Eligibility of patients in a community HIV setting for switching rilpivirine/emtricitabine /tenofovir disoprixolfumurate (R/F/TDF) to tenofovir alafenamide(TAF)

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Introduction :

NHS(E) guidance on switching to TAF containing regimens for kidney disease recommends an eGFR < 60 ml/min or heavy proteinuria (albumin creatinine ratio(ACR)) > 30mg/mmol as a definite contraindication for TDF containing regimens. Moderately reduced eGFR 60-90 ml/min in presence of other recognised risk factors for chronic kidney disease (CKD) as relative contraindications.[1].Applying these criteria estimates of 30% have been proposed for switch consideration on TDF.

Aims:

To establish proportion of a sub-group of patients on TDF regimen (Eviplera) switched or considered eligible for TAF containing regimen (Odefsey) based on NHS (E) criteria.
To assess where possible any change in renal parameters of individual patients on switching to TAF. Sub analysis of association of serum phosphate levels with renal impairment and intention to TAF switch.

Methods:

Electronic patient records used to obtain a cross-sectional review of all patients commenced on Eviplera for minimum of 12 months. Data was collected retrospectively including demographics, CKD risk factors, eGFR, serum phosphate, urine dipstix, urinary protein creatinine ratio (UPCR), ACR and other markers of tubular function, with post switch data where applicable.

Results:

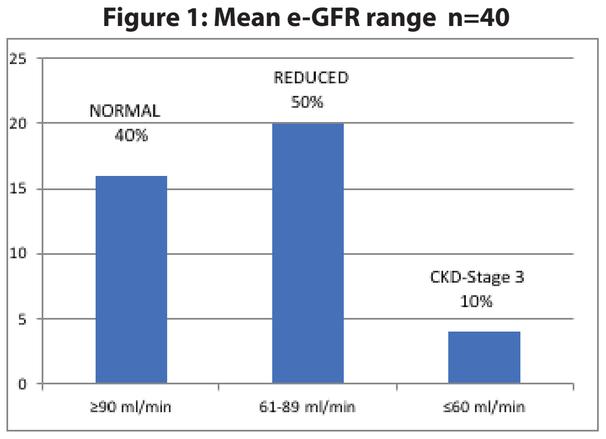
Baseline characteristics- -40 adults were recruited, 47% on 1st regimen and 53 % previously switched regimen. Mean age was 42 years with Male/female ratio 4:1 and White/Black ethnic minority 3:1. Mean duration on eviplera was 4.2 years.

eGFR range-10% of pts on Eviplera were classed as CKD stage 3a on basis of e GFR ≤ 60ml/min and/or proteinuria with 50% reduced eGFR (61-89ml/min) without proteinuria. (Fig 1)

Conclusion:

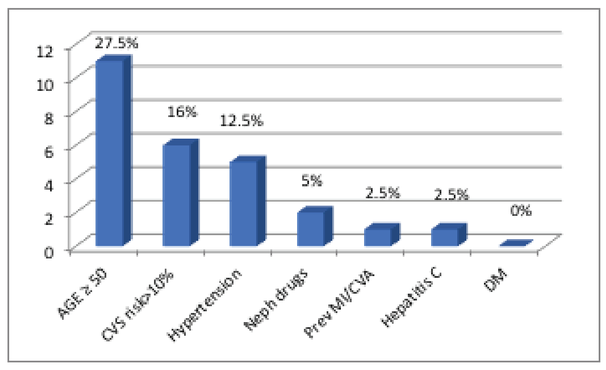
- CKD in PLWHIV is known to be multifactorial in origin and associated with a range of risk factors including usage of anti-retroviral drugs notably TDF based regimens. It is therefore advisable to switch to TAF containing regimens in these pts to avoid further deterioation of renal function where Abacavir is not a suitable alternative.
- Patients with relative contraindications to TDF should be considered for TAF switch in presence of other CKD risk factors.In this cohort our approach was the presence of 2 or more CKD risk factors should prompt consideration for switching to TAF.
- Our cohort reflects the NHS (E) estimate of 30% eligible for switch. It is reassuring that the 3 switch patients analysed to date show gradual improvement in renal function and this is most marked in suspected TDF associated tubulopathy (pt 4).
- Our limited data suggests phosphate levels unless extremely low in association with CKD -3 has little correlation with predicting TDF to TAF switch and alternative causes such as nutritional, alcohol intake and Vit D deficiency should be considered.[2]

Figure 1: Mean e-GFR range n=40



CKD risk factors- Overall 38% of cohort had at least one recognised risk factor(Fig 2) with Age >50, high CVS risk and hypertension accounting for the vast majority. There were no diabetics and most common nephrotoxic drug was NSAID usage.

Figure 2: Overall distribution of CKD risk factors. n=16 (38%)



TAF switch due to definite contraindications – 12.5 % were switched to Odefsey in view of deteriorating renal parameters (Table 1) of e-GFR ≤ 60 ml/min or heavy proteinuria on dipstix with confirmatory UPCR or ACR where available. 3 patients (1, 3 and 5) had additional CKD risk factors with pt 4 having suspected proximal renal tubulopathy with abnormal urinary markers of renal tubular function (glycosuria,-phosphaturia)

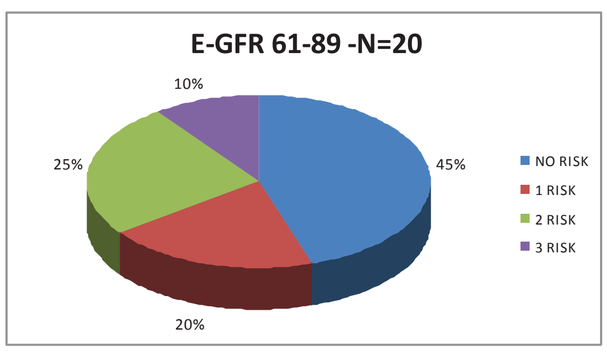
Table 1 : Renal parameters of switch patients due to definite C/I

eGFR/ Pt no	Serum phosphate (mmol/L)	Dipstick / Proteinuria	uPCR	uACR	Tubular markers
1.*56.	0.51	nad	nad	N/D	N/D
2. 60.	0.67	++ 1 g/l	↑ 25-30mg/mmol	nad	↑ gluc
3.*59.	0.6	nad	nad	N/D	N/D
4. 65.	0.89	+++ 3g/l	↑↑↑ >100mg/mmol	↑ 3>10 mg/mol	↑glucose ↑phosphate
5.*69.	0.56	+++	nad	N/D	N/D

NAD: No abnormality Detected, N/D: No Data * ≥ 2 CKD risk factors

TAF switch consideration due to relative contraindications- Of the 20 pts with mildly reduced eGFR 55% were classified as having one or more CKD risk factors and 10% 3 risks .(Fig 3) Overall 27.5% of the cohort had ≥ 1 CKD and 17.5% ≥2 risk factors in addition to 12.5% with definite C/I to TDF, equals 30% estimated for TAF switch.

Figure 3: Relative contraindications - Mildly reducede GFR (no proteinuria) and CKD risk factors



Utility of serum phosphate (Fig 4-) Very low phosphate levels (<0.6mm/l) were strongly associated with CKD stage 3 and all of these pts switched to TAF regimens. Moderate levels were weakly associated with mild reduction in e-GFR (41%) and normal phosphate levels in 34.5%.

Fig 4 - Serum phosphate range n=40

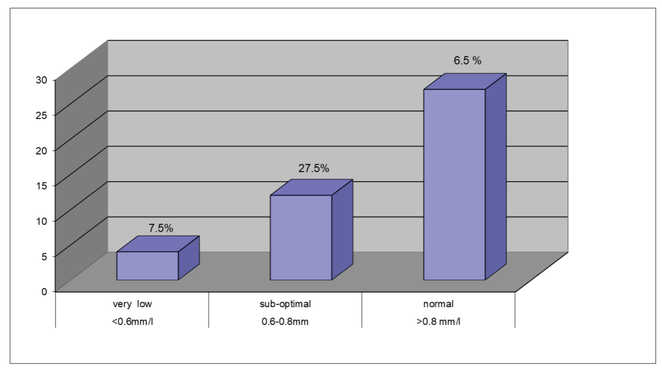
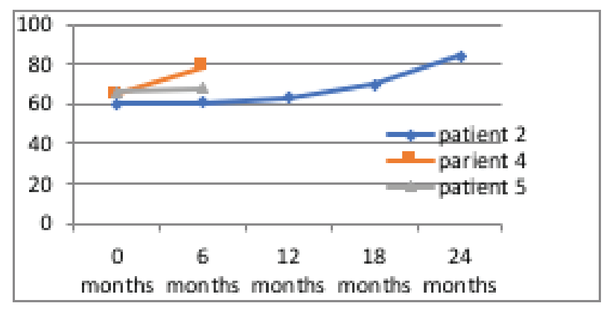
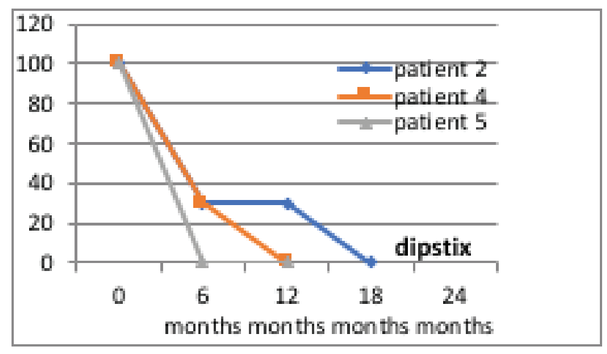


Figure 5: Improvement of renal parameters in patients 2,4 & 5 post TAF switch (c Table 1).

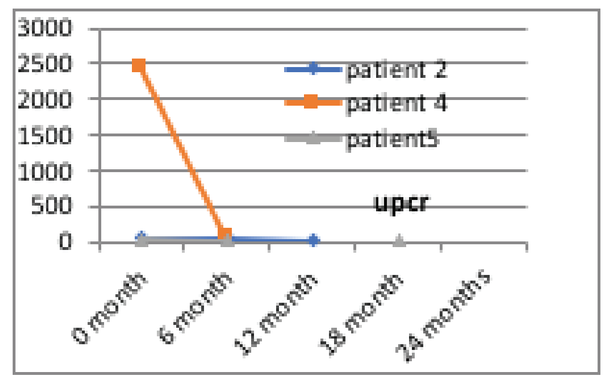
A . e-GFR (ml/min)



B . Urinalysis dipstix(mg/dl)



C. UPCR (mg/mmol)



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2.Bagnis CI et al: Hypophosphataemia:an easy strategy for diagnosis and Rx in HIV pts. Antiviral Therapy 14:481-488