

Patients treated for HCV and listed for LT in a French multicenter study: what happens at 3 years ?

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1 INTRODUCTION

Combinations of DAA have shown excellent results to treat HCV-infection in cirrhotic patient but some issues remain unresolved regarding efficacy in patients awaiting liver transplantation (LT) and impact on access to LT. Indeed, previous study found a delisting rate between 16-24% for patients with HCV-related decompensated cirrhosis treated while awaiting LT (1-3). However, there are few data about the outcome of patients on the waiting list for LT, especially patients listed for hepatocellular carcinoma (HCC) (3).

2 AIM

The aims of this study were

1. to assess the efficacy and tolerability of DAA in HCV patients awaiting LT
2. To determine the long-term outcome after viral eradication (3 years)
3. To evaluate survival, transplant rate, delisting rate for patient with decompensated cirrhosis
4. To determine risk of drop out, recurrence after LT for patient with HCC

3 METHOD

This is an observational, multicenter, and retrospective analysis of prospectively collected data from 18 hospitals in France. All HCV-positive patients who received antiviral therapy with an IFN-free regimen while awaiting LT were enrolled in this study. Data on comorbidities (diabetes, dyslipidaemia, alcohol consumption, arterial hypertension, BMI) were collected. Complete clinical and biological response (CBR) to HCV treatment was defined by improvement until Child A, stable response by Child A stability, partial response by change of Child score class and no response by stability or aggravation (Child B or C).

4 RESULTS

179 HCV-positive patients who received antiviral therapy with an IFN-free regimen while awaiting LT between **November 2013 and June 2015** were enrolled in this study. The mean follow-up since the end of treatment was **43,3 months**.

The LT indication was **HCC in 104 (58%)** patients and **decompensated cirrhosis in 75 (42%)** patients.

Baseline characteristics of the patients included and regimen of HCV-treatment are presented in **table 1**.

Most of the patients were male (144, (80,5%)) with a median age of 55,7 years-old (\pm 6,9). Comorbidities were also collected: diabetes (48, (27%)), alcohol consumption (39, (22%)), arterial hypertension (44, (25%)) and dyslipidaemia (8, (5%)). Majority of patients were genotype 1 (102, (57%)) treated with DAA plus ribavirin for 96 patients. SVR rate was 84%. At baseline, mean MELD was 11 (6-32) and mean Child B8 (5-14) for patients listed for decompensated cirrhosis (**Table 1**). 75 patients listed for HCC had an AFP score \leq 2.

Among patients listed for **decompensated cirrhosis**, 13 (25%), 8 (15%), 7 (13%) and 25 (47%) had respectively a CBR complete, partial, stable and no response (**Figure 2**).

37 patients (49%) with decompensated cirrhosis were transplanted, 33 are alive. 38 patients (51%) were not transplanted: 7 are inactive and 30 were delisted (20 for improvement) and 5 developed HCC during the follow up (**Figure 1**).

Among patients listed for **HCC**, 78 (75%) were transplanted, 71 are alive. Only 6 patients (5,8%) have been delisted for HCC progression (**Figure 1**).

No case of HCC recurrence post LT has been reported.

Table 1: Baseline characteristics of the patients included in the study according to the presence of decompensated cirrhosis or HCC

	Overall n=179 (%)	Decompensated cirrhosis n=75 (%)	HCC n=104 (%)
Male	144 (80,5)	56 (74,7)	88 (84,6)
Age (years)	54,7 (\pm 6,9)	53,2 (\pm 7,9)	55,8 (\pm 5,9)
BMI (kg/m²)	25,6 (\pm 4,2)	25,4 (\pm 4,4)	25,7 (\pm 4,4)
Diabetes	48 (27,4)	25 (34,3)	23 (22,6)
Arterial hypertension	44 (25,1)	13 (17,8)	31 (31,4)
Alcohol consumption	39 (22,2)	14 (18,9)	25 (24,5)
Dyslipidemia	8 (95,4)	2 (2,7)	6 (5,9)
HIV positive	12 (6,7)	7 (9,3)	5 (4,8)
HCV Genotype			
1	102 (57)	45 (60)	57 (76)
2	7 (3,9)	5 (6,7)	2 (1,9)
3	41 (23)	12 (16)	29 (28,2)
4	26 (14,6)	12 (16)	14 (13,6)
5	2 (1,1)	1 (1,3)	1 (1)
Previous HCV-treatment	133 (74,3)	55 (73,3)	78 (75)
Current HCV-treatment			
Sofosbuvir	179 (100)	75 (100)	104 (100)
Simeprevir	11 (6,2)	2 (2,7)	9 (8,7)
Daclatasvir	111 (62)	47 (62,7)	64 (61,5)
Ledipasvir	18 (10)	10 (13,3)	8 (7,7)
Abbvie 2D - 3D	0 (0)	0 (0)	0 (0)
Ribavirin	96 (53,6)	38 (50,7)	58 (55,8)
Meld baseline	12 (\pm 5)	15 (\pm 5)	10 (\pm 4)
Child Pugh class baseline	A: 83 (48) / B:51(29,5) / C: 39 (22,5)	A: 15 (20) / B: 30 (40) / C: 30 (40)	A: 68 (69,4) / B: 21 (21,4) / C: 9 (9,2)
SVR rate	151 (84,4)	69 (92)	82 (78,9)
Liver transplant	115 (64,3)	37 (49,3)	78 (75)

Figure 1: Flow chart

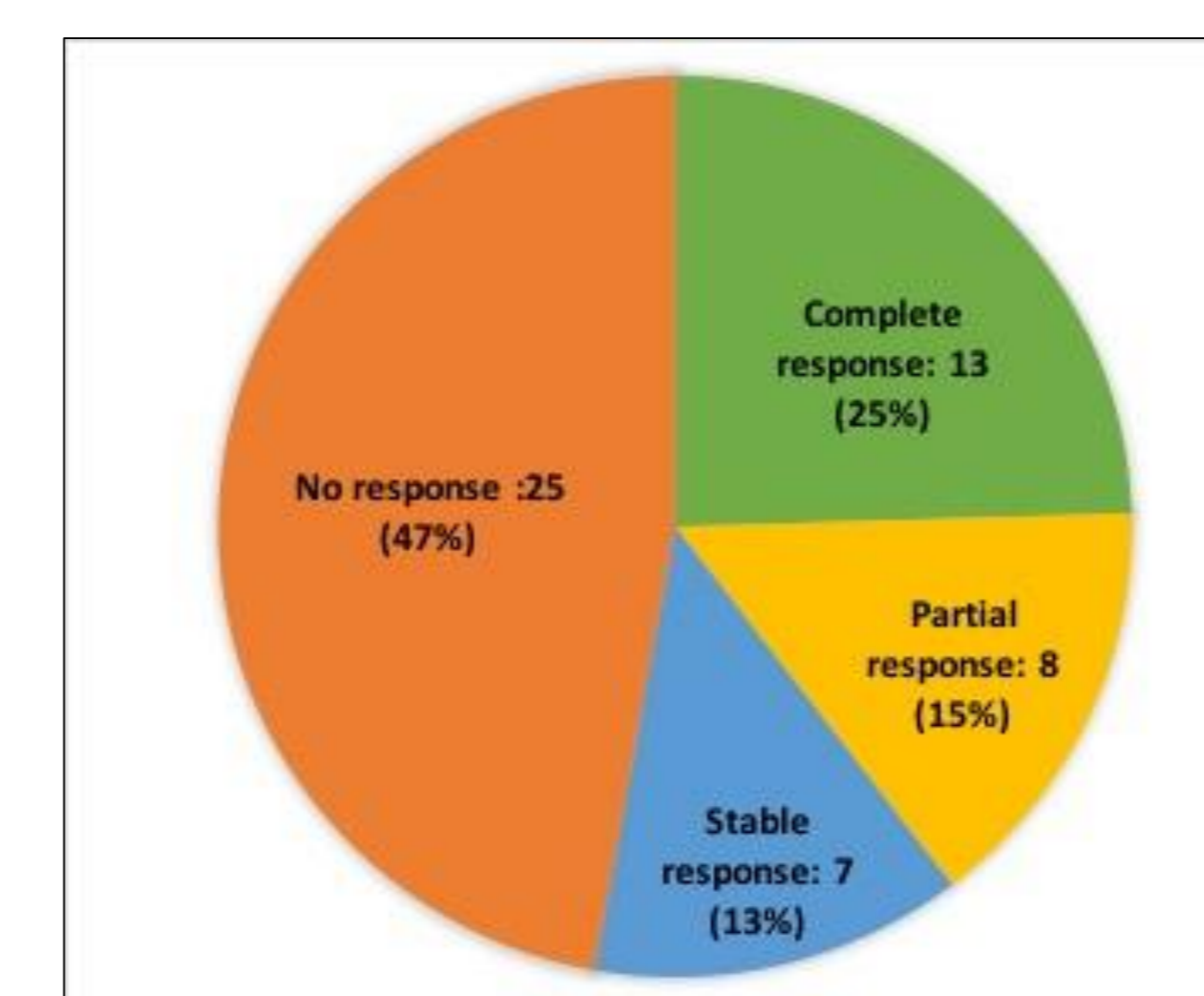
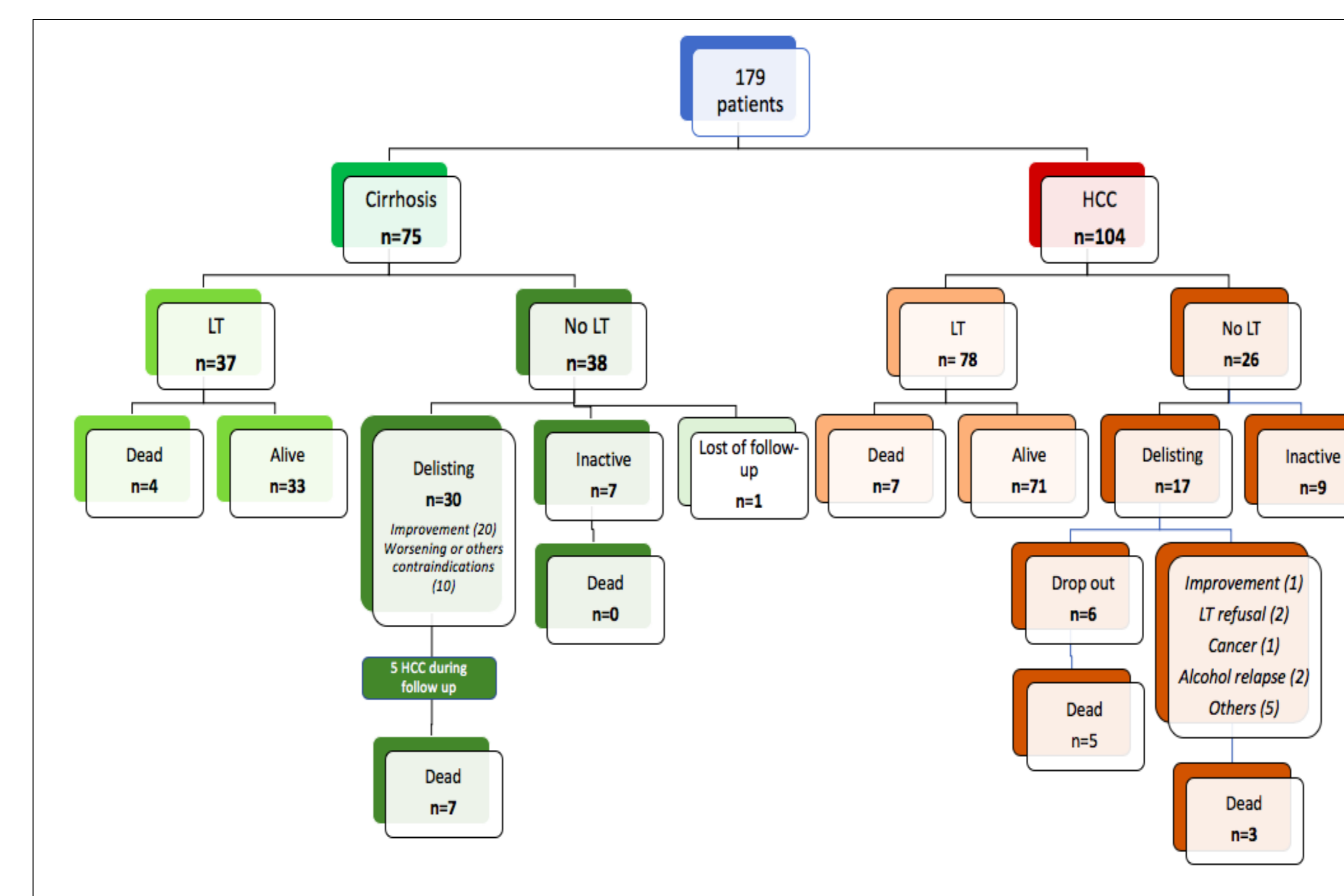
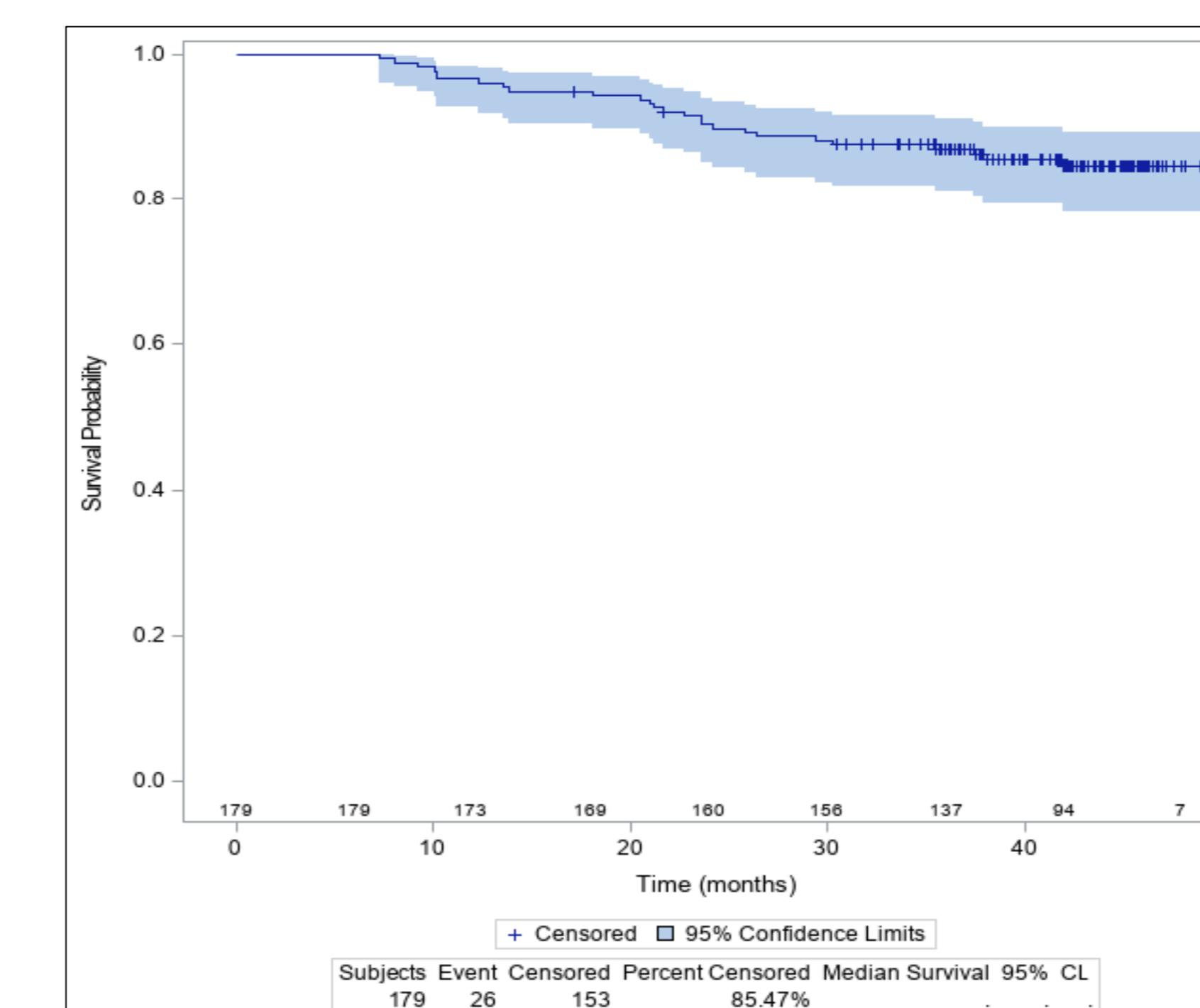


Figure 2: Clinical and biological response for patients listed for decompensated cirrhosis

Figure 3: Overall survival

In total, during follow-up **26 (14,5%)** patients had been died without statistical difference between HCC (15/104) or decompensated cirrhosis (11/75). The overall survival is presented **figure 3**.



5 CONCLUSIONS

- HCV-treatment in patients awaiting LT allows **delisting for improvement in 27%** (20/75) of cases.
- After treatment only 5,8% (6/104) of HCC-patients were delisted for drop out.
- We did not collect any HCC recurrence post-LT.

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7 REFERENCES

- (1) Coilly A et al. Improving liver function and delisting of patients awaiting liver transplantation for HCV cirrhosis: do we ask too much to DAAs? *Hepatology* 2015;62:257A.
- (2) Belli LS et al. Delisting of liver transplant candidates with chronic hepatitis C after viral eradication: A European study. *J Hepatol* 2016;65:524-531.
- (3) Pascasio JM et al. Clinical outcomes of patients undergoing antiviral therapy while awaiting liver transplantation. *J Hepatol* 2017;67:1168-1176.

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