My Patient is Diagnosed with Hep C. What Do I Do?

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Nanaimo Division of Family Practice
A GPSC initiative

Primary Health Care
Chronic Disease Management
Rural Health Services
Laying the Foundation
Regional Support Program

Chronic HCV Infection

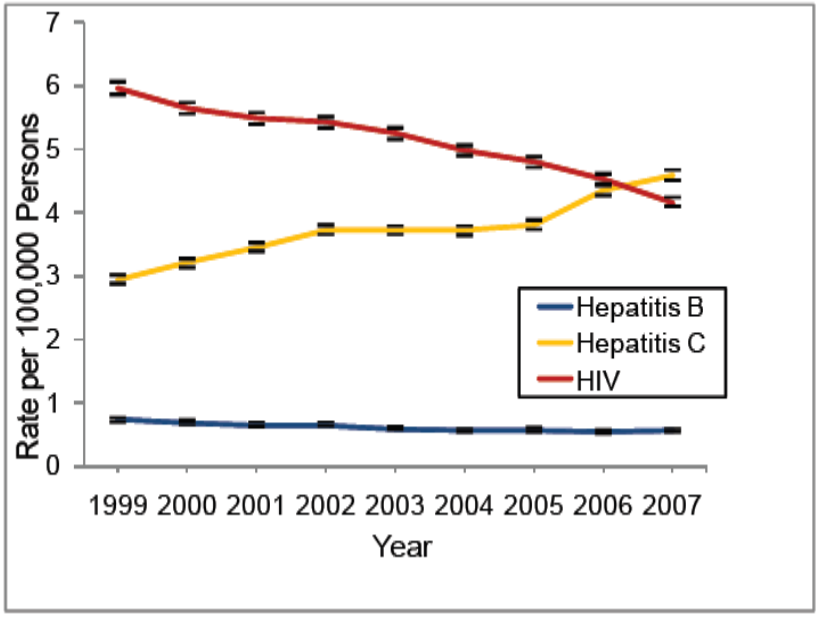
- Definition:
  HCV-RNA detected in blood after 6 months

- RNA rarely clears after 6 months (< 1% /year)
- Not all chronic HCV have elevated ALT, AST
- HIV patients may not have Anti-HCV

Importance of Screening for, and Treating of, HCV

Increase in mortality in HCV vs. HIV[1]

- HIV-related deaths have been decreasing, while HCV-related deaths have significantly increased
- In 2007, mortality from HCV exceeded that of HIV in the US



HIV: human immunodeficiency virus

1. Ly et al. Ann Intern Med. 2012;156:271-278

Hepatitis C: Concept of Proportionality

As healthcare providers, how many HCV (+ive) patients do you have in your practice?

A. 0-5
B. 5-10
C. 10-15
D. more

HCV Epidemiology in Canada

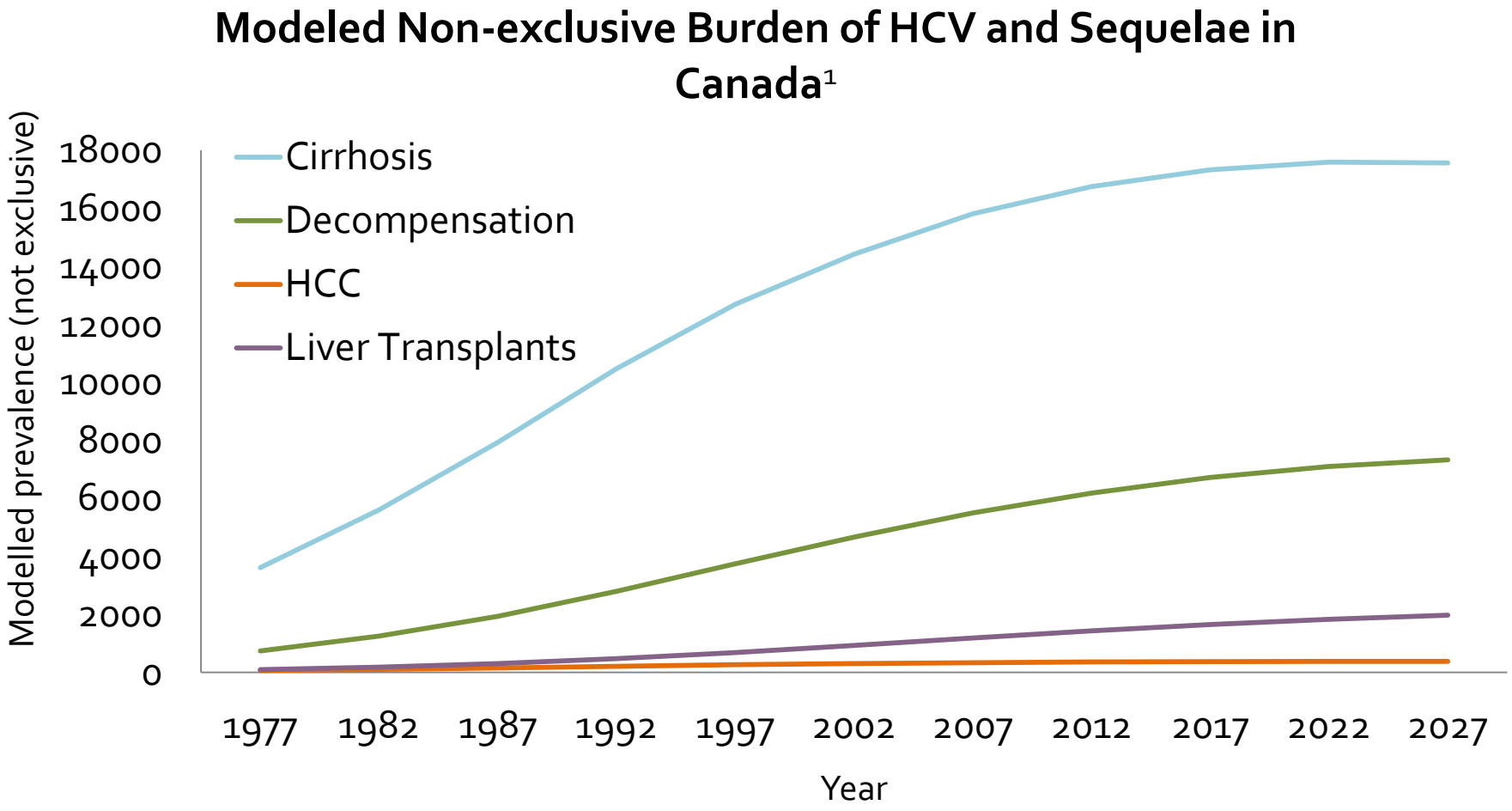
Prevalence in Canada[1,2]

- Health Canada estimates an overall prevalence of **0.78%** in Canada
  - 242 500 infected individuals

Fraction Diagnosed

- "Silent epidemic": often asymptomatic for years[3]
- HCV-associated disease is the primary indication for liver transplantation[4]
  - Accounts for 50% of hepatocellular carcinoma (HCC) in the US[4], the fastest growing cause of cancer-related mortality[5]

Importance of Screening and Treating HCV



HCC: hepatocellular carcinoma; CDC: Centers for Disease Control and Prevention

1. Remis RS. Final Report. Public Health Agency of Canada. 2007. Available from: http://www.phac-aspc.gc.ca/sti-its-surv-epi/model/pdf/model07-eng.pdf.

Course Objectives

After this case based presentation the attendee will:

- Have an improved understanding of who to refer for treatment of Hepatitis C.
- Have an increased awareness of the referral process for potential treatment of Hepatitis C patients.

Course Objectives

- Have a better understanding of the important role of the GP while the patient is being treated for Hepatitis C.

- Have increased knowledge of primary care management for patients with Hepatitis C.

Case

55 year old female : moved here from Ontario . Says has been told has stable hepatitis C diagnosed 10 years earlier. Her doctor in Ontario has reassured her that she should keen an eye on it, but not to worry about it as her ALT levels are always below the upper limit of normal on routine checking.

Chronic Hepatitis C (CHC) and ‘Normal’ Alanine Aminotransferase (ALT)

“Persistently ‘normal’ ALT”

PNALT

Case

Your workup reveals normal Alt at 55, platelets 145, and normal CBC.

What would be your advice?

Case

Advise patient that having a normal ALT is a contraindication for treatment.

Carry on, simply check the ALT every 6 months to make sure it remains stable.

Advise patient to consider the possibility of treatment even though she feels fine.

True or False

Approximately one-half

of patients with persistently normal ALT levels have moderate to severe liver disease on biopsy

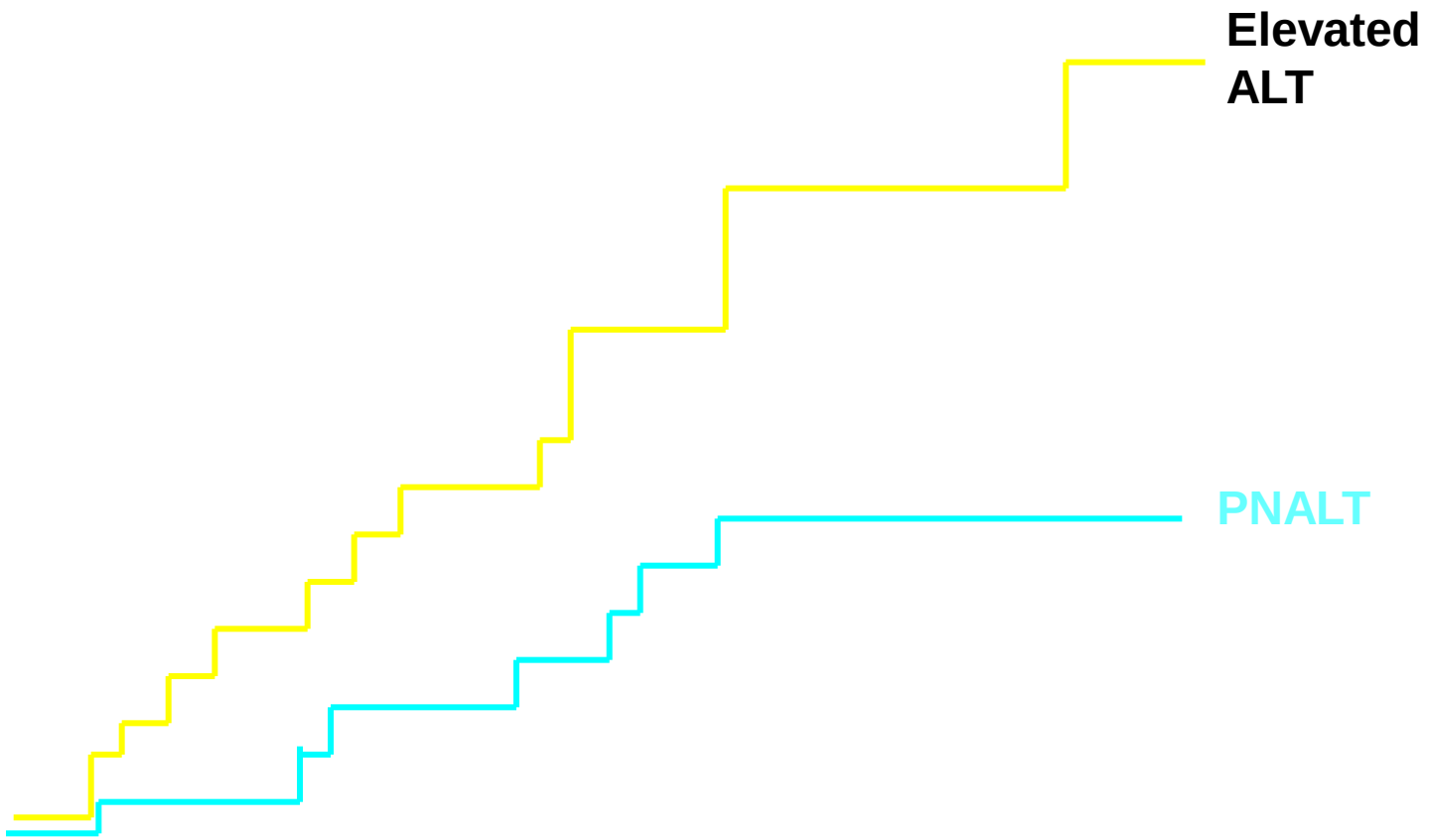
False

Approximately one-quarter of patients with persistently normal ALT levels have moderate to severe liver disease on biopsy

PNALT

Comprises approximately one-third of chronically infected individuals.

Probability of Fibrosis Progression: ‘Normal’ vs Elevated ALT Levels

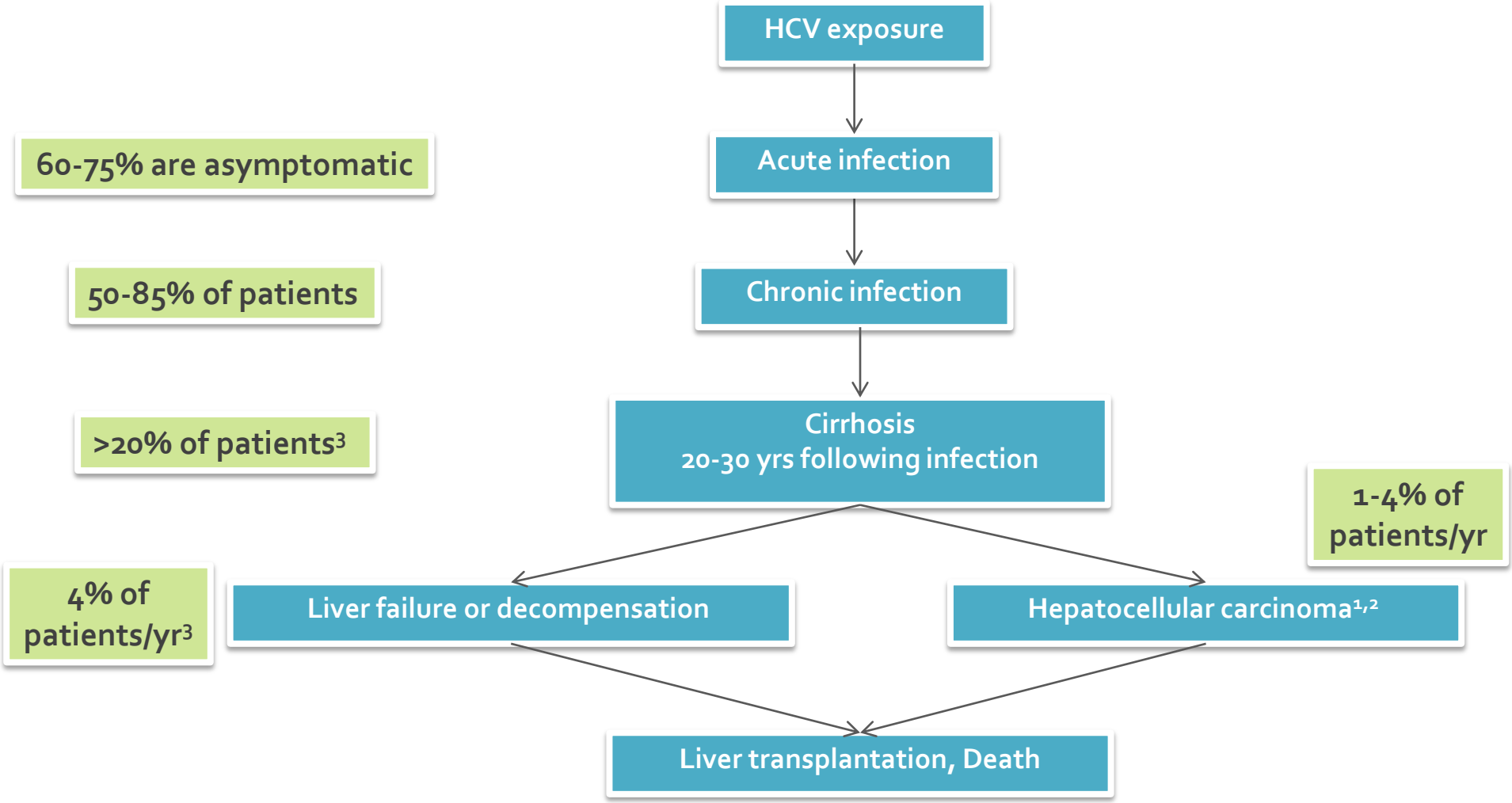


What happens no treatment?

- Educating your patient regarding the pros and cons of treatment.

- The diagnosis is NOT a death sentence for the average person.

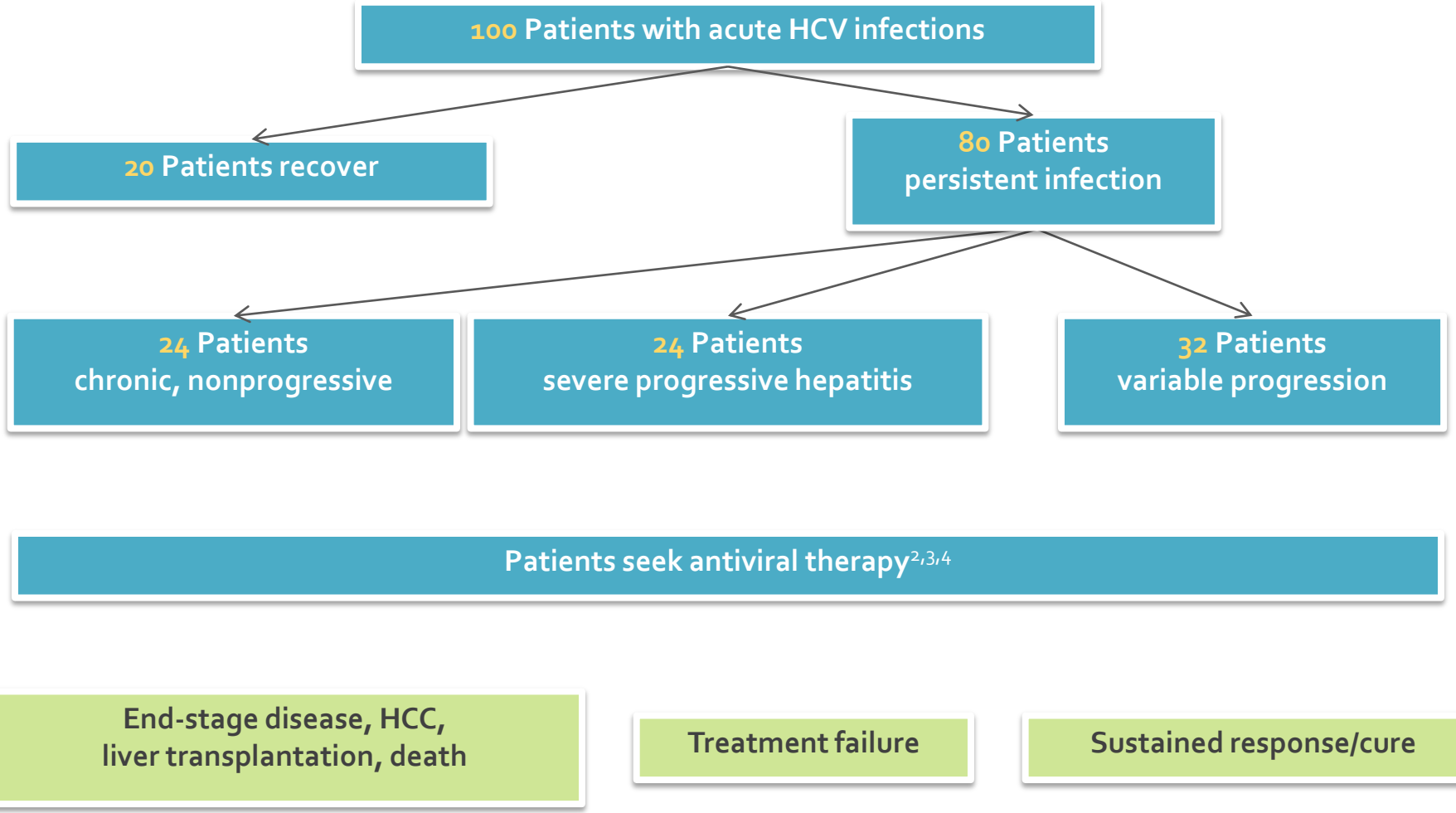
Natural History of HCV[1]



1. Seeff LB. Hepatology 2002;36(Suppl 1):S35-46; 2. Sherman et al. Curr Oncol. 2011;18(5):228-40; 3.

Patient Counseling:

Projection of Lifetime Outcomes[1]



Evaluation:
Laboratory Testing[1-2]

Virological tests to confirm HCV infection

- Anti-HCV
- HCV-RNA
- HCV genotype
- (Viral load if considering treatment)

Bloodwork

- CBC
- Liver enzyme & function tests: ALT, AST, GGT, alkaline phosphatase, **bilirubin, INR (or PT), albumin**
  - Normal ALT is <u>not</u> a contraindication to treatment
- Creatinine

Evaluation:

Laboratory Testing[1-2]

The score employs five clinical measures of liver disease. Each measure is scored 1-3, with 3 indicating most severe derangement.

Measure	1 point	2 points	3 points
Total bilirubin, µmol/l (mg/dl)	<34 (<2)	34-50 (2-3)	>50 (>3)
Serum albumin, g/l	>35	28-35	<28
PT INR	<1.7	1.71-2.30	> 2.30
Ascites	None	Mild	Moderate to Severe
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)

Different textbooks and publications use different measures. Some older reference works substitute PT prolongation for INR.

In primary sclerosing cholangitis (PSC) and primary biliary cirrhosis (PBC), the bilirubin references are changed to reflect the fact that these diseases feature high conjugated bilirubin levels. The upper limit for 1 point is 68 µmol/l (4 mg/dl) and the upper limit for 2 points is 170 µmol/l (10 mg/dl).

Interpretation [edit]

Chronic liver disease is classified into Child-Pugh class A to C, employing the added score from above.

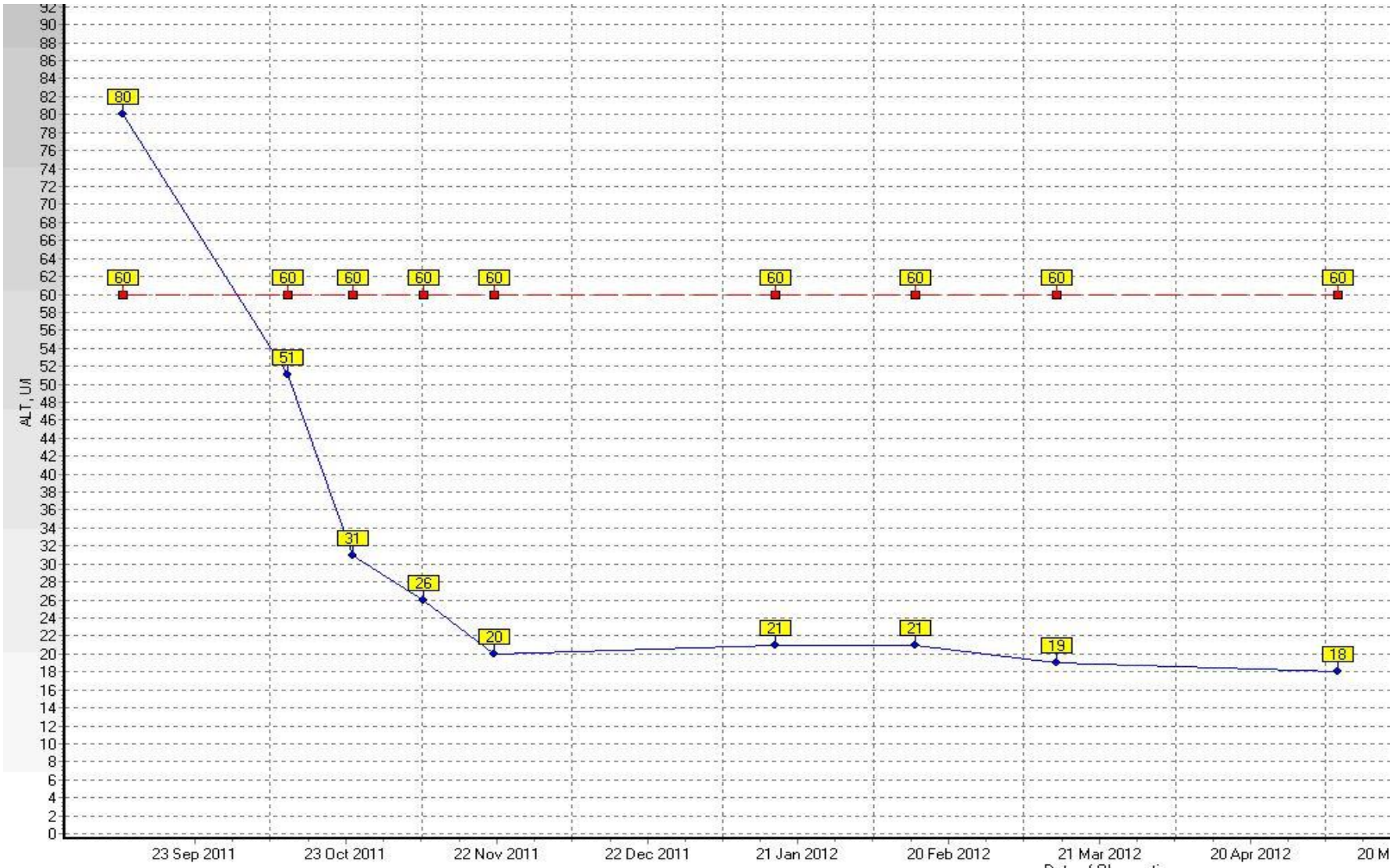
Points	Class	One year survival	Two year survival
5-6	A	100%	85%
7-9	B	81%	57%
10-15	C	45%	35%

Child-Pugh Score

Lab Tests

- **ALT**
  - Is often elevated in Hepatitis C
  - Can fluctuate over months and years
    - Possibly due to ongoing waves of injury to the liver from the virus
  - ALT level may <u>not</u> correlate with the extent of inflammation found on liver biopsy
    - People with cirrhosis may have normal ALTs
  - ~30% of people with chronic Hepatitis C have normal ALT
  - **“Surrogate marker.”**

ALT IMPROVEMENT DURING TREATMENT



Evaluation: Laboratory Testing[1-2]

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  - Normal ALT is <u>not</u> a contraindication to treatment –⅓[2]
- Creatinine

Abdominal ultrasound

- To test for cirrhosis and exclude hepatocellular carcinoma

Tests to rule out coinfections

- Hepatitis A (Anti-HAV IgG)
- Hepatitis B (HBsAg, Anti-HBs)
- HIV (Anti-HIV)

Tests to exclude other causes of liver disease

- The high fatality rate among our patients with chronic hepatitis C and HAV superinfection (35 percent) is thus surprising.
- As is the even higher percentage of such patients with fulminant hepatitis (41 percent).

Evaluation:

Laboratory Testing[1-2]

- **Tests to exclude other causes of liver disease**

Routine testing of patients with chronic hepatitis C virus (HCV)*

Category of testing	Tests	Comments
Confirmation and characterization of chronic infection	HCV RNA	Confirms chronicity and baseline for treatment response
	HCV genotype	Directs choice and duration of therapy
Assessment of liver disease	Complete blood count, ALT, AST, GGT, Alkaline phosphatase	Thrombocytopenia may indicate cirrhosis and portal hypertension. Platelets needed for APRI calculation. Normal value does not preclude significant fibrosis. AST needed for calculation of APRI
	Bilirubin, INR (or PT), Albumin	Elevated bilirubin or INR, or hypoalbuminemia may indicate significant liver dysfunction
	CT scan, abdominal ultrasound	May suggest cirrhosis, in which case, serves as a baseline for HCC surveillance
Viral coinfections	Immunoglobulin G anti-HAV	If negative, vaccinate against hepatitis A virus (HAV)
	HBsAg	Exclude hepatitis B coinfection.
	anti-HBs	If negative (and HBsAg-negative), vaccinate against hepatitis B
	anti-HIV	Exclude HIV coinfection
Exclude other causes of liver disease†	Alpha-1-antitrypsin	Alpha-1-antitrypsin deficiency
	Ceruloplasmin	Wilson disease
	Ferritin, serum iron, total iron-binding capacity	Iron overload
	Antinuclear antibody, smooth muscle antibody	Autoimmune hepatitis (AIH)
	Antimitochondrial antibody	Primary biliary cirrhosis (PBC)
	Immunoglobulin G	Often elevated in AIH and cirrhosis of any cause
	Immunoglobulin A	Often elevated in fatty liver and alcoholic liver disease
	Immunoglobulin M	Often elevated in PBC
Contraindications to treatment	Serum or urine β-HCG	Exclude pregnancy in women of reproductive age
	Electrocardiogram	If >50 years or history of cardiac disease
	Thyroid-stimulating hormone	Exclude thyroid disease, which may be exacerbated by IFN
	Fundoscopy	Exclude retinopathy in patients >50 years or with hypertension or diabetes mellitus

*Confirmed anti-HCV antibody positive. †Suggested tests only; tailor testing to individual case. Anti-HBs Hepatitis B surface antibody, ALT Alanine aminotransferase, AST Aspartate aminotransferase, APRI AST/platelet ratio index, β-HCG Beta-human chorionic gonadotropin, GGT Gamma-glutamyltransferase, HBsAg Hepatitis B surface antigen, HCC Hepatocellular carcinoma, IFN Interferon, INR International normalized ratio, PT Prothrombin time

Why Treat Now?

- **Dawn of a new era in chronic HCV therapy "** Direct-acting antivirals (**DAAs**),
  - **Dual therapy** (peg-interferon [PEG-IFN] and ribavirin [RBV]) is utilized to eradicate HCV in **non-genotype 1** patients[2]
  - Introduction of direct-acting antivirals for treatment of genotype 1
    - **Triple therapy** (boceprevir or telaprevir + PEG-IFN/RBV)[3,4]
    - Low discontinuation rates due to adverse events (anemia, neutropenia, rash and fever)[5-7]
    - Potential for shorter treatment duration (24-48 weeks)[3,4]

HCV can now be eradicated in 70-80% of all treatment naïve patients[3,4,8]

Low discontinuation rates due to adverse events (anemia, neutropenia, rash and fever)[5-7]

- **Triple therapy** (boceprevir or telaprevir + PEG-IFN/RBV)[3,4]

ADVERSE EVENTS OF TELAPREVIR AND BOCEPREVIR
Patients treated with PI-based combination therapy experience more adverse effects than those treated with PEG-IFN and RBV alone.

Clinical trial and postmarketing experience suggest that the transfusion of packed red blood cells is more frequently required to manage severe symptomatic anemia in patients undergoing PI-based therapy (both boceprevir and telaprevir), particularly those with cirrhosis

Direct-acting antivirals (**DAAs**),

Hepatitis C Genotypes

HCV genotype directs choice and duration of therapy

Chronic Hepatitis C: Considerations of Treatment

Independent predictors of SVR

- Genotype
- Viral load
- Age
- Fibrosis / Cirrhosis

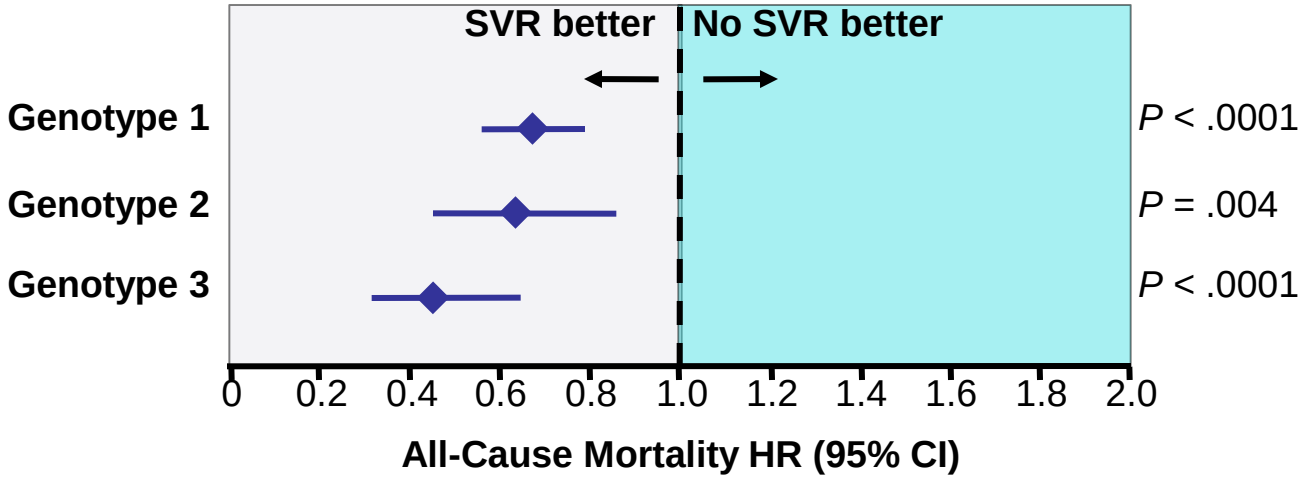
Adherence to Therapy

Aims of Treatment

- **Virologic response**
  - Sustained Virologic Response (SVR) = patient tests HCV-PRR negative 6 months after completing therapy
  - There is no evidence of HCV in liver or the blood
  - There appears to be less than a 2% relapse rate 7 years post-treatment
  - Suppression of HCV activity
    - Delay progression to cirrhosis
    - Decrease incidence of Hepatocellular Cancer (HCC)

SVR : Important Clinical Endpoint

- Achieving an SVR results in a significant reduction of HCV-associated complications and mortality[1,2]



1. Morgan TR, et al. Hepatology. 2010;52:833-844.
2. Backus L, et al. 2010 AASLD. Abstract 213.

Quantitative PCR: Viral Load.

True or false: HCV viral load is useful in predicting the achievement of a SVR

1. True
2. False

Quantitative PCR: Viral Load.

- Is useful in predicting the achievement of a SVR ie if < or > 800,000.

- Will be measured at 4, 8, 12, 24, 48 and 72 weeks in patients on triple therapy of their genotype 1 HCV. The results guide treatment with Peg/Rib/DAA “Response based therapy” RGT

Quantitative PCR: Viral Load.

ACC#: H41974 COLL: 08/Sep/2011 14:24 REC: 12/Sep/2011 15:54
FINAL CLIENT OR ORD. PHYS: 05532 PHILLIPS,RONALD KEITH
COPY TO: Steele,Dale Robert
NANAIMO VIRAL HEPATITIS,X
BC PHARMACARE,x

Submitter's Ref. Or Comment: %700054001

	RESULT	FLAG	REFERENCE RANGE	UNITS	RESULTED
Hepatitis C Quant NAT					
Specimen Description	Plasma				12/Sep/2011{L}
HCV RNA (IU/mL)	1162998				21/Sep/2011{D}
HCV RNA (log10 IU/mL)	6.07				21/Sep/2011{D}

The lower limit of detection is 15 IU/mL and the assay is linear between 43 to 69,000,000 IU/mL. Quantitative assay variability may result in up to 5 fold (0.5 log10) differences between specimens.

{D} Testing performed or reported by BC Centre for Disease Control Laboratory
{L} Testing performed or reported by Central Processing + Receiving Laboratory

Quantitative PCR: Viral Load.

ACC#: H59724 COLL: 12/Jul/2012 10:54 REC: 16/Jul/2012 12:40
FINAL CLIENT OR ORD. PHYS: 05532 PHILLIPS,RONALD KEITH
COPY TO: CENTRAL ISLAND CD HUB,VHI

	RESULT	FLAG	REFERENCE RANGE	UNITS	RESULTED
Hepatitis C Quant NAT					
Specimen Description	Plasma				16/Jul/2012{L}
HCV RNA (IU/mL)	500448				20/Jul/2012{D}
	HCV RNA DETECTED				
	The qualitative HCV RNA assay used to confirm HCV infection has been replaced by an equally sensitive quantitative assay (detection limit 10 to 15 IU/mL).				
	The magnitude of the HCV RNA viral load is used to predict and monitor treatment response but does not correlate with disease progression.				
HCV RNA (log10 IU/mL)	5.70				20/Jul/2012{D}
	The lower limit of detection is 10 to 15 IU/mL and the assay is linear between 43 to 69,000,000 IU/mL. Quantitative assay variability may result in up to 5 fold (0.5 log10) differences between specimens.				

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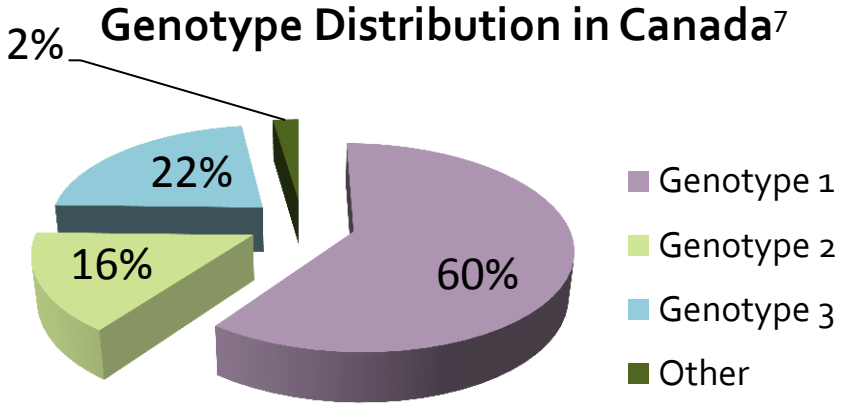
Curing Hepatitis C

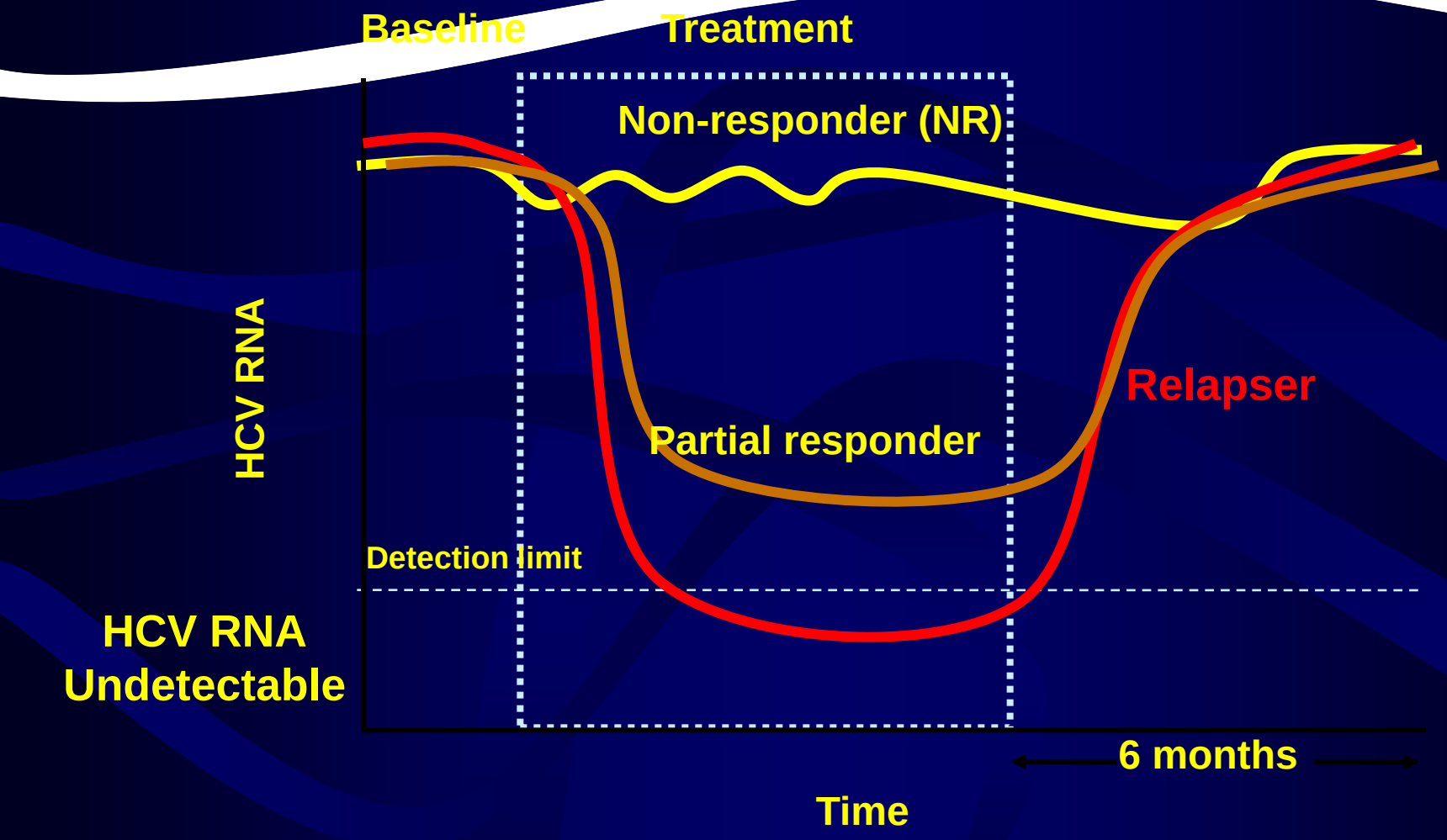
- HCV eradication rate and treatment is dependent upon viral genotype and the stage of fibrosis[1,2]



- **Genotype 1** has an SVR rate of **~70%** with triple therapy[3]
- **Genotypes 2 and 3** have an SVR rate of **~80% with dual** therapy[1,2]

- Treatment is less effective in patients with advanced liver disease (i.e. cirrhosis) and in those who were unresponsive to dual therapy[1,4-6]
  - Can still be cured with therapy

Patterns of Virological 'Non-Response'



Partial responder – 2 log decrease in HCV RNA but still RNA positive at wk 24 or 48

Course Objectives

"After this case based presentation the attendee will have an improved understanding of **who to refer** for treatment of Hepatitis C:"

Noncirrhotic patients with HCV genotype 1 who have demonstrated relapse to previous PEG-IFN and RBV therapy should be offered retreatment with RGT including PEG-IFN, RBV, and boceprevir or telaprevir.

Patterns of Virological 'Non-Response'

Duration of therapy using response-guided therapy guidelines in patients treated with boceprevir- or telaprevir-based triple therapy

	HCV RNA result*		
Boceprevir†	**Week 8**	**Week 24**	**Action**
Previously untreated patients	Undetectable	Undetectable	Stop boceprevir, PEG-IFN and RBV at treatment week 28. Treatment is completed.
	Detectable	Undetectable	Continue boceprevir, PEG-IFN and RBV until treatment week 28 and then administer PEG-IFN and RBV until week 48.
Previous treatment failures (relapsers and partial responders)	Undetectable	Undetectable	Stop boceprevir, PEG-IFN and RBV at treatment week 36. Treatment is completed.
	Detectable	Undetectable	Continue boceprevir, PEG-IFN and RBV until treatment week 36 and then administer PEG-IFN and RBV until week 48.
	HCV RNA result		
Telaprevir‡	**Week 4**	**Week 12**	**Action**
Previously untreated patients and relapsers	Undetectable	Undetectable	Stop telaprevir at treatment week 12 and then continue PEG-IFN and RBV until week 24.
	Detectable§	Undetectable or detectable§	Stop telaprevir at treatment week 12 and then continue PEG-IFN and RBV until week 48.

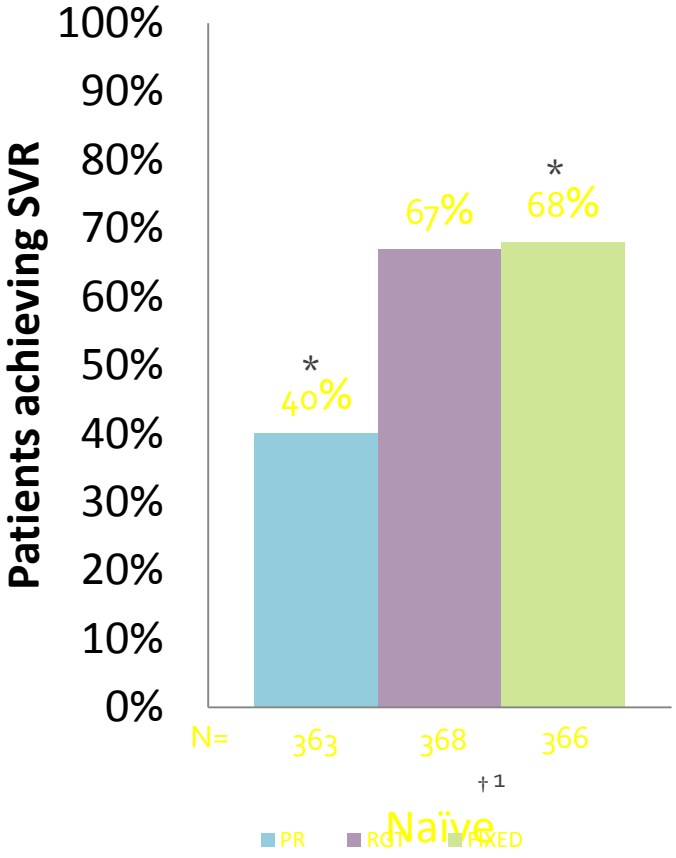
**Hepatitis C virus (HCV) RNA should be quantified using an assay with a lower limit of detection of no greater than 10 IU/mL to 15 IU/mL; †Response-guided therapy to boceprevir is not recommended for patients with cirrhosis (F4), null responders to previous pegylated interferon (PEG-IFN) and ribavirin (RBV) therapy, or patients with a less than 1 $\log_{10}$ decline in HCV RNA at treatment week 4 compared with baseline; ‡Response-guided therapy to telaprevir is not recommended for patients with cirrhosis (F4) or previous partial or null responders to PEG-IFN and RBV therapy; §Detectable, but ≤1000 IU/mL. Higher values necessitate discontinuation of all therapy (see Table 7).*

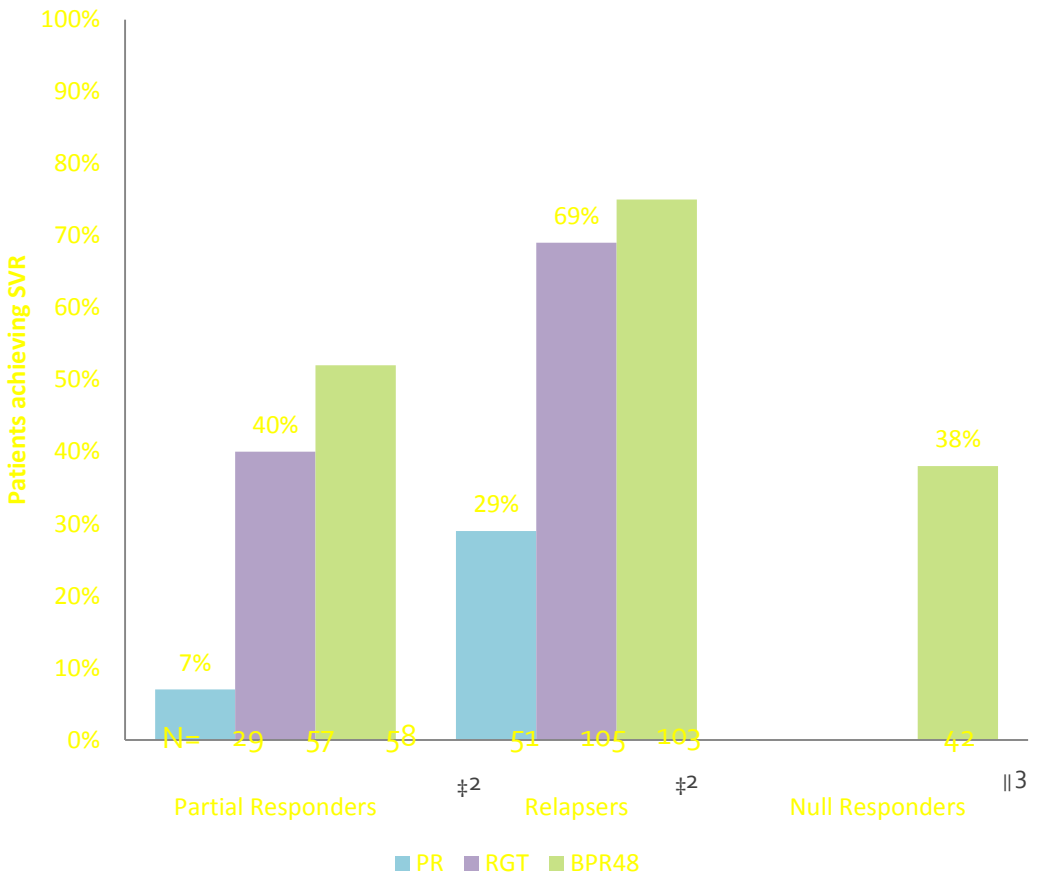
Partial responder – 2 log decrease in HCV RNA but still RNA positive at wk 24 or 48

Treatment:

Boceprevir

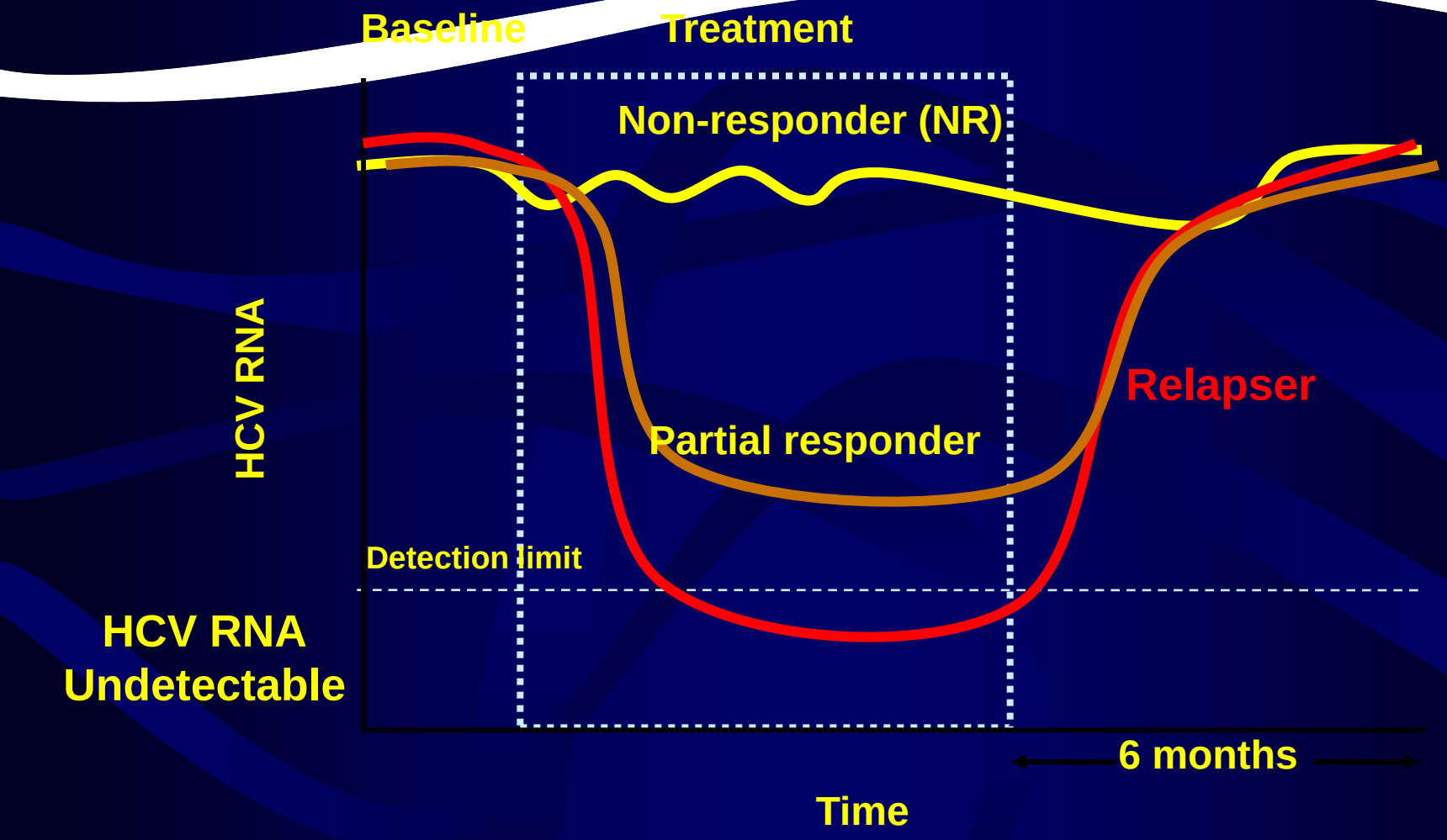
SVR rates following boceprevir treatment in various patient cohorts





PR: peginterferon-alpha and ribavirin; RGT: response-guided therapy; SVR: sustained viral response

Patterns of Virological 'Non-Response'



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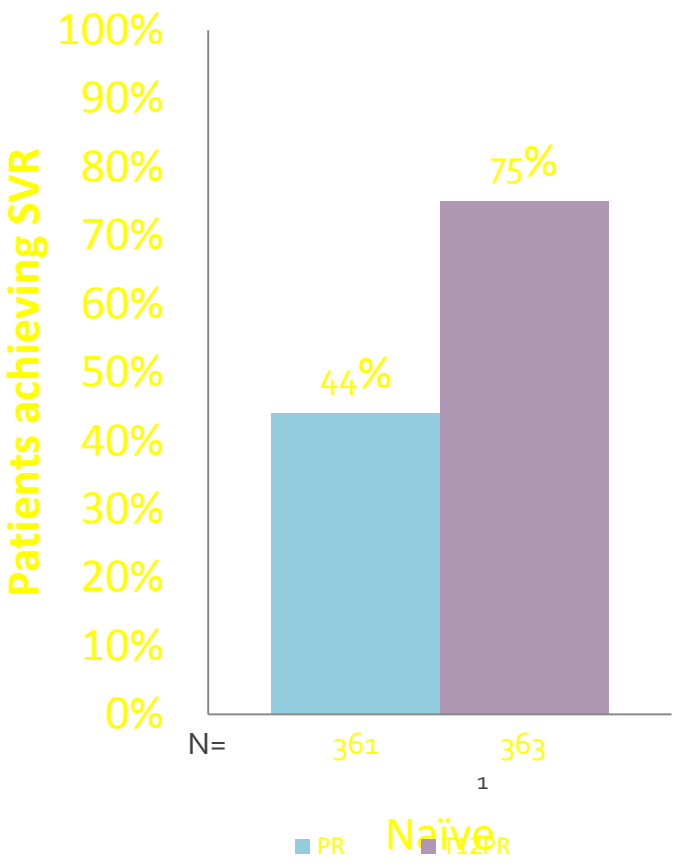
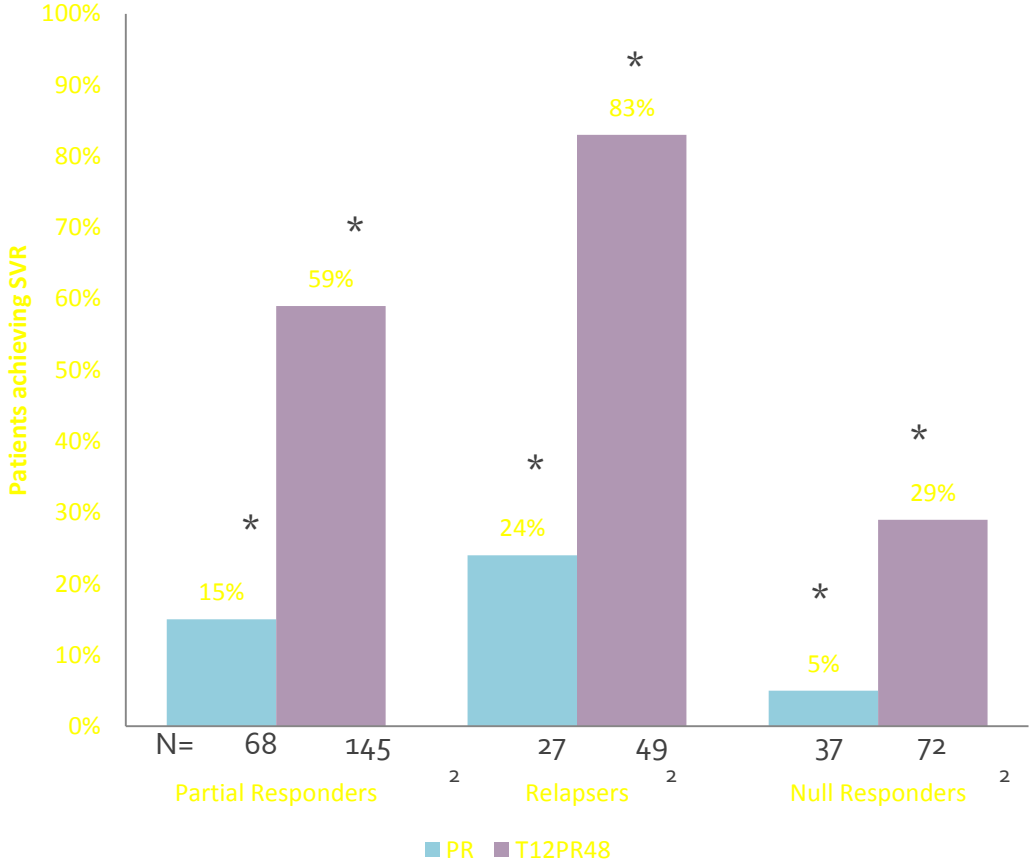
Telaprevir

SVR rates following telaprevir treatment in various patient cohorts



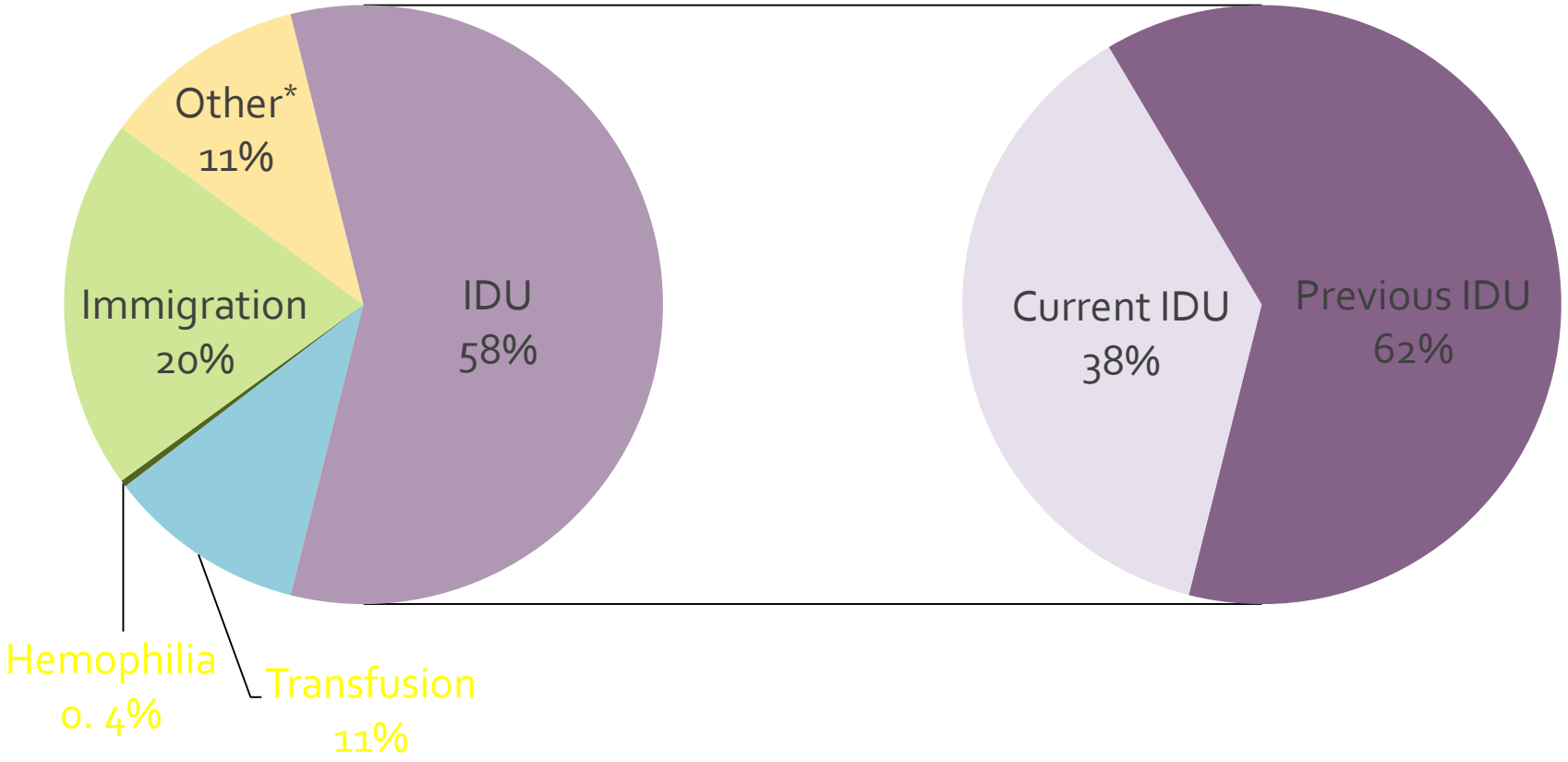


PR: peginterferon-alpha and ribavirin; SVR: sustained viral response

What are the most prevalent risk factors associated with HCV?

1. **Born between 1945-1965**
2. **Injection drug use**
3. **Resided in a country with high prevalence of HCV**
4. **2 and 3**
5. **All of the above**

Proportion of Canadian Prevalence According to Exposure



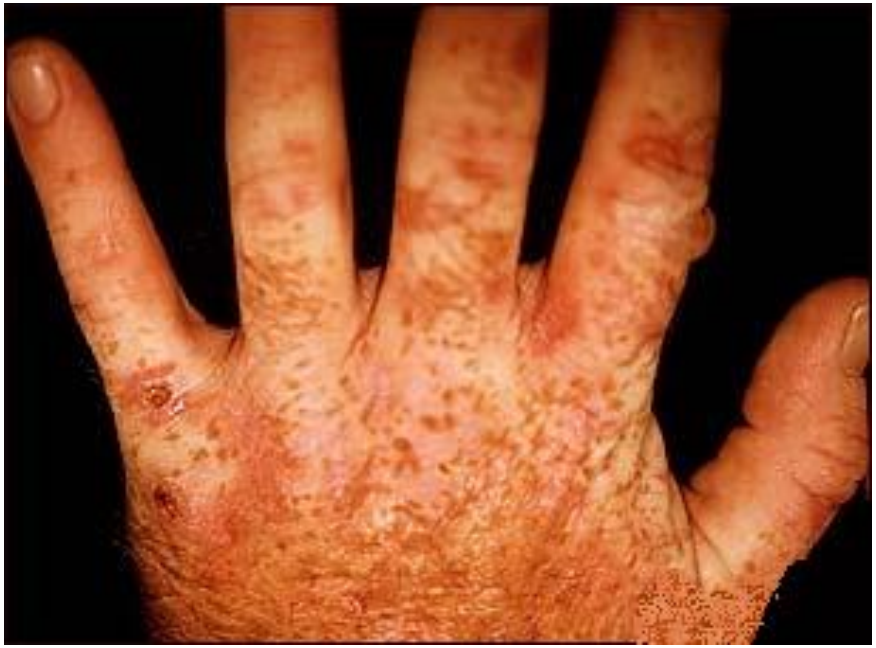
Screening:
Other Risk Factors[1]

- Sharing sharp instruments or personal hygiene materials with an infected individual
- Shared contaminated materials involved in tattooing, piercing, ceremonial rituals, or intranasal/inhalation drug use
- Homelessness or residency in group homes or shelters
- Higher-risk sexual activity

In a recent CDC survey, 45% of infected individuals reported no known exposure to risk factors[2]

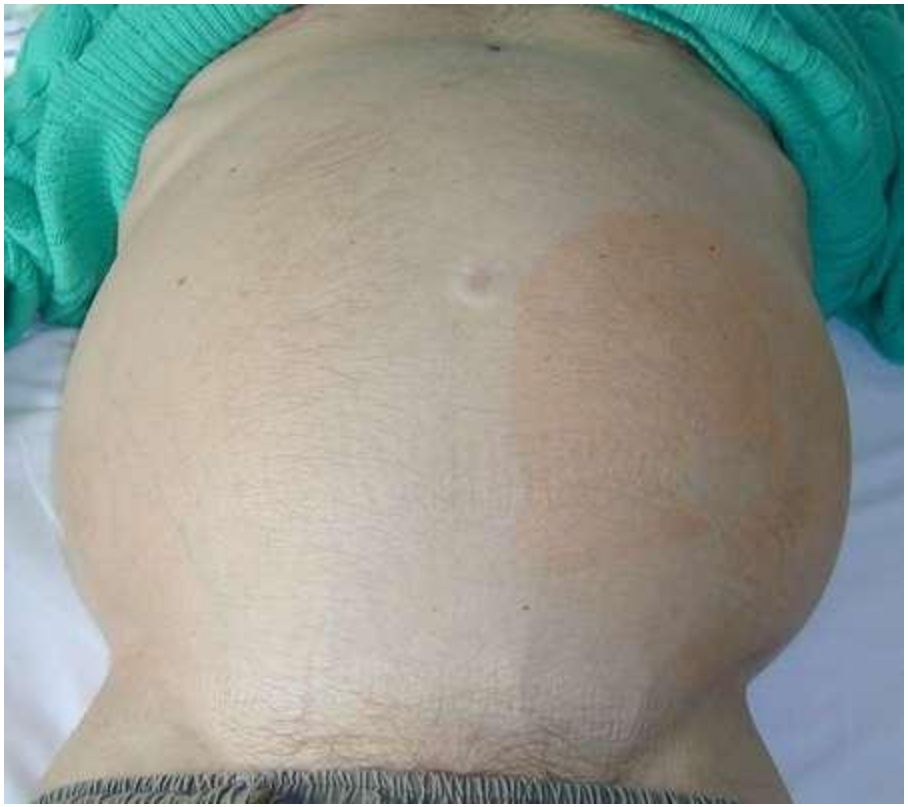
Other Diseases Associated with Hepatitis C

Porphyria Cutanea Tarda



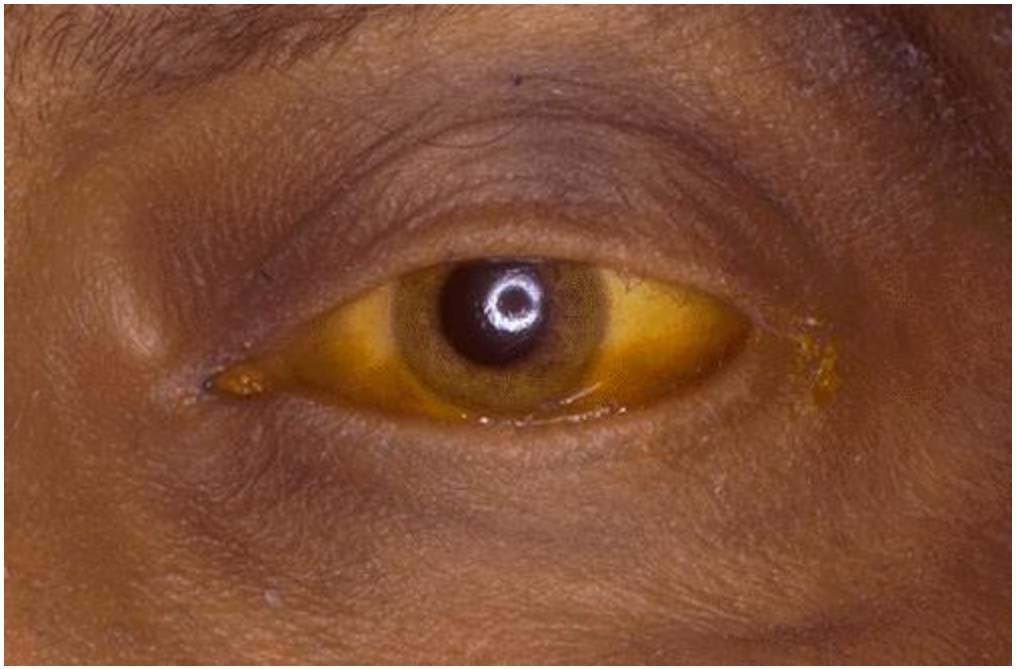
Signs of Advanced Liver Disease

Ascites



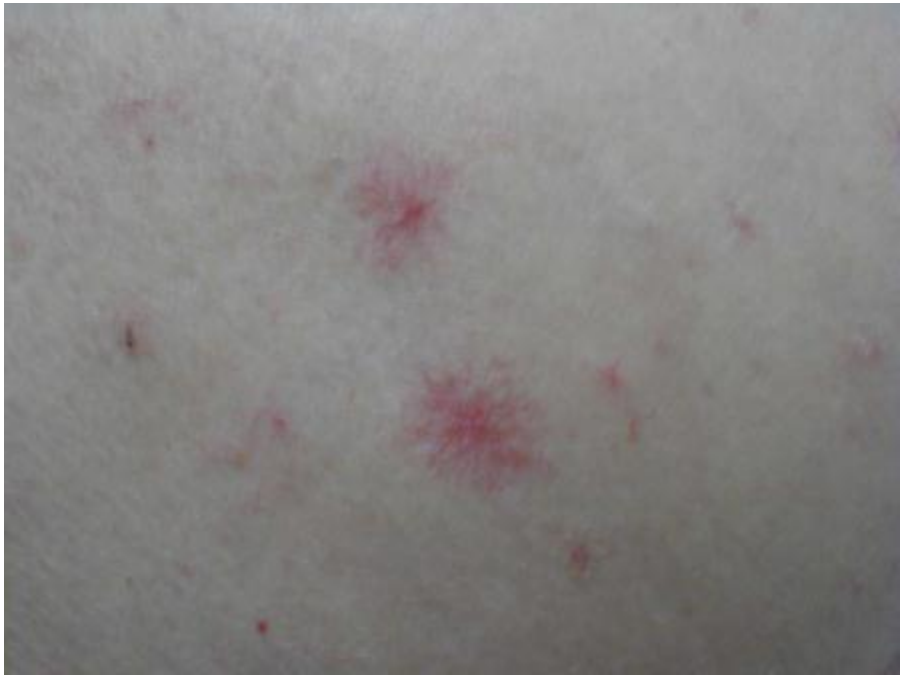
Signs of Advanced Liver Disease

Jaundice



Signs of Advanced Liver Disease

Spider angioma



Course Objectives

- Have increased knowledge of primary care management for patients with Hepatitis C.

- Who should we be screening for HCV infection?

Screening:
Risk Factors

High Risk[2,3]

- Injection drug use (IDU) (58% of chronic infections)
- Receipt of healthcare where there is a lack of universal safety precautions or where there is a higher incidence of HCV
- Incarceration
- Blood transfusion or organ transplant in Canada given prior to 1992

High-risk populations:

Refugees and immigrants	21%[4]
Prisoners	18.7%[4]
Baby boomers (1943-1967)	~5.98%[4]

Intermediate Risk[3]

- Hemodialysis
- Infant born to infected mother
- Needle stick injuries

CDC Recommendations[1,2]

(August 2012)

Screening of all those born between 1945-1965

→ One-time testing during a yearly checkup or as a part of insurance blood work

- Prevalence of HCV in this population is 5 times greater than in other age groups
- In the US, >75% of adults with chronic hepatitis C are baby boomers
- In 2007, 73.4% of HCV-related deaths were in persons between the ages of 45 and 64 years

CDC: Centers for Disease Control and Prevention

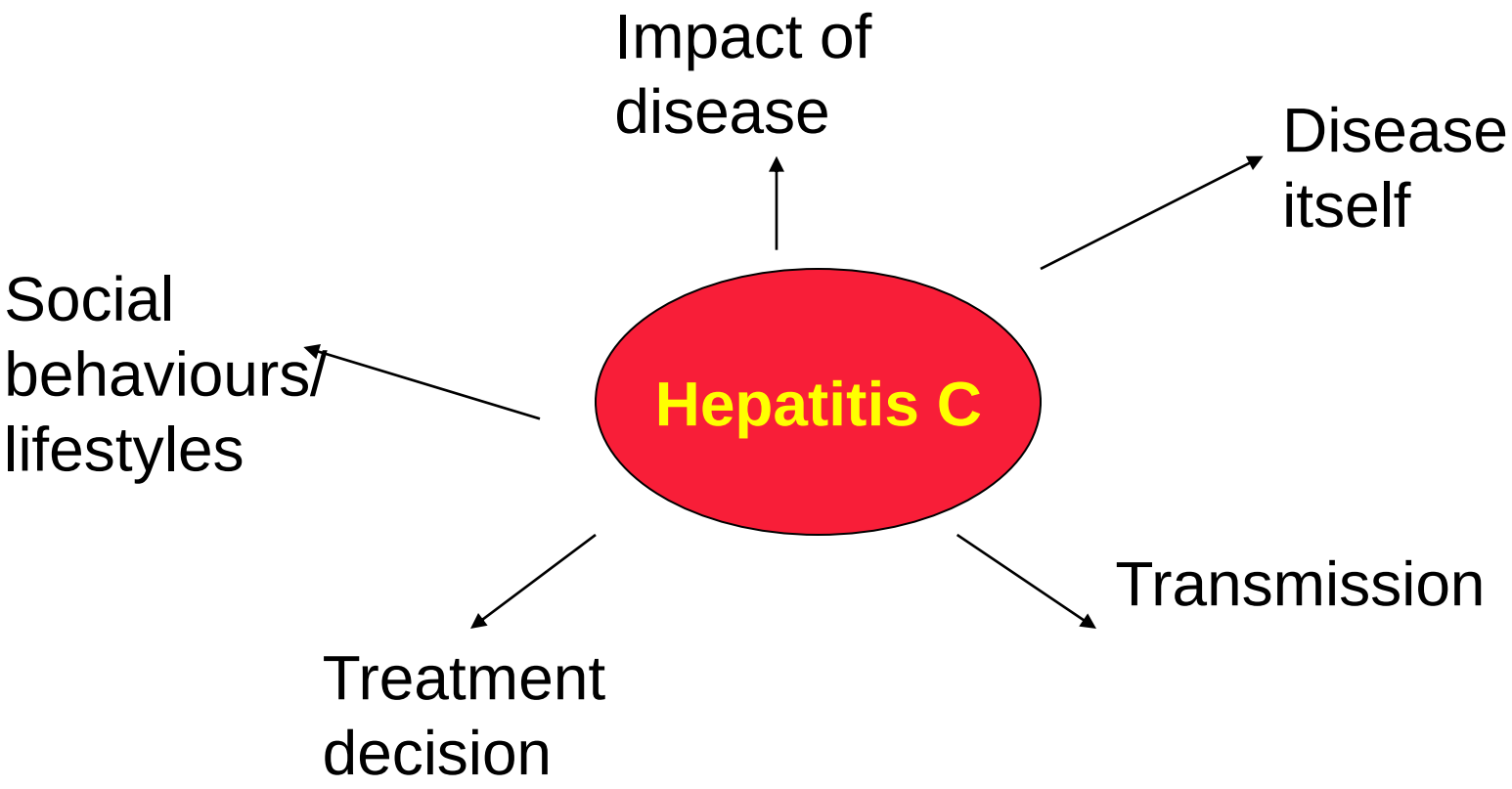
1. Hepatitis C: Proposed Expansion of Testing Recommendations, 2012. Available from: http://www.cdc.gov/nchhstp/newsroom/docs/HCV-TestingFactSheetNoEmbargo508.pdf; 2. Centers for Disease Control and Prevention. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6104a1.htm?s_cid=rr6104a1_w.

HCV Patient Education:
Role of the Primary Care Physician[1]

The role includes:

- Providing information regarding
  - Reduction of liver damage
  - Prevention of transmission and re-infection
  - How to live well while infected
- Educating the patient on HCV, informing about support resources and treatments available and supporting through treatment.

Patient Education & Counseling



Counseling the Patient; Impact of Disease

- Physical: minimal to moderate symptoms
- Emotional: shock, guilt, fear, stress, uncertainty
- Social: stigma, labeling of disease
- Financial: loss of work or income, treatment cost

Course Objectives

After this case based presentation the attendee will:

- Have an improved understanding of who to refer for treatment of Hepatitis C.

Referral Guidelines:
Criteria for Referral and Referral Network

- All patients with chronic HCV should be considered for antiviral therapy, especially those with evidence of liver fibrosis[2,4]
  - Patients with evidence of advanced liver fibrosis or cirrhosis (F_3/F_4) should be treated immediately[2,4]
- Refer to an experienced colleague such as hepatologist, gastroenterologist, infectious diseases specialist, or physician with experience in HCV management.

Consensus Guideline 2011

All patients with chronic hepatitis C who have compensated liver disease, are willing to undergo therapy and have no contraindications, should be considered candidates for antiviral treatment.

Who to refer for treatment of Hepatitis C.

Patient characteristics that are no longer considered to be contraindications:

- Normal alanine aminotransferase level
- Injection drug use
- Stable methadone maintenance
- Neutropenia, anemia or thrombocytopenia
- Controlled seizure disorder
- Older than 65 years of age
- Alcohol use

Patient Counseling:
Chronic Infection[1]

Reducing liver damage

- Limit **alcohol** intake[1,2]
- Maintain a healthy body weight* [1,2]
- Ensure HAV & HBV immunity
- Consider therapy for hepatitis C

Living well with HCV

- Adhere to, and be actively involved in, the follow-up and monitoring of your hepatitis C infection
- Be informed – obtain current/accurate information about hepatitis C

Counseling: Healthy Liver Care

- Careful use of medications & alternative meds

  Some are potentially hepatotoxic

  (e.g., acetaminophen >2 or 3 Gram/day, Senna, Vitamin A)

- Recommend Hep A & B vaccine if susceptible

Q What are the most prevalent risk factors associated with HCV?

A

Born between 1945-1965

Injection drug use

Resided in a country with high prevalence of HCV

Egypt, Somalia, Pakistan, Bangladesh, Vietnam or non-recent immigration from Italy, Greece, Spain[1]

1. Sherman et al. Can J Gastroenterol. 2007;21(Suppl C):25C-34C.

SVR True or False?

Achieving a SVR sustained virologic response with treatment is considered a cure of hepatitis C.

Criteria for Screening:
Symptoms*[1-3]

•Fatigue •Nausea, loss of appetite • Arthralgia

•Abdominal pain •Mild hepatosplenomegaly

60%-75% of patients are asymptomatic[4]

Possible dermatological signs:

- •Mixed essential cryoglobulinemia
- •Lichen planus
- •Porphyria cutanea tarda
- •Maculopapular rash
- •Jaundice (past or present)

Other possible extrahepatic manifestations:

- • Membranous or membranoproliferative glomerulonephritis
- • Non-Hodgkin's lymphoma
- • Sjögren's syndrome

*Symptoms described are non-specific and not strongly associated with hepatitis C.

1. Wong and Lee. CMAJ. 2006 Feb 28;174(5):649-59; 2. Centers for Disease Control and Prevention. Available from: www.cdc.gov/hepatitis/resources/professionals/pdfs/abctable.pdf; 3. 4. Seeff LB. Hepatology 2002;36(Suppl 1):S35-46.

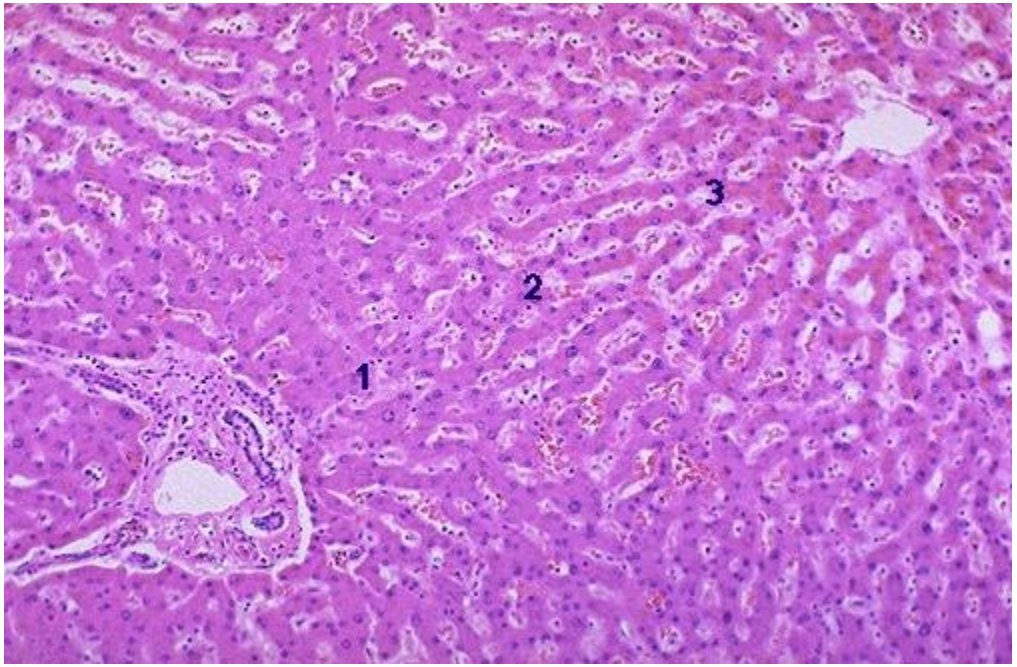
Evaluation:
Assessing Degree of Fibrosis[1,2]

- Methods for assessing presence of fibrosis/cirrhosis:
  - Non-invasive alternatives: FibroScan, FibroTest, serum biomarker panels (liver function tests), ultrasound-elastography
  - Liver biopsy (only in certain cases)*[3]
- Indications of cirrhosis:
  - Low platelets[2,3]
  - Splenomegaly
  - Nodular shrunken liver

Not all patients require a liver biopsy.

1. Myers et al. Can J Gastroenterol. 2012;26(6):359-75; 2. Pinette et al. Public Health Agency of Canada. Available from: http://www.phac-aspc.gc.ca/hepc/pubs/pdf/hepc_guide-eng.pdf; 3. Consensus recommendations of the Steering Committee.

Normal Liver

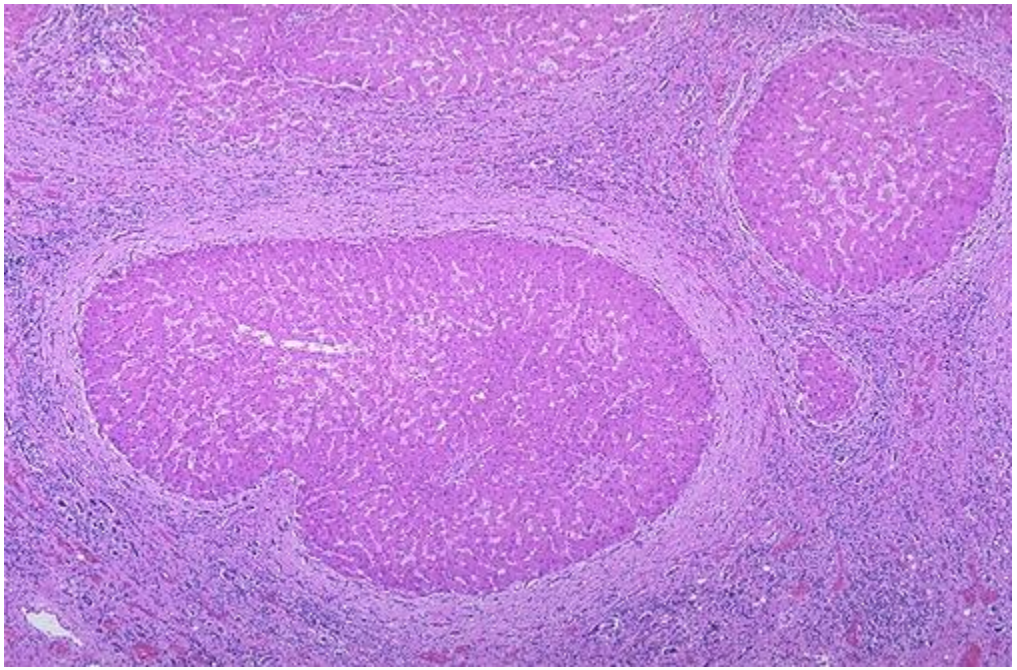


F4=Cirrhosis

Stage	Histologic criteria
1	Zone 3 perivenular perisinusoidal/pericellular fibrosis, focal or extensive · 1A - delicate perisinusoidal fibrosis · 1B - dense perisinusoidal fibrosis · 1C - portal-only fibrosis
2	As above with focal or extensive periportal fibrosis
3	Bridging fibrosis, focal or extensive
4	Cirrhosis

Kleiner DE, et al. Design and validation of histologic scoring system for nonalcoholic fatty liver disease. Hepatology 2005;41:1313-21.

Cirrhotic Liver



Evaluation:
Assessing Degree of Fibrosis[1,2]

Clinical History

Request for review by Dr Hamid Masoudi.
History of hepatitis C, genotype 1. "Core biopsy shows fairly advanced stage of fibrosis and portal inflammation. There is also some bile duct damage as well as neutrophilic infiltration within the lobules in the portal tract. Please rule out concomitant biliary disease"

DIAGNOSIS

(Review of slides, NRGH NS12-7324)
Core biopsy of liver:

- Chronic hepatitis C with mild activity (grade 2), with advanced septal fibrosis (stage 3)
- Mild steatohepatitis

Electronically Signed By: Dr. C Wright 250-370-8836
Date Reported: 28-May-2012

FibroScan®

TECHNOLOGIE

plus la fibrose est sévère.

CONFORT

Absence de risque pour le patient

1. L'examen est totalement non-invasif.
2. L'examen est parfaitement indolore.
3. Il n'y a aucun effet secondaire.

PALPATION QUANTITATIVE

Foie mou : pas de fibrose

Foie dur : fibrose sévère

Sonde à ultrasons montée sur un système vibrant appliquée à la surface de la peau

Durée maximum de l'examen : 5 minutes

APPLICATION

Meilleure prise en charge thérapeutique

1. Le diagnostic peut être élargi aux sujets à risque pour lesquels la biopsie n'est pas prescrite comme les hémophiles, ou aux patients qui la refusent comme les toxicomanes ou les alcoolo-dépendants.
2. Le suivi est renforcé : l'examen, dont le résultat est instantané, peut être réalisé autant de fois que nécessaire.
3. Le diagnostic n'est pas perturbé par un traitement ou par une pathologie associée.

SANTÉ PUBLIQUE

Prévention accrue et réduction des dépenses

1. Des campagnes de dépistage de la cirrhose dans la population générale sont désormais possibles.
2. Le coût de l'examen est très faible :
   - pas de consommable,
   - pas d'hospitalisation,
   - pas d'infrastructure dédiée.

Treatment:
Role of Primary Care Physician During Treatment[1-3]

- Counsel and inform patient.
- Watch for concomitant medications
  - Assess potential DDIs which may impact treatment success or lead to adverse events; patient must avoid herbal supplements.[4]
- Aid patient in management of side effects
- Ensure adherence to treatment schedule[1]
  - Adherence is associated with higher rates of SVR
  - Non-adherence may cause resistance

DDIs: drug-drug interactions; HCC: hepatocellular carcinoma; SVR: sustained viral response.

1. Myers et al. Can J Gastroenterol. 2012;26(6):359-75; 2. European Association for the Study of the Liver. J Hepatol. 2011;55(2):245-64; 3. Group. Hepatology.

Drug Interaction Charts

Printable Charts | View All | View all Protease Inhibitors | View all Interferons | View all Nucleoside/tide Analogues | Back to start

Step 1	Searching by: **Boceprevir**	Amend Selection
Step 2	Searching by: **All classes**	Amend Selection
Step 3	Searching by: **Boceprevir, Buprenorphine**	Amend Selection
Step 4	View results	

Key to symbols:

Clicking on a solid symbol within a table will give further information on the interaction.
Empty symbols indicate that the combination has not been assessed (either by study or within the product label) and an interaction has been predicted based on the metabolic profiles of the drugs.

● / ○	These drugs should not be coadministered
■ / □	Potential interaction – may require close monitoring, alteration of drug dosage or timing of administration
◆ / ◇	No clinically significant interaction expected
✦ / ✧	This interaction has not been assessed
n/a	Data not available

If a drug is not listed it cannot automatically be assumed it is safe to coadminister.

NEW - click here to generate a personalised report in PDF format

Analgesics	Boceprevir
Buprenorphine	◇
Hepatitis C Protease Inhibitors	Boceprevir
Boceprevir	n/a

Course Objectives

- Have a better understanding of the important role of the GP while the patient is being treated for Hepatitis C.

Improving Adherence to HCV Therapy

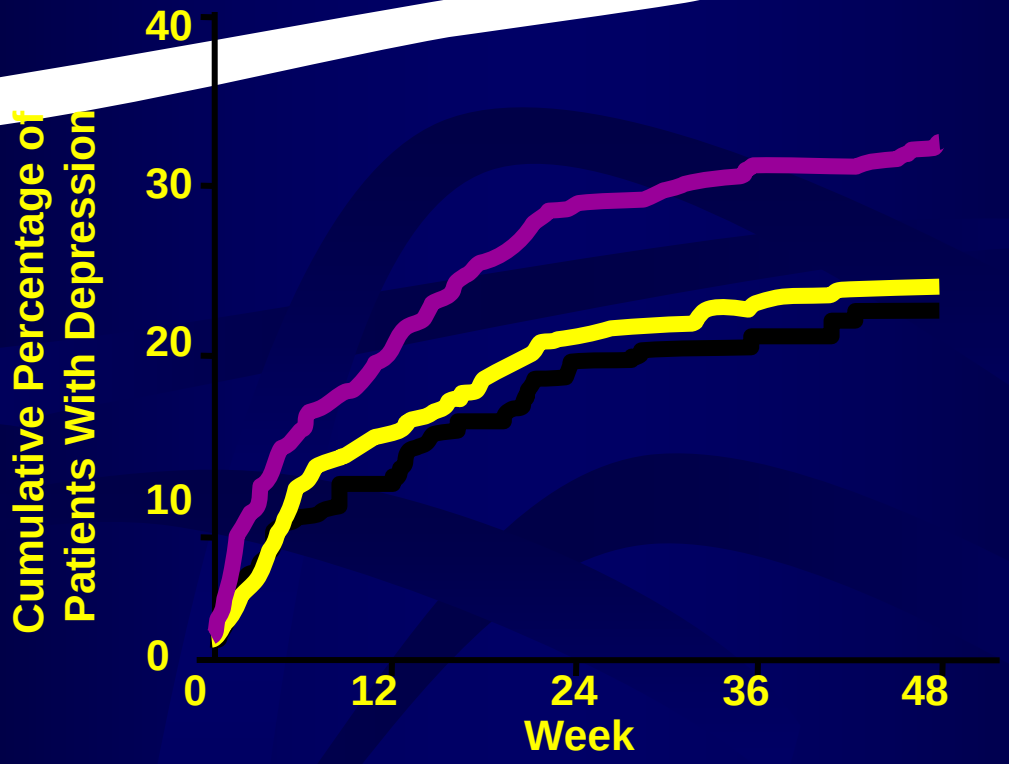
- **Address depression/substance abuse first**
- **Patient education**
  - -HCV disease
  - -Treatment regimen
  - -Side effect management
  - -Consequences of non**-**adherence
- **Patient support systems**
  - -Hepatitis Support Nurses
  - -Pharmacists
  - -Peers
- **Ask about adherence**
- **Manage side effects**

COMPLICATIONS OF TREATMENT

- Neuropsychiatric

- Headache
- Loss of concentration and memory "Brain fog."
- Depression
- Insomnia
- Psychosis
- Suicidal ideation
- Seizures

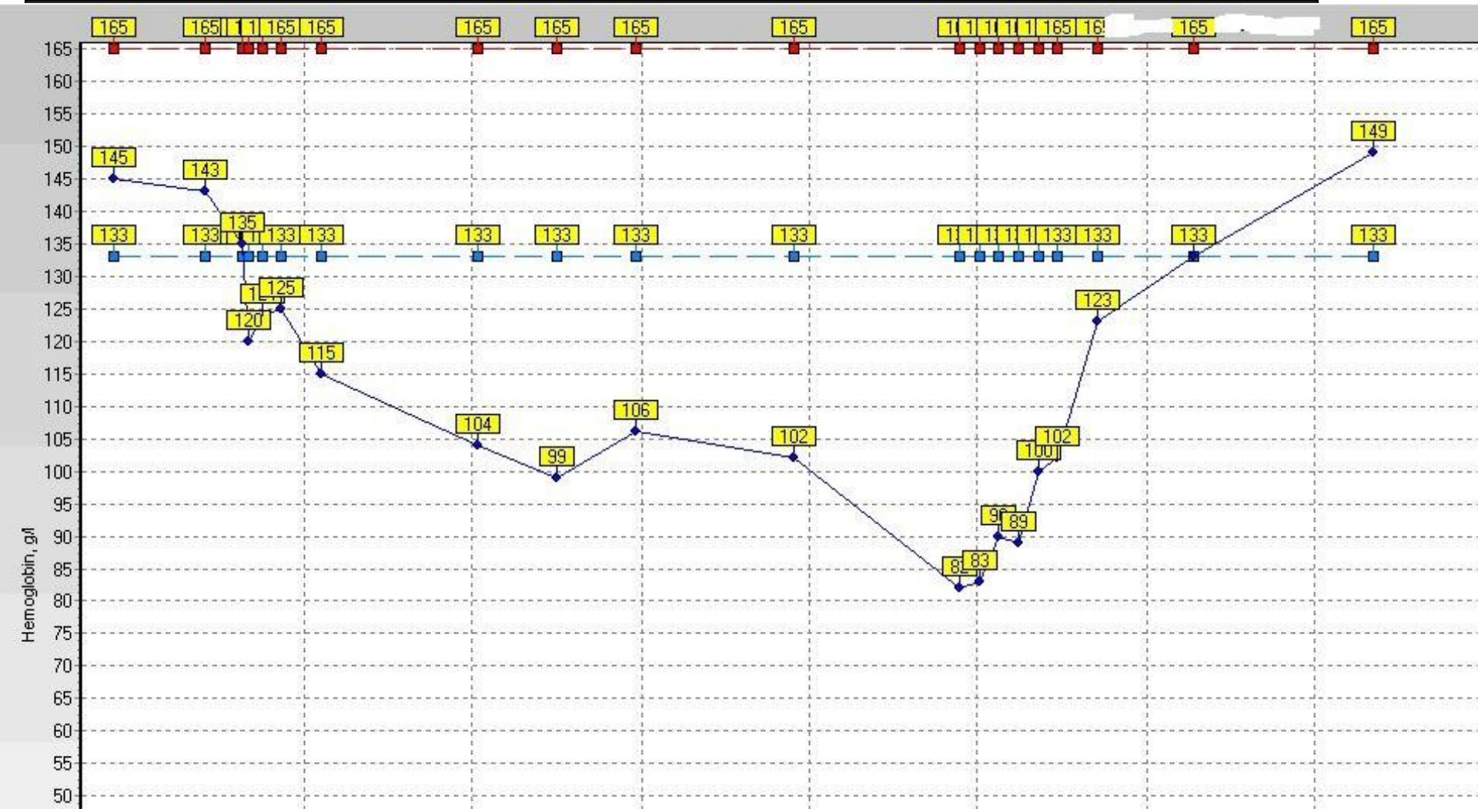
Peginterferon Alfa-2a and Interferon Alfa-2b Plus RBV: Relative Rates of Depression



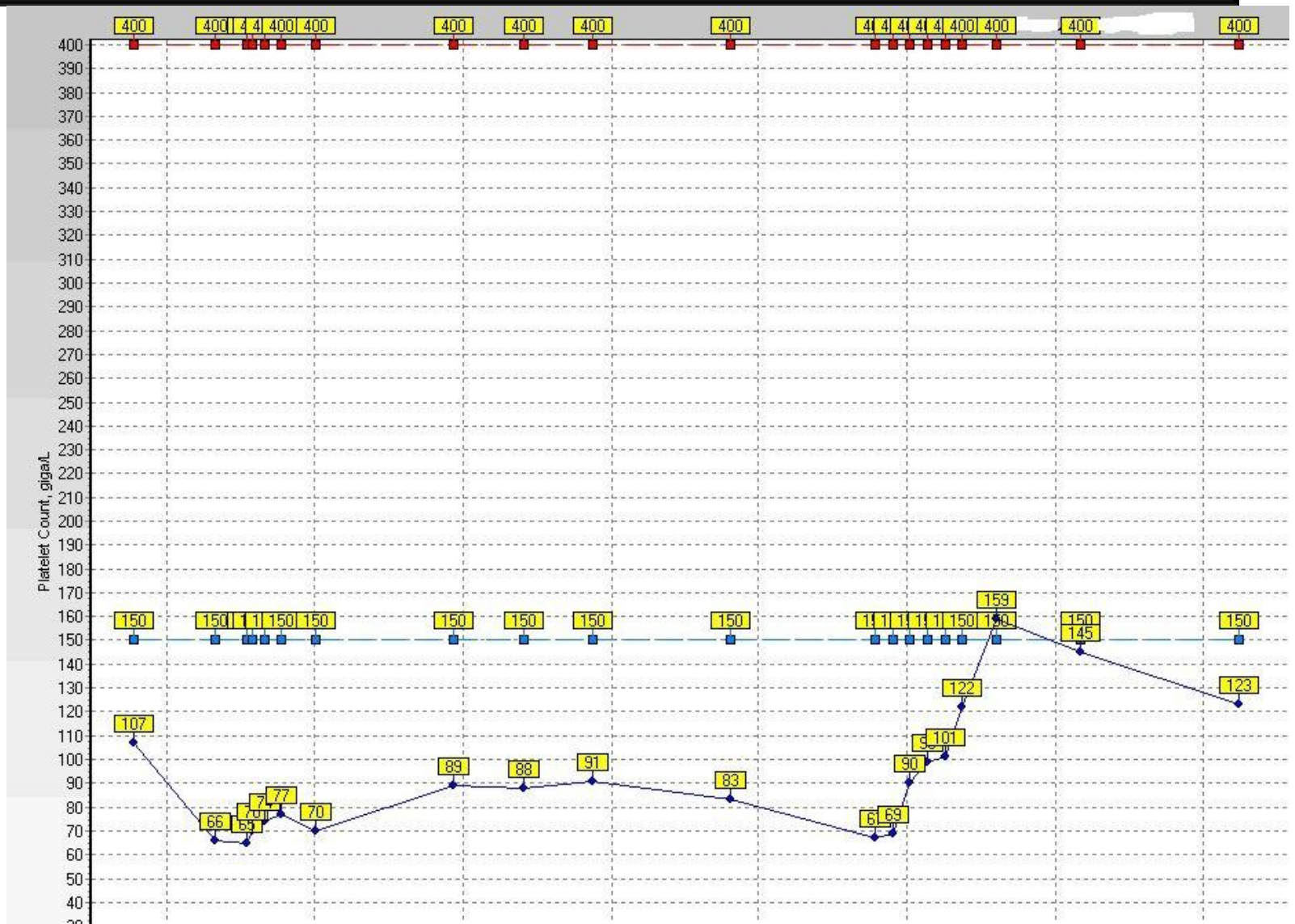
Treatment Group	n	Rate of Depression
IFN + RBV	443	30% (n = 134)
PEG-IFN 〈 -2a + RBV	451	22% (n = 100)
PEG-IFN 〈 -2a + placebo	223	20% (n = 45)

Fried MW. DDW Annual Meeting. 2001.

COMPLICATIONS OF TREATMENT



COMPLICATIONS OF TREATMENT



COMPLICATIONS OF TREATMENT

Futility rules in treatment-naive and previous treatment failure patients treated with boceprevir- or telaprevir-based triple therapy

Boceprevir	**HCV RNA result***	**Action**
Week 12	≥100 IU/mL	Stop all therapy
Week 24	Detectable	Stop all therapy
Telaprevir	**HCV RNA result***	**Action**
Week 4	>1000 IU/mL	Stop all therapy
Week 12	>1000 IU/mL	Stop all therapy
Week 24	Detectable	Stop all therapy

**Hepatitis C virus (HCV) RNA should be quantified using an assay with a lower limit of detection of no greater than 10 IU/mL to 15 IU/mL*

Course Objectives

After this case based presentation the attendee will:

- Have an improved understanding of who to refer for treatment of Hepatitis C.
- Have an increased awareness of the referral process for potential treatment of Hepatitis C patients.

Course Objectives

- Have a better understanding of the important role of the GP while the patient is being treated for Hepatitis C.
- Have increased knowledge of primary care management for patients with Hepatitis C.