Kidney disease in ageing people with HIV

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Overview

- Chronic kidney disease in HIV+ patients
- ART/renal toxicity (TDF and ATV)
- ART/inhibition of creatinine secretion
- TAF

Chronic Kidney Disease (CKD) in HIV+ patients

- HIV-associated kidney disease
  - HIV-associated nephropathy (HIVAN)
  - Immune complex kidney disease (HIVICK)
  - Thrombotic microangiopathy (TMA)

- Non-HIV associated
  - CKD related to HPT,
  - CKD related to expo
  - IgA nephropathy
  - Amyloidosis
    - Variable reduction in eGFR
    - Variable severity of proteinuria

- HIV implicated in the pathogenesis
- More common in HIV
- Associated with low CD4 / high VL
- Responsive to ART

Chronic Kidney Disease (CKD) in HIV+ patients

- HIV-associated kidney disease
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  - Immune complex kidney disease (HIVICK)
  - Thrombotic microangiopathy (TMA)

- Non-HIV associated aetiologies
  - CKD related to HPT, DM, cardiovascular/urological disease
  - CKD related to exposure to ARV and non-ARV drugs
  - IgA nephropathy
  - Amyloidosis
    - Variable reduction in eGFR
    - Variable severity of proteinuria

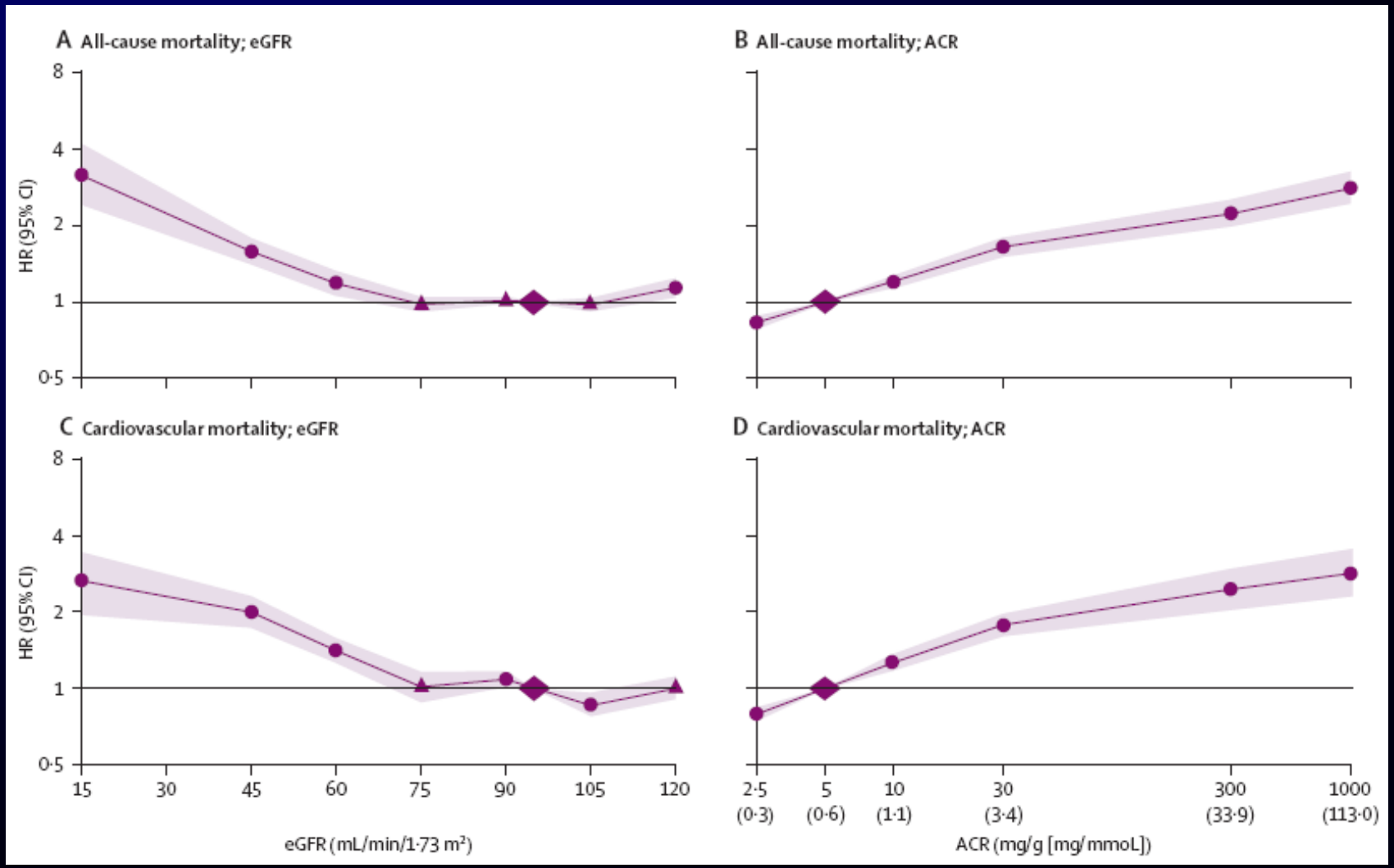
Factors associated with CKD in the EuroSIDA cohort

Table 2. Progression to chronic kidney disease; univariate and multivariate analysis.

		Univariate			Multivariate		
		IRR	95% CI	*P*	RH	95% CI	*P*
eGFR at baseline	Per 5 ml/min per 1.73 m^2	0.75	0.73–0.78	<0.0001	0.84	0.80–0.87	<0.0001
AIDS at baseline	Yes vs. no	1.90	1.46–2.47	<0.0001	1.25	0.95–1.65	0.11
AIDS during follow-up[a]	Yes vs. no	2.78	1.48–5.25	0.0016	2.22	1.14–4.32	0.019
Nephrotoxic drugs[a]	Yes vs. no	1.81	1.33–2.46	0.0002	1.01	0.73–1.40	0.94
Current CD4 cell count[a]	Per doubling	0.85	0.75–0.95	0.0065	0.92	0.79–1.07	0.30
Current age[a]	Per 10 years older	2.57	2.30–2.87	<0.0001	1.54	1.31–1.80	<0.0001
Current HIV-RNA viral load[a]	Per $\log_{10}$ copies/ml higher	0.67	0.55–0.80	<0.0001	0.81	0.67–0.99	0.040
Any CVD event[a]	Yes vs. no/unknown	4.80	3.34–6.92	<0.0001	1.33	0.90–1.98	0.15
Hypertension[a]	Yes vs. no/unknown	3.19	2.45–4.16	<0.0001	1.69	1.26–2.27	0.0005
Diabetes[a]	Yes vs. no/unknown	3.82	2.73–5.31	<0.0001	1.50	1.05–2.16	0.028
Hepatitis C antibody positive[a]	Yes vs. no/unknown	1.23	0.82–1.65	0.17	1.98	1.44–2.71	<0.0001
Sex	Female vs. male	1.01	0.75–1.37	0.93	1.68	1.22–2.30	0.0013
Non-AIDS malignancy[a]	Yes vs. no	3.63	2.36–5.59	<0.0001	1.72	1.10–2.70	0.018
Cumulative Exposure[a]	Tenofovir	1.32	1.21–1.41	<0.0001	1.16	1.06–1.25	<0.0001
	Indinavir	1.18	1.13–1.24	<0.0001	1.12	1.06–1.18	<0.0001
	Atazanavir	1.48	1.35–1.62	<0.0001	1.21	1.09–1.34	0.0003
	Lopinavir/r	1.15	1.07–1.23	<0.0001	1.08	1.01–1.16	0.030

Mocroft et al. AIDS 2010

Reduced eGFR, albuminuria, and (cardiovascular) mortality



Lancet 2010; 375: 2073

CKD progression to death/ESKD

N=27,998 with eGFR <90 for >3 months
Median FU: 66 months

		Proportion alive:
CKD 2 (eGFR 60-89)	ESKD: 1.1% Death: 19.5%	79.4%
CKD 3 (eGFR 30-59)	ESKD: 1.3% Death: 24.3%	74.4%
CKD 4 (eGFR 15-29)	ESKD: 19.9% Death: 45.7%	34.4%

Keith DS et al. Arch Intern Med 2004:164:659–63

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Mocroft et al. AIDS 2010

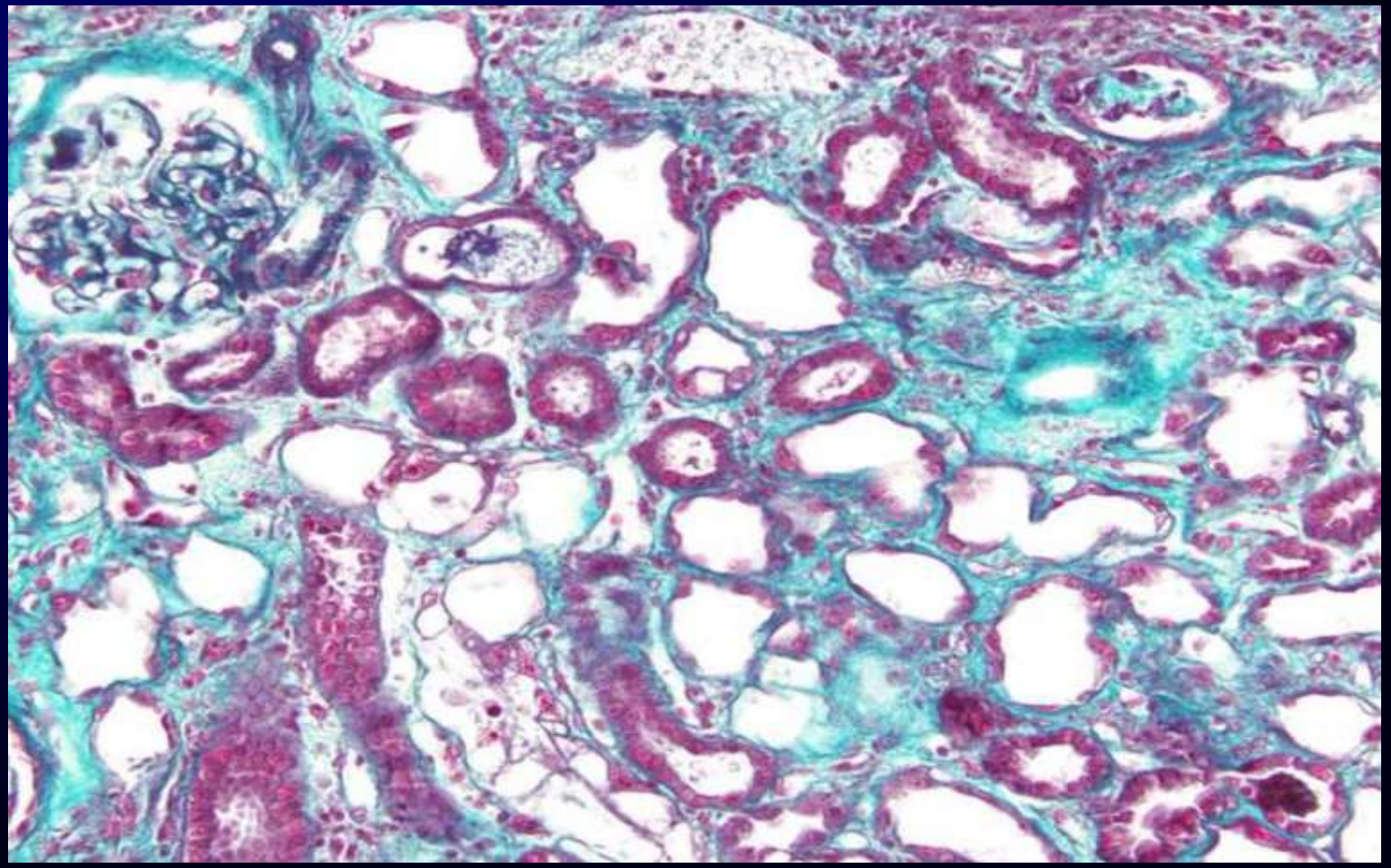
ARV's and the kidney: Treatment-limiting renal toxicity

Antiretroviral drug(s)	Alteration of renal function (not treatment-limiting)	Treatment-limiting renal toxicity
Tenofovir DF	Renal tubular dysfunction Rapid eGFR decline	**Acute kidney injury** Tubulo-interstitial nephritis **Renal tubular disease/Fanconi syndrome** CKD with progressive eGFR decline
Riton	etion on	Acute kidney injury (rare) Tubulo-interstitial nephritis **Nephrolithiasis**
Cobic (TDF/ Cobic (TDF/FTC)	etion etion	AKI Renal tubular disease/Fanconi syndrome AKI Renal tubular disease/Fanconi syndrome
Rilpivirine	Inhib. of creatinine secretion	None reported
Raltegravir	Inhib. of creatinine secretion?	None reported
Ritonavir/lopinavir	Chronic kidney disease	Nephrolithiasis
Ritonavir/darunavir	Crystalluria	Nephrolithiasis

- **Tenofovir (TDF)**
  - **Acute tubular injury**
  - **Fanconi syndrome**
- **Atazanavir**
  - **Nephrolithiasis**
  - **Interstitial nephritis**

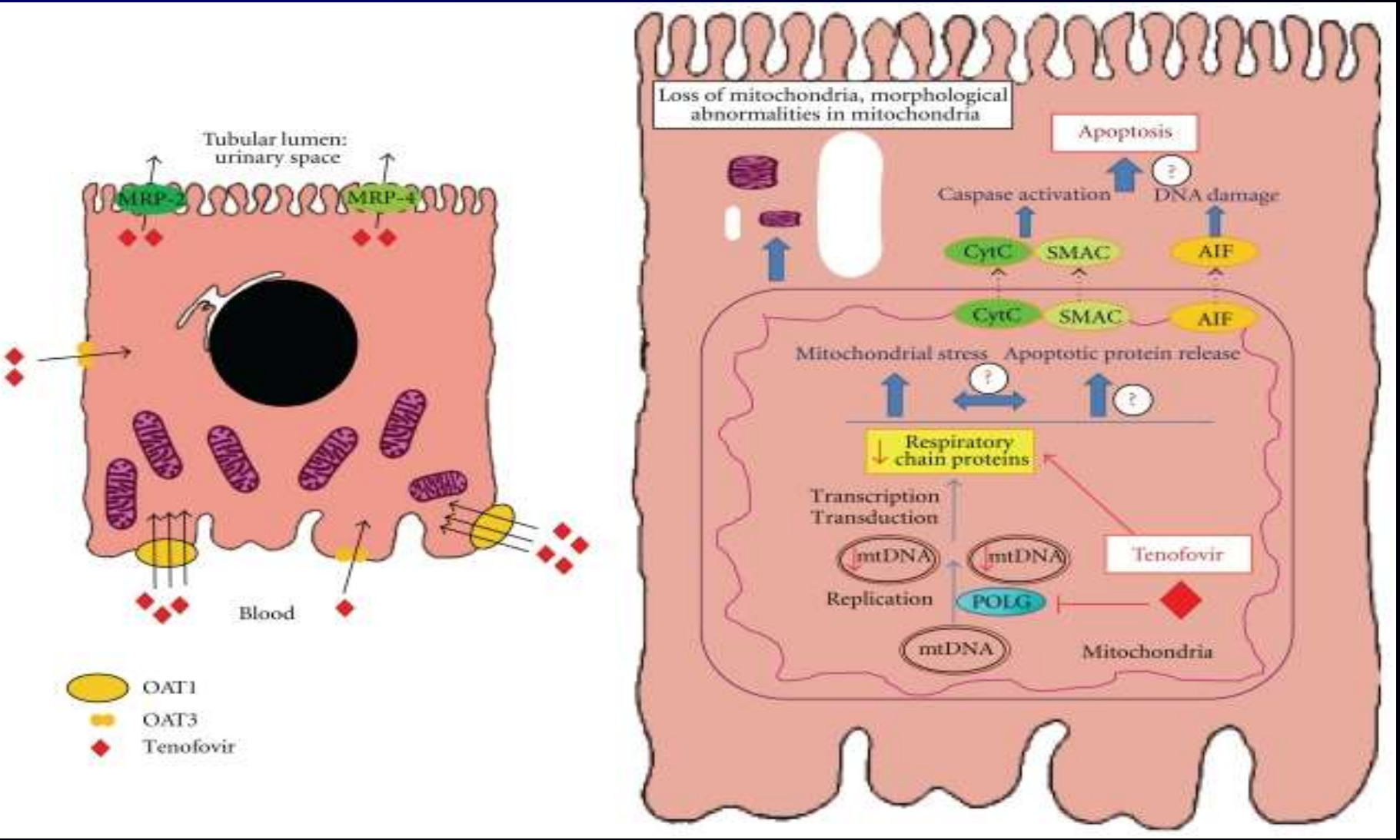
AIDS 2014; 28: 621-32

Case of acute tubular injury and Fanconi syndrome with tenofovir (TDF)



AIDS 2016, in press

Tenofovir: Renal tubular toxicity



AIDS Res Treat 2011; 2011: 354908

Renal tubular disease: associations with ART

Table 1. Clinical characteristics of patients with acute tubular injury, tubulo-interstitial nephritis and interstitial fibrosis and tubular atrophy at the time of kidney biopsy.

		ATI ($n=22$)	TIN ($n=20$)	IFTA ($n=12$)	P value
Age (years)	Mean (SD)	50.6 (11.0)	47.0 (11.9)	49.9 (9.9)	0.6
Sex (men)	*N* (%)	21 (96)	14 (70)	11 (92)	0.06
Ethnicity (Black)	*N* (%)	2 (10)	11 (55)	5 (42)	**0.006**
HIV risk (MSM)	*N* (%)	3 (14)	11 (58)	6 (50)	**0.008**
HBV surface antigen positive	*N* (%)	2 (10)	1 (5)	2 (17)	0.6
HCV antibody positive	*N* (%)	1 (5)	2 (10)	1 (8)	0.8
Time since HIV diagnosis (years)	Median (IQR)	10.7 (7.0, 14.7)	3.8 (0.2, 11.5)	12.8 (0.3, 17.2)	0.07
On ART at biopsy	*N* (%)	22 (100)	11 (55)	8 (67)	**0.001**
Current/recent use of TDF[a]	*N* (%)	19 (86)*	4 (20)	3 (25)	**<0.001**
Past use of TDF	*N* (%)	3 (14)	0	1 (8)	0.2
Current/recent use of ATV[a]	*N* (%)	4 (18)	2 (10)	3 (25)	0.5
Past use of ATV	*N* (%)	4 (18)	0	0	0.3
Current/recent use of IDV[a]	*N* (%)	0	1 (5)	0	0.5
Past use of IDV	*N* (%)	6 (27)	2 (10)	3 (25)	0.7
Current/recent use of LPV[a]	*N* (%)	8 (36)	1 (5)	3 (25)	0.2
Past use of LPV	*N* (%)	3 (14)	2 (10)	0	0.7
$CD4^+$ cell count nadir (cells/μl)	Median (IQR)	154 (57, 245)	102 (14, 210)	87 (55, 176)	0.4
$CD4^+$ cell count (cells/μl)	Median (IQR)	364 (240, 582)	262 (131, 500)	227 (123, 551)	0.4
AIDS	*N* (%)	5 (24)	7 (35)	8 (67)	0.06
VL (log copies/ml)	Median (IQR)	1.7 (1.7, 1.7)	1.9 (1.7, 5.1)	1.7 (1.7, 4.3)	0.07
VL <200 copies/ml	*N* (%)	22 (100)	10 (54)	7 (58)	**<0.001**
Diabetes mellitus	*N* (%)	7 (32)	3 (15)	1 (8)	0.3
Hypertension	*N* (%)	9 (43)	5 (26)	6 (50)	0.4
eGFR (CKD-EPI, ml/min/1.73 m^2)	Median (IQR)	47 (10, 60)	25 (16, 37)	42 (32, 67)	**0.049**
Proteinuria (g/24 h)	Median (IQR)	1.4 (0.7, 2.2)	1.8 (0.7, 2.3)	1.2 (0.3, 4.8)	0.9

AIDS 2015; 29: 1831-6

Risk factors for severe TDF-associated Renal Tubulopathy

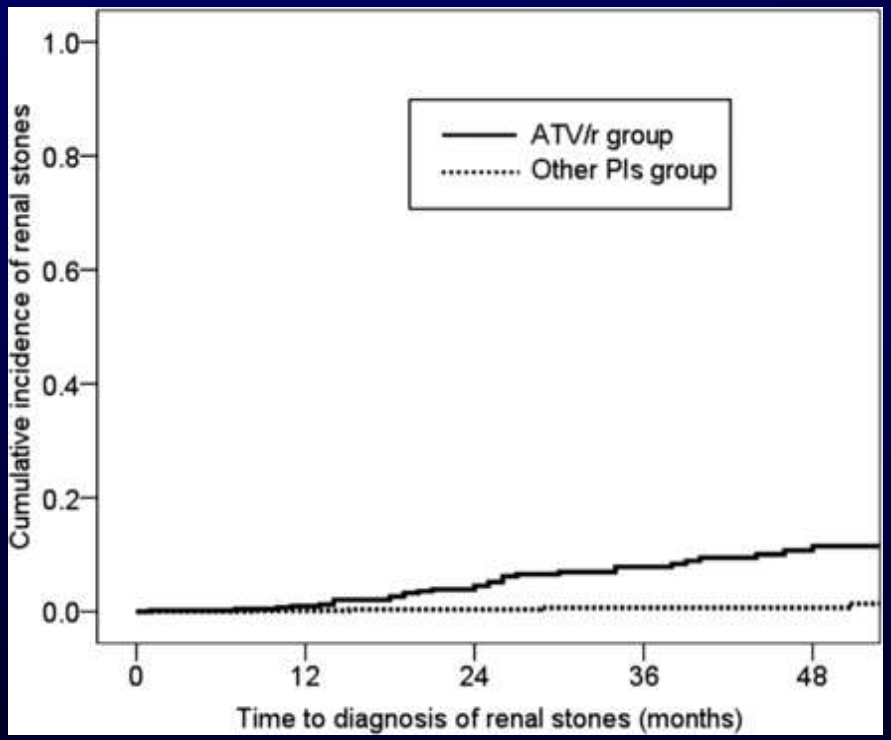
- 15983 subjects received TDF for >4 weeks between Oct 2002-July 2013
  - 69 (0.4%) developed tubulopathy (PT: n=52; ATI: n=17) after a median (IQR) of 43 (26, 67) months of TDF exposure
  - At RT diagnosis, 83% were taking ritonavir-boosted PI
    - 44% lopinavir, 35% atazanavir, 16% darunavir, 5% other

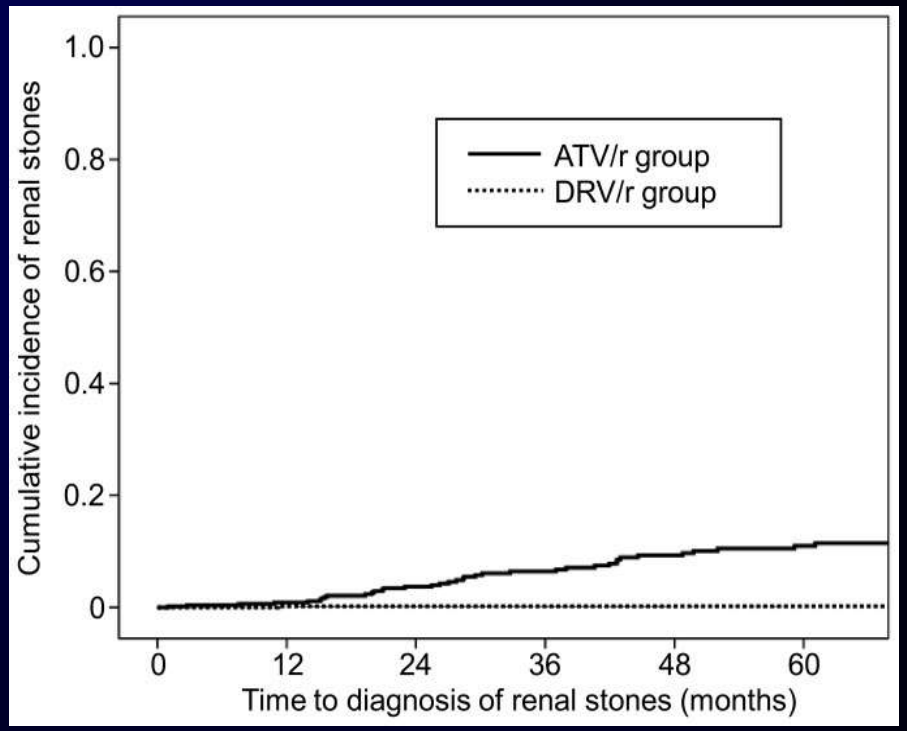
Table 1: Factors associated with developing TDF associated renal tubulopathy

	Univariate			Multivariate$		
	RR	95% CI	P-value	RR	95% CI	P-value
Age at baseline	**1.30**	**(1.16, 1.46)**	**<0.0001**	**1.33**	**(1.18, 1.50)**	**<0.0001**
Ethnicity (black vs. white/other)	**0.28**	**(0.12, 0.64)**	**0.003**	**0.27**	**(0.12, 0.63)**	**0.003**
Calendar year at TDF start						
2000-2003	1			1		
2004-2007	0.46	(0.26, 0.81)	**0.007**	0.60	(0.33, 1.07)	0.083
2008-2010	0.31	(0.15, 0.63)	**0.001**	0.54	(0.25, 1.17)	0.116
2011-2014	0.39	(0.15, 0.97)	**0.043**	0.72	(0.26, 2.00)	0.532
Time on TDF (per year increase)*	**1.11**	**(1.01, 1.21)**	**0.025**	**1.12**	**(1.01, 1.23)**	**0.026**
Years on ARVs at TDF start	1.06	(1.01,1.11)	**0.030**	1.00	(0.94, 1.05)	0.900
ARV regime (PI based vs NNRTI based)*	**4.05**	**(2.44, 6.72)**	**<0.0001**	**3.99**	**(2.38, 6.68)**	**<0.0001**
CD4 cell count (per 50 cell increase)*	**0.93**	**(0.88, 0.98)**	**0.006**	**0.92**	**(0.88, 0.97)**	**0.003**

Hamzah et al, CROI 2016 (poster #683)

Atazanavir and kidney stones





Clin Infect Dis 2012; 55: 1262-9
PLoS One 2013; 8: e77268

ATV and interstitial nephritis

Table 3 Patients with acute renal failure and acute interstitial nephritis

Patients	Diagnosis	Drugs
51-year-old man	Acute interstitial nephritis	Atazanavir, tenofovir, ritonavir, lamivudine (all since 3 months); amoxicillin/clavulanic acid, oxazepane, methadone, esomeprazole
44-year-old woman	Chronic interstitial nephritis with acute component	Atazanavir, tenofovir, ritonavir, emtricitabine (all since 6 weeks)
63-year-old man	Chronic interstitial nephritis with acute component and focal tubular necrosis	Atazanavir (since 4 months), lopinavir/ritonavir (since 4.5 years), tenofovir (since 17 months), lamivudine (since 4 years), didanosine (since 4 months), acidum salicylicum, clopidogrelum, calcium acetate, spironolactone, metoprololi succinas, epoetinum beta, insuline, atorvastatine, rosiglitazone

C&W cohort

- 42% of C&W patients who developed stones had eGFR <60 at baseline

Italian cohort

- Stone formers had higher ATV concentrations (1098 vs. 218 ng/mL)

N Engl J Med 2006; 355:2158, AIDS 2006; 20:2131, AIDS 2007; 21:1060, AIDS 2007; 21:1215, AIDS 2007; 21:2357
Virchows Arch 2007; 450: 665, Antiviral Ther 2011; 16: 119, Am J Kid Dis 2004; 44: e81, AIDS 2011; 25: 1671-3; PLoS One 2015; 10: e0123670

Tubulo-interstitial nephritis: ARV's are an infrequent cause

Table 2. Clinical outcomes.

		ATI ($n=22$)	TIN ($n=20$)	IFTA ($n=12$)
Renal syndrome[a]	Proteinuria >1.5 g/24 h and eGFR <60	3	12	6
	Proteinuria >1.5 g/24 h and stable eGFR >60	3	0	0
	Unexplained chronic kidney disease	3	3	1
	Sub-acute eGFR decline	0	0	3
	Acute kidney injury	7	11	1
	Proximal tubulopathy/Fanconi syndrome	5	0	0
	Other	1	0	1
Suspected cause	Infection/drugs (non-ART)	4	11	0
	Malignancy/chemotherapy	1	1	0
	Other	0	3	1
	ART drugs (atazanavir, indinavir)	5	2	1
	ART drugs (tenofovir)	20	0	0
	Unclear	1	3	10
Management	Immunosuppression[b]	2	11	0
	Tenofovir discontinued[c]	20	4	1
	Atazanavir/indinavir discontinued[c]	4	3	2
	Renal replacement therapy	5	9	1
Renal outcome (eGFR)	Return to baseline[d]	17 (77)	10 (50)	7 (58)
	Chronic kidney disease(eGFR 30–59)	2	3	2
	chronic kidney disease(eGFR <30)	2	1	1
	End-stage kidney disease	1	5	2
	Death	3	3	1

AIDS 2015; 29: 1831-6

ARV's associated with rapid eGFR decline in the VA cohort

Table 4. Association of cumulative antiretroviral exposure (per year) with risk[a] of kidney disease outcomes, ordered by prevalence of use.

Antiretroviral	% of participants with any exposure at end of study	Proteinuria		Rapid Decline[c]		Chronic Kidney Disease	
		Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Tenofovir	39.7	1.34 (1.25, 1.45)	<0.0001	1.11 (1.03, 1.18)	0.0033	1.33 (1.18, 1.51)	<0.0001
Lamivudine	89.5	0.98 (0.94, 1.03)	0.50	1.02 (0.97, 1.06)	0.44	0.93 (0.85, 1.02)	0.11
Zidovudine	68.3	0.98 (0.93, 1.03)	0.42	0.98 (0.93, 1.02)	0.29	0.89 (0.81, 0.98)	0.020
Efavirenz	49.0	0.94 (0.90, 0.99)	0.026	1.01 (0.97, 1.05)	0.64	0.88 (0.79, 0.98)	0.018
Stavudine	43.0	1.02 (0.97, 1.07)	0.54	1.02 (0.97, 1.06)	0.43	0.98 (0.89, 1.07)	0.61
Ritonavir[b]	35.7	1.18 (1.09, 1.27)	<0.0001	0.96 (0.89, 1.04)	0.34	0.97 (0.84, 1.14)	0.74
Nelfinavir	31.6	0.99 (0.95, 1.04)	0.68	1.02 (0.98, 1.06)	0.39	1.01 (0.92, 1.11)	0.76
Abacavir	29.6	1.01 (0.96, 1.07)	0.73	1.01 (0.96, 1.06)	0.65	1.07 (0.97, 1.18)	0.20
Indinavir	24.6	1.04 (0.99, 1.09)	0.15	0.99 (0.95, 1.04)	0.67	1.16 (1.06, 1.27)	0.0019
Didanosine	23.0	0.94 (0.88, 1.00)	0.051	0.98 (0.93, 1.04)	0.49	0.95 (0.84, 1.07)	0.37
Nevirapine	22.8	1.01 (0.96, 1.06)	0.69	1.02 (0.97, 1.06)	0.52	0.93 (0.84, 1.03)	0.18
Atazanavir	17.1	0.93 (0.79, 1.08)	0.34	1.22 (1.07, 1.40)	0.0035	0.96 (0.77, 1.18)	0.69
Lopinavir/r	15.3	0.77 (0.68, 0.86)	<0.0001	1.05 (0.94, 1.17)	0.39	1.21 (0.91, 1.60)	0.18
Saquinavir	10.7	0.91 (0.83, 0.99)	0.035	1.00 (0.92, 1.08)	0.97	0.89 (0.72, 1.09)	0.24
Amprenavir	4.3	0.90 (0.78, 1.05)	0.20	1.03 (0.90, 1.18)	0.67	1.17 (0.94, 1.46)	0.16
Fosamprenavir	3.3	0.91 (0.63, 1.32)	0.63	1.29 (0.90, 1.85)	0.16	1.00 (0.67, 1.47)	0.98
Zalcitabine	1.5	1.11 (0.92, 1.35)	0.29	0.91 (0.72, 1.14)	0.41	1.24 (0.70, 2.19)	0.46
Delavirdine	1.5	1.10 (0.90, 1.35)	0.35	0.85 (0.66, 1.10)	0.21	1.24 (0.84, 1.81)	0.28
Tipranavir	0.6	0.87 (0.29, 2.68)	0.81	0.34 (0.05, 2.34)	0.27	0.06 (0.00, 66.0)	0.43

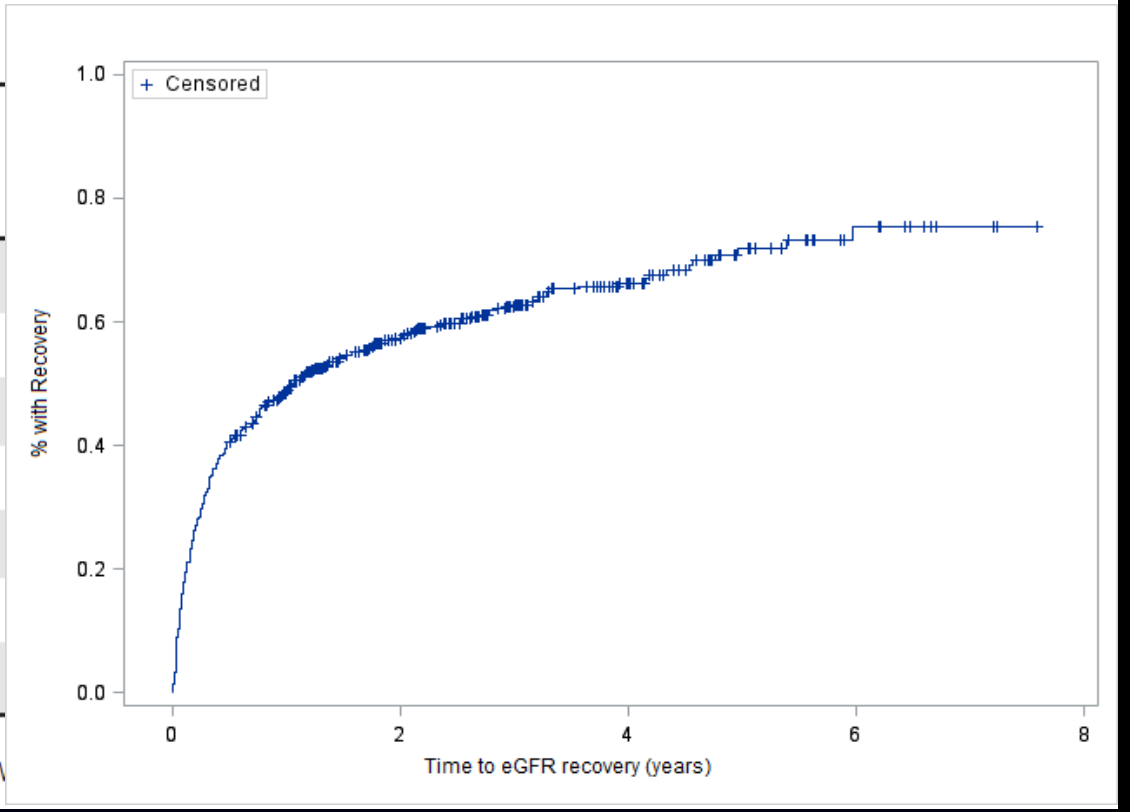
Scherzer et al, AIDS 2012

eGFR slopes in patients who discontinued TDF

Table 2. Estimated Glomerular Filtration Rate (eGFR) Slopes Before Initiation of, During, and After Discontinuation of Tenofovi Disoproxil Fumarate (TDF) Exposure

Interval, Relative to TDF Exposure	Overall (n = 834)
Before initiation	−0.9 (−1.6 to −0.2)
During	
≤3 mo	−15.7 (−20.5 to −10.9)
>3 mo	−3.1 (−4.6 to −1.7)
After discontinuation	
≤3 mo	12.5 (8.9–16.1)
>3 mo	0.8 (0.1–1.5)

Data are mean values (95% confidence intervals) from a piecev



JID 2014; 210: 363-373

ARV's and the kidney: Alteration of renal function

Antiretroviral drug(s)	Alteration of renal function (not treatment-limiting)	Treatment-limiting renal disease
Tenofovir DF	Renal tubular dysfunction Rapid eGFR decline Proteinuria Chronic kidney disease	Acute kidney injury Tubulo-interstitial nephritis **Renal tubular disease/Fanconi syndrome** CKD with progressive eGFR decline
Ritonavir/atazanavir	Inhib. of creatinine secretion Renal tubular dysfunction Rapid eGFR decline Chronic kidney disease	Acute kidney injury (rare) Tubulo-interstitial nephritis **Nephrolithiasis**
Cobicistat/elvitegravir (TDF/FTC)	Inhib. of creatinine se	Renal tubular disease/Fanconi syndrome
Cobicistat/atazanavir (TDF/FTC)	Inhib. of creatinine secretion	AKI Renal tubular disease/Fanconi syndrome
Rilpivirine	Inhib. of creatinine secretion	None reported
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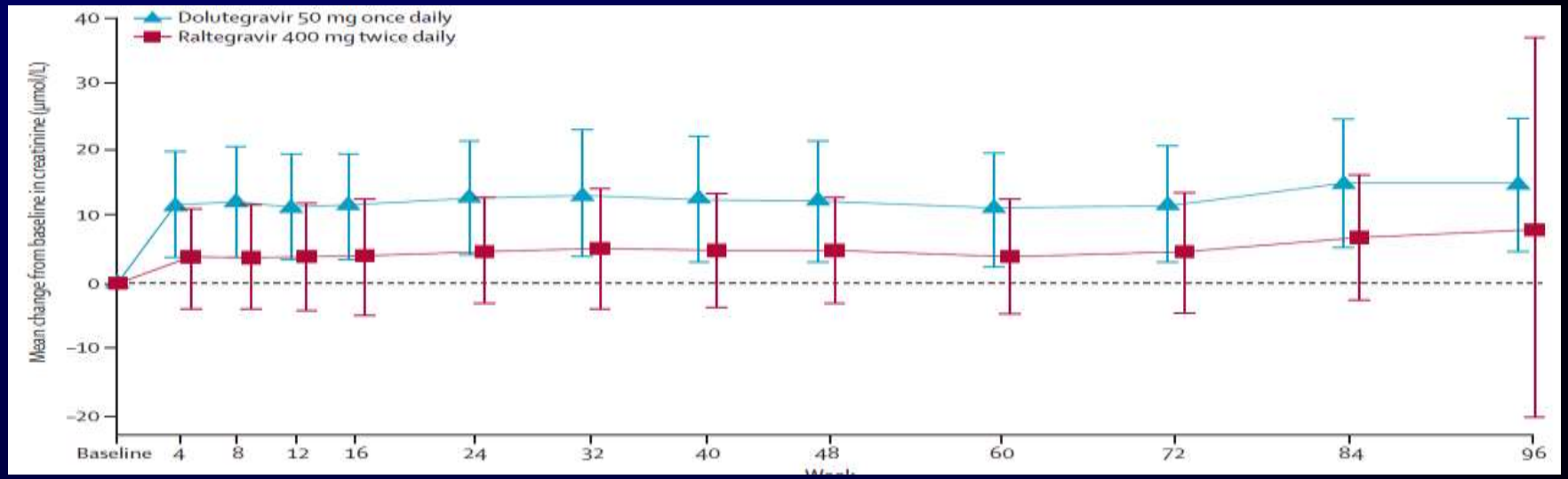
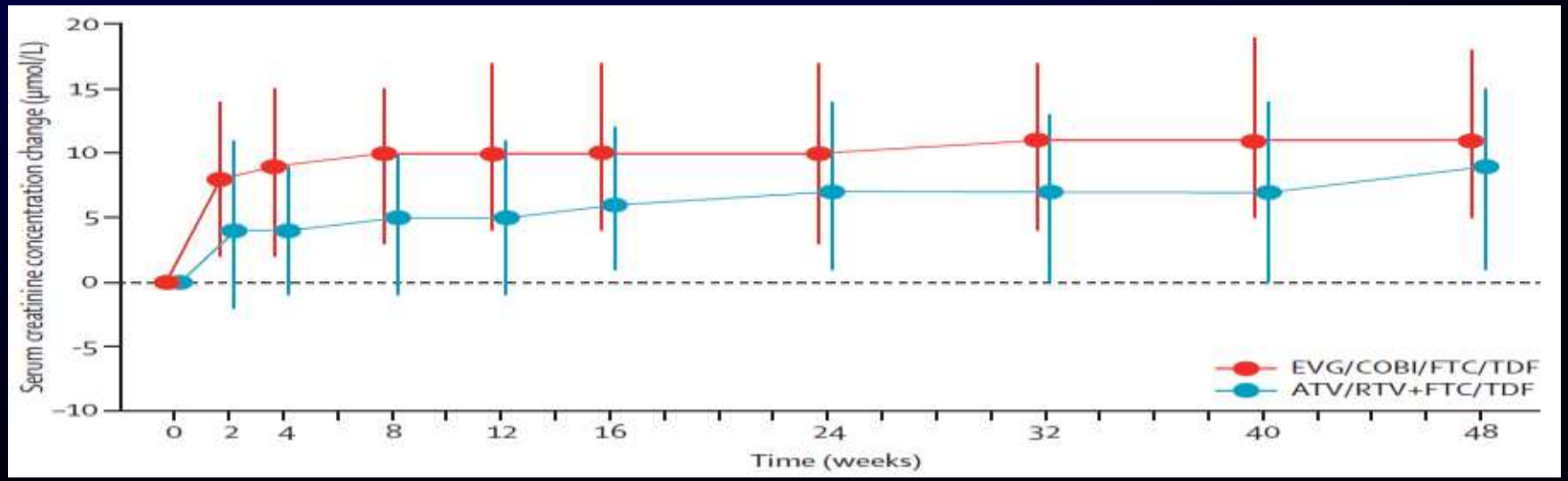
- **Inhibition of creatinine secretion**

AIDS 2014; 28: 621-32

Changes in creatinine clearance with RTV/ATV and Cobi/EVG





Lancet Inf Dis 2013; 13: 927-35, Lancet 2012; 379: 2429-38

Effects of ART on creatinine clearance

Table 3. Changes in creatinine clearance in tenofovir disoproxil fumarate/emtricitabine-treated patients with commonly used antiretrovirals.

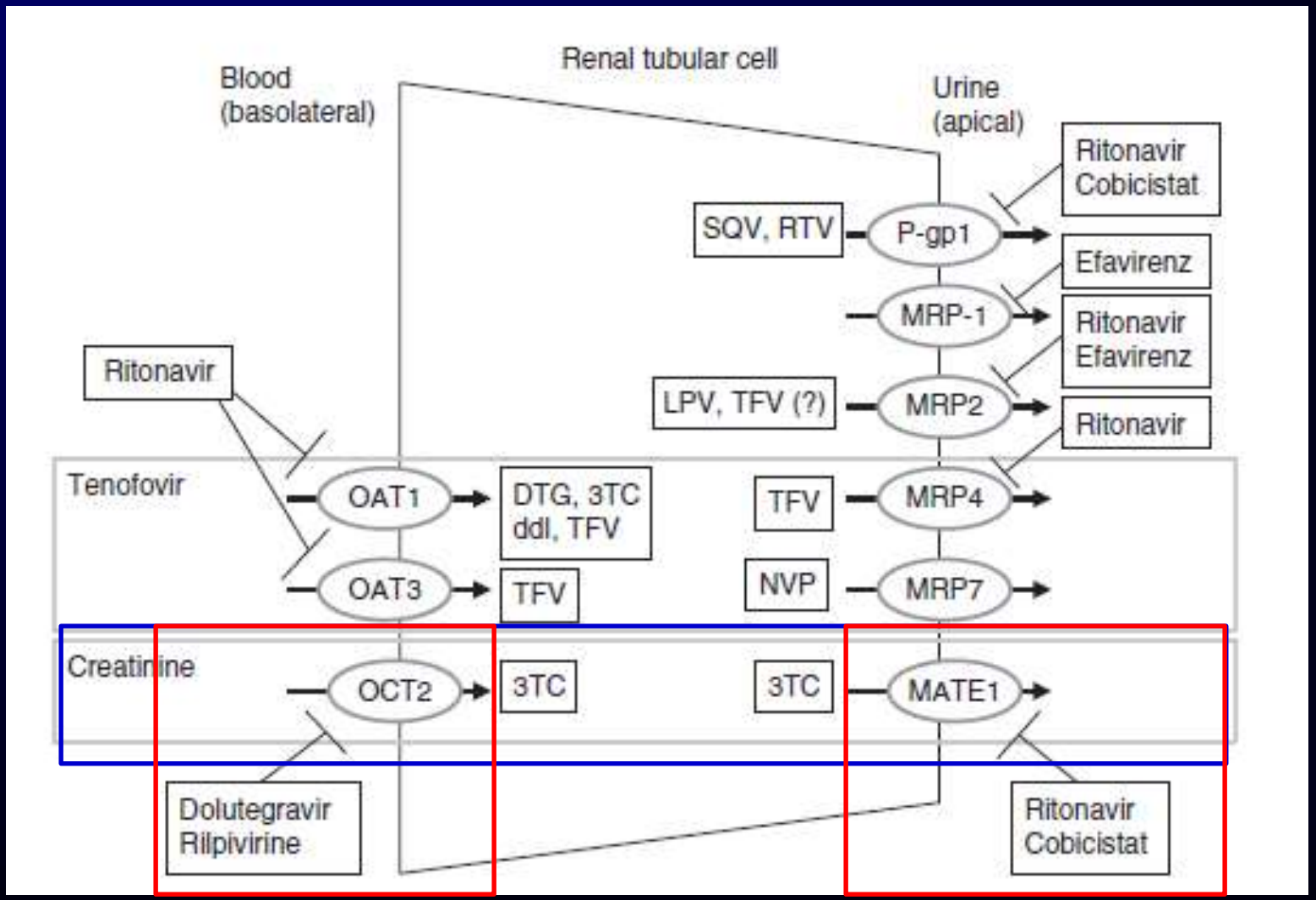
	Antiretroviral drug(s)	Change in creatinine clearance (ml/min) up to 192 weeks	Reference
Minimal or no change	Efavirenz	−0.8	[22,53]
Moderate decrease	Rilpivirine[a]	−5 to −11	[53,107]
	Raltegravir	−5.4	[34]
	Ritonavir/lopinavir	−7.0	[32]
	Ritonavir/atazanavir	−9.1 to −9.5	[23,36]
	Ritonavir/darunavir	−9.3	[32]
Greatest decrease	Cobicistat/elvitegravir	−12.7 to −14.3	[22,23]
	Cobicistat/atazanavir	−12.9	[36]
	Dolutegravir[a]	−16.5	[34]

[a]Includes patients on abacavir/lamivudine and/or zidovudine/lamivudine.

Not associated with (worsening) proteinuria, haematuria or glycosuria

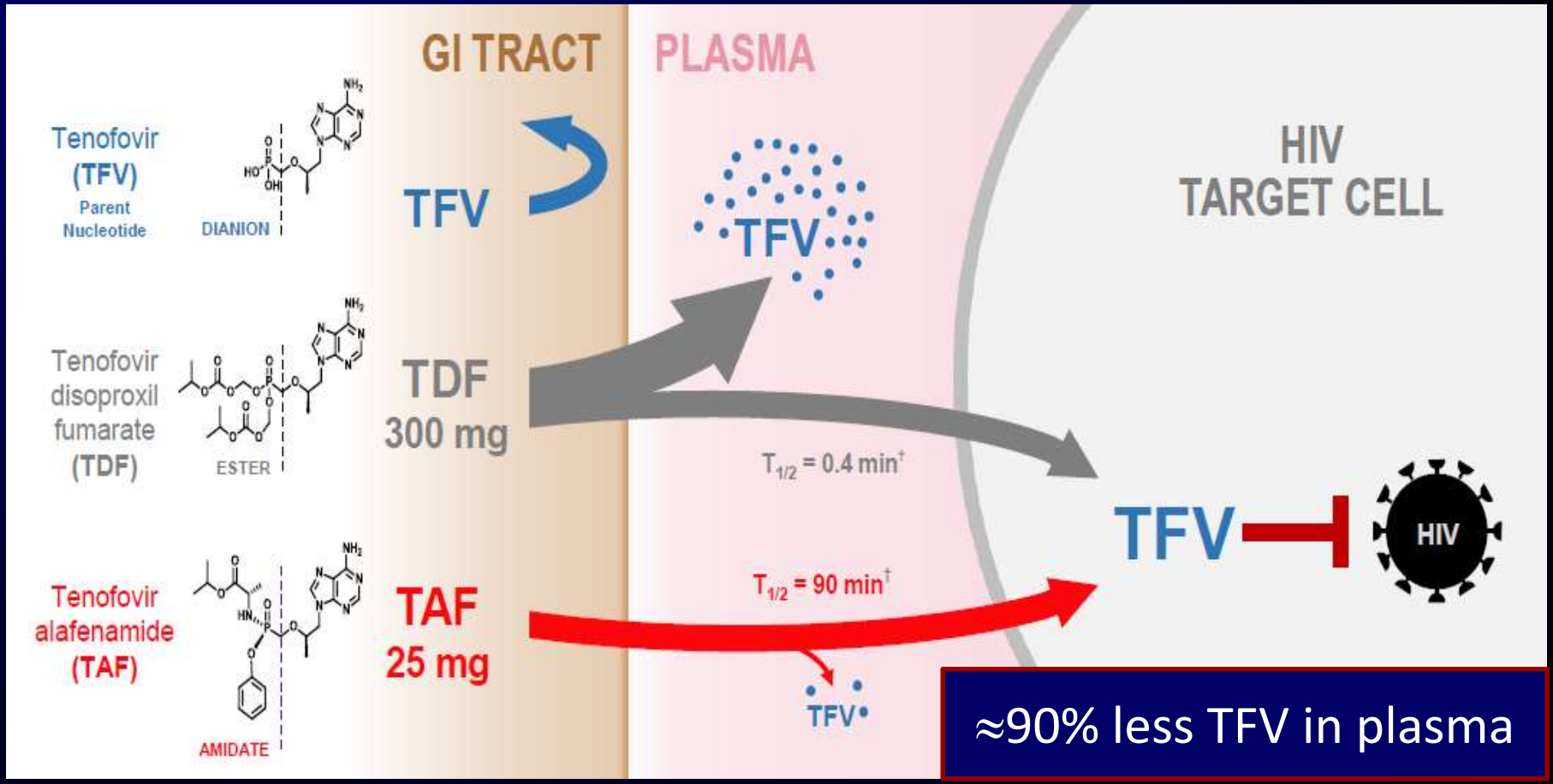
AIDS 2014; 28: 621-32

Cobicistat, ritonavir, rilpivirine and dolutegravir inhibit tubular secretion of creatinine



AIDS 2014; 28: 621-32

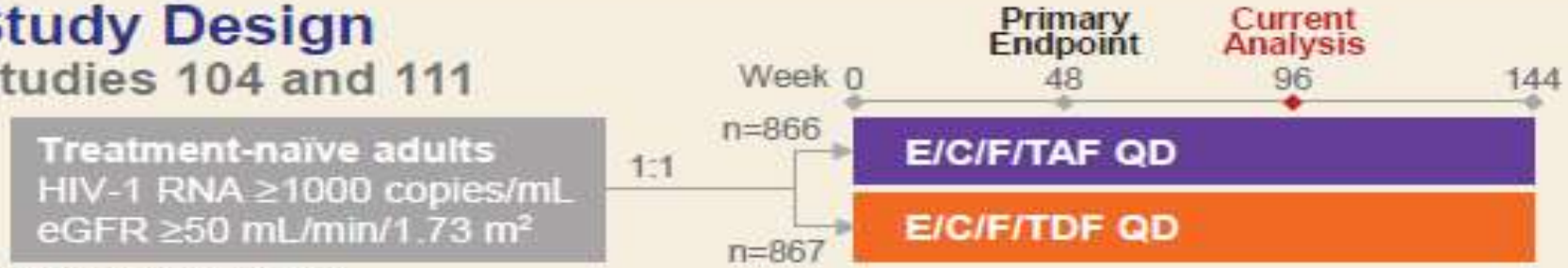
Tenofovir alafenamide (TAF)



TAF is not a substrate for renal tubular transporters:
Use of TAF results in greatly reduced TFV exposure to kidneys and bone

Comparison of ECF-TAF vs. ECF-TDF in ART-naïve patients (GS-0104/0111)

Study Design
Studies 104 and 111

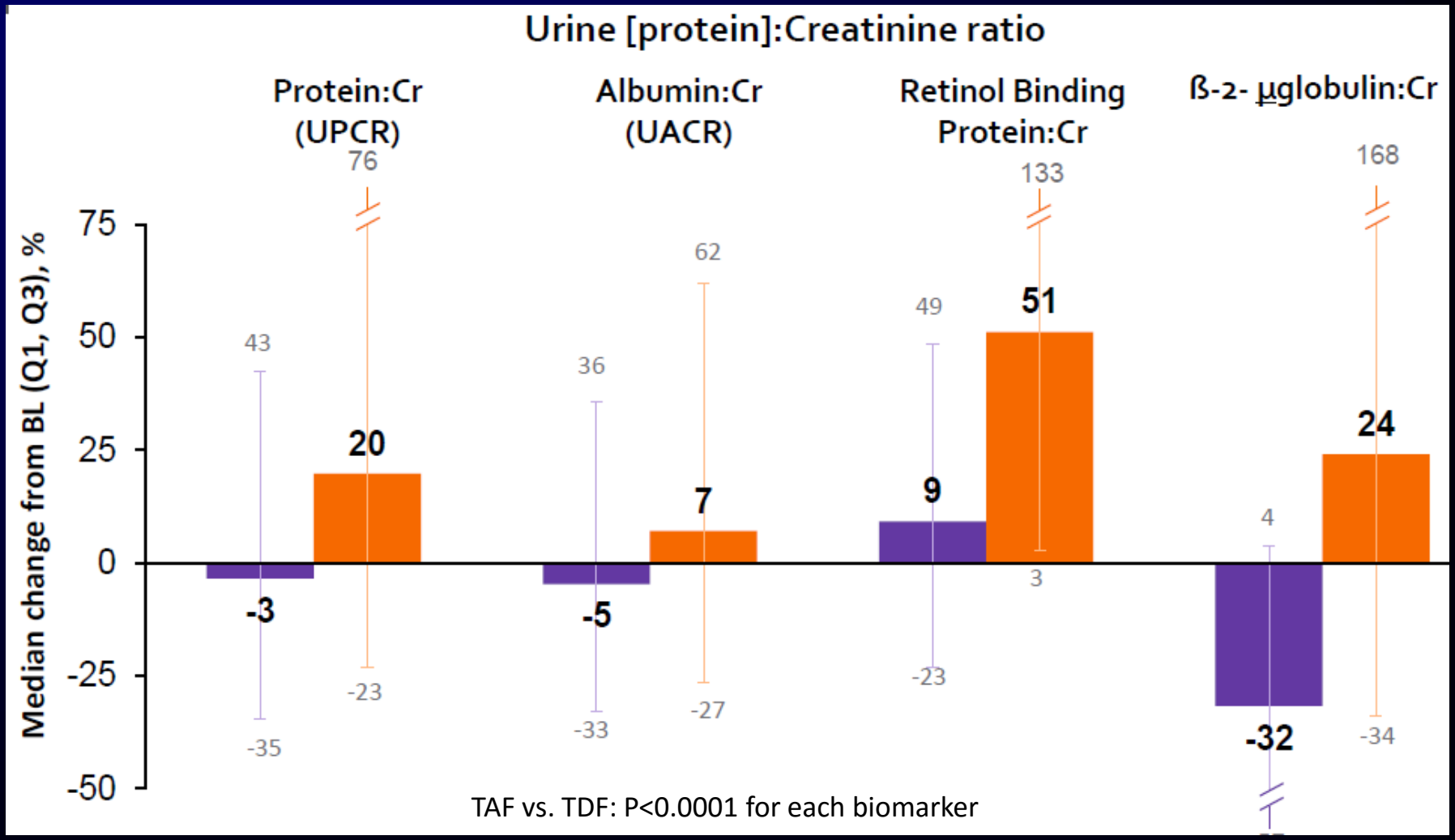


eGFR, estimated glomerular filtration rate.

Baseline Demographics and Renal Parameters

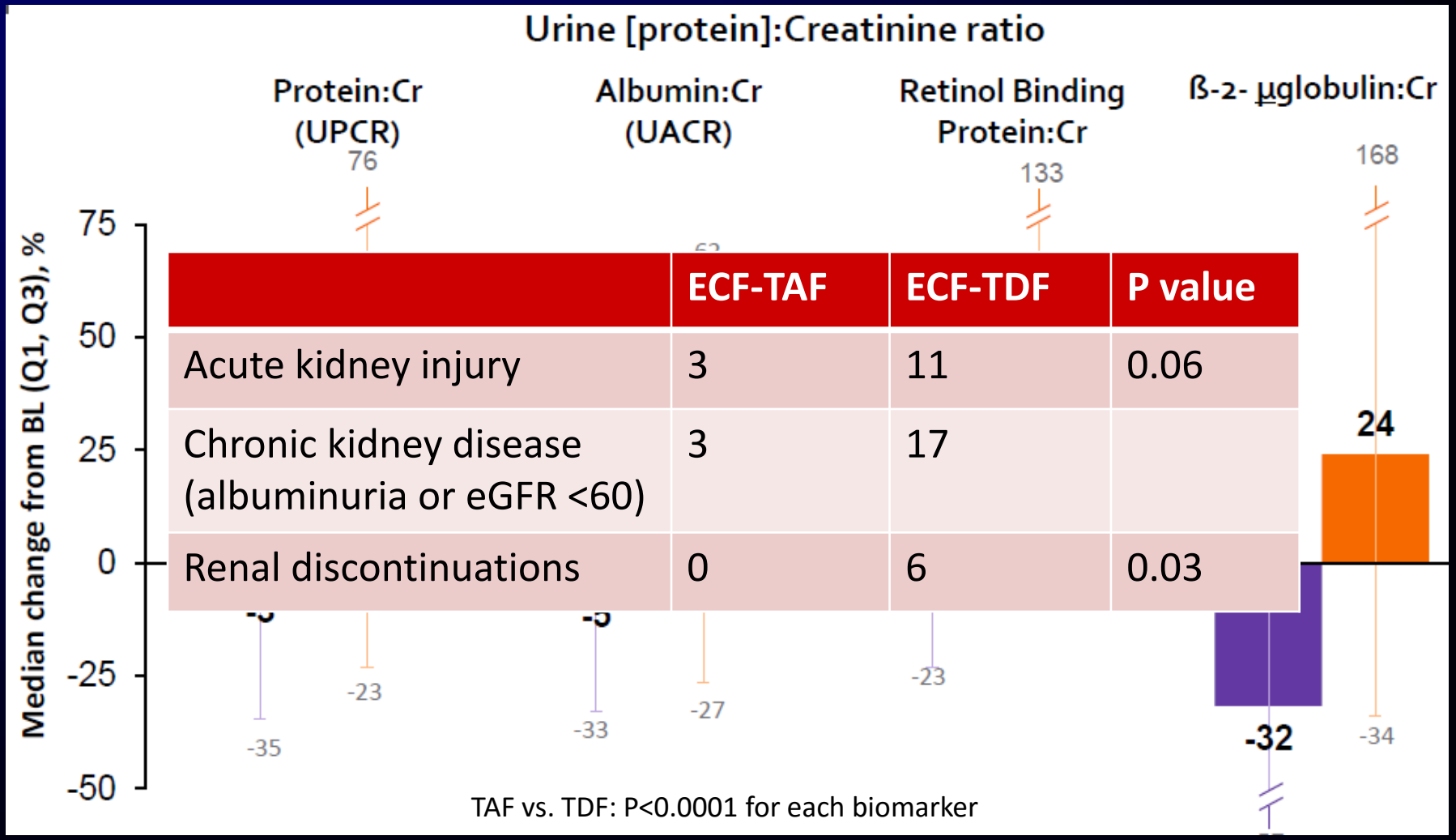
	E/C/F/TAF n=866	E/C/F/TDF n=867
Median age, y (Q1, Q3)	33 (26, 42)	35 (28, 44)
Female, n (%)	133 (15)	127 (15)
Race and ethnicity, n (%)		
White	485 (56)	498 (57)
Black or African heritage	223 (26)	213 (25)
Asian	91 (11)	89 (10)
Hispanic or Latino	167 (19)	167 (19)
Median HIV-1 RNA, $\log_{10}$ copies/mL (Q1, Q3)	4.6 (4.1, 5.0)	4.6 (4.1, 5.0)
Mean CD4 cell count, /μL (SD)	426 (216)	429 (220)
HIV disease status, n (%)		
Asymptomatic	779 (90)	800 (93)
Symptomatic HIV infection	53 (6)	34 (4)
AIDS	31 (4)	29 (3)
Unknown	3 (<1)	4 (<1)
Median eGFR by CKD-EPI, mL/min/1.73 m² (Q1, Q3)	106.5 (94.8, 118.0)	104.8 (93.2, 115.4)
Proteinuria grade by urinalysis, n (%)		
0	778 (90)	780 (90)
1	80 (9)	67 (8)
2	8 (<1)	18 (2)
3	0	1 (<1)
Missing	0	1 (<1)
Diabetes mellitus, n (%)	25 (3)	40 (5)
Hypertension, n (%)	119 (14)	147 (17)
Cardiovascular disease, n (%)	10 (1)	14 (2)
Hyperlipidemia, n (%)	91 (11)	104 (12)

104/111 studies: Tenofovir alafenamide (TAF) has no effect on renal tubular function



Lancet 2015;385:2606-15

104/111 studies: Tenofovir alafenamide (TAF) has no effect on renal tubular function

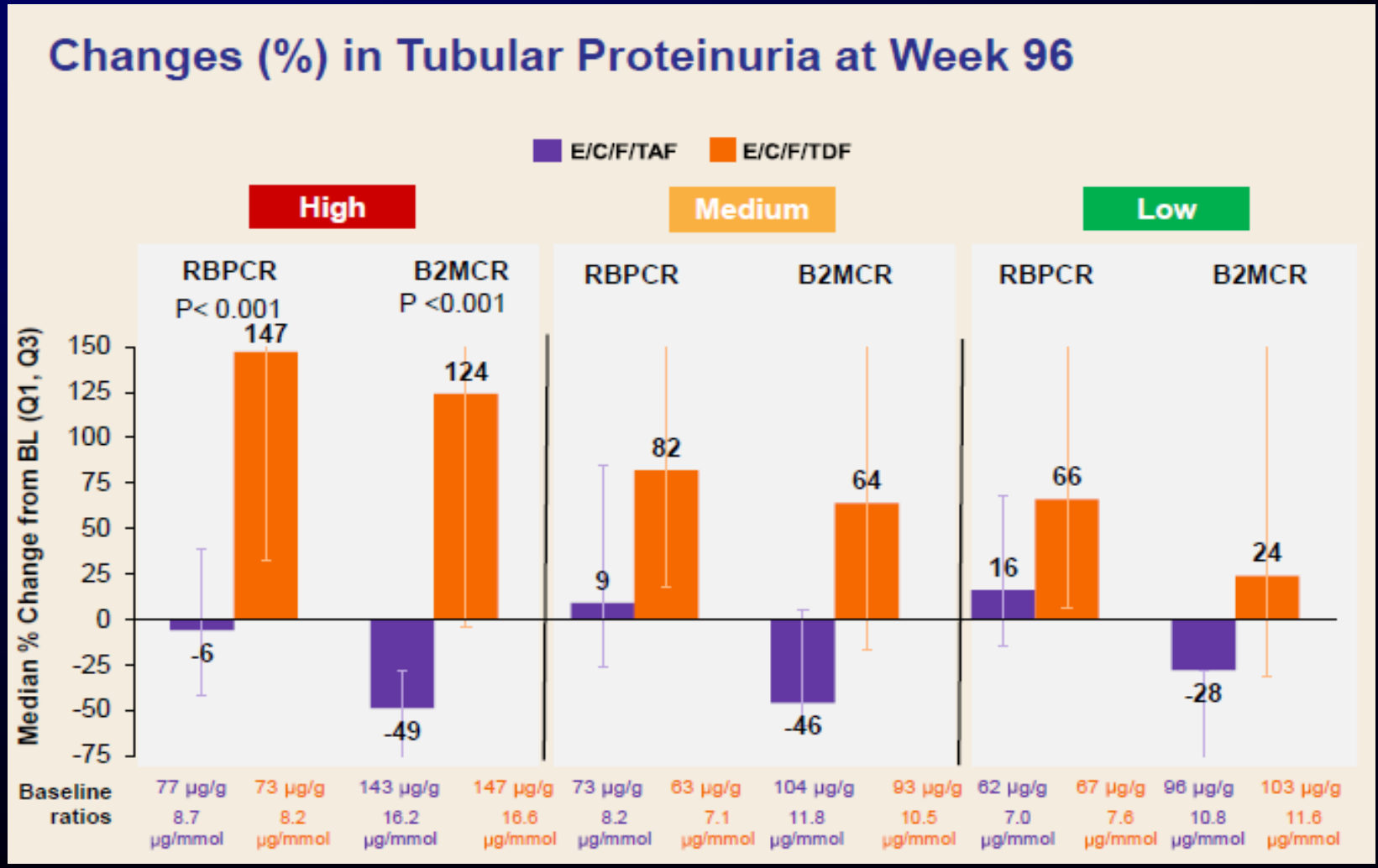


	ECF-TAF	ECF-TDF	P value
Acute kidney injury	3	11	0.06
Chronic kidney disease (albuminuria or eGFR <60)	3	17	
Renal discontinuations	0	6	0.03

TAF vs. TDF: P<0.0001 for each biomarker

CROI 2016 (poster 682)

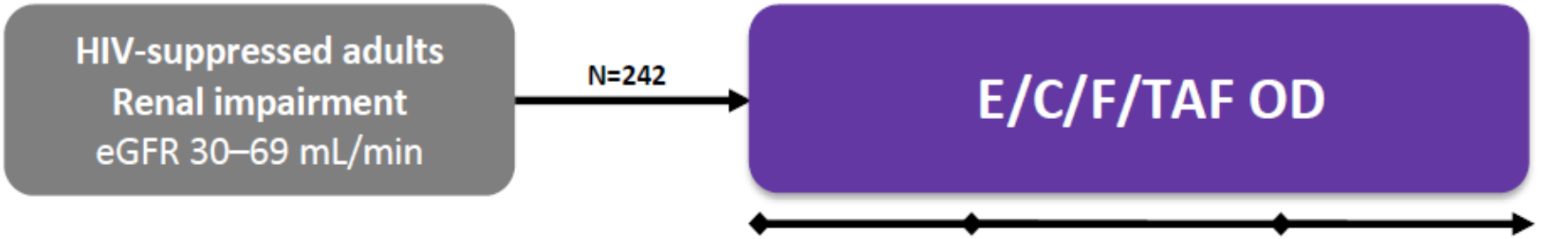
104/111 studies: Effects of TAF vs. TDF on renal tubular function (stratified by D:A:D CKD risk score)



CROI 2016 (poster 681)

Study 112: Safety of Genvoya in patients with renal impairment

Phase III, 96-week, multi-centred, single-arm, open label study



Key inclusion criteria

- CD4 ≥50 cells/μL
- No HCV or HBV infection
- HIV-1 RNA <50 c/mL for ≥6 months

ClinicalTrials.gov identifier: NCT01818596

Primary endpoint

- Change from baseline in glomerular filtration rate*† at Week 24

Secondary endpoints

- Efficacy, safety, and tolerability observed through Weeks 48 and 96
- Proportion of subjects with HIV-1 RNA <50 c/mL by FDA Snapshot analysis

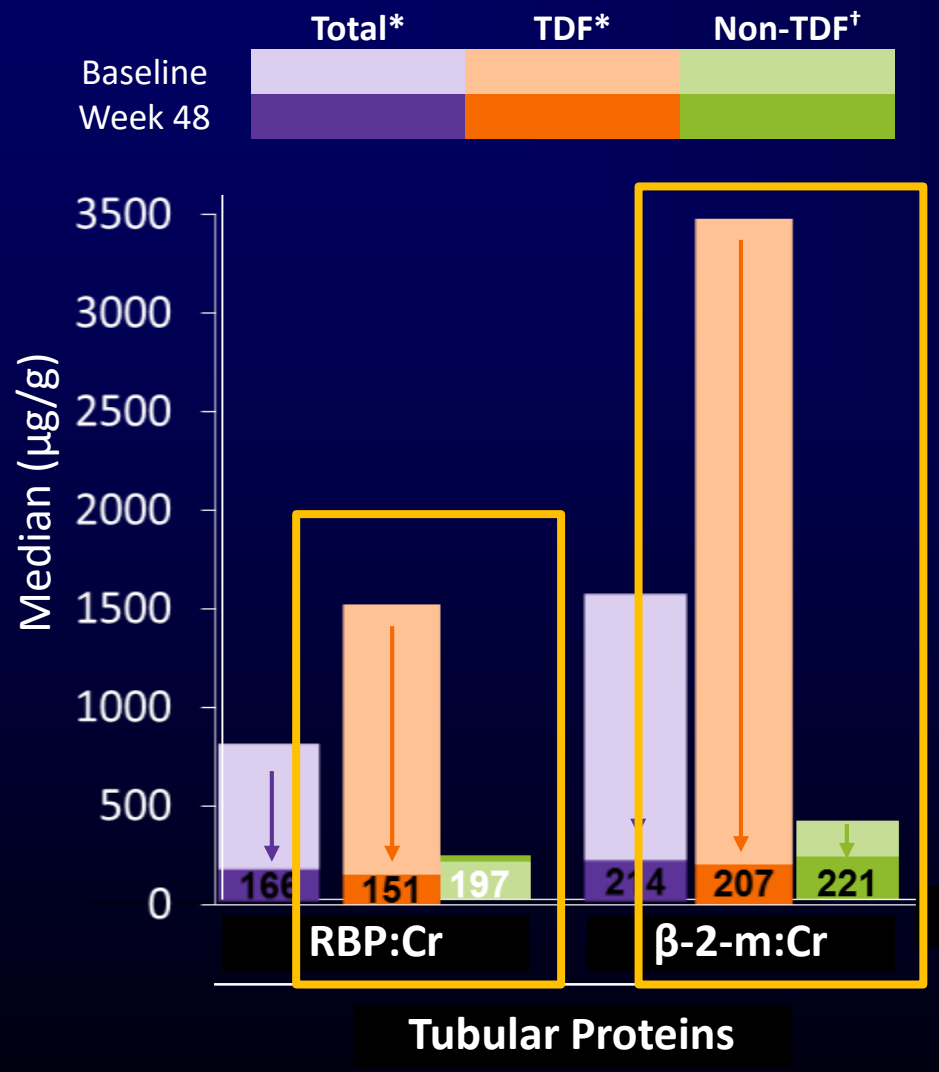
JAIDS, in press

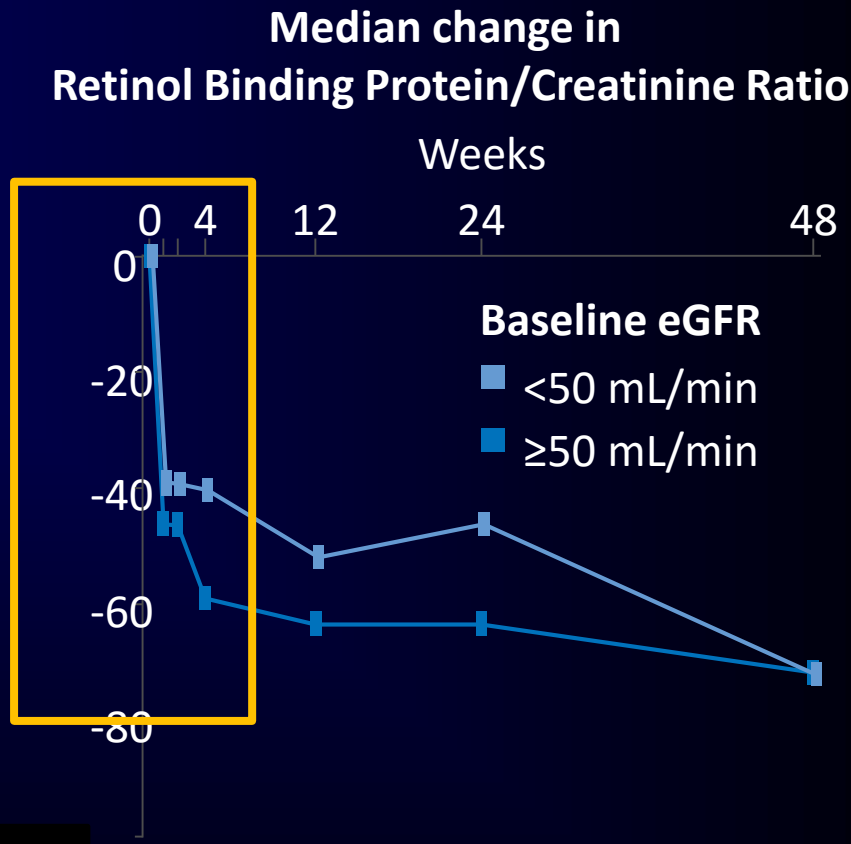
Patient characteristics

	Baseline eGFR		
	30–49 mL/min n=80	50–69 mL/min n=162	Total N=242
Median age, year (IQR)	59 (52, 66)	58 (51, 64)	58 (52, 65)
Age >65 years, n (%)	25 (31)	38 (23)	63 (26)
Females, n (%)	21 (26)	29 (18)	50 (21)
Black or African descent, %	18	19	18
Median CD4 count, cells/µL	622	635	632
Pre-switch TDF use, %	58	69	65
Hypertension, %	50	34	39
Diabetes, %	15	13	14
Median $eGFR_{CG}$, mL/min	43	60	56
Median $eGFR_{CKD\text{-}EPI,\ creatinine}$, mL/min/1.73 m^2 *	45	58	54
Median $eGFR_{CKD\text{-}EPI,\ cystatin\ C}$, mL/min/1.73 m^2 †	57	77	70
Dipstick proteinuria (grade 1 or 2), % ‡	44	27	33

JAIDS, in press

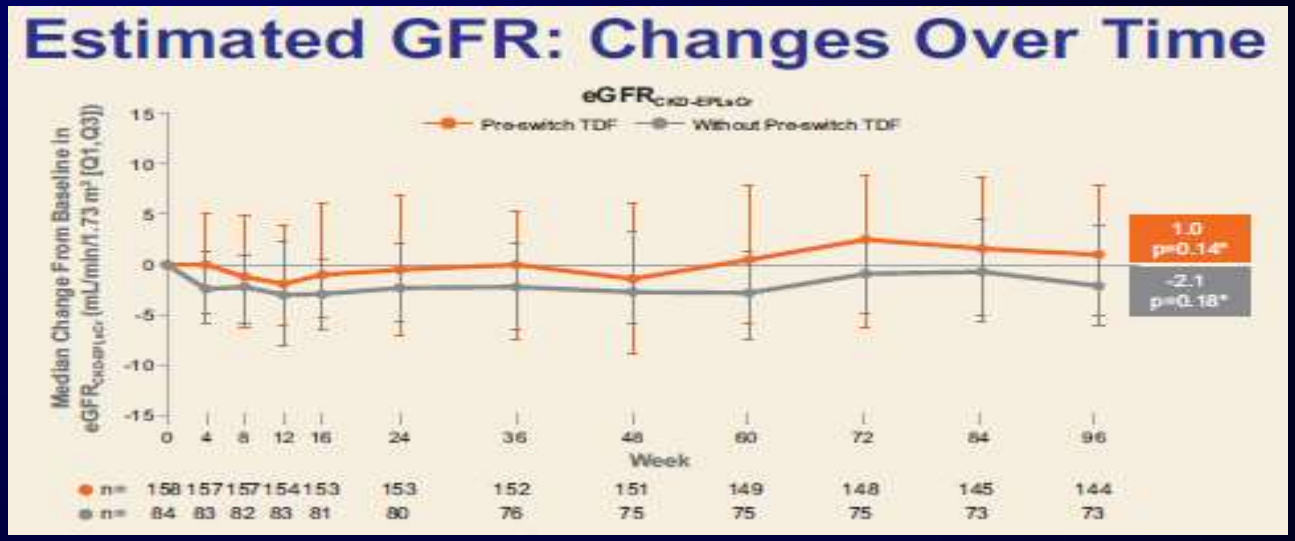
Switching from TDF to Genvoya improved tubular proteinuria

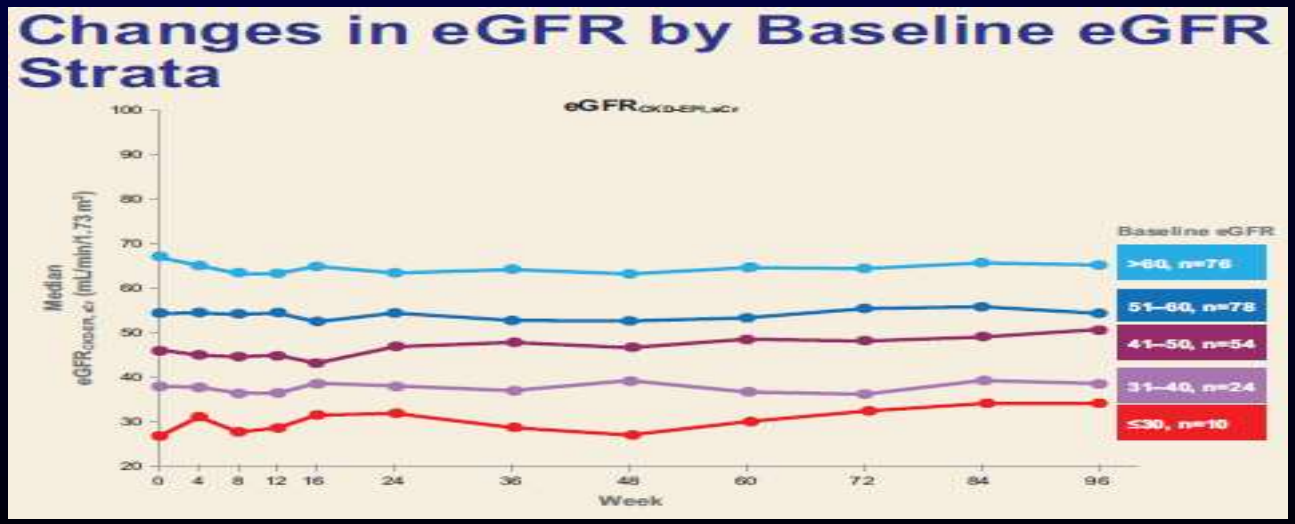




JAIDS, in press

GS-0112: ECF-TAF switch in patients with renal impairment





CROI 2016 (poster 680)

Summary

- The incidence of CKD increases as HIV+ patients age
- CKD is an important CVD risk factor and affects ARV choice
- TDF and ATV may cause renal injury and are best avoided in patient with, or at risk of, CKD
- Several ARV's may inhibit creatinine secretion
- TAF is a new treatment option for patients with mild-moderate renal impairment