

Background

Before initiating of long-acting (LA) cabotegravir and rilpivirine (CAB/RPV), oral lead-in (OLI) is an option, intending to rule out potential (systemic) side effects.

The desire of people with HIV (PWH) to skip this phase is often in contrast to the wish of health care professionals (HCP) to 'test' the drug in a short acting form before administering the first LA dose.

This study aimed to add to the understanding of the relevance of OLI with regards to persistence on CAB/RPV by performing a retrospective analysis of routine clinical data from a single, large HIV outpatient center in Munich, Germany, focusing not only on overall persistence, but in particular on early discontinuation which might be attributable to unexpected side effects.

Methods

Retrospective cohort study in PWH exposed to at least one dose of CAB/RPV orally (as OLI) and/or intramuscularly from January 2021 onwards. Persistence on CAB/RPV LA was compared between PWH, receiving at least one dose of CAB/RPV LA with or without OLI.

Analysis was repeated after stratification for previous antiretroviral regimen (dolutegravir [DTG] containing yes/no).

Standard and modified log-rank tests (using Peto-Peto-Prentice weighing), were used to compare event-times in the overall and the early time on treatment, respectively.

Statistical analysis was performed using R 4.2.0 (The R-project).

$\alpha = 0.05$ was used as the level of significance.

Results

161 PWH were included into the analysis, of which 56.8% switched from a DTG-containing regimen. 122 PWH (75.8%) received OLI.

While 8 (6.6 %) did not proceed to LA after OLI, in only one (0.8 %) a potential side effect was the reason. No severe adverse event was observed.

Times of persistence on CAB/RPV LA was not significantly different for PWH with and without OLI ($p=0.917$). This was also true when focusing on the early episode after initiation ($p=0.936$).

Stratifying for ART prior to initiation of CAB/RPV yielded similar results, whether the previous ART was DTG-containing ($p=0.650$) or not ($p=0.665$).

Conclusion

Rate of discontinuation during OLI was low in our study sample and due to mild side effects.

Time of persistence on CAB/RPV LA was not significantly different between PWH with and without OLI. This was also true when particularly focusing on the early period after therapy initiation, where most of the drug-related side effects might be expected.

Our findings suggest, that OLI does not affect the persistence on CAB/RPV LA, in particular in PWH with prior DTG exposure.

Particularly in the subgroup of PWH without prior DTG-containing ART, the validity of our findings might be limited by low sample size.

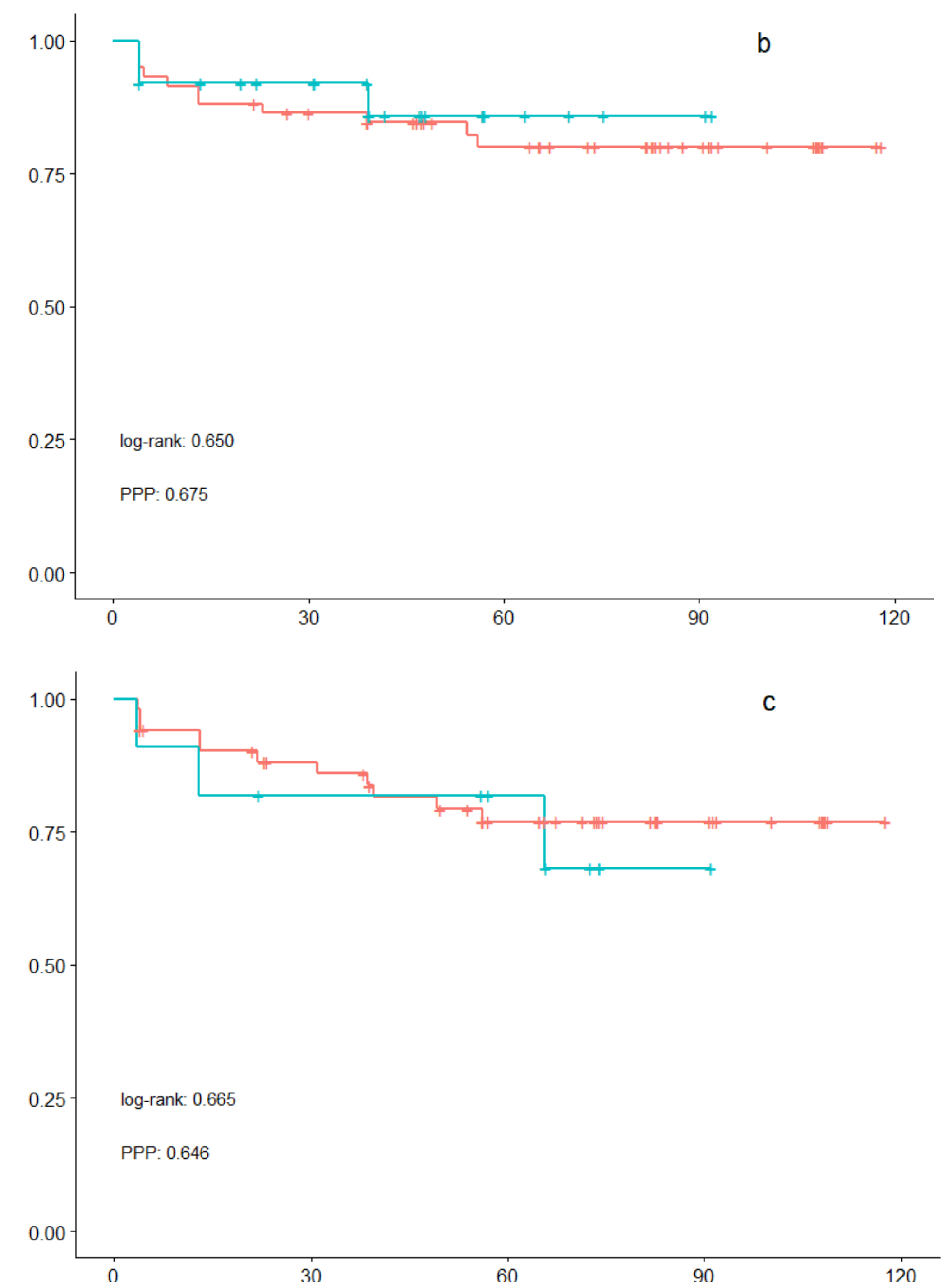
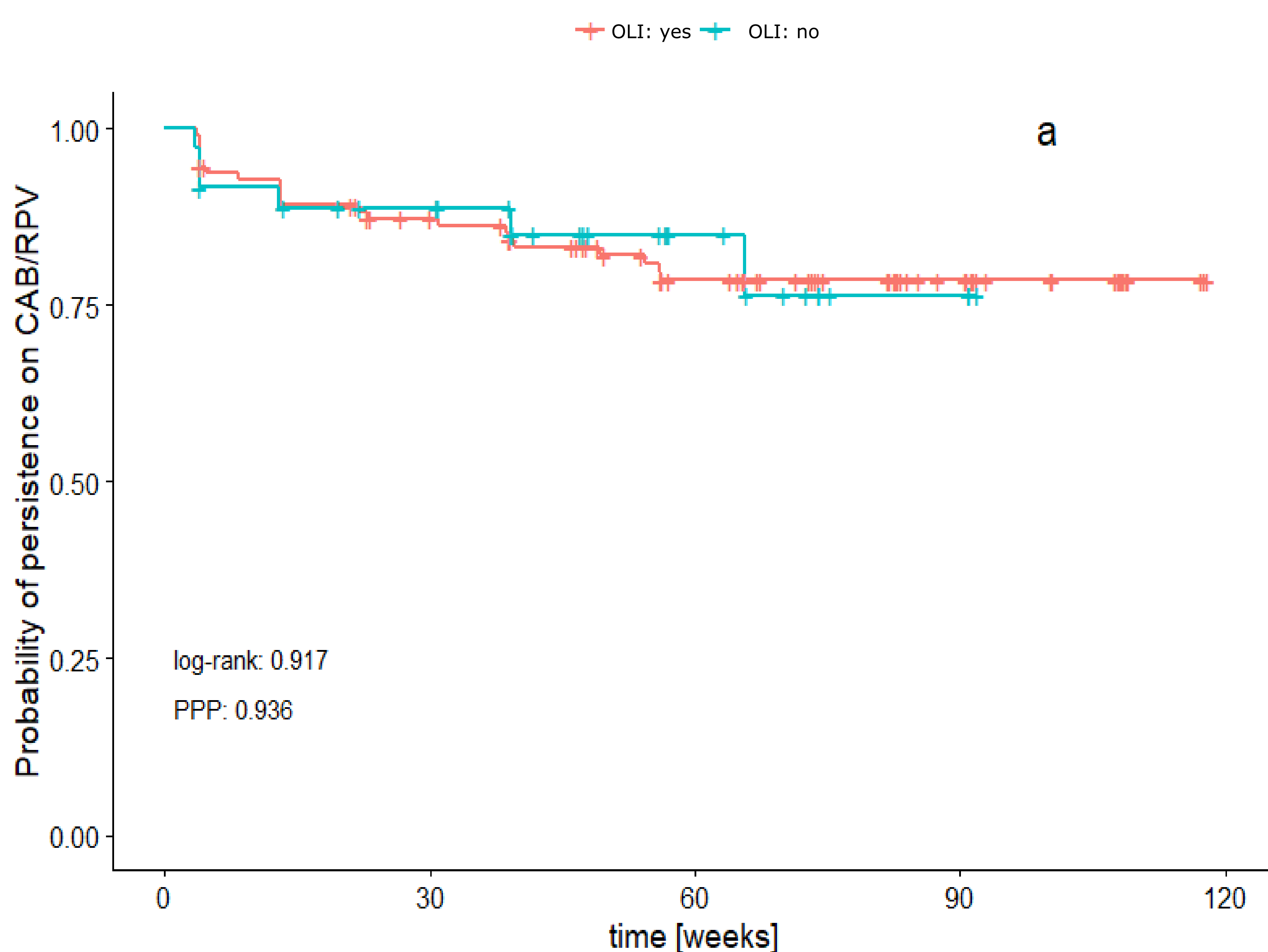


Figure 1: Kaplan-Meier curves for the times of persistence on CAB/RPV LA in the overall study sample (a), as well as the subsets of PWH with DTG-containing (b) and non-DTG-containing (c) antiretroviral regimens prior to initiation of CAB/RPV. P-values for each group are given for the log-rank test as well as the Peto-Peto-Prentice (PPP) test; DTG: dolutegravir; OLI: oral lead-in.

Key findings

- **Adverse events during oral lead-in that lead to discontinuation / not-initiation of CAB/RPV LA are rare. No severe adverse events were observed.**
- **Discontinuation from CAB/RPV LA does not seem to depend on whether or not oral lead-in was used.**
- **These findings result from a cohort of PWH with high exposure to dolutegravir, which shows a high level of analogy to CAB. Therefore our data must be generalized with care for PWH without prior dolutegravir exposure.**