Introduction

Tenofovir disoproxil fumarate (TDF) is associated with nephrotoxicity, bone mineral density (BMD) decline, and it decreases LDL.

TDF-associated nephrotoxicity can lead to an estimated Glomerular Filtration Rate (eGFR) decline and/or proximal tubular dysfunction (PTD).

Besides BMD, the trabecular bone score (TBS) is a relatively new measure of bone strength that also includes information about bone-microarchitecture. Both BMD and TBS are useful in predicting fracture risk.

In the DOMONO-study (NCT02401828), patients on cART switched to dolutegravir (DTG) monotherapy, 85 of whom switched from a TDF containing cART regimen.

Several secondary endpoints were predefined, of which those related to metabolism and inflammation are described here:

1. To evaluate the metabolic effects of a switch from TDF containing cART to DTG monotherapy.
2. To evaluate the impact of a switch from cART to DTG monotherapy on inflammation markers.

Aim

To describe the effects on lipids, renal, bone, and inflammation markers of switching from TDF-containing cART to DTG maintenance monotherapy.

Methods

DOMONO was a randomized, clinical, non-inferiority trial, switching patients from cART to DTG maintenance monotherapy. The primary endpoint (not discussed here) was virological suppression across 24 weeks during DTG maintenance monotherapy.

Renal markers evaluated were: eGFR, protein:creatinine ratio (UPCR), albumin:creatinine ratio (UACR) and beta2-microglobulin:creatinine ratio (B2M/GFR).

Bone markers were: lumbar and hip BMD, proportions of normal BMD osteopenia/osteoporosis, and lumbar TBS, and these were only measured in patients that had been on a TDF containing cART regimen.

Inflammation markers evaluated were: CD4:CD8 ratio and C-reactive protein (CRP).

A Bonferroni-corrected significance level was defined as p<0.0017. Paired T-tests, Wilcoxon Rank Sum tests, and McNemar tests were used when appropriate.

Results

95 patients started DTG maintenance monotherapy. 78 had reached the week 48 endpoint, when the study was discontinued prematurely as 8 patients had been observed with virological failure (VF) and 3 of them developed integrase inhibitor associated mutations. 85 patients had been on a TDF-containing cART regimen.

No significant changes in any of the lipid markers nor any of the inflammation markers were observed during the 48 weeks of DTG maintenance monotherapy.

Discussion and Conclusions

In patients without virological failure during DTG monotherapy, a switch from TDF containing cART to DTG monotherapy improved renal tubular and bone markers, whereas lipids and inflammation markers remained stable.

As expected, the discontinuation of TDF improved proteinuria and improved BMD.

During DTG monotherapy, inflammation markers remained stable. Because patients with virological failure restarted cART, this conclusion can only be made for patients without virological failure while on DTG. The inflammation markers remaining stable suggests that as long as virological control is maintained, dolutegravir or monotherapy has no negative impact on inflammation.