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# Real-life renal safety of “boosted TDF” in HIV/HCV-patients on SOF/LDV

Poster # 452

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## Background

Ledipasvir increases tenofovir (TDF) exposures. In individuals taking EVG/COBI/TDF/FTC or TDF with a ritonavir (RTV)-boosted HIV PI, higher TDF exposures may increase the risk of renal toxicity. The safety of increased tenofovir concentrations in these settings has not been establised*.

## Objectives

To evaluate the renal safety of 12 or 24 weeks of Sofosbuvir/Ledispasvir (SOF/LDV), according to boosted TDF exposure, in a cohort 398 HIV/HCV co-infected DAAs treated patients at a tertiary center in Madrid (Spain).

## Methods

From March 2015, 225 patients started SOF/LDV. We included all consecutive patients with complete renal function and overall safety follow-up data during therapy. Paired baseline and at the end of treatment eGFR (CKD-EPI) comparisons were made regarding TDF-boosted or not populations.

**Table 1. Baseline Characteristics of the 69 patients treated with TDF and SOF/LDV .**
At baseline there were no significant differences with respect to demographic data, genotype or HCV viral load, eGFR (CKD-EPI), or % of subjects with eGFR<70mil/min.
Of note, more patients on boosted TDF received a 24w course of SOF/LDV (20% vs 2%, p=0.018).

| Baseline characteristics | TDF-No boosted N=44 | TDF-Boosted N=25 |
|---|---|---|
| Patients, men, n (%) | 36 (82%) | 21 (84%) |
| Age, years, mean±SD | 49±7 | 50±4 |
| HVC genotype 1, n (%) | 30 (68%) | 17 (68%) |
| Cirrhosis, n (%) | 13 (29%) | 9 (36%) |
| Fibroscan®, kPA±SD | 13.6±13 | 11±9 |
| HCV viral load at baseline Log10 IU/L, mean±SD | 5.96±1.2 | 6.31±0.7 |
| CD4 cels/mm3, mean±SD | 618±268 | 549±419 |
| SOF/LDV 24 w, n (%) | 1(2%) | 5 (20%) |
| RBV use | 4 (9%) | 1 (4%) |
| TDF suspension, n (%) | 0 (0%) | 1 (4%) |

**Table 2. Glomerular filtration rate at baseline and at the end of treatment.**
Rates of eGFR<70 ml/min at the end of SOF/LDV were similiar with no significant differences :
2 patients (4%) in the no-boosted TDF group vs 3 patients (12%) in the TDF-boosted group (p=0.32).

| CKD-EPI eGFR (ml/min) | Baseline eGFR (ml/min) mean±SD | Baseline <70 ml/min n (%) | End-treatment eGFR (ml/min) mean±SD | End-treatment <70 ml/min n (%) |
|---|---|---|---|---|
| TDF-No boosted (n=44) | 96±12 | **1** (2%) | 90±15 | **1**+1 (4%)* |
| TDF-Boosted (n=25) | 96±11 | 0 (0%) | 88±17 | 3 (12%)** |

* eGFR: 63ml/min; 69 ml/min **eGFR: 56 ml/min; 61 ml/min; 63 ml/min

**Abbreviations:**
**ARV: Antiretroviral; EVG/COBI: Elvitegravir/Cobicistat; TDF: Tenofovir; FTC: Emtricitabine; SOF/LDV: Sofosbuvir/Ledipasvir; RBV: Ribavirine; INI: Integrase Inhibitors; NNRTIs: Non-Nucleoside Reverse Transcriptase Inhibitor; PI: Protease Inhibitor; eGFR: estimated glomerular filtration rate;**

**Table 3: Characteristics of 5* patients with eGFR<70 ml/min during SOF/LDV.**
Only one patient on boosted-TDF (1.4%) stopped TDF due to renal impairment after 74 days of therapy (eGFR 56 ml/min).

| TDF-No Boosted | Case 1 | Case 2 |
|---|---|---|
| ARV regimen | FTC / RPV / TDF | FTC / RPV / TDF |
| Baseline FibroScan™ (kPa) | 10 | 9 |
| Comorbidities | - | DM-Cholesterol |
| Baseline eGFR ml/min | 63 | 82 |
| Maximun decrease eGFR (ml/min) | 53 | 69 |
| After SOF/LDV eGFR (ml/min) | 74 | 76 |

| TDF-Boosted | Case 3 | Case 4 | Case 5 |
|---|---|---|---|
| ARV regimen | EVG/COBI/FTC/TDF | ATV/r+FTC/TDF | EVG/COBI/FTC/TDF |
| Baseline FibroScan™(kPa) | 8 | 9 | 7 |
| Comorbidities | - | - | - |
| Baseline eGFR ml/min | 93 | 71 | 89 |
| Maximun decrease eGFR (ml/min) | 61 | 63 | 56 |
| After SOF/LDV eGFR (ml/min) | 72 | 71 | 85 |

*None with RBV

**Figure 2: TDF based regimens during SOF/LDV and SVR rates.**
HAART included TDF/FTC in 69 (31%); of them, 44 patients did not receive a boosted TDF regimen, whereas a “boosted TDF” regimen was used in 25 (36%): EVG/COBI/FTC/TDF in 15 (60%), FTC/TDF plus a RTV-boosted PI in 8 (32%), and simultaneous EVG/COBI/FTC/TDF and darunavir in two (8%).

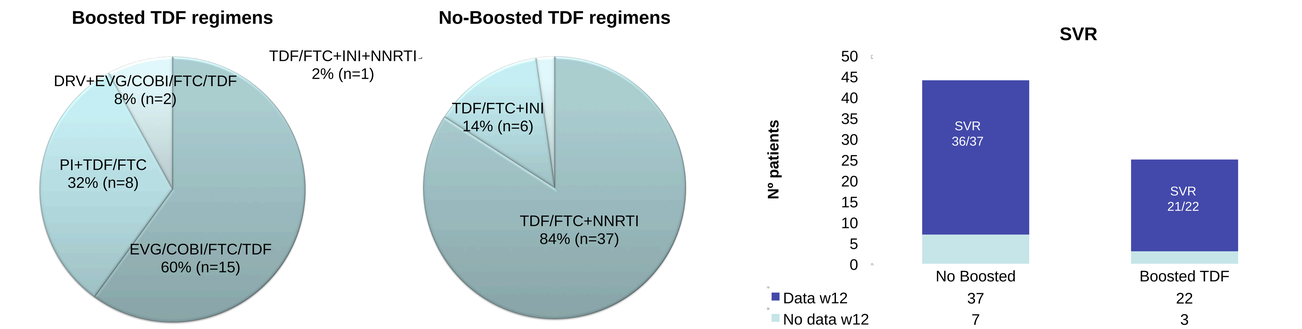
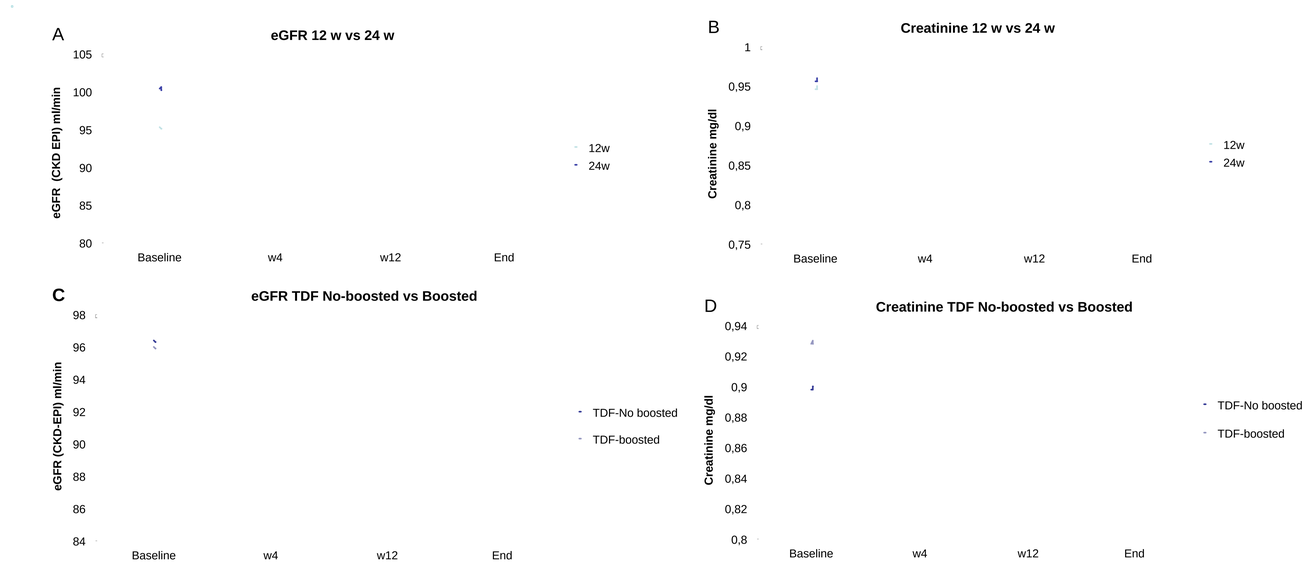



**Figure 1: Effect of Boosted TDF or 24 weeks of SOF/LDV.**
During therapy we did not find significant differences in Creatinine or eGFR between no boosted TDF or TDF-boosted, nor in 12 vs 24 weeks of SOF/LDV.
None of the 69 patients on TDF reached eGFR below 50ml/min.




**Conclusions:** In our “real life” population, SOF/LDV did not significantly worsen renal function in patients on “boosted TDF” (EVG/COBI/FTC/TDF or TDF with a RTV-boosted HIV PI).

**Coadministration of elvitegravir/cobicistat (150/150 mg once daily) and ledipasvir/sofosbuvir (90/400 mg once daily) decreased elvitegravir Cmax by 12%, but increased AUC and Cmin by 2% and 36%; cobicistat Cmax, AUC and Cmin increased by 25%, 59% and 325%, respectively. Ledipasvir Cmax, AUC and Cmin increased by 63%, 78% and 91%, respectively and sofosbuvir Cmax and AUC increased by 33% and 36%. The combination is also expected to increase tenofovir concentrations. The safety of increased tenofovir concentrations in this setting has not been established and coadministration is not recommended. The combination should be used with caution with frequent renal monitoring if other alternatives are not available. www.hep-druginteractions.org report*