| **Author year Country*Quality*** | **Treatment Regimen (1x/day unless otherwise noted)** | **Clinical Outcomes** | **Adverse Events** | **Funding Source** |
| --- | --- | --- | --- | --- |
| Abergel 2016a142France*Fair* | Ledipasvir 90 mg + sofosbuvir 400 mg | Mortality: 0% (0/21) | *Entire study cohort (n=44; 23% cirrhosis)*Any adverse event: 71% (31/44)Serious adverse events: 0%Withdrawal due to adverse events: 0%Headache: 25% (11/44)Fatigue: 20% (9/44)Nausea: 9% (4/44)Diarrhea: 9% (4/44)Hemoglobin 10.0 to 10.9 g/dL: 2% (1/44)ALT >1.25-2.50x ULN: 2% (1/44)Bilirubin >1.0-1.5x ULN: 5% (2/44) | Gilead |
| Abergel 2016b141France*Good* | Ledipasvir 90 mg + sofosbuvir 400 mg | Mortality: 0% (0/22) | *Entire study cohort (n=41; 22% cirrhosis)*Any adverse event: 80% (33/41)Serious adverse events: 2% (1/41; worsening depression)Withdrawal due to adverse events: 0%Headache: 27% (11/41)Fatigue: 10% (4/41)Diarrhea: 7% (3/41)Hemoglobin 100-109 g/dL: 2% (1/41)Bilirubin >1.0-1.5 ULN: 10% (4/41) | Gilead |
| Afdhal 2014185ION-1U.S. and Europe*Fair* | A. Ledipasvir 90 mg + sofosbuvir 400 mgB. Ledipasvir 90 mg + sofosbuvir 400 mg + ribavirin | NR | A vs. B12-week intervention groupAny adverse event: 79% (169/214) vs. 85% (185/217)Serious adverse event\*: 0.5% (1/214) vs. 3% (7/217)Withdrawal due to adverse events: 0% vs. 0%Headache: 25% (53/214) vs. 23% (49/217)Fatigue: 21% (44/214) vs. 36% (79/217)Nausea: 11% (24/214) vs. 17% (37/217)Diarrhea: 11% (24/214) vs. 8% (18/217)Insomnia: 8% (17/214) vs. 21% (45/217)Anemia: 0% vs. 12% (25/217)Rash: 7% (16/214) vs. 10% (21/217) 24-week intervention groupAny adverse event: 82% (178/217) vs. 92% (200/217)Serious adverse event\*: 8% (8% (18/217) vs. 3% (7/217)Withdrawal due to adverse events: 2% (4/217) vs. 3% (6/217)Headache: 24% (54/217) vs. 30% (65/217)Fatigue: 24% (24% (53/217) vs. 38% (82/217)Nausea: 13% (29/217) vs. 15% (32/217)Diarrhea: 11% (24/217) vs. 6% (14/217)Insomnia: 12% (26/217) vs. 22% (47/217)Anemia: 0% vs. 10% (22/217)Rash: 7% (16/217) vs. 12% (25/217) | Gilead |
| Ahmed 2018195Egypt*Fair* | Ledipasvir 90 mg + sofosbuvir 400 mg | NR | Any adverse event: 26% (26/100)Headache: 2% (2/100)Fatigue: 18% (18/100)Nausea: 2% (2/100)Diarrhea: 1% (1/100)Insomnia: 2% (2/100) | NR |
| Andreone 2014186PEARL-IIAustria, Belgium, Italy, The Netherlands, Portugal, Puerto Rico, Sweden, Switzerland, U.S.*Fair* | A. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/dayB. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/day + ribavirin | NR | A vs. BAny adverse event: 77.9% (74/95) vs. 79% (72/91)Withdrawals due to adverse events: 0% (0/95) vs. 2% (2/91)Serious adverse events (Pancreatitis, cellulitis, nephrolithiasis, osteoarthritis): 2% (2/95) vs. 2% (2/91)Headache: 23.3% (22/95) vs. 24.2% (22/91)Fatigue: 15.8% (15/95) vs. 31.9% (29/91)Nausea: 6.3% (6/95) vs. 20.9% (19/91)Diarrhea: 12.6% (12/95) vs. 13.2 (12/91)Anemia: 0% (0/95) vs. 11% (10/91)Rash: 1% (1/95) vs. 9% (8/91) | AbbVie |
| Asselah 2018196SURVEYOR II Part 4, Multinational (Asia, Europe, U.S. [specific countries NR])*Fair* | Glecaprevir 300 mg + pibrentasvir 120 mg | NR | Any adverse event: 63% (128/203)Serious adverse events (cholecystitis, urosepsis): 1% (2/203)Withdrawal due to adverse events: 0% (0/203)Headache: 18% (37/203)Fatigue: 14% (28/203)Nausea: 11% (23/203) | AbbVie |
| Asselah 2019143ENDURANCE-5Multinational (Australia, Belgium, Canada, France, New Zealand, Singapore, South Africa, Vietnam, U.S.)*Fair* | Glecaprevir 300 mg + pibrentasvir 120 mg | Mortality: 0% (0/23) | *Total population (n=84, genotype 5 and 6 combined)*Any adverse event: 55% (46/84)Serious adverse events (gastric ulcer, pyelonephritis, giardiasis and depression, pulmonary tuberculosis, viral infection): 6% (5/84)Withdrawal due to Adverse events: 0% (0/84)Headache: 13% (11/84)Fatigue:13% (11/84) | AbbVie |
| Asselah 2019143ENDURANCE-6 (same publication as ENDURANCE-5)*Fair* | See Asselah 2019 ENDURANCE-5 | Mortality: 0% (0/61) | See Asselah 2019 ENDURANCE-5 | See Asselah 2019 ENDURANCE-5 |
| Brown 2018144C-SCAPE (Genotype 4 only)Multinational (Australia, Belgium, France, Israel, Spain, U.K., U.S.)*Fair* | A. Elbasvir 50 mg + grazoprevir 100 mg (n=10)B. Elbasvir 50 mg + grazoprevir 100 mg + ribavirin (n=10) | Mortality: 0% (0/20) | *Total population (genotypes 2, 4, 5, 6)*Any adverse event: 79% (15/19) vs. 95% (18/19)Serious adverse events: 0% (0/19) vs. 0% (0/19)Withdrawal due to adverse events: 5% (1/19) vs. 0% (0/19)Headache: 26% (5/19) vs. 32% (6/19)Fatigue: 16% (3/19) vs. 26% (5/19)Nausea: 5% (1/19) vs. 11% (2/19)Asthenia: 21% (4/19) vs. 16% (3/19) | Merck |
| Chayama 2018197CERTAIN-1 (Arm A only)Japan*Fair* | Glecaprevir 300 mg + pibrentasvir 120 mg | NR | Any adverse event: 57% (74/129)Serious adverse events: 0% (0/129)Withdrawal due to adverse events: 0% (0/129)Headache: 5% (6/129)Rash: 2% (3/129) | AbbVie |
| Chuang 2016145Taiwan*Fair* | Ledipasvir 90 mg + sofosbuvir 400 mg  | *Total population (treatment-naïve and treatment-experienced)*Mortality: 0% (0/85) | *Total population (treatment-naïve and treatment-experienced)*Any adverse event: 60% (51/60)Withdrawals due to adverse events: 1% (1/85)Headache: 14% (12/85)Fatigue: 9% (8/85)Nausea: 6% (5/85) | Gilead |
| Dore 2016137MALACHITE-1Australia, Canada, Europe, South America*Good* | Genotype 1aA. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/day + weight-based ribavirin B. Telaprevir 750 mg 3x/day + subcutaneous pegylated IFN 180 ug 1/week + weight-based ribavirinGenotype 1bC. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/day + weight-based ribavirin D. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/dayE. Telaprevir 750 mg 3x/day + subcutaneous pegylated IFN 180 ug 1/week + weight-based ribavirin | Genotype 1aA vs. B SF-36 mental component score, mean change from baseline at 12 weeks post-treatment: -1.1 (SD 12) vs. -2.1 (SD 10.1) SF-36 physical component score, mean change from baseline at 12 weeks post-treatment: 3.1 (SD 8.7) vs. 0.7 (SD 7.6) Genotype 1bC vs. D vs. ESF-36 mental component score, mean change from baseline at 12 weeks post-treatment: 1.9 (SD 9.6) vs. 1.4 (SD 8.1) vs. -0.3 (SD 10.3)SF-36 physical component score, mean change from baseline at 12 weeks post-treatment: 2.3 (SD 5.3) vs. 2.5 (SD 5.7) vs. 1.0 (SD 8.4) | (A + C [with ribavirin]) vs. D (without ribavirin) vs. (B + E [telaprevir])Any adverse event: 75% (115/153) vs. 49% (41/83) vs. 99% (74/75); (A+C) vs. (B+E): RR 0.76 (95% CI, 0.69 to 0.84); D vs. (B+E): RR 0.50 (95% CI, 0.40 to 0.62)Withdrawals due to adverse events: 1% (1/153) vs. 0% (0/83) vs. 8% (6/75); (A+C) vs. (B+E): RR 0.08 (95% CI, 0.01 to 0.67)Serious adverse events (one each: prostate cancer, overdose, anemia, cough, chest pain, hematochezia, retinopathy, toxic skin eruption, cellulitis): 1% (1/153) vs. 0% (0/83) vs. 12% (9/75); (A+C) vs. (B+E): RR 0.05 (95% CI, 0.007 to 0.42); D vs. (B+E): RR 0.05 (95% CI, 0.003 to 0.80)Headache: 27% (41/153) vs. 19% (16/83) vs. 31% (23/75); (A+C) vs. (B+E): RR 0.87 (95% CI, 0.57 to 1.34); D vs. (B+E): RR 0.63 (95% CI, 0.36 to 1.10)Fatigue: 14% (21/153) vs. 5% (4/83) vs. 31% (23/75); (A+C) vs. (B+E): RR 0.45, (95% CI, 0.27 to 0.76); D vs. (B +E): RR 0.16 (95% CI, 0.06 to 0.43)Nausea: 21% (32/153) vs. 8% (7/83) vs. 40% (30/75); (A+C) vs. (B+E): RR 0.52 (95% CI, 0.35 to 0.79); D vs. (B+E): RR 0.21 (95% CI, 0.10 to 0.45)Anemia: 7% (10/153) vs. 1% (1/83) vs. 45% (34/75); (A+C) vs. (B+E): RR 0.14 (95% CI, 0.08 to 0.28); D vs. (B+E): RR 0.03 (95% CI, 0.004 to 0.19)Rash: 8% (12/153) vs. 0% vs. 23% (17/75); (A+C) vs. (B+E): RR 0.37 (95% CI, 0.19 to 0.73); D vs. (B+E): RR 0.03 (95% CI, 0.00 to 0.42) | AbbVie |
| Dore 2016137MALACHITE-2Australia, Canada, Europe, South America*Good* | A. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/day + weight-based ribavirin B. Telaprevir 750 mg 3x/day + subcutaneous pegylated IFN 180 ug 1/week + weight-based ribavirin | A vs. BSF-36 mental component score, mean change from baseline at 12 weeks post-treatment: 0.8 (SD 8.0) vs. -1.5 (SD 7.5)SF-36 physical component score, mean change from baseline at 12 weeks post-treatment: 3.0 (SD 6.4) vs. -1.3 (5.3) | A vs. BAny adverse event: 62% (63/101) vs. 91% (43/47); RR 0.68 (95% CI, 0.57 to 0.81)Serious adverse events (epilepsy, anemia [2 people], abdominal pain, infectious diarrhea, staphylococcal : 1% (1/101) vs. 5% (11/47); RR 0.04 (95% CI, 0.006 to 0.32)Withdrawal due to adverse events: 0% (0/101) vs. 11% (5/47); RR 0.04 (95% CI, 0.002 to 0.76)Headache: 29% (29/101) vs. 45% (21/47); RR 0.64 (95% CI, 0.41 to 1.00)Fatigue: 12% (12/101) vs. 26% (12/47); RR 0.47 (95% CI, 0.23 to 0.96)Nausea: 10% (10/101) vs. 43% (20/47); RR 0.23 (95% CI, 0.12 to 0.46)Insomnia: 6% (6/101) vs. 21% (10/47); RR 0.28 (95% CI, 0.11 to 0.72)Anemia: 3% (3/101) vs. 34% (16/47); RR 0.09 (95% CI, 0.03 to 0.28)Rash: 3% (3/101) vs. 17% (8/47); RR 0.06 (95% CI, 0.02 to 0.21) | AbbVie |
| Everson 2015 (Part A)146U.S.*Good* | Part A (trial phase)A. Sofosbuvir 400 mg + velpatasvir 25 mg (Genotype 1)B. Sofosbuvir 400 mg + velpatasvir 100 mg (Genotype 1)C. Sofosbuvir 400 mg + velpatasvir 25 mg (Genotype 3)D. Sofosbuvir 400 mg + velpatasvir 100 mg (Genotype 3)E. Sofosbuvir 400 mg + velpatasvir 25 mg (Genotype 2; 4-6)F. Sofosbuvir 400 mg + velpatasvir 100 mg (Genotype 2; 4-6) | A vs. B vs. C vs. D vs. E vs. FMortality: 0% (0/27) vs. 0% (0/28) vs. 0% (0/27) vs. 0% (0/27) vs. 4% (1/23) vs. 0% (0/22) | (A + C + E) vs. (B + D + F)Any adverse event: 68% (52/77) vs. 70% (54/77)Withdrawal due to adverse events: 0% (0/77) vs. 0% (0/77)Serious adverse events (not described): 3% (2/77) vs. 1% (1/77)Headache: 21% (16/77) vs. 18% (14/77)Fatigue: 25% (19/77) vs. 18% (14/77)Nausea: 13% (10/77) vs. 10% (8/77)Diarrhea: 6% (5/77) vs. 9% (7/77)Constipation: 12% (9/77 vs. 8% (6/77)Insomnia: 4% (3/77) vs. 6% (5/77)Hemoglobin <100g/L: 0% vs. 0%Bilirubin >2.5x ULN: 0% vs. 0%Rash: 5% (4/77) vs. 5% (4/77) | Gilead |
| Feld 2014187SAPPHIRE-1Australia, New Zealand; Austria, France, Germany, Hungary, Great Britain, Italy, Spain, Sweden, Switzerland; Canada, U.S.*Good* | A. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x day + weight-based ribavirinB. Placebo for 12 weeks followed by open-label ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x day + weight-based ribavirin | NR | A vs. B Any adverse event: 86% (414/473) vs. 73% (116/158); RR 1.19 (95% CI, 1.08 to 1.32)Withdrawal due to adverse event: 0.6% (3/473) vs. 0.6% (1/158); RR 1.00 (95% CI, 0.10 to 9.56)Serious adverse events (appendicitis, lobar pneumonia, cholecystitis, lumbar vertebral fracture in one patient each; aortic stenosis and postoperative wound infection in one; overdose and encephalopathy in one; mediastinal mass and non–small-cell lung cancer in one; acute respiratory failure and hypoxemia in one; abdominal pain, sinus tachycardia, diarrhea, chills, vomiting, nausea, and ventricular extrasystoles in one; and anemia and noncardiac chest pain in one): 2% (10/473) vs. 0%; RR 7.04 (95% CI, 0.42 to 120)Diarrhea: 14% (65/473) vs. 7% (11/158); RR 1.97 (95% CI, 1.07 to 3.64)Fatigue: 35% (164/473) vs. 29% (45/158); RR 1.22 (95% CI, 0.92 to 1.60)Headache: 33% (156/473) vs. 27% (42/158); RR 1.24 (95% CI, 0.93 to 1.66)Nausea: 24% (112/473) vs. 13% (21/158); RR 1.78 (95% CI, 1.16 to 2.74) Insomnia: 14% (66/473) vs. 8% (12/158); RR 1.84 (95% CI, 1.02 to 3.31)Grade 3 or 4 hemoglobin: 0% vs. 0% Rash: 11% (51/473) vs. 6% (9/158); RR 1.89 (95% CI, 0.95 to 3.76) | AbbVie |
| Feld 2015139ASTRAL-1U.S., Canada, Europe, Hong Kong*Good* | A. Sofosbuvir 400 mg + velpatasvir 100 mgB. Placebo | A vs. BMortality: 0.2% (1/624) vs. 0% (0/116)Mean change from baseline in patient-reported outcomes (composite SF-36, FACIT-F, CLDQ-HCV, WPAI:SHP; scale 0 to 100), 24-weeks post-treatment: 5.4; p<0.05 for all individual components except WPAI:SHP work productivity and WPAI:SHP absenteeism | A vs. BAny adverse event: 78% (485/624) vs. 77% (89/116); RR 1.01, 95% CI, 0.91 to 1.13Serious adverse events (19 events in 15 patients: abscess limb, acute myocardial infarction, appendicitis, bronchitis, cellulitis, chronic obstructive pulmonary disease, epilepsy, extremity necrosis, gastroenteritis, influenza, ligament sprain, lung cancer, mania, palpitations, rotatorcuff syndrome, small intestinal obstruction, sudden death from unknown cause, upper limb fracture, and vestibular neuronitis): 2% (15/624) vs. 0% (0/116); RR 5.80, 95% CI, 0.35 to 96Withdrawals due to adverse events: 0.2% (1/624) vs. 2% (2/116); RR 0.09 (95% CI, 0.01 to 1.02)Headache: 29% (182/624) vs. 28% (33/116); RR 1.03 (95% CI, 0.75 to 1.40)Fatigue: 20% (126/624) vs. 20% (23/116); RR 1.02 (95% CI, 0.68 to 1.52)Nausea: 12% (75/624) vs. 11% (13/116)Diarrhea: 8% (48/624) vs. 7% (8/116); RR 1.12 (95% CI, 0.54 to 2.30)Insomnia: 8% (50/624) vs. 9% (11/116); RR 0.84 (95% CI, 0.45 to 1.57)Hemoglobin <10 g/dL: 0.4% (2/624) vs. 0% (0/116); RR 2.21 (95% CI, 0.11 to 46) | Gilead |
| Ferenci 2014188PEARL IIIAustria, Belgium, Hungary, Israel, Italy, Poland, Portugal, Romania, Russia, Spain, U.S.*Good**Same publication as PEARL IV* | A. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/dayB. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/day + ribavirin | NR | A vs. BAny adverse event: 67.0% (140/209) vs. 80% (168/210)Serious adverse events (coronary artery disease, atrial fibrillation, nephrolithiasis, epididymitis, arthritis, breast lesion, uterine polyp, myalgia): 2% (4/209) vs. 2% (4/210)Withdrawal due to adverse events: noneHeadache: 23% (49/209) vs. 24% (51/210)Fatigue: 23% (48/209) vs. 21% (45/210)Nausea: 4% (9/209) vs. 23% (11/210)Diarrhea: 6% (13/209) vs. 4% (9/210)Rash: 3% (8/209) vs. 6% (12/210) | AbbVie |
| Ferenci 2014188PEARL IVCanada, U.K., U.S.*Good**Same publication as PEARL III* | A. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/dayB. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/day + ribavirin | NR | Any adverse event: 82% (169/205) vs. 92.0% (92/100)Serious adverse events (pancreatitis, anemia, intestinal obstruction, diverticulitis): 0.5% (1/205) vs. 3.0% (3/100)Withdrawal due to adverse events: noneHeadache: 28% (58/205) vs. 25.0% (25/100)Fatigue: 35% (72/205) vs. 46.0% (46/100)Nausea: 14% (28/205) vs. 21.0% (21/100)Diarrhea: 16.1% (33/205) vs. 14.0% (14/100)Rash: 5% (10/205) vs. 5% (5/100) | AbbVie |
| Foster 2015147 ASTRAL-2U.S.*Fair* | A. Sofosbuvir 400 mg + velpatasvir 100 mgB. Sofosbuvir 400 mg + ribavirin | A vs. BMortality: 1% (2/134) vs. 0% (0/132) | A vs. BAny adverse event: 69% (92/134) vs. 77% (101/132)Serious adverse events (pneumonia, enteritis, abdominal pain, arthralgia, depression): 1% (2/134) vs. 2% (2/132)Withdrawals due to adverse events: 1% (1/134) vs. 0% (0/132)Dyspepsia: 1% (1/134) vs. 4% (5/132)Headache: 18% (24/134) vs. 22% (29/132)Fatigue: 15% (20/134) vs. 35% (47/132)Nausea: 10% (14/134) vs. 14% (19/132)Grade 3 or 4 bilirubin elevation: 0% (0/134) vs. 0% (0/132)Insomnia: 4% (6/134) vs. 14% (18/132 | Gilead |
| Foster 2015147 ASTRAL-3U.S.*Fair**Same publication as ASTRAL-2* | Same as Foster 2015 ASTRAL-2 | A vs. BMortality: 0% (0/278) vs. 0.7% (2/280) | A vs. BAny adverse event: 88% (245/277) vs. 95% (260/275)Serious adverse events (myocardial infarction, bursitis, cellulitis, cardiovascular accident, cholecystitis, chronic obstructive pulmonary disease, depression, food poisoning, gunshot wound, hematochezia, overdose, intervertebral disc protrusion, aneurysm, lung infection, ovarian cyst rupture, stenosis, infection, psychotic disorder, rash): 2% (6/277) vs. 5% (15/275)Withdrawal due to adverse events: 0% (0/277) vs. 3% (9/275)Dyspepsia: 3% (9/277) vs. 11% (30/275)Headache: 32% (90/277) vs. 32% (89/275)Fatigue: 26% (71/277) vs. 38% (105/275)Nausea: 17% (46/277) vs. 21% (58/275)Insomnia: 11% (31/277) vs. 27% (74/275) | Gilead |
| Gane 2015148New Zealand (Genotype 6 subset)*Fair* | Ledipasvir 90 mg + sofosbuvir 400 mg | Mortality: 0% (0/25) | Any adverse event: 84% (21/25)Serious adverse events (not described): 4% (1/25)Withdrawal due to adverse events: 0% (0/25)Headache: 8% (2/25)Fatigue: 24% (6/25)Nausea: 0% (0/25)Diarrhea: 16% (4/25)Gastroenteritis: 0% (0/25)Vomiting: 0% (0/25)Hemoglobin 7.0 to <9.0 g/dL: 0% (0/25)Total bilirubin >2.5 to 5x ULN: 0% (0/25)ALT elevation >5 to 10x ULN: 4% (1/25)AST elevation >5 to 10x ULN: 4% (1/25)Rash: 8% (2/25) | Gilead |
| Grebely 2018a150SIMPLIFYMultinational (Australia, Canada, New Zealand, Norway, Switzerland, U.K., U.S.)*Fair* | Sofosbuvir 400 mg + velpatasvir 100 mg | Mortality: 4% (4/103) | Any adverse event: 83% (85/103)Serious adverse events (rhabdomyolysis; other serious adverse events NR): 7% (7/103)Withdrawal due to adverse events: 1% (1/103)Headache: 18% (19/103)Fatigue: 22% (23/103)Nausea: 14% (14/103)Vomiting: 4% (4/103)Diarrhea: 4% (4/103)Insomnia: 9% (9/103) | Gilead |
| Grebely 2018b149D3FEATMultinational (Australia, Canada, France, New Zealand, Norway, Switzerland)*Fair* | Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg + 1000-1200 mg ribavirin | Mortality: 3% (3/87) | Any adverse event: 61% (53/87)Serious adverse events (NR): 6% (5/87)Withdrawal due to adverse events: 0% (0/87)Headache: 5% (12/87)Fatigue: 10% (25/87)Nausea: 8% (20/87)Vomiting: 4% (11/87)Anemia: 5% (12/87)Insomnia: 4% (11/87) | AbbVie |
| Hezode 2015189PEARL I (Treatment-naïve population)France, Hungary, Italy, Poland, Romania, Spain, Turkey, U.S.*Good**See also Lawitz 2015155 (PEARL I - Genotype 1b)* | Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + ribavirin (weight-based; dose NR) | NR | Any adverse event: 88% (37/42)Serious adverse events: 0%Withdrawal due to adverse events: 0%Headache: 33% (14/42)Fatigue: 12% (5/42)Nausea: 17% (7/42)Diarrhea: 14% (6/42)Insomnia: 10% (4/42)Hemoglobin <100 g/L: 2% (1/42)Total bilirubin, grade 3 elevation: 0% ALT elevation >5x ULN and ≥2x baseline: 0%AST elevation >5x ULN and ≥2x baseline: 0% |  AbbVie |
| Hezode 2015189PEARL I (Treatment experienced population)France, Hungary, Italy, Poland, Romania, Spain, Turkey, U.S.*Good**See also Lawitz 2015155 (PEARL I - Genotype 1b)* | Same as Hezode 2015 (Treatment naïve population) | NR | Any adverse event: 88% (43/49)Serious adverse events: 0%Withdrawal due to adverse events: 0%Headache: 29% (14/49)Fatigue: 18% (9/49)Nausea: 12% (6/49)Diarrhea: 6% (3/49)Insomnia: 16% (8/49)Hemoglobin <100 g/L: 2% (1/49)Total bilirubin, grade 3 elevation: 6% (3/49)ALT elevation >5x ULN and ≥2x baseline: 0%AST elevation >5x ULN and ≥2x baseline: 0%  | AbbVie |
| Kowdley 2014a190ION-3U.S.*Fair* | Ledipasvir 90 mg + sofosbuvir 400 mg | NR | 8-week intervention groupAny adverse event: 67% (145/215)Serious adverse events (anaphylaxis, colitis, inadequately controlled diabetes, gastrointestinal hemorrhage, hypertension, pituitary tumor): 2% (4/215)Withdrawal due to adverse events: 0%Headache: 14% (30/215)Fatigue: 21% (45/215)Nausea: 7% (15/215)Diarrhea: 7% (15/215)Insomnia: 5% (11/215)Anemia: 1% (2/215)Rash: 1% (3/215)12-week intervention groupAny adverse event: 69% (149/216)Serious adverse events (abdominal pain, bile duct stone, hemothorax, hypoglycemia, intestinal perforation, mental illness, respiratory failure, rhabdomyolysis, traffic accident, bone injury, lung cancer): 2% (5/216)Withdrawal due to adverse events: 1% (2/216)Headache: 15% (33/216)Fatigue: 23% (49/216)Nausea: 11% (24/216)Diarrhea: 4% (9/216)Insomnia: 7% (15/216)Anemia: 1% (2/216)Rash: 2% (5/216) | Gilead |
| Kowdley 2014b191AVIATORAustralia, Canada, France, Germany, New Zealand, Puerto Rico, Spain, U.K., U.S.*Good* | A. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 150 mg + dasabuvir 800 mg B. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100-150 mg + dasabuvir 800 mg + ribavirin 1000-1200 mg  | NR | A vs. BAny adverse event: NRSerious adverse events (affective disorder, animal bite, arthralgia, acute cholecystitis, and facial paresis (occurring in one patient each); increased blood creatinine level and bronchitis occurring in the same patient; the cervicobrachial syndrome, neck pain, and osteoarthritis of the spine occurring in the same patient; lung disorder and pneumonia occurring in the same patient): 3% (2/79) vs. 1% (1/79)Withdrawals due to adverse events: 0% (0/79) vs. 3% (2/79)Headache: 19% (15/79) vs. 27% (21/79)Fatigue: 20% (16/79) vs. 28% (22/79)Nausea: 14% (11/79) vs. 24% (19/79)Diarrhea: 16% (13/79) vs. 13% (10/79)Grade 3 or 4 bilirubin elevation: 0% (0.79) vs. 5% (4/79)Grade 3 or 4 ALT elevation: 0% (0/79) vs. 1% (1/79)Anemia: 1% (1/79) vs. 9% (7/79) | AbbVie |
| Kumada 2017 (Part 2 only)152Japan*Good* | Elbasvir 50 mg + grazoprevir 100 mg | Mortality: 0% (0/227) | Serious adverse events (not described): 5% (11/227)Withdrawal due to adverse events: 1% (3/227)Clinically significant adverse event: 4% (8/227) | Merck |
| Kumada 2015151GIFT-1 (Substudy 1)Japan*Fair* | A. Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg (double-blind treatment)B. Placebo for 12 weeks, followed by ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg (open-label treatment) | A vs. BMortality: 0% (0/255 vs. 0% (0/106) | A vs. B (placebo-controlled phase only) Any adverse event: 68.8% (148/215) vs. 56.6% (60/106); RR 1.22 (95% CI, 1.01 to 1.47)Serious adverse events (not described): 3.3% (7/215) vs. 1.9% (2/106); RR 1.73 (95% CI, 0.36 to 8.16)Withdrawals due to adverse events: 0.9% (2/215) vs. 0% (0/106); RR 2.48 (95% CI, 0.12 to 51)Headache: 8.8% (19/215) vs. 9.4% (10/106); RR 0.94 (95% CI, 0.45 to 1.94)Nausea: 4.3% (9/215) vs. 3.8% (4/106); RR 1.11 (95% CI, 0.35 to 3.52)Hemoglobin <8g/dL: 0% vs. 0% | AbbVie |
| Kwo 2016153OPTIMIST-1Canada, U.S.*Fair* | Simeprevir 150 mg + sofosbuvir 400 mg | Mortality: 0% (0/155)Quality of life, mean change from baseline (among 141/155 with SVR) --HCV-SIQv4 overall body symptom score -3.9 (SE 0.96)-Fatigue Severity Scale: -0.5 (SE 0.15)-Center for Epidemiologic Studies-Depression Scale: -0.2 (SE 0.73)-EQ-5D VAS: 4.1 (SE 1.4) | Any adverse event: 66% (103/155)Serious adverse events (colitis): 1% (1/155)Withdrawals due to adverse events: 0% (0/155)Nausea: 15% (23/155)Headache: 14% (22/155)Fatigue: 12% (19/155)Increased bilirubin: 1% (1/155)Rash: 6% (10/155) | Janssen |
| Lalezari 2015192U.S.*Fair* | Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + dasabuvir 250 mg 2x/day + ribavirin 1000-1200 mg | NR | Any adverse event: 92.1% (35/38)Serious adverse events (cerebrovascular accident, sarcoma, acute myeloid leukemia): 7.9% (3/38)Withdrawal due to adverse events: 2.6% (1/38)Headache: 31.6% (12/38)Fatigue: 47.4% (18/38)Nausea: 50% (19/38)Vomiting: 10.5% (4/38)Insomnia: 18.4% (7/38)Anemia: 10.5% (4/38)Rash: 15.8% (6/38) | AbbVie |
| Lawitz 2014a154COSMOS U.S.*Fair* | A. Simeprevir 150 mg + sofosbuvir 400 mgB. Simeprevir 150 mg + sofosbuvir 400 mg + ribavirin | Mortality: 0% (0/81) | Any adverse event: 79% (11/14) vs. 89% (24/27)Serious adverse events: 0% vs. 0%Withdrawals due to adverse events: 0% vs. 0%Anemia: 0% vs. 0%Rash: 7% (1/14) vs. 22% (6/27) | Janssen |
| Lawitz 2014b193LONESTAR (Cohort A)U.S.*Fair* | A. Ledipasvir 90 mg + sofosbuvir 400 mg, 8 weeksB. Ledipasvir 90 mg + sofosbuvir 400 mg, 12 weeksC. Ledipasvir 90 mg + sofosbuvir 400 mg + ribavirin  | NR | 8-week intervention groupAny adverse event: 45% (9/20)Serious adverse events: 0%Withdrawal due to adverse events: 0%Headache: 10% (2/20)Nausea: 10% (2/20)Rash: 5% (1/20)12-week intervention groupAny adverse event: 42% (8/19)Serious adverse events (exacerbation of peptic ulcer disease): 5% (1/19)Withdrawal due to adverse events: 0%Headache: 0%Nausea: 5% (1/19)Rash: 0% | Gilead |
| Lawitz 2015155PEARL-1France, Hungary, Italy, Poland, Puerto Rico, Romania, Spain, Turkey, U.S.*Fair* | Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg | Mortality: 0% (0/82) | Any adverse event: 76.8% (63/82)Serious adverse events (unclear; NR according to treatment group): 2.4% (2/82)Severe adverse events: 2.4% (2/82)Withdrawals due to adverse events: 0% (0/82)Asthenia: 6.1% (5/82)Diarrhea: 7.3% (6/82)Dry skin: 8/5% (7/82)Fatigue: 7.2% (6/82)Headache: 29.3% (24/82)Hypertension: 1.2% (1/82)Nausea: 9.8% (8/82)Pruritus: 7.3% (6/82) | AbbVie |
| Lim 2016156Korea*Fair* | Ledipasvir 90 mg + sofosbuvir 400 mg | *Includes all patients (n=93, including treatment experienced, 28% cirrhosis)*Mortality: 0% (093) | *Includes all patients (n=93, including treatment experienced, 28% cirrhosis)*Any adverse event: 49% (46/93)Serious adverse event (contact dermatitis, erysipelas, inguinal hernia): 3% (3/93)Withdrawals due to adverse events: (1/93)Headache: 8% (7/93)Fatigue: 6% (6/93) | Gilead |
| Nelson 2015157ALLY-3U.S.*Fair* | Daclatasvir 60 mg + sofosbuvir 400 mg | Mortality: 0% (0/152) | Any adverse event: NRSerious adverse events (gastrointestinal hemorrhage): 0.7% (1/152)Headache: 20% (30/152)Fatigue: 19% (29/152)Nausea: 12% (18/152)Diarrhea: 9% (13/152)Insomnia: 6% (9/152) | Bristol-Myers Squibb |
| Pianko 2015158Australia, New Zealand, U.S.*Fair* | A. Sofosbuvir 400 mg + velpatasvir 100 mg (Group 3)B. Sofosbuvir 400 mg + velpatasvir 100 mg + ribavirin (Group 4) | *Includes Genotype 3 patients with cirrhosis and Genotype 1 patients*A vs. BMortality: 0% (0/80) | *Includes Genotype 3 patients with cirrhosis and Genotype 1 patients (n=80; 41% cirrhosis)*A vs. BAny adverse event: 79% (63/80) vs. 86% (69/80)Serious adverse events (group A only: cholecystitis, suicide, rib fracture, contusion; group B not described): 5% (4/80) vs. 4% (3/80)Withdrawal due to adverse events: 0% (0/80) vs. 0% (0/80)Headache: 23% (18/80) vs. 30% (24/80)Fatigue: 24% (19/80) vs. 34% (27/80)Nausea: 9% (7/80) vs. 23% (18/80)Diarrhea: 11% (9/80) vs. 5% (4/80)Insomnia: 8% (6/80) vs. 20% (16/80)Rash: 3% (2/80) vs. 11% (9/80) | Gilead |
| Poordad 2017194MAGELLAN-1U.S.*Fair* | A. Glecapravir 200 mg + pibrentasvir 80 mgB. Glecapravir 200 mg + pibrentasvir 120 mgC. Glecapravir 200 mg + pibrentasvir 120 mg + ribavirin | NR | A vs. B vs. CAny adverse event: 83.3% (5/6) vs. 81.8% (18/22) vs. 86.4% (19/22) Serious adverse events (fracture, breast cancer): 16.7% (1/6) vs. 0% vs. 4.5% (1/22)Withdrawal due to adverse events: 0% vs. 0% vs. 0%Headache: 16.7% (1/6) vs. 36.4% (8/22) vs. 22.7% (5/22) Fatigue: 16.7% (1/6) vs. 18.2% (4/22) vs. 36.4% (8/22)Nausea: 16.7% (1/6) vs. 13.6% (3/22) vs. 27.3% (6/22)Insomnia: 0% vs. 0% vs. 27.3% (6/22)ALT >3x ULN: 0% vs. 0% vs. 0%AST >3x ULN: 0% vs. 0% vs. 0%Bilirubin >3x ULN: 0% vs. 0% vs. 0%Hemoglobin <10 g/dL: 0% vs. 0% vs. 0% | AbbVie |
| Pott-Junior 2019 (Group A - daclatasvir/ sofosbuvir arm)159Brazil*Good* | Daclatasvir 60 mg + sofosbuvir 400 mg  | Mortality: 0% (0/127) | Headache: 15% (10/65)Fatigue: 23% (15/65) Nausea: 6% (4/65) Vomiting: 2% (1/65) Insomnia: 6% (4/65)Rash: 2% (1/65) | Federal University of São Paulo |
| Pott-Junior 2019 (Group B - simeprevir/ sofosbuvir arm)159Brazil*Good* | Simeprevir 150 mg + sofosbuvir 400 mg  | See Pott-Junior 2019 Group A | Headache: 28% (17/60)Fatigue: 28% (17/60)Nausea: 13% (8/60)Vomiting: 5% (3/60)Insomnia: 10% (6/60)Rash: 10% (6/60) | See Pott-Junior 2019 Group A |
| Sperl 2016198 and Ng 2018138C-EDGE Head-2-Head (elbasvir/grazoprevir arm only)Multinational (Europe, Turkey)*Fair* | Elbasvir 50 mg + grazoprevir 100 mg | SF-36 physical component score, mean change from baseline: 2.0SF-36 mental component score, mean change from baseline: 2.0FACIT-F score, mean change from baseline: 1.75 | Any adverse event: 52% (67/129)Serious adverse events (type of adverse event NR): 0.8% (1/129)Withdrawal due to adverse events: 0.8% (1/129) | Merck |
| Sulkowski 2014161A1444040 StudyU.S.*Fair* | A. Sofosbuvir 400 mg + daclatasvir 60 mgB. Sofosbuvir 400 mg + daclatasvir 60 mg + ribavirin | Mortality: 0% (0/41) | Any adverse event: 93% (38/41)Serious adverse events (psychiatric disorder): 2% (1/41)Withdrawal due to adverse events: 0%Headache: 34% (14/41)Fatigue: 39% (16/41)Nausea: 20% (8/41)Vomiting: 2% (1/41)Diarrhea: 5% (2/41)Insomnia: 10% (4/41)Grade 3 or 4 lab abnormality: 0% | Bristol-Myers Squibb; Gilead |
| Sulkowski 2015160C-WORTHYAustralia, Canada, Denmark France, Hungary, Israel, New Zealand, Puerto Rico, Spain, Sweden, Turkey, U.S.*Fair* | A. Grazoprevir 100 mg + elbasvir 50 mgB. Grazoprevir 100 mg + elbasvir 50 mg + ribavirin | Mortality: 0% (0/44) | Any adverse event: NR; drug-related adverse events 56% (24/43†)Serious adverse events: 0%Withdrawal due to adverse events: 0%Headache: 35% (15/43)Fatigue: 23% (10/43)Nausea: 16% (7/43)Diarrhea: 12% (5/43)Hemoglobin <8.5 g/dL: 0%ALT >2.5x baseline value: 0%AST >2.5x baseline value: 0%Bilirubin >5x baseline value: 0% | Merck |
| Toyoda 2018199CERTAIN-2 (Arm A only)Japan*Fair* | Glecaprevir 300 mg + pibrentasvir 120 mg | NR | Any adverse event: 48% (43/90)Serious adverse events (pneumothorax, unstable angina): 2% (2/90)Withdrawal due to adverse events: 1% (1/90)Headache: 7% (6/90)Nausea: 3% (3/90)Anemia: 0% (0/90) | AbbVie |
| Waked 2016162AGATE-IIEgypt*Good* | Ombitasvir 25 mg + paritaprevir 150 mg + ritonavir 100 mg + 1000-1200 mg ribavirin | Mortality: 1% (1/100) | Any adverse event: 80% (80/100)Serious adverse events (deep venous thrombosis, cardiac arrest): 2% (2/100)Headache: 41% (41/100)Fatigue: 35% (35/100)Dyspepsia: 17% (17/100)Insomnia: 9% (9/100)Grade 2 hemoglobin abnormality: 7% (7/100)Grade ≥2 total bilirubin elevation: 19% (19/100) | AbbVie |
| Wei 2018163China*Fair* | Ledipasvir 90 mg + sofosbuvir 400 mg +  | Mortality: 0% (0/206) | Any adverse event: 58% (120/206)Serious adverse events (epicondylitis, asthma, bone contusion): 1% (3/206)Withdrawal due to adverse events: 0% (0/206) | Gilead |
| Wei 2019a164C-CORAL (Genotype 1 and 4 only)Multinational (Australia, China, Korea, Russia, Taiwan, Thailand, Vietnam)*Good* | A. Elbasvir 50 mg + grazoprevir 100 mg (n=326)B. Placebo (n=123; harms assessment only) | A vs. BMortality: 0.2% (1/486) vs. 0% (0/123) | A vs. BAny adverse event: 47% (230/486) vs. 50% (62/123)Serious adverse events (suicide, contusion, Evans syndrome, lymphoma, enteritis vs. influenza, fracture): 2% (8/486) vs. 2% (2/123)Withdrawal due to adverse events: 0.6% (3/486) vs. 2% (2/123)Headache: 6% (27/486) vs. 5% (6/123)Fatigue: 5% (22/486) vs. 7% (9/123) | Merck |
| Wei 2019b165Multinational (China, Malaysia, Singapore, Thailand, Vietnam)*Fair* | Sofosbuvir 400 mg + velpatasvir 100 mg | Mortality: 0% (0/375) | Any adverse event: 50% (189/375)Serious adverse events (foot infection, pneumonia, ligament rupture): 1% (3/375)Withdrawal due to adverse events: 0% (0/375)Headache: 5% (18/375) | Gilead |
| Zeuzem 2015166C-EDGEMultinational (Australia, Czech Republic, France, Germany, Israel, Puerto Rico, South Korea, Taiwan, U.S.)*Good* | Grazoprevir 100 mg + elbasvir 50 mg | *Patients without cirrhosis only*Mortality: 0.4% (1/246) | *Patients without cirrhosis only*Any adverse event: 71% (175/246)Serious adverse events (not described): 3% (7/246)Withdrawal due to adverse event: 0.8% (2/246) | Merck |
| Zeuzem 2018167ENDURANCE-1Multinational (Australia, Austria, Belgium, Canada, Chile, France, Germany, Hungary, Israel, Italy, Lithuania, Mexico, New Zealand, Poland, Portugal, Puerto Rico, Romania, Russian Federation, Spain, South Korea, Sweden, Switzerland, Taiwan, U.K., U.S.)*Fair* | Glecaprevir 300 mg + pibrentasvir 120 mg | 8-week intervention groupMortality: 0% (0/351)12-week intervention groupMortality: 0.3% (1/352) | 8-week intervention groupAny adverse event: 62% (216/351)Serious adverse events (suicide attempt, unstable angina, fracture, uterine leiomyoma, transient ischemic attack): 1% (5/351)Withdrawal due to adverse events: 0% (0/351)Headache: 19% (68/351)Fatigue: 9% (31/351)Nausea: 5% (19/351)12-week intervention groupAny adverse event: 66% (234/352)Serious adverse events (irritable bowel syndrome, pneumonia/death, bronchitis, atrial fibrillation): 1% (4/352)Withdrawal due to adverse events: 0.3% (1/352)Headache: 18% (62/352)Fatigue: 12% (43/352)Nausea: 8% (29/352) | AbbVie |
| Zeuzem 2018167ENDURANCE-3 (same publication as ENDURANCE-1)*Fair* | A. Glecaprevir 300 mg + pibrentasvir 120 mg, 8 weeksB. Glecaprevir 300 mg + pibrentasvir 120 mg, 12 weeks3. Sofosbuvir 400 mg + daclatasvir 60 mg. 12 weeks | A vs. B vs. CMortality: 0.6% (1/157) vs. 0% (0/233) vs. 0.9% (1/115) | A vs. B vs. CAny adverse event: 62% (98/157) vs. 76% (177/233) vs. 70% (80/115)Serious adverse events (ulcerative keratitis, overdose, substance-abuse dependence): 2% (3/157) vs. 2% (5/233) vs. 2% (2/115)Withdrawal due to adverse events: 0% (0/157) vs. 1% (3/233) vs. 0.9% (1/115)Headache: 20% (31/157) vs. 26% (60/233) vs. 20% (23/115)Fatigue: 13% (20/157) vs. 19% (44/233) vs. 14% (16/115)Nausea: 12% (19/157) vs. 14% (32/233) vs. 13% (15/115)  | Same as Zeuzem 2018 |

**\***Serious adverse events occurring in more than one person (each occurred in 2 people; NR by intervention group): cellulitis, chest pain, gastroenteritis, hand fracture, noncardiac chest pain, pneumonia.

**†**One patient excluded from analysis due to receiving the ineligible intervention.

**Abbreviations:** ALT = alanine aminotransferase; AST = aspartate amino transferase; CI = confidence interval; CLDQ-HCV = Chronic Liver Disease Questionnaire-Hepatitis C Version; EQ-5D VAS = EuroQoL 5-Dimensions questionnaire visual analog scale; FACIT-F = Functional Assessment of Chronic Illness Therapy-Fatigue; HCV-SIQv4 = Hepatitis C Symptom and Impact Questionnaire; NR = not reported; RR = relative risk; SD = standard deviation; SE = standard error; SF = short form; SVR = sustained virologic response; U.K. = United Kingdom; ULN = upper limit of normal; U.S. = United States; WPAI:SHP = Work Productivity and Activity Impairment Questionnaire: Specific Health Problem. Study names are not acronyms.