Renal Function Monitoring of Patients Living with HIV on Efavirenz/Emtricitabine/Tenofovir disoproxil (EFV/FTC/TDF) at an Ambulatory HIV Clinic

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Objective

1. Identify any association between EFV/FTC/TDF use and renal function decline while accounting for normal ageing, and specifically to determine whether it is significant enough to consider switching to a TAF regimen.

2. Audit UHL HIV OPD compliance with EACS guidelines for monitoring of renal function.

Background

Regular assessment of renal function is increasingly important in the care of patients living with HIV, an ageing cohort with a range of comorbidities that can compound their risk of kidney injury. The newer TAF (tenofovir alafenamide) containing regimens have been shown in some studies to be relatively safer compared with TDF (Tenofovir disoproxil)

Methods

- A list of patients on the tenofovir combination pill (*600mg EFV/200mg FTC/245mg TDF*) in UHL HIV OPD was compiled by pharmacy.
- The following data was collected from clinic flowsheets: eGFR, viral load, CD4 count and urinalysis results.
- If only the creatinine value was noted then the MDRD calculation was manually used
- *MDRD 4-variable GFR Equation; GFR in mL/min per 1.73 m2 = 175 x SerumCr-1.154 x age-0.203 x 1.212 (if patient is black) x 0.742 (if female).*
- Charts and OPD letters were reviewed to determine start and end dates of this regimen and, if available, date of diagnosis and any treatment received.

Diagnosis of kidney disease

		eGFR[ii]			
		> 60 mL/min	> 60 mL/min, but accelerated decline of eGFR*	> 30 - ≤ 60 mL/min	≤ 30 mL/min
Proteinuria (mg/mmol)[iii]	UA/C[iii] < 3	Regular follow-up			
	UA/C[iii] 3-30	• Check risk factors for CKD[iv] and nephrotoxic medicines including ART[iv, v] • Discontinue or adjust drug dosages where appropriate[iv] • Perform renal ultrasound • If haematuria present with any level of proteinuria refer to nephrologist • Refer to nephrologist if new CKD or progressive decline in eGFR			• Check risk factors for CKD and nephrotoxic medicines including ART[iv] • Discontinue or adjust drug dosages where appropriate[iv] • Perform renal ultrasound • Urgent referral to nephrologist
	UA/C[iii] > 30				

* Defined as decrease in eGFR of 5 mL/min per year for ≥3 consecutive years or confirmed 25% eGFR decline from baseline

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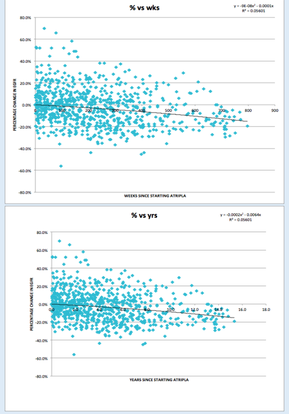
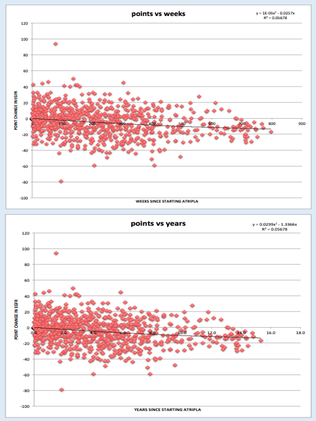
Results

- 41 patients in total were identified, the majority were Irish or Afro-Carribean in origin. They ranged in age from 28 to 75 years old, with the median age being 43.
- 9 patients were started on EFV/FTC/TDF as ART naïve subjects. 5 patients had eGFR<90 on starting ART. The duration of EFV/FTC/TDF use averaged 7.4 years (389 weeks) to a maximum of 15.3 years.
- Of note, no patient started with what would be considered a low eGFR (<60) or dropped to a level that required a switch, although this decision was borderline in some patients and reviewed at a series of visits.
- From initiation of EFV/FTC/TDF to the end of time interval studied, eGFR did not significantly change in any patient outside of the expected ranges associated with normal ageing. Significant change defined as per EACS Guidelines 2020 (Fig 2)

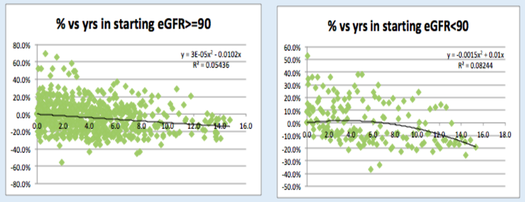
Weeks and Years % drop in eGFR



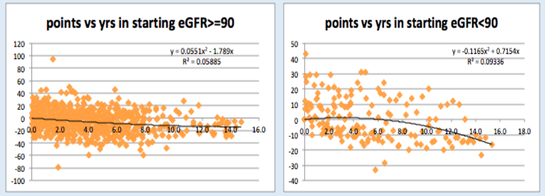
Weeks and Years Point drop in eGFR



Subset analysis of patients with eGFR<90 vs eGFR= >90 when starting ART



Subset analysis of patients with eGFR<90 vs eGFR= >90 when starting ART



Management of HIV-associated kidney disease[vii]

Prevention of progressive renal disease	Comment
1. ART	Start ART immediately where HIV-associated nephropathy (HIVAN) [viii] or HIV immune complex disease strongly suspected. Immunosuppressive therapy may have a role in immune complex diseases. Renal biopsy to confirm histological diagnosis recommended **Consider replacing TDF** by non-tenofovir drug or TAF*** if:** • UP/C 15-50 mg/mmol (see tubulopathy section) • eGFR > 60 mL/min, but decrease in eGFR by 5 mL/min per year for at least 3 consecutive years or confirmed 25% eGFR decline from baseline • co-morbidities with a high risk of CKD (i.e. diabetes and hypertension) • body weight < 60 kg • use of a PI/r as a third agent **Replace TDF** by non-tenofovir drug or TAF*** if:** • eGFR ≤ 60 mL/min • UP/C > 50 mg/mmol • nephrotoxic comedication • previous TDF toxicity (proximal renal tubulopathy) ** Expert opinion pending clinical data ***There are limited data on use of TAF with eGFR ≤ 30 mL/min, and longer term outcomes are unknown

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Conclusions

- No need to switch from EFV/FTC/TDF to newer TAF containing drugs in our stable patients.
- We identified a need to involve other medical specialties when reasons for renal function decline were identified that were not causally related to medication or HIV complications.
- Clinic was compliant with EACS guidelines in terms of frequency and timing of monitoring of renal function.

References

1. Gameiro J, Jorge S, Lopes JA. HIV and renal disease: a contemporary review. *Int J STD AIDS*. 2018;29(7):714-719. doi:10.1177/0956462417750710
2. Yombi JC, Pozniak A, Boffito M, et al. Antiretrovirals and the kidney in current clinical practice: renal pharmacokinetics, alterations of renal function and renal toxicity. *AIDS*. 2014;28(5):621-632. doi:10.1097/QAD.0000000000000103
3. Baba M, Longitudinal study of the decline in renal function in healthy subjects. PloS one. 2015 Jun 10;10(6):e0129036.
4. Horberg M. Impact of tenofovir on renal function in HIV-infected, antiretroviral-naive patients." *JAIDS Journal of Acquired Immune Deficiency Syndromes* 53, no. 1 (2010): 62-69
5. European AIDS Clinical Society Treatment Guidelines October 2020 Available From: https://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html
6. Lê MP, DAYANA Study Group. Tenofovir plasma concentrations related to estimated glomerular filtration rate changes in first-line regimens in African HIV-infected patients: ANRS 12115 DAYANA substudy. J Antimicrob Chemother. 2015 May;70(5):1517-21. doi: 10.1093/jac/dku532. Epub 2015 Jan 11. PMID: 25583749.