ABBREVIATED CLINICAL STUDY REPORT

Study Title:	**ROCKET** - **R**andomized **O**pen Label Switch for **C**holesterol Elevation on **K**ivexa **E**valuation **T**rial A Phase 4, Open Label, Randomized, Controlled Study to Assess the Effect on Lipid Profile of Switching from a Stable HAART Regimen of fixed dose Abacavir/Lamivudine (Kivexa) Plus Efavirenz, to Once Daily Atripla in Adult HIV-1 Infected Subjects With Raised Cholesterol
Name of Test Drug:	Atripla® (efavirenz/emtricitabine/tenofovir disoproxil fumarate)
Dose and Formulation:	Fixed-dose tablet containing efavirenz 600 mg, emtricitabine 200 mg, and tenofovir disoproxil fumarate 300 mg
Indication:	HIV-1 Infection
Sponsor:	Gilead Sciences Limited Granta Park, Abington, Cambridge, CB21 6GT, United Kingdom
Study No.:	GS-UK-177-0109
Phase of Development:	Phase 4
IND No.: **EudraCT No.:**	Not applicable 2007-003354-28
Study Start Date: **Study End Date:**	27 March 2008 (First Subject Screened) 12 January 2010 (Last Subject Observation)
Principal or Coordinating Investigator:	Name: Graeme Moyle, MB, BS, Dip GUM Affiliation: [redacted] PPD
Gilead Responsible Medical Monitor:	Name: Cham Herath, MD Telephone: [redacted] PPD Fax: [redacted] PPD
Report Date:	30 June 2010

CONFIDENTIAL AND PROPRIETARY INFORMATION

This study was conducted in accordance with the guidelines of Good Clinical Practice, including archiving of essential documents.

STUDY SYNOPSIS

Gilead Sciences Limited
Granta Park, Abington
Cambridge, CB21 6GT, United Kingdom

Title of Study:

ROCKET - **R**andomized **O**pen Label Switch for **C**holesterol Elevation on **K**ivexa **E**valuation **T**rial

A Phase 4, Open Label, Randomized, Controlled Study to Assess the Effect on Lipid Profile of Switching from a Stable HAART Regimen of fixed dose Abacavir/Lamivudine (Kivexa) Plus Efavirenz, to Once Daily Atripla in Adult HIV-1 Infected Subjects With Raised Cholesterol

Investigators: Multicenter

Study Centers: Subjects were enrolled at 17 centers in the United Kingdom.

Publications:

Orkin C, Moyle G, Fisher M, Wang H, Ewan J. Switching from Kivexa [KVX] ABC/3TC + efavirenz [EFV] to Atripla [ATR] (EFV/FTC/TDF) reduces cholesterol in hypercholesterolemic subjects: preliminary results of a 24-week randomized study [Abstract O10]. HIV Med 2010;11 (Suppl. 1):1-119.

Orkin C, Moyle G, Fisher M, Wang H, Ewan J. Switching from Kivexa [KVX] (ABC/3TC) + Efavirenz [EFV] to Atripla [ATR] (EFV/FTC/TDF) Reduces Cholesterol in Hypercholesterolaemic Subjects: Primary Endpoint Results of a 24-Week Randomised Study [Abstract No. 0417] [Oral Presentation]. Second Joint Conference of the British HIV Association (BHIVA) with the British Association for Sexual Health and HIV (BASHH); 2010 April 20–23; Manchester, UK.

Study Period:

27 March 2008 (first subject screened)
12 January 2010 (last subject observation)

Phase of Development: Phase 4

Objectives:

The primary objective of this study was as follows:

- To determine if switching from a stable highly active antiretroviral therapy (HAART) regimen of Kivexa (KVX) + efavirenz (EFV) to once-daily Atripla (ATR) leads to a reduction in fasting total cholesterol at 12 weeks.

The secondary objectives of this study were as follows:

- Evaluation of fasting metabolic parameters (e.g., low-density lipoprotein [LDL], high-density lipoprotein [HDL], non-HDL cholesterol, triglycerides, and cholesterol ratios).
- Evaluation of efficacy and safety by assessing adverse events (AEs), clinical laboratory tests, physical examinations, and vital signs at every visit.
- Evaluation of changes in the 10-year risk factor for coronary heart disease (CHD) outcomes.

Methodology: This was a Phase 4, open-label, randomized, multicenter, controlled study to assess the effect on lipid profile of switching from a stable HAART regimen of KVX+EFV to ATR in adult human immunodeficiency virus type 1 (HIV-1) infected subjects with raised cholesterol.

Subjects were randomized 1:1 to either switch to ATR (Group 1) or remain on KVX+EFV (Group 2) at baseline. Concomitant lipid regulating therapy was permitted but subjects had to be on a stable lipid-regulating regimen for ≥ 12 weeks prior to screening and had to remain on that regimen throughout the treatment phase of the study. At Week 12, subjects in Group 2 (continuation of KVX+EFV) switched to ATR (the Delayed Switch to ATR group). Treatment continued through Week 24.

Postbaseline assessments were completed during visits at Weeks 4, 12, 16, and 24.

Number of Subjects (Planned and Analyzed):
Planned: 180
Analyzed (by analysis set and treatment group):

Intent-to-treat (ITT) and treated analysis sets: 157 (ATR 79, KVX+EFV 78; Delayed Switch to ATR 73, All ATR 152)

Modified ITT (MITT) analysis set: 153 (ATR 79, KVX+EFV 74; Delayed Switch to ATR 69, All ATR 148)

Diagnosis and Main Criteria for Inclusion: HIV-1 infected adults, virologically suppressed (HIV-1 ribonucleic acid [RNA] < 50 copies/mL at screening and for ≥ 12 weeks prior to screening) on a stable HAART regimen of KVX+EFV for ≥ 24 weeks prior to screening, with documented confirmed raised total cholesterol ≥ 5.2 mmol/L (≥ 200 mg/dL) for the last 2 consecutive tests (at least 4 weeks apart), and with fasted total cholesterol ≥ 5.2 mmol/L (≥ 200 mg/dL) at screening.

Duration of Treatment: 24 weeks

Test Product, Dose, Mode of Administration, and Batch No.: ATR (efavirenz 600 mg/emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg), 1 tablet, orally, once daily. It was recommended that ATR tablets were taken with water, on an empty stomach, at bedtime.

ATR Lot Numbers: AA510B2, AA0602B1, AA0603B1, AA0603B1-A

Reference Therapy, Dose, Mode of Administration, and Batch No.: Kivexa (abacavir [as sulfate] 600 mg/lamivudine 300 mg) plus Sustiva (efavirenz 600 mg), orally, once daily (commercial supply - batch numbers not collected).

Criteria for Evaluation:

Efficacy: Metabolic endpoints were assessed by monitoring fasting lipid profiles. Virologic efficacy was assessed by monitoring plasma HIV-1 RNA levels. Immunologic efficacy was assessed by monitoring cluster determinant 4 (CD4) and CD8 cell counts and percentages.

Safety: Safety was assessed by monitoring AEs, clinical laboratory tests, and physical examinations including vital signs and body weight. Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA), Version 12.1.

Outcomes Research: Changes in the 10-year risk for CHD outcomes were assessed using Framingham risk score. Treatment adherence was assessed using pill counts, a visual analog scale (VAS), and questions regarding missed doses. Treatment acceptability was assessed using the Preference of Medicine (POM) questionnaire; the Treatment Satisfaction and Symptoms (TSS) questionnaire; the HAART Intrusiveness Scale (m-HIS); and the Perceived Ease of Regimen for Condition (PERC) questionnaire.

Statistical Methods:

Efficacy: The MITT analysis set was used for analyses of fasting lipid parameters. It included subjects who were randomized and received at least 1 dose of study drug and had no major protocol violation (defined as fasting total cholesterol < 4.2 mmol/L at baseline). The ITT analysis set was used for analyses of HIV-1 RNA, CD4, and CD8 endpoints. It included subjects who were randomized and received at least 1 dose of study drug. Subjects were grouped by treatment assigned.

The primary endpoint was the change from baseline in fasting total cholesterol at Week 12. The primary analysis of the primary endpoint was based on the MITT analysis set and used last postbaseline observation carried forward [LOCF] methodology. Changes from baseline were analyzed within each treatment group using a Wilcoxon signed rank test, and differences between ATR and KVX+EFV groups were analyzed using a Wilcoxon rank sum test. Confidence intervals (CIs, 95%) for the differences in changes between the 2 groups (ATR minus KVX+EFV) were constructed based on normal approximation. A secondary analysis of the primary endpoint was based on observed data (i.e., no imputation for missing). Sensitivity analyses were conducted for the primary endpoint using LOCF methodology in the MITT analysis excluding data for subjects who started or modified lipid-lowering therapy during the study, and using observed data in the treated analysis set. Other fasting lipid parameters were analyzed in a similar manner to the primary endpoint.

The proportions of subjects with plasma HIV-1 RNA < 50, < 200, and < 400 copies/mL at Week 12 were compared between ATR and KVX+EFV groups using Fisher exact test. The exact 95% CIs were estimated based on unconditional exact methods using inverted 2 1-sided tests with the standardized statistic. The p-values and 95% CIs were based on 2 response categories: success (HIV-1 RNA less than the specified level) and failure (HIV-1 RNA equal or above the specified level). The following methods were used for treating missing values in calculating proportions: missing = failure, LOCF, and missing = excluded.

For CD4 and CD8 cell counts and percentages, absolute values and change from baseline were summarized by visit. Differences between ATR and KVX+EFV groups in change from baseline were tested using the Wilcoxon rank sum test at Week 12.

Safety: All safety analyses were based on the treated analysis set and were summarized using descriptive statistics by treatment group according to the study drug received. Data collected up to the date of last dose of study drug plus 30 days were included in safety analyses.

Outcomes Research: The observed values and changes from baseline at Week 12 in the 10-year risk for CHD outcomes were summarized by treatment group using the treated analysis set. The change from baseline was tested using the Wilcoxon signed rank test within treatment group and was compared between ATR and KVX+EFV groups using the Wilcoxon rank sum test at Week 12. Other outcomes research endpoints were summarized; changes from baseline were summarized and differences between ATR and KVX+EFV groups were performed using appropriate statistical tests.

SUMMARY – RESULTS:

A total of 157 subjects received study drug in the randomized phase; 79 subjects received ATR and 78 subjects continued KVX+EFV. Seventy-three subjects switched to ATR from KVX+EFV at Week 12. Of the 157 subjects who received study drug, 143 subjects completed 24 weeks of study treatment and 14 subjects discontinued study drug prematurely. Reasons for discontinuation were AE (6 subjects), protocol violation (3 subjects), pregnancy (2 subjects), withdrawal of consent (2 subjects), and investigator's decision (1 subject).

There were no clinically relevant differences in demographic and baseline characteristics between the randomized ATR and KVX+EFV groups. Subjects were predominantly male (79.6%) and white (59.2%) with a mean age of 43.8 years (range 28 to 73 years). Mean (standard deviation, SD) fasting total cholesterol at baseline was 6.46 (0.929) mmol/L. Subjects had been receiving Kivexa for a mean (SD) of 2.2 (1.24) years at study baseline.

Efficacy Results: In the primary analysis (LOCF, MITT analysis set) of fasting total cholesterol, the difference between groups (ATR minus KVX+EFV) for the change from baseline to Week 12 was −0.74 mmol/L (95% CI −1.00, −0.47); the difference was statistically significant ($p < 0.001$). In the ATR group, there was a statistically significant decrease from baseline to Week 12 in fasting total cholesterol (median change −0.86 mmol/L, $p < 0.001$), while in the KVX+EFV group there was no statistically significant change from baseline to Week 12 in fasting total cholesterol (median change 0.01 mmol/L, $p = 0.45$). Results were similar to those for the primary analysis when assessed according to the secondary analysis based on observed data, for the sensitivity analysis of the MITT set excluding 3 subjects in the ATR group who started/modified lipid-lowering medication during the study, and for the sensitivity analysis of observed data in the treated analysis set. A statistically significant decrease from ATR baseline to ATR Week 12 in fasting total cholesterol was also seen in the Delayed Switch to ATR group (median change −0.73 mmol/L, $p < 0.001$).

In the ATR group, the decreases from baseline in fasting total cholesterol seen at Week 12 were maintained at Week 24 (treated analysis set, median change from baseline −0.71 mmol/L, $p < 0.001$).

Results of analyses of secondary fasting lipid parameters were similar to those for fasting total cholesterol. For each parameter (LOCF, MITT analysis set), there was a statistically significant decrease from baseline to Week 12 in the ATR group while there was no statistically significant change from baseline to Week 12 in the KVX+EFV group. Differences between groups (mean [95% CI]) for the changes from baseline to Week 12 in secondary fasting lipid parameters were statistically significant ($p < 0.001$) for LDL cholesterol (−0.47 mmol/L [−0.70, −0.25]), HDL cholesterol (−0.15 mmol/L [−0.21, −0.08]), triglycerides (−0.43 mmol/L [−0.75, −0.11]), and non-HDL cholesterol (−0.56 mmol/L [−0.80, −0.31]), but not for total/HDL cholesterol ratio. Results in the Delayed Switch to ATR group were similar to those in the ATR group; however, the decrease from ATR baseline to ATR Week 12 in triglycerides was not statistically significant (median change −0.13 mmol/L, $p = 0.063$).

Virologic suppression and immunologic control were maintained in subjects who switched therapy to ATR or who remained on KVX+EFV. No subjects met protocol-defined criteria for virologic failure (2 consecutive HIV-1 RNA values ≥ 400 copies/mL within 2 to 4 weeks).

Safety Results: Description of safety data is focused on the All ATR group that provides an overview of the safety profile of ATR in the study as a whole. Separate description is provided for the KVX+EFV group. Comparisons of AE data between ATR and KVX+EFV groups are not considered appropriate since exposure to study drug is not balanced in the respective groups. In accordance with the study design, the median duration of treatment was 24.0 weeks in the ATR group, 12.0 weeks in the KVX+EFV group, 12.0 weeks in the Delayed Switch to ATR group, and 15.5 weeks in the All ATR group (planned duration of treatment: 24 weeks for the ATR group and 12 weeks for the KVX+EFV and Delayed Switch to ATR groups). When appropriate (when comparisons were planned in the protocol/analysis plan), differences between the randomized ATR and KVX+EFV groups are provided.

Atripla was adequately tolerated in this study. No subjects died. Serious AEs (SAEs) were reported for 1 subject in the All ATR group (ATR subgroup) and 1 subject in the KVX+EFV group; no SAE was considered related to study drug by the investigator. Six subjects discontinued study drug due to an AE, including 5 subjects in the All ATR group (3 ATR, 2 Delayed Switch to ATR) and 1 subject in the KVX+EFV group. At least 1 AE was reported for 71.7% of subjects (109 subjects [62 ATR, 47 Delayed Switch to ATR]) in the All ATR group and 51.3% of subjects (40 subjects) in the KVX+EFV group. In the All ATR group, AEs were most frequently reported in the gastrointestinal disorders (26.3%, 40 subjects), nervous system disorders (26.3%, 40 subjects), and infections and infestations (25.0%, 38 subjects) system organ classes (SOCs). In the KVX+EFV group, AEs were most frequently reported in the infections and infestations SOC (24.4%, 19 subjects).

In the All ATR group, the most frequently reported AEs were headache (15.8%, 24 subjects) and diarrhea (9.9%, 15 subjects). In the KVX+EFV group, the most frequently reported AEs were lower respiratory tract infection (5.1%, 4 subjects) and nasopharyngitis (3.8%, 3 subjects).

Adverse events considered related to study drug were reported for 30.3% of subjects (46 subjects [25 ATR, 21 Delayed Switch to ATR]) in the All ATR group and for 3.8% of subjects (3 subjects) in the KVX+EFV group. In the All ATR group, the most frequently reported AEs considered related to study drug were abnormal dreams (12 subjects [7 ATR, 5 Delayed Switch to ATR]) and fatigue (8 subjects [2 ATR, 6 Delayed Switch to ATR]). No AE considered related to study drug was reported for more than 1 subject in the KVX+EFV group.

Grade 3 or 4 AEs were reported for 2 subjects in the All ATR group (ATR subgroup) and for 1 subject in the KVX+EFV group; no Grade 3 or 4 AEs were considered related to study drug.

Pollakiuria, reported for 1 subject in the All ATR group (ATR subgroup), was the only AE reported in the renal and urinary disorders SOC. The event was nonserious, Grade 2 in severity, and was not considered related to study drug by the investigator.

No fractures or other bone events, AEs of skin hyperpigmentation, or Grade 3 or 4 skin events were reported.

Hepatic steatosis (Grade 1) was reported as an AE for 1 subject in the All ATR group (ATR subgroup). Hepatic enzyme increased (Grade 2) was reported as an AE for 1 subject in the All ATR group. Neither of these AEs was considered related to study drug by an investigator. No high-grade (Grade 3 or 4) hepatic enzyme elevations were reported.

In the upper respiratory tract infections high-level term (HLT), AEs were reported for 17 subjects in the All ATR group (13 ATR, 4 Delayed Switch to ATR) and for 5 subjects in the KVX+EFV group. In the upper respiratory tract signs and symptoms HLT, AEs were reported for 1 subject in the All ATR group (Delayed Switch to ATR subgroup) and for 2 subjects in the KVX+EFV group. In addition, viral upper respiratory tract infection was reported as an AE for 3 subjects in the All ATR group (2 ATR, 1 Delayed Switch to ATR). All AEs related to upper respiratory tract infections were nonserious, mild or moderate in severity, and were not considered related to study drug by investigators.

Treatment-emergent AEs in the nervous system disorders SOC were reported for 40 subjects in the All ATR group (23 ATR, 17 Delayed Switch to ATR) and for 2 subjects in the KVX+EFV group. Nervous system AEs considered related to study drug were reported for 12 subjects in the All ATR group (5 ATR, 7 Delayed Switch to ATR). The most frequently reported nervous system AEs considered related to study drug were dizziness (5 subjects [2 ATR, 3 Delayed Switch to ATR]) and headache (5 subjects [3 ATR, 2 Delayed Switch to ATR]). All nervous system AEs were nonserious and Grade 1 or Grade 2 in severity. No action was taken with study drug in relation to any nervous system AE.

Treatment-emergent AEs in the psychiatric disorders SOC were reported for 31 subjects in the All ATR group (18 ATR, 13 Delayed Switch to ATR) and for 6 subjects in the KVX+EFV group. Psychiatric disorder AEs considered related to study drug were reported for 24 subjects in the All ATR group (16 ATR, 8 Delayed Switch to ATR) and for 2 subjects in the KVX+EFV group. In the All ATR group, the most frequently reported psychiatric disorder AEs considered related to study drug were abnormal dreams (12 subjects [7 ATR, 5 Delayed Switch to ATR]) and sleep disorder (6 subjects [4 ATR, 2 Delayed Switch to ATR]). In the KVX+EFV group, psychiatric disorder AEs considered related to study drug were nightmare and depression (each reported for 1 subject). An event of suicide attempt was reported as an SAE for 1 subject in the KVX+EFV group; this was the only psychiatric disorder AE reported that was Grade 3 or 4 in severity (Grade 4). Psychiatric disorder AEs resulted in study drug discontinuation for 3 subjects in the All ATR group (2 ATR, 1 Delayed Switch to ATR; AEs of anxiety, insomnia, and sleep disorder each reported for 1 subject) and for 1 subject in the KVX+EFV group (depression). Events of sleep disorder, depression, and insomnia were considered related to study drug by investigators.

There were no clinically relevant changes from baseline in median values for hematology and (nonlipid) chemistry parameters during the study (including renal parameters: serum creatinine, serum phosphorus, estimated creatinine clearance [using the Cockcroft-Gault method], and estimated glomerular filtration rate [using the Modification of Diet in Renal Disease formula]). Treatment-emergent Grade 3 laboratory abnormalities were reported for 5 subjects in the All ATR group (3 ATR, 2 Delayed Switch to ATR) and for 6 subjects in the KVX+EFV group. Grade 3 treatment-emergent laboratory abnormalities reported for more than 1 subject were for cholesterol (2 subjects in the All ATR group [1 ATR, 1 Delayed Switch to ATR] and 4 subjects in the KVX+EFV group) and triglycerides (1 subject in the All ATR group [ATR subgroup] and 2 subjects in the KVX+EFV group). Grade 4 glycosuria was reported for 1 subject in the All ATR group (ATR subgroup).

There were no clinically relevant changes from baseline in body weight, body mass index, or vital signs.

Outcomes Research Results: Changes from baseline to Week 12 in the 10-year risk for CHD outcomes were not statistically significant within any treatment group or between randomized treatment groups; however, there was a slight decrease in the 10-year risk for CHD outcomes in the ATR group compared to the KVX+EFV group, evident in a lower first quartile and a larger mean reduction from baseline in the ATR group compared to the KVX+EFV group. Median (interquartile range, IQR) changes from baseline at Week 12 were 0.0 (–3.0, 0.0) in the ATR group and 0.0 (–1.0, 0.0) in the KVX+EFV group. Mean (SD) changes from baseline at Week 12 were –0.6 (3.85) in the ATR group and –0.1 (2.69) in the KVX+EFV group.

Adherence to ATR was high in this study, whether assessed based on pill counts (median 100%), VAS assessments (median ≥ 98.0%), or self-reported adherence based on the number of missed doses of study drug (≥ 93.2% of subjects with < 2 days missed in the last 30 days).

Results from subject self-assessments of treatment satisfaction and symptoms showed benefits in taking ATR, as demonstrated by statistically significant differences between the ATR and KVX+EFV groups at Week 12 for satisfaction with convenience and simplicity (very satisfied: 90.7% ATR, 76.7% KVX+EFV), and the ability to tolerate the regimen (very satisfied: 81.1% ATR, 61.6% KVX+EFV). In addition, there was a statistically significant difference between groups in the proportion of subjects who were bothered by side effects of the regimen at Week 12 (bothered: 39.2% ATR, 61.6% KVX+EFV). There were no significant differences between groups in satisfaction with the ability of the regimen to control HIV, or with general satisfaction of the regimen. There were sustained reductions (improvement) in satisfaction with their ability to tolerate the regimen for subjects who received 24 weeks of treatment with ATR. There were statistically significant improvements in a number of treatment symptoms from baseline to Week 12 in the ATR group, with accompanying differences between the ATR and KVX+EFV group; however, improvements from baseline to Week 24 were seen only for symptoms of difficulty in falling or staying asleep (with symptom: 53.4% at baseline, 45.3% at Week 12, and 31.4% at Week 24).

HIV-1 infected subjects in this study considered ATR an easier regimen to follow than their previous HIV-1 regimen, as assessed using the PERC survey. In the All ATR group, the proportion of subjects who considered their regimen very easy to take increased from 78.9% at baseline to 90.1% at Week 12 ($p = 0.004$). There were increases in the proportions of subjects who considered their regimen very easy to take in the ATR (from 75.3% at baseline to 90.5% at Week 12, $p = 0.002$) and Delayed Switch to ATR subgroups (from 82.9% at ATR baseline to 89.6% at ATR Week 12, $p = 0.37$). The difference between ATR and KVX+EFV groups at Week 12 was not statistically significant (very easy: 90.5% ATR vs 80.3% KVX+EFV, $p = 0.10$). At Week 24, 85.5% of subjects in the ATR subgroup consider ATR a very easy regimen to take ($p = 0.035$).

The majority of subjects who received Atripla preferred it to their previous medication, as assessed using the POM questionnaire. In the ATR group, 54.5% of subjects considered ATR to be much better than their previous regimen, and 14.3% of subjects considered ATR to be slightly better than their previous regimen ($p < 0.001$). In the Delayed Switch to ATR group, 51.4% of subjects considered ATR to be much better than their previous regimen, and 16.7% of subjects considered ATR to be slightly better than their previous regimen ($p < 0.001$). No subjects receiving ATR considered it to be much worse than their previous regimen.

Study medication acceptability was good at baseline, as assessed by overall m-HIS index scores, and improved during the study for subjects who received ATR. In the All ATR group, there was a statistically significant reduction (improvement) in overall m-HIS index score from baseline to Week 12 (median [IQR] change 0.0 [−0.2, 0.0]; mean [SD] change −0.1 [0.44], $p < 0.001$). The changes in the ATR and Delayed Switch to ATR subgroups were consistent with those in the All ATR group; however, the change from baseline to Week 12 was not statistically significant in the ATR subgroup. The difference between ATR and KVX+EFV groups at Week 12 was statistically significant (median [IQR] changes were 0.0 [−0.1, 0.0] in the ATR group and 0.0 [0.0, 0.1] in the KVX+EFV group; mean [SD] changes were −0.1 [0.52] in the ATR group and 0.0 [0.38] in the KVX+EFV group; $p = 0.037$). In the ATR group, there was a statistically significant reduction (improvement) in overall m-HIS index score from baseline to Week 24 (median [IQR] change 0.0 [−0.2, 0.0]; mean [SD] change −0.1 [0.39], $p < 0.001$).

CONCLUSIONS: The conclusions of Study GS-UK-177-0109 are as follows:

- In virologically suppressed HIV-1 infected subjects with raised cholesterol, switching to ATR from KVX+EFV led to a reduction in fasting total cholesterol and other fasting lipid parameters (LDL cholesterol, HDL cholesterol, triglycerides, non-HDL cholesterol, and total/HDL cholesterol ratio). For all fasting lipid parameters, statistically significant decreases from baseline were seen at Week 12 in the ATR group; differences between ATR and KVX+EFV groups were statistically significant for the changes from baseline to Week 12 in fasting total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, and non-HDL cholesterol. Similar decreases from baseline were seen for subjects who switched to ATR at Week 12. Decreases seen at Week 12 were maintained for subjects who received 24 weeks of treatment with ATR.
- HIV-1 infected subjects who switched to ATR from KVX+EFV maintained virologic and immunologic control.
- Changes from baseline to Week 12 in the 10-year risk for CHD outcomes were not statistically significant within any treatment group or between randomized treatment groups.