HCV Treatment Options

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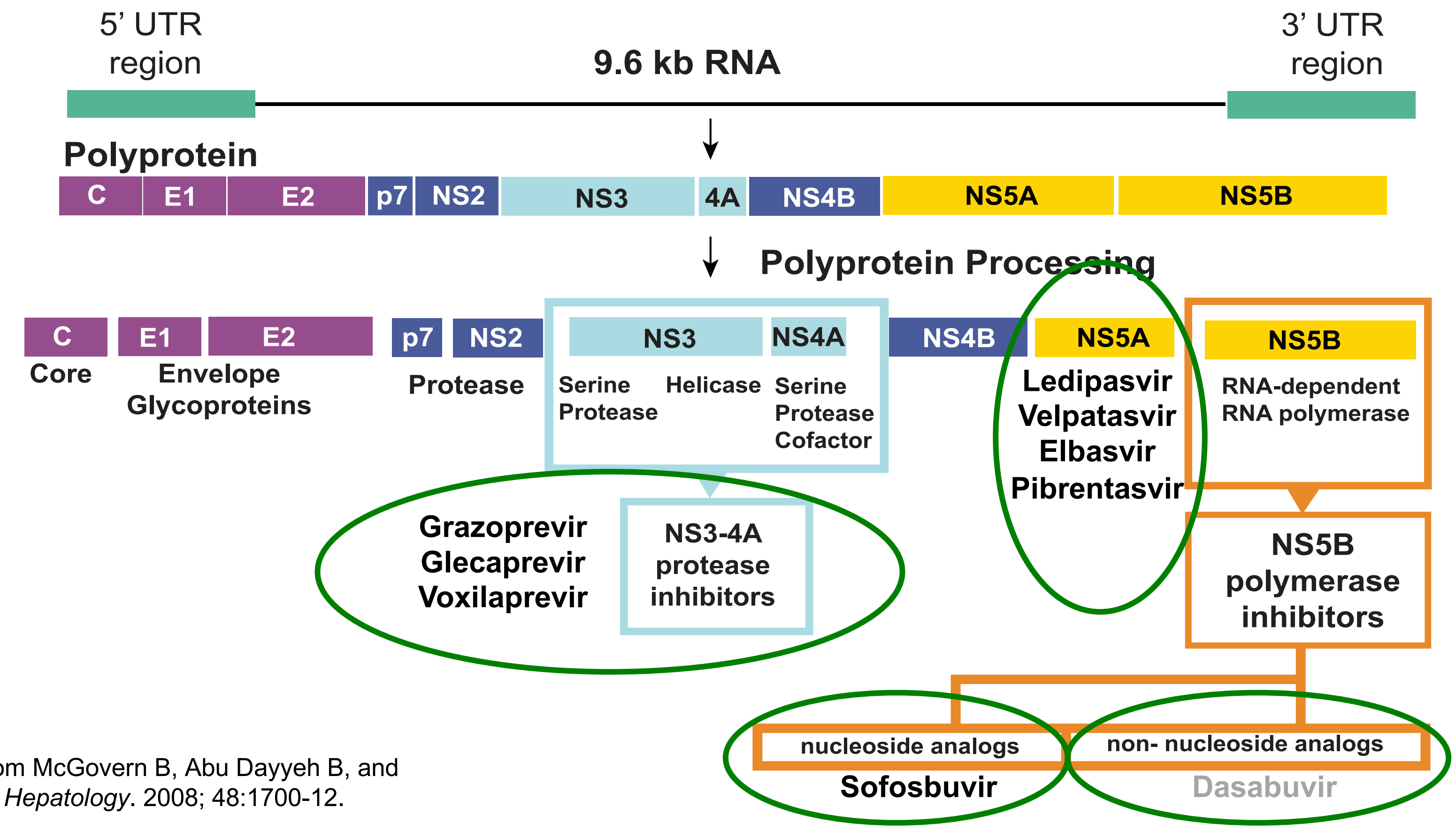
January 15, 2021

Harm Reduction ECHO: HCV and Liver Health

Increased in LFT during treatment.

- Compliance
- Concurrent infections.
- DILI (Drug Induced Liver Injury)
- DDI (Drug and Drug Interaction).
- Other causes of hepatitis.
- Increased bilirubin in patient taking Mavyret:
  - In creased total bilirubin more than 2x ULN noted in 3.5% of the initial clinical trial compared to 0% in placebo. 1.2% in Phase 2/3 trial but no concurrent elevation of transaminases.
  - Inhibition of Organic Anion Transporting Polypeptides 1B 1/3. And to a lesser degree UGT 1A1 (Uridine Glucuronosyltransferase).
  - Estrogen containing agent cause increased hepatitis in young women during the clinical trial.

Multi-targeted Approach for Treatment: Approved Protease, Polymerase and NS5A Inhibitors



Adapted from McGovern B, Abu Dayyeh B, and Chung RT. *Hepatology*. 2008; 48:1700-12.

HCV Landscape: Select All-Oral DAA Options for Treatment-Naïve Non-Cirrhotic Patients

- These products differ with respect to indications, patient populations studied, and clinical safety and efficacy profile. No conclusions regarding comparative safety or efficacy should be drawn from the information presented.

	Ledipasvir/sofosbuvir[1]	Elbasvir/grazoprevir[2]	Sofosbuvir/velpatasvir[3]	Glecaprevir/pibrentasvir[4]
Manufacturer	Gilead	Merck	Gilead	AbbVie
FDA approval	October 2014	January 2016	June 2016	August 2017
Boxed warning	RISK OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS COINFECTED WITH HCV AND HBV: Test all patients for evidence of current or prior HBV infection before initiating HCV treatment. HBV reactivation has been reported, in some cases resulting in fulminant hepatitis, hepatic failure, and death.			
HCV genotype	1 2 3 4 5 6	1 2 3 4 5 6	1 2 3 4 5 6	1 2 3 4 5 6
Treatment duration	12 or 24 weeks*	12 or 16 weeks	12 weeks	8, 12, or 16 weeks
Dosing and administration	1 tablet once daily with or without food	1 tablet once daily with or without food	1 tablet once daily with or without food	3 tablets once daily with food
Compensated cirrhosis	Yes	Yes	Yes	Yes
Decomp. cirrhosis (Child-Pugh B or C)	GT1	No	Yes	No
Severe renal impairment or ESRD	Yes	Yes	yes	Yes
HIV coinfection	Yes	Yes	Yes	Yes
Concomitant RBV	Decomp. cirrhosis Liver transplant	GT1a with resistance GT1 or 4 P/R-experienced	Decomp. cirrhosis	Not indicated for any population

*8 weeks can be considered in GT1 treatment naïve, non-cirrhotic patients with <6 million IU/mL baseline viral load

AbbVie Inc. manufactures, markets, and sells MAVYRET.

Please see Mavyret Product Information on slide 34. For further information, please refer to the full US Prescribing Information at www.rxabbvie.com

ESRD=end-stage renal disease; HBV=hepatitis B virus; P/R=pegylated interferon + ribavirin; .

1. Harvoni Prescribing Information. November 2017; 2. Zepatier Prescribing Information. June 2018; 3. Epclusa Prescribing Information. November 2017; 4. Mavyret Prescribing Information. April 2019.

- Glecaprevir/pibrentasvir (300/120 mg qd) for 8 weeks
  - Adolescents aged ≥12 years or weighing ≥45 kg
  - Any genotype, without cirrhosis or with compensated cirrhosis (Child-Pugh A)
- Ledipasvir/sofosbuvir (weight-based dosing) for 12 weeks
  - Children aged ≥3 years
  - Genotypes 1, 4, 5, or 6
  - Without cirrhosis or with compensated cirrhosis (Child-Pugh A)
- Sofosbuvir/velpatasvir (weight-based dosing) for 12 weeks*
  - Children ≥6 years
  - Genotype 1, 2, 3, 4, 6 without cirrhosis or with compensated cirrhosis

*July 2020 update to full prescribing information.

AASLD-IDSA. http://www.hcvguidelines.org/full-report-view. Version November 6, 2019.

- SVR12 rates for all recommended regimens for HCV : ≥95%

Treatment Duration (weeks)

Genotype	Regimen	No Cirrhosis	Compensated Cirrhosis
1-6	Glecaprevir/pibrentasvir	8	8
1-6	Sofosbuvir/velpatasvir	12	12
1,4-6	Ledipasvir/sofosbuvir	8* or 12	12
1 or 4	Elbasvir/grazoprevir	12†	12†

*Only for patients who are HIV-uninfected and have a baseline HCV RNA <6M IU/mL.
†Only for genotype 1a patients without baseline NS5A RASs for elbasvir.

AASLD-IDSA. http://www.hcvguidelines.org/full-report-view. Version November 6, 2019.

	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Sofosbuvir/Velpatasvir/ Voxilaprevir
Antacids	√			√	
Cimetidine				√	
Esomeprazole				√	
Famotidine				√	
Lansoprazole				√	
Omeprazole				√	
Pantoprazole				√	
Rabeprazole				√	
Ranitidine				√	

No clinically significant interaction expected | Potential weak interaction | Potential interaction | Do not coadminister

https://www.hep-druginteractions.org/.

	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Sofosbuvir/Velpatasvir/ Voxilaprevir
Desogestrel	√	√	√	√	√
Dienogest	√	√	√	√	√
Drospirenone	√	√	√	√	√
Estradiol			√	√	
Etonogestrel (implant)	√	√	√	√	√
Etonogestrel (vaginal ring)	x	√	√	√	x
Levonorgestrel (COC)	x		√	√	x
Levonorgestrel (implant, IUD)	√	√	√	√	√
Levonorgestrel (POP)		√	√		√
Levonorgestrel (emergency contraception)	√	√	√	√	√
Norethindrone	√	√	√	√	√

No clinically significant interaction expected | Potential weak interaction | Potential interaction | Do not coadminister

https://www.hep-druginteractions.org/.

	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Ledipasvir/ Sofosbuvir	Elbasvir/ Grazoprevir	Sofosbuvir/Velpatasvir/ Voxilaprevir
Atorvastatin	x				x
Bezafibrate	√	√	√	√	√
Ezetimibe		√	√	√	
Fenofibrate	√	√	√	√	√
Fish oils	√	√	√	√	√
Fluvastatin					x
Gemfibrozil		√	√		√
Lovastatin	x				x
Pitavastatin				√	x
Pravastatin		√		√	
Rosuvastatin			x		x
Simvastatin	x				x

No clinically significant interaction expected   Potential weak interaction   Potential interaction   Do not coadminister

https://www.hep-druginteractions.org/.

- No dose adjustment is required in patients with CKD stage 1, 2, 3, 4, or 5
  - In November 2019, the FDA amended the package inserts for sofosbuvir-containing regimens to allow use in patients with renal disease, including those with an eGFR ≤30 mL/min and those on dialysis

Duration (weeks)

Genotype	Regimen	No Cirrhosis	Compensated Cirrhosis
1	Glecaprevir/pibrentasvir	8	8
	Sofosbuvir/velpatasvir	12	12
	Ledipasvir/sofosbuvir	8* or 12	12
	Elbasvir/grazoprevir	12†	12†
2/3	Glecaprevir/pibrentasvir	8	8
	Sofosbuvir/velpatasvir	12	12‡
4	Glecaprevir/pibrentasvir	8	8
	Sofosbuvir/velpatasvir	12	12
	Ledipasvir/sofosbuvir	12	12
	Elbasvir/grazoprevir	12	12
5/6	Glecaprevir/pibrentasvir	8	8
	Sofosbuvir/velpatasvir	12	12
	Ledipasvir/sofosbuvir	12	12

*Only for patients who are HIV-uninfected and have a baseline HCV RNA <6M IU/mL.
†Only for genotype 1a patients without baseline NS5A RASs for elbasvir.
‡In genotype 3: only for patients without baseline NS5A RAS Y95H.

AASLD-IDSA. http://www.hcvguidelines.org/full-report-view. Version November 6, 2019.

	Glecaprevir/ Pibrentasvir	Sofosbuvir/ Velpatasvir	Ledipasvir/ Sofosbuvir	Daclatasvir
Anti-proliferative				
Azathioprine	√	√	√	√
Mycophenolate	√	√	√	√
Calcineurin inhibitors				
Cyclosporine		√	√	
Tacrolimus		√	√	
mTOR inhibitors				
Everolimus				
Sirolimus		√	√	
IL-2 receptor antagonists				
Basiliximab	√	√	√	√

No clinically significant interaction expected | Potential weak interaction | Potential interaction | Do not coadminister

Sofosbuvir/velpatasvir: no dose adjustment required when given with cyclosporin or tacrolimus (Summary of Product Characteristics).
*May require a dosage adjustment, altered timining of administration, or additional monitoring. DDI: drug-drug interaction.

https://www.hep-druginteractions.org/.