Case Presentation: Kidney Disease

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Disclosures

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  Gilead Sciences

- Honoraria for internal education
  Bristol Myers Squibb
Kidney Disease is Common in HIV

- Both acute & chronic kidney disease are more common in HIV-infected adults

Wyatt *et al.* AIDS 2008
Choi *et al.* JASN 2007
Medapalli *et al.* JAIDS 2012
Acute Kidney Injury is Associated with Adverse Outcomes in HIV

Choi et al. KI 2010
Chronic Kidney Disease (CKD) is Associated with Adverse Outcomes

Wyatt et al. JAIDS 2010
Choi et al. Circ 2010*
Case Presentation

- 46 year old HIV-HCV+ black man referred for rising creatinine

Baseline 0.9 mg/dL $\rightarrow$ 1.3 four months ago $\rightarrow$ 1.5
(80 mmol/L $\rightarrow$ 133)

eGFR 118 $\rightarrow$ 64 mL/min/1.73m$^2$

CrCl (70kg man) 102 $\rightarrow$ 61 mL/min
Case Presentation

- HIV-HCV diagnosed 2010
  - Risk factor MSM, no history of IDU
  - Nadir CD4 > 200; on ARVs since diagnosis
  - CD4 > 500; HIV-RNA undetectable
- No other medical history
- Family history of DM and HTN, no CKD
- Current meds: FTC/TDF, dolutegravir
Case Presentation

- Thin, well-groomed man
  - BP 112/64
  - Weight 57 kg

| eGFR 118 | 76 | 64 mL/min/1.73m² |
| CrCl 83  | 57 | 50 mL/min       |
GFR Estimates are Just That

- Serum creatinine is not an ideal marker
  - Influenced by muscle mass
  - Both filtered and secreted

- Estimates perform ‘OK’ in stable HIV
  - Studies have included few ART-naïve patients

Inker et al. JAIDS 2012
Gagneux-Brunon et al. AIDS 2013
Best Choice of GFR Estimate Varies

- FDA dosing guidelines are based on CrCl
- CKD-EPI is usually the most accurate
- Near dosing thresholds, clinical judgment is essential. For example:
  - 3TC has a wider therapeutic window
  - Ask about diet/ supplements
  - Consider meds that inhibit creatinine secretion

Inker et al. JAIDS 2012
Drugs used in HIV Interfere with Creatinine Secretion

- Dolutegravir
- Rilpivirine
- OCT2

Creatinine

Blood

Urine

- MATE2
- Trimethoprim

- MATE1
- Cobicistat
- Ritonavir

Lepist et al, Kidney Int 2014
Moss et al, Antimicrob Agents Chemother 2013
ART & Low GFR: Role of RTV?

EUROSIDA (CrCl<60)

Mocroft et al. AIDS 2010*
Sherzer et al. AIDS 2012
Ryom et al. JID 2013
Cystatin C-based GFR estimates?

- Potential advantages in unique settings:
  - Extremes of muscle mass
  - Drugs that interfere with creatinine secretion

- Stronger association with mortality in HIV
  - May reflect systemic inflammation

Choi et al, AJKD 2010
Lucas et al, HIV Med 2014
Cystatin C-based GFR estimates?

- Lower accuracy & higher bias in HIV

May still be useful if normal/low

Inker et al. JAIDS 2012
Back to Our Case

- 46 year old HIV-HCV+ black man referred for rising creatinine

Baseline 0.9 mg/dL $\rightarrow$ 1.3 four months ago $\rightarrow$ 1.5

Creatine/ high protein diet

Darunavir/r $\rightarrow$ Dolutegravir (FTC/TDF continued)
Case Presentation

**Creatinine** 0.9 mg/dL → 1.3 → 1.5 → 1.3 mg/dL

Off creatine/ diet

**Cystatin C** 0.77 mg/L (normal range 0.5-1.0)

**Urinalysis**: no protein, no glucose; UPCR 0.09

**eGFR (Cr)**: 76 mL/min/1.73m²

**eGFR (CysC)**: 113 mL/min/1.73m²
Our Case: Alternate Ending

- 46 year old HIV-HCV+ black man referred for rising creatinine

Baseline 0.9 mg/dL $\rightarrow$ 1.3 four months ago $\rightarrow$ 1.5

No changes in diet/ meds

Urinalysis: 2+ protein, no glucose, no cells
Case Presentation: Ending 2

- 46 year old HIV-HCV+ black man with rising creatinine and proteinuria
  - HIV-related disease?
  - HCV-related disease?
  - Comorbid disease?
  - Medication nephrotoxicity?
HIV-Associated Nephropathy?

![Bar chart showing proportion of biopsies with HIVAN from 1995 to 2004.](Image)
Case Presentation: Ending 2

- 46 year old HIV-HCV+ black man with rising creatinine and proteinuria
  - HIV-related disease: probably not
  - HCV-related disease?
  - Comorbid disease?
  - Medication nephrotoxicity?
Case Presentation: Critics’ Choice

- Urine protein: creatinine 1.1
- UA: 1+ protein, otherwise negative
- Serum complements normal
- Serum cryoglobulin negative
- Rheumatoid factor slightly elevated
- Serum bicarbonate, phosphorus & uric acid wnl
Kidney Biopsy Can Provide a Definitive Diagnosis

- Unclear diagnosis
- Limited alternatives
- HBV co-infection

Courtesy of Glen Markowitz & Vivette D’Agati
Potential for ↓ Nephrotoxicity with Tenofovir Alafenamide?

- Median (Q1, Q3) change from baseline eGFR Cockroft-Gault (mL/min)

- Cobicistat effect
- Tenofovir effect

E/C/F/TAF
STB

Zolopa et al. CROI 2013*
Sax et al. Lancet 2014
Potential for ↘ Toxicity with TAF: Switch Studies

- Phase 3 trial of full-dose E/C/F/TAF in stable patients with GFR 30-69 (80 with GFR < 50)
- No significant change in eGFR with switch
- Reduction in proteinuria/albuminuria
- Rapid decline in RBP & β2-microglobulin?

Fordyce et al. CROI 2015
Our Case: The Hollywood Ending

- Increased risk for TDF toxicity, particularly with planned HCV therapy?
  - Low body weight, uncertain GFR estimates
  - Regimen already switched to avoid PI/r
- A candidate for TAF when approved?
Our Case: Alternate Ending

- Safety of re-challenge with TAF in patients with known or suspected TDF toxicity is unknown