1.0 Abstract

Title

Post-Marketing Surveillance of Safety and Efficacy of Kaletra® Tablet in Korean Patients under the "New Drug Re-Examination"

Keywords

HIV-1, AIDS, Kaletra®, Post marketing surveillance

Rationale and Background

This surveillance was conducted in compliance with the Korean regulations on New Drug Re-examination. Typically, limited safety and effectiveness clinical data are included in New Drug Application; therefore additional information should be obtained via long-term surveillance in a broader patient population after marketing approval is granted for a new drug. The purpose of the New Drug Re-examination is to investigate and confirm the type and incidence of newly identified adverse events and any other factors affecting safety and effectiveness of the new drug so that the regulatory authority can manage the marketing approval properly.

Research Question and Objectives

The objective of this surveillance study was to evaluate the following items in relation to the use of Kaletra® in routine medical practice settings:

(1) Serious adverse events and serious adverse drug reaction profile

(2) Unexpected adverse events and unexpected adverse drug reaction profile

(3) Known adverse drug reaction profile

(4) Non-serious adverse drug reaction profile

(5) Other information related to the product safety and effectiveness

Study Design

Non-interventional, prospective, single-country, multi-center, post marketing observational study in Korea.

Setting

The use of Kaletra® (Lopinavir/Ritonavir 200mg/50mg and 100mg/25mg) tablet in routine medical practice settings

Subjects and Study Size, Including Dropouts

According to the regulation, information on 555 or more Korean subjects who were administered Kaletra® (Lopinavir/Ritonavir 200mg/50mg and 100mg/25mg) tablet was collected over a period of up to 6 years.

Variables and Data Sources

Variables and data sources included demographics, HIV-1 diagnosis history, clinical/immunological/virological/laboratory status, other prior and concurrent disease history, prior anti-retroviral (ARV) therapy history, Kaletra®-containing regimen information, concomitant medication information and information on adverse events.

Results

First patient first visit date was 15 Oct 2009 and Last patient last visit date was 31 Oct 2014 during the re-examination report period. The database was locked on 24 Feb 2015 after evaluation of last patient.

Five hundred ninety-five (595) subjects completed protocol-defined follow-up during the study period (28 Apr 2009 ~ 27 Apr 2015); 580 subjects were included in the safety analyses while 15 subjects were excluded from the safety analyses due to violation of the inclusion/exclusion criteria (off-label use) and incorrect usage/dosage.

Of the 580 subjects evaluated, 524 subjects were male (524/580 subjects, 90.34%) and 56 subjects were female (56/580 subjects, 9.66%); age ranged from 18 to 82 years.

Among the female subjects, 9 subjects (9/56 subjects, 16.07%) were pregnant at the start of treatment. The mean (± SD) duration of time since HIV diagnosis was 462.62 days (± 861.29). The proportions of subjects with time since HIV diagnosis of less than one year, between 1 and 3 years, and over 3 years were 71.95%, 9.76%, and 18.29% respectively. 283 subjects (283/580 subjects, 48.79%) had concurrent diseases. 128 subjects (128/580 subjects, 22.07%) had previous ARV treatment which was discontinued before enrollment.

927 adverse events were reported in 363 subjects (363/580 subjects, 62.59%). Among the reported adverse events, 627 adverse drug reactions were reported in 279 subjects (279/580 subjects, 48.10%).

During this regulatory post-marketing observational study period, 88 serious adverse events were reported in 51 subjects (51/580 subjects, 8.79%). Among the reported SAEs, there were 28 serious adverse drug reactions (ADRs) in 19 subjects (19/580 subjects, 3.28%).

232 unexpected adverse events were reported in 139 subjects (139/580 subjects, 23.97%). Among the reported unexpected adverse events, 102 ADRs occurred in 74 subjects (74/580 subjects, 12.76%).

Among the 580 subjects included in the safety evaluation, effectiveness evaluation was performed in 198 subjects whose Week 24 (± 4 weeks) laboratory data were available and who received Kaletra® tablet for at least 24 weeks.

183 subjects (183/198 subjects, 92.42%) achieved viral load less than 400 copies/mL at Week 24. CD4 counts were increased by a mean of 145.47 cells/mm^3 (±144.28) at Week 24 from baseline ($p < 0.0001$). Of the 198 subjects with resistance testing during the initial 24-week observation period, one subject exhibited genotypic resistance to lopinavir. 198 subjects were analyzed for the time to treatment failure (i.e. permanent discontinuation of Kaletra® tablet due to lack of effectiveness). The median value of time to treatment failure was 761 days.

Discussion

This post marketing observational study was a regulatory requirement that assessed the safety and effectiveness of Kaletra® tablet in Korean subjects. 927 adverse events were reported in 363 subjects during this re-examination period. 695 unexpected adverse events (including 525 unexpected ADRs) and 88 serious adverse events (including 28 serious ADRs) were reported in this re-examination period. The safety information from this report is consistent with the safety profile described in the approved label of Kaletra® tablet. The safety and effectiveness of Kaletra® tablet will be continuously monitored.

Marketing Authorisation Holder(s)

AbbVie Korea

Names and Affiliations of Principal Investigators

[redacted]