Tenofovir Disoproxil Fumarate-Associated Nephrotoxicity in HIV-Infected Patients: A Prospective Controlled Study

Khobchok Woratanarat MD*,
Talerngsak Kanjanabuch MD**, Chusana Suankratay MD, PhD*

** Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
*** Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

Objective: *To evaluate all renal functions in patients receiving TDF and other nucleoside analogues.*
Material and Method: *A prospective controlled study evaluating glomerular and tubular functions was conducted in patients receiving either TDF- or AZT-containing antiretroviral therapy regimen between 2008 and 2009 at King Chulalongkorn Memorial Hospital, Bangkok, Thailand.*
Results: *Of 51 patients, there were 39 and 12 patients, with the mean age of 40.03±7.7 and 37.2±7.6 years in the TDF and AZT groups. There was no difference between the two groups, except longer HIV infection duration, higher patient number with previous antiretroviral therapy and undetectable HIV RNA, and higher CD4 count in the TDF group. All and most patients had received lamivudine and a non-nucleoside analogue. The mean change of eGFR from the baseline to the six months of follow-up was +1.32 and +5.88 mL/minute in the TDF and AZT groups. Proximal tubular dysfunction was not noted at three and six months of follow-up. However, patients in the TDF group had lower serum phosphate and higher renal potassium loss than the AZT group at six months of follow-up (p = 0.08 and p = 0.09, respectively). No patients in the two groups with distal tubular dysfunctions were noted.*
Conclusion: *To our knowledge, this is the first prospective controlled study extensively evaluating all renal functions in patients receiving TDF and AZT. There are no differences in the eGFR decline between the two groups during the six months of follow-up. However, a trend towards greater renal loss of potassium and phosphate is noted in the TDF group. A study with longer duration of follow-up is needed.*

Keywords: *Tenofovir disoproxil fumarate, Nephrotoxicity, HIV, AIDS, Fanconi syndrome, Thailand*

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The association between antiretroviral agents and the development of nephrotoxicity remains unclear[1-3]. Tenofovir disoproxil fumarate (TDF) has been recommended as the first-line agent in highly active antiretroviral therapy (HAART) regimen in most countries including Thailand[4-6]. Many patients with TDF-associated nephrotoxicity including acute renal failure, renal proximal tubulopathy (Fanconi syndrome), and nephrogenic diabetes insipidus have been reported[7-14]. Even though most of these patients had preexisting renal impairment, these complications were observed in the patients without any identified risks. TDF shares the similar structure with other acyclic nucleotide analogues including adefovir and cidofovir, which are established nephrotoxic agents in a dose-dependent fashion[15,16], raising concerns regarding the long-term renal safety of TDF.

Correspondence to:
Suankratay C, Division of Infectious Diseases, Department of Medicine, Chulalongkorn University Hospital, Bangkok 10330, Thailand.
Phone & Fax: 0-2256-4578
E-mail: chusana.s@chula.ac.th

To our knowledge, no prospective controlled study evaluating all renal functions in patients receiving TDF in comparison with those receiving other nucleoside analogues has been performed. The objective of the present study was to determine the incidence of renal failure, renal proximal tubulopathy, and distal tubulopathy in HIV-infected adults receiving TDF-containing HAART regimen, compared to those receiving zidovudine (AZT)-containing HAART regimen.

Material and Method

Study design

A prospective controlled study evaluating all renal functions including creatinine clearance (CrCl) and tubular functions was carried out in HIV-infected adult patients receiving either TDF- or AZT-containing HAART regimen at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. The present study period was between January 1, 2008 and February 28, 2009. Written informed consent was obtained from all patients, and the institutional review board approved the protocol.

Patients

The inclusion criteria included HIV-infected patients aged between 18 and 60 years attending the Infectious Diseases clinic who had the estimated glomerular filtration rate (eGFR) of more than 60 mL/minute and had received HAART containing two nucleoside analogues (TDF or AZT as one component) and one non-nucleoside analogues or one ritonavir-boosted protease inhibitor. It should be noted that TDF was never prescribed in accompanying with didanosine or stavudine due to the increased nephrotoxicity risk. The exclusion criteria included 1) contraindications to perform short ammonium chloride loading test, 2) contraindications to perform water deprivation test, and 3) current use of any medications that may lead to the development of renal toxicities.

Regarding the designation as the case or control patients, the case and control patients were those who had received TDF- and AZT-containing HAART regimens, respectively.

Routine data of each patient were collected in the case record form that included demographics, HIV condition [baseline plasma HIV RNA (RT_PCR; Amplicor, Roche Molecular System, CA, the US), CD4 cell count, duration of HIV infection and HARRT therapy, previous antiretroviral use, current HAART regimen], renal function tests, and concomitant medications. All patients made a regular visit, and all renal functions were tested at baseline, three and six months of follow-up.

Renal function tests

All renal function tests including glomerular and both proximal and distal tubular functions were performed. The eGFR was calculated using the Cockcroft-Gault (CG) formula and the Modification of Diet in Renal Disease (MDRD) equation[2]. In addition, it was measured as creatinine clearance using the 24-hour urine collection.

Proximal tubular function tests were determined according to the measurement of daily urine glucose, fractional excretion of phosphate ($FEPO_4$) (normal value was 5 to 12%, and should not exceed 20%), and fractional excretion of potassium (FEK) (normal value should not exceed 20%, and if more than 40% indicated the renal loss)[17].

Distal tubular function tests were determined according to the measurement of 24-hour urine volume in accompanying with urine and serum osmolarities, and the performance of short ammonium chloride loading and water deprivation tests[17].

Statistical analysis

A sample size of 39 patients was calculated to achieve the 80% power to detect the 15% difference in the decline of eGFR at six months of follow-up between the case and control groups (the authors' unpublished data from the pilot study), and alpha and beta errors were 0.05 and 0.20, respectively. The assumed dropout rate was 10%.

The values were presented as the mean±SD and the percentage for the categorical variables. The continuous variables were compared using the Student's t test or Mann-Whitney U test. The Chi-square or Fisher's exact test was used to compare the categorical variables. An analysis of covariances (ANCOVA) was performed to compare the differences of creatinine clearance and all renal function tests ($FEPO_4$, FEK, and urine volume). All P values of less than 0.05 were considered statistically significant. The SPSS software version 13 was used for these analyses.

Results

Baseline characteristics (Table 1)

Thirty-nine and 12 patients were in the TDF and AZT groups, respectively. The mean age was 40.03±7.66 and 37.17±7.55 years in the TDF and AZT groups, respectively. There was no statistical difference between the two groups, except the longer duration of HIV infection, the higher number of patients with previous antiretroviral therapy and undetectable HIV RNA, and the higher CD4 cell count in the TDF group than the AZT group. All patients in the two groups had received lamivudine (3TC) as the second nucleoside analogue. Among non-nucleoside analogues used, there were no significant difference between the two groups (21 (53.8%) and 11 (87.2%) patients had received efavirenz in the TDF and AZT groups, respectively). Only three (7.7%) and one (8.3%) patients in the TDF and AZT groups, respectively, had received lopinavir/ritonavir as the third antiretroviral agent. In addition, all patients in the two groups had no concomitant HBV and HCV infections

Renal functions

Baseline renal functions (Table 2)

Baseline renal functions including serum creatinine, eGFR, proximal tubular functions, and distal tubular functions between the two groups are shown in Table 2. There was no significant difference between eGFR either calculated using the CG formula, the MDRD equation, or 24-hour urine creatinine. The median value and interquartile range of eGFR

Table 1. Baseline characteristic of the study patients

Variables	TDF group (39 patients)	AZT group (12 patients)	p-value
Demography			
Male gender (%)	23 (59.0)	7 (58.3)	0.61
Mean age (years) (±SD)	40.03±7.66	37.00±7.55	0.26
Body mass index (kg/m^2) (±SD)	22.05±3.64	22.25±3.66	0.87
Diabetes (%)	0 (0)	0 (0)	
Hypertension (%)	0 (0)	0 (0)	
HIV data			
Duration of infection (years) (±SD)	7.01±3.88	4.12±2.97	0.02
HIV risk (%)			0.43
Heterosexual	37 (94.9)	12 (100)	
Homosexual	2 (5.1)	0 (0)	
Prior antiretrovirals (%)			0.001
Naive	5 (12.8)	8 (66.7)	
Concomitant antiretroviral (%)			0.94
NRTI			
Lamivudine	39 (10.0)	12 (100)	
NNRTI			
Efavirenz	21 (53.8)	11 (87.2)	
Nevirapine	15 (38.5)	0 (0)	
PI			
Lopinavir/ritronavir	3 (7.7)	1 (8.3)	
Median CD4 count (cell/μL) (IQR)	359 (234-448)	225 (145-289)	0.02
HIV RNA <50 copies/mL (%)	31 (79.5)	3 (25.0)	0.001
Concomitant drug (%)			0.32
Cotrimoxazole	5 (12.8)	3 (25.0)	
No	34 (87.2)	9 (75.0)	
HBV infection (%)	0 (0)	0 (0)	
HCV infection (%)	0 (0)	0 (0)	

IQR = interquartile range; NRTI = nucleoside reverse transcriptase inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; HBV = hepatitis B virus; SD = standard deviation; TDF = tenofovir disoproxil fumarate; AZT = zidovudine

calculated using the CG formula in the two groups was relatively lower than those calculated using the MDRD and 24-hour urine creatinine. In addition, the quantity of daily proteinuria was not significantly different between the two groups.

Baseline proximal tubular functions including glucosuria in the absence of hyperglycemia, $FEPO_4$, and FEK were assessed. There were no patients with abnormal proximal tubular function tests in the two groups. $FEPO_4$, FEK, serum uric acid, serum phosphate, serum magnesium, and serum potassium were not significantly different between the two groups.

Baseline distal tubular functions including the measurement of 24-hour urine volume in accompanying with urine and serum osmolarities, and the performance of short ammonium chloride loading and water deprivation tests were assessed. There was no significant difference in daily urine volume between the two groups. No patients with impaired acid excretion and urine concentrating ability upon ammonium chloride loading and water deprivation tests, respectively, were observed in the two groups.

Renal functions at three and six months of follow-up (Table 3)

eGFR as calculated using the CG formula, the MDRD equation, and 24-hour urine creatinine at three and six months of follow-up was overall normal and not significantly different between the two groups. A decline of eGFR at three and six months of follow-up was not observed in the two groups. The mean change of eGFR calculated using 24-hour urine creatinine between the baseline and six months of follow-up was +1.32 mL/minute in the TDF group, compared with +5.88 mL/minute in the AZT group. In

Table 2. Baseline renal functions between the TDF and AZT groups

Variables[a]	TDF group (n = 39)	AZT group (n = 12)	p-value
eGFR (mL/min)			
24-hour urine volume	114.5±37.3	115.88±27.8	0.91
Cockcroft-Gault formula	106.6±23.2	109.9±23.9	0.67
MDRD equation	112.9±21.1	112.4±20.1	0.94
Preximal tubular functions (median, interquartile range)			
Normoglycemia glucosuria (n,%)	0 (0)	0 (0)	NS
$FEPO_4$ (%)	11.7 (9.5-14.7)	12.6 (10.3-14.6)	0.42
FEK (%)	6.03 (4.9-7.6)	5.2 (4.4-5.95)	0.07
Abnormal NH_4Cl loading test (n,%)	0 (0)	0 (0)	NS
Distal tubular functions			
Abnormal water deprivation test (n,%)	0 (0)	0 (0)	NS
Urine volume (mL/day)	2,027.6±786.0	1,732.5±649.4	0.24
Serum			
Creatinine (mg/dL)	0.76±0.2	0.78±0.2	0.78
Phosphate (mg/dL)	3.2±0.5	3.5±0.6	0.15
Potassium (mEq/L)	3.9±0.2	3.9±0.3	0.42
Magnesium (mg/dL)	2.2±0.15	2.1±0.1	0.78
Uric acid (mg/dL)	5.5±2.0	6.1±1.5	0.42
Urine protein (g/day) (median, interquartile range)	0.06 (0.02-0.13)	0.03 (0.003-0.115)	0.57

[a] Data are expressed as mean±SD, unless otherwise indicated.
eGFR = estimated glomerular filtration rate; MDRD = modification of diet in renal disease; $FEPO_4$ = functional excretion of phosphate; FEK = fractional excretion of potassium; TDF = tenofovir disoproxil fumarate; AZT = zidovudine; NS = not significant

addition, the quantity of daily proteinuria was not significantly different between the two groups at three and six months of follow-up.

Proximal tubular dysfunction was not observed at three and six months of follow-up in the two groups of patients. $FEPO_4$, FEK, serum uric acid, serum phosphate, serum magnesium, and serum potassium at three and six months of follow-up were not significantly different between the two groups. In addition, a trend towards greater renal loss of phosphate ($FEPO_4$), potassium (FEK), uric acid, and magnesium between the baseline and six months of follow-up was not observed in the two groups. Even though patients in the TDF group had non-statistically lower serum phosphate and higher FEK than the AZT group at six months of follow-up ($p = 0.083$ and $p = 0.086$, respectively).

At three and six months of follow-up, no patients with distal tubular dysfunctions were observed in the two groups. There was no significant difference in daily urine volume between the two groups. No patients with impaired acid excretion and urine concentrating ability upon ammonium chloride loading and water deprivation tests, respectively, were observed in the two groups.

Discussion

The authors' prospective controlled study has demonstrated that exposures to TDF-containing HAART regimen over a 6-month duration is not associated with an increased risk of nephrotoxicity both glomerular and tubular dysfunctions, compared to that to AZT-containing HAART regimen. Regarding glomerular function, our results are in consistent with a recent cross-sectional study by Labarga et al, which demonstrated that no significant eGFR impairment was observed in HIV-infected patients treated with TDF-containing HAART, compared to those treated with TDF-sparing HAART[18]. Another study was an observational longitudinal cohort study which compared eGFR between the TDF-treated and non-TDF-treated patients with baseline eGFR of more than 50 mL/minute[11]. There was no significant difference in a decline of eGFR between the patients receiving TDF-containing HAART, compared to TDF-sparing HAART. In contrast, a recent prospective observational cohort was carried out in Italian patients by Tordato and colleagues[3]. They found that current exposure of TDF was associated with a greater risk of an eGFR decline. A recent study was retrospectively carried out in 24 HIV-infected male patients who discontinued

Table 3. Renal functions at three and six months of the follow-up between TDF and AZT group

Variables[a]	TDF group (n = 39)		AZT group (n = 12)		p-value[b]
	3 M	6 M	3 M	6 M	
eGFR (mL/min)					
24-hour urine volume	114.1±33.1	116.2±30.5	114.8±32.7	112.4±30.1	0.71
Cockcroft-Gault formula	104.3±26.1	105.6±23.9	115.6±25.9	114.9±25.5	0.19
MDRD equation	108.8±22.9	111.3±22.5	119.4±20.9	118.3±21.5	0.35
Proximal tubular functions (median, interquartile range)					
Normoglycemia glucosuria (n,%)	0 (0)	0 (0)	0 (0)	0 (0)	NS
$FEPO_4$ (%)	12.8 (9.6-15.9)	12.8 (9.0-14.9)	9.6 (8.3-11.6)	12.1 (8.2-14.95)	0.71
FEK (%)	5.6 (4.9-7.9)	6.03 (4.9-7.6)	5.1 (4.1-6.5)	5.2 (4.4-5.91)	0.08
Abnormal NH_4Cl loading test (n,%)	0 (0)	0 (0)	0 (0)	0 (0)	NS
Distal tubular functions (median, interquartile range)					
Abnormal water deprivation test (n,%)	0 (0)	0 (0)	0 (0)	0 (0)	NS
Urine volume (mL/day)	1,890.0 (1,500.0-2,800.0)	2,100.0 (1,600.0-2,530.0)	1,530.0 (1,187.0-2,262.0)	1,325.0 (1,055.0-2,652.0)	0.14
Serum					
Creatinine (mg/dL)	0.8±0.2	0.8±0.2	0.7±0.2	0.7±0.2	0.60
Phosphate (mg/dL)	3.3±0.6	3.3±0.6	3.7±0.6	3.5±0.6	0.08
Potassium (mEq/L)	3.9±0.2	3.9±0.3	3.9±0.2	3.9±0.4	0.83
Magnesium (mg/dL)	2.2±0.2	2.2±0.2	2.2±0.1	2.2±0.2	0.62
Uric acid (mg/dL)	5.1±1.7	4.9±1.6	5.5±1.6	5.6±1.6	0.18
Urine protein (g/day) (median, interquartile range)	0.11 (0.03-0.21)	0.12 (0.08-0.2)	0.08 (0.02-0.17)	0.11 (0.01-0.14)	0.18

[a] Data are expressed as mean±SD, unless otherwise indicated.

[b] The difference between the TDF and AZT groups at six months of the follow-up.

M = month; eGFR = estimated glomerular filtration rate; MDRD = modification of diet in renal disease; $FEPO_4$ = functional excretion of phosphate; FEK = fractional excretion of potassium; TDF = tenofovir disoproxil fumarate; AZT = zidovudine; NS = not significant

TDF because of a decline of eGFR (using the MDRD equation and CG formula)[19]. They found that there was an incomplete improvement of eGFR after TDF cessation, and factors related to greater eGFR improvement included shorter duration of TDF receipt, more rapid decline of eGFR, and the patients receiving TDF with a protease inhibitor. The median duration of TDF therapy in the present study was 21 and 40 months in the patients with greater and less eGFR improvement, respectively. A recent non-randomized cohort study by Mocroft and colleagues in 6,843 HIV-infected patients showed that TDF exposure was an increased risk associated with chronic kidney disease[2]. The median follow-up in the present study was 3.7 years. A recent meta-analysis of all 17 prospective studies was performed by Cooper et al to evaluate the renal safety between TDF-containing and TDF-sparing HAART[8]. They found that there was a statistically significant decline of eGFR among the patients receiving TDF-containing HAART, compared with TDF-sparing HAART. These conflicting results are probably due to the difference in study design, definition of eGFR used, gender, race and age group of the study patients, associated traditional risks for nephrotoxicity, concomitant anti-retrovirals and nephrotoxic agents, and duration of follow-up. There is the difference in eGFR calculated using the CG formula, the MDRD equation, and 24-hour urine creatinine[20]. An excellent review by Rodriguez-Novoa et al concluded that the occurrence of compromised glomerular function without tubulopathy associated with TDF use is very uncommon[9]. In conclusion, our prospective controlled study confirmed that there was no decline of glomerular function in the patients taking TDF-containing HAART at least for short-term duration.

Regarding renal tubular functions associated with TDF use, there was no significant difference between the patients taking TDF-containing and AZT-containing HAART. However, a trend towards greater renal loss of potassium (FEK) and lower serum phosphate was noted in the TDF group, compared with the AZT group. These results were in consistent with a cross-sectional study by Labarga and colleagues, which showed that there were reduced tubular reabsorption of phosphorus and increased tubular excretion of uric acid in the patients treated with TDF, compared with the control group[18]. A recent pathologic study showed a reversible mitochondrial toxicity of proximal renal tubules in the patients taking TDF[21]. In contrast, a recent meta-analysis of all 17 prospective studies by Cooper et al also showed that there was no significantly increased incidence of hypophosphatemia among the TDF recipients, compared with the control group[8]. A recent analysis of two randomized controlled studies by Gallant and colleagues in 1,111 patients has shown that there was no significant difference in the change of serum phosphate from baseline to week 144 in the TDF group, compared with the control group[22]. A review by Rodriguez-Novoa et al concluded that the occurrence of severe TDF-associated tubulopathy was uncommon and was probably of multifactorial nature[9]. The pathogenesis of TDF-associated proximal renal tubulopathy is probably due to multiple factors including the genetic predispositions[7,9,15,23], race, sex, age, underlying kidney disease, and concomitant nephrotoxic agents. Tenofovir is excreted by both glomerular filtration and proximal tubular secretion. It is transported via organic anion transporter-1 (OAT-1) from the circulation into the proximal tubular cytoplasm, where it is then secreted into the tubular lumen via multidrug resistance protein-2 (MRP-2) and MRP-4 efflux pumps[7,15,23]. It has been demonstrated that a single nucleotide polymorphism in the MRP gene may be associated with TDF-induced renal tubulopathy[24]. In addition, ritonavir can increase tenofovir intracellular concentration within proximal tubules by inhibiting MRP efflux pumps, enhancing risk for TDF-induced mitochondrial toxicity[7]. In our study, only mild renal loss of potassium and phosphate were noted, probably due to a minority of patients receiving ritonavir. In any case, the present study showed that short-term exposure of TDF might be associated with mild proximal renal tubulopathy.

The present study has some limitations. The follow-up duration is only six months, which is short to make a conclusion regarding TDF-associated nephrotoxicity. However, the authors' plan to reevaluate the renal functions especially proximal tubular functions at nine and 12 months. The sample size in the controlled group was small, in comparison with the TDF group, probably due to less long-term mitochondrial toxicity, availability and much convenience of TDF during the study period in our institute. However, apart from a comparison of renal functions between the TDF and AZT group, our study was also designed to compare renal functions in the TDF group between at baseline before and after initiation of HAART. Furthermore, the present study was carried out in a single center, and all patients older than 60 years, with baseline eGFR of less than 60 mL/min, and receiving concomitant nephrotoxic drugs were excluded from the present study. In

addition, most of the patients had received non-nucleoside analogue. Our observation is hence limited to HIV-infected patients with relatively young age group and receiving two nucleoside analogues and one non-nucleoside analogue. Despite these limitations, the present study has some strength including the first prospective controlled study extensively assessing all renal functions between before and after TDF exposure, as well as between after TDF and AZT exposure.

In conclusion, to the best of our knowledge, this is the first prospective controlled study evaluating all renal functions in HIV-infected patients receiving TDF- and AZT-containing HAART. There are no significant differences in the decline of eGFR, proximal and distal tubular functions between the two groups during the 6-month period of follow-up. However, a trend towards greater renal loss of potassium and low serum phosphate is observed in the TDF group than the AZT group. A study with longer duration of follow-up is needed to determine the potential proximal renal tubulopathy of TDF.

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Potential conflict of interest

None.

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ความเป็นพิษต่อไตจาก tenofovir disoproxil fumarate ในผู้ป่วยติดเชื้อเอชไอวีที่โรงพยาบาลจุฬาลงกรณ์

กอบโชค วรธนารัตน์, เถลิงศักดิ์ กาญจนบุษย์, ชุษณา สวนกระต่าย

วัตถุประสงค์: *ต้องการประเมินการทำงานของไตทุกส่วนในผู้ป่วยที่ได้รับ tenofovir disoproxil fumarate (TDF) และยากลุ่ม nucleoside analogues อื่น*

วัสดุและวิธีการ: *การศึกษาชนิดไปข้างหน้าและควบคุม โดยประเมินการทำงานของ glomerulus และท่อไตทุกส่วน ในผู้ป่วยที่ได้รับสูตรยาต้านไวรัสที่มี TDF หรือ zidovudine (AZT) ตั้งแต่ พ.ศ. 2551 ถึง พ.ศ. 2552 ที่โรงพยาบาลจุฬาลงกรณ์*

ผลการศึกษา: *มีผู้ป่วยทั้งสิ้น 51 ราย โดยมีผู้ป่วย 39 และ 12 ราย และมีอายุเฉลี่ย 40.03±7.7 และ 37.2±7.6 ปี ที่อยู่ในกลุ่ม TDF และ AZT ระยะเวลาติดเชื้อเอชไอวีที่นานกว่า จำนวนผู้ป่วยมากกว่าที่ได้ยาต้านไวรัสมาก่อนและตรวจไม่พบไวรัสเอชไอวีในเลือด และจำนวน CD4 สูงกว่า ในกลุ่ม TDF นอกจากนั้นไม่พบความแตกต่างระหว่างทั้ง 2 กลุ่ม ผู้ป่วยทั้งหมดได้รับ lamivudine และส่วนใหญ่ได้ non-nucleoside analogue อีก 1 ชนิด การเปลี่ยนแปลงของอัตราการกรองของไตจากเริ่มต้นจนครบ 6 เดือนของการติดตามเป็น +1.32 และ +5.88 มิลลิลิตร/นาที ในกลุ่ม TDF และ AZT ไม่พบมีการสูญเสียการทำงานของท่อไตส่วนต้นที่ 3 และ 6 เดือนของการติดตามในทั้ง 2 กลุ่ม อย่างไรก็ตามผู้ป่วยในกลุ่ม TDF มีระดับฟอสเฟตในซีรัมต่ำกว่าและการสูญเสียโพแทสเซียมทางไตสูงกว่าเมื่อเทียบกับผู้ป่วยในกลุ่ม AZT ที่ 6 เดือนของการติดตาม (p = 0.08 และ p = 0.09 ตามลำดับ) ไม่พบมีการสูญเสียการทำงานของท่อไตส่วนปลายในผู้ป่วยทั้ง 2 กลุ่ม*

สรุป: *การศึกษานี้เป็นการศึกษาแรกที่เป็นชนิดไปข้างหน้าและควบคุมที่มีการประเมินหน้าที่การทำงานของไตอย่างละเอียดทุกด้านในผู้ป่วยที่ได้ TDF เทียบกับ AZT ไม่พบความแตกต่างของของอัตราการกรองของไตในทั้ง 2 กลุ่ม เมื่อครบ 6 เดือนของการติดตาม อย่างไรก็ตามมีแนวโน้มที่จะสูญเสียโพแทสเซียมและฟอสเฟตทางไตในกลุ่ม TDF จำเป็นต้องการการศึกษาที่เฝ้าติดตามผู้ป่วยในระยะยาวนานกว่านี้*
