1.0 Abstract

Title

Use of KALETRA® tablets in adult HIV-infected patients:

Data from the multicenter Star/Stella cohort

Keywords

HIV, ART-naïve, treatment experienced, lopinavir/ritonavir, LPV/r, Star, Stella, Star/Stella

Rationale and Background

Star/Stella was a non-interventional prospective open cohort study including ART-naïve and treatment-experienced male and female HIV-1-infected patients initiated on LPV/r based ART in routine clinical care between 2006 and 2014. Patients were observed for a period of 3 years. Since 2006 the tablet formulation has been available in routine clinical care enabling a reduced pill count in comparison to the soft gel capsules, elimination of food effects and storage without refrigeration. Eligibility for Star/Stella was not restricted concerning the use of additional antiretrovirals. Assignment of a patient to a particular cART was part of routine clinical care and was independent from the conduct of Star/Stella.

Research Question and Objectives

The goal of this study was to observe and collect data on the usage, dosing, tolerability, and effectiveness of KALETRA® tablets when used in accordance with the terms of the marketing authorization. In the Star/Stella cohort, it was of specific interest to evaluate the effectiveness, persistence, and safety of KALETRA® tablet and the quality of life of the patients when used in daily clinical routine in either ART-naïve patients or in patients switching from other PIs or other non-PI based regimens.

Study Design:

Prospective, multicenter, observational, non-interventional open cohort study

Setting:

Routine clinical practice in Germany, Belgium, and Israel

Subjects and Study Size, Including Dropouts

The study population consisted of ART-naïve, PI-naïve and PI-experienced HIV-infected patients initiated on LPV/r based combination regimens. By the end of the recruitment phase, 3039 eligible patients were included.

Variables and Data Sources

The electronic case report forms included demographic data, HIV-related variables such as the time since first HIV diagnosis, HIV subtype, past and current antiretroviral therapy, reasons for switch to new LPV/r based ART, reasons for discontinuation as well as effectiveness and safety laboratory parameters (HIV-1 RNA, CD4 cell count, and specific serum chemistry parameters [which were documented in a small subgroup of centres]. Clinical variables included height, weight, comorbidities and the prevalence of specific clinical and laboratory adverse events (AEs; including WHO grades) at the time of the patients' visits. Only data available in the patient files which were assessed during the usual clinical management of patients were documented. The study protocol did not mandate visits or laboratory measurements beyond those performed in clinical routine. All patient data entered in the electronic case report form were pseudonymised.

Results

The full analysis set consisted of 3039 adult patients, 20% of female gender and 66% of Caucasian ethnicity. Median age was 40 years (interquartile range, IQR 33 – 47). In 25% of patients, HIV associated diseases were documented at baseline. Chronic hepatitis C and B were present in 9% and 4% of patients, respectively.

The majority of patients (77%) were ART-naïve prior to initiation of LPV/r based ART, 20% were ART-experienced, but PI-naïve, and 3.0% were ART-experienced with one protease inhibitor (other than LPV/r). The most common antiretroviral combination partners of LPV/r were TDF/FTC (68%), 3TC/ABC (13%) and 3TC/AZT (7%).

In ART-experienced patients, the main reasons for switch to LPV/r based ART (in > 20% of patients; multiple responses permitted) were failure of previous ART, adverse events, re-start of ART after treatment interruption, patient's wish and drug resistance.

Baseline HIV-1 RNA levels were > 100,000 copies/mL in 44% of patients, (51% of ART-naïve, 20% of PI-naïve, 17% of PI-experienced patients). Of ART-experienced patients, 20% were on suppressive ART at study entry. Median baseline CD4 cell count was 240/µl (224/µl in ART-naïve and between 300/µl and 350/µl in the ART-experienced subgroups).

After 48 weeks, 78% of the patients were still on LPV/r based ART, after 96 and 144 weeks 64% and 56% were still on LPV/r (Kaplan-Meier estimates). The main reasons for discontinuation were adverse advents (17% of the cohort), patient's wish (7%), therapy simplification (6%), and resistance/virologic failure (2%). The (restricted) mean time to discontinuation was 159 weeks.

In modified ITT-analysis, HIV-1 RNA level was < 400 (< 50) copies/mL in 69% (58%) of patients at Week 48, in 52% (46%) of patients at Week 96, and in 46% (41%) of patients at Week 144, respectively. The (restricted) mean time to virologic failure censoring discontinuations at HIV-1 RNA levels < 50 copies/mL was 175 weeks.

In ART-naïve patients, the median CD4 cell increases from baseline were +217/µL, +279/µL and +317/µL at Weeks 48, 96 and 144, respectively. In ART-experienced PI-naïve patients, median CD4 cell changes were +120/µL, +175/µL, and +224/µL,

respectively; in PI-experienced patients, median changes were +122/µL, +208/µL, and +171/µL, respectively.

Regarding the whole study period from Weeks 0 to Week 144, the most common adverse events (in > 5% of patients) documented as being present in a patient at least once were diarrhea (in 33% of patients), hypercholesterolemia (16%), hypertriglyceridemia (14%), nausea (12%), elevated gamma-GT (9%), mood disorders (9%), fatigue (9%), abdominal pain (8%), elevated ALT/SGPT (8%), elevated AST/GOT (7%), hyperglycemia (6%) and headache (5%).

The total baseline ASDM score as indicator for quality of life (QoL; high score = high distress; with minimum and maximum possible scores of 0 and 88, respectively) was 15.0 (IQR 6.0 – 29.3) (ART-naïve patients 15.0, PI-naïve 13.0, PI-experienced 13.5). Overall median changes from baseline in ASDM scores using the LOCF method were 0.0 (IQR: –8.0 – 0.0), 0.0 (–9.0 – 0.0), and –0.4 (–9.0 – 0.0) at Weeks 48, 96 and 144, respectively. Of note, PI-experienced patients showed an improvement in the ASDM score in at least 50% of patients with median changes from baseline of –2.5 (–9.0 – 0.0), –1.5 (–10.0 – 0.0), and –1.5 (–10.0 – 0.0) at Weeks 48, 96 and 144, respectively. In the *as-treated* analyses, changes in the ASDM scores were more pronounced in all three groups with median changes between –1.0 and –10.0 across groups and Week 48, 96, and 144 visits, reflecting an improvement in symptom distress in the majority of patients remaining on LPV/r based ART.

Discussion

This large cohort of patients reflects the management of HIV-1 infected patients initiated on LPV/r based first- or further-line ART in routine clinical care. Discontinuation of LPV/r based ART prior to the end of the planned observation period of 3 years was mainly triggered by adverse events and reasons other than virologic failure.

Marketing Authorisation Holder(s)

AbbVie Ltd. (formerly Abbott)

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