

Predictive Factors for Liver Disease Progression Following the Direct Acting Antivirals Induced Sustained Virological Response: Data from the Italian Platform for the Study of Viral Hepatitis Therapies (PITER) Cohort



LA Kondili¹, MG Quaranta¹, S Rosato¹, LE Weimer¹, F D'Angelo¹, C Coppola², AL Zignego³, MR Brunetto⁴, G Raimondo⁵, TA Santantonio⁶, A Iannone⁷, G Taliani⁸, M Zuin⁹, L Chessa¹⁰, A Craxi¹¹, G Borgia¹², P Andreone¹³, FP Russo¹⁴, P Blanc¹⁵, F Morisco¹², G Parruti¹⁶, F Barbaro¹⁷, S Madonia¹⁸, F Capra¹⁹, M Vinci²⁰, M Persico²¹, L Chemello¹⁴, A Gori²², M Massari²³, M Puoti²⁰, A Licata²⁴, E Villa²⁵ and PITER Collaborating Group (available at www.progettopiter.it)

¹Istituto Superiore di Sanità, Rome, ²Gragnano Hospital, Naples, ³University of Florence, ⁴University Hospital of Pisa, ⁵University Hospital of Messina, ⁶Ospedali Riuniti, Foggia, ⁷University Hospital of Bari, ⁸Umberto I Hospital-Sapienza University, Rome, ⁹ASST Santi Paolo e Carlo, Milan, ¹⁰University of Cagliari, ¹¹University of Palermo, ¹²Federico II University, Naples, ¹³University of Bologna, ¹⁴University of Padua, ¹⁵S.M. Annunziata Hospital, Florence, ¹⁶Spirito Santo General Hospital, Pescara, ¹⁷University Hospital of Padua, ¹⁸Villa Sofia-Cervello Hospital, Palermo, ¹⁹University Hospital of Verona, ²⁰Niguarda Hospital, Milan, ²¹University of Salerno, ²²San Gerardo Hospital, Monza, ²³Azienda Unità Sanitaria Locale – IRCCS di Reggio Emilia, ²⁴University Hospital P. Giaccone, Palermo, ²⁵ University of Modena and Reggio Emilia

INTRODUCTION

The real life use of the Direct Acting Antivirals (DAAs) has brought excellent efficacy results, with a high efficacy and safety profile in real life use very similar compared to what has been reported by the clinical trials (1). However the effectiveness in terms of the role of Sustained Virological Response (SVR) in the liver disease progression according to the severity of liver disease need to be further explored.

AIM

The aim of this analysis was to evaluate in a real life cohort of patients with chronic hepatitis C in care, the potential liver disease progression, in terms of Child Pugh Class and/or score deterioration and or Hepatocellular Carcinoma (HCC) appearance, following viral eradication due to DAA treatment and the predictive factors which could influence it.

METHODS

Data from treated patients with liver cirrhosis and with available follow up (at least 6 months) after having achieved SVR12, in the PITER cohort were evaluated (2). Changes in the severity of liver disease in terms of Child Pugh (C-P) Class and/or score and/or HCC appearance were evaluated during an available follow up of at least 6 months following the SVR12. Age, gender, HCV genotype, Body Mass Index, alcohol use, presence of diabetes, bilirubin and albumin levels and platelets counts were evaluated as potential factors related to C-P Class and/or score deterioration and *de-novo* HCC appearance.

RESULTS

Of overall treated patients in the PITER cohort, 1539 with liver cirrhosis, [median age: 61±14 years; 862 (56%) were men with a pre-treatment C-P Class distribution: 1308 (85%) C-P class A; 200 (13%) C-P class B and 31 (2%) C-P class C] whom achieved SVR12 and had an available follow up (followed up for a median time of 12 months: Range: 10-30 months) were evaluated in this study. Of the overall patients evaluated, 923 (60%) did not change the C-P Class and Score (98% of them were pre-treatment C-P class A and 2% C-P class B); 432 (28%) improved C-P Class and/or Score (from B to A in 40% of patients, from C to B in 2%, from C to A in 1% and in the remaining 58% of patients the C-P score was improved within the same pre-treatment and at the end of follow up). In the remaining 184 patients (12%) C-P class and/or score were deteriorated: from A to B in 55 (30%), from B to C in 3 (2%) and in the remaining 126 (68%) the score was deteriorated within the same pre-treatment and end of follow up C-P class.

Tab 1. Variables independently associated to deterioration of Child Pugh Score

Variables	Crude OR	CI 95%	Adjusted OR	CI 95%
Age	0.9	0.98 1.0	1	1 1
Gender M/F	0.9	0.64 1.3	1	0.7 1.5
HCC	1.7	0.9 3.0	1.8	1.1 3.3
Genotype 3/Others	1.1	0.6 1.9	1	0.5 1.9
Diabetes	0.9	0.9 1.9	1	0.6 1.5
Albumin <3.5mg/dl	2.4	0.4 3.6	1.4	0.5 5.0
Bilirubin>1.5	1.4	0.9 2.0	1.1	0.7 1.7
BMI>25 vs≤25	1.01	0.69 1.4	0.9	0.7 1.4
Liver fat	0.89	0.6 1.4	1.1	0.7 1.8
Platelets ≤10,000	1.6	1.1 2.3	1.7	1.2 2.4

Tab 2. Variables independently associated to *de-novo* HCC appearance following the DAA therapy

Variables	Crude OR	CI 95%	Adjusted OR	CI 95%
Age	1.04	1.02 1.07	1.05	1.02 1.08
Gender M/F	0.8	0.5 1.3	0.72	0.42 1.24
Genotype 3/Others	1.1	0.4 2.1	1.6	0.5 1.9
Diabetes	1.7	1.01 3	1.3	0.6 1.5
Albumin <2.8mg/dl	3.3	1.1 12.5	4.4	1.4 14
Bilirubin>1.5	2.68	1.7 4.4	1.9	1.1 3.39
BMI>25 vs≤25	1.4	0.9 2.3	1.4	0.8 2.4
Liver fat	0.7	0.4 1.3	0.9	0.5 2.4
Platelets ≤10,000	3.0	1.8 4.9	2.3	1.4 4.0

The only factors independently associated to the C-P score deterioration by the logistic regression analysis were the presence of pre-treatment HCC (OR 1.8 CI 95% 1.1-3.3) and platelets count lower than 10,000 (OR 1.7 CI 95% 1.1-2.4). Regarding *de novo* HCC appearance, the incidence was 62 (4.3%) patients during a median follow up time of 15 months (range 8-23 months). Factors independently associated to the HCC development were platelets count lower than 10,000; (OR 2.3 CI 95% 1.3-4); bilirubin level higher than 2 mg/dl (OR 1.1-3-3) and albumin level lower than 2.8 mg/dl (OR 4.4: CI 95% 1.4-14).

CONCLUSION

The effectiveness of DAAs treatment in patients with advanced liver cirrhosis is not as high as its efficacy. In real life practice only part of treated patients with cirrhosis improved C-P score after achieving SVR. Most patients remained stable, while a substantial portion (12%), who was characterised by an advanced pre-treatment liver disease (low platelets levels as surrogate of portal hypertension and/or HCC), deteriorated liver function regardless HCV eradication. Advanced liver disease was also an independent predictive factor for HCC appearance.

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DISCLOSURES

Nothing to disclosure

Contact information

Loreta Kondili MD, PhD. Center for Global Health, Istituto Superiore di Sanità, Rome-Italy.
Email: loreta.kondili@iss.it