Patient Adherence to Long-Acting CAB and RPV Injections Through 96 Weeks of Maintenance Therapy in LATTE-2

THPEB084

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Introduction

- Cabotegravir (CAB) and rilpivirine (RPV), formulated as long-acting (LA) injectable suspensions, are currently under evaluation as a once-monthly or every-2-month dosing regimen for the treatment of HIV
- Upon authorization, CAB LA + RPV LA will be the first long-acting regimen that can minimize the burden of daily dosing
- Safety and efficacy data from the LATTE-2 study have demonstrated the tolerability and viral suppression of CAB LA + RPV LA in treatment-experienced, HIV-1–infected adults
- Adherence to injection visits and patient-reported outcomes (PRO) data from the LATTE-2 study have been collected in parallel to further explore participants' behavior and experience with the new form of administration

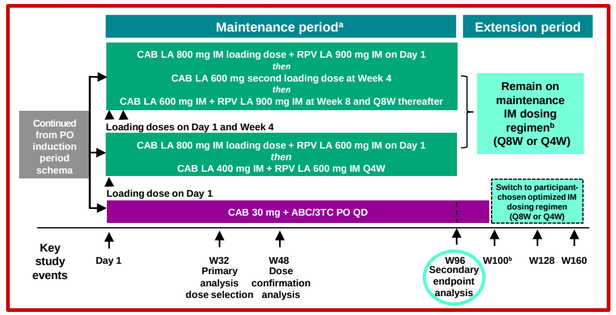
Objective

- To evaluate the adherence to injection visits and patient-reported experience of 230 participants receiving CAB LA + RPV LA in the LATTE-2 study

Methods

- LATTE-2 is a phase IIb, multicenter, open-label study in ART-naive HIV-1–infected adults
- Participants completing the 20-week induction period were randomized 2:2:1 on Day 1 to IM CAB LA + RPV LA every 8 weeks (Q8W) or every 4 weeks (Q4W) or to oral CAB + abacavir/lamivudine (ABC/3TC) in the maintenance period
- The target date for subsequent injection visits was projected from the Day 1 visit date
- Protocol-defined virologic failure (PDVF) is defined as 2 consecutive HIV-1 RNA levels ≥200 c/mL after prior suppression to <200 c/mL

Figure 1. LATTE-2 Study Design



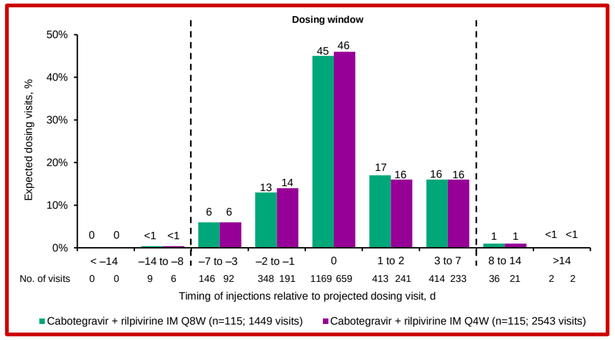
ABC/3TC, abacavir/lamivudine; CAB, cabotegravir; IM, intramuscular; LA, long-acting; PO, oral; QD, once daily; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine. [a]Participants who withdraw after receiving at least 1 IM dose will be followed on study via long-term follow-up period with quarterly visits for 52 weeks. [b]If eligible.

Adherence measures

- Adherence to LA therapy was calculated as the proportion of injection visits occurring within protocol-defined ± 7-day dosing window over the expected visits up to Week 96 (injection visits occurring within the dosing window from date of projected visit divided by number of expected dosing visits up to Week 96 or early withdrawal)
  - Individual CAB and RPV injections administered at the same visit were counted once, and additional unscheduled injections were excluded
- In addition, patient-reported medication adherence was assessed by the HIV Medication Questionnaire (HIVMQ)
  - The HIVMQ included 6 questions asked separately about each LA injectable and oral tablet medication and was used to evaluate acceptability, tolerability, and participant-reported medication adherence
  - Responses are evaluated on an individual-item basis with scores ranging from 0 to 6 (0 refers to "none of the time" or "none at all," and 6 refers to "all of the time" or "a very great deal")

Results

Figure 2. Timeliness of Injections Relative to Date of Projected Dosing Visits*



IM, intramuscular; Q4W, every 4 weeks; Q8W, every 8 weeks.

- 309 participants were enrolled: 91% male, 20% non-white, and 19% HIV-1 RNA >100,000 c/mL; 286 participants were randomized into the maintenance phase, and 258 participants completed the maintenance phase
- Through 96 weeks of maintenance treatment, 94% (108/115) of Q8W and 87% (100/115) of Q4W participants were virologically suppressed (HIV-1 RNA <50 c/mL) compared with 84% (47/56) of oral CAB participants by FDA snapshot
- 78% (179/230) of participants were fully adherent to the prespecified dosing schedule, with 82% (188/230) having no late injection visits and 13% (31/230) having only 1 late injection visit (Table 1)
- Relative to the projected visit date, 3906 (98%) injection visits took place within the ± 7-day window, 15 (<1%) injection visits were >7 days early, and 61 (2%) injection visits were >7 days late (Table 2)
  - 7 missed visits were preplanned and covered by oral CAB/RPV therapy
  - No PDVFs for any participant with an injection visit outside of the ± 7-day window

Table 1. Adherence for Selected Q8W IM and Q4W IM Treatment Arms

% of Participants	Q8W IM (N=115)	Q4W IM (N=115)	IM subtotal (N=230)
Adherence to dosing window (projected visit dates relative to Day 1, ± 7 days)[a]			
<75%	1/115 (<1%)	0/115	1/230 (<1%)
75% to <85%	5/115 (4%)	1/115 (<1%)	6/230 (3%)
85% to <90%	0/115	3/115 (3%)	3/230 (1%)
90% to <95%	16/115 (14%)	10/115 (9%)	26/230 (11%)
95% to ≤99%	0/115	15/115 (13%)	15/230 (7%)
100%	93/115 (81%)	86/115 (75%)	179/230 (78%)
Number of late injections outside of dosing window (>7 days late relative to projected visit dates)			
0	96/115 (83%)	92/115 (80%)	188/230 (82%)
1	17/115 (15%)	14/115 (12%)	31/230 (13%)
2	1/115 (<1%)	5/115 (4%)	6/230 (3%)
3	0/115	3/115 (3%)	3/230 (1%)
≥4	1/115 (<1%)	1/115 (<1%)	2/230 (<1%)

[a]Adherence percentage = number of injection visits occurring within the ± 7-day dosing window from date of projected visit divided by number of expected dosing visits up to Week 96 or early withdrawal (excluding periods of oral bridging).

- By HIVMQ (item D), 96% (104/108) of Q8W and 96% (95/99) of Q4W participants at Week 96 reported they always took/received medication exactly as recommended vs 70% (32/46) of oral CAB participants (with respect to the oral CAB tablet)
- By HIVMQ (item E), 76% (82/108) of Q8W and 68% (67/99) of Q4W participants at Week 96 reported it was never inconvenient or difficult to take/receive medication as recommended vs 39% (18/46) of oral CAB participants (with respect to the oral CAB tablet)
  - Note: Data presented for the HIVMQ, items D and E, for Q8W and Q4W are the mean of the CAB LA and RPV LA item scores for each participant, rounded to the nearest integer

Table 2. Timeliness of Injections Relative to Date of Projected Dosing Visits[a]

% of Injection Visits	Q8W IM (N=115)	Q4W IM (N=115)	IM Subtotal (N=230)
Total number of expected dosing visits	**1449**	**2543**	**3992**
Early out-of-window injection (more than 7 days early relative to projected visit date)	6/1449 (<1%)	9/2543 (<1%)	15/3992 (<1%)
Within-window injection (± 7 days relative to projected visit date)	1416/1449 (98%)	2490/2543 (98%)	3906/3992 (98%)
Late out-of-window injection (more than 7 days late relative to projected visit date)	23/1449 (2%)	38/2543 (2%)	61/3992 (2%)
Missed injection with oral bridging	3/1449 (<1%)	4/2543 (<1%)	7/3992 (<1%)
Unverifiable	1/1449 (<1%)	2/2543 (<1%)	3/3992 (<1%)

[a]Calculated by using actual injection visit date minus projected visit date from Day 1.
Note: Additional unscheduled injections are excluded from all derivations.

Conclusions

- CAB LA + RPV LA injectable regimens, when administered within the prespecified ± 7-day dosing window, demonstrated comparable antiviral activity compared to daily oral CAB + 2 NRTIs through 96 weeks of treatment in virologically suppressed patients
- Patients participating in the LATTE-2 study demonstrated high rates of adherence to injection visits through 96 weeks of follow-up, with 98% of injections occurring within the ± 7-day window
- HIVMQ results demonstrated similar treatment adherence in the 2 groups, with 96% of Q8W and 96% of Q4W patients reporting that they always took their medication exactly as recommended
- These results suggest that LA injectable therapy may provide an alternate, directly observed therapeutic option, which may help improve adherence in some patients

Acknowledgments:

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