

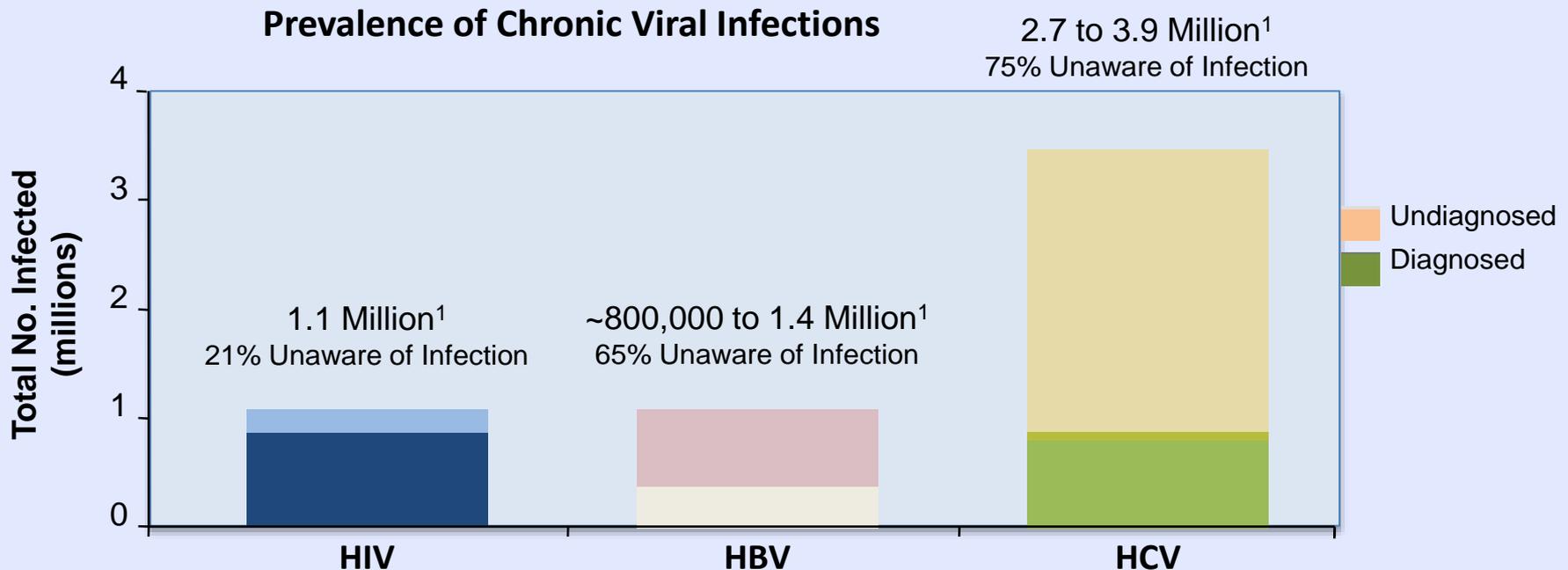
The Hitchhiker's Guide to HCV Therapy

Julio Gutierrez, MD
Assistant Professor
Texas Liver Institute
UTHSCSA
San Antonio, TX

Disclosures

- Scientific advisor, research funds or speaker for Janssen, Gilead, BMS, and Abbvie.
- Slides are available if you email me:
gutierrez@txliver.com

HCV is nearly 4 times as prevalent as HIV and HBV



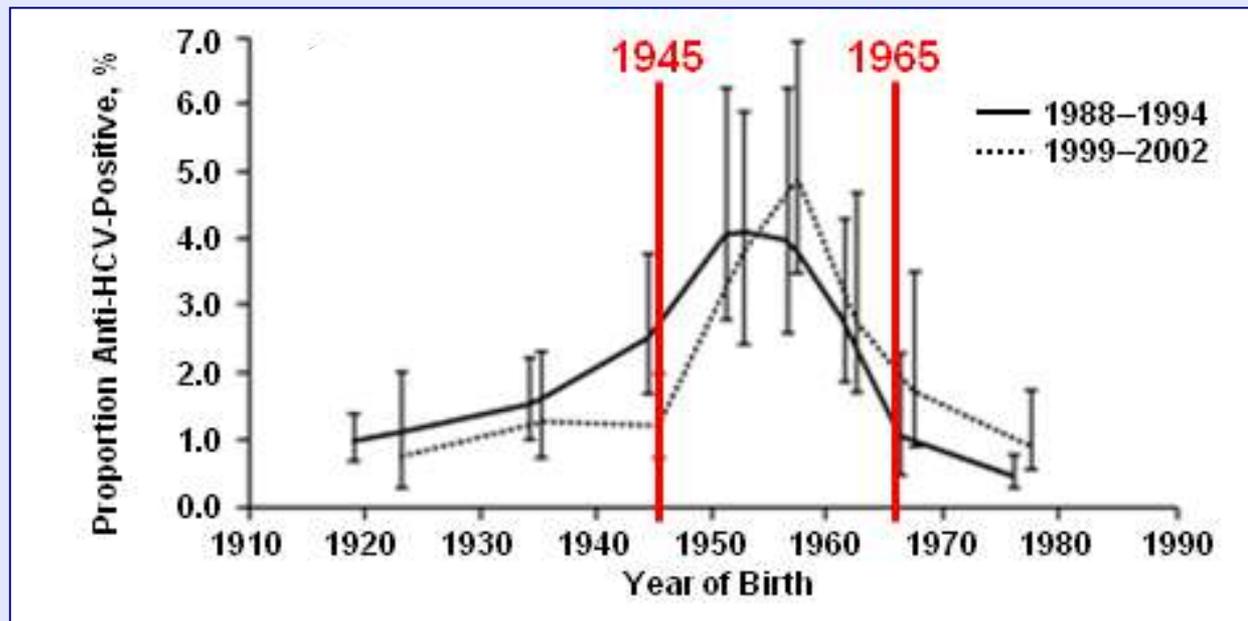
- A 2011 study estimated that as many as 5.2 million persons are living with HCV in the United States²

HBV=hepatitis B virus; HCV=hepatitis C virus; HIV=human immunodeficiency virus.

1. Institute of Medicine. Washington, DC: The National Academies Press; 2010.
2. Chak E, et al. *Liver Int.* 2011;31(8):1090-1101.

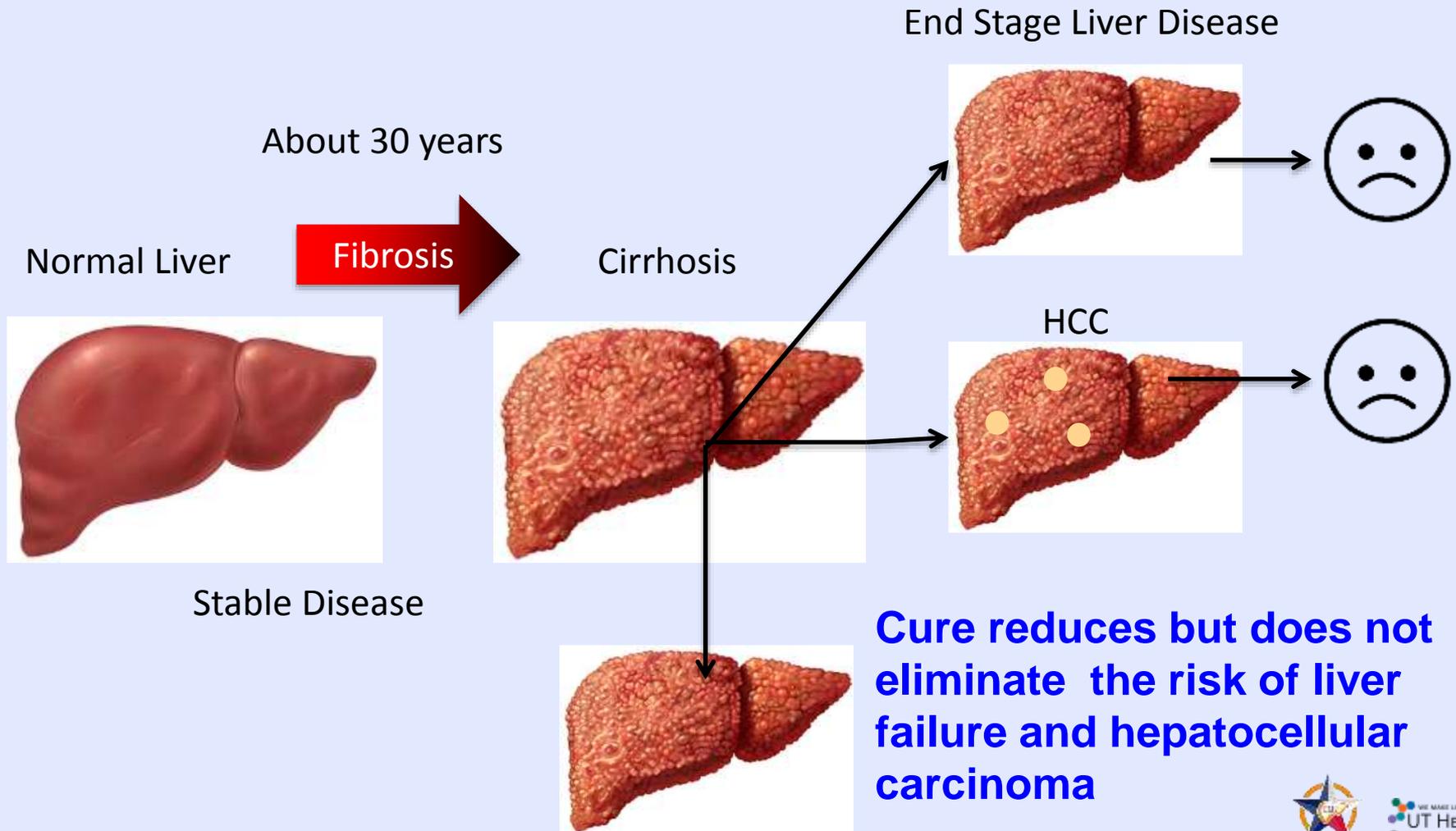
Two of three Americans infected with HCV were born from 1945-1965

- Reflects high incidence in past
- 5x higher prevalence than other birth cohorts (3.4 vs. 0.5%)
- 81% of HCV infected adults and 73% of HCV mortality.



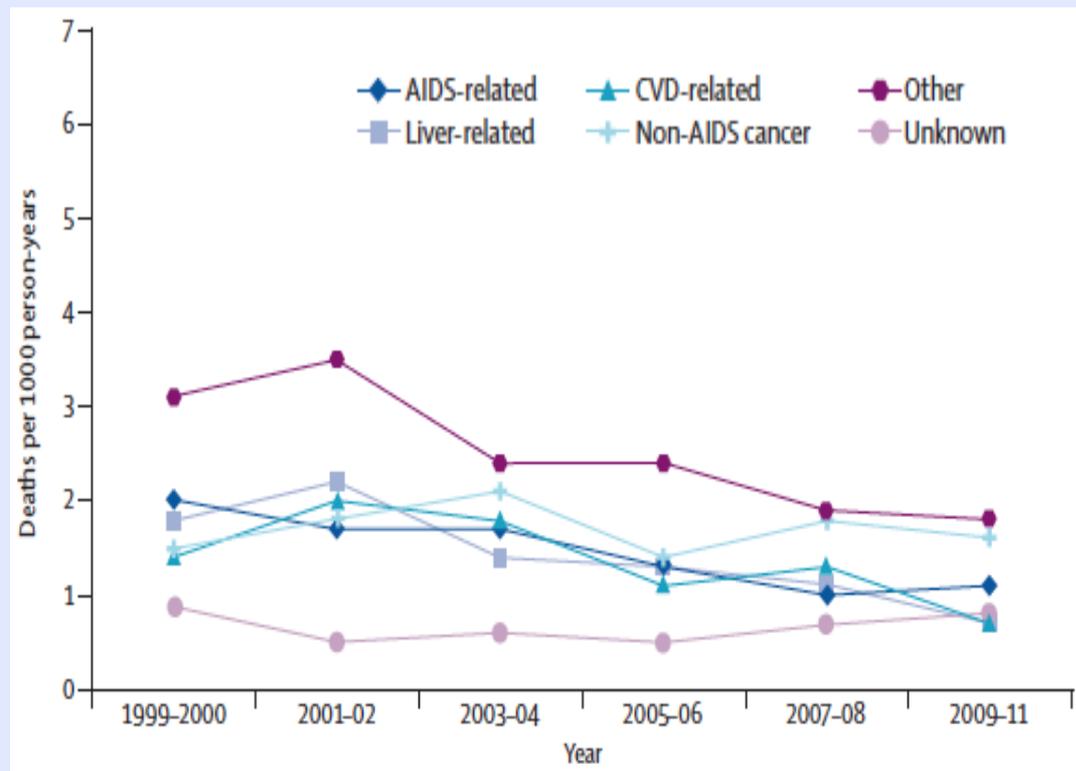
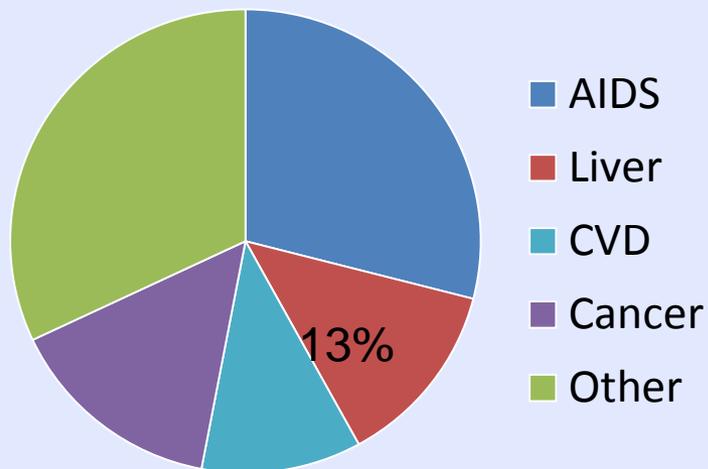
CDC RECOMMENDATION: Screen all individuals born between 1945-1965

Liver disease progresses over time with chronic HCV infection

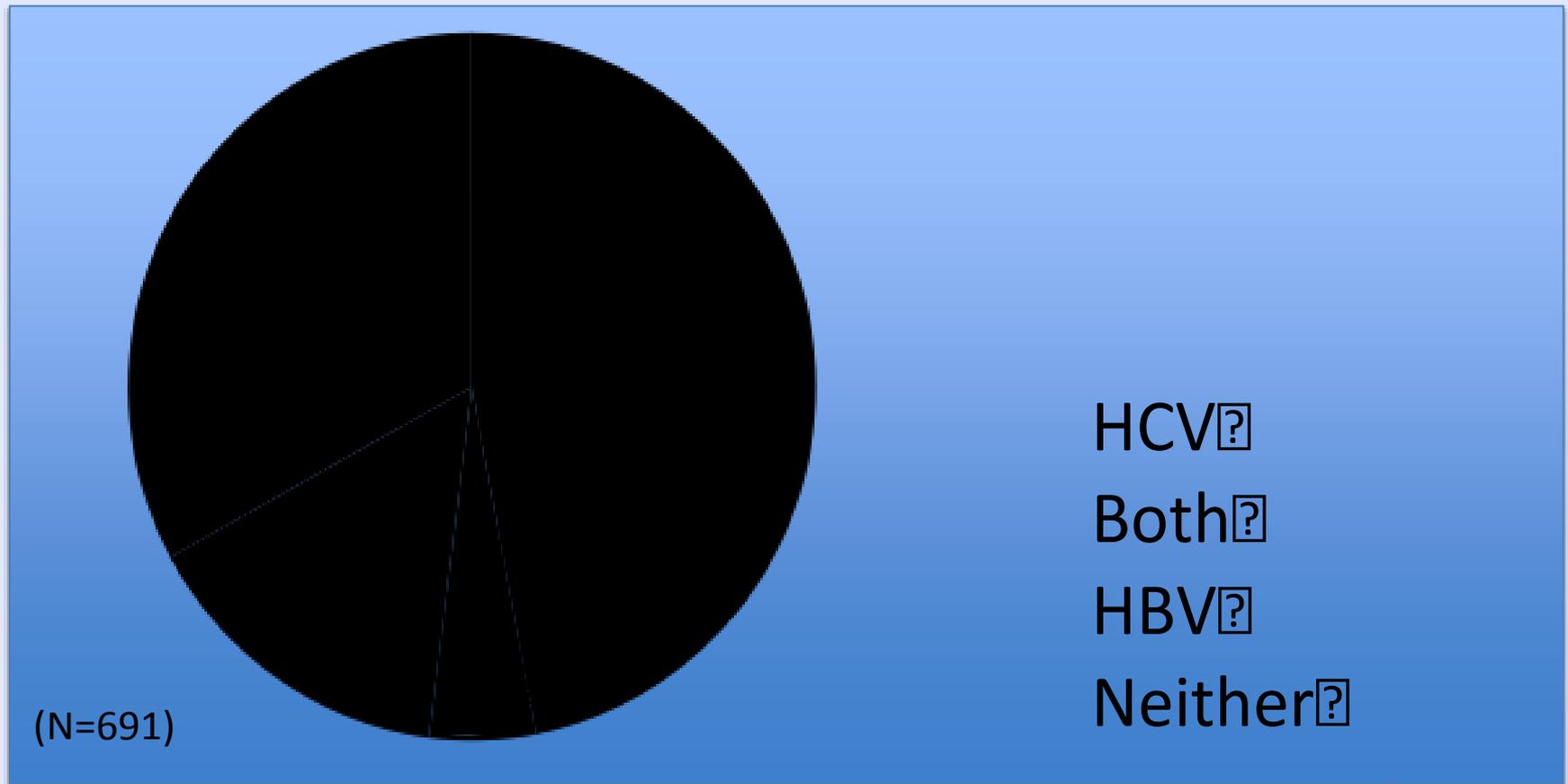


Liver Disease Remains a Major Cause of Mortality in HIV

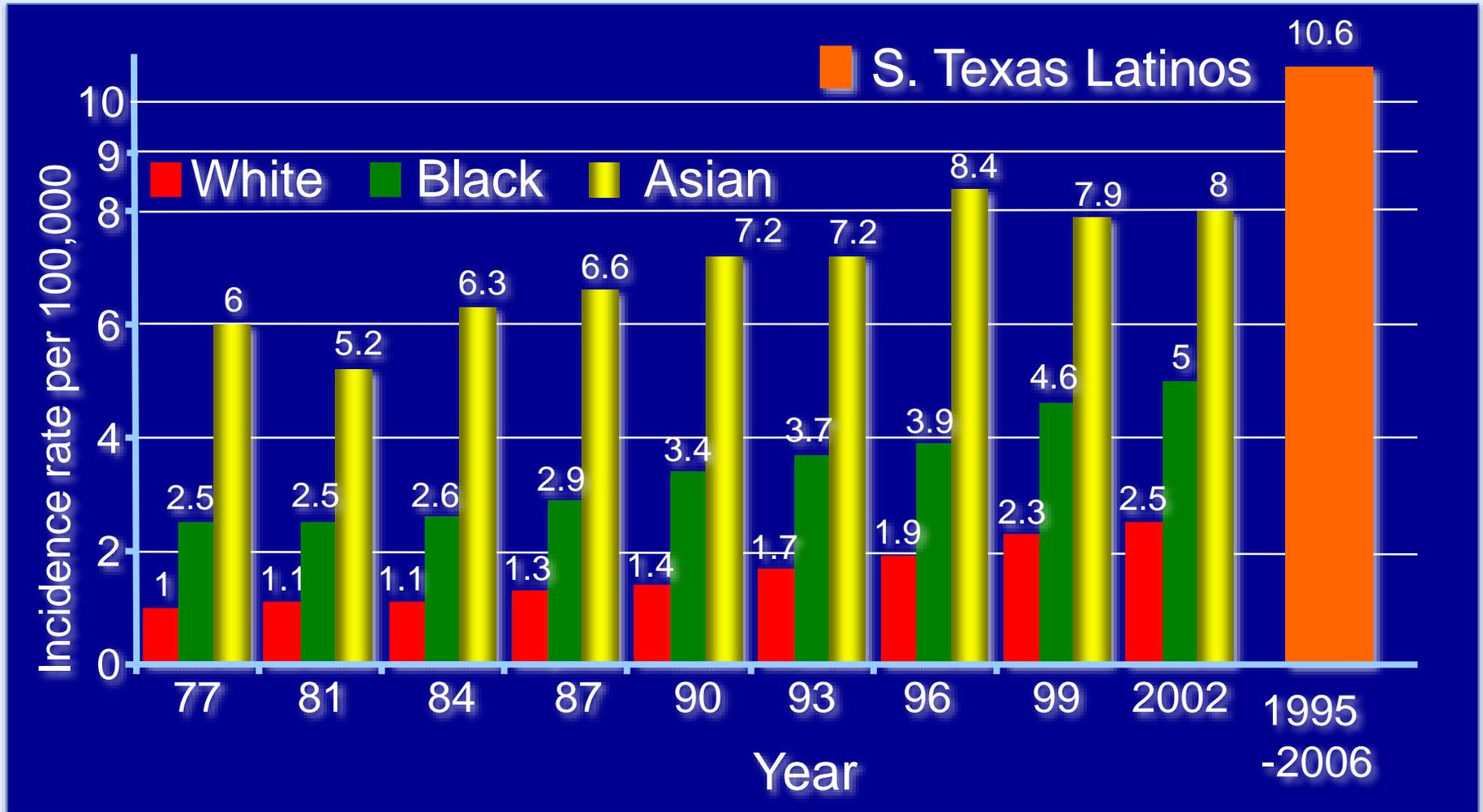
Cause of Death



HBV and HCV are the Dominant Causes for HCC in the US



Racial-ethnic incidence rates* for HCC in U.S. and Latinos in S. Texas



El-Serag HB et al, Ann Intern Med 2003

Ramirez AG, PloS one 7: e35573.

* Per 100,000

Key Points: History and Physical Exam: Looking for Signs of Cirrhosis

HISTORY

- History of jaundice, ascites/edema, GI bleeding/varices or hepatic encephalopathy.
- Being told they have cirrhosis, or previous biopsy.
- Heart and kidney disease may impact.

PHYSICAL EXAM

- Jaundice
- Temporal wasting
- Spider angiomas
- Gynecomastia
- Ascites
- Hepatomegaly or splenomegaly.
- Edema
- Asterixis or confusion

Excluding Cirrhosis is Important

- Presence of cirrhosis:
 - Triggers routine cirrhosis care
 - Evaluation for varices
 - Surveillance for hepatocellular carcinoma
 - Negatively affects likelihood of achieving sustained viral response (SVR) with treatment
 - May increase treatment duration
 - May require additional treatment with ribavirin

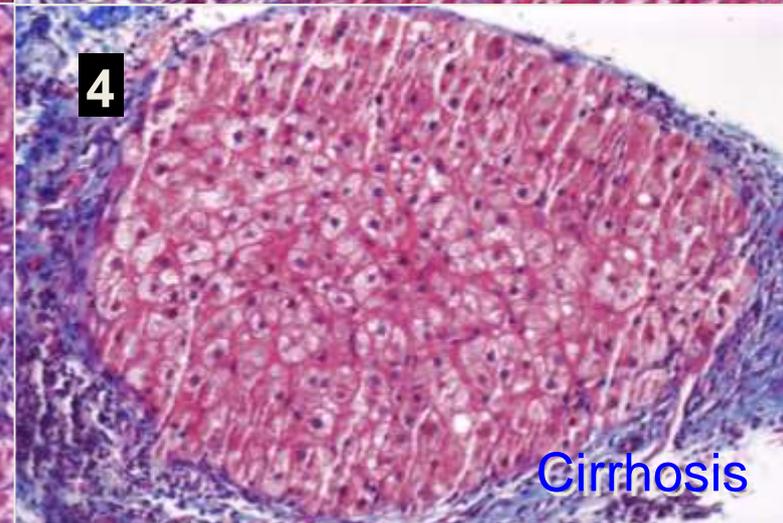
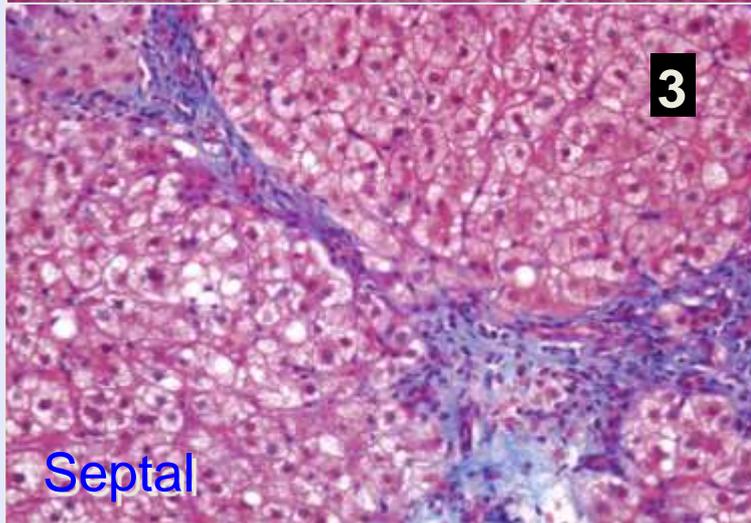
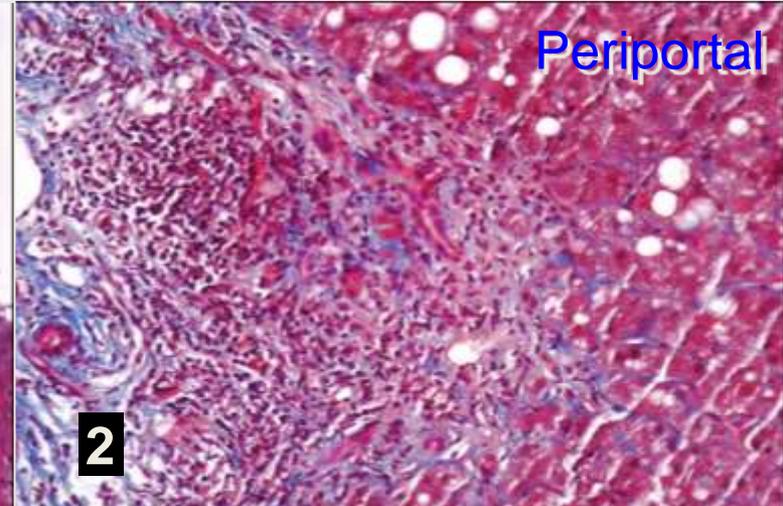
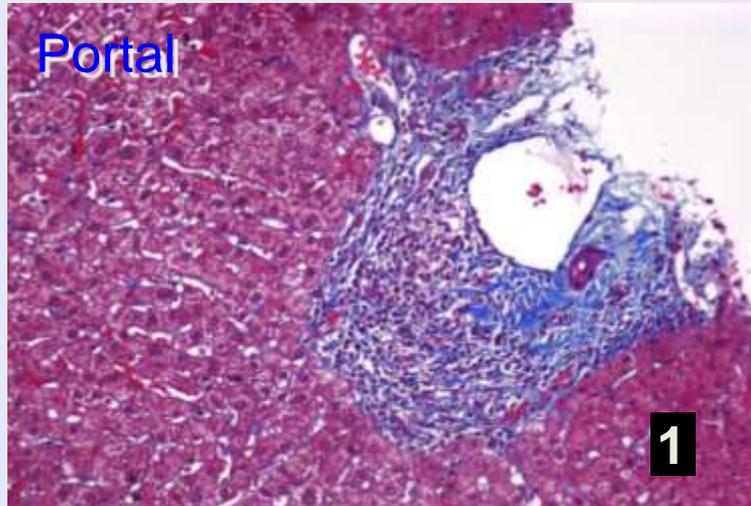
Other Relevant Data: Planning for Therapy

- Medications:
 - Start considering significant drug-drug interactions (DDIs)
- Pre-Treatment Evaluation:
 - Alcohol use.
 - Signs of non-compliance (elevated A1C, or unclear of medications that are being taken)
 - Social support, substance abuse
 - Pregnancy risk
 - Psychiatric evaluation no longer needed (severe depression was a risk for suicide with interferon),
 - Although patients with known issues should be in care.

Interpreting Labs in Patients with HCV

- HCV Labs:
 - HCV RNA and Genotype.
- Liver Function: Albumin, bilirubin and prothrombin time.
 - Alert: Albumin <3.5g/dL or INR/TB above ULN.
- Liver Enzymes: AST, ALT and ALK Phos
 - May be up to 10 X ULN in HCV infection or normal.
- Marker or Portal Hypertension: Platelet Count.
 - Alert: Platelet <170 suspicious, and <140 highly suspicious for cirrhosis.
- Anemia: If patient requires ribavirin.
 - Average drop about 2.5 g/dL with ribavirin.

Four Stages of Fibrosis



Staging Liver Fibrosis

- Liver biopsy is gold standard but excluding cirrhosis may also be possible with noninvasive estimates of liver fibrosis
 - **Fib-4 or APRI** or equivalent serum tests are widely available.
 - Fibroscan in special centers
 - MRI elastography not widely available.

Calculating Fib-4

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = \text{1.45}$$

Non-cirrhotic

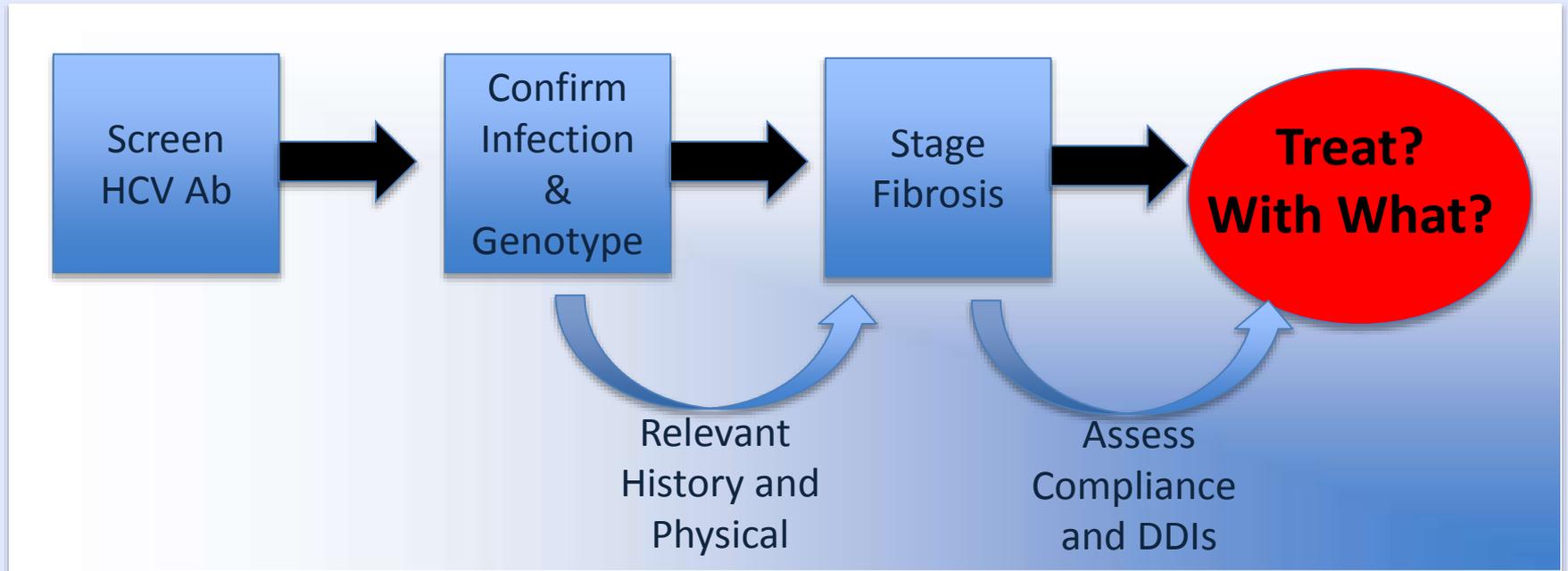
3.25

Cirrhotic

Interpretation:

Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

Preparing for HCV Therapy

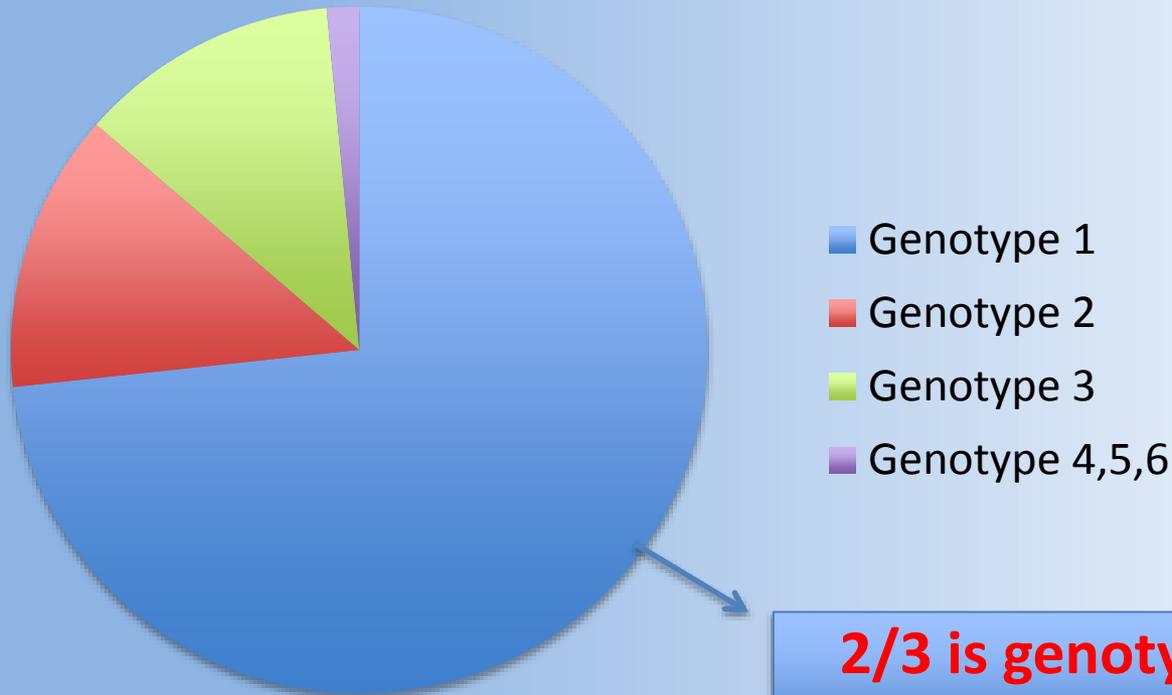


HCV Evaluation and Staging

- Treatment history (interferon therapy or DAA)
- Genotype (1, 2, 3..) and subgenotype (1a vs 1b).
- Imaging
- Viral load (copies/mL)
- Fibrosis score (i.e. Fib-4)
- Drug-drug interactions (DDIs)

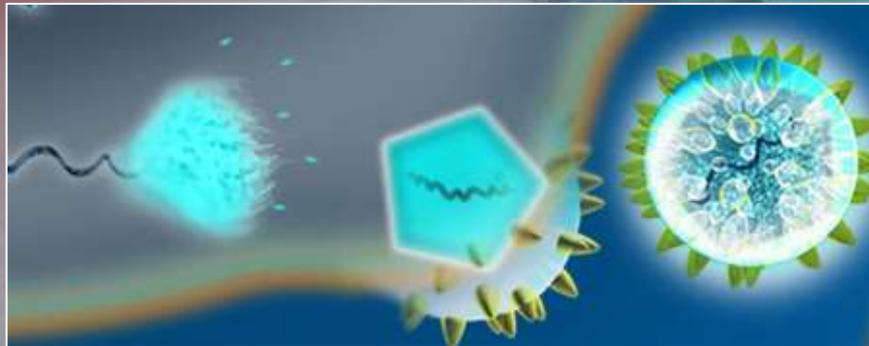
HCV Genotype 1a: Most Common in US

US Distribution



2/3 is genotype 1a
1/3 is genotype 1b

HCV Genome



HCV DAA Nomenclature

- DAA= Direct-acting Antivirals
- HCV Protease Inhibitors: ending in **previr**
 - e.g. Paritaprevir
- HCV NS5A Inhibitors: ending in **asvir**
 - e.g. Ledipasvir
- HCV Polymerase Inhibitors: ending in **buvir**
 - e.g. Sofosbuvir
 - Includes nucleotide/non-nucleoside analogs

HCV Novel DAAs



NS3/4A Protease inhibitors

- Simeprevir-SIM (COSMOS)
- Paritaprevir-PTV (Viekira)

NS5A Inhibitors

- Ledipasvir-LDV (Harvoni)
- Ombitasvir-OBV (Viekira)
- Daclatasvir-DCV (Daklinza)

NS5B Nucleos(t)ide inhibitors (NI)

- Sofosbuvir-SOF (COSMOS or Harvoni)

NS5B Non-nucleoside inhibitors (NNI)

- Dasabuvir-DSV (Viekira)

Principles of all Oral Regimens for HCV

- Combine drugs from different classes
 - Hit multiple viral targets to increase efficacy
 - Diminishes risk of viral resistance
- Benefits of multi-drug strategies
 - Backbone/anchor drug plus additional agent(s)
 - Superior efficacy than expected from individual drugs
- If done properly
 - Near universal efficacy
 - Short duration of therapy
 - Side effects have minimal impact on QOL

HCV Novel DAAs: Genotype 1



NS3/4A Protease inhibitors

- High potency
- Limited genotypic coverage
- Low barrier to resistance

NS5A

- Promiscuous protein
- Part of replication complex
- Serendipitously discovered

NS5B

- RNA dependent RNA Polymerase
- Copies HCV RNA

HCV Drug Targets



Target	Potency	Barrier to Resistance	Genotypic Coverage
NS3/4A	High	Low	Limited
NS5A	High	Intermediate	Multi
NS5B NUC	Intermediate	High	Pan-genotypic
NS5B Non-NUC	Intermediate	Low	Limited

HCV Novel DAAs



NS3/4A Protease inhibitors

- Simeprevir-SIM (COSMOS)
- Paritaprevir-PTV (Viekira)

NS5A Inhibitors

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- Ombitasvir-OBV (Viekira)
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NS5B Nucleos(t)ide inhibitors (NI)

- Sofosbuvir-SOF (COSMOS or Harvoni)

NS5B Non-nucleoside inhibitors (NNI)

- Dasabuvir-DSV (Viekira)

General concepts about selecting HCV regimens

- Interferon-free, all-oral regimens with cure rates >90%
- Choice of regimen, treatment duration, and use of ribavirin depends on:
 - Presence of cirrhosis
 - Prior treatment experience (uncommon in your patients)
 - PEG-RBV failure
 - Prior protease inhibitor failure
 - Prior sofosbuvir failure
 - Genotype

HCV Regimens: Treatment Varies By Genotype

- Genotype 1:
 - Sofosbuvir/Simeprevir (COSMOS)
 - Sofosbuvir/Ledipasvir (Harvoni)
 - Paritaprevir/r, Ombitasvir, Dasabuvir (Viekira Pak)
 - +/- Ribavirin (RBV)
- Genotype 2:
 - Sofosbuvir + RBV
- Genotype 3:
 - Sofosbuvir + RBV
 - Sofosbuvir + Daclatasvir (\pm RBV)
- Genotype 4:
 - Similar to GT 1.

HCV Cure: Sustained Virologic Response (SVR)

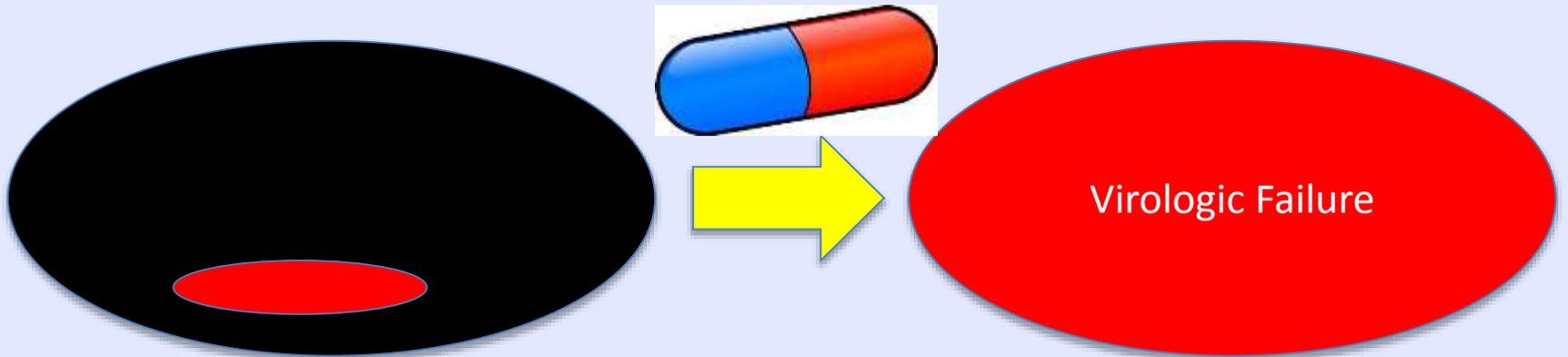
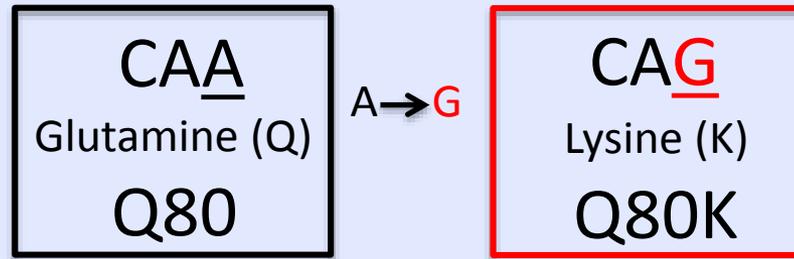
- Early Marker TW 4: (-)HCV RNA is a Rapid Virologic Response (RVR)
- Bad Sign: Viral Breakthrough, late TND or relapse after treatment.
- End of Treatment (EOT): HCV RNA at end of therapy.
- Durable **CURE**: Known as Sustained Virologic Response (SVR). Determined 12 weeks after treatment (**SVR 12**).

TW=Treatment week

TND=Target Not Detectable

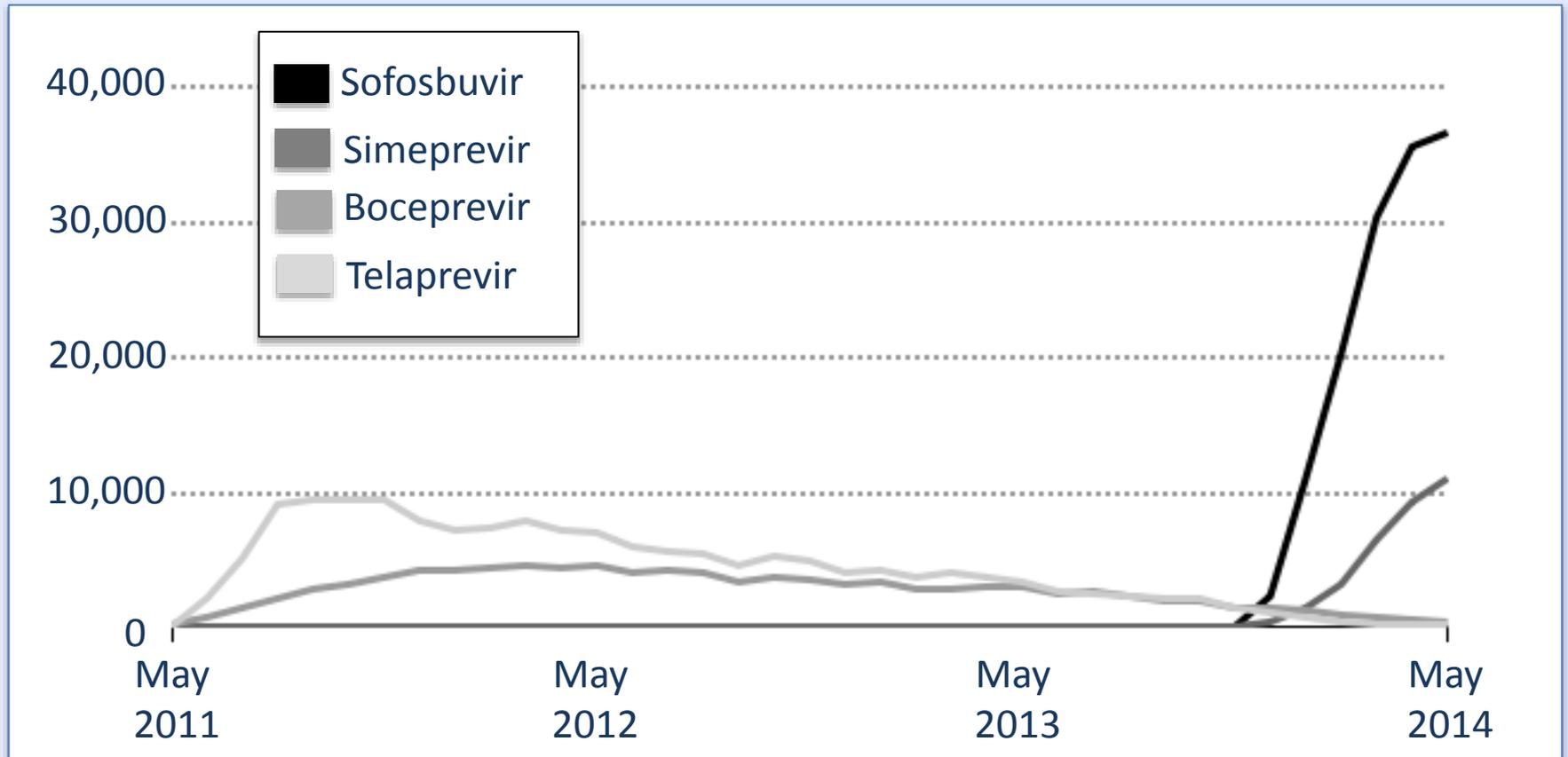


HCV Resistance



Viral Quasispecies Population

Monthly Prescriptions of DAAs (2011-2014) in the US



Sofosbuvir/Simeprevir (SOF/SIM)

- Dubbed “COSMOS” or SOF/SIM
- Use limited by cost now, but widely used in 2013.
- SMV primarily metabolized by the liver
 - In moderate or severe hepatic impairment (Child-Pugh Class B and C), post marketing reports of hepatic decompensation, liver failure and death; higher exposures associated with rash and photosensitivity in clinical trials
- No dosage adjustment of SIM required with mild, moderate or severe renal impairment
- Drug-drug interactions
 - Moderate/strong inducers or inhibitors of CYP3A (e.g., St. Johns Wort) may increase plasma concentrations of SMV
 - Amiodarone with sofosbuvir and SMV may result in symptomatic bradycardia

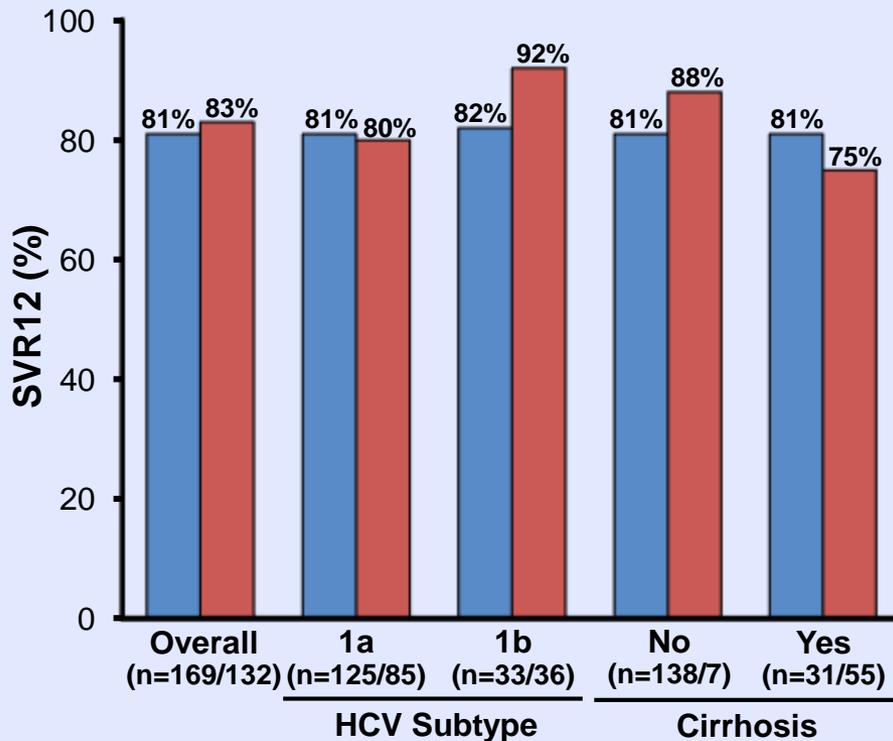
Trio: SOF/SIM SVR12 Rates in GT 1 Patients



Treatment-Naïve

Sofosbuvir plus

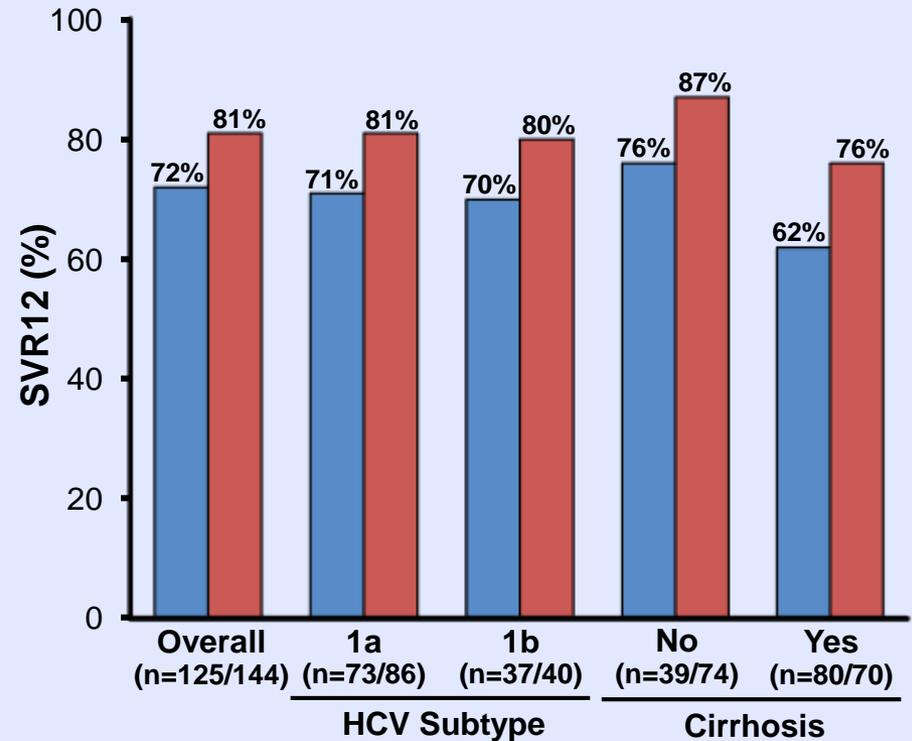
PR Simeprevir ± RBV



Treatment-Experienced

Sofosbuvir plus

PR Simeprevir ± RBV



PR: pegIFN + RBV.

SVR12 rates (sofosbuvir + PR and sofosbuvir + simeprevir ± RBV):

Prior PR failure (73% and 82%; prior PI failure (67% and 87%).

How To Manage HCV in Your Practice

AUGUST 2015

- Resource Poor
 - Lack of staging ability.
 - No local HCV experts, including ID, GI, or Hepatologist
 - Uninsured or underfunded.
 - When obtaining meds from PAP
- Resource Rich
 - Invasive and non-invasive testing at hand.
 - Plenty of local expertise.
 - Drugs are easily obtainable.
- Blended Resources
 - May have access to some but not all.

Case: Genotype 1A

- **55 Y M, HCV GT 1A**
- Naïve, Newly diagnosed
Non-cirrhotic.
- Has DM, A1C is 8.5%.
- Social: ETOH daily (2~24oz,
cigarettes daily). With
girlfriend. Has tattoos from
high school. Denies IVDU.
- Meds: Omeprazole (PPI),
Metformin, and
carbamazepine.. (when
questioned reports distant
seizure)
- PEX: No
hepatosplenomegaly.
- PLT 255 ALB 3.8 INR 1 TB
0.7
- AST 55 ALT 62 SALP 124
- HCV RNA: 2,170,342
copies/mL
- FIB-4 1.43 (<1.45=low
likelihood for cirrhosis/ F4-
6)
- US: No Masses

What Are the Considerations for Treatment

- Stage of liver disease?
- HCV GT and viral load?
- DDIs? Issues with pharmacokinetics?
- What is a good therapy for the patient?
- Is sofosbuvir/ledipasvir a good option?
- Would you treat someone who is drinking ETOH?

Ledipasvir/Sofosbuvir: Harvoni®

- Fixed dose combination, 1 pill/daily (Harvoni®).
- AKA LDV/SOF
- 400 mg/ Sofosbuvir
 - NUC: Inhibits the RNA-dependent RNA-polymerase.
 - Minimal resistance.
- 90 mg/Ledipasvir
 - NS5A inhibitor.
 - Baseline resistance (RAVs) may diminish SVR.

Ledipasvir/Sofosbuvir

- *Not* approved for severe renal disease, dialysis
 - GFR <30
- Drug – drug interactions (DDIs):
 - Amiodarone and digoxin
 - PPIs and other therapies that lower gut pH
 - Anticonvulsants
 - Rifampin
 - HIV ARVs
 - St. John's Wort
 - Rouvastatin

Treatment Duration and SVR Rates with LDV/SOF

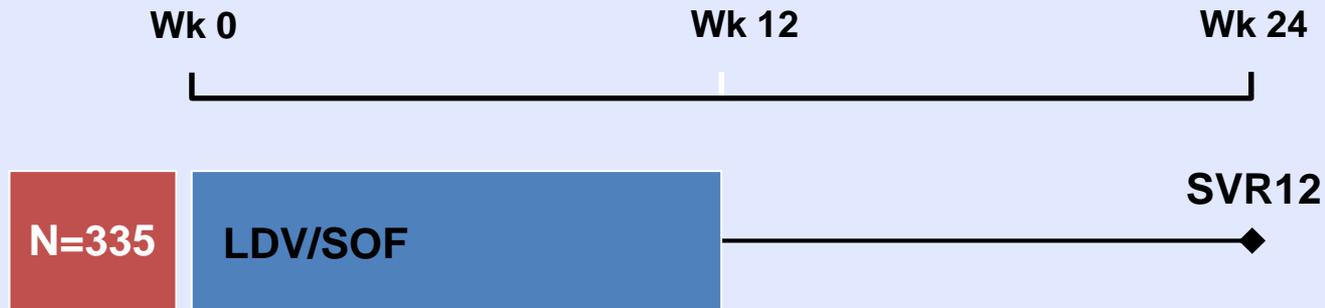
Fibrosis	Treatment Hx	VL	Duration	SVR 12
Non-Cirrhotic	Treatment naive	VL <6,000,000	8 weeks	98%
Non-Cirrhotic	Treatment naive	VL >6,000,000	12 weeks	98%
Non-Cirrhotic	Treatment Experienced	--	12 weeks	95%
Cirrhotic	Treatment naive	--	12 weeks	94%
Cirrhotic	Treatment Experienced	--	24 weeks	99%

Ledipasvir-Sofosbuvir: Adverse event rates

	8 Weeks	12 Weeks	24 Weeks
	N=215	N=539	N=326
Fatigue	16%	13%	18%
Headache	11%	14%	17%
Nausea	6%	7%	9%
Diarrhea	4%	3%	7%
Insomnia	3%	5%	6%

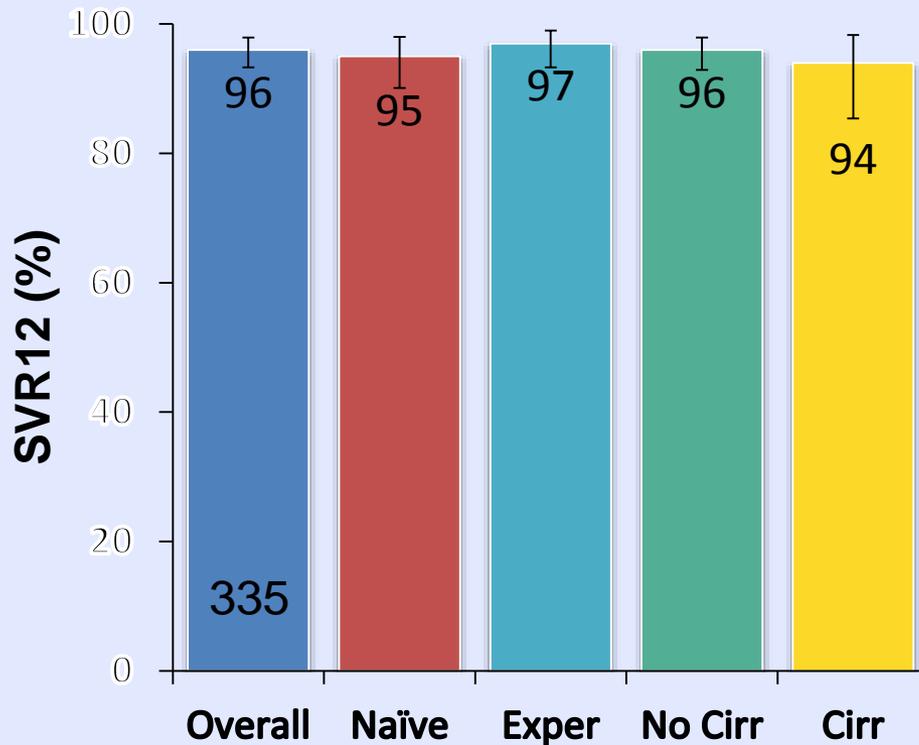
- Source: *Harvoni* Prescribing Information. Gilead Sciences

SOF/LDV in HIV Co-Infection: ION-4



- HCV GT 1 or 4
- Naïve or experienced
- Cirrhosis up to 20%
- TDF/FTC plus
 - EFV
 - RAL
 - RPV
- Subjects
 - 82% male
 - 34% African/American
 - 55% experienced
 - 20% cirrhosis

High SVR with 12 Weeks of SOF/LDV



- **Failures:**
 - 10 relapses
 - 2 on-treatment VF
 - 1 lost
 - 1 death
- **Safety and tolerability:**
 - 2% Serious AEs
 - No discontinuations due to AEs
 - 1 death

Case: Genotype 1A

- 55 Y M, HCV GT 1A
- Naïve, Newly diagnosed Non-cirrhotic.
- Has DM, A1C is 8.5%.
- Social: ETOH daily (2~24oz, cigarettes daily). With girlfriend. Has tattoos from high school. Denies IVDU.
- Meds: Omeprazole, Metformin, and carbamazepine.. (when questioned reports distant seizure)
- PEX: No hepatosplenomegaly.
- PLT 255 ALB 3.8 INR 1 TB 0.7
- AST 55 ALT 62 SALP 124
- HCV RNA: 2,170,342 copies/mL
- FIB-4 1.43 (<1.45=low likelihood for cirrhosis/ F4-6)
- US: No Masses

8 Weeks Harvoni IF:

-STOP PPI, SWITCH carbamazepine
Otherwise.. Consider alternate therapy

Case: Genotype 1b

- 62 YO Hispanic F HCV GT 1b
- Cirrhosis by biopsy in 2009. Doing well, no history of liver complications (ascites, varices, or encephalopathy).
- Social: Lives with son, no toxic habits.
- Meds: Milk thistle, pravastatin, amlodipine.
- PEX: No icterus, Spider telangectasia+, Palmar erythema+, and splenomegaly. No ascites.
- PLT 121 ALB 3.2 INR 1.2 TB 1.2
- AST 95 ALT 101 SALP 125
- HCV RNA: 7,170,342 copies/mL
- FIB-4: 4.84
- US: Cirrhosis, No Masses

Paritaprevir/ Ritonavir/ Ombitasvir/Dasabuvir (POD): Viekira Pak[®]

- 1 packet daily: 3 tablets in AM, 1 tablet in PM (3D= Viekira Pak[®]).
- AKA: 3D or POD
- Paritaprevir (boosted w/ritonavir): Protease inhibitor.
- Ombitasvir: NS5A inhibitor.
- Dasabuvir: Non-nuc.
- RBV daily required for GT 1a patients:
 - 1200mg for >75Kg (165lbs) and 1000mg <75kg.
 - Dose reduce RBV by 200-400 mg if Hgb drops 2 g/dL
 - Dose reduce with chronic kidney disease/dialysis
 - Average drop on therapy is 2.4 g/dL.

Key CIs and DDIs with POD

- Approved for severe renal disease but not dialysis*
- **Contraindicated in decompensated cirrhosis.**
- DDIs (CYP3A inhibitors & CYP2C8 inhibitors)**:
 - Ethinyl Estradiol (birth control with 2 medications)
 - Anticonvulsants
 - Statins and gemfibrozil
 - St. Johns Wort
 - Some anti-retroviral drugs.
 - Ergots
 - May need dose reduction of CCB, lasix.
- **Most of these drugs have alternatives or can be stopped for the duration of the therapy except anticonvulsants**

*Awaiting results of RUBY trial

**Not a complete list of DDIs.

POD +/- Ribavirin

Fibrosis	GT	RBV (Y/N)	Duration	SVR
Non-cirrhotic	1a	Y	12 weeks	96%
Non-cirrhotic	1b	N	12 weeks	100%
Cirrhotic	1a	Y	24 weeks	95%
Cirrhotic	1b	N*	12 weeks	100%

*Pending FDA, but data from Turquoise III shows 100% SVR.

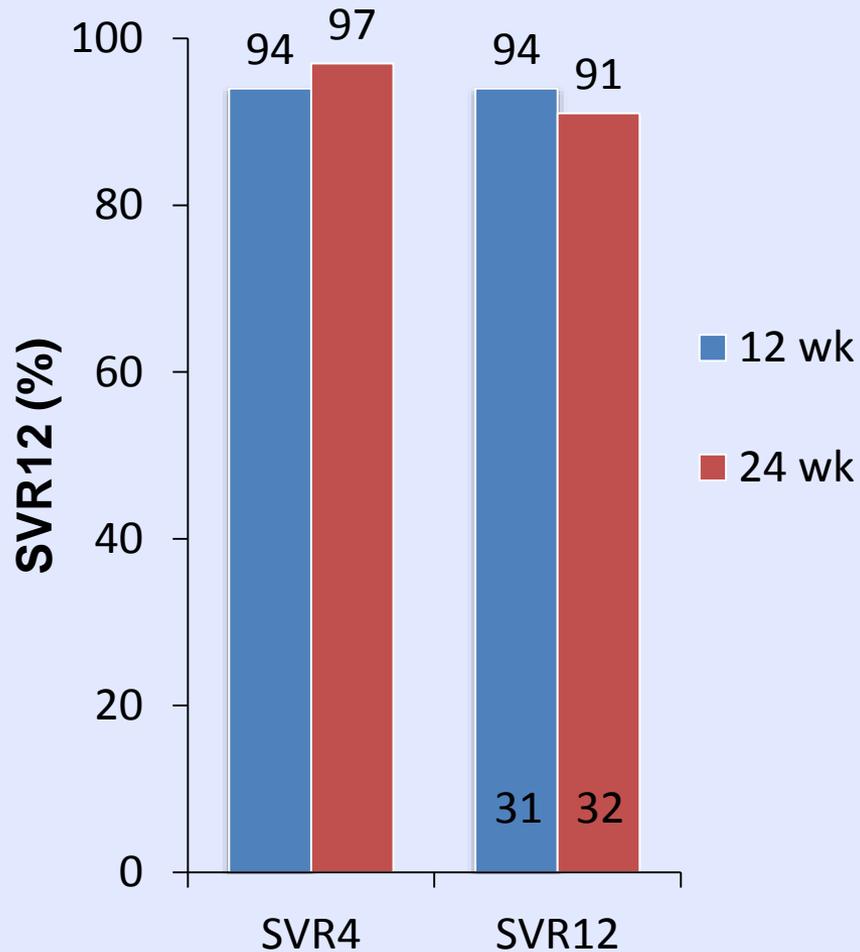
Treatment history and VL does not affect duration.

Adverse events: 3D+RBV vs. 3D

Event	GT1a		GT1b	
	3D + RBV (n=100)	3D (n=205)	3D + RBV (n=210)	3D (n=209)
Any adverse event %	92.0	82.4	80.0	67
Any serious adverse event %	3.0	0.5	1.9	1.9
Common adverse events:				
Headache %	25.0	28.3	24.3	23.4
Fatigue %	46.0	35.1	21.4	23.0
Pruritus %	10.0	5.9	11.9	5.3
Nausea %	21.0	13.7	11.0	4.3
Insomnia %	17.0	7.8	9.0	3.3
Diarrhea %	14.0	16.1	4.3	6.2
Laboratory abnormalities (%):				
Hemoglobin < 10 g/dl	4.0	0	9.0	0
Total bilirubin > 3x ULN	3.0	0.5	5.7	0.5

3D = Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir; **RBV** = ribavirin

TURQUOISE I: 3D + RBV in HIV/HCV



- 2 Virologic failures
 - 1a cirrhotic null responders
 - Relapse in 12-wk arm
 - BT at week 16
- 2 Re-infections
- Well tolerated
 - No discontinuation due to AEs
 - 5 HIV VL ≥ 40 copies/mL
 - None ≥ 200 copies/mL
 - All re-suppressed

RUBY: Efficacy of POD in ESRD

- All patients completing treatment to date had virologic response
- Virologic response has been sustained in all patients who have reached post-treatment weeks 4 and 12 in this ongoing study

Timepoint	N	Virologic Response (n)	Percent
End of Treatment	14	14	100
Post-treatment Week 4	10	10	100
Post-treatment Week 12	2	2	100

3D +/- RBV: Points to Consider

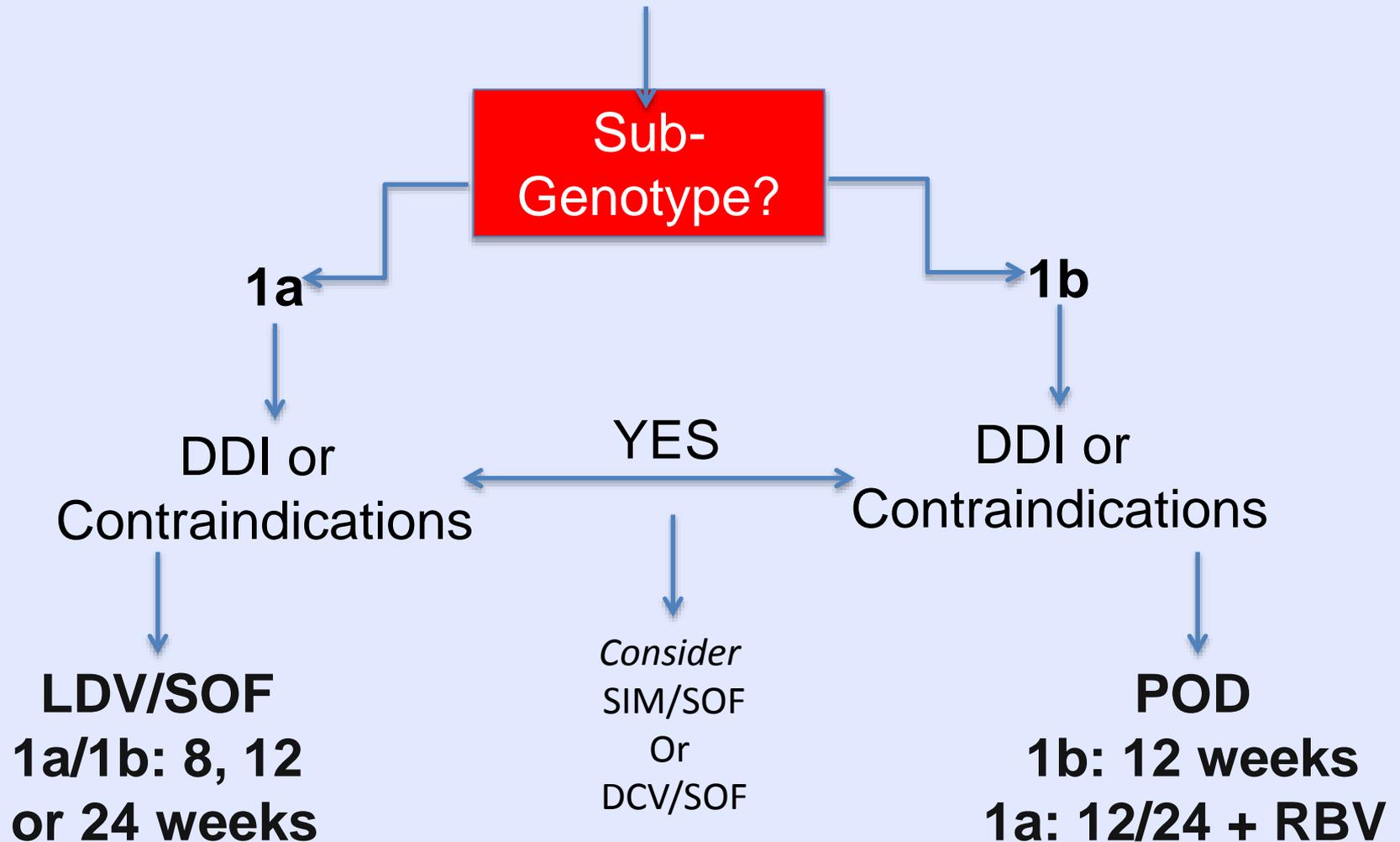
- Need careful review of DDIs because of RBV
- Avoid ribavirin if patient (or spouse) might become pregnant on treatment or 6 months after
- Avoid in patients with a history of ascites, variceal bleeding or encephalopathy
- No ethinyl estradiol
- Need labs in the first 4 weeks, if ALT is >10 upper limit of normal must stop therapy

Case: Genotype 1b

- 62 YO Hispanic F HCV GT 1b, Interferon experienced.
- Cirrhosis by biopsy in 2009. Doing well, no history of liver complications (ascites, varices, or encephalopathy).
- Social: Lives with son, no toxic habits.
- Meds: Milk thistle, pravastatin, amlodipine.
- PEX: No icterus, Spider telangectasia+, Palmar erythema+, and splenomegaly. No ascites.
- PLT 121 ALB 3.2 INR 1.2 TB 1.2
- AST 95 ALT 101 SALP 125
- HCV RNA: 7,170,342 copies/mL
- FIB-4
- US: Cirrhosis, No Masses

12 Weeks POD:
Stop Pravastatin,
reduce amlodipine

HCV Genotype 1 Algorithm*



*Not including decompensated cirrhosis

Case: Genotype 3

- 54 Y M with HCV GT 3, interferon/RBV experienced male.
- Failed SOF+ RBV, 24 weeks in 2013.
- Social: Non-toxic, mailman. Former marine. Tattoo on left forearm says USMC with a bird below.
- Medical: Biopsy showed stage 2/4 in 2010, 5/8 steatohepatitis. Diabetic on metformin/glipizide
- PEX: Appears healthy. Midline incisional hernia from a MVA with laparotomy in 1975. Obese.
- Labs: PLT 211 ALB 3.8 INR 1.1 TB 1.1
- AST 45 ALT 41 SALP 125
- HCV RNA: 751,325 copies/mL
- FIB-4: 1.8
- US: Fibrosis vs Steatosis, No Masses, Spleen is 15 cm.

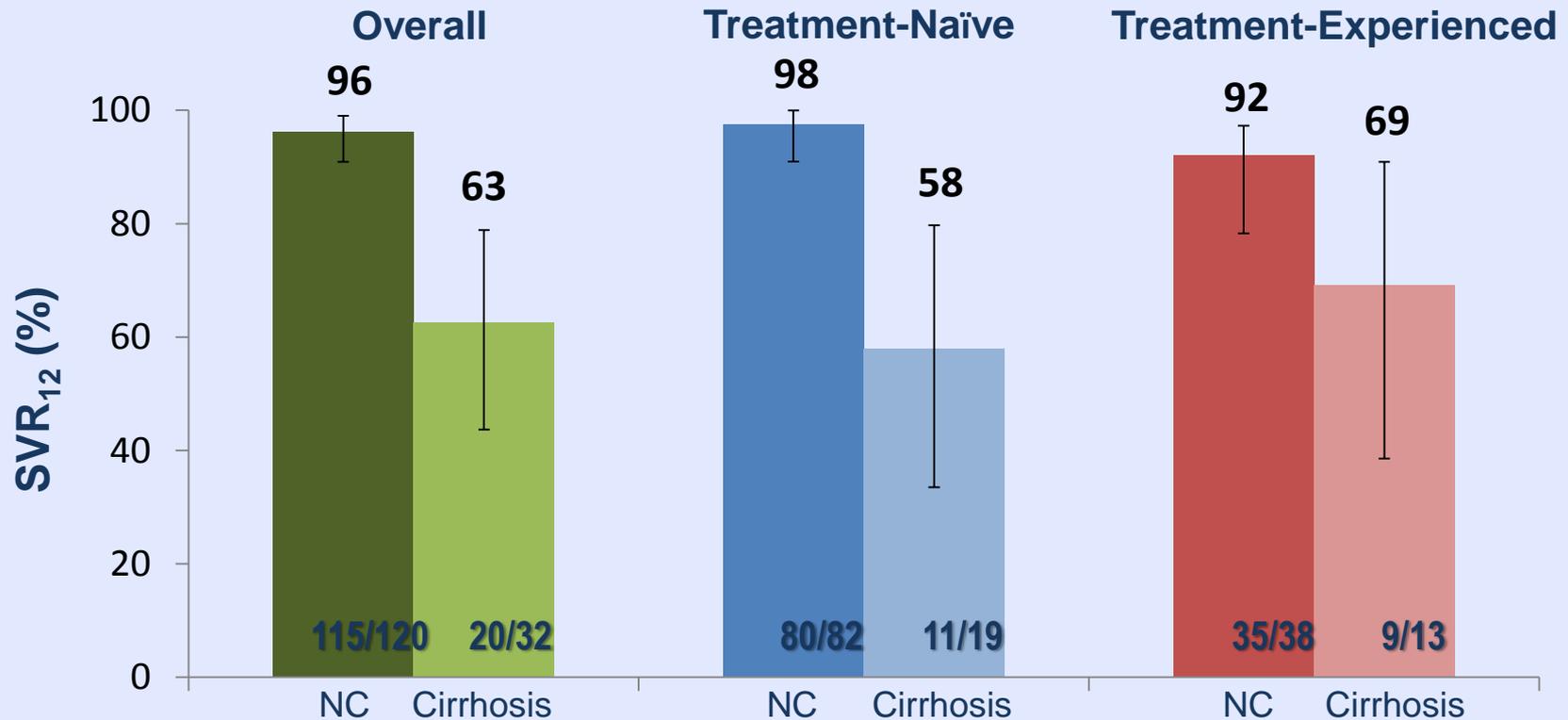
Genotype 3: Considerations

- What are the available regimens?
- Is the patient a good candidate for RBV? Does he need it?
- Even though he did not have advanced fibrosis on prior biopsy, might be benefit from HCV therapy in other ways?
- Would you restage with biopsy?

Sofosbuvir/Daclatasvir

- Sofosbuvir (Sovaldi) has same considerations as in other regimens.
- Daclatasvir (DCV; Daklinza) is an NS5A inhibitor.
- FDA approved for GT3; however, DCV is pangenotypic.

Sofosbuvir/Daclatasvir: GT3, for 12 Weeks



NC* = Non-cirrhotic

Nelson DR, et al. ALLY-3 Phase 3 Study. *Hepatology*.
2015;61(4):1127-1135

Cirrhotic GT 3: Optimal Duration of Therapy and RBV Use

Fibrosis	Author	N	Weeks	RBV	SVR
Non-cirrhotic	Nelson	120	12	No	96%
Cirrhotic	Nelson	32	12	No	63%
Cirrhotic	Foster	114	12	YES	70%
Cirrhotic	Foster	7	12	NO	71%
Cirrhotic	Poordad	6	12	YES	83%
Cirrhotic	Hezode	29	12	+/-	76%
Cirrhotic	Hezode	59	24	+/-	88%

AASLD/IDSA Guidelines (Aug 2015): 12 weeks of SOF/DCV + RBV, or if RBV intolerant 24 weeks of SOF/DCV

Nelson DR, et al. *Hepatology*. 2015;61(4):1127-1135.

Foster. *J. Hepatol*. 2015. EASL Vienna, Austria; abstract O002.

Hezode. *J. Hepatol*. 2015. EASL Vienna, Austria; abstract LP05

Poordad. *J. Hepatol*. 2015. EASL Vienna, Austria; abstract L08

Considerations with DCV Use

- Strong CYP3A inhibitors may alter plasma levels of DCV.
 - Majority are ARV, and DCV 30 mg dose can be substituted.
- Strong CYP3A inducers are contraindicated.
 - Phenytoin, carbamazepine, rifampin, St. John's wort (*Hypericum perforatum*).
- AASLD Guidelines recommend consideration with decompensated cirrhosis.

Case: Genotype 3

- 54 Y M with HCV GT 3, interferon/RBV experienced male.
- Failed SOF+ RBV, 24 weeks in 2013.
- Social: Non-toxic, mailman. Former marine. Tattoo on left forearm says USMC with a bird below.
- Medical: Biopsy showed stage 2/4 in 2010, 5/8 steatohepatitis. Diabetic on metformin/glipizide
- PEX: Appears healthy. Midline incisional hernia from a MVA with laparotomy in 1975. Obese.
- Labs: PLT 211 ALB 3.8 INR 1.1 TB 1.1
- AST 45 ALT 41 SALP 125
- HCV RNA: 751,325 copies/mL
- FIB-4: 1.8
- US: Fibrosis vs Steatosis, No Masses, Spleen is 15 cm.

-Restage
-Consider SOF/DCV
x 12 weeks.

Selected Drug Interactions with DAAs

Con Med	LDV	3D/PO D	SIM	SOF	DCV
Acid Reducers	X	-	-	-	-
Alfuzosin/Tamsulosin	-	X	-	-	-
Amiodarone	-	-	X	X	-
Anticonvulsants	X	X	X	X	X
Buprenorphine	-	X	-	-	-
Calcineurin inhibitors	-	X	X	-	-
Calcium channel blockers	-	X	X	-	-
Ethinyl estradiol products	-	X	-	-	-
St. John's Wort	-	X	X	X	X
Milk Thistle	-	-	X	-	X
Tenofovir	X	-	-	-	-
Statins	X	X	X	-	-

3D regimen= paritaprevir/r + ombitasvir + dasabuvir

Adapted from: hcvguidelines.org



Drug Interaction Scorecard (Kisergram)

	SOF	SOF/LD V	SMV	DCV	3D
TDF		RAL/DTG			
		HIV PI/EFV (↑TDF)			
EFV		(↑TDF)	↓SMV	DCV 90mg	
RLP					↑RLP
RAL/DTG					
ATV/r		ABC	↑SMV	DCV 30mg	
		↑TDF			
DRV/r		ABC	↑SMV		↓DRV
		↑TDF			
TDF/FTC/ ELV/Cobi			↑SMV*	DCV 30mg*	

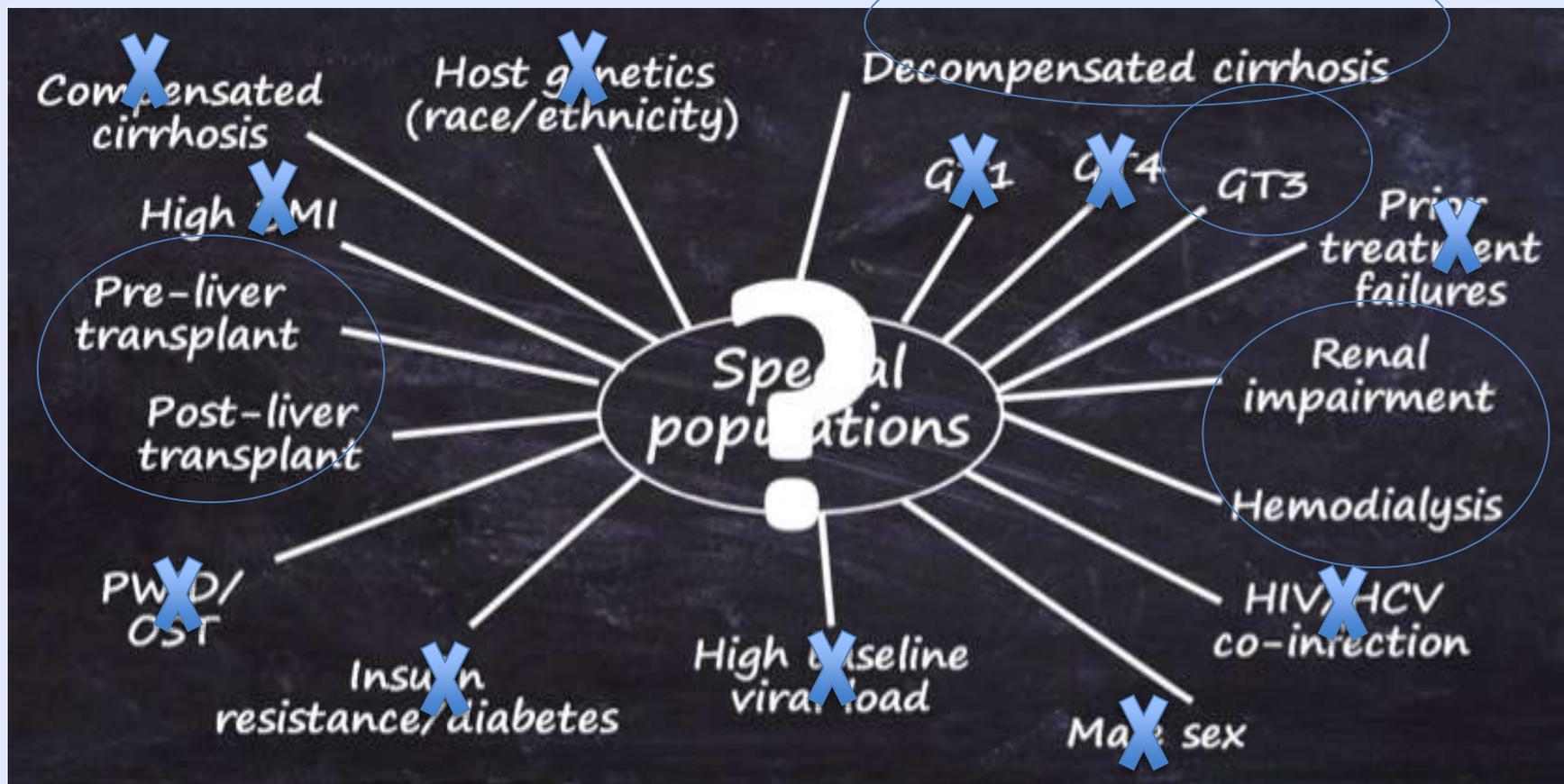
 No expected issues with co-administration

 Caution- potentially significant interactions or interactions of unknown significance. Additional monitoring may be necessary.

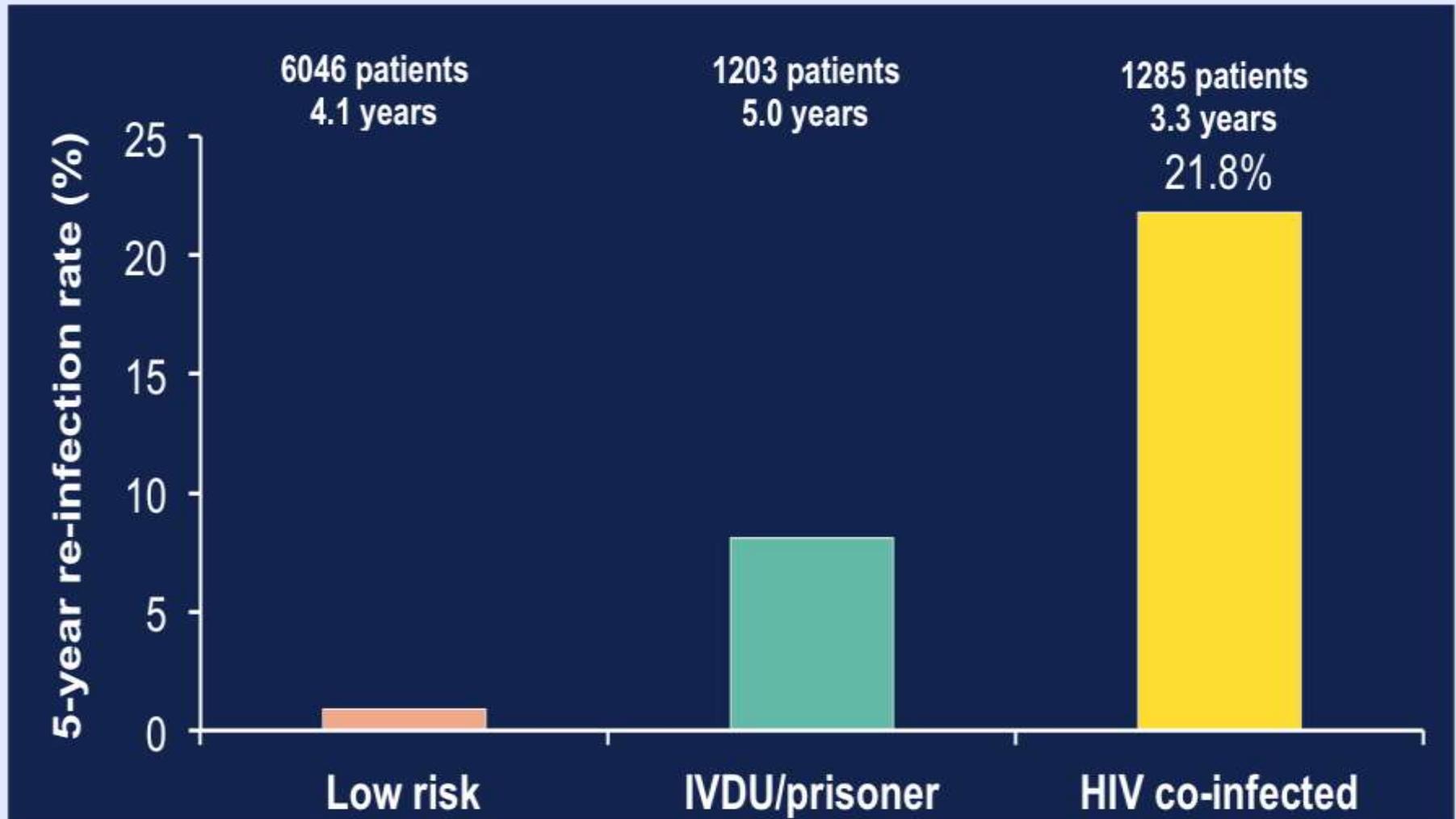
 Do not co-administer

*not studied, based on predicted interactions.

Who are the new special populations?



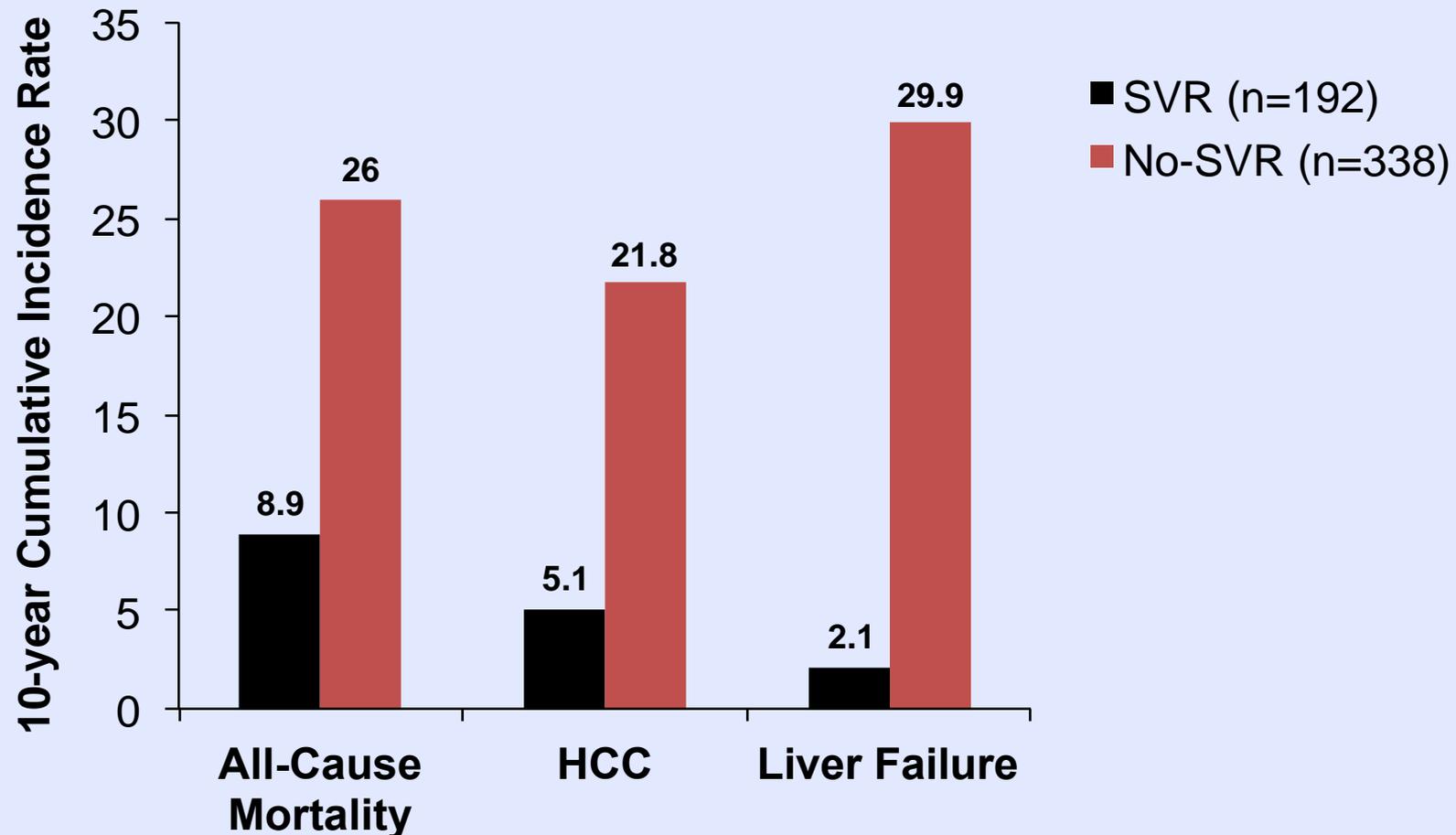
How Big of an Issue is Re-Infection?



Barriers to Treat (Texas) Medicaid Patients

- High number of patients expected over the next 10 years.
 - At minimum, there might be 80,000 Medicaid patients with HCV in Texas.
 - 1,000 individuals planned for treatment in 2015.
- F0, F1 and F2 excluded from treatment now.
- F3 has 7% risk of HCC over 5 year after cure.
- Cirrhotics are often difficult to treat
 - Benefit of treatment in decompensated liver disease of question. Most likely they need transplant first.

SVR (Cure) Associated with Decreased All-Cause Mortality



Summary

- HCV GT 1 is most common in US (1a>1b)
- FDA approved therapies are available for GT 1, 2, 3 and 4.
- HCV therapy treatment and duration needs to be individualized in each patient.
- Side effects and drug-drug interactions are manageable.
- Cure rates are high for all regimens selected.
- No clear medical rationale for withholding treatment from low fibrosis score patients.

The Hitchhiker's Guide to HCV Therapy

Julio Gutierrez, MD
Assistant Professor
Texas Liver Institute
UTHSCSA
San Antonio, TX

EMAIL: Gutierrez@txliver.com

cell: 646-345-2492

Office Number: 210-253-3426 (SAN ANTONIO &
McAllen)

512-454-7883 (AUSTIN)