37 – Non AIDS-Defining Complications of HIV/AIDS

Speaker: Michael Saag, MD

2020 INFECTIOUS DISEASE BOARD REVIEW

Non AIDS-Defining Complications of HIV/AIDS

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Disclosures of Financial Relationships with Relevant Commercial Interests

- None

CASE 1

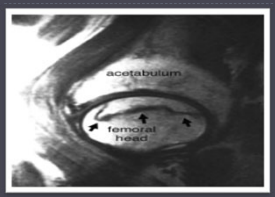
- 55 year old man presents with R hip pain
- H/o COPD requiring steroids frequently
- HIV diagnosed 17 years ago
- On TDF / FTC / EFV for 10 years; originally on IND / AZT / 3TC
- Initial HIV RNA 340,000; CD4 43 cells/ul
  - Now HIV RNA < 50 c/ml; CD4 385 cells/ul
- Electrolytes NL; Creat 1.3; Phos 3.5 Ca 8.5
- Mg 2.1, alk phos 130; U/A neg
- R Hip film unremarkable

QUESTION #1

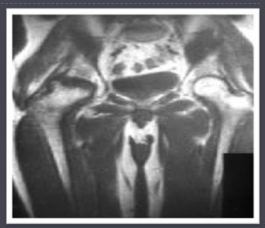
Which if the following is the most likely underlying cause of his hip pain?

A. Osetonecrosis of Femoral Head
B. Fanconi's syndrome
C. Vitamin D deficiency
D. Tenofovir bone disease
E. Hypogonadism

Osteonecrosis



This image demonstrates a classic segmental area of osteonecrosis with a dark line denoting the border between dead bone and living bone.



M. Levine. Ostoenecrosis of the hip- emedicine.com

Avascular necrosis in HIV

- Reported prior to the HAART era; increasing in HAART era.
- Rates of AVN 4.8/1000 person years >> general population.
  - Age ~ 35 yrs
  - Male predominance
  - H/o IDU
  - Increased duration of HIV
  - Low CD4
  - Elevated lipids
  - Glucocorticoid steroid use
  - Alcohol use

Monier et al, CID 2000;31:1488-92, Moore et al, AIDS 2003

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CASE 2

- 46yowf c/o (CD4 582, VL <50 c/ml) c/o 1 week cramps in calves, tingling in hands, feet
- Today awoke and can't move except hands/feet
- No F/C, chest pain, SOB, incontinence
- + chronic diarrhea 4x/day
- Chronic fatigue, poor appetite
- Meds
  - TDF/FTC/EFV (2008), on TDF/FTC/Elv/cobi since 2014
  - zoloft, buproprion, norco, prilosec, trazodone, pravachol ibuprofen

CASE 2: Exam

- VS: T 98.2 P 79 BP 112/73
- RR 16, O2 sat 97%
- Pertinent findings
- Neuro: CNII-XII intact, strength 1+ all extremities except 4+ hand/wrist and ankles.
- NI reflexes. Alert, oriented.

CASE 2: Labs

137|116|5 Gluc 83
1.6 |18 |1.0 AG 3

Ca 8.3 Phos 1.8 Mg 2.1
Lactate 1.5 CK 186
UDS +cocaine/benzo/opiate
UA: 1.015 pH 6.5 2+ pro
Neg: gluc/ketones

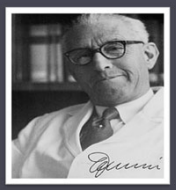
QUESTION #2

Which of the following is the most likely diagnosis?

A. Cocaine toxicity
B. Nucleoside-induced myopathy (ragged red fiber disease)
C. Serotonin Syndrome
D. Statin toxicity
E. Fanconi's syndrome

Fanconi syndrome

- Type II RTA
- Generalized proximal tubule dysfunction
- Hypophosphotemia, renal glucosuria, hypouricemia, aminoaciduria
  - Not all have present at once
- Osteomalacia can occur
- Recovery is the rule; can take months



CASE 3

- 35 year old man presents with complaints of increasing fatigue, headache, SOB / DOE
- HIV diagnosed 4 mos ago with PCP; intolerant to TMP/SMX
- Now on TAF / FTC / BIC + PCP Prophylaxis with Dapsone
- Claims adherence to all meds;
  "Doesn't miss a dose!"
- Normal PE
- Pulse Ox 85%; CXR no abnormalities
- ABG: 7.40 / 38 / 94/ 96% (room air)

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QUESTION #3

Which of the following is the most likely underlying cause of his symptoms?

A. Recurrent PCP
B. IRIS Reaction
C. Drug toxicity
D. Pulmonary Embolus
E. Patent Foramen Ovale

Hemoglobin and Methemoglobin

Methemoglobinemia: Therapy

- Discontinue offending agent
- Methylene blue
  - Action: reduces methemoglobin by NADPH-pathway
  - Indication: methemoglobin level > 30%
  - Dose: 1-2 mg/kg IV given over 5 minutes
  - Avoid: do not give to patients with G6PD deficiency (won't work)

CASE 4

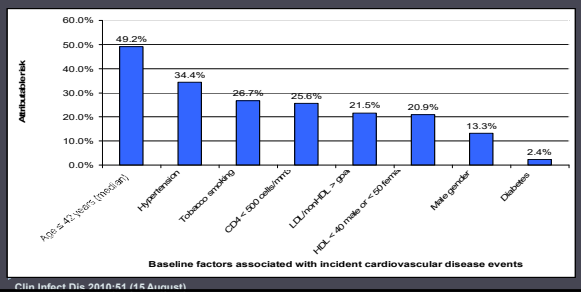
- 55 year old man presents with complaints of crushing chest pain
- HIV diagnosed 10 years ago
- Initial HIV RNA 340,000; CD4 43 cells/ul
  - Now HIV RNA < 50 c/ml; CD4 385 cells/ul
- Initally Rx with ZDV/3TC / EFV;
  now on ABC/3TC/ EFV
- On no other medications / smoker
- ECG shows acute myocardial infarction

QUESTION #4

Which of the following is the highest relative risk for his Acute MI?

A. Cigarette smoking
B. Lipid levels (LDL level of 180 / HDL 30)
C. Abacavir use
D. Lack of use of aspirin
E. HIV infection

Low CD4⁺ T Cell Count Is a Risk Factor for Cardiovascular Disease Events in the HIV Outpatient Study



Clin Infect Dis 2010;51 (15 August)

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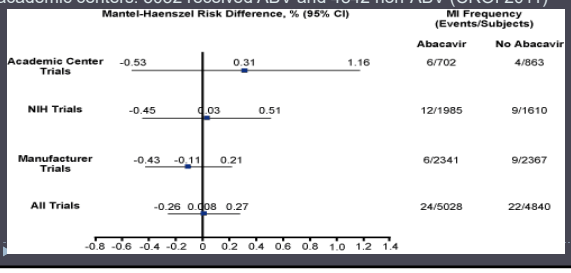
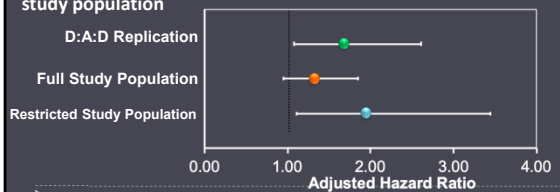
FDA meta-analysis

26 randomized, controlled ART trials of abacavir. 16 GSK studies, 5 NIH, 5 academic centers. 5032 received ABV and 4842 non-ABV (CROI 2011)



Abacavir and Risk for Myocardial Infarction- Analysis of NA-ACCORD

Adjusted hazard ratios of MI among persons with recent ABC use (vs. no recent ABC use): replication of the D:A:D model, NA-ACCORD model in the Full study population, and NA-ACCORD model in the Restricted study population



Palella FJ *et al*, Abstract 749 CROI Seattle 2015

MI Classification Protocol

Universal Definition of MI:

Primary MI (Type 1 'traditional' MI atherosclerosis)

Plaque rupture with thrombus

Secondary MI (Type 2 supply-demand mismatch)

Vasospasm

Secondary MIs common in HIV-infected individuals before age 50

Causes of Secondary MI in HIV-infected Individuals*	N (%)
Sepsis/bacteremia	100 (35%)
Cocaine induced/illicit drug	39 (14%)
Hypertensive urgency/emergency	28 (10%)
Respiratory failure	26 (9%)
Non-coronary cardiac	23 (8%)
Hypotension	15 (5%)
Procedure related	12 (4%)
GI bleed	11 (4%)
Neurologic	6 (2%)
Overdose	5 (2%)
Other/unknown	23 (8%)

*Crane et al. *Am J Epidemiol* Apr 15 2014

CASE 5

- 25 year old black woman presents with fatigue
- History of IV Heroin use; intermittently takes TDF/FTC PreP
- Exam no edema
- Work up in ER shows creatinine 8.4 BUN 79; mild anemia; mild acidemia
- In ER 10 weeks earlier; normal renal function
- U/A high grade proteinuria
- US of kidneys: Normal to increase size; no obstruction
- Rapid HIV test positive

QUESTION #5

Which of the following is the most likely cause of her renal failure?

A. Volume depletion / ATN
B. Heroin Associated Nephropathy
C. HIVAN
D. Membranous glomerulonephritis
E. Tenofovir Toxicity (PrEP)

Bonus Question:

In a patient with HIV Associated Nephropathy, which of the following is the most effective intervention to prevent progression to ESRD?

A. An ACE inhibitor
B. Corticosteroids
C. High Molecular Weight Dextran
D. Antiretroviral Therapy
E. A calcium channel blocker

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CASE 6

- 55 year old man presents with complaints of fever / volume depletion
- HIV diagnosed in ER on rapid test
- Lymphadenopathy / splenomegaly / few petechiae / Oriented X 3
- HIV RNA 340,000; CD4= 3 cells/ul
- On no medications

Hb 8.2 gm/dl; Plt count 21,000; Creatinine 2.0

Rare schizocytes on peripheral blood smear

QUESTION #6

Which of the following is the most effective intervention to increase the platelet count?

A. Splenectomy
B. Corticosteroids
C. Plasmapheresis
D. Ethambutol + Azithromycin
E. Antiretroviral Therapy

CASE 7

- 45 year old recently diagnosed with HIV
- HIV RNA 140,000; CD4= 230 cells/ul
- Baseline labs:
- Hb 11.2 gm/dl; AST 310 / ALT 120

140|101 | 5 Gluc 100

4.2 | 28 |1.1 eGFR = 65 ml/min

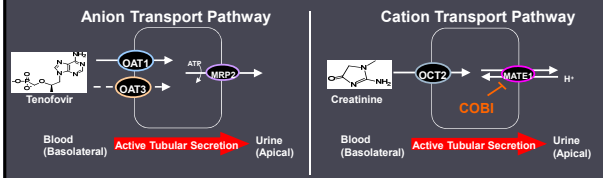
- Started on TAF/FTC+ Dolutegravir; No other medications
- Returns 4 weeks later, labs unchanged except creatinine now 1.3 mg/dl (eGFR 55)

QUESTION #7

Which of the following is the most likely cause of her increased creatinine / reduced eGFR?

A. Glomerular lesion
B. Proximal Tubule damage
C. Proximal Tubule inhibition
D. Distal Tubule damage
E. Distal Tubule inhibition

Tenofovir and COBI Interact with Distinct Renal Transport Pathways

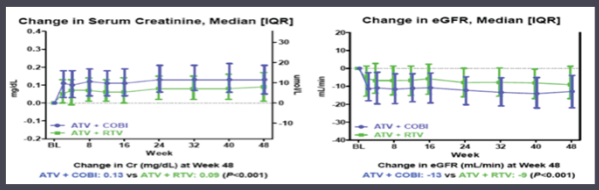


The active tubular secretion of tenofovir and the effect of COBI on creatinine are mediated by distinct transport pathways in renal proximal tubules

Ray A, et al. Antimicro Agents Chemo 2006;3297-3304
Lepist E, et al. ICAAC 2011; Chicago. #A1-1724

Changes in Serum Creatinine and eGFR Study 114

- COBI increases serum creatinine by inhibiting renal creatinine secretion[1]
- COBI does not affect actual glomerular filtration rate[2]



Gallant IAS 2012

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CASE 8

- 26 year old presents with cryptococcal meningitis and newly diagnosed HIV (Rx with AMB +5FC; to fluconazole)
- HIV RNA 740,000; CD4= 23 cells/ul
- Baseline labs:
- CSF: 2 lymphocytes / protein 54 / glu 87 (serum 102)
  OP = 430 mm H_20
  Started on TAF/FTC /Bictegravir at week 2
- Returns 6 weeks later, Fever 103 and a mass in supra-clavicular region (3 x 4 cm)

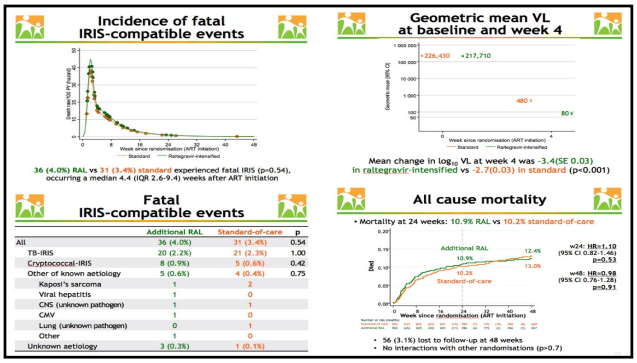
QUESTION #8

Which of the following is the most likely cause of the new mass?

A. B Cell Lymphoma
B. Multicentric Castleman's Disease
C. IRIS reaction to cryptococcus
D. Mycobacteria Avium Complex
E. Bacterial Abscess from prior PICC line

IRIS

- Immune Reconstitution Inflammatory Syndrome
- Occurs 4 – 12 weeks after initial ARV administration
- Most often in patients with advanced HIV infection
- High viral load / low CD4 count
- TB, MAC, crypto, PML, KS are most common OIs
- Is **NOT** related to type of ARV therapy



CASE 9

- 48 yo Male presents with newly diagnosed HIV infection
- Asymptomatic
- **Initial: HIV RNA 160,000 c/ml**
  CD4 count 221 cells/ul
- Other labs are normal; Started on ARV Rx with DTG + TAF/FTC
- Returns for a 3 month follow up visit
- **HIV RNA < 20 c/ml; CD4 390 cells/ul**

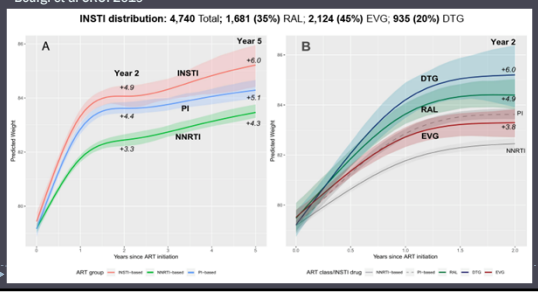
QUESTION # 9

Which of the following will most likely be present on his 3 month visit from use of dolutegravir:

A. Morbilliform skin rash (extremities)
B. 3 kg weight gain
C. Mild cognitive impairment
D. Depression
E. Anemia

Change in Weight Overtime – NA-ACCORD

Bourgi et al CROI 2019



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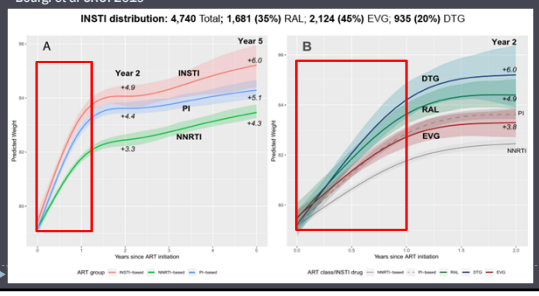

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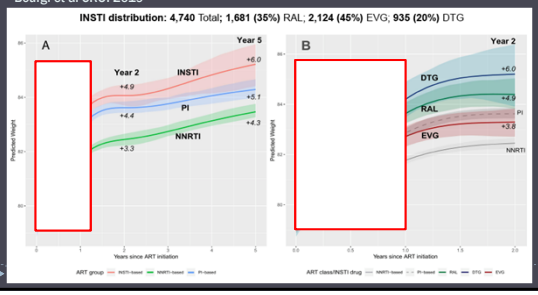

CASE 10

- 48 yo Male presents with newly diagnosed HIV infection
- Asymptomatic except for weight loss / fatigue
- **Initial: HIV RNA 160,000 c/ml**
  CD4 count 221 cells/ul
- Other labs are normal; Started on ARV Rx
- Returns for a 3 month follow up visit
- **HIV RNA < 20 c/ml; CD4 390 cells/ul**

QUESTION # 10

Assuming he remains undetectable, you tell him that his risk of transmitting HIV to his seroneg partner via sex is:

A. Virtually zero risk (< 0.2%)
B. Very low risk (< 2%)
C. Possible (<10 %)
D. It depends on which ARV regimen he's on

PARTNERS Study

- 548 heterosexual and 972 discordant gay couples followed up to 8 years
- Seropositive partner had VL < 200 c/ml
- 77,000 sexual acts without condoms
- Zero transmissions (from seropositive partner)
- Upper bound of 95% CI: 0.23 /100 CYFU
- **Sexual Transmission from a person with Undetectable Viral Load is Effectively Zero**

Rodger AJ, et al. Lancet 393: 2428-38, 2019

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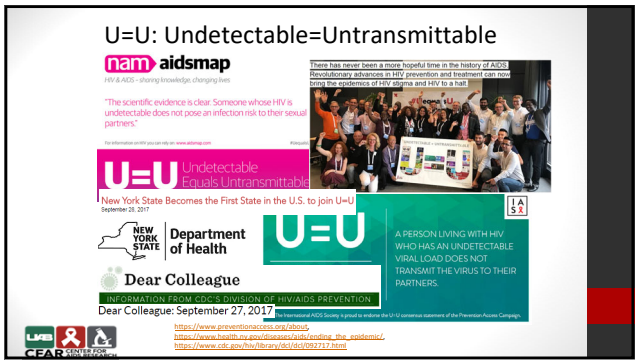

CASE 11

- 48 yo Male presents with cough, fever, loss of snese of smell, diarrhea and fatigue for 10 days
- On ARV Rx:
- **HIV RNA < 20 c/ml; CD4 590 cells/ul**
- **SARS-CoV-2 PCR test is positive**

QUESTION # 11

Which of the following is true regarding COVID-19 in PLWH vs non-HIV individuals:

COVID-19:

A. Occurs more often in PLWH and is more severe
B. Occurs less often in PLWH and is less severe
C. Occurs more often in PLWH but is less severe
D. Occurs less often in PLWH but is more severe
E. Neither occurs more often in PLWH nor is more severe

Few studies on how HIV influences COVID-19 outcomes to date

Case report of pt with HIV, HCV, and COVID-19 showed RT-PCR repeatedly negative, IgM peak prolonged (42 days) & IgG titers blunted compared to those without HIV[1]
Case series of 9 patients in Bronx COVID-19 had severe disease but all had co-morbidities[1]
Mount Sinai- PWH admitted with COVID-19 (n = 88) matched to people without HIV (n=405) by age, race/ethnicity, sex, week of COVID-19 hospitalization admission: No differences in disease severity on admission or adverse outcomes (mechanical ventilation or death)[3]

[1]Zhao CID 2020; [2]Suwanwongse K. J Med Virol 2020; [3]Sigel. JID in press;