Telaprevir in Treatment-Experienced HIV-HCV G1 Coinfected Patients (ANRS HC26 TelapreVIH)

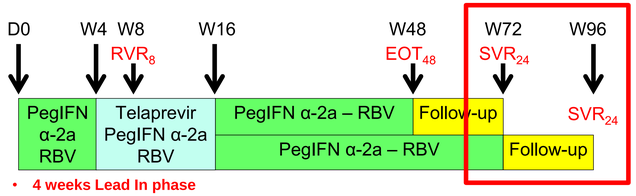
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Background

The majority (58%) of HIV/HCV coinfected patients in France are infected with HCV genotype 1. Due to poor response to PegIFN/RBV, the majority of previously treated patients are not cured. Retreatment with PegIFN + RBV results in poor SVR rates in these patients. We conducted a single-arm, phase 2 trial with Telaprevir-PegIFN-RBV in HIV/HCV genotype 1 coinfected patients who had failed a previous treatment with PegIFN + RBV. We report here the final results of this study (SVR_{24})

Study design



- **4 weeks Lead In phase**
- **Complete RVR_8** (HCV-RNA <15 IU/mL at W8) : 32 weeks PegIFN/RBV phase **(Total treatment duration: 48 weeks)**
- **Partial RVR_8** (15 IU/mL < HCV-RNA < 1000 IU/mL) : 56 weeks PegIFN/RBV phase **(Total treatment duration: 72 weeks)**

Inclusion/exclusion criteria

Main inclusion criteria

- Male and female patients, ≥ 18 years
- Controlled HIV-1 infection, stable cART ≥ 3 months.
- Authorized antiretrovirals: ATV, ATVr, EFV, RAL, TDF, FTC, 3TC
- Chronic HCV genotype 1 infection
- Previous virological failure after ≥ 12 weeks PegIFN + RBV

Main exclusion criteria

- HBV coinfection, HIV-2 infection
- Past history of decompensated cirrhosis
- Previous Null Response with cirrhosis

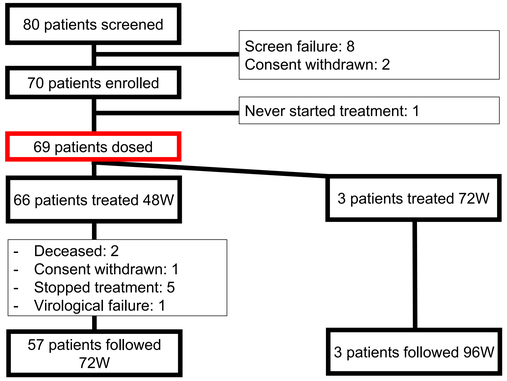
Treatment

- Telaprevir 750 mg q8h (1125 mg q8h with Efavirenz)
- PegIFN α-2a 180 µg sc / week
- Ribavirin 1000 mg / day (≤75 kg), 1200 mg /day (>75 kg)
- EPO, G-CSF, TPO-R agonists allowed

Futility rules for Telaprevir

- HCV-RNA > 1000 IU/mL at week 8 or week 12, virological breakthrough at any time

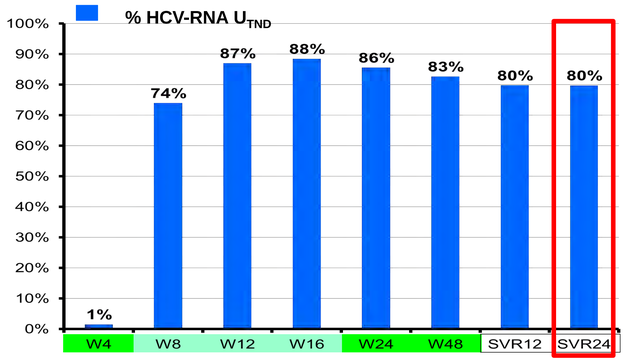
Study flow diagram



Baseline characteristics

	N (%), n=69
Age, median [IQR]	50 years [47-52]
Male	55 (80 %)
Non-Black	59 (85 %)
IVDU	38 (55 %)
BMI ≥ 25 %	26 (38 %)
CDC stage C	13 (19 %)
CD4 cells/mm^3, median [IQR]	630 [459-736]
HIV-RNA <50 copies/mL	68 (99 %)
Antiretroviral treatment	
TDF-FTC-ATVr	34 (49 %)
TDF-FTC-EFV	13 (19 %)
TDF-FTC-RAL	12 (17 %)
HCV genotype 1a / 1b	48 (70 %) / 21 (30%)
Log HCV-RNA, IU/mL, median [IQR]	6.2 [5.8-6.7]
IL 28B polymorphism (n=68)	
CC	21 (31%)
CT	34 (50%)
TT	13 (19%)
Fibrosis score (METAVIR)	
F3	11 (16%)
F4	16 (23%)
Response to previous HCV treatment	
Relapse	27 (39 %)
Breakthrough	6 (9 %)
Partial responder	15 (22 %)
Null-responder	21 (30 %)

Virological response (ITT, n=69)

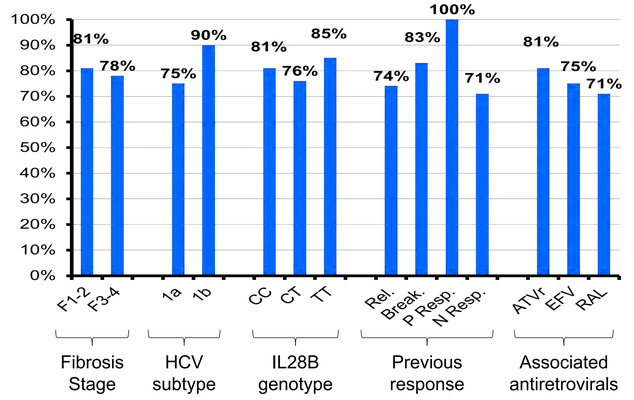


HCV-RNA decrease ≥ 1 log at W4 : 72%
HCV-RNA decrease < 1 log at W4 : 28%

Complete RVR_8 : 66 patients (96%)
Partial RVR_8 : 3 patients (4%)

Null response : 1 (W8)
Breakthrough : 3 (W28, W36, W40)
Relapse : 1 (W52, patient with a partial RVR_8 who stopped the treatment at W48)

SVR_{24} by baseline characteristic

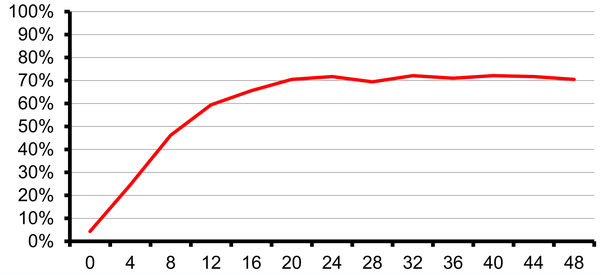


Safety

	N (%), n=69	
Grade 4 AEs	14 (20%)	
Hematological AEs	11 (16%)	
Psychiatric AEs	1 (1.4%)	
Cutaneous AEs	0 (0%)	
Infectious Aes	2 (3%)	
Death	2 (3%)	
W40 : intracerebral hemorrhage secondary to autoimmune thrombocytopenia)		
W55 : upper gastrointestinal hemorrhage		
Grade 4 anemia (< 65 g/L)	4 (6%)	
EPO use	45 (65%)	
RBC transfusion	16 (23%)	
Grade 4 neutropenia (< 0.50 giga/L)	3 (4%)	
G-CSF use	4 (6%)	
Grade 4 thrombocytopenia (< 20 giga/L)	1 (1.4%)	
TPO-R agonist use	1 (1.4%)	
Platelet transfusion	1 (1.4%)	
Telaprevir dose reduction	4 (6%)	
PegIFN dose reduction	15 (22%)	
RBV dose reduction	30 (43%)	
Treatment interruption	Failure	AE
W0-W16	1 (1.4%)	7 (10%)
> W16	3 (4%)	7 (10%)

Cumulative hematological toxicity

Cumulative proportion of patients presenting at least Hb <70 g/L, prescription of EPO, transfusion, or RBV dose reduction



Conclusion

Despite a 20% discontinuation rate related to toxicity, a SVR_{24} rate of 80% was achieved with TVR-PegIFN-RBV in PegIFN-RBV-experienced HIV-HCV genotype 1 coinfected patients.