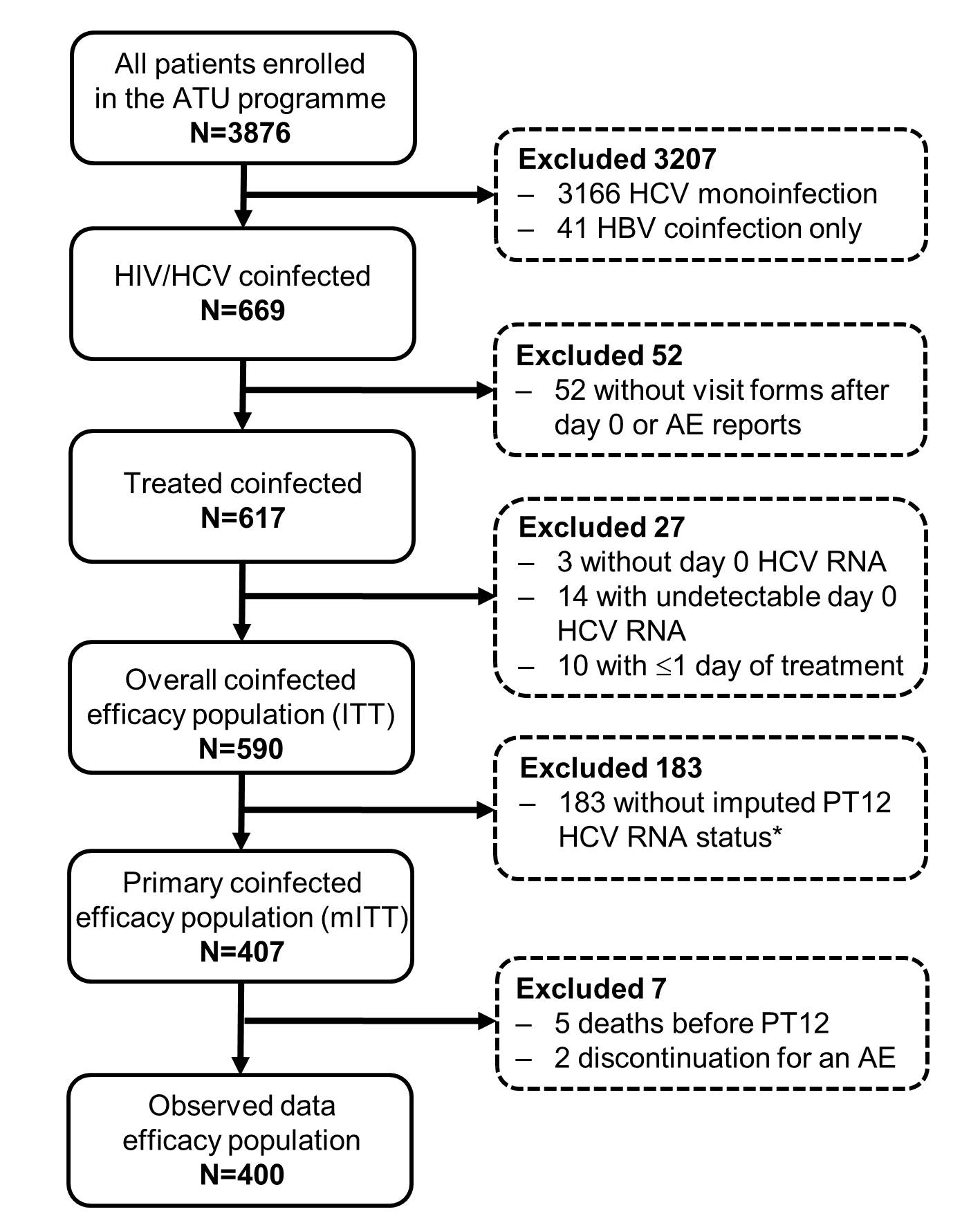
**SUPPLEMENTAL DIGITAL CONTENT**

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‡ |
| Ascites  Slight/moderate or medically controlled  Severe/not controlled | 19 (5)  3 (1) | 11 (6)  2 (1) | 0.652|| |
| Encephalopathy  Slight/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 weeks  10–<14 weeks  14–<20 weeks  ≥20 weeks | 17 (4)  86 (21)  14 (3)  290 (71) | 23 (13)  37 (20)  19 (10)  104 (57) | **<0.001†** |
| Antiretroviral use  NRTI  NNRTI  PI  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/L  Albumin, g/L  ALT, IU/L  AST, IU/L  Total bilirubin, μmol/L  Gamma 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 TAR  Platelets <25 ×109/L  Albumin <35 g/L  ALT >175 IU/L  AST >200 IU/L  Total bilirubin >60 μmol/L  Gamma GT >90 (women) or >140 (men) IU/L | 2 (1)  86 (25)  23 (6)  11 (3)  11 (3)  151 (40) | 0  34 (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)¶  <10  10–<15  ≥15 | 35 (53)  14 (21)  17 (26) | 12 (57)  6 (29)  3 (14) | 0.564|| |
| Ascites  Slight/moderate or medically controlled  Severe/not controlled | 10 (4)  1 (<1) | 4 (10)  1 (3) | 0.061|| |
| Encephalopathy  Slight/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 use  NRTI  NNRTI  PI  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/L  Albumin, g/L  ALT, IU/L  AST, IU/L  Total bilirubin, μmol/L  Gamma 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/L  Albumin <35 g/L  ALT >175 IU/L  AST >200 IU/L  Total bilirubin >60 μmol/L  Gamma GT >90 (women) or >140 (men) IU/L | 2 (1)  48 (24)  16 (6)  7 (3)  5 (3)  81 (36) | 0  11 (37)  0  1 (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**  mITT  Observed values† | 203  200 | 29  29 | 11  10 | 141  139 | 22  22 |
| **SVR12, n (%) [95% CI]**  mITT  Observed 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 breakthrough  Relapse  Undefined virologic failure§  Non-virologic failure | 15  1  7  4  3 | 5  1  1  3  0 | 3  0  1  1  1 | 7  0  5  0  2 | 0  -  -  -  - |
| **Patients with Child-Pugh B cirrhosis\*** | | | | | |
| **N**  mITT  Observed values† | 40‡  38‡ | 8  7 | 0  0 | 27  26 | 3  3 |
| **SVR12, n (%) [95% CI]**  mITT  Observed 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 breakthrough  Relapse  Undefined virologic failure§  Non-virologic failure | 6  0  2  2  2 | 4  0  1  2  1 | -  -  -  -  - | 2  0  1  0  1 | 0  -  **-**  -  - |
| **Patients with Child-Pugh C cirrhosis\*** | | | | | |
| **N**  mITT  Observed values† | 5  4 | 2  1 | 0  0 | 2  2 | 1  1 |
| **SVR12, n (%) [95% CI]**  mITT  Observed 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 breakthrough  Relapse  Undefined virologic failure§  Non-virologic failure | 2  0  0  1  1 | 2  0  0  1  1 | -  -  -  -  - | 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 genotype  1 overall  1a  1b  2  3  4  6 | 256 (69)\*  194 (53)  55 (15)  1 (<1)  42 (11)  69 (19)  1 (<1) | 18 (69)  16 (59)  2 (7)  0  3 (11)  5 (19)  0 | 11 (73)  10 (63)  1 (6)  0  2 (13)  2 (13)  0 | 4 (57)  3 (43)  1 (14)  0  2 (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  <10  10 to <15  ≥15 | 57 (55)  25 (24)  22 (21) | 5 (50)  3 (30)  2 (20) | 2 (40)  2 (40)  1 (20) | 1 (25)  0  3 (75) |
| Hepatocellular carcinoma | 10 (3) | 2 (7) | 1 (6) | 0 |
| Extra-hepatic manifestations  Without F3 or F4 fibrosis | 43 (12)  23 (6) | 2 (7)  1 (4) | 2 (13)  1 (6) | 0  0 |
| 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 initiation  30 mg  60 mg  90 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 inhibitors  Non-nucleoside RT inhibitors  Integrase inhibitors  Maraviroc  Other | 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)  0  4 (57)  0  0 |
| Laboratory results at TAR, median (IQR)  Platelets, × 109/L  Albumin, g/L  ALT, IU/L  AST, IU/L  Total bilirubin, μmol /L  Gamma 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/L  Albumin <35 g/L  ALT >175 IU/L  AST >200 IU/L  Total bilirubin >60 μmol/L  Gamma GT >90 (women) or >140 (men) IU/L | 20 (6)  68 (24)  20 (6)  11 (3)  9 (3)  118 (37) | 1 (4)  8 (36)  0  1 (4)  0  12 (50) | 0  3 (27)  0  0  0  8 (62) | 1 (14)  2 (33)  0  0  2 (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)  0  1 (<1)  1 (<1)  1 (<1)  1 (<1)  0 | 0  0  0  0  0  0  0  1 (1)  0  0  0  0  1 (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)  0  0  0  0  0  0  0  0  0  0  0  0  0 |
| **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)  0  1 (<1)  1 (<1)  1 (<1)  1 (<1)  1 (<1)  0  1 (<1)  0  1 (<1) | 1 (1)  0  0  0  1 (1)  0  0  0  0  0  1 (1)  0  1 (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 | 0  1 (1)  0  0  0  0  0  0  1 (<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)  0  1 (<1)  0  1 (<1) | 0  0  0  1 (1)  0  1 (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)  0  1 (<1) | 0  0  0  0  0  0  0  1 (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)  0  0  0  0  0 |
| **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) | 0  0  0  0  0  0  0 |
| **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)  0  0  0 |
| **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) | 0  0  0 |
| **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) | 0  0  0  0  0 |
| **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) | 0  1 (<1)  1 (<1)  1 (<1)  1 (<1) | 1 (1)  0  0  0  0 |
| **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)  0  0 | 0  0  0  1 (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) | 0  0  0  0 |
| **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) | 0  0  0 |
| **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 failure  Asthenia  Pain | 1 (<1)  1 (<1)  1 (<1) | 0  1 (<1)  1 (<1) | 1 (1)  0  0 |
| **Neoplasms benign, malignant, and unspecified** | **4 (1)** | **3 (1)** | **0** |
| Hepatocellular carcinoma  Hodgkin's disease | 3 (<1)  1 (<1) | 3 (1)  0 | 0  0 |
| **Gastrointestinal disorders** | **4 (1)** | **2 (<1)** | **2 (1)** |
| Ascites  Diarrhea hemorrhagic  Gastrointestinal disorder  Upper gastrointestinal hemorrhage | 2 (<1)  1 (<1)  1 (<1)  1 (<1) | 2 (<1)  0  1 (<1)  0 | 0  1 (1)  0  1 (1) |
| **Injury, poisoning, and procedural complications** | **4 (1)** | **4 (1)** | **0** |
| Fall  Femoral neck fracture  Overdose  Road traffic accident | 1 (<1)  1 (<1)  1 (<1)  1 (<1) | 1 (<1)  1 (<1)  1 (<1)  1 (<1) | 0  0  0  0 |
| **Cardiac disorders** | **3 (<1)** | **2 (<1)** | **1 (1)** |
| Acute coronary syndrome  Atrioventricular block complete  Bundle branch block | 1 (<1)  1 (<1)  1 (<1) | 0  1 (<1)  1 (<1) | 1 (1)  0  0 |
| **Hepatobiliary disorders** | **2 (<1)** | **2 (<1)** | **0** |
| Hepatic cirrhosis  Portal vein thrombosis | 1 (<1)  1 (<1) | 1 (<1)  1 (<1) | 0  0 |
| **Metabolism and nutrition disorders** | **3 (<1)** | **2 (<1)** | **0** |
| Cell death  Hypertriglyceridemia  Malnutrition | 1 (<1)  1 (<1)  1 (<1) | 0  1 (<1)  1 (<1) | 0  0  0 |
| **Nervous system disorders** | **2 (<1)** | **2 (<1)** | **0** |
| Hepatic encephalopathy  Coma | 2 (<1)  1 (<1) | 2 (<1)  1 (<1) | 0  0 |
| **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** |
| Pneumonia  Pyelonephritis acute  Sepsis | 1 (<1)  1 (<1)  1 (<1) | 1 (<1)  1 (<1)  1 (<1) | 0  0  0 |
| **Psychiatric disorders** | **2 (<1)** | **1 (<1)** | **1 (1)** |
| Depression  Insomnia  Suicide attempt | 1 (<1)  1 (<1)  1 (<1) | 1 (<1)  1 (<1)  0 | 0  0  1 (1) |
| **Respiratory, thoracic, and mediastinal disorders** | **2 (<1)** | **1 (<1)** | **1 (1)** |
| Dyspnea  Respiratory distress | 1 (<1)  1 (<1) | 0  1 (<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 failure  Hepatorenal syndrome | Not related |
| 3 | 49/F | B | 15 | 236 | Septic shock  Acute respiratory distress syndrome | Not related |
| 4 | 55/F | B | NR | 72 | Multi-organ failure  Septic shock  Intestinal 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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