

1.0 Abstract

Title

Real-Life Effectiveness of the Kaletra Adherence Support Assistance (KASA) Program: A Prospective Observational Cohort Study (KASA PMOS)

Keywords

Kaletra, real-life, adherence, effectiveness, safety

Rationale and Background

Patients treated for human immunodeficiency virus (HIV) sometimes require adaptation of their life-style to take several medications with very strict regimens. While adherence to highly-active antiretroviral therapy (HAART) regimens is essential to achieve and maintain long-term virological suppression, suboptimal adherence is often observed due to the complexity of the treatment regimens as well as their associated short- and long-term toxicities. The Kaletra Adherence Support Assistance (KASA) Program is a customized support network that has been offered to patients treated with lopinavir / ritonavir (LPV/r; Kaletra[®]). KASA offers individual counseling with an HIV experienced nurse who assists patients with various aspects of their therapy including life-style changes, emotional stress, and adverse events. Patients enrolled in KASA may also have access to various healthcare professionals (dietician, social worker, psychologist, etc.) or may be offered other types of support (transportation, exercise, etc.), which may help improve their quality of life as well as adherence or compliance while taking LPV/r. This observational study was developed to assess the effectiveness of the KASA support program on improving or maintaining treatment adherence in HIV-positive patients who are receiving treatment with LPV/r in real-life conditions.

Research Question and Objectives

The overall purpose of the study was to describe the real-life adherence, effectiveness and safety of the KASA support program in HIV-positive patients who are receiving treatment with LPV/r in Canada.

The primary objective of this study was to assess the real-life effectiveness of KASA in improving or maintaining adherence of HIV-positive patients treated with LPV/r at six months as measured by the Adherence Self-Efficacy Scale (ASES) questionnaire.

Secondary objectives included the assessment of: the real-life effectiveness of KASA in improving or maintaining adherence of HIV-positive patients treated with LPV/r at 12 months; the effect of KASA on patients' quality of life (Health Status Assessment questionnaire – HSA), perception of stress (Perceived Stress Scale – PSS), psychological well-being (Centre for Epidemiologic Studies – Depression scale – CES-D), coping self-efficacy (Coping Self-Efficacy scale - CSE), as well as health care resource utilization (HRU) and clinical status (measured CD4+ cells counts and viral load) at 6 and 12 months. In addition, the study surveyed health care providers' satisfaction with the KASA program.

Study Design

This was a 12-month, multi-center, Canadian Post Marketing Observational Study utilizing a prospective single cohort design. All treatments including participation in the KASA program were according to the decision of the treating physician and the patients and were not affected in any way by their decision to participate in the study. Follow-up was for 12 months at an interval of every six months.

Setting

Patients were recruited from the practices of 8 physicians in Canada between 29 June 2012 and 06 August 2015.

Subjects and Study Size, Including Dropouts

One-hundred seventy-three (n = 173) patients were enrolled in the study. All 173 patients received at least 1 dose of LPV/r and were, therefore, included in the ITT population. Of the 173 patients, 26 patients started LPV/r the same month as their baseline visit (new LPV/r starts). The overall mean follow-up duration was 11.3 months with 142 (82.5%) and 109 (63.0%) patients completing the month 6 and month 12 visits, respectively.

Overall, 66 (38.1%) patients discontinued the study, 19.2% of LPV/r starts (5/26) vs. 41.5% of LPV/r stable patients (61/147), with 31 (LPV/r starts n=3 vs. LPV/r stable n=28), 33 (LPV/r starts n=2 vs. LPV/r stable n=31), and 2 (LPV/r starts n=0 vs. LPV/r stable n=2) patients discontinuing before month 6, between months 6 and 12, and at month 12, respectively. The reasons of discontinuation were being no longer on LPV/r [30 (17.3%)], withdrawal of consent [6 (3.5%)], due to adverse event [1 (0.6%)], and other reasons [29 (16.8%)].

Variables and Data Sources

The primary outcome measure was the adherence with LPV/r treatment at month 6, assessed by the ASES questionnaire where adherence was defined as a change in the ASES summative score greater than or equal to zero. Secondary outcome variables included the change in adherence at month 12, and change in patient quality of life (HSA), patient perception of stress (PSS), psychological well-being (CES-D), coping self-efficacy (CSE), and in health resource utilization at months 6 and 12, as well as the healthcare providers' (HCPs) satisfaction with the KASA program at months 6 and 12. The CD4+ cell counts and viral load at each visit were also described.

Results

The 3 mean ASES summative, adherence integration and adherence perseverance scores remained relatively stable from baseline to month 6 and month 12. Using an intent-to-treat (ITT) population, where patients previously discontinuing from the study or lost to follow-up (n=31) were considered as non-adherent but still included in the analysis, the adherence rate at month 6 was 43.3% (68/157, 95% CI: 35.9%, 50.7%); patients not

discontinued from the study or lost to follow-up but with missing information on the absolute change in the ASES summative score (n=16) were excluded from this analysis. In a per-protocol (PP) population, excluding patients previously discontinued or lost to follow-up (n=31) and patients with missing information on the absolute change in the ASES summative score (n=16), the adherence rate at month 6 was 54.0% (68/126, 95% CI: 45.8%, 62.2%). At month 12, the treatment adherence rate was 30.2% (48/159, 95% CI: 23.3%, 37.0%) and 51.6% (48/93, 95% CI: 42.2%, 61.0%) for the ITT and PP populations, respectively. When focusing on the subgroup of patients initiating LPV/r at study enrollment, the adherence rates were higher, specifically 64.0% (16/25, 95% CI: 56.8%, 71.2%) and 60% (12/20, 95% CI: 52.7%, 67.3%) for the ITT population at months 6 and 12, respectively. For the PP population, these rates were 70.0% (14/20, 95% CI: 62.5%, 77.5%) and 60.0% (12/20, 95% CI: 50.8%, 69.2%), respectively.

Overall, the HSA Questionnaire scores remained stable over time. Similarly, the PSS, CES-D, and CSE scores were also generally stable over time, with median absolute changes from baseline of approximately zero. The mean viral load decreased over time from 111.3 copies/mL at baseline to 55.7 copies/mL at month 6, and to 47.2 copies/mL at month 12. The mean CD4+ cell count increased from 547.0 cells/mm³ at baseline to 620.8 cells/mm³ at month 6 and then stabilized.

In terms of health resource utilization, at baseline, the most commonly utilized resource was visits to a doctor's office or clinic (55.5% of patients), followed by visits to a specialist (16.2%), nursing services (12.7%), visits to a psychiatrist, psychologist or counselor (9.2%) and visits to the emergency room (ER) (8.1%). Health utilization rates remained relatively stable over time, with the exception of visits to the ER which decreased over time (baseline vs. month 12: 8.1% vs. 5.5%) and physiotherapist/rehabilitation consultations which increased over time (3.5% vs. 8.3%).

With respect to healthcare provider's satisfaction with the KASA program, where the possible range of scores for each parameter was 0 to 100, scores indicated moderate-to-high satisfaction with the program (mean scores of 74.1 and 73.3 at month 6 and month 12, respectively), benefits regarding HIV medication compliance and adherence (mean

scores of 65.6 and 62.7, respectively) and likelihood that the HCPs would recommend the KASA program in the future (mean scores of 74.7 and 70.0, respectively).

Three patients reported 3 serious adverse events (SAEs) during the study including cardiac disorder, depression, and death. Two of these patients died while the other SAE had an unspecified outcome.

Discussion

Overall, the current study has reported a relatively low patient adherence rate with the treatment. Most patients (85%) enrolled in the study had already been treated with LPV/r for an average of 6 years prior to study entry. When focusing on new LPV/r starts, the adherence rate was higher and similar to what was expected, namely 60% to 70% with a variability of up to $\pm 10\%$ based on the 95% confidence intervals. Despite the low adherence observed, viral counts and CD4+ cell counts remained stable and only 17% discontinued LPV/r during the study, indicating that patients were well controlled.

The present results must be interpreted with caution in consideration of the study's limitations. In the absence of a comparator group, the eventual impact of the KASA program on patient adherence with treatment cannot be properly evaluated. In addition, no information regarding the patients' use of the KASA program was collected in order to assess the association between the extent of use of the program and adherence with LPV/r.

However, despite these limitations, HCP satisfaction with the KASA program was good with HCPs reporting at 6 months that the KASA program was 66% beneficial in helping their patients maintain compliance and adherence with HIV treatments.