NON-INTERVENTIONAL POST-AUTHORIZATION SAFETY STUDY REPORT

Title	Real-life study of single tablet regimen (STR) and multi tablet regimen (MTR) usage in Germany on persistency of initial HIV therapy in adult patients – STRingent Protocol ID: GS-DE-236-1272
Version identifier of the final study report	Version 1, Final
Date of last version of the final study report	08 Dec 2016
EU PAS register number	ENCEPP/SDPP/6118
Active substance	J05AR09 emtricitabine, tenofovir disoproxil, elvitegravir and Cobicistat J05AR08 emtricitabine, tenofovir disoproxil and rilpivirine J05AR13 abacavir, dolutegravir and lamivudine and multi tablet regimens consisting of various approved HIV medications
Medicinal product	STR: Stribild®, Eviplera®, Triumeq® MTR: multi tablet regimens consisting of various approved HIV medications in various combinations consisting of at least 2 tablets/dosing forms
Product reference	EU/1/13/830/001 EU/1/13/830/002 EU/1/11/737/001 EU/1/11/737/002 EU/1/14/940/001 EU/1/14/940/002
Procedure number	Not applicable
Marketing authorisation holder for Stribild® and Eviplera®	Gilead Sciences International Limited Cambridge CB21 6GT, United Kingdom
Joint PASS	No

Research question and objectives	The primary objective of this study was as follows: • To evaluate persistency of initial HIV therapy in patients starting with a STR or a MTR during the first year of therapy. The secondary objectives of this study were as follows: • To describe and evaluate real-life effectiveness of STR and MTR – by describing the characteristics of HIV-infected patients with initial therapy in an HIV-specialized practice or outpatient setting – by describing the treatment motivation (early treatment according to guidelines, treatment as prevention (TasP) or other) and the specific treatment regimen (STR or MTR) in Germany with respect to patient characteristics and factors driving treatment decision (such as side effect profile, co-morbidities/co-medications, resistance, anticipated patient adherence, and patient preference) – by describing STR/MTR efficacy using HIV-RNA and CD4 cell count changes • To describe reasons for treatment discontinuation or change of therapy • To describe adherence to ART medication • To describe physical and mental health-related quality of life and health status using standardized questionnaires (Health Survey Short Form (SF-36) and HIV Symptom Index) • To describe rates of severe and/or unexpected toxicities and drug-drug interactions derived from reported ADRs/SADRs
Country(-ies) of study	Germany
Author	Crispin Bennett PhD, CROMSOURCE

Marketing authorisation holder(s)

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1 ABSTRACT

1.1 Title

Real-life study of single tablet regimen (STR) and multi tablet regimen (MTR) usage in Germany on persistency of initial HIV therapy in adult patients – STRingent.

1.2 Keywords

HIV therapy regimen Germany adult.

1.3 Rationale and background

To evaluate persistency of initial HIV therapy in patients starting with a STR or a MTR during the first year of therapy.

1.4 Study design

Non-interventional cohort study.

1.5 Setting

Specialized HIV practitioners throughout Germany.

1.6 Patients and study size, including dropouts

Three hundred and fifty five patients provided informed consent, were enrolled into the study and contributed data while on therapy (236 STR; 119 MTR).

1.7 Variables and data sources

Whether the patient has taken STR or MTR was the exposure of interest. Descriptive and outcome variables are the collected clinical and laboratory parameters as available.

1.8 Results

Primary outcome

In patients starting with a STR, 90.5% (171/189) persisted on the initial HIV therapy for the observational period, while 9.5% (18/189) switched or discontinued the initial therapy.
For patients starting with a MTR, 75.5% (77/102) persisted on the initial HIV therapy for the observational period, while 24.5% (25/102) switched or discontinued initial therapy.

A greater proportion of patients starting with a MTR switched or discontinued therapy (24.5%, 25/102) than patients starting with a STR (9.5%, 18/189): p =0.001. Note that this p-value is to be interpreted as a descriptive measure.

The mean (95% CI) rate of therapy switch, or discontinuation, was markedly higher among patients starting with MTR versus those starting with STR (3.76 [2.44-5.56] vs 1.53 [0.91-2.42] per patient-year of treatment, respectively).

The mean person time of follow-up in the STR and MTR patients was similar.

HIV-1 RNA viral load

HIV-1 RNA viral load at baseline was lower in patients starting with a STR than with MTR: STR mean (median) 141,656.1 (24,000.0) copies/mL; MTR 755,780.2 (56,700.0) copies/mL.

In the STR-treatment arm, 81.6% (177/217) of patients had an HIV-1 RNA viral load of <= 100.000 copies/mL at baseline, while 18.4% (40/217) had a viral load of > 100.000 copies/mL. In the MTR-treatment arm, these figures were 60.7% (68/112) and 39.3% (44/112) respectively.

The mean (median) viral loads subsequently reduced for both STR- and MTR- treated patients with no apparent difference between treatment arms (to 53.2 (49.0) at month 12 for STR-treated patients and to 49.0 (49.0) at month 12 for MTR-treated patients). It should be noted that all non-missing values less than 50 were set to 49 and this was the lowest median that could occur.

CD4 Cell Count

CD4 cell counts were similar in both treatment arms at baseline [STR mean (median) 499.7 (461.0) cells/µL; MTR 481.3 (427.0)].

However, when categorized, a higher proportion of STR-treated patients than MTR-treated patients had >=500 cells/µL at baseline: 45.7% (101/221), compared to 34.2% (39/114).

Other Analyses

Quality of Life: Quality of life was evaluated using the SF 36. There was no change in physical component scores with therapy, with a possible small improvement in mental component scores at month 12.

AIDS defining events: One patient (0.6%, 1/165) in the STR-treatment arm had a new AIDS defining event at month 3, with no events reported by patients in the MTR-treatment arm.

HIV symptom index: HIV symptom index was similar for patients in the STR- and MTR-treatment arms.

Adverse Events: The rate (95% CI) of total Treatment Emergent (TE) Adverse Drug Reactions (ADR) per patient year was similar in both treatment arms: [1.78 (1.10 - 2.73) STR arm; 1.81 (0.93 - 3.16) MTR arm].

In the STR-treatment arm, 10 TE ADRs were reported in the Gastrointestinal disorders SOC, with the most common PT in this SOC being “nausea”, with 5 events reported by 5 (2.1%) patients. In the MTR-treatment arm there were 4 TE ADRs in this SOC with diarrhea being the only reported PT, reported by 4 (3.4%) patients.

Very few TE ADRs were reported in each group, with overall similar rates. Therefore, no conclusions regarding the benefit-risk balance of STR versus MTR can be drawn.

Driver for therapy start and choice of regimen: The most common reasons for therapy start were "Patient Driven - Patient explicit wish to start therapy" in 71 (30.2%) of STR patients [32 (26.9%) of MTR patients] and "Physician Driven - Guidelines (CD4 cells 200-350 cells/µl)" in 33 (27.7%) of MTR patients [53 (22.6%) of STR patients]. There were no notable differences between the treatment groups for the primary driver for therapy start.

For STR, "Patient preference for this regimen" was the most common reason for the choice of regime (55.9%, 132/236). For MTR, "Anticipated adherence" was the most common reason, recorded (32.8%, 39/119). For STR patients the STR regimen was chosen due to "Patient wish for STR" in 59.3% (140/236) of patients.

1.9 Discussion

Due to early termination of the study, the number of patients recruited was fewer than the 1000 that was planned. The conclusions that can be drawn are limited by the relatively small number of patients that completed the study.

1.10 Marketing Authorisation Holder(s)

The Marketing Authorisation Holder for Stribild® and Eviplera® is Gilead Sciences International Limited, Cambridge, CB21 6GT, United Kingdom.

1.11 Names and affiliations of principal investigators

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