

The PVT risk is still considerable after SVR among patients with cirrhosis.

Severity of liver disease remains the main determinant of PVT development.



De-novo occurrence thrombosis in patients with HCV-related sustained after cirrhosis medium response: to observations from the ongoing PITER cohort

Introduction

Achievement of sustained virological response (SVR) by direct-acting antiviral therapy (DAAs) in patients with cirrhosis (both compensated and decompensated) is associated with reduced risks of decompensation, liver-related mortality and hepatocellular carcinoma (HCC). In addition, SVR ameliorates portal hypertension, and may reverse hyper-coagulability driven by cirrhosis. However, an unexpected incidence of portal vein thrombosis (PVT) immediately after antiviral therapy has recently been reported.

Aim

Based on the prospective multicenter design of the ongoing PITER cohort, representative of HCV patients in care in Italy, we aimed to 1) determine the incidence of PVT in patients with HCV cirrhosis who achieved SVR after DAAs vs those who didn't and vs untreated patients; 2) investigate predictive factors for development of PVT in these patients.

Method

Study population: All consecutively enrolled patients in the PITER cohort diagnosed with liver cirrhosis independently by DAA therapy were evaluated. Patients with a previous diagnosis of PVT, previous liver transplantation or on the waiting list, were excluded. Neoplastic PVT were excluded from this analysis. IFN-free DAA-treated patients with at least a 12-weeks F.U. after the end of treatment were included. For treated patients, follow-up started when DAA therapy was finished. Untreated patients with at least F.U. after enrolment were included.

Statistical Analysis: The Mann-Whitney U test was used for continuous variables to assess differences between distribution, and the Chi-squared test was used to compare proportions. De-novo PVT occurrences were examined using Kaplan-Meier survival analyses and the log-rank test. Cox proportional hazard model was used to evaluate predictive factors independently associated with *de-novo* PVT adopting a forward stepwise selection, adding terms with $p \le 0.1$ and removing those with $p \ge 0.2$. A propensity score was calculated to take into account the imbalance between the untreated group and the successfully treated group. A p value <0.05 was considered statistically significant. Statistical analysis was performed with STATA version 16.1 (StataCorp, College Station, TX, USA).

Conclusions

The risk of *de-novo* non-neoplastic PVT in patients with cirrhosis who achieved the SVR is low and mainly related to the liver disease severity. PVT development following the SVR may identify patients with higher decompensation and mortality risks.

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References

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of portal vein virological term long

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Results

PVT de-novo occurrence in DAA treated and untreated patients

Of overall 1626 consecutive patients with liver cirrhosis who undergone the antiviral therapy (median follow-up time was 35.6 months after EOT; IQR 23.3 - 44.3 months), 34 (2.1%) developed non-neoplastic PVT following DAA treatment. The two year PVT cumulative incidence rates were 0.7% for SVR patients and 6.4% for those who failed to achieve the SVR (p<0.001) (Figure 1). A total of 508 untreated patients with at least 1-year FU after enrolment and 1386 patients who achieved the SVR with the availability of values for each pre-treatment variables considered, were compared for PVT development. All the variables analyzed were well matched between the two groups after Inverse Probability Weighting (IPW) (Weighted SMD < 0.1) (data not shown). Considering the EOT as the starting time point for treated patients and the enrollment date for untreated patients, in the first 36 months, there are 12 de-novo PVT diagnoses in the untreated patients, with a weighted incidence rate of 0.09% (CI95%: 0.05-0.18) and 15 new diagnoses in the successfully treated patients with an incidence rate of 0.04% (CI 95%: 0.02-0.06). Treated patients with SVR report a weighted HR=0.41 (CI 95% 0.18-0.93) p=0.033, which indicates that in the first 36 months following viral eradication, the PVT development risk is halved compared to the risk observed in untreated patients. The two year PVT cumulative incidence rates were 2.4% for the untreated patients and 0.8% in treated patients with SVR (Figure 2).

Baseline characteristics of cirrhotic DAA successfully treated patients by PVT occurrence

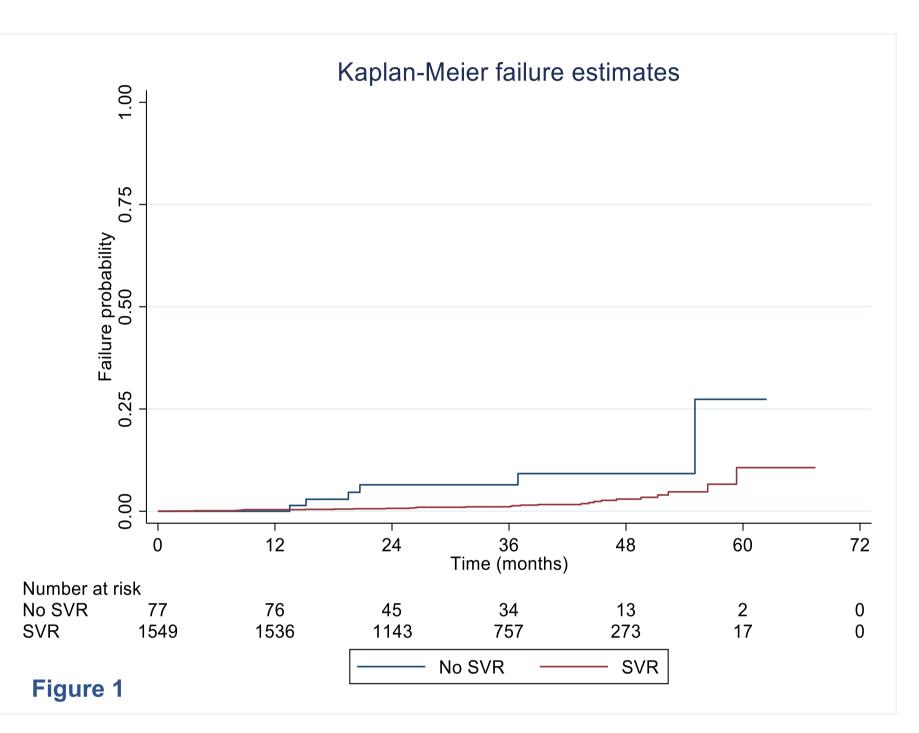
Of 1549 SVR patients, 28 (1.8%) experienced non-neoplastic PVT (median time of PVT occurrence was 33.8 months after EOT; IQR 17-45 months). Of them, 12 reported HCC (3 previous and 9 after achieving

| | | | No thrombosis (N=1521*) | | Thrombosis occurrence (N=28*) | | TOTAL (N=1549*) Median (IQR) | | 0.75 - | | | | |
|--|---|---|---|---|---|---|--|--|--|--|--|--|---|
| Epidemiological features | | Median (IQR) | | Median (IQR) | | p** | | | | | | | |
| Age (years) | | 65 (56 | 5 - 72) | 67 (58 | 3 - 71) | 0.616 | 65 (56 | 5 - 72) | | | | | |
| | | N. | % | N. | % | p*** | Ν. | % | 0.50 - | | | | |
| Sex | Male | 842 | 55.4 | 13 | 46.4 | 0.346 | 855 | 55.2 | | | | | |
| | Female | 679 | 44.6 | 15 | 53.6 | | 694 | 44.8 | | | | | |
| BMI | Underweight-Normal | 661 | 43.5 | 11 | 39.3 | 0.329 | 672 | 43.4 | 0.25 - | | | | |
| | Qxerweight. | 634 | 41.7 | 10 | 35.7 | | 644 | 41.6 | | | | | |
| Alcoholuso | Obese | 226 | 14.9 | 7 | 25.0 | 0.200 | 233 | 15.0 | | | | | |
| Alcohol use | Never | 1023 | 68.1 | 22 | 78.6 10.7 | 0.369 | 1045 156 | 68.3 | 0.00 - | | | | |
| | Current | 153 326 | 10.2 21.7 | 2 | 10.7 | | 329 | 10.2 21.5 | 0 6 | 12 18 | 3 24 | 30 | 36 |
| HCV-genotype | Past. 1a | 171 | 11.2 | 5 | 3.6 | 0.507 | 172 | 11.1 | 0 0 | Mont | | 30 | 50 |
| | 1a 1b | 911 | 58.9 | 18 | 64.3 | 0.507 | 929 | 60.0 | Number at risk | | _ | | |
| | 2 | 219 | 14.4 | 6 | 21.4 | | 225 | 14.5 | No treated 508 506.4 Treated 1386 1378 | 501.3 350. 1373 116 | | 235.1 861.5 | 193.2 676.2 |
| | 3 | 128 | 8.4 | 1 | 3.6 | | 129 | 8.3 | | | | | |
| | Other. | 92 | 6.1 | 2 | 7.1 | | 94 | 6.1 | | No treated | | eated | |
| HIV+ | Yes | 55 | 3.6 | 1 | 3.6 | 0.990 | 56 | 3.6 | | | | | |
| | No | 1466 | 96.4 | 27 | 96.4 | | 1493 | 96.4 | | | | | |
| HBV Infection | Anti-HBc+/HBsAg+ | 16 | 1.1 | 0 | 0.0 | 0.675 | 16 | 1.0 | | | | | |
| | Anti-HBc+/HBsAg- | 294 | 19.3 | 4 | 14.3 | | 298 | 19.2 | Figure 2 | | | | |
| | | 1211 | 70.0 | 24 | 05.7 | | | | | | | | |
| | No | 1211 | 79.6 | 24 | 85.7 | | 1235 | 79.7 | | | | | |
| Metabolic syndrom | | 207 | 79.6 13.6 | 24 | 85.7 | 0.321 | 1235 209 | 79.7 13.5 | | | | | |
| Metabolic syndrom | | | | 24 2 26 | | 0.321 | | | Pre-treatment variable | es associ | ated wit | :h <i>de-no</i> | vo PV |
| | e Yes | 207 | 13.6 | 2 | 7.1 | 0.321 | 209 | 13.5 | | | | | |
| | e Yes No | 207 1314 | 13.6 86.4 | 2 | 7.1 92.9 | | 209 1340 | 13.5 86.5 | occurrence in cirrhotic | DAA suc | cessfully | | |
| History of HCC | e Yes No Yes | 207 1314 120 1401 725 | 13.6 86.4 7.9 92.1 47.7 | 2 26 3 25 13 | 7.1 92.9 10.7 89.3 46.4 | | 209 1340 123 1426 738 | 13.5 86.5 7.9 92.1 47.6 | | DAA suc | cessfully | | |
| History of HCC Previous | e Yes No Yes No | 207 1314 120 1401 725 796 | 13.6 86.4 7.9 92.1 47.7 52.3 | 2 26 3 25 | 7.1 92.9 10.7 89.3 46.4 53.6 | 0.584 | 209 1340 123 1426 738 811 | 13.5 86.5 7.9 92.1 47.6 52.4 | occurrence in cirrhotic Univariate and multivar | DAA suc | cessfully sis. | treated | patients |
| History of HCC Previous nterferon use | e Yes No Yes No Yes No Yes | 207 1314 120 1401 725 796 345 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 | 2 26 3 25 13 15 9 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 | 0.584 | 209 1340 123 1426 738 811 354 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 | occurrence in cirrhotic Univariate and multivar Pre-treatment factors | Crude HR | sis. 95% CI | Adjusted HR* | patients |
| History of HCC Previous Interferon use Diabetes | e Yes No Yes No Yes No | 207 1314 120 1401 725 796 345 1176 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 | 2 26 3 25 13 15 9 19 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 | 0.584 0.897 0.237 | 209 1340 123 1426 738 811 354 1195 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 | occurrence in cirrhotic Univariate and multivar | DAA suc | cessfully sis. | treated | patients |
| History of HCC Previous nterferon use Diabetes Clinical features | e Yes No Yes No Yes No Yes No | 207 1314 120 1401 725 796 345 1176 N. | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 % | 2 26 3 25 13 15 9 19 N. | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % | 0.584 0.897 0.237 p*** | 209 1340 123 1426 738 811 354 1195 N. | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % | occurrence in cirrhotic Univariate and multivar Pre-treatment factors | Crude HR | sis. 95% CI | Adjusted HR* | 95% CI 0.97 - 1.06 |
| History of HCC Previous nterferon use Diabetes Clinical features | e Yes No Yes No Yes No Yes No <u>Yes</u> No | 207 1314 120 1401 725 796 345 1176 N. 1075 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 % 71.3 | 2 26 3 25 13 15 9 19 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 | 0.584 0.897 0.237 | 209 1340 123 1426 738 811 354 1195 N. 1102 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 | occurrence in cirrhotic Univariate and multivar Pre-treatment factors Age (increasing years) | Crude HR 1.02 | cessfully sis . 95% Cl 0.98 - 1.06 | Adjusted HR* | 95% CI 0.97 - 1.06 |
| History of HCC Previous nterferon use Diabetes Clinical features Platelets count | Yes No Yes No Yes No Yes No Yes No 4 150,000/μL > 150,000/μL | 207 1314 120 1401 725 796 345 1176 N. 1075 432 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 % 71.3 28.7 | 2 26 3 25 13 15 9 19 N. 27 1 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 | 0.584 0.897 0.237 p*** 0.003 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 | occurrence in cirrhotic Univariate and multivar Pre-treatment factors Age (increasing years) Gender (ref. male) | Crude HR 1.02 1.39 | cessfully sis . 95% Cl 0.98 - 1.06 0.66 - 2.93 | Adjusted HR* | 95% Cl 0.97 - 1.06 0.64 - 2.97 |
| History of HCC Previous Interferon use Diabetes Clinical features Platelets count | Yes No Yes No Yes No Yes No Yes No ≤ 150,000/μL > 150,000/μL ≤ 3.5 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 % 71.3 28.7 24.1 | 2 26 3 25 13 15 9 19 N. 27 1 1 8 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 | 0.584 0.897 0.237 p*** | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 | Occurrence in cirrhotic Univariate and multivar Pre-treatment factors Age (increasing years) Gender (ref. male) BMI: overweight (ref. under-normalweight) | Crude HR 1.02 1.39 0.97 | cessfully sis . 95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 | Adjusted HR* 1.02 1.38 | patients |
| History of HCC Previous Interferon use Diabetes Clinical features Platelets count Albumin (g/dL) | Yes No Yes No Yes No Yes No Yes No So,000/μL ≤ 3.5 > 3.5 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 % 71.3 28.7 24.1 75.9 | 2 26 3 25 13 15 9 19 N. 27 1 1 18 10 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 | 0.584 0.897 0.237 p*** 0.003 < 0.001 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 | Occurrence in cirrhotic Univariate and multivar Pre-treatment factors Age (increasing years) Gender (ref. male) BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight) | Crude HR 1.02 0.97 2.33 | Cessfully 5is . 95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 | Adjusted HR* 1.02 1.38 | 95% Cl 0.97 - 1.06 0.64 - 2.97 |
| History of HCC Previous nterferon use Diabetes Clinical features Platelets count Albumin (g/dL) | e Yes No Yes No Yes No Yes No $\leq 150,000/\mu$ L $\leq 150,000/\mu$ L ≤ 3.5 > 3.5 > 3.5 ≥ 1.1 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 460 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 % 71.3 28.7 24.1 75.9 31.3 | 2 26 3 25 13 15 9 19 N. 27 1 1 18 10 20 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 71.4 | 0.584 0.897 0.237 p*** 0.003 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 480 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 32.0 | occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never) | Crude HR Crude HR 1.02 1.39 0.97 2.33 1.29 0.44 | Cessfully sis. 95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 | Adjusted HR* 1.02 1.38 | 95% Cl 0.97 - 1.06 0.64 - 2.97 |
| History of HCC Previous nterferon use Diabetes Clinical features Platelets count Albumin (g/dL) Bilirubin (mg/dL) | Yes No Yes No Yes No Yes No Yes No ≤ 150,000/μL ≤ 150,000/μL ≤ 3.5 > 3.5 ≥ 1.1 < 1.1 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 % 71.3 28.7 24.1 75.9 | 2 26 3 25 13 15 9 19 N. 27 1 1 18 10 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 | 0.584 0.897 0.237 p*** 0.003 < 0.001 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 | occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never)HCV-genotype (3 vs others) | Crude HR 1.02 1.39 0.97 2.33 1.29 0.44 0.43 | Cessfully sis. 95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 0.06 - 3.15 | Adjusted HR* 1.02 1.38 | 95% Cl 0.97 - 1.06 0.64 - 2.97 |
| History of HCC Previous nterferon use Diabetes Clinical features Platelets count Albumin (g/dL) Bilirubin (mg/dL) | No Yes No Yes No Yes No Yes No Yes No Yes No ≤ 150,000/µL ≤ 3.5 > 3.5 ≥ 1.1 < 1.1 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 460 1012 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 22.7 77.3 28.7 24.1 75.9 31.3 68.8 | 2 26 3 25 13 15 9 19 N. 27 1 1 8 10 20 8 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 71.4 28.6 | 0.584 0.897 0.237 0.003 < 0.001 < 0.001 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 480 1020 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 32.0 68.0 | occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never)HCV-genotype (3 vs others)HCC | Crude HR 1.02 1.39 0.97 2.33 1.29 0.44 0.43 1.12 | Cessfully sis. 95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 0.06 - 3.15 0.27 - 4.73 | Adjusted HR* 1.02 1.38 | 95% Cl 0.97 - 1.06 0.64 - 2.97 |
| History of HCC Previous nterferon use Diabetes Diabetes Clinical features Platelets count Albumin (g/dL) Bilirubin (mg/dL) NR | Yes No Yes No Yes No Yes No Yes No ≤ 150,000/μL ≤ 150,000/μL ≤ 3.5 > 3.5 ≥ 1.1 < 1.1 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 460 1012 737 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 22.7 77.3 28.7 24.1 75.9 31.3 68.8 51.4 | 2 26 3 25 13 15 9 19 N. 27 1 1 8 10 20 8 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 71.4 28.6 71.4 | 0.584 0.897 0.237 0.003 < 0.001 < 0.001 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 480 1020 757 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 32.0 68.0 51.8 | Occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never)HCV-genotype (3 vs others)HCCPrevious Interferon treatment | Crude HR Crude HR 1.02 1.39 0.97 2.33 1.29 0.44 0.43 1.12 0.81 | Cessfully sis. 95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 0.06 - 3.15 0.27 - 4.73 0.38 - 1.71 | Adjusted HR* 1.02 1.38 2.18 | 95% Cl 0.97 - 1.06 0.64 - 2.97 0.89 - 5.32 |
| History of HCC Previous nterferon use Diabetes Diabetes Clinical features Datelets count Albumin (g/dL) Bilirubin (mg/dL) NR | e Yes No Yes No Yes No Yes No Yes Yes No $\leq 150,000/\mu L$ ≤ 3.5 > 3.5 > 3.5 > 1.1 < 1.1 ≤ 1.1 < 1.1 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 460 1012 737 696 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 22.7 77.3 28.7 24.1 75.9 31.3 68.8 51.4 48.6 | 2 26 3 25 13 15 9 19 N. 27 1 1 8 10 20 8 20 8 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 71.4 28.6 71.4 28.6 | 0.584 0.897 0.237 0.003 < 0.001 < 0.001 0.036 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 480 1020 757 704 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 32.0 68.0 51.8 48.2 | Occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never)HCV-genotype (3 vs others)HCCPrevious Interferon treatmentPlatelets (ref. >120,000/µL) | Crude HR 1.02 1.39 0.97 2.33 1.29 0.44 0.43 1.12 0.81 9.48 | 95% Cl 0.95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 0.066 - 3.15 0.27 - 4.73 0.38 - 1.71 1.29 - 69.78 | Adjusted HR* 1.02 1.38 2.18 3.56 | 95% Cl 0.97 - 1.06 0.64 - 2.97 0.89 - 5.32 |
| History of HCC Previous nterferon use Diabetes Clinical features Platelets count Albumin (g/dL) Bilirubin (mg/dL) NR Liver Stiffness Measurement (kPa) | Pe Yes No Yes No Yes No Yes No ≤ 150,000/μL ≤ 150,000/μL ≤ 3.5 > 3.5 > 3.5 ≥ 1.1 < 1.1 ≥ 1.1 < 1.1 ≥ 20 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 460 1012 737 696 586 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 22.7 77.3 28.7 24.1 75.9 31.3 68.8 51.4 48.6 48.8 | 2 26 3 25 13 15 9 19 N. 27 1 1 8 10 20 8 20 8 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 71.4 28.6 71.4 28.6 71.4 28.6 66.7 | 0.584 0.897 0.237 0.003 < 0.001 < 0.001 0.036 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 480 1020 757 704 596 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 32.0 68.0 51.8 48.2 49.0 | Occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never)HCV-genotype (3 vs others)HCCPrevious Interferon treatmentPlatelets (ref. >120,000/µL)Albumin (ref. > 3.5 g/dL) | Crude HR I.02 1.39 0.97 2.33 0.97 2.33 1.29 0.44 0.43 1.12 0.81 9.48 5.75 | 95% Cl 0.95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 0.066 - 3.15 0.27 - 4.73 0.38 - 1.71 1.29 - 69.78 2.65 - 12.47 | Adjusted HR* 1.02 1.38 2.18 3.56 2.66 | 95% Cl 0.97 - 1.06 0.64 - 2.97 0.89 - 5.32 |
| History of HCC Previous Interferon use Diabetes Clinical features Platelets count Albumin (g/dL) Bilirubin (mg/dL) INR Liver Stiffness Measurement (kPa) | Pe Yes No Yes No Yes No Yes No Yes No ≤ 150,000/μL ≤ 150,000/μL ≤ 3.5 > 3.5 > 3.5 > 1.1 < 1.1 ≤ 1.1 < 1.1 ≥ 20 < 20 > 3.25 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 460 1012 737 696 586 615 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 22.7 77.3 28.7 24.1 75.9 31.3 68.8 51.4 48.6 48.8 51.2 | 2 26 3 25 13 15 9 19 N. 27 1 1 8 10 20 8 20 8 20 8 20 8 10 5 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 71.4 28.6 71.4 28.6 71.4 28.6 66.7 33.3 | 0.584 0.897 0.237 p*** 0.003 <0.001 <0.001 0.169 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 480 1020 757 704 596 620 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 32.0 68.0 51.8 48.2 49.0 51.0 | Occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never)HCV-genotype (3 vs others)HCCPrevious Interferon treatmentPlatelets (ref. >120,000/µL) | Crude HR 1.02 1.39 0.97 2.33 1.29 0.44 0.43 1.12 0.81 9.48 | 95% Cl 0.95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 0.066 - 3.15 0.27 - 4.73 0.38 - 1.71 1.29 - 69.78 | Adjusted HR* 1.02 1.38 2.18 3.56 | 95% Cl 0.97 - 1.06 0.64 - 2.97 |
| History of HCC Previous Interferon use Diabetes Clinical features Platelets count Albumin (g/dL) Bilirubin (mg/dL) Bilirubin (mg/dL) INR Liver Stiffness Measurement (kPa) FIB4 | e Yes No Yes No Yes No Yes No Yes No Yes $\leq 150,000/\mu L$ ≤ 3.5 > 3.5 > 3.5 > 1.1 < 1.1 < 1.1 < 1.1 < 20 < 20 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 460 1012 737 696 586 615 1025 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 22.7 77.3 28.7 24.1 75.9 31.3 68.8 51.4 48.6 48.8 51.4 48.6 48.8 51.2 68.5 | 2 26 3 25 13 15 9 19 N. 27 1 1 8 10 20 8 20 8 20 8 20 8 10 5 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 71.4 28.6 71.4 28.6 71.4 28.6 66.7 33.3 89.3 | 0.584 0.897 0.237 p*** 0.003 <0.001 <0.001 0.169 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 480 1020 757 704 596 620 1050 474 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 32.0 68.0 51.8 48.2 49.0 51.0 68.9 | Occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never)HCV-genotype (3 vs others)HCCPrevious Interferon treatmentPlatelets (ref. >120,000/µL)Albumin (ref. > 3.5 g/dL) | Crude HR I.02 1.39 0.97 2.33 0.97 2.33 1.29 0.44 0.43 1.12 0.81 9.48 5.75 | 95% Cl 0.95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 0.066 - 3.15 0.27 - 4.73 0.38 - 1.71 1.29 - 69.78 2.65 - 12.47 | Adjusted HR* 1.02 1.38 2.18 3.56 2.66 | 95% Cl 0.97 - 1.06 0.64 - 2.97 0.89 - 5.32 |
| History of HCC Previous nterferon use Diabetes Clinical features Platelets count Albumin (g/dL) Albumin (g/dL) Albumin (mg/dL) NR Liver Stiffness Measurement (kPa) FIB4 | Pe Yes No Yes No Yes No Yes No Yes No ≤ 150,000/μL ≤ 150,000/μL ≤ 3.5 > 3.5 > 3.5 > 1.1 < 1.1 ≤ 1.1 < 1.1 ≥ 20 < 20 > 3.25 | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 460 1012 737 696 586 615 1025 471 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 22.7 77.3 28.7 24.1 75.9 31.3 68.8 51.4 48.6 48.8 51.4 48.6 48.8 51.2 68.5 31.5 | 2 26 3 25 13 15 9 19 N. 27 1 1 8 10 20 8 20 8 20 8 20 8 20 8 10 5 25 3 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 71.4 28.6 71.4 28.6 71.4 28.6 66.7 33.3 89.3 10.7 | 0.584 0.897 0.237 p*** 0.003 <0.001 <0.036 0.169 0.019 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 480 1020 757 704 596 620 1050 474 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 32.0 68.0 51.8 48.2 49.0 51.0 68.9 31.1 | occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never)HCV-genotype (3 vs others)HCCPrevious Interferon treatmentPlatelets (ref. >120,000/µL)Albumin (ref. > 3.5 g/dL)Bilirubin (ref. > 1.1 mg/dL) | Crude HR 1.02 1.39 0.97 2.33 0.97 2.33 1.29 0.44 0.43 1.12 0.81 9.48 5.75 5.32 | Cessfully sis. 95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 0.06 - 3.15 0.27 - 4.73 0.38 - 1.71 1.29 - 69.78 2.65 - 12.47 2.34 - 12.09 | Adjusted HR* 1.02 1.38 2.18 3.56 2.66 | 95% Cl 0.97 - 1.06 0.64 - 2.97 0.89 - 5.32 |
| Metabolic syndrom History of HCC Previous Interferon use Diabetes Clinical features Platelets count Albumin (g/dL) Bilirubin (mg/dL) Bilirubin (mg/dL) INR Liver Stiffness Measurement (kPa) FIB4 Child-Pugh Class | e Yes No Yes No Yes No Yes No ≤ 150,000/μL ≤ 150,000/μL ≤ 3.5 > 3.5 > 3.5 > 1.1 < 1.1 ≤ 1.1 < 1.1 ≥ 1.1 < 1.1 ≥ 20 < 20 > 3.25 ≤ 3.25 A | 207 1314 120 1401 725 796 345 1176 N. 1075 432 346 1088 460 1012 737 696 586 615 586 615 1025 471 1305 | 13.6 86.4 7.9 92.1 47.7 52.3 22.7 77.3 28.7 24.1 75.9 31.3 68.8 51.4 48.6 48.8 51.4 48.6 48.8 51.2 68.5 31.5 | 2 26 3 25 13 15 9 19 N. 27 1 1 8 10 20 8 20 8 20 8 20 8 20 8 10 5 25 3 17 | 7.1 92.9 10.7 89.3 46.4 53.6 32.1 67.9 % 96.4 3.6 64.3 35.7 71.4 28.6 71.4 28.6 71.4 28.6 66.7 33.3 89.3 10.7 60.7 | 0.584 0.897 0.237 p*** 0.003 <0.001 <0.036 0.169 0.019 | 209 1340 123 1426 738 811 354 1195 N. 1102 433 364 1098 480 1020 757 704 596 620 1050 474 1322 227 | 13.5 86.5 7.9 92.1 47.6 52.4 22.9 77.1 % 71.8 28.2 24.9 75.1 32.0 68.0 51.8 48.2 49.0 51.8 48.2 49.0 51.0 68.9 31.1 85.3 | occurrence in cirrhotic Univariate and multivarPre-treatment factorsAge (increasing years)Gender (ref. male)BMI: overweight (ref. under-normalweight) obese (ref. under-normalweight)Alcohol use: current (ref. never) past (ref. never)HCV-genotype (3 vs others)HCCPrevious Interferon treatmentPlatelets (ref. >120,000/µL)Albumin (ref. > 3.5 g/dL)Bilirubin (ref. > 1.1 mg/dL)INR (ref. < 1.1) | Crude HR I.02 1.39 0.97 2.33 1.29 0.44 0.43 1.12 0.81 9.48 5.75 5.32 2.44 | Cessfully sis. 95% Cl 0.98 - 1.06 0.66 - 2.93 0.41 - 2.29 0.90 - 6.04 0.38 - 4.33 0.13 - 1.46 0.06 - 3.15 0.27 - 4.73 0.38 - 1.71 1.29 - 69.78 2.65 - 12.47 2.34 - 12.09 1.07 - 5.55 | Adjusted HR* 1.02 1.38 2.18 3.56 2.66 2.70 | 95% Cl 0.97 - 1.0 0.64 - 2.9 0.89 - 5.3 1.03 - 12.3 1.15 - 6.1 1.10 - 6.6 |



Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali.

PVT cumulative incidence rates in cirrhotic treated patients by SVR



PVT cumulative incidence rates in cirrhotic successfully treated vs untreated patients

