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Impairment of Renal Function associated with Tenofovir Therapy

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Introduction

- Tenofovir (TDF): nucleotide reverse transcriptase inhibitor (NRTI)
- Used in treatment of HIV and Hepatitis B
- Potential for accumulation of high concentration of TDF in renal tubular cells
- Impaired renal function first reported as side-effect in 2005

Aims of Study

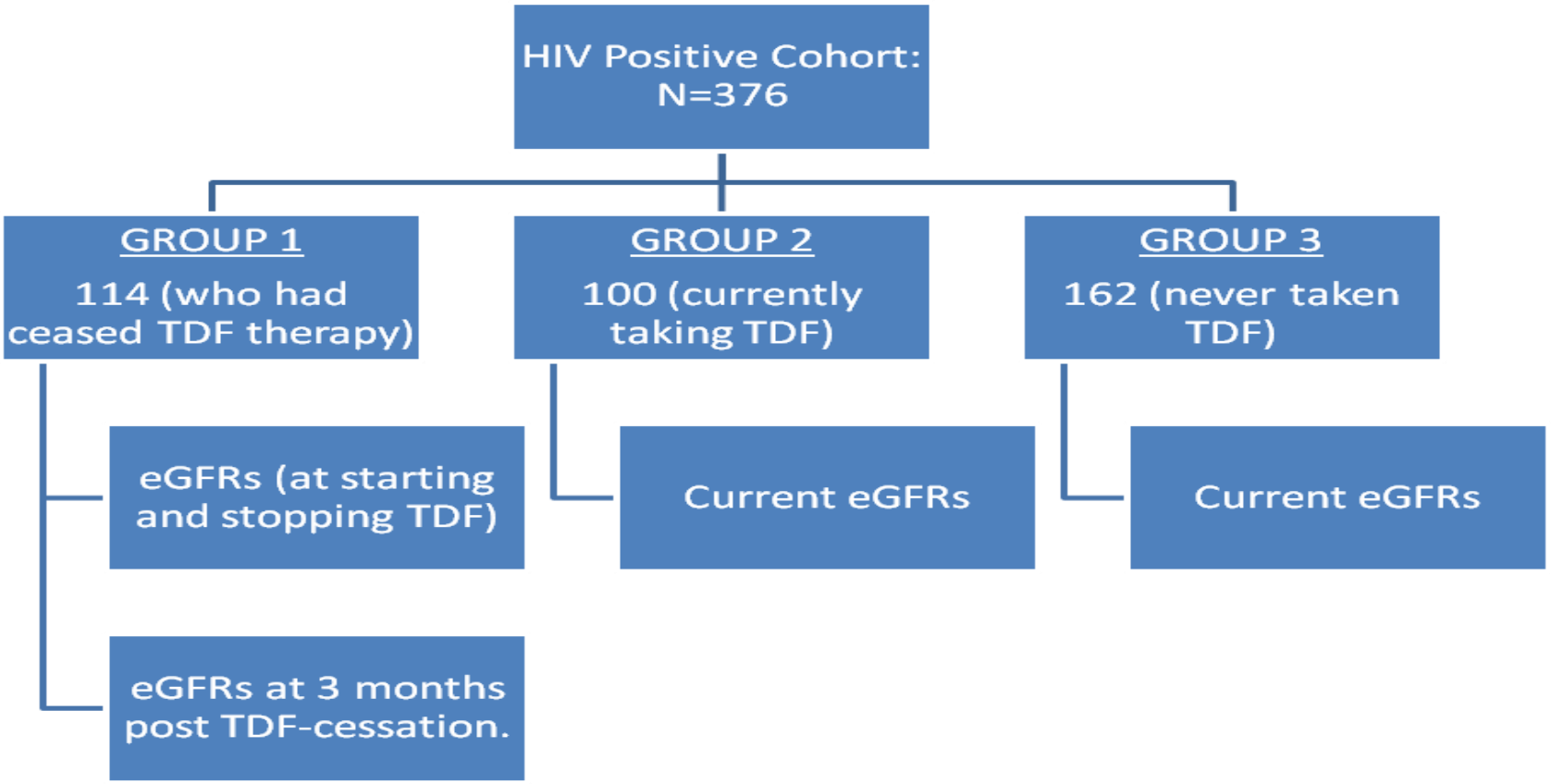
To further investigate impact of TDF therapy on renal function in HIV positive patients, looking specifically at:

- Reversibility of renal impairment at 3 months post cessation of treatment
- Effect of HCV co-infection
- Confounding factors, such as concurrent protease inhibitor(s) therapy

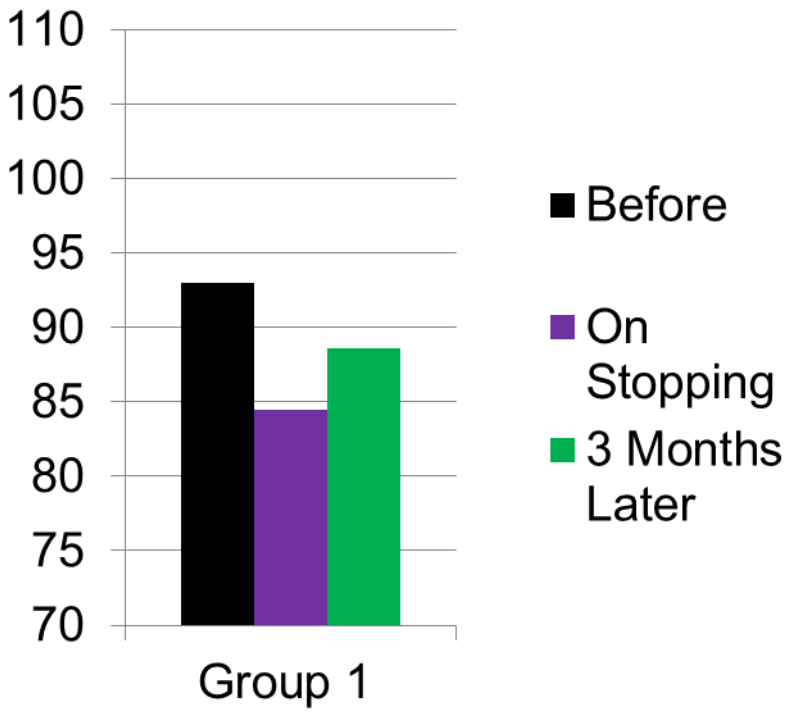
Methods

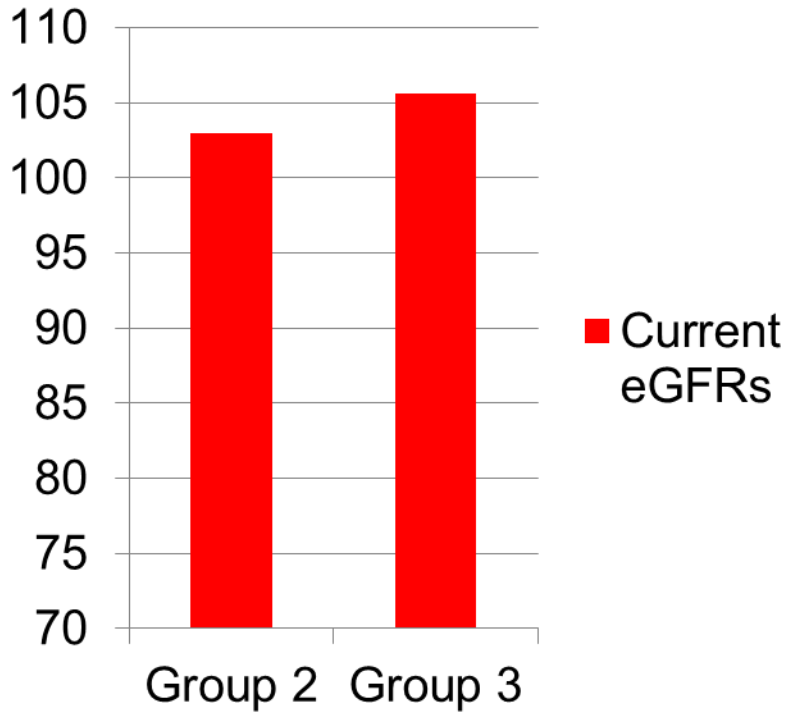
- Renal function assessed retrospectively (eGFR and proteinuria) in HIV +ve patients (n=214) treated for >3 months with TDF at RIDU
- MDRD equation used to calculate eGFR from serum creatinine, age, race and sex
- Controls (n=162) had never received TDF
- Data analysed using SPSS version 19

Patient Selection



Results: Mean eGFRs





Group 1

Before: 93.0 (+/- 21.1)

On stopping: 84.5 (+/- 32.1)

Post-cessation: 88.6 (+/- 30.1)

Group 2 103.0 (+/-23.0)

Group 3 105.6 (+/-26.35)

Results: Reversibility (Group 1)

- 26 patients died whilst receiving TDF. A further 2 patients died following in the 3 months follow-up

- In 58/86 (67.4%) of patients, eGFRs did not return to baseline level by 3 months post-cessation
- 30/86 (34.9%) did not return to within 10% of baseline eGFR at 3 months post-cessation

Results: Group 1

CKD Stage*	GFR	Before TDF	On Stopping TDF	3 Months post-cessation
1	>/= 90	-	-	-
2	60-89	-	-	-
3	30-59	4 (3.5%)	20 (22.7%)	9 (10.5%)
4	15-29	0	1 (1.1%)	0
5	<15	0	2 (2.3%)	1 (1.2%)

***NICE, Chronic Kidney Disease**

Results: Proteinuria

- Median protein:creatinine ratio of 12 (IQ range 8.5-18) in group 2 compared to 10 (IQ range 7-15) in group 3

- No evidence of increase in proteinuria in patients receiving TDF

Results: HCV co-infection

- Did not impact the decline in renal function in any group
- Did not impact the reversibility of impairment of renal function (13/39 HCV +ve (33%) returned to baseline eGFR compared with 16/47 (34 %) HCV -ve)

Results: Confounding Factors

- Protease inhibitor therapy: no significant difference ($p>0.05$) in impairment of renal function or reversibility
- Duration of treatment, age, gender and ethnicity were not significant confounders ($p>0.05$)

Conclusions

- Results provide further support for previous studies [1,2]

1. Scherzer R, Estrella M, Li Y, et al. Association of tenofovir exposure with kidney disease in HIV infection. *AIDS.* 2012 April; 26(7):867-875.

2. Wever K, van Agtmaei M.A, Carr A. Incomplete reversibility of tenofovir-related renal toxicity in HIV-infected men. *J Acquir Immune Defic Syndr.* 2010; 55(1):78-81.

- The use of TDF is associated with impairment of renal function
- This impairment was not fully reversible in the majority of patients following cessation of TDF

- Further work required into benefits of treatment with TDF versus dangers of renal impairment.

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