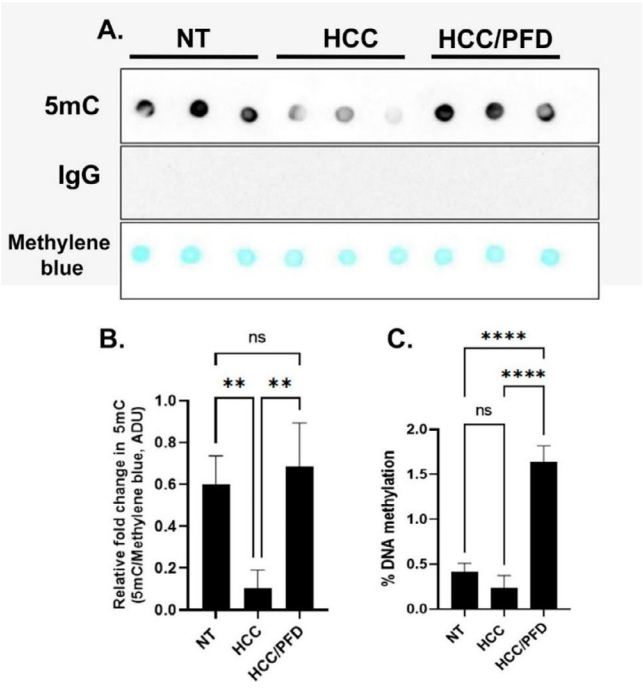
Finally, global DNA methylation was determined by Dot-blot and ELISA. The data obtained were analyzed using one-way ANOVA, and a Tukey post hoc test.

**Results:** We demonstrate that PFD treatment reduces the number and size of neoplastic lesions, prevents damage to hepatic architecture and collagen deposition, and decreases the presence of the histopathological marker Glypican-3. On the other hand, it positively regulates antioxidant markers such as GSH, MDA, Nrf2, GSTP1 and Catalase. It was also effective to decrease c-Myc expression and $\beta$-catenin redistribution from the nucleus to the cytoplasm. Finally, PFD stimulated the nuclear transfer of several isoforms of PPARs, SIRT1 and DNMT1, increasing epigenetic mechanisms of global DNA methylation (figure 1).

**Conclusions:** PFD prevents neoplastic lesions development by modulating antifibrogenic, antioxidant, and antiproliferative processes and modulating epigenetic marks to reverse global DNA hypomethylation.

Figure 1. Analysis of global DNA methylation. A) Representative dot blot using anti-5mC which recognizes global methylated DNA, anti-IgG as negative control and methylene blue staining as total DNA loading control. B) Graphs shows mean ± standard deviation of 5mC densitometry brand intensity of study groups. C) Graph that represents the percentage of global methylation of the DNA analyzed with ELISA.A one-way ANOVA statistical test and a Tukey post hoc test were performed. Group NT: only received vehicle; Group HCC: damage group induced by weekly administration of DEN and 2-AAF for 12 weeks; and Group HCC/PFD: which received the same treatment as Group HCC, plus PFD (300 mg/kg) (**p<0.005)




https://doi.org/10.1016/j.aohep.2023.101034

## O-25 ASSESSMENT OF MODELS FOR PREDICTING RESPONSE TO CORTICOIDS TREATMENT IN ALCOHOL-ASSOCIATED HEPATITIS: A GLOBAL COHORT STUDY

Francisco Idalsoaga[1], Luis Antonio Díaz[1], Gustavo Ayares[1], Jorge Arnold[1], Winston Dunn[2], Yanming Li[2], Ashwani Singal[3], Doug Simonetto[4], María Ayala-Valverde[5], Diego Perez[4], Jaime Gomez[5], Rodrigo Escarate[5], Eduardo Fuentes-López[6], Carolina A Ramirez[7], Dalia Morales-Arraez[8], Wei Zhang[9], Steve Qian[9], Joseph Ahn[4], Seth Buryska[4], Heer Mehta[2], Muhammad Waleed[3], Horia Stefanescu[10], Adelina Horhat[10], Andreea Bumbu[10], Bashar Attar[11], Rohit Grawal[12], Joaquín Cabezas[13], Inés García-Carrera[13], Berta Cuyàs[14], Maria Poca[14], German Soriano Pastor[14], Shiv K Sarin[15], Rakhi Maiwall[15], Prasun K Jalal[16], María Fátima Higuera-De La Tijera[17], Anand Kulkarni[18], Nagaraja Rao P[18], Patricia Guerra Salazar[19], Lubomir Skladaný[20], Natália Bystrianska[20], Veronica Prado[21], Ana Clemente-Sanchez[22], Diego Rincón[22], Tehseen Haider[23], Kristina R Chacko[23], Gustavo A Romero[24], Florencia D Pollarsky[24], Juan Carlos Restrepo[25], Luis G Toro[26], Pamela Yaquich[27], Manuel Mendizabal[28], Maria Laura Garrido[29], Sebastian Marciano[30], Melisa Dirchwolf[31], Victor Vargas[32], Cesar Jimenez[32], Guadalupe García-Tsao[33], Guillermo Ortiz[33], Juan G Abraldes[34], Patrick Kamath[4], Marco Arrese[1], Vijay Shah[4], Ramon Bataller[8], Juan Pablo Arab[1,35,36]

[1] *Department of Gastroenterology, Medical School, Pontifical Catholic University of Chile, Santiago, Chile*
[2] *Division of Gastroenterology and Hepatology, University of Kansas Medical Center, KS, USA*
[3] *Division of Gastroenterology and Hepatology, Department of Medicine, University of South Dakota Sanford School of Medicine, Sioux Falls, SD, USA*
[4] *Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA*
[5] *Internal Medicine Service, El Pino Hospital, Santiago, Chile*
[6] *Department of Health Sciences, Faculty of Medicine, Pontifical Catholic University of Chile, Santiago, Chile*
[7] *Department of Anesthesiology, Las Condes Clinic, Santiago, Chile*
[8] *Center for Liver Diseases, Division of Gastroenterology, Hepatology and Nutrition, University of Pittsburgh Medical Center, PA, USA*
[9] *Division of Gastroenterology and Hepatology, University of Florida, Gainesville, FL, USA*
[10] *Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca, Romania*
[11] *Division of Gastroenterology & Hepatology, Cook County Health and Hospital Systems, Chicago, Illinois, USA*
[12] *Division of Gastroenterology and Hepatology, University of Illinois, Chicago, Illinois, USA*
[13] *Gastroenterology and Hepatology Department. University Hospital Marques de Valdecilla. Santander. Spain; Research Institute Valdecilla (IDIVAL). Santander. Spain*
[14] *Department of Gastroenterology, Hospital de La Santa Creu I Sant Pau, Ciberehd, Barcelona, Spain*
[15] *Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi, India*
[16] *Department of Gastroenterology and Hepatology, Baylor College of Medicine, Houston, TX, USA*
[17] *Gastroenterology Service, General Hospital of México, National Autonomous University of México, México City, México*

[18] *Department of Hepatology, Asian Institute of Gastroenterology, Hyderabad, India*
[19] *Gastroenterology Department, Gastroenterology Institute Bolivian-Japanese, La Paz, Bolivia*
[20] *Division of Hepatology, Gastroenterology and Liver Transplantation, Department of Internal Medicine II, Slovak Medical University, F. D. Roosevelt University Hospital, Banska Bystrica, Slovak Republic*
[21] *Hepatology, Centre Hospitalier de Luxembourg, Luxembourg*
[22] *Liver Unit, Department of Digestive Diseases University General Hospital Gregorio Marañón Madrid, Spain; Ciberehd Biomedical Research Center in the Liver and Digestive Diseases Network Madrid, Spain*
[23] *Division of Gastroenterology and Hepatology, Montefiore Medical Center, Bronx, NY, USA*
[24] *Hepatology Section, Gastroenterology Hospital Dr. Carlos Bonorino Udaondo, Buenos Aires, Argentina*
[25] *Hepatology Unit, Pablo Tobon Uribe Hospital, university of Antioquia, Medellín, Colombia*
[26] *Hepatology and Liver Transplant Unit, Hospitals of San Vicente Fundación, Medellín-Rionegro, Antioquia, Colombia*
[27] *gastroenterology Department, San Juan de Dios Hospital, Santiago, Chile*
[28] *Hepatology and Liver Transplant Unit, Austral University Hospital, Pilar, Argentina*
[29] *Central Hospital San Luis, San Luis, Argentina*
[30] *Liver Unit, Buenos Aires Italian Hospital, Buenos Aires, Argentina*
[31] *Liver Unit, Rosario Private Hospital, Rosario, Argentina*
[32] *Liver Unit, Hospital Vall D'hebron, Universitat Autonoma Barcelona, Ciberehd, Barcelona, Spain*
[33] *Section of Digestive Diseases, Yale University School of Medicine/VA-CT Healthcare System, New Haven/ West Haven, USA*
[34] *Division of Gastroenterology, Liver Unit, University of Alberta, Edmonton, Canada*
[35] *Division of Gastroenterology, Department of Medicine, Schulich School of Medicine, Western University & London Health Sciences Centre, London, Ontario, Canada*
[36] *Department of Epidemiology and Biostatistics, Schulich School of Medicine, Western University, London, Ontario, Canada*

**Introduction and Objectives:** Alcohol-associated hepatitis (AH) is a severe entity associated with high mortality. Corticosteroids might be used in cases with severe disease and several dynamic models can predict mortality and response to corticosteroids in AH patients. However, there is no consensus on the best of them. This study aimed to evaluate dynamic models to predict response to corticosteroid treatment based on short-term mortality in patients with severe AH based on a worldwide cohort.

**Materials and Methods:** A retrospective cohort study of patients with severe AH (between 2009 – 2019). We included patients who received corticosteroid treatment and calculated the Lille model of day 4 (Lille-4), day 7 (Lille-7) (cut-off value ≥0.45), and the Trajectory of Serum Bilirubin (TSB)(cut-off value ≥0.8 of the ratio between bilirubin at admission and day 7) to predict mortality. We estimated up to 30-day survival using Kaplan-Meier curves, and we performed multivariable analyzes using Cox regression. Specifically, we constructed two models to compare Lille-4 vs. TSB and Lille-7 vs. TSB, adjusting by well-known clinical variables associated with higher mortality in AH (age, sex, and creatinine at admission).

**Results:** 1,066 patients were included (30 centers, 10 countries), age 47.7 ± 10.9 years, 30% women. The MELD score on admission was 25 [21-30]. Responders were considered by Lille-4 49.1%, Lille-7 46.6%, and TSB 55.4%. In the first Cox regression, we observed that Lille-4 and TSB predicted 30-day mortality (HR 3.0, 95%CI: 1.7-5.1; p<0.0001, and HR 2.1, 95%CI: 1.3-3.5; p=0.005, respectively) (Table A). In the second Cox regression, Lille-7 also predicted 30-day mortality (HR 3.7, 95%CI: 2.1-6.7; p<0.0001) but not TSB (HR 1.5, 95% CI: 0.8-2.6; p=0.180) (Table B). Creatinine at admission was also statistically significant in both Cox-regressions.

**Conclusions:** Different dynamic models can determine the response to corticosteroids in patients with severe AH. However, Lille-7 and Lille-4 have the best performance. New models are needed for better prognostication in AH.

**Table 1:** Models to compare Lille-4 vs. TSB (Table A) and Lille-7 vs. TSB (Table B)

Table A

| Variable | Hazard Ratio | P value | 95 % Conf. Interval |
|---|---|---|---|
| **Age** | 0.999 | 0.933 | 0.98 - 1.01 |
| **Gender** | 0.954 | 0.829 | 0.62 - 1.45 |
| **Creatinine in Admission** | 1.195 | **0.00** | 1.08 - 1.31 |
| **Lille- 7 Response** | 3.706 | **0.00** | 2.05 - 6.68 |
| **TSB Response** | 1.476 | 0.180 | 0.83 - 2.60 |

Table B

| Variable | Hazard Ratio | P value | 95 % Conf. Interval |
|---|---|---|---|
| **Age** | 0.999 | 0.948 | 0.98 - 1.01 |
| **Gender** | 0.911 | 0.678 | 0.58 - 1.40 |
| **Creatinine in Admission** | 1.193 | **0.001** | 1.07 - 1.31 |
| **Lille- 4 Response** | 2.99 | **0.00** | 1.74 - 5.14 |
| **TSB Response** | 2.08 | **0.005** | 1.25 - 3.45 |

https://doi.org/10.1016/j.aohep.2023.101035

## O-26 IMMUNE PROFILING PROVIDES A SET OF 5 CYTOKINES TO DETECT HEPATOCELLULAR CARCINOMA RELATED TO VIRAL HEPATITIS IN SOUTH AMERICAN PATIENTS

Jose Debes[1], Enrique Carrera Estupinan[2], Melina Rocio Ferreiro[3], Angelo Mattos[4], Domingo Balderramo[5], Maria Massotti[6], Joe Koopmeiners[7], Andre Boonstra[8]

[1] *Department of Medicine, University of Minnesota, Minneapolis, MN, USA*
[2] *Department of Gastroenterology, Eugenio Espejo Hospital, Quito, Ecuador*
[3] *Department of Gastroenterology, Clinic National Hospital, Buenos Aires, Argentina*
[4] *Department of Gastroenterology, Federal University of Health Sciences of Porto Alegre, Porto Alegre, Brazil*
[5] *Department of Gastroenterology, University Private Hospital of Córdoba. University Institute of Biomedical Sciences of Córdoba, Argentina*
[6] *Division of Biostatistics, University of Minnesota, Minneapolis, MN, USA*
[7] *Division of Biostatistics, University of Minnesota, Minneapolis, MN, USA*
[8] *Department of Gastroenterology, Erasmus MC, Rotterdam, the Netherlands*

**Introduction and Objectives:** New peripheral markers are needed for the early detection of hepatocellular carcinoma (HCC). Currently, the only accepted biomarker is alpha-fetoprotein (AFP) which by itself is suboptimal for early HCC detection. We investigated