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Changes in the profile and therapeutic care of people who use drugs with HCV mono-infection – a retrospective study between 2015 and 2019 from a monocentric tertiary referent center in France.

Short title: HCV mono-infection in people who use drugs.

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Abstract (250 words)

Background and aims: People who use drugs (PWUDs) are the main group at risk for HCV transmission and a key population for hepatitis C elimination. Multidisciplinary team (MDT) meetings were set up in France in December 2014 within regional reference centers to supervise the prescriptions and delivery of direct acting antivirals (DAAs) in order to optimize the management of HCV infection. The aim of this retrospective study was to analyze the changes in the profile and therapeutic care of PWUDs with HCV mono-infection according with the evolution of MDT meetings in a regional tertiary reference center.

Methods: Between 2015 and 2019, overall 1912 HCV infected patients presented at the MDT meetings, 547 were PWUDs with HCV mono-infection treated with DAAs. Five periods were defined according to the evolution of MDT meetings. The profile and management of PWUDs were compared among these five periods.

Results: Over time, the frequency of advanced stage of fibrosis decreased from 90.8% to 36.3% ($p < 0.001$), whereas the therapeutic care of the patients in primary addictology centers and networks of general practitioners increased from 17.4% to 55% ($p < 0.001$). The frequency of excessive alcohol consumption varied between 9.1% and 30% ($p = 0.003$) and that of opioid substitution therapy between 42.5% and 70% ($p < 0.001$). The SVR 12 rate was above 95% for the five periods.

Conclusion: Between 2015 and 2019, the changes in the profile and management of PWUDs have followed the evolution of MDT meetings concerning patients with less advanced fibrosis and more therapeutic hepatitis C care made by the primary care centers.

Key-words: hepatitis C, people who use drugs, multidisciplinary team meetings, hepatic fibrosis, primary care centers

Introduction

People who use drugs (PWUDs) are the main risk group for hepatitis C virus (HCV) transmission. If HCV is to be eliminated, then they represent a key target group (1,2). According to the criteria of the French ANRS-Coquelicot study, PWUDs are defined as any person who has injected or sniffed a drug at least once in their life (3). The clinical pathway of PWUDs has improved since the advent of direct-acting antivirals (DAAs) (4-6). Multidisciplinary team (MDT) meetings were set up in France in December 2014 within regional viral hepatitis centers (7) in order to coordinate the prescription and dispensing of DAAs and optimize patient follow-up, regardless of their mode of infection. Efforts were also made to ensure equal access to such meetings across the country. The treatment decisions of MDT meetings evolved between 2014 and 2019, as the indications and rules for prescribing and dispensing DAAs changed. Initially, DAAs were prescribed by a hospital practitioner like a gastroenterologist, infectious disease specialist, or internist and then dispensed by a hospital pharmacist. As regards the indications for DAAs, they were restricted to adults with: 1) chronic HCV with advanced fibrosis (F3/F4) or severe F2 fibrosis (depending on clinical status and rate of progression of fibrosis) or 2) chronic HCV with concurrent HIV infection; systemic, symptomatic mixed cryoglobulinemia; or B-cell lymphoma regardless of fibrosis score (7). Then, in July 2016, the indications were expanded to any F2 fibrosis (8). By August 2017, the indications had been further expanded to all stages of fibrosis, but MDT meetings were restricted to complex cases involving advanced F3/F4 fibrosis or patients with comorbidities (9). In March 2018, community pharmacists were granted the authorization to dispense DAAs as well (10). Finally, in May 2019, pangenotypic DAAs became the norm, and primary care physicians could now also prescribe DAAs under a program for simplified access to HCV treatment so long as the patient had no advanced fibrosis, HIV or hepatitis B virus coinfection, severe kidney failure, organ transplantation, or poorly controlled

comorbidities such as unhealthy alcohol consumption, diabetes, or obesity (11). Our aim was to retrospectively analyze how the profile and treatment of PWUDs with HCV mono-infection changed as MDT practices evolved in a French tertiary care setting between 2015 and 2019.

Patients and methods

All PWUDs included in the study exhibited HCV mono-infection and received a 8- to 24-week DAA treatment that complied with the successive treatment recommendations of the AFEF (Association Française pour l'Etude du Foie), the French Hepatology Society, between January 2015 and February 2019 (12). The DAAs was either a first-line treatment or second-line treatment following resistance or relapse with an interferon-based treatment. PWUDs who had HIV coinfection were excluded from the study since they were treated under a different clinical pathway. Similarly, those with hepatitis B virus infection were also excluded since their hepatitis B treatment was heterogeneous.

To retrospectively study the profile and treatment of PWUDs between January 2015 and December 2019, the data was divided into five periods that coincided with changes in MDT practices. These periods were P1 (January 2015–June 2016), P2 (July 2016–July 2017), P3 (August 2017–February 2018), P4 (March 2018–April 2019), and P5 (May 2019–December 2019). All data were collected by the Alsace Viral Hepatitis Center (SELHVA), a tertiary referral center for the Alsace region. This data was obtained from computerized summary reports of MDT decisions which were drawn up using an AFEF template (13). MDT meetings took place once or twice a month depending on the number of files submitted. They involved a hospital hepatologist, a hospital internist or infectious disease specialist, an addictologist, a virologist, a hospital pharmacist, a clinical research associate and a health professional in charge of therapeutic education. On an ad hoc

basis and according to needs, a private hepatogastroenterologist, a general practitioner and a social worker were associated. The following data were collected about the profile of PWUDs: i) demographic data regarding age, sex, and country of birth; as well as ii) clinical and paraclinical data regarding active injectors, viral genotype; stage of fibrosis, which was mostly ascertained using a FibroScan® device (advanced F3/F4 fibrosis defined as elasticity $\geq 10\text{kP}$) (12); concomitant cirrhosis and hepatocellular carcinoma; prior liver transplantation; symptomatic cryoglobulinemia; body mass index (BMI) in kg/m^2 ; comorbidities, namely obesity ($\text{BMI} \geq 30\text{Kg/m}^2$), type 2 diabetes, excessive alcohol consumption ($> 20\text{g/day}$) (14), and psychiatric disorders; and, lastly, use of harmful substances besides drugs, namely alcohol (non-drinker/occasional drinker, regular drinker with an intake $< \text{or} > 20\text{g/day}$), tobacco (number of cigarettes/day), and cannabis (number of joints/day). The following data were collected about the patients' treatment: treatment center (gastroenterology department of Strasbourg University Hospital, to which the SELHVA is affiliated; gastroenterology department of a general hospital; or primary care centers, including addiction centers with an advanced hepatology consultation for some and networks of general practitioners oriented towards the prevention and treatment of drug addiction or vulnerable populations, the selection of patients coming from these primary care centers being unknown; patient education program (University Hospital patients only); first-line or second-line DAA after failure of an interferon-based treatment; type of DAA (pangenotypic or not); opioid substitution therapy (OST); and drug interactions with the DAAs. Sustained virologic response assessed 12 weeks after the end of treatment (SVR12) is a measure of full viral clearance, and it too was investigated.

All summary reports stored on Strasbourg University Hospital's server were collated into an Excel spreadsheet by the SELHVA and anonymized for statistical analysis. Approval was obtained from the Strasbourg Faculty of Medicine's institutional review board on

December 17, 2020 (CE-2020-171). The processing of data was registered in the processing activities records of Strasbourg University Hospital on January 22, 2021 (record number 21-009).

The statistical analysis was entrusted to the Clinical Research Methodology Unit of the Public Health, Occupational Health, and Hospital Hygiene Department of Strasbourg University Hospital. The analyses were run through R Studio. Binary/category variables were expressed as number and 95% confidence interval, and continuous variables as median and interquartile range. The study periods were compared using the chi-squared test for binary/category variables and Kruskal–Wallis test for continuous ones.

Results

Of the 1912 patients discussed in MDT meetings between January 2015 and December 2019, overall 1667 exhibited HCV mono-infection treated with DAAs. The majority of PWUDs were active injectors. When broken down by study period, 637 patients were discussed in P1, 694 in P2, 113 in P3, 143 in P4, and 80 in P5. Some 547 patients were PWUDs (32.8%). The proportion of PWUDs per study period is shown in *Figure 1*. It varied between extremes of 27.4% in P2 and 41.2% in P5 ($p < 0.001$).

The changes in the profile of PWUDs over the five study periods are shown in *Table 1*. A significant difference was observed in six variables. Median age gradually decreased from 51 to 44 years between P1 and P4, before rising again to 47 years in P5 ($p < 0.001$). Most of the PWUDs were born in France. The proportion of Eastern European migrants rose from 8.7% to 22.5% between P1 and P3, before falling to 15.2% in P5 ($p = 0.02$). The proportion of cases with advanced fibrosis plummeted from 90.8% to 36.3% between P1 and P2, after which it varied between 27.3% and 42.5% (*Figure 2*, $p < 0.001$). The proportion

of obese patients fluctuated across the study periods, falling from 12.9% to 0% between P1 and P3, and then rising to more than 9% thereafter ($p=0.001$). The prevalence of excessive alcohol consumption also fluctuated, rising from 12.9% to 30% between P1 and P3, falling to 9.1% during P4, and then climbing again to 21.2% during P5 ($p=0.003$). The proportion of cannabis smokers rose steadily from 15.8% to 29.5% between P2 and P4, before falling to less than 20% during P5 ($p<0.001$).

The changes in the treatment of PWUDs over the five study periods are shown in *Table 2*. While the proportion of patients treated at the University Hospital varied, it stayed at or above 30%. In contrast, the proportion of patients treated in the general hospitals gradually fell from 52.9% in P1 to 6.8% in P4 before rising again to 18.2% in P5 (*Figure 3*, $p<0.001$). The proportion of patients treated in the primary care addiction centers increased from 3.7% to 47.7% between P1 and P4 before falling to 18.2% in P5 (*Figure 3*, $p<0.001$). Likewise, the proportion of patients treated in the networks of general practitioners doubled between P1 and P3 before returning to its initial P1 level in P5 (*Figure 3*, $p<0.001$). Overall, the proportion of patients treated in primary care settings varied between 17.4% in P1 and 55% in P3. The proportion of patients who followed a patient education program decreased steadily from 60.6% in P1 to 5.9% in P5 ($p=0.002$). The number of patients receiving first-line treatment steadily increased from 60% to 81.8% between P1 and P4, but then returned to its initial level during P5 ($p<0.001$). The proportion of patients treated with pangenotypic DAAs increased tenfold between P2 and P5, when it reached 100% ($p<0.001$). The proportion of patients receiving OST increased from 42.5% to 70% between P1 and P3 before falling to 57.6% during P5 ($p<0.001$). As regards the prevalence of drug interactions with the DAAs, a decrease from 11.2% to 2.5% was

observed between P1 and P3, followed by a rise to 21.2% during P5 ($p=0.015$).

The proportion of patients who achieved SVR12 did not significantly differ between the study periods (*Table 2*). Nor were there any significant differences in the prevalence of hepatocellular carcinoma, liver transplantation, cryoglobulinemia, diabetes, or concomitant psychiatric disorders; in tobacco consumption; in the sex ratio; or the proportion of each genotype (*Table 1*).

Discussion

This study, which concerns a large number of patients, shows that the profile and treatment of PWUDs with HCV, mostly active injectors, changed between 2015 and 2019 as MDT practices evolved. That said, SVR12 rates did not vary significantly among the study periods, remaining steady at more than 95%.

The proportion of patients who were PWUDs fluctuated significantly between 2015 and 2019, being very low in P2. A delay in informing primary care physicians about the expansion of the indications for DAAs to F2 fibrosis may have been behind this. It is thus logical that the proportion of patients treated in networks of general practitioners did not change between P1 and P2 (around 13%), while the proportion of those treated in addiction centers barely exceeded 10% in P2. Conversely, the proportion of PWUDs was highest in P5, when DAAs became the norm. Here again, the delay in informing primary care physicians about the simplified treatment access program may have been to blame. The small proportion of patients treated in addiction centers and networks of general practitioners during that period supports this hypothesis, particularly since most MDT patients did not have advanced fibrosis or comorbidities. Hence the movement of PWUDs from specialized hospital departments to primary care centers was not immediate. These results show why the communication of

information to primary care physicians needs to be better. However, the proportion of PWUD referred to MDT meetings compared to all PWUDs followed by the primary care centers was unknown. Thus, the “test and treat” strategy, currently recommended for PWUDs, cannot be evaluated in our study.

Of the variables that differed significantly over the five periods, only those directly related to changes in MDT practices will be discussed. These are advanced fibrosis, certain comorbidities (obesity and excessive alcohol consumption), treatment center, and type of DAA (pangenotypic or not).

Fibrosis stage was a key element in the changing French MDT practices. Initially, priority was given to the most severe cases of chronic HCV with advanced fibrosis (F3/F4), a policy borne out in our study, in which the proportion of cases with advanced fibrosis exceeded 90% in P1 (2,7). The expansion of MDT meetings to F2 fibrosis explains why the proportion of advanced fibrosis cases plummeted to 36.3% in P2 (8). That proportion then varied but remained much lower, fluctuating between 27.3% and 42.5%, as MDT meetings were restricted to complex HCV cases from P3 onward (9). Using FibroScan® to assess hepatic fibrosis may have represented a limitation of our study, since that modality is of predictive diagnostic value only (15). That said, the technique is widely known and was used in one study to encourage PWUDs to undergo screening for HCV before the rapid diagnostic orientation tests became available (16). FibroScan® was also investigated in Alsace in a research project coordinated by the SELHVA and approved by the ARS, the regional health agency (6). In our study, the technique was used to identify advanced fibrosis without distinction between F3 and F4, the key element in the changes in MDT practices. For such uses the diagnostic performance of FibroScan® is excellent (17).

Of the comorbidities, obesity and excessive alcohol consumption are known to worsen fibrosis (2). In our study, obesity rates were highest

in P1 (like advanced fibrosis) and in P4, when MDT meetings were restricted to complex HCV cases with advanced fibrosis and/or comorbidities. The changes in excessive alcohol consumption levels were difficult to interpret, being patient-reported. It was highest in P2 and P3 just as access to DAAs was expanded to all fibrosis stages (8,9). Initially, concurrent alcohol abuse and drug use blocked access to HCV treatment, even if it proved to be just as effective in this population (18).

Most HCV patients were treated in hospital during P1 and P2. This was probably because a large existing cohort of patients were waiting for new, more effective, better tolerated treatments, and that cohort included both treatment-naïve patients *and* second-line patients who had been treated with interferon. However, the changes in treatment center trended in different directions between the University Hospital and general hospitals, the number of patients being treated in the University Hospital rising between P1 and P5, whereas that of those treated in general hospitals fell between P1 and P4. When MDT meetings became restricted to complex HCV cases, the University Hospital became the predominant treatment center, its role as a referral center being further enhanced by the SELHVA. Patients moved to the addiction centers and networks of general practitioners once treatment was expanded to all stages of fibrosis and once DAAs could be prescribed by community pharmacists (9,10), with more than half of patients being treated in primary care settings from that point on. However, this trend differed between the addiction centers and the networks of general practitioners. There was a constant, marked increase in the number of patients treated in addiction centers between P1 and P4, with that number increasing more than twelvefold. In contrast, the increase in the number of patients treated in networks of general practitioners was less pronounced and of shorter duration, increasing only twofold between P1 and P3. After that, the numbers fell in both addiction centers and networks of general practitioners, even though the prevalence of advanced fibrosis

remained steady at around 30%. It is worth sounding a note of caution with the interpretation of these results, as the number of patients fell considerably overall between P1 and P5.

The steady rise in the proportion of pangenotypic DAAs prescribed – with that proportion reaching 100% in P5 – reflected the uptake among prescribing physicians for simpler treatment regimens (2).

Conclusions

Evolving MDT practices directly impacted the HCV characteristics of PWUDs. For instance, the rate of advanced fibrosis decreased from the second half of 2015 onward, with that decrease then having a knock-on effect on the age of patients. The impact on patient treatment began to be seen in the second half of 2017, when patients moved to primary care settings such as addiction centers and networks of general practitioners. The proportion of patients treated at Strasbourg University Hospital, the referral hospital for Alsace, rose between January 2015 and December 2019. To screen for and facilitate the management of hepatitis C in PWUDs among the primary care centers the widespread implementation of training actions and advanced hepatology consultations should be encouraged.

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Legends of figures and tables

Figure 1. Change in the proportion of PWUD over the five periods. (P1 from January 2015 to June 2016, P2 from July 2016 to July 2017, P3 from August 2017 to February 2018, P4 from March 2018 to April 2019 and P5 from May 2019 to December 2019).

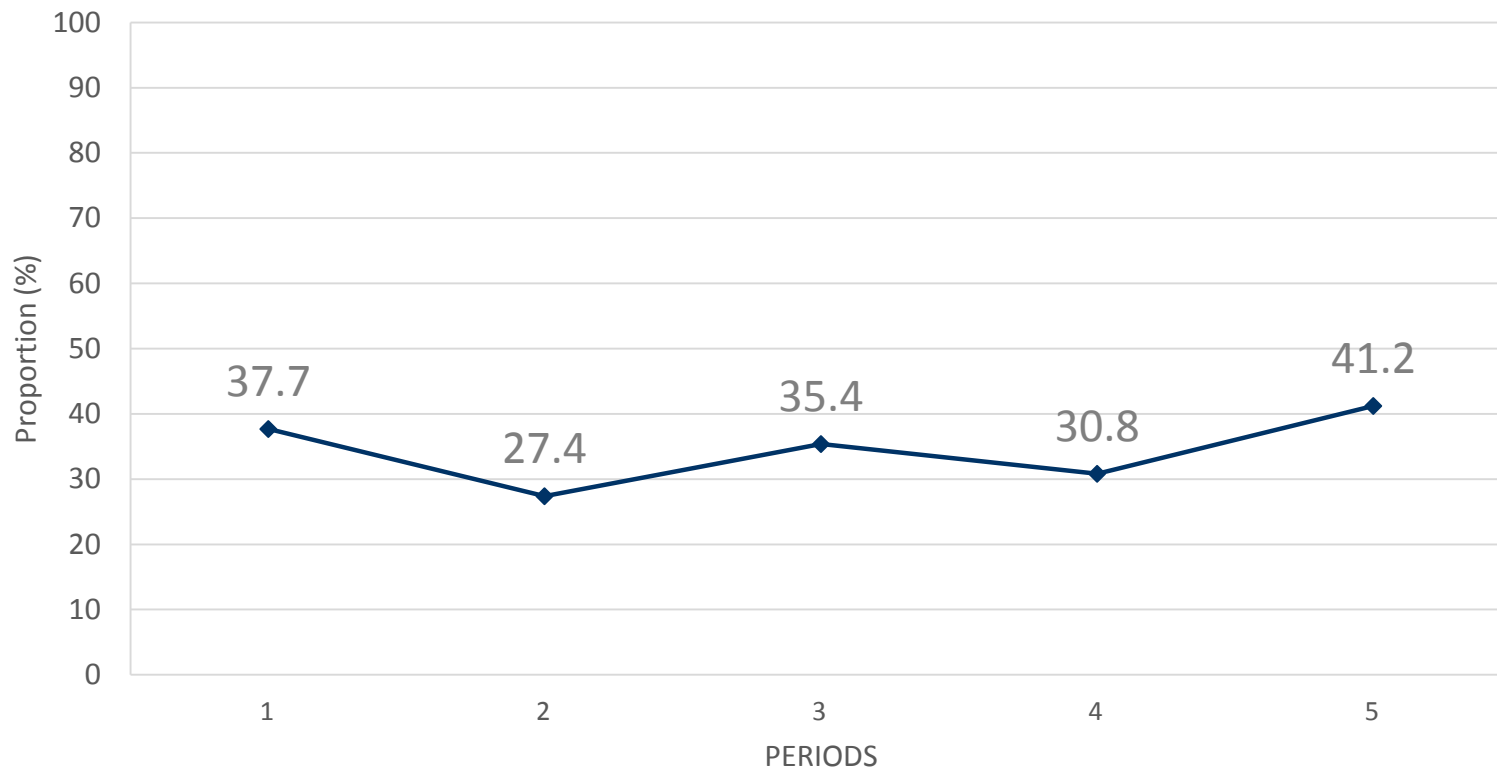
Figure 2. Change in the proportion of advanced fibrosis over the 5 periods (See Table 1 for details).

Figure 3. Change in the proportion of different therapeutic care structures over the five periods (See Table 2 for details)

Table 1. Evolution of PWUD profile over the five periods. Abbreviation: (a) and (b) d for drinks.

Table 2. Evolution of PWUD therapeutic care over the 5 periods. Abbreviations: (a) TPE: Therapeutic Patient Education, (b) Primary TTT: Primary Treatment, (c) Type of DDAs: Type of Direct-Acting-Antivirals, (d) OST : Opioid substitution treatment, (e) SVR 12 : Sustained Viral Response at week 12

Figure 1 :



Periods	1	2	3	4	5
N PWUD	240	190	40	44	33
N total	637	694	113	143	80

Figure 2 :

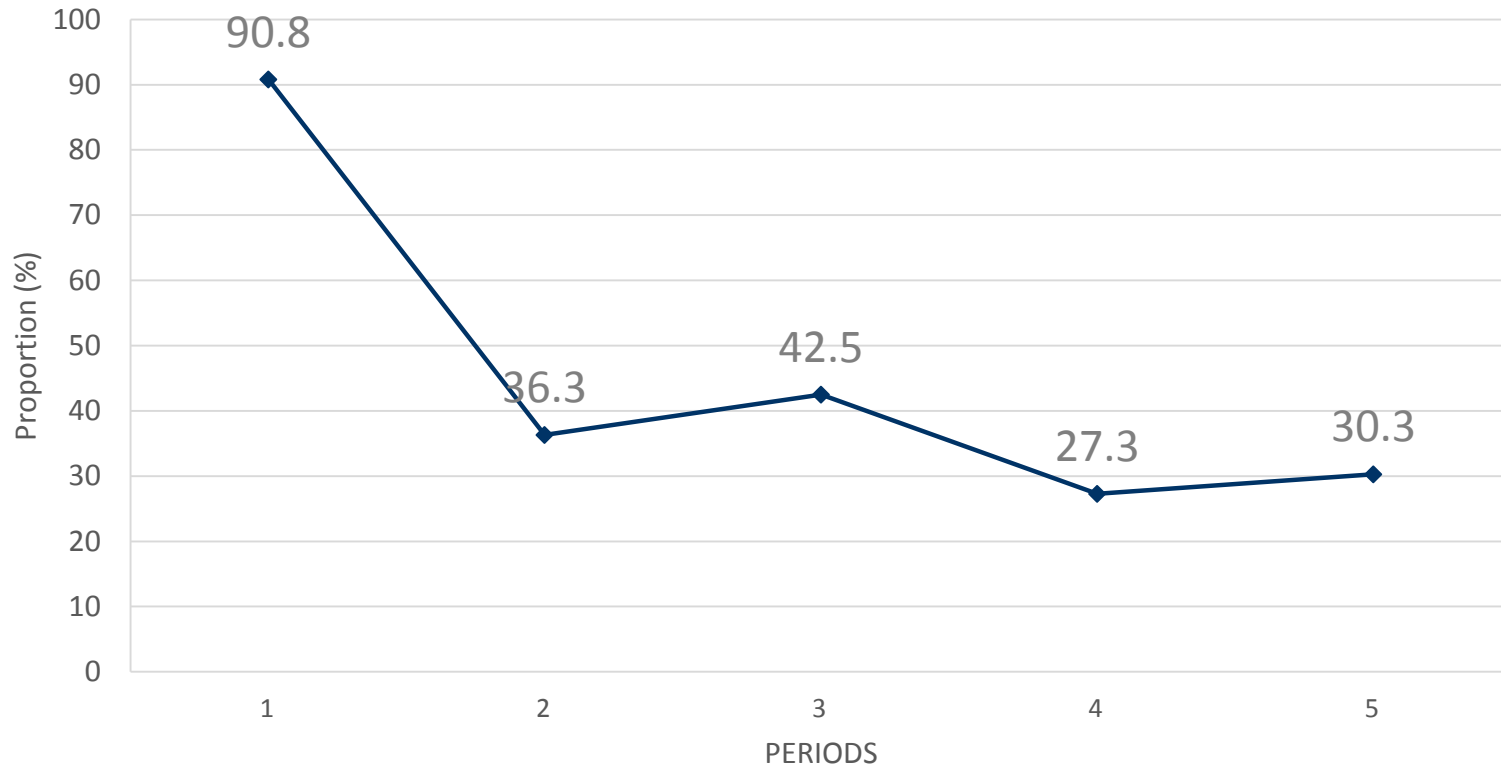


Figure 3:

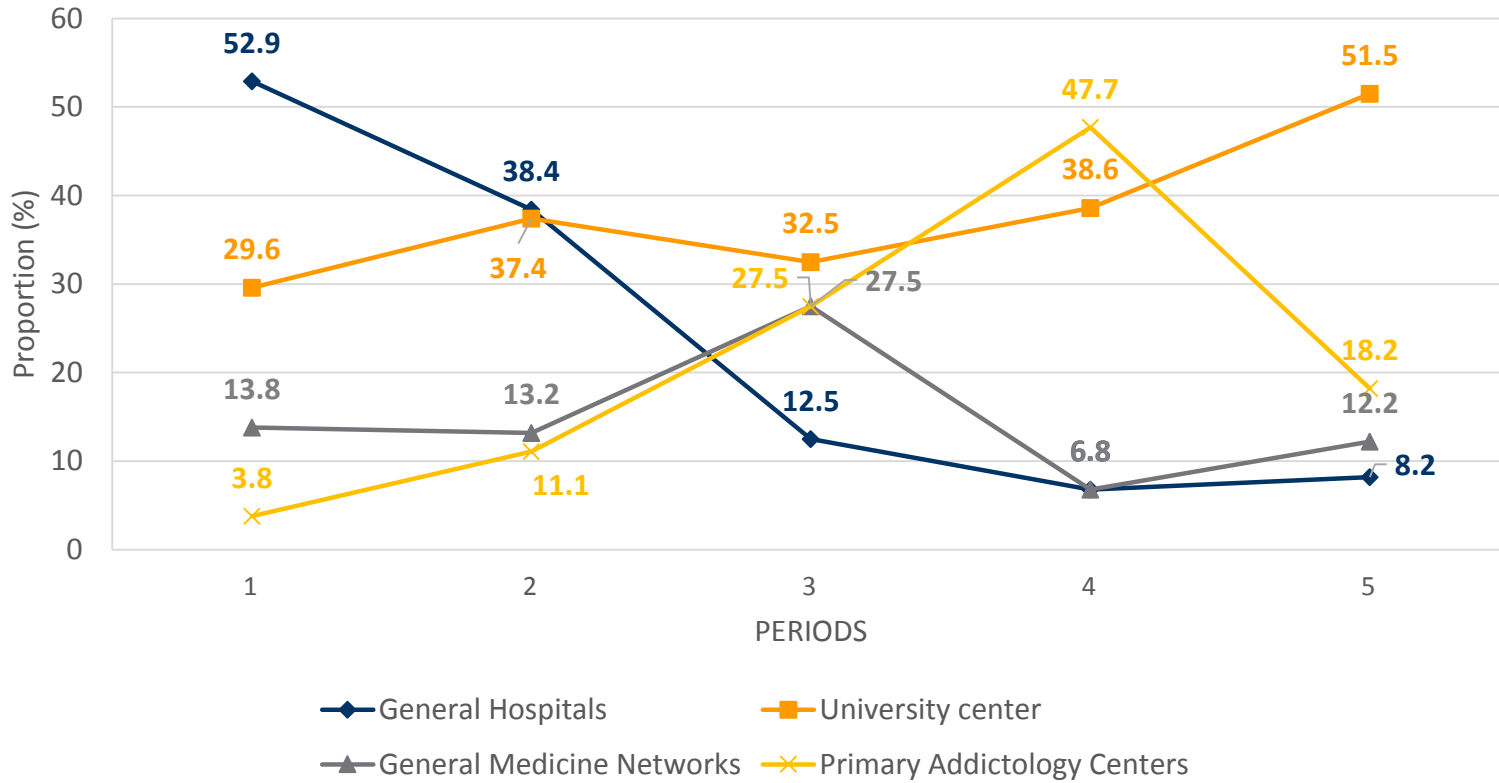


Table 1

Characteristics	P1 (N=240)			P2(N=190)			P3 (N=40)			P4 (N=44)			P5(N=33)			P
	n	%	IC	n	%	IC	n	%	IC	n	%	IC	n	%	IC	
Age	236	51	[35.7-63]	187	48	[30.6-63.0]	40	46.0	[31.9-60.1]	44	44.0	[26.2-58.9]	33	47.0	[32.2-62.4]	<0.001
Sex																NS
male	203	84.6	79.4-88.9	167	87.9	82.4-92.2	35	87.5	73.2-95.8	36	81.8	67.3-91.8	28	84.8	68.1-94.9	
female	37	15.4	11.1-20.6	23	12.1	7.8-17.6	5	12.5	4.2-26.8	8	18.2	8.2-32.7	5	15.2	5.1-31.9	
Native country																0,02
France	219	91.2	86.9-94.5	159	83.7	77.6-88.6	30	75.0	58.8-87.3	35	79.5	64.7-90.2	28	84.8	68.1-94.9	
Eastern Europe	21	8.7	5.5-13.1	26	13.7	9.1-19.4	9	22.5	10.8-38.4	9	20.4	9.8-35.3	5	15.2	5.1-31.9	
others	0	0.0		5	2.6	0.9-6.0	1	2.5	0.1-13.2	0	0.0		0	0.0		
Genotype																
1	134	55.8	49.3-62.2	90	47.4	40.1-54.7	22	55.0	38.5-70.7	17	38.6	24.4-54.5	14	42.4	25.5-60.8	NS
3	76	31.7	25.8-38.0	75	39.5	32.5-46.8	11	27.5	14.6-43.9	12	27.3	15.0-42.8	8	24.2	11.1-42.3	
others	30	12.5	8.6-17.4	23	12.1	7.8-17.6	6	15.0	5.7-29.8	3	6.8	1.4-18.7	3	9.1	1.9-24.3	
Advanced fibrosis																<0.001
yes	218	90.8	86.4-94.2	69	36.3	29.5-43.6	17	42.5	27.0-59.1	12	27.3	15.0-42.8	10	30.3	15.6-48.7	
no	22	9.2	5.8-13.5	117	61.6	54.3-68.5	23	57.5	40.9-73.0	30	68.2	52.4-81.4	21	63.6	45.1-79.6	
Hepatocellular carcinoma																NS
yes	6	2.5	0.9-5.4	2	1.0	0.1-3.7	0	0.0		1	2.3	0.1-12.0	1	3.0	0.1-15.8	
no	234	97.5	34.6-99.1	188	98.9	96.2-99.9	40	100.0	91.2-100	43	97.7	88.0-99.9	32	97.0	84.2-99.9	
Liver Transplantation																NS
yes	3	1.2	0.3-3.6	2	1.0	0.1-3.75	0	0.0		0	0.0		0	0.0		
no	237	98.7	96.4-99.7	188	98.9	96.2-99.9	40	100.0	91.2-100	44	100.0	91.7-100	33	100.0	89.4-100	
Cryoglobulin																NS
yes	21	8.7	5.5-13.1	11	5.8	2.9-10.1	1	2.5	0.1-13.1	2	4.5	0.6-15.5	1	3.0	0.1-15.8	
no	192	80.0	74.4-84.9	179	94.2	89.9-97.1	39	97.5	86.8-99.9	42	95.4	84.5-99.4	31	93.9	79.8-99.3	
BMI																
median [IQR]	222	25.4	[18.3-35.4]	178	24.2	[17.9-37.6]	39	24.7	[19.5-39.1]	36	24.1	[20.5-33.5]	28	24.3	[16.3-42.1]	NS
<25	112	46.7	40.2-53.2	125	65.8	58.6-72.5	26	65.0	48.3-79.4	22	50.0	34.6-65.4	15	45.4	28.1-63.6	0,001
25-29,9	78	32.5	26.6-38.8	35	18.4	13.2-24.7	8	20.0	9.0-35.6	7	15.9	6.6-30.1	10	30.3	15.6-48.7	
≥30	31	12.9	8.9-17.8	18	9.5	5.7-14.6	0	0.0		6	13.6	5.2-27.3	3	9.1	1.9-24.3	
Diabetes																NS
yes	25	10.4	6.9-15.0	9	4.7	2.2-8.8	1	2.5	0.1-13.2	3	6.8	1.4-18.7	2	6.1	0.7-20.2	
no	215	89.6	85.0-93.1	181	95.3	91.2-97.8	39	97.5	86.8-99.9	41	93.2	81.3-98.6	31	93.9	79.8-99.3	
Psychiatric condition																NS
yes	58	24.2	18.9-30.1	51	26.8	20.7-33.7	10	25.0	12.7-41.2	10	22.7	11.5-37.8	10	30.3	15.6-48.7	
no	100	41.7	35.4-48.2	133	70.0	62.9-76.4	30	75.0	58.8-87.3	34	77.3	62.2-88.5	22	66.7	48.2-82.0	
Alcohol																0,003
no or occasional	146	60.8	54.3-67.0	117	61.6	54.3-68.5	27	67.5	50.9-81.4	36	81.8	67.3-91.8	24	72.7	54.5-86.7	
<10 d/ week (a)	47	19.6	14.8-25.2	34	17.9	12.7-24.1	1	2.5	0.1-13.2	4	9.1	2.5-21.7	1	3.0	0.1-15.8	
>10 d/week (b)	31	12.9	8.9-17.8	37	19.5	14.1-25.8	12	30.0	16.6-46.5	4	9.1	2.5-21.7	7	21.2	9.0-38.9	
Tobacco																NS
yes	19	7.9	4.8-12.1	88	46.3	39.1-53.7	27	67.5	50.9-81.4	31	70.4	54.8-83.2	18	54.5	36.3-71.9	
no	2	0.8	0.1-3.0	60	31.6	25.0-38.7	13	32.5	18.6-49.1	12	27.3	15.0-42.8	11	33.3	18.0-51.8	
Cannabis																<0,001
yes	15	6.2	3.5-10.1	30	15.8	10.9-21.8	7	17.5	7.3-32.8	13	29.5	16.8-45.2	6	18.2	7.0-35.5	
no	10	4.2	2.0-7.5	115	60.5	53.2-67.5	33	82.5	67.2-92.7	31	70.4	54.8-83.2	23	69.7	51.3-84.4	

Table 2

Therapeutic care	P1 (N=240)			P2(N=190)			P3 (N=40)			P4 (N=44)			P5(N=33)			P
	n	%	IC	n	%	IC	n	%	IC	n	%	IC	n	%	IC	
Structures																<0.001
university hospital center	71	29.6	23.9-35.8	71	37.4	30.5-44.7	13	32.5	18.6-49.1	17	38.6	24.4-54.5	17	51.5	33.5-69.2	
generals hospitals	127	52.9	46.4-59.4	73	38.4	31.5-45.7	5	12.5	4.2-26.8	3	6.8	1.4-18.7	6	18.2	7.0-35.5	
primary addict centers	9	3.7	1.7-7.0	21	11.1	7.0-16.4	11	27.5	14.6-43.9	21	47.7	32.5-63.3	6	18.2	7.0-35.5	
generals medecine network	33	13.8	9.7-18.8	25	13.2	8.7-18.8	11	27.5	14.6-43.9	3	6.8	1.4-18.7	4	12.1	3.4-28.2	
TPE (a)																0.002
yes	43	60.6	48.2-72.0	33	46.5	34.5-58.7	5	38.5	13.9-68.4	2	11.8	1.5-36.4	1	5.9	0.1-28.7	
no	28	39.4	28.0-51.7	38	53.5	41.3-65.4	8	61.5	31.6-86.1	15	88.2	63.6-98.5	5	29.4	10.3-56.0	
Primary TTT (b)																<0.001
yes	144	60	53.5-66.2	151	79.5	73.0-85.0	32	80.0	64.3-90.9	36	81.8	67.3-91.8	20	60.6	42.1-77.1	
no	96	40	33.7-46.5	39	20.5	15.0-27.0	8	20.0	9.1-35.6	8	18.2	8.2-32.7	13	39.4	22.9-57.9	
Type of DAAs (c)																<0.001
pangenotypic	0	0		20	10.5	6.5-15.8	24	60.0	43.3-75.1	39	88.6	75.4-96.2	33	100.0	89.4-100	
no pangenotypic	240	100	98.5-100	170	89.5	84.2-93.4	16	40.0	24.9-56.7	5	11.4	3.8-24.6	0	0.0		
OST (d)																<0.001
yes	102	42.5	36.2-49.0	119	62.6	55.3-69.5	28	70.0	53.5-83.4	29	65.9	50.1-79.5	19	57.6	39.2-74.5	
no	138	57.5	51.0-63.8	71	37.4	30.5-44.7	12	30.0	16.6-46.5	15	34.1	20.5-49.9	14	42.4	25.5-60.8	
Drug interactions																0.015
yes	27	11.2	7.5-15.9	12	6.3	3.3-10.8	1	2.5	0.1-13.2	2	4.5	0.6-15.5	7	21.2	9.0-38.9	
no	213	88.7	84.1-92.4	178	93.7	89.2-96.7	39	97.5	86.8-99.9	42	95.5	84.5-99.4	26	78.8	61.1-91.0	
SVR12 (e)																NS
yes	233	97.1	94.1-98.8	183	96.3	92.6-98.5	38	95.0	83.1-99.4	44	100.0	92.0-100	33	100.0	89.4-100	
no	3	1.2	0.3-3.6	4	2.1	0.6-5.3	1	2.5	0.1-13.2	0	0.0		0	0.0		