Response to DAA-based regimens in HIV-HCV co-infected patients in real-life, France

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Abstract

Background: Several new oral direct active agent (DAA)-based regimens are available in France for HCV-HIV co-infected patients. We report on efficacy and safety of DAA-based regimen in real-life settings.
Methods: HIV-HCV co-infected patients enrolled in the French nationwide ANRS CO13 HEPAVIH cohort were included in this analysis if an oral DAA-based regimen without peg-interferon was initiated before March 1st 2015 (3-month regimen) or before December 1st 2014 (6-month regimen) and if the patients had sufficient follow-up data to evaluate DAA efficacy. Treatment success was defined as an undetectable HCV-RNA (<15 UI/mL) at 12 weeks or thereafter (SVR12). Patients with premature treatment stops, detectable HCV-RNA and those who died during treatment were considered as treatment failures.
Results: We included 215 patients in 25 clinics with a median age of 53 years (IQR: 50-56), 76% men and 98% on antiretroviral therapy. HIV viral load was <50 copies/mL in 87% and median CD4 was 530 cells/mm³ (IQR: 342-730). Sixty-seven percent of the patients were cirrhotic, and 71% had failed previous anti-HCV treatment. HCV genotype (Gt) distribution was as follows: Gt1, 61%; Gt2, 3%; Gt3, 14%; Gt4, 21%; Gt6, 1%. Overall, we observed SVR12 in 92% of patients (95% CI: 87-95): 92% (CI: 87-96) in cirrhotic and 90% (CI: 80-96) in non-cirrhotic patients. In a subgroup analysis of 106 cirrhotic patients receiving a regimen without ribavirin, SVR12 for 12 or 24 weeks of treatment were 93% (CI: 76-99) and 92% (CI: 84-97), respectively. Furthermore, in cirrhotic patients receiving a DAA regimen with ribavirin for 12 and 24 weeks, SVR12 rates were 83% (CI: 36-100) and 94% (CI: 78-99), respectively. Of 18 patients with treatment failure, there were 15 relapses, two premature stops and one death. Patients with treatment failure had a median age of 54 years (IQR: 51-57), were mainly men (78%); 12 of them were Gt1, 3 Gt3 and 3 Gt 4; 61% were cirrhotic. Planned treatment duration was 24 weeks in 10 of these patients and 12 weeks for the remaining 8 patients.
Conclusion: In this real-life prospective French nationwide cohort of HIV-HCV co-infected patients, oral-DAA based regimens showed high efficacy and excellent tolerability. In cirrhotic patients neither a longer duration of treatment nor the addition of ribavirin seemed to have an impact on treatment response.

Background

- It is widely recommended to treat chronic hepatitis C in HIV co-infected patients, considering its worse evolution and prognosis in these patients. Several new oral direct active agents (DAA)-based regimens are available in France for HIV-HCV co-infected patients since 2014.

Aims

- To describe DAA-based treatments prescribed to HIV-HCV co-infected patients.
- To describe virological responses 12 weeks after end of treatment, according to DAA prescribed, genotypes, cirrhosis, treatment duration and use of Ribavirin.
- To describe adverse events and treatment failures.

Methods

➢ Study population:

HIV-HCV co-infected patients enrolled in the French nationwide ANRS CO13 HEPAVIH cohort were included in this analysis if:

- an all-oral DAA-based regimen without peg-interferon was initiated,
- DAA-based treatment started before March 1st 2015 (if planned duration was 3 months) or before December 1st 2014 (if planned duration was 6 months),
- treatment was outside clinical trial,
- sufficient follow-up data were available to evaluate treatment efficacy.

➢ Statistical analysis:

- Treatment efficacy was evaluated at end of treatment (EOT) and at least 12 weeks after end of treatment (SVR12).
- Treatment success was defined as an undetectable HCV-RNA (< 15 UI/mL) at SVR12.
- A patient was considered as a relapser when his HCV-RNA was undetectable at EOT but detectable at SVR12 (or before).
- Treatments of patients with detectable HCV-RNA at EOT or before 12 weeks after treatment stop, or who died during treatment, were considered as failures in this analysis.
- Descriptive results are presented as numbers (%) for qualitative variables and median (interquartile range, IQR) for quantitative variables. 95% confidence intervals for treatment outcomes were calculated.
- Factors associated with HCV treatment success were evaluated with exact logistic regression.

Results

Study population

- Among the 477 patients who initiated a DAA-based regimen, 215 fulfilled the inclusion criteria.
- DAA-based treatment repartition was as follows: Sofosbuvir (SOF) + Daclatasvir (DCV) ± Ribavirin (RBV) n=145, SOF + RBV n=32, SOF + Ledipasvir (LDV) ± RBV n=25, SOF + Simeprevir (SMV) ± RBV n=13

Characteristics	Overall (n=215)
Age (years)	53 (50-56)
Male sex	164 (76)
CD4 (/mm³)	530 (342-730)
HIV-RNA < 50 copies/mL	187 (87)
cART	211 (98)
HCV genotype (Gt)	
1 (overall)	131 (61)
including 1a	85 (65)
including 1b	28 (21)
2	7 (3)
3	30 (14)
4	46 (21)
6	1 (1)
Cirrhosis	145 (67)
Elastometry (measured by Fibroscan®, kPa) (n=118)	14.2 (10.1-21.8)
Failure to previous HCV treatment	153 (71)
HCV viral load (log_{10} UI/mL)	6.0 (5.6-6.4)
Planned treatment duration	
12 weeks	78 (36)
24 weeks	137 (64)

Notes: Results are presented in n (%) or median (IQR). IQR: inter-quartile range. cART: combination antiretroviral therapy.

Adverse events and characteristics of patients failing treatment

- Among the 215 patients, 4 patients stopped their treatment prematurely.
- Among 211 patients with available safety data, adverse events related to anti-HCV treatment occurred in 61 patients (29%), corresponding to 22 patients receiving RBV and to 39 without RBV. Anemia was reported for 15% of the cases and occurred in 13% of patients receiving RBV and in 1% of patients without RBV.
- Overall, eighteen patients (8%) failed to respond to anti-HCV treatment due to relapse (15 cases), premature stops (2), or death (1), their characteristics are presented in Table 2.
- Patients in HCV treatment failure were taking SOF + DCV ± RBV in 56% of the cases, SOF + RBV in 22%, SOF + LDV ± RBV in 17%, and SOF + SMV in 6%.

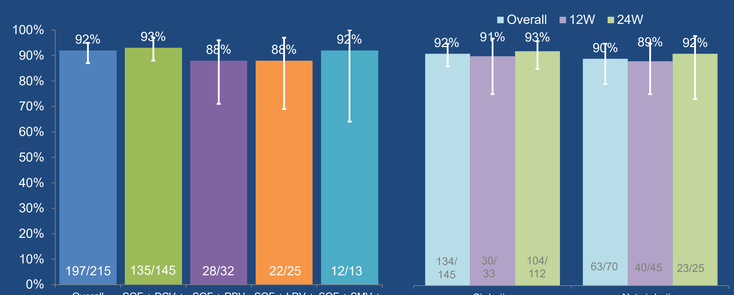
Characteristics	Failures (n=18)
Age (years)	54 (51-57)
Male sex	14 (78)
CD4 (/mm³)	525 (266-853)
HIV-RNA < 50 copies/mL	13 (72)
HCV Gt 1, 3, 4	12 (66), 3 (17), 3 (17)
Cirrhosis	11 (61)
Failure to previous HCV treatment	13 (72)
Planned treatment duration	
12 weeks	8 (44)
24 weeks	10 (56)

Notes: Results are presented in n (%) or median (IQR). IQR: inter-quartile range.

- Among 10 patients who failed to respond to anti-HCV treatment with SOF + DCV ± RBV, 6 (60%) were taking 30 mg/day of DCV, 3 were taking 60 mg/day and one 90 mg/day.

Response to treatment

- Among 215 patients, 196/198 (99%) with available data had undetectable HCV-RNA at EOT.
- SVR12 rates according to anti-HCV treatment, cirrhosis and treatment duration are presented below (Legend: vertical bars represent 95% confidence intervals).



Univariable analysis of factors associated with treatment success.

Covariates	OR (95% CI)	p-value
Age	0.98 (0.91-1.06)	0.593
Male sex vs female	0.91 (0.21-3.09)	1.000
CD4	1.00 (0.99-1.00)	0.984
HCV Gt 1 vs others	0.76 (0.23-2.31)	0.800
Cirrhotic vs not cirrhotic	1.35 (0.42-4.03)	0.721
HIV RNA at treatment initiation < 50 copies/mL vs > 50	2.89 (0.74-9.69)	0.132
HCV pre-treated vs naive	0.95 (0.25-2.99)	1.000
Treatment duration 24 weeks vs 12	1.39 (0.45-4.10)	0.673

Conclusion

- In this real-life prospective French national cohort of HIV-HCV co-infected patients, oral-DAA based regimens (without peg-interferon) showed high SVR12 rates and good tolerability in a large variety of clinical settings.
- None of the following factors: sex, age, CD4 cell count, HCV genotype, cirrhosis, HCV treatment status (naive/pretreated) or treatment duration were associated with treatment outcome. HIV RNA undetectability (<50 copies/mL) as a proxy for treatment adherence may be in favour for HCV treatment success.
- The small number of treatment events may have limited the power for identifying factors associated to treatment outcome.
- Longer follow-up or collaborative studies are needed to study disease progression in patients treated with DAAs.

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