



Poster H-169

# Renal Safety of Tenofovir DF in HIV Treatment-experienced Patients with Adverse Events Related to NRTI Use

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## BACKGROUND

Tenofovir DF (TDF) is the only nucleotide analogue reverse transcriptase inhibitor (NtRTI) approved for HIV treatment. TDF is excreted by glomerular filtration and active tubular secretion. Acute renal failure, Fanconi syndrome and other renal disorders have been reported in association with TDF use. The risk of a patient developing nephrotoxicity with TDF is approximately 0.02%\*. Most cases have been associated with renal disease risk factors. At present, it is recommended that the creatinine clearance (CrCl) be measured before starting TDF, and if lower than 50mL/min to adjust TDF dosing interval.

\* Izzedine H, Isnard-Bagnis C, Hulot JS, et al. AIDS 2004; 18(7):1074-6

## OBJECTIVES

To assess the incidence of renal events associated with TDF use in the RECOVER cohort, and to identify the presence of risk factors.

## METHODS

RECOVER is a prospective and multicenter Spanish cohort including patients who developed NRTI-related toxicity that led to the substitution of this NRTI by TDF. No other drug substitutions were allowed. TDF-associated renal impairment that lead to discontinuation of the drug were prospectively collected and followed.

## RESULTS

1350 patients were included in the RECOVER cohort between Sep2002 and May2003. We have available data through Sep 2004 of 1193 patients who have reached an median of 36 weeks of follow-up (12 to 48 weeks) (1507 patient-years). Five patients discontinued treatment as a result of acute renal failure during this period, all of them with concomitant renal risk factors (Table 1). Three out of 5 were male, 2/5 were IVDU and 3/5 were on 4th line of treatment or higher. Before administration of TDF, CrCl was only determined in 2/5 patients and in both cases was <50mL/min and TDF dosing interval was not modified.

## RESULTS (Cont.)

TABLE 1

Main characteristics and outcome of patients who interrupted TDF treatment due to renal disorders

(Recover Cohort: Sep 2002 to May 2003).

| CASE | NRTI SWITCHED | TOXICITY ASSOCIATED TO THE NRTI SWITCHED | CURRENT ANTIRETROVIRAL TREATMENT | RENAL PREDISPOSING FACTORS                                               | ADVERSE EVENT                   | TAKEN ACTION               | OUTCOME                                                              |
|------|---------------|------------------------------------------|----------------------------------|--------------------------------------------------------------------------|---------------------------------|----------------------------|----------------------------------------------------------------------|
| 1    | AZT           | Severe anemia                            | TDF+3TC+EFV                      | Diabetes Mellitus<br>Chronic renal failure (Basal CrCl<50 mL/min)        | Worsening of renal function     | Stop TDF                   | Death due to myocardial infarction at the second day of TDF stopping |
| 2    | AZT           | Severe anemia                            | TDF+3TC+EFV                      | Chronic renal failure due to pre-renal causes (Basal Cr Cl<50 mL/min)    | Worsening of renal function     | Stop TDF                   | Favorable                                                            |
| 3    | AZT           | Severe anemia                            | TDF+3TC+NFV                      | Nephrolithiasis and nephrocalcinosis due to indinavir previous treatment | Acute renal failure             | Stop TDF                   | Favorable                                                            |
| 4    | d4T           | Severe Neuropathy                        | TDF+ddI+EFV                      | Nephrolithiasis                                                          | Obstructive uropathy and sepsis | Renal surgery and Stop TDF | Favorable                                                            |
| 5    | ddI           | Asymptomatic hyperlactatemia             | TDF+3TC+LPV/rvt                  | Previous renal failure secondary to didanosine                           | Acute renal failure             | Stop TDF                   | Favorable                                                            |

## CONCLUSIONS

After a median of 36 weeks of follow-up in highly-experienced patients, the incidence of renal impairment leading to discontinuation of TDF was 0.4% (0.3 per 100 patient-years). This conclusion is in concordance with available data from clinical trials, which suggest that TDF is a renal safe drug