**Supplemental Tables and Figures**

**Supplemental Table 1.** Direct-acting antiviral (DAA) regimen generation categories

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Generation 1** | **Generation 2** | **Pangenotypic** |
| **Drug Name** | sofosbuvir | daclatasvir + sofosbuvir | velpatasvir + sofosbuvir |
| grazoprevir + elbasvir |
| paritoprevir + ritonavir + ombitasvir  (+/- dasabuvir) | voxilaprevir + velpatasvir + sofosbuvir |
| simeprevir + sofosbuvir | glecaprevir + pibrentasvir |
| sofosbuvir + ledipasvir |

**Supplemental Table 2.** Adjuvant ribavirin (RBV) treatment status and p-values before and after adjustment for propensity scores across patient, viral, and previous treatment characteristics.

| **Variable** | **Response** | **NoRBV (N= 2998)** | **RBV-treated**  **(N= 1135)** | **p-value: Unweighted** | **p-value: Weighted** |
| --- | --- | --- | --- | --- | --- |
| Age Group (in years) | <40 | 194 (6%) | 58 (5%) | **0.007** | 0.857 |
| 40<50 | 232 (8%) | 81 (7%) |  |  |
| 50<60 | 955 (32%) | 439 (39%) |  |  |
| ≥60 | 1617 (54%) | 557 (49%) |  |  |
| Sex | Female | 1170 (39%) | 408 (36%) | 0.309 | 0.660 |
| Male | 1828 (61%) | 727 (64%) |  |  |
| Race Category | Asian American/ Pacific Islander | 167 (6%) | 68 (6%) | **0.021** | 0.891 |
| Black/ African American | 885 (30%) | 180 (16%) |  |  |
| White | 1827 (61%) | 824 (73%) |  |  |
| Unknown/Other | 119 (4%) | 63 (6%) |  |  |
| Insurance Type | Medicaid | 512 (17%) | 207 (18%) | **0.028** | 0.964 |
| Medicare | 1076 (36%) | 356 (31%) |  |  |
| Private | 1356 (45%) | 556 (49%) |  |  |
| None | 48 (2%) | 13 (1%) |  |  |
| Prior Treatment Status | Treatment Naive | 2333 (78%) | 691 (61%) | **<.001** | 0.065 |
| IFN-based TF | 604 (20%) | 375 (33%) |  |  |
| DAA-based TF | 61 (2%) | 69 (6%) |  |  |
| HCV Genotype | 1 | 2485 (83%) | 582 (51%) | **<.001** | 0.239 |
| 2 | 161 (5%) | 270 (24%) |  |  |
| 3 | 36 (1%) | 28 (2%) |  |  |
| other | 316 (11%) | 255 (22%) |  |  |
| HIV at Index Date | No | 2917 (97%) | 1109 (98%) | 0.545 | 0.552 |
| Yes | 81 (3%) | 26 (2%) |  |  |
| HBV at Index Date | No | 2991 (100%) | 1126 (99%) | 0.102 | 0.486 |
| Yes | 7 (0%) | 9 (1%) |  |  |
| Diabetes at Index Date | No | 2023 (67%) | 788 (69%) | 0.517 | 0.156 |
| Yes | 975 (33%) | 347 (31%) |  |  |
| Median Household Income | <$15K | 92 (3%) | 31 (3%) | **<.001** | 0.387 |
| $15<30K | 477 (16%) | 148 (13%) |  |  |
| $30<50K | 1039 (35%) | 461 (41%) |  |  |
| $50<75K | 695 (23%) | 297 (26%) |  |  |
| ≥$75K | 286 (10%) | 116 (10%) |  |  |
| Missing | 409 (14%) | 82 (7%) |  |  |
| Charlson-Deyo Comorbidity Score | 0 | 1430 (48%) | 395 (35%) | **0.029** | 0.989 |
| 1 | 705 (24%) | 303 (27%) |  |  |
| 2 | 261 (9%) | 93 (8%) |  |  |
| 3 | 602 (20%) | 344 (30%) |  |  |
| Fibrosis-4 Index Category | ≤1.21 | 477 (16%) | 115 (10%) | **<.001** | 0.653 |
| 1.21≥5.88 | 1791 (60%) | 660 (58%) |  |  |
| >5.88 | 328 (11%) | 270 (24%) |  |  |
| Missing | 402 (13%) | 90 (8%) |  |  |
| Cirrhosis Status | Non-Cirrhosis | 1945 (65%) | 476 (42%) | **<.001** | 0.630 |
| Compensated Cirrhosis | 964 (32%) | 518 (46%) |  |  |
| Decompensated Cirrhosis | 89 (3%) | 141 (12%) |  |  |
| BMI Category (kg/m2) | <25 | 733 (24%) | 271 (24%) | 0.480 | 0.852 |
| 25>30 | 966 (32%) | 384 (34%) |  |  |
| ≥30 | 1231 (41%) | 456 (40%) |  |  |
| CHeCS Site | KPNW | 629 (21%) | 302 (27%) | **<.001** | 0.146 |
| KPHI | 267 (9%) | 155 (14%) |  |  |
| HFHS | 1486 (50%) | 467 (41%) |  |  |
| GHS | 616 (21%) | 211 (19%) |  |  |

Generation 1: sofosbuvir (SOF) with ribavirin (RBV); Generation 2: daclatasvir +SOF, grezoprevir +elbasvir, paritoprevir +ritonavir +ombitasvir (with and without dasabuvir), simeprevir +SOF, and SOF +ledipasvir; and Pangenotypic: velpatasavir+SOF, voxilaprevir+velpatasvir+SOF, and glecaprevir+pibrentasvir. DAA: direct-acting antiviral; TF: treatment failure; IFN: interferon-based treatment; PPI: proton-pump inhibitors; GT: hepatitis C genotype; HBV: chronic hepatitis B infection; Diab: type 2 diabetes; RBV: ribavirin. BMI: body mass index (kg/m2); GHS: Geisinger Clinic (Danville PA); HFHS: Henry Ford Health System (Detroit MI); KPHI: Kaiser-Permanente, Hawai’I (Honolulu, HI); KPNW: Kaiser-Permanente Northwest (Portland, OR);

**Supplemental Table 3.** Adverse Event (AE) distribution by DAA generation and use of ribavirin

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Adverse event** | **Gen1** | **Gen2** | | **Pangenotypic** | | **Total events** |
| **+RBV** | **No RBV** | **+RBV** | **No RBV** | **+RBV** |
| n (%) | n (%) | n (%) | n (%) | n (%) | n (%) |
| **Overall toxicity** | 135 (32.3) | 146 (5.5) | 184 (28.4) | 19 (5.5) | 10 (14.5) | 494 (12) |
| **Anemia** | 67 (16) | 7 (0.3) | 100 (15.4) | 3 (0.9) | 3 (4.3) | 180 (4.4) |
| **Appetite-decreased** | 2 (0.5) | 1 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (0.1) |
| **Bradycardia** | 7 (1.7) | 0 (0) | 3 (0.5) | 0 (0) | 0 (0) | 10 (0.2) |
| **Chills** | 0 (0) | 0 (0) | 1 (0.2) | 0 (0) | 0 (0) | 1 (0) |
| **Depression** | 6 (1.4) | 9 (0.3) | 5 (0.8) | 0 (0) | 1 (1.4) | 21 (0.5) |
| **Diarrhea** | 3 (0.7) | 7 (0.3) | 3 (0.5) | 0 (0) | 1 (1.4) | 14 (0.3) |
| **Dyspnea** | 1 (0.2) | 10 (0.4) | 6 (0.9) | 1 (0.3) | 0 (0) | 18 (0.4) |
| **Fatigue** | 18 (4.3) | 4 (0.2) | 21 (3.2) | 1 (0.3) | 1 (1.4) | 45 (1.1) |
| **Fever** | 0 (0) | 1 (0) | 4 (0.6) | 0 (0) | 0 (0) | 5 (0.1) |
| **Flu-like symptoms** | 3 (0.7) | 5 (0.2) | 3 (0.5) | 1 (0.3) | 0 (0) | 12 (0.3) |
| **Headache** | 4 (1) | 13 (0.5) | 4 (0.6) | 1 (0.3) | 0 (0) | 22 (0.5) |
| **Hepatic decompensation** | 1 (0.2) | 10 (0.4) | 4 (0.6) | 1 (0.3) | 0 (0) | 16 (0.4) |
| **Insomnia** | 12 (2.9) | 13 (0.5) | 15 (2.3) | 4 (1.2) | 0 (0) | 44 (1.1) |
| **Irritability** | 6 (1.4) | 0 (0) | 1 (0.2) | 0 (0) | 0 (0) | 7 (0.2) |
| **Jaundice** | 0 (0) | 0 (0) | 1 (0.2) | 0 (0) | 0 (0) | 1 (0) |
| **Muscle aches/ pain** | 4 (1) | 6 (0.2) | 3 (0.5) | 0 (0) | 0 (0) | 13 (0.3) |
| **Myocardial infarction** | 0 (0) | 1 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0) |
| **Nausea** | 14 (3.3) | 21 (0.8) | 19 (2.9) | 6 (1.7) | 2 (2.9) | 62 (1.5) |
| **Neutropenia** | 1 (0.2) | 1 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (0) |
| **Other** | 0 (0) | 0 (0) | 9 (1.4) | 0 (0) | 0 (0) | 9 (0.2) |
| **Pancreatitis** | 0 (0) | 4 (0.2) | 0 (0) | 0 (0) | 0 (0) | 4 (0.1) |
| **Pancytopenia** | 0 (0) | 1 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0) |
| **Pneumonia** | 3 (0.7) | 5 (0.2) | 1 (0.2) | 0 (0) | 0 (0) | 9 (0.2) |
| **Pruritis** | 0 (0) | 1 (0) | 2 (0.3) | 0 (0) | 0 (0) | 3 (0.1) |
| **Skin reaction** | 13 (3.1) | 15 (0.6) | 25 (3.9) | 1 (0.3) | 1 (1.4) | 55 (1.3) |
| **Suicidal ideation/ attempt** | 0 (0) | 1 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0) |
| **Vomiting** | 3 (0.7) | 13 (0.5) | 10 (1.5) | 3 (0.9) | 1 (1.4) | 30 (0.7) |
| **Total** | 418 (100) | 2653 (100) | 648 (100) | 343 (100) | 69 (100) | 4131 (100) |

Generation 1: sofosbuvir (SOF) with ribavirin (RBV); Generation 2: daclatasvir +SOF, grezoprevir +elbasvir, paritoprevir +ritonavir +ombitasvir (with and without dasabuvir), simeprevir +SOF, and SOF +ledipasvir; and Pangenotypic: velpatasavir+SOF, voxilaprevir+velpatasvir+SOF, and glecaprevir+ pibrentasvir.

**Supplemental Table 4.** Severe Adverse Event (SAE) distribution by DAA generations

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Severe adverse event** | **Gen1** | **Gen2** | | **Gen3** | | **Total events** |
| **+RBV** | **no RBV** | **+RBV** | **no RBV** | **+RBV** |
| **Overall toxicity** | 19 (4.5) | 60 (2.3) | 26 (4) | 4 (1.2) | 0 (0) | 109 (2.6) |
| **Anemia** | 3 (0.7) | 3 (0.1) | 3 (0.5) | 3 (0.9) | 0 (0) | 12 (0.3) |
| **Appetite-decreased** | 1 (0.2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0) |
| **Bradycardia** | 1 (0.2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0) |
| **Chills** | 0 (0) | 0 (0) | 1 (0.2) | 0 (0) | 0 (0) | 1 (0) |
| **Depression** | 0 (0) | 1 (0) | 1 (0.2) | 0 (0) | 0 (0) | 2 (0) |
| **Diarrhea** | 0 (0) | 3 (0.1) | 2 (0.3) | 0 (0) | 0 (0) | 5 (0.1) |
| **Dyspnea** | 1 (0.2) | 3 (0.1) | 2 (0.3) | 0 (0) | 0 (0) | 6 (0.1) |
| **Fatigue** | 1 (0.2) | 0 (0) | 2 (0.3) | 0 (0) | 0 (0) | 3 (0.1) |
| **Fever** | 0 (0) | 0 (0) | 2 (0.3) | 0 (0) | 0 (0) | 2 (0) |
| **Headache** | 1 (0.2) | 1 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (0) |
| **Hepatic decompensation** | 1 (0.2) | 10 (0.4) | 4 (0.6) | 1 (0.3) | 0 (0) | 16 (0.4) |
| **Insomnia** | 1 (0.2) | 2 (0.1) | 0 (0) | 0 (0) | 0 (0) | 3 (0.1) |
| **Jaundice** | 0 (0) | 0 (0) | 1 (0.2) | 0 (0) | 0 (0) | 1 (0) |
| **Muscle aches/ pain** | 2 (0.5) | 1 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (0.1) |
| **Myocardial infarction** | 0 (0) | 1 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0) |
| **Nausea** | 2 (0.5) | 5 (0.2) | 2 (0.3) | 0 (0) | 0 (0) | 9 (0.2) |
| **Other** | 6 (1.4) | 24 (0.9) | 10 (1.5) | 0 (0) | 0 (0) | 40 (1) |
| **Pancreatitis** | 0 (0) | 4 (0.2) | 0 (0) | 0 (0) | 0 (0) | 4 (0.1) |
| **Pneumonia** | 2 (0.5) | 2 (0.1) | 0 (0) | 0 (0) | 0 (0) | 4 (0.1) |
| **Pneumonitis** | 0 (0) | 0 (0) | 1 (0.2) | 0 (0) | 0 (0) | 1 (0) |
| **Skin reaction** | 0 (0) | 3 (0.1) | 1 (0.2) | 0 (0) | 0 (0) | 4 (0.1) |
| **Suicidal ideation/ attempt** | 0 (0) | 1 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (0) |
| **Vomiting** | 1 (0.2) | 6 (0.2) | 2 (0.3) | 0 (0) | 0 (0) | 9 (0.2) |
| **Total** | 418 (100) | 2653 (100) | 648 (100) | 343 (100) | 69 (100) | 4131 (100) |

Generation 1: sofosbuvir (SOF) with ribavirin (RBV); Generation 2: daclatasvir +SOF, grezoprevir +elbasvir, paritoprevir +ritonavir +ombitasvir (with and without dasabuvir), simeprevir +SOF, and SOF +ledipasvir; and Pangenotypic 3: velpatasavir+SOF, voxilaprevir+velpatasvir+SOF, and glecaprevir+ pibrentasvir.

**Supplemental Figure 1.** Pairwise comparisons of the effect of ribavirin and cirrhosis category on the likelihood of sustained virological response (SVR) at 12 weeks after the end of treatment.

aOR: adjusted odds ratio; CI: confidence interval; RBV: ribavirin.

C:\Users\strudea1\Downloads\SVR_RBV_odds_OR_043019_cirr2 (1).tiff