



**Ready or Not, Here It Comes:
Updates for Management of Hepatitis C Virus
across Practice Settings**

Moderator:

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Disclosure

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Gilead: Advisory Board

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AbbVie: Stockholder/Ownership Interest (excluding diversified mutual funds);
Gilead: Advisory Board, Stockholder/Ownership Interest (excluding diversified mutual funds); Merck: Stockholder/Ownership Interest (excluding diversified mutual funds)

All other planners, presenters, and reviewers of this session report no financial relationships relevant to this activity.

Learning Objectives

- Given a patient case, analyze emerging data on currently approved and anticipated hepatitis C virus (HCV) therapies.
- Discuss the challenges faced with HCV treatment across practice settings, including management of drug interactions, avoidance of treatment interruptions, and challenges encountered with specialty pharmacy medication coverage.
- Select resources for screening and management of HCV, medication selection, drug-drug interactions, pipeline agents, and continuing education.

Session Roadmap

- Dr. Martin
 - Overview of HCV / comparison of treatment options
 - Case studies in ambulatory care
- Dr. Spooner:
 - Management of HCV infection in the inpatient setting
 - Challenges/case studies
- Dr. Deming
 - Emerging data
 - Telemedicine
 - Anticipated challenges



Management of HCV Infection in the Ambulatory Care Setting

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Which resource offers guidance for HCV treatment selection?

- A. <https://www.clinicaloptions.com/Hepatitis.aspx>
- B. <http://www.hep-druginteractions.org/checker>
- C. <http://www.hcvguidelines.org/>
- D. <http://www.hepatitisc.uw.edu/>

Which of the following pieces of information is (are) necessary when selecting appropriate HCV treatment for a patient?

- A.** HCV genotype
- B.** HCV treatment history
- C.** Stage of disease (presence / absence of cirrhosis)
- D.** Concurrent medications

Which of the following is (are) an all-oral, pangenotypic, single tablet regimen(s) currently approved by the FDA for the treatment of adults with genotypes 1-6 chronic HCV infection?

- A.** Elbasvir/grazoprevir
- B.** Glecaprevir/pibrentasvir
- C.** Sofosbuvir/velpatasvir/voxilaprevir
- D.** Paritaprevir/ritonavir/ombitasvir/dasabuvir

Glecaprevir/pibrentasvir offers an 8-week treatment course for treatment-naïve, non-cirrhotic patients with any HCV genotype.

- A. True
- B. False

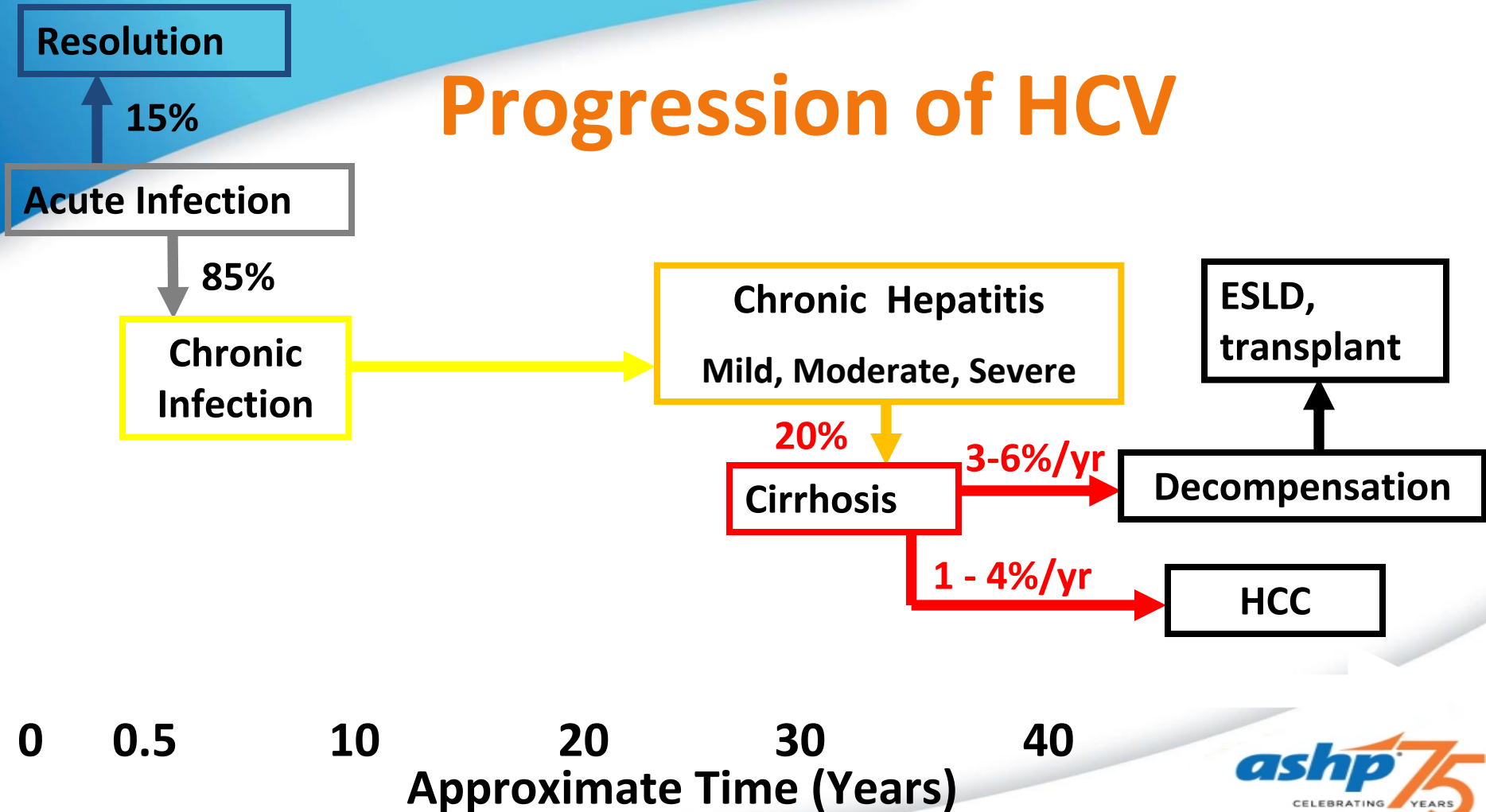
Abbreviation	Definition	Brand (if applicable)
CTP	Child-Turcotte-Pugh	
DAA	Direct-acting antiviral	
DCV	Daclatasvir	Daklinza®
EBR/GZR	Elbasvir/grazoprevir	Zepatier®
ESLD	End-stage liver disease	
G/P	Glecaprevir/pibrentasvir	Mavyret®
GT	Genotype	
HCC	Hepatocellular carcinoma	
LDV/SOF	Ledipasvir/sofosbuvir	Harvoni®
PegIFN	Pegylated interferon	Pegasys®, PegIntron®
PrOD	Paritaprevir/ritonavir/ombitasvir + dasabuvir	Viekira XR®
RBV	Ribavirin	
SMV	Simeprevir	Olysio®
SOF	Sofosbuvir	Sovaldi®
SOF/VEL	Sofosbuvir/velpatasvir	Epclusa®
SOF/VEL/VOX	Sofosbuvir/velpatasvir/voxilaprevir	Vosevi®
SVR	Sustained virologic response	

Hepatitis C Virus (HCV)

- Single-stranded RNA virus
- Multiple HCV genotypes and subtypes
- Most common blood-borne infection in the United States
 - Leading known reason for liver transplant
 - Main cause of liver-related death, end-stage liver disease (ESLD), and hepatocellular carcinoma (HCC)
- No vaccine available

Global Prevalence	Global Death Rate	US Prevalence	US Death Rate
~177.5 million	~399,000 / year	~2.5 – 4.7 million	19,629 in 2015

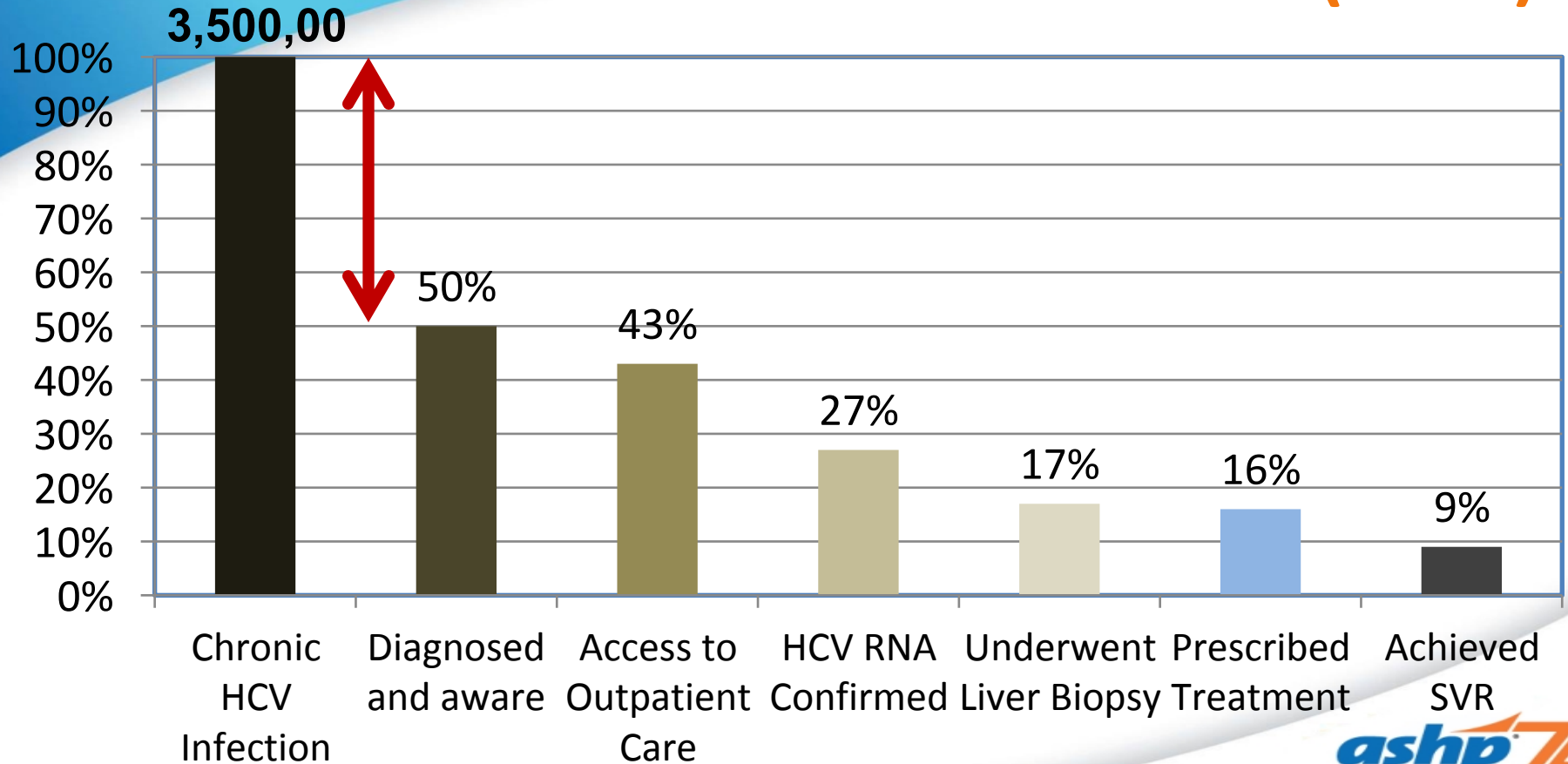
Progression of HCV



HCV Screening Recommendations

1. All patients with risk factors for HCV infection
2. Everyone born between 1945 and 1965 should get tested for HCV once regardless of risk factors
3. Annual testing of patients with ongoing risk factors
 - Persons who inject drugs
 - HIV+ men who have sex with men patients who have unprotected sex

HCV Treatment Cascade in US (2014)



Selecting HCV Treatment

- To ensure correct HCV agent and length of treatment, you need to know (at minimum):
 - 1) Genotype
 - 2) Previous treatment history
 - 3) Presence/absence of cirrhosis
 - Also need to know:
 - Concomitant comorbidities (e.g., renal impairment, post-transplant)
 - Check concomitant medications to avoid/manage DDIs
- Use HCV guidance to select appropriate regimen

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



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



- www.hcvguidelines.org
- First published on January 29, 2014
- Updated several times since

The screenshot shows the website's navigation menu with options: Home, Test, Evaluate, Monitor, Treatment-naïve, Treatment-experienced, Unique Populations, and About. Below the menu is a banner image of two healthcare professionals. A yellow notification box says "Start Here: Choose a patient profile from the menu above." The main content area features a "Welcome to the New HCVGuidelines.org" message, a search bar, and a list of guidance sections: "Contents and Introduction", "Testing, Evaluation, and Monitoring of Hepatitis C", "Initial Treatment of HCV Infection", "Retreatment of Persons in Whom Prior Therapy Has Failed", and "Management of Unique Populations". A "Recent Announcements" section highlights the FDA approval of glecaprevir/pibrentasvir and sofosbuvir/velpatasvir/voxilaprevir. At the bottom, there is a section for mobile device access with buttons for iPhone/iPad and Android.

Drug-Drug Interaction Evaluation

HEP Drug Interactions

UNIVERSITY OF LIVERPOOL

Interaction Checker →

Interaction Charts Site Updates Interaction Query Service About Us Pharmacology Resources Contact Us

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

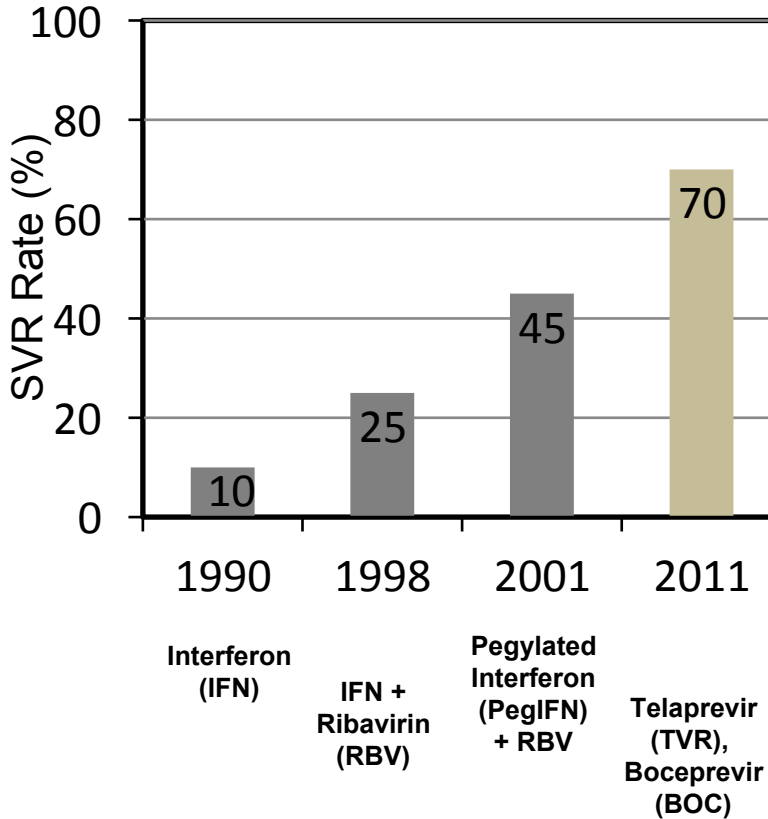
Start Now →

Legend:

- Do Not Coadminister (Red circle)
- Potential Interaction (Orange square)
- No Interaction Expected (Green diamond)
- No Clear Data (Grey diamond)

	Daclatasvir	Eltasvir/Grazoprevir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Simeprevir	Sofosbuvir
Amiodarone	Do Not Coadminister	Potential Interaction	Do Not Coadminister	Do Not Coadminister	Potential Interaction	Do Not Coadminister
Antacids	No Interaction Expected	No Interaction Expected	Potential Interaction	No Interaction Expected	No Interaction Expected	Potential Interaction
Aspirin	No Interaction Expected	No Interaction Expected	No Interaction Expected	No Interaction Expected	No Interaction Expected	No Interaction Expected
Cannabis	No Interaction Expected	No Interaction Expected	No Interaction Expected	Potential Interaction	Potential Interaction	No Interaction Expected
Carbamazepine	Do Not Coadminister	Do Not Coadminister	Do Not Coadminister	Do Not Coadminister	Do Not Coadminister	Do Not Coadminister
Ciclosporin	No Interaction Expected	Do Not Coadminister	Potential Interaction	Potential Interaction	Do Not Coadminister	No Interaction Expected
Dabigatren	Potential Interaction	Potential Interaction	Potential Interaction	Potential Interaction	Potential Interaction	No Interaction Expected

HCV Treatment Evolution



Ahn J, et al. *Gastroenterol Hepatol*. 2014;10(2):90-100. W
2015;373:714-725. Zeuzem A, et al. *Ann Intern Med*. 2015;163:1-13. Feld JJ, et al. *N Engl J Med*. 2015;373(27):2599-2607. Bourliere M, et al. *N Engl J Med*. 2017;376(22):2134-2146. Forns X, et al. *Lancet Infect Dis*. 2017; Epub ahead of print.

HCV DAA Medication Class Suffixes 2011-Present

<p><u>-previr =</u> NS3/4A Protease Inhibitors (PIs)</p> <p>(1st generation: telaprevir + boceprevir – not used in US)</p>	<ul style="list-style-type: none">• simeprevir• paritaprevir• grazoprevir• voxilaprevir• glecaprevir
<p><u>-asvir =</u> NS5A Replication Complex Inhibitors</p>	<ul style="list-style-type: none">• ledipaasvir• ombitaasvir• daclataasvir• elbaasvir• pibrentaasvir
<p><u>-buvir =</u> NS5B Inhibitors</p>	<ul style="list-style-type: none">• sofosbuvir• dasabuvir

HCV Treatment Comparison

	SMV + SOF 2013	LDV / SOF 2014	PrOD 2014	DCV + SOF 2015	EBR / GZR 2016	SOF / VEL 2016	SOF / VEL / VOX 2017	G/P 2017
DAA Class	PI + NS5B	NS5A / NS5B	PI / NS5A / NS5B	NS5A + NS5B	NS5A / PI	NS5B / NS5A	NS5B / NS5A / PI	PI / NS5A
Genotype (GT)	1	1, 4 – 6	1	1 – 3	1, 4	1 – 6	1 – 6	1 – 6
Length of Therapy: GT1, naïve, non-cirrhotic	12 weeks	8 – 12 weeks	12 weeks	12 weeks	12 – 16 weeks	12 weeks	12 weeks	8 weeks

HCV Treatment Comparison

	SMV + SOF 2013	LDV / SOF 2014	PrOD 2014	DCV + SOF 2015	EBR / GZR 2016	SOF / VEL 2016	SOF / VEL / VOX 2017	G/P 2017
Use in CKD, ESRD?	≥ 30 mL/min	≥ 30 mL/min	Used in dialysis	≥ 30 mL/min	Safe in dialysis	≥ 30 mL/min	≥ 30 mL/min	Safe in dialysis
Safety in cirrhosis CTP B, C	No	Yes	No	Yes	No	Yes	No	No

HCV Treatment Comparison

	SMV + SOF 2013	LDV / SOF 2014	PrOD 2014	DCV + SOF 2015	EBR / GZR 2016	SOF / VEL 2016	SOF / VEL / VOX 2017	G/P 2017
Daily DAA Pill Burden	2	1	3	2	1	1	1	3
Administra- tion	With food	+/- food	With food	+/- food	+/- food	+/- food	With food	With food
ADRs	Fatigue, HA, rash, photosen- sitivity, pruritus, nausea	Fatigue, HA	Nausea, pruritis, insomnia	Fatigue, HA	Fatigue, HA, nausea	Fatigue, HA	Fatigue, HA, nausea, diarrhea	Fatigue, HA

HCV Treatment Comparison

	SMV + SOF 2013	LDV / SOF 2014	PrOD 2014	DCV + SOF 2015	EBR / GZR 2016	SOF / VEL 2016	SOF / VEL / VOX 2017	G/P 2017
Cost	\$\$\$\$ - 2 copays	\$\$ - 1 copay	\$\$ - 1 copay	\$\$\$\$ - 2 copays	\$ - 1 copay	\$\$ - 1 copay	\$\$ - 1 copay	\$ - 1 copay
Role	Used less after 2014	Highest used in 2015	DDIs limit use	Less use due to cost	1 st approval for use in dialysis	1 st pan- geno- typic regimen	NS5A or NS3 failures	NS5A or NS3 failures (not both)

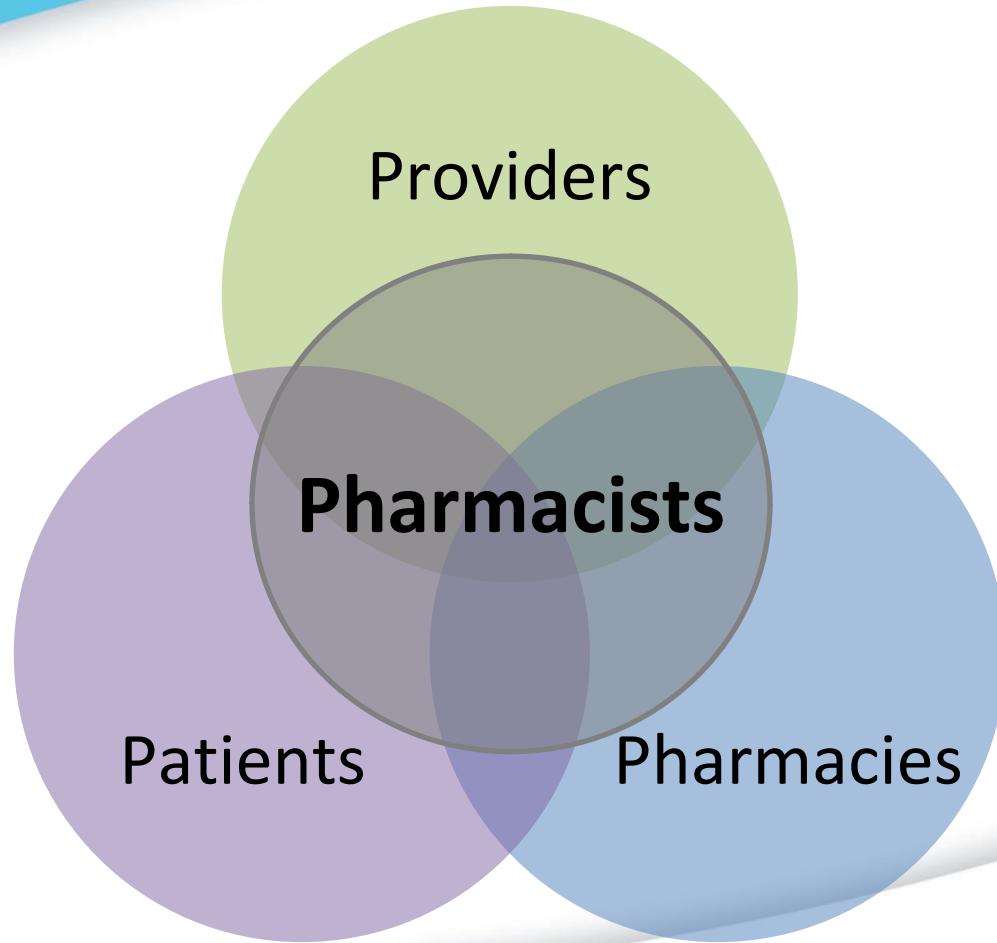
HCV Treatment Comparison

	SMV + SOF 2013	LDV / SOF 2014	PrOD 2014	DCV + SOF 2015
DDIs	<p><u>SMV</u>: CYP 3A4 inhibitor, inducer, mild inhibitor of CYP 1A2, inhibitor P-gp, and OATP1B1/3</p> <p><u>SOE</u>: P-gp and BCRP substrates</p>	<p><u>LDV</u>: Requires acidic environment for absorption; discuss antacid/H₂RA/PPI use</p> <p><u>SOE</u>: P-gp and BCRP substrates</p>	<p><u>All</u>: P-gp substrates; <u>Paritaprevir</u>: CYP 3A4 inhibitor, inducer; <u>ritonavir</u>: CYP 3A4, 2D6 substrate;</p> <p><u>Dasabuvir</u>: CYP 2C8, 3A substrates;</p> <p><u>Ombitasvir</u>: metab hydrolysis, oxidative</p>	<p><u>DCV</u>: P-gp substrate and inhibitor; CYP 3A4 substrate (*decrease dose to 30 mg daily with strong inhibitors, increase dose to 90 mg daily with moderate inducers)</p> <p><u>SOE</u>: P-gp and BCRP substrates</p>
Genetic Testing	Not for use in GT 1a <u>with</u> Q80K polymorphism			

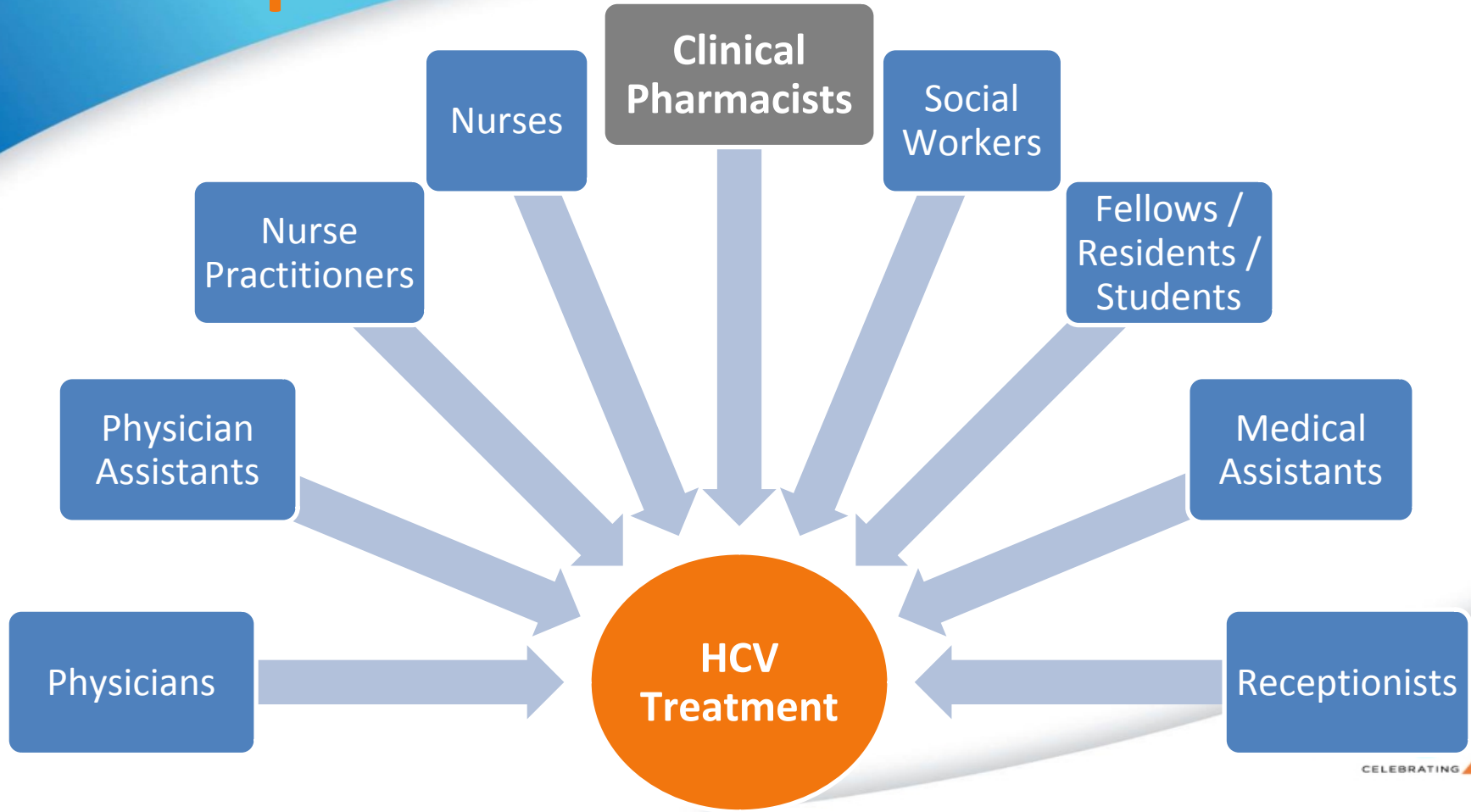
HCV Treatment Comparison

	EBR / GZR 2016	SOF / VEL 2016	SOF / VEL / VOX 2017	G/P 2017
DDIs	<p><u>EBR</u>: CYP 3A4 and P-gp substrate</p> <p><u>GRZ</u>: Weak CYP 3A4 inhibitor, CYP 3A4, and P-gp substrate</p>	<p><u>SOF/VEL</u>: P-gp and BCRP substrates</p> <p><u>VEL</u>: Requires acidic GI for absorption; discuss antacids/H₂RA/PPI use; inhibitor of P-gp and OATP181/3 (weak), BCRP (mod); substrate of OATP181/3; metab'd by CYP3A4, CYP2B6, CYP2C8</p>	<p><u>SOF/VEL/VOX</u>: P-gp and BCRP substrates</p> <p><u>VEL</u>: discuss antacid/H₂RA/PPI use; see SOF/VEL for additional info</p> <p><u>VOX</u>: substrate of OATP1B1/3; metab'd by CYP3A4, CYP1A2, CYP2C8</p>	<p><u>G/P</u>: P-gp, BCRP, OATP1B1/3 inhibitors; weak inhibitors of CYP3A4, CYP1A2, and UGT1A1</p>
Genetic Testing	<p>If GT1a – must check <u>baseline NS5A resistance</u></p>			

The Center of HCV Treatment



Sample Ambulatory Care Clinic Staff



Ambulatory Care HCV Management Pearls

- Recommend screening, team involvement
- Aid in medication selection
 - Use guidance to confirm/select regimen
- Drug-drug interaction (DDI) screening and management
- Liaison for medication assistance programs
- Pt management
 - Clinic visits
 - Provide education – adverse drug reactions (ADRs), dosing, adherence, lifestyle changes
 - Monitor labs

Case Study 1

- DS is a 59-year-old African American woman with HCV GT 1b, stage F3. She is treatment-naïve and her HCV RNA is 799,715 IU/mL.
 - PMH: HCV, COPD, peripheral neuropathy, Non-Hodgkin's Lymphoma; Laryngopharyngeal reflux
 - SH: Denies etoh, tob, illicit
 - Labs: tbili: 1.2; Alk Phos: 94; AST: 39; ALT 22; Albumin: 4; Hgb 15.3g/dL; PLT: 158; INR: 1.1; Scr: 0.56; CrCl 97.3 mL/min; Tox screen negative
 - Hep A IgG positive; Hep B surf Ag negative, Hep B surf Ab negative, Hep B core Ab total negative
 - Vitals: Wt: 79.3 kg; Ht: 68", BMI 26.81

Case Study 1 (Continued)

- Stage F3 African American woman
 - HCV GT 1b
 - Treatment-naïve
 - HCV RNA 799,715 IU/mL
- All: None
- Insurance:
 - Blue Cross Medicaid Managed Care
- Medications:
 - Albuterol HFA – 2 puffs every 4 hours as needed
 - Fluticasone 44mcg HFA – 2 puffs every 12 hours
 - Ranitidine 150mg twice daily
 - Gabapentin 600mg three times daily

Case Study 1 (Continued)

Question 1: What potential struggles do you anticipate with obtaining treatment approval?

Question 2: What treatment regimen(s) is(are) appropriate for her?

Question 3: Any drug-drug interactions (DDIs) to manage?

Question 4: What is (are) the shortest HCV treatment regimen(s) available for this patient?

Question 5: What is the least expensive HCV treatment regimen available for this patient?

Case Study 2

- CT is a 62-year-old cirrhotic man (Child Pugh Class A) with HCV GT 1a. He relapsed after 12-weeks of treatment with ledipasvir/sofosbuvir in 2015. His HCV RNA is 7,956,694 IU/mL.
 - PMH: HCV, HTN, T2DM, HL
 - SH: Denies etoh, tob. Smokes marijuana 3x/week
 - Labs: tbili: 0.4; Alk Phos: 116; AST: 70; ALT 93; Albumin: 3.7; Hgb 13g/dL; PLT: 270; INR: 1; Scr: 1.08; CrCl 36.3mL/min; NS5A Resistance: No mutations; Fibrosure (2016): F4
 - Hep A IgG positive; Hep B surf Ag negative, Hep B surf Ab positive, Hep B core Ab total positive
 - Vitals: Wt: 52.27 kg; Ht: 59", BMI 23.29

Case Study 2 (Continued)

- Compensated cirrhotic man
 - HCV GT 1a
 - Treatment-experienced with NS5A
 - HCV RNA is 7,956,694 IU/mL
- ALL: penicillin (hives)
- Insurance:
 - State Medicaid
- Medications:
 - Amlodipine 10mg daily
 - Aspirin 81mg daily
 - Furosemide 40mg daily
 - Insulin glargine 22 units daily
 - Insulin lispro 10-15 units TID AC
 - Losartan 10mg daily
 - Metoprolol succinate 200mg daily
 - Simvastatin 20mg daily

Case Study 2 (Continued)

Question 1: What potential struggles do you anticipate with obtaining treatment approval?

Question 2: What treatment regimen(s) is(are) appropriate for him?

Question 3: Any drug-drug interactions (DDIs) to manage?

Question 4: If this patient had decompensated cirrhosis, what treatment regimen(s) is(are) appropriate for him?



Management of HCV Infection in the Inpatient Setting

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Optimizing Outcomes for Inpatients Receiving Treatment for HCV Infection

- Case study
- Overview
- Unique medication safety concerns
- Ideas for error prevention

Case Study 3

- JS is a 40 year old man with NKDA who presents to the Emergency Department (ED) complaining of a red, swollen left lower extremity and fever. He notes that 3 days ago, he fell forward on cement stairs and cut his leg, and that redness and warmth began to creep up his shin over the past day
 - PMH:
 - HTN
 - Genotype 1a HCV infection, treatment-naïve, non-cirrhotic
 - Initiated treatment 2 weeks ago with ledipasvir/sofosbuvir
 - Plan is for 12 weeks of treatment
- The admitting resident diagnoses JS with cellulitis, and decides he will be admitted to the general medical floor for IV antibiotics.

Case Study 3 (Continued)

- JS is admitted to the floor
 - Initial labwork shows normal renal and hepatic function
 - The resident orders an HCV RNA (viral load)
 - Results pending
 - The following orders are entered and verified:
 - Vancomycin 1250 mg IV Q12H
 - Hydrochlorothiazide 25 mg PO daily
 - Pantoprazole 40 mg PO daily
 - Patient's own medication (ledipasvir/sofosbuvir, Harvoni[®]) once daily
 - Acetaminophen 1000 mg PO Q6H PRN headache

Discussion Questions

- How would you have performed medication reconciliation?
- Are there medication errors occurring here?
 - Underlying reasons for errors?
- How could these errors be prevented?

Medication Safety Concerns for Inpatients Taking HCV Pharmacotherapy

- Potential for treatment interruptions
 - At transitions of care
 - Admission to hospital
 - Documentation
 - Communication issues
 - Medication access
 - Discharge to home or rehabilitation facility
 - Lost medications
 - Communication issues
 - Why are interruptions problematic?

Medication Safety Concerns for Inpatients Taking HCV Pharmacotherapy

- Documentation as “Patient’s Own Med” in medication administration record (MAR)
 - Lack of automated drug interactions assessment
 - Missed drug interactions
 - Brand name or acronym use
 - Consistency
 - Confusion
 - Separate handling of the medication
 - Storage
 - Access

Medication Safety Concerns for Inpatients Taking HCV Pharmacotherapy

Drug interactions with inpatient medications

- Proton pump inhibitor (PPI)/H2-receptor antagonist/antacid issues
 - Ledipasvir/sofosbuvir
 - Sofosbuvir/velpatasvir
 - Sofosbuvir/velpatasvir/voxilaprevir
- Cytochrome P450 issues
 - Regimens containing protease inhibitors
- Enzyme/transporter induction
 - Antiepileptic drugs
 - Rifampin
- Antiarrhythmic medications issues
 - Amiodarone, digoxin
 - Sofosbuvir-containing regimens
- Autosubstitutions
 - Statins
 - PPIs

Medication Safety Concerns for Inpatients Taking HCV Pharmacotherapy

- Lack of familiarity with HCV medications
 - Regimens and durations used, drug interactions, patient counseling points
 - Potential for omission of ribavirin
 - Lack of knowledge varies among
 - Medical residents
 - Hospitalists
 - Nurses
 - Pharmacists
 - Look alike/sound alike names/acronyms
 - An issue with order entry, progress notes, discharge summaries

Ideas for Prevention of Medication Errors for Inpatients

- Education
 - Empowering patients
 - Interdisciplinary inservicing
- Pocket guides and wall charts
- Provision of electronic resources that are easy to access
- Order entry options
 - Customized order entry sets
 - Restricted prescribing
 - Entry of drug names from library rather than “patient’s own med”
 - Clinical pharmacist review

Case Study 3, Epilogue

- After 4 days in the hospital, JS is discharged home with orders to return to the infusion center daily for IV antibiotics.
 - How can the pharmacist assist with this transition of care?
 - What patient counseling points should be made?
- How can we apply lessons learned during JS's hospitalization to improve care for our inpatients with HCV infection?



Challenges in HCV Treatment

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Remaining Challenges in HCV Therapy

- HCV treatment in patients with decompensated cirrhosis
- Treatment interruptions
- HCV resistance
- Access to HCV therapy

Case Study 4: A 54 yo woman who previously failed HCV treatment with ledipasvir/sofosbuvir.

- Her past medical history is significant for cirrhosis, CTP Class A.
- What therapeutic options exist for retreatment?

Glecaprevir/Pibrentasvir: Indications and Duration of Therapy

HCV Genotype	Prior Treatment Experience	Without Cirrhosis	With Compensated Cirrhosis
1,2,3,4,5,6	Naïve	8 weeks	12 weeks
1,2,4,5,6	Pegylated interferon, ribavirin and/or sofosbuvir	8 weeks	12 weeks
3	Pegylated interferon, ribavirin and/or sofosbuvir	16 weeks	16 weeks
1	NS3/4A (NS5A naïve)	12 weeks	12 weeks
	NS5A (NS3/4A naïve)	16 weeks	16 weeks

Studies Evaluating the Efficacy of Mavyret in Patients with HCV GT1, 2, 4-6 Infection with or without Compensated Cirrhosis

Mavyret for 8 Weeks in TN/TE NC Patients: ENDURANCE-1 and SURVEYOR-2

Mavyret for 12 Weeks in TN/TE CC Patients: EXPEDITION-1



BT

Relapse

Non-VF*

	Overall	GT1	GT2	GT4	GT5	GT6
BT	1	1				
Relapse	2		2			
Non-VF*	7	2	2	3		

All analyses are using the ITT population.

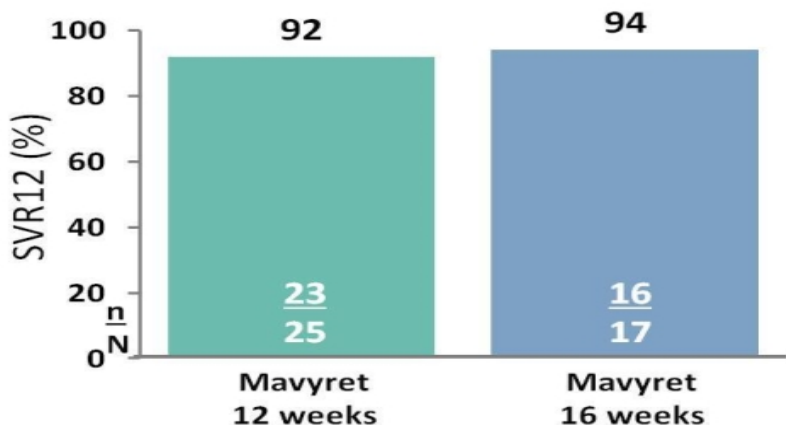
TN, treatment-naïve; TE, treatment-experienced with IFN or pegIFN ± RBV, or SOF + RBV ± pegIFN; NC, non-cirrhotic; CC, compensated cirrhotic; ITT, intent-to-treat; BT, breakthrough; VF, virologic failure.

*Includes patients who discontinued due to adverse events, lost to follow-up, or withdrew.

MAVYRET US Prescribing Information; Accessed August 2017.

Efficacy of Mavyret in GT1 Patients who have Previously Failed an NS3/4A PI or NS5A Inhibitor Containing DAA Regimen

Mavyret for 12 or 16 Weeks in GT1 Patients with Prior NS3/4A PI or NS5A Inhibitor Failure: MAGELLAN-1



G/P is not indicated for patients experienced to both NS5A inhibitors *and* NS3/4A PIs

BT	1
Relapse	
Non-VF [‡]	2

- PI-experienced (NS5A inhibitor-naïve)*
- NS5A inhibitor-experienced (PI-naïve)[†]

All analyses are using the ITT population.

BT, breakthrough; PI, protease inhibitor; VF, virologic failure.

*Regimens containing simeprevir and sofosbuvir or simeprevir, boceprevir, or telaprevir with interferon or pegylated interferon and ribavirin.

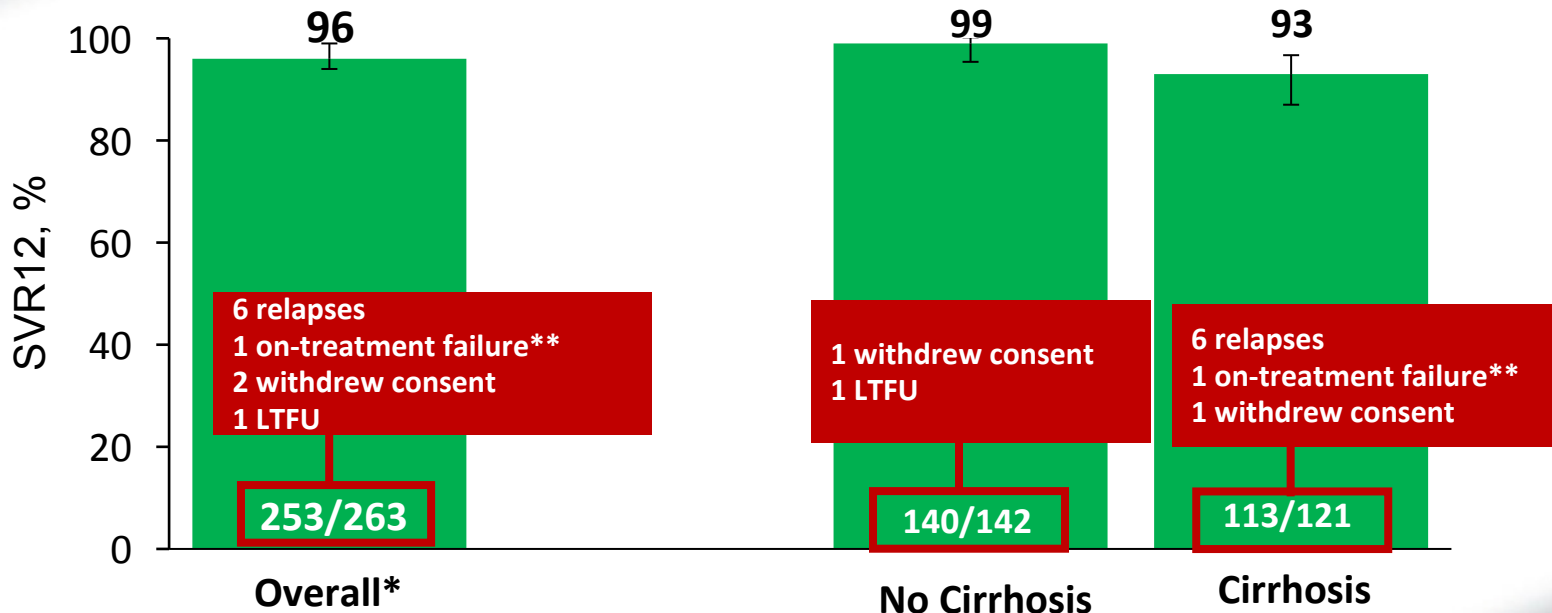
[†]Regimens containing ledipasvir and sofosbuvir or daclatasvir with pegylated interferon and ribavirin.

[‡]Includes patients who discontinued due to adverse events, lost to follow-up, or withdrew.

Sofosbuvir/Velpatasvir/Voxilaprevir Indications: DAA Treatment Experienced Patients

- Patients with genotype 1, 2, 3, 4, 5, or 6 who were **previously treated with an NS5A inhibitor**
- Patients with genotype 1a or 3 infection previously treated without an NS5A inhibitor
 - No advantage of using sofosbuvir/velpatasvir/voxilaprevir over sofosbuvir/velpatasvir for retreatment of patients with GT 1b, 2, 4, 5, or 6

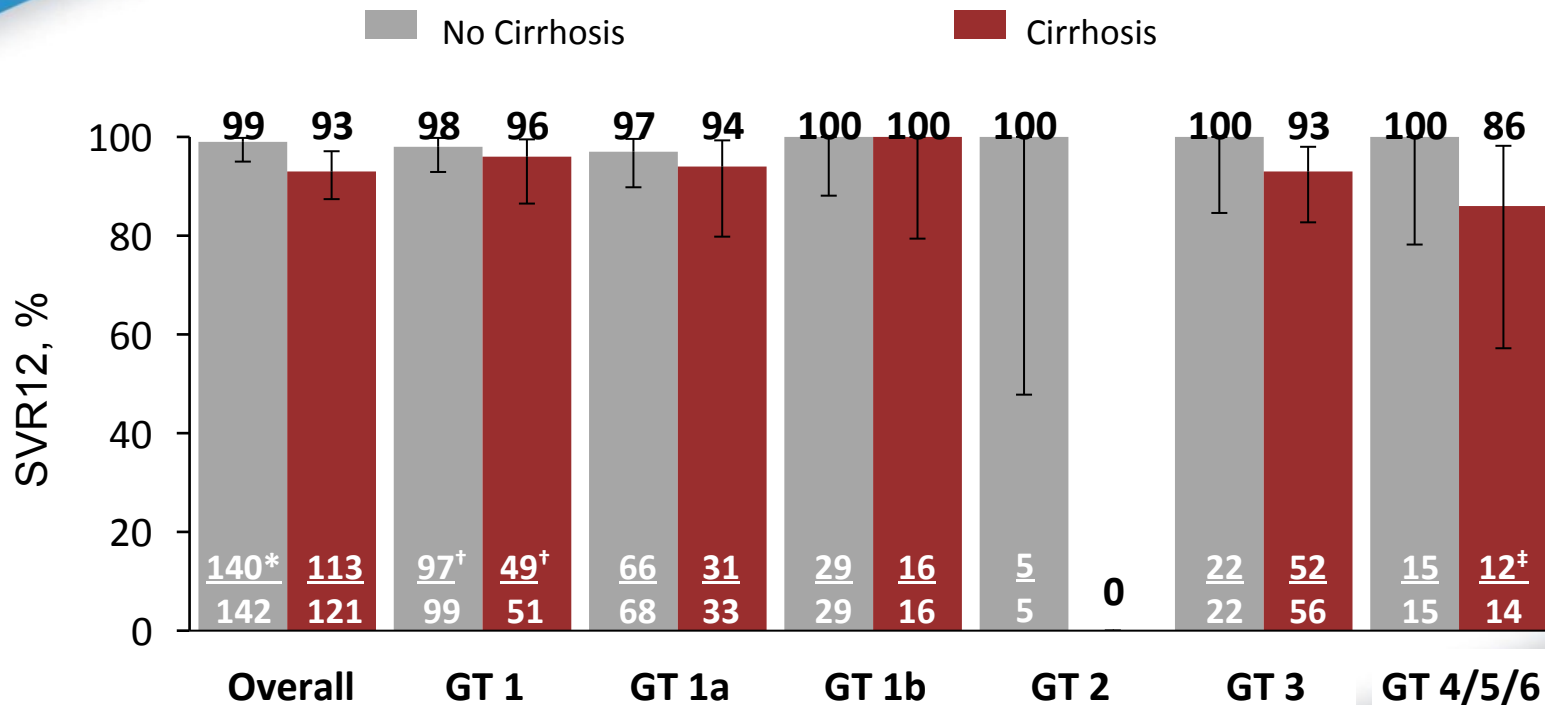
SVR12 Results Overall and by Cirrhosis Status



* $p < 0.001$ for superiority compared with prespecified 85% performance goal for SOF/VEL/VOX

** Exposure was consistent with non-adherence

SVR12 by Genotype and Cirrhosis Status



*1/1 patient with GT unknown achieved SVR12; [†]4/4 patients with GT 1 other (cirrhosis, n=2; no cirrhosis, n=2) achieved SVR12; [‡]Includes only GT 4 patients.

Case Study 5: 47 yo female with HCV GT3. She previously failed daclatasvir plus sofosbuvir. What are her treatment options?

- Currently on lactulose for encephalopathy and spironolactone and furosemide for ascites
- Laboratories: albumin 3.4 mg/dL, bilirubin 1.6 mg/dL, and INR of 1.11

Case Study 6: Which of the following is an effective approach to minimize the costs of HCV therapy?

- A. Reauthorization of the therapy at week 4
- B. Require HCV RNA viral load at week 4 prior to sending refill
- C. Limit refills to 14 days to document adherence
- D. None of the above

What's the Big Deal?

- Interruptions in HCV therapy can lead to HCV resistance
- The development of resistance can compromise current treatment AND future attempts at retreatment
- Treatment interruptions compromise HCV therapy!

AASLD Guidelines Regarding HCV RNA Monitoring

“The significance of a positive HCV RNA test result at week 4 that remains positive, but lower, at week 6 or week 8 is unknown. No recommendation to stop therapy or extend therapy can be provided at this time”

HCV Therapies

HCV Class	Therapies
NS3/4A inhibitors	Simeprevir, Paritaprevir, Grazoprevir, Voxilaprevir, Glecaprevir
NS5A inhibitors	Ledipasvir, Elbasvir, Ombitasvir, Velpatasvir, Pibrentasvir Ruzasvir*
NS5B inhibitors	Sofosbuvir, Dasabuvir Uprifosbuvir*

*Investigational agents

The Project ECHO (Extension for Community Healthcare Outcomes) Model



Moving Knowledge Instead of Patients

Hepatitis C in New Mexico (2004)



- More than 35,000 reported HCV cases
- Less than 5% had been treated
- Only one academic health center treated HCV
- Highest rate of cirrhosis deaths in the nation

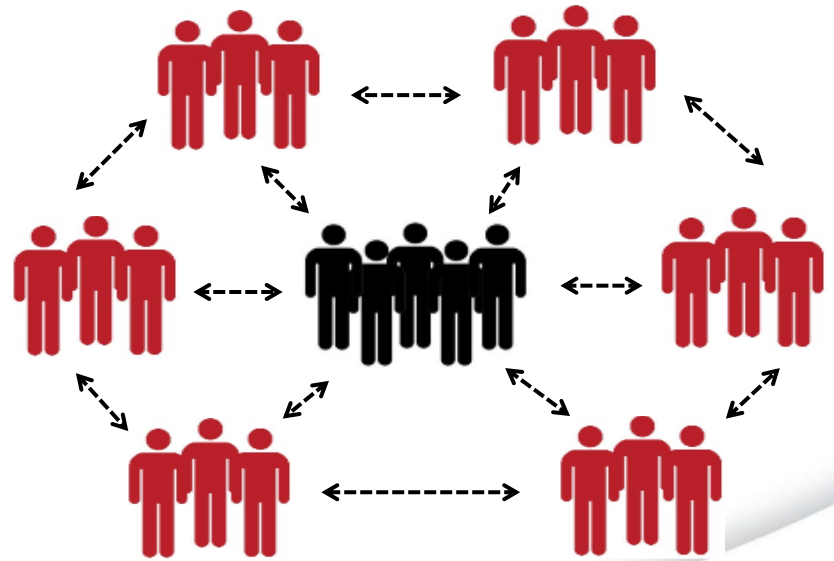
Methods

- Use technology to leverage scarce healthcare resources (specialty knowledge and expertise)
 - Train physicians, nurses, pharmacists, and their teams in HCV care
- Share best practices- reduce variation in care
 - Conduct teleECHO clinics- “Knowledge Network”
- Case based learning (learning by doing)
 - Initiate case-based guided practice- “Learning Loops”
- Centralized database to monitor outcomes
 - Collect data and monitor outcomes centrally



Learning Loops

- Interactive Learning Environment
- Co-management of Cases
- Learning by doing
- Learning from didactics
- Learning from each other
- Collaborative Problem Solving
- ACPE continuing education credits for pharmacists



ECHO vs. Telemedicine



Traditional
Telemedicine



Specialist Manages Patient Remotely



ECHO and Indian Health Services



- >70 sessions
- >130 new patient cases
- Predominantly pharmacists managing HCV patients

Pharmacists' Roles

Ambulatory Care	Inpatient	Community/Specialty
Screening and referrals	Screening + linkage to care	Screening + linkage to care
Medication selection	Prevent interruption of treatment	Verify medication selection and length of treatment
DDI screening, management	DDI screening, management	DDI screening, management
Education	Education – adherence, administration, ADRs	Education – adherence, administration, ADRs
Liaison with pharmacy and assistance programs	Liaison with clinic	Liaison with clinic and assistance programs
Labs and follow-up	Labs	Refill management

Which resource offers guidance for HCV treatment selection?

- A. <https://www.clinicaloptions.com/Hepatitis.aspx>
- B. <http://www.hep-druginteractions.org/checker>
- C. <http://www.hcvguidelines.org/>
- D. <http://www.hepatitisc.uw.edu/>

Which of the following pieces of information is (are) necessary when selecting appropriate HCV treatment for a patient?

- A.** HCV genotype
- B.** HCV treatment history
- C.** Stage of disease (presence / absence of cirrhosis)
- D.** Concurrent medications

Which of the following is (are) an all-oral, pangenotypic, single tablet regimen(s) currently approved by the FDA for the treatment of adults with genotypes 1-6 chronic HCV infection?

- A.** Elbasvir/grazoprevir
- B.** Glecaprevir/pibrentasvir
- C.** Sofosbuvir/velpatasvir/voxilaprevir
- D.** Paritaprevir/ritonavir/ombitasvir/dasabuvir

Glecaprevir/pibrentasvir offers an 8-week treatment course for treatment-naïve, non-cirrhotic patients with any HCV genotype.

- A. True
- B. False

Key Takeaways

- Medication errors and drug interactions may occur in those patients taking HCV pharmacotherapy
 - Determining risk factors for your population will permit identification and prevention
- Maintaining current knowledge in HCV pharmacotherapy will permit optimal care of patients in all practice settings
 - Development of inservices, medication charts, pocket guides will facilitate accurate review of regimens

Q&A

HCV Resources for Patients and Providers

HCV Guidelines

- American Association for the Study of Liver Diseases, Infectious Disease Society of America, and International Antiviral Society-USA: www.hcvguidelines.org

Drug-Drug Interactions

- University of Liverpool: www.hep-druginteractions.org

HCV Clinical Information

- Clinical Care Options: www.clinicaloptions.com/Hepatitis.aspx
- National AIDS Treatment Advocacy Project: www.natap.org
- ViralEd: www.viraled.com

Online Courses / Certificate Programs

- National Association of Specialty Pharmacy:
<http://education.nasprx.org/products/1204/hepatitis-c-certificate-program>
- University of Washington: <http://hepatitisc.uw.edu>

Free Online Hepatitis Textbook

- inPractice Hepatology: www.inpractice.com/Textbooks/Hepatology.aspx

Patient Support Groups

- American Liver Foundation: www.liverfoundation.org/support
- HCV Advocate: <http://hcvadvocate.org/resources/support-groups>
- HCV Support: www.hcvsupport.org