**Sustained virologic response to direct-acting antiviral agents predicts better outcomes in HCV-infected patients: a retrospective study**

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**SUPPLEMENTAL MATERIAL**

**Table S1. Inclusion criteria for direct-acting antiviral agents use by the Italian Medicines Agency (AIFA) recommendations and according to the sustained virologic response achievement and hepatocellular carcinoma development.**

| N. | Criterium | No SVR n = 18 | SVR n = 362 | No HCC n = 363 | HCC* n = 17 |
|---|---|---|---|---|---|
| 1 | Patients with cirrhosis of class A or B Child-Pugh and/or with the presence of a hepatocellular carcinoma that has been cured by surgery or local therapy and that are not potential candidate to liver transplantation [n (%)] | 12 (66.7) | 118 (32.6) | 116 (31.9) | 14 (82.3) |
| 2 | HCV viremia recurrent after liver transplantation in patients clinically stable and with an optimal immunosuppressive therapy [n (%)] | 1 (5.6) | 9 (2.5) | 9 (2.5) | 1 (5.9) |
| 3 | Serious extrahepatic manifestations independently of grade of liver fibrosis evaluated by the Metavir score system [n (%)] | 0 | 19 (5.2) | 19 (5.2) | 0 |
| 4 | Chronic liver inflammation with a Metavir score of more than F2 [n (%)] | 3 (16.7) | 90 (24.8) | 92 (25.3) | 1 (5.9) |
| 5 | Patients in waiting list for liver transplantation with a Model for End-Stage Liver Disease (MELD) score of less than 25, and/or with a hepatocellular carcinoma that can be cured according to Milan criteria, and that can wait in list for at least 2 months [n (%)] | 0 | 1 (0.3) | 1 (0.3) | 0 |
| 6 | Patients with transplantation of bone marrow or solid organ other than liver with liver fibrosis more than Metavir score F1 [n (%)] | 0 | 4 (1.1) | 4 (1.1) | 0 |
| 7 | Patients with chronic hepatitis with fibrosis Metavir more than F2 and/or the presence of chronic pathological conditions that can participate to liver damage such as HIV or HBV coinfection, non-viral chronic liver disease, drug-treated diabetes, obesity, or congenital hemoglobin or coagulation diseases [n (%)] | 0 | 38 (10.5) | 38 (10.5) | 0 |
| 8 | Chronic hepatitis with fibrosis Metavir F0-F1 and/or the presence of chronic pathological conditions that can participate to liver damage such as HIV or HBV coinfection, non-viral chronic liver disease, drug-treated diabetes, obesity, or congenital hemoglobin or coagulation diseases [n (%)] | 2 (11.1) | 83 (22.9) | 84 (23.1) | 1 (5.9) |

DAAs, direct-acting antiviral agents; SVR, sustained virologic response; HCC, hepatocellular carcinoma. *P=0.007 by Fisher exact test between HCC and inclusion criteria.

**Table S2. Frequencies of direct-acting antiviral agents use according to the sustained virologic response achievement and hepatocellular carcinoma development**

| Drugs association | No SVR n= 18 | SVR* n = 362 | No HCC n = 363 | HCC** n = 17 |
|---|---|---|---|---|
| Daclatasvir + Ribavirin [n (%)] | 3 (16.7) | 47 (13.0) | 47 (12.9) | 3 (17.6) |
| Sofosbuvir + Velpatasvir [n (%)] | 2 (11.1) | 84 (23.2) | 86 (23.7) | 0 |
| Ledipasvir + Ribavirin [n (%)] | 1 (5.6) | 57 (15.7) | 57 (15.7) | 1 (5.9) |
| Glecaprevir + Pibrentasvir [n (%)] | 0 | 57 (15.7) | 57 (15.7) | 0 |
| Simeprevir + Sofosbuvir [n (%)] | 5 (27.8) | 21 (7.7) | 28 (7.7) | 8 (47.0) |
| Sofosbuvir + Ribavirin [n (%)] | 4 (22.2) | 35 (9.9) | 36 (9.9) | 3 (17.6) |
| Elbasvir + Grazoprevir [n (%)] | 2 (11.1) | 24 (6.6) | 24 (6.6) | 2 (11.8) |
| Ombitasvir + Paritaprevir + Ritonavir [n (%)] | 1 (5.6) | 27 (7.7) | 28 (7.7) | 0 |

DAAs, direct-acting antiviral agents; SVR, sustained virologic response; HCC, hepatocellular carcinoma. *P=0.010 and **P<0.001 by Fisher exact test between drug association and SVR or HCC, respectively.

**Table S3. Frequencies of hepatitis C virus genotypes according to the sustained virologic response achievement and hepatocellular carcinoma development**

| HCV genotype | No SVR n = 18 | SVR n = 362 | No HCC n = 363 | HCC n = 17 |
|---|---|---|---|---|
| 1a [n (%)] | 0 | 61 (16.8) | 61 (16.8) | 0 |
| 1b [n (%)] | 7 (38.9) | 137 (37.8) | 136 (37.5) | 8 (47.1) |
| 2 [n (%)] | 5 (27.8) | 78 (21.5) | 81 (22.3) | 2 (11.8) |
| 3 [n (%)] | 3 (16.7) | 51 (14.1) | 50 (13.8) | 4 (23.5) |
| 4 [n (%)] | 3 (16.7) | 22 (6.1) | 22 (6.1) | 3 (17.6) |
| 5 [n (%)] | 0 | 12 (3.3) | 12 (3.3) | 0 |
| 6 [n (%)] | 0 | 1 (0.3) | 1 (0.3) | 0 |

DAAs, direct-acting antiviral agents; SVR, sustained virologic response; HCC, hepatocellular carcinoma.

**Table S4. Frequency of adverse events occurred during the treatment with direct-acting antiviral agents.**

| Adverse event | No SVR n = 18 | SVR n = 362 | P |
|---|---|---|---|
| Lymphomas [n (%)] | 1 (5.6) | 0 | NS |
| Acute liver failure [n (%)] | 2 (11.1) | 0 | 0.015 |
| Acute kidney disease [n (%)] | 1 (5.6) | 0 | NS |
| Abdominal pain [n (%)] | 2 (11.1) | 1 | 0.043 |
| Cutaneous rash or itching [n (%)] | 1 (5.6) | 1 (0.3) | NS |
| Severe thrombocytopenia (< 50 x $10^3$/ml) [n (%)] | 0 | 1 (0.3) | NS |
| Hypotension [n (%)] | 1 (5.6) | 0 | NS |
| Hypertension crisis [n (%)] | 1 (5.6) | 0 | NS |
| Anxiety, insomnia, or agitation [n (%)] | 2 (11.1) | 0 | 0.015 |
| DAAs interruption [n (%)] | 4 (22.2) | 1 (0.3) | <0.001 |
| Ribavirin interruption [n (%)] | 0 | 2 (0.6) | NS |

DAAs, direct-acting antiviral agents; SVR, sustained virologic response.

**Figure S1**

Kaplan-Meier curves of hepatocellular carcinoma (HCC) or mortality free probability by sustained virologic response (SVR) achievement and the presence of cirrhosis