

Appointments and Disclosures

- Clinical Pharmacist
 - Bobby and Marvin Fink Family Liver Clinic
 - University of Illinois Hospital and Health Sciences System
- Clinical Assistant Professor
 University of Illinois at Chicago College of Pharmacy
- I have no financial conflicts of interest related to the content of this presentation.

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• The live presentation will include additional slides

Learning Objectives

- 1) Choose a medication regimen for treatment of hepatitis C virus (HCV) for genotypes 1, 2, and 3
- Recognize the role of the pharmacist in HCV management
- 3) Discuss the HCV agents in late-stage development
- 4) Calculate the costs of HCV treatment regimens

Why is HCV a "Hot Topic" Now?

- Updated screening recommendations / increased awareness
- More people have HCV than HIV in the US
- Since 2006 in the US, more people die from HCV than HIV annually
- Aging baby boomers / disease progression
- Expensive medications!

Ann Intern Med. 2013

Screening Recommendations

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- Patients with a high risk of HCV infection
- Current guidelines recommend that everyone born between 1945 and 1965 get tested for HCV once, <u>regardless</u> of risk factors
 - The CDC updated its guidelines in August 2012
 - The USPSTF updated its guidelines (Grade B) in June 2013
 - AASLD / IDSA / IAS-USA updated their guidelines (Class 1 Level B) in January 2014

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- CMS updated its guidelines June 2014

ttp://www.uspreventiveservicestasl ttp://www.hcvguidelines.org/



- 67 subtypes (denoted a, b, etc)

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- Genotypes 1a and 1b most common; ~75% in US:
- Genotypes 2 and 3 account for ~20-25% in US

McHutchison JG, et al. Am J Manag Care. 2005 Smith DB, et al. Hepatology. 2014.





















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Clinical Pharmacist's Role: Interaction with Internal Specialty Pharmacy

- Sends all HCV prescriptions to institution's Specialty Pharmacy
- Coordinates with Specialty Pharmacy for medication benefits review and approval

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- · Acts as a medication acquisition liaison
- Sends HCV prescriptions to outside pharmacies if necessary

Clinical Pharmacist's Role: Interaction with Patients

- Once medication is approved, coordinates treatment initiation visit
- Conducts HCV education and treatment initiation visit
- Orders labs and follow-up clinic visits for entire course of HCV treatment
- Serves as direct phone contact for patients on HCV treatment

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- Holds patient education classes
- Administers vaccinations







LDV / SOF

- Regimen: fixed dose combination (FDC) of NS5A LDV 90mg / NS5B SOF 400mg; 1 tablet daily
- Gilead submitted NDA: 2/10/2014
- Prescription Drug User Fee Act (PDUFA) date: 10/10/2014

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Study	Characteristics (N)	Regimen	SVR	Discontinuations (D/C's) / Relapses / Breakthrough (BT)
ION-1	N-1 GT 1 TN (865), included pts with compensated cirrhosis (136/865)	LDV/SOF +RBV 12 wks (217)	97%	0 D/C's / 0 relapse / 0 BT
		LDV/SOF 12 wks (214)	99%	0 D/C's / 1 relapse (NS5A mutation) / 0 BT
		LDV/SOF +RBV 24 wks (217)	99%	6 D/C's / 0 relapse / 0 BT
		LDV/SOF 24 wks (217)	98%	4 D/C's / 1 relapse (NS5A mutation)/ 1 BT (non-adherent)
			94-100% in cirrhotics	

	LDV/SOF – ION Trials							
Study	Characteristics (N)	Regimen	SVR	D/C's / Relapses / BT				
ION-2	GT1 TE (with PI) (440), included 20	LDV/SOF +RBV 12 wks (111)	96% 82% in cirrhotics	0 D/C's due to ADRs / 4 (4%) relapses / 0 BT				
	cirrhotic pts per arm (80/440)	LDV/SOF 12 wks (109)	94% 86% in cirrhotics	0 D/C's / 7 (6%) relapses / 0 BT				
		LDV/SOF +RBV 24 wks (111)	99%	0 D/C's / 0 relapses / 1 BT				
		LDV/SOF 24 wks (109)	99%	0 D/C's / 0 Relapses / 0 BT				
Afdhal N, Rec	ddy R, et al. N Engl J Med.	overall	Ave 98% without cirrhosis and 92% with cirrhosis					
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DCV and ASV

- NS5A inhibitor daclatasvir (DCV) 60mg daily + NS3 PI asunaprevir (ASV) 100mg BID for 24 weeks → GT 1b
- Daclatasvir in combination with other DAAs to treat other GTs (ex. DCV and SOF)
- Bristol-Myers Squibb submitted NDA 4/7/2014; given "breakthrough therapy designation"

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• PDUFA date: 11/30/2014

DCV and ASV

- 2 phase III trials
- Other ongoing phase III trials:
 - ALLY 1 and 2 (DCV + SOF + RBV x 12 wks): cirrhotic pre- and posttransplant patients GT 1-6
 - ALLY 2 (DCV + SOF): TN and TE non-cirrhotic HIV/HCV co-infected patients, GT 1-6
 - UNITY 1 (DCV + ASV + BMS 791325 x 12 wks): TN, TE non-cirrhotic GT 1
 - UNITY 2 (DCV + ASV + BMS 791325 + RBV x 12 wks): TN cirrhotic GT 1
 - UNITY 3 (2D or 3D x 12 or 24 wks): TN non-cirrhotics in Japan; GT 1b
- DDIs: PI: CYP3A4 interactions
- Common ADRs: increased ALT and AST, headache, diarrhea, nausea, nasopharyngitis, and pyrexia
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Study	Characteristics (N)	Regimen	SVR	D/C's / Relapses / BT
Kumada GT 1b TE in et al Japan; include compensated cirrhotic s	GT 1b TE in Japan; included compensated cirrhotic s	DCV + ASV 24 wks; IFN-ineligible (135)	87.4%; 90.9% cirrhotics	9 D/C's / 11 relapses / 4 BT (+2 failures)
	(22/223)	DCV + ASV 24 wks; non- responders (87)	80.5%; 90.9% cirrhotics	2 D/C's / 6 relapses / 10 BT (+1 failure)
			Ave 84.7%	

DCV and ASV – HALLMARK-DUAL

Study Cha (N)	aracteristics	Regimen	SVR24	D/C's / Relapses / BT
HALL GT MARK TE - inc	HALL GT 1b TN and MARK TE (745); included DUAL cirrhotics (223/745)	DCV + ASV 24 wks TN (203)	90%	6 (3%) D/C's / 5 (3%) relapses / 9 (4%) BT
DUAL cirr		Placebo TN (102)	were treated after study	
(22		DCV + ASV 24 wks TE nonresponders (205) 31% cirrhotic	82%	2 (1%) D/C's / 7 (4%) relapses / 26 (13%) BT
		DCV + ASV 24 wks TE IFN- intolerant /ineligible (235) 47% cirrhotic	82%	2 (1%) D/C's / 12 (6%) relapses / 20 (9%) BT
lanns M, et al. I	Lancet. 2014		85% non-cirrhotic, 83% cirrhotic (ave)	

ABT-450/r + Ombitasvir+ Dasabuvir

- 3D regimen components \rightarrow GT 1
 - fixed-dose combination of the PI ABT-450 100mg/ritonavir 100mg with the NS5A inhibitor ombitasvir (ABT-267) 25mg daily, + NS5B dasabuvir (ABT-333) 250mg BID, +/- RBV x 12 wks

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- AbbVie submitted NDA 4/21/2014; given "breakthrough therapy designation"
- PDUFA date: 12/21/2014

ABT-450/r + Ombitasvir+ Dasabuvir

- 6 Phase III studies (>2,300 patients)
- Ongoing/future study populations: GT 2, GT3, CKD, HIV, post-transplant
- Most common ADRs: fatigue, headache, pruritis, nausea

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• DDIs: PI: CYP3A4 interactions

ABT-450/r + Ombitasvir+ Dasabuvir – Phase III Trials									
Trial	Characteristics (N)	Regimen	SVR	D/C's / Relapses / BT					
PEARL-II	GT 1b, TE (186) non-cirrhotic	3D +RBV (95) 12 wks	96.6%	2 (2.2%)D/C's / 0 relapse / 0 BT (1 lost to follow up)					
		3D (91) 12 wks	100%	0 D/C / 0 relapse / 0 BT					
PEARL- III	GT 1b, TN (419) non-cirrhotic	3D +RBV (210) 12 wks	99.5%	0 D/C's / 0 relapses / 1 BT					
		3D (209) 12 wks	99%	0 D/C's / 0 relapses / 0 BT					
PEARL- IV	GT 1a, TN (305) non-cirrhotic	3D +RBV (100) 12 wks	97%	0 D/C's / 1 (1%) relapse / 1 BT (1%)					
3D (205) 90.2% 3 D/C / 10 (5.2%) relapses / dreane P. et al. Gastroenterology. 2014 12 Wks 6 BT (2.9%)									
enci P, et al. 1	NEngl J Med. 2014. Illinois Council of H	lealth-System Pha	rmacists 2	014 Annual Meeting					

ABT-450/r + Ombitasvir+ Dasabuvir – Phase III Trials						
Trial	Characteristics (N)	Regimen	SVR	D/C's / Relapses / BT		
SAPPHIRE -I	GT1, TN (631) non-cirrhotic	3D + RBV (473) 12 wks	96.2% (95.3% GT 1a, 98% GT1b)	3 (0.6%) D/C's / 7 (1.5%) relapses / 1 BT		
		placebo (158) 12 wks	Were offered treatment later	1 (0.6%) D/C / N/A / N/A		
SAPPHIRE -II	GT1, TE (394) non-cirrhotic	3D + RBV (297) 12 wks	96.3% (96% GT 1a, 96.7% GT1b)	3 (1%) D/C 's / 7 relapses (4 stopped tx early) / 0 BT		
		placebo (97) 12 wks	Were offered treatment later			
JJ, et al. N En em S, et al. N	gl J Med. 2014. Engl J Med. 2014.					
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ABT-450/r + Ombitasvir+ Dasabuvir – Phase III Trials							
	Trial	Characteristics (N)	Regimen	SVR	D/C's / Relapses / BT		
	TURQUOISE -II	GT1 TN and TE with compensated cirrhosis (380)	3D+RBV for 12 weeks (208)	91.8% (TN: 92.2% GT 1a, 100% GT 1b)	4 (1.9%) D/Cs / 12 (5.9%) relapses / 1 BT		
			3D+RBV 24 weeks (172)	95.9% (TN: 92.9% GT 1a, 100% GT 1b)	4 (2.3%) D/Cs / 1 (0.6%) relapse / 3 BT		
or	dad F, et al. N E	ngl J Med. 2014.					
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The Future of HCV Treatment

- All-oral therapy (elimination of PegIFN) for all genotype
- Combination DAAs
- Shortened treatment duration
- Simpler regimens
- Preventing relapses
- Addressing viral resistance / previous DAA failures

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Current Cost of HCV Meds (as of 7/16/14)							
Medication	Cost per 4 weeks	Cost per 12 weeks	Cost per 24 weeks				
PegIFN2a	\$ 3,569.73	\$10,709.19	\$21,418.38				
PegIFN2b	\$ 3,905.89	\$11,717.67	\$23,435.34				
Ribavirin	\$ 1,255.60	\$3,766.80	\$7,533.60				
Simeprevir	\$ 23,894.20	\$71,682.6	Not applicable				
Sofosbuvir	\$ 30,244.60	\$90,733.80	\$181,467.60				
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Cost	Cost of HCV Treatment Courses						
(GT 1, 2, 3)							
Regimen	Cost per 4 weeks	Cost per 12 weeks	Cost per 24 weeks				
SOF + SMV	\$54,138.80	\$162,416.40 (GT 1)	Not applicable				
SOF + SMV + RBV	\$55,394.40	\$166,183.20 (GT 1)	Not applicable				
SOF + PegIFN2a / 2b + RBV	\$35,069.93 / \$35,406.09	\$105,209.79 / \$106,218.27 (GT 1,2,3)	SOF x 12; PegIFN + RBV x 24 = \$119,685.78 / \$121,702.74 (GT 1)				
SMV + PegIFN2a / 2b + RBV	\$28,719.53 / \$29,055.69	\$86,158.59 / \$87,167.07	SMV x 12; PegIFN + RBV x 24 = \$100,634.58 / \$102,651.54 (GT 1)				
SOF + RBV	\$31,500.20	\$94,500.60 (GT 2)	\$189,001.20 (GT 1,3)				

Co	Cost Analysis of SOF + SMV versus SOF + RBV for GT 1							
Regimen	Cost of Rxs / SVR rates	Base Case Cost	QALYs	Cost / QALY	Cost / SVR	Cost Savings per SVR with SMV + SOF		
SMV + SOF	~\$150,000 / 52 - 84%	\$165,336	14.69	\$11,255	\$170,456	\$91,590		
SOF + RBV	~\$169,000 / 89 - 100%	\$243,586	14.45	\$16,857	\$262,046			
Hagen LM, et al.	oen LM. et al. Heeatoloov. 2014.							
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How do Payors Handle High Cost of HCV Treatment?

- Prioritization of patients for treatment
 - IL Medicaid imposes strict guidelines on coverage for HCV medication
 - Medicaid Managed Care and Cook County also have strict criteria for use of HCV medications
- Some insurance plans cover only one course of HCV treatment

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• Want to prevent treatment failure and encourage successful treatment



Summary

- HCV is a major public health concern
- HCV treatment is advancing rapidly; 6 more DAA approvals are anticipated in 2014 Q4
- Future developments include additional oral DAA agents, with the goal of IFN-free treatment for all genotypes, and shorter treatment duration
- Pharmacists have an important role in educating patients and providers about HCV medications and appropriate timing of treatment

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Cost and DDIs will continue to complicate HCV treatment

Going Viral! Hepatitis C Treatment in the Age of Direct-Acting Antivirals

> Michelle T. Martin, PharmD, BCPS, BCACP

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Panelists

- Payor Perspective: Mary Lynn Moody from UIC
- Specialty Pharmacy: Phoebe Sebhatu from Rush Specialty Pharmacy
- Inpatient Pharmacy: Hannah Brooks from Northwestern
- Clinic Perspective: Michelle Martin from UIC

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Payor Considerations

Mary Lynn Moody, BSPharm Manager, Medicaid 4 Prescription Policy Clinical Associate Professor University of Illinois at Chicago The speaker has no conflict of interest to disclose.





Oregon Medicaid Criteria August 2014

- Only for patients with later stages of liver damage
- Drug-free for at least six months
- Prescribed by a liver or gastrointestinal specialist
- Often requires months of waiting for an appointment

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Key Illinois Medicaid Criteria July 2014

- Only for Patients with Metavir score of 4
- Drug and alcohol-free for 12 months
- Only FDA approved regimens
- Patients who are Genotype 1, not considered interferon-ineligible

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 The patient has no history of a full or incomplete course of Sovaldi treatment ("Once in a lifetime" treatment policy)

Key Illinois Medicaid Criteria July 2014

- Non-compliance will result in discontinuation of previous prior approval
- Sovaldi will be dispensed as 2 weeks supply
- Any MD may prescribe. If the prescriber is NOT a board-certified gastroenterologist, transplant hepatologist or infectious disease specialist, a one-time written consultation report from a specialist required.
- Requests will not be accepted from mid-level practitioners and pharmacies

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Specialty Pharmacy Considerations

Phoebe Sebhatu, PharmD Clinical Pharmacy Specialist Rush University Medical Center The speaker has no conflict of interest to disclose.

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Formulary Considerations

Hannah Brooks, PharmD, BCPS Northwestern Medicine The speaker has no conflict of interest to disclose.

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Northwestern Medicine: Hepatitis C Clinical Services

- Developed and implemented program for treatment
 - pre and post transplant
- Established HCV Treatment Protocol
- Pharmacy completes Prior Authorization process
- Pharmacist provides face-to-face in clinic or phone initiation education
- Monthly phone call follow up and monitoring

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Hepatitis C Clinical Services Outcomes

- More than 70 patients started treatment
- Assisted in starting treatment for 126 patients:
 - 27 completed treatment course
 - End of therapy cure rate = 96% (26/27)
 - 66 currently on treatment
 - 33 pending start of treatment/ approval

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Inpatient Formulary Process: Sofosbuvir and Simeprevir

- April 2014 P&T Committee
- · Simeprevir/Sofosbuvir added to the formulary
- Approved as CONTINUATION of outpatient therapy only
- Utilize patient's own medication supply
- NMH Pharmacy does NOT stock Simeprevir or Sofosbuvir

Panelist Discussion Question and Answer Session

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Going Viral! Hepatitis C Treatment in the Age of Direct-Acting Antivirals ICHP Annual Meeting September 12, 2014 Michelle T. Martin, PharmD, BCPS, BCACP

Self-Assessment Questions

1. A non-cirrhotic patient with HCV genotype 1a failed treatment with PegIFN and RBV

in 2006-2007. Which one of the following regimens is best to recommend for this patient

for retreatment per the AASLD guidelines?

- A. SOF + PegIFN + RBV for 12 weeks
- B. SMV + PegIFN + RBV for 24 weeks
- C. SOF + SMV for 12 weeks
- D. SOF + RBV for 24 weeks

2. A 47-year-old woman with HCV genotype 2 presents to her physician. She has cirrhosis and has not been treated for HCV in the past. Which treatment regimen is best for this patient?

- A. SOF + PegIFN + RBV for 12 weeks
- B. SMV + PegIFN + RBV for 24 weeks
- C. SOF + SMV for 12 weeks
- D. SOF + RBV for 12 weeks

3. A 42-year-old treatment naïve, non-cirrhotic HCV/HIV coinfected patient presents to liver clinic for HCV treatment evaluation. The patient's HIV regimen consists of atazanavir (Reyataz) 300 mg QHS, ritonavir 100 mg daily, and emtricitabine-tenofovir (Truvada) 200 mg-300 mg tablet daily. He is also well controlled on sertraline 25 mg daily, levetiracetam 500 mg twice daily, and sildenafil 25 mg prn. Assuming all treatment regimens are FDA-approved and available, which one of the following regimens is best to recommend for this patient's HCV GT 1a treatment?

- A. SOF + PegIFN + RBV for 12 weeks
- B. SOF + SMV for 12 weeks
- C. ABT-450/r + Ombitasvir + Dasabuvir + RBV for 12 weeks
- D. DCV + ASV for 24 weeks

4. Which of the following treatment regimens is only pursuing FDA approval for HCV genotype 1b?

- A. ABT-450/r + Ombitasvir + Dasabuvir + RBV for 12 weeks
- B. DCV + ASV for 24 weeks
- C. SOF + LDV for 12 weeks
- D. SOF + SMV for 12 weeks

5. Which of the following best describes the role of an ambulatory care pharmacist in

HCV treatment?

- A. Educating providers and patients, and acting as a liaison with specialty pharmacies in order to facilitate HCV treatment.
- B. Performing benefit verification
- C. Dispensing HCV treatment
- D. Participating in research

6. As of July 2014, In order to limit funds spent on HCV treatment, Illinois Medicaid is restricting HCV treatment coverage to only cover which patient population?

- A. Pre-transplant patients
- B. Post-transplant patients
- C. Patients that have cirrhosis
- D. Patients with hepatocellular carcinoma
- 7. Which HCV treatment regimen is most costly?
 - A. SOF + PegIFN + RBV for 12 weeks
 - B. SMV + PegIFN + RBV for 24 weeks
 - C. SOF + SMV for 12 weeks
 - D. SOF + RBV for 24 weeks

Answer Key: 1. C; 2. D; 3. A; 4. B; 5. A; 6. C; 7. D

Going Viral! Hepatitis C Treatment in the Age of Direct-Acting Antivirals ICHP Annual Meeting September 12, 2014 Michelle T. Martin, PharmD, BCPS, BCACP

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