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ORIGINAL ARTICLE

Outcome of Decompensated Hepatitis C Virus Cirrhotic Patients Treated with Direct Acting Antiviral Drugs

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ABSTRACT

Background: All oral direct-acting antivirals (DAAs) effectively treat chronic hepatitis C infection (HCV) and widely used for patients with compensated cirrhosis. However, data regarding their safety and efficacy in patients with decompensated cirrhosis are insufficient .

The aim of this work was to test efficacy, safety and outcome of DAAs in the treatment of decompensated HCV related cirrhotic patients (CTP-B).

Methods: prospective study among 62 chronic HCV cirrhotic patients, divided into two groups. Group I(the study group) included 32 patients with CTP-B treated for 12 weeks by sofosbuvir (SOF) 400 mg once daily plus Daclatasvir (DCV) 60 mg once daily plus Ribavirin (RBV) with initial dose 600 mg /day), while group II (the control group) included 30 patients with CTP-A treated by (SOF 400 mg once daily + DCV 60 mg once daily +RBV dosed according to body weight) for 12 weeks. According to the National Committee for control of viral hepatitis (NCCVH). Follow up after end of treatment (EOT) for 24weeks so the total period of the study 36 weeks **Results:** cases achieved SVR in Group I: 93.75% and in group II:100%, Liver parameters were improved from baseline to 24 weeks after end of treatment. The most common adverse effects were anemia, no patients died by the end of the study, but one case 3.1% in group I stopped treatment due to severe complications. **Conclusion:** Treatment with DAAs in patients with CTP-B is effective and safe, but patients remain at risk of life-threatening complications as HCC and liver-related morbidity.

Key words:

HCV, Sofosbuvir, Ribavirin, SVR, DAA.

INTRODUCTION

Cirrhosis is an increasing cause of morbidity and mortality being the 14th most common cause of death worldwide, with one-year mortality ranging from 1% to 57% depending on the Class[1]. Globally, more than 350 000 HCV-infected patients die each year from HCV, mostly as a result of decompensation of liver cirrhosis or HCC[2].

In Egypt 2015, the prevalence of HCV antibody was found to be 10% and that of HCV RNA to be 7%, in the age group 15–59-year. Approximately, 3.7 million patients have chronic HCV infection in the same age group. An estimated 29% reduction in HCV RNA prevalence has been seen since 2008 [3].

DAAs are licensed and target three viral

proteins: the NS3-4A protease which needed for processing the viral polyprotein, the NS5A phosphoprotein that regulates RNA replication and virus assembly, and the viral RNA-dependent RNA polymerase (NS5B) that catalyzes genome replication. Combination therapies cure > 95% of treated patients with excellent safety and tolerability[4].

The protocol of the treatment of HCV patients with DAAs depends on the stage of fibrosis. Treatment must be considered without delay in patients with cirrhosis, including decompensated cirrhosis[5].

Non-invasive tests to diagnose cirrhosis were now widely used in clinical practice and recommended by international and EASL guidelines [5], FIB-4 score >3.25 indicate advanced fibrosis and cirrhosis (specificity 98.2%, positive predictive value 82.1%) [6], Distorted liver architecture and nodular liver Surface on the abdominal ultrasonography showed a sensitivity and specificity for diagnosing cirrhosis of 98% and 85% [7].

The risk of HCC and liver-related mortality is significantly reduced, but not eliminated, in patients with cirrhosis who clear HCV [8].

SOF-based combinations, either with ledipasvir (LDV), DCV or velpatasvir (VEL) ± RBV, showed to be safe and effective in clinical trials when used in cases with decompensated cirrhosis [9].

We aimed in this study to test the efficacy, safety and outcome of DAAs regimens in the treatment of decompensated HCV cirrhotic patients (CTP-B) in Egypt.

METHODS

Study design and Settings:

We carried out a prospective cohort study in collaboration between Internal Medicine Department(Hepato-gastro-enterology unit), Faculty of Medicine, Zagazig University, and Al Ahrar Teaching Hospital, Sharqia Governorate, during the period from January 2018 to March 2019.

A total number of 62 chronic HCV related cirrhotic Egyptian patients up to CTP-9 were divided into two groups. Group I included 32

patients with CTP-B (the study group) while group II included 30 patients with CTP-A (the control group).

Inclusion criteria:

The age was from 18 to 75years, chronic Naive HCV related cirrhotic patients up to CTP-9 eligible for treatment by DAAs, female patient practicing adequate contraception during the treatment period and at least 6 months after treatment stoppage. The wife of a male patient practicing adequate contraception.

Exclusion criteria:

CTP-C patients, causes of liver cirrhosis other than HCV (HBV, Wilson, autoimmune hepatitis, alcoholic and hemochromatosis), HCC, patient with platelet count <50.000, patient with renal impairment (creatinine clearance < 30 ml/min), extra-hepatic malignancy, patient refused to be involved in the study, pregnancy and lactation, inadequately controlled diabetes mellitus (HbA1c > 9%).

Therapy:

According to the NCCVH (December 2016): **group I** patients treated for 12 weeks by SOF 400 mg once daily plus DCV 60 mg once daily + RBV with initial dose 600 mg /day, the dose increased gradually 200 mg each week till a dose 1000 mg/day based on the patient tolerability, while **group II** patients treated by SOF 400 mg once daily + DCV 60 mg once daily +RBV dosed according to body weight 1000 mg if < 75 kg, 1200 mg if > 75 kg, for 12 weeks.

Administrative Design :

Study was approved by Faculty of Medicine, Zagazig University institutional review board (IRB), The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Process:

All subjects of the study were subjected to: Written informed consent, detailed history taking, full physical examination, laboratory investigations (complete blood picture by automated blood counter, diagnosis of viral markers: HCV by HCV abs by ELISA and HBV by HBsAg, quantitative

PCR for HCV RNA if HCV abs test was positive, liver function tests: serum bilirubin, serum albumin, serum alanine transferase [ALT] and aspartate transferase [AST] measured by kinetic methods, coagulation profile : PT and INR, markers for autoimmune hepatitis as [Antinuclear antibody] in suspected cases, markers for Wilson disease as [serum copper, serum ceruloplasmin and urinary copper] in suspected cases, markers for Hemochromatosis [serum iron, serum ferritin and transferrin saturation] in selected cases, kidney function tests: serum creatinine and GFR was calculated by MDRD equation: $186 \times [\text{Creatinine}/88.4]^{-1.154} \times [\text{Age}]^{-0.203} \times [0.742 \text{ if female}] \times [1.210 \text{ if black}]$, Fasting blood glucose, HbA1c% in diabetic cases, alfa fetoprotein [AFP], pregnancy test for females in childbearing period), radiological investigations including: abdominal and pelvic ultrasonography and triphasic CT of the liver if focal lesion is suspected by ultrasound or AFP more than 100, calculation of CTP score for assessment the severity of liver disease, non-invasive markers of liver cirrhosis like fibrosis-4 (FIB-4) score.

Assessment of efficacy, safety and outcome:

Diagnosis of SVR following treatment is currently defined by the absence of viral RNA in the blood 12 weeks after stopping treatment. Safety during the study period in the form of clinical adverse effects (either related to chronic liver disease and not related).

Diagnosis of complications as the development of HCC is done by (contrast-enhanced triphasic CT).

Timeline of the treatment regimens, the control group and the study group were subjected to treatment for 12 weeks then followed up for another 12 weeks (SVR), and then followed up for another 12 weeks so the total period of the study was 36 weeks.

Follow up:

We performed: serum(ALT, AST, albumin, bilirubin, creatinine), CBC, INR, FIB-4, and CTP score at (during treatment plus 12 and 24 weeks after EOT), a quantitative PCR at EOT and 12 weeks after EOT, pelvi-abdominal US at EOT plus 12 and 24 weeks after EOT, and triphasic CT abdomen in patients who developed focal lesion by the US .

Stoppage of treatment: When the patients finished the treatment, or on the occurrence of severe decompensation.

Statistical analysis:

Data were analyzed with SPSS for version 15.0 (Statistical Package for the Social Science, Chicago, IL). Quantitative data were expressed as mean \pm standard deviation (SD), Data were analyzed by independent sample, paired t-test. While qualitative data were expressed as number and percentage and were analyzed by Chi-square (χ^2) test. P-value was considered significant if <0.05 and highly significant if <0.001 .

Results:

There is statistically non-significant difference between the studied groups regarding age, BMI or gender (table 1), There is statistically non-significant difference between the studied groups regarding baseline Hb level, platelet count, serum creatinine, AST level and ALT level. However There is statistically significant difference between them regarding baseline INR level, serum albumin level, total serum bilirubin level and FIB-4 score (table 2), There is non-significant difference between the studied groups regarding SVR By the end of treatment, patients achieved SVR in Group I (93.75%) and in group II (100%) (table 3).

As regard side effects regarding Hb level during therapy there is significant decrease in Hb level (table 4) and In **group I**: During therapy only 3 cases 9.4% stop RBV (1 case at 4th week and 2 cases at 8th week) As Hb level less than 8.5 gm% and take blood transfusion and Erythropoietin), But in **group II**: only one case 3.3% stop RBV at 8th week of therapy.

As regard mortality and morbidity (table 5) No patient within the study groups had died by the end of the study. But only one case 3.1% from **group I**: stop treatment at 4th week as he developed severe side effects and complications as (HE Grade 2 ,3) . moreover 3 cases 9.4% from **group I** developed HE after EOT but in **group II**: no any case developed HE during treatment or after EOT, In **group I**: only one patient 3.1% had new onset ascites at 4th week of therapy and one patient 3.1% showed

moderate ascites progression to tense ascites 24 weeks after EOT. Also in **group II**: 2 cases 6.6% had new onset ascites at 12, 24 weeks after EOT. regarding complication development of focal lesion we had 2 cases 6.2% In **group I** detected at 12, 24 weeks after EOT, And only one case 3.3% in **group II** detected at 12 week after EOT.

As regard Outcome of therapy in both studied groups(table 6) There is statistically non-significant difference between the studied groups regarding AST and ALT levels during treatment and also after EOT, On measuring change over time in each group separately, there is significant decrease in AST and ALT levels.

There is statistically significant difference between the studied groups regarding serum albumin and bilirubin levels during treatment. However, there is non-significant difference between both groups in it at last observation (24 week after EOT). On measuring change over

time in each group separately, there is significant improvement in serum albumin and bilirubin specially in Group I.

There is statistically significant difference between the studied groups regarding INR level during therapy and after EOT. In Group I, there is significant change INR level over time while there is non-significant change over time in Group II.

There is statistically non-significant difference between the studied groups regarding platelet count during therapy and also after EOT. In each group separately, there is non-significant change in platelet count over time but There is significant decrease in FIB-4 overtime among both groups.

As regard CTP There is statistically significant difference between the studied groups regarding CTP classification and there is significant improvement in CTP over time especially in group I (table 7).

Table 1. Comparison between the studied groups regarding demographic data.

Demographic and laboratories characteristics		Study groups		Test	P-value
		Group I N=32	Group II N=30	χ^2/t	
Gender:	N (%)				
	Male	12 (37.5)	12 (40)	0.041	0.84
Female	20 (62.5)	18 (60)			
BMI:	N (%)				
	Average	20 (62.5)	20 (66.7)	0.117	0.732
	Obsess	12 (37.5)	10 (33.3)		
Age (years):	Mean \pm SD	55.5 \pm 8.62	53.2 \pm 9.5	0.999	0.322
	Range	37 – 69	33 - 66		

N (%)=Number of cases as apercentage of total, BMI=Body mass index

Table 2. Comparison between the studied groups regarding Mean laboratories value at time of presentation

Demographic and laboratories characteristics	Study groups		Test	P-value
	Group I Mean ± SD	Group II Mean ± SD	t-test	
Hb level (gm/dL):	12.05 ± 1.68	12.6 ± 1.33	1.423	0.159
INR level:	1.41 ± 0.25	1.29 ± 0.15	2.243	0.029
Serum albumin (g/dl):	2.88 ± 0.4	3.28 ± 0.28	4.533	<0.001
Total bilirubin (mg/dL):	2.12 ± 0.75	1.41 ± 0.29	4.854	<0.001
platelet count: cells/µl ×10³	115.75 ± 56.87	126.43 ±45.16	0.815	0.418
AST level (U/L) :	91.69 ± 59.18	84.7 ± 23.83	0.602	0.549
ALTlevel(U/L):	68.97 ± 35.09	70.97 ± 20.13	0.273	0.785
Serum creatinine (mg/dL):	0.91 ± 0.2	1 ± 0.15	1.994	0.051
FIB-4:	6.25 ± 3.48	4.7±2.17	2.088	0.041
CTP score:	7.81 ± 0.78	5.87 ± 0.35	12.827	<0.001

Hb=Haemoglobin, AST=aspartate aminotransferase, ALT= alanine aminotransferase, INR=international normalization ratio, FIB4=fibrosis index based on 4 parameters. CTP = Child turcotte pugh.

Table 3. SVR(as apercentage of total) at EOT and at 12weeks after EOT

SVR	Study groups	
	Group I N=32 (%)	Group II N=30 (%)
At EOT:		
No	2 (6.2)	0 (0)
Yes	30 (93.8)	30 (100)
At 12weeks after EOT:		
No	2(6.2)	0 (0)
Yes	30 (93.8)	30 (100)

N (%)=Number of cases as apercentage of total
SVR=sustained virological response, EOT= end of treatment

Table 4. Comparison between the studied groups regarding hemoglobin level before and after therapy.

Hemoglobin level	Study groups		Test	
	Group I	Group II	t-test	P-value
	Mean \pm SD	Mean \pm SD		
Baseline	12.05 \pm 1.68	12.6 \pm 1.33	-1.425	0.159
At 4 weeks	11.57 \pm 1.73	12.06 \pm 1.28	-1.27	0.209
At 8 weeks	11.12 \pm 1.76	11.75 \pm 1.23	-1.642	0.106
At 12 weeks	10.6 \pm 1.58	10.96 \pm 1.36	-0.970	0.336
12 week after EOT	11.33 \pm 1.5	10.96 \pm 1.31	1.032	0.306
24 week after EOT	11.25 \pm 1.36	11.2 \pm 1.41	0.164	0.871

EOT= end of treatment

Table 5. Comparison between both groups as regard mortality and morbidity during and after therapy.

Time of observation	During therapy		During follow up Up to 24 week after EOT	
	Group I N (%)	Group II N (%)	Group I N (%)	Group II N (%)
Mortality	0 (0)	0 (0)	0 (0)	0 (0)
New onset HE	1 (3.1)	0 (0)	3 (9.4)	0 (0)
New onset or worsening of ascites	1 (3.1)	0 (0)	1 (3.1)	2 (6.6)
CTP worsen	3 (9.4)	1 (3.3)	4 (12.5)	2 (6.6)
HCC	0 (0)	0 (0)	2 (6.2)	1 (3.3)

N (%)=Number of cases as a percentage of total

EOT= end of treatment, HE= Hepatic encephalopathy, CTP = Child turcotte pugh, HCC = Hepatocellular carcinoma .

Table 6. Outcome of therapy in both studied groups as regard INR level, serum albumin, serum total bilirubin, platelet count, liver enzymes and FIB-4 score during therapy after EOT.

Time of observation	At EOT				At LO (24 weeks after EOT)				
	Study group	Group I Mean ± SD	Group II Mean ± SD	t-test	p-value	Group I Mean ± SD	Group II Mean ± SD	t-test	p-value
INR		1.39 ± 0.21	1.29 ± 0.13	2.159	0.035	1.32 ± 0.16	1.24 ± 0.15	2.164	0.035
Serum albumin(g/dl)		3.22 ± 0.64	3.37 ± 0.32	1.155	0.268	3.48 ± 0.7	3.66 ± 0.46	1.188	0.268
Total bilirubin (mg/dL)		1.75 ± 0.66	1.33 ± 0.27	3.239	0.002	1.43 ± 0.57	1.2 ± 0.29	1.982	0.052
Platelet cells/ $\mu\text{l} \times 10^3$	118.6 ± 50.1		129.7 ± 48.51	0.885	0.379	125.5 ± 55.9	133.2 ± 46.3	0.588	0.558
AST level (U/L)		37.26 ± 13.1	37.63 ± 9.81	0.125	0.901	34.39 ± 13.36	31.07 ± 6.89	1.217	0.228
ALT level (U/L)		32.03 ± 10.64	34.27 ± 10.44	0.836	0.406	28.22 ± 9.08	27.73 ± 6.68	0.240	0.810
FIB-4		3.74 ± 2.22	3.46 ± 1.49	0.579	0.564	3.54 ± 2.03	2.76 ± 1.54	1.695	0.095

EOT= end of treatment, LO= Last observation, AST=aspartate aminotransferase, ALT= alanine aminotransferase, INR=international normalization ratio, FIB4=fibrosis index based on 4 parameters.

Table 7. Comparison between the studied groups regarding CTP change over time.

CTP	Study groups		t-test	P-value
	Group I	Group II		
	N=32 (%)	N=30 (%)		
Baseline				
Mean ± SD	7.81 ± 0.78	5.87 ± 0.35	12.827	<0.001
At 4th week				
Improved	8 (25)	6 ((20)		
The same	21 (65.6)	24 (80)		
Worsen	3 (9.4)	0(0)		
Mean ± SD	7.72 ± 1.14	5.87 ± 0.35	8.752	<0.001
To 8th week				
Improved	10 (31.25)	6 (20)		
The same	20 (62.5)	24 (80)		
Worsen	2 (6.25)	0(0)		

Mean ± SD	7.42 ± 1.09	5.87 ± 0.35	7.558	<0.001
To EOT				
Improved	21 (65.6)	12 (40)		
The same	9 (28.2)	17 (56.7)		
Worsen	2 (6.2)	1 (3.3)		
Mean ± SD	6.74 ± 1.39	5.67 ± 0.48	4.065	<0.001
12 week after EOT				
Improved	19 (59.4)	12 (40)		
The same	11 (34.4)	17 (56.7)		
Worsen	2 (6.2)	1 (3.3)		
Mean ± SD	6.35 ± 1.38	5.5 ± 0.57	3.179	0.003
24 week after EOT				
Improved	22 (68.7)	15 (50)		
the same	6 (18.8)	13 (43.4)		
Worsen	4 (12.5)	2 (6.6)		
Mean ± SD	6.32 ± 1.83	5.5 ± 0.73	2.316	0.026

N (%)=Number of cases as a percentage of total, EOT= end of treatment , CTP = Child turcotte pugh.

DISCUSSION

The studies which included decompensated cirrhotic HCV patients treated with DAAs were scarce so, the aim of our study tested the efficacy, safety and outcome of DAAs in the treatment of decompensated hepatitis C related cirrhotic patients. Our study included 62 patients with decompensated cirrhosis (group I) and compensated cirrhosis (group II) treated with DAAs for 12 weeks.

Our results regarding SVR12 were similar to results of **Poordad et al, [9]**. Their study on patients with decompensated cirrhosis when treated with a 12-week regimen of SOF-DCV plus RBV, SVR12 rates of 94% were observed. Similar results were from **Curry et al., [10]** with SVR12 rates of 94% in patients with decompensated cirrhosis when treated with DAAs, and **Gentile et al., [11]** the rate of SVR 12 was 95.5%.

And not agreed with **Ahmed et al., [12]** SVR12 rates were 84.54% in Egyptian HCV cirrhotic patients treated by SOF - DCV ± RBV for 12

weeks and **Foster et al., [13]** the SVR12 rates were 71% after 12 weeks of SOF-DCV ± RBV, In our opinion, this difference due to not all cases in their study take RBV which cause significant increase in SVR rate.

As regard laboratory parameters (serum albumin and bilirubin) there were improvement in serum albumin, bilirubin during therapy and follow up especially in group I in our study was nearly similar to results recorded by **Van der Meer et al, [14]** who detected an improvement of liver function (albumin and bilirubin levels) during and shortly after therapy among patients with decompensated cirrhosis treated with SOF/DCV and RBV.

And similar results from **Pascasio et al, [15]** in patients with decompensated cirrhosis, there was a significant improvement in bilirubin, albumin during treatment and 12 weeks after (EOT). And **Gentile et al, [11]** who detected an increase in albumin levels (from 3.1 at the start of therapy to 3.6 at 12 week post-treatment).

As regard CTP score in our study, In group I at

12, 24 weeks after EOT (59.4% and 68.7%) of cases were improved to CTP-A cirrhosis. Those results were in agreement with results recorded from **Charlton et al, [16]** who detected an improvement in the CTP score in a significant proportion of patients after relatively short follow up.

Also, near results of **Gentile et al, [11]** the number of patients who switched from a decompensated to a compensated liver cirrhosis progressively increased during the observation from 45.5% at one-month treatment to 61.8% at last observation.

Also were away from **Kimura et al, [17]** patients with decompensated cirrhosis who achieved SVR 12, approximately 25% of them showed improvement from CTP-B to CTP-A even in a short period of time. This difference in our opinion because of most of our CTP-B cases was (CTP-B7).

AS regard Change in FIB-4 score, our results were in agreement with results of **Bachofner et al, [18]** treatment with DAAs regimens cause rapid regression of fibrosis markers as FIB-4 (3–6 months post-treatment), also was similar to results recorded by **Chan et al, [19]**. The main cause of improvement in our opinion was an improvement in liver inflammation especially in patients who achieve an SVR.

As regard change in ALT and AST over time in our study, there is a significant decrease in AST and ALT levels in both groups these results were in agreement with a study from **Gentile et al, [11]** and **Mauss et al, [20]** which had confirmed the same results.

Our results regarding INR level, there is significant decrease in INR level over time in group I patients, it was similar to results recorded by **Flamm et al, [21]** and **Fernandez Carrillo et al, [22]** which had confirmed the same results in decompensated cirrhotic patients treated with DAAs. But were not in agreement with a study from **Gentile et al, [11]** who detected no significant change in INR over time.

The most important adverse effects during therapy in our study is anemia $Hb(\leq 10)$ especially in group I > group II. This was

nearly similar to results recorded by **Guardigni et al, [23]** who detected CTP-B patients displayed significantly higher level of anemia than those with compensated cirrhosis.

Also, were in Agreement with **Attia et al, [24]** who detected adverse events in 149,816 chronic HCV patients treated with different regimens in the (NCCVH) in Egypt, Anemia was the most commonly reported adverse event in patients with cirrhosis especially decompensated cases treated with SOF and RBV.

As regard ascites in our study, there was a significant difference between the studied groups regarding the development of ascites. In group I at baseline most cases (45.2%) had mild ascites and only 2 cases (6.5%) had moderate ascites, with no cases had severe ascites). most of these cases showed clinical improvement especially after EOT. This was in consistent with **El-Sherif et al., [25]** who detected, severe ascites have a lower chance of achieving clinical improvement in comparison to mild to moderate ascites.

Our results regarding the development of focal lesion we had 2 cases 6.2% In group I detected at (12 and 24 weeks after EOT) and one case 3.3% in group II detected at (12 weeks after EOT). was nearly similar to results recorded by **Calvaruso et al, [26]** who detected overall incidence of HCC in cirrhotic patients with SVR was 3-fold higher in CTP- B patients than in those with compensated cirrhosis (7.8% vs. 2.1%). Also, were in agreement with results from **Bang and Song [27]** who detected post-SVR follow-up studies showed that the risk of developing HCC remains in patients with cirrhosis who eliminate HCV.

As regard time of occurrence of HCC in our study was nearly similar to results recorded by **Nault et al, [28]** who detected the median latency period between exposure to DAA and occurrence of HCC was very short from 2.7 to 5.6 months. And the same results from **Foster et al, [13]** who detected HCC developed over a short time period after DAAs therapy. This would suggest that some or all of these HCCs were present but not detected on enrolment into the study.

In our study as regard mortality, no patient within the study groups had died by the end of the study. Was in agreement with **Poordad et al, [9]** who detected that SOF-based combinations, either with LDV, DCV or VEL±RBV, showed to be safe in clinical trials when used in cases with decompensated cirrhosis and were consistent with **Backus et al, [29]** who detected that patients with chronic HCV infection, treated with DAAs achievement of SVR12, there was a reduction in the risk of death, including liver-related and non-liver-related deaths. In contrast, the results recorded by **Maan et al, [30]** who had Six patients in their study (1.4%) (1 CTP score of A, 3 CTP scores of B, and 2 CTP scores of C) died between starting therapy and SVR12. In our opinion, this difference due to a large number of patients achieving SVR in our study that reduce mortality and also due to the relatively short period of follow up (only 6 months after the end of therapy), in addition to CTP scores of C is excluded from our study.

Post-treatment assessment of cirrhosis by FIB-4 score is not accurate as it indicate only improvement of liver inflammation, slightly limited numbers of cases and relatively short period of follow up.

CONCLUSION

In conclusion, treatment with DAAs in CTP-B cirrhosis is safe and leads to high rate of viral clearance, a significant rate of improvement in liver function within 6 months after EOT, however, Patients with cirrhosis remains at risk of liver-related complications as HCC, So Further studies are needed to assess the impact of therapy on survival and quality of life in long-term follow-up.

Conflict of interest: Nothing to declare

Financial disclosure: Nothing to declare

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