Same same but different? Risk of DAA therapy failure in real-life HCV/HIV coinfection: The GECCO Cohort

551

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Background

Directly-acting agents (DAA) against HCV have impressively improved treatment of chronic hepatitis C coinfection. However, relapses still occur. Therefore we assessed the influence of traditional risk factors on treatment outcome in HCV/HIV coinfected patients in the German hepatitis C cohort (GECCO).

Methods

The GECCO cohort is a multicenter cohort from 9 sites in Germany. All HCV mono- and coinfected patients with complete follow-up having received one of the following DAA regimen were analysed (n=1505): Pegylated interferon plus ribavirin (RBV) + sofosbuvir (SOF); SOF + RBV; SOF + simeprevir; SOF + daclatasvir +/- RBV; SOF + ledipasvir; paritaprevir/ritonavir, ombitasvir +/- RBV and +/- dasabuvir. Treatment outcome was measured as sustained virologic response 12 weeks after end of therapy (SVR12). Liver cirrhosis was assessed mainly by transient elastography (FibroScan®) or APRI score. Fisher's exact, chi-square and Mann-Whitney U test were used for statistical analysis.

Results

Baseline characteristics of 1505 patients are shown in table 1.

Table 1. Baseline characteristics

	All n=1505	HCV mono n=1156	HCV/ HIV n=349	p-value
Male sex [%]	63	55	89	**≤0.001**
Median age [years] (IQR)	52 (45-59)	54 (46-61)	48 (42-53)	0.095
HCV GT 1/2/3/4 [%]	72/4/18/6	73/3/21/3	70/3/9/18	**≤0.001**
Baseline HCV-RNA >6 Mio. IU/ml [%]	20	17	27	**≤0.001**
Median baseline ALT [U/l] (IQR)	67 (43-111)	67 (42-111)	65 (43-109)	0.982
Treatment-experienced [%]	46	45	52	0.107
Liver cirrhosis [%]	29	31	22	**0.003**
OST [%]	19	18	21	0.309

349/1505 (23%) were HIV coinfected. Among HCV/HIV coinfected patients median CD4 nadir was 206/ul (123-360). 69/349 (20%) were diagnosed with HIV at CDC stage C (clinical AIDS) of which 55 were diagnosed at CDC stage C3. 61/349 (17%) had baseline CD4 <350/ul, 53/349 (15%) baseline CD4 <20%. 345/349 (99%) were on cART.

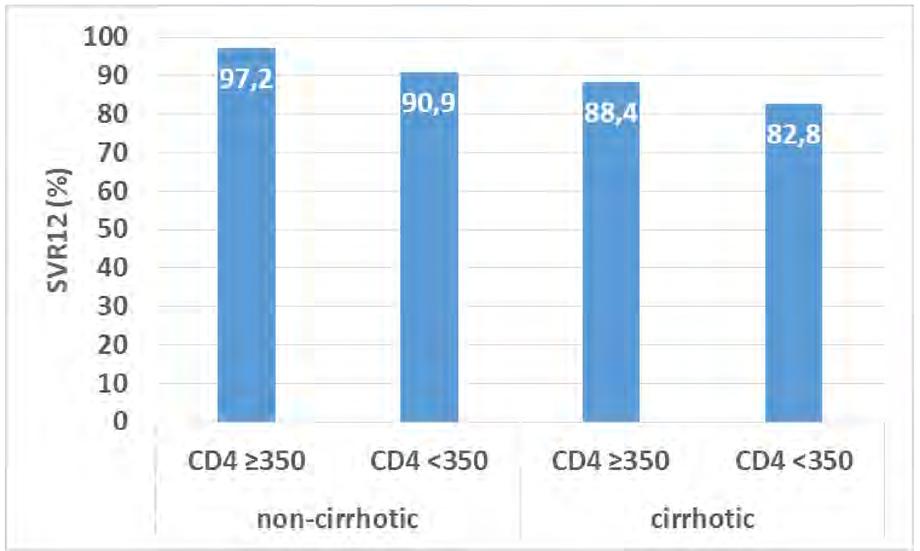
Results

Overall SVR rate was 95% (1425/1505), 95% (1096/1156) in HCV mono- and 94% (329/349) in HCV/HIV coinfected (p=0.684).

10 patients stopped treatment (1 non-response, 2 viral breakthroughs, 7 toxicities). 3 re-infections and 67 relapsers were noted.

Among the 349 coinfected patients, neither sex (p=0.708), age (p=0.876), GT (p=0.594), high HCV RNA (p=0.873), ALT (p=0.262), TE (p=0.360), CD4 nadir (p=0.473) or OST (p=0.391) were statistically significantly associated with SVR in univariate analysis. However, patients with CD4 <350/ul (p=0.012), CD4 <20% (p=0.005) and liver cirrhosis (p=0.003) were less likely to achieve SVR (see figure 1). In multivariate analysis only liver cirrhosis (p=0.02, OR 3.5 (95%CI 1.2-9.9)) remained statistically significantly associated with Non-SVR.

Figure 1. SVR12 according to cirrhosis status and CD4 T cell count (/ul)



Treatment was stopped in 4 patients due to clinical adverse events (dyspnea, rash, panic attacks, insomnia). No grade 3 or 4 laboratory adverse event was reported.

Conclusions

Despite considerably improved safety and efficacy of treatment of chronic hepatitis C with DAA in HCV/HIV-coinfection liver cirrhosis remains as a risk factor for DAA treatment failure in patients with additional impaired immune function. Low CD4 cells were highly correlated with liver cirrhosis probably due to splenomegaly causing lymphopenia. This highlights the need for early initiation of DAA therapy in HCV/HIV coinfected patients before the onset of higher liver fibrosis/cirrhosis to allow for optimal rates of viral eradication and to substantially reduce morbidity and mortality in this patient population.