Hepatitis C Training Program for Healthcare in Ontario Corrections

Designed and delivered by:

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Updated: January 1, 2024

In collaboration with: Ministry of Health, Ministry of Solicitor General, CATIE

Disclosures

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Jordan Feld, MD, MPH	Consultancy fees: Abbvie, Gilead Research grants (to institution): Abbvie, Gilead, Cepheid
Mia Biondi, PhD, NP-PHC	Consultancy fees and/or honoraria from: Specialty Rx Solutions, McKesson Investigator initiated grants: Gilead, AbbVie, Cepheid Ad boards and speaker bureaux: Gilead, AbbVie, Abbott, ViiV
Hemant Shah, MD, MSc	Employee: Specialty Rx Solutions

Four Modules – 20 Minutes Each

1. Implications for Public Health, HCV Transmission and Prevention
2. HCV Screening, Diagnosis and Linkage to Care
3. HCV Assessment: Getting A Person Ready for Treatment
4. HCV Treatment: Making the Right Choice and Monitoring Afterwards

Module Four – HCV Treatment: Making the Right Choice and Monitoring Afterwards

Updated: January 1, 2024

Learning Objectives

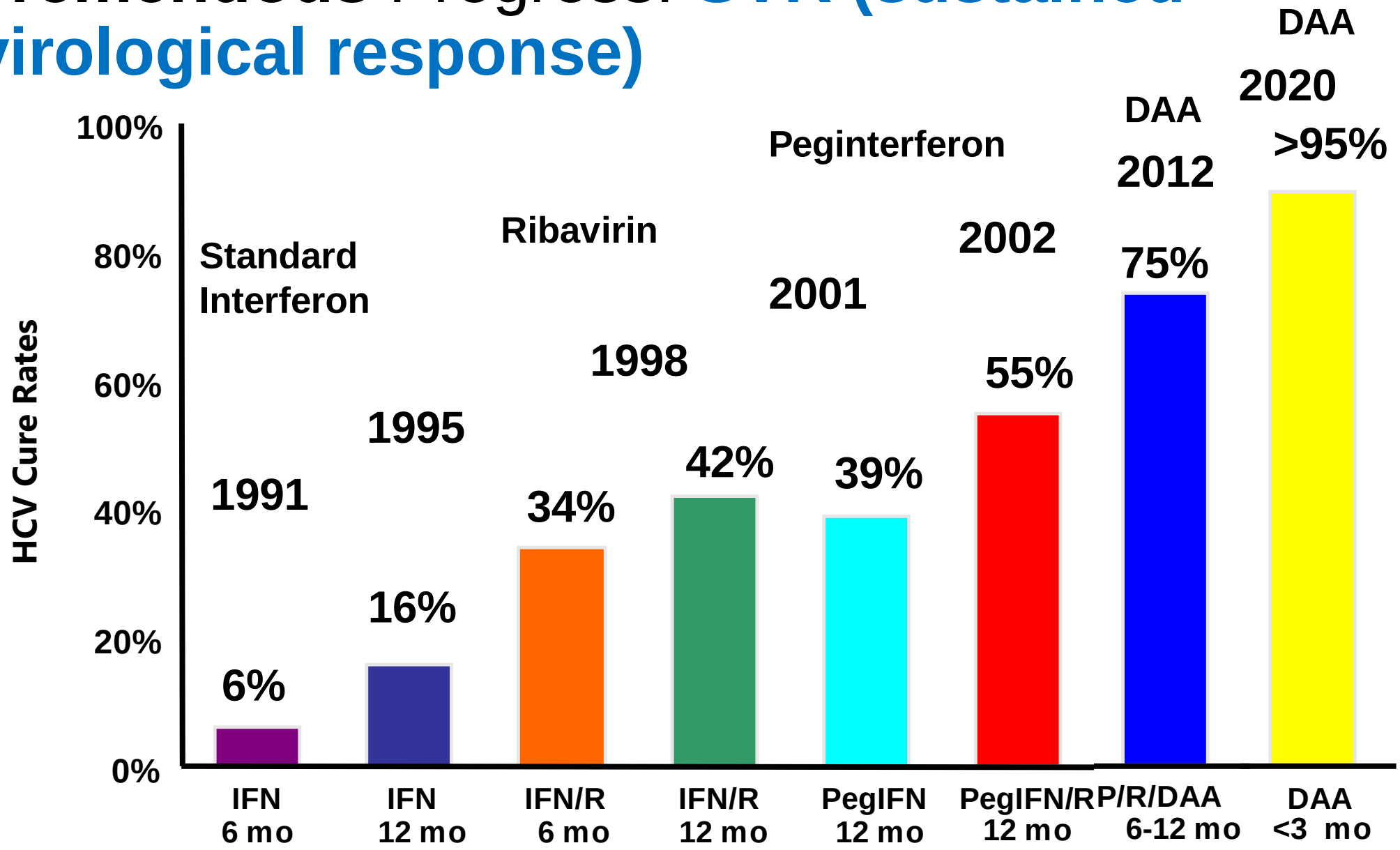
- **If you are a prescriber (MD, NP)**
  - Understand the rationale for treating hepatitis C – liver and non-liver benefits
  - Understand how to treat HCV with the commonly used regimens
  - Appreciate pitfalls of therapy and where to get support

- **If you are a nurse or allied health professional**
  - Understand the rationale for treating hepatitis C – liver and non-liver benefits
  - Appreciate the simplicity of current HCV treatment
  - Recognize where support during treatment may be useful

Module 4 - Hepatitis C Treatment: Making the Right Choice and Monitoring Afterwards

1. Treatment Options
2. Simplified Treatment Approach
3. On-Treatment Monitoring

Tremendous Progress: **SVR (sustained virological response)**



Treatment has changed (dramatically!)

Interferon Era

- Difficult treatment
- Weekly injections x 1 yr
- Many side effects
- Not very effective
- Careful monitoring required
- **Treatment only recommended for those with liver damage**

Direct acting antivirals

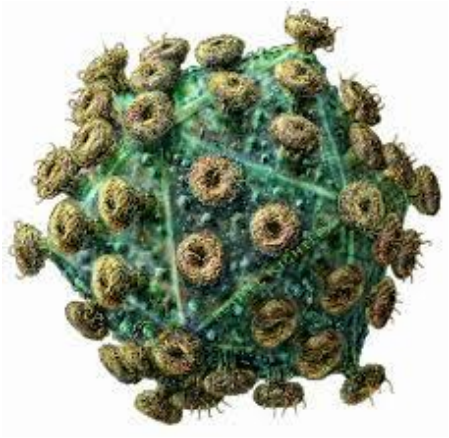
- Easy treatment
- 1-3 pills per day x 2-3 months
- Few or no side effects
- Highly effective (>95% cure)
- Minimal or no monitoring required
- **Treatment recommended for everyone with HCV**

Important to remember – many still 'afraid' of HCV treatment

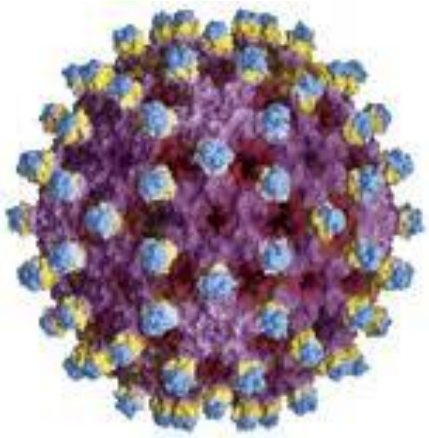
The goal of treatment is cure!

Controllable

Curable



HIV



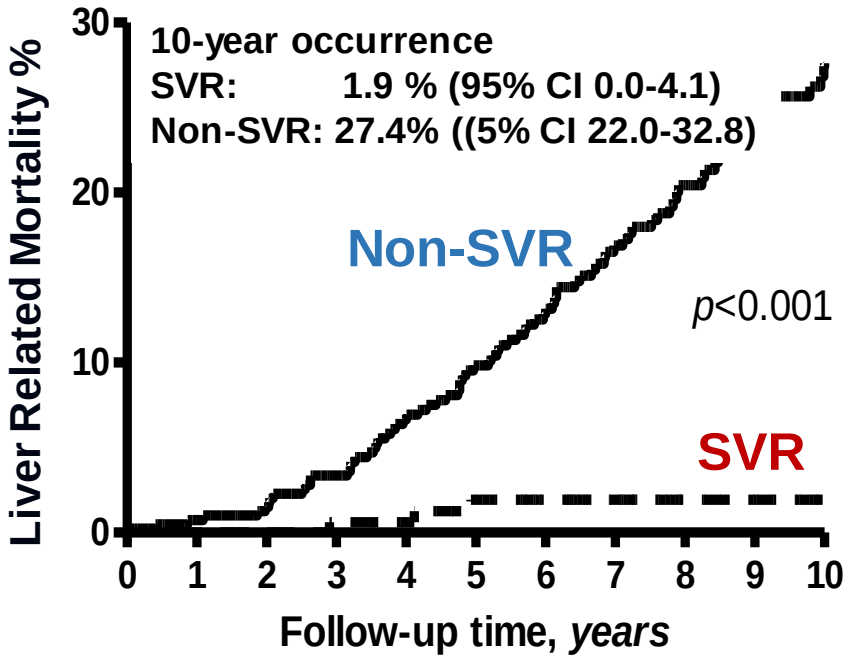
Hep B

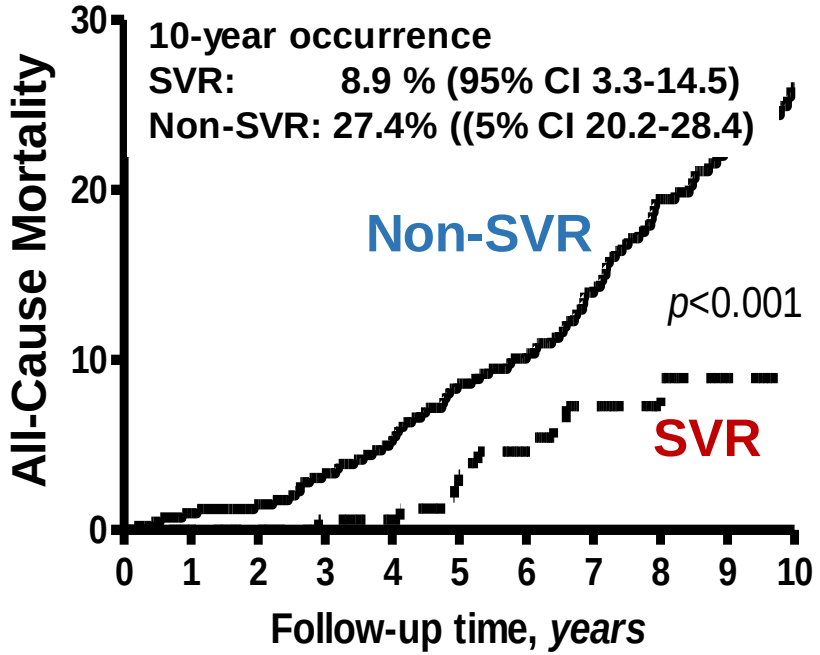
Hep C

Hep C is the first curable chronic viral infection

Liver benefits of sustained virological response (cure)

Long-term follow-up of 534 patients with F3/F4 post-treatment

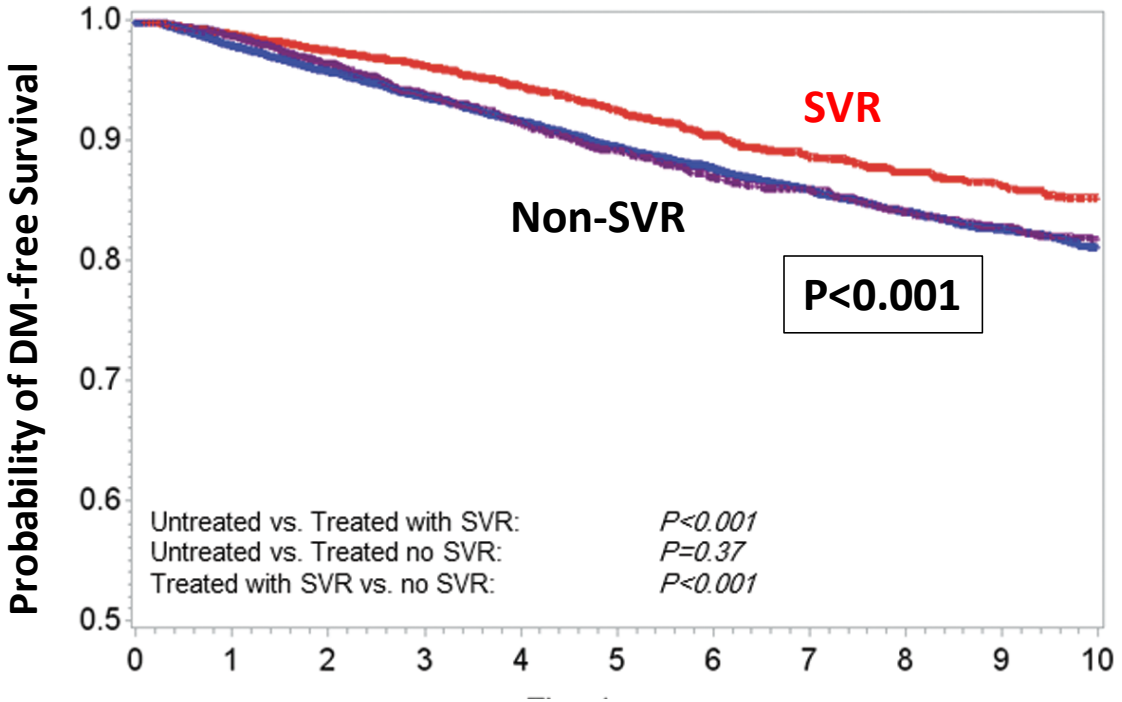




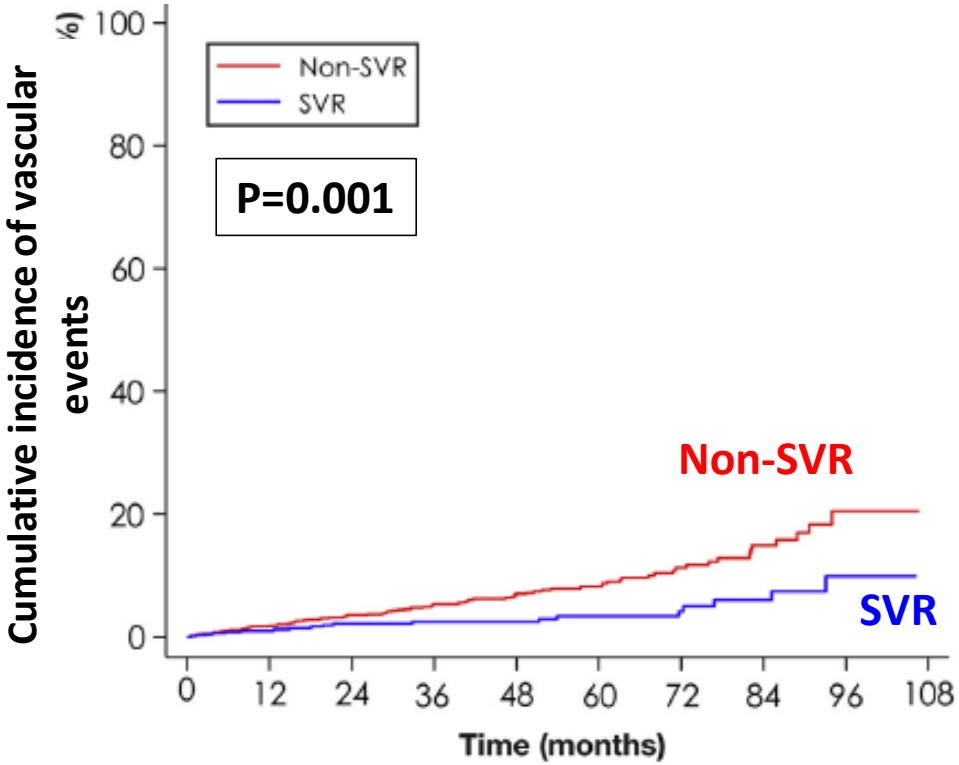
- SVR eliminates liver failure & liver-related death
- **SVR is not a surrogate** = reduced ***all-cause*** mortality

HCV Treatment Has Benefits Beyond the Liver

Risk of Diabetes



Risk of MI & Stroke



Sustained Virologic Response (cure) reduces **diabetes** and **heart disease**

Bottom line on SVR

Without cirrhosis

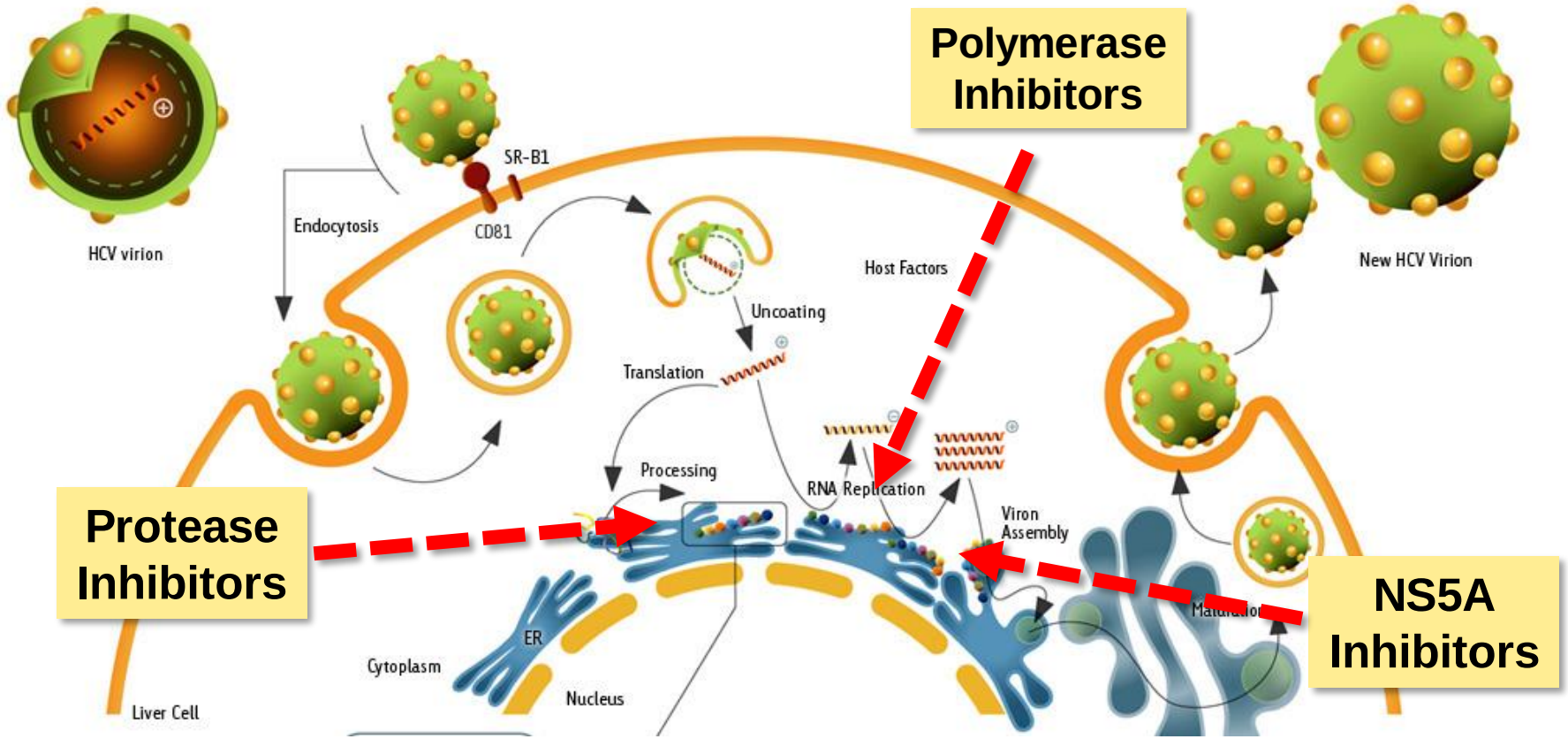
- SVR = cure → normal life expectancy

Profile
HCV Ab+ (lifelong) but
HCV RNA-negative → virus is gone!

With cirrhosis

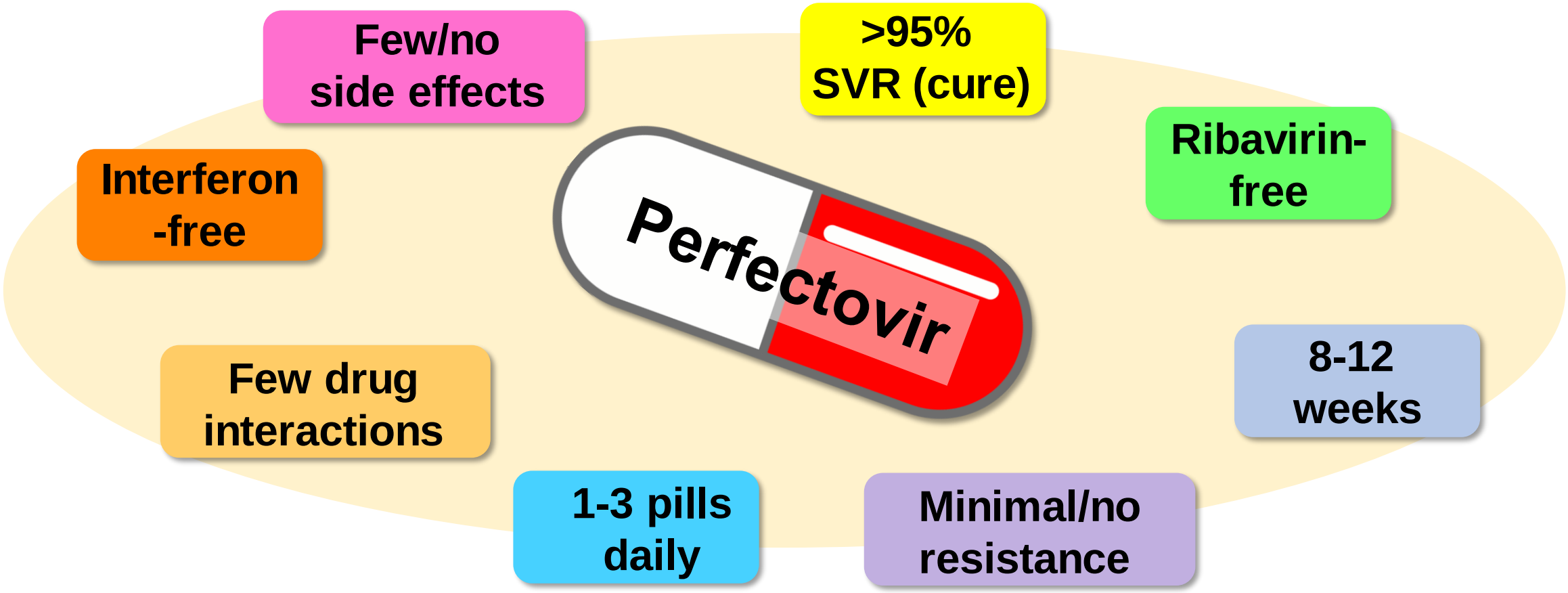
- SVR eliminates liver failure
- SVR greatly reduces the risk of liver cancer (HCC)
- SVR improves liver-related ***AND*** overall survival
- Reduces risk of non-liver complications of HCV

The Hepatitis C Virus Lifecycle - Lots of Targets for Therapy



Manns Nat Rev 2007

“Perfectovir” now close to a reality



Currently Recommended Treatment Regimens

- **Genotype-specific**
  - Ledipasvir/Sofosbuvir (Harvoni) – GT 1, 4, 5, 6
- **Pangenotypic (all genotypes)**
  - Sofosbuvir/Velpatasvir (Epclusa) – GT 1-6
  - Glecaprevir/Pibrentasvir (Maviret) – GT 1-6
- **Retreatment:** Sofosbuvir/Velpatasvir/Voxilaprevir (Vosevi) – GT 1-6

AASLD/IDSA. HCV Guidance. 2018. Shah et al CMAJ

Amongst the Excellent Options… How Do You Choose the Right One?

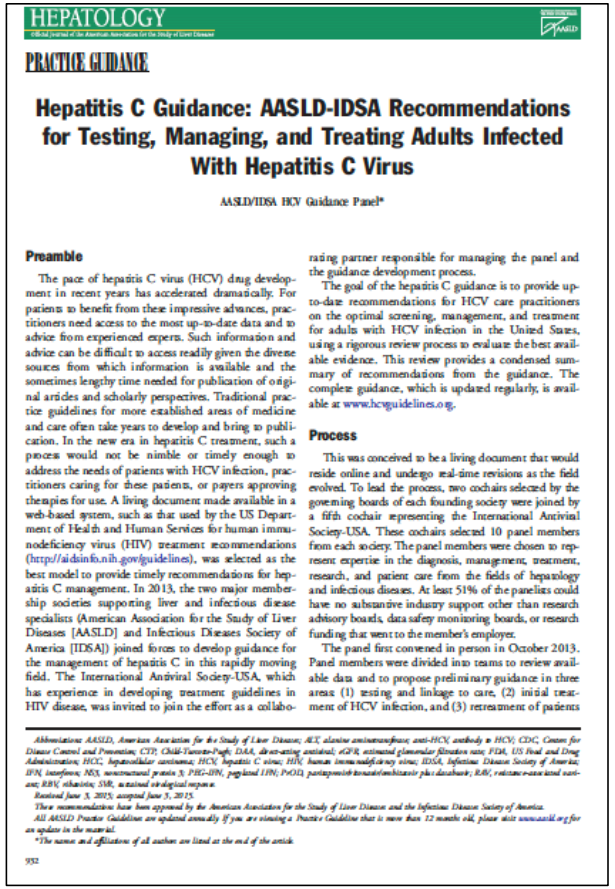
- All very effective, safe and well tolerated
- Cure rates consistently **> 95%** in clinical trials and real-world studies
- Safety/tolerability excellent
- Used successfully in hard-to-reach populations (active substance use, jails, etc.)
- **For most patients, any of the recommended options are fine**

Considerations

- ***Drug Interactions*** *– important to check*
- ***Duration*** **–** *8 vs 12 weeks*
- ***Pill burden*** **–** *1 vs 3 pills once daily*
- ***Food requirement*** **–** *an issue for some*

Treatment guidelines – down to 1 page!

2015→ 22 pages



HEPATOLOGY

PRACTICE GUIDANCE

Hepatitis C Guidance: AASLD-IDSA Recommendations for Testing, Managing, and Treating Adults Infected With Hepatitis C Virus

AASLD/IDSA HCV Guidance Panel*

Preamble

The pace of hepatitis C virus (HCV) drug development in recent years has accelerated dramatically. For patients to benefit from these impressive advances, practitioners need access to the most up-to-date data and to advice from experienced experts. Such information and advice can be difficult to access readily given the diverse sources from which information is available and the sometimes lengthy time needed for publication of original articles and scholarly perspectives. Traditional practice guidelines for more established areas of medicine and care often take years to develop and bring to publication. In the new era in hepatitis C treatment, such a process would not be nimble or timely enough to address the needs of patients with HCV infection, practitioners caring for these patients, or payers approving therapies for use. A living document made available in a web-based system, such as that used by the US Department of Health and Human Services for human immunodeficiency virus (HIV) treatment recommendations (http://aidsinfo.nih.gov/guidelines), was selected as the best model to provide timely recommendations for hepatitis C management. In 2013, the two major membership societies supporting liver and infectious disease specialists (American Association for the Study of Liver Diseases [AASLD] and Infectious Diseases Society of America [IDSA]) joined forces to develop guidance for the management of hepatitis C in this rapidly moving field. The International Antiviral Society-USA, which has experience in developing treatment guidelines in HIV disease, was invited to join the effort as a collaborating partner responsible for managing the panel and the guidance development process.

The goal of the hepatitis C guidance is to provide up-to-date recommendations for HCV care practitioners on the optimal screening, management, and treatment for adults with HCV infection in the United States, using a rigorous review process to evaluate the best available evidence. This review provides a condensed summary of recommendations from the guidance. The complete guidance, which is updated regularly, is available at www.hcvguidelines.org.

Process

This was conceived to be a living document that would reside online and undergo real-time revisions as the field evolved. To lead the process, two cochairs selected by the governing boards of each founding society were joined by a fifth cochair representing the International Antiviral Society-USA. These cochairs selected 10 panel members from each society. The panel members were chosen to represent expertise in the diagnosis, management, treatment, research, and patient care from the fields of hepatology and infectious diseases. At least 51% of the panelists could have no substantive industry support other than research advisory boards, data safety monitoring boards, or research funding that went to the member's employer.

The panel first convened in person in October 2013. Panel members were divided into teams to review available data and to propose preliminary guidance in three areas: (1) testing and linkage to care, (2) initial treatment of HCV infection, and (3) retreatment of patients

Abbreviations: AASLD, American Association for the Study of Liver Diseases; ALT, alanine aminotransferase; anti-HCV, antibody to HCV; CDC, Centers for Disease Control and Prevention; CTP, Child-Turcotte-Pugh; DAA, direct-acting antiviral; eGFR, estimated glomerular filtration rate; FDA, US Food and Drug Administration; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDSA, Infectious Diseases Society of America; IFN, interferon; NS5, nonstructural protein 5; PEG-IFN, pegylated IFN; PrOD, paritaprevir-ritonavir-ombitasvir plus dasabuvir; RBV, ribavirin; SVR, sustained virological response.

Received June 3, 2015; accepted June 5, 2015.

This recommendation has been approved by the American Association for the Study of Liver Disease and the Infectious Disease Society of America.

All AASLD Practice Guidelines are updated annually. If you are viewing a Practice Guideline that is more than 12 months old, please visit www.aasld.org for an update to the material.

*The names and affiliations of all authors are listed at the end of the article.

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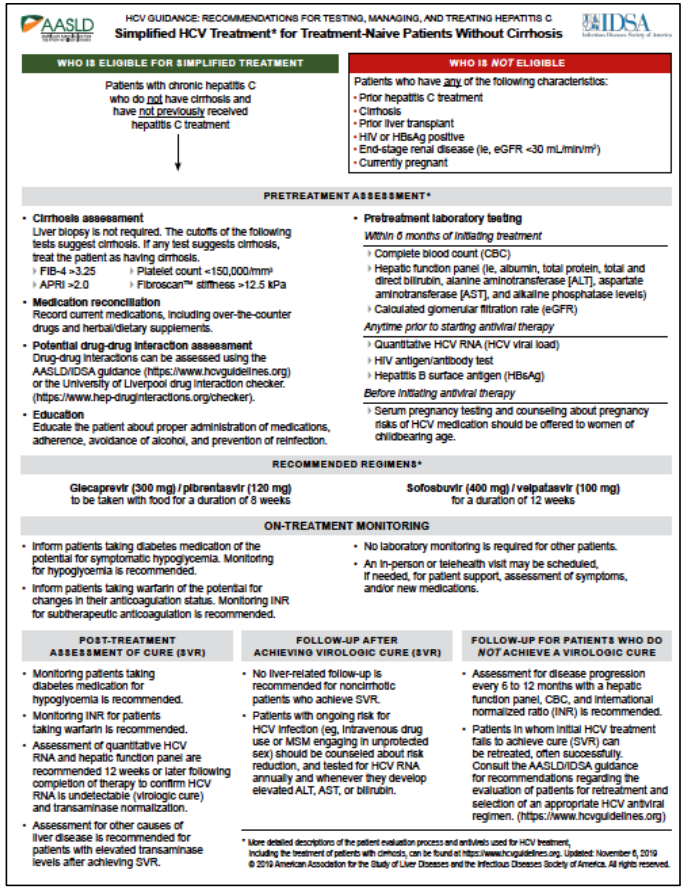
https://www.hcvguidelines.org/
(or google: "HCV guidelines")

2019→ 1 page



AASLD | IDSA

HCV GUIDANCE: RECOMMENDATIONS FOR TESTING, MANAGING, AND TREATING HEPATITIS C

Simplified HCV Treatment* for Treatment-Naive Patients Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients with chronic hepatitis C who do not have cirrhosis and have not previously received hepatitis C treatment

WHO IS *NOT* ELIGIBLE

Patients who have any of the following characteristics:
- Prior hepatitis C treatment
- Cirrhosis
- Prior liver transplant
- HIV or HBsAg positive
- End-stage renal disease (ie, eGFR <30 mL/min/m²)
- Currently pregnant

PRETREATMENT ASSESSMENT*

- **Cirrhosis assessment**
  Liver biopsy is not required. The cutoffs of the following tests suggest cirrhosis. If any test suggests cirrhosis, treat the patient as having cirrhosis.
  - FIB-4 >3.25
  - Platelet count <150,000/mm³
  - APRI >2.0
  - Fibroscan™ stiffness >12.5 kPa
- **Medication reconciliation**
  Record current medications, including over-the-counter drugs and herbal/dietary supplements.
- **Potential drug-drug interaction assessment**
  Drug-drug interactions can be assessed using the AASLD/IDSA guidance (https://www.hcvguidelines.org) or the University of Liverpool drug interaction checker. (https://www.hep-druginteractions.org/checker).
- **Education**
  Educate the patient about proper administration of medications, adherence, avoidance of alcohol, and prevention of reinfection.
- **Pretreatment laboratory testing**

  Within 6 months of initiating treatment
  - Complete blood count (CBC)
  - Hepatic function panel (ie, albumin, total protein, total and direct bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], and alkaline phosphatase levels)
  - Calculated glomerular filtration rate (eGFR)

  Anytime prior to starting antiviral therapy
  - Quantitative HCV RNA (HCV viral load)
  - HIV antigen/antibody test
  - Hepatitis B surface antigen (HBsAg)

  Before initiating antiviral therapy
  - Serum pregnancy testing and counseling about pregnancy risks of HCV medication should be offered to women of childbearing age.

RECOMMENDED REGIMENS*

Glecaprevir (300 mg) / pibrentasvir (120 mg) to be taken with food for a duration of 8 weeks

Sofosbuvir (400 mg) / velpatasvir (100 mg) for a duration of 12 weeks

ON-TREATMENT MONITORING

- Inform patients taking diabetes medication of the potential for symptomatic hypoglycemia. Monitoring for hypoglycemia is recommended.
- Inform patients taking warfarin of the potential for changes in their anticoagulation status. Monitoring INR for subtherapeutic anticoagulation is recommended.
- No laboratory monitoring is required for other patients.
- An in-person or telehealth visit may be scheduled, if needed, for patient support, assessment of symptoms, and/or new medications.

POST-TREATMENT ASSESSMENT OF CURE (SVR)

- Monitoring patients taking diabetes medication for hypoglycemia is recommended.
- Monitoring INR for patients taking warfarin is recommended.
- Assessment of quantitative HCV RNA and hepatic function panel are recommended 12 weeks or later following completion of therapy to confirm HCV RNA is undetectable (virologic cure) and transaminase normalization.
- Assessment for other causes of liver disease is recommended for patients with elevated transaminase levels after achieving SVR.

FOLLOW-UP AFTER ACHIEVING VIROLOGIC CURE (SVR)

- No liver-related follow-up is recommended for noncirrhotic patients who achieve SVR.
- Patients with ongoing risk for HCV infection (eg, intravenous drug use or MSM engaging in unprotected sex) should be counseled about risk reduction, and tested for HCV RNA annually and whenever they develop elevated ALT, AST, or bilirubin.

FOLLOW-UP FOR PATIENTS WHO DO *NOT* ACHIEVE A VIROLOGIC CURE

- Assessment for disease progression every 6 to 12 months with a hepatic function panel, CBC, and international normalized ratio (INR) is recommended.
- Patients in whom initial HCV treatment fails to achieve cure (SVR) can be retreated, often successfully. Consult the AASLD/IDSA guidance for recommendations regarding the evaluation of patients for retreatment and selection of an appropriate HCV antiviral regimen. (https://www.hcvguidelines.org)

* More detailed descriptions of the patient evaluation process and antivirals used for HCV treatment, including the treatment of patients with cirrhosis, can be found at https://www.hcvguidelines.org. Updated: November 6, 2019

What is on the 1 page?

Eligible for simplified treatment IF: No cirrhosis, no prior DAAs, no HIV/HBV

Pre-treatment assessment

Exclude cirrhosis – any of the following suggests cirrhosis

- FIB4 >3.25
- APRI >2.0
- Fibroscan >12.5 KPa
- Plt <150,000

Drug interactions → look them up

Other labs

- Liver panel – ALT/AST, INR, Bili, Albumin + Creatinine
- HCV RNA
- HIV, HBsAg
- Pregnancy test

Treatment

- **GLE/PIB (Marviret) x 8 weeks or SOF/VEL (Epclusa) x 12 weeks (no genotyping required)**
- No monitoring required (blood sugar if DM, INR if on warfarin)

Post-treatment follow-up

- SVR12 HCV RNA – if no SVR, retreat with different regimen (2nd line)
- HCV RNA periodically if ongoing risk exposures

Sofosbuvir/velpatasvir (Epclusa)

- **Single tablet regimen**
- **Well tolerated:**
  - Fatigue, headache common, rarely severe
  - Some patients report more than expected
- **Drug-drug Interactions:**
  - **Acid Suppression** meds (PPIs, antacids, H2 blockers): Reduce absorption up to 80%!
  - **Seizure** meds: Many seizure meds difficult except Keppra & valproate
  - **HBV/HIV** medications can interact
  - Cardiac: **Digoxin, Amiodarone**
  - **Statins**

Glecaprevir/Pibrentasvir (Maviret)

- Three tablets taken together once per day ***with food*** x 8 weeks
- Well tolerated
  - Fatigue, headache common – rarely severe
  - **Cannot be used in decompensated cirrhosis**
- Drug-drug Interactions:
  - No **acid suppression** (PPI) issue
  - **Seizure** meds challenging
  - **Psychiatric meds** may be challenging
  - **Estrogen-containing birth control pill**
  - Safe in renal failure including **dialysis**

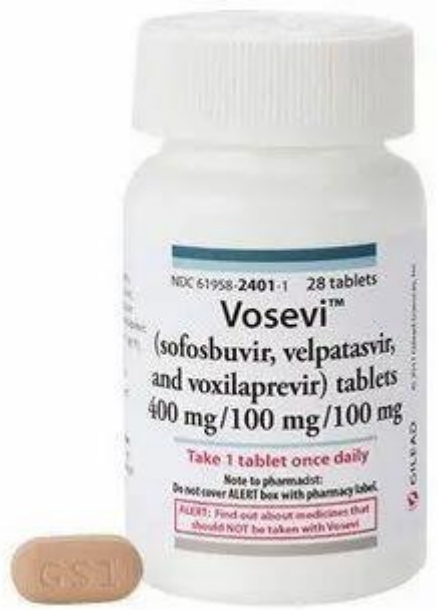
Comparison of first-line Pangenotypic Regimens

Sofosbuvir/Velpatasvir (Epclusa)	Glecaprevir/Pibrentasvir (Maviret)

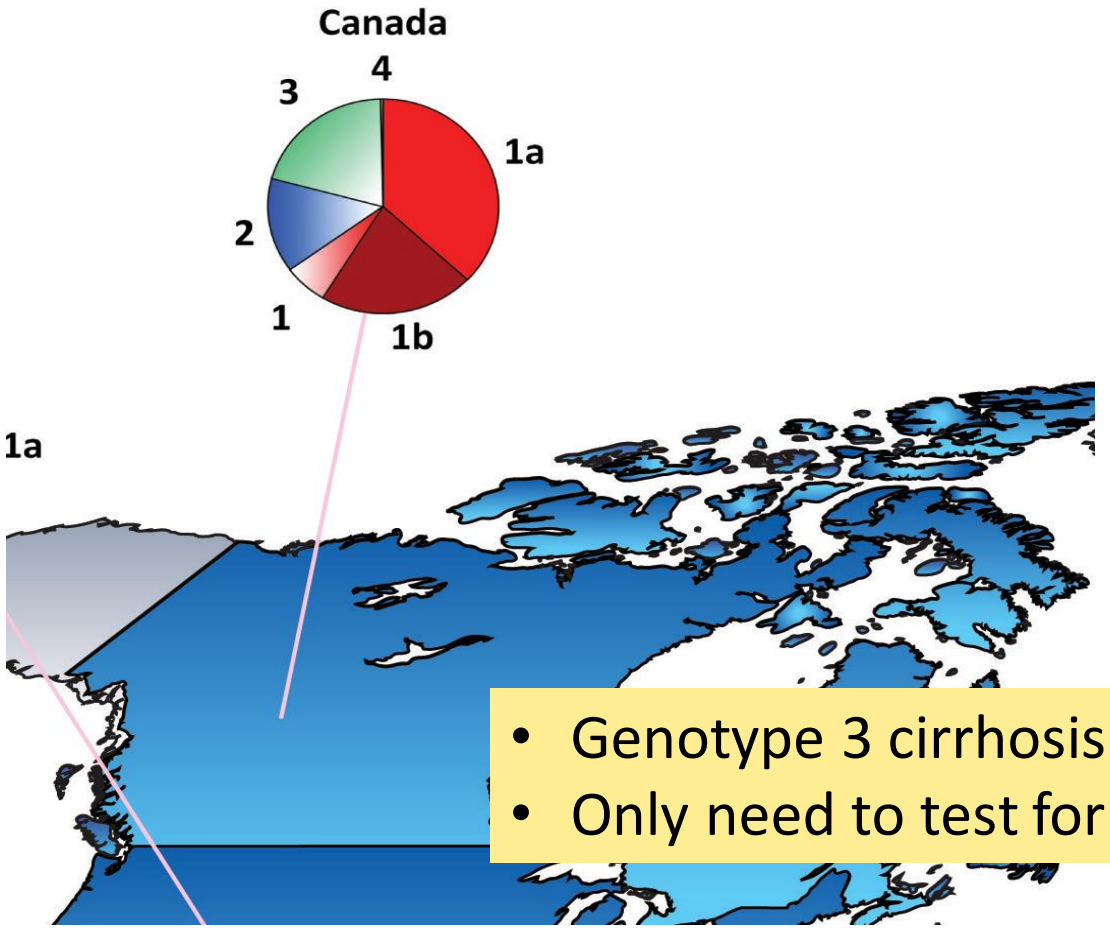
• 1 pill per day
• 12-week course for all
• Drug interactions
  • PPIs
  • Statins
  • Seizure meds
  • Amiodarone
	• 3 pills once per day **with food**
	• 8-week course for all
	• Drug interactions
	  • Estrogen-containing birth control pills
	  • Statins
	  • Seizure meds

Sofosbuvir/velpatasvir/voxilaprevir (Vosevi)

- **Single tablet regimen**
- **Well tolerated**
  - Fatigue, headache common, rarely severe
  - Additional side effect of mild diarrhea in about 15-20% of patients
- **Drug-Drug Interactions (**similar to Epclusa):
  - **Acid Suppression** meds: Reduce drug absorption up to 80%
  - **Seizure** meds: All seizure meds except Keppra
  - HBV/HIV – **tenofovir** – increase levels (renal toxicity)
  - Cardiac: Avoid **digoxin**
  - **Statins**
- Because of Voxilaprevir, **cannot use in decompensated cirrhosis**



Genotypes in Canada



But do we care?

ONLY IF CIRRHOSIS IS PRESENT…

- Genotype 3 cirrhosis is a bit more complicated
- Only need to test for genotype **if cirrhosis is present**

A Very Simplified Approach

**Assume refer decompensated to specialist

- **G1, 2, 3*, 4, 5, 6**
  - SOF/VEL (Epclusa) x 12 weeks
  - GLE/PIB (Maviret) x 8 weeks
- **G3 Cirrhosis:**
  - GLE/PIB (Maviret) x 8 weeks – first line
  - SOF/VEL (Epclusa) + Ribavirin x 12 weeks – second line
- **Treatment Failures – relapse/non-response:**
  - SOF/VEL/VOX (Vosevi) x 12 weeks

On-treatment Monitoring

For people ***without*** **cirrhosis** – **VERY minimal**

- **No blood testing required**
- Consider - Week 4 – CBC, ALT, creatinine (no HCV RNA)
- If any concerns – retest week 8, 12 or as indicated
- **12 weeks post-treatment** – CBC, ALT, creatinine, HCV RNA
  - **HCV RNA negative = cure!**

For people ***with*** **cirrhosis**

- **Week 4 –** CBC, ALT, AST, Bilirubin, Albumin, Creatinine
- Very small risk of worsening liver function during treatment - rare
- **If current or past decompensation…get specialists involved**

Adherence

- Always an important consideration…BUT, **the drugs are fairly forgiving!**
- Cure rates still extremely high with imperfect adherence
- Important to finish full course even if takes longer than planned, such as taking missed doses at the end
- Interruptions of less than 7 days, unlikely to affect outcome
- If **>7 day** interruption **within first 4 weeks** → consider restart
- If **>7 day** interruption **beyond 4 weeks** → before restart, check for cure
- Lost meds can usually be replaced by manufacturers – contact companies for reissue of meds

Issues After Treatment

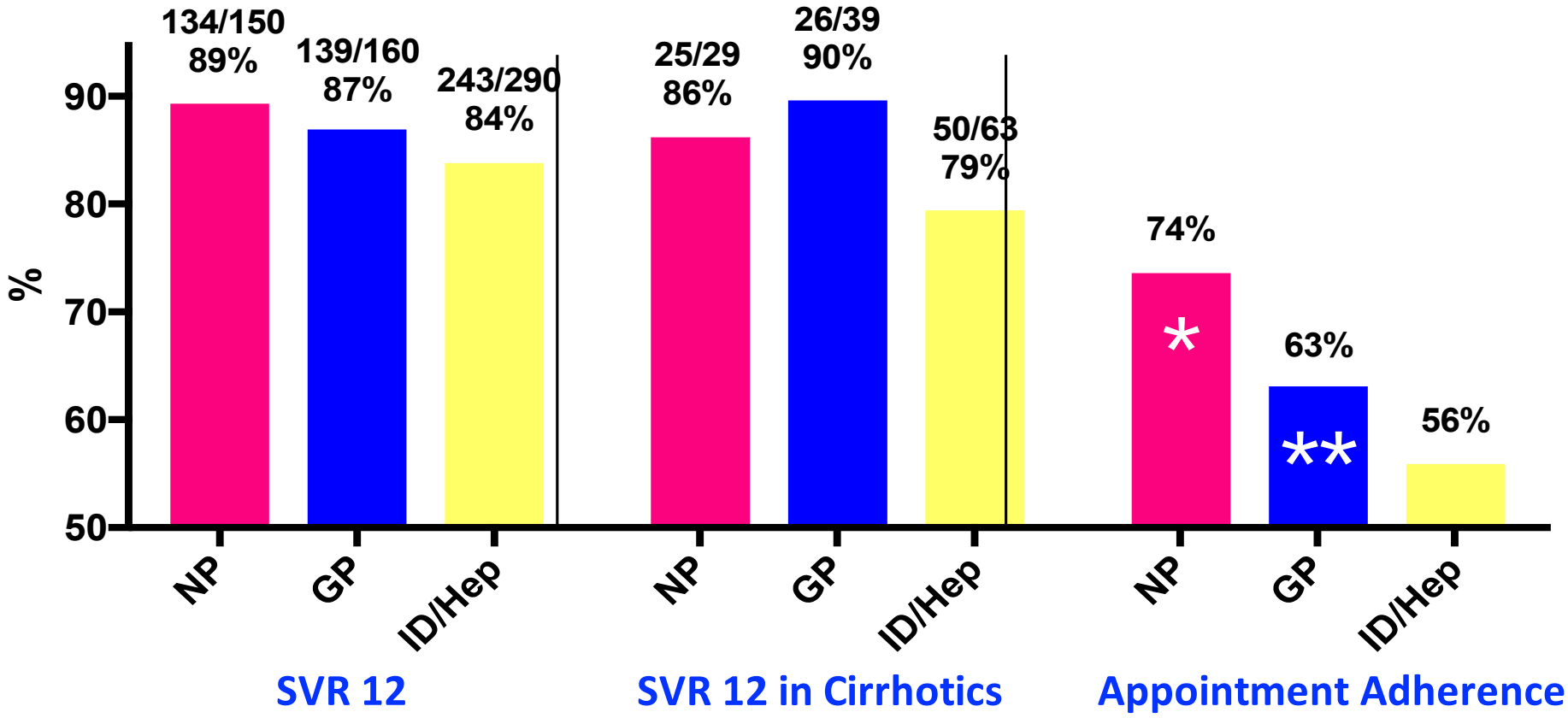
1. **Consequences of liver disease**
   - If no cirrhosis – liver effectively back to normal – no follow-up required
   - If cirrhosis – continue liver cancer surveillance with ultrasound q6m indefinitely (risk persists long-term even if numbers/fibroscan normalize)
2. **Reinfection risk**
   - Ongoing exposures – HCV RNA testing q6-12 m → **Harm Reduction – OAT maintenance KEY!**
   - No ongoing exposures – annual ALT, promote liver health (diet & alcohol) and *nothing else!*

Communicate information well

- if cured while in custody – key to ensure other providers aware
- if not cured, **connection to post-release care critical**

Treatment Should (and has) Move Out of Specialty Clinics

Treatment outcomes if led by NP, GP, or Specialist



Successful models of treatment in prisons e.g. federal prisons in Canada

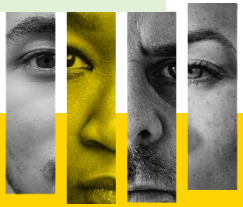
If you need some support…

ECHO Liver Ontario – please join
https://uhn.echoontario.ca/Our-Programs/Liver

Project ECHO
- Linking PCPs to specialists
- Brief didactic + case presentations
- Telementoring – support before, during & after treatment

ECHO Liver Ontario
- Monday 12-1:30 pm (EST)
- Free
- CPD Credits

HepCNet
- MOH program to support HepC Teams
- Available to SOLGEN providers
- Thursday 1-2 pm (EST) – free



Treatment Summary

- Very simple, high cure rates
- Usually comes down to:
  - **1 pill x 12 weeks (SOF/VEL – Epclusa)** vs. **3 pills with food x 8 weeks (GLE/PIB – Maviret)**
- Occasionally drug-drug interactions/medical issues favour one regimen
- Genotyping rarely required – only if cirrhotic and want to use SOF/VEL (G3)
- On-treatment monitoring is very limited
- Post-treatment follow-up
  - Cirrhosis – HCC surveillance
  - No cirrhosis – None except testing HCV RNA if ongoing risk exposures
- Support to help you get started
  - ECHO Liver
  - HepCNet
  - CATIE on-line resources

Module 4: 3-minute Self-Reflection

1. What resources would I need to prescribe and administer hepatitis C treatment to patients?

2. Who else needs to learn more about hepatitis C in my workplace so that we can better look after people/patients with infection?

3. What supports can I provide to help people successfully complete hepatitis C treatment?

Next Steps

This completes **Module Four.**

Additional Learning

Live Virtual Group Session

- Review key concepts and answer your questions with a hepatitis C specialist
- Visit the Live Session tab for more information at http://hcvtraining.ca/live-session/
- Talk to your manager on how to sign up for a session

Discussion Board

- Share your ideas and post your questions

Thank you!

Please complete the post-course quiz and access the resource page for more information