Case Presentation: Kidney Disease

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Disclosures

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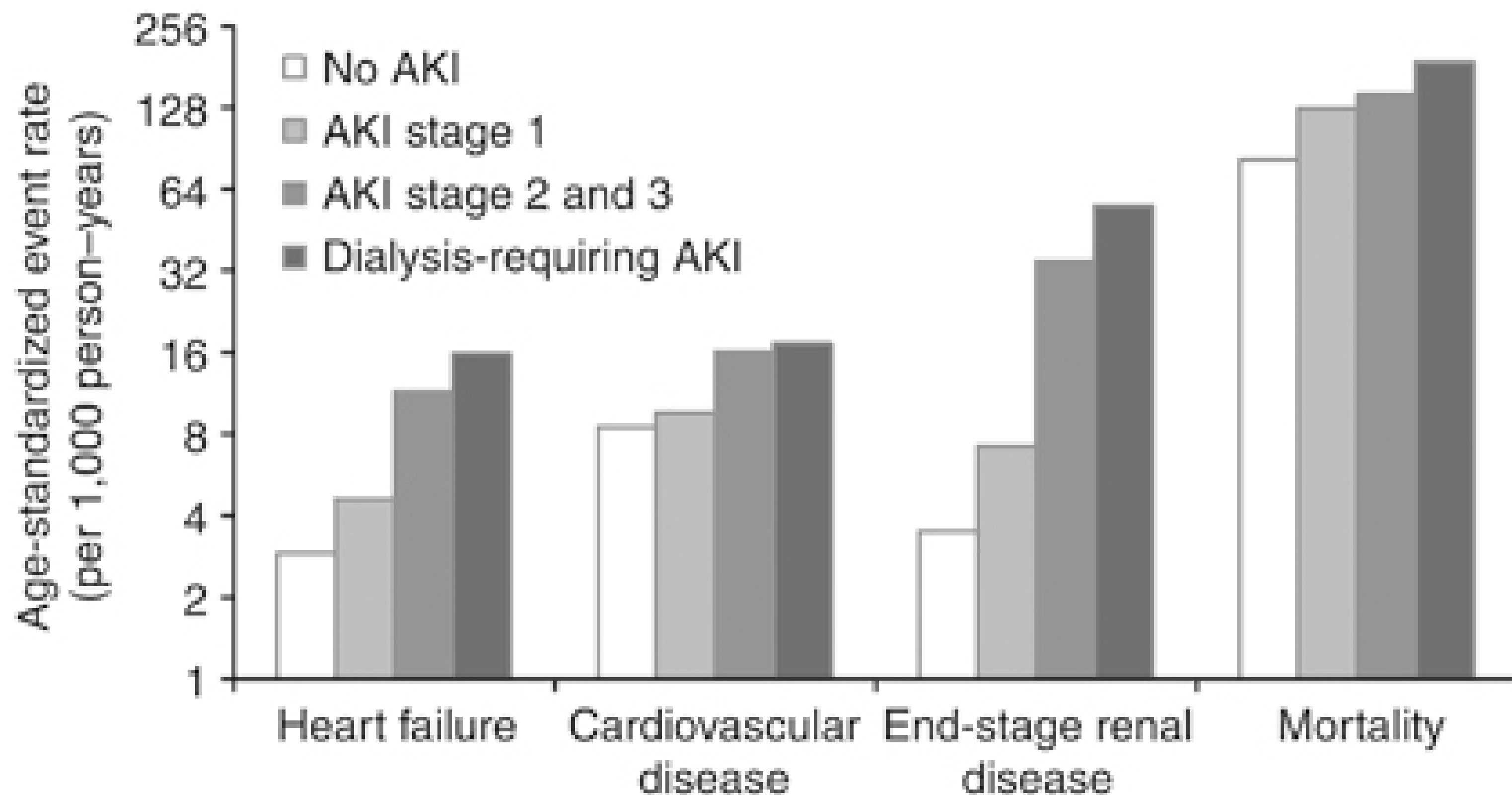
- Honoraria for internal education Bristol Myers Squibb

Kidney Disease is Common in HIV

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

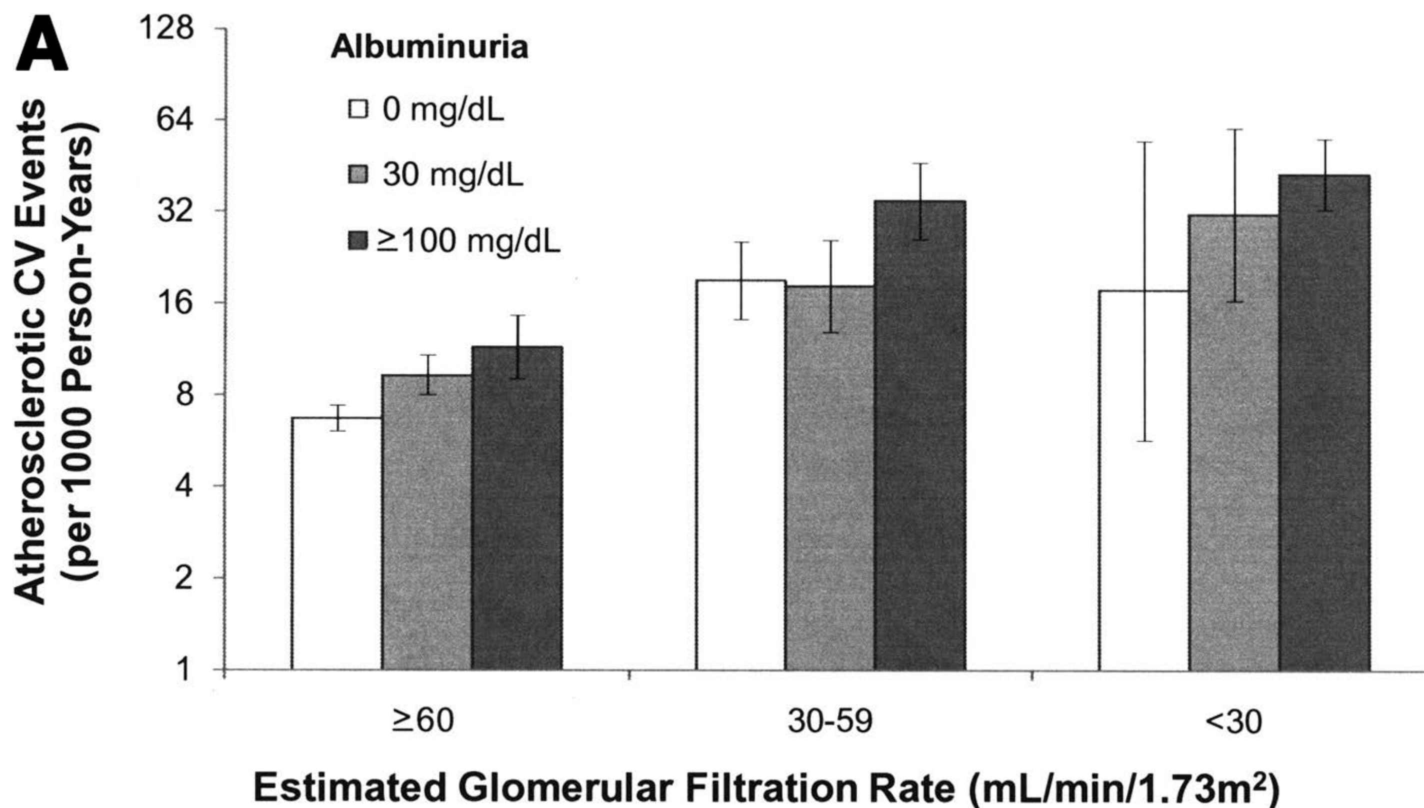
Wyatt *et al*. AIDS 2008
Choi *et al*. JASN 2007
Medapalli *et al*. JAIDS 2012

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 → **1.3** four months ago → **1.5**
(80 mmol/L →→ 133)

eGFR 118 → 64 mL/min/1.73m^2

CrCl (70kg man) 102 → 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/1.73m^2

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

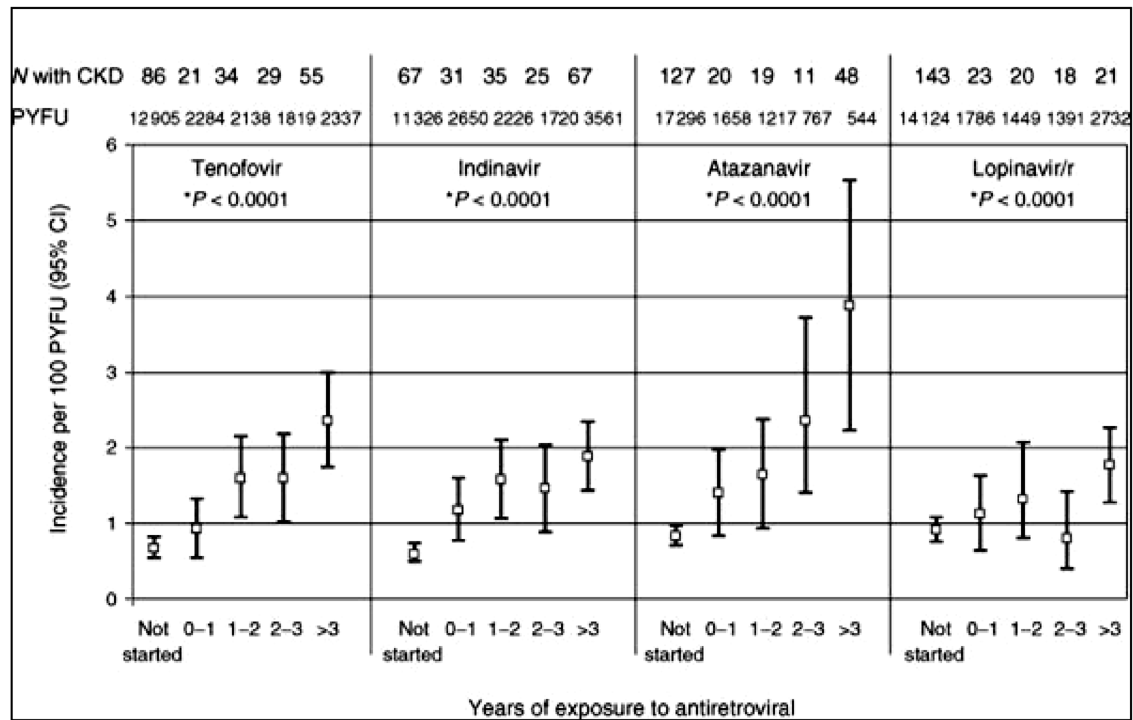
- FDA dosing guidelines are based on CrCl
- CKD-EPI is usually the most accurate
- Near dosing thresholds, clinical judgment is essential. For example:
  - 3TC has a wider therapeutic window
  - Ask about diet/ supplements
  - Consider meds that inhibit creatinine secretion

Inker *et al*. JAIDS 2012
Vrouenraets *et al*. Clin Nephrol 2012

Drugs used in HIV Interfere with Creatinine Secretion

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

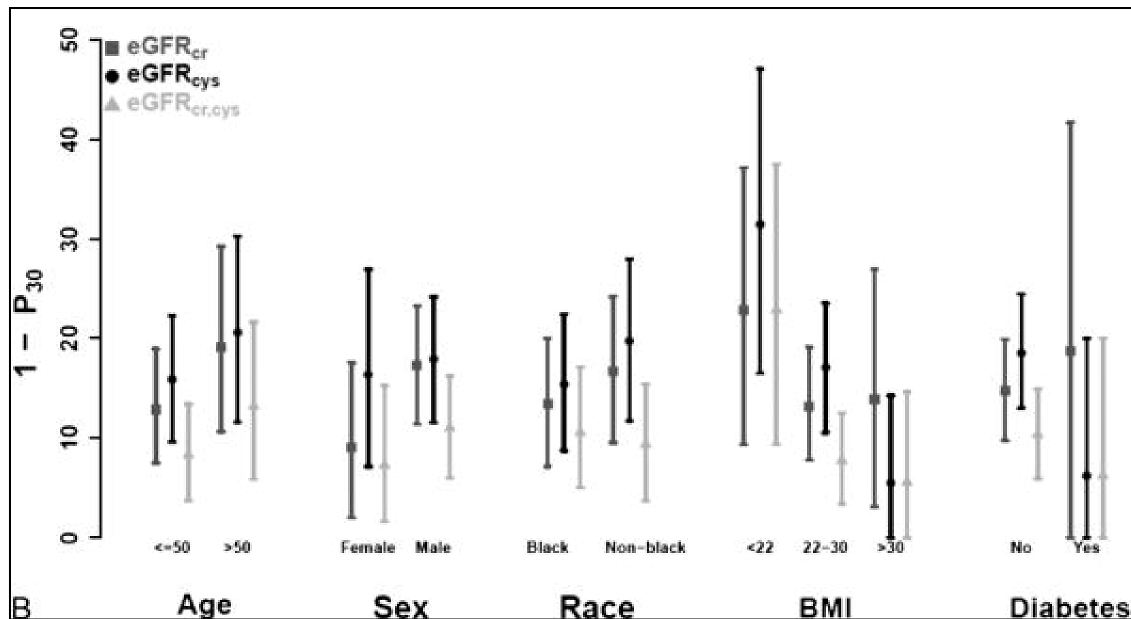
Cystatin C-based GFR estimates?

- 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

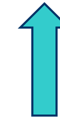
Baseline 0.9 mg/dL → 1.3 four months ago → 1.5

Creatine/ high protein diet

Darunavir/r → 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/1.73m^2
eGFR (CysC): 113 mL/min/1.73m^2

Our Case: Alternate Ending

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

Baseline 0.9 mg/dL → 1.3 four months ago → 1.5

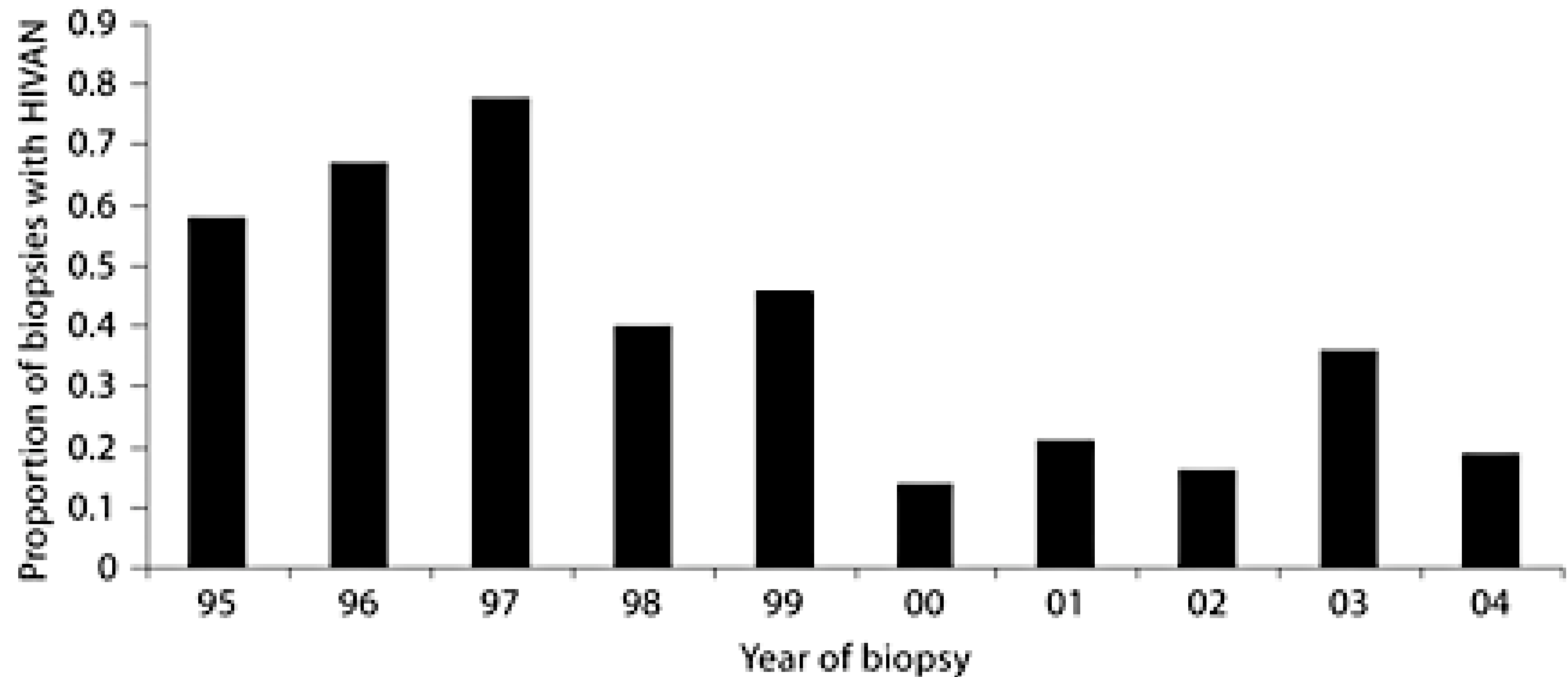
No changes in diet/ meds

Urinalysis: <u>2+ protein</u>, 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?



Berliner *et al.* Am J Nephrol 2008

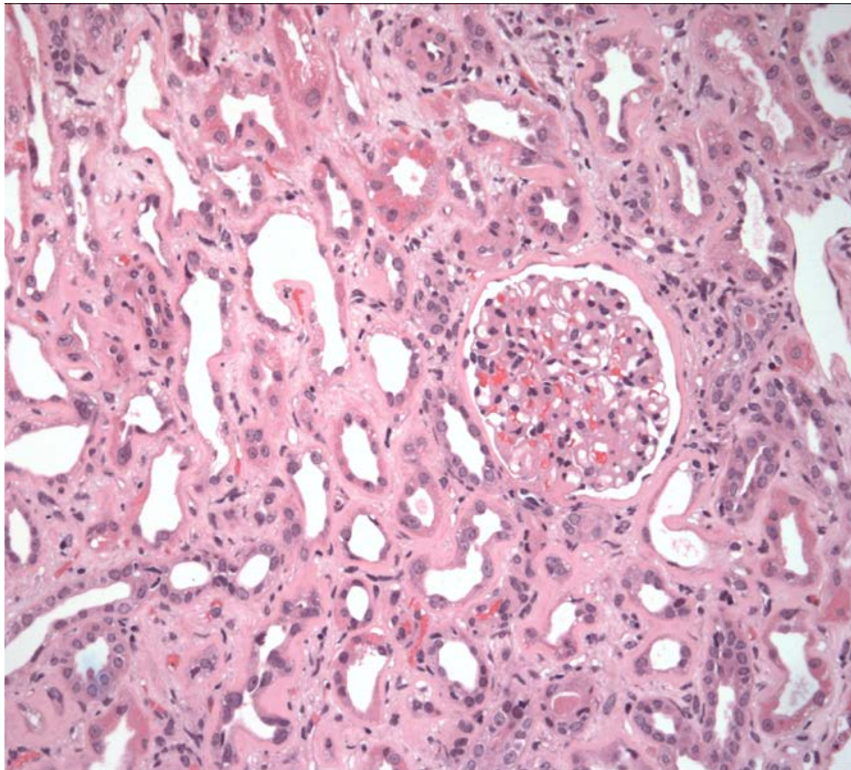
Case Presentation: Ending 2

- 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

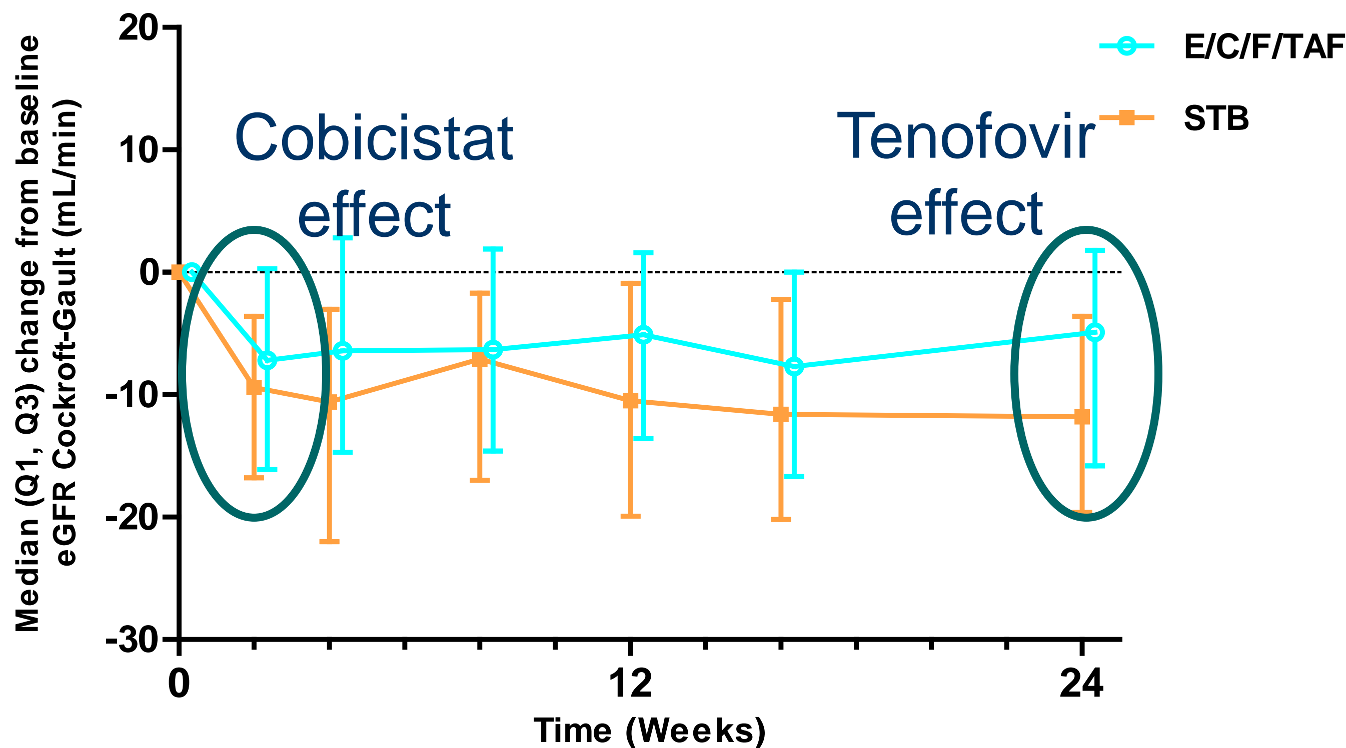
Kidney Biopsy Can Provide a Definitive Diagnosis



Courtesy of Glen Markowitz & Vivette D’Agati

- Unclear diagnosis
- Limited alternatives
- HBV co-infection

Potential for ↓ Nephrotoxicity with Tenofovir Alafenamide?



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