Effect of Detectable HIV-RNA at Baseline on the Response to Treatment With PegIFN and RBV in Patients Coinfected With HIV and HCV

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Background

- Baseline predictors of sustained virologic response (SVR) after therapy with PegIFN and RBV (PR) in HIV/HCV+ patients include virus-related factors (e.g. HCV genotype and HCV-RNA), and host-related factors (e.g. liver fibrosis stage, and polymorphisms in *IL28B*).
- HIV can infect hepatic stellate cells[1], promoting collagen I expression and secretion of the proinflammatory cytokine monocyte chemoattractant protein-1, raising the question as to whether detectable HIV viral load (VL) can compromise PR efficacy in coinfected patients
- Paradoxically, in one clinical trial of PR in coinfected patients, detectable HIV VL at baseline was associated with an increased odds of SVR[2]

1. Tuyama AC, et al. **Hepatology** 2010; 52: 612
2. Chung et al. **NEJM** 2004; 351: 451

Aims

- We assessed whether HIV-VL that is detectable at baseline has an effect on treatment response to PR therapy.

Methods

- Pooled analysis of two large cohorts of HIV/HCV+ patients treated with PR in Spain between 2000 and 2008 (GESIDA 3603[1] and GESIDA 5006[2]).
- SVR was defined as an undetectable HCV RNA 24 weeks after discontinuation of PEG-IFN + RBV.
- Patients were categorized in 4 subgroups according to whether or nor were on cART and whether or not had detectable HIV-VL at the initiation of PEG-IFN + RBV
- Logistic regression models were used to test possible associations between SVR and pretreatment characteristics, including concomitant antiretroviral drugs.
- All analyses were performed on an ITT basis.

1 Berenguer J, et al. Hepatology 2009; 50:407-413
2 González-García JJ, et al. 15th CROI, 2008; Paper #

Patients characteristics (I)

Characteristic	HIV-VL (-) cART	HIV-VL (-) No-cART	HIV-VL (+) cART	HIV-VL (+) No-cART	Total
Patients*	1183 (70)	62 (4)	288 (17)	149 (9)	1682
Male sex*	891 (76)	45 (74)	212 (74)	105 (70)	1253 (75)
Age – yr	41 (37 – 44)	39 (36 - 43)	40 (37 - 43)	39 (36 - 43)	40 (37 - 44)
History of IDU*	966 (82)	50 (81)	238 (83)	115 (77)	1369 (82)
CDC category C*	285 (25)	4 (7)	76 (27)	13 (9)	378 (23)
CD4 + cells nadir – n/mm^3♯	187 (100 - 283)	370 (265 - 500)	187 (96 - 287)	389 (262 - 500)	204 (110 - 308)
CD4 + cells baseline – n/mm^3♯	519 (391 - 725)	645 (478 - 1036)	475.5 (333 - 664)	520 (421 - 699)	515 (390 - 720)
HIV viral load – Log c/mL♯	-	-	2.37 (2.06 – 3.36)	3.84 (3.04 – 4.42)	-
Methadone use*	126 (12)	9 (16)	31 (12)	24 (17)	190 (12.5)
Type of cART*					
3-4 nRTI	142 (12)	NA	46 (16)	NA	188 (11)
2 nRTI + nnRTI	354 (30)	NA	105 (36)	NA	459 (27)
2 nRTI + PI	584 (49)	NA	105 (36)	NA	689 (41)
Other regimens	103 (9)	NA	32 (12)	NA	135 (8)

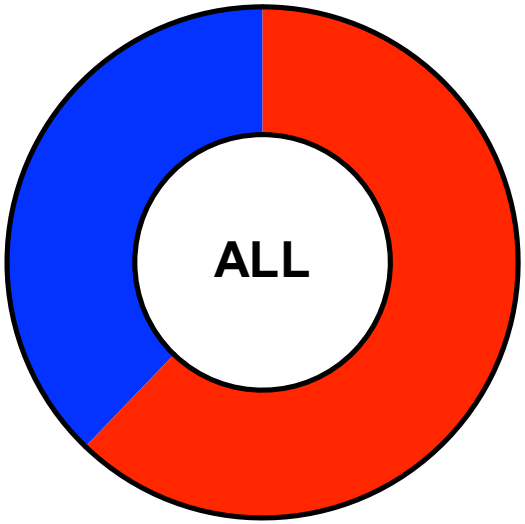
*n (%); ♯median (IQR)

Patients characteristics (II)

Characteristic	HIV-VL (-) cART	HIV-VL (-) No-cART	HIV-VL (+) cART	HIV-VL (+) No-cART	Total
Patients*	1183 (70)	62 (4)	288 (17)	149 (9)	1682
HCV genotype*					
1	598 (50)	25(40)	153 (53)	59 (39)	835 (50)
2	24 (2)	4 (6)	5 (2)	6 (4)	39 (2)
3	380 (32)	21 (34)	87 (30)	53 (35)	541 (32)
4	155 (13)	9 (14)	31 (11)	26 (17)	221 (13)
Unknown	26 (2)	3 (5)	12 (4)	5 (3)	46 (3)
HCV-RNA ≥ 500,000 IU/mL*	341 (30)	22 (40)	77 (28)	30 (21)	470 (30)
Liver Biopsy*	789 (67)	37(60)	212 (74)	104 (70)	1142 (68)
METAVIR F≥3*	317 (41)	11(30)	89 (42)	28 (27)	445 (40)
EtOH intake > 50 mg/d*	472 (40)	24 (39)	107 (37)	57 (38)	660 (39)
Type of IFN*					
Pegylated a2a	453 (38)	23 (37)	143 (49.6)	71 (48)	690 (41)
Pegylated a2b	730 (62)	39 (63)	145 (50.4)	78 (52)	992 (59)
RBV dose mg/kg/day♯	14 (12.6-15.6)	13 (11.8-15.3)	14 (12.3-15.3)	13.6 (12.3-15.3)	14 (12.6-15.3)

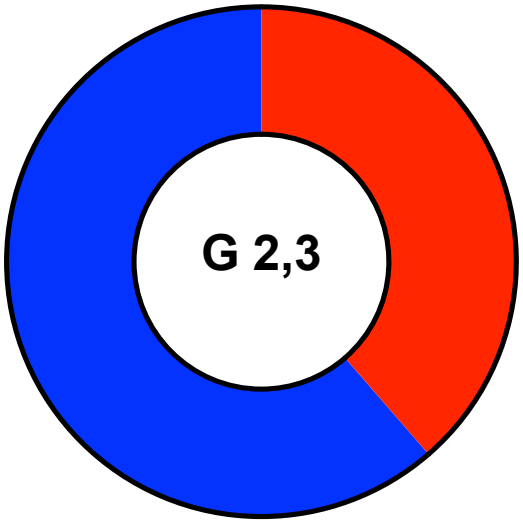
*n (%); ♯median (IQR)

SVR by Genotypes



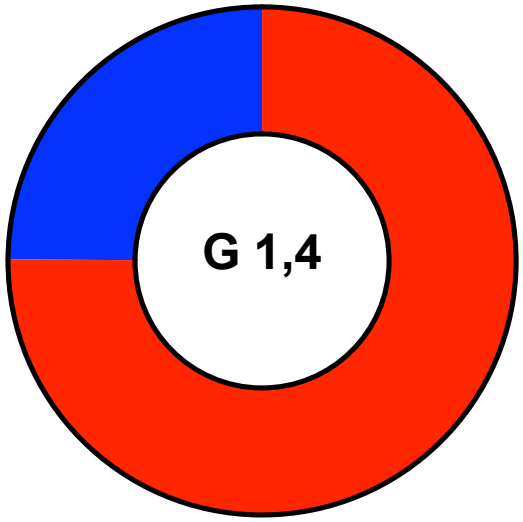
N = 1682

SVR 37.8%



N = 580

SVR 61.4%

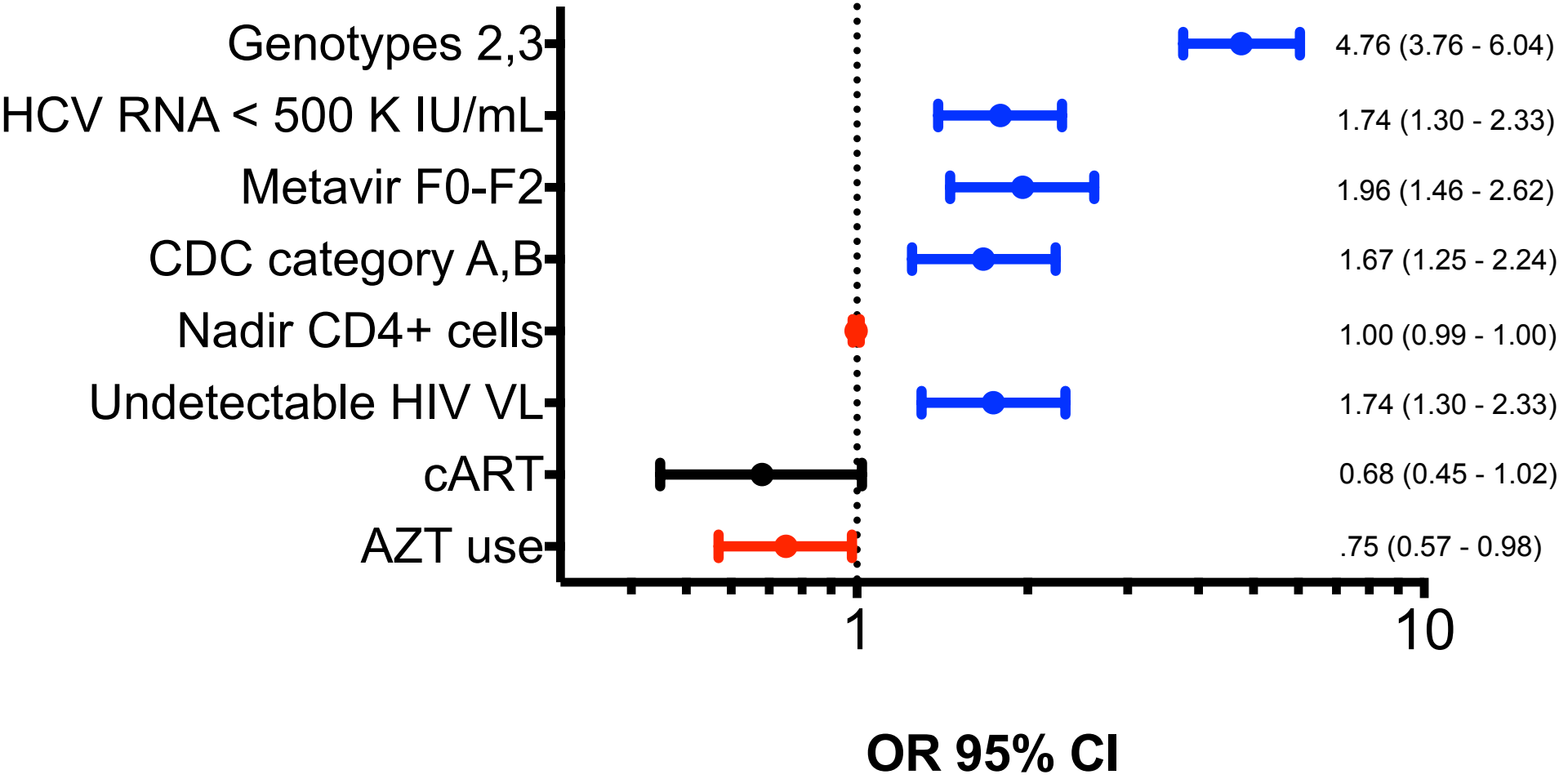


N = 1056

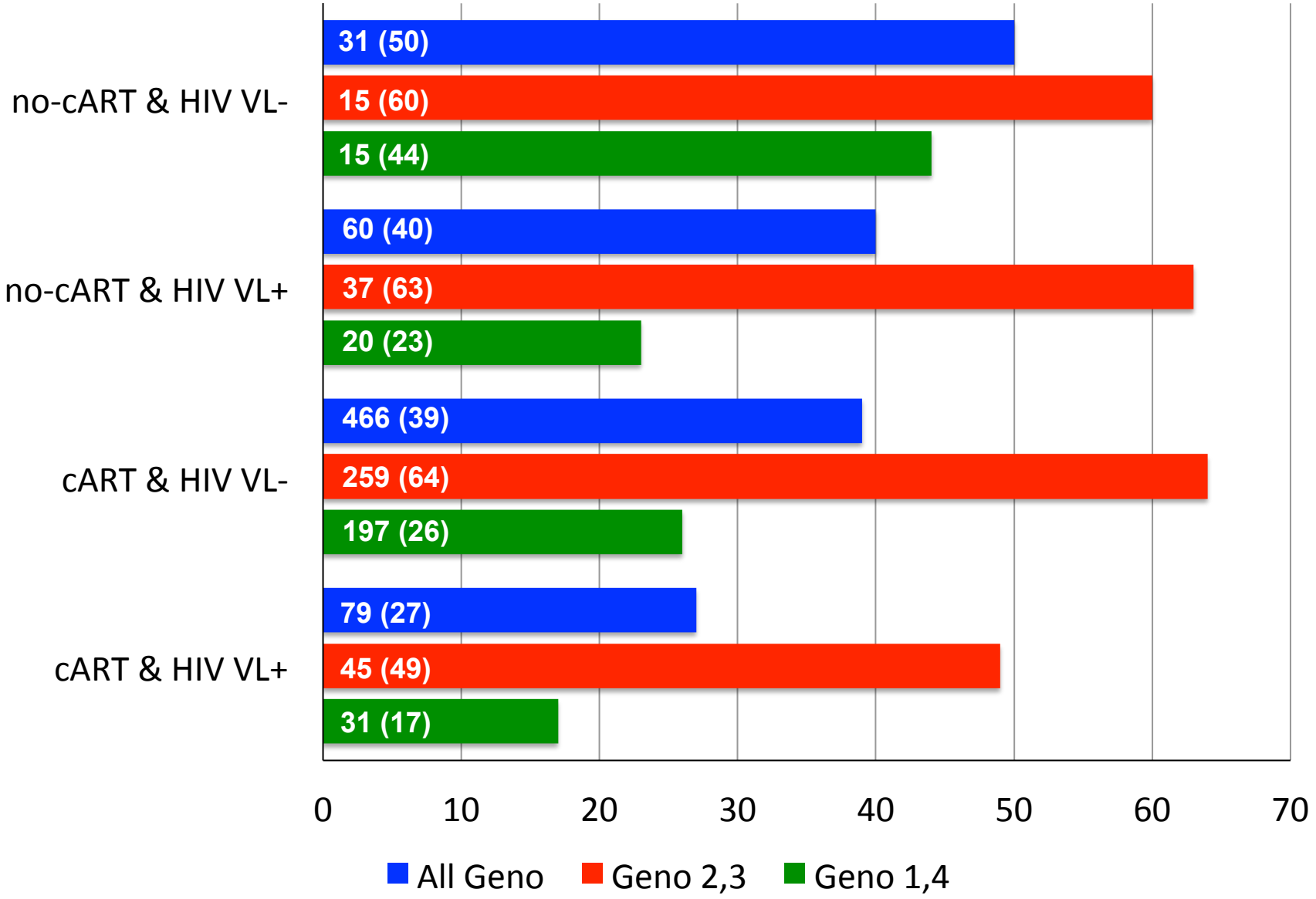
SVR 24.9%

Baseline Predictors of SVR

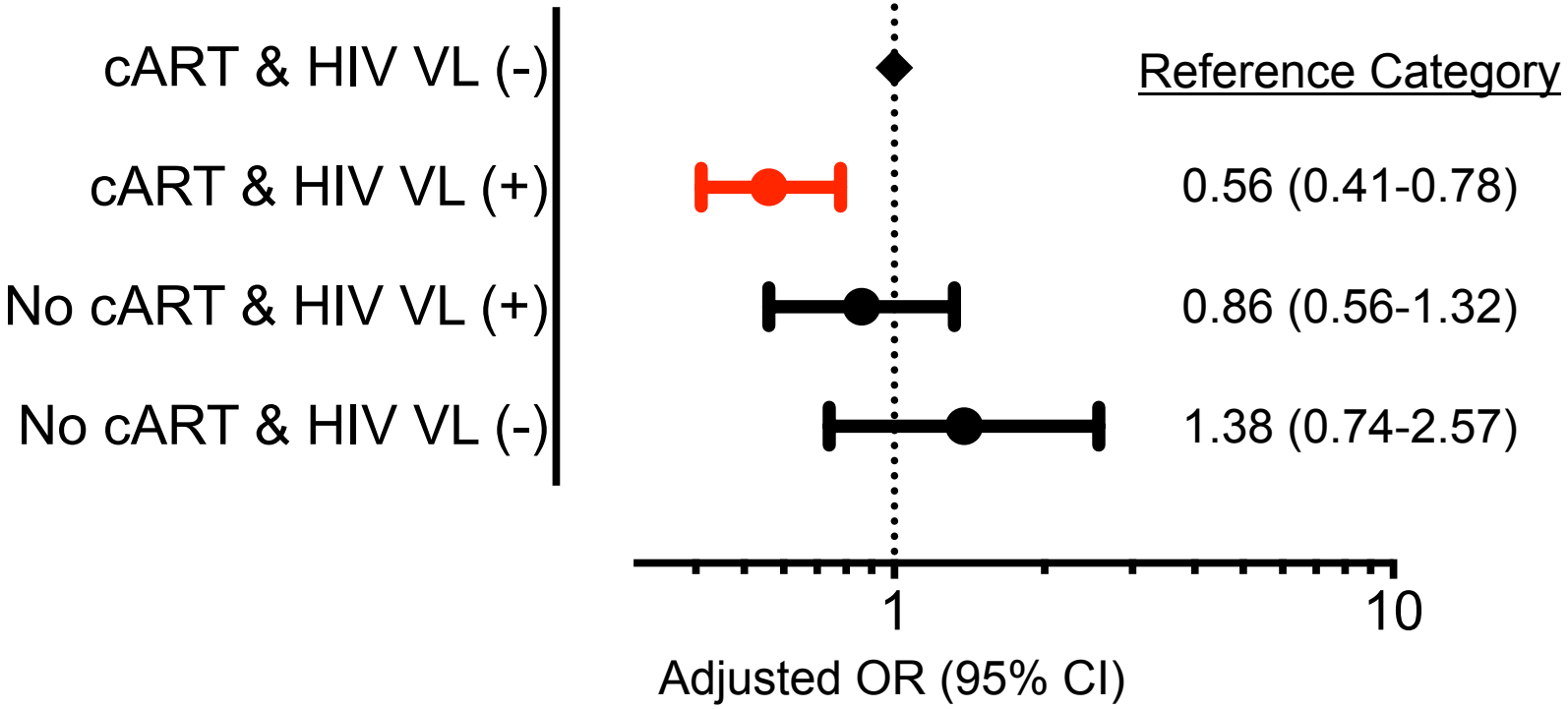
(Multivariate Logistic Regression Analysis)



SVR Subgroup Analysis



Adjusted OR (95% CI) for SVR
According to different categories



Adjusted by nadir CD4+ cell count, CDC clinical category, AZT use, HCV genotype, HCV-RNA, and liver fibrosis stage

Conclusions

① Detectable HIV-RNA at baseline was independently associated with a reduced likelihood of SVR.

② However, subgroup analysis adjusted by important baseline covariates indicated that this was only true in patients with detectable HIV-VL and cART.

③ It remains to be determined whether this last finding represents a true effect of HIV-VL on response to PR or a spurious association due to poor adherence to treatment

④ The finding that treatment response to PR among patients without cART and detectable HIV-VL was not compromised, support the notion that treating HCV before HIV can be an option in co-infected patients with high CD4+ cell counts

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