**SUPPLEMENTAL DIGITAL CONTENT**

Lacombe K,et al. Real-world efficacy of daclatasvir and sofosbuvir, with and without ribavirin, in HIV/HCV co-infected patients with advanced liver disease in a French early-access cohort.

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**Supplemental Fig. 1. Derivation of the Analysis Populations.**

AE, adverse event; ATU, Autorisation Temporaire d'Utilisation; HBV, hepatitis B virus; HCV, hepatitis C virus; ITT, intention-to-treat; mITT, modified ITT; PT12, post-treatment week 12.
\*Discontinued without virologic failure for reasons undocumented or other than death or discontinuation for AEs.



**Supplemental Table 1. Derivation of Patient Cirrhosis Status According to Treatment Access Request Details**

|  |  |
| --- | --- |
| **Treatment Access Request entries** | ***Derived cirrhosis status*** |
| **Fibrosis stage assessment\***  | **FibroScan value** | **Stage of disease for ATU eligibility\*** |
| F4 | *NA* | *NA* | *Cirrhotic* |
| F3/F4 | <14.5 or missing | *NA* | *Noncirrhotic* |
| F3/F4 | ≥14.5 | *NA* | *Cirrhotic* |
| ≤F3 | <14.5 or missing | *NA* | *Noncirrhotic* |
| ≤F3 | ≥14.5  | F4 | *Cirrhotic* |
| ≤F3  | ≥14.5  | F3 | *Noncirrhotic* |
| Missing | ≥14.5 | *NA* | *Cirrhotic* |
| Missing | <14.5 | *NA* | *Noncirrhotic* |
| Missing | Missing | F4 | *Cirrhotic* |
| Missing | Missing | F3 or HCV extra-hepatic manifestations alone | *Noncirrhotic* |
| Missing | Missing | Missing | *Missing cirrhosis status* |

ATU, Autorisation Temporaire d'Utilisation *NA*, not assessed; value (if present) is not used to determine cirrhosis status.
\*Physician-assessed.

**Supplemental Table 2.** **Comparison of Baseline Characteristics Between ITT Population Patients Included and Excluded From the Primary mITT Analysis**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter, n (%) unless otherwise indicated** | **mITT****(N=407)** | **Excluded from mITT****(N=183)** | ***P*** |
| Age, median (range) years  | 52.1 (34–74) | 52.6(30–74) | 0.993\* |
| Male | 288 (72) | 139 (78) | 0.180† |
| Time since HCV diagnosis, median (IQR) years | 18.7 (14–23) | 18.9 (15–23) | 0.901\* |
| HCV-RNA, median (IQR) log10 IU/mL  | 6.1 (5.5–6.5) | 6.1 (5.6–6.5) | 0.315‡ |
| Cirrhosis | 290 (72) | 126 (69) | 0.442† |
| Child-Pugh class§A B C | 204 (82) 39 (16) 5 (2) | 82 (88)8 (9) 3 (3) | 0.182|| |
| MELD score, median (IQR)¶ | 9 (7–14) | 9 (7–13) | 0.527‡ |
| AscitesSlight/moderate or medically controlledSevere/not controlled  | 19 (5)3 (1) | 11 (6)2 (1) | 0.652|| |
| EncephalopathySlight/moderate or medically controlled | 7 (2) | 3 (2) | 1.000|| |
| Post-liver transplant HCV recurrence | 13 (3) | 4 (2) | 0.498† |
| Treatment experienced | 330 (82) | 146 (80) | 0.545† |
| RBV use | 58 (14) | 12 (7) | **0.007†** |
| Treatment duration<10 weeks10–<14 weeks14–<20 weeks≥20 weeks | 17 (4)86 (21)14 (3)290 (71) | 23 (13)37 (20)19 (10)104 (57) | **<0.001†** |
| Antiretroviral useNRTINNRTIPI INI | 352 (90)91 (23)136 (35)255 (65) | 151 (83)46 (25)75 (41)104 (57) | **0.038†**0.555†0.115†0.088† |
| HIV RNA <50 copies/mL | 322 (95) | 144 (92) | 0.186† |
| CD4, median (IQR) cells/mm3<500 cells/mm3<350 cells/mm3<200 cells/mm3 | 555 (335–765)158 (43)99 (27)32 (9) | 551 (350–794)75 (44)41 (24)16 (9) | 0.784‡0.884†0.449†0.817† |
| Laboratory parameters at TAR, median (IQR)Platelets, × 109/LAlbumin, g/LALT, IU/LAST, IU/LTotal bilirubin, μmol/LGamma GT, IU/L | 135 (87–193)39 (35–43)62 (43–102)64 (42–95)13 (8–24)106 (60–176) | 123 (87–188)39 (35–42)68 (44–93)66 (44–100)13 (9–24)98 (51–178) | 0.455†0.986‡0.368‡0.605‡0.973‡0.274‡ |
| Laboratory abnormalities at TARPlatelets <25 ×109/LAlbumin <35 g/LALT >175 IU/LAST >200 IU/LTotal bilirubin >60 μmol/LGamma GT >90 (women) or >140 (men) IU/L | 2 (1)86 (25)23 (6)11 (3)11 (3)151 (40) | 034 (22)12 (7)7 (4)8 (6)64 (39) | 1.000||0.517†0.698†0.476†0.198†0.827† |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; gamma GT, gamma- glutamyl transferase; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; INI, integrase inhibitor; IQR, interquartile (25th–75th) range; ITT, intention-to-treat; MELD, Model for End-Stage Liver Disease; mITT, modified ITT; NRTI, nucleoside analog reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RBV, ribavirin; TAR, Treatment Access Request.

ITT patients were excluded from the mITT population for missing data at post-treatment week 12 due to undocumented discontinuation or discontinuation for reasons other than death or adverse events, without virologic failure. All percentages are of patients with available data in indicated category. Missing data for percentages quoted were:

* **mITT population** —sex (n=9); cirrhosis status (n=4); Child-Pugh class (n=42); ascites (n=8); encephalopathy (n=8); previous HCV treatment status (n=4); RBV use (n=2); Antiretroviral use (n=14); HIV RNA (n=69); CD4 cells (n=39); platelets (n=9); albumin (n=64); ALT (n=6); AST (n=6); total bilirubin (n=64); gamma GT (n=32).
* **Excluded from mITT population**—sex (n=4); Child-Pugh class (n=33); ascites (n=2); encephalopathy (n=2); antiretroviral use (n=2); HIV RNA (n=27); CD4 cells (n=11); platelets (n=6); albumin (n=31); AST (n=1); total bilirubin (n=43); gamma GT (n=20).

\*Student’s T test. †Chi-square test. ‡Wilcoxon test. §Cirrhotic patients only. ||Fisher’s exact test. ¶Cirrhotic and pre-transplant patients only.

**Supplemental Table 3. Comparison of Baseline Characteristics Between Patients Treated for 24 Weeks With or Without Ribavirin**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter, n (%) unless otherwise indicated** | **DCV+SOF****(N=260)** | **DCV+SOF+RBV****(N=42)** | ***P*** |
| Age, median (range) years  | 52.1 (34–70) | 51.4(42–74) | 0.936\* |
| Male | 188 (73) | 32 (80) | 0.358† |
| Time since HCV diagnosis, median (IQR) years | 19.4 (15.3–23.3) | 19.3 (14.3–23.7) | 0.515‡ |
| HCV-RNA, median (IQR) log10 IU/mL  | 6.1 (5.6–6.5) | 6.1 (5.6–6.7) | 0.412‡ |
| Cirrhosis | 195 (75) | 33 (83) | 0.301† |
| Initial Child-Pugh class§A B C | 141 (83) 27 (16) 2 (1) | 22 (85)3 (12) 1 (4) | 0.371|| |
| MELD score (day 0)¶<1010–<15≥15 | 35 (53)14 (21)17 (26) | 12 (57)6 (29)3 (14) | 0.564|| |
| AscitesSlight/moderate or medically controlledSevere/not controlled  | 10 (4)1 (<1) | 4 (10)1 (3) | 0.061|| |
| EncephalopathySlight/moderate or medically controlled | 3 (1) | 3 (8) | **0.034||** |
| Post-liver transplant HCV recurrence | 7 (3) | 5 (12) | **0.015||** |
| Treatment experienced | 221 (85) | 39 (95) | 0.087‡ |
| Antiretroviral useNRTINNRTIPI INI | 224 (89)61 (24)86 (34)162 (64) | 36 (88)9 (22)10 (24)33 (80) | 0.792||0.753†0.218†**0.041†** |
| HIV-RNA <50 copies/mL | 203 (95) | 34 (97) | 1.000|| |
| CD4, median (IQR) cells/mm3<500 cells/mm3<350 cells/mm3<200 cells/mm3 | 569 (350–763)100 (42)59 (25)16 (7) | 363 (230–588)22 (58)18 (47)6 (16) | **0.004‡**0.064†**0.004†**0.096|| |
| Laboratory parameters (day 0), median (IQR)Platelets, × 109/LAlbumin, g/LALT, IU/LAST, IU/LTotal bilirubin, μmol/LGamma GT, IU/L | 133 (84–184)40 (35–43)66 (43–103)70 (44–107)14 (9–26)96 (55–155) | 116 (70–180)37 (32–41)67 (40–114)62 (46–93)17 (10–28)138 (81–226) | 0.263‡0.089‡0.874‡0.566‡0.235‡**0.028‡** |
| Laboratory abnormalities (day 0)Platelets <25 × 109/LAlbumin <35 g/LALT >175 IU/LAST >200 IU/LTotal bilirubin >60 μmol/LGamma GT >90 (women) or >140 (men) IU/L | 2 (1)48 (24)16 (6)7 (3)5 (3)81 (36) | 011 (37)01 (2)3 (10)19 (51) | 1.000||0.138†0.140||1.000||0.082||0.068† |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; DCV, daclatasvir; gamma GT, gamma- glutamyl transferase; HCV, hepatitis C virus; HIV, human immunodeficiency virus; INI, integrase inhibitor; IQR, interquartile (25th–75th) range; MELD, Model for End-Stage Liver Disease; NRTI, nucleoside analog reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RBV, ribavirin; SOF, sofosbuvir.
All percentages are of patients with available data in indicated category. Missing data for percentages quoted were:

**DCV+SOF** —sex (n=3); Child-Pugh class (n=25); MELD score (n=129); ascites (n=2); encephalopathy (n=2); previous HCV treatment status (n=1); Antiretroviral use (n=8); HIV RNA (n=46); CD4 cells (n=21); platelets (n=15); albumin (n=60); ALT (n=9); AST (n=9); total bilirubin (n=72); gamma GT (n=33).

**DCV+SOF+RBV**—sex (n=2); cirrhosis status (n=2); Child-Pugh class (n=7); MELD score (n=12); ascites (n=2); encephalopathy (n=2); previous HCV treatment status (n=1); antiretroviral use (n=1); HIV RNA (n=7); CD4 cells (n=4); platelets (n=1); albumin (n=12); AST (n=1); total bilirubin (n=12); gamma GT (n=5).

\*Student’s T test. †Chi-square test. ‡Wilcoxon test. §Cirrhotic patients only. ||Fisher’s exact test. ¶Cirrhotic and pre-transplant patients only.

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**Supplemental Table 4. Sustained Virologic Response and Treatment Failure Among Patients With Cirrhosis By Initial Child-Pugh Status**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **All Treated** | **DCV+SOF****12 weeks** | **DCV+SOF****+RBV****12 weeks** | **DCV+SOF****24 weeks** | **DCV+SOF****+RBV****24 weeks** |
| **Patients with Child-Pugh A cirrhosis\*** |
| **N**mITTObserved values† | 203200 | 2929 | 1110 | 141139 | 2222 |
| **SVR12, n (%) [95% CI]**mITTObserved values† | 188 (93) [88.2–95.5]188 (94) [89.8–96.5] | 24 (83) [65.5–92.4]24 (83) [65.5–92.4] | 8 (73) [43.4–90.3]8 (80) [49.0–94.3] | 134 (95.0) [90.1–97.6]134 (96) [91.9–98.5] | 22 (100) [85.1–100]22 (100) [85.1–100] |
| **Treatment failure, n**Virologic breakthroughRelapseUndefined virologic failure§Non-virologic failure | 151743 | 51130 | 30111 | 70502 | 0---- |
| **Patients with Child-Pugh B cirrhosis\*** |
| **N**mITTObserved values† | 40‡38‡ | 87 | 00 | 2726 | 33 |
| **SVR12, n (%) [95% CI]**mITTObserved values† | 34 (85) [70.9–92.9]34 (89) [75.9–95.8] | 4 (50) [21.5–78.5]4 (57) [25.0–84.2] | -- | 25 (93) [76.6–97.9]26 (96) [81.1–99.3] | 3 (100) [43.9–100]3 (100) [43.9–100] |
| **Treatment failure, n**Virologic breakthroughRelapseUndefined virologic failure§Non-virologic failure | 60222 | 40121 | ----- | 20101 | 0-**-**-- |
| **Patients with Child-Pugh C cirrhosis\*** |
| **N**mITTObserved values† | 54 | 21 | 00 | 22 | 11 |
| **SVR12, n (%) [95% CI]**mITTObserved values† | 3 (60) [23.1–88.2]3 (75) [30.1–95.4] | 0 (0) [0–65.8]0 (0) [0–79.3] | -- | 2 (100) [34.2–100]2 (100) [34.2–100] | 1 (100) [20.7–100]1 (100) [20.7–100] |
| **Treatment failure, n**Virologic breakthroughRelapseUndefined virologic failure§Non-virologic failure | 20011 | 20011 | ----- | 0---- | 0---- |

CI, confidence interval; DCV, daclatasvir; HBV, hepatitis B virus; HCV, hepatitis C virus; MELD, Model for End-Stage Liver Disease; RBV, ribavirin; SOF, sofosbuvir; SVR12, sustained virologic response at post-treatment week 12.
Non-virologic failure is defined as treatment discontinuation for adverse events or death before post-treatment week 12.
\*For patients with available data: 14% (11/76) Child-Pugh A, 48% (12/25) Child-Pugh B, and 100% (3/3) Child-Pugh C patients had a MELD score ≥15 at day 0.
†Observed values analysis excludes non-virologic treatment failure.

‡Total includes two patients with missing regimen data, both achieved SVR12.

§Last reported HCV-RNA through post-treatment week 12 was at treatment week 2 or 4 (quantifiable) in four undefined virologic failures for Child-Pugh A, two for Child-Pugh B, and one for Child-Pugh C.

**Supplemental Table 5. Baseline characteristics of treatment failures**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **#** | **Age/Sex** | **Derived Regimen** | **Daclatasvir Dose****(mg)** | **Actual Treatment****(weeks)** | **Prior HCV Tx (Y/N)** | **HCV-RNA****log10 IU/mL** | **Cirrhosis****(Y/N)** | **Child-Pugh Class** | **MELD Score** | **Type of Failure** |
| **Virologic failures** |
| 1 | 50/F | D+S 12w | 60 | 2 | Y | 5.70 | Y | B | NR | Undefined |
| 2 | 55/F | D+S 12w | 60 | 12 | N | 5.97 | Y | A | 7 | Breakthrough |
| 3 | 49/M | D+S 12w | 60 | 12 | N | 5.28 | N | – | 7 | Relapse |
| 4 | 48/F | D+S 12w | 30 | 12 | Y | 3.79 | Y | A | NR | Relapse |
| 5 | 55/M | D+S 24w | 30 | 24 | Y | 6.56 | Y | A | NR | Relapse |
| 6 | 53/NR | D+S 24w | 60 | 24 | Y | 5.73 | N | – | NR | Relapse |
| 7 | 52/F | D+S 24w | 60 | 26 | Y | 5.91 | Y | A | 10 | Relapse |
| 8a | 64/M | D+S 24w | 30 | 24 | Y | 6.49 | Y | A | NR | Relapse |
| 9 | 57/M | D+S+R 12w | 30 | 12 | Y | 6.52 | Y | A | NR | Relapse |
| 10 | 50/F | D+S 24w | 60 | 24 | Y | 7.13 | Y | A | NR | Relapse |
| 11 | 55/M | D+S 12w | 60 | 12 | Y | 6.00 | Y | NR | NR | Relapse |
| 12 | 54/M | D+S 24w | 30 | 24 | Y | 6.24 | Y | A | 20 | Relapse |
| 13 | 43/M | D+S 12w | 60 | 7 | Y | 6.15 | Y | NR | NR | Undefined |
| 14 | 49/M | D+S 12w | 60 | 4 | Y | 7.10 | N | – | NR | Undefined |
| 15 | 46/F | D+S+R 12w | 30 | 2 | Y | 7.19 | Y | A | 7 | Undefined |
| 16\* | 62/M | D+S 12w | 30 | 5 | N | 5.49 | Y | A | 14 | Undefined |
| 17 | 50/M | D+S 24w | 60 | 24 | Y | 5.92 | Y | B | NR | Relapse |
| 18 | 50/F | D+S 12w | 60 | 11 | Y | 6.68 | Y | A | NR | Undefined |
| 19 | 44/M | D+S 12w | 60 | 6 | Y | 6.46 | Y | B | 13 | Relapse |
| 20 | 42/F | D+S 12w | 30 | 8 | Y | 5.46 | Y | A | NR | Undefined |
| 21 | 52/M | D+S 12w | 30 | 12 | N | 6.00 | N | – | NR | Relapse |
| 22 | 44/M | D+S 12w | 60 | 8 | Y | 6.23 | Y | NR | 7 | Undefined |
| 23 | 51/M | D+S 12w | 90 | 2 | Y | 5.1 | Y | C | 17 | Undefined |
| 24 | 51/M | D+S 24w | 60 | 25 | Y | 5.90 | Y | NR | NR | Relapse |
| 25 | 61/M | D+S 12w | 30 | 4 | Y | 6.10 | Y | NR | 7 | Undefined |
| 26 | 53/F | D+S 12w | 90 | 12 | Y | 3.44 | N | – | NR | Relapse |
| 27 | 50/M | D+S 12w | 60 | 9 | Y | 2.30 | Y | B | NR | Undefined |
| **Non-virologic failures** |
| 28 | 50/M | D+S 24w | 30 | 22 | Y | 6.02 | Y | A | NR | Death |
| 29 | 54/M | D+S+R 12w | 30 | 8 | Y | 5.52 | Y | A | 7 | Disc. for AEs |
| 30 | 58/M | D+S 12w | 30 | 11 | Y | 2.82 | N | – | NR | Disc. for AEs |
| 31 | 49/F | D+S 24w | 30 | 15 | N | 5.91 | Y | B | 15 | Death |
| 32 | 48/M | D+S 24w | 30 | 24 | Y | 6.24 | Y | A | NR | Death |
| 33 | 58/M | D+S 12w | 30 | 10 | Y | 4.91 | Y | C | 15 | Death |
| 34 | 56/M | D+S 12w | 60 | 2 | Y | 5.51 | Y | B | 19 | Death |

AE, adverse event; D, daclatasvir; Disc., discontinuation; HCV, hepatitis C virus; MELD, model for end-stage liver disease; NR, not reported; S, sofosbuvir; R, ribavirin; Tx, treatment; w, weeks.

\*Hepatocellular carcinoma at treatment access request.

**Supplemental Table 6. Baseline Characteristics by SVR12 Success or Failure**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter, n (%) unless otherwise indicated** | **Achieved SVR12****(N=373)** | **All Virologic Failures****(N=27)** | **Breakthrough or Relapse Only****(N=16)** | **Non-Virologic Failures****(N=7)** |
| Age, median (range) years  | 52.2 (34–74) | 51.2(42–64) | 52.5 (44–64) | 53.9 (48–58) |
| Male | 265 (73) | 17(65) | 10 (67) | 6 (86) |
| HCV-RNA at Day 0, median (IQR) log10 IU/mL HCV-RNA ≥6 log10 IU/mL | 6.1 (5.6–6.5)207 (55) | 6.0 (5.5–6.5)14 (52) | 6.0 (5.8–6.5)8 (50) | 5.5 (4.9–6.0)2 (29) |
| HCV genotype1 overall1a1b2346 | 256 (69)\*194 (53)55 (15)1 (<1)42 (11)69 (19)1 (<1) | 18 (69)16 (59)2 (7)03 (11)5 (19)0 | 11 (73)10 (63)1 (6)02 (13)2 (13)0 | 4 (57)3 (43)1 (14)02 (29)1 (14)0 |
| Advanced fibrosis (F3) | 72 (20) | 4 (15) | 3 (19) | 1 (14) |
| Cirrhosis  | 262 (71)  | 22 (81) | 12 (75) | 6 (86) |
| Child-Pugh stage†A B C | 188 (84) 34 (15) 3 (1) | 12 (71)4(24) 1 (6) | 8 (80) 2 (20) 0 | 3 (50) 2 (33) 1 (17) |
| MELD category at Day 0<1010 to <15≥15 | 57 (55)25 (24)22 (21) | 5 (50)3 (30)2 (20) | 2 (40)2 (40)1 (20) | 1 (25)03 (75) |
| Hepatocellular carcinoma  | 10 (3) | 2 (7) | 1 (6) | 0 |
| Extra-hepatic manifestationsWithout F3 or F4 fibrosis | 43 (12)23 (6) | 2 (7)1 (4) | 2 (13)1 (6) | 00 |
| Post-liver transplant HCV recurrence | 13 (3) | 0 | 0 | 0 |
| Pre-liver/renal transplant | 9 (2) | 4 (15) | 3 (19) | 0 |
| Treatment-experienced | 301 (82) | 23 (85) | 13 (81) | 6 (86) |
| DCV dose at initiation30 mg60 mg90 mg | 106 (28)230 (62)37 (10) | 10 (37)15 (56)2 (7) | 6 (38)9 (56)1 (6) | 6 (86)1 (14)0 |
| HIV RNA <50 copies/mL | 289 (95) | 26 (100) | 15 (100) | 7 (100) |
| CD4 cells/mm3, median (IQR) <200 cells/mm3 | 560 (336–763)26 (8) | 631 (380–792)3 (12) | 655 (371–796)3 (19) | 236 (158–390)3 (43) |
| Antiretroviral regimen‡Protease inhibitorsNon-nucleoside RT inhibitorsIntegrase inhibitorsMaravirocOther | 115 (32)85 (24)236 (66)16 (4)2 (1) | 15 (56)6 (22)15 (56)1 (4)0 | 8 (50)2 (13)9 (56)1 (6)0 | 6 (86)04 (57)00 |
| Laboratory results at TAR, median (IQR)Platelets, × 109/L Albumin, g/LALT, IU/LAST, IU/LTotal bilirubin, μmol /LGamma GT, IU/L | 137.0 (89–194)39.9 (35–43)61.0 (42–101)64.0 (41–93)12.5 (8–22)102.5 (60–172) | 128.5 (85–179)38.0 (32–41)71.0 (49–108)78.0 (47–132)14.0 (8–29)125.5 (45–201) | 146.0 (83–190)38.5 (34–43)71.0 (49–158)77.0 (41–169)14.0 (9–36)182.0 (45–216) | 92.0 (40–115)34.0 (30–38)52.0 (37–106)99.0 (61–147)50.0 (14–58)121.0 (51–182) |
| Laboratory abnormalities at day 0§Platelets <50 × 109/LAlbumin <35 g/LALT >175 IU/LAST >200 IU/LTotal bilirubin >60 μmol/LGamma GT >90 (women) or >140 (men) IU/L | 20 (6)68 (24)20 (6)11 (3)9 (3)118 (37) | 1 (4)8 (36)01 (4)012 (50) | 03 (27)0008 (62) | 1 (14)2 (33)002 (33)5 (83) |

ALT, alanine aminotransferase; AST, aspartate aminotransferase; DCV, daclatasvir; gamma GT, gamma glutamyl transferase; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile (25th–75th) range; MELD, model for end-stage liver disease; RBV, ribavirin; RT, reverse transcriptase; SOF, sofosbuvir; TAR, Treatment Access Request.

\*Includes seven genotype 1 patients of unknown/unspecified subtype.

†Determined for cirrhotic patients only

‡Excludes nucleoside analogs. Patients could receive more than one agent or class of agent.

§Data represent abnormalities grade ≥3 except for albumin.

Characteristics are at treatment access request except where indicated as day 0 (pre-treatment baseline). All percentages are of patients with available data in indicated category. Missing data for quoted percentages were:

* **Achieved SVR12** – sex (n=8); HCV genotype (n=4); advanced fibrosis (n=10); cirrhosis status (n=4); Child-Pugh class (n=37); MELD score (n=159); hepatocellular carcinoma (n=4); extra-hepatic manifestations (n=4); previous HCV treatment status (n=4); HIV RNA (n=68); CD4 cells (n=38); antiretroviral regimen (n=14); platelets (n=18); albumin (n=88); ALT (n=13); AST (n=14); total bilirubin (n=115); gamma GT (n=50).
* **All virologic failures** – sex (n = 1); Child-Pugh class (n = 5); MELD score (n = 14); HIV RNA (n = 1); CD4 cells (n = 1); platelets (n = 2); albumin (n = 5); ALT (n = 1); AST (n = 1); total bilirubin (n = 5); gamma GT (n = 3).
* **Breakthrough or relapse only** – sex (n = 1); Child-Pugh class (n = 2); MELD score (n = 9); platelets (n = 1); albumin (n = 5); HIV RNA (n = 1); ALT (n = 1); AST (n = 1); total bilirubin (n = 4); gamma GT (n = 3).
* **Non-virologic failures** – MELD score (n=2); total bilirubin (n=1); gamma GT (n=1).

**Supplemental Table 7. Adverse Events Reported as Serious**

| **n (%)** | **All Treated(N=617)\*** | **DCV+SOF (N=531)** | **DCV+SOF+RBV(N=74)** |
| --- | --- | --- | --- |
| **Patients with ≥1 serious adverse event** | **55 (9)** | **47 (9)** | **7 (10)** |
| **General disorders and administration site conditions** | **19 (3)** | **16 (3)** | **2 (3)** |
|  Asthenia Fatigue Multi-organ failure Pyrexia Unspecified Chills Death Drug ineffective Influenza like illness Edema Edema peripheral Pain Ulcer hemorrhage | 6 (1)4 (1)3 (<1)2 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 6 (1)3 (1)3 (1)2 (<1)1 (<1)1 (<1)1 (<1)01 (<1)1 (<1)1 (<1)1 (<1)0 | 00000001 (1)00001 (1) |
| **Gastrointestinal disorders** | **15 (2)** | **13 (2)** | **1 (1)** |
|  Ascites Abdominal pain Abdominal pain upper Constipation Diarrhea Nausea Abdominal distension Diarrhea hemorrhagic Gastrointestinal disorder Hemorrhoids Intestinal obstruction Subileus Upper gastrointestinal hemorrhage Vomiting | 4 (1)2 (<1)2 (<1)2 (<1)2 (<1)2 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 3 (1)2 (<1)1 (<1)2 (<1)1 (<1)2 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 1 (1)0000000000000 |
| **Infections and infestations** | **13 (2)** | **10 (2)** | **3 (4)** |
|  Bronchitis Sepsis Septic shock Gastroenteritis Herpes zoster Influenza Lung infection Nasopharyngitis Parotitis Pharyngeal abscess Pneumonia Pyelonephritis acute Upper respiratory tract infection Urinary tract infection | 2 (<1)2 (<1)2 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 1 (<1)2 (<1)2 (<1)1 (<1)01 (<1)1 (<1)1 (<1)1 (<1)1 (<1)01 (<1)01 (<1) | 1 (1)0001 (1)000001 (1)01 (1)0 |
| **Nervous system disorders** | **13 (2)** | **11 (2)** | **2 (3)** |
|  Headache Hepatic encephalopathy Cerebral hematoma Coma Disturbance in attention Dysesthesia Epilepsy Generalized tonic-clonic seizure Transient ischemic attack | 5 (1)2 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 5 (1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)0 | 01 (1)0000001 (<1) |
| **Psychiatric disorders** | **11 (2)** | **8 (2)** | **2 (3)** |
|  Insomnia Sleep disorder Abnormal behavior Affective disorder Anxiety Delirium Depression Suicide attempt | 4 (1) | 2 (<1) | 1 (1) |
| 3 (0.5)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 3 (1)1 (<1)1 (<1)01 (<1)01 (<1) | 0001 (1)01 (1)0 |
| **Injury, poisoning, and procedural complications** | **9 (1)** | **8 (2)** | **1 (1)** |
|  Fall Overdose Ankle fracture Contusion Femoral neck fracture Foot fracture Road traffic accident Tibia fracture Underdose | 2 (<1)2 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 2 (<1)2 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)01 (<1) | 00000001 (1)0 |
| **Neoplasms benign, malignant, and unspecified**  | **8 (1)** | **7 (1)** | **1 (1)** |
|  Hepatocellular carcinoma Castleman's disease Hepatic cancer Hodgkin's disease Lymphoma Malignant neoplasm progression | 4 (1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 3 (1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 1 (1)00000 |
| **Respiratory, thoracic, and mediastinal disorders** | **8 (1)** | **8 (2)** | **0** |
|  Dyspnea Acute respiratory distress syndrome Cough Dyspnea exertional Lung disorder Pulmonary arterial hypertension Respiratory distress | 3 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 3 (1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 0000000 |
| **Vascular disorders** | **8 (1)** | **7 (1)** | **1 (1)** |
|  Hypertension Cryoglobulinemia Hypovolemic shock Phlebitis superficial | 5 (1)1 (<1)1 (<1)1 (<1) | 4 (1)1 (<1)1 (<1)1 (<1) | 1 (1)000 |
| **Blood and lymphatic system disorders** | **6 (1)** | **6 (1)** | **0** |
|  Anemia Thrombocytopenia Leukopenia | 3 (<1)3 (<1)1 (<1) | 3 (1)3 (1)1 (<1) | 000 |
| **Hepatobiliary disorders** | **6 (1)** | **6 (1)** | **0** |
|  Hepatic cirrhosis Bile duct stenosis Hepatorenal syndrome Jaundice Portal vein thrombosis | 2 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 2 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 00000 |
| **Musculoskeletal and connective tissue disorders** | **6 (1)** | **6 (1)** | **0** |
|  Arthralgia Myalgia Hypercreatinemia Muscle spasms Pain in extremity Torticollis | 2 (<1) | 2 (<1) | 0 |
| 2 (<1) | 2 (<1) | 0 |
| 1 (<1) | 1 (<1) | 0 |
| 1 (<1) | 1 (<1) | 0 |
| 1 (<1) | 1 (<1) | 0 |
| 1 (<1) | 1 (<1) | 0 |
| **Metabolism and nutrition disorders** | **5 (1)** | **4 (1)** | **1 (1)** |
|  Cell death Diabetes mellitus Diabetes mellitus inadequate control Hypertriglyceridemia Malnutrition | 1 (<1)1 (<1)1 (<1)1 (<1)1 (<1) | 01 (<1)1 (<1)1 (<1)1 (<1) | 1 (1)0000 |
| **Cardiac disorders** | **4 (1)** | **2 (<1)** | **1 (1)** |
|  Acute coronary syndrome Atrioventricular block complete Bundle branch block Tachycardia | 1 (<1)1 (<1)1 (<1)1 (<1) | 1 (<1)1 (<1)00 | 0001 (1) |
| **Renal and urinary disorders** | **4 (1)** | **4 (1)** | **0** |
|  Acute kidney injury Calculus ureteric Glomerulonephritis Renal failure | 2 (<1)1 (<1)1 (<1)1 (<1) | 2 (<1)1 (<1)1 (<1)1 (<1) | 0000 |
| **Skin and subcutaneous tissue disorders** | **3 (<1)** | **3 (1)** | **0** |
|  Skin lesion Pruritus Rash | 2 (<1)1 (<1)1 (<1) | 2 (<1)1 (<1)1 (<1) | 000 |
| **Surgical and medical procedures** | **2 (<1)** | **2 (<1)** | **0** |
|  Surgery | 2 (<1) | 2 (<1) | 0 |
| **Endocrine disorders** | **1 (<1)** | **1 (<1)** | **0** |
|  Basedow's disease | 1 (<1) | 1 (<1) | 0 |
| **Investigations** | **1 (<1)** | **1 (<1)** | **0** |
|  Blood creatine phosphokinase increased | 1 (<1) | 1 (<1) | 0 |
| **Reproductive system and breast disorders** | **1 (<1)** | **1 (<1)** | **0** |
|  Gynecomastia | 1 (<1) | 1 (<1) | 0 |

DCV, daclatasvir; RBV, ribavirin; SOF, sofosbuvir.\*Includes 12 patients with missing regimen details.

**Supplemental Table 8. Adverse Events Reported as Grade 3 (Severe) or Grade 4 (Life-Threatening) by Cirrhosis Status**

| **n (%)** | **Total(N=617)\*** | **Cirrhotic(N=435)** | **Noncirrhotic(N=177)** |
| --- | --- | --- | --- |
| **Patients with at least one grade 3-4 AE** | 26 (4) | 19 (4) | 5 (3) |
| **General disorders and administration site conditions** | **3 (<1)** | **2 (<1)** | **1 (1)** |
| Multi-organ failureAstheniaPain | 1 (<1)1 (<1)1 (<1) | 01 (<1)1 (<1) | 1 (1)00 |
| **Neoplasms benign, malignant, and unspecified**  | **4 (1)** | **3 (1)** | **0** |
| Hepatocellular carcinomaHodgkin's disease | 3 (<1)1 (<1) | 3 (1)0 | 00 |
| **Gastrointestinal disorders** | **4 (1)** | **2 (<1)** | **2 (1)** |
| AscitesDiarrhea hemorrhagicGastrointestinal disorderUpper gastrointestinal hemorrhage | 2 (<1)1 (<1)1 (<1)1 (<1) | 2 (<1)01 (<1)0 | 01 (1)01 (1) |
| **Injury, poisoning, and procedural complications** | **4 (1)** | **4 (1)** | **0** |
| FallFemoral neck fractureOverdoseRoad traffic accident | 1 (<1)1 (<1)1 (<1)1 (<1) | 1 (<1)1 (<1)1 (<1)1 (<1) | 0000 |
| **Cardiac disorders** | **3 (<1)** | **2 (<1)** | **1 (1)** |
| Acute coronary syndromeAtrioventricular block completeBundle branch block | 1 (<1)1 (<1)1 (<1) | 01 (<1)1 (<1) | 1 (1)00 |
| **Hepatobiliary disorders** | **2 (<1)** | **2 (<1)** | **0** |
| Hepatic cirrhosisPortal vein thrombosis | 1 (<1)1 (<1) | 1 (<1)1 (<1) | 00 |
| **Metabolism and nutrition disorders** | **3 (<1)** | **2 (<1)** | **0** |
| Cell deathHypertriglyceridemiaMalnutrition | 1 (<1)1 (<1)1 (<1) | 01 (<1)1 (<1) | 000 |
| **Nervous system disorders** | **2 (<1)** | **2 (<1)** | **0** |
| Hepatic encephalopathyComa | 2 (<1)1 (<1) | 2 (<1)1 (<1) | 00 |
| **Blood and lymphatic system disorders** | **2 (<1)** | **1 (<1)** | **1 (1)** |
| Anemia | 2 (<1) | 1 (<1) | 1 (1) |
| **Infections and infestations** | **2 (<1)** | **2 (<1)** | **0** |
| PneumoniaPyelonephritis acuteSepsis | 1 (<1)1 (<1)1 (<1) | 1 (<1)1 (<1)1 (<1) | 000 |
| **Psychiatric disorders** | **2 (<1)** | **1 (<1)** | **1 (1)** |
| DepressionInsomniaSuicide attempt | 1 (<1)1 (<1)1 (<1) | 1 (<1)1 (<1)0 | 001 (1) |
| **Respiratory, thoracic, and mediastinal disorders** | **2 (<1)** | **1 (<1)** | **1 (1)** |
| DyspneaRespiratory distress | 1 (<1)1 (<1) | 01 (<1) | 1 (1)0 |
| **Investigations** | **1 (<1)** | **1 (<1)** | **0** |
| Blood creatine phosphokinase increased | 1 (<1) | 1 (<1) | 0 |
| **Renal and urinary disorders** | **1 (<1)** | **1 (<1)** | **0** |
| Acute kidney injury | 1 (<1) | 1 (<1) | 0 |
| **Vascular disorders** | **1 (<1)** | **1 (<1)** | **0** |
| Hypertension | 1 (<1) | 1 (<1) | 0 |

AE, adverse event.
\*Includes five patients of unknown cirrhosis status

**Supplemental Table 9. Summary of Patient Deaths**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **No.** | **Age/Sex** | **Child-Pugh****Class** | **MELD****Score****(Day 0)** | **CD4****Cells/mm3****(Day 0)** | **Cause of Death** | **Relatedness to Treatment****(as Reported)** |
| 1 | 55/M | B | 19 | 135 | Decompensated cirrhosis | Possibly related\* |
| Multi-organ failure | NR† |
| 2 | 58/M | C | 15 | 188 | Multi-organ failureHepatorenal syndrome | Not related |
| 3 | 49/F | B | 15 | 236 | Septic shockAcute respiratory distress syndrome | Not related |
| 4 | 55/F | B | NR | 72 | Multi-organ failureSeptic shockIntestinal obstruction | NR† |
| 5 | 54/F | A | 7 | NR | Unknown | Not related |
| 6 | 44/M | B | 13 | 1138 | Respiratory distress | Not related |
| 7 | 48/M | A | NR | 390 | Carcinoma | Not related |
| 8 | 47/M | A | NR | NR | Road traffic accident | Not related |
| 9 | 50/M | A | NR | 358 | Undifferentiated carcinoma (hepatic) | NR† |
| 10 | 49/M | B | NR | 314 | Intracerebral hematoma (due to fall)  | Not related |

MELD, model for end-stage liver diease; NR, not reported.

All patients were receiving daclatasvir and sofosbuvir without ribavirin.

\*Considered possibly related to HCV or HIV treatment (tenofovir disoproxil fumarate, emtricitabine, dolutegravir) by attending physician.

†Imputed as treatment-related.

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