NEW YORK STATE

HCV PROVIDER CLASSIFICATION TRAINING

Empire Liver FOUNDATION

New York State HCV Provider Webinar Series

Monitoring Prior, During, and After Treatment

Empire Liver FOUNDATION

Objectives

- Describe the appropriate evaluation prior to initiation of DAA therapy
- Discuss the process for obtaining DAA approval from payors
- Recognize the appropriate monitoring on DAA therapy
- Describe the appropriate monitoring following treatment with DAA therapy

The New World of HCV Therapy

- Interferon-free therapy is here
- Cure is an almost certain outcome
- Hand-holding is no longer needed

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Patient assessment prior to therapy continues to be of paramount importance

Pre-Therapy Assessment 2017
Predictors of Response

WHAT'S OUT	WHAT'S IN

Pre-Therapy Assessment 2017
Predictors of Response

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- **Race**
- **BMI**
- **IL28b**
- **HIV co-infection**
- **Type of prior non-response**

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Predictors of Response

WHAT'S OUT	WHAT'S IN
• Race • BMI • IL28b • HIV co-infection • Type of prior non-response	• Fibrosis • Genotype • Resistance

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Advanced fibrosis has remained as an important significant negative predictor of response

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  - Hepatocellular carcinoma (FOR LIFE)

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- Allows for selection of proper treatment plan and duration of therapy
- Used by many payors as a way to restrict access to therapy
- Following cure, patients with cirrhosis need to continued to be screened for HCC

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  - Fibrosure, APRI, AST/ALT ratio, Forns index, FIB-4, etc.
    - Work well in cases of no fibrosis or established cirrhosis

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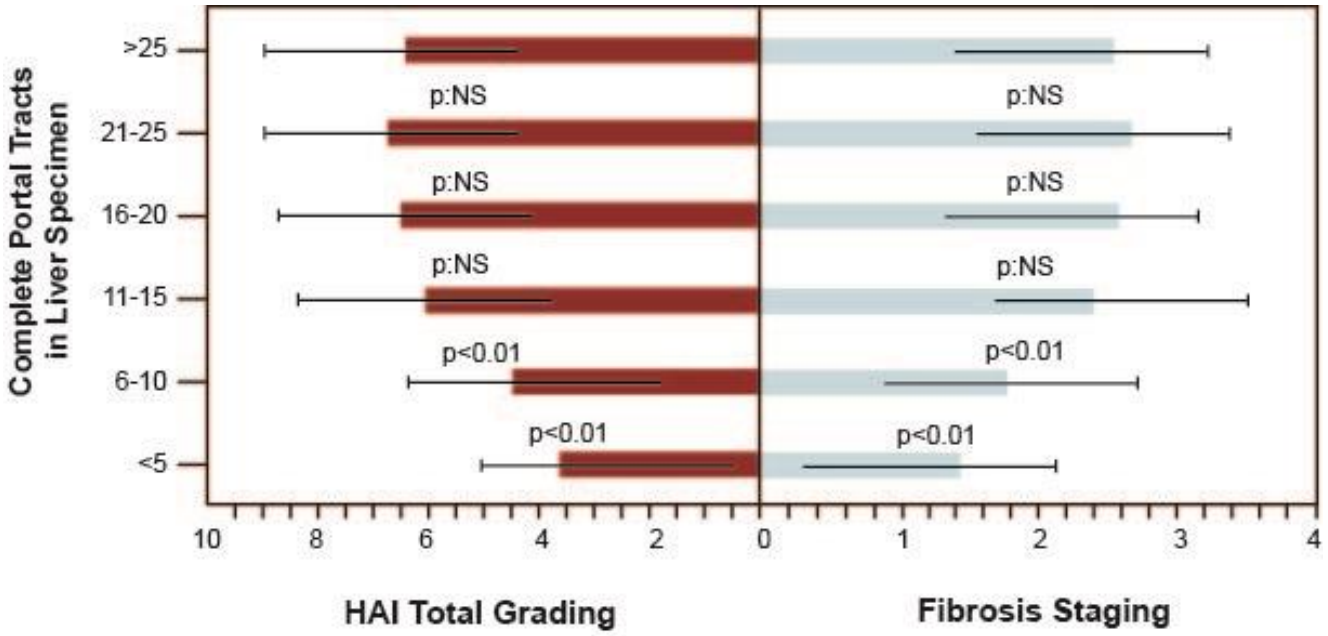
No single test is accurate enough!

How Good Is Liver Biopsy?

- Widely regarded as the “Gold Standard”
  - Compared to what?
- Published data may not represent real-life results
- What is an optimal liver biopsy?

Liver Biopsy in HCV

- Specimen size matters
  - ≥11 portal tracts should be represented



Colloredo G, et al. *J Hepatol.* 2003;39:239-244.

How Can You Get an Accurate Liver Biopsy Interpretation?

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- **Pathologist matters!**
- 391 HCV patients underwent liver biopsies
- 2 hepatopathologists read the biopsies, reading compared to community pathologist
  - Agreement among readings: 50%
  - **Community pathologists under-staged fibrosis in 73% of cases**

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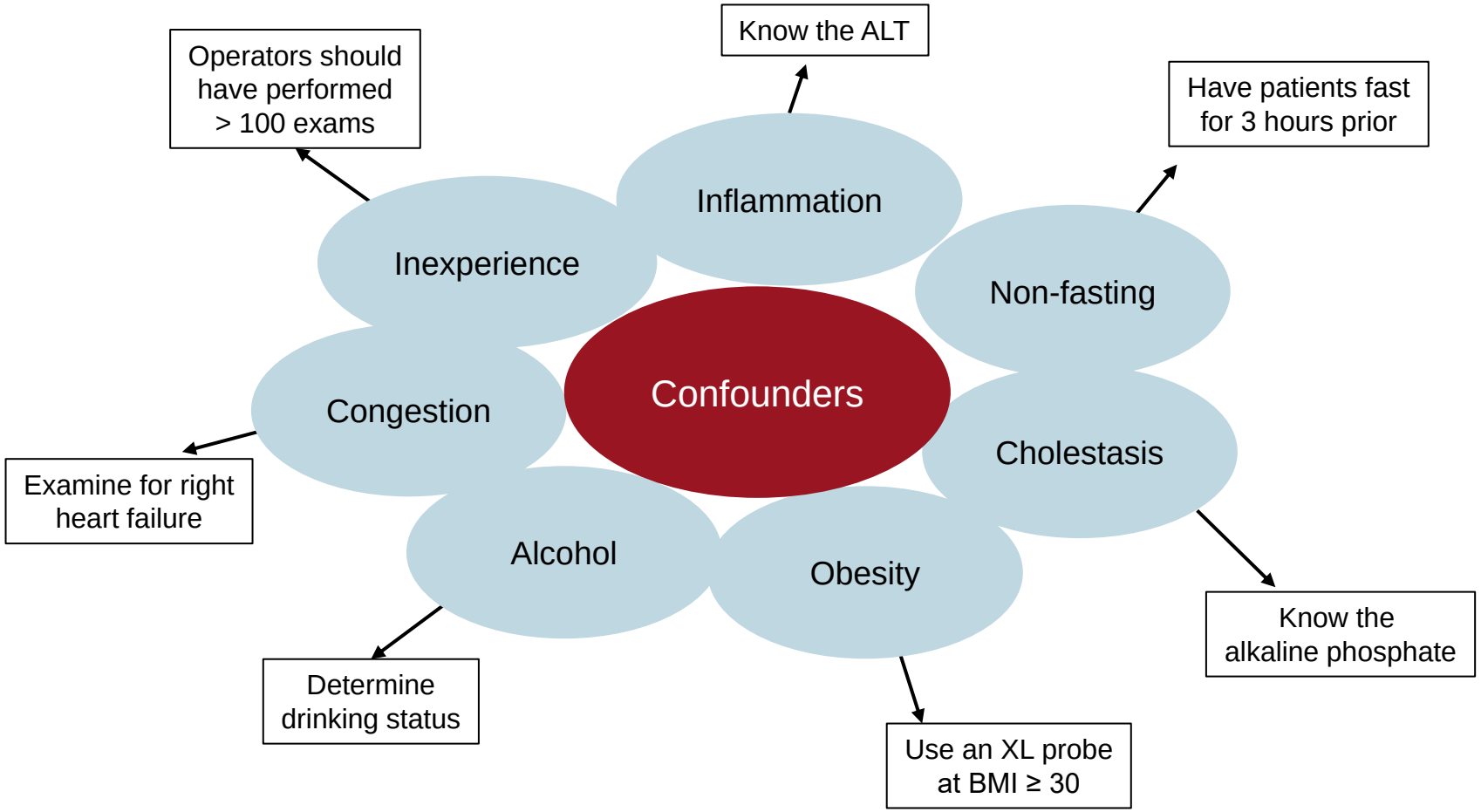
Liver biopsy is one of several components of fibrosis assessment

Vibration-Controlled Transient Elastography (VCTE)FIBROSCAN™

- Non-invasive method to assess fibrosis



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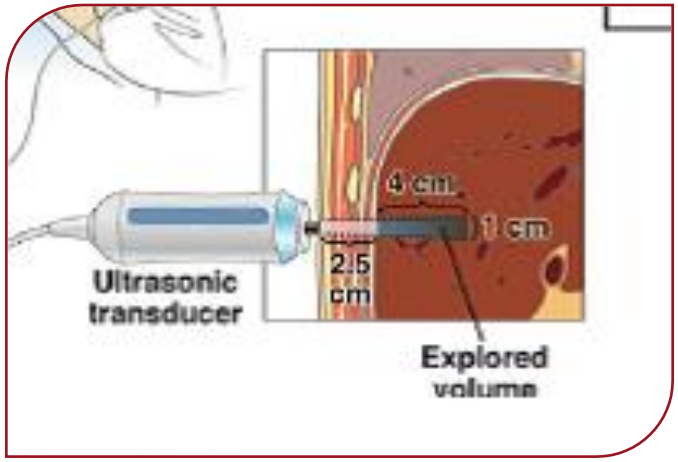
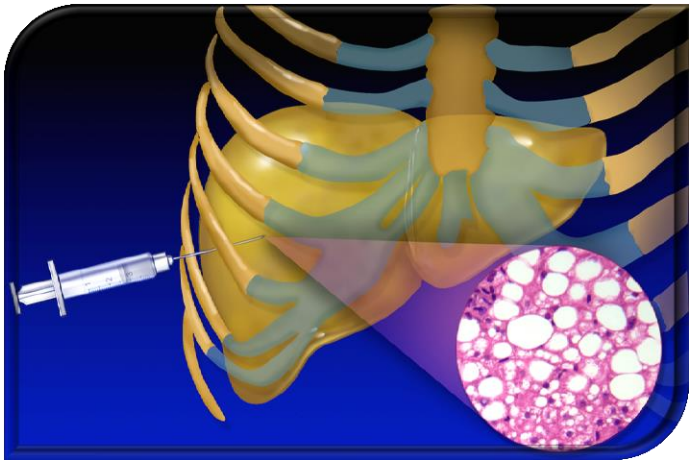
VCTE Analyzes a Larger Volume of Liver Tissue

VCTE	Liver Biopsy
~ 1 cm x 4 cm	~ 0.14 cm x 2-3 cm





VCTE vs. Liver Biopsy

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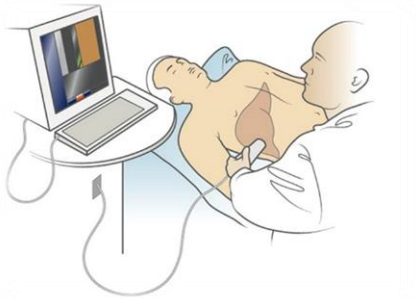

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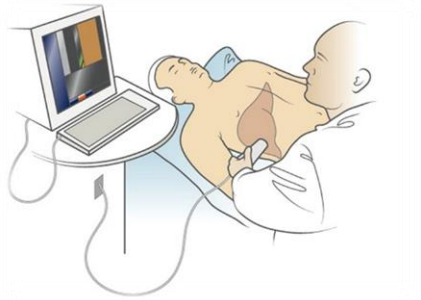

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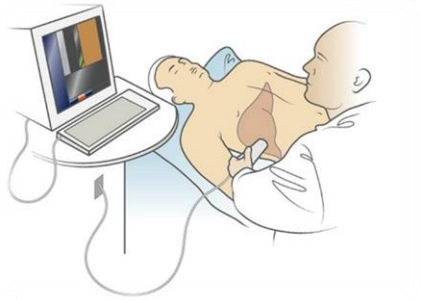

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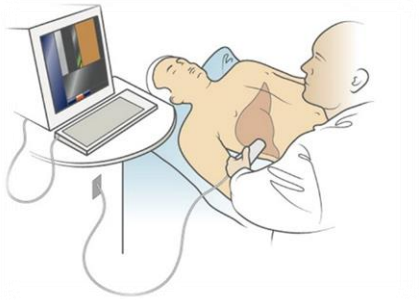

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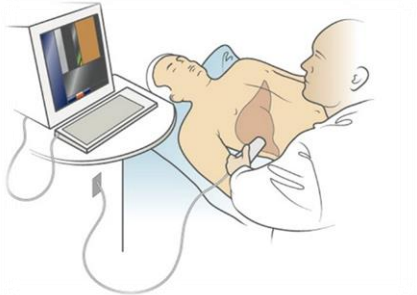

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HCV: ≥7.3 kPa suggests significant fibrosis; ≥12.5 kPa suggests cirrhosis

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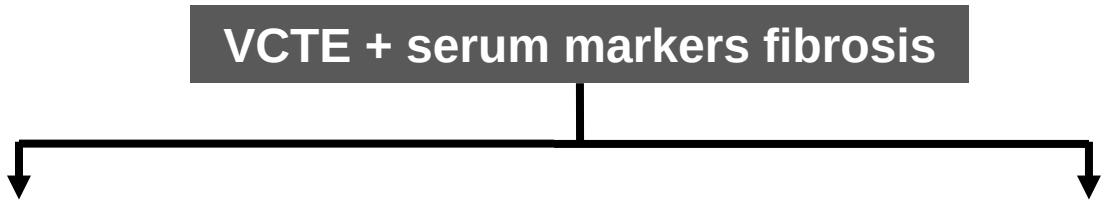
Take Home Message: Use All Your Tools!

- **Serum fibrosis tests**
- **AST/ALT ratio**
  - >0.8 suggests advanced fibrosis if no alcohol
- **APRI**
  - AST/ULN divided by platelet count x 100; ≥2 suggests cirrhosis
- **Platelet count**
  - <150,000 suggests portal hypertension
- **Ultrasound**
  - Splenomegaly or PV diameter ≥13mm suggests portal hypertension
- **VTCE in HCV**
  - ≥7.3 kPa suggests advanced fibrosis, > 12.5 kPa suggests cirrhosis

Non-Invasive Assessment of Fibrosis



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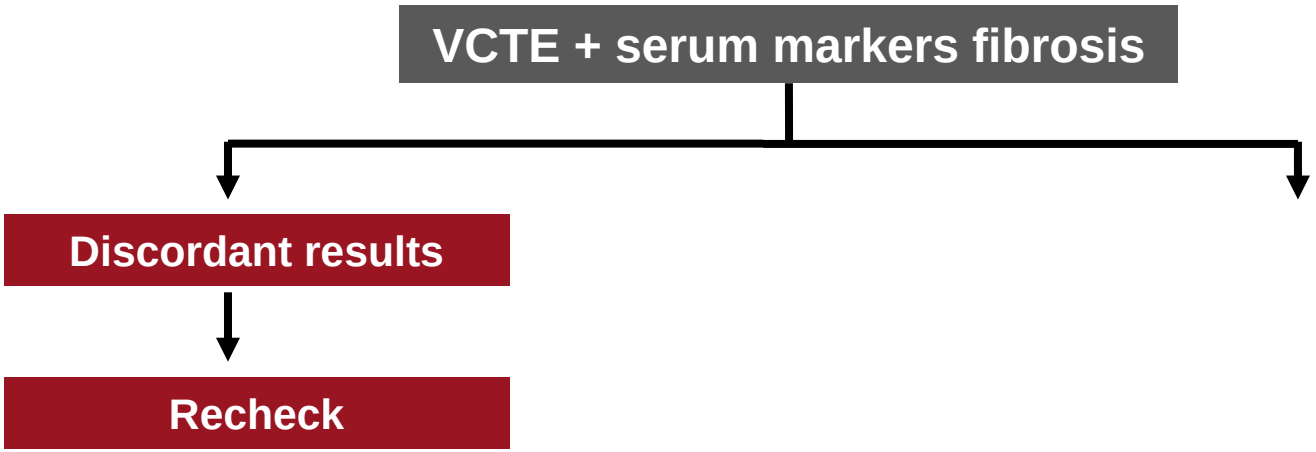

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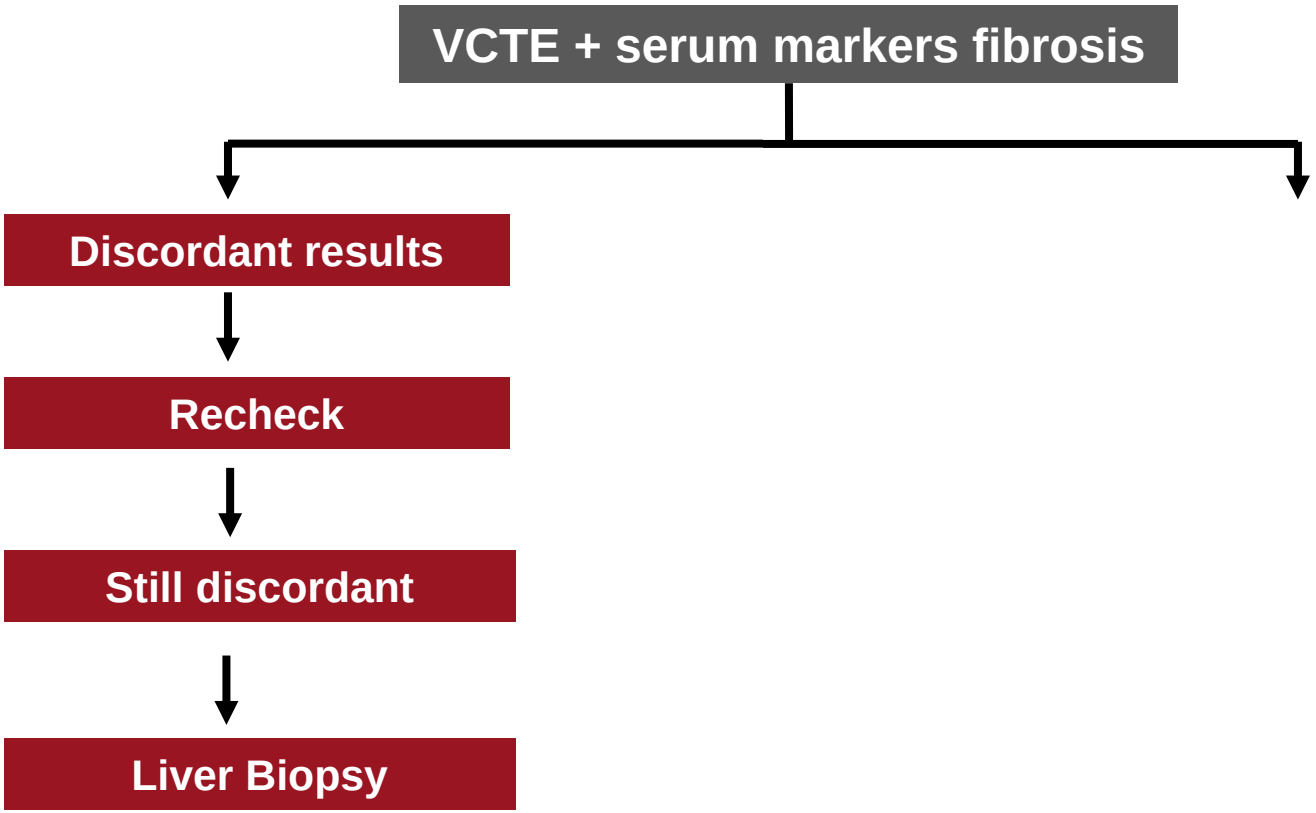

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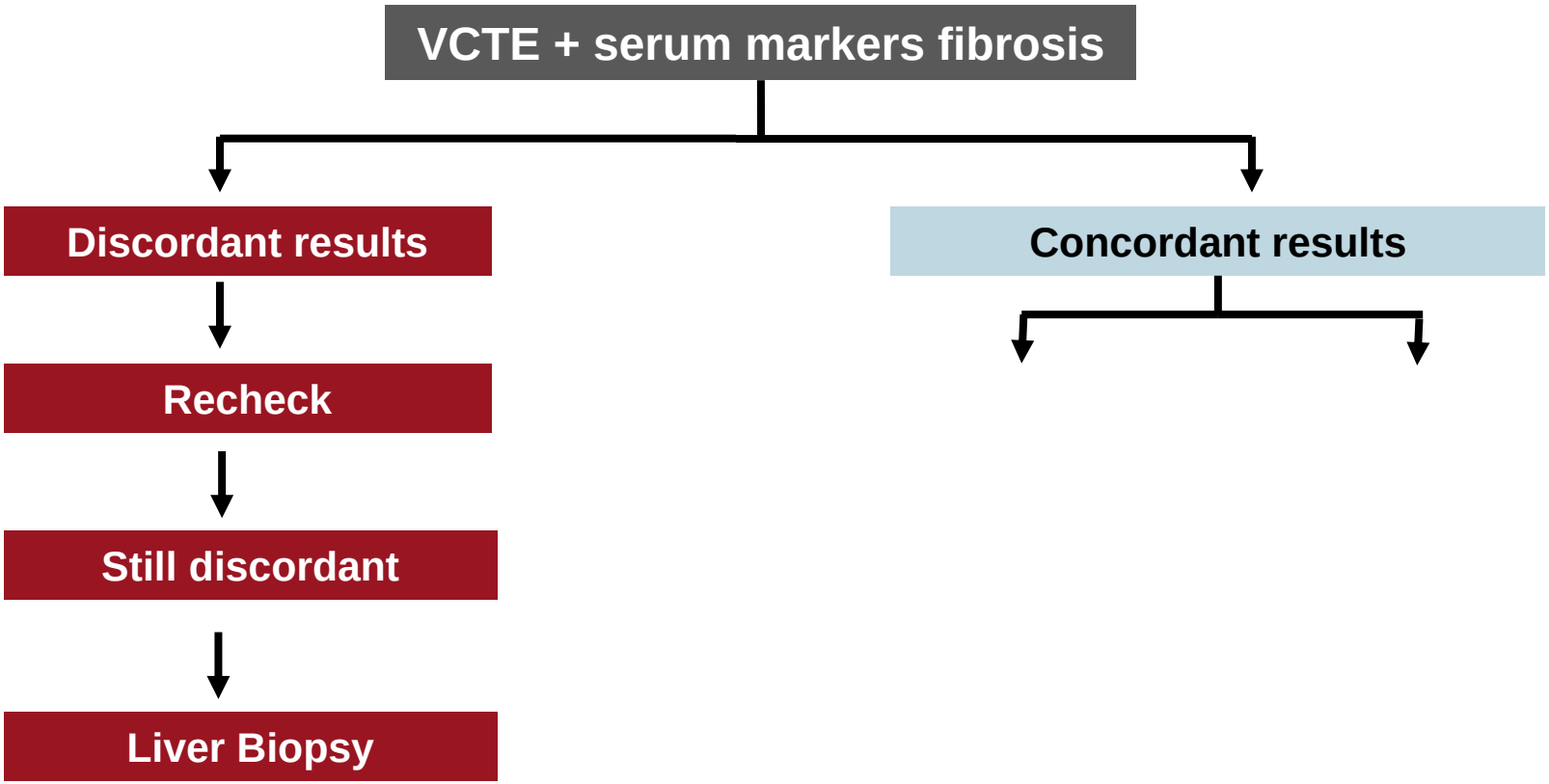

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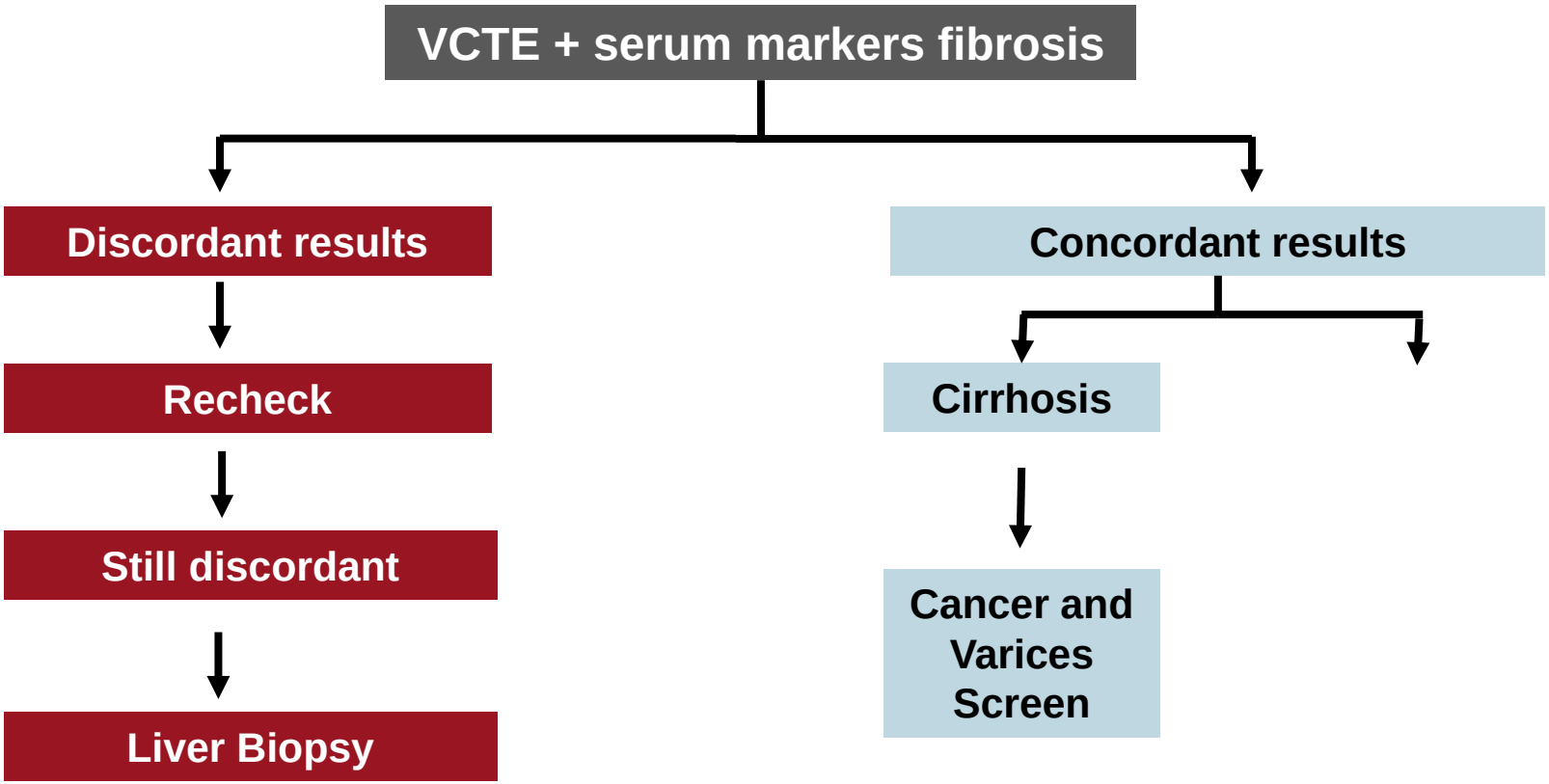

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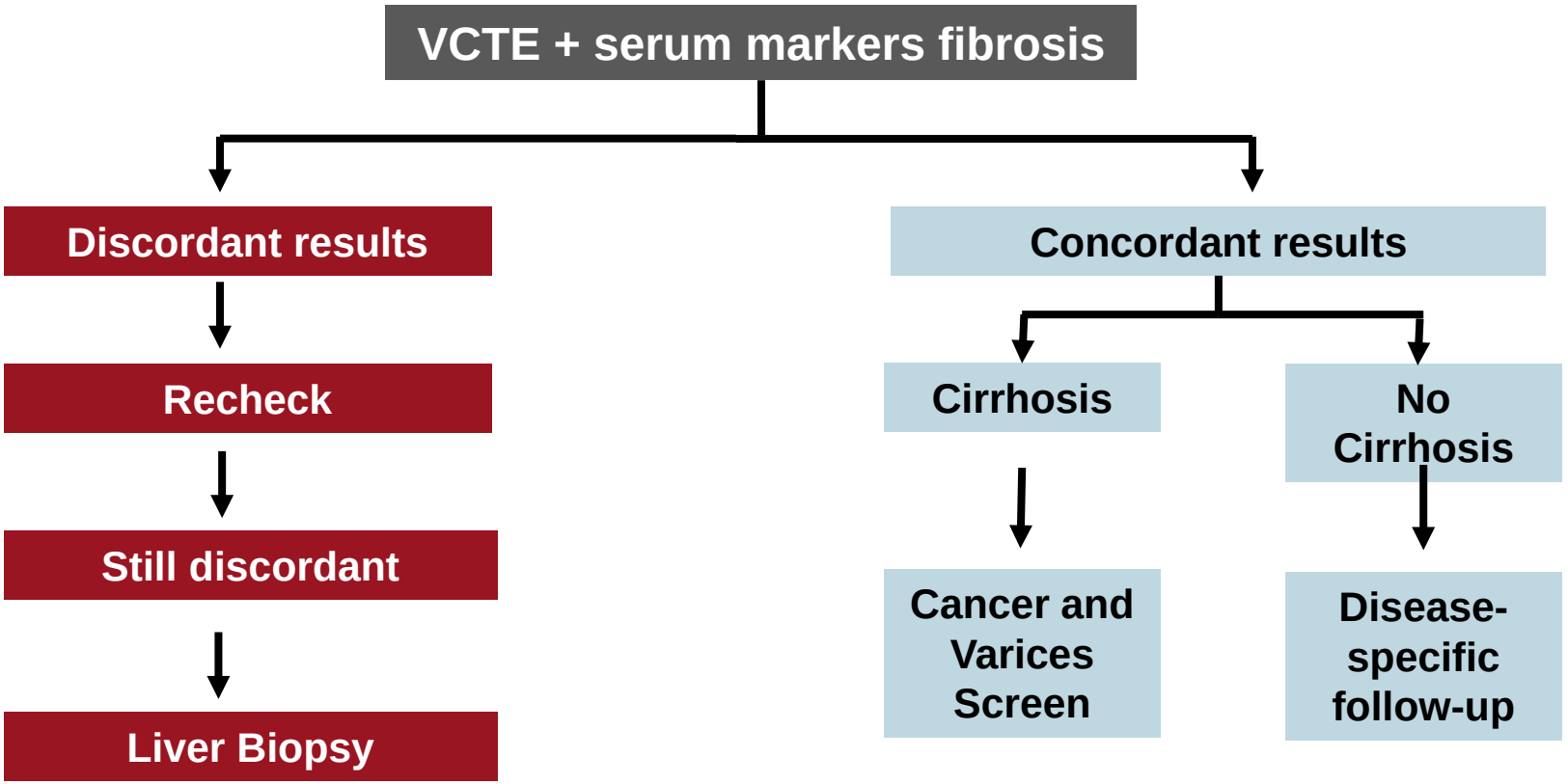

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Co-Morbidities

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- Need for family/friend support system
- Avoidance of therapy in patients with psychiatric illness

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  - Understands the implications of HCV infection?
  - Understands the importance of a cure?

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Starting therapy on the initial visit is usually not a good idea, even in 2017

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Need to understand the pharmacology of new agents to select the best treatment

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Remember: Patients rarely tell you all the pills they are taking!

Pre-Therapy Assessment 2017

Pregnancy Issues

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Pregnancy Issues

- **Ribavirin containing regimens are teratogenic**
  - Two contraceptive methods
    - NO OCP containing ethinyl estradiol if using ombitasvir/paritaprevir/ritonavir with dasabuvir
  - Continue contraception for up to 6 months after completion of therapy

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- **Ribavirin free regimens**
  - Pregnancy Category B
  - Avoid therapy during pregnancy or lactation
  - Recommend contraception during therapy

Pre-Therapy Assessment 2017
Pre-Treatment Laboratory Assessment

- **Basic labs should include**
  - Genotype assessment at least once in the RECENT pastViral load relatively recent
    - Some insurances require within 3 months
  - Hepatitis BsAg, Hepatitis B sAb, Hepatitis BcAb
    - HBVDNA if HBsAg positive
  - HIV Ab
  - Assessment of liver function
  - Assessment of renal function (creatinine, GFR)
  - CBC for patients who will be on ribavirin
  - Assessment of liver fibrosis
  - Drug/alcohol screening if required by payors
  - BASELINE RESISTANCE TESTING FOR GENOTYPE 1A IF GRZ/ELB CONSIDERED or Genotype 3 cirrhotics

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- Many issues should be addressed:
  - Importance of adherence
  - Review of concurrent medications
  - Pregnancy issues
  - Proper storage of medications
  - Instructions on how to manage missed doses
  - Arranging follow up lab tests and visits
  - STAGE OF CIRRHOSIS

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This is very expensive therapy – Do it right the first time!

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  - Appealing a denial may get your patient approved

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    - Fibrosis assessment may have underestimated true fibrosis stage
    - Patient may develop extra-hepatic complications of HCV
  - Approval rules change frequently – you will be the last one to know
  - Appealing a denial may get your patient approved

Having a denial letter in the medical record will help you when your patient develops unexpected complications of untreated HCV!

Getting Medications Approved

- **Use a specialty pharmacy**
  - Not all are the same

Getting Medications Approved

- **Use a specialty pharmacy**
  - Not all are the same
- **Appeal the first denial**
  - Some will get automatically approved
  - Your letter should state the specific reasons you want to treat your patient
    - Therapy is FDA-approved
    - Recommended by the AASLD/ISDA/NYS guidelines
    - Increased risk of non-hepatic complications
    - Recently published data
  - **Provide a copy of the letter to the patient**


Monitoring on Therapy
Empire Liver
FOUNDATION

The Treatment Initiation Visit

- Continued patient education
- Obtaining follow-up data
- This visit is particularly important for those with cirrhosis
- Age appropriate cancer screening
- Counseling regarding alcohol abstinence, transmission and reinfection
- Counseling regarding adherence and consequences of treatment failure

The Treatment Initiation Visit

- If advanced fibrosis (F3 or F4) is noted:
  - Upper endoscopy to evaluate varices
  - Alpha fetoprotein
  - Cross-sectional abdominal imaging with contrast if ultrasound inadequate
  - Referral to liver transplant program if MELD > 15

On Treatment Monitoring for 8 Week Course

- Week 4*:
  - HCVRNA, creatinine, eGFR, albumin, ALT, AST
- Week 8* after end of treatment: HCVRNA
- Week 20* (12 weeks after completing therapy)
  - HCV RNA
  - INR, AFP if cirrhotic

* HBVDNA if HBsAg and/or HBcAb positive

On Treatment Monitoring for 12 Week Course

- Week 4*:
  - HCVRNA, creatinine, eGFR, albumin, ALT, AST
- Week 8*:
  - HCVRNA, creatinine, eGFR, albumin, ALT, AST
- Week 12* after end of treatment: HCVRNA
- Week 24* (12 weeks after completing therapy)
  - HCV RNA
  - INR, AFP if cirrhotic

* HBVDNA if HBsAg and/or HBcAb positive

On Treatment Monitoring for 16 Week Course

- Week 4*:
  - HCVRNA, CBC, creatinine, eGFR, albumin, ALT, AST
- Week 8*:
  - HCVRNA, CBC, creatinine, eGFR, albumin, ALT, AST
- Week 12*
  - HCVRNA, CBC, creatinine, eGFR, albumin, ALT, AST, alk phos
- Week 16*
  - HCV RNA
- Week 28* (12 weeks after completing therapy)
  - HCV RNA
  - INR, AFP if cirrhotic

* HBVDNA if HBsAg and/or HBcAb positive

On Treatment Monitoring for 24 Week Course

- Week 4*:
  - HCVRNA, CBC, creatinine, eGFR, albumin, ALT, AST
- Week 8*:
  - HCVRNA, CBC, creatinine, eGFR, albumin, ALT, AST
- Week 12*
  - HCVRNA, CBC, creatinine, eGFR, albumin, ALT, AST
- Week 16*
  - HCVRNA, CBC, creatinine, eGFR, albumin, ALT, AST
- Week 20*
  - HCVRNA, CBC, creatinine, eGFR, albumin, ALT, AST
- Week 24*
  - HCV RNA, CBC
- Week 36* (12 weeks after stopping therapy)
  - HCVRNA, CBC, creatinine

* HBVDNA if HBsAg and/or HBcAb positive

Post Treatment Monitoring and Follow up Care

- For those patients who do not achieve SVR, referral to an specialist/hepatologist is warranted
- New therapies for treatment failure are on the horizon
- Consider clinical trials for relapsers or viral failure to current DAA regimens
- Reinfection would restart the entire process

Post Treatment Monitoring and Follow up Care of Those Achieving SVR (F0-F2)

- Will depend on level of pre-treatment fibrosis
- In those who achieve SVR and have F2 or less, completion of a care course will be adequate to not require long-term follow up by a specialist
- In patients with HbSag and/or HBcAb positive, continued monitoring
- Patients with ongoing high-risk behaviors should be educated about the risk of reinfection
- Those with excessive alcohol intake and NAFLD should be counseled accordingly

Post Treatment Monitoring and Follow up Care of Those Achieving SVR (F3-F4)

- Liver related care should continue
- In patients with HbSag and/or HBcAb positive, continued monitoring
  - All HBVDNA positive patients should be treated
- Screening for HCC and monitoring of liver function every 6 months
- Annual follow-up with specialist
- Those with cirrhosis should be screened periodically for varices according to AGA guidelines

Monitoring of Patients Who Have Had Antiviral Therapy Deferred

- Viral resistance to available agents
- Patient refusal
- DDIs which cannot be overcome
- Psychosocial issues
- Regular monitoring of liver function
- Consideration of treatment when underlying reason has been resolved

Summary

- DAA therapies cure almost all treated patients
- Pre-treatment evaluation remains important
- DDI increasingly important
- On-treatment monitoring remains important
- Fibrosis stage helps determine therapy and post-treatment follow up
- Following SVR:
  - F 0-2 may be discharged from care
  - F 3-4 needs to be continued to be screened for HCC