# Satisfaction, Tolerability, and Acceptability of Cabotegravir (CAB) + Rilpivirine (RPV) Long-Acting Therapy: LATTE-2 Results

THPEB052

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## Background

While there have been considerable advances in the treatment of HIV in the development of new antiretroviral therapies (ART), chronic HIV infection in adults continues to be characterized by the development of resistant virus, transmission of resistant virus, and issues associated with long-term toxicity of ART.

The current HIV treatment paradigm involves life-long therapy with multiple antiretrovirals. There is a need to develop new agents with improved safety and resistance profiles with different modes of administration for both antiretroviral treatment-naive and treatment-experienced patients.

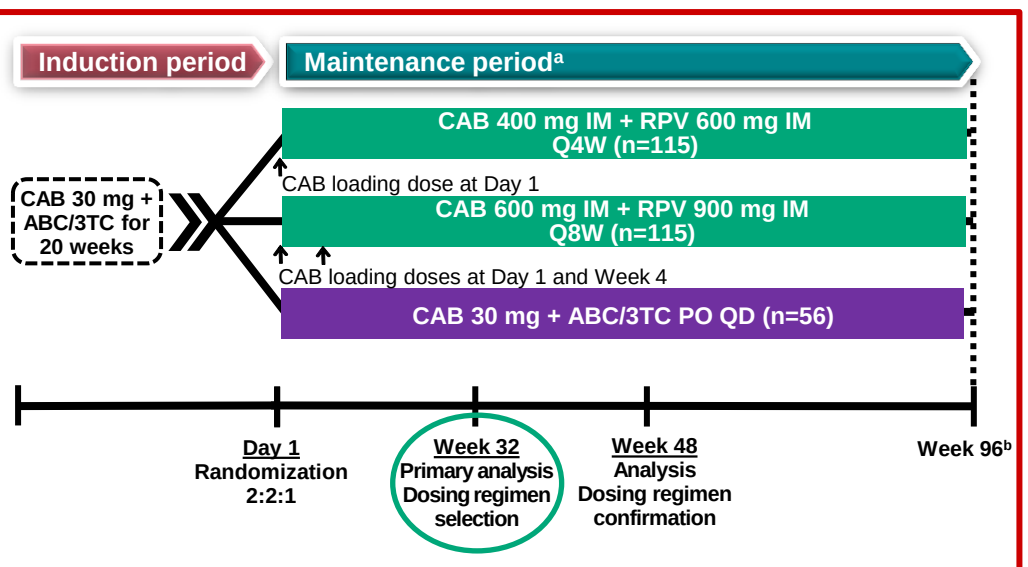
## Methods

- LATTE-2 is a phase IIb, randomized, multicenter, parallel-group, open-label, 3-part study conducted in 309 HIV-1–infected ART-naive adults

### Study periods

- **Part 1:** *Screening period*: 28 days
- **Part 2:** *Induction period*: Eligible subjects were enrolled into the study and began a 20-week induction period of an oral regimen of CAB 30 mg plus ABC/3TC 600/300 mg once daily
- **Part 3:** *Maintenance period*: Subjects with undetectable HIV-1 RNA (<50 c/mL) at Week -4 were randomly assigned on a 2:2:1 basis to an IM regimen of CAB LA 400 mg + RPV LA 600 mg every 4 weeks (Q4W) for 96 weeks
  - IM regimen of CAB LA 600 mg + RPV LA 900 mg every 8 weeks (Q8W) for 96 weeks
  - Continue oral CAB 30 mg plus ABC/3TC for 96 weeks

**Figure 1. LATTE-2 Study Design**




ABC/3TC, abacavir/lamivudine; ALT, alanine aminotransferase; IM, intramuscular; PO, orally; Q4W, every 4 weeks; Q8W, every 8 weeks; QD, once daily; ULN, upper limit of normal. [a]Subjects who withdrew after at least 1 IM dose entered the long-term follow-up period. [b]Subjects can elect to enter LA extension phase beyond Week 96.

### Study objectives

- **Primary objectives**
  - Assess the safety and efficacy of 2-drug ART administered by IM injection compared with 3-drug oral ART (CAB + ABC/3TC)
  - Select a CAB LA + RPV LA dosing schedule for phase III studies
- **Key secondary objectives**
  - Characterize the pharmacokinetics of CAB LA + RPV LA
  - Evaluate the tolerability and acceptability of injectable dosing

### Assessment of acceptability, tolerability, and satisfaction

- Self-assessed at Weeks -16 and -4 during the induction period and at Day 1, Week 8, and Week 32 during the maintenance period
- Results presented are based on an observed case data set of subjects who completed questionnaires at the stated visit (no imputation for missing values)
- **HIV-Medication Questionnaire (HIV-MQ)**
  - Contains 5 questions and is used to evaluate acceptability, tolerability, and subject-reported medication adherence
  - Data are presented separately for the CAB LA and RPV LA arms of the study
  - Responses are evaluated on an individual-item basis with scores ranging from 0 to 6 (6 refers to “none at all” and 0 refers to “a very great deal”)
- **HIV-Treatment Satisfaction Questionnaire (HIV-TSQ)**
  - Developed to evaluate patient satisfaction with HIV treatment
    - Two versions of the HIV-TSQ were used: HIV-TSQ (s) status version and the HIV-TSQ (c) change version. The latter was used to compare patients’ views on LA therapy with oral ART used during the induction phase
  - Contains 10 standard and 2 additional (adapted) items, with an individual satisfaction rating for each item ranging from 0 to 6
    - Higher scores indicate greater improvement in treatment satisfaction
  - Adapted with 2 additional items
    - Pain or discomfort with treatment
    - Ease/Difficulty of the treatment

## Results

- LATTE-2 included 309 patients (91% male, 20% non-white), of which 286 qualified and entered the maintenance period
- In the maintenance period, 95% (Q8W) and 94% (Q4W) of patients on CAB LA + RPV LA maintained HIV-1 RNA <50 c/mL at Week 32 compared with 91% on 3-drug oral ART (ITT-ME)
- To Week 32 of the injection phase, injection intolerability led to study withdrawal in 2 of 230 IM recipients (both in the Q8W arm)
- Drug-related adverse events (AEs) through Week 32 included injection site pain (92% of patients on IM arms) with 99% of injection site reactions (ISRs) being mild (82%) or moderate (17%), lasting a median of 3 days, and decreasing in frequency after the first injection

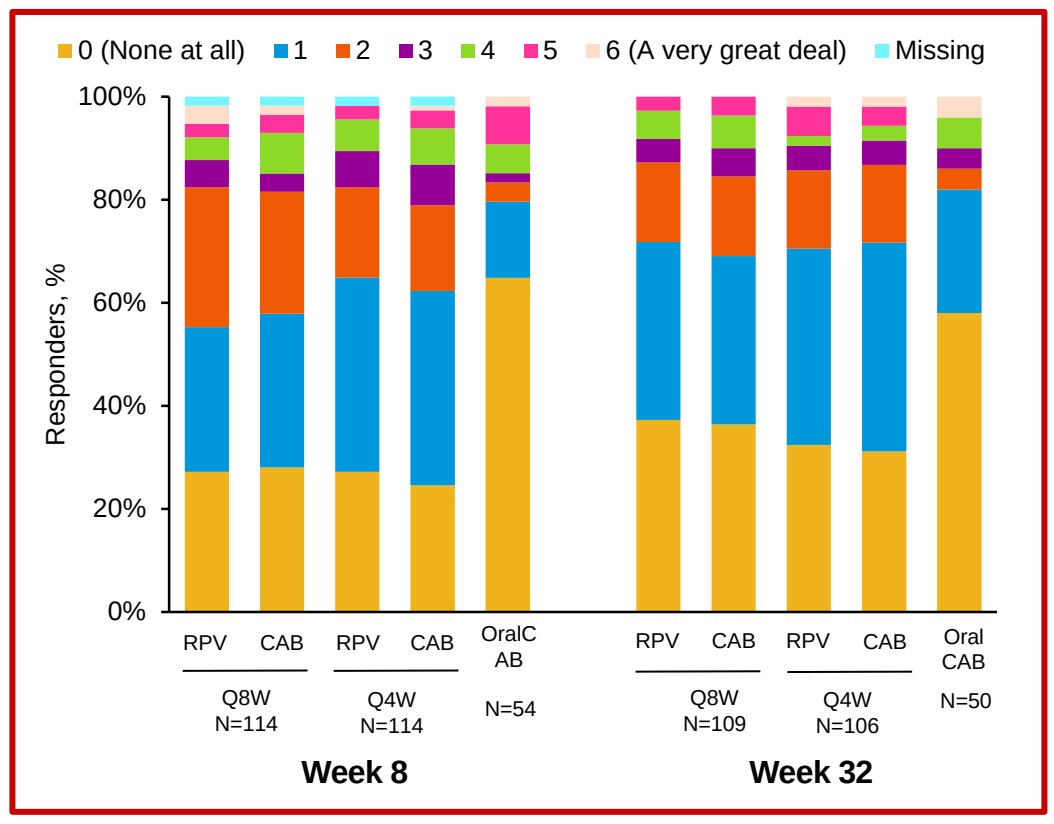
**Table 1. Adverse Events During Maintenance Period**

| | Q8W IM (n=115) | Q4W IM (n=115) | IM subtotal (N=230) |
|---|---|---|---|
| Number of injections | 1623 | 2663 | 4286 |
| Number of ISRs (events/injection) | 1054 (0.65) | 1228 (0.46) | 2282 (0.53) |
| **Grades** | | | |
| Grade 1 | 839 (80%) | 1021 (83%) | 1860 (82%) |
| Grade 2 | 202 (19%) | 197 (16%) | 399 (17%) |
| Grade 3 | 12 (1%) | 10 (<1%) | 22 (<1%) |
| Grade 4 | 0 | 0 | 0 |
| **Duration, days** | | | |
| ≤7 | 943 (89%) | 1121 (91%) | 2064 (90%) |
| Median | 3.0 | 3.0 | 3.0 |

- Number of subjects reporting ISRs decreased over time, from 86% (Day 1) to 33% (Week 32)[a,b]

[a]Represents percent of participants with a Week 32 visit (n=220). [b]Data through data cutoff for the Week 32 primary analysis.

**Figure 2. Amount of Pain and Discomfort With CAB LA + RPV LA and Oral CAB at Week 8 and Week 32 (HIV-MQ)**




- The percentage of subjects rating their pain/discomfort as 0 (“none at all”) was similar for CAB LA + RPV LA with both the Q8W and Q4W arms, with decreasing pain/discomfort over time; Week 8: Q8W (CAB LA=28%; RPV LA=27%), Q4W (CAB LA=25%; RPV LA=27%); Week 32: Q8W (CAB LA=37%; RPV LA=38%), Q4W (CAB LA=31%; RPV LA=32%)

**Figure 3. Satisfaction With Treatment at Week 32 and Comparing LA With Oral Induction Phase (HIV-TSQ [c])**

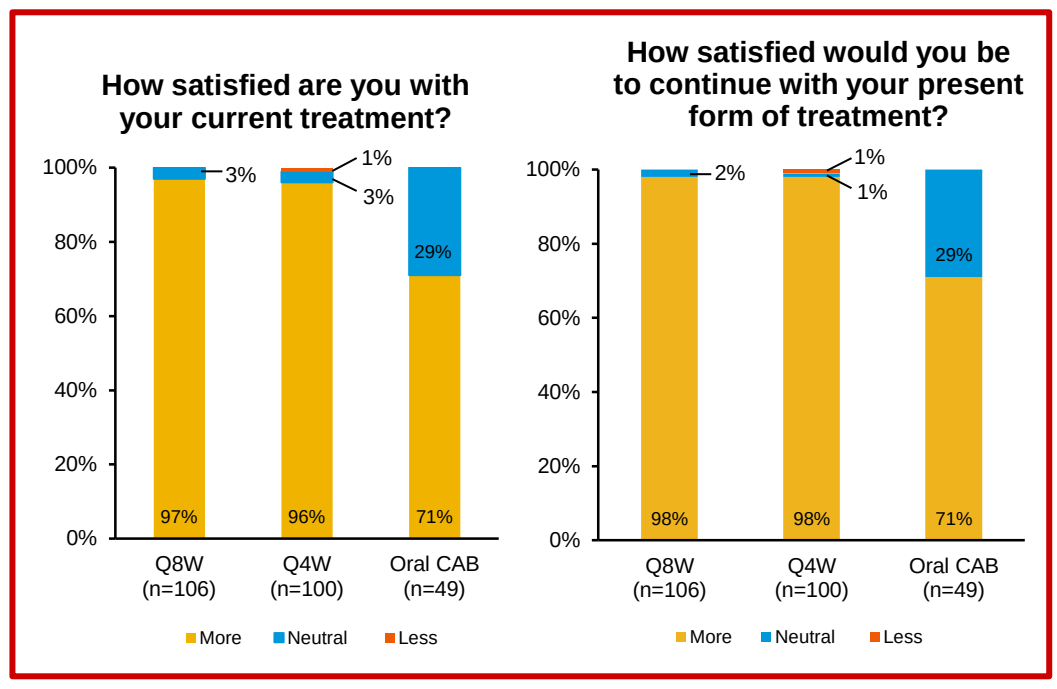
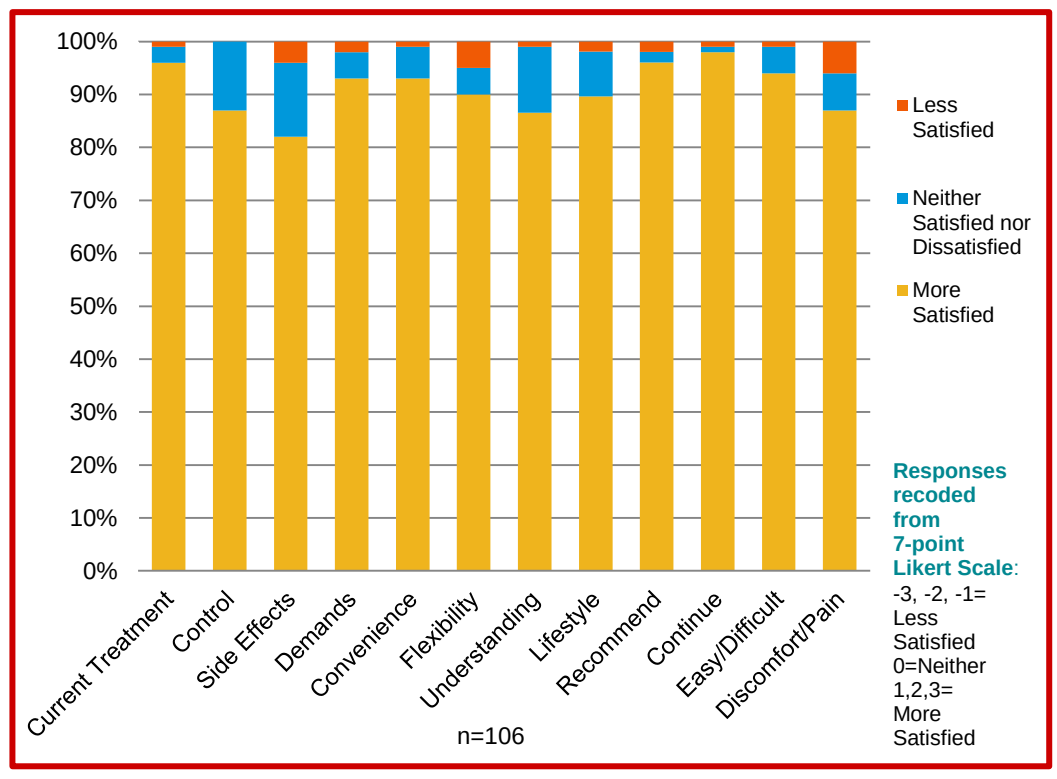



**Figure 4. Individual Item Scores for Patients on LA Therapy, Q4W, Week 32 Compared With the Induction Phase (HIV-TSQ [c])**




- At Week 32, participants in the Q4W reported being more satisfied with their LA therapy, compared with the oral CAB + 2NRTI treatment received in the 20-week induction phase, on all 12 items on the HIV-TSQ (c). The greatest satisfaction was on the item related to “willingness to continue therapy” followed by “would recommend to a friend”

## Discussion

- In the LATTE-2 study, the tolerability, acceptability, AEs, and pain associated with long-acting injectables (LAIs) were assessed from participants’ diaries as well as from participant-reported outcome measures (ie, HIV-TSQ and HIV-MQ). The results demonstrated that while participants experienced pain with injectable CAB+RPV, the majority were satisfied with the treatment and were willing to continue with LA therapy
- Overall, LATTE-2 participants reported a high degree of satisfaction with their study medication; most participants in the Q4W LA arm (98%) were willing to continue treatment at Week 32. Likewise, when comparing the views of participants on the LA arm, the participants on the LA arm were more satisfied compared to participants taking oral CAB+2NRTI, especially with regard to items related to convenience, flexibility, and lifestyle
- The specific measures in LATTE-2 underpin the importance of evaluating tolerability, acceptability, and satisfaction with participants on LA therapy. These secondary endpoints help contextualize the safety data from the trial

## Conclusions

- While low-grade CAB LA + RPV LA injection site pain was common among LATTE-2 participants, the results suggested participants experienced a high level of overall satisfaction and a preference for LA therapy on dimensions such as convenience, flexibility, and ease of use

**Acknowledgment**

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