584 Directly Acting Agents Against HCV - Results From the German Hepatitis C Cohort (GECCO)

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Objective

In January 2014, the EMA approval of sofosbuvir heralded a new era in the management of hepatitis C patients in Europe. Henceforward, interferon-sparing or interferon-free regimens became the standard-of-care in Germany. However, the data available from clinical trials was very limited, especially with regards to certain patient populations such as HIV-HCV coinfected patients or patients treated with sofosbuvir (SOF) and ledipasvir (LDV) for 8 weeks (SL8). The multicentric GErman hepatitis C COhort – GECCO – was initiated in February 2014, to rapidly generate a reliable real-life dataset on the treatment outcome with directly-acting agents (DAA) from Germany.

Methods

The GECCO cohort is a multicenter cohort from 9 sites in Germany. All patients started on the following DAAs were included in the analysis (Figure 1): Sofosbuvir (SOF), pegylated interferon and ribavirin (RBV); SOF and RBV; SOF and simeprevir (SMV); SOF and daclatasvir (DCV) +/- RBV; SOF and ledipasvir (LDV); paritaprevir/ritonavir (PTV/r), ombitasvir (OBV)+/- RBV and +/- dasabuvir (DSV).

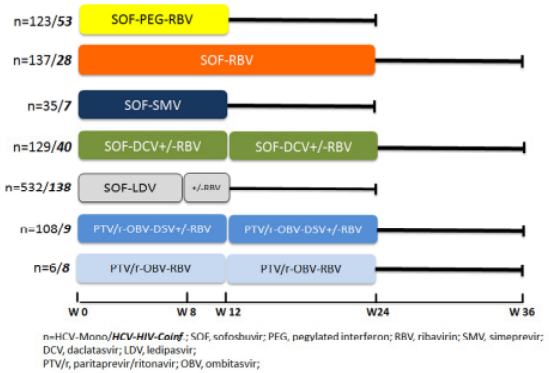

Figure 1: DAA regimes and duration of treatment documented in GECCO

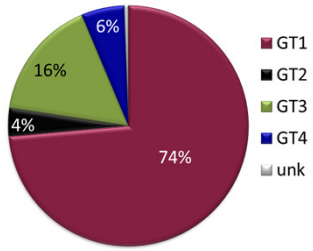

Figure 2: HCV-genotype distribution (n=1353)

Results

Up to date, 1346 patients were included into the cohort. The HCV genotype (GT) distribution was as follows (**Figure 2**): 996 (74%) GT 1, 51 (4%) GT 2, 221 (16%) GT 3, 78 (6%) GT4. The basline characteristics are shown in **Table 1**. N=282 were HIV-coinfected patients with a median CD4+ cell count of 606/mm^3. SVR12 rates for the whole cohort according to genotype and DAA regimen are shown in **Figure 3**. Relapse rates did not differ in HCV-mono (4%) or HIV-HCV-coinfected (6%) patients.

Results cont.

Pretreatment status, presence of liver cirrhosis or diabetes at baseline or a HIV-coinfection did not influence SVR12 rates (P =NS). N=258 patients were treated for SL8, n=191 reached FU12 time point with 92% SVR12, 2% (n=4) relapse and 6% (n=11) lost to follow up. Although not recommended for patients with high VL at baseline (measured with either Roche Taqman v2.0 or Abbott Real Time PCR), pretreated or cirrhotic patients, no statistical significant difference of the SVR12 rate could be detected in either of these subgroups **(Figure 5**).

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Table 1: Baseline patient characteristics

	HCV (n=1070)	HIV/HCV (n=283)	p
Male sex	612/1070 (79%)	254/283 (90%)	<0.001
Median age [years] (IQR)	53 (45 – 61)	48 (42 – 53)	<0.001
Median HCV RNA [IU/mL] (IQR)	1.1x10^6 (0.4x10^6 – 2.9 x10^6)	1.2x10^6 (0.2x10^6 – 3.3 x10^6)	ns
Median ALT [U/L] (IQR)	68 (48 – 118)	69 (45 – 124)	ns
Median platelets [/nL] (IQR)	195 (142 – 241)	195 (149 – 235)	ns
Median haemoglobin [g/dL] (IQR)	14.6 (13.5 – 15.5)	14.9 (13.9 – 15.7)	<0.05
Median bilirubin [mg/dL] (IQR)	0.58 (0.4 – 0.8)	0.57 (0.4 – 0.8)	ns
Median HIV RNA <20 [copies/mL] (IQR)		244/271 (90%)	
Median CD4+ [cells/µL] (IQR)		606 (402 – 777)	
FibroScan >12,5 kPa or APRI>2	272/1055 (26%)	47/276 (17%)	<0.001
Diabetes	68/1070 (6%)	11/283 (4%)	ns
Opioid substitution	220/1070 (21%)	63/283 (22%)	ns
Prior HCV treatment	489/967 (51%)	143/283 (51%)	ns
Genotype 1	798/1066 (75%)	198/280 (71%)	ns
Genotype 2	42/1066 (4%)	9/280 (3%)	ns
Genotype 3	198/1066 (19%)	23/280 (8%)	<0.001
Genotype 4	28/1066 (3%)	50/280 (18%)	<0.001

Figure 3: Treatment efficacy stratified by genotype and DAA regimen (with at least n=10 treated, ITT)

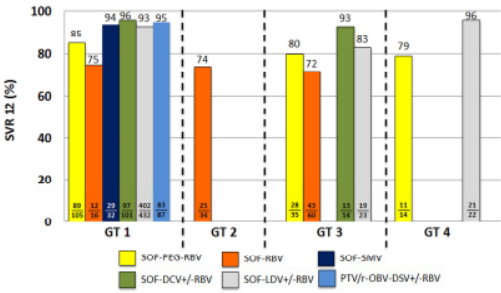
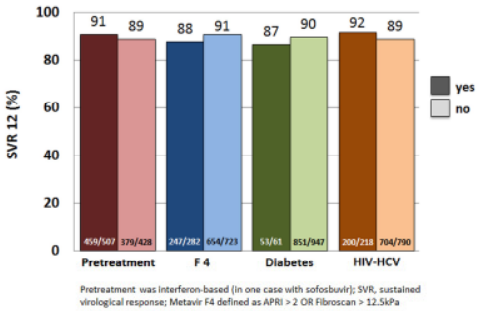
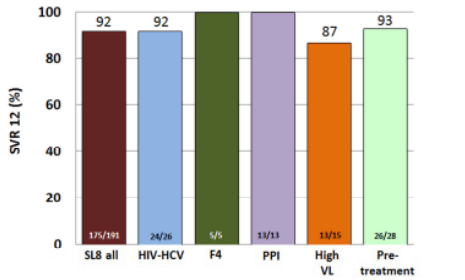


Figure 4: Treatment efficacy for different subgroups (ITT) [p=ns for all subgroups]



Pretreatment was interferon-based (in one case with sofosbuvir); SVR, sustained virological response; Metavir F4 defined as APRI > 2 OR Fibroscan > 12.5kPa

Figure 5: Treatment efficacy SOF-LDV for 8 weeks (SL8) for different subgroups (ITT) [p=ns for all subgroups]



Metavir F4 defined as APRI > 2 OR Fibroscan > 12.5kPa, high VL load defined as > 2mio IU/ml (Abbott PCR) or 6 mio IU/ml (Roche PCR), pretreatment was interferon-based (in one case with sofosbuvir); SVR, sustained virological response; APRI, AST-to-platelets ratio index; VL, viral load; PPI, Protonpump inhibitor use at baseline

Conclusion

Real-life DAA-based treatment regimens are highly effective in HCV-mono- as well as HIV-HCV-coinfected patients. Relapse occurred in only 4% of the patients. All DAA combinations were generally well tolerated. In particular, SOF/LDV for 8 weeks seems highly effective in selected patients in this population.