A New Era in Hepatitis C: 

Direct Acting Antivirals and Primary Care Based Treatment

Colleen S. Lynch MD MPH

January 26, 2016
Disclosures

- No disclosures
- Medication names
Overview

• Hepatitis C natural history and epidemiology
• Assessing treatment readiness
• Treatment eligible vs. treatment priority
• New direct acting antivirals (DAAs)
• SFHN HCV Treatment Expansion
  – eReferral for Primary Care-Based HCV Treatment
The Challenge- 2016

• ~4 million chronically infected
• New treatments are effective, well tolerated and safe
• SFHN uniquely positioned
• HUGE opportunity to end the epidemic
How many chronic diseases can you CURE in your practice?
NATURAL HISTORY
HCV Infection

Acute Infection, 20-30% with symptoms

Clearance of HCV RNA, 15%-25% ↔ Fulminant Hepatitis, Rare

Chronic Infection, 75%-85%

Extrahepatic Manifestations

Chronic Active Hepatitis

Cirrhosis, 10%-20% over 20 years

 Decompensated Cirrhosis, 5-year survival rate of 50% ↔ HCC, 1%-4% per year

Hector

- 40 y/o Latino man
- In ED for trauma after an MVA
- HCV ab +
- Remote h/o cocaine use
- Remote h/o incarceration
You see Hector as a new patient

In addition to confirmatory HCV Antibody, which of the following tests would you order for him?

a. HCV viral load
b. HCV genotype
c. HCV resistance testing
You see Hector as a new patient

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b. HCV genotype
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## Types of HCV Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV Antibody</td>
<td>• Screening test</td>
</tr>
<tr>
<td></td>
<td>• Positive in past or current infection</td>
</tr>
<tr>
<td>HCV Viral load</td>
<td>• RNA PCR test</td>
</tr>
<tr>
<td></td>
<td>• Does not correlate with degree of liver disease</td>
</tr>
<tr>
<td></td>
<td>• Only recheck if treating</td>
</tr>
<tr>
<td>HCV Genotype</td>
<td>• “Strain” of HCV</td>
</tr>
<tr>
<td></td>
<td>• 1-6</td>
</tr>
<tr>
<td></td>
<td>• NOT like HIV genotype</td>
</tr>
<tr>
<td>HCV Resistance testing</td>
<td>• Currently only used for DAA failures</td>
</tr>
</tbody>
</table>
Risk factors

- IVDU (even once)
- HD
- Solid organ transplant or blood transfusion pre-1992
- Hemophilia with product <1987
- Body piercing/tattoos in unregulated/unlicensed setting
- HIV (30% HIV pos are co-infected)

- Born 1945-1965
- Intranasal drugs
- Incarceration
- Needle stick/occupational
- Endemic countries
- Sexual transmission (most often MSM)
- Maternal transmission (low)
- Household contact (low)
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EPIDEMIOLOGY
Prevalence

1.3-2% of the US population (NHANES data vs expanded prevalence model)

Baby boom prevalence ~4%
Question

What estimated percentage of people living with chronic HCV in the US are unaware?

a. 5-10%
b. 10-20%
c. 20-50%
d. 40-80%
Question

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Prevalence of cirrhosis in 2010 = 24.8%
Projected prevalence of cirrhosis in 2030 = 44.9%

CDC HCV Epidemiology 2013.
Davis et al., Gastroenterology 2010.
Risks

• 2x all cause mortality
• Even higher risk of death: co-infection (HBV/HIV), EtOH, minorities. liver disease
• #1 indication for liver transplant
• 50% of HCC cases are HCV associated
Annual Age-Adjusted Mortality Rates: HCV and HIV

U.S. HCV Epidemiology

Prevalence: 4.1M
Diagnosed: 1.7M (~41%)
Under Treater Care: 385 (~22%)
Treated: 58 (~17%)

ASSESSING TREATMENT READINESS/ TREATMENT PRIORITY
Who is a treatment candidate?

Recommendations for when and in whom to initiate treatment

Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.

Rating: Class I, Level A
Jeanne

- 61 year old woman
- HTN, DM, COPD, HCV
- Lisinopril, metformin, glipizide, advair, ASA
- Intermittent crack cocaine
- Stable housing, good social support
- Missed 4 appt/year
Jeanne

“Can I get treated for my hepatitis, doc?”

<table>
<thead>
<tr>
<th>Lab</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype</td>
<td>1b</td>
</tr>
<tr>
<td>VL</td>
<td>5 million</td>
</tr>
<tr>
<td>Cr</td>
<td>1.1</td>
</tr>
<tr>
<td>K</td>
<td>5.0</td>
</tr>
<tr>
<td>AST/ALT</td>
<td>47/58</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.2</td>
</tr>
<tr>
<td>Platelets</td>
<td>166</td>
</tr>
<tr>
<td>INR</td>
<td>1.1</td>
</tr>
<tr>
<td>A1c</td>
<td>10.2</td>
</tr>
<tr>
<td>LDL</td>
<td>110</td>
</tr>
<tr>
<td>Utox</td>
<td>Pos cocaine</td>
</tr>
</tbody>
</table>
In considering HCV treatment for Jeanne, what factors are the most concerning?

a. No cirrhosis
b. Positive cocaine
c. Missed appointments
d. Uncontrolled diabetes
In considering HCV treatment for Jeanne, what factors are the most concerning?

a. No cirrhosis
b. Positive cocaine
c. Missed appointments
d. Uncontrolled diabetes
Treatment readiness

✓ Patient wants HCV treatment
Treatment readiness

✓ Patient wants HCV treatment
✓ Reasonably stable social situation
Treatment readiness

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✓ Reasonably stable social situation
✓ Takes Rx’d meds
Treatment readiness

✓ Patient wants HCV treatment
✓ Reasonably stable social situation
✓ Takes Rx’d meds
✓ Other medical issues are reasonably stabilized
Treatment readiness

✓ Makes scheduled appointments
Treatment readiness

✓ Makes scheduled appointments
✓ Can articulate a plan to avoid reinfection
Treatment readiness

✓ Makes scheduled appointments
✓ Can articulate a plan to avoid reinfection
✓ Able to contact patient by phone or have reliable communication (get email, multiple #s)
Treatment readiness

✓ Makes scheduled appointments
✓ Can articulate a plan to avoid reinfection
✓ Able to contact patient by phone or have reliable communication (get email, multiple #s)
✓ Stabilized from substance use/mental health standpoint
Eligibility

Anyone!

– Life expectancy > 12 months
– Must be “treatment ready”
Treatment priority: advanced disease

- Stage 2 fibrosis or greater
- Extra-hepatic manifestations
  - Cryoglobulinemia/vasculitis
  - Kidney disease (Proteinuria/nephrotic/MPGN)
- Organ transplant
- HCC with >12 month life expectancy
- HIV co-infection
- HBV co-infection
- Other liver disease (ex. steatohepatitis)
- Debilitating fatigue
- Diabetes mellitus or insulin resistance (pre-diabetes)
Treatment priority: risk of transmission

- MSM in high-risk sex practices
- Active IVDU
- Incarcerated
- Long term HD
- Women of child-bearing potential
- Health care workers
So we have some work to do
Direct Acting Antivirals (DAAs)
DAAs + YOU

HCV PCBT team
New Hepatitis C treatments

DIRECT ACTING ANTIVIRALS
To compare...

**Peg-IFN + RBV**

- Unknown mechanism
- 40-80% effective
- 1 year of treatment
- Severe side effects
  - Fatigue
  - Depression
  - Cytopenias
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**New meds**
- Viral polymerase/protease inhibitors
- 90-100% effective
- 2-6 months treatment
- Mild side effects
  - Fatigue
  - Headache
  - GI symptoms
  - Insomnia
To compare...

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  - Headache
  - GI symptoms
  - Insomnia

SVR= Sustained viral response
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Site of Action</th>
<th>Diagram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclatasvir (Daklinza®)</td>
<td>NS5a</td>
<td>DAC</td>
</tr>
<tr>
<td>Sofosbuvir (Sovaldi®)</td>
<td>NS5B</td>
<td>SOF</td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir (Harvoni®)</td>
<td>NS5A/NS5B</td>
<td>LDV/SOF</td>
</tr>
<tr>
<td>Paritaprevir/ritonavir/ombitasvir + dasabuvir (Viekira®)</td>
<td>NS3/4A/NS5A + NS5B</td>
<td>P/r/O, D</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>Not applicable</td>
<td>R</td>
</tr>
</tbody>
</table>

*Also: Simeprevir, Telaprevir, Boceprevir*
# HCV without cirrhosis

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Regimen</th>
<th>Duration</th>
<th>SVR Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DAC</td>
<td>12 weeks</td>
<td>96-100%</td>
</tr>
<tr>
<td></td>
<td>SOF</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LDV/SOF</td>
<td>8-12 weeks</td>
<td>93-100%</td>
</tr>
<tr>
<td></td>
<td>P/r/O</td>
<td>12 weeks</td>
<td>95-98%</td>
</tr>
<tr>
<td></td>
<td>D +/-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>DAC</td>
<td>12 weeks</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td>SOF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>DAC</td>
<td>12 weeks</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td>SOF</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SOF</td>
<td>24 weeks</td>
<td>93%</td>
</tr>
</tbody>
</table>
### HCV with compensated cirrhosis

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Regimen</th>
<th>Duration</th>
<th>SVR Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DAC</td>
<td>SOF +/-</td>
<td>24 weeks</td>
</tr>
<tr>
<td>1</td>
<td>LDV/SOF</td>
<td>SOF +/-</td>
<td>12 weeks</td>
</tr>
<tr>
<td>1</td>
<td>P/r/O</td>
<td>D +/-</td>
<td>12-24 weeks*</td>
</tr>
<tr>
<td>2</td>
<td>DAC</td>
<td>SOF +/-</td>
<td>12-24 weeks</td>
</tr>
<tr>
<td>2</td>
<td>SOF</td>
<td></td>
<td>16 weeks</td>
</tr>
<tr>
<td>3</td>
<td>DAC</td>
<td>SOF +/-</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>

*higher risk of drug induced liver injury, not often used
In general...

Prevalence:
- Gt 1 $\rightarrow$ 70%
- Gt 2 $\rightarrow$ 15%
- Gt 3 $\rightarrow$ 10%

Most patients are candidates for two medication regimens

Often limited by insurance (daclatasvir)
Treatments

www.hcvguidelines.org
Initial Treatment Box. Summary of Recommendations for Patients Who are Initiating Therapy for HCV Infection by HCV Genotype

Several options with similar efficacy in general are recommended for treatment-naïve patients with HCV genotype 1a infection (listed in alphabetic order; see text).

Daily daclatasvir (60 mg*) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks with or without weight-based RBV (1000 mg [<75 kg] to 1200 mg [>75 kg]) (cirrhosis) is recommended for treatment-naïve patients with HCV genotype 1a infection.

Rating: Class I, Level B (no cirrhosis); Class IIa, Level B (cirrhosis)

Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for 12 weeks is recommended for treatment-naïve patients with HCV genotype 1a infection.

Rating: Class I, Level A

Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) and weight-based RBV for 12 weeks (no cirrhosis) or 24 weeks (cirrhosis) is recommended for treatment-naïve patients with HCV genotype 1a infection.

Rating: Class I, Level A

Daily simeprevir (150 mg) and sofosbuvir (400 mg) for 12 weeks (no cirrhosis) or 24 weeks (cirrhosis) without the Q80K polymorphism with or without weight-based RBV is recommended for treatment-naïve patients with HCV genotype 1a infection.

Rating: Class I, Level A
Drug-Drug Interactions

- PPI/acid blockers (led/sof)
- ARVs
- Statins
- Beta blockers, CCBs
- Anticonvulsants
- Amiodarone

HIV co-infected patients

• Not special!
• Same meds and duration
• More medication interactions
Special Populations

• Decompensated cirrhotics (Childs-Pugh Class B or C)
• Renal failure (eGFR < 30, stage 4-5)
• Patients previously treated with DAAs
• Compensated cirrhotics with peg-IFN/rbv failure
HCV Primary Care-Based Treatment
Goals

• Increase PCP comfort with HCV treatment
• Support multidisciplinary teams
• Increase in HCV treatment rates
• Maintaining patient safety
  – Collaborating with SFGH Liver clinic
SFHN Model for Primary Care-Based HCV Treatment

**Primary Care Roles**
- Adherence and Monitoring Support
- Med Access Support

**Centralized Roles**
- Regimen Selection eReferral Consultation (Primary Care MD and PharmD)
- Specialty Pharmacy
- Insurance Companies
- Patient Assistance Programs

**SFGH Liver Clinic**
## SFHG Adult Portal

Welcome to the eReferral site, which has been developed to handle appointment requests from Community Health Network (CHN) and CHN-affiliated providers for outpatient specialty consultations. Routine consultation requests for the below clinics will no longer be accepted by handcopy, facsimile, or phone. Please follow the steps outlined below in submitting your referral request.

Begin by selecting an eReferral type for **WILLIAMS, DENISE**

### Medical Specialty Clinics
- Allergy Adult Clinic
- Cardiology Clinic
- Chest Clinic (Pulmonary)
- Diabetes Services
- Endocrinology Clinic
- Gastroenterology Clinic
- Geriatrics Clinic
- Hematology Clinic
- Infectious Disease at LHH
- Liver Clinic
- Neurology Clinic
- Oncology Clinic
- Renal Clinic
- Rheumatology Clinic
- TB Clinic
- Weight Management Clinic

### Women's Health Specialty Clinics
- 3M Breast Evaluation Clinic (Non Surgical)
- Gynecology Clinic
- Obstetric Clinic

### Other Programs
- 1M Anticoagulation Clinic (No Review)
- Anticoagulation PHC (No Review)
- Comprehensive Pharmacy Care
- Asthma and COPD Group Education Classes (No Review)
- Back Class (No Review)
- Cancer Risk Program (Genetic Counseling)
- Financial Fitness Program (No Review)
- Health At Home (Home Health Services)
- Medical-Legal Partnership (No Review)
- Neuropsychology Service
- Respite Program
- Stop Smoking Program (No Review)
- Cancer Support CARE Program (No Review)
- Transgender Health Services
- Wellness Center Classes/Services (No Review)
- CRANUM (PCP for Citywide Focus ONLY)
- Primary Care Psychiatry Service (Maxine Hall Health Center ONLY)
- SFHN Primary Care (Overall/Well, 6M, 1Y, 6G, UC & Respite ONLY)
- Therapeutic Food Pantry (EM clinic ONLY)

### Surgical Specialty Clinics
- Minor Procedure (No Review)
- IM/Surgical Clinic
- Anesthesia PreOp Clinic (No Review)
- Cardiac Anesthesia Clinic
- Concussion Clinic (No Review)
- General Surgery Clinic
- Neurosurgery Clinic
- Ophthalmology/Optometry Clinic (No Review)
- Diabetic Telemedicine Screening Service (No Review)
- Orthopedic Surgery Clinic
- Otolaryngology (Head and Neck Surgery) Clinic
- Plastic Surgery Clinic
- Podiatry Clinic
- Radiology - Interventional Radiology (No Review)
- Urology Clinic
- Vascular Surgery
- Vasectomy Service (No Review)

### Diagnostic Services
- Audiology Clinic (No Review)
- Echocardiography (No Review)
- EEG (No Review)
- Ambulatory ECG Monitoring (Ze Patch) (No Review)
- Exercise Treadmill Testing (ETT) (No Review)
- Sleep Study
- Radiology - CT
- Radiology - Fluoroscopy
- Radiology - Mammography Screening (No Review)
- Radiology Mobile MammoVan Screening (CMHC and MHC)
- MRCP ONLY (No Review)
- Radiology - Breast Mammography Diagnostic
- Radiology - MRI
- Pulmonary Function Testing (PFT) (No Review)
- Radiology - Ultrasound
- Vascular Ultrasound Lab (No Review)

### Rehabilitation Services
- Aquatic Therapy (No Review)
- Occupational Therapy
- Physical Therapy (Physical Medicine & Rehabilitation) Clinic (No Review)
- Speech Therapy
Electronic Referral (eReferral) for Primary Care-Based Hepatitis C Treatment

Treatment of chronic hepatitis C infection in the primary care setting is safe, effective and possible for many patients. The purpose of this eReferral is to provide the primary care provider assistance to select an appropriate medication regimen for HCV treatment within the primary care setting, and to provide monitoring recommendations that are compatible with the patient’s medical history and current medications. Note: if you are currently a resident physician or a clinician working outside the SFHN Primary Care system, please refer your patient to Liver Clinic for treatment. We cannot take referrals from these prescribers at this time.

This referral is appropriate for individuals for whom treatment will be prescribed and managed by you, the primary care provider, within the primary care setting, without a face-to-face visit with a specialist. Individuals not appropriate for primary care-based treatment using this referral include those with:

- Cirrhosis and a history of decompensated liver disease (ascites, variceal bleeding, hepatic encephalopathy) or Childs Pugh B or C (http://www.mdcalc.com/child-pugh-score-for-cirrhosis-mortality)
- Cirrhosis with complex medical history
Eligible

• They will NOT be seen in a specialty clinic → patients you want to treat yourself in clinic
• Assessed and treatment-ready
• Should have a HCV viral load, genotype, and labs such as CBC, CMP, INR within the last 6 months
Ineligible

• You don’t want to treat them yourself
• Resident patients/those outside SFHN
• Too sick or complicated:
  – History of decompensated cirrhosis
  – Cirrhosis with other complex medical problems
  – CKD stage 4 or 5 (eGFR <30)
  – HCC
  – Prior failed treatment with DAAs

Refer to SFGH Liver Clinic!
eReferral: What you’ll get

• Readiness assessment
• Liver staging
• Regimen selection
• Navigating insurance
  – Team roles
  – Language for notes
  – PA process
• Monitoring on treatment
eReferral: What you’ll get

• Initial detailed recommendations ➔ 1 week
• Supported through process with back and forth
• eReferral stays open for the duration of treatment if necessary
• Monitoring issues ➔ 2 days

• Reminder: patient will not be seen in a specialty clinic
SFHN Primary Care-Based HCV Treatment

– PC team training (today!)
– Conferences
– Project coordinator
  • Team building support
  • Patient tracking
– Liver Clinic
In Sum...

• Hepatitis C is prevalent & high mortality
• Improve screening and engagement in care
• We should assess all patients for treatment readiness
  – Stability, med. adherence, shows up
• Many conditions are “treatment priority” → good medication access
• Many resources for new medications
• SFHN Primary Care-Based HCV Treatment Model
  – eReferral
“Opportunity paged me, beeped me, linked me, e-mailed me, faxed me, and spammed me. But I was expecting it to knock!”
Thanks to...

• Kelly Eagen MD
• Annie Luetkemeyer MD
• Joanna Eveland MS MD
• Donald Gardenier DNP FNP-BC
QUESTIONS?