Summary Tables
NEW DRUGS IN HCV
(+ new data)

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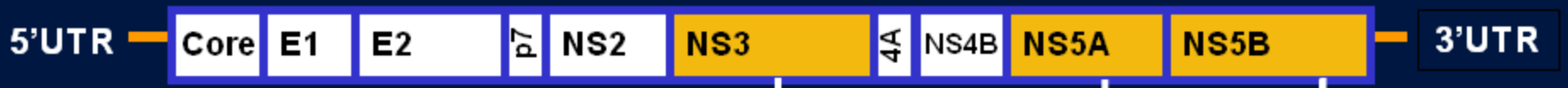
Multiple Direct Acting Antivirals



Protease

Polymerase

HCV PIs

Viral enzyme
Active site

Telaprevir
Boceprevir
Simeprevir
Faldaprevir
Asunaprevir
ABT-450
MK-5172
Sovaprevir
ACH-2684

NS5A Inhibitors

Non-enzyme
Replication complex

Daclatasvir
Ledipasvir
ABT-267
GS-5816
ACH-3102
PPI-668
GSK2336805
Samatasvir
MK-8742

NS5B Nucs

Viral enzyme
Active site

Sofosbuvir
VX-135
IDX20963
ACH-3422

NS5B Non-nucs

Viral enzyme
Allosteric site

ABT-333
Deleobuvir
BMS-791325
PPI-383
GS-9669
TMC647055

Direct-Acting Antiviral Profiles

	Direct-Acting Antiviral					
	NS3[1]	NS3[2]	NS5A[1]	NS5A[2]	Non Nuc NS5B	Nuc NS5B
Resistance profile						
Pan-genotypic efficacy						
Efficacy						
Adverse events						
Drug-drug interactions						

 Good profile  Average profile  Least favorable profile

[1] 1st generation.
[2] 2nd generation.

	Simeprivir (OLYSIO)	Sofosbuvir (SOVALDI)
Drug Group	NS3/4A Protease inhibitor	NS5B polymerase inhibitor Nucleotide analog
Genotypes affected	1a Q80K(-); 1b; (2, 4, 5, 6)	1,2,3,4 (5 & 6)
Dose	150 mg/d with food	400 mg a day
Associated drugs; dose reduction	Peg-IFN; standard RBV (as in RBV prescribing info)	Peg-IFN; standard RBV 1200/1000 by weight; 600 dose reduction
Regimens approved by FDA (see effectiveness in tables; some non-approved regimens may be superior)	G1 Naïve or Relapser: S+P+R x 12 w + PR x 12 w G1 NR, Part R & Null: S+P+R x 12w + PR x 36 w	**G1 & 4: S+P+R 12 w**, G1: S+R x 24 w (IFN Ineligible) **G1 & 4 pre-OLTx: S+R x 48 w** **G2: S+R x 12 w** **G3: S+R x 24 w *(Cirrhosis: S+P+R x 12 is superior but no FDA approved).*** ***HIV: S+P+R x 12 w (all G) is best regimen but no FDA approved.*** HIV G1 & 3: S+R x 24 HIV G2: S+R x 12 w
Renal impairment	No dose change. Not studied in GFR < 30	No if GFR < 30
Stop Rules and Precautions	STOP: if >/= 25 @ 4, 12, or 24 w Precaution: East Asian ancestry.	None
Liver Impairment	No in C-P B or C or decompensation.	MELD</= 14; Compensated C-P A, B, or C. No in decompensation.
Pregnancy	2 anti-conceptives during & until 6 months after.	2 anti-conceptives during &until 6 months after
Ages	19-73	19-75

	Simeprivir	Sofosbuvir
DAA increases drug levels **but can be used with caution and monitoring**	**Antiarrhytmics:** Digoxin, Amiodarone, Disopyramide, Flecainide, Mexiletine, Propafenone, Quinidine **Ca Channel blockers:** Amlodipine, Diltiazem , Felodipine, Nicardipine, Nifedipine, Nisoldipine, Verapamil **Statins**: Rosuvastatin max 10 mg, Atorvastatin max 40 mg, Simvastatin lowest possible dose, Pitavastatin lowest possible dose, Pravastatin lowest possible dose, Lovastatin lowest possible dose **Phosphodiesterase 5 inh:** Sildenafil , Tadalafil , Vardenafil all need dose adjustment when treating pulmonary hypertension **Sedatives:** Oral Midazolam and Triazolam	
DAA increases drug levels and **SHOULD NOT BE USED**	Erythromycin, Cisapride	
Drug **increases DAA** level and **SHOULD NOT BE USED**	**Milk Thistle** **Antibiotics:** Erythromycin, Clarithromycin, Telithromycin, **Antifungals (systemic):** Itraconazole, Ketoconazole, Posaconazole, Fluconazole , Voriconazole, **Anti-retrovirals:** Cobicistat-containing product (elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil fumarate), Darunavir, Ritonavir	
Drug **decreases DAA** level and **SHOULD NOT BE USED**	**St John's wort** **Anticonvulsants:** Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin **Antibiotics:** Rifampin, Rifabutin, Rifapentine **Corticosteroids:** Dexamethasone. **Antiretrovirals:** Efavirenz	**St John's wort** **Anticonvulsants:** Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin **Antibiotics:** Rifampin, Rifabutin, Rifapentine **Antiretrovirals:** tipranavir//ritonavir
Drug has **variable effect in DAA** and **SHOULD NOT BE USED**	**Antiretrovirals:** Atazanavir, Fosamprenavir, Lopinavir, Indinavir, Nelfinavir, Saquinavir, Tipranavir, Delavirdine, Etravirine, Nevirapine	
DAA has modest effect that requires monitoring	Cyclosporine, Tacrolimus, Sirolimus, Warfarin	

Treatment of HCV
AASLD/IDSA Guidelines

Who should be Tested for HCV?

- **HCV testing is recommended at least once for persons born between 1945 and 1965. Rating:** Class I, Level B
- **Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviors, exposures, and conditions associated with an increased risk of HCV infection. Rating:** Class I, Level B
  - ***Risk behaviors***
    - **Injection-drug use (current or ever, including those who injected once)**
    - **Intranasal illicit drug use**
  - ***Risk exposures***
    - **Long-term hemodialysis (ever)**
    - **Getting a tattoo in an unregulated setting**
    - **Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-infected blood**
    - **Children born to HCV-infected women**
    - **Prior recipients of transfusions or organ transplants, including persons who:**
      - **were notified that they received blood from a donor who later tested positive for HCV infection**
      - **received a transfusion of blood or blood components, or underwent an organ transplant before July 1992**
      - **received clotting factor concentrates produced before 1987**
      - **were ever incarcerated**
  - ***Other medical conditions***
    - **HIV infection**
    - **Unexplained chronic liver disease and chronic hepatitis including elevated alanine aminotransferase levels**

Recommendations for patients with HCV

- Avoid sharing toothbrushes and dental or shaving equipment, and cover any bleeding wound to prevent the possibility of others coming into contact with their blood.
- Stop using illicit drugs and enter substance abuse treatment. If continue to inject drugs should avoid reusing or sharing syringes, needles, water, cotton, and other drug preparation equipment; use new sterile syringes and filters and disinfected cookers; clean the injection site with a new alcohol swab; and dispose of syringes and needles after one use in a safe, puncture-proof container.
- Do not donate blood and discuss HCV serostatus prior to donation of body organs, other tissue, or semen.
- MSM with HIV infection and those with multiple sexual partners or sexually transmitted infections should use barrier precautions to prevent sexual transmission. Other persons with HCV infection should be counseled that the risk of sexual transmission is low and may not warrant barrier protection.
- Household surfaces and implements contaminated with visible blood from an HCV-infected person should be cleaned using a dilution of 1 part household bleach to 9 parts water. Gloves should be worn when cleaning up blood spills.

Who should be treated for HCV

Highest Priority due to Highest Risk for Severe Complications

- **Advanced fibrosis (Metavir F3) or compensated cirrhosis (Metavir F4)**
  - **Rating:** Class I, Level A
- **Organ transplant**
  - **Rating:** Class I, Level B
- **Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (eg, vasculitis)**
  - **Rating:** Class I, Level B
- **Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis**
  - **Rating:** Class IIa, Level B
- *Transient Liver Elastograpy (TLE) & serum fibrosis markers:*
  - *A cutoff value of 8.7 kPa correlates with Metavir F2 or higher fibrosis stage;*
  - *greater than 9.5 kPa with F3; and*
  - *14.5 or higher kPa with F4 or cirrhosis.*
  - *The measurement range does overlap between stages. If serum fibrosis markers (e.g.: Fibrosure) are discordant with TLE, do liver biopsy.*

Who should be treated for HCV

High Priority

Owing to High Risk for Complications

- **Fibrosis (Metavir F2)**
  - **Rating:** Class I, level B
- **HIV-1 coinfection**
  - **Rating:** Class I, Level B
- **HBV coinfection**
  - **Rating:** Class IIa, Level C
- **Other coexistent liver disease (eg, NASH)**
  - **Rating:** Class IIa, Level C
- **Debilitating fatigue**
  - **Rating:** Class IIa, Level B
- **Type 2 Diabetes mellitus (insulin resistant)**
  - **Rating:** Class IIa, Level B
- **Porphyria cutanea tarda**
  - **Rating:** Class IIb, Level C

Owing to Transmission Risk

- **MSM with high-risk sexual practices**
- **Active injection drug users**
- **Incarcerated persons**
- **HCV-infected women of child-bearing potential wishing to get pregnant**
- **Persons on long-term hemodialysis**
  - **Rating:** Class IIa, Level C
  - Should be counseled on ways to decrease transmission and minimize the risk of reinfection.

Factors Associated with Accelerated Fibrosis in HCV

Host Factors

- **Non-Modifiable**
  Fibrosis stage
  Inflammation grade
  Older age at time of infection
  Male sex
  Organ transplant
- **Modifiable**
  Alcohol consumption
  Nonalcoholic fatty liver disease
  Obesity
  Insulin resistance

Viral Factors

- Genotype 3
- Coinfection with HBV or HIV

Interferon Ineligible
Definition

- Intolerance to IFN
- Autoimmune hepatitis and other autoimmune disorders
- Hypersensitivity to PEG or any of its components
- Decompensated hepatic disease
- History of depression
- Clinical features consistent with depression
- A baseline neutrophil count below 1500/µL
- A baseline platelet count below 90,000/µL
- A baseline hemoglobin below 10 g/dL
- A history of preexisting cardiac disease

Grading of the Evidence

Classification	Description
Class I	Conditions for which there is evidence and/or general agreement that a given diagnostic evaluation, procedure, or treatment is beneficial, useful, and effective
Class II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness and efficacy of a diagnostic evaluation, procedure, or treatment
Class IIa	Weight of evidence and/or opinion is in favor of usefulness and efficacy
Class IIb	Usefulness and efficacy are less well established by evidence and/or opinion
Class III	Conditions for which there is evidence and/or general agreement that a diagnostic evaluation, procedure, or treatment is not useful and effective or if it in some cases may be harmful
Level of Evidence	**Description**
Level A	Data derived from multiple randomized clinical trials or meta-analyses
Level B	Data derived from a single randomized trial, or nonrandomized studies
Level C	Consensus opinion of experts, case studies, or standard of care

Concomitant Medications	Ledipasvir	Paritaprevir / Ritonavir / Ombitasvir + Dasabuvir	Simeprevir	Sofosbuvir
Acid-reducing agents*	-Decrease Omeprazole not to exceed 20 mg a day.	-Increase Omeprazole but do not exceed 40 mg a day ; decreases effect of Omeprazole.		
Alfuzosin/tamsulosin		-Do not take with Viekira; can cause hypotension.		
Anticonvulsants	-AVOID: Carbamazepine, Phenytoin; decrease Ledispavir	-Do not take with Carbamazepine, phenytoin, Phenobarbital. Loss of effectiveness of Viekira.	-DO NOT USE; DECREASES SIMEPREVIR EFFECT: Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin.	-DO NOT USE; DECREASES SOFASBUVIR EFFECT: Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin
Antiretrovirals*	-with tenofovir only if CrCl >/= 60; -DO NOT USE with cobicistat, elvitegravir nor tipranavir	-Atazanavir without Ritonavir: give only 300 mg and only in am. Likely to elevate bilirubin. -Do not give Darunavir/Ritonavir -Do not give Lopinavir/Ritonavir -Do not give Rilpivirine (QT prolongation) -Do not give with Efavirenz (liver enzyme elevation).	-DO NOT USE; INCREASES SIMEPREVIR LEVELS: Cobicistat-containing product (elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil fumarate), Darunavir, Ritonavir -DO NOT USE; DECREASES SIMEPREVIR EFFECT: Efavirenz -DO NOT USE; VARIABLE EFFECT ON SIMEPREVIR: Atazanavir, Fosamprenavir, Lopinavir, Indinavir, Nelfinavir, Saquinavir, Tipranavir, Delavirdine, Etravirine, Nevirapine	-DO NOT USE; DECREASES SOFOSBIVIR EFFECT: tipranavir / ritonavir only.
Azole antifungals*		-Do not exceed Fluconazole 200 mg a day. -Avoid using Voriconazole.	-DO NOT USE; INCREASES SIMEPREVIR LEVELS: Itraconazole, Ketoconazole, Posaconazole, Fluconazole , Voriconazole.	
Buprenorphine/ naloxone		-No dose modification, BUT monitor closely for sedation and cognitive effects.		

Concomitant Medications	Ledipasvir	Paritaprevir / Ritonavir / Ombitasvir + Dasabuvir	Simeprevir	Sofosbuvir
Calcineurin inhibitors*		-Reduce CSA to 1/5th of original dose and monitor levels; readjust by blood levels at EOT. Monitor renal function. -Tacrolimus: do not give in day 1 of Viekira; start day 2 with 0.5 mg a week adjusting dose and frequency by blood levels. Monitor renal function.	-MODEST EFFECT AND REQUIRES MONITORING: Cyclosporine, Tacrolimus, Sirolimus	
Calcium channel blockers*		- Dose reduce Amlodipine and monitor BP.	-USE WITH CAUTION AND MONITORING: Amlodipine, Diltiazem , Felodipine, Nicardipine, Nifedipine, Nisoldipine, Verapamil	
Cisapride		X	-Increases Cisapride level	
Digoxin	-AVOID: increases Digoxin levels.		-Increases Digoxin levels; reduce dose and monitor levels.	
Ergot derivatives		-Do not give with Ergotamine, dihydroergotamine, methylergonovine.; can cause ergot toxicity (vasospasm + ischemia).		
Ethinyl estradiol–containing products		-Do not give with BCPs or patches (Lo Estrin, FE, Norinyl, Ortho Tri-Cyclen Lo, Ortho Evra), or Rings (NuvaRing), or hormone replacement (FEM HRT); Causes ALT elevation.		
Furosemide		-Increases effect of furosemide; reduce dose or monitor.		

Concomitant Medications	Ledipasvir	Paritaprevir / Ritonavir / Ombitasvir + Dasabuvir	Simeprevir	Sofosbuvir
Gemfibrozil		-Do not take with Gemfibrozil (Lopid); causes QT prolongation.		
Glucocorticoids		-Inhaled, or Intranasal Fluticasone is absolved in excess and causes decreased cortisol levels.	-Decreases Simeprivir effect: Dexamethasone.	
Herbals St. John's wort Milk thistle		-Causes loss of activity of Viekira: St. John's wort	-DO NOT USE; DECREASES SIMEPREVIR LEVEL: St John's wort. -DO NOT USE; INCREASE SIMEPREVIR LEVEL: Milk Thistle	-DO NOT USE; DECREASES SOFOSBUVIR EFFECT: St. John's wort
Macrolide antimicrobials*			-DO NOT USE: Erythromycin, Clarithromycin, Telithromycin; increases Simeprivir levels. -Simeprevir also increases antibiotic level.	
Other antiarrythmics*	-DO NOT TAKE HARVONI WITH AMIODARONE	-USE WITH CAUTION AND MONITORING: Amiodarone, Bepridil, Disipyramide, Flecainidine, Lidocaine (systemic), Mexiletine, Propafenone, Quinidine; increases antiarrhythmic effect; follow drug levels.	-USE WITH CAUTION AND MONITORING: Digoxin, Amiodarone, Disopyramide, Flecainide, Mexiletine, Propafenone, Quinidine	-DO NOT TAKE WITH AMIODARONE (especially when combined with Simeprivir or Daclatasvir)
Phosphodiesterase type 5 inhibitors*		-Revatio CONTRAINDICATED because effect is increased; risk of visual disturbance, hypotension, priapism, and syncope.	-USE WITH CAUTION AND MONITORING: Sildenafil , Tadalafil , Vardenafil all need dose adjustment when treating pulmonary hypertension.	

Concomitant Medications	Ledipasvir	Paritaprevir / Ritonavir / Ombitasvir + Dasabuvir	Simeprevir	Sofosbuvir
Pimozide		-Do not give Pimozide with Viekira; risk of cardiac arrhythmias.		
Rifamycin antimicrobials	-AVOID; Decreases Ledipasvir level.	-Rifampin causes loss of effect of Viekira.	-DO NOT USE; Decrease Simeprivir level: Rifampin, Rifabutin, Rifapentine	-DO NOT USE; DECREASES SOFOSBUVIR EFFECT: Rifampin, Rifabutin, Rifapentine
Salmeterol		-Not recommended due to increased risk of QT prolongation and sinus tachycardia.		
Sedatives		- Do not give with Oral Midazolam nor Triazolam; prolonged sedation and respiratory depression. -Alprazolam : consider dose reduction; effect is increased.	-USE WITH CAUTION AND MONITORING: Oral Midazolam and Triazolam	
Simeprevir	-AVOID: Increases levels of both drugs.			
Statins	-Rosuvastatin: AVOID; Increases rosuvastatin level and risk of myopathy and rhabdomyolysis.	-CONTRAINDICATED with Lovastatin and Simvastatin ; risk of myopathy and rhabdomyolysis. -Limit Rosuvastatin to 10 mg/d . -Limit Pravastatin to 40 mg/d.	-Rosuvastatin max 10 mg, -Atorvastatin max 40 mg, -Simvastatin lowest possible dose, -Pitavastatin lowest possible dose, -Pravastatin lowest possible dose, -Lovastatin lowest possible dose	

Treatment Naïve or Relapsers after Peg-IFN/RBV

Genotype	Recommended	Alternative	NOT Recommended
1	-**SOF 400 + SMV* 150 ± RBV** 1-1.2g x 12 weeks (24 weeks in cirrhosis) (all: 93%-96%). -**SOF/LED 400/90** (Naive F0-2, < 6 Million x 8 weeks: 97%); (Naive F0-2,> 6 Million x 12 weeks: 96%); (F3-4 x 12w: 94%) -**VIEKIRA +/- RBV**: **1a** F0-2 with RBV 1-1.2 x 12 weeks (96%);F3-4 with RBV 1-1.2 x 24 weeks (95%); **1b** F0-2 (without RBV) x 12 weeks (100%);F3-4 with RBV 1-1.2 x 12 weeks (99%). -**GZR 100 + EBR 50** x 12 weeks (1a:92%; 1b:99%)	-None	-SOF 400 + PEG/RBV 1-1.2g x 12 weeks (Cir:80%; NCir:92%) -TVR + PEG/RBV x 24 or 48 weeks (RGT) -BOC + PEG/RBV x 28 or 48 weeks (RGT) -PEG/RBV x 48 weeks -Monotherapy with PEG, RBV, or a DAA -Do not treat decompensated cirrhosis with PEG or SMV
2	-**SOF 400 + RBV** 1-1.2g x 12 weeks ; 16 weeks in cirrhosis (Naive:94%)	-**SOF/LED 400/90** x 12 weeks (96%)	-PEG/RBV x 24 weeks -Monotherapy with PEG, RBV, or a DAA -Any regimen with TVR, BOC, or SMV
3	-**SOF 400 + RBV** 1-1.2g x 24 weeks (Naive:93%; Rlap:77%; C: 82-92%) -**DCV 60 + SOF 400** x 12 weeks Naïve: NC: 97%, NOT in *Cirrhosis: SVR only 58%*)	-**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks (compensated F3/F4 cirrhosis) (Naive:97%; if **Cirrhosis: 92%**) -**GZR + EBR + SOF** x 12 weeks in cirrhosis (SVR 91%)	-PEG/RBV x 24-48 weeks -Monotherapy with PEG, RBV, or a DAA -Any regimen with TVR, BOC, or SMV
4	-**SOF 400 + RBV** 1-1.2g x 24 weeks (Naive: 92-100%) -**SOF/LED 400/90** x 12 weeks (95-100%) -**TECHNIVIE + RBV** 1-1.2g/d x 12 weeks (100%) -**SOF/SMV 400/150 +/- RBV** x 12 weeks (100%)	-<u>IFN eligible Naive</u>**:** -**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks (Naive:96%) -**GZR 100 + EBV 60 +/- RBV** x 12 weeks (SVR: 90-100%)	-PEG/RBV x 48 weeks -Monotherapy with PEG, RBV, or a DAA -Any regimen with TVR or BOC
5	-**SOF/LED 400/90** x 12 weeks (SVR 95%) -**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks	-**PEG/RBV** 1-1.2g x 48 weeks -**GZR 100 + EBV 60 + RBV** x 12 weeks (100%)	Monotherapy with PEG, RBV, or a DAA -Any regimen with TVR or BOC
6	-**SOF/LED 400/90** x 12 weeks (SVR: 96%)	-**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks (100 %) -**GZR 100 + EBV 60** x 12 weeks (SVR: 80%)	

* Do not use in Q80K polymorphism

Previous Peg-IFN/RBV Failures (Non-responders or Null-Responders)

Genotype	Recommended	Alternative	NOT Recommended
1	-**SOF/LED 400/90 +/- RBV**: In 1a or b: F0-2: SOF/LED 400/90 x 12 weeks (95%);F3-4: SOF/LED 400/90 **+ RBV** 1-1.2 g x 12 weeks (SVR 96%), or SOF/LED 400/90 x 24 weeks (100%) -**SOF 400 + SMV* 150 ± RBV** 1-1.2g x 12 weeks (24 weeks in cirrhosis) (all:93%-96%) -**VIEKIRA +/- RBV**: **1a** F0-2 with RBV 1-1.2 x 12 weeks (96%);F3-4 with RBV 1-1.2 x 24 weeks (95%); **1b** F0-2 (without RBV) x 12 weeks (100%); F3-4 with RBV 1-1.2 x 12 weeks (99%) -**GZR 100 + EBR 50 + RBV** x 16 weeks (F0-4: SVR 97%)	-None -In previous **SOFOSBUVIR FAILURES (after RAV testing)** **If NS5A RVA is negative:** -**with ADVANCED FIBROSIS**: **SOF/LED 400/90 + RBV** 1-1.2 x 24 weeks (unknown SVR) F0-F2 in need of URGENT therapy: **SOF/LED 400/90 + RBV** 1-1.2 x 12 weeks **If NS5A RAV is (+) but NS3A is (-) for RAVs:** -**SIM/SOF** 150/400 x 24 weeks	-PEG/RBV ± telaprevir or boceprevir -Monotherapy with PEG, RBV, or a DAA -Do not treat decompensated cirrhosis with PEG or SMV -SOF x 12 weeks + PEG/RBV 1-1.2g x 12-24 weeks (C:80%; NC:92%) -SOF 400 + RBV 1-1.2g x 24 weeks (all:70%) -SIM x 12 weeks + PEG/RBV 1-1.2 x 48 weeks (null:53%,Partl:65%)
2	-**SOF 400 + RBV** 1-1.2g x 12-16 weeks (88%-91%) (16 weeks in cirrhosis)	-**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks (96%)	-PEG/RBV ± telaprevir or boceprevir -Monotherapy with PEG, RBV, or a direct-acting antiviral agent -Do not treat decompensated cirrhosis with PEG
3	-F0-2: **SOF 400 + RBV** 1-1.2g x 24 weeks (87%) -F3-4: **SOF 400 + Peg/RBV** 1-1.2 g/d x 12 weeks (83-86%) -**SOF/LED 400/90 + RBV 1-1.2** x 12 weeks (F0-2: 89%; F3-4: 73%)	-F0-2: **SOF 400 + PEG/RBV** 1-1.2g x 12 weeks (83%) -F3-4: **SOF 400 + RBV** 1-1.2g/d x 24 weeks (60%) -**DCV 60 + SOF 400** x 12 weeks; All SVR 86%; NC: 94%; C: 69% (higher with 24 weeks + RBV)	-PEG/RBV ± any current protease inhibitor -Monotherapy with PEG, RBV, or a DAA -Do not treat decompensated cirrhosis with PEG
4	-**TECHNIVIE + RBV** 1-1.2 g x 12 weeks (100%) -**SOF/LED 400/90** x 12 weeks (95%) (24 w for C) -**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks (96%) -**SOF 400 + RBV** 1-1.2g x 24 weeks (89%) -**GZR 100 + EBR 50 + RBV** x 16 weeks (F0-4: SVR 97%)		-PEG/RBV ± any current HCV protease inhibitor -Monotherapy with PEG, RBV, or a DAA -Do not treat decompensated cirrhosis with PEG
5	-**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks -**SOF/LED** 400/900 x 12 weeks	-**PEG/RBV** 1-1.2 g/d x 48 weeks	-PEG/RBV ± any current HCV protease inhibitor -Monotherapy with PEG, RBV, or a DAA -Do not treat decompensated cirrhosis with PEG
6	-**SOF/LED 400/90** x 12 weeks (SVR: 96%) -**GZR 100 + EBR 50 + RBV** x 16 weeks (F0-4: SVR 97%)	-**SOF + Peg/RBV** 1-1.2 g/d x 12 weeks (100%)	

* Do Not use in Q80K polymorphism

Previous Failure with Peg-IFN/RBV + Telaprevir or Boceprevir

Genotype	Recommended	Alternative	NOT Recommended
1a or b	-F0-2: **SOF/LED 400/90** x 12 weeks (SVR 96%) -F3-4: **SOF/LED 400/90 + RBV** 1-1.2 g/d x 12 weeks, or **SOF/LED 400/90** x 24 weeks (SVR 97%) -F0-4: **GZR 100 + EBR 50 + RBV** 1-1.2 x 12 weeks (SVR 96%)	-None	-PEG/RBV ± telaprevir or boceprevir or SMV -Monotherapy with PEG, RBV, or a DAA -Do not treat decompensated cirrhosis with PEG or SMV

Treatment in Cirrhosis

- **Treatment-naive patients with compensated cirrhosis, including those with hepatocellular carcinoma**: should receive the same treatment as recommended for patients without cirrhosis. **Rating: Class I, Level A**
- ***Patients with decompensated cirrhosis (moderate or severe hepatic impairment; CTP class B or C):*** *should be referred to a medical practitioner with expertise in that condition (ideally in a liver transplant center).* **Rating: Class I, Level C**
- ***Patients with any HCV genotype who have DECOMPENSATED cirrhosis (moderate or severe hepatic impairment; CTP class B or C)*** *who may or may not be candidates for liver transplantation,* ***including those with hepatocellular carcinoma****. This regimen should be used only by highly experienced HCV providers*
  - **Genotype 2 or 3: Daily Sofosbuvir (400 mg) plus weight-based RBV** (with consideration of the patient's creatinine clearance and hemoglobin level) **for up to 48 weeks. Rating: Class IIb, Level B**
  - **Genotype 1 or 4: Daily SOF/LED 400/90 + RBV 600 escalated up as tolerated x 12 weeks (SVR 86%) (24 weeks if previous SOF failure, or if RBV intolerant)** (Treatment naïve or experienced; Child-Pugh A, B, and C up to CPT 12; MELD up to 20; most had PSE and/or ascites). MELD and CPT improved in most patients during therapy.
  - **Genotype 1,2,3, or 4: Daily SOF 400/DCV 60 + RBV 600-1000 x 12 weeks; in G1: SVR 82%; in G3: SVR 70% (higher if for 24 weeks; SVR 4: 88%). The SVR in Child-Pugh = A: 92%, B: 94%, C: 56%.**
- *The following regimens are* ***NOT recommended for patients with decompensated cirrhosis*** *(moderate or severe hepatic impairment; CTP class B or C):*
  - Any IFN-based therapy. **Rating: Class III, Level A**
  - Monotherapy with PEG, RBV, or a DAA. Rating: **Class III, Level A**
  - Telaprevir-, boceprevir-, or simeprevir-based regimens. **Rating: Class III, Level A**
  - Viekira regimens

Child-Pugh Classification (non-Cholestatic)

"Decompensated Cirrhosis" = Child-Pugh B or C

	Class A	Class B	Class C
Total points	5–6	7–9	10–15
Factor	**1 Point**	**2 Points**	**3 Points**
Total bilirubin (mg/dL)	< 2	2 to 3	> 3
Serum albumin (g/L)	>35	28–35	<28
Prothrombin time/international normalized ratio	<1.7	1.71–2.30	>2.30
Ascites	None	Mild	Moderate to Severe
Hepatic encephalopathy	None	Grade I–II (or suppressed with medication)	Grade III–IV (or refractory)

Treatment Post-Liver Transplant

Genotype	Recommended	Alternative	NOT Recommended
1, & 4 (including compensated cirrhosis)	**-For Genotype 1 or 4:** -**SOF/LED 400/90 + RBV 1-1.2g x 12 weeks (96%)** (in decompensated, increasing dose weekly as tolerated from 600 mg) Rating: Class I, Level B -**SOF/LED 400/90 x 24 weeks** **-SOF 400 + DCV 60 + RBV** 600-1000 x 24 weeks (91%)	-None	-Monotherapy with PEG, RBV, or a DAA Rating: Class III, Level A -Telaprevir- or boceprevir- based regimens should not be used for patients with compensated allograft hepatitis C infection. Rating: Class III, Level A
	-For genotype 1 only: **-SOF 400 + SIM 150 +/- RBV 1-1.2 g x 12 weeks (92%)** (weight-based dose of 1000 mg [<75 kg] to 1200 mg [≥75 kg] 1200 mg). Rating: Class IIb, Level C -**For F0-2 only: VIEKIRA + RBV 1-1.2 g/day x 24 weeks** (start at 600-800 and increase weekly as tolerated) (1a: 97%; 1b: 100%) [CSA 1/5 of daily dose when starting Viekira; TAC none on 1st Viekira day, 0.5 mg/week starting day-after starting Viekira] Rating: Class I, Level B **-SOF 400 + DCV 60 + RBV** 600-1000 x 12 weeks (1a:97%; 1b: 90%)		
2 (including compensated cirrhosis)	**Daily sofosbuvir (400 mg) and RBV 1-1.2 g x 24 weeks** (if decompensated, initial dose 600 mg/day, increased weekly by 200 mg/day as tolerated to weight-based dose of 1000 mg [<75 kg] to 1200 mg [≥75 kg] 1200 mg) with consideration of the patient's CrCL value and hemoglobin level. Rating: Class IIb, Level C	-**SOF/LED 400/90** x 12 weeks if RBV intolerant.	
3 (including compensated cirrhosis)	**Daily sofosbuvir (400 mg) and RBV 1-1.2 g x 24 weeks** (if decompensated, initial dose 600 mg/day, increased weekly by 200 mg/day as tolerated to weight-based dose of 1000 mg [<75 kg] to 1200 mg [≥75 kg] 1200 mg) with consideration of the patient's CrCL value and hemoglobin level. Rating: Class I, Level B **-SOF 400 + DCV 60 + RBV** 600-1000 x 12 weeks (SVR 91%)	-**SOF/LED + RBV** (?) no enough data	
Any with decompensated cirrhosis	Treatment-naive patients with decompensated allograft HCV infection should receive the same treatment as recommended for patients with decompensated cirrhosis (moderate or severe hepatic impairment; CTP class B or C). Rating: Class I, Level C		

Treatment of HIV/HCV Co-infection

Genotype	Recommended	Alternative	NOT Recommended	Allowable Antiretroviral Therapy
1 Treatment Naïve or PEG/RBV Relapsers	-**SOF 400 + SMV* 150 ± RBV** 1-1.2g x 12 weeks (24 weeks in cirrhosis) (all: 93%-96%) -**SOF/LED 400/90** (N F0-2 <6M; 8w: 97%); (N F0-2,>6M; 12w: 96%); (F3-4 12w: 94%) -**VIEKIRA +/- RBV**: **1b** F0-2 x 12 weeks (100%);F3-4 with RBV 1-1.2 x 12 weeks (99%); **1a** F0-2 with RBV 1-1.2 x 12 weeks (96%);F3-4 with RBV 1-1.2 x 24 weeks (95%) -**GZR 100 + EBR 50** x 12 weeks (F0-4: SVR 95%)	-**SOF + DCV** x 12 weeks (F0-4 compensated) (SVR 96%),	-TVR + PEG/RBV x 24 or 48 weeks (RGT) -BOC + PEG/RBV x 28 or 48 weeks (RGT) -PEG/RBV x 48 weeks -SMV x 12 weeks + PEG/RBV x 48 weeks	**For SOF use:** ALL except didanosine, zidovudine, tipranavir **For SMV use:** Only in raltegravir, rilpivirine, maraviroc, enfuvirtide, tenofovir, emtricitabine, lamivudine, abacavir. NO with efavirenz, etravirine nevirapine, cobicistat or any HIV protease inhibitor **For LED use:** with tenofovir only if CrCl >/= 60; NO with cobicistat, elvitegravir nor tipranavir **For Viekira use:** NO with efavirenz,rilpiviride, darunavir, nor ritonavir-boosted lopinavir NO IN PATIENTS NOT TAKING HAART **For RBV use:** NO in didanoside, stavudine, nor zidovudine
1 PEG/RBV Nonresponders	-**SOF/LED 400/90 +/- RBV**: In 1a or b: F0-2: SOF/LED 400/90 x 12 weeks (95%);F3-4: SOF/LED 400/90 **+ RBV** 1-1.2 g x 12 weeks (SVR 96%), or SOF/LED 400/90 x 24 weeks (100%) -**SOF 400 + SMV* 150 ± RBV** 1-1.2g x 12 weeks (24 weeks in cirrhosis) (all:93%-96%) -**VIEKIRA +/- RBV**: **1a** F0-2 with RBV 1-1.2 x 12 weeks (96%);F3-4 with RBV 1-1.2 x 24 weeks (95%); **1b** F0-2 x 12 weeks (100%); F3-4 with RBV 1-1.2 x 12 weeks (99%)	-**SOF + DCV** x 12 weeks (F0-4 compensated) (SVR 98%), -In previous **SOFOSBUVIR FAILURES with ADVANCED FIBROSIS**: -**SOF/LED 400/90 +/- RBV** 1-1.2 x 24 weeks		Same as above
4	-**SOF 400 + RBV** 1-1.2g x 24 weeks (Naive: 84 %) -**SOF/LED 400/90** x 12 weeks -**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks -**VIEKIRA + RBV** 1-1.2g/d x 12 weeks -**GZR 100 + EBR 50** x 12 weeks (F0-4: SVR 96%)	-**SOF 400 + DCV 60 + RBV** 600-1000 x 12 weeks (Naïve or NR: SVR 97-98%)	-PEG/RBV x 48 weeks -Any regimen with TVR or BOC	**For SOF/RBV:** ALL except didanosine, zidovudine, stavudine, tipranavir **For Viekira use:** NO with efavirenz,rilpiviride, darunavir, nor ritonavir-boosted lopinavir NO IN PATIENTS NOT TAKING HAART For **GZR/EBR** OK with: Abacavir,Tenofovir, Raltegravir, Dolutegravir, Rilpivirine.
5	**Regardless of treatment history:** **-SOF 400 + PEG/RBV 1-1.2g** x 12 weeks	-**PEG/RBV** 1-1.2g x 48 weeks	-Any regimen with TVR, BOC, or SMV	**For SOF/RBV:** ALL except didanosine, zidovudine, stavudine, tipranavir
6	-**SOF/LED 400/90 x 12 weeks**	-**SOF + Peg/RBV** 1-1.2 g/d x 12 weeks		**For SOF/RBV:** ALL except didanosine, zidovudine, stavudine, tipranavir

HIV-HCV Genotype 1 Cheat Sheet

(Dr. Matt Cave)

	HIV Backbone	HIV Brand Name	HIV Generic Names	Compatible HCV regimen
Recommended HIV Regimens DHHS - 2015	Integrase	**Triumeq**	dtg/abc/3tc	Harvoni, dcv/sof, sim/sof, Merck regimen, Viekira Pak probably OK (AASLD/IDSA)
		Tivicay/Truvada	dtg/tdf/ftc	Harvoni, dcv/sof, sim/sof. Merck regimen, Viekira Pak probably OK (AASLD/IDSA)
		Stribild	evg/cobi/tdf/ftc	NO DATA; ? dcv (30 mg) / sof
		Isentress/Truvada	ral/tdf/ftc	Harvoni, Viekira Pak, dcv/sof, sim/sof, Merck regimen
	PI	**Prezista/r/Truvada**	drv/r/ftc/tdf	Harvoni, dcv/sof (dcv 30 mg given in Ally-2 but dose reduction not recommended in prescribing information).
Alternate HIV Regimens DHHS - 2015	NNRTI	**Atripla**	efv/tdf/ftc	dcv (90 mg) / sof, Harvoni
		Complera	rpv/tdv/ftc	Harvoni, dcv/sof, sim/sof, Merck regimen
	PI	**Reyataz/r/Truvada**	atv/r+tdv/ftc	Viekira Pak (hold r), dcv (30mg) / sof
		Prezista/r/Ziagen/Epivir	drv/r/abc/3tc	Harvoni, dcv/sof (dcv 30 mg given in Ally-2 but dose reduction not recommended in prescribing information).

Black patients may do less well with Harvoni.
Viekira Pak should not be given to patients not on HIV meds.
Patients on darunavir/r may do less well with dcv/sof.
No riba if didanosine, stavudine, or zidovudine.
Theoretic risk of tenofovir-mediated renal toxicity when Harvoni is given with Atripla not seen in clinical trials.
Harvoni should not be given with tenofovir if GFR < 60 or co-administered with protease inhibitor/r.
Eight week duration of therapy with Harvoni or dcv/sof may not be sufficient for co-infected patients.
Listed Merck regimens were from the list allowable in clinical trials.
Do not interrupt HIV therapy.

Treatment of HIV/HCV Co-infection

Genotype	Recommended	Alternative	NOT Recommended	Allowable Antiretroviral Therapy
2 **Treatment Naïve or Peg/RBV Relapsers**	-**SOF 400 + RBV** 1-1.2g x 12 weeks (94%)	-None	-PEG/RBV x 24-48 weeks -Any regimen with TVR, BOC, or SMV	ALL except didanosine, zidovudine, stavudine, nor tripanavir
2 **Peg/RBV Nonresponders**	**SOF 400 + RBV** 1-1.2 g/d x 12-16 weeks (91%)	-**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks (96%)		-SOF cannot be used with tipranavir -RBV cannot be used with didanoside, stavudine, nor zidovudine.
3 **Treatment Naïve or Peg/RBV Relapsers**	-**SOF 400 + RBV** 1-1.2 x 24 weeks regardless of treatment history	-**SOF 400 + PEG/RBV** 1-1.2g x 12 weeks (compensated F3/F4 cirrhosis) (Naive:97%; if C:92%)	-PEG/RBV x 24 - 48 weeks -Any regimen with TVR, BOC, or SMV	ALL except didanosine, zidovudine, stavudine, nor tripanavir
3 **Peg/RBV Nonresponders**	-F0-2: **SOF 400 + RBV** 1-1.2g x 24 weeks (87%) -F3-4: **SOF 400 + Peg/RBV** 1-1.2 g/d x 12 weeks (83%) -SOF/LED 400/90 + RBV 1-1200 x 12 weeks (?)	-F0-2: **SOF 400 + PEG/RBV** 1-1.2g x 12 weeks (83%) -F3-4: **SOF 400 + RBV** 1-1.2g/d x 24 weeks (60%)		-SOF cannot be used with tipranavir -RBV cannot be used with didanoside, stavudine, nor zidovudine.

Dose Adjustment for Renal Impairment

Renal Impairment	eGFR/CrCl level (mL/min/ 1.73 m^2)	Interferon	Ribavirin	Sofosfovir	Simeprevir
Mild	50-80	180 µg PEG (2a); PEG (2b) 1.5 µg/kg	Standard	Standard	Standard
Moderate	30-50	180 µg PEG (2a); PEG alfa-2b1 µg/kg or 25% reduction	Alternating doses 200 and 400 mg every other day	Standard	Standard
Severe	<30	135 µg PEG (2a); PEG (2b)1 µg/kg or 50% reduction	200 mg/d	Data not available	Standard
ESRD/HD		PEG (2a) 135 µg/wk or PEG (2b) 1 µg/kg/wk or standard IFN 3 mU 3x/wk	200 mg/d	Data not available	Data not available

Dose Adjustment for Renal Impairment

- In HCV g-1a or b, naïve or treatment experienced (relapser), non-cirrhotics (7% compensated cirrhosis), with CKD4/5 +/- HD: **GZR + EBR** without dose modification x 12 weeks: SVR 99%.
- In g 1a or 1b, CKD 4/5 +/- HD, **Viekira + RBV 200 in 1a (no in 1b)** x 12 wks: "high SVR 4"
- When using sofosbuvir to treat or retreat HCV infection in patients with appropriate genotypes, no dosage adjustment is required for patients with mild to moderate renal impairment (CrCl ≥30 mL/min). Sofosbuvir is not recommended in patients with severe renal impairment/ESRD (CrCl <30 mL/min) or those who require hemodialysis, because no dosing data are currently available for this patient population. **Rating: Class IIa, level B**
- When using simeprevir in treatment/retreatment of HCV-infected patients, no dosage adjustment is required for patients with mild to moderate to severe renal impairment. Simeprevir has not been studied in patients with ESRD, including those requiring hemodialysis. **Rating: Class IIa, level B**
- In patients with renal impairment/ESRD/HD, dosing of PEG and RBV should follow updated FDA recommendations or package insert recommendations based on calculated GFR. Caution should be used in administering RBV to these patients, and close monitoring of hemoglobin is required. **Rating: Class IIa, level B**

Suggested RBV dose by Creatinine Clearance

Kamar N et al. Am J Kidney Dis. 2004;43:140-146 &
Bruchfeld A et al. Drug Monit. 2002;24:701-708

Creatinine Clearance (Cockcroft-Gault)	>/= 100 mL/min	80 mL/min	60 mL/min	40 mL/min	20 mL/min	< 20 mL/min
RBV (mg/day)	1200	1000	800	600	400	200

SVR by Treatment Regimen

Genotype 1 Naive

Genotype	Status	Fibrosis	Regimen	Weeks	% SVR
1 all	naive	all	Sof+R	24	52-68
1a	**naive**	**F0-2**	**Sof+P+R**	**12**	**91-100**
		F3/F4	**“**		**89/78**
1b		**F0-2**	**“**		**92**
		F3-4	**“**		**80**
1a	Naïve Q80K(-)	All	Sim12+P+R	24(92%)-48	84
	Q80K(+)	All	“		58
1b	Naive	All	“		85
1 all		F0-2	“		84
		F3/4	“		73/60
1 all	**Naive**	**All**	**Sof+Ledipasvir**	**8**	**100**

Genotype 1 Relapser, Null, & Experienced

Genotype	Status	Fibrosis	Regimen	Weeks	% SVR
1a	**Relapser**	**All**	**Sim12+P+R**	**24-48**	**70**
1b		**All**			**86**
1 all		F0-2			82
1 all		F3			73
1 all		F4			74
1 all	**Null**	**F0-2**	**Sof+Sim+/-R**	**12**	**93/96** (90% in 1a Q80K(+))
1 all		**F3-4**			**93/96** (90% in 1a Q80K(+))
1 all	Experienced	All	Sof+Ledipasvir	12	95

Genotype 2

Genotype	Status	Fibrosis	Regimen	Weeks	% SVR
2 all	**Naive**	**F0-2**	**Sof+R**	**12**	**97**
2 all		**F3-4**	**“**		**100**
2 all	Experienced	F0-2	Sof+R	12	91
2 all		F3-4	“		88
2 all	**Experienced**	**F0-2**	**Sof+P+R**	**12**	**100**
2 all		**F3-4**	**“**		**93**

Genotype 3

Genotype	Status	Fibrosis	Regimen	Weeks	% SVR
3 all	**Naive**	**F0-2**	**Sof+R**	**24**	**94**
		F3-4	**“**		**92**
3 all	**Experienced**	**F0-2**	**Sof+R**	**24**	**87**
		F3-4	“		60
3 all	Experienced	F0-2	Sof+P+R	12	83
3 all	**Experienced**	**F3-4**	**Sof+P+R**	**12**	**83**

Genotype 4

Genotype	Status	Fibrosis	Regimen	Weeks	% SVR
4 all	**Naive**	**All**	**Sof+R**	**12**	**79**
				24	**100**
4 all	Experienced	All	Sof+R	12	59
4 all	**Experienced**	**All**	**Sof+R**	**24**	**93**

HCV + HIV Naive

Genotype	Status	Fibrosis	Regimen	Weeks	% SVR
1 all	Naive	All	Sof+R	24	76
2 all	"	"	"	12	88
3 all	"	"	"	12	67
1a	**Naive**	**All**	**Sof+P+R**	**12**	**87-89**
1b	"	"	"	**12**	**100**
2	"	"	"	**12**	**100**
3	"	"	"	**12**	**100**
4	"	"	"	**12**	**100**

HIV/HCV Coinfection

- Broad inclusion criteria
  - Cirrhosis permitted with no platelet cutoff
  - Hemoglobin: ≥12 mg/dL (males); ≥11 mg/dL (females)
- Wide range of ART regimens allowed
  - Undetectable HIV RNA for >8 weeks on stable ART regimen
- Baseline CD4 count
  - ART treated: CD4 T-cell count >200 cells/mm^3 and HIV RNA < 50 c/mL
  - ART untreated: CD4 T-cell count >500 cells/mm^3
- Tenofovir DF/emtricitabine plus
  - Efavirenz
  - Atazanavir/ritonavir
  - Darunavir/ritonavir
  - Raltegravir
  - Rilpivirine