

Chronic hepatitis C infection treated with direct-acting antiviral agents and occurrence/recurrence of hepatocellular carcinoma: does it still matter?

Carlo Smirne, Maria Grazia Crobu, Irene Landi, Nicole Vercellino, Daria Apostolo, David James Pinato, Federica Vincenzi, Rosalba Minisini, Stelvio Tonello, Davide D'Onghia, Antonio Ottobrelli, Silvia Martini, Christian Bracco, Luigi Maria Fenoglio, Mauro Campanini, Alessandro Maria Berton, Alessia Ciancio and Mario Pirisi

Supplementary Table S4. HCC risk calculators.

Tool	Description
FIB-4 ¹	$\text{Age (years)} \times \text{AST [U/L]} / (\text{platelet count [10}^9\text{/L]} \times (\text{ALT [U/L]})^{1/2})$
aMAP ²	$((\text{age [years]} \times 0.06 + \text{gender} \times 0.89 (\text{male: 1, female: 0}) + 0.48 \times ((\log_{10} \text{bilirubin } [\mu\text{mol/L}] + (\text{albumin [g/L]} \times -0.085)) - 0.01 \times \text{platelet count [10}^3\text{/mm}^3]) + 7.4) / 14.77 \times 100$
GALAD ²	$-10.08 + 1.67 \times \text{gender (male: 1, female: 0)} + 0.09 \times \text{age} + 0.04 \times \text{AFP-L3\%}^3 + 2.34 \times \log_{10}\text{AFP} \times \log_{10}\text{DCP}$

Tool	Predictors	Predictor categories
VA HCC model ^{2,4}	AFP, ng/mL	≤ 4
		> 4 - 6.5
		> 6.5 - 10.5
		> 10.5 - 14.71
		> 14.71
	Sex	Male
		Female
	Age, years	≤ 56
		> 56 - 60
		> 60 - 64
		> 64 - 67
		> 67

BMI, Kg/m ²	< 20 20- 25 25 - 30 30- 35 > 35
Race/Ethnicity	White, non-Hispanic Black, non-Hispanic Hispanic Other Declined to answer, missing
HCV Genotype	Non-3 Genotype 3
Hemoglobin, g/dL	> 15.7 > 14.8 - 15.7 > 13.7 - 14.8 > 12.7 - 13.7 ≤ 12.7
Platelet count, x 10 ⁹ /L	> 167 > 123 - 167 > 87 - 123 > 61 - 87 ≤ 61
Albumin, g/dL	> 4.0 > 3.7 - 4.0 > 3.3 - 3.7 > 2.9 - 3.3 ≤ 2.9
INR, Units	≤ 1.00 > 1.00 - 1.20 > 1.20 - 1.34 > 1.34
AST/ \sqrt ALT	≤ 6.50 6.50 - 8.49 8.49 - 11.01 11.01 - 13.90 > 13.90
GES score ²	Sex Male Female
Age, years	≤ 54

	> 54
Fibrosis stage	F3
	F4
Albumin, g/dL	≥ 3.8
	< 3.8
AFP, ng/mL	≤ 20
	> 20
<hr/>	
ADRESS-HCC model ²	Age, years
	Diabetes
	Present
	Absent
	Race/Ethnicity
	Non-Hispanic white
	Non-white or Hispanic
	Etiology
	Autoimmune
	Alcohol/metabolic
	Viral
	Sex
	Male
	Female
	Child-Pugh score (severity of liver disease)
	5 → 15
<hr/>	
Watanabe score ²	Sex
	Male
	Female
	Diabetes mellitus
	Present
	Absent
	White blood cell count, n × μL
	≥ 5,600
	4,223–5,600
	≤ 4,223
	Prothrombin activity, %
	≥ 99.7
	87.1–99.7
	≤ 87.1
	FIB-4 index at EOT ⁵
	≤ 1.7
	1.7–2.8
	≥ 2.8
	FIB-4 index at SVR
	≤ 1.84
	1.84–2.90
	≥ 2.90
	AFP at EOT, ng/mL
	≤ 3.0
	3.0–4.6
	≥ 4.6
	AFP at SVR, ng/mL
	≤ 2.8

2.8–4.0

≥ 4.0

RNN HCC model ²

Age ⁶, sex, race, HCV genotype ⁷

Cirrhosis development, SVR achievement, BMI ⁸

Bilirubin, AST, AST/ULN, ALT, ALT/ULN, AFP, AFP/ULN, ALP, ALP/ULN, albumin, AST/ALT, FIB-4 score, APRI, blood urea nitrogen, creatinine, glucose, INR, hemoglobin, white blood cell count, platelet count, sodium, potassium, chloride, total protein ^{8,9}

Abbreviations: α -fetoprotein (AFP); α -fetoprotein L1 glycoform (AFP-L1); LCA-reactive α -fetoprotein L3 glycoform (AFP-L3); alkaline phosphatase (ALP); AST-platelet ratio index (APRI); aspartate transaminase (AST); alanine aminotransferase (ALT); body mass index (BMI); des-gamma-carboxy-prothrombin (DCP); advanced liver fibrosis (F3); liver cirrhosis (F4); fibrosis-4 (FIB-4); hepatocellular carcinoma (HCC); hepatitis C virus (HCV); international normalized ratio (INR); lens culinaris agglutinin (LCA); recurrent Neural Network (RNN); sustained virologic response (SVR); upper limit of normal (ULN); Veterans Affairs (VA). ¹ simplified scoring system. ² multivariable HCC risk calculator. ³ calculated as follows: $\text{AFP-L3\%} = \frac{\text{AFP-L3 concentration}}{(\text{AFP-L1 concentration} + \text{AFP-L3 concentration})} \times 100$. ⁴ Four groups (cirrhosis/SVR, cirrhosis/no SVR, no cirrhosis/SVR, no cirrhosis/no SVR). Available online: www.hccrisk.com (accessed on 23 September 2024). ⁵ at end of treatment (EOT). ⁶ at cirrhosis diagnosis. ⁷ all baseline predictors. ⁸ all longitudinal predictors. ⁹ all laboratory blood tests.