Simplified Treatment for Hepatitis C

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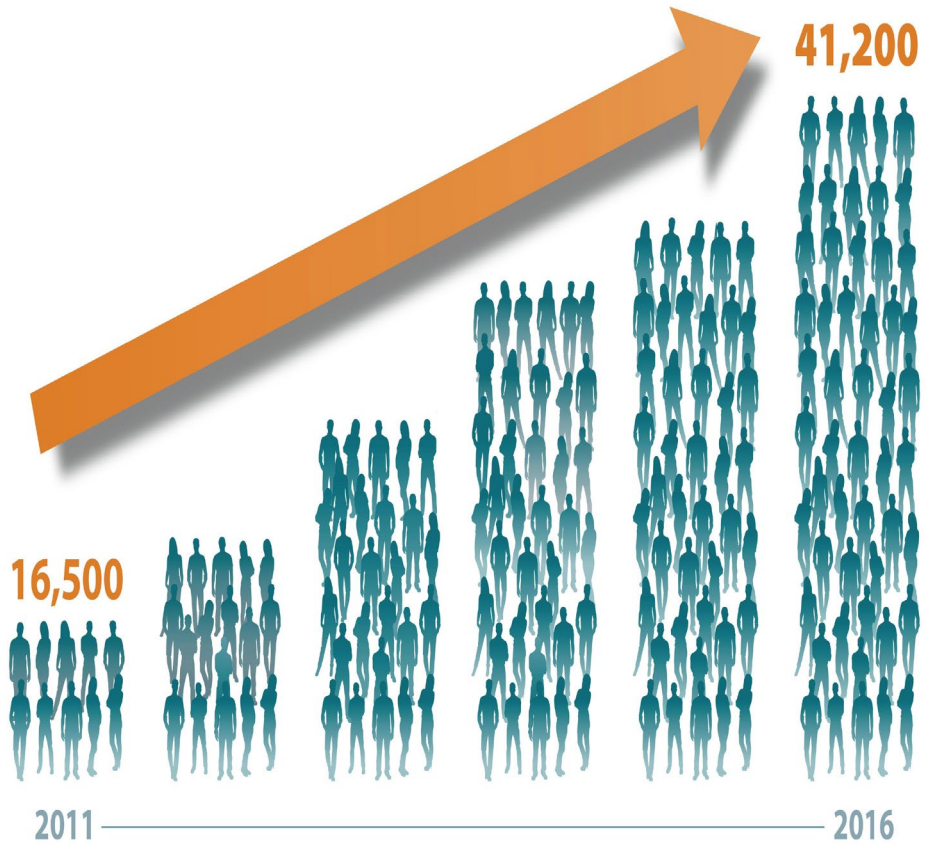
INTRODUCTION

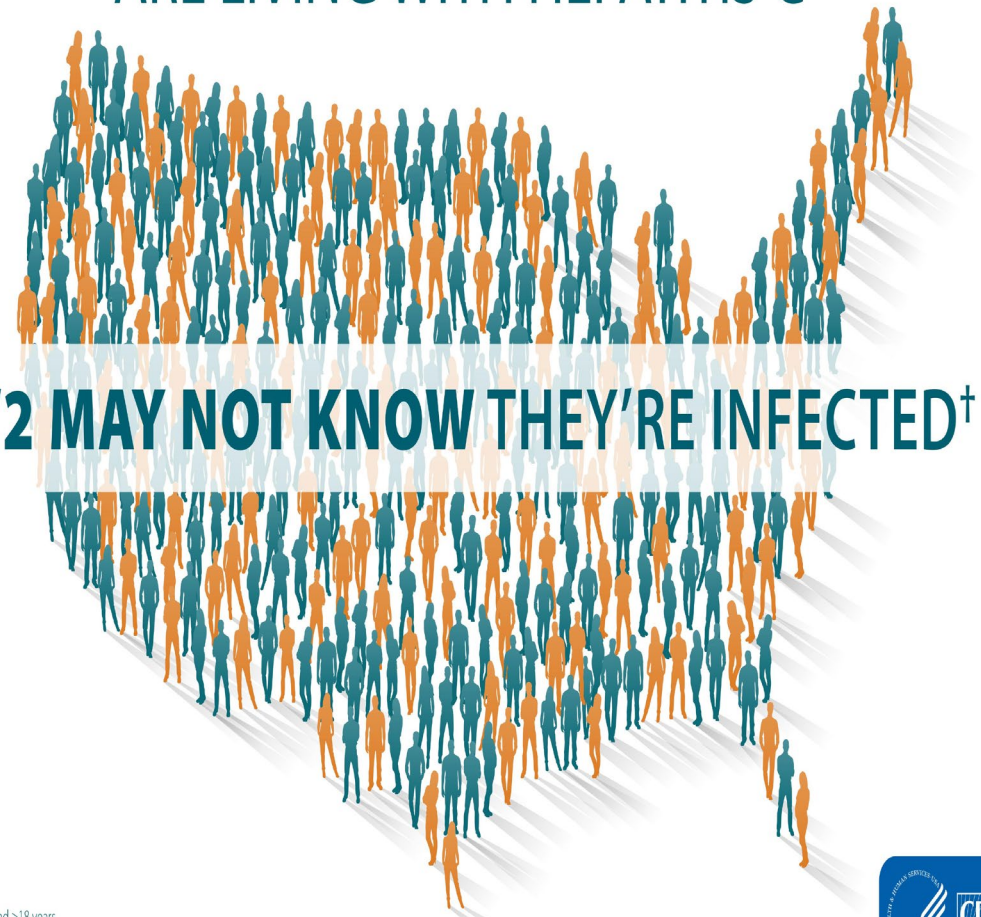
- Natural History of Hepatitis C infection
  - chronic hepatitis, liver cirrhosis, liver cancer.
- Slowly progressive disease.
- 20 – 30% of chronic HCV patients develop liver Cirrhosis over a 20 years period.
- Aim of antiviral treatment is to cure chronic hepatitis C infection.
- Viral cure - sustained virologic response (SVR)
  - undetectable HCV RNA in blood 12- 24 wks after completing anti-viral treatment.
- No immunity from prior exposure

IN THE SHADOW OF THE OPIOID CRISIS, NEW HEPATITIS C INFECTIONS HAVE **INCREASED**



Visit www.cdc.gov/hepatitis for more information

NEARLY **2.4 MILLION** AMERICANS ARE LIVING WITH HEPATITIS C*



1/2 MAY NOT KNOW THEY'RE INFECTED†

*Among adults aged ≥18 years
†According to 2014 study: *The Treatment Cascade for Chronic Hepatitis C Virus Infection in the United States: A Systematic Review and Meta-Analysis*

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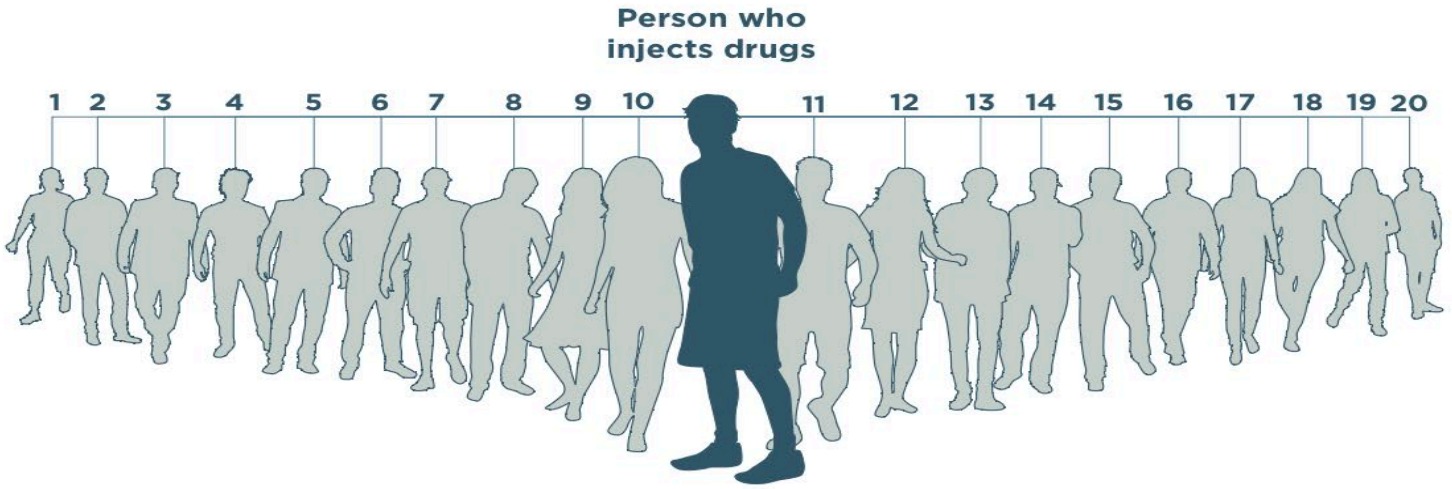
HCV IS THE ONLY CHRONIC VIRAL INFECTION THAT CAN BE CURED, AND HCV ELIMINATION IS POSSIBLE[9-13]

Each person who injects drugs living with HCV is likely to infect ~20 other people within the first 3 years of initial infection[14,15]



Based on the 2021 NIH National Institute on Drug Abuse *Heroin Research Report*

Oral direct-acting antivirals have allowed more individuals to be successfully treated and cured[13]

2030 WORLD HEALTH ORGANIZATION TARGETS FOR HEPATITIS C ELIMINATION[13]

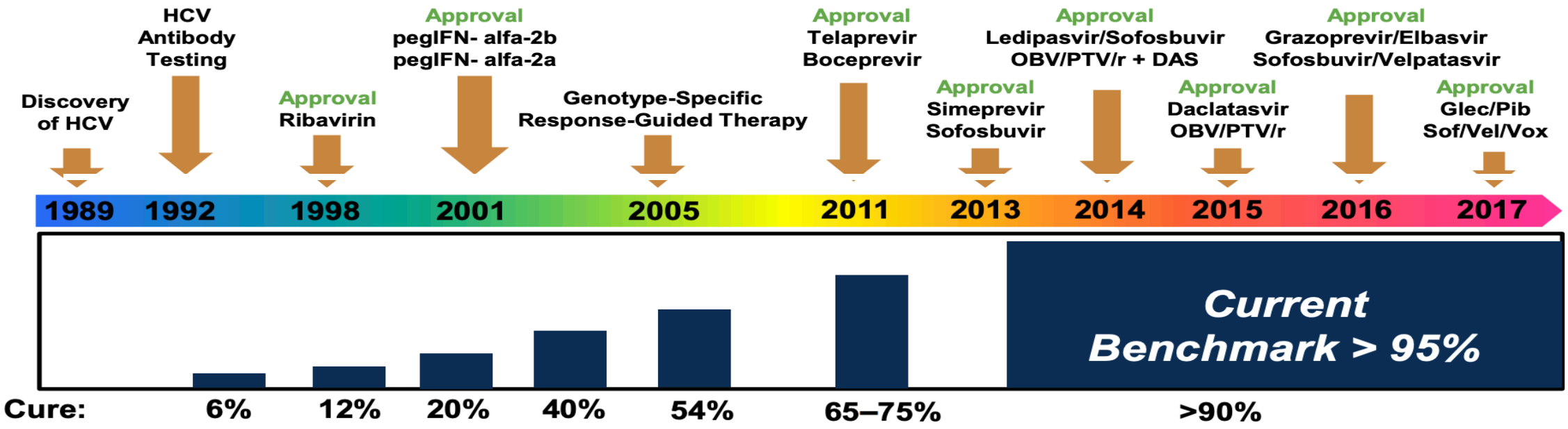
of those living with chronic HCV

of those diagnosed with chronic HCV

These targets are set to minimize new chronic infections and decrease HCV-related mortality[13]

Screenshot

Discovery of Direct Acting Antivirals (DAAs) Revolutionized HCV Therapy



- Patients can be cured in 8-12 weeks
- Therapy with oral DAAs have very few adverse events
- Interferon and ribavirin rarely used

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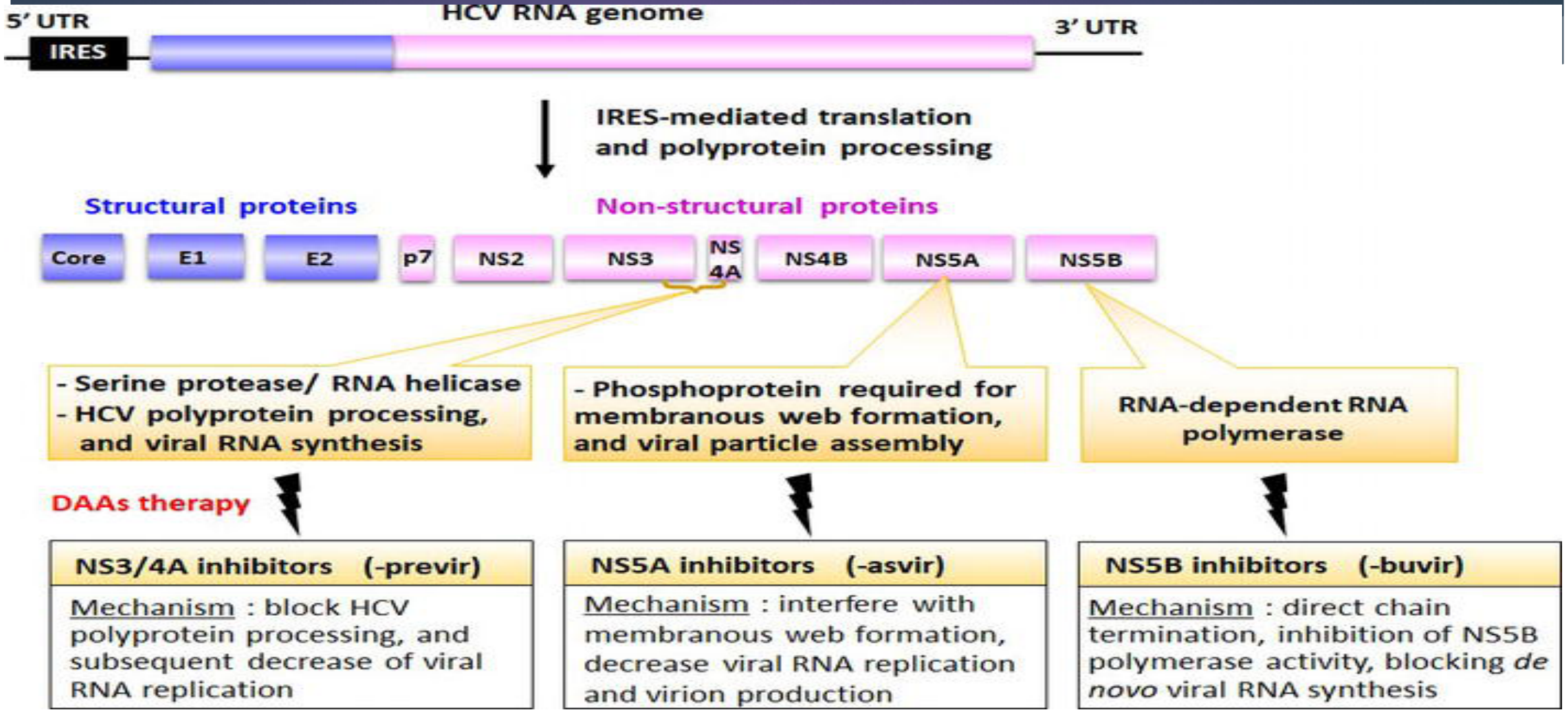
Pol, S., Lagaye, S. The remarkable history of the hepatitis C virus. *Genes Immun* **20**, 436–446 (2019). https://doi.org/10.1038/s41435-019-0066-z

GHAPP
Gastroenterology & Hepatology Advanced Practice Providers

HCV genomic RNA and encoded viral proteins; virological functions of targeted non-structural proteins for direct-acting antivirals (DAAs) therapy. UTR, untranslated region; IRES, internal ribosome entry site.



Kitab, B., Kohara, M., & Tsukiyama-Kohara, K. (2021). Host-Targeting Antivirals for Treatment of Hepatitis C. IntechOpen. doi: 10.5772/intechopen.95373

Testing

Screening

- UNIVERSAL SCREENING is recommended at least once in all adults aged ≥18 years.
- One time HCV testing for all persons less that 18 yrs old with high risk activities associated with HCV infection
- Prenatal HCV testing
- Periodic repeat HCV testing should be offered to all persons with an increased risk of HCV exposure.

Testing

- **HCV antibody** screening with reflex **HCV RNA testing** to establish the presence of active infection.

Future

- Innovative new test such as HCV core Antigen

Simplified Treatment algorithm

Who is eligible for simplified treatment?

- Adults with chronic HCV infection, regardless of HCV genotype.
- HCV treatment naïve
- Compensated Cirrhosis

Unique features

- ? PWID: No dosage adjustment is recommended for PWID
- ? on MAT for opioid use disorder
- ? ESRD: No dosage adjustment is recommended for patients with mild, moderate, or severe renal impairment, including ESRD requiring dialysis.

Pre Treatment Assessment

1. Calculate a FIB-4
2. Assess for cirrhosis
3. Medication reconciliation, including over the counter medications
4. Assess for potential drug-drug interactions
5. Educate the patient on medication administration, adherence and risk for reinfection
6. Pre-treatment laboratory assessment

Pretreatment Laboratory Assessment

- Within 6 months of treatment initiation for patients without cirrhosis and within 3 month of treatment initiation for those with compensated cirrhosis:
  - Complete blood count
  - Hepatic function panel
  - Calculate glomerular filtration rate
  - HIV antigen/antibody test
  - Hepatitis B surface antigen

Recommended DAA Medications for Treatment of HCV in the Simplified Treatment Algorithm

Glecaprevir-Pibrentasvir (*Mavyret*)

3 tablets daily for 8 weeks

Taken with food

Sofosbuvir-Velpatasvir (*Epclusa*)

- 1 tablet daily for 12 weeks

Glecaprevir-Pibrentasvir

- First pangenotypic NS3/4A protease inhibitor-NS5A inhibitor combination to be approved
- Not an option for patients with decompensated cirrhosis due to the presence of a protease inhibitor.
- SVR-12 rates ≥95% for treatment naïve individuals with and without compensated cirrhosis

Glecaprevir-Pibrentasvir: Notable Drug-Drug Interactions

1. **Statins:** Co-administrations leads to increased plasma concentrations of statins and can increase the risk for myopathy, including rhabdomyolysis.

2. **Ethinylestradiol:** Co-administration increase levels of ethinylestradiol, leading to increased risk of ALT elevation.

3. **Select HIV ART:** Protease inhibitors and pharmacologic boosters (e.g., ritonavir and cobicistat) can increase serum concentrations of glecaprevir. Select NNRTIs, including efavirenz and etravirine, which can decrease plasma concentrations of glecaprevir-pibrentasvir.

Sofosbuvir-Velpatasvir

- Pangenotypic NS5A-NS5B inhibitor, given as a single pill combination.
- Safe for use in patients with decompensated cirrhosis.
- SVR-12 rates ≥95% for treatment naïve individuals with and without compensated cirrhosis

Sofosbuvir-Velpatasvir: Notable Drug-Drug Interactions

- **Proton pump inhibitors:** Co-administration leads to decreased plasma concentrations of sofosbuvir-velpatasvir.
- Amiodarone
- St. Johns Worts

Summary of Glecaprevir-Pibrentasvir vs. Sofosbuvir-Velpatasvir

Medication	Glecaprevir-Pibrentasvir	Sofosbuvir-Velpatasvir
Trade Name	Mavyret	Epclusa
Adult Dose (oral)	Glecaprevir 300 mg and pibrentasvir 120 mg as 3 tablets once daily	Sofosbuvir 400 mg and velpatasvir 100 mg as one single tablet once daily
Duration	8 weeks	12 weeks
Food Requirement	Yes	No
Hepatic Impairment	Contraindicated in patients with decompensated cirrhosis (Child B or C)	No dose adjustment necessary for any degree of cirrhosis (Child A, B or C)
Renal Impairment	No dosage adjustment in patients with any degree of renal impairment, including dialysis	No dosage adjustment in patients with any degree of renal impairment, including dialysis
Notable Drug interactions	- Statins - Ethinylestradiol - HIV protease inhibitors and select NNRTIs	- Proton pump inhibitors (PPIs)

Laboratory Monitoring

- Most patients will not require any on-treatment laboratory monitoring.
- Compensated cirrhosis: may order liver function testing to monitor for liver injury during treatment.
- SVR: HCV RNA and liver function testing 12 weeks post-treatment to assess for HCV cure and transaminase normalization.
- NO IMMUNITY ACQUIRED FROM TREATMENT.
- Assess for HCV Recurrence
- SVR: 94% among both adherent and nonadherent participants (taken <90% of the total dosage).

HBV Coinfection

High risk for Reactivation of Hepatitis B Virus Infection:

- Hep BsAg: Pos
- Treat Hepatitis B

- Hep B c Positive
- Treat Hepatitis C, Monitor for reactivation for Hepatitis B

Pregnancy

Testing

Recommendation for Universal Hepatitis C Screening in Pregnancy	
RECOMMENDED	RATING
All pregnant women should be tested for HCV infection (see Recommendations for Initial HCV Testing and Follow-Up), ideally at the initiation of prenatal care.	IIb, C

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 69 / No. 2
April 3, 2020

CDC Recommendations for Hepatitis C Screening Among Adults — United States, 2020

"Hepatitis C screening is recommended for all pregnant women during each pregnancy except in settings where the prevalence of HCV infection is < 0.1%"

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

IDSA
Infectious Diseases Society of America

Decompensated Cirrhosis

- Mavyret contraindicated
- Referral for transplant evaluation
- Treatment decision based on liver transplant evaluation
- Treatment of HCV delayed for the benefit of Hepatitis C donor liver

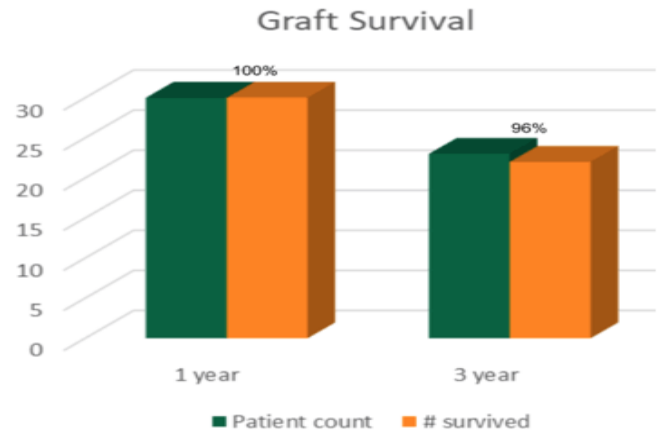
Transplant

Safety and efficacy of oral direct-acting antiviral in liver transplant infected HCV patients: a real-world experience from a satellite clinic in the Southern United States

Richard Trieu M.D., Phillip Henderson D.O., and Rajab Idriss M.D.
University of South Alabama Division of Gastroenterology and Hepatology Mobile, Alabama

CONCLUSION

- In our population of patients with recurrent HCV post-OLT, DAAs are an efficacious and safe treatment therapy for those after transplant.
- Patients with recurrent HCV post OLT showed great survivability and response to DAA treatment.



Case

- A 35 yrs old Male presenting for wellness exam for clearance for applying for graduate school. No significant past medical history.
- Labs:
  - Hepatitis C Ab: Positive, Hepatitis Bs Ag neg, HIV Ag/Ab neg, AST/ALT: 67/88, T.Bili: 1.5, HCV RNA: 10,00,000IU/ml.
  - FIB 4 score: <1.30 (no cirrhosis)
  - ? Treatment
  - Epclusa x 12wks
  - Mavyret x 8 wks

Acknowledgements

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HEPATITIS B ONLINE

HEPATITIS C ONLINE

IDEA INFECTIOUS DISEASES EDUCATION & ASSESSMENT

AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

THANKS