 24 wk, no ribavirin					12 wk with ribavirin* or 24 wk, no ribavirin	
Genotype 1b	Treatment-naïve	8-12 wk, no ribavirin	12 wk, no ribavirin	8-12 wk, no ribavirin	No	12 wk, no ribavirin	12 wk, no ribavirin	No
	Treatment-experienced	12 wk, no ribavirin		12 wk, no ribavirin				
Genotype 2	Both	No	12 wk, no ribavirin	No	No	No	12 wk, no ribavirin	No
Genotype 3	Treatment-naïve	No	12 wk, no ribavirin	No	No	No	12 wk, no ribavirin	No
	Treatment-experienced		12 wk with ribavirin[c]				12 wk with ribavirin[c]	

J Hepatology 2017; 66: 153–194

Major issues leading to recognition of HCV/HIV coinfected as a population of „special attention”

- More advanced liver disease
- Risk of DDI between DAA and ART
- Reduced SVR rate during IFN era
- Non adherence
- Risk of HCV spread

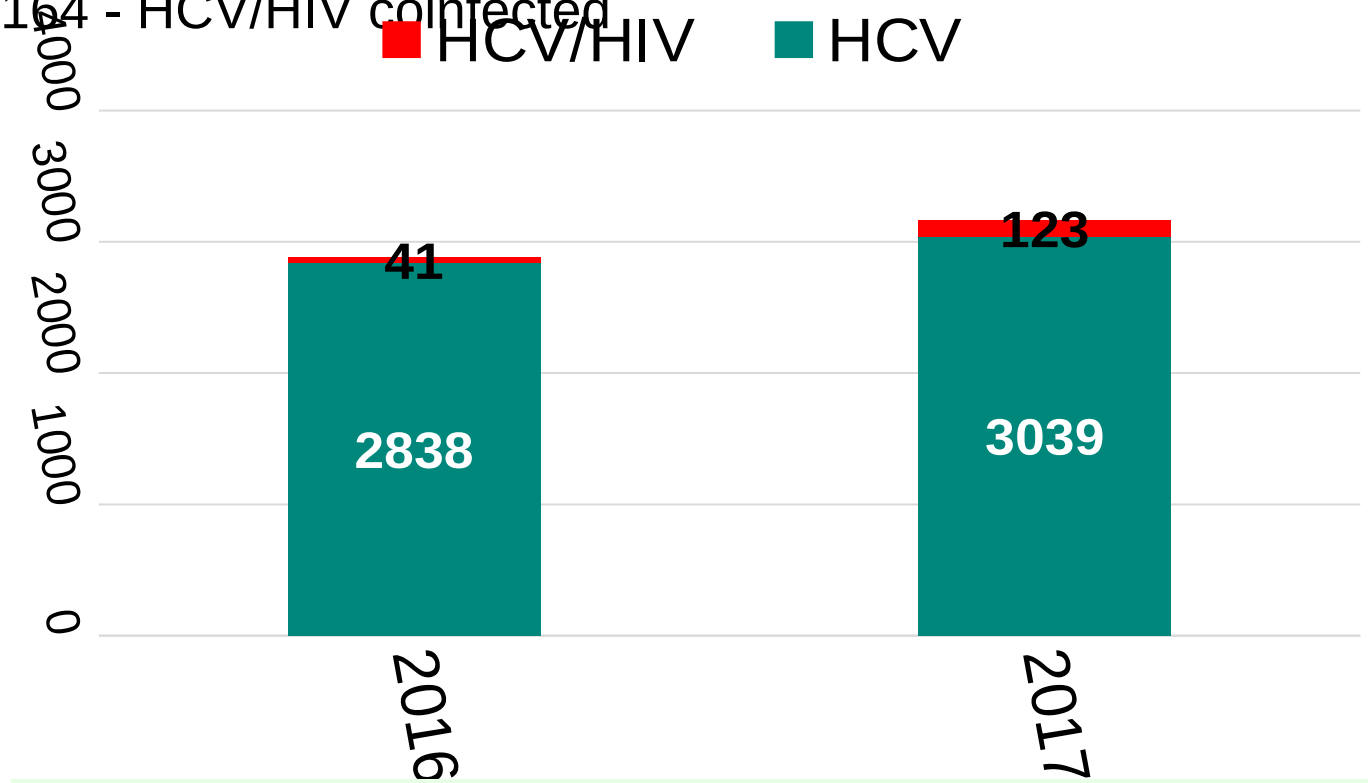
EpiTer-2

- Real world, database of patients treated for HCV in Poland within Narodowy Fundusz Zdrowia (NFZ-National Health Fund) reimbursement therapeutic program (from mid 2015).
- Independent, initiated and supported by Polish Association of Epidemiologists and Infectiologists.
- 22 HCV treating centers, including:
  - 20 infectious diseases,
    - 13 both HCV and HIV treating centers,
  - 1 gastroenterology,
  - 1 transplant.
- Priority of treatment according to national guidelines:
  - advanced liver disease
  - accompanying disease which can be affected by HCV infection

Proportion of HIV coinfected in the EpiTer-2

6041 patients registered in 2016 and 2017, ~40% all treated

- 5877 - HCV monoinfected
- 164 - HCV/HIV coinfected

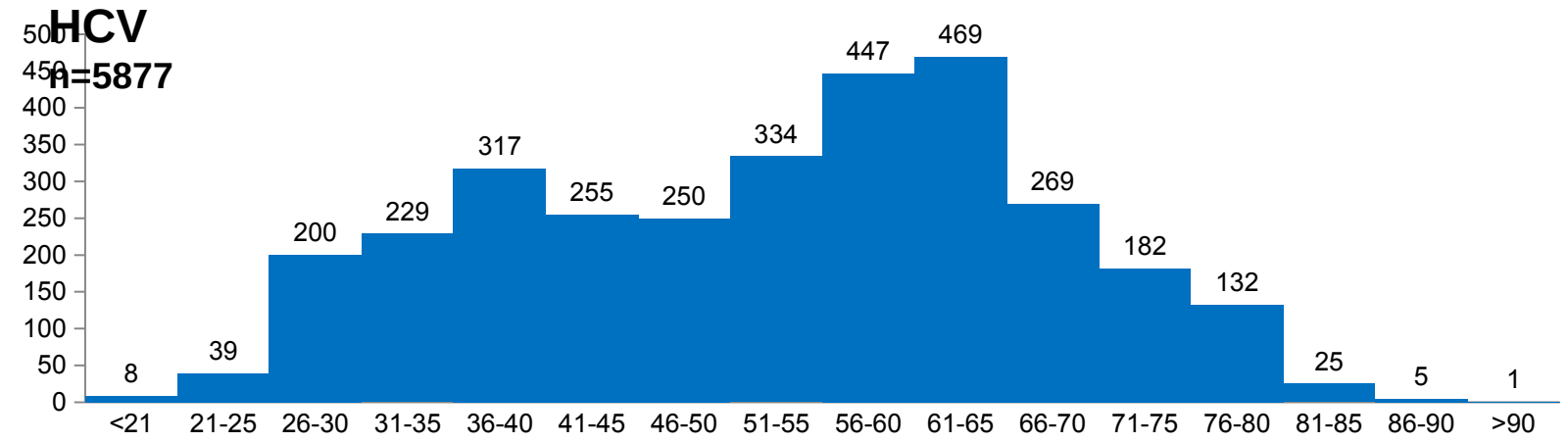


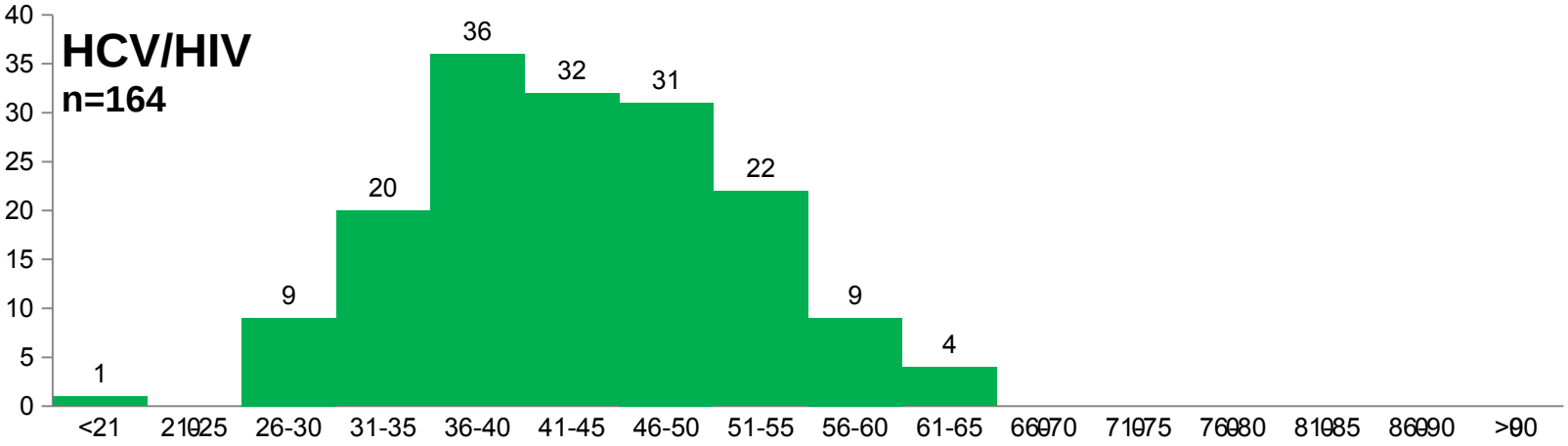
Why proportion of HIV coinfected was lower in 2016?

- *Patients not interested*
- *Doctors not interested*
- *Less advanced disease – no need of priority*

Age distribution among currently treated

EpiTer-2



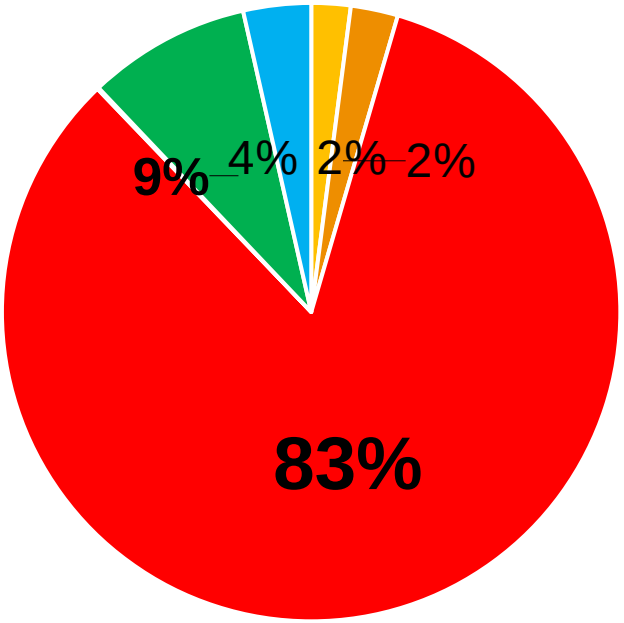


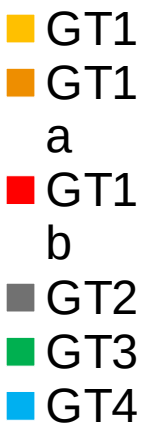
- HCV/HIV are younger.
- ~10% of 25-50 years old HCV population is HIV coinfected.
- **Should we expect them to be dominant in the**

Genotypes distribution

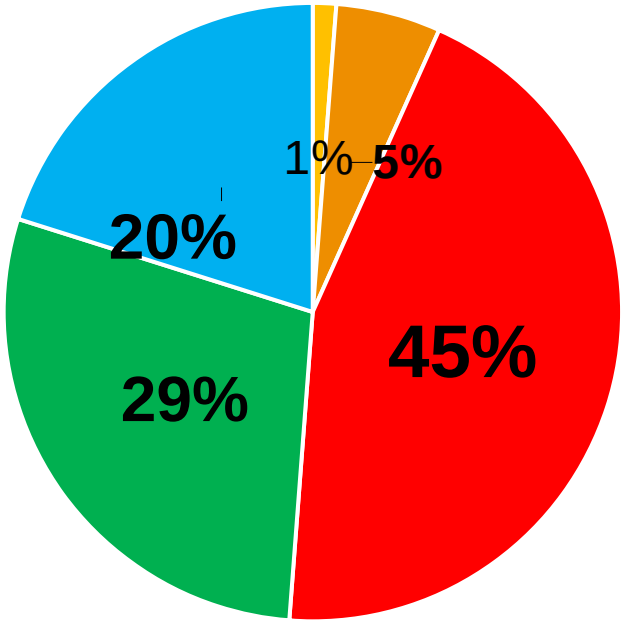
EpiTer-2

HCV
n=5877





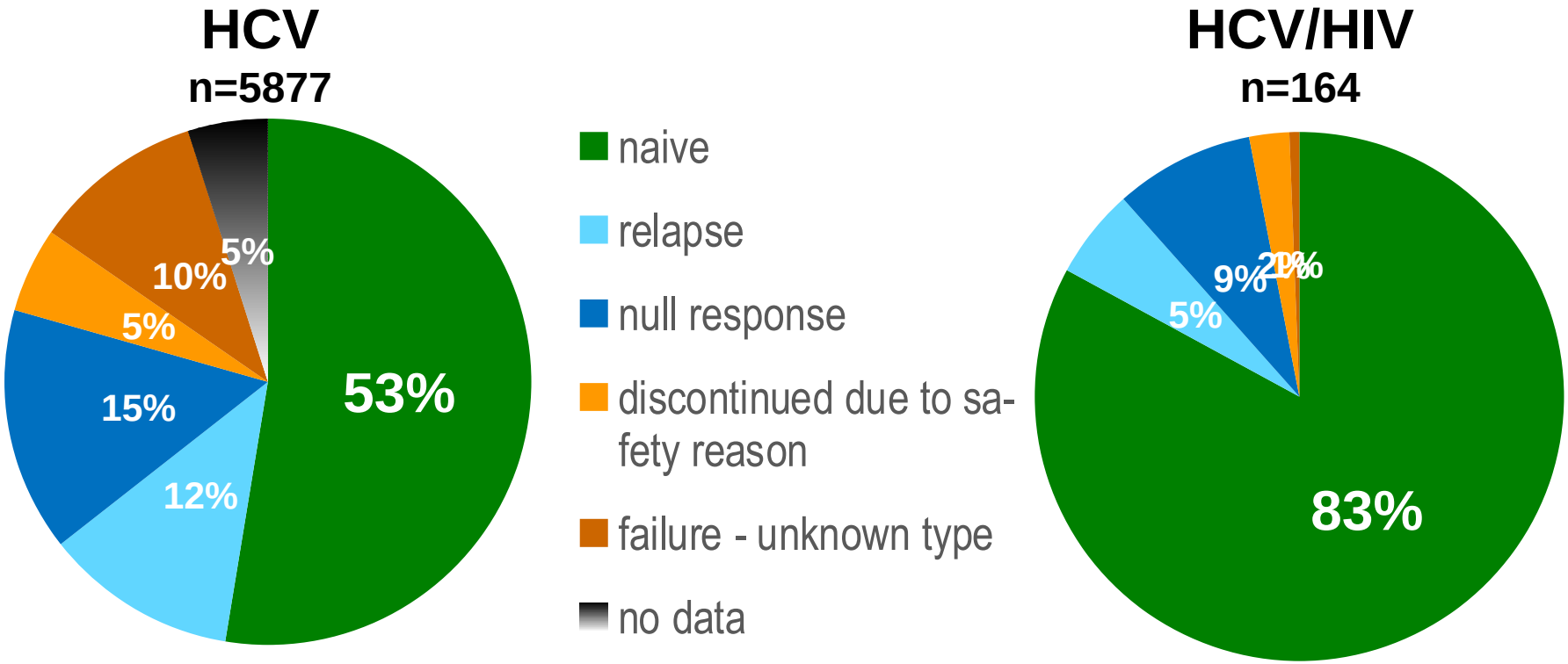
HCV/HIV
n=164



GT3 and GT4 are recognized as more frequently related to IVDU in Poland

History of previous treatment

EpiTer-2

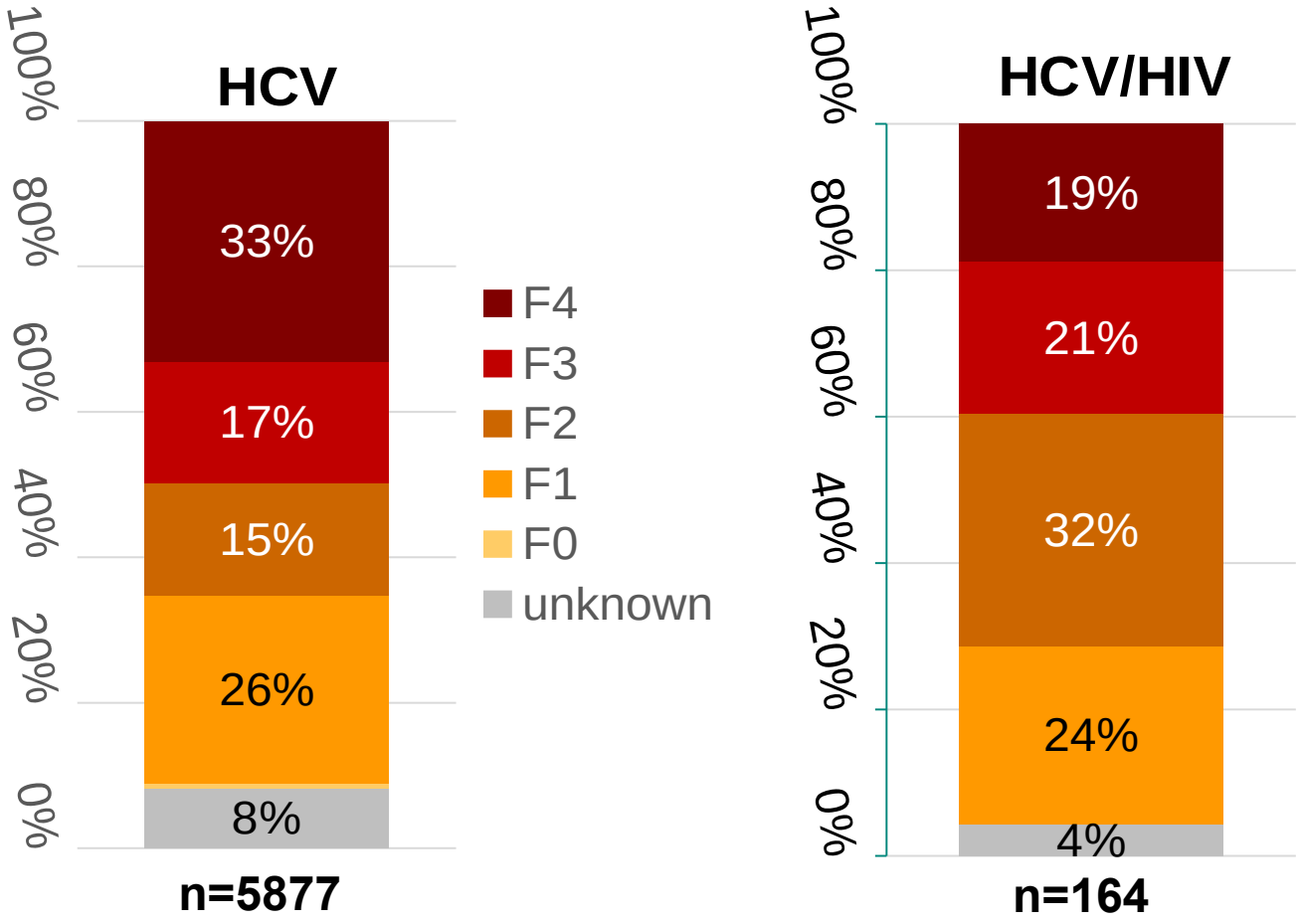


In the IFN era (<2015):

- ❖ HIV coinfected patients (mostly IVDU) were not interested in HCV treatment
  - complicated, long regimen, side effects
- ❖ Physicians (even ID) did not push them
  - reimbursement of ~3 500 IFN based therapies annualy (in 2017 >10 000)
  - non-adherence = waste of money

Fibrosis in HCV/HIV

EpiTer-2



Less advanced fibrosis in HCV/HIV !!!

Patients characteristics
EpiTer-2

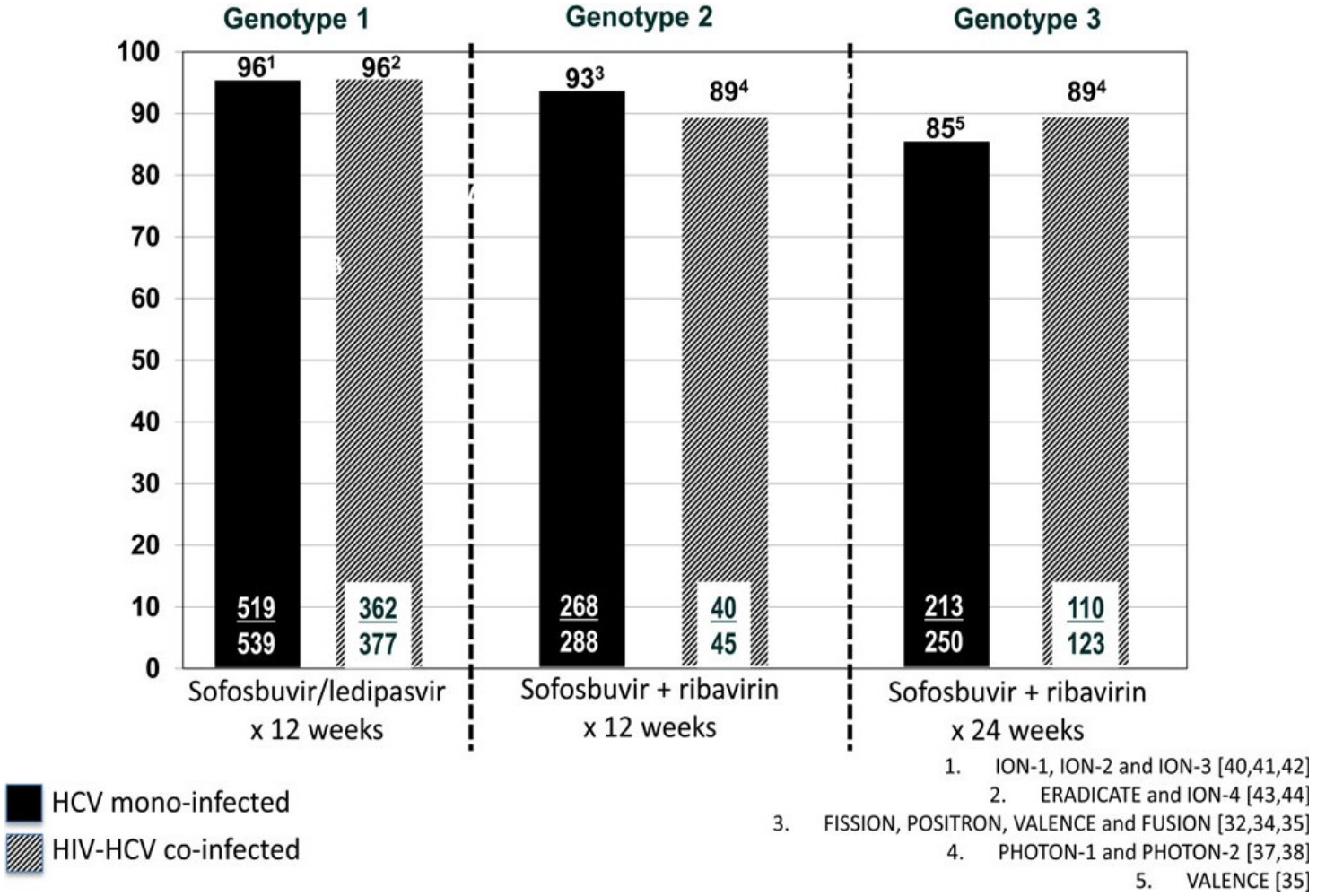
	HCV n=5877	HCV/HIV n=164
Decompensation history	269 (4.6%)	5 (3.0%)
HCC history	149 (2.5%)	1 (1.2%)
OLTx history	140 (2.4%)	0
Oesophageal varices	767 (13.1%)	14 (8.5%)
Ascites at baseline	96 (1.7%)	1 (0.6%)
Encephalopathy at baseline	54 (0.9%)	0
Patients with accompanying diseases	3897 (66.3%)	61 (41.5%)
GFR <30 ml/min	169 (2.9%)	0
MELD >18	128 (2.2%)	1 (0.6%)
Child-Pugh >A		3 (1.8%)

Less complicated disease !!!

SVR in clinical trials

HIV coinfected have similar SVR rates as HCV monoinfected with DAAs (SOF based regimens):

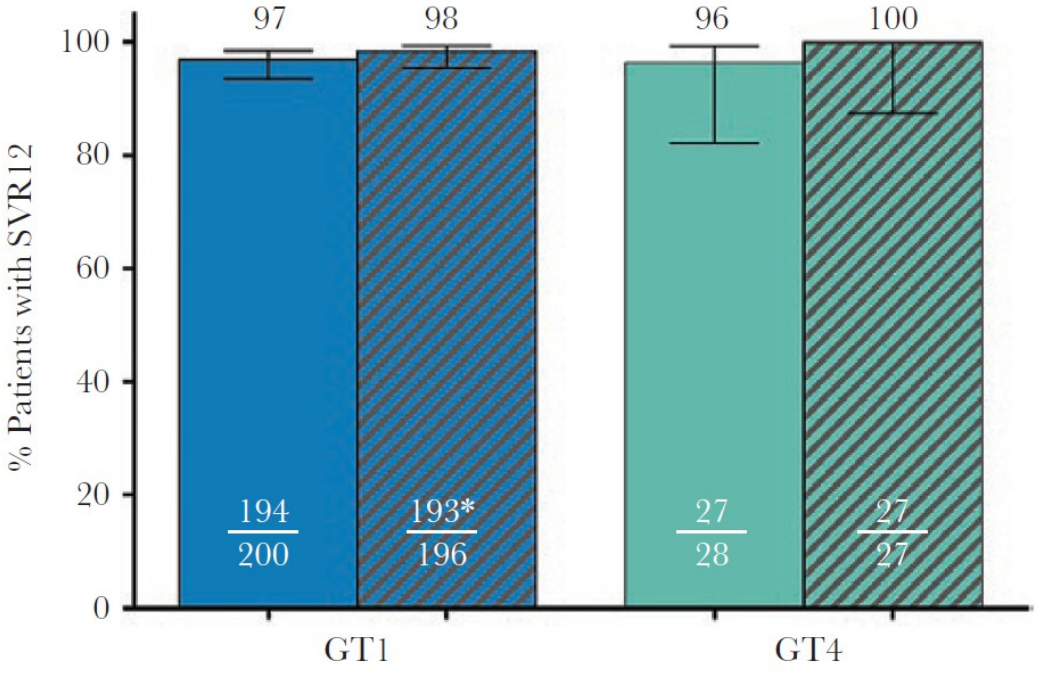
it's time to end segregation and integrate HIV patients into HCV trials



hafran SD et al.. Clinical Infectious Diseases 2015; 61:1127–34

SVR in clinical trials

Ombitasvir, Paritaprevir with Ritonavir ± Dasabuvir with or without Ribavirin in patients with HIV-1 and HCV GT1 or GT4 coinfection:
TURQUOISE-I Part 2



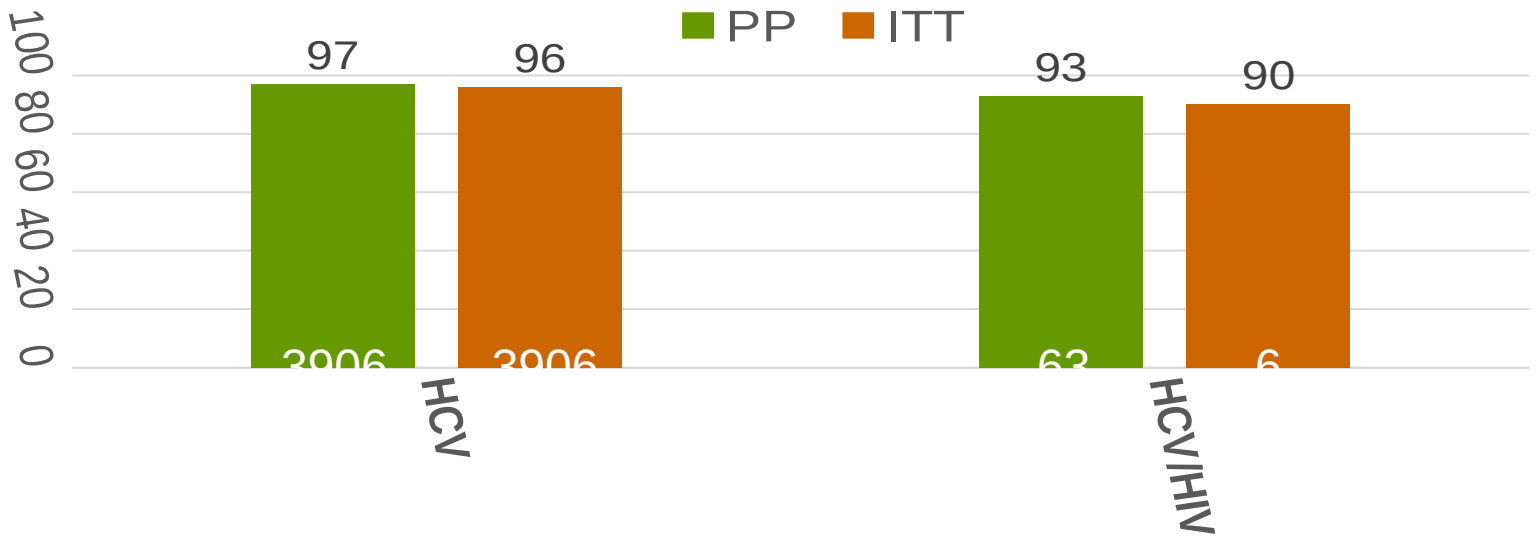
	GT1		GT4	
Breakthrogh	1	1	0	0
Relapse	1	1	0	0
Reinfection	1	1	0	0
Premature D/C	2	N/A	1	N/A
Missing SVR12 Data	1	N/A	0	N/A

: ITT analysis
: mITT analysis

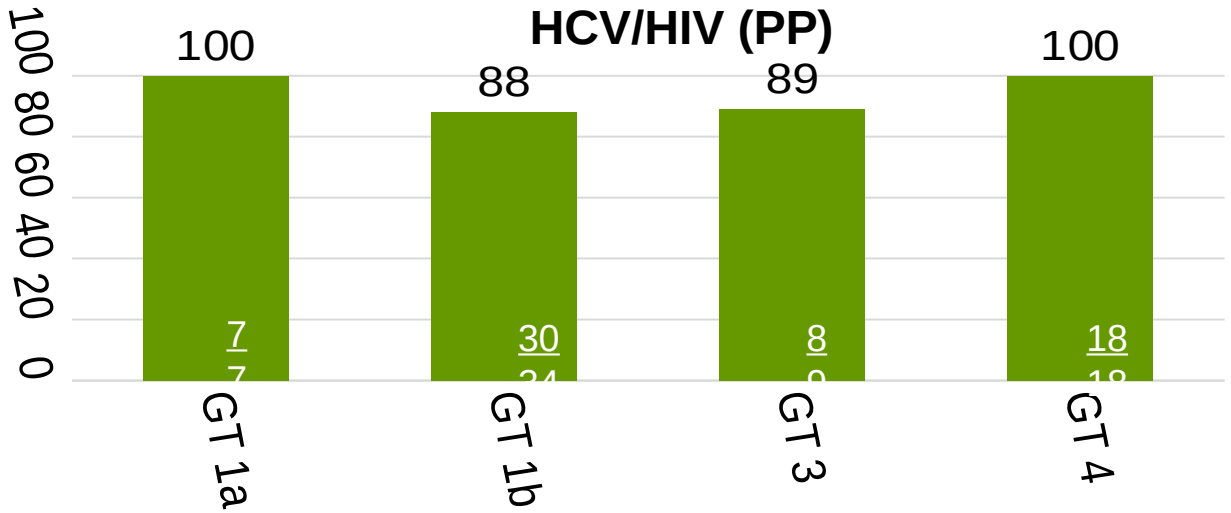
ockstroh JK et al. Open Forum Infectious Diseases 2017 in press

SVR in real world exerience

EpiTer-2

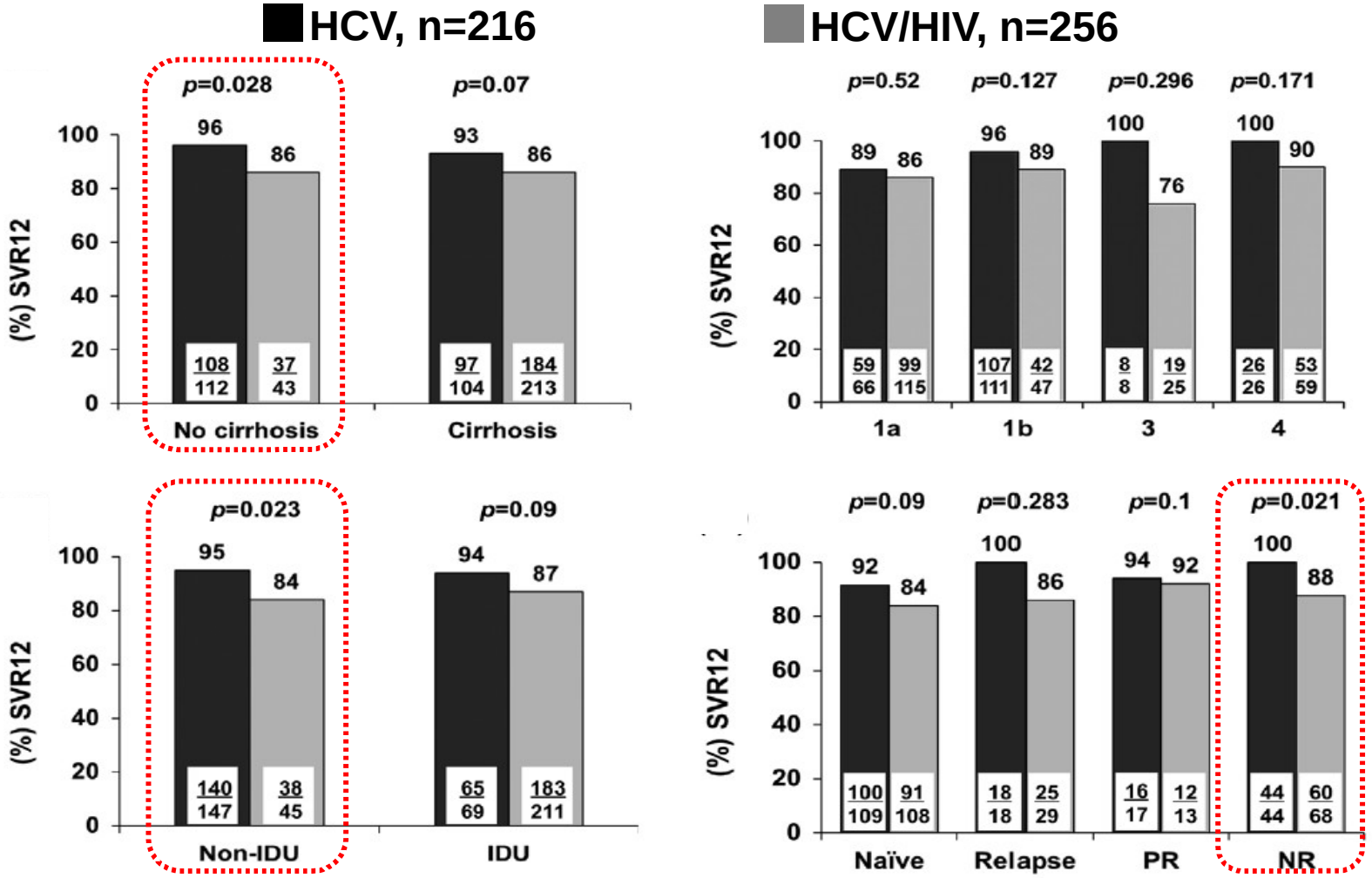


Available data: 70% 43%



SVR in real world experience

HCV vs. HCV/HIV, RWE data from the Spanish cohort

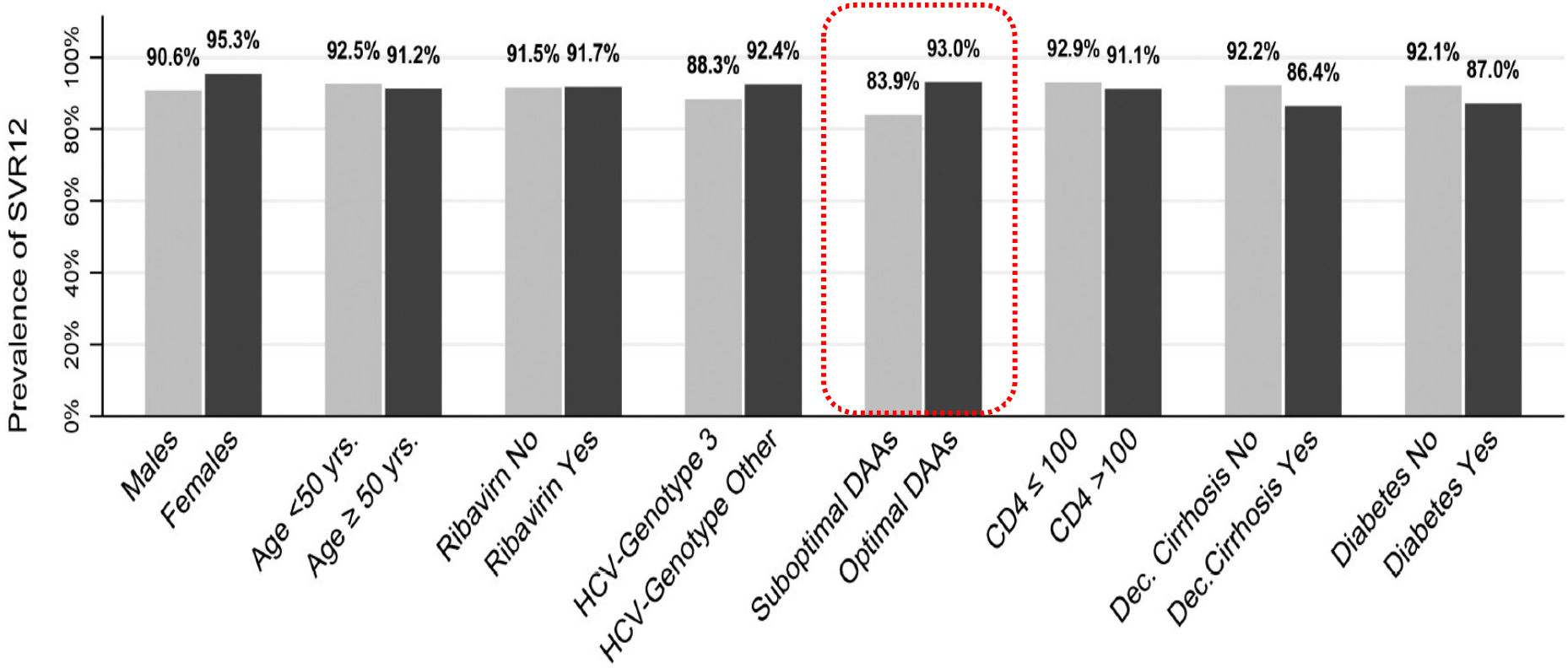


SVR was significantly reduced in
HIV coinfected non-cirrhotics, non-IDU and non-responders (???)

Neukam K et al. HIV Clinical Trials 2017; 18: 126-134

SVR in real world experience

RWE data from the Italian ICONA HCV/HIV cohort (n=1090)

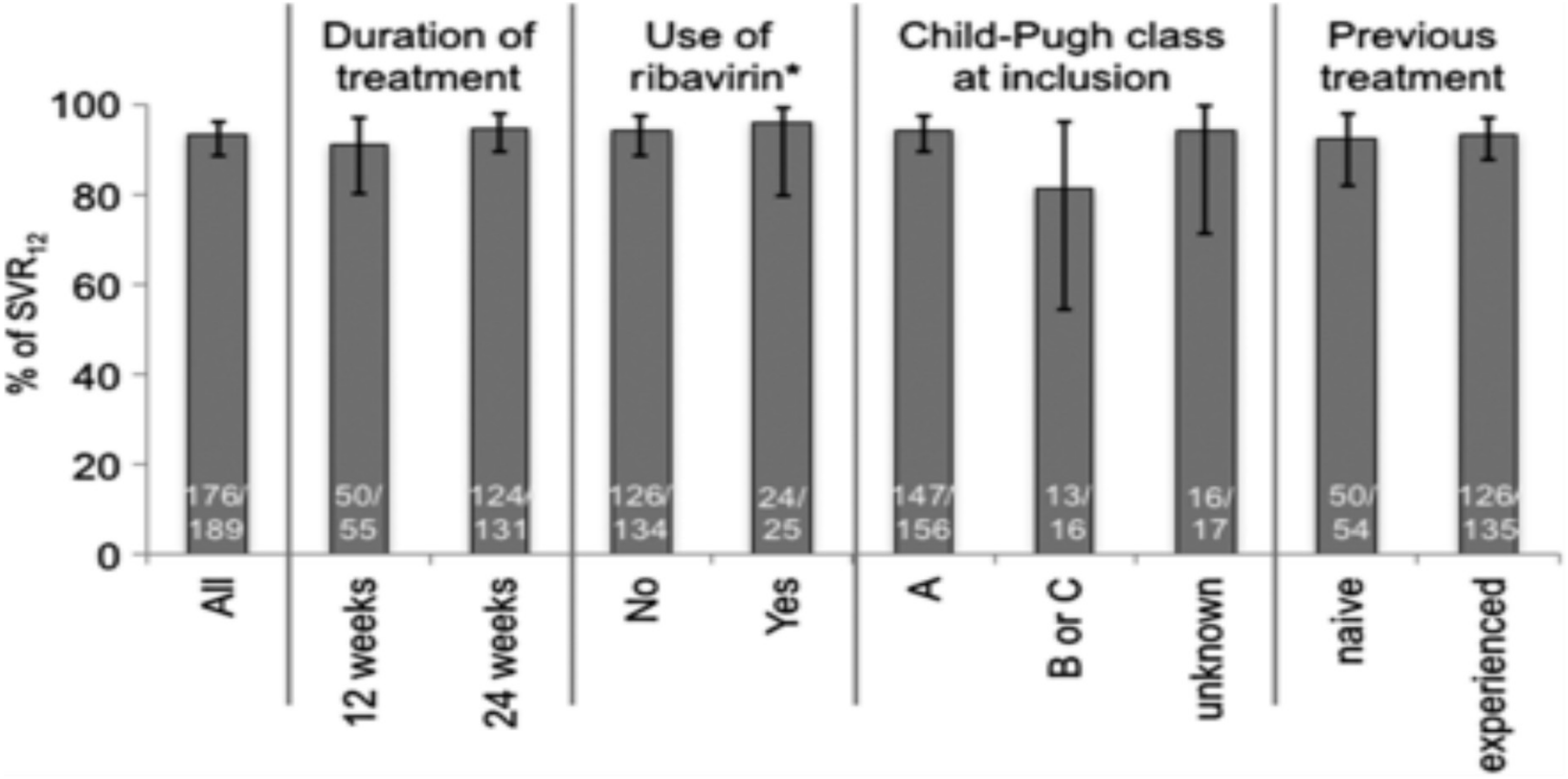


Suboptimal therapy was the only independent predictor of treatment failure

l'Arminio Monforte A et al. PLoS ONE 2017; 12(5): e0177402

SVR in real world experience

RWE data from the ANRS CO13–HEPAVIH Cohort (n=189)



No clear predictors of possible failure

Sogni P et al. Clin Infect Dis 2016; 63: 763–770

Drug-drug interaction

EASL | JOURNAL OF HEPATOLOGY

Table 4A. Drug-drug interactions between HCV DAAs 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	◆	◆	◆	◆	◆	◆	◆

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.

Colour legend

◆ No clinically significant interaction expected.

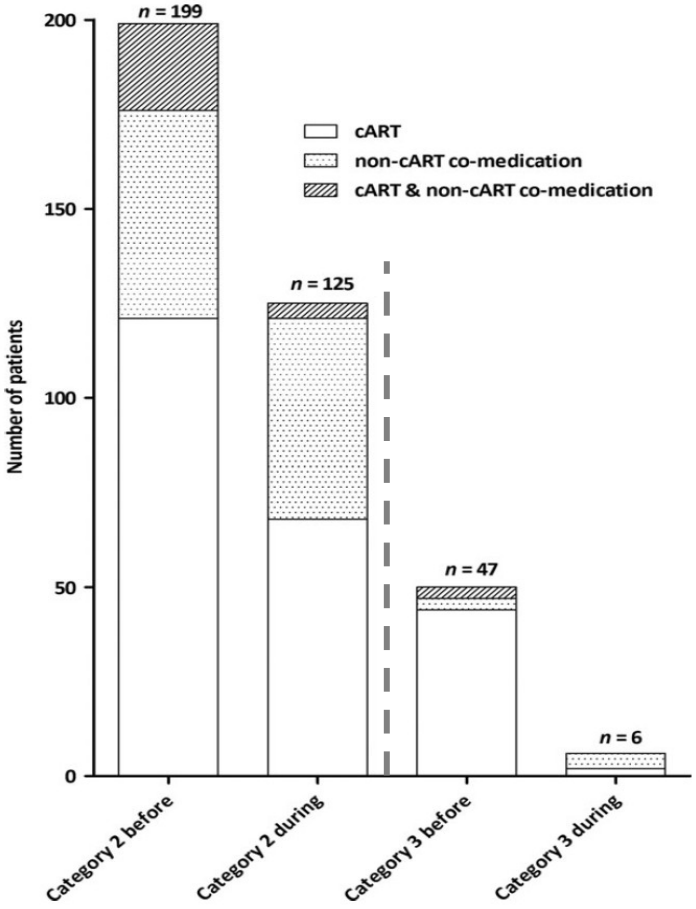
■ Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring.

● These drugs should not be co-administered.

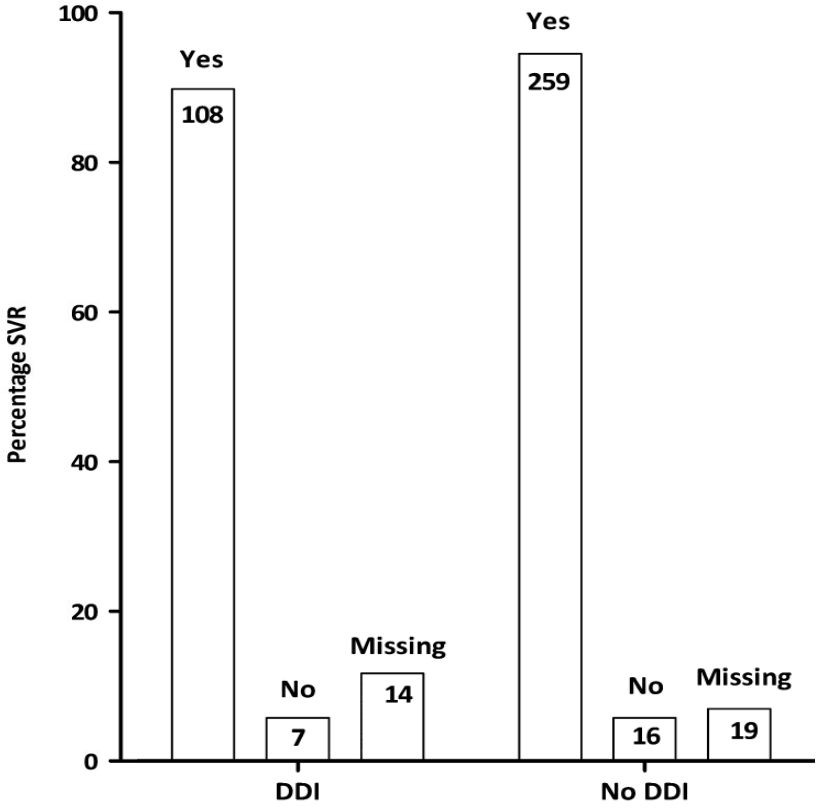
Journal of Hepatology 2017; 66: 153–194

Awareness of DDI among HCV/HIV treaters

Dutch experience, n=423



Reduced number of potential DDI related to cART during DAA therapy

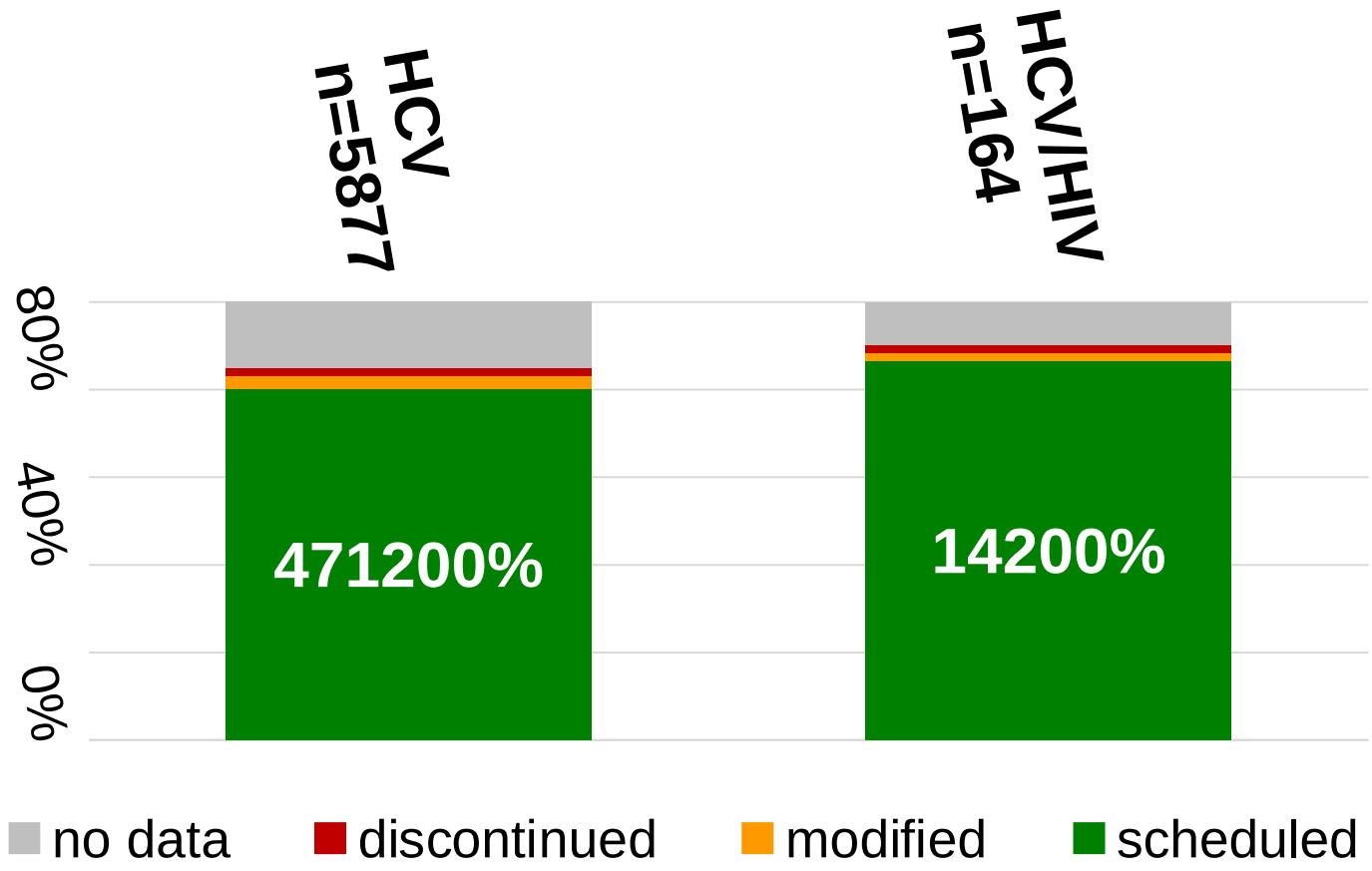


No effect of DDI on SVR

Smolders EJ et al. HIV Medicine 2017: DOI: 10.1111/hiv.12570

Need of DAA modification

EpiTer-2



Need of DAA modification due to risk of DDI similar to monoinfected

Need of cART modification due to DDI risk in 25 consecutive HCV/HIV patients from Białystok

HCV regimen	cART before HCV treatment	cART modified due to risk of DDI
VR	raltegrawir, abakawir, lamiwudyna	
VER	emtrycytabina, TDF, atazanawir, rytonawir	emtrycytabina, TDF, atazanawir
VR	lopinawir, rytonawir, abakawir, lamiwudyna	atazanawir, abakawir, lamiwudyna
VE	lopinawir, rytonawir, abakawir, lamiwudyna	dolutegrawir, abakawir, lamiwudyna
SoPR	emtrycytabina, TDF, atazanawir, kobicystat	
VE	emtrycytabina, TDF, raltegrawir	
HR	lopinawir, rytonawir, lamiwudyna, zydowudyna	dolutegrawir, abakawir, lamiwudyna
GE	emtrycytabina, rylpiwiryna, TDF	
VR		
SoPR	emtrycytabina, rylpiwiryna, TDF	
GER	emtrycytabina, rylpiwiryna, TAF	
H	emtrycytabina, TDF, newirapina	emtrycytabina, TAF, newirapina
SoR	kobicystat, elwitegrawir, emtrycytabina, TAF	
SoPR	emtrycytabina, rylpiwiryna, TAF	
SoR	emtrycytabina, rylpiwiryna, TDF	
VR	dolutegrawir, abakawir, lamiwudyna	
VR	darunawir, abakawir, lamiwudyna, rytonawir	raltegrawir, emtrycytabina, TAF
SoPR	emtrycytabina, rylpiwiryna, TDF	
SoPR	emtrycytabina, rylpiwiryna, TDF	

Need of cART modification due to DDI risk

in 7 among 25 consecutive HCV/HIV patients from Białystok

cART before HCV treatment	cART modified
emtricitabin, TDF, atazanavir, ~~ritonavir~~	emtricitabin, TDF, atazanavir
~~lopinavir~~, ~~ritonavir~~, abacavir, lamivudin	atazanavir, abacavir, lamivudin
~~lopinavir~~, ~~ritonavir~~, abacavir, lamivudin	dolutegravir, abacavir, lamivudin
~~lopinavir~~, ~~ritonavir~~, lamivudin, ~~zidovudin~~	dolutegravir, abacavir, lamivudin
emtricitabin, ~~TDF~~, nevirapin	emtrycytabina, TAF, nevirapin
~~darunawir~~, ~~abakawir~~, ~~lamiwudyna, rytonawir~~	raltegravir, emtricitabin, TAF
emtricitabin, rylpivirine, ~~TDF~~	emtricitabin, rylpivirine, TAF

Ritonavir removal or switch to newer regimens were major consequences of DDI preventing cART modification before start of DAA therapy.

Should we treat HCV/HIV coinfected as a „special” population?