Management of Hepatitis C and Chronic Liver Disease: Beyond Universal Screening

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Educational Objectives

- 1- Discuss a hepatitis C universal screening and treatment program that maximizes efficiency and ensures quality outcomes
- 2- Describe treatment of liver disease beyond antiviral treatment of infectious hepatitis
- 3- Design protocols to safely and efficiently management liver disease

Background

- Kansas Department of Corrections receives dedicated funding to treat Hepatitis C
- This is authorized by the Kansas State Legislature
- Universal screening for Hepatitis C, at intake to prison, was initiated in 2018.
- However, due to the COVID pandemic, initiation of new treatment for patients had slowed creating a large backlog of patients.

Background

- With 100s of patients waiting to be assessed as assigned a treatment course, and transition of healthcare vendors, a need for additional resources was identified
- A new regional office position was created to dedicate an RN to manage the program
- Assessment, diagnosis, and treatment were then streamlined and standardized according to AASLD (American Association for the Study of Liver Disease) and Infectious Disease Society of America (IDSA) Simplified Treatment Guidelines.

AASLD/IDSA Guideline HCVguidelines.org

- Simplified treatment algorithm by genotype, history of past treatment, and severity of liver disease
- Additional guidance for special populations (co-occurring HIV, Hep B, etc), and situations such as non-adherence.

Simplified HCV Treatment Algorithm for Treatment-Naive Adults Without Cirrhosis

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

Adults with chronic hepatitis C (any genotype)
who do not have cirrhosis
and have not previously received hepatitis C treatment

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

- Prior hepatitis C treatment
- Cirrhosis (see simplified treatment for treatment-naive adults with compensated cirrhosis)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

PRETREATMENT ASSESSMENT*

- **Calculate FIB-4 score.**
- **Cirrhosis assessment**: Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
  - Prior liver biopsy showing cirrhosis

- **Pretreatment laboratory testing**

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

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

Simplified HCV Treatment Algorithm for Treatment-Naive Adults With Compensated Cirrhosis

WHO IS *NOT* ELIGIBLE FOR SIMPLIFIED TREATMENT

Patients who have any of the following characteristics:

- **Current or prior** episode of decompensated cirrhosis, defined as Child-Turcotte-Pugh (CTP) score ≥7 (ascites, hepatic encephalopathy, total bilirubin >2.0 mg/dL, albumin ≤3.5 g/dL, or INR ≥1.7)
- Prior hepatitis C treatment
- End-stage renal disease (ie, eGFR <30 mL/min/m^2)
  (see Patients with Renal Impairment section)
- HIV or HBsAg positive
- Current pregnancy
- Known or suspected hepatocellular carcinoma
- Prior liver transplantation

(See HCV guidance for treatment recommendations for these patients.)

WHO IS ELIGIBLE FOR SIMPLIFIED TREATMENT

- Adults with chronic hepatitis C (any genotype) who have compensated cirrhosis (Child-Pugh A) and have not previously received hepatitis C treatment
- Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 **or** any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
  - Prior liver biopsy showing cirrhosis

PRETREATMENT ASSESSMENT *

- **Calculate FIB-4 score.**
- **Calculate CTP score:** Patients with a CTP score ≥7 (ie, CTP B or C) have decompensated cirrhosis and this simplified treatment approach is not recommended.
- **Ultrasound of the liver** (conducted within the prior 6 months): Evaluate to exclude HCC and subclinical ascites.
- **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 or the University of Liverpool drug interaction checker.

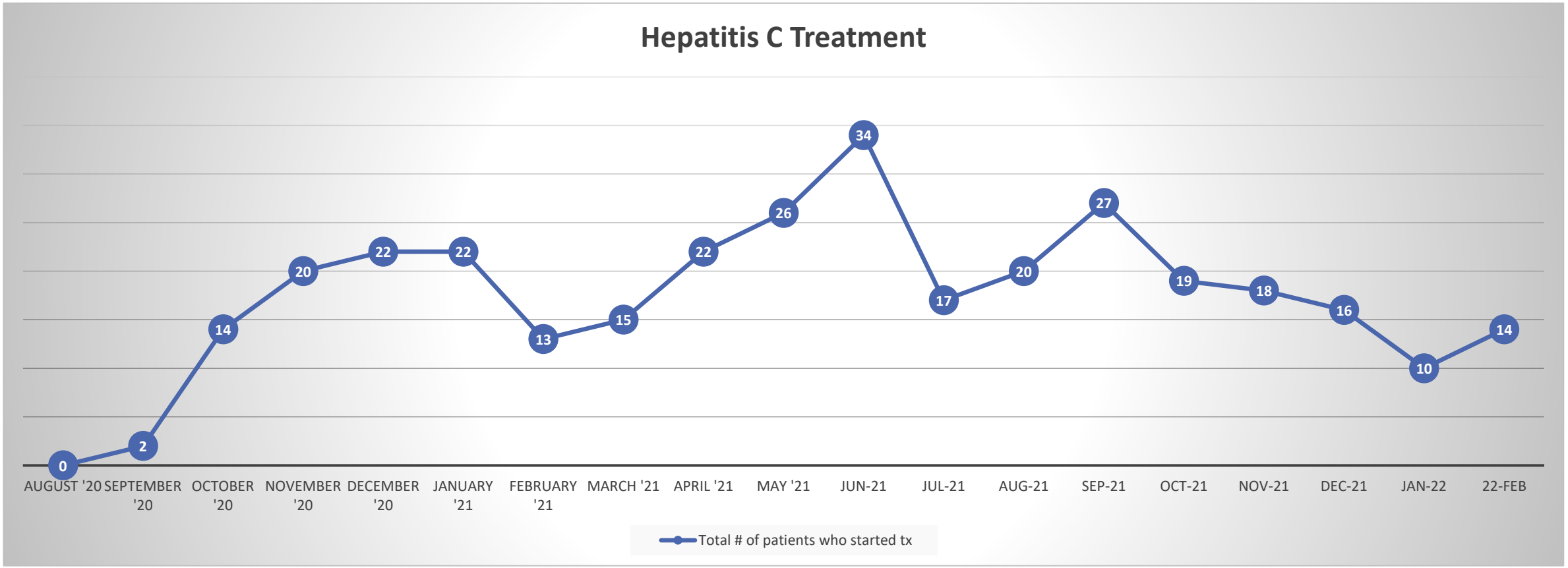
Within 3 months of initiating treatment

- Complete blood count (CBC)
- International normalized ratio (INR)
- Hepatic function panel (ie, albumin, total and direct bilirubin, alanine aminotransferase [ALT], and aspartate aminotransferase [AST])
- Calculated glomerular filtration rate (eGFR)

Any time prior to starting antiviral therapy

- Quantitative HCV RNA (HCV viral load)
- HIV antigen/antibody test
- Hepatitis B surface antigen
- HCV genotype (if treating with sofosbuvir/velpatasvir)

Treatment for Hep C population



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Treatment for Hep C population

Site	# Positive	In Review	Ready to Start	Currently being Treated	Spontaneoulsy Cleared Virus	Evaluated but not eligible	No time to TX	Refusing TX	Out to Court	Jail Program	TX Completed for FY 21	TX Completed for FY 22	SVR	Unable to F/U	Released prior to TX since 7/1/2020
EDCF	26	5	2	2	7		6	2			17	12	19	8	36
ECF	1	0	0	1	1		0				7	12	15	2	4
HCF	27	1	1	13	9		4	6			28	21	34	11	32
LCF	25	5	0	7	2		7	2			17	40	37	12	19
LCMHF	3	0	0	1	1		0				7	10	10	6	13
NCF	8	2	0	5	4		1	0	1		18	40	25	18	15
TCF	12	4	4	1	3		2	1			19	19	21	12	23
WFC	10	2	1	4	3		0	1			24	13	28	5	16
KJCC															
Total	112	19	8	34	30	0	20	12	1	0	137	167	189	74	158

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Simplified Workup

- US +/- AFP:
  - Q 6 months,
  - but doesn't have to occur before Hep C treatment if patient has no physical signs of cirrhosis
- EGD:
  - unless liver elastography is normal
  - Then q 1-5 years depending on findings

Simplified Workup

- Child-Pugh Score
- APRI score
- Fibrotest
- MELD
- CBC and CMP prior to and at 4 weeks of treatment

Simplified Workup

Finding	+ Likelihood Ratio
Terry's nails	16.0-22.0
Gynecomastia	5.8-35.0
Distended abdominal wall veins	11.0
Ascites	7.2
Palmar erythema	5.0
Spider nevi	4.3
Jaundice	3.8

Simplified Treatment

Recommended regimens listed by evidence level and alphabetically for: Treatment-Naive Genotype 2 Patients Without Cirrhosis		
RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[a]	8 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A

[a] Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

Simplified Treatment

- 8 week vs 12 week treatment courses
- Less potential for interruptions with a shorter time course:
  - Lockdowns
  - Out to court
  - Short time to release
- Some savings in costs due to nursing/med line DOT administration

Simplified Treatment

- Track 12 week post-treatment VL for resistance
- One drug choice = less med errors

Program Impacts

- Most patients have a complete workup and initiation of treatment before they leave the RDU.
- Off-site trips for imaging and specialty consult no longer delay initiation of treatment
- Reinfection rates after admission have declined
- Patients are also being re-screened at periodic assessments or if symptomatic and new Hep C cases are being identified after intake

Prioritization for treatment

- Previously, 6 month waiting period to see if acute infection would cleared achieved recovery spontaneously
- New guidelines suggest treating all patients, even in acute infection
- Mostly newly diagnosed infections are chronic

Prioritization for treatment

- Positive factors associated with spontaneous clearance include:
  - VL 10000 or lower
  - Jaundice
  - elevated ALT
  - female sex
  - younger age, and
  - genotype 1 infection

Prioritization for Treatment

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING
Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.	I, A

Prioritization for Treatment

- 1/3 of all US persons with HCV have contact with the correctional system each year
- Most incarcerated persons will transition back to the community
- Correctional facilities thus serve as a reservoir or “sink” that prevents the elimination of Hepatitis C

Treatment Experienced Patients

- Patients previously treated with interferon and/or ribavirin, before the availability to DAAs (Direct-acting antiretroviral drugs), should not be resistant to the new, much more effective treatments, and are treated as if they are naïve!!

Treatment Experienced Patients

Recommended and alternative regimens listed by evidence level and alphabetically for:

Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)[b]	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) except for NS3/4 protease inhibitor inclusive combination DAA regimen failures[c] • Not recommended for genotype 3 infection with sofosbuvir/NS5A inhibitor experience.	16 weeks	I, A

[a] For decompensated cirrhosis, please refer to the appropriate section.

[b] Genotype 3: Add weight-based ribavirin if cirrhosis is present and there are no contraindications.

[c] This regimen is not recommended for patients with prior exposure to an NS5A inhibitor plus NS3/4 PI regimens (eg. Elbasvir/grazoprevir).

Patients with confirmed or possible decompensated cirrhosis

Recommended regimens listed by evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] Who Have Genotype 1-6 and Are Ribavirin Ineligible

RECOMMENDED	DURATION	RATING
Genotype 1, 4, 5, or 6 only: Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	24 weeks	I, A[b]
Genotype 1-6: Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	24 weeks	I, A[c]

[a] Includes CTP class B and class C patients who may or may not be candidates for liver transplantation, including those with hepatocellular carcinoma.

[b] Only available data for genotypes 5 and 6 are in a small number of patients with compensated cirrhosis.

[c] Only available data for genotype 6 are in patients with compensated cirrhosis.

Program Impacts

- Most patients with cirrhosis have now completed treatment and management can now be more appropriately directed
- Several unique co-occurring diseases have been identified

Post-treatment surveillance

- If F0, and US is normal, can be removed from CC. Likely doesn't need future surveillance for HCC or varices.
- If F0 and US is not normal, or F1- there are no clear recommendations for follow up!
- F2 and greater should be followed at least Q 6 months indefinitely

Screening for other causes of liver disease

- Alpha-1-antitrypsin, ANA, Hep B, hemochromatosis, DM, HIV
- Clotting disorders and Budd-Chairi Syndrome
- History- alcohol use, family history
- Obesity = non-alcoholic fatty liver disease
- Co-management with GI/Hepatology
  - second diagnosis,
  - mismatch in serum and US testing,
  - F3 and greater fibrotic scores,
  - uncompensated cirrhosis, and
  - young patients who might quality for transplant

Screening for other causes of liver disease

- ANA +
  - screened for DM (HgbA1c),
  - lupus (as them about symptoms),
  - and thyroid disease (ask them about symptoms).
  - This follow up needs to be documented
  - If F0 and F1, follow over time, could resolve

Screening for other causes of liver disease

- Elevated Ferritin
- Hemochromatosis is underdiagnosed
  - 1 in 300 non-Hispanic whites
  - 1 in 10 of these men will develop severe liver disease
  - If Hct/Hgb elevated, refer at diagnosis of Hep C.
  - With normal Hct/Hgb, follow over time, may resolve with treatment of Hep C
  - https://www.cdc.gov/genomics/disease/hemochromatosis.htm
  - Joint pain is frequent complaint

General recommendations for treatment of liver disease

- Coffee/caffeine may be protective and 3-4 cups daily is recommended
- 2 gms daily Tylenol, baclofen and tramadol also ok, NSAIDs contraindicated
- Low dose ASA ok if needed for CAD
- Avoid PPIs: Blocking stomach acid may promote chronic liver disease | National Institutes of Health (NIH)

General recommendations for treatment of liver disease

- Ammonia levels are not helpful for serial monitoring or even acute decompensation (shouldn't impact decision to send out).
- Encephalopathy- treat with lactulose, with separate second episode, add rifaximin
- MELD score > greater than 14 = avoid elective surgery
- Imaging: Don't get CTs, US with Doppler or MRI
- Gold standard for diagnosis is still biopsy

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