HCV treatment with new direct acting antivirals (DAAs): characteristics of patients failing new DAA combinations.

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Background

With the recent development of new potent DAA combinations, sustained virological response (SVR) rates >90% are achievable for almost all HCV genotypes and stages of liver disease. In the case of treatment failure, the appearance of resistance mutations is likely. However, it is important to document the characteristics of patients in case of treatment failure with new DAA in order to know other possible causes that may trigger therapeutic failure.

Objectives

To describe the principal characteristics of patients failing treatment with DAA.

Material/Methods

We included all consecutive patients treated of HCV infection in our hospital (Complejo Hospitalario Navarra, Pamplona; Spain) and failing an all-oral DAA regimen started between october 2014 and october 2016 (some of them still ongoing).

Treatment failure was classified as virological therapeutic failure (null-response, breakthrough or relapse) or non-virological therapeutic failure (adverse drug reaction, death and other causes non-related with treatment).

The HCV-RNA detection was performed during treatment (4th week of treatment and end of treatment) and 12 weeks after completion of treatment and/or thereafter.

Cobas® HCV (Roche Diagnostics, Mannheim, Germany (Roche®) was used to perform HCV-RNA detection and VERSANT® HCV Genotype 2.0 Assay (LiPA) (Siemens Healthcare Diagnostics, Tarrytown, NY, USA) to determine HCV genotype.

Results

Of 635 patients who initiated an oral DAA regimen, 23 patients (3,6%) failed therapy. We observed 7 relapses, 4 null-response, 3 breakthrough, 6 stopped treatment (5 adverse drug reaction and 1 voluntary-stop) and 3 deaths. We could observed differences between global and DAA-failure populations. In general, Global population characteristics: median age: 53 years, 69% male, 24,6% cirrhotic (60% FibroScan≥F3) and 61,4% had received previous treatment. DAA failure population: median age 52 years, 78,6% male, 14,3% cirrhotic (57% FibroScan≥F3) and 35,7% received previous treatment. According to genotype we observed that the 3,2% of 1a genotype failed, followed by the genotype 4 with a 3% of failures, genotype 3 (1,6%) and finally genotype 1b with a 1,4% of failures. Patients´characteristic are displayed in table1 and 2.

Table 1. Epidemiological and clinical patients´characteristics.

	DAA Treatment		Failed therapy		DAA faiulure	
	Total	Co-HIV	Total	Co-HIV	Total	Co-HIV
	n=635	n=121	n=23	n=5	n=14	n=2
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Gender (male)	439 (69,1)	92 (76)	17 (81)	4 (80)	11 (78,6)	2 (100)
Age (median, ICR)	52 (16-85)	52 (38-76)	53 (37-79)	51 (38-76)	52 (37-63)	52 (51-53)
Genotype						
1	436 (68,6)	70 (58,7)	16 (69,6)	1(20)	10 (71,4)	1 (50)
1a	217 (34,2)	54 (44,6)	10 (43,5)	1 (20)	7 (50)	1 (50)
1b	213 (33,5)	17 (14,1)	6 (26,1)	0	3 (21,4)	0
2	9 (1,4)	2 (1,6)	0	0	0	0
3	123 (19,4)	33 (27,3)	3 (13)	2 (40)	2 (14,3)	1 (50)
4	66 (10,4)	15 (12,4)	4 (17,4)	2 (40)	2 (14,3)	0
5	1 (0,2)	0	0	0	0	0
IL-28						
CT	126 (19,8)	31 (25,6)	6 (28,6)	0	6 (42,9)	0
CC	77 (12,1)	31 (25,6)	4 (19)	1 (20)	3 (21.4)	0
TT	21 (3,3)	10 (8,3)	4 (19)	3 (60)	2 (14,3)	1 (50)
Unknown	409 (64,4)	49 (40,5)				1 (50)
Cirrhosis	156 (24,6)	51 (41,1)	8 (38,1)	2 (40)	2 (14,3)	0
Fibrosis						
F0	13 (2)	0	0	0	0	0
F1	69 (10,9)	2 (1,6)	1 (4,8)	0	1 (7,2)	0
F2	171 (26,9)	21 (17,4)	6 (28,6)	1 (20)	5 (35,7)	0
F3	149 (23,5)	37 (30,6)	6 (28,6)	1 (20)	4 (28,6)	1 (50)
F4	233 (36,7)	61 (50,4)	8 (38,1)	3 (60)	4 (28,6)	1 (50)
Co-HIV	121 (19,1)	12 (100)	5 (23,8)	5 (100)	2 (16,7)	2 (100)

Table 2. Pharmacological patients´characteristics.

	DAA Treatment		Failed therapy		DAA faiulure	
	Total	Co-HIV	Total	Co-HIV	Total	Co-HIV
	n=635	n=121	n=23	n=5	n=14	n=2
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
Previous anti-HCV therapy	390 (61,4)	81 (66,9)	5 (23,8)	3 (60)	5 (35,7)	2 (100)
DAA combination						
2D	27 (4,3)	2 (1,6)	1 (4,3)	0	1 (7,1)	0
3D	246 (38,7)	33 (27,3)	6 (26,1)	1 (20)	6 (42,9)	1 (50)
SMP	17 (2,7)	3 (2,5)	6 (26,1)	1 (20)	5 (35,7)	0
SMP-SOF	54 (8,5)	10 (8,3)	0	0	0	0
SOF	12 (1,9)	2 (1,6)	0	0	0	0
SOF-DCV	139 (21,9)	41 (33,9)	3 (13)	2 (40)	2 (14,3)	1 (50)
SOF-LDP	139 (21,9)	30 (24,8)	7 (30,4)	1 (20)	0	0
TEL	1 (0,2)	0	0	0	0	0
DAA+RBV	378 (59,5)	63 (52,1)	17 (73,9)	5 (100)	11 (78,6)	2 (100)
Cause failure						
Breakthrough	3 (0,5)	1 (0,8)	3 (13)	1 (20)	3 (21,4)	1 (50)
Null-response	4 (0,6)	0	4 (17,4)	0	4 (28,6)	0
Relapse	7 (1,1)	1 (0,8)	7 (30,4)	1 (20)	7 (50)	1 (50)
STOP (abandon)	1 (0,2)	1 (0,8)	1 (4,3)	1 (20)	-	-
STOP (RAM)	5 (0,8)	2 (1,6)	5 (23,8)	2 (40)	-	-
Death	3 (0,5)	0	3 (13)	0	-	-
RAV sequence	4 (0,6)	0	4 (17,4)	2 (40)	4 (28,57)	0

2D: ombitasvir, paritaprevir, ritonavir; **3D:** 2D+ dasabuvir; **SMP:**simeprevir; **SOF:** sofosbuvir; **DCV:** daclastavir; **LDP:** ledipasvir; **TEL:** telaprevir; **RBV**: ribavirin.

Bibliography

- Actualización en la terapia de la hepatitis C. Nuevos fármacos, monitorización de la respuesta y resistencias. Chueca Porcuna N. et al. Enferm Infecc Microbiol Clin. 2013:31(Supl 1):40-47.
- The importance of resistance to direct antiviral drugs in HCV infection in clinical practice. Sarrazin C. Journal of Hepatology 2016 vol.64:486-504.

Conclusions

- **In this prospective real-life cohort, failure to an oral DAA regimen occurred in 3,6% of the patients and was mainly due to relapses or adverse drug reactions.**
- **In our study, patients with DAA failure were mainly male (79%), mono-infected (83%), were genotype 1a (50%), have received 3D (42,9%), and most of them (79%) were treated with a combination of DAA plus ribavirin.**