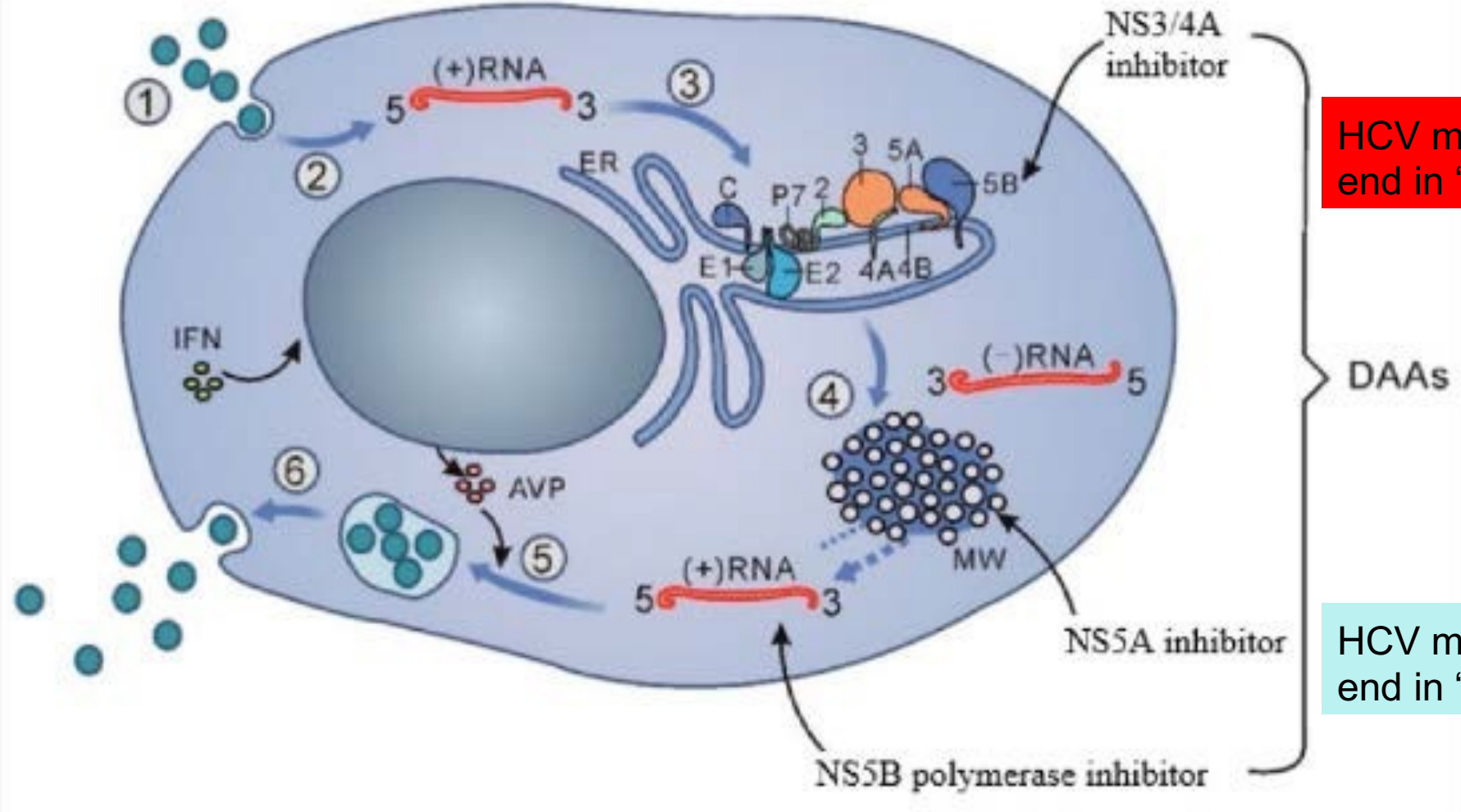


HCV 101: Meds and Management

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Direct Acting Antivirals (DAAs) Work on the Hepatitis C Virus



HCV meds that end in "buvir"

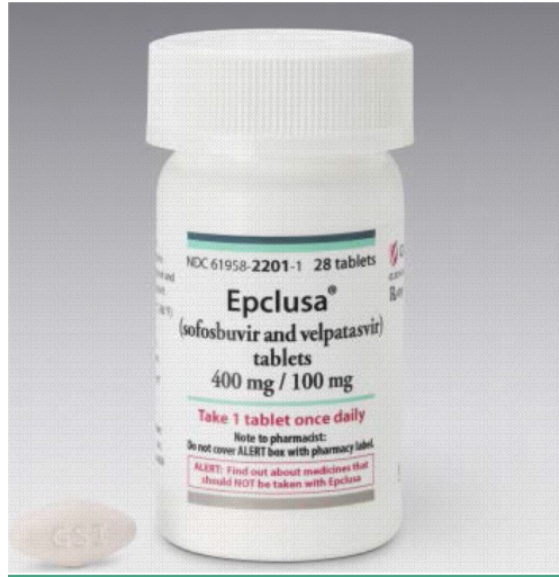
HCV Direct
Acting
Antivirals
(DAAs):
Name shows
where the drug
is working on
the virus

Target	NS3/4A: Protease Inhibitors (-previr)	NS5A: Replication Complex Inhibitors (-asvir)	NS5B: Polymerase Inhibitors (-buvir)
	Grazoprevir Glecaprevir Voxilaprevir	Ledipasvir Elbasvir Velpatasvir Pibrentasvir	Nucleotide: Sofosbuvir
	Boceprevir* Telaprevir* Simeprevir*	Ombitasvir* Daclatasvir*	Non-nucleoside: Dasabuvir*
	Paritaprevir*		

*no longer available in US

HCV Direct Acting Antivirals (DAAs) Generic Name	Brand Name	Comments
Glecaprevir/Pibrentasvir	Mavyret®	Pan-genotypic
Sofosbuvir/ Velpatasvir	Epclusa® agEpclusa®	Pan-genotypic
Sofosbuvir/ Velpatasvir/ Voxilaprevir	Vosevi®	Pan-genotypic
<i>Other Therapies</i>		
Ribavirin	Ribasphere®, RibaPak®, Copegus®, Rebetol®	

Sofosbuvir/ Velpatasvir (SOF/VEL)



**AUTHORIZED GENERIC OF
EPCLUSA®
(SOFOSBUVIR/VELPATASVIR)**

Prescribing information,
including **BOXED WARNING** ▶

BLISTER PACK

NDC: 72626-2701-1

Tablet: 400/100 mg

28 count

- Fixed-dose combination of sofosbuvir (NS5B inhibitor) and velpatasvir (NS5A inhibitor)
- Approved for chronic HCV genotypes 1, 2, 3, 4, 5, or 6 for 12 weeks
- Administration
 - 1 tablet once daily with or without food
 - Requires acidic environment for absorption

Who Can Be Treated with Sofosbuvir/Velpatasvir?

- Patients without cirrhosis
- Patients with cirrhosis, including Child's class A, B or C cirrhosis
- Patients with renal insufficiency including patients on dialysis
- Approved for use in pediatric patients 3 years old and older

Glecaprevir/ Pibrentasvir (G/P)



- Glecaprevir an NS3/4A protease inhibitor
- Pibrentasvir an NS5A inhibitor

- Dosage and administration: 3 tablets once daily with food
- Indicated for 8-12 weeks

Who Can Be Treated with Glecaprevir/Pibrentasvir?

- Patients without cirrhosis
- Patients with Child's class A cirrhosis (compensated cirrhosis)
- Do not use in patients with Child's Class B or Child's Class C cirrhosis (decompensated cirrhosis)
- Patients with renal insufficiency including patients on dialysis

- Approved for use in children 3 yo and older

Sofosbuvir/ Velpatasvir/ Voxilaprevir



- Combination of
 - NS5B polymerase inhibitor (Sofosbuvir);
 - NS5A inhibitor (Velpatasvir);
 - NS3/4A protease inhibitor (Voxilaprevir)
- Administration
 - One tablet once daily with food
- Indicated for patients who were previously failed by DAA therapy

Who Can Be Treated with SOF/VEL/VOX?

- Patients without cirrhosis
- Patients with Child's class A cirrhosis (compensated cirrhosis)
- Patients with renal insufficiency including hemodialysis

- Not recommended in patients with Child's Class B or C cirrhosis

Ribavirin

- **Limited use**

- Added to treatment in specific clinical scenarios
 - Patients with decompensated cirrhosis who can tolerate ribavirin

- Well-known toxicity profile
 - Hemolytic anemia
 - Teratogenic
 - Pregnancy category X

Side Effect Profile of DAAs

- Prior treatments:
 - Interferon:
 - Flu-like symptoms: fever, headache, myalgia
 - Fatigue
 - Depression
 - Irritability
 - Insomnia
 - Nausea/ vomiting
 - Anorexia
 - Cognitive dysfunction
 - Ribavirin:
 - Rash
 - Nausea/vomiting
 - Headache
- DAAs:
 - Overall very well tolerated
 - Most commonly reported side effects:
 - Headache
 - Fatigue
 - Nausea
 - Diarrhea (reported with voxilaprevir)

Laboratory Abnormalities with DAAs

- Overall not common
- Observed laboratory abnormalities:
 - Anemia with concomitant use of ribavirin
 - Ribavirin causes hemolytic anemia
- Potential laboratory abnormalities:
 - Improvement in liver disease can affect other medications:
 - Hypoglycemia: Patients on diabetic medications may require closer follow up and reduction in diabetic medication- *particularly true for diabetic medications known to cause hypoglycemia*
 - Changes in INR with warfarin

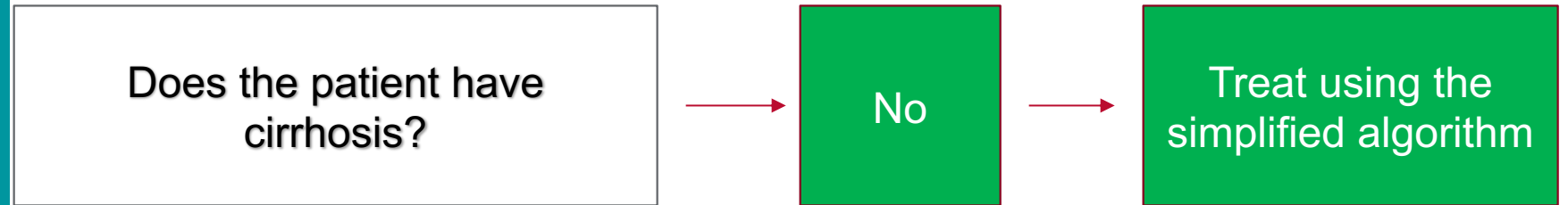
HBV Reactivation Risk in HCV

- FDA warning issued 2016 following 24 reported cases of HBV reactivation in patients treated with HCV DAAs
 - 2 deaths
 - 1 liver transplant
- Mechanism of reactivation unclear
 - HCV DAAs do not have immunosuppressive effects
- Current recommendations are to “evaluate patients for potential coinfection of HCV and HBV”
 - ***All patients should be tested for anti-HBc, HBsAg, anti-HBs***

What Predicts Treatment Success or Failure?

- Patients who are treatment naïve and non-cirrhotic have very high SVR rates
- Underlying cirrhosis can decrease SVR
- Medication adherence

General Approach to HCV Treatment



Perform Baseline Assessment

Within 6 months:

1. CBC
2. Hepatic panel (albumin, AST, ALT, total & direct bilirubin)
3. Chem7
4. PT/INR

Documentation of:

1. HCV RNA and genotype
2. HIV Ab
3. HBsAg, anti-HBc (IgG or total), anti-HBs
4. HAV Ab (IgG or total)

Does this patient have:

- Prior HCV treatment
- Cirrhosis (on imaging or labs)
- ESRD (GFR \leq 30 ml/min/m²)
- HBsAg positivity
- Prior liver transplant
- Pregnancy
- Hepatocellular carcinoma (known or suspected)

YES

NO

STOP
Do not use this algorithm

Check for drug-drug interactions:
hep-druginteractions.org
Check current medications and any over-the-counter products
Avoid herbals/supplements during HCV treatment
Patients on diabetic medications may develop symptomatic hypoglycemia

Counsel on avoiding pregnancy

Counsel on medication adherence and follow up with patient as clinically indicated

Counsel on avoiding acid suppressive therapy (especially important for Epclusa)

Start HCV Treatment

**(Mavyret)
G/P
x 8 wks**

OR

**(Epclusa)
SOF/VEL
x 12 wks**

Repeat HCV RNA and LFTs \geq 12 wks after end of treatment

If LFTs remain elevated after SVR, investigate for other causes of liver disease

What About Medications in Patients with HCV?

Current Medications:

Medication name:	Dosage:	Frequency	Medication name:	Dosage:	Frequency

Current Method of Birth Control: _____

If oral contraceptive, does it contain ethinyl estradiol? Yes No

- Avoid herbals
- Verify potential drug interactions using Liverpool website
- In patients with cirrhosis
 - Avoid NSAIDs
 - Acetaminophen preferred for short-term pain management at <2 grams per day

Other Main Drug Interaction Concerns for DAAs

- Statins:
 - Interactions vary by DAA and statin
 - Safest option may be to hold statin during HCV therapy
- Acid suppressive therapy:
 - **Velpatasvir requires acidity for absorption**
 - Recommend minimizing acid suppressive therapy in all patients undergoing HCV therapy
- Avoid amiodarone
 - Amiodarone with sofosbuvir and other DAA: Serious symptomatic bradycardia

Major Drug- Drug Interactions for all Direct Acting Antivirals

- **Carbamazepine**
- **Oxcarbazepine**
- **Phenytoin**
- **Phenobarbital**
- **Rifampin**
- Expected to ↓ concentrations
- **DO NOT USE WITH HCV THERAPY!**

What About Medications in Patients with HCV?

Current Medications:

Medication name:	Dosage:	Frequency	Medication name:	Dosage:	Frequency

Current Method of Birth Control: _____

If oral contraceptive, does it contain ethinyl estradiol? Yes No



Avoid ethinyl estradiol with glecaprevir/pibrentasvir

- Studies in pregnancy currently enrolling

“Despite the lack of a recommendation, treatment can be considered during pregnancy on an individual basis after a patient-physician discussion about the potential risks and benefits”

- **Bottom line: Recommend birth control in all female patients of childbearing age/capacity**

HCVguidelines.org. Accessed January 25, 2022

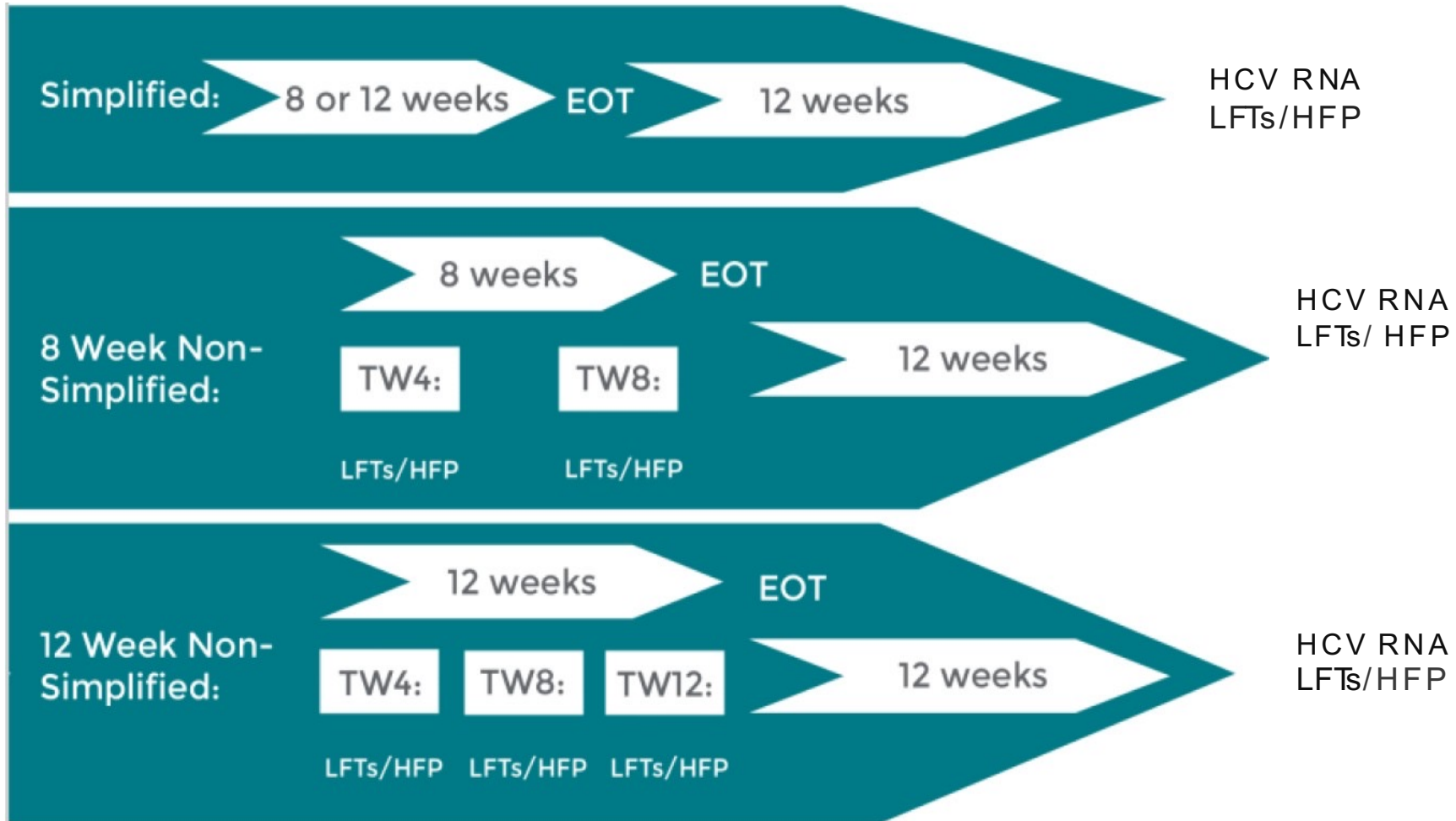
Baseline Labs

CBC
Chem7
LFTs/ HFP
HCV RNA and GT
Anti-HAV
Anti-HBc (IgG or total)
Anti-HBs
HBsAg
Ant-HIV
PT/ INR (only if presumed cirrhosis)

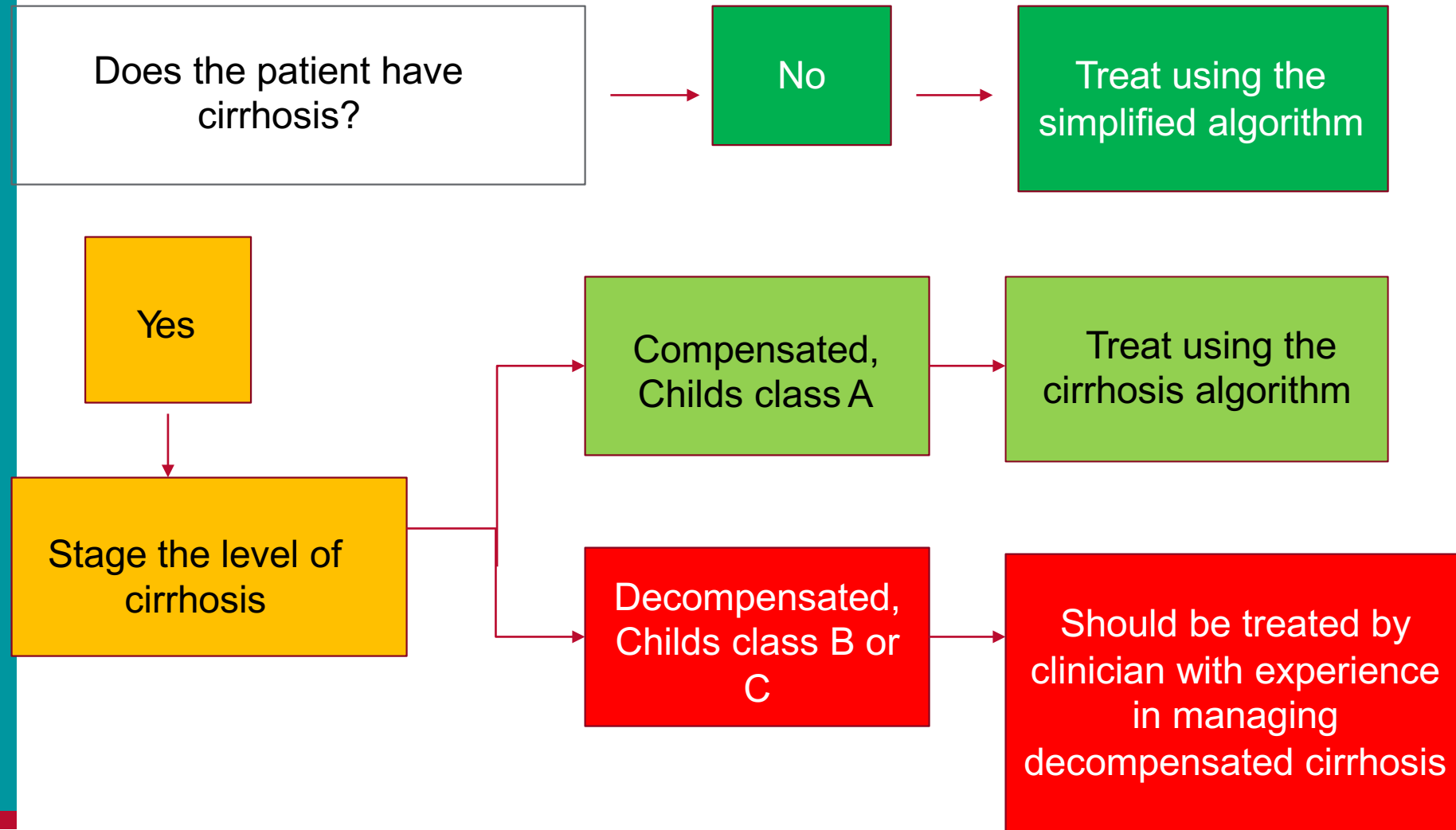


HCV On-Treatment Monitoring*

EOT: End of Treatment. TW: Treatment Week, *Does not apply to patients on OAA therapy plus ribavirin



General Approach to HCV Treatment



Treatment Options for Patients with Decompensated Cirrhosis

- Sofosbuvir/velpatasvir plus ribavirin x 12 weeks
 - Use of ribavirin requires frequent monitoring for hemolytic anemia
- Sofosbuvir/velpatasvir x 24 weeks
- All protease inhibitor therapy is contraindicated in decompensated cirrhosis due to reports of serious liver injury