P070

Patient-Reported Outcomes After 152 Weeks of HIV Maintenance Therapy With Long-Acting Cabotegravir + Rilpivirine in the Phase 3b ATLAS-2M Study

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Key Takeaways

- **ATLAS-2M is a multicenter, Phase 3b, randomized, open-label study investigating cabotegravir + rilpivirine long-acting (CAB + RPV LA) dosed every 8 weeks (Q8W) and every 4 weeks (Q4W) as a maintenance regimen for people living with HIV-1.**
- **Participants were found to be satisfied with CAB + RPV LA Q8W and Q4W as a treatment for the maintenance of virologic suppression across a range of patient-reported outcomes (PROs).**
- **Participants with no previous experience with CAB + RPV LA reported increases in treatment satisfaction over their previous daily oral regimen through 3 years of therapy.**
- **Participants with prior exposure to CAB + RPV LA reported high satisfaction at baseline, which remained high through 3 years of therapy.**

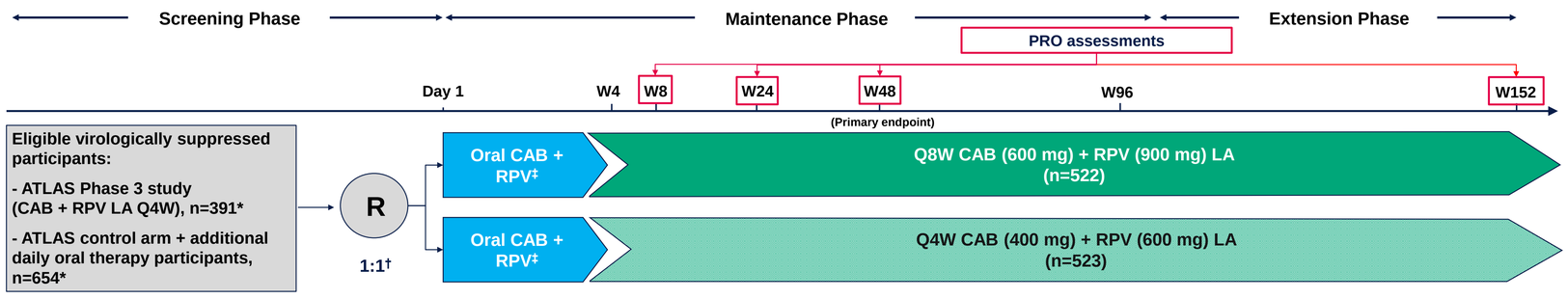
Background

- CAB + RPV LA administered monthly[1,2] or every 2 months[3] is the first complete LA regimen recommended by treatment guidelines for the maintenance of HIV-1 virologic suppression in people living with HIV-1.[4–6]
- CAB + RPV LA reduces dosing frequency compared with daily oral antiretroviral therapy (ART), and may help address concerns including fear of disclosure, anxiety around medication adherence, and daily reminders of HIV status.
- Durable noninferior efficacy of CAB + RPV LA was demonstrated between Q4W dosing and oral comparator ART at Week 48 in the ATLAS (NCT02951052) study,[1] and at Week 48 and Week 96 in the FLAIR (NCT02938520) study.[2,7]
- Noninferior efficacy was also established between Q8W and Q4W dosing at Weeks 48, 96, and 152 in the ATLAS-2M study (NCT03299049).[3,8,9]
- PROs in ATLAS-2M,[10] an important element to understand participants' preferences and experiences with this novel LA treatment regimen, updated through Week 152 are presented.

Methods

- ATLAS-2M is a multicenter, Phase 3b, randomized, open-label study investigating whether CAB + RPV LA dosed Q8W is noninferior to CAB + RPV LA dosed Q4W (**Figure 1**).
- The study was conducted across 13 countries: Argentina, Australia, Canada, France, Germany, Italy, Mexico, Russia, South Africa, South Korea, Spain, Sweden, and the United States.
- The primary endpoint was the proportion of participants with plasma HIV-1 RNA ≥50 copies/mL at Week 48 (FDA Snapshot).[1]
- Several PRO instruments were included at pre-specified time points in ATLAS-2M to assess tolerability and acceptability of injections, treatment satisfaction, acceptance, and treatment preference (**Table 1**).
  - PRO instruments were selected based on patient feedback from qualitative interviews conducted with a subset of patients from the LATTE-2 Phase 2b study (NCT02120352).[11]
  - Results were stratified by prior CAB + RPV exposure in the pre-specified statistical analysis, as a subset of participants rolled over from the Phase 3 ATLAS study.[1]

Figure 1. Study Design



*ITT-E population. †Randomization was stratified by prior exposure to CAB + RPV (0 weeks, 1–24 weeks, >24 weeks). ‡Excluding participants with prior CAB + RPV exposure in ATLAS (n=391). For further study design details, please see Overton ET, et al. *Lancet.* 2020;396(10267):1994–2005.
CAB, cabotegravir; ITT-E, intention-to-treat exposed; LA, long-acting; PRO, patient-reported outcome; Q4W, every 4 weeks; Q8W, every 8 weeks; R, randomized; RPV, rilpivirine; W, week.

Table 1. 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 movement. 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.[12]*	"Acceptance of ISRs" over time from Week 8 to Weeks 24, 48, and 152 (or withdrawal). This dimension only was selected for statistical analysis to avoid multiplicity. LOCF.
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, 48, and 152 (or withdrawal). LOCF.
HIV Treatment Satisfaction Questionnaire status version (HIVTSQs)	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[1,2,11,13]	Change from baseline in total treatment satisfaction score at Weeks 24, 48, and 152 (or withdrawal) with HIVTSQs. LOCF.
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 oral therapy for patients who received oral therapy to cover missed LA doses.	Preference for CAB + RPV LA compared with daily oral therapy for patients who received oral therapy to cover missed doses at Week 152 (or withdrawal). LOCF.

*VAPI contact information and permission to use: Mapi Research Trust, Lyon, France.
Email: PROinformation@mapi-trust.org; internet: www.mapi-trust.org.
CAB, cabotegravir; HIVTSQ, HIV Treatment Satisfaction Questionnaire; ISR, injection site reaction; LA, long-acting; LOCF, last observation carried forward; PRO, patient-reported outcome; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

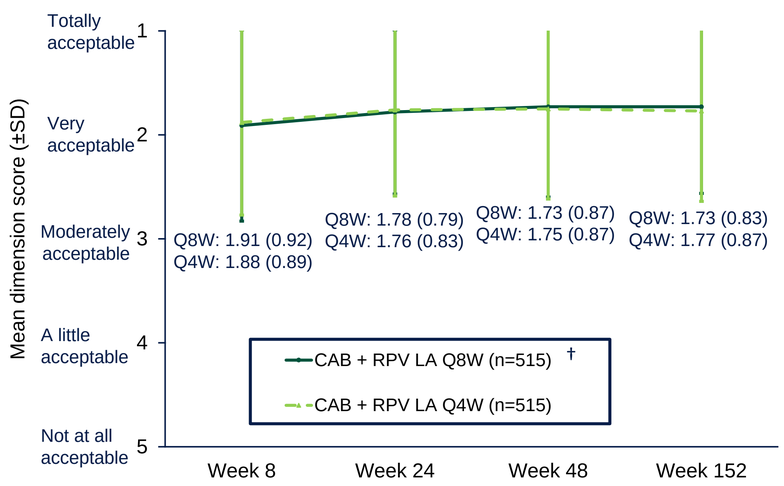
Results

Baseline Characteristics (Intention-to-Treat Exposed Population)*

- Baseline characteristics were similar between the Q8W and Q4W arms:[3]
  - Median age of 42 years (interquartile range [IQR] 34–50).
  - 27% (n=280/1045) were female (sex at birth).
  - 73% (n=764/1045) were White.
  - Median (IQR) CD4+ count was 642 cells/μL (499–827) and 688 cells/μL (523–878) in the Q8W and Q4W arms, respectively.
  - 37% (n=391/1045) of participants had prior exposure to CAB + RPV from participation in the Phase 3 ATLAS study.

*1049 participants were randomized. However, four participants did not receive study drug and therefore were not part of the intention-to-treat exposed population.

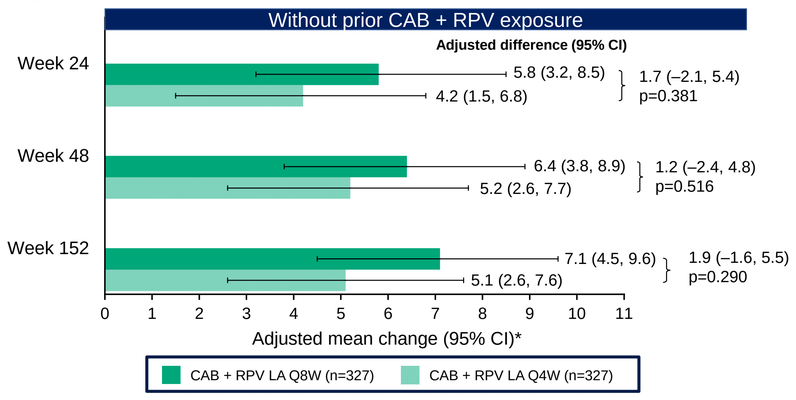
Figure 2. Acceptability of Injection Site Reactions* (PIN Questionnaire) – LOCF



*The acceptance of ISRs dimension consists of two items: acceptance of local reactions and acceptance of pain.
†n=514 for Week 8.
CAB, cabotegravir; ISR, injection site reaction; LA, long-acting; LOCF, last observation carried forward; PIN, Perception of Injection; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine; SD, standard deviation.

- Overall, 78% of participants in both dosing arms rated pain as "totally" or "very acceptable" at Week 152 in the acceptance of ISRs dimension of the PIN questionnaire, with small but statistically significant (p<0.005) improvements observed from Week 8 (4 weeks post first injection) to Weeks 24, 48, and 152 for Q8W and Q4W dosing.
- There was no statistically significant difference observed between the Q8W and Q4W dosing arms in the acceptability of ISRs per the adjusted mean change from Week 8 to Weeks 24 (p=0.767), 48 (p=0.394), and 152 (p=0.256) (**Figure 2**).

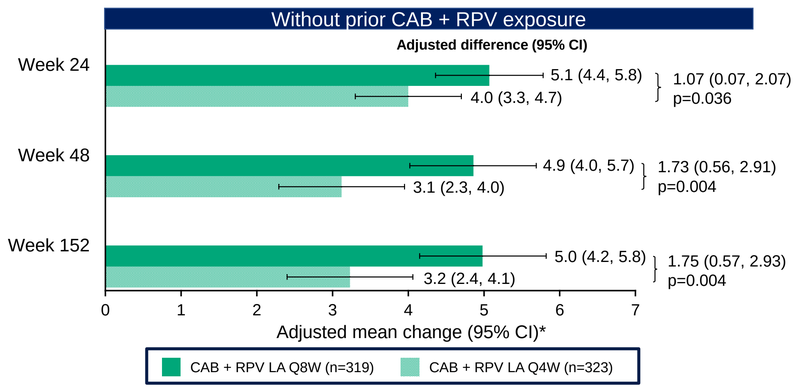
Figure 3. Treatment Acceptance (ACCEPT© Questionnaire) – LOCF



*Adjusted mean change from baseline calculated from an ANCOVA model including the following covariates: baseline score, sex at birth (female, male), age (<50, ≥50 years), and race (White, non-White) for participants with no prior exposure; baseline score, sex at birth (female, male), age (<50, ≥50 years), race (White, non-White), and prior exposure to CAB + RPV (1–24, >24 weeks) for participants with prior exposure.
CAB, cabotegravir; CI, confidence interval; LA, long-acting; LOCF, last observation carried forward; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

- For participants without prior CAB + RPV exposure, general acceptance scores at baseline were similar between arms (mean baseline [SD]: Q8W, 81.5 [25.23]; Q4W, 81.8 [25.98]; scores range from 0 [not at all acceptable] to 100 [totally acceptable]). Marked improvements from baseline were observed in both arms through Week 152, with neither significantly favored at any time point (**Figure 3**).
- 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 152 weeks in both LA arms (adjusted mean change from baseline at Week 152 [95% CI]: Q8W, –0.5 [–3.7, 2.7]; Q4W, –2.0 [–5.2, 1.1]).

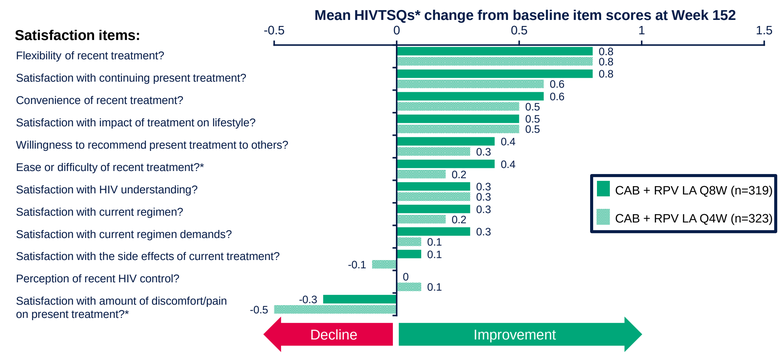
Figure 4. Treatment Satisfaction (HIVTSQs) – LOCF



*Adjusted mean change from baseline calculated from an ANCOVA model including the following covariates: baseline score, sex at birth (female, male), age (<50, ≥50 years), and race (White, non-White) for participants with no prior exposure; baseline score, sex at birth (female, male), age (<50, ≥50 years), race (White, non-White), and prior exposure to CAB + RPV (1–24, >24 weeks) for participants with prior exposure.
CAB, cabotegravir; CI, confidence interval; HIVTSQs, HIV Treatment Satisfaction Questionnaire status version; LA, long-acting; LOCF, last observation carried forward; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

- In participants without prior CAB + RPV exposure, mean (SD) HIVTSQs scores were similar at baseline (Q8W, 57.7 [9.21]; Q4W, 56.7 [9.34]; scores range from 0 [very dissatisfied] to 66 [very satisfied]).
  - Treatment satisfaction markedly increased from baseline in both LA arms; a statistically significantly greater improvement in treatment satisfaction was observed for participants randomized to the Q8W arm compared with the Q4W arm at Weeks 48 and 152 (**Figure 4**).
- In participants with prior CAB + RPV exposure, mean (SD) baseline treatment satisfaction scores were high for both treatment arms (Q8W, 62.2 [5.41]; Q4W, 62.0 [6.72]), and remained at high levels over 152 weeks (adjusted mean change from baseline at Week 152 [95% CI]: Q8W, +0.42 [–0.36, 1.21]; Q4W, +0.16 [–0.62, 0.94]).

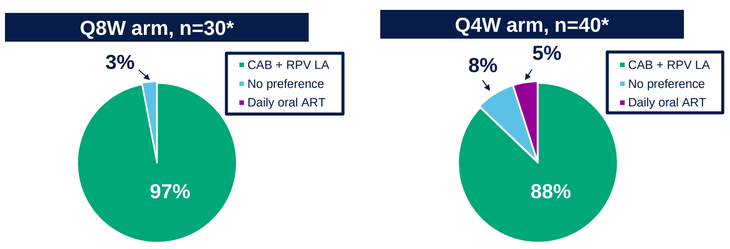
Figure 5. Treatment Satisfaction (HIVTSQs Individual Items, Without Prior CAB + RPV Exposure) – LOCF



*HIVTSQ was adapted to include two additional questions relating to injectable treatment.
CAB, cabotegravir; HIVTSQ, HIV Treatment Satisfaction Questionnaire; HIVTSQs, HIV Treatment Satisfaction Questionnaire status version; LA, long-acting; LOCF, last observation carried forward; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

- In participants without prior exposure, satisfaction improved from baseline to Week 152 across both arms in nine of the 12 individual items, with Q8W and Q4W scoring similarly across the 12 individual items (**Figure 5**), consistent with the Week 48 results.[10]

Figure 6. Treatment Preference (Subset of Participants Who Received Oral Therapy to Cover Missed Injections, n=70) at Week 152



*Preference for CAB + RPV LA Q8W or CAB + RPV LA Q4W compared with daily oral therapy for participants receiving oral therapy was assessed using a preference questionnaire. Participants utilized oral therapy when they were unable to comply with the injection visit schedule, including oral therapy to cover missed doses due to COVID-19 pandemic–related interruptions (oral CAB + RPV or other standard of care oral therapies were allowed during this time).
ART, antiretroviral therapy; CAB, cabotegravir; LA, long-acting; Q4W, every 4 weeks; Q8W, every 8 weeks; RPV, rilpivirine.

- At the Week 152 analysis, the preference questionnaire was limited to those who had received recent oral therapy (to cover missed injections during LA treatment). This was done to allow for meaningful comparisons between treatment regimens, as participants who did not miss any injections during the study had not experienced oral therapy for at least 3 years by the Week 152 analysis.
- Most participants across both arms preferred LA therapy vs. the daily oral ART they received to cover missed injections (**Figure 6**); the most common reasons supporting LA preference were convenience (81% [n=57/70]) and not having to worry as much about remembering to take medication (74% [n=52/70])

Conclusions

- Participants entered ATLAS-2M with generally high levels of treatment satisfaction, having previously received either LA treatment in the ATLAS study or daily oral ART.
- CAB + RPV LA was associated with high levels of treatment satisfaction and acceptance across both treatment arms, 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 ART substantially increased for both LA dosing schedules.
- For those transitioning from LA in ATLAS, high levels of treatment satisfaction were maintained after more than 152 weeks on CAB + RPV LA therapy.
- The majority of participants who received oral ART to cover missed injection visits preferred LA dosing over daily oral 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.
- These findings contextualize the high retention and low discontinuation rates observed in ATLAS-2M.[9]

Acknowledgments: The authors thank everyone who has contributed to the success of ATLAS-2M, all study participants and their families, and the clinical investigators and their staff. This analysis was funded by ViiV Healthcare and Janssen Pharmaceuticals. Professional medical writing support was provided by Euan Paul of Scimentum (Nucleus Global), funded by ViiV Healthcare.

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