SUPPLEMENTARY INFORMATION

Statistics

Statistical analyses were performed using IBM SPSS Statistics 25 (SPSS Inc., Armonk, New York, USA), GraphPad Prism 8 (GraphPad Software, La Jolla, California, USA) and R 3.6.2 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were reported as mean ± standard deviation or median (interquartile range (IQR)) depending on their distribution, while categorical variables were shown as numbers and proportions of patients. Comparisons of continuous variables were performed using Student’s t-test or Mann-Whitney U test, as applicable. For comparisons of more than two groups, Chi-squared test was used. Areas under the receiver operating characteristic curves (AUROC) were calculated to assess the diagnostic accuracy of non-invasive markers for the prediction of hepatic decompensation, transplant-free mortality, and de-novo HCC, and also included 95% confidence intervals (95%CI) to quantify uncertainty. Youden’s index was used to obtain optimized cut-offs. Survival analyses were performed using the Kaplan-Meier method and log-rank test to compare the incidence of hepatic decompensation. Cox regression analysis was performed to determine factors associated with hepatic decompensation. Patients were censored at the time of HCC diagnosis/OLT/death in analyses investigating hepatic decompensation and at the time of OLT/death in the analyses on HCC development. In addition, we conducted a competing risks analysis (cmprsk: subdistribution analysis of competing risks, https://CRAN.R-project.org/package=cmprsk) considering hepatic decompensation as the event of interest and HCC development, OLT, and death as competing risks. Group comparisons were performed using Gray’s test (1).

A two-sided p-value ≤0.05 was considered as statistically significant.
Internal validation cohort

Except for a larger proportion of CTP B/C patients (18.6% vs. 7.2%; \(P=0.002\)) and higher BL-MELD (9.9±4.4 vs. 8.6±2.6 points; \(P=0.012\)), as well as a more pronounced male predominance (n=67, 77.9% vs. n=174, 63.0%; \(P=0.011\)), patient characteristics of the internal validation cohort were comparable to the derivation cohort (Supplementary Table 4).

Patients in the internal validation cohort were followed for a median of 39.6 (IQR: 36.3) months after end of IFN-free therapy. Seven (8.1%) patients experienced hepatic decompensation during FU: Variceal bleeding in 1 (1.2%) patient, ascites in 5 (5.8%) patients, and HE in 1 (1.2%) patient.

External validation cohort

Compared to the derivation cohort, patients in the external validation cohort (n=162) were older (60.1±11.1 vs. 56.0±10.6 years; \(P<0.001\)), more commonly female (n=76, 46.9% vs. n=102, 37.0%; \(P=0.041\)), and also showed a lower BL-MELD (7.9±2.2 vs. 8.6±2.6 points; \(P=0.001\)) (Supplementary table 5).

Patients in the external validation cohort were followed for a median of 38.7 (IQR: 26.7) months after treatment cessation. Seven (4.3%) patients experienced hepatic decompensation during post-treatment FU: Variceal bleeding in 2 (1.2%) patients, ascites in 4 (2.5%) patients, and HE in 1 (0.6%) patient.

Non-invasive prediction of de-novo HCC and liver-related transplant-free mortality in the derivation cohort

The predictive performances of non-invasive parameters for HCC development during FU tended to be worse than those reported for hepatic decompensation, with BL-
VITRO (AUROC=0.806 (95%CI: 0.723-0.889)) achieving the best result, followed by BL-PLT (AUROC=0.798 (95%CI: 0.697-0.899)), and FU-VITRO (AUROC=0.786 (95CI: 0.682-0.890)); Supplementary table 6). Interestingly, although LSM at BL or FU was not predictive of HCC, absolute/relative changes in LSM showed some predictive capacity, with AUROC values of 0.709/0.705, respectively. BL-VITRO (>2.66; 0% vs. 15.3% at 3 years; \( P<0.001 \)) and FU-VITRO (>1.82; 1.3% vs. 11.8% at 3 years; \( P<0.001 \)) cut-offs obtained by Youden's index discriminated between patients at a very low-risk of HCC (more than two thirds of patients) and patients at high-risk for de-novo HCC development (less than one third of patients) (Supplementary figure 9).

Although several parameters achieved AUROC values >0.8 for liver-related transplant-free mortality, we abstained from conducting detailed analyses, as the number of events was low (Supplementary table 7).

Recompensation in dACLD patients of the derivation cohort

Of 26 dACLD patients (9.4%) in our derivation cohort, 5 patients had a history of variceal bleeding as the only decompensating event. Of the remaining 21 patients, all were either on diuretics for ascites control or on HE medication at treatment initiation. Of these, 9 patients recompensated and the proportion of patients with recompensation was twice as high in patients in the gray-zone (66.7% (4/6)), as compared to patients in the high-risk group (33.3% (5/15)), although the difference did not attain statistical significance (\( P=0.331 \)). Of note, none of the dACLD patients had been assigned to the low-risk group according to our FU-LSM and -VITRO-based algorithm.
### Supplementary tables

#### Supplementary table 1

| Patient characteristics | All patients, n=276 | No hepatic decompensation during FU, n=264 | Hepatic decompensation during FU, n=12 | P value |
|-------------------------|---------------------|---------------------------------------------|------------------------------------------|---------|
| BMI, kg x m⁻²²           | 26.8±5.0            | 26.8±5.0                                    | 27.6±4.9                                  | 0.566   |
| ≥25kg x m⁻²²             | 165 (59.8%)         | 157 (59.5%)                                 | 8 (66.7%)                                 | 0.788   |
| ≥30kg x m⁻²²             | 62 (22.5%)          | 59 (22.3%)                                  | 3 (25.0%)                                 | 0.736   |
| Prediabetes¹             | 25 (9.1%)           | 24 (9.1%)                                   | 1 (8.3%)                                  | 1.000   |
| Diabetes²                | 45 (16.3%)          | 42 (16.0%)                                  | 3 (25.0%)                                 | 0.423   |
| Arterial hypertension³   | 102 (37.0%)         | 100 (37.9%)                                 | 2 (16.7%)                                 | 0.221   |
| Hypertriglyceridemia⁴    | 27 (9.8%)           | 27 (10.2%)                                  | 0 (0.0%)                                  | 0.615   |
| HDL below threshold⁵     | 49 (17.8%)          | 47 (17.8%)                                  | 2 (16.7%)                                 | 1.000   |
| Statin use               | 13 (4.7%)           | 13 (4.9%)                                   | 0 (0.0%)                                  | 1.000   |
| Hepatic steatosis⁶       | 141 (53.6%)         | 136 (54.0%)                                 | 5 (45.5%)                                 | 0.579   |
| Alcohol consumption      |                     |                                             |                                          |         |
| Abstinent                | 224 (81.2%)         | 218 (82.6%)                                 | 6 (50.0%)                                 |         |
| Non-abstinent but below the threshold⁷ | 22 (8.0%) | 22 (8.3%) | 0 (0.0%) | <0.001 |
| Above the threshold⁷     | 30 (10.9%)          | 24 (9.1%)                                   | 6 (50.0%)                                 |         |

¹ Fasting blood glucose 100-125mg x dL⁻¹.
² Fasting blood glucose >125mg x dL⁻¹, HbA1c ≥6.5%, or antidiabetic medication.
³ Blood pressure >140/90mmHg, or antihypertensive medication.
⁴ Fasting triglyceride levels >150mg x dL⁻¹.
⁵ <35mg x dL⁻¹ for males and <39mg x dL⁻¹ for females.
⁶ Controlled attenuation parameter >248dB/m. Data were available in 263 patients.
⁷ >30g/day and >20g/day for males and females, respectively (2).

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**Supplementary table 1.** Comparison of factors related to the metabolic syndrome (3) and alcohol consumption between patients with and without hepatic decompensation during follow-up (FU).

**Abbreviations:**

BMI body mass index
FU follow-up
### Supplementary table 2

| Parameter                                      | Model A |       |       | Model B |       |       |
|-----------------------------------------------|---------|-------|-------|---------|-------|-------|
|                                               | aHR     | 95%CI | P value | aHR     | 95%CI | P value |
| History of hepatic decompensation             | 2.605   | 0.618-10.972 | 0.192 | 3.110   | 0.748-12.930 | 0.119 |
| FU-MELD, per point                            | 1.041   | 0.903-1.200 | 0.582 | 1.074   | 0.929-1.240 | 0.336 |
| FU-albumin, per g x L⁻¹                        | 0.846   | 0.782-0.914 | <0.001 | 0.846   | 0.779-0.920 | <0.001 |
| Alcohol consumption above the threshold¹      | 10.593  | 2.849-39.387 | <0.001 | 7.554   | 1.955-29.193 | 0.003 |
| FU-LSM, per kPa                                | 1.045   | 1.018-1.074 | 0.001 | -       | -       | -       |
| FU-VITRO per point                            | -       | -       | -       | 1.315   | 1.128-1.533 | <0.001 |

¹ >30g/day and >20g/day for males and females, respectively (2).

**Supplementary table 2.** Cox regression analyses investigating factors associated with hepatic decompensation during follow-up (FU) in the derivation cohort. Model A included FU-LSM and was adjusted for history of hepatic decompensation and indicators of hepatic dysfunction (FU-MELD score and serum FU-albumin levels) and alcohol consumption above the threshold¹, while model B included FU-VITRO and was adjusted for the same factors.

**Abbreviations:**
- FU follow-up
- LSM liver stiffness measurement
- VITRO von Willebrand factor antigen/platelet count ratio
- MELD model for end-stage liver disease
Supplementary table 3

| Parameter                | Model A |          |          | Model B |          |          |
|--------------------------|---------|----------|----------|---------|----------|----------|
|                          | aHR     | 95% CI   | P value  | aHR     | 95% CI   | P value  |
| Ascites                  | 2.427   | 0.611-9.643 | 0.208   | 1.750   | 0.460-6.662 | 0.412   |
| FU-MELD, per point       | 1.085   | 0.952-1.235 | 0.220   | 1.135   | 1.000-1.289 | 0.050   |
| FU-albumin, per g x L^{-1} | 0.866   | 0.805-0.932 | <0.001 | 0.852   | 0.790-0.919 | <0.001 |
| FU-LSM, per kPa          | 1.043   | 1.017-1.070 | 0.001   | -       | -       | -       |
| FU-VITRO, per point      | -       | -        | -        | 1.384   | 1.186-1.614 | <0.001 |

**Supplementary table 3.** Cox regression analyses investigating factors associated with hepatic decompensation during follow-up (FU) in the derivation cohort. Model A included FU-LSM and was adjusted for ascites and indicators of hepatic dysfunction (FU-MELD score and serum FU-albumin levels), while model B included FU-VITRO and was adjusted for the same factors.

Abbreviations: FU follow-up  
LSM liver stiffness measurement  
VITRO von Willebrand factor antigen/platelet count ratio
## Supplementary table 4

| Patients characteristics | Derivation cohort, n=276 | Internal validation cohort, n=86 | \( P \) value |
|--------------------------|--------------------------|----------------------------------|---------------|
| Age, years               | 56.0±10.6                | 55.8±11.2                        | 0.11          |
| Sex                      |                          |                                  |               |
| Male                     | 174 (63.0%)              | 67 (77.9%)                       | 0.011         |
| Female                   | 102 (37.0%)              | 19 (22.1%)                       |               |
| History of hepatic decompensation | 26 (9.4%)              | 14 (16.3%)                       | 0.076         |
| Varices                  | 62 (22.5%)               | 19 (22.1%)                       | 0.943         |
| Small                    | 33 (12.0%)               | 11 (12.8%)                       | 0.936         |
| Large                    | 29 (10.5%)               | 8 (9.3%)                         |               |
| BL-CTP, points           | 5±1                      | 6±1                              | 0.020         |
| Stage A                  | 256 (92.8%)              | 70 (81.4%)                       | 0.002         |
| Stage B/C                | 20 (7.2%)                | 16 (18.6%)                       |               |
| \( \Delta \) CTP, points | 0 (0)                    | 0 (0)                            | 0.014         |
| FU-CTP, points           | 5±1                      | 5±1                              | 0.271         |
| BL-MELD, points          | 8.6±2.6                  | 9.9±4.4                          | 0.012         |
| \( \Delta \) MELD, points | 0 (2)                  | 0 (2)                            | 0.949         |
| FU-MELD, points          | 8.8±3.3                  | 9.9±5.0                          | 0.048         |
| BL-albumin, g x L\(^{-1}\) | 41.1±4.6                | 41.3±4.9                         | 0.759         |
| Absolute \( \Delta \) albumin, g x L\(^{-1}\) | 1.9 (4.5)                | 2.0 (5.2)                        | 0.820         |
| Relative \( \Delta \) albumin, % | 4.4 (11.9)               | 4.6 (12.5)                       | 0.786         |
| FU-albumin, g x L\(^{-1}\) | 43.1±4.5                 | 43.3±4.7                         | 0.735         |
| BL-LSM, kPa              | 17.1 (15.6)              | 18.4 (20.3)                      | 0.353         |
| Absolute \( \Delta \) LSM, kPa | -3.6 (7.4)               | -4.4 (11.2)                      | 0.153         |
| Relative \( \Delta \) LSM, % | -20.7 (39.2)             | -26.3 (46.9)                     | 0.119         |
| FU-LSM, kPa              | 12.7 (14.3)              | 14.8 (18.5)                      | 0.203         |
| BL-PLT, G x L\(^{-1}\)  | 146±69                   | 149±66                           | 0.741         |
| Absolute \( \Delta \) PLT, G x L\(^{-1}\) | 9 (28)                   | 11 (39)                          | 0.897         |
| Relative \( \Delta \) PLT, % | 6.8 (20.8)               | 9.4 (30.2)                       | 0.960         |
| FU-PLT, G x L\(^{-1}\)  | 158±72                   | 168±76                           | 0.274         |
| BL-VWF, %                | 233 (144)                | 237 (171)                        | 0.532         |
| Absolute \( \Delta \) VWF, % | -38 (68)               | -45 (78)                         | 0.337         |
| Relative \( \Delta \) VWF, % | -18.4 (25.2)             | -20.0 (26.8)                     | 0.514         |
| FU-VWF, %                | 180 (105)                | 180 (133)                        | 0.724         |
| BL-VITRO                 | 1.69 (2.08)              | 1.74 (2.34)                      | 0.952         |
Supplementary table 4. Comparison of patient characteristics between the derivation and the internal validation cohort.

|                           | Derivation | Internal validation | p-value |
|---------------------------|------------|---------------------|---------|
| Absolute Δ VITRO          | -0.32 (0.80) | -0.37 (0.79)        | 0.649   |
| Relative Δ VITRO, %       | -23.3 (32.4) | -25.6 (30.5)        | 0.780   |
| FU-VITRO                  | 1.15 (1.52)  | 1.14 (1.60)         | 0.629   |

Abbreviations: ACLD advanced chronic liver disease, BL baseline, CTP Child-Turcotte-Pugh score, FU follow-up, HVPG hepatic venous pressure gradient, LSM liver stiffness measurement, MELD model for end-stage liver disease score, PLT platelet count, VITRO von Willebrand factor antigen/platelet count ratio, VWF von Willebrand factor.
## Supplementary table 5

| Patients characteristics | Derivation cohort, n=276 | External validation cohort, n=162 | \( P \) value |
|--------------------------|--------------------------|-----------------------------------|--------------|
| Age, years               | 56.0±10.6                | 60.1±11.1                         | <0.001       |
| Sex                      |                          |                                   |              |
| Male                     | 174 (63.0%)              | 86 (53.1%)                        | 0.041        |
| Female                   | 102 (37.0%)              | 76 (46.9%)                        |              |
| History of hepatic decompensation |              |                                   |              |
| Varices                  | 62 (22.5%)               | 38 (23.5%)                        | 0.811        |
| Small                    | 33 (12.0%)               | 25 (15.4%)                        | 0.449        |
| Large                    | 29 (10.5%)               | 13 (8.0%)                         |              |
| BL-CTP, points           | 5±1                      | 5±1                               | 0.158        |
| Stage A                  | 256 (92.8%)              | 154 (95.1%)                       | 0.340        |
| Stage B/C                | 20 (7.2%)                | 8 (4.9%)                          |              |
| Δ CTP, points            | 0 (0)                    | 0 (0)                             | <0.001       |
| FU-CTP, points           | 5±1                      | 5±0                               | 0.034        |
| BL-MELD, points          | 8.6±2.6                  | 7.9±2.2                           | 0.001        |
| Δ MELD, points           | 0 (2)                    | 0 (2)                             | 0.224        |
| FU-MELD, points          | 8.8±3.3                  | 7.8±2.1                           | <0.001       |
| BL-albumin, g x L\(^{-1}\) | 41.1±4.6                | 40.4±4.3                          | 0.082        |
| Absolute Δ albumin, g x L\(^{-1}\) | 1.9 (4.5)               | 2.0 (5.0)                         | 0.981        |
| Relative Δ albumin, %    | 4.4 (11.9)               | 4.8 (12.4)                        | 0.982        |
| FU-albumin, g x L\(^{-1}\) | 43.1±4.5                | 42.5±3.8                          | 0.177        |
| BL-LSM, kPa              | 17.1 (15.6)              | 15.9 (11.4)                       | 0.998        |
| Absolute Δ LSM, kPa      | -3.6 (7.4)               | -5.4 (6.8)                        | <0.001       |
| Relative Δ LSM, %        | -20.7 (39.2)             | -34.3 (30.4)                      | <0.001       |
| FU-LSM, kPa              | 12.7 (14.3)              | 11.4 (9.8)                        | 0.004        |
| BL-PLT, G x L\(^{-1}\)  | 146±69                   | 152±63                            | 0.482        |
| Absolute Δ PLT, G x L\(^{-1}\) | 9 (28)                  | 9 (31)                            | 0.633        |
| Relative Δ PLT, %        | 6.8 (20.8)               | 8.1 (21.9)                        | 0.582        |
| FU-PLT, G x L\(^{-1}\)  | 158±72                   | 160±69                            | 0.712        |
| BL-VWF, %                | 233 (144)                | 225 (143)                         | 0.667        |
| Absolute Δ VWF, %        | -38 (68)                 | -50 (72)                          | 0.092        |
| Relative Δ VWF, %        | -18.4 (25.2)             | -21.5 (24.7)                      | 0.115        |
| FU-VWF, %                | 180 (105)                | 170 (89)                          | 0.398        |
| BL-VITRO                 | 1.69 (2.08)              | 1.57 (1.59)                       | 0.379        |
Absolute Δ VITRO | -0.32 (0.80) | -0.35 (0.64) | 0.949  
Relative Δ VITRO, % | -23.3 (32.4) | -26.4 (32.9) | 0.544  
FU-VITRO | 1.15 (1.52) | 1.07 (1.27) | 0.530  

**Supplementary table 5.** Comparison of patient characteristics between the derivation and the external validation cohort.

Abbreviations:  
ACLD advanced chronic liver disease  
BL baseline  
CTP Child-Turcotte-Pugh score  
FU follow-up  
HVPG hepatic venous pressure gradient  
LSM liver stiffness measurement  
MELD model of end-stage liver disease score  
PLT platelet count  
VITRO von Willebrand factor antigen/platelet count ratio  
VWF von Willebrand factor
## Supplementary table 6

| Parameter    | AUROC (95% CI) | Youden’s index-optimized cut-off | Sensitivity | Specificity | PPV  | NPV  |
|--------------|----------------|---------------------------------|-------------|-------------|------|------|
| BL-MELD      | 0.673 (0.524-0.823) | >9 points                       | 57.1%       | 76.0%       | 11.3% | 97.1% |
| FU-MELD      | 0.646 (0.472-0.821)  | -                               | -           | -           | -    | -    |
| BL-albumin   | 0.753 (0.615-0.890)  | <39.6 g x L⁻¹                    | 71.4%       | 72.4%       | 12.0% | 97.9% |
| FU-albumin   | 0.786 (0.651-0.922)  | <41.8 g x L⁻¹                    | 78.6%       | 70.8%       | 12.6% | 98.4% |
| BL-LSM       | 0.497 (0.365-0.629)  | -                               | -           | -           | -    | -    |
| FU-LSM       | 0.597 (0.474-0.721)  | -                               | -           | -           | -    | -    |
| Absolute Δ LSM | 0.709 (0.600-0.818)  | > -3.7kPa                        | 92.9%       | 50.8%       | 9.2%  | 99.3% |
| Relative Δ LSM | 0.705 (0.600-0.810)  | > -37.6%                        | 100%        | 29.0%       | 7.0%  | 100% |
| BL-PLT       | 0.798 (0.697-0.899)  | <103 G x L⁻¹                     | 78.6%       | 72.5%       | 13.3% | 98.4% |
| FU-PLT       | 0.778 (0.672-0.884)  | <154 G x L⁻¹                     | 92.9%       | 53.1%       | 9.6%  | 99.3% |
| BL-VWF       | 0.680 (0.544-0.817)  | >266%                           | 78.6%       | 63.4%       | 10.3% | 98.2% |
| FU-VWF       | 0.689 (0.548-0.830)  | >236%                           | 57.1%       | 75.6%       | 11.1% | 97.1% |
| BL-VITRO     | 0.806 (0.723-0.889)  | >2.66                           | 85.7%       | 71.4%       | 13.8% | 98.9% |
| FU-VITRO     | 0.786 (0.682-0.890)  | >1.82                           | 78.6%       | 69.8%       | 12.2% | 98.4% |

**Supplementary table 6.** Area under the receiver operating characteristic curve (AUROC) values, Youden’s index-optimized cut-offs, and diagnostic indices of potential non-invasive predictors of de-novo hepatocellular carcinoma in the derivation cohort.
| Abbreviations | Description |
|---------------|-------------|
| 95%CI         | 95% confidence interval |
| AUROC         | area under the receiver operator characteristic curve |
| BL            | baseline |
| FU            | follow-up |
| LSM           | liver stiffness measurement |
| NPV           | negative predictive value |
| PLT           | platelet count |
| PPV           | positive predictive value |
| VITRO         | von Willebrand factor antigen/platelet count ratio |
| VWF           | von Willebrand factor |
### Supplementary table 7

| Parameter | AUROC (95%CI) | Cut-off | Sensitivity | Specificity | PPV  | NPV  |
|-----------|---------------|---------|-------------|-------------|------|------|
| BL-MELD   | 0.746 (0.532-0.959) | > 9 points* | 80.0% | 75.3% | 5.6% | 99.5% |
| FU-MELD   | 0.621 (0.294-0.948) | -       | -           | -           | -    | -    |
| BL-albumin| 0.829 (0.666-0.992) | <33.1 g x L⁻¹* | 60.0% | 95.2% | 18.8% | 99.2% |
| FU-albumin| 0.766 (0.585-0.947) | <43.8 g x L⁻¹* | 100% | 50.4% | 2.9% | 100% |
| BL-LSM    | 0.550 (0.348-0.752) | -       | -           | -           | -    | -    |
|           |               | >12.4 kPa | 80.0% | 48.7% | 2.9% | 99.2% |
|           |               | >25.3 kPa | 40.0% | 79.0% | 3.4% | 98.6% |
| BL-PLT    | 0.829 (0.741-0.917) | <86 G x L⁻¹* | 100% | 68.6% | 5.6% | 100% |
| FU-PLT    | 0.839 (0.724-0.955) | <129 G x L⁻¹* | 100% | 63.5% | 4.8% | 100% |
| BL-VWF    | 0.730 (0.456-1.000) | -       | -           | -           | -    | -    |
| FU-VWF    | 0.832 (0.678-0.986) | >221%*  | 80.0% | 74.9% | 5.6% | 99.5% |
| BL-VITRO  | 0.824 (0.691-0.957) | >3.35*  | 80.0% | 80.1% | 6.9% | 99.5% |
|           |               | >0.95   | 100% | 41.3% | 3.0% | 100% |
| FU-VITRO  | 0.873 (0.771-0.975) | >3.3    | 60.0% | 86.7% | 7.7% | 99.2% |

* Youden’s index-optimized cut-off.

### Supplementary table 7.

Area under the receiver operating characteristic curve (AUROC) values, Youden’s index-optimized cut-offs, and diagnostic indices of potential predictors of liver-related mortality in the derivation cohort.

**Abbreviations:**

95%CI 95% confidence interval
AUROC area under the receiver operating characteristic curve
BL baseline
FU follow-up
LSM liver stiffness measurement
NPV negative predictive value
PLT platelet count
PPV positive predictive value
VITRO von Willebrand factor antigen/platelet count ratio
VWF von Willebrand factor
Supplementary figures

Supplementary figure 1

A

\[ \text{BL-LSM} \]
\[ \text{AUROC} = 0.812 \quad (95\% \text{ CI: 0.721-0.904}) \]

\[ \text{FU-LSM} \]
\[ \text{AUROC} = 0.875 \quad (95\% \text{ CI: 0.796-0.954}) \]

\[ \Delta \text{LSM (abs.)} \]
\[ \text{AUROC} = 0.658 \quad (95\% \text{ CI: 0.427-0.890}) \]

\[ \Delta \text{LSM (rel.)} \]
\[ \text{AUROC} = 0.721 \quad (95\% \text{ CI: 0.546-0.897}) \]

B

\[ \text{BL-PLT} \]
\[ \text{AUROC} = 0.837 \quad (95\% \text{ CI: 0.739-0.935}) \]

\[ \text{FU-PLT} \]
\[ \text{AUROC} = 0.883 \quad (95\% \text{ CI: 0.815-0.951}) \]

\[ \Delta \text{PLT (abs.)} \]
\[ \text{AUROC} = 0.697 \quad (95\% \text{ CI: 0.536-0.858}) \]

\[ \Delta \text{PLT (rel.)} \]
\[ \text{AUROC} = 0.704 \quad (95\% \text{ CI: 0.496-0.911}) \]
BL-VWF  AUROC = 0.758 (95% CI: 0.604-0.911)
FU-VWF  AUROC = 0.871 (95% CI: 0.757-0.986)
\( \Delta \, \text{VWF (abs.)} \)  AUROC = 0.787 (95% CI: 0.671-0.904)
\( \Delta \, \text{VWF (rel.)} \)  AUROC = 0.820 (95% CI: 0.745-0.896)

BL-VITRO  AUROC = 0.857 (95% CI: 0.762-0.952)
FU-VITRO  AUROC = 0.925 (95% CI: 0.874-0.977)
\( \Delta \, \text{VITRO (abs.)} \)  AUROC = 0.756 (95% CI: 0.574-0.938)
\( \Delta \, \text{VITRO (rel.)} \)  AUROC = 0.715 (95% CI: 0.681-0.949)
Supplementary figure 1. Area under the receiver operator characteristics curve (AUROC) of A liver stiffness measurement (LSM), B platelet count (PLT), C von Willebrand factor (VWF), D von Willebrand factor antigen/platelet count ratio (VITRO), and E serum albumin levels for predicting hepatic decompensation after HCV-cure in the derivation cohort.

Abbreviations: AUROC area under the receiver operator characteristics curve  
BL baseline  
FU follow-up
LSM liver stiffness measurement
PLT platelet count
SVR sustained virological response
VITRO von Willebrand factor antigen/platelet count ratio
VWF von Willebrand factor
**Supplementary figure 2.** Assignment of patients to risk groups at baseline (BL) and follow-up (FU), as well as stage migration occurring between these two timepoints in the derivation cohort.

Abbreviations:  
BL baseline  
FU follow-up
Supplementary figure 3. Competing risk regression analyses of hepatic decompensation in the derivation cohort. Patients were stratified according to their probability of post-treatment clinically significant portal hypertension (CSPH, hepatic venous pressure gradient (HVPG)≥10mmHg).

Abbreviations:
- CSPH: clinically significant portal hypertension
- HVPG: hepatic venous pressure gradient
- FU: follow-up
- LSM: liver stiffness measurement
- VITRO: von Willebrand factor antigen/platelet count ratio
Supplementary figure 4

Kaplan-Meier analysis of hepatic decompensation in patients with cirrhosis included in the derivation cohort, stratified according to their risk of post-treatment clinically significant portal hypertension (CSPH, hepatic venous pressure gradient (HVPG)≥10mmHg).

Subjects at risk

| CSPH ruled-in | 65 | 52 | 37 | 23 |
| Gray-zone     | 44 | 40 | 35 | 28 |
| CSPH ruled-out| 59 | 53 | 43 | 34 |

Time (months)

Cumulative incidence rates at 3 years: 18.4% vs. 2.9% vs. 0%; P=0.001

Abbreviations:

CSPH clinically significant portal hypertension
HVPG hepatic venous pressure gradient
FU follow-up
LSM liver stiffness measurement
VITRO von Willebrand factor antigen/platelet count ratio
Supplementary figure 5. Kaplan-Meier analysis of hepatic decompensation in patients of the derivation cohort, stratified according to their risk of post-treatment clinically significant portal hypertension (CSPH, hepatic venous pressure gradient (HVPG)≥10mmHg) by applying liver stiffness measurement (LSM) cut-offs that were not specifically developed for patients who achieved HCV-cure.

Abbreviations: CSPH clinically significant portal hypertension
HVPG hepatic venous pressure gradient
FU follow-up
LSM liver stiffness measurement
VITRO von Willebrand factor antigen/platelet count ratio
**Supplementary figure 6.** Kaplan-Meier analyses of hepatic decompensation in patients of the internal validation cohort, stratified according to their risk of post-treatment clinically significant portal hypertension (CSPH, hepatic venous pressure gradient (HVPG)≥10mmHg).

**Abbreviations:**

CSPH clinically significant portal hypertension

HVPG hepatic venous pressure gradient

FU follow-up

LSM liver stiffness measurement

VITRO von Willebrand factor antigen/platelet count ratio
Supplementary figure 7. Prevalence of clinically significant portal hypertension (HVPG≥10mmHg) and high-risk portal hypertension (HVPG≥16mmHg) and comparison of HVPG levels throughout the risk groups in the internal validation cohort, as defined by non-invasive tests.

Abbreviations:  
CSPH clinically significant portal hypertension  
HVPG hepatic venous pressure gradient  
IQR interquartile range  
PH portal hypertension
**Supplementary figure 8.** Kaplan-Meier analyses of hepatic decompensation in patients of the external validation cohort, stratified according to their risk of post-treatment clinically significant portal hypertension (CSPH, hepatic venous pressure gradient (HVPG) ≥ 10 mmHg).

1 Comparing only high-risk vs. low-risk due to crossing curves.

Abbreviations: CSPH clinically significant portal hypertension
HVPG hepatic venous pressure gradient
FU follow-up
LSM liver stiffness measurement
VITRO von Willebrand factor antigen/platelet count ratio
Supplementary figure 9. Kaplan-Meier analyses of de-novo hepatocellular carcinoma in the derivation cohort stratified by Youden’s index-optimized cut-offs for A baseline (BL)-VITRO (>2.66) and B) follow-up (FU)-VITRO (>1.82).
Abbreviations:

BL baseline

FU follow-up

VITRO von Willebrand factor antigen/platelet count ratio
References

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