Long-Acting Cabotegravir + Rilpivirine as Maintenance Therapy: ATLAS Week 48 Results

DA Margolis,1 S Swindells,1 JF Andrade-Villanueva,2 GJ Richmond,3 G Rizzardi,4 A Baumgarten,5 D Del Mar Masiá,6 G Latiff,7 V Pokrovsky,1 JM Mrs,1 JO Huang,1 KJ Hudson,1 KY Smith,1 P Williams,7 WR Spreen1

1ViiV Healthcare, Research Triangle Park, NC, USA; 2University of Nebraska Medical Center, Omaha, NE, USA; 3University of Guadalajara, Guadalajara, Mexico; 4Broward Health Medical Center, Broward Health Imperial Point, Fort Lauderdale, FL, USA; 5Fanwood Medical Center, Fanwood, NJ, USA; 6MIB Infectious Diseases Medical Center, Berlin, Germany; 7Hospital General Universitario de Elche, Alicante, Spain; 8Maxwell Centre, Durban, South Africa; 9Russian Federal Centre of AIDS, Moscow, Russia, 10GaelleSmKsllMe, Mississauga, ON, Canada; 11Janssen Research and Development, Beerse, Belgium

Introduction

In a randomized, phase 2b, open-label study of treatment-naïve adults with HIV-1 infection (LATTE-2), long-acting (LA) cabotegravir (CAB) + rilpivirine (RPV) LA given every 4 or 8 weeks maintained HIV-1 RNA <50 c/mL for >3 years.1 ATLAS is an ongoing phase III, randomized, open-label study designed to establish whether switching to monthly intramuscular (IM) injections of CAB + RPV LA is noninferior to continuing current 3-drug oral antiretroviral therapy (ART) in virologically suppressed adults with HIV-1 infection

Methods

Eligible participants (pts) had HIV-1 RNA <50 c/mL for ≥6 months without virologic failure on oral regimens of at least 2 nucleoside reverse transcriptase inhibitors (NNRTIs) + 1 integrase strand transfer inhibitor (INSTI), non-INSTI (NRTI), or protease inhibitor

Pts were randomly (1:1) assigned to continue their current ART regimen (CAR) or switch to CAB LA + RPV LA

In the CAR arm and CAB LA + RPV LA groups, 308 pts each, HIV RNA levels were <50 c/mL at Week 48. pts receiving oral Cab were given the option to switch to CAB LA + RPV LA by transitioning to the ATLAS weekly dosing regimen

The primary endpoint was HIV-1 RNA <50 c/mL at Week 48 (US Food and Drug Administration snapshot algorithm, 6% noninferiority margin)

Select secondary endpoints included HIV-1 RNA <50 c/mL at Week 48 (~10% noninferiority margin), viral resistance in the setting of confirmed virologic failure (2 consecutive HIV-1 RNA measurements ≥200 c/mL, safety and tolerability, and patient-reported outcomes (HIV Treatment Satisfaction Questionnaire, status version (HTSv2a), and single-item question for patient-reported preference)

Results

Virologic Snapshots for Week 48 in Intention to Treat–Exposed

5 pts (1.6%) receiving CAB + RPV LA and 3 (1%) receiving CAR had HIV RNA 50 c/mL, precluding noninferiority criteria for the primary endpoint (adjusted treatment difference 0.8% [95% confidence interval –1.2 to 2.5] Figure)

Of the pts with HIV-1 RNA 50 c/mL, in the CAB LA + RPV LA and CAR groups, respectively, 4 (0.2%) and 1 (0.3%) had data in the window red below the threshold, 3 (0.1%) and 2 (0.6%) discontinued the study due to lack of efficacy and 0.1% and 0.3% discontinued for another reason while not below the threshold

18 pts (5.8%) in the CAB LA + RPV LA and 11 (3.6%) in the CAR group did not have virologic failure, with the primary reason for study discontinuation due to adverse events (AEs) followed by discontinuation for other reasons

Virologic Failure

3 CAB LA + RPV LA and 4 CAR pts had confirmed virologic failure

1 of 2 pts in the CAB LA + RPV LA group had no “on treatment” resistance mutations; 1 pt had “on treatment” INSTI and NRTI-INSTI associated resistance mutations (B3L8K and N159S) at failure that were not seen in peripheral blood mononuclear cell at baseline

Plasma CAB and RPV concentrations at the time of failure were below the population means within the range for the vast majority of individuals who maintained virologic suppression

In the CAR arm, 99% (1439/1460) of injection site reactions (ISRs) were grade 1/2; most (88%) occurred within 7 days, and 4 pts (1%) withdrew from the study as a result

48/88 (95%) of CAB LA + RPV LA pts with any drug-related adverse event (exceeding ISRs) had a maximum grade 1/2 AE (Table 2)

No cases of drug-related serious AEs, drug hypersensitivity, or drug-induced liver injury were observed in the CAB LA + RPV LA group

Adverse Events

In pts receiving CAB LA + RPV LA, 231 (75%) had injection-site pain

The majority (90%, 1439/1600) of injection-site reactions (ISRs) were grade 1/2; most (88%) occurred within 7 days, and 4 pts (1%) withdrew from the study as a result

48/88 (95%) of CAB LA + RPV LA pts with any drug-related event (excluding ISRs) had a maximum grade 1/2 AE (Table 2)

No cases of drug-related serious AEs, drug hypersensitivity, or drug-induced liver injury were observed in the CAB LA + RPV LA group

Conclusions

Increases from baseline to Week 42 and 44 in treatment satisfaction were significantly greater in pts receiving CAB LA + RPV LA compared with pts receiving CAR (P<0.001)

A single-blind, open-label, safety substudy was performed on 25% of responding pts receiving the CAB LA + RPV LA regimen preferred LA over their previous oral regimen

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