# PATIENT-REPORTED OUTCOMES THROUGH WEEK 48 OF ATLAS-2M: A STUDY OF LONG-ACTING CABOTEGRAVIR AND RILPIVIRINE ADMINISTERED EVERY FOUR OR EIGHT WEEKS

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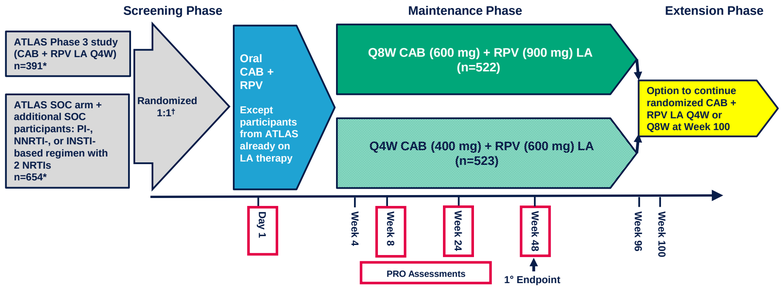
## Introduction

- Despite the success of daily oral antiretroviral therapy (ART), challenges still exist for some people living with HIV around pill burden, stigma, drug/food interactions, and adherence.
  - Thus, there is considerable interest in developing long-acting (LA) therapeutics for HIV-1 infection.
- The ATLAS (NCT02951052) and FLAIR (NCT02938520) Phase 3 studies demonstrated that switching to LA formulations of cabotegravir + rilpivirine (CAB + RPV LA) dosed every 4 weeks (Q4W) showed noninferior efficacy versus continuing current ART in virologically suppressed people living with HIV-1.[1,2]
- In the Phase 3b ATLAS-2M (NCT03299049) study (Figure 1), CAB + RPV LA dosed every 8 weeks (Q8W) was proven noninferior to Q4W dosing on the primary endpoint as per the FDA Snapshot algorithm, with an adjusted difference in proportion of participants with plasma HIV-1 RNA ≥50 copies/mL (95% confidence [CI]) of 0.8 (−0.6–2.2).[3]
  - CAB + RPV LA dosed Q8W was well tolerated; while injection site reactions (ISRs) were common, they were mostly of low grade and short lived (median duration: 3 days).[3]
- Patient-reported outcomes (PROs) in ATLAS-2M, an important element to understand participants' preferences and experiences with the new LA formulation, are presented herein.

### Figure 1. Study Design and PRO Assessments

**Phase 3, randomized, multicenter, parallel-group, noninferiority, open-label study**




*ITT-E population. For further study design details, please see Overton et al. CROI 2020; Boston, MA. Presentation 3334.[3] INSTI, integrase strand transfer inhibitor; ITT-E, intention-to-treat exposed; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; SOC, standard of care.

### Baseline Characteristics in the Intention-to-Treat Exposed (ITT-E) Population Were Similar Between Treatment Arms

- Baseline characteristics were similar between the Q8W and Q4W arms (Table 1).
- Overall, 37% (n=391) of participants had prior exposure to CAB + RPV.

### Table 1. Baseline Characteristics (ITT-E Population)

| Parameter | Q8W n=522 | Q4W n=523 | Total N=1045* |
|---|---|---|---|
| Prior exposure to CAB + RPV, n (%) | | | |
| None | 327 (63) | 327 (63) | 654 (63) |
| 1–24 weeks | 69 (13) | 68 (13) | 137 (13) |
| >24 weeks | 126 (24) | 128 (24) | 254 (24) |
| Median age (range), years | 42 (20–83) | 42 (19–75) | 42 (19–83) |
| Age ≥50 years, n (%) | 143 (27) | 139 (27) | 282 (27) |
| Female (sex at birth), n (%) | 137 (26) | 143 (27) | 280 (27) |
| Female (participant-reported gender), n (%) | 142 (27) | 146 (28) | 288 (28) |
| Race, n (%) | | | |
| White | 370 (71) | 393 (75) | 763 (73) |
| Black or African American | 101 (19) | 90 (17) | 191 (18) |
| Other | 51 (10) | 40 (8) | 91 (9) |
| Median body mass index (IQR), kg/m$^2$ | 26 (23–29) | 26 (23–29) | 26 (23–29) |
| ≥30, n (%) | 113 (22) | 98 (19) | 211 (20) |
| Median CD4 count (IQR), cells/mm$^3$ | 642 (499–827) | 688 (523–878) | 661 (508–849) |

*1049 participants were randomized. However, four participants did not receive study drug and therefore were not part of the ITT-E population. IQR, interquartile range.

## Methods

- Secondary endpoints included acceptability of ISRs, treatment acceptance, treatment satisfaction, and treatment preference (Table 2).

### Table 2. PRO Measures

| PRO | Description | Endpoint |
|---|---|---|
| **Perception of Injection Questionnaire (PIN)** | 4 dimensions that measure acceptability of ISRs, bother of ISRs, impact of sleep, and leg functioning. 5 individual items measuring pain during injection, anxiety before and after injections, willingness to be injected in the future, and overall satisfaction with mode of administration. Modified from a Vaccinees' Perception of Injection (VAPI) questionnaire; VAPI© Sanofi Pasteur 2009, all rights reserved.[5]* | "Acceptance of ISRs" over time from Week 8 to Weeks 24 and 48 (or withdrawal). This dimension only was selected for statistical analysis to avoid multiplicity. |
| **Chronic Treatment Acceptance Questionnaire (ACCEPT©)** | 3 items that produce the general acceptance score were included, which measure general acceptance of study medication based on overall advantages and disadvantages. | Change from baseline in treatment acceptance using the "general acceptance" dimension at Weeks 24 and 48 (or withdrawal). |
| **HIV Treatment Satisfaction Questionnaire status (HIVTSQs) and change versions (HIVTSQc)** | 12-item questionnaire that produces the treatment satisfaction total score (11 items) and 1 standalone item on pain/discomfort. Previously used in the ATLAS and FLAIR studies and adapted from the 10-item HIVTSQ and validated in the LATTE-2 study (NCT02120352).[1,2,4,6] | Change from baseline in total treatment satisfaction score at Weeks 24 and 48 (or withdrawal) with HIVTSQs and at Week 48 (or withdrawal) with HIVTSQc. |
| **Preference for HIV Treatment** | 3-item questionnaire comprising a single question assessing patients' preference, along with questions evaluating attributes supporting this preference, for CAB + RPV LA compared with daily CAB + RPV oral therapy and preference for the Q8W or Q4W regimen. | Preference for CAB + RPV LA Q8W compared with Q4W; preference for CAB + RPV LA Q8W or Q4W compared with CAB + RPV oral therapy at Week 48 (or withdrawal). |
| **HIV/AIDS-Targeted Quality of Life (HAT-QoL)†** | 3 out of 9 dimensions of the HAT-QoL were selected, measuring life satisfaction, disclosure worries, and HIV medication. | Change from baseline at Weeks 24 and 48 (or withdrawal). |

*VAPI contact information and permission to use: Mapi Research Trust, Lyon, France. E-mail: PROinformation@mapi-trust.org – Internet: www.mapi-trust.org. †HAT-QoL results not included here – no statistical differences between treatment groups were observed.

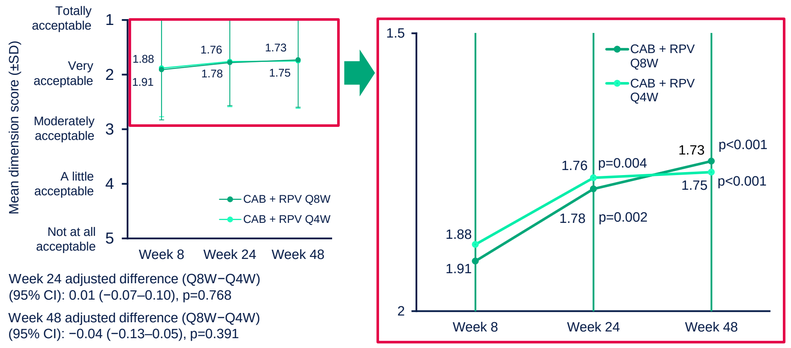
- Participants' experience with CAB + RPV LA was assessed using PRO instruments that were selected based on patient feedback from qualitative interviews conducted with a subset of patients from the LATTE-2 Phase 2b study.[4]
- PRO endpoints measuring treatment satisfaction, treatment acceptance, and aspects of quality of life were stratified by prior CAB + RPV exposure in the pre-specified statistical analysis.
- The objective of this analysis was to present the PRO data from the ATLAS-2M study.

## Results

### Increase in Acceptability of ISRs Through 48 Weeks

- Statistically significant improvements in the "acceptance of ISRs" domain of the PIN questionnaire were observed from Week 8 to Weeks 24 and 48 for Q8W and Q4W dosing (Figure 2), with 77% of participants in both dosing arms rating pain as "totally" or "very acceptable" at Week 48.
  - This observation coincides with the reduction in the frequency of ISRs over time seen in this study.[3]
- No statistically significant difference in adjusted mean change from Week 8 to Weeks 24 and 48 in acceptability of ISRs was observed between the Q8W and Q4W dosing arms.

### Figure 2. Summary of Acceptability of ISRs per Visit (ITT-E Population)




Week 24 adjusted difference (Q8W−Q4W) (95% CI): 0.01 (−0.07–0.10), p=0.768

Week 48 adjusted difference (Q8W−Q4W) (95% CI): −0.04 (−0.13–0.05), p=0.391

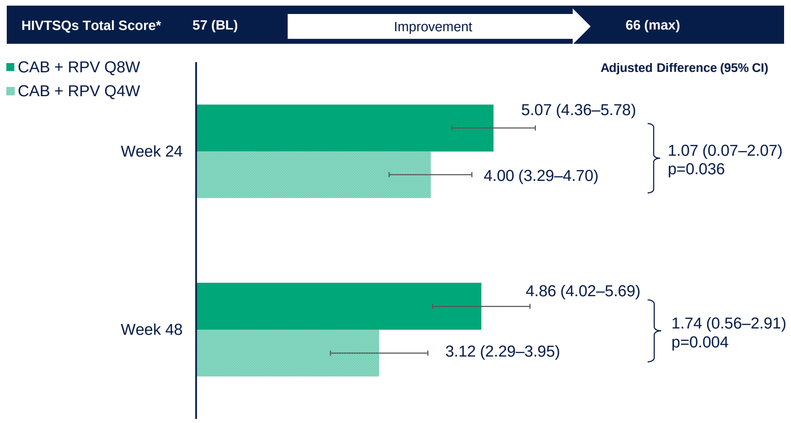
### Treatment Acceptance Improved From Baseline in Both Arms

- In participants without prior CAB + RPV exposure, marked improvements from baseline (mean baseline [standard deviation {SD}] for Q8W, 81.5 [25.23]; Q4W, 81.8 [25.98]) were observed in the general acceptance domain of the ACCEPT© questionnaire in both LA arms at Week 48 (adjusted mean change from baseline [95% CI]: Q8W, 6.8 [4.3–9.3]; Q4W, 5.7 [3.2–8.1]).
- Change from baseline scores did not significantly favor any LA group at Week 48 (adjusted difference [Q8W−Q4W] [95% CI]: 1.1 [−2.4–4.6], p=0.525).
- For participants with prior CAB + RPV exposure, general acceptance scores were high at baseline (mean baseline [SD]: Q8W, 89.3 [20.03]; Q4W, 91.2 [16.74]) and remained high through 48 weeks in both LA groups.

### High Levels of Treatment Satisfaction Were Observed with Long-Acting Therapy

- In participants without prior CAB + RPV exposure, mean (SD) HIVTSQs scores were similar at baseline, with 57.7 (9.21) and 56.7 (9.34) points for the Q8W and Q4W arms, respectively.
  - Treatment satisfaction markedly increased from baseline in both LA arms (Figure 3).
  - Statistically significantly greater improvement in treatment satisfaction was observed for participants randomized to the Q8W arm compared with the Q4W arm at Weeks 24 and 48 (Figure 3).
  - Satisfaction improved from baseline to Week 48 in nine of the 12 individual items, with Q8W scoring equal to or higher than the Q4W dosing arm (Figure 4).
- In participants with prior CAB + RPV exposure, mean (SD) baseline treatment satisfaction scores were high for both treatment groups at 62.2 (5.41) points for the Q8W arm and 62.0 (6.72) points for the Q4W arm out of a maximum of 66, and remained at high levels over 48 weeks.

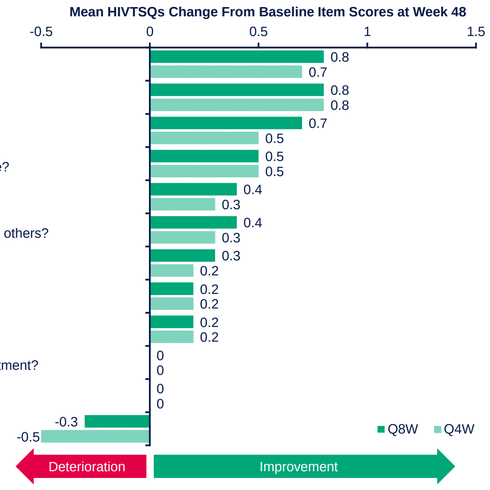
### Figure 3. Participant Satisfaction (HIVTSQs) Change From Baseline at Weeks 24 and 48 for Participants Without Prior CAB + RPV Exposure




*Adjusted mean change from baseline; calculated from an ANCOVA model including the covariates: baseline score, sex at birth (female, male), age (<50, ≥50 years), and race (white, non-white). BL, baseline.

- Overall, 96% (Q8W, n=493/512) and 92% (Q4W, n=474/518) reported they were satisfied or very satisfied to continue current treatment (HIVTSQs).

### Figure 4. Mean HIVTSQs Change From Baseline in Those Without Prior CAB + RPV Exposure

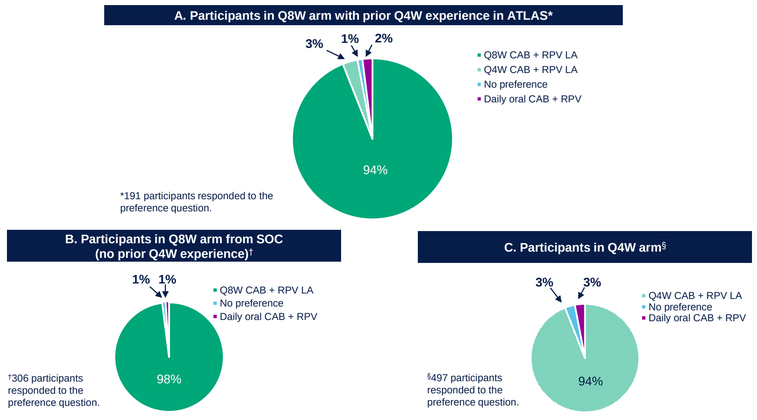



*HIVTSQ was adapted to include two additional questions relating to injectable treatment.

### The Majority of Participants Preferred LA Dosing

- Among those participants in the Q8W arm with prior CAB + RPV exposure, 94% (n=179/191) preferred CAB + RPV Q8W dosing versus Q4W (3% [n=6/191]) or daily oral dosing (2% [n=4/191]) (Figure 5A).
- Participants without prior CAB + RPV exposure who received CAB + RPV Q8W dosing preferred this regimen over daily oral dosing (98% [n=300/306]) (Figure 5B).
- Participants in the Q4W group (no experience of Q8W dosing) preferred CAB + RPV Q4W dosing over daily oral dosing (94% [n=468/497]) (Figure 5C).
- The most common reasons supporting preference were administration frequency and convenience.

### Figure 5. Treatment Preference at Week 48 in the Q8W Arm (A and B) and Q4W Arm (C)




## Conclusions

- CAB + RPV LA was associated with high levels of treatment satisfaction and acceptance irrespective of prior CAB + RPV exposure at study entry.
- Of those without prior experience of CAB + RPV, treatment satisfaction and acceptance for LA treatment over prior daily oral treatment substantially increased for both Q8W and Q4W dosing schedules.
- For participants transitioning from the Q4W arm in ATLAS, high levels of treatment satisfaction were maintained after more than 96 weeks on CAB + RPV LA therapy.
- The vast majority of participants preferred Q8W and Q4W dosing over daily oral dosing, with Q8W also preferred over Q4W dosing.
- The PRO data, along with safety and efficacy data, support the therapeutic potential of monthly or every 2 months CAB + RPV and highlight participants' preference for LA therapy over daily oral dosing.

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**References: 1.** Swindells S, et al. *N Engl J Med.* 2020;382(12):1112–1123. **2.** Orkin C, et al. *N Engl J Med.* 2020;382(12):1124–1135. **3.** Overton ET, et al. Conference on Retroviruses and Opportunistic Infections 2020; Boston, MA; March 8–11, 2020. Presentation 3334. Available at: www.croiwebcasts.org/p/2020croi/croi34. **4.** Margolis DA, et al. *Lancet.* 2017;390(10101):1499–1510. **5.** Chevat C, et al. *Health Qual Life Outcomes.* 2009;7:21. **6.** Woodcock A, Bradley C. *Value Health.* 2006;9(5):320–333.

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