Study Synopsis

Name of sponsor: Gilead Sciences, Lda. Portugal	
Title of Study:	An observational cohort study to evaluate the impact of the tenofovir disoproxil fumarate (TDF)-based single tablet regimens on adherence, quality of life and cost-effectiveness in HIV-1 infected patients
Study centre(s):	PPD PPD PPD PPD PPD PPD PPD PPD PPD PPD PPD PPD PPD
Investigator(s):	PPD PPD PPD PPD PPD PPD PPD PPD PPD PPD PPD PPD PPD
Publication:	Lebre, J.G. Saraiva da Cunha, M.J. Aleixo, K. Mansinho, M. Abreu, M. Doroana, P. Pacheco, F. Aragão, M. Cavaco, C. Delgado, V. Andreozzi, F. Antunes. Metabolic syndrome, cardiovascular risk and renal impairment in HIV infected patients initiating antiretroviral therapy in Portugal. 5th EACS Barcelona, Spain, October 21-24. 2015. Poster PE8/28
Study period:	From: 1st January 2008 To: 17th May 2017
Phase of development:	Phase IV

Objectives:	Primary Objective: To prospectively evaluate the impact of TDF-based single tablet regimens (STR) on adherence in HIV-1 infected subjects. Secondary Objective: To prospectively evaluate the impact of the TDF-based STR on health-related quality of life in HIV-1 infected patients; To evaluate concordance of the main adherence measure (CEAT-VIH) with: ▪ Visual analogue scale (VAS) adherence questionnaire; ▪ Proportion of days covered (PDC) using the pharmacy's refill electronic database; ▪ To evaluate the impact of TDF-based STR on selective adherence and non-adherence; ▪ To evaluate the clinical and economic consequences of selective adherence and non-adherence; ▪ To evaluate the impact of switching to TDF-based STR on effectiveness, safety and tolerability; ▪ To compare persistence among patients on TDF-based STR with that observed in patients on other combined antiretroviral therapy (cART); ▪ To estimate the impact of TDF-based STR on the probability of hospitalization; ▪ To estimate the cost differential between cohorts, including: o The cART cost; o Monthly (inpatient and outpatient) non-cART costs; o Monthly total (SRT plus non-cART) costs.
Methodology:	This was a multicentre observational study with a control cohort, with retrospective observation and prospective follow-up periods. The cohort under investigation (STR Cohort) consisted of patients who switched to or initiated a TDF-based STR (Atripla®, Eviplera® or Stribild®). The multiple tablet regimen (MTR) Cohort comprised subjects who initiated cART with any multi-tablet recommended regimen according to EACS Guidelines, in force at the time of treatment initiation, and who did not switch to any STR up to the final date of study inclusion.
Number of patients	**Planned:** 860 adult patients (400 in the STR Cohort and 460 in the MTR Cohort) **Screened**: 460 adult patients (234 STR; 199 MTR; 27 missing) **Analysed:** 431 adult patients (234 STR; 197 MTR)
Main eligibility criteria	HIV-1 infected subjects, aged 18 years or older at the time of the introduction of first cART (STR or MTR), availability of complete cART clinical history and pharmacy refills (pharmacy's electronic database) and subjects who initiated therapy according to EACS Guidelines, in force at the time. To be eligible to STR cohort, patients had to start a TDF-based STR up to 30th June 2015. To be eligible to MTR cohort, patients should have never refilled a TDF-based STR up to the time of inclusion in the study.
Study duration:	The retrospective period covered the time between 1st January 2008 and the enrolment date. After the enrolment date, patients were prospectively evaluated for a maximum (max) period of 24 months.

	However, this study was terminated early due to very slow participant recruitment. As the planned sample size would not be reachable and the proportion of missing data overall and also for the primary endpoint was significant, it was decided to terminate the study earlier. This meant that the majority of the outcomes proposed could not be evaluated and several objectives could not be analysed.
Planned Endpoints	Primary: Adherence was to be evaluated through the CEAT-VIH questionnaire, comparing the mean score in the STR cohort with the mean score in the MTR cohort. Secondary: Quality of life, measured through SF-6D and Modified HAART Intrusiveness Scale (m-HIS) questionnaire, comparing the mean score between STR and MTR cohorts; Mean score of VAS questionnaire, comparing STR and MTR cohorts; PDC based on pharmacy refills among patients of the STR cohort (while on STR), compared with PDC in the MTR cohort. However, none of these endpoints were reached due to large volume of missing data and minimum (min) sample size not achieved. As such, the study variables were only descriptively analysed and no conclusions drawn out of this study.
Statistical methods	Due to the above-mentioned reasons, only descriptive analyses were conducted. For continuous variables, measures of central tendency, such as mean and median, and measures of variability, namely standard error and range were calculated. The number of observations for each outcome was also included and reflects all the responses available for each outcome. When applicable, continuous outcomes were categorized. For categorical outcomes, were presented tables with frequencies and percentages, where the denominator included observed and missing data. Missing values for continuous and categorical variables will be clearly indicated, including the number of missing values and their percentage on the overall total of eligible records. The descriptive statistics were stratified by cohort (STR and MTR) and, when possible, were also stratified by visit (baseline, screening, month 12 and month 24). In the contingent tables, the percentages were calculated by total column, unless otherwise specified.
Results:	A total of 460 patients were screened, of which 431 patients met eligibility criteria: 234 were in the STR cohort and 197 were in the MTR cohort. However, due to the reduced number of included patients and missing information for several variables the study endpoints, namely, adherence, quality of life and costs, could not be answered. The majority of patients included were male in both STR cohort (74.5%) and MTR cohort (67.3%). Mean age of patients was 41.6 and 43.3 years in the STR and MTR cohort, respectively. The most likely mode of infection was heterosexual contact for both the STR (50.0%) and the MTR (47.2%) cohorts. As for drug therapy, the most commonly used backbone was emtricitabine+tenofovir disoproxil fumarate (FTC+TDF), both for the STR (75.2%) and for the MRT (25.4%). The most frequently third agent used was efavirenz (EFV) in the STR cohort and ritonavir-boosted lopinavir (LPV/r) in the MTR cohort. At baseline, 8.1% and 4.0% of patients had moderate to high 10-year risk of cardiovascular disease in the STR and MTR cohorts, respectively, according to the Framingham risk

	score. When considering the estimation of 10-year risk of fatal cardiovascular disease, according to Systematic COronary Risk Evaluation (SCORE) system, 1.7% and 2.0% of patients showed high risk (>5%). Renal function, in accordance with the Cockcroft-Gault equation, 9.9% in the STR and 13.7% in the MTR had and estimated glomerular filtration rate (eGFR) below 90 ml/min.
Conclusion	Due to the high proportion of missing information is not possible to interpret the results. Nonetheless, this study suggests that patients with HIV should be carefully monitored due to considerable proportion of several comorbidities.
Report version/date:	Version 2.2, 16th January 2019