

HEPATITIS C WHAT'S NEW?

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Disclosure

- We have nothing to disclose

Objectives

- Discuss prevalence of Hepatitis C in Alaska
- Review when treatment for Hepatitis C is appropriate
- Describe first line treatment options for Hepatitis C

Treatment Guidelines

- HCV Guidance
 - *American Association for the Study of Liver Diseases and the Infectious Diseases Society of America*

HEP-COAA HCV Guidance: Recommendations for Managing and Treating Hepatitis C, 2017 (Final)

HCV Statistics

Global Prevalence	United States Prevalence	Global Death Rate	United States Deaths	Alaska Prevalence
~177.5 million	~2.7-3.9 million	~399,000 / year	19,629 in 2015	~1,600

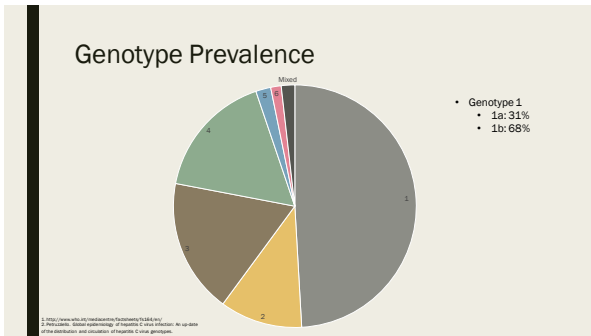
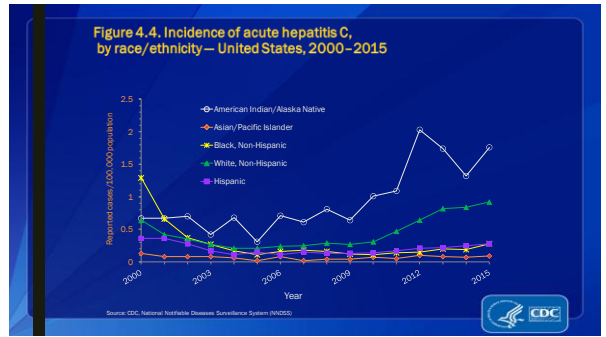
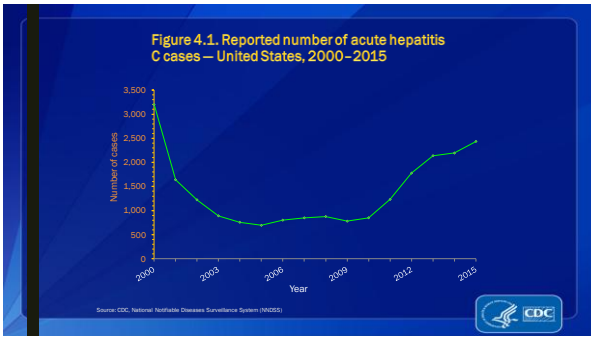
- Higher burden than HIV
 - 2016 Worldwide Prevalence HIV: 36.7 million
 - 2015 United States Prevalence HIV: 1.1 million

1. WHO Surveillance Report, CDC. <http://www.who.int/surveillance-reports/2016-05-2017>. November 05, 2017.
2. 2016 Hepatitis Surveillance Report, Alaska, 2016. CDC. <https://www.cdc.gov/hepatitis/2016-surveillance-reports/2016-hepatitis-surveillance-report-alaska/>.
3. WHO. <http://www.who.int/mediacentre/factsheets/fs104/en/>.
4. Perisic, M. Global epidemiology of hepatitis C virus infection: An update on the distribution and circulation of hepatitis C virus genotypes.

HCV Statistics

	Past/present HCV cases reported	2015 Number of HCV Related Deaths	2015 Death Rate per 100,000
White	19,874 (35.5%)	12,355	4.38
Black	3,617 (6.5%)	3,606	8.14
Hispanic	2,458 (4.4%)	2,699	6.40
American Indian/Alaska Native	151 (0.3%)	367	12.95
Asian/Pacific Islander	404 (0.7%)	445	2.49
Unknown/missing	28,772 (51.0%)		

1. 2016 Hepatitis Surveillance Report, Alaska, 2016. CDC. <https://www.cdc.gov/hepatitis/2016-surveillance-reports/2016-hepatitis-surveillance-report-alaska/>.
2. <http://www.who.int/mediacentre/factsheets/fs104/en/>.
3. WHO. <http://www.who.int/mediacentre/factsheets/fs104/en/>.
4. Perisic, M. Global epidemiology of hepatitis C virus infection: An update on the distribution and circulation of hepatitis C virus genotypes.



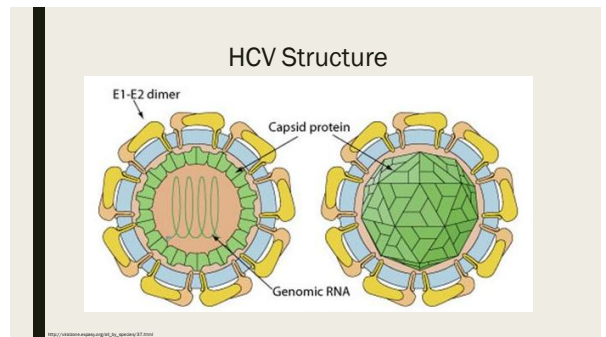
Hepatitis Infection

	Hepatitis A	Hepatitis B	Hepatitis C
Acute vs Chronic	Acute	Both	Both
Transmission	Fecal-oral	Blood, body fluid	Blood, body fluid
Vaccine	Yes	Yes	No
1 st Line Tx	Supportive	PEG-INF or NRTI	DAA Combo
2 nd Line Tx	-	-	Add Ribavirin

Reprints: Nishi, et al. Hepatol. 2010; 52: 1000-1008

Hepatitis C Virus

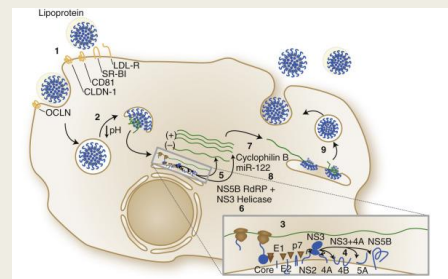
- Single-strand, positive sense RNA virus
- Outer - Enveloped glycoproteins in a lipid bilayer
- Inner - Protein layer encapsulating core known as capsid protein
- Single strand of viral genomic RNA



Pathophysiology

- Binds hepatocyte and undergoes endocytosis
- Uses host ribosomes and endoplasmic reticulum to make single polyprotein molecule
- Cleaved into 10 mature viral proteins
 - Structural: E1, E2, p7 and NS2
 - Non-structural: NS3, NS4A, NS4B, NS5A and NS5B
- Non-structural: post-translational processing (drug targets)
- Structural: pieces incorporated into new viral structure

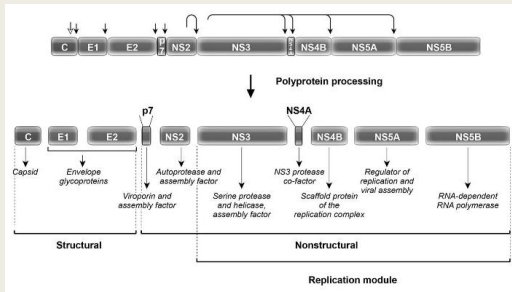
1. Hsu, Troy, et al. "Hepatitis C in a New Era: Review of Current Therapies." *Pharmacy and Therapeutics*, vol. 42, no. 5, May 2017, pp. 348-360.
 2. Schuster, T. "The New Old Understanding of the Hepatitis C Virus Life Cycle Opens the Way for Highly Effective Therapies." *Ann Hepatol* 2012; 11:88-117.



1. Entry
2. Uncoating
3. NS2/NS3 cysteine protease
4. NS3/NS4A serine protease
5. NS5B RdRP
6. NS3 Helicase
7. NS5B interaction with CypB
8. MicroRNA-122 requirement
9. Virion maturation and release

Worsham, Douglas, and Robert's Principles and Practice of Infectious Diseases, Updated Edition. Published January 5, 2015. Pages 1064-1077 e11. © 2015.

Structural/Non-Structural Proteins



1. Schuster, Troy, "Virology and Cell Biology of the Hepatitis C Virus Life Cycle - An Update." *Journal of Hepatology*, Elsevier, 3 Nov 2014.

Drug Targets – NS3/4A Protease Complex

- Heterodimeric serine protease complex
 - Made up of NS3 and NS4A proteins
- NS3: possesses the **proteolytic** activity
- NS4A: membrane bound; acts as a **cofactor**
- Enzyme involved in post-translational processing and HCV replication

Schuster, Troy, "Virology and Cell Biology of the Hepatitis C Virus Life Cycle - An Update." *Journal of Hepatology*, Elsevier, 3 Nov 2014.

Drug Targets – NS5A Protein

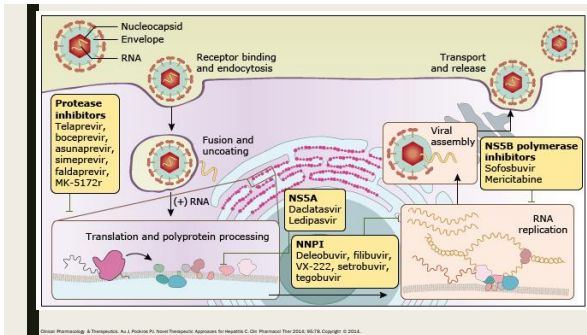
- Known as "replication complex" protein
- Critical role in both:
 - Viral replication
 - Assembly of viral complex
- Exact mechanism by which this is accomplished is uncertain

Schuster, Troy, "Virology and Cell Biology of the Hepatitis C Virus Life Cycle - An Update." *Journal of Hepatology*, Elsevier, 3 Nov 2014.

Drug Targets – NS5B Polymerase

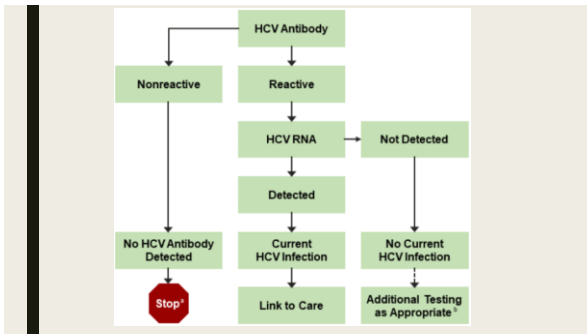
- RNA-dependent RNA polymerase
- Enzyme involved in post-translational processing and HCV replication
- Has multiple catalytic binding sites for drug therapy
 - 1 nucleoside site
 - 4 known non-nucleoside sites
- Structure itself is conserved across all HCV genotypes
 - Polymerase inhibitors (PIs) - have activity against all genotypes

Schuster, Troy, "Virology and Cell Biology of the Hepatitis C Virus Life Cycle - An Update." *Journal of Hepatology*, Elsevier, 3 Nov 2014.



Who Gets Tested?

- Anyone born from 1945 – 1965
- Illicit drug use – IV or intranasal
- Long term hemodialysis
- Needle sticks
- Children born to HCV infected women
- Incarcerated – ever
- HIV
- Yearly testing for persons who have continued risk factors
 - Drug use



Who to Treat?

- Chronic HCV infection
- Earlier treatment = better SVR
 - F0 or F1. 15 year survival rate = 92% with SVR
- F3 – 2x increase in liver related mortality after treatment
- F4 – 5x increase in liver related mortality after treatment
- Recommended to treat earlier

HEP-054: HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. 2017

Selecting Treatment

- Genotype
- Previous treatment
- Cirrhosis
- Co-morbid conditions

HEP-054: HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. 2017

Co-Morbidities

- Prior Liver Transplantation
 - Treat prior to treatment and after
- HIV Co-infection
 - Accelerates fibrosis
- HBV Co-infection
 - Treat both as if mono-infection

HEP-054: HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C. 2017

Risk factors for accelerated fibrosis progression

Non-Modifiable	Modifiable	Viral
Fibrosis stage	Alcohol consumption	Genotype 3
Inflammation grade	Nonalcoholic fatty liver disease	Co-infection
Older age	Obesity	- Hepatitis B
Male	Diabetes	- HIV
Organ transplant		

HBV/HCV Substrate Recommendations for Testing, Monitoring, and Treating Hepatitis C 2017

Hepatitis C Regimen Roadmap



Direct Acting Antiviral (DAA) Classes

TARGET	SUFFIX	EXAMPLE
NS3/4A P rotease	"- P revir"	Sime P revir
NS5 A Protein	"- A svir"	Daclat A svir
NS5 B Polymerase	"- B uvir"	Sofos B uvir

Hepatitis Treatment

NS3/4A Inhibitors	NS5A Inhibitors	NS5B Inhibitors
Simeprevir*	Daclatasvir*	Sofosbuvir**
Telaprevir*	Ombitasvir	Dasabuvir
Boceprevir*	Elbasavir	
Paritaprevir	Ledipasvir	
Glecaprevir	Velpatasvir	
Grazoprevir	Pibrentasvir	
Voxilaprevir		

DAA Adverse Effects

- Overall well tolerated
- Fatigue
- Weakness
- Headache
- Rash (photosensitivity)

Epstein, Nelson, et al. Hepatitis C Virus. Nelson, H.C., 2016.

Warnings and Monitoring

- October 2016:
 - FDA Boxed Warning added to all DAAs
- **Hepatitis B virus (HBV) reactivation** has been reported in hepatitis C virus (HCV)/HBV co-infected patients who were **receiving or had completed treatment with HCV DAA and were not receiving HBV antiviral therapy**; some cases have resulted in **fulminant hepatitis, hepatic failure and death**. **Test all patients for evidence of current or prior HBV infection** prior to initiation of DAA. Monitor co-infected patients for hepatitis flare or HBV reactivation during and following treatment.

Lexi-Comp, Inc. Lexi-Comp. Lexi-Comp, Inc. January 03, 2018.

Drug-Drug Interactions

- Contraindicated with strong 3A4 inducers
 - Carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, St. John's wort
 - May decrease drug levels and result in treatment failure
- Amiodarone
 - Serious symptomatic bradycardia with certain DAAs
- Acid suppressive therapy
 - May decrease drug levels and result in treatment failure with certain DAAs

Shapiro, Nelson, et al. Hepatology Clinical Practice, 2014, 18(1), 1-10

Drug Interactions

- Check all new medications
- Keep a list of medications
- Always ask about supplements and over the counter medications
- Helpful resources
 - www.hep-druginteractions.org

Ledipasvir/Sofosbuvir (Harvoni®)

- N5SA + NS5B Combination
- FDA approved October 2014
- **Dose:** Once daily with or without food
- **Genotypes:** 1, 4, 5 or 6
- **Adverse Effects:** Insomnia (3-6%), Irritability (9%), Myalgia (9%)

Harvoni (ledipasvir and sofosbuvir) tablets and oral suspension, Janssen-Cilag, Inc., January 10, 2015

Ledipasvir/Sofosbuvir (Harvoni®)

- Sofosbuvir Component
 - Serious **symptomatic bradycardia** when used in combination with Amiodarone and another DAA
 - Generally occurs within **hours to a few days** following administration
 - Risk may increase when taking other negative inotropic/chronotropic medications or patients with cardiac comorbidities
 - May also increase risk of myopathy with statins

Harvoni (ledipasvir and sofosbuvir) tablets and oral suspension, Janssen-Cilag, Inc., January 10, 2015

Ledipasvir/Sofosbuvir (Harvoni®)

- Ledipasvir Component
 - Avoid or minimize acid suppressive therapy
 - **Antacids** - Separate by 4 hours
 - **H₂RAs** - Take at same time or 12 hours apart
Use ≤ famotidine 40 mg BID or equivalent
 - **PPIs** - Take at same time
Avoid ≥ omeprazole 20 mg/day or equivalent

Shapiro, Nelson, et al. Hepatology Clinical Practice, 2014, 18(1), 1-10

Ledipasvir/Sofosbuvir (Harvoni®)

- | | |
|--|--|
| <ul style="list-style-type: none"> ■ ION-1 ■ 865 treatment-naïve patients <ul style="list-style-type: none"> - Cirrhotic patients included ■ 12 weeks vs 24 weeks treatment ■ SVR was 97.99% across all study arms <ul style="list-style-type: none"> - No difference based on length of treatment ■ No difference in cirrhosis vs no cirrhosis <ul style="list-style-type: none"> - 97% vs 98% respectively | <ul style="list-style-type: none"> ■ ION-3 ■ 647 treatment-naïve patients <ul style="list-style-type: none"> - Excluded cirrhotic patients ■ 12 weeks vs 8 weeks treatment ■ SVR was 93.95% across all study arms <ul style="list-style-type: none"> - No difference based on length of treatment ■ Relapse rate were higher in 8-week arm (20/431) vs 12-week arm (3/216) |
|--|--|

ION-1 USA, ION-3 Subgroup: Recommendations for Managing and Treating Hepatitis C, 2013 Meeting

Grazoprevir/Elbasvir (Zepatier®)

- NS3/4A + NS5A Combination
- FDA approved January 2016
- **Dose:** Once daily with or without food
- **Genotypes:** 1 and 4
- **Adverse Effects:** Elevated ALT (1%), Night sweats (2%), Insomnia (2-3%)

1. Leung TW, et al. *Hepatology*. 2016;62(1):1-10.
 2. HCV, et al. *Hepatology*. 2016;62(1):1-10.

Grazoprevir/Elbasvir (Zepatier®)

- Screening for NS5A polymorphism is recommended
- **Contraindicated** with efavirenz, HIZ protease inhibitors and cyclosporine
- Increase risk of **myopathy** with **statins**
 - *Grazoprevir/Elbasvir may increase serum concentrations of statins that are major 3A4 substrates*

Shapiro, et al. *Hepatology*. 2016;62(1):1-10.

Grazoprevir/Elbasvir (Zepatier®)

- **C-Edge**
- 382 treatment-naïve patients
- Genotypes 1, 4 and 6
- 12-weeks total treatment
- 92% SVR in genotype 1a
- 99% SVR in genotype 1b

1. HCV, et al. *Hepatology*. 2016;62(1):1-10.

Velpatasvir/Sofosbuvir (Epclusa®)

- NS5A + NS5B Combination
- FDA approved June 2016
- **Dose:** Once daily with or without food
- **Genotypes:** First DAA approved for all genotypes
- **Adverse Effects:** Headache (22%), Fatigue (15%), Nausea (9%)

Leung TW, et al. *Hepatology*. 2016;62(1):1-10.

Velpatasvir/Sofosbuvir (Epclusa®)

- **Contraindicated** in Child-Pugh Class B or C
- Velpatasvir Component
 - *Avoid or minimize acid suppressive therapy*
 - **Antacids** - Separate by 4 hours
 - **H₂RAs** - Take at same time or 12 hours apart
Use ≤ famotidine 40 mg BID or equivalent
 - **PPIs** - Use is not recommended

Shapiro, et al. *Hepatology*. 2016;62(1):1-10.

Velpatasvir/Sofosbuvir (Epclusa®)

- **Astral-1**
- 624 patients with genotypes 1, 2, 4, 5 or 6
- Placebo-controlled trial
 - 12-weeks total treatment
- 328/323 genotype 1 achieved SVR
- 120/121 cirrhotic patients achieved SVR

1. HCV, et al. *Hepatology*. 2016;62(1):1-10.

Glecaprevir/Pibrentasvir (Mavyret®)

- NS3/4A + NS5A Combination
- FDA approved August 2017
- **Dose:** 3 tablets once daily **With** food
- **Genotypes:** Second DAA approved for all genotypes
- **Adverse Effects:** Headache (9-17%), Fatigue (11-14%), Diarrhea (3-7%)

Lexington, Inc. 2016 (right) | Lexington, Inc. January 10, 2016

Glecaprevir/Pibrentasvir (Mavyret®)

- **Contraindicated** in Child-Pugh Class C
- **Avoid** co-administration with atazanavir or rifampin
- Other interactions still unknown or theorized
 - Minor substrate CYP3A4
 - Inhibits BRCP/ABCG2, CYP1A2 (weak), CYP3A4 (weak)

Lexington, Inc. 2016 (right) | Lexington, Inc. January 10, 2016

Glecaprevir/Pibrentasvir (Mavyret®)

- | | |
|--|---|
| <ul style="list-style-type: none"> ■ Surveyor-1 ■ Phase 2 trial; 8-week treatment ■ 33/34 with SVR <ul style="list-style-type: none"> - No virologic failures ■ Endurance-1 ■ 703 noncirrhotic, genotype 1 patients ■ 8-weeks vs 12-weeks <ul style="list-style-type: none"> - SVR 99% vs 99.7% respectively | <ul style="list-style-type: none"> ■ Expedition-1 ■ 146 compensated cirrhotic patients ■ Genotype 1, 2, 4, 5 or 6 ■ SVR of 99% ■ Expedition-2 ■ 153 HIV/HCV co-infected patients ■ Any genotype ■ 8-weeks (noncirrhotic patients) and 12-weeks cirrhotic patients ■ SVR of 98% |
|--|---|

MSD-DAA, HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C, 2017

Monitoring During Therapy

- Labs
 - CBC, SCr, hepatic function panel
- 10x increase in ALT – discontinue therapy
- HCV viral load
 - 4 and 12 weeks after completion of therapy

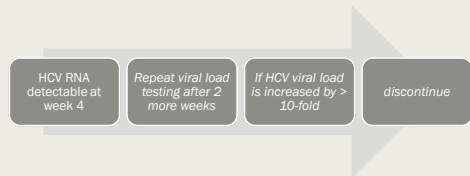
MSD-DAA, HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C, 2017

Monitoring After Response

- Sustained Virologic Response (SVR) = continued absence of detectable HCV RNA for 12 weeks or more after completion of therapy
- No advanced fibrosis – monitor as if never infected
- Assess for recurrence if ongoing risk for HCV
- Advanced fibrosis – assess for hepatocellular carcinoma twice yearly

MSD-DAA, HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C, 2017

Discontinuation from Lack of Efficacy



MSD-DAA, HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C, 2017

Monitoring After Treatment Failures

- Disease progression every 6 - 12 months
 - CBC, INR and LFTs
- Screening for hepatocellular carcinoma every 6 months
 - If F3 or F4
- Esophageal varices screening if cirrhosis present
- Evaluate retreatment options as new therapies are developed

AASLD-HBV Guidelines: Recommendations for Testing, Managing, and Treating Hepatitis B 2017

Treatment failures

- 2nd line therapy dependent on previous exposure
- Peg-interferon or ribavirin exposure
- NS3 Protease Inhibitor exposure
- Sofosbuvir exposure
- NS5A inhibitor exposure

AASLD-HBV Guidelines: Recommendations for Testing, Managing, and Treating Hepatitis B 2017

Genotype 1a/1b

Recommended	Duration	Rating
Treatment-Naïve Genotype 1a/1b		
Elbasvir/grazoprevir 50-100mg*	12 weeks	1A
Glecaprevir/pibrentasvir 300-120 mg	8 weeks	1A
Ledipasvir/sofosbuvir 90-400 mg	12 weeks	1A
Ledipasvir/sofosbuvir 90-400mg**	8 weeks	1B
Sofosbuvir/velpatasvir 400-100 mg	12 weeks	1A
Treatment-Naïve Genotype 1a/1b with cirrhosis		
Elbasvir/grazoprevir 50-100mg*	12 weeks	1A
Glecaprevir/pibrentasvir 300-120 mg	12 weeks	1A
Ledipasvir/sofosbuvir 90-400 mg	12 weeks	1A
Sofosbuvir/velpatasvir 400-100 mg	12 weeks	1A

* For Genotype 1a: Without baseline NS5A RAS for elbasvir

** For patients who are non-black, HIV-uninfected and HCV RNA level < 6 million IU/mL

AASLD-HBV Guidelines: Recommendations for Testing, Managing, and Treating Hepatitis B 2017

Genotype 1 recap

- Similar recommendations for type 1a and 1b
- Glecaprevir/Pibrentasvir, ledipasvir/sofosbuvir, sofosbuvir/velpatasvir
 - If NS5A RAS or unknown resistance
- May shorten duration of ledipasvir/sofosbuvir
 - Non-black, HIV-uninfected, HCV RNA level < 6 million IU/mL

AASLD-HBV Guidelines: Recommendations for Testing, Managing, and Treating Hepatitis B 2017

Genotype 2

Recommended	Duration	Rating
Treatment-Naïve Genotype 2		
Glecaprevir/pibrentasvir 300-120 mg	8 weeks	1,A
Sofosbuvir/velpatasvir 400-100 mg	12 weeks	1,A
Treatment-Naïve Genotype 2 with Cirrhosis		
Sofosbuvir/velpatasvir 400-100 mg	12 weeks	1,A
Glecaprevir/pibrentasvir 300-120 mg	12 weeks	1,B

AASLD-HBV Guidelines: Recommendations for Testing, Managing, and Treating Hepatitis B 2017

Genotype 3

Recommended	Duration	Rating
Treatment-Naïve Genotype 3		
Glecaprevir/pibrentasvir 300-120 mg	8 weeks	1,A
Sofosbuvir/velpatasvir 400-100 mg	12 weeks	1,A
Treatment-Naïve Genotype 3 with Cirrhosis		
Glecaprevir/pibrentasvir 300-120 mg	12 weeks	1,A
Sofosbuvir/velpatasvir 400-100 mg	12 weeks	1,A

AASLD-HBV Guidelines: Recommendations for Testing, Managing, and Treating Hepatitis B 2017

Genotype 4

Recommended	Duration	Rating
Treatment-Naïve Genotype 4		
Glecaprevir/pibrentasvir 300-120 mg	8 weeks	I,A
Sofosbuvir/velpatasvir 400-100 mg	12 weeks	I,A
Elbasvir/grazoprevir 50-100 mg	12 weeks	Ila,B
Ledipasvir/sofosbuvir 90-400 mg	12 weeks	Ila,B
Treatment-Naïve Genotype 4 with cirrhosis		
Sofosbuvir/velpatasvir 400-100 mg	12 weeks	I,A
Glecaprevir/pibrentasvir 300-120 mg	12 weeks	I,B
Elbasvir/grazoprevir 50-100 mg	12 weeks	Ila,B
Ledipasvir/sofosbuvir 90-400 mg	12 weeks	Ila,B

MSD-USA, MSD-BioPharma. Recommendations for Testing, Monitoring, and Treatment Reports © 2017

Genotype 5 or 6

Recommended	Duration	Rating
Glecaprevir/pibrentasvir 300-120 mg	8 weeks (no cirrhosis)	I,A
Glecaprevir/pibrentasvir 300-120 mg	12 weeks (cirrhosis)	I,A
Sofosbuvir/velpatasvir 400-100 mg	12 weeks	I,B
Ledipasvir/sofosbuvir 90-400 mg	12 weeks	Ila,B

MSD-USA, MSD-BioPharma. Recommendations for Testing, Monitoring, and Treatment Reports © 2017

Resistance-Associated Substitution Testing

N55A Testing Recommended	N55A Testing NOT Recommended
Elbasvir/grazoprevir – genotype 1a	Elbasvir/grazoprevir – genotype 1b
Ledipasvir/sofosbuvir – genotype 1a consider if treatment experienced	Glecaprevir/pibrentasvir – any genotype
Sofosbuvir/velpatasvir – genotype 3 treatment-experienced	Ledipasvir/sofosbuvir – genotype 1b
Daclatasvir plus sofosbuvir – genotype 3	Paritaprevir/ritonavir/ombitasvir ± dasabuvir ± weight based ribavirin
	Sofosbuvir/velpatasvir – genotype 1, 2, 4, 5, 6
	Sofosbuvir/velpatasvir/voxilaprevir – any genotype

Other Available Treatment Options

Single Agent Products	Combination Products
Simeprevir (Olysio®)	Paritaprevir/Ombitasvir/Ritonavir (Technivie®)
Daclatasvir (Daklinza®)	Paritaprevir/Ombitasvir/Ritonavir/Dasabuvir (Viekira Pak®)
Sofosbuvir (Sovaldi®)	Voxilaprevir/Velpatasvir/Sofosbuvir (Vosevi®)

Regimens in Special Populations

Drugs	Kidney Disease	Safety in CTP B, C
Ledipasvir/Sofosbuvir	≥30 mL/min	Yes
Dasabuvir/ombitasvir/paritaprevir/ritonavir	Used in Dialysis	No
Elbasvir/grazoprevir	Safe in Dialysis	No
Sofosbuvir/Velpatasvir	≥30 mL/min	Yes
Sofosbuvir/Velpatasvir/Voxilaprevir	≥30 mL/min	No
Glecaprevir/pibrentasvir	Safe in Dialysis	No

1. Ledipasvir, Inc. (Ledipasvir) | Ledipasvir, Inc. January 20, 2016.
2. AAS, Nig, et al. "Regimen C is a New Era of Chronic Hepatitis C Treatment." Pharmacy and Therapeutics, vol. 43, no. 5, May 2017, pp. 558-560.

Treatment Costs Based on Average Wholesale Price (AWP)

Drug	Daily Cost	12-week Treatment
Daclatasvir	\$900	\$75,600
Dasabuvir/ombitasvir/paritaprevir/ritonavir	\$1190	\$99,980
Elbasvir/grazoprevir	\$780	\$65,520
Ledipasvir/sofosbuvir	\$1350	\$113,400
Ombitasvir/paritaprevir/ritonavir	\$1095	\$91,983
Simeprevir	\$948	\$79,632
Sofosbuvir	\$1200	\$100,800
Sofosbuvir/velpatasvir	\$1068	\$89,712
Glecaprevir/pibrentasvir*	\$565	\$47,520

1. Ledipasvir, Inc. (Ledipasvir) | Ledipasvir, Inc. January 20, 2016.
2. AAS, Nig, et al. "Regimen C is a New Era of Chronic Hepatitis C Treatment." Pharmacy and Therapeutics, vol. 43, no. 5, May 2017, pp. 558-560.

Assisting in Cost

- Gilead Sciences offers "SUPPORT PATH" program
 - Sofosbuvir
 - Sofosbuvir/Ledipasvir
 - Sofosbuvir/Velpatasvir
- AbbVie offers assistance through ProCeed program
 - Dasabuvir/ombitasvir/paritaprevir/ritonavir
 - Ombitasvir/paritaprevir/ritonavir
- Other companies have similar programs
 - The American Liver Foundation
 - hepc.liverfoundation.org/resources/what-if-i-need-financial-assistance-to-pay-for-treatment

1. Hsu, Ting, et al. "Sustained C in a New Era: A Review of Current Therapies." *Hepatology and Transplantation*. vol. 43, no. 5, May 2017. pp. 838-850

Conclusion

- Importance of compliance
- Co-morbidities
- Many drug-drug interactions
- Continued education
- Refill reminders
- Be a positive resource

