

MEDICATIONS FOR THE TREATMENT OF CHRONIC HEPATITIS C



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CONFLICT OF INTEREST DISCLOSURE STATEMENT

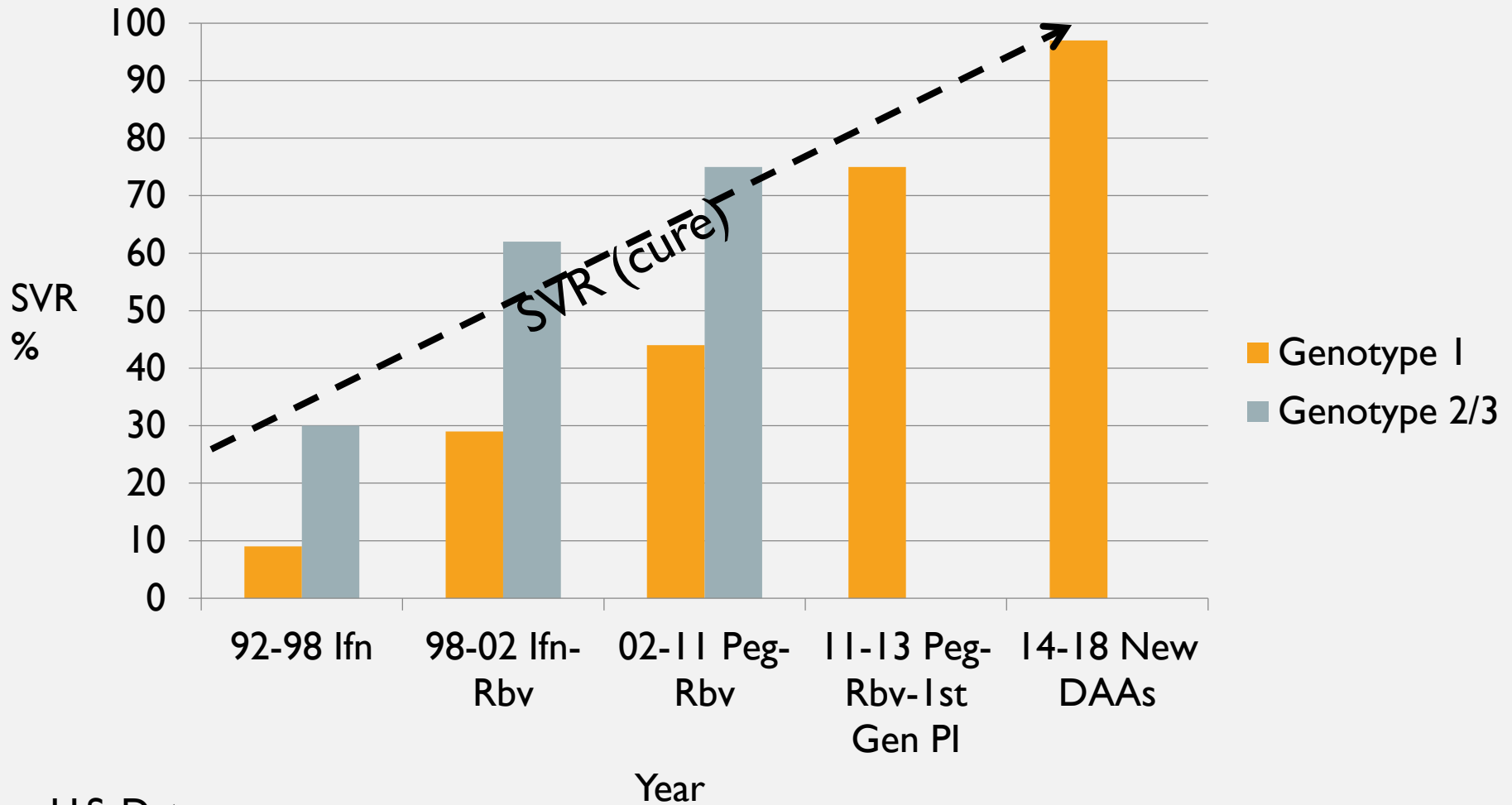
None.

I will only discuss licensed medications
and on-label use during this talk.

HEPATITIS C REVOLUTION

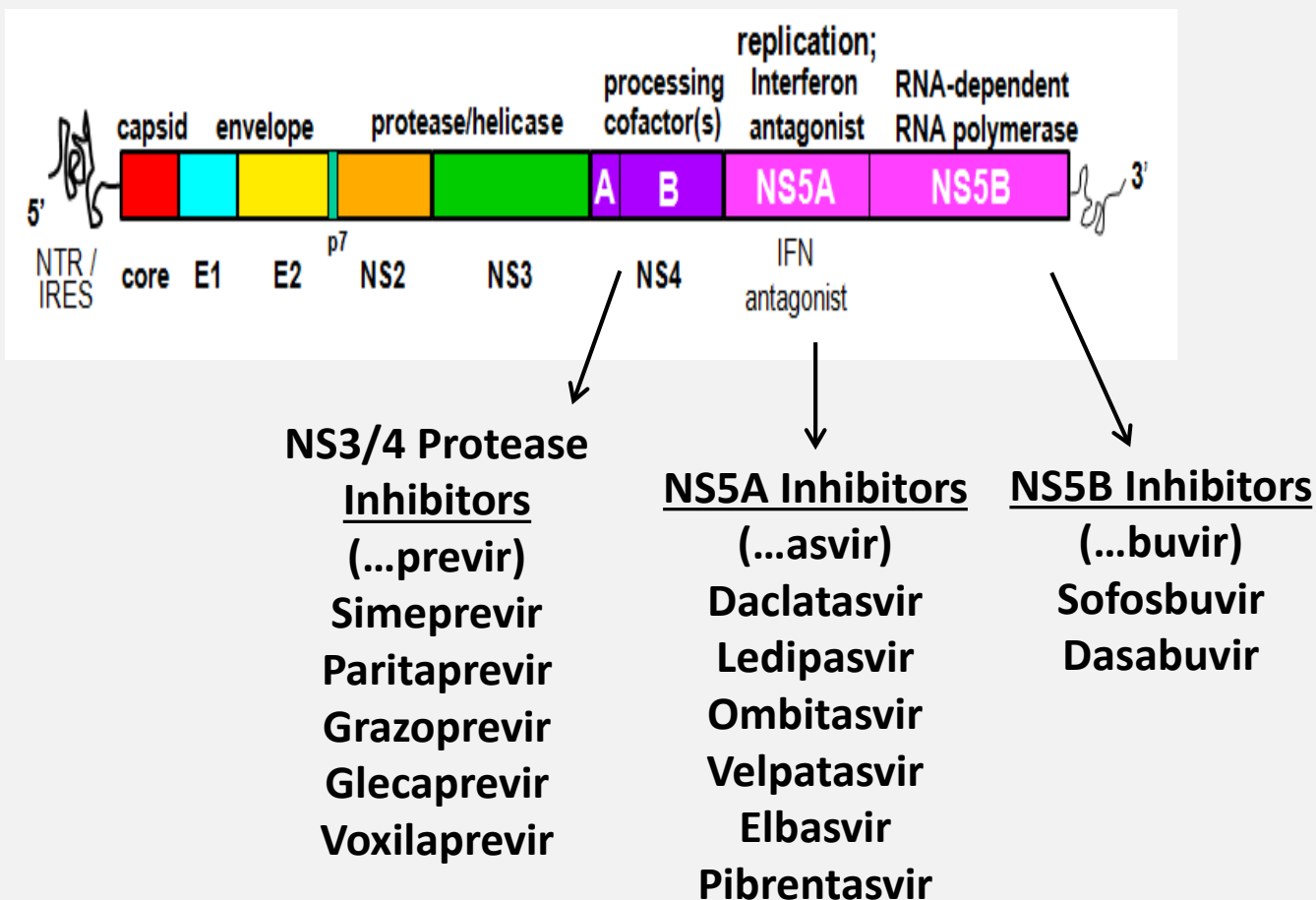
- Short Treatments
- Once daily dosing
- Few Side effects
- Minimal monitoring on treatment
- >95% cure for most

HISTORY OF HEPATITIS C TREATMENT RESPONSE



U.S. Data

WHERE DIRECT ACTING ANTI-VIRALS (DAAS) TARGET THE HEPATITIS C VIRUS



TREATMENT REGIMENS AVAILABLE TO TREAT HEPATITIS C

sofosbuvir/velpatasvir

Daclatasvir/sofosbuvir

Glecaprevir/pibrentasvir

Ledipasvir/sofosbuvir

Sofosbuvir/velpatasvir/voxilaprevir

Elbasvir/grazoprevir

Ombitasvir, paritaprevir, ritonavir

Simeprevir/sofosbuvir



IT'S AS EASY AS THESE 3

Glecaprevir/pibrentasvir

Ledipasvir/sofosbuvir

Sofosbuvir/velpatasvir



AASLD/IDSA RECOMMENDATIONS FOR FIRST-LINE HCV TREATMENT

HCV GT	Regimen	Duration, Wks	
		No Cirrhosis	Compensated Cirrhosis
1	GLE/PIB	8	12
	EBR/GZR*	12	12
	SOF/LDV	8 or 12 [†]	12
	SOF/VEL	12	12
2 or 3	GLE/PIB	8	12
	SOF/VEL	12	12 [‡]
4	GLE/PIB	8	12
	SOF/VEL	12	12
	EBR/GZR	12	12
	SOF/LDV	12	12
5 or 6	GLE/PIB	8	12
	SOF/LDV	12	12
	SOF/VEL	12	12

*If GT1a, use only if no baseline NS5A elbasvir RASs detected.

[†]If nonblack, no HIV, and HCV RNA < 6 million IU/mL, 8-wk duration recommended.

[‡]For GT3, if Y93H RAS detected, add RBV or consider SOF/VEL/VOX.



GLECAPREVIR/PIBRENTASVIR

- Glecaprevir 100mg
 - NS3/4A protease inhibitor
- Pibrentasvir 40mg
 - NS5A inhibitor
- Total daily dose 300mg/120mg
- Pangenotypic
(Treats all genotypes 1, 2, 3, 4, 5, & 6)
- Treatment duration 8 or 12 weeks for most



GLECAPREVIR/PIBRENTASVIR

- Treatment naïve or retreatment
- Safe to use in severe renal disease (eGFR<30)
- Not safe in decompensated cirrhosis
- Side effects – headache (18%), fatigue (15%), nausea (12%) and comparable in patients with or without cirrhosis
- Do not co-administer with rifampin, atazanavir
- Not recommended with ethinyl estradiol, atorvastatin, lovastatin, simvastatin

LEDIPASVIR/SOFOSBUVIR

First combination Direct Acting Antiviral (DAA)

NS5A inhibitor and NS5B polymerase inhibitor

Genotypes 1, 4, 5, and 6

Side effects:

fatigue (16%)

headache (14%)

Treatment duration 8-12 weeks

Safe in mild /moderate renal impairment (GFR \geq 30)

Safe in severe liver disease (decompensated)

Interactions with acid-suppressing medications:

- Omeprazole 20mg/day ok – Take at same time
- Famotidine 40mg BID ok – Take at same time +/- or 12 hrs apart
- Separate aluminum, magnesium containing antacids 4 hrs apart from LED/SOF



1 pill/day

SOFOSBUVIR/VELPATASVIR

- First pangenotypic Direct Acting Antiviral (DAA)
 - Combination NS5B polymerase inhibitor and NS5A inhibitor
- Treatment duration 12 weeks
- Side effects
 - Headache (~22%)
 - Fatigue (~16%)
 - Nausea (~9%)
- Safe in mild to moderate renal impairment (GFR \geq 30)
- Safe in severe liver disease (decompensated)



1 pill/day

Interactions with acid-suppressing medications:

- Omeprazole 20mg/day ok – Take 4 hrs after SOF/VEL
- Famotidine 40mg BID – Take at same time +/- or 12 hrs apart
- Separate aluminum, magnesium containing antacids 4 hours apart from SOF/VEL

CASE #1

A 59 year old female patient of yours agreed to Baby Boomer HCV screening with her annual labs earlier this year. The HCV antibody was reactive and HCV RNA was 68,000 iu/mL. Pre treatment labs were drawn and she returns to clinic today to review the results.

YOUR PATIENT'S LAB RESULTS

HCV RNA (viral count): 8,987,654 iu/mL. (confirms active infection)

Genotype: 1a

CBC: plt 256

CMP: ALT 39, AST 24, bili, alk phos and albumin normal,

Creat 0.6, eGFR >60

APRI: 0.234, FIB-4: 0.89 (none or minimal fibrosis)

PT/INR: 13/0.9

HIV screen: negative

HBsAg: negative HBcAb: negative HBsAb: negative

HAV Total antibody: negative

WHAT YOU KNOW

- Treatment naïve
- Minimal liver fibrosis
- Hepatitis A and B vaccinations needed

You review her current medications with her and she tells you she is taking –

- Omeprazole 20mg bid
- Lisinopril 10 mg daily
- Atorvastatin 20 mg daily

HEP iChart app users - please update to the newest version to ensure up-to-date information

HEP Drug Interaction Checker

Access our comprehensive, user-friendly, free drug interaction charts. Providing clinically useful, reliable, up-to date, evidence-based information

Start Now →

● Do Not Coadminister
■ Potential Interaction
◆ No Interaction Expected
◇ No Clear Data

	Daclatasvir	Elbasvir/Grazoprevir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Simeprevir	Sofosbuvir
Amiodarone	●	■	●	●	■	●
Antacids	◆	◆	■	◆	◆	■
Aspirin	◆	◆	◆	◆	◆	◆
Cannabis	◆	◆	◆	■	■	◆
Carbamazepine	●	●	●	●	●	●
Ciclosporin	◆	●	■	■	●	◆
Dabigatran	■	■	■	■	■	◆

DRUG-DRUG INTERACTIONS

- Antacids/PPIs

- Ledipasvir/sofosbuvir, Sofosbuvir/



- Antacid/PPI affect absorption and decrease cure if not dosed correctly.

- Give patient dosing instructions

- Decrease omeprazole to 20mg

- Consider elbasvir/grazoprevir if unable to decrease dose

CORRECTLY DOSING ACID SUPPRESSING DRUGS W/LED/SOF OR SOF/VEL

Acid reducing agents decrease absorption (of NS5A) negatively affecting cure if not dosed correctly.

- Antacids – [Al(OH)₃ and Mg(OH)₃] separate dosing from LED/SOF or SOF/VEL by 4 hours
- H₂-receptor antagonists (famotidine) admin simultaneously with or 12 hours apart. Dose not to exceed equivalent to famotidine 40mg bid
- PPI's (equivalent to omeprazole 20mg)
 - Not rec w/SOF/VEL
 - If necessary take SOF/VEL w/food & 4 hours later take PPI
 - Admin simultaneously with LED/SOF

WHAT ABOUT STATINS?

- Watch interaction w/some DAA's due to increased concentration of the statin
 - GLE/PIB
 - Do not give w/ atorvastatin, lovastatin or simvastatin.
 - Low dose rosuvastatin, pravastatin, fluvastatin, pitavastatin ok.
 - LED/SOF or SOF/VEL
 - Monitor closely if on atorvastatin and consider lowering dose.
 - Do not give with rosuvastatin



TREATMENT OPTIONS FOR GENOTYPE I, TREATMENT NAÏVE, NONCIRRHOTIC

- <https://anthc.org/what-we-do/clinical-and-research-services/hep/hep-c-treatment-information/>
- After this conference, the AKCureHCV.org website will bring you to this page.

MONITORING ON TREATMENT

Your patient starts treatment and comes to see you 4 weeks later.

What will you review at today's visit?

- 1. Adherence
- 2. Side effects
- 3. Any new medications
- 4. Labs – CBC, Creat, GFR, LFT and HCV RNA

<https://www.hcvguidelines.org/evaluate/monitoring>

MONITORING HCV RNA ON TREATMENT

- If detected at week 4
 - Repeat in 2 weeks
 - If > 10 fold --- discontinue treatment
 - If lower continue treatment
 - Not much guidance...if any questions consult

MONITORING ALT ON TREATMENT

- 10 fold increase – discontinue treatment
- < 10 fold increase with weakness, nausea, vomiting, jaundice; or bilirubin, alkaline phosphatase or INR increase – discontinue treatment
- Asymptomatic increase < 10 fold retest at 2 week intervals and consider discontinuing treatment if it remains elevated

END OF TREATMENT

Your patient has finished all of her medication. She returns for an end of treatment appointment.



1. Document last day of medication
2. Consider obtaining an HCV RNA to show suppression of virus (determine relapse or not)
3. Check for sustained virologic response (SVR) in 12 weeks.

SVR

- No HCV RNA 12 weeks or later after the end of treatment
- Some patients will achieve this even if they do not complete treatment
- Benefit
 - 70% reduction in risk of HCC
 - 90% reduction in liver related mortality and transplant



Decreased risk of diabetes and heart disease

<https://www.hcvguidelines.org/evaluate/monitoring>
Van Der Meer, et al. JAMA 2012: 308:2584-2593

MONITORING AFTER SVR

- For those without advanced liver disease
 - Follow up same as though they were never infected with hepatitis C
 - Assess for recurrence only if risk factors are present or unexplained elevation of ALT
 - HCV RNA preferred test as HCV antibody will remain positive
- Cirrhotic and advanced fibrosis patients

Continue HCC surveillance RUQ US every 6 months (consider AFP)

CASE #2

- Katy is a 22 year old female, diagnosed at age 18 with HCV, GT 2a. She has a history of IVDU. She just returned from treatment (sober from drugs and alcohol for 4 months), working in landscaping and is living with an older sibling. She has no health care coverage. She made today's appointment to discuss hepatitis C treatment.

Chart review shows she's fully vaccinated against Hepatitis A and B. Hep B surface antigen and core antibody are negative.

Medications: ethinyl estradiol/norethindrone OCP, St. John's Wort

PE: Without stigmata of liver disease

You get pretreatment labs...

PRE TREATMENT LAB REVIEW

HCV RNA - 1,003,458 iu/ml, GT 2

CBC- WNL, Plt 340

ALT - 49, AST 34, Alk 69, Alb 4.6, t. bili 0.4,

eGFR - 112

PT/INR - 13/1.0

HIV – negative

HBsAg and HBcAb – negative

Pregnancy test – negative

APRI: 0.250; FIB-4: 0.31 (no or mild fibrosis)

DDI'S

Ethinyl Estradiol Containing Products w/ GLE/PIB

May increase risk of ALT elevations

Co-administration not recommended

St John's Wort

Decreases absorption of all DAA's

Do not co-administer



PATIENT ASSISTANCE PROGRAMS FOR FREE DRUG

Pharmaceutical Company Sponsored Programs:

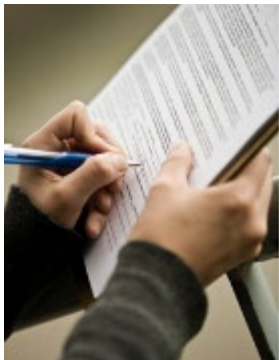
AbbVie (Mavyret) Patient Assistance

1-877-628-9738 - Call for Patient Assistance form



Gilead Support Path (Harvoni, Epclusa)

1-855-769-7284 or mysupportpath.com



GENOTYPE 2 TREATMENT NAÏVE, NONCIRRHOTIC OPTIONS

- <https://anthc.org/what-we-do/clinical-and-research-services/hep/hep-c-treatment-information/>
- After this conference, the AKCureHCV.org website will bring you to this page.

CASE #3

- 58 yo male with a history of htn, hld, type 2 DM and CKD. Known HCV infection since 1996. Never wanted to take interferon. Asks if you will treat his Hepatitis C with “that new pill I see on TV”.
- He is fully vaccinated against hepatitis A and B.
- Hepatitis screen shows hep B core antibody +, surface antigen -, indicating immune by past exposure.

RISK OF REACTIVATING HBV W/DAA THERAPY

- Assess and Refer if co-infected HBV/HCV
- Isolated anti-HBc+ ?
 - Not much guidance
 - What ANTHC does

Check HBV DNA

Pretreatment

At treatment completion

Refer/consult GI/hepatology if HBV DNA (+)

<https://www.hcvguidelines.org/evaluate/monitoring>

<https://anthc.org/wp-content/uploads/2017/11/Treatment-Checklists-Outside-ASU.pdf>

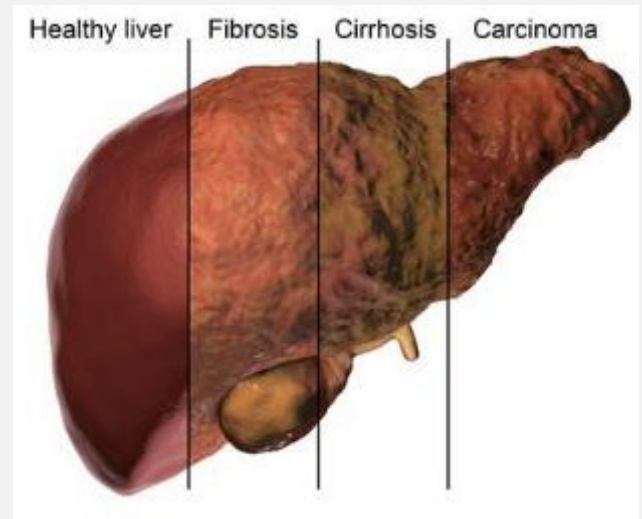
FIBROSIS STAGING

Calculated APRI= 0.604 (indeterminant)

FIB-4= 1.34 (no/minimal fibrosis)

Fibrotest-Actitest (Quest)= 0.43 (F2/moderate)

Consider FibroScan if
available



KIDNEY FUNCTION AND HCV TREATMENT MEDICATIONS

	Ledipasvir/ Sofosbuvir	Sofosbuvir/ Velpatasvir	Glecaprevir/ Pibrentasvir
eGFR	<30*	<30*	No dose adjustment required

*LED/SOF and SOF/VEL– For severe renal impairment, no dosage recommendation can be given. Consult nephrologist and Liver Disease provider before beginning treatment.

GENOTYPE 3 TREATMENT OPTIONS ALGORITHM

- <https://anthc.org/what-we-do/clinical-and-research-services/hep/hep-c-treatment-information/>
- Treatment naïve
- Fibrosis – F2
- CKD – eGFR 29

CASE #4

- Bill is 57 yo, he was diagnosed with hepatitis C in 2012 at a routine physical. He was screened per CDC recommendations that all baby boomers have a one time screening for hepatitis C. Upon questioning he doesn't recall a history of risk behavior or exposure.

PRETREATMENT LABS

HCV RNA 1,003,458 iu/ml, Genotype 1b

CBC- Plt 120

ALT 49, AST 100, Alk 69, Alb 3.6, t. bili 1.0,

eGFR 65

PT/INR 13/1.2

HIV – negative

HBsAg and HBcAb - negative

APRI score 2.083 (cirrhosis), FIB-4 3.49
(advanced fibrosis). Fibrotest 0.84 (cirrhosis)

CIRRHOSIS - COMPENSATED OR DECOMPENSATED?

Child-Turcotte Pugh Score

	POINTS*		
	1	2	3
Encephalopathy	None	Grade 1-2 (or precipitant-induced)	Grade 3-4 (or chronic)
Ascites	None	Mild/Moderate (diuretic-responsive)	Severe (diuretic-refractory)
Bilirubin (mg/dL)	<2	2-3	>3
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
INR	<1.7	1.7-2.3	>2.3

Add score for each parameter.
CTP class:
 A = 5-6 points
 (compensated)
 B = 7-9 points
 (decompensated)
 C = 10-15 points
 (decompensated)

CIRRHOTIC?

Compensated

Child-Pugh score 5-6

Decompensated

Child Pugh score ≥ 7

Refer to Specialist for treatment

Recommendations

- HCC* surveillance – US every 6 mo (consider afp)
- Varices screening – EGD (if plts ≤ 150 or FibroScan > 20)
- Hep A & B and pneumococcal vaccinations

*HCC – Hepatocellular Carcinoma

GENOTYPE I, TREATMENT NAÏVE, COMPENSATED CIRRHOSIS

- <https://anthc.org/what-we-do/clinical-and-research-services/hep/hep-c-treatment-information/>
- Remember – RUQ US and AFP every 6 months for HCC screening continues after treatment even if fibrosis scores improve

CASE #5

Shelly is a 24 yo client being seen for annual well woman exam. During the interview she shares with you –"I use heroin most days" . You determine that she's been using injecting drugs for over 4 years.

STI screening –, HCV ab +; HCV RNA
2,000,000 iu/mL

PWIDS WHO ARE HCV +

- Current guidelines recommend treating active drug users
- Refer to syringe exchange, substance use treatment, medication assisted treatment
- Stigma...treat as a person w/ a health issue

PRETREATMENT LABS

HCV Genotype 1b, HCV RNA 2,000,000 iu/mL

CBC- Plt 320

ALT 49, AST 40, Alk 69, Alb 3.8, t. bili 1.0

eGFR 65

PT/INR 11/1.0

HIV – negative

HBsAg and HBcAb – negative

Fully vaccinated against hepatitis A and B

Pregnancy test positive

APRI score: 0.31, FIB-4: 0.47 = no or minimal fibrosis

PREGNANCY AND HCV TREATMENT

- Delay treatment until after delivery and breastfeeding
- Safety of DAAs in pregnancy unknown
- Refer for or initiate MAT (bupre



MONITORING ON TREATMENT HCV GUIDELINES

Clinic visit or phone call weekly/monthly to ensure medication adherence

Monitor for adverse effects

Check for DDI's

Week 4

CBC, CMP (monitor renal and liver functions)

HCV RNA

if detectable at week 4 repeat at week 6 and if increased > 10 fold: discontinue treatment.*

Week 8 (ELB/GRA)

LFT

End of treatment

Consider HCV RNA

12 weeks after Treatment completion

HCV RNA for test of cure

*<http://hcvguidelines.org/full-report/monitoring-patients-who-are-starting-hepatitis-c-treatment-are-treatment-or-have>

POST SVR – HCV GUIDELINES

- For those without advanced liver disease
 - Follow up same as though they were never infected with hepatitis C
 - Assess for recurrence only if risk factors are present or unexplained elevation of ALT
 - HCV RNA preferred test as HCV antibody will remain positive
- Cirrhotic and advanced fibrosis patients
 - Continue HCC surveillance RUQ US every 6 months (consider AFP)

POST SVR – WHAT WE DO



1 year post-treatment for 5 years:

- Zero to minimal scarring (F0-F2): yearly CBC & LFTs
- |• Advanced Fibrosis (F3): RUQ US & AFP q 6 months; yearly CBC, LFTs, & AFP
 - Liver Field Clinic appointment every 2-3 years
- Cirrhosis (F4): RUQ US & AFP q 6 months; yearly CBC, CMP, AFP, PT/INR
 - Yearly Liver Field Clinic appointment

TAKE-HOME POINTS

- Only 3 regimens now recommended for first-line treatment of HCV
 - GLE/PIB LDV/SOF SOF/VEL
- GLE/PIB and SOF/VEL indicated for treatment-naive pts with GT1-6 HCV
 - GLE/PIB -No cirrhosis: 8 wks; cirrhosis: 12 wks
 - No dose adjustment for pts with renal impairment
 - SOF/VEL – 12 wks
- LDV/SOF – GT 1,4,5,6. 8-12 wks

RESOURCES

- Clinical calculators - Calculate APRI, FIB-4, MELD, Child's Pugh Score
 - Hepatitis C Score Calculator – free App for your phone
 - <https://www.hepatitisc.uw.edu/page/clinical-calculators/meld>
- AASLD/IDSA guidelines
 - <https://www.hcvguidelines.org/>
- Viral Hepatitis Drug Interactions
 - <https://hep-druginteractions.org/checker>
- ANTHC Liver Disease and Hepatitis Program
 - <https://anthc.org/hep/>

THANK-YOU



• Questions?

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