Interactive ART Case-Based Panel Discussion

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Acknowledgements: Drs. William Short, Sarah Turbett, Virginia Pierce and Robert Goldstein; Delaney Taylor for help with preparing slides

Panelists

Constance Benson
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Connie Celum
Eric Daar
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Learning Objectives

After attending this presentation, learners will be able to:

- Evaluate options for initial treatment of HIV
- Assess regimens for managing drug-resistant HIV
- Summarize potential complications of antiretroviral therapy

Case 1: What to Start in a Person with Newly Diagnosed HIV

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ARS Question 1: What to Start

- 40 yo MSM with fever, sore throat for 1 week. Recent new sexual partner.
- No other medical conditions. Exam normal.
- HIV Ab/Ag positive; HIV differentiation Ab negative; HIV RNA 10 million.
- Pending: creatinine; CD4 cell count; HIV genotype; HLA-B5701.
- He's willing to start treatment.

What do you start?

1. Dolutegravir + FTC/tenofovir AF
2. Bictegravir/FTC/TAF
3. Dolutegravir/abacavir/lamivudine
4. Dolutegravir + lamivudine
5. Doravirine/3TC/tenofovir DF
6. Darunavir/cobi/FTC/tenofovir AF
7. Something else

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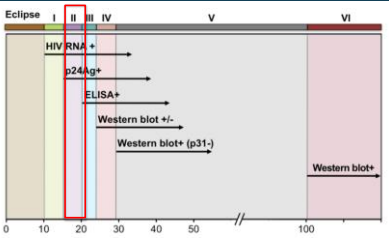
Acute HIV Infection: Fiebig Stages



Fiebig EW et al AIDS. 2003;17:1871-9

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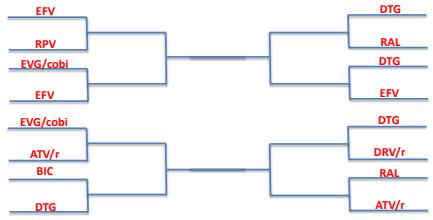
Choosing An Initial Regimen



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First line treatment: Integrase Inhibitor + 2 NRTI

DHHS (10/2018) Recommended for Most People with HIV	IAS-USA (7/2018) Recommended Initial Regimens
• Bictegravir/TAF/FTC	• Bictegravir/TAF/FTC
• Dolutegravir/abacavir/3TC	• Dolutegravir/abacavir/3TC
• Dolutegravir + TAF/FTC or TDF/FTC	• Dolutegravir + TAF/FTC
• Raltegravir + TAF/FTC or TDF/FTC	

- Fewer long-term safety and efficacy data with BIC than with DTG
- If substantial cost difference, TDF (with FTC/3TC) is effective and generally well-tolerated, esp. if pt not at high risk for bone, renal disease
- Differences between TAF and TDF accentuated when TDF is used with RTV or cobicistat

DHHS.http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Revision October 25, 2018.

Saag MS, et al. *JAMA*. 2018;320:379-396.

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Other Treatment Options When You Don't Think an Integrase Inhibitor is Optimal

- Generic EFV/TDF/3TC
- Rilpivirine/FTC/TDF or Rilpivirine/FTC/TAF
  - Food requirement (about 400 calorie meal)
  - Do not use with proton-pump inhibitor; stagger dosing if on H2 blocker
- Doravirine/3TC/TDF or Doravirine + FTC/TAF
- Darunavir/cobi/FTC/TAF

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Doravirine (DOR): A New NNRTI

- Active *in vitro* against HIV resistant to first-generation non-nucleoside reverse transcriptase inhibitors (NNRTI) (K103N, Y181C, G190A, E101K, E138K)[1]
- Once daily. Low potential for drug interactions
- Phase 3 randomized trials (DRIVE-FORWARD[2], DRIVE-AHEAD[3,4]): DOR non-inferior to darunavir/ritonavir and efavirenz in virologic suppression
  - DOR: better lipid effects than DRV/r; fewer neuropsychiatric effects than EFV
- In switch study (DRIVE-SHIFT)[5], changing to DOR/3TC/TDF non-inferior to continuing baseline ART
- DOR available alone and coformulated with TDF/3TC
- Option for people in whom integrase inhibitor therapy not optimal – eg, frequent multivalent cation use; side effects from integrase inhibitor

[1]Lai AAC 2014;58:1652-1663. [2]Molina JM, 22nd IAC, Abstract LBPEB017. [3]Orkin. IDWeek 2018. Abstr LB1. [4]Orkin. Clin Infect Dis. 2018;[Epub]. [5]Kumar P. IDWeek 2018. Abstr LB2.

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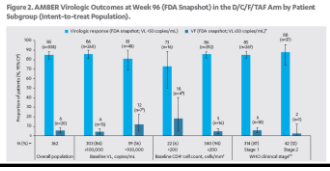
Darunavir/cobi/FTC/TAF

- High virologic suppression rate
- High barrier to resistance: no participant in phase 3 AMBER study developed tenofovir or DRV resistance
- Single arm DIAMOND study of rapid initiation (n=109): ~90% virologic suppression rate



Huhn GD et al, CROI 2019, abstract 500; Huhn GD et al, 22nd International AIDS Conference, WEPEC200

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ARS Question 2 – Resistance Testing

- 40 yo MSM with fever, sore throat for 1 week. Recent new sexual partner.
- Exam normal.
- HIV Ab/Ag positive; HIV differentiation Ab negative; HIV RNA 10 million.
- In addition to ordering RT/PR genotype, which of the following would you order?

1. HIV Integrase genotype
2. Trofile
3. Proviral DNA
4. Trofile DNA
5. None of the above
6. All of the above

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ARS Question 3: Have you seen a case of transmitted INSTI resistance?

1. Yes
2. No
3. I'm not looking

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Clinical Infectious Diseases

MAJOR ARTICLE

IDSA hivma

Should We Be Testing for Baseline Integrase Resistance in Patients Newly Diagnosed With Human Immunodeficiency Virus?

Yiannis Koullias,[1,2] Paul E. Sax,[3,4] Naomi F. Fields,[3] Rochelle P. Walensky,[3,4,5] and Emily P. Hyle[3,4,5]

[1]Department of Medicine, Brigham and Women's Hospital, [2]Harvard Medical School, [3]Division of Infectious Diseases, Brigham and Women's Hospital, and [4]Medical Practice Evaluation Center, Department of Medicine and [5]Division of Infectious Diseases, Massachusetts General Hospital, Boston

- Compared 96-week clinical outcomes and cost-effectiveness of integrase resistance testing in newly diagnosed patients
- Conclusion: Integrase resistance testing projected to result in worse outcomes and was not cost effective

Koullias et al, CID, 2017

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Open Forum Infectious Diseases

BRIEF REPORT

Canary in the Coal Mine? Transmitted Mutations Conferring Resistance to All Integrase Strand Transfer Inhibitors in a Treatment-Naive Patient

Kara S. McGee,[1] Nwora Lance Okeke,[1] Christopher B. Hurt,[1] and Mehri S. McKellar[2]

[1]Department of Medicine, Division of Infectious Diseases, Duke University Medical Center, Durham, North Carolina, [2]Institute for Global Health and Infectious Diseases, University of North Carolina at Chapel Hill

- Woman diagnosed with HIV in May 2018
- No previous ART treatment
- Pre-treatment genotype: 3 INSTI mutations: E138A, G140S, and Q148H.
- Sexual partner with HIV had the same mutations. He had previously received RAL and DTG

McGee KS et al, OFID, 2018

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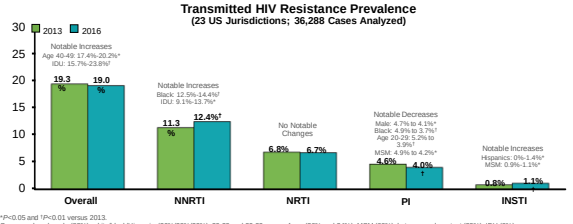
CDC (2013-2016): Transmitted HIV Drug Resistance



McClung RP, et al. 26th CROI. Seattle, 2019. Abstract 526.

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Case 2: What to Start in a Person with M184V HIV?

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ARS Question 4: What to use in someone with M184V?

- 60 yo M with HIV diagnosed in 1980s
  - CD4 cell count nadir 100
  - AZT monotherapy
  - TDF/FTC/EFV
- Reverse transcriptase genotype: M184I/V, K103N

Which regimen would you choose?

1. DTG/ABC/3TC
2. DTG + FTC/TAF
3. BIC/FTC/TAF
4. DTG + RPV/FTC/TAF
5. DRV/c/FTC/TAF
6. Something else

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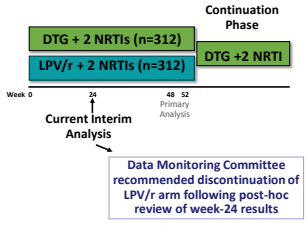
DTG + 2 NRTIs for People Failing 1st line NNRTI therapy

DAWNING study
Phase 3b

Open-label, non-inferiority
Virologic failure with NNRTI + 2 NRTIs
No primary resistance to
PIs or INSTIs
Investigator-selected NRTIs
(≥1 fully active)

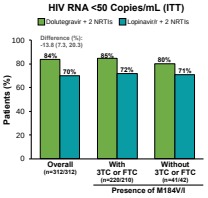
Baseline demographics:
HIV RNA >100K copies/mL: 21%.
CD4 <200 cells/mm^3: 50%.
AIDS: 32%.

Duration of 1st line ART: 36 months.
Prior therapy agent:
EFV (78%), TDF (59%), AZT (29%), abacavir (2%).



DAWNING: DTG + 2 NRTI superior to LPV/r + 2 NRTI

- DTG + 2 NRTIs superior to LPV/r + 2 NRTIs in terms of HIV RNA <50
- High rate of suppression with DTG + 2 NRTI even when M184V/I present and 3TC/FTC used



Brown D, et al. 26th CROI. Seattle, 2019. Abstract 144.
Aboud M, et al. *Lancet Infect Dis*. 2019;19:253-264.

What about switching a person with M184V who is suppressed?

- 100% virologic suppression at wk 24 in participants (n=37) with isolated M184V/I who switched to EVG/cobi/FTC/TAF
- Randomized study
  - People (n=563) suppressed on DTG + FTC/TDF or DTG + FTC/TAF switched to BIC/FTC/TAF or DTG + FTC/TAF
  - 14% had baseline M184V/I (in isolation or with other mutations)
  - Week 12 results: 99% remained virologically suppressed; similar results regardless of presence of baseline M184V/I

Zhang W, et al. AIDS 2018, Abst. TUAB0104B39; Acosta RK, et al. 26th CROI, 2019, Abstract 551

Case 3: What regimen to use in someone with virologic failure?

What to use in someone with virologic failure?

- 40 yo M with HIV with virologic suppression on DRV/cobi + FTC/TDF. No previous ARV regimens
- Serum creatinine 1.4
- You discuss switching him DRV/cobi + FTC/TAF; he plans to make this change in a few weeks and return for labs in 6 weeks
- Misses 6 week follow up for labs. Comes back about 3 months later
  - HIV RNA **3500** copies/ml. Denies any missed doses
  - You review his medications and he is only taking FTC/TAF (thought it was a new single tablet regimen with all components)

Case courtesy of William Short, MD

ARS Question 5

Would you add back DRV/c right now while awaiting genotype?

1. Yes
2. No
3. Not sure

Case courtesy of William Short, MD

Panel

- What resistance mutations do you expect?
- What regimen would you keep him on while awaiting the genotype?

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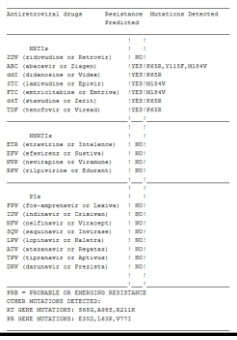
Genotype:
K65R, Y115F, M184V

What regimen would you recommend?



Antiretroviral drugs	Resistance Predicted	Mutations Detected
NRTIs		
3TC (lamivudine or Epivir)	YES	M184V
ABC (abacavir or Ziagen)	YES	K65R,Y115F,M184V
AZT (zidovudine or Retrovir)	NO	
D4T (stavudine or Zerit)	YES	K65R
DDI (didanosine or Videx)	YES	K65R
FTC (emtricitabine or Emtriva)	YES	M184V
TDF (tenofovir or Viread)	YES	K65R
NNRTIs		
DOR (doravirine or Pifeltro)	NO	
EFV (efavirenz or Sustiva)	NO	
ETR (etravirine or Intelence)	NO	
NVP (nevirapine or Viramune)	NO	
RPV (rilpivirine or Edurant)	NO	
PIs		
ATV (atazanavir or Reyataz)	NO	
DRV (darunavir or Prezista)	NO	
FPV (fos-amprenavir or Lexiva)	NO	
IDV (indinavir or Crixivan)	NO	
LPV (lopinavir or Kaletra)	NO	
NFV (nelfinavir or Viracept)	NO	
SQV (saquinavir or Invirase)	NO	
TPV (tipranavir or Aptivus)	NO	

PRB = PROBABLE OR EMERGING RESISTANCE
OTHER MUTATIONS DETECTED:
RT GENE MUTATIONS: S68G,A98S,R211K
PR GENE MUTATIONS: E35D,L63P,V77I

Case courtesy of William Short, MD

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Follow-up

- Started on DRV/cobi/TAF/FTC plus dolutegravir while genotype results pending
- 4 weeks later, HIV RNA <20
- 3 months later, HIV RNA <20
- 9 months later, HIV RNA <20

Case courtesy of William Short, MD

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Case 4: What do you do in someone on ART with persistent low-level viremia?

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Case

- 63 yo diagnosed with HIV in the 1990s
- CD4 nadir 180, HIV RNA 60,000 copies/mL
- Multiple regimens in the 1990s; no known drug resistance
- 2010 to 2015: DRV/r + TDF/FTC
- HIV RNA 50-200 copies/mL
- 2015 to present: DTG + FTC/tenofovir
- HIV RNA 40-200 copies/mL
- Reports 100% adherence; does not take other medicines

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ARS Question 6: What should you do?

1. Change his ART regimen
2. Intensify his ART regimen
3. Leave him alone
4. Something else

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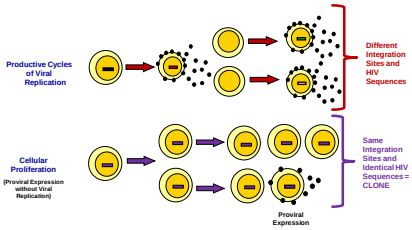
Non-suppressible viremia: Viral Replication vs. Cellular Proliferation



Halvas E et al, CROI 2019, #23

Non-suppressible viremia due to large clones producing HIV particles

- 10 participants; no suspected non-adherence
- Median VL: 98 (range: 43, 378); median duration viremia on ART: 3.2 yr
- Sequencing and integration site analyses:
  - Plasma viremia due to clonal proliferation of CD4 cells carrying replication-competent proviruses ("repliclones")
  - No evidence for drug resistance, inadequate drug levels
- Implications:
  - Intensification or ART changes would not be effective
  - Repliclones may need to be eliminated to cure HIV

Halvas E et al, CROI 2019, #23; Also Zhang X et al, CROI 2019, #348

Case 5: What should you do in someone who gains weight after starting ART?

Case

- 63 yo African American woman diagnosed with HIV in the 1990s
- Previous regimens: TDF/FTC/EFV; DRV/r + ETR + TAF/FTC (because of drug resistant virus)
- Switched to DTG + DRV/r + TAF/FTC
- Gained 40 lb over ensuing 2 years (from 210 lb to 250 lb)
- She asks you if her weight gain is related to her medicines

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Case—ARS Question 7: Weight Gain and ART

Weight gain is associated with:

1. All antiretroviral regimens
2. Integrase inhibitor-based regimens
3. Protease inhibitor-based regimens
4. Non-nucleoside reverse transcriptase inhibitor-based regimens
5. The jury is still out

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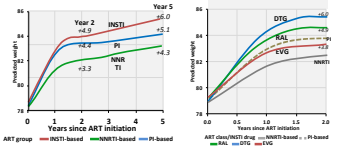
Weight Gain and Integrase Inhibitors: Initial Rx

- NA-ACCORD: observational study of 24,001 participants initiating ART
  - INSTIs and PIs associated with greater increase in weight than NNRTI
  - DTG and RAL associated with greater weight gain than EVG



Bourgi K et al, CROI 2019, #670

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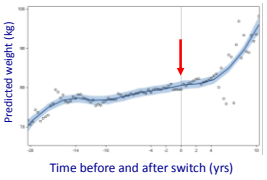
Weight Gain & Integrase Inhibitors: Switch study

- ACTG study
  - 972 adults who switched to INSTI-based ART (observational study)
  - Women, blacks and those >60 years had greatest weight gain
  - DTG associated with greatest increase in annual weight (1.0 kg per year compared with 0.5 and -0.2 for EVG and RAL, respectively)



Lake J et al, CROI 2019, #669

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Weight Gain and Integrase Inhibitors

- Other recent studies showing association:
  - HOPS: observational switch study
    - BMI trajectory slopes: DTG > RAL or EVG
  - WIHS: observational switch study in women
- Studies showing mixed result or no association
  - TRIO study: associated in bivariate analysis, not in multivariable model
  - HPTN 077: Cabotegravir in people without HIV: no association

Kerchberger A et al, CROI 2019, #672; Pallela FJ et al, CROI 2019, #674; McComsey G et al, CROI 2019, #671; Landovitz R et al, CROI 2019, #34

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My Take: Is Weight Gain More Common and Significant With INSTI-Based Regimens?

- Accumulating data that INSTI-based regimens may be associated with greater weight gain than some other regimens; randomized data from initial therapy trials needed
- Whether there are differences between INSTIs and the role of NRTIs in the regimen are uncertain
- Mechanism of weight gain and distribution of fat after initiation of modern regimens, including INSTI-based therapies, should be evaluated
- In patients with significant weight gain, the impact of changing to a non-INSTI based regimen needs to be studied

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Case Follow-up

- 43 yo African American woman diagnosed with HIV in the 1990s
- Previous regimens: TDF/FTC/EFV; DRV/r + ETR + TAF/FTC
- Switched to DTG + DRV/r + TAF/FTC
- Gained 40 lb over the ensuing year (from 210 lb to 250 lb)
- **She asks you if her weight gain is related to her medicines**
- **Over the ensuing 3 months, without changing her ART regimen, she begins to diet and exercise: loses 30 lb!**

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Surprises

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Case 7

- 40 yo M with well controlled HIV on ABC/3TC/DTG
- Presented with 6 days of abdominal cramping and diarrhea: 1-3 bowel movements per hour throughout day and night
- Noted blood on toilet paper but not in stool
- Mild chills; temperature 100.7
- Travel: Cape Cod. Ate at cookouts, including salads with mayonnaise
- Three new male sexual partners; oral anal stimulation

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Specimen Source/ Description	STOOL
SPECIAL REQUESTS	No Special Requests
CULTURE / TEST	SHIGELLA SONNEI (GROUP D) (*)
CULTURE / TEST	RESULT CALLED TO CARE UNIT AND/OR MD (*)
CULTURE / TEST	Identification confirmed by STATE LAB, MA Dept of Public Health, 305 South Street, Jamaica Plain, MA 02130
CULTURE / TEST	NORMAL ENTERIC FLORA PRESENT
REPORT STATUS	08242017 FINAL
ORGANISM	SHIGELLA SONNEI (GROUP D)
ORGANISM	SHIGELLA SONNEI (GROUP D)

ARS Question 8: Would you treat this patient?

1. Yes
2. No
3. Only if he doesn't improve

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			Shigella sonnei (group d) (ZZ00) GRADIENT METHOD		Shigella sonnei (group d) (ZZ01) RAPID MIC METHOD	
Specimen Source/ Description	STOOL					
SPECIAL REQUESTS	No Special Requests					
CULTURE / TEST	SHIGELLA SONNEI (GROUP D) (*)					
CULTURE / TEST	RESULT CALLED TO CARE UNIT AND/OR MD (*)					
CULTURE / TEST	Identification confirmed by STATE LAB, MA Dept of Public Health, 305 South Street, Jamaica Plain, MA 02130					
CULTURE / TEST	NORMAL ENTERIC FLORA PRESENT					
REPORT STATUS	08242017 FINAL					
ORGANISM	SHIGELLA SONNEI (GROUP D)					
ORGANISM	SHIGELLA SONNEI (GROUP D)					
Susceptibility						
		Ampicillin			>=32	Resistant
		Azithromycin	>256	No Interpretation		
		Ciprofloxacin	4	Resistant		
		Trimethoprim/sulfamethoxazole			>=320	Resistant
Susceptibility Comments						
Shigella sonnei (group d) (ZZ00)						
SHIGELLA SONNEI (GROUP D)						
Shigella sonnei (group d) (ZZ01)						
SHIGELLA SONNEI (GROUP D)						

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Case 8

- 50 yo HIV negative MSM on PrEP presents with 4 days of watery diarrhea, abdominal cramping
- Denies blood in stools, fevers, chills
- Reports recent oral anal contact

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Specimen Source/ Description	STOOL WATERY STOOL
SPECIAL REQUESTS	No Special Requests
CULTURE / TEST	SHIGELLA FLEXNERI (GROUP B) SEROTYPE: 3a (*)
CULTURE / TEST	RESULT CALLED TO CARE UNIT AND/OR MD (*)
CULTURE / TEST	Serotyping performed by STATE LAB, MA Dept of Public Health, 305 South Street, Jamaica Plain, MA 02130
CULTURE / TEST	NORMAL ENTERIC FLORA PRESENT
REPORT STATUS	08242017 FINAL
ORGANISM	SHIGELLA FLEXNERI (GROUP B)
ORGANISM	SHIGELLA FLEXNERI (GROUP B)

Susceptibility

	Shigella flexneri (group b) (Z290) GRADIENT METHOD		Shigella flexneri (group b) (Z281) RAPID MIC METHOD	
Ampicillin			>=32	Resistant
Ciprofloxacin	0.12	No Interpretation		
Trimethoprim/sulfamethoxazole			<=20	Susceptible

ARS 9: How would you treat this patient?

1. Oral Cipro
2. Oral TMP/SMX
3. No treatment
4. IV ceftriaxone

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Antibiotic-resistant Shigella

- Increased risk of antibiotic-resistant Shigella in MSM[1]
  - 7 outbreaks between 2011 and 2015
  - 6 outbreaks: azithromycin resistance
  - 3 outbreaks: multi-drug resistance
- ~20% of Shigella isolates tested in NYC during 2013–2015: decreased azithromycin susceptibility (>=32 ug/mL)[2]
  - Almost exclusively among MSM, most infected with HIV

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1. Bowen A et al, Emerg Infect Dis, 2016; 2. Murray K et al, MMWR, 2017

Update – CDC Recommendations for Managing and Reporting *Shigella* Infections with Possible Reduced Susceptibility to Ciprofloxacin

HAN

This is an official CDC HEALTH UPDATE

June 7, 2018

- Increasing number of Shigella isolates that test susceptible to cipro (MIC 0.12 to 1 mcg/mL) but harbor resistance genes
  - Unclear whether FQ associated with worse clinical outcome, increased transmission
- Increasing number of isolates with azithromycin MIC that exceed epidemiologic cutoff value (ECV)
- CDC: antibiotics if immunocompromised, severe illness, outbreaks
- If treatment failure suspected: report to local health department, send stool isolate to CDC for further testing
- Counsel patients to wait to have sex for 1-2 wk after diarrhea resolves

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Recent MGH Cases

- *Shigella sonnei* (group D): resistant to ampicillin, TMP/SMX, azithromycin (>256) and ciprofloxacin (MIC 8); CTX susceptible
  - Patient 1: treated for Giardia, not Shigella
  - Patient 2: treated with cefixime
  - Patient 3: not treated
  - Patient 4: not treated (partner also infected)
- *Shigella flexneri* (group B): resistant to amp, susceptible to TMP/SMX, cipro MIC 0.12
  - Patient 5: not treated

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Case 9: Pulmonary and Hepatic Nodules in a Man with HIV

- Middle-aged man with HIV
- CD4 count >500, VL <50 for many years on TDF/FTC + ATV/r
- Patient presented with 3-4 weeks of abdominal pain and chest wall discomfort
- Admitted to outside hospital for evaluation of chest discomfort. Found to have pulmonary nodules and rim-enhancing lesions in the liver

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Case - continued

- Past medical history: secondary syphilis several years ago, s/p treatment; non-reactive RPR 4 months prior to presentation
- Multiple sexual partners, does not always use condoms. No TB exposures.
- Afebrile. No rash or adenopathy. No abdominal tenderness, HSM
- AP 695. ALT 119. AST 70. Bilirubin 2.5/0.3 (LFTs had been normal 4 months ago)

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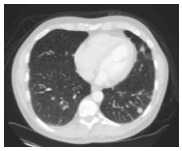
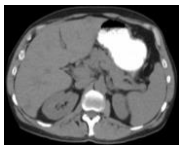
Question: What is the diagnosis?

1. Malignancy
2. Syphilis
3. Peliosis hepatis (Bartonella)
4. Fungal infection
5. Mycobacterial infection



Multiple pulmonary nodules, measuring 2-10 mm



Multiple rim-enhancing lesions in the liver

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Tests

- Blood cultures negative.
- Cryptococcal antigen negative
- Urine histoplasma antigen negative
- Serologic testing for Bartonella, Brucella, Coxiella negative
- Interferon-gamma release assay negative
- HIV RNA undetectable. CD4 cell count 500
- HCV RNA undetectable. HCV Ab negative

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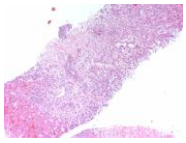
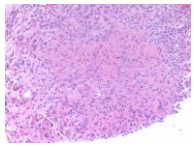
Liver biopsy

- Periportal inflammation and edema; granulomas; microbiologic stains negative



Periportal inflammation and edema



Granuloma

Slides courtesy of Dr. Joseph Misdraji, Mass. General

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Follow-up

- RPR + 1:64
- Treated with 3 weekly shots of IM penicillin
- AP declined from 695 to normal
- ALT declined from 119 to normal
- Repeating imaging revealed markedly decreased size of pulmonary nodules and liver lesions!

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Syphilitic hepatitis

- LFT abnormalities may occur during secondary syphilis
- AP may be disproportionately elevated, but not always
  - In one series, median AP 186 (129-1836), median ALT 105 (82-614)
  - LFTs normalized after penicillin (within 5 d to 3 mo.)
- Pathology: pericholangiolar inflammation, periportal hepatocyte necrosis; spirochetes seen on liver biopsy in some but not all cases
- Rare cases of hepatic gumma mimicking cancer reported

Crum-Cianflone N et al Int J STD AIDS, 2009. Mullick CJ et al, CID, 2004. Shim HJ. World J Hepatol, 2010

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Take home points

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Take Home Points

- Integrase inhibitor-based regimens optimal for most people with HIV; newer NNRTI- and PI-based therapies are good alternatives
- Transmitted integrase inhibitor resistance uncommon; monitoring needed
- Most people with M184V HIV will have virologic suppression on 2 NRTI + dolutegravir (and probably bictegravir) as long as there is active NRTI
- Stable low-level viremia in people on ART may not represent ongoing viral replication
- CDC has updated its guidance on diagnosing and managing Shigella
- Look out for unusual manifestations of syphilis: #itsalwayssyphilis

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Extra Case

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Case: When should you use a 2-drug regimen for initial therapy?

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ARS Question: Two-drug therapy

- 50 yo HIV+ M with diabetes, hypertension, chronic renal insufficiency (creatinine clearance of 25)
- HIV RNA 30,000, CD4 cell count 450
- HLA-B5701 positive
- You want to choose a regimen that avoids TAF, TDF, ABC

1. Darunavir/cobicistat + FTC
2. Darunavir/ritonavir + raltegravir
3. Darunavir/ritonavir + dolutegravir
4. Darunavir/ritonavir + 3TC
5. Dolutegravir + 3TC
6. Dolutegravir + rilpivirine
7. Atazanavir + elvitegravir/cobicistat

NRTI-limiting Regimens for Initial Therapy

- **DRV/r + RAL (NEAT001)[1,2]**
  - –Non-inferior to DRV/r + TDF/FTC
  - –CD4 <200: DRV/r + RAL inferior to DRV/r + 2 NRTI
  - –VL >100 K: more failures with DRV/r + RAL
- **DRV/r + 3TC[3] (ANDES)**
  - –Non-inferior to DRV/r + FTC/TDF (n=145)

[1]Raffi F et al, Lancet, 2014; [2]Lambert-Niclot S et al, J Antimicrob Chemother, 2016; [3]Figueroa et al, CROI 2018, Abstract 489

NRTI-limiting Regimens for Initial Therapy

- **DTG + 3TC**
  - –Non-inferior to DTG + TDF/FTC (GEMINI-1 and -2)
- **Long-acting injectable cabotegravir + rilpivirine (after virologic suppression on oral therapy)**
  - –Non-inferior to oral ART (FLAIR)

My take: Are 2-Drug Regimens Optimal Initial Therapy for Most Persons With HIV?

- For initial therapy, DTG + 3TC looks promising at week 48
  - Single-tablet formulation approved on April 8, 2019 for initial treatment of adults with no known or suspected resistance to its components
    - One pill once daily with or without food
    - Should not be used in people with HIV/HBV (test for HBV)
  - Longer term data awaited before recommended by guidelines for most persons with HIV
- Other NRTI-limiting options for initial therapy
  - DRV/r + RAL (if CD4 count >200, VL <100K); DRV/r + 3TC; in the future, perhaps long-acting cabotegravir + rilpivirine

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Question-and-Answer

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