Use of *Apretude* for Pre-Exposure Prophylaxis Without Use of the Oral Lead-In

Summary

- An oral lead-in with oral cabotegravir prior to initiation of *Apretude* (long-acting cabotegravir, CAB LA) to assess tolerability of cabotegravir is optional.
- No safety and efficacy data are available for use of CAB LA for pre-exposure prophylaxis without an oral lead-in.
- In FLAIR, after Week 96, HIV patients originally randomized to abacavir/dolutegravir/lamivudine (ABC/DTG/3TC) were eligible to transition to long-acting cabotegravir and rilpivirine (CAB + RPV LA) with or without an OLI period beginning at Week 100 (extension phase).[1]
    - Virologic outcomes at Week 124 (after 24 weeks of CAB + RPV LA) during the extension phase of FLAIR were similar between patients who received the oral lead-in (OLI) and those who did not.
    - No clinically meaningful differences in median CAB and RPV concentrations were observed between the treatment arms.
    - The rates of drug-related adverse events between the two treatment arms were similar.
- Important Safety Information and Boxed Warning can be found in the Prescribing Information and can also be accessed from the Our HIV Medicines section of viivhealthcare.com/us.

To access additional scientific information related to ViiV Healthcare medicines, visit the ViiV US Medical Portal at viivhcmedinfo.com.

FLAIR

FLAIR is an ongoing phase 3 trial originally designed to assess the efficacy and safety of CAB + RPV LA versus ABC/DTG/3TC in virologically suppressed patients with HIV-1.[1] Please click here for more details about the study design of FLAIR.

After Week 96, patients originally randomized to ABC/DTG/3TC were eligible to transition to CAB + RPV LA with or without an OLI period beginning at Week 100 (extension phase).[1]

The objectives of this analysis were to evaluate the antiviral and immunologic effects, pharmacokinetics, safety and tolerability, and viral resistance of CAB + RPV LA among patients switching from ABC/DTG/3TC.[1]

Results

A total of 232 patients [oral lead-in (OLI) arm, n=121; direct to injection (DTI) am, n=111] out of the original 283 chose to transition to CAB + RPV LA during the extension phase. [1]

Virologic outcomes at Week 124 (after 24 weeks of CAB + RPV LA) were similar between the OLI and DTI arms.[1]

One patient in the DTI arm met the criteria for confirmed virologic failure (CVF; 2 consecutive HIV-1 RNA ≥200 copies/mL) on Week 12 of CAB + RPV LA.[1] No integrase or non-nucleoside reverse transcriptase inhibitor (NNRTI) RAMs were detected at baseline and no integrase RAMs were detected at the timepoint of the suspected virologic failure.

Assay for CAB and RPV concentrations was conducted 1 and 4 weeks after the loading dose injections were administered.[1] No clinically meaningful differences in median CAB and RPV concentrations were observed between the treatment arms.

A summary of adverse events reported in FLAIR through Week 124 can be found in Table 1.[1] The most common adverse events reported in both arms (excluding ISRs) were pyrexia and dizziness.

There were no liver stopping events, confirmed hypersensitivity reactions, or other dermatological manifestations in either treatment arm.[1]

Table 1. Summary of Adverse Events (Excluding ISRs) in FLAIR through Week 124[1]

Paramter, n (%)	OLI Arm (n=121)	DTI Arm (n=111)
Any AE	85 (70)	88 (79)
Any Grade 3 to 4 AE	5 (4)	4 (4)
Drug-related AE	23 (19)	22 (20)
Drug-related Grade 3 to 4 AE	0	1 (<1)[a]
AEs leading to withdrawal	1 (<1)[b]	1 (<1) [a]
Any SAE	5 (4)	4 (4)
Drug-related SAE	0	1 (<1) [a]
Fatal SAE	0	0

[a] Grade 4 drug-related SAE leading to withdrawal in the DTI arm was Hodgkin's disease mixed cellularity; [b] One participant discontinued from the OLI arm due to AE of weight gain (8 kg).

OLI = oral lead-in; DTI = direct-to-injection; AE = adverse event; SAE = serious adverse event

The reporting of ISRs was similar to what has been reported for FLAIR previously and for other phase 2 and 3 trials more broadly.[1] A total of 4442 injections were administered leading to 914 (21%) ISR events. ISRs were numerically less common in the OLI arm (16%) than the DTI arm (25%). The most common event reported was pain. There were 2 withdrawals due to ISRs (both in OLI arm). Most ISRs were mild to moderate in severity and decreased over the course of the study.

ONGOING STUDIES WITH OPTIONAL ORAL LEAD-IN OF CABOTEGRAVIR FOR HIV-1 PREEXPOSURE PROPHYLAXIS

HPTN 083 is a randomized, double-blind, double-dummy, phase 2b/3, non-inferiority study designed to assess the safety and efficacy of CAB LA compared to daily oral TDF/FTC for PrEP in HIV-uninfected cisgender men and transgender women who have sex with men.[2]

HPTN 084 is a double-blind, placebo-controlled, phase 3, superiority trial evaluating the safety and efficacy of long-acting injectable cabotegravir compared to daily oral TDF/FTC for pre-exposure prophylaxis in HIV-uninfected cisgender women.[3]

Both studies are ongoing in an open-label extension phase and allow for participants to transition directly to CAB LA without the use of the OLI.[4,5]

REFERENCES

1. D'Amico R, et al. Safety and efficacy of cabotegravir + rilpivirine long-acting with and without oral lead-

in: FLAIR Week 124 results. Presented at HIV Drug Therapy Glasgow, October 5-8, 2020, Glasgow, UK. Oral Presentation O414.
2. Landovitz R DD, Clement ME, et al. Cabotegravir for HIV prevention in cisgender men and transgender women. *NEJM*. 2021;385(7):595-609. doi:http://dx.doi.org/10.1056/NEJMoa2101016.
3. Delany-Moretlwe S. Long acting injectable cabotegravir is safe and effective in preventing HIV infection in cisgender women: results from HPTN 084. Presented at HIV Research for Prevention Conference (HIVR4P), January 27-28 and February 3-4, 2021 (Virtual).
4. NCT02720094 (HPTN 083). Available at: https://clinicaltrials.gov/ct2/show/NCT02720094?term=cabotegravir+prep&rank=1. Accessed October 3, 2019.
5. NCT03164564 (HPTN 084). Available at: https://clinicaltrials.gov/ct2/show/NCT03164564?term=cabotegravir+prep&rank=3. Accessed October 3, 2019.