Managing Hepatitis C and Diabetes: The Impact of a Cure

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Disclosure Declaration

I do not have (nor does any immediate family member have) a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation.

Objectives

Pharmacists and Technicians

1. Identify risk factors for hepatitis C virus (HCV) exposure and the two-way association
2. Summarize the evidence and recommendations surrounding the co-management of HCV and diabetes
3. Recognize and be aware of potential drug interactions and contraindications for patients with HCV and diabetes

Outline

Pathophysiology and complications of HCV and diabetes

Overlapping risk factors

Current literature and research
- Effects of HCV on diabetes
- Impact of the cure

Recommendations and management
- Scenarios that could affect treatment

Pharmacotherapy and risk factors for drug-drug interactions

Question 1

_____ have increased risk of hepatocellular carcinoma.

A. GLP1s

B. Sulfonylureas

C. DPP4s

D. DAAs

Question 2

The hepatitis C virus has been shown to infect the _____

A. Kidney

B. Gallbladder

C. Pancreas

D. Brain

Question 3

Insulin resistance in hepatitis C only affects patients with diabetes

A. True

B. False

Viral Hepatitis

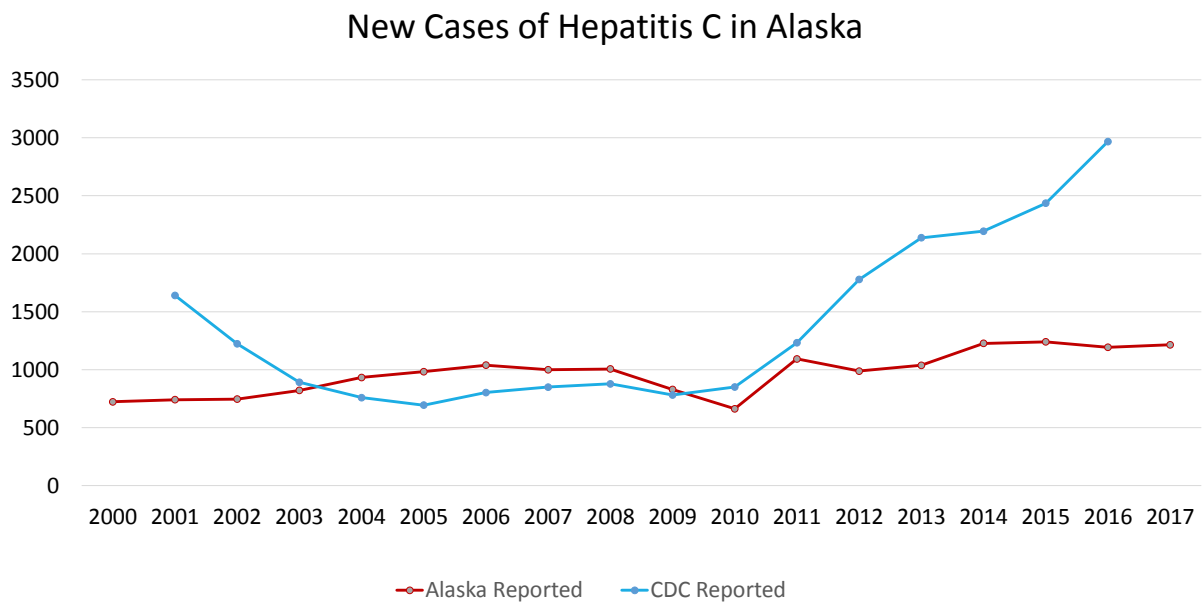
	Hepatitis A	Hepatitis B	Hepatitis C
Route of transmission	Fecal-oral	Bodily fluids	Bodily fluids
Acute/Chronic	Acute	Chronic	Chronic
Re-infection	No	Yes	Yes
Vaccine?	Yes	Yes	No
New cases in 2014	2,500	19,200	30,500
Total infections	-	850,000 – 2 million	2.7 – 4 million
Potential for Chronic Infection	No	Yes	Yes

"The ABCs of Hepatitis" CDC, 2016

Hepatitis C

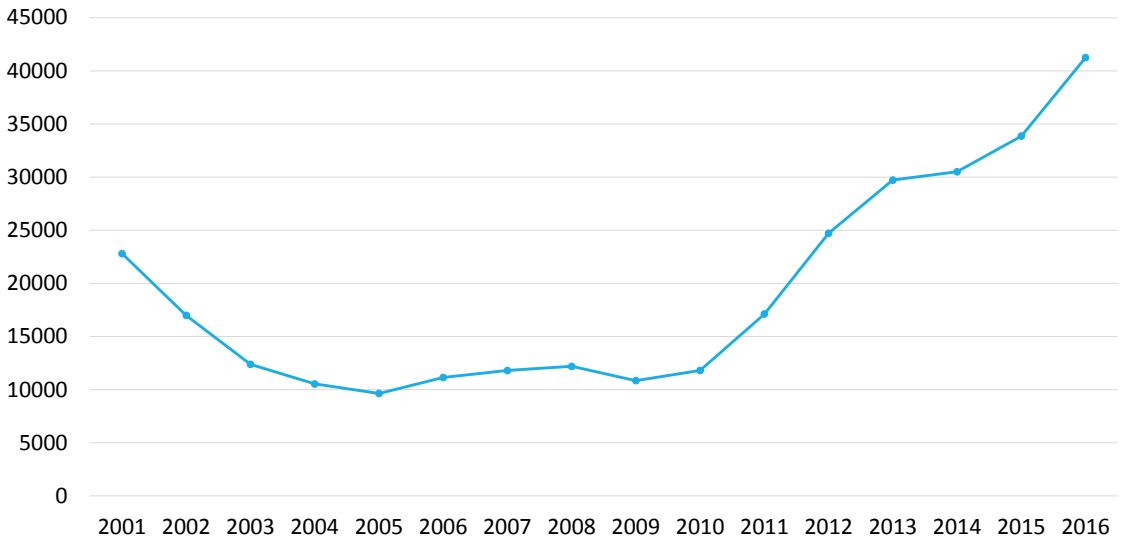
- Most common infectious disease in the world
- Leading cause of hepatocellular carcinoma and liver transplantation
- Largely undiagnosed due to lack of symptoms
- 1945-1965 birth years
  - Make up 27% of US population but 75% of all HCV infections
- Changes in demographics

Sebastiani, G., Chronic hepatitis C and liver fibrosis. *World Journal of Gastroenterology*, *2014*.



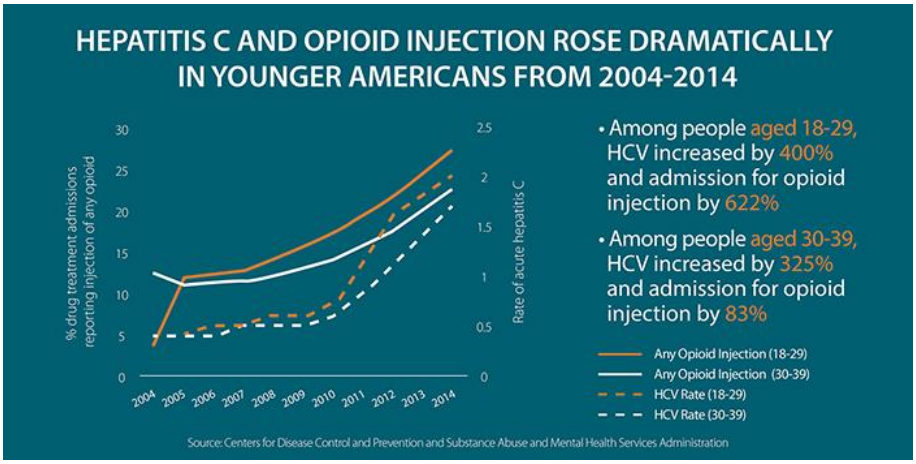
Centers for Disease Control
Alaska Department of Health and Human Services

CDC Estimated New Cases of HCV



Centers for Disease Control

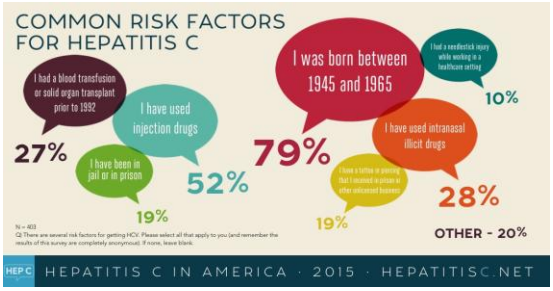
Behind the Data



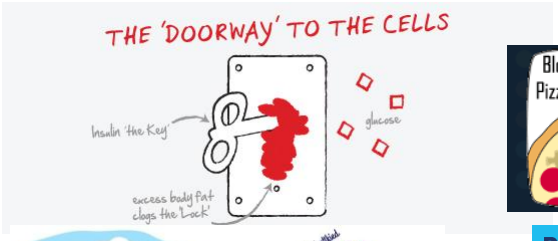
Jon E. Zibbell et al. American Journal of Public Health, 2018

Risk Factors for Hepatitis C

- IV drug misuse
- Born between 1945 – 1965
- Blood transfusions and hemodialysis
  - Before 1992
- Known exposures to HCV
  - Health care workers
- HIV infection
- Children born to HCV infected mothers
- Incarceration
- Intranasal drug misuse
- Body piercing or tattoos done with non-sterile instruments/ink



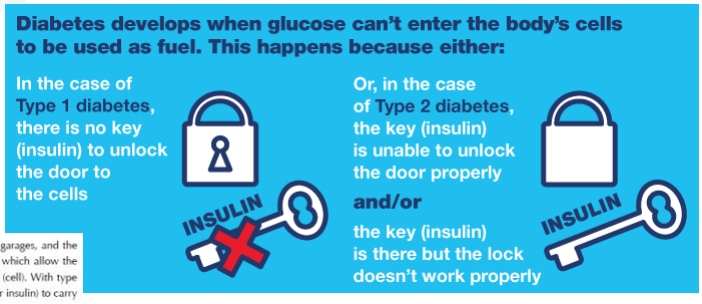
Diabetes



"I often say managing type 1 diabetes is like flying a plane. A plane is off-course most of the time and the pilot checks his instruments to bring it back on course. That's type 1 diabetes."

Your pancreas makes the hormone, insulin, and releases it into your blood.

Put differently, think of the blood vessels as streets, the cells as garages, and the glucose as cars that travel on the street. Insulin acts as the driveways, which allow the cars (glucose) to leave the street (blood vessels) and go into the garage (cell). With type I, the cars (glucose) stay on the street because there are no driveways (or insulin) to carry the glucose into the cell (garage).



Diabetes Data

	Alaska	US
Prevalence	7.3	9.4
Incidence	6.0	7.9
High Blood Pressure	75.9	62.4
High Cholesterol	68.0	60.8
Activities of Daily Living	13.9	16.7
Coronary Heart Disease	10.7	17.2
Hospitalization*		
CHF	6.4	9.5
Stroke	5.4	6.0
Heart Attack	5.0	5.6
Amputations	3.9	3.4
Total Cost	865.5 million	42.2 billion
Years of Life Lost	4.7 years	4.4

Centers for Disease Control Diabetes State Burden Toolkit

Risk Factors for Diabetes

- Age
- Sex
- Gestational diabetes
- Family history
- Hypertension
- Sedentary lifestyle
- Obesity

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Risk Factors for Hepatitis C

- IV drug abuse
- Born between 1945 – 1965
- Blood transfusions and hemodialysis
- Health care workers
- HIV infection
- Children born to HCV infected mothers
- Incarceration
- Intranasal drug abuse
- Tattoos and piercings with unsterile tools

How Diabetes and Hepatitis C are Related

HCV positive patients are 2-3 times as likely to have diabetes

- Risk increases with length of infection and cirrhosis
- Regardless of other factors
  - BMI
  - Age
  - HBV
  - Liver diseases

The reverse is also true

- Increased prevalence of HCV in patients with diabetes compared to rest of population
- Patients with diabetes had poorer HCV outcomes

White et. al. Journal of Hepatology 2009
Hammerstad et. al. Frontiers of Endocrinology 2015

How Diabetes and Hepatitis C are Related

A Southeast Asian Study

- Differences between diabetic and non-diabetic patients with HCV
  - BMI was not statistically different between the two
  - Patients with diabetes were twice as likely to be cirrhotic (OR: 2.05, CI: 1.15-3.43)
  - Age, fasting blood sugar, cholesterol and renal function were different
- Limitations:
  - Size (361 patients), single center, external validity

Memon et. al. Journal of Diabetes Research, *2013*

How Diabetes and Hepatitis C are Related

Large 2018 meta analysis

- 31 studies
- Diabetes was increased in patients with chronic hepatitis C and cirrhotic hepatitis C
- Risk was also increased in cirrhotic patients
- "On the whole the results show an unequivocal association of HCV chronic infection and T2DM."

Fabiani et. al. Reviews in Endocrine and Metabolic Disorders, 2018

The Two Way Association

Same meta analysis

- The prevalence of HCV infection in diabetic patients is higher than in non-diabetic
- Diabetes seems to have an impact on hepatocellular carcinoma (HCC) development

The prevalence of T2D was shown to increase with every rise in the fibrosis score of HCV patients with an OR of 3.83

Hammerstad et. al. Frontiers of Endocrinology 2015

Hepatitis C Virus

RNA virus
- 10 proteins

6 genotypes multiple subtypes

Genotype matters
- Prevalence
- Outcomes
- Treatment
- Mixed infections

Acute Infection vs Chronic Infection

Acute infection – mostly asymptomatic
- Unlikely to lead to diagnosis
- 15-25% of patients can clear the disease and have undetectable virus
  - Depends on age, sex, genetic polymorphisms, and liver enzymes

Chronic infection
- Presence of HCV after 6 months
- Left untreated leads to long term liver cirrhosis and death
  - After 20 years of infection, 20% of patients will die from HCC
- Rate of progression to cirrhosis varies
  - Males, age over 50, alcohol use, coinfection and immunosuppression

Centers for Disease Control, 2018

Liver Fibrosis and Cirrhosis

As virus infects and spreads in the liver, hepatic stellate cells (HSC) are activated
- Leads to proliferation of myofibroblasts

Fibrosis
- Reversible wound healing
- Due to cell regeneration the deposition of extracellular matrix (ECM) is reduced

Progression of fibrosis to cirrhosis
- Increasing damage leads to disruption in the equilibrium between deposition and dissolution of ECM proteins

Insulin Resistance in Hepatitis C

Insulin resistance is significantly increased in patients with HCV

Prospective case–control study of 133 patients with advanced liver fibrosis (F3–F4) without type 2 diabetes

At baseline patients had similar liver fibrosis levels

Homeostatic model assessment for insulin resistance

Pretreatment HOMA-IR was 4.90 ± 4.62

Post-treatment HOMA-IR was 2.38 ± 1.642
- $p<0.0001$

Adinolfi et. al. Journal of Gastroenterology and Hepatology, 2017

However, the Exact Mechanism is Unknown

Increase in reactive oxygen species

- NS3 and NS5, in particular, were shown to trigger oxidative stress responses.
- leads to the release of an array of cytokines, including TNFα, TGFβ, IL-6, and IL-8.

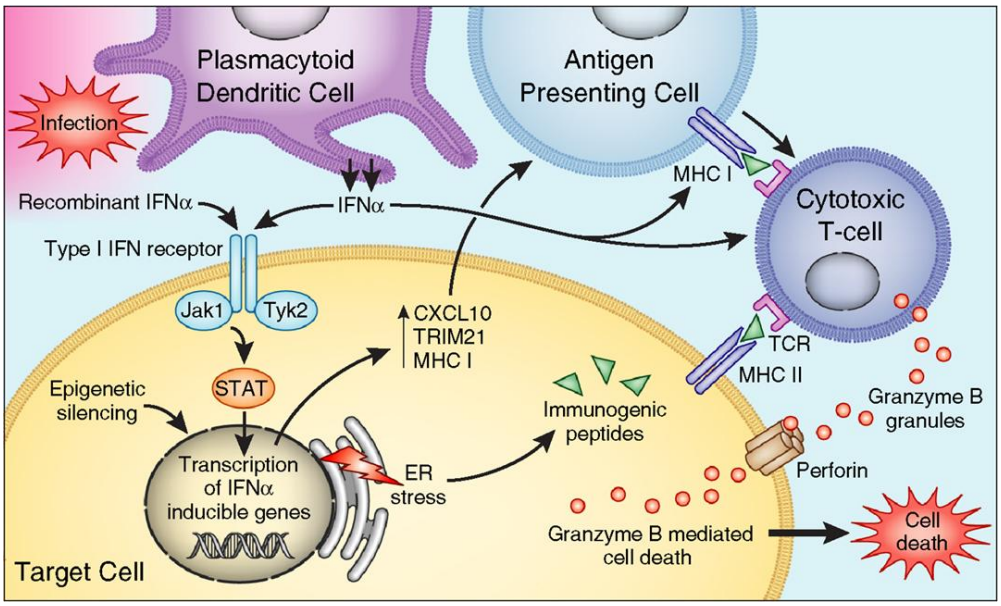
TNF-α and other inflammatory cytokines

- Higher serum TNFα in diabetic HCV patients than in non-diabetic HCV patients (74 vs 64%; p-value <0.0001)

Beta cell dysfunction

- Pancreatic β-cells are infected with HCV and have morphological and functional defects, including a blunted insulin response to glucose

Hammerstad et. al. Frontiers of Endocrinology 2015



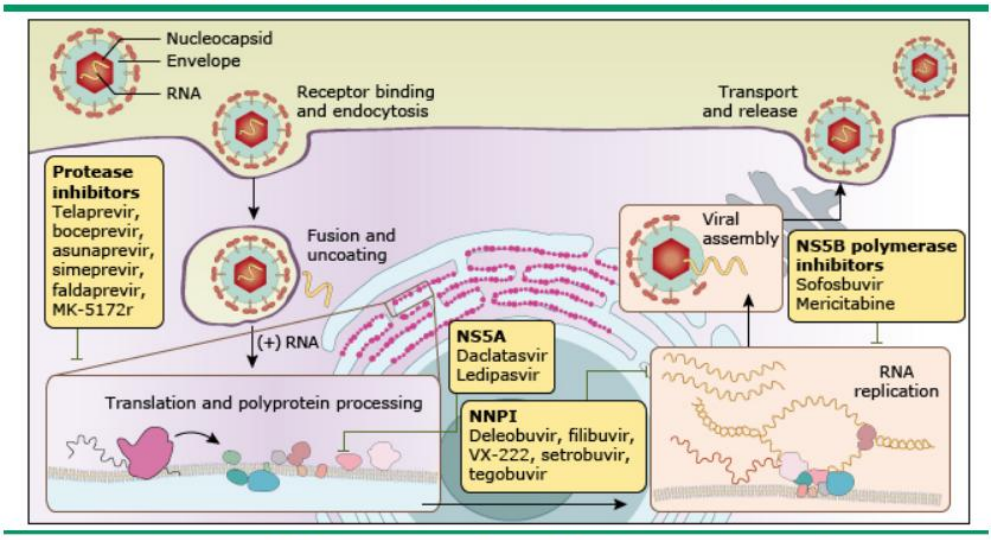
Hammerstad et. al. Frontiers of Endocrinology 2015

Hepatitis C Treatment

Direct Acting Antivirals (DAA)

- Highly effective
- Treatment and duration is dependent on:
  - Genotype and subtype
  - Presence of cirrhosis
  - Treatment naïve or treatment experienced
  - Race
  - Recommended drug
  - Other disease states
  - Viral load

Mechanism of action of direct acting antivirals for hepatitis C virus



NS5A: nonstructural protein 5A; NS5B: nonstructural protein 5B; NNPI: non-nucleoside polymerase inhibitor.

Au J, Pockros PJ. Novel Therapeutic Approaces for Hepatitis C. Clin Pharmacol Ther 2014; 95:78.

	Protease inhibitors	Nucleos(t)ide polymerase inhibitors	Non-nucleoside polymerase inhibitors	NS5A inhibitors
Potency	High (varies by HCV genotype)	Moderate-to-high (consistent across HCV genotypes and subtypes)	Varies by HCV genotype	High (against multiple HCV genotypes)
Barrier to resistance	Low (1a <1b)	High (1a = 1b)	Very low (1a <1b)	Low (1a <1b)
Potential for drug interactions	High	Low	Variable	Low-to-moderate
Toxicity	Rash, anemia, ↑ bilirubin	Mitochondrial toxicity, interactions with HIV antiretrovirals (nucleoside reverse transcriptase inhibitors) and ribavirin*	Variable	Variable
Dosing	Daily to three times daily	Daily to twice daily	Daily to three times daily	Daily
Comments	Later generation protease inhibitors are expected to have higher barriers to resistance and be pan-genotype	Single target for binding at the active site	Many targets for binding at allosteric sites	Multiple antiviral mechanisms of action

Outcomes in Patients with HCV and Diabetes

Overall, most studies support the notion that insulin resistance (IR) and diabetes predispose to liver fibrosis and cirrhosis.

HCV patients with diabetes had a hazard ratio of 1.73 for HCC compared to non-diabetic HCV patients

A recent meta-analysis of 14 studies showed that patients with IR treated with peg IFN–RBV had a 20% lower rate of SVR compared to patients without IR (95% CI: −29.9 to −9.4%, $p < 0.001$).

- In addition, responders had a lower HOMA-IR compared to non-responders (mean difference: −0.92, 95% CI: −1.53 to −0.32, $p < 0.001$)

Deltenre et al. Journal of Hepatology, 2011
Lai et al. American Journal of Gastroenterology, 2012

Guideline Recommendations

American Association for the Study of Liver Diseases (AASLD)

- The relationship between chronic hepatitis C and diabetes (most notably type 2 diabetes and insulin resistance) is complex and incompletely understood.
- Treatment should be initiated as early as possible to reduce insulin resistance, liver fibrosis and hepatocellular carcinoma.

American Gastroenterological Association

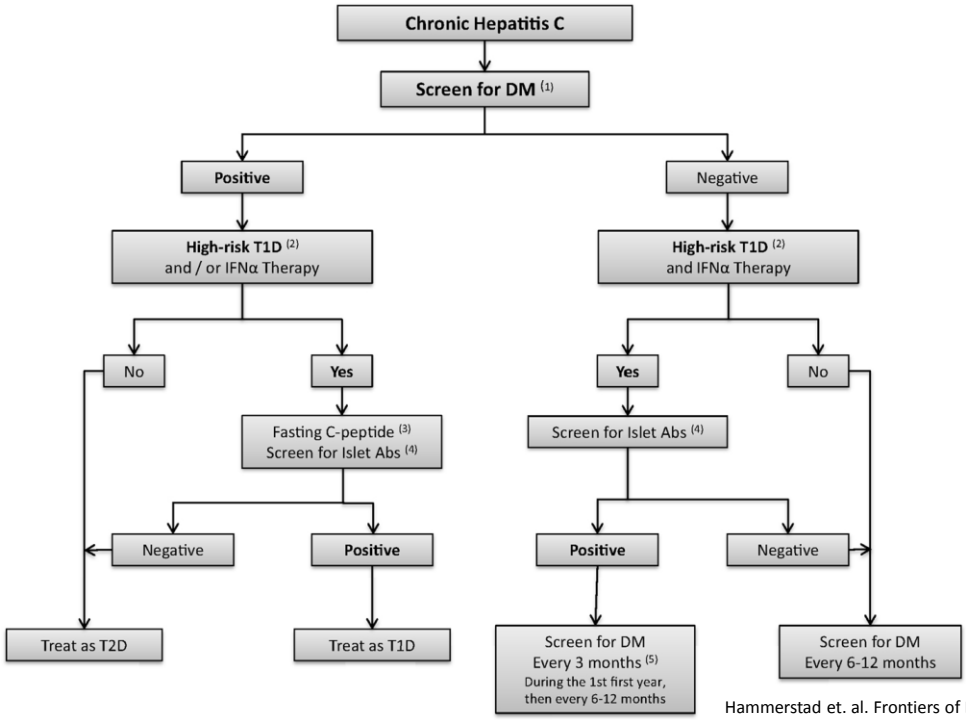
- Until more data become available to provide evidence-based recommendations for addressing diabetes and fatty liver in patients post-SVR, patients at risk or with a known diagnosis should be advised of the risk of liver-related complications, and continue disease-specific management to optimize weight loss and glycemic control.

Screening and Therapeutic Considerations

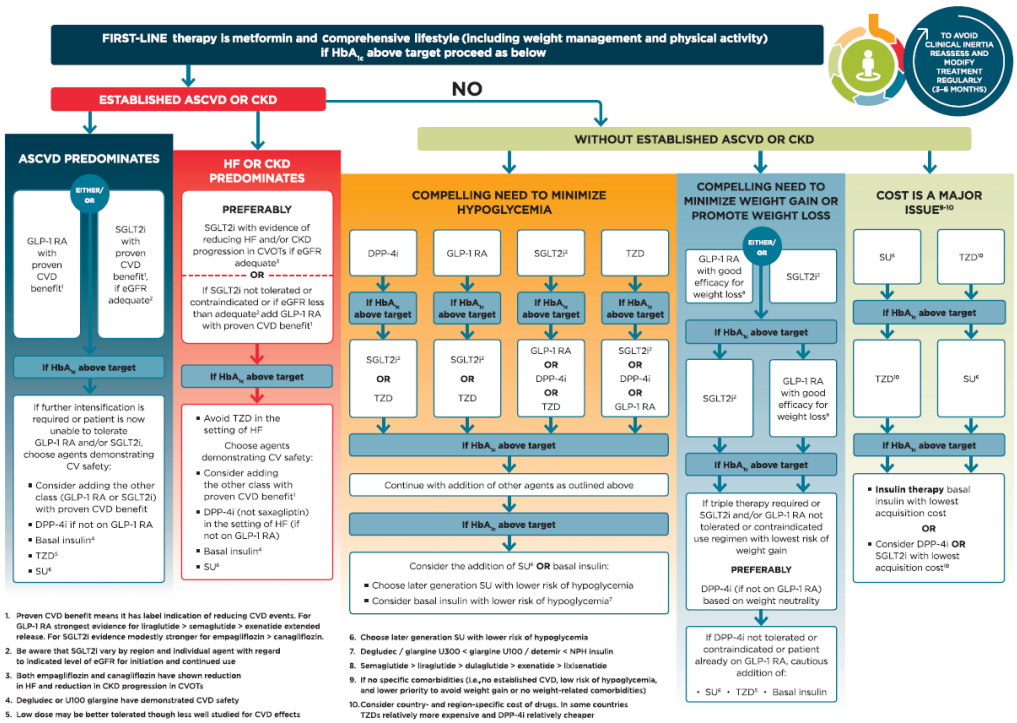
Literature commonly recommends screening for diabetes in all HCV patients

Screening diabetic patients at risk is also reasonable

- Persistently elevated ALT
- Or in cases that do not have evidence of non alcoholic fatty liver disease



Hammerstad et. al. Frontiers of Endocrinology 2015



Treatment Considerations

Not much room for change in HCV treatment

What about diabetes treatment?

Therapy Considerations

Metformin is still the drug of choice

- increasing evidence that metformin is independently associated with reduced risk for HCC and liver-related death/transplantation
- not recommended in advanced hepatic disease because of increased risk for lactic acidosis

Interestingly, GLP-1 levels were decreased and DPP-4 levels are significantly increased in HCV patients

- Does not affect

Small study in Japan found that insulin and second-generation SU were independent variables associated with incidence of HCC

Impact of Curing Hepatitis C

Treating HCV and achieving SVR impacts insulin resistance and glycemic control
- But…

SVR may decrease medication needs in patients cleared of HCV

Post SVR hepatocellular carcinoma is still increased in patients with diabetes
- Patients without diabetes have a 70% decrease in HCC risk

Positive Glycemic Results from Treatment

Improvement in Glycemic Control of Type 2 Diabetes After Successful Treatment of Hepatitis C Virus

Large Veteran's Affair's study showed improvement in HgbA1c
- 2,435 patients with diabetes who underwent interferon-free and ribavirin-free DAA-based antiviral treatment for HCV
- Average A1c of 7.2%
- The mean of the HbA1c measurements of patients was calculated for the 12-month period prior to treatment ("pretreatment") and the 12-month period from 3 to 15 months after treatment ("post-treatment").

Results showed patients had a decrease in A1c, insulin use and metformin use
- Were less likely to receive antidiabetic medication (74.8% vs 78.0%) or insulin (41.3% vs 49.8%) – not significant
- The number of patients receiving treatment with insulin decreased more significantly in patients who achieved SVR (from 41.3% to 38%) than in patients who did not (who actually had a slight increase in the proportion of patients receiving treatment with insulin)
  - Amount not reported

Hum et al. Diabetes Care, 2017

Positive Glycemic Results from Treatment

There was a significant drop in fasting glucose in the group of patients who received treatment compared to the group that received placebo.

In overall, notable drop in fasting glucose was observed (–8.87 mg/dL by week 12; $p < 0.0001$).

The most significant drop in fasting glucose was recorded in the group of patients with type II diabetes (–22.1 mg/dL by week 12; $p < 0.0001$).

Followed by still significant drop of fasting glucose in the group of patients with pre-diabetes

(–5.78 mg/dL by week 12; $p < 0.0001$).

On the contrary, there was slight, not significant increase of fasting glucose in the group of patients with normal baseline fasting glucose levels (1.34 mg/dL by week 12; $p = 0.057$)

Drazilova et al. Canadian Journal of Gastroenterology and Hepatology, 2018

Table 1: Studies reporting the changes of fasting glucose, HbA1C, and antidiabetic treatment after DAA treatment.

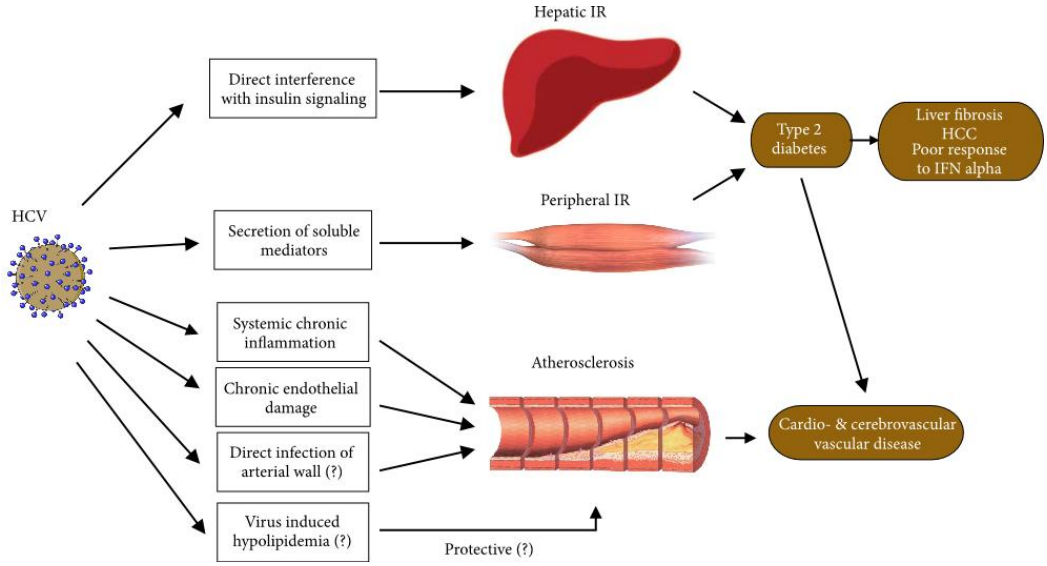
Author	Country	Patients	Genotype	Treatment	Decrease of the fasting glucose during or after DAA treatment	Decrease of the HbA1C during or after DAA treatment	Proportion of patients with the reduction of antidiabetic treatment
Tran,2017 [54]	Multi-ethnic	General HCV population, 25.4% prediabetes 5.9% T2DM	Genotype 1	Paritaprevir/ ritonavir + dasabuvir + ombitasvir	Yes, in all patients, patients with prediabetes and T2DM	NA	NA
Ikeda, 2017 [55]	Japan	T2DM	Genotype 1b	Sofosbuvir + ledipasvir	NA	Yes	NA
Meissner, 2015 [56]	USA	T2DM	Genotype 1	Sofosbuvir + ribavirin	NA	Yes	NA
Hum [57]	USA	T2DM	Mostly genotype 1	Sofosbuvir + simeprevir or Sofosbuvir + ledipasvir or Paritaprevit/ritonavir + dasabuvir + ombitasvir	NA	Yes	9%

Drazilova et al. Canadian Journal of Gastroenterology and Hepatology, 2018

				ombitasvir			
Morales, 2016 [58]	USA	T2DM	Mostly genotype 1	Only sofosbuvir based	NA	Yes	25%
Ciancio, 2018 [59]	Italy	T2DM	Mostly genotype 1	Mostly sofosbuvir based	Yes	Yes	21%
Fabrizio, 2017 [60]	Italy	T2DM	Mostly genotype 1	Mostly sofosbuvir based	Yes	NA	NA
Pavone, 2016 [61]	Italy	T2DM	Mostly genotype 1	Mostly sofosbuvir based	Yes	Yes	23%
Abdel Alem, 2017 [62]	Egypt	T2DM	Mostly genotype 4	Only sofosbuvir based	Yes	Yes	NA
Dawood, 2017 [63]	Egypt	T2DM	Genotype 4	Sofosbuvir + daclatasvir	Yes	Yes	27%
El Sagher, 2018 [64]	Egypt	T2DM	Genotype 4	Sofosbuvir + simeprevir	Yes	NA	NA
Beig, 2018 [65]	New Zealand	LTx patients, only patients without antidiabetic treatment	Mostly genotype 1	Mostly sofosbuvir based	yes	Yes	40%
Chaudhury, 2017 [66]	USA	General population, 31% HIV positive, 17%T2DM	Genotype 1	Multiple DAA	NA	No	3%

NA: not available; T2DM: type 2 diabetes mellitus.

Drazilova et al. Canadian Journal of Gastroenterology and Hepatology, 2018



Drazilova et al. Canadian Journal of Gastroenterology and Hepatology, 2018

Some Interesting Studies

Meta-analysis of 34 studies, all of which followed patients with coronary artery disease, unstable angina pectoris, myocardial infarction, and stroke, patients with chronic HCV infection were at significantly higher risk for cardio-cerebrovascular disease than noninfected patients (OR: 1.43; 95%CI: 1.21 - 1.68).

Petta et al. Journal of Hepatology, 2018

Direct Acting Antivirals and Interactions

DAAs have many interactions with medications that are common used for diabetes

- Statins
- Antiplatelet therapy

Other common medications

- Acid lowering agents
- Analgesics
- Macrolides

Less common medications

- Antiarrhythmic
- Anticoagulants
- Anticonvulsants

Role of the Pharmacy

Depending on practice site

- Transitions of care
- Continuous follow up and education
  - Adherence
  - Administration
  - Adverse reactions
- Monitoring interactions
  - Drugs
  - Herbal products

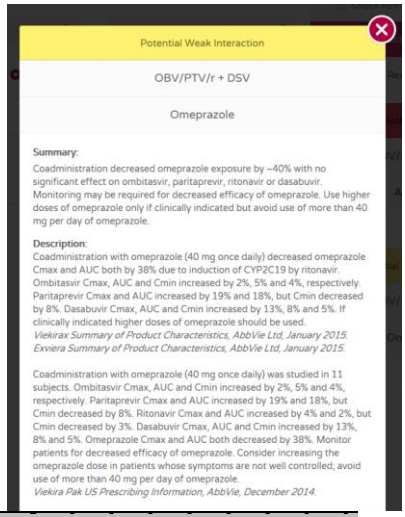
Behind the scenes factors

- Prior authorization
- Billing and reimbursement

Resources

Interaction checkers

- Hep Drug Interactions
  - Comprehensive check for large number of drugs
  - Provides potential actions to take
  - Individualized patient reports
  - https://www.hep-druginteractions.org/
- Hepatitis C Online
  - Funded by CDC and ran by universities
  - Large collection of drug guides
  - Free modules and CE in HCV topics
  - Clinical tools and calculators
  - https://www.hepatitisc.uw.edu/



Potential Weak Interaction

OBV/PTV/r + DSV

Omeprazole

Summary:

Coadministration decreased omeprazole exposure by ~40% with no significant effect on ombitasvir, paritaprevir, ritonavir or dasabuvir. Monitoring may be required for decreased efficacy of omeprazole. Use higher doses of omeprazole only if clinically indicated but avoid use of more than 40 mg per day of omeprazole.

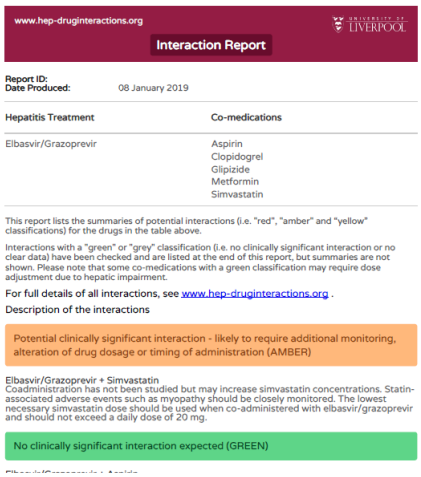
Description:

Coadministration with omeprazole (40 mg once daily) decreased omeprazole Cmax and AUC both by 38% due to induction of CYP2C19 by ritonavir. Ombitasvir Cmax, AUC and Cmin increased by 2%, 5% and 4%, respectively. Paritaprevir Cmax and AUC increased by 19% and 18%, but Cmin decreased by 8%. Dasabuvir Cmax, AUC and Cmin increased by 13%, 8% and 5%. If clinically indicated higher doses of omeprazole should be used.

Viekirax Summary of Product Characteristics, AbbVie Ltd, January 2015.
Exviera Summary of Product Characteristics, AbbVie Ltd, January 2015.

Coadministration with omeprazole (40 mg once daily) was studied in 11 subjects. Ombitasvir Cmax, AUC and Cmin increased by 2%, 5% and 4%, respectively. Paritaprevir Cmax and AUC increased by 19% and 18%, but Cmin decreased by 8%. Ritonavir Cmax and AUC increased by 4% and 2%, but Cmin decreased by 3%. Dasabuvir Cmax, AUC and Cmin increased by 13%, 8% and 5%. Omeprazole Cmax and AUC both decreased by 38%. Monitor patients for decreased efficacy of omeprazole. Consider increasing the omeprazole dose in patients whose symptoms are not well controlled; avoid use of more than 40 mg per day of omeprazole.

Viekira Pak US Prescribing Information, AbbVie, December 2014.



www.hep-druginteractions.org — UNIVERSITY OF LIVERPOOL

Interaction Report

Report ID:
Date Produced: 08 January 2019

Hepatitis Treatment	Co-medications
Elbasvir/Grazoprevir	Aspirin Clopidogrel Glipizide Metformin Simvastatin

This report lists the summaries of potential interactions (i.e. "red", "amber" and "yellow" classifications) for the drugs in the table above.

Interactions with a "green" or "grey" classification (i.e. no clinically significant interaction or no clear data) have been checked and are listed at the end of this report, but summaries are not shown. Please note that some co-medications with a green classification may require dose adjustment due to hepatic impairment.

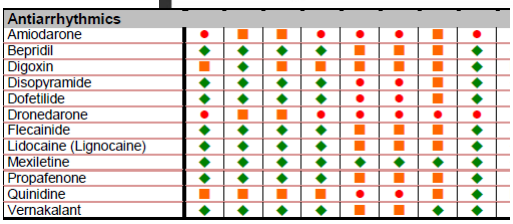
For full details of all interactions, see www.hep-druginteractions.org .

Description of the interactions

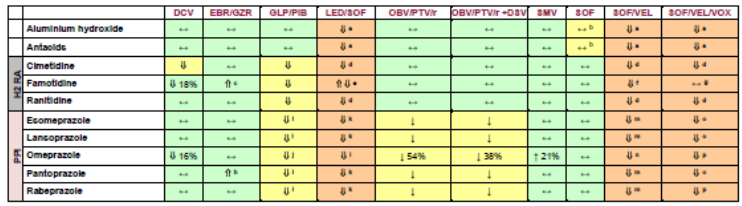
Potential clinically significant interaction - likely to require additional monitoring, alteration of drug dosage or timing of administration (AMBER)

Elbasvir/Grazoprevir + Simvastatin
Coadministration has not been studied but may increase simvastatin concentrations. Statin-associated adverse events such as myopathy should be closely monitored. The lowest necessary simvastatin dose should be used when co-administered with elbasvir/grazoprevir and should not exceed a daily dose of 20 mg.

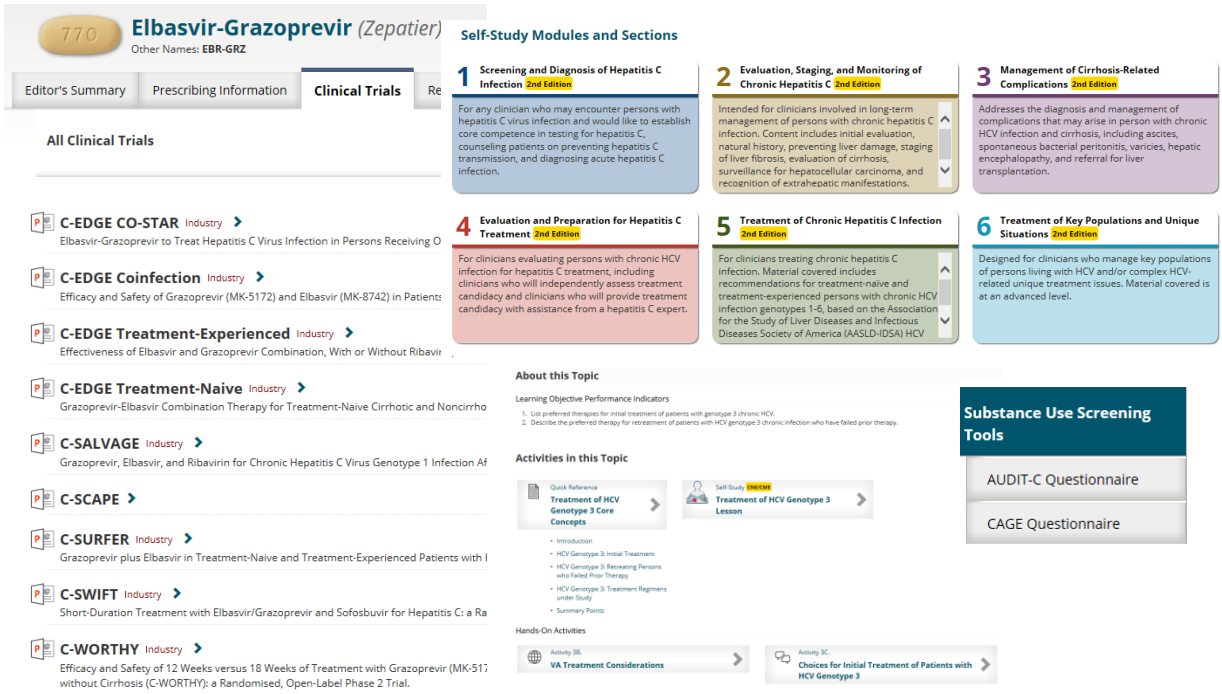
No clinically significant interaction expected (GREEN)



Antiarrhythmics								
Amiodarone	●	■	■	●	●	●	■	●
Bepridil	◆	◆	◆	◆	■	■	■	◆
Digoxin	■	◆	■	■	■	■	■	◆
Disopyramide	◆	◆	◆	◆	●	●	■	◆
Dofetilide	◆	◆	◆	◆	●	●	■	◆
Dronedarone	●	■	■	●	●	●	●	●
Flecainide	◆	◆	◆	◆	■	■	■	◆
Lidocaine (Lignocaine)	◆	◆	◆	◆	■	■	■	◆
Mexiletine	◆	◆	◆	◆	◆	◆	◆	◆
Propafenone	◆	◆	◆	◆	■	■	■	◆
Quinidine	■	■	■	■	●	●	■	◆
Vernakalant	◆	◆	◆	◆	■	■	◆	◆



		DCV	EBR/GZR	GLP/PIB	LED/SOF	OBV/PTV/r	OBV/PTV/r +DSV	SMV	SOF	SOF/VEL	SOF/VEL/VOX
	Aluminium hydroxide	↔	↔	↔	⇩*	↔	↔	↔	↔[5]	⇩*	⇩*
	Antacids	↔	↔	↔	⇩*	↔	↔	↔	↔[5]	⇩*	⇩*
H2RA	Cimetidine	⇩	↔	⇩	⇩[d]	↔	↔	↔	↔	⇩[d]	⇩[d]
H2RA	Famotidine	⇩ 18%	⇧[c]	⇩	⇧⇩*	↔	↔	↔	↔	⇩[f]	↔[g]
H2RA	Ranitidine	↔	↔	⇩	⇩[d]	↔	↔	↔	↔	⇩[d]	⇩[d]
PPI	Esomeprazole	↔	↔	⇩[i]	⇩*	↓	↓	↔	↔	⇩[m]	⇩[o]
PPI	Lansoprazole	↔	↔	⇩[i]	⇩*	↓	↓	↔	↔	⇩[m]	⇩[o]
PPI	Omeprazole	⇩ 16%	↔	⇩[j]	⇩[i]	↓ 54%	↓ 38%	↑ 21%	↔	⇩[n]	⇩[p]
PPI	Pantoprazole	↔	⇧[k]	⇩[i]	⇩*	↓	↓	↔	↔	⇩[m]	⇩[o]
PPI	Rabeprazole	↔	↔	⇩[i]	⇩*	↓	↓	↔	↔	⇩[m]	⇩[p]



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Elbasvir-Grazoprevir *(Zepatier)*

Other Names: **EBR-GRZ**

Editor's Summary | Prescribing Information | **Clinical Trials** | Re

All Clinical Trials

C-EDGE CO-STAR Industry
Elbasvir-Grazoprevir to Treat Hepatitis C Virus Infection in Persons Receiving O

C-EDGE Coinfection Industry
Efficacy and Safety of Grazoprevir (MK-5172) and Elbasvir (MK-8742) in Patients

C-EDGE Treatment-Experienced Industry
Effectiveness of Elbasvir and Grazoprevir Combination, With or Without Ribavi

C-EDGE Treatment-Naive Industry
Grazoprevir-Elbasvir Combination Therapy for Treatment-Naive Cirrhotic and Noncirrho

C-SALVAGE Industry
Grazoprevir, Elbasvir, and Ribavirin for Chronic Hepatitis C Virus Genotype 1 Infection Af

C-SCAPE

C-SURFER Industry
Grazoprevir plus Elbasvir in Treatment-Naive and Treatment-Experienced Patients with I

C-SWIFT Industry
Short-Duration Treatment with Elbasvir/Grazoprevir and Sofosbuvir for Hepatitis C: a Ra

C-WORTHY Industry
Efficacy and Safety of 12 Weeks versus 18 Weeks of Treatment with Grazoprevir (MK-517 without Cirrhosis (C-WORTHY): a Randomised, Open-Label Phase 2 Trial.

Self-Study Modules and Sections

1 Screening and Diagnosis of Hepatitis C Infection 2nd Edition
For any clinician who may encounter persons with hepatitis C virus infection and would like to establish core competence in testing for hepatitis C, counseling patients on preventing hepatitis C transmission, and diagnosing acute hepatitis C infection.

2 Evaluation, Staging, and Monitoring of Chronic Hepatitis C 2nd Edition
Intended for clinicians involved in long-term management of persons with chronic hepatitis C infection. Content includes initial evaluation, natural history, preventing liver damage, staging of liver fibrosis, evaluation of cirrhosis, surveillance for hepatocellular carcinoma, and recognition of extrahepatic manifestations.

3 Management of Cirrhosis-Related Complications 2nd Edition
Addresses the diagnosis and management of complications that may arise in person with chronic HCV infection and cirrhosis, including ascites, spontaneous bacterial peritonitis, varicies, hepatic encephalopathy, and referral for liver transplantation.

4 Evaluation and Preparation for Hepatitis C Treatment 2nd Edition
For clinicians evaluating persons with chronic HCV infection for hepatitis C treatment, including clinicians who will independently assess treatment candidacy and clinicians who will provide treatment candidacy with assistance from a hepatitis C expert.

5 Treatment of Chronic Hepatitis C Infection 2nd Edition
For clinicians treating chronic hepatitis C infection. Material covered includes recommendations for treatment-naive and treatment-experienced persons with chronic HCV infection genotypes 1-6, based on the Association for the Study of Liver Diseases and Infectious Diseases Society of America (AASLD-IDSA) HCV

6 Treatment of Key Populations and Unique Situations 2nd Edition
Designed for clinicians who manage key populations of persons living with HCV and/or complex HCV-related unique treatment issues. Material covered is at an advanced level.

About this Topic

Learning Objective Performance Indicators
1. List preferred therapies for initial treatment of patients with genotype 3 chronic HCV.
2. Describe the preferred therapy for retreatment of patients with HCV genotype 3 chronic infection who have failed prior therapy.

Activities in this Topic

Quick Reference
Treatment of HCV Genotype 3 Core Concepts
- Introduction
- HCV Genotype 3: Initial Treatment
- HCV Genotype 3: Retreating Persons who Failed Prior Therapy
- HCV Genotype 3: Treatment Regimens under Study
- Summary Points

Self-Study CME/CNE
Treatment of HCV Genotype 3 Lesson

Hands-On Activities

Activity 3B.
VA Treatment Considerations

Activity 3C.
Choices for Initial Treatment of Patients with HCV Genotype 3

Substance Use Screening Tools

AUDIT-C Questionnaire

CAGE Questionnaire

Question 1

_____ have increased risk of hepatocellular carcinoma.

A. GLP1s

B. Sulfonylureas

C. DPP4s

D. DAAs

Question 1

_____ have increased risk of hepatocellular carcinoma.

A. GLP1s

B. Sulfonylureas

C. DPP4s

D. DAAs

Question 2

The hepatitis C virus has been shown to infect the _____

A. Kidney

B. Gallbladder

C. Pancreas

D. Brain

Question 2

The hepatitis C virus has been shown to infect the _____

A. Kidney

B. Gallbladder

C. Pancreas

D. Brain

Question 3

Insulin resistance in hepatitis C only affects patients with diabetes

A. True

B. False

Question 3

Insulin resistance in hepatitis C only affects patients with diabetes

A. True

B. False

Summary

There is a two way association between hepatitis C and diabetes

- There is a higher prevalence of diabetes in patients with HCV
- Diabetes increases the risk of poor outcomes from HCV

HCV is associated with insulin resistance

- Including non-diabetic patients

Treating HCV provides some benefit to glycemic control

More data is needed for formal guideline recommendations

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Questions?