Efficacy and safety of the switch of Triumeq® to generic (abacavir + lamivudine) + Tivicay®: data at 48 weeks

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ABSTRACT

Introduction: Generic drugs are helpful to enhance the efficiency of the sanitary system. A generic coformulation of abacavir (ABC) and lamivudine (3TC) is available since 2016 in Spain. A report of our experience with its use is exposed.

Methods: Patients between February 2017 and June 2017 who were taking Triumeq® were switched to the generic ABC + 3TC plus DTG. Efficacy, safety, reasons for discontinuation and costs savings were evaluated at 48 weeks.

Results: Switch was made in 93 patients, with a median age of 47 years and a mean time of 12.33 years with HIV infection. Six patients (6.5%) discontinued the new ART, being toxicity of the central nervous system the most frequent reason. The effective saving derived from the change after 1 year of treatment was 151.127 €.

Conclusions: The change from Triumeq® to a generic regimen of ABC + 3TC and another pill of DTG seems to be safe and efficient at 48 weeks.

KEYWORDS
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Introduction

HIV infection is a chronic disease that is not curable nowadays. The main goal of treatment is maintaining an undetectable viral load in blood, which can be achieved in the majority of cases with highly active antiretroviral therapy based on three drugs. The economic burden of the antiretroviral treatment (ART) is high. A prompt initiation of ART reduces mortality and HIV-defining illnesses [1]. It has been proved that a single tablet regimen (STR) favours the adherence and consequently the efficacy [2]. Nevertheless, these studies were done mainly with tenofovir + emtricitabine + efavirenz, a combination that has been removed from the recommended initial therapies in the main guidelines [3,4].

Generic drugs are the name given to the drugs that have the same active ingredients and pharmaceutical presentation as well as similar bioequivalence than the reference drug, demonstrated by studies of bioavailability. The main reason for introducing generic drugs is the save in costs, which could lead to an easier accessibility to ART in low-income countries. In 2016, a generic coformulation of ABC + 3TC was commercialized. We reported the results at 24 weeks and both treatments were similar in safety and efficacy [5]. In this paper, we analyse the results after 48 weeks of follow up.

Methods

A decision in our hospital committee was made to systematically switch the patients taking the Triumeq® to the generic coformulation (ABC + 3TC) and DTG 50 mg, which is a 25% cheaper in our hospital. The doctor explained the switch to the patient and then the information was reinforced in the hospital's pharmacy. The frequency of clinical follow-up was identical to any other patient. A transversal retrospective analysis at 48 weeks was made to evaluate their evolution in terms of viroimmunological, biochemical and clinical control.

The demographic and biochemical variables were extracted from the electronic records of the hospital, while the start data of the different antiretroviral treatments were extracted from the pharmacy’s computer system. When an interruption of the new treatment happened, we analysed the reasons and predicting factors.

Quantitative data are shown as mean and 95% confidence interval, and qualitative variables as percentages. A non-parametric test was done to identify factors that could contribute to the interruption. SPSS 20.0 was used to analyse data. We calculated the saving costs at one year since the switch multiplying the difference between the two alternatives and the number of patients.

Results

Ninety-three patients were switched from Triumeq® to the generic coformulation of ABC + 3TC with DTG. The mean age was 47 years (95% CI: 45–49), with 76% of males. Eighty per cent were Spanish, 11% south Americans and 9% from the rest of the world. Forty-eight per cent were men who had sex with men, 34% heterosexuals and 16% intravenous drug users. Near 40% of patients had active smoking, 7.5% had active alcohol consumption and 5% had active drug use.

The mean of the Charlson’s index was 1.76 (95% CI: 1.23–2.30) and that of the infection age was 12.33 years (95% CI: 10.53–14.12). The mean time using ART was 7.29 years (95% CI: 5.80–8.78); 11% of patients were naïve and 89% used previously other ART. The mean CD4 recount was 852 cells/microL. There was a previous virological failure in 34% of patients. Twenty-nine per cent had suffered an AIDS event throughout the course of their disease and a quarter had suffered a non-AIDS event. Twenty-three per cent had past Hepatitis B infection and 21% hepatitis C infection with negative viral load; none of them with active disease. Fifty-five per cent did not take other medications besides ART, while 16% took statins, 11% antihypertensive drugs and 10% antidepressants.

After 48 weeks of follow-up, 6 patients (6.5%) interrupted the new treatment. Four of them did it in the first 24 weeks. The mean duration before discontinuation was 31 weeks (95% CI: 15.18–46.82). Four patients discontinued because of toxicity and the other 2 because of physician’s decision. Two patients lost follow-up. The toxicity was related to the central nervous system in three cases: 2 of headache and 1 of burning mouth syndrome. The other case was a suspicion of stroke that was ruled out after neuroimaging studies. There was no significant statistical relationship between discontinuation and age, Charlson’s index, years with ART, years with HIV infection, previous virological failures or previous ART toxicities.

At baseline, there were 2 patients (2.2%) with detectable viral load (190 and 54 copies/mL), while at 48 weeks there were 7 (7.5%). Their values were 204, 104, 98, 82, 78, 68 and 51 copies/mL. One of them was detectable already at the time of change. In the next measurement done in less than 3 months, none of these patients had a detectable viral load. There were no differences
between the basal and 48 weeks levels of total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, transaminases, glomerular filtrate, CD4 recount or viral load.

After 48 weeks of treatment with the new combination, there was a saving of 151.127 € taking into account only the medication expenses.

Discussion

In this study, the change from the Triumeq® to the generic coformulation ABC + 3TC plus DTG was safe and effective. The incidence of discontinuations was 6.5% and there were no statistically significant changes in HIV viral load or CD4 population. A meta-analysis showed the advantages of STR against multi-tablet regimens in terms of adherence and achieving virological suppression [2]. Nevertheless, our results showed that the new coformulation was more cost-effective without compromising the viroimmunological status. Krentz et al. reported 177 patients who voluntarily accepted switching from Triumeq® to the generic coformulation of ABC + 3TC and DTG with similar results as ours [6].

There were two patients that experienced a new onset of headache attributable to the new ART. One of them had a detectable viral load at week 48 but not at week 24 when the side effect was not reported. In the other two discontinuations related to the central nervous system, (the burning mouth syndrome and suspicion of stroke), at least the second one could be ruled out after complementary tests. The percentage of central nervous system related toxicity in our study was lower than the reported in the SINGLE trial [7]. In the two changes because of clinical judgement, one of them was justified because the patient preferred a STR; in the other, the reason is not specified.

Seven patients had a detectable viral load at 48 weeks, the highest being 204 copies/mL. The adherence measured in the pharmacy for these patients was at least 90%. In the next blood test control after 48 weeks, none of these patients had detectable viral load, so we assume they were blips. In consequence, no cases of interruption of the new treatment regimen due to virological failure were described.

Our study has limitations. First, it is a retrospective study with a small sample size, so we are not able to make strong statements. Second, there was a special motivation within the pharmacy employees to monitor the adherence to the new treatment; it would be necessary to confirm the results after a longer period of observation.

Nowadays, one of the most efficient antiretroviral treatment for HIV infection in Spain is Triumeq® [8]. The inclusion of generic drugs in ART could improve efficiency.

Conclusion

The switch from a STR to a generic coformulation plus a second pill with the same components is safe and more cost-effective at 48 weeks.

Disclosure statement

No potential conflict of interest was reported by the authors.

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