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HIV/HCV/STI cases

Marshal Miller, MD, AAHIVS
Thomas Jefferson University

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HIV/HCV/STI cases

Marshal Miller, MD, AAHIVS

Department of Family & Community Medicine
Thomas Jefferson University

September 10, 2020

Disclosures

I have no financial relationships to disclose.

Any drug or brand names included in this talk are included for educational purposes only.

Zoom lectures are no fun. Unless there's participation from EVERYONE.

Objectives

- Discuss approach to Syphilis testing and management in persons infected with HIV and HIV negative patients
- Review strategies to improve ART adherence
- Review ART options and considerations for initiating and modifying ART and clinically relevant Rx-Rx interactions
- Assess patients for HCV treatment and review simplified treatment strategies for patients with chronic HCV infection

22 yo M presents with CC: I think I have syphilis



What else do you want to know?

HPI/PMH

Patient had been lost to care since 9/2019.
Labs at that time: HIV VL 124 , CD4 696 (38%).

Recently hospitalized 5/2020 and admitted to rehab for schizophreniform d/o, crystal meth use. Started on haldol, cogentin and sertraline and currently in outpatient psychiatric Tx

Other history?

Prior Syphilis Hx:

7/2018: Syphilis EIA Ab+, RPR 1:64
(asymptomatic)

8/2018: RPR 1:512-> Treated with Bicillin IM x
1 dose

9/23/19: Syphilis EIA Ab+, RPR NR, Particle
Agglutination Reactive

Other history?

How would you treat him? (He has NKDA)

Follow up visit:

He reports adherence to ART and denies missing any doses in the last month. You decide to obtain repeat labs and follow up the next week. Interim labs return:

HIV VL: 82,400 CD4 776 (36%)

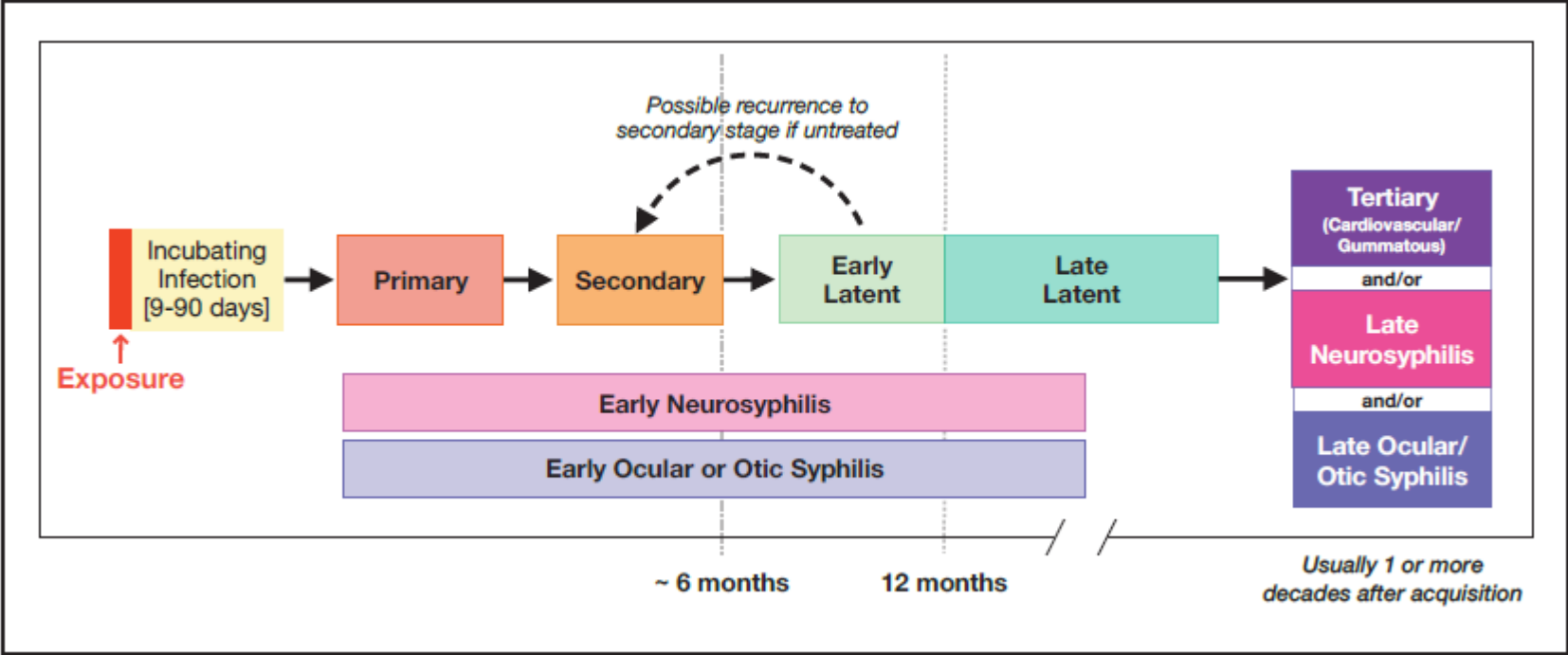
RPR: 1:512

Does this change your treatment plan for syphilis?

How would you address his HIV?

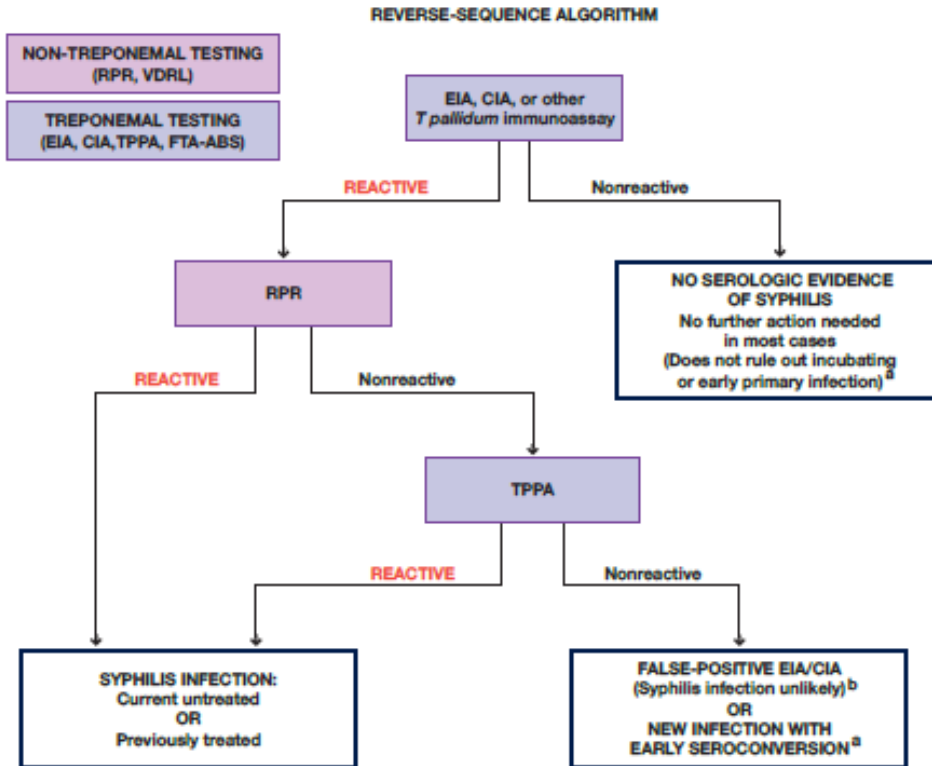
On exam you note mild bilateral upper extremity postural tremor and dysmetria. His neuro exam is otherwise unremarkable. He reports tremor has been present since hospitalization in May and preceded current rash.

Syphilis Natural history



	Non-treponemal	Treponeme-Specific
Assays	RPR (Rapid Plasma Reagin) VDRL (Venereal Disease Research Laboratory)	TPPA (T Pallidum Particle Agglutination) EIA (T Pallidum Enzyme Immunoassay)
Ab Detected	cardiolipin-cholesterol-lecithin ag	recombinant treponemal antigen
Sensitivity (False neg)	Poor in early infection Long-standing w/ prolonged latency	Earlier seroconversion Remains + after treatment or prolonged latency
Specificity (False +)	Lower- need to confirm + with Treponemal test	Higher
Clinical Use:	Initial test in lower prevalence areas (traditional seq) Treatment response Detecting re-infection in previously Tx'd patients	Initial screening test in higher prevalence areas (rev. seq) Detection of early primary, old latent infections

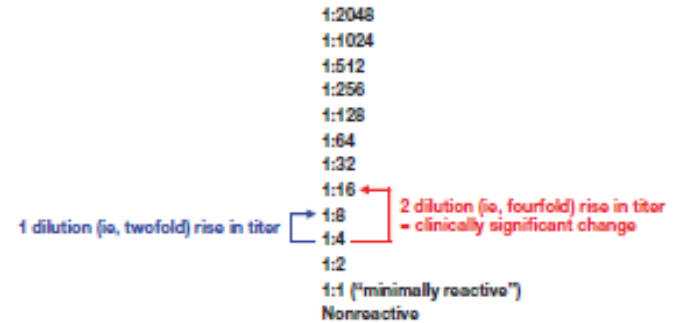
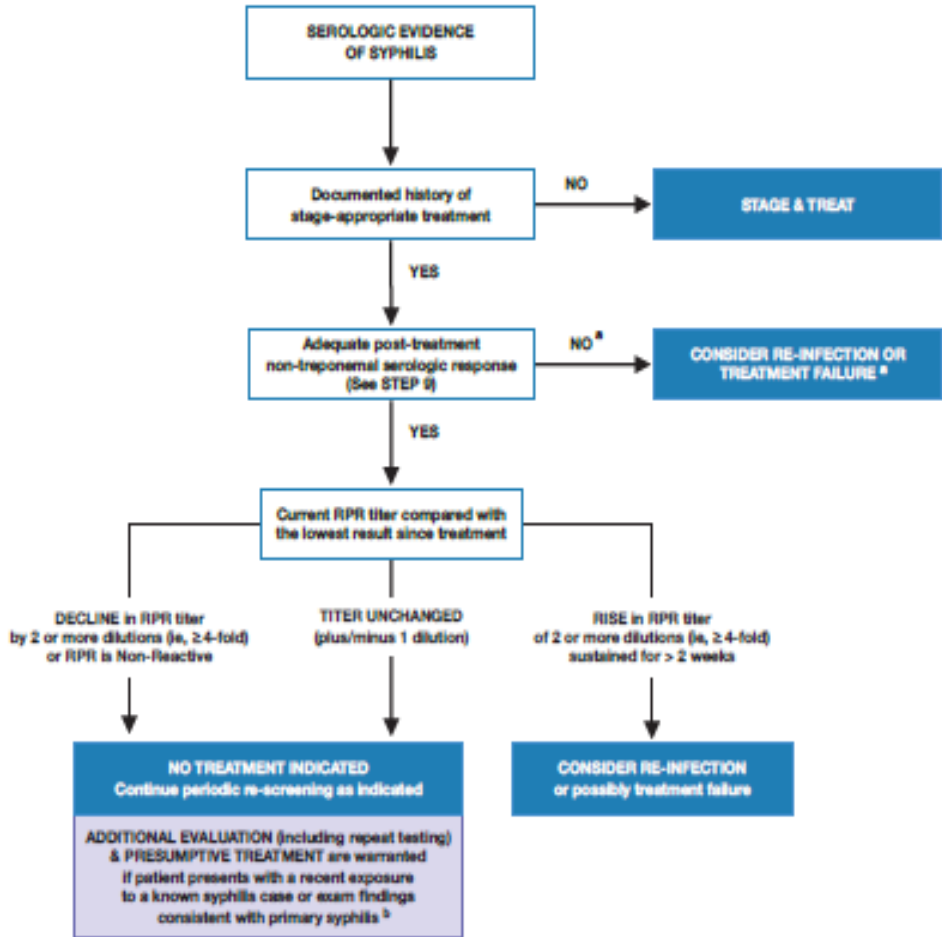
Reverse Sequence Testing Algorithm



In what scenarios would negative testing warrant treatment?

- Exposure within 90 days to partner with confirmed active infection
 - ◆ retest 1,3 mo
- Skin lesion c/w primary syphilis
 - ◆ Retest at 2-4 weeks if not treated

Treatment Algorithm



Syphilis Staging and Treatment:

Stage of Infection	CDC 2015 Recommended Treatment Regimen
Incubating Infection	Benzathine penicillin G 2.4 million units as a single intramuscular injection
Primary	Alternatives Regimens (for <u>nonpregnant patients</u> with a documented penicillin allergy) <ul style="list-style-type: none"> • Oral doxycycline 100mg twice daily for 14 days
Secondary	OR
Early Latent	<ul style="list-style-type: none"> • Oral tetracycline 500mg 4 times each day for 14 days
Late Latent or Latent of Unknown Duration	Benzathine penicillin G 7.2 million units total, administered as 3 separate doses of 2.4 million units intramuscularly, each at 1-week intervals • Alternative Regimens (for <u>nonpregnant patients</u> with a documented penicillin allergy) Note: Close serologic follow-up is critical, especially in patients living with HIV <ul style="list-style-type: none"> • Oral doxycycline 100mg twice daily for 28 days OR <ul style="list-style-type: none"> • Oral tetracycline 500mg 4 times daily for 28 days
Neurosyphilis or Ocular/Otic Syphilis	Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units intravenously every 4 hours, or by continuous infusion, for 10–14 days Alternative Regimen <ul style="list-style-type: none"> • Procaine penicillin G 2.4 million units intramuscularly once daily for 10–14 days PLUS <ul style="list-style-type: none"> • Probenecid 500mg orally 4 times daily for 10–14 days
Tertiary	Tertiary syphilis should be managed in consultation with an infectious disease specialist. Testing for HIV infection and CSF examination should be performed before therapy is initiated.

Summary:

Primary, Secondary, early latent = 1 dose Penicillin

Late/Unknown Latent: 3 weekly doses

Neurosyphilis: 10-14 days IV

Treat with Penicillin whenever possible. Only agent with good data in pregnancy, persons with HIV or neurosyphilis

Monitoring Response to Treatment:

Follow up testing:

- Obtain repeat RPR w/ titer at 6&12 months
- Consider 3,6,9,12 &24 if HIV+
- Should see 2 dilution (4-fold) decrease in titer

When to Worry about Treatment Failure:

- Persistent Si/sx after Tx
- Sustained 2+ week rise in titer (4 fold) s/p Tx
- Failure of RPR to decrease 4 fold in 6-12 mo

How to address possible Treatment Failure:

- Rule out unrecognized HIV infection
- Evaluate for re-infection (by symptoms or exposures)
- Assess adherence if Tx'd w/ oral regimen
- Rule out neuro, ocular, otosyphilis

Retreat with 3 weekly doses of benzathine Penicillin G if no evidence of CNS infection

HIV and Syphilis:

- Interpretation of treponemal and nontreponemal testing the same
- Stage-based treatment is the same for those who are HIV negative
 - Penicillin alternatives not well studied in HIV+ individuals
- May have higher rates of serologic failure or “high serofast” state
- Higher risk for neurological complications in early (primary/secondary) infection
- CSF abnormalities associated with CD4 <350, RPR > 1:32
 - No clear indication for LP in the absence of neuro signs/sx

Is anyone paying attention?

Syphilis Kahoots!

HIV Treatment

He reports adherence to ART and denies missing any doses in the last month. You decide to obtain repeat labs and follow up the next week. Interim labs return:

HIV VL: 82,400

CD4 776 (36%)

Prior HIV labs and treatment history:

HIV Dx 7/2018: VL: 402,626, CD4 698 (26%)

Started on B/TAF/FTC (lost to care),

8/27/19: VL 21,159 (reported 2 week Tx lapse)

HIV genotype: NRTI: no RAMs, NNRTI: E138A, PI: no RAMs, INSTI: No RAMs

9/23/19: VL 124 CD4 696 (38%)

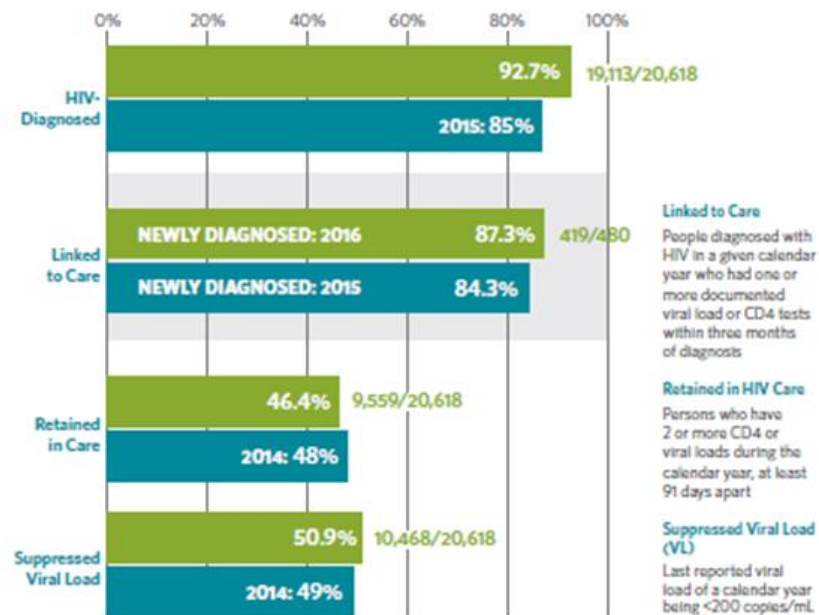
How can we promote ART adherence?

How would you address his viremia?

Linkage & Retention:

HIV Care Continuum

FIGURE 1
Philadelphia 2016 vs the United States



Sources

Philadelphia Data: Philadelphia Department of Public Health, AIDS Activities Coordinating Office.

U.S. Data: Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2015. HIV Surveillance Supplemental Report 2012;22(No. 2). <http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Published July 2012. Accessed August 2017.

Adherence Strategies:

- • Regularly assess adherence to ART and appointments.
 - ◆ Engage patients with a constructive, collaborative, nonjudgmental, and problem-solving approach
- Elicit an individual's barriers to adherence:
 - ◆ personal barriers (e.g., substance use, housing instability, stigma, lack of transportation)
 - ◆ clinic barriers (e.g., limited clinic hours, processes that make it more difficult to obtain prescriptions or schedule appointments)
 - ◆ system barriers (e.g. copays/assistance, PAT ,other Rx coverage/refill processes)
- Tailor ART to improve adherence:
 - ◆ Involve patient in treatment decisions/ART selection
 - ◆ simplify dosing or reduce side effects
 - ◆ Choose regimens without food requirements
 - ◆ Choose ART regimen with high genetic barrier to resistance (dolutegravir (bictegravir), boosted-darunavir)
 - ◆ Consider out of pocket costs/copays
- Link patients to counseling to overcome stigma, substance use, or depression
- Multidisciplinary approaches and time to understand and address barriers are needed with help of social work and case management when available

HIV Treatment

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How would you address his viremia?

ARV Viremia ?s

Terminology Review

Virologic suppression: A confirmed HIV RNA level below level of detection

Virologic failure: The inability to achieve or maintain suppression of viral replication to an HIV RNA level <200 copies/mL

Incomplete virologic response: Two HIV RNA levels ≥ 200 copies/mL after 24 weeks on an ARV regimen w/o documented suppression

Virologic rebound: Confirmed HIV RNA ≥ 200 copies/mL after virologic suppression

Virologic blip: After virologic suppression, an isolated detectable HIV RNA level that is followed by a return to virologic suppression

Potential Causes of Viremia:

- Suboptimal adherence
- Viral blip
- Drug resistance:
 - Inherited/Transmitted
 - Acquired
 - Suboptimal adherence
 - Rx-Rx or Food-Rx interactions

Addressing Detectable Viral Load: Clinical Situations

- **HIV RNA above the LLOD and <200 copies/mL.** Confirm VL and assess adherence, drug-drug and drug-food interactions.
 - a. Viral blip does not require change in treatment(All)
 - b. Persistent viremia <200 copies/mL- risk of resistance low but requires closer monitoring (All)
- **HIV RNA \geq 200 and <1,000 copies/mL.** Confirm VL and assess as per above
 - a. Persistently >200 copies/mL- higher risk of resistance
 - b. If confirmatory VL > 1000 copies/mL- obtain resistance testing (consider if >500)
- **HIV RNA >1,000 copies/mL and no drug resistance identified.**
 - a. Patient is likely not taking meds - confirm timing of test relative to patient stopping meds
 - b. If the current regimen is well tolerated- restart old regimen- repeat VL 2-4 weeks after restarting and if VL >500 get resistance testing
- **HIV RNA >1,000 copies/mL and drug resistance identified.**
 - a. Change ART regimen

Case 2: JW 51yo M presents for f/u of HIV and chronic conditions

He takes the following medications:

HIV: Elvitegravir/cobicistat/tenofovir AF/Emtricitabine (Genvoya)

Mod-persistent Asthma/Allergy: albuterol HFA, montelukast 10mg, fluticasone furoate/vilanterol (Breo) 200mcg/25mcg, Fluticasone prop. nasal

DM2: glipizide XL 20mg daily, Metformin XR 750mg BID, januvia 100mg daily

HTN/HL: lisinopril 10mg daily, chlorthalidone 25mg daily atorvastatin 40mg daily

GERD: Omeprazole 40mg daily

Case 2: JW 51yo M presents for f/u of HIV and chronic conditions

He obtained the Following labs prior to his visit:

HIV VL <40, CD4 1165 (44%)

HbA1c: 9.2%

Cr: 1.4 (eGFR 45)

LDL 51, TG 81, HDL 59 (ASCVD 20%)

He is reluctant to start insulin or other injectable medications for DM. How can we optimize his regimen?

Moore Kahoots!

ARVs and Glucocorticoids

https://www.hiv-druginteractions.org/drug_queries/472812/drug_query_interactions/table_view

Medication Interactions

- Do Not Coadminister ■ Potential Interaction ▲ Potential Weak Interaction ◆ No Interaction Expected ✦ No Clear Data
- Do Not Coadminister □ Potential Interaction △ Potential Weak Interaction ◇ No Interaction Expected ✧ No Clear Data

Results Key

	Darunavir	Emtricitabine/TAF	Ritonavir
Atorvastatin	■	◆	■
Fluvastatin	◆	◆	◆
Lovastatin	●	◆	●
Pitavastatin	◆	◆	◆
Pravastatin	■	◆	◆
Simvastatin	●	◆	●

Statins and PK inhibitors

- Most PIs (and boosted INSTI) inhibit the metabolism of most statins
- Increased risk of toxicity
- Simvastatin and Lovastatin have the most interactions
- **Fluvastatin and Pitavastatin have a safer profile**
- **Atorvastatin had the most data with Darunavir/r - need to dose adjust**

ARV and GERD Treatments

ARV Class	ARV Drugs	PPI	H2 blockers	Antacids	Effects
NRTI	None				
NNRTI	Rilpivirine (RPV)	Contrain.	Give 12h before or 4h after RPV	Give 2h before or 4h after RPV	Dec RPV conc.
PI	Atazanavir (ATV)	Contrain if Tx exper. or unboosted	Give H2 10h before or 1-2h after ATV	Give 2h before or 1-2h after ATV	Dec ATV conc. *No dose adj w/ Darunavir
INSTI	Raltegravir (RAL)			RAL: C/i Other INSTI: 2 hrs before/6hrs after	Al-Mg cont agents

Food-Drug Interactions

- No Food Requirement:
 - Bictegravir, Dolutegravir or Raltegravir- based regimens (INSTI)

- Take with Food:
 - Atazanavir/r, Darunavir/r (PI)
 - Elvitegravir based regimen (INSTI)
 - Rilpivirine (NNRTI)

- Take without food:
 - Efavirenz (NNRTI)

Note on Rilpivirine (RPV):

- Requires acid for adequate absorption
 - Requires >390 kcal meal
 - Contraindicated with PPIs
 - Separate H2 or antacids

HCV Case- RS

63yo M Hx of chronic HCV, Seizure d/o, Latent TB (untreated), DM2, GERD, HTN, CKD and remote CVA presents for routine follow up.

Hx of chronic HCV first Dx'd in 2015. Tx naive. Remote hx of IDU.

Current meds: Amlodipine 5 mg, keppra 1500 mg TID. Valproic acid 750 MG BID, Atorvastatin 40mg, Pantoprazole 40mg daily

How would you evaluate him for treatment?

Labs/Studies:

HCV PCR: 5,290,000 copies/mL

Genotype: 1b, NS5a resistance not predicted

HIV Ab/Ag: NR

HbsAg: NR, HbsAb: NR, HbcAb: Reactive

HepA IgG,IgM: NR

Hgb 11.9, Plt 295

AST: 39, ALT 34, ALP 57, Tbil 0.4, Alb 4.3

Elastography: Median liver stiffness 6.59 kPa, mod risk of clinically significant fibrosis (F2-F3), hepatic steatosis

Steps before treatment HCV Ab+ patients:

- 1) Are they infected? Get HCV PCR
- 2) Have they been treated before?
- 3) Do they have Cirrhosis?:
 - a) ***[Calculate FIB-4 score](#). >3.25 OR
 - b) ***Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
 - c) Noninvasive serologic tests above cutoffs (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
 - d) Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm³)
 - e) Prior liver biopsy showing cirrhosis
- 4) If yes, is it decompensated?:
 - a) [Calculate CTP score](#): ≥ 7 or ascites, encephalopathy, Tbili≥2, INR≥1.7, Albumin <3.5 -> If yes then refer
- 5) Is there evidence of HCC? Eval with US
- 6) Medication reconciliation & review interactions:
 - a) [AASLD/IDSA guidance](#)
 - b) [Liverpool drug interaction checker](#).
 - c) Pretreatment laboratory testing:
- 7) Do they have HIV? Order Ab/Ag test
- 8) Do they have chronic hep B? Order HbSAg
- 9) Get additional Labs (if needed)
 - a) Complete blood count (CBC)
 - b) Hepatic function panel
 - c) eGFR (Cr)
- 10) Are they or can they get pregnant? Pregnancy Test & counsel

Treatment of HCV

- 1) Glecaprevir (300 mg) / pibrentasvir (120 mg) (Mavyret) for 8 weeks
 - a) Needs to be taken with food
 - b) PI raises potential for Rx-Rx interactions
 - c) 3 tablets daily
- 2) Sofosbuvir (400 mg) / velpatasvir (100 mg) (Epclusa) for 12 weeks
 - a) In compensated cirrhosis need NS5A resistance testing for genotype 3
 - b) Single tablet

Be mindful of Rx interactions:

- Statins
- PPI, H2RA, Antacids
- Anticoagulants
- Antiepileptics
- Hypoglycemic drugs

Treatment monitoring:

- Assess adherence and treatment side effects
- Monitor hypoglycemia in diabetic patients
- INR if on warfarin
- Cirrhosis: consider LFTs in patients

Post-treatment evaluation:

- Confirm SVR-12 with HCV PCR 12 weeks after treatment along with LFTs
- Assess reinfection risk
- Limit/avoid ETOH
- Cirrhosis: HCC screening w/ US q6mo, variceal screening with EGD q2-3yr

HCV Kahoots

Resources

DHHS: <https://aidsinfo.nih.gov/>

IAS-USA: <https://www.iasusa.org/>

Ward 86 :<https://hiv.ucsf.edu/education/recommendations.html>

Liverpool HIV interactions: <http://www.hiv-druginteractions.org/>

Liverpool HCV interactions: <https://www.hep-druginteractions.org/>

HIV and Aging: <http://hiv-age.org/>

Stanford University HIV Resistance Database: <http://hivdb.stanford.edu>

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