

ORIGINAL ARTICLE



WILEY

Gene signature-MELD score and alcohol relapse determine long-term prognosis of patients with severe alcoholic hepatitis

Pierre Deltenre^{1,2}  | Eric Trépo^{1,3} | Naoto Fujiwara⁴ | Nicolas Goossens^{4,5} | Astrid Marot⁶  | Margaux Dubois⁷  | Laurent Spahr⁵  | Jean Henrion⁸ | Christophe Moreno^{1,3} | Yujin Hoshida⁴

¹Department of Gastroenterology, Hepatopancreatology, and Digestive Oncology, C.U.B. Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium

²Department of Gastroenterology and Hepatology, Clinique St Luc, Bouge, Belgium

³Laboratory of Experimental Gastroenterology, Université Libre de Bruxelles, Brussels, Belgium

⁴Division of Digestive and Liver Diseases, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, USA

⁵Division of Gastroenterology and Hepatology, Geneva University Hospital, Geneva, Switzerland

⁶Department of Gastroenterology and Hepatology, CHU UCL Namur, Université Catholique de Louvain, Yvoir, Belgium

⁷Division of Gastroenterology and Hepatology, Centre Hospitalier Universitaire Vaudois, University of Lausanne, Lausanne, Switzerland

⁸Department of Gastroenterology and Hepatology, Hôpital de Jolimont, Haine-Saint-Paul, Belgium

Correspondence

Yujin Hoshida, Division of Digestive and Liver Diseases, Department of Internal Medicine, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390, USA.
Email: Yujin.Hoshida@UTSouthwestern.edu

Funding information

NIH/U.S. National Institute of Diabetes and Digestive and Kidney Diseases, Grant/Award Number: DK099558; European Commission, Grant/Award Number: ERC-2014-AdG-671231; Cancer Prevention

Abstract

Background: The gene-signature-model for end stage liver disease (gs-MELD) score has been shown to be a strong predictor of 6-month survival in severe alcoholic hepatitis (AH). Currently, only a few studies have evaluated the long-term prognosis of patients with severe AH.

Aim: To assess the prognostic value of the gs-MELD score at 5 years in patients with severe AH.

Methods: Forty-eight consecutive patients with AH (25 males, median age 52 years [95% CI: 48-56]) were included.

Results: The median gs-MELD score was 2.6 (95% CI: 2.2-3.0). According to the gs-MELD score, 22 patients (46%) were considered to have a poor prognosis. During a median follow-up of 29 months (95% CI: 4-43), 19 patients (40%) were abstinent and 24 patients (50%) died. At 5 years, rates of survival were 61% (95% CI: 41-81) and 26% (95% CI: 11-55) in patients with low and high gs-MELD scores ($P = .001$), and 81% (95% CI: 58-96) and 22% (95% CI: 10-47) in abstainers and in consumers ($P < .001$) respectively. In multivariable competing risk regression modelling, gs-MELD score (subdistribution hazard ratio: 5.78, 95% CI: 2.17-15.38, $P < .001$) and recurrent alcohol consumption (subdistribution hazard ratio: 12.18, 95% CI: 3.16-46.95, $P < .001$) were independently associated with 5-year mortality.

Conclusions: Both gs-MELD score and alcohol consumption drive AH long-term prognosis. The gs-MELD score may guide the development of molecularly targeted therapies in AH.

KEYWORDS

cirrhosis, MELD, prognosis

1 | INTRODUCTION

Severe alcoholic hepatitis (AH) is defined by a Maddrey's discriminant function of 32 or higher¹ and is the form of alcoholic liver disease that carries the poorest prognosis. Mortality rates as high as 50% have been reported at 3 months without treatment.² Currently, corticosteroid therapy is the only available option that provides a limited (albeit significant) reduction in short-term mortality.³⁻⁵ The Lille score or the combination of the Lille and the model for end stage liver disease (MELD) scores have been proposed as tools for helping physicians to decide whether or not corticosteroids should be maintained after one week of treatment according to the probability of improvement in survival if corticosteroids are maintained.^{6,7} However, the incidence of infections is increased during corticosteroid treatment, even if administered for only a short period of time, and the negative impact of the development of infection during a course of corticosteroids on patient prognosis has been well-demonstrated in this setting.⁸

Recently, the gene signature-MELD (gs-MELD) score, a combination of a gene signature obtained from a liver biopsy and the MELD score calculated at baseline, has been proposed as a new prognostic tool for predicting short-term survival of AH patients treated with corticosteroids. The gs-MELD score has the advantage over the Lille score or the combination of the Lille and the MELD scores of being available before any therapeutic intervention. In addition, this score outperformed other clinical models for prediction of short-term survival of patients with severe AH in 2 validation cohorts.⁹

Up to now, most studies on patients with severe AH have focused on short-term survival. As alcoholic liver disease has a deep impact on public health and on the liver transplantation waiting list, accurate prediction of both short- and long-term prognosis of patients with severe AH is mandatory for guiding therapeutic strategy.^{6,7} However, only a few studies have evaluated the long-term prognosis of patients with severe AH.^{10,11} The aim of the present study was to assess the long-term prognostic value of the gs-MELD score among patients with severe AH.

2 | MATERIALS AND METHODS

2.1 | Patients

Patient characteristics have already been extensively described elsewhere.⁹ Forty-eight consecutive patients were recruited at four European institutions in Belgium and Switzerland. These patients were those who constituted the validation cohort for the initial study.⁹ Patients included in the derivation cohort were not considered in the primary analysis to avoid a biased estimation of the performance of the gs-MELD score as the derivation cohort was the one used to derive the gs-MELD score. However, analyses in the

Key points

- Only a few studies have evaluated the long-term prognosis of patients with severe alcoholic hepatitis.
- The gene-signature-model for end stage liver disease score has been shown to be a strong predictor of 6-month survival in severe alcoholic hepatitis.
- In this study, gs-model for end stage liver disease score and recurrent alcohol consumption were independently associated with 5-year mortality.
- The gs-model for end stage liver disease score may guide the development of molecularly targeted therapies in alcoholic hepatitis.

derivation cohort were also preformed and results are presented in Supplementary Figure 1A and 1B. Briefly, all patients were chronic alcohol consumers (>60 g/d for males and >40 g/d for females), had recent (<90 days) onset of jaundice (bilirubin level > 5 mg/dL), and less than 60 days of abstinence before the onset of jaundice. All patients had histologically confirmed AH and a Maddrey's discriminant function ≥ 32 .¹ Histological criteria included the presence of steatosis, ballooned hepatocytes and Mallory bodies, with infiltration of polymorphonuclear neutrophils.¹² Needle biopsy specimens of the liver were obtained from all patients before corticosteroid therapy and archived as formalin-fixed, paraffin-embedded (FFPE) tissue blocks. Patients with viral or autoimmune hepatitis, hemochromatosis or co-infection with human immunodeficiency virus were excluded. All received methylprednisolone orally at a dose of 32 mg/d for a maximum of 28 days. None had active infection at the start of corticosteroids. Written informed consent was obtained from all individuals. The Ethical Committees at CUB Hôpital Erasme, Hôpital de Jolimont, Centre Hospitalier Universitaire Vaudois, University Hospitals of Geneva, and Mount Sinai Medical Center approved the study.

2.2 | Data collection and study endpoints

Day 0 was defined as the date of corticosteroid initiation. The gs-MELD score was generated as described previously.⁹ Briefly, using five 10-micron-thick FFPE liver biopsy tissue sections, total RNA was extracted using the AllPrepDNA/RNA Mini Kit (Qiagen), 250 ng of total RNA with sufficient quality (RPL13A qPCR Ct value < 30) was assayed using the Affymetrix GeneTitan Human Genome U219 microarray (Affymetrix). Raw scan data were normalized using the Robust Multiarray Average algorithm¹³ and poor quality transcriptome profiles were defined by inter-sample correlation <0.70.¹⁴ Less variable genes across the samples, based on coefficient of variation <0.4, were excluded. A 123-gene prognostic gene signature was defined in the derivation cohort

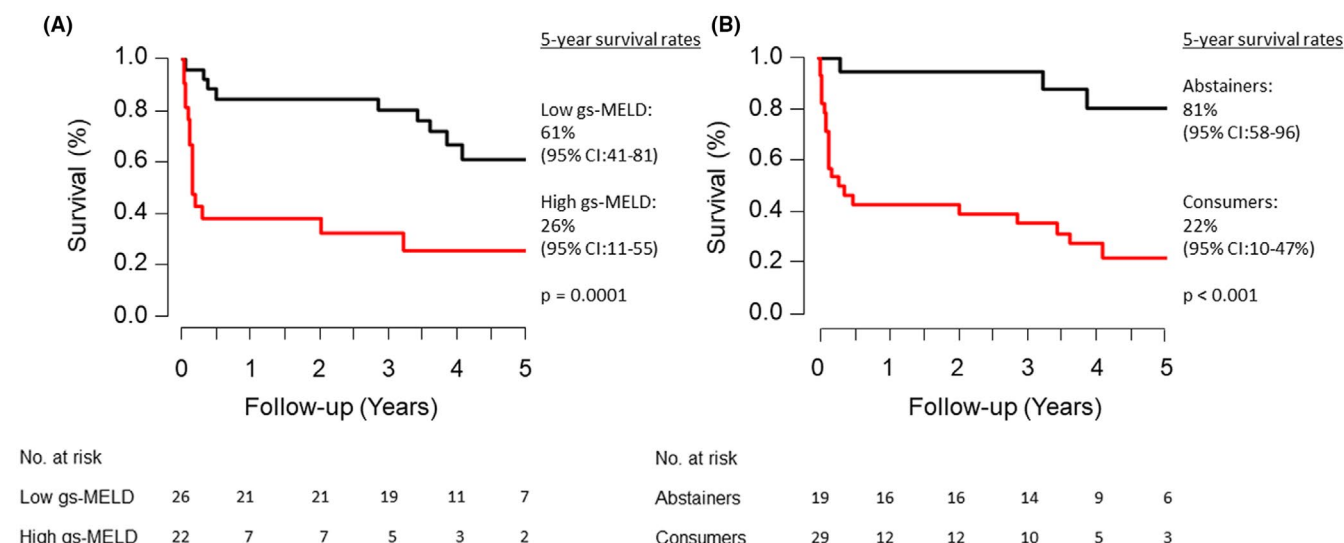


FIGURE 1 Survival curves according to gs-model for end stage liver disease (MELD) score and to alcohol consumption. A, According to gs-MELD score. B, According to alcohol consumption

as previously described.¹⁴ One hundred fourteen genes with the largest absolute Cox scores (to fit the assay format) were implemented in an nCounter Elements assay (NanoString), and 200 to 500 ng of total RNA samples was assayed. Gene signature-based outcome prediction was performed using the Nearest Template Prediction algorithm, based on a prediction confidence of $P < .05$ defining the poor-prognosis group, while the rest of the subjects were designated to the good-prognosis group. A prognostic score, integrating the gene signature and the MELD score, was developed by using regression coefficients from the multivariable Cox regression model in the derivation cohort as follows:

$$\begin{aligned} \text{gs-MELD score} = & 1.102 \times (1 \text{ if poor prognosis} \\ & 123\text{-signature prediction or } 0 \\ & \text{if non-poor prognosis prediction}) \\ & + 0.102 \times \text{MELD score} \end{aligned}$$

Patients with a gs-MELD score >2.66 (the median value of the gs-MELD score in the derivation cohort of the initial study⁹) were considered to have a poor prognosis.

Patients were considered abstinent if they had no alcohol consumption during follow-up. As a minimal period of abstinence is necessary to have a positive impact on survival,¹⁵⁻¹⁷ patients with <3 months of follow-up were considered non-abstinent. The primary endpoint was 5-year overall mortality.

2.3 | Statistical analysis

Inter-group differences for continuous and categorical variables were tested using the Wilcoxon rank-sum test and Fisher's exact

test respectively. Follow-up time was defined as the period from the first day of initiation of therapy to 5 years after treatment started. Data for patients who had not died, including those lost to follow-up, were censored at the date of the last follow-up visit. The risk of death was estimated taking into account liver transplantation as a competing risk. We conducted univariable and multivariable Fine and Gray competing risk regression to identify factors associated with death.¹⁸ Subdistribution hazard ratios (SHR) are reported with their 95% confidence intervals (CI). To avoid bias related to the effect of collinearity, when Child-Pugh or MELD scores were included in multivariable analysis, their constituent variables were not considered. A two-tailed $P < .05$ was considered statistically significant.

All data analyses were performed using NCSS 2016 software (NCSS, Kaysville, UT, USA) and R (R Foundation for Statistical Computing, Vienna, Austria).

3 | RESULTS

3.1 | Patients

The clinical demographics of the 48 patients included in the primary analyses of the study are described in Table 1. Three (6%), 1 (2%), and 1 (2%) patients were lost to follow-up at 1, 2, and 3 years respectively. The median gs-MELD score was 2.6 (95% CI: 2.2-3.0). According to the gs-MELD score, 22 patients (46%) were considered to have a poor prognosis. During a median follow-up of 29 months (95% CI: 4-43), 19 patients (40%) were abstinent and 24 patients (50%) died. Among the 38 non-abstinent patients, 13 had <3 months of follow-up and were thus considered non-abstinent, and 16 returned to alcohol consumption after a median delay of 105 days (95% CI: 14-547 days, range 14-952 days), most of them within the

TABLE 1 Characteristics of patients and clinical outcomes

Characteristics	n = 48
Age, y	52 (48-56)
Male gender, n	25 (52%)
INR	1.7 (1.5-1.8)
Bilirubin, mg/dL	12.8 (11.5-16.0)
Creatinine, mg/dL	0.8 (0.7-0.8)
Albumin, g/L	26 (25-28)
Maddrey discriminant function	50 (45-58)
Child-pugh score	11 (10-12)
MELD score	22 (21-23)
Lille score ^a	
Median score	0.30 (0.21-0.39)
Non-responders, n	14 (30%)
gs-MELD	
Median score	2.6 (2.2-3.0)
Poor prognosis, n	22 (46%)
Abstinence, n	19 (40%)
Death, n	24 (50%) ^b
Liver transplantation, n	4 (8%) ^c

^aLille score could not be calculated in 2 patients since they died before 7 days of treatment.

^bAll deaths were liver-related;

^cLiver transplantation was performed for hepatocellular carcinoma and for liver failure in 2 and 2 patients respectively.

Abbreviations: gs-MELD, gene signature-MELD; INR: international normalized ratio; MELD: model for end-stage liver disease.

Note: Continuous variables are presented as median (interquartile range).

first 6 months following inclusion. All deaths were liver-related. Four patients underwent a liver transplantation, 2 for hepatocellular carcinoma and 2 for liver failure.

3.2 | Prognostic value of the gs-MELD score and recurrent alcohol use at 5 years

At 5 years, rates of survival were 61% (95% CI: 41-81) and 26% (95% CI: 11-55) in patients with low and with high gs-MELD score ($P = .001$, Figure 1A), and 81% (95% CI: 58-96) and 22% (95% CI: 10-47) in abstainers and in consumers ($P < .001$, Figure 1B) respectively. In multivariable competing risk regression, the gs-MELD score (SHR: 5.78, 95% CI: 2.17-15.38, $P < .001$) and recurrent alcohol consumption (SHR: 12.18, 95% CI: 3.16-46.95, $P < .001$) were independently associated with 5-year mortality (Table 2). Of note, gs-MELD score and alcohol consumption were not correlated ($P = .14$). Results in the derivation cohort of the initial study⁹ are presented in Figure S1A and B. In multivariable competing risk regression, the gs-MELD score (SHR: 2.04, 95% CI: 1.42-2.93, $P < .001$) and recurrent alcohol consumption (SHR: 2.54, 95% CI: 1.17-5.51, $P = .002$) were independently associated with 5-year mortality.

Association between the gs-MELD prognostic classification and the Lille score categorized according to the 0.45 cut-off.

Table 3 indicates the relationship between the gs-MELD prognostic classification and the Lille score. The gs-MELD prognostic classification was not significantly associated with Lille score-based corticosteroid response ($P = .9$).

TABLE 2 Risk factors for death at 5 years

Baseline characteristics	Comparison group	Mortality at 5 years			
		Univariable		Multivariable	
		SHR (95% CI)	P-value	SHR (95% CI)	P-value
Age	1-year increase	1.04 (1.00-1.09)	.06		
Gender	Male vs female	1.93 (0.87-4.32)	.11		
INR	1-point increase	2.36 (0.83-6.76)	.11		
Bilirubin	1 mg/dL increase	0.96 (0.90-1.03)	.26		
Creatinine	1 mg/dL increase	4.44 (0.95-20.70)	.06		
Albumin	1 g/dL increase	0.94 (0.85-1.03)	.17		
Maddrey score	1-point increase	1.03 (1.00-1.05)	.03	1.01 (0.98-1.03)	.7
Child-Pugh score	1-point increase	1.25 (0.90-1.74)	.18		
MELD score	1-point increase	1.07 (0.94-1.22)	.28		
Lille score	1-point increase	2.67 (0.66-10.80)	.17		
gs-MELD score	1-point increase	2.29 (1.16-4.55)	.02		
gs-MELD score	Poor vs favorable	3.92 (1.73-8.87)	.001	5.78 (2.17-15.38)	<.001
Alcohol consumption	Yes vs no	8.21 (2.64-25.50)	<.001	12.18 (3.16-46.95)	<.001

Abbreviations: CI: confidence interval. Scores are presented as median (interquartile range); gs-MELD, gene signature-MELD; MELD: model for end-stage liver disease; SHR, subdistribution hazard ratio.

TABLE 3 Association between the gene-signature-model for end stage liver disease (gs-MELD) prognostic classification and the Lille score categorized according to the 0.45 cut-off

		gs-MELD-based prognostic classification	
		Good prognosis (n = 26)	Poor prognosis (n = 20)
Lille score-based corticosteroid response	Response (n = 32)	18	14
	Non-response (n = 14)	8	6

4 | DISCUSSION

Among patients with AH, an accurate prediction of the risk of death is required to guide therapeutic strategy. While many studies have focused on short-term risk of death, few efforts have been made to assess long-term prognosis. In this study, gs-MELD score and alcohol relapse were the 2 factors independently associated with the risk of death at 5 years in patients with severe AH treated with corticosteroids.

Two studies have already identified alcohol consumption as the main driver of long-term prognosis in AH patients. In these studies, the other factor associated with outcome was the Lille score in one study,¹¹ and the MELD score in the other.¹⁰ The present study has the advantage over these 2 studies of using the gs-MELD score, which has shown better predictive value than either the Lille score or the MELD score alone for short-term prognosis assessment,⁹ as highlighted in the last American Association for the Study of the Liver guidelines.¹⁹ Interestingly, Altamirano and colleagues have emphasized the need to investigate whether genetic factors impact long-term outcomes.¹⁰ Therefore, the present study was required to assess this important issue. Using a cut-off of 2.66, survival rates were more than twice as high in patients with a favourable gs-MELD score compared to those with a poor score. As the gs-MELD score is available at baseline, it may help to guide therapeutic strategy early on and may be used as a stratification factor for patient inclusion in clinical trials designed to test new pharmaceutical drugs in AH, as surrogate markers of outcome are required for these patients.²⁰

From a practical point of view, the gs-MELD score combines a 123-gene prognostic gene signature and the MELD score. Five 10-mm-thick formalin-fixed, paraffin-embedded liver biopsy tissue sections, allowing extraction of 250 ng of total RNA with sufficient quality, are needed to get the gene signature. Thus, calculation of this score requires a liver biopsy and this currently limits its widespread use in clinical practice. Even if histological confirmation of AH may not be mandatory in many cases with typical presentation,¹⁹ European Association for the Study of the Liver guidelines recommend the use of histologic analysis because it has been demonstrated that relying only on clinical criteria is associated with a significant risk of misclassification.²¹ Of note, the gs-MELD score

remains predictive of outcome when implemented in an independent assay platform and can be calculated in 2 days using this FDA-approved platform, which can accommodate up to 800 genes in a single reaction.⁹

In this study, gs-MELD and Lille scores were not correlated. Even if both scores were designed to predict survival, neither of these scores can be recommended as a predictor of the response assessed by the other. In addition, the Lille score does not predict survival perfectly as, in the original study aimed at deriving the Lille score, 25% of non-responders were alive and 15% of responders were dead at 6 months.⁷ Lastly, the independent relationship between the Lille score and survival has not been well-established in real-world cohorts, especially in non-French centres.²²

We acknowledge that this study is a post-hoc analysis and that one potential limitation is related to its small sample size. However, severe AH remains a rare complication among heavy drinkers.² Furthermore, all patients were consecutively included across 4 European centres and all were treated with corticosteroids, as recommended.²¹ Overall, we believe that the patient population represents a valuable cohort for the assessment of long-term prognosis in severe AH.

In conclusion, although these findings should be validated in independent prospective cohorts, the gs-MELD score is a strong short- and long-term prognostic tool in patients with severe AH treated with corticosteroids. Alcohol consumption is the other factor that negatively impacts patient outcomes at 5 years, and this can be improved by clinical intervention. The gs-MELD score may guide the development of molecularly targeted therapies to improve long-term outcomes.

WRITING ASSISTANCE

We acknowledge the contribution of Sandy Field, PhD, for her assistance concerning English-language editing.

DISCLOSURE

The authors declare no competing interests in the present study.

AUTHORS' CONTRIBUTIONS

PD: study concept and design; statistical analysis; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; study supervision. ET: study concept and design; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content. NF: statistical analysis; acquisition of data, analysis and interpretation of data; critical revision of the manuscript for important intellectual content. NG, AM, MD, LS, JH, CM: acquisition of data, analysis and interpretation of data; critical revision of the manuscript for important intellectual content. YH: study concept and design; statistical analysis; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; study supervision.

ORCID

Pierre Deltenre  <https://orcid.org/0000-0002-4253-6028>Astrid Marot  <https://orcid.org/0000-0001-8961-4006>Margaux Dubois  <https://orcid.org/0000-0002-9856-8379>Laurent Spahr  <https://orcid.org/0000-0001-8407-2463>

REFERENCES

1. Maddrey WC, Boitnott JK, Bedine MS, Weber FL, Mezey E, White RI. Corticosteroid therapy of alcoholic hepatitis. *Gastroenterology*. 1978;75:193-199.
2. Lucey MR, Mathurin P, Morgan TR. Alcoholic hepatitis. *New Engl J Med*. 2009;360:2758-2769.
3. Mathurin P, O'Grady J, Carithers RL, et al. Corticosteroids improve short-term survival in patients with severe alcoholic hepatitis: meta-analysis of individual patient data. *Gut*. 2011;60:255-260.
4. Thursz MR, Richardson P, Allison M, et al. Prednisolone or pentoxifylline for alcoholic hepatitis. *N Engl J Med*. 2015;372:1619-1628.
5. Louvet A, Thursz MR, Kim DJ, et al. Corticosteroids reduce risk of death within 28 days for patients with severe alcoholic hepatitis, compared with pentoxifylline or placebo—a meta-analysis of individual data from controlled trials. *Gastroenterology*. 2018;155(458-68):e8.
6. Louvet A, Labreuche J, Artru F, et al. Combining data from liver disease scoring systems better predicts outcomes of patients with alcoholic hepatitis. *Gastroenterology*. 2015;149(2):398-406.
7. Louvet A, Naveau S, Abdelnour M, et al. The Lille model: a new tool for therapeutic strategy in patients with severe alcoholic hepatitis treated with steroids. *Hepatology*. 2007;45:1348-1354.
8. Louvet A, Wartel F, Castel H, et al. Infection in patients with severe alcoholic hepatitis treated with steroids: early response to therapy is the key factor. *Gastroenterology*. 2009;137:541-548.
9. Trepo E, Goossens N, Fujiwara N, et al. Combination of gene expression signature and model for end-stage liver disease score predicts survival of patients with severe alcoholic hepatitis. *Gastroenterology*. 2018;154:965-975.
10. Altamirano J, López-Pelayo H, Michelena J, et al. Alcohol abstinence in patients surviving an episode of alcoholic hepatitis: prediction and impact on long-term survival. *Hepatology*. 2017;66:1842-1853.
11. Louvet A, Labreuche J, Artru F, et al. Main drivers of outcome differ between short term and long term in severe alcoholic hepatitis: a prospective study. *Hepatology*. 2017;66:1464-1473.
12. European Association for the Study of L. EASL clinical practical guidelines: management of alcoholic liver disease. *J Hepatol*. 2012;57:399-420.
13. Irizarry RA, Hobbs B, Collin F, et al. Exploration, normalization, and summaries of high density oligonucleotide array probe level data. *Biostatistics*. 2003;4:249-264.
14. Hoshida Y, Villanueva A, Kobayashi M, et al. Gene expression in fixed tissues and outcome in hepatocellular carcinoma. *N Engl J Med*. 2008;359:1995-2004.
15. Im GY, Cameron AM, Lucey MR. Liver transplantation for alcoholic hepatitis. *J Hepatol*. 2019;70:328-334.
16. Lucey MR, Brown KA, Everson GT, et al. Minimal criteria for placement of adults on the liver transplant waiting list: a report of a national conference organized by the American Society of Transplant Physicians and the American Association for the Study of Liver Diseases. *Liver Transpl Surg*. 1997;3:628-637.
17. Marot A, Dubois M, Trepo E, Moreno C, Deltenre P. Liver transplantation for alcoholic hepatitis: a systematic review with meta-analysis. *PLoS ONE*. 2018;13:e0190823.
18. Jepsen P, Vilstrup H, Andersen PK. The clinical course of cirrhosis: the importance of multistate models and competing risks analysis. *Hepatology*. 2015;62:292-302.
19. Crabb DW, Im GY, Szabo G, Mellinger JL, Lucey MR. Diagnosis and treatment of alcohol-related liver diseases: 2019 practice guidance from the American Association for the Study of Liver Diseases. *Hepatology*. 2019. <https://doi.org/10.1002/hep.30866>. [Epub ahead of print]
20. Mathurin P, Thursz M. Endpoints and patient stratification in clinical trials for alcoholic hepatitis. *J Hepatol*. 2019;70:314-318.
21. European Association for the Study of the Liver. EASL clinical practice guidelines: management of alcohol-related liver disease. *J Hepatol*. 2018;69:154-181.
22. Moreno C, Deltenre P, Senterre C, et al. Intensive enteral nutrition is ineffective for patients with severe alcoholic hepatitis treated with corticosteroids. *Gastroenterology*. 2016;150(903-10):e8.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Deltenre P, Trépo E, Fujiwara N, et al. Gene signature-MELD score and alcohol relapse determine long-term prognosis of patients with severe alcoholic hepatitis. *Liver Int*. 2019;00:1-6. <https://doi.org/10.1111/liv.14265>