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LONG-ACTING CABOTEGRAVIR + RILPIVIRINE FOR HIV MAINTENANCE: FLAIR WEEK 48 RESULTS

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Background:
The 2-drug long-acting (LA) injectable regimen of the INSTI cabotegravir (CAB) and the NNRTI rilpivirine (RPV) is being developed to reduce dose frequency, pill taking and drug exposure. FLAIR, a phase 3, open-label, multicenter study is investigating whether switching to monthly CAB+RPV is noninferior to dolutegravir/abacavir/lamivudine (DTG/ABC/3TC).

Methods:
ART-naïve participants received induction therapy with oral DTG/ABC/3TC (CAR&) for 20 weeks. Those with HIV-1 RNA <50 c/mL at 16 weeks were eligible to enter the maintenance phase and randomly assigned (1:1) to continue CAR or switch to LA. Participants in the LA arm received an oral lead-in of CAB 30mg + RPV 25mg once daily for 4 weeks to assess tolerability before receiving CAB+RPV as intramuscular monthly LA injectable therapy. The primary endpoint was viral load (VL) ≥50 c/mL at W48 by FDA snapshot algorithm (NI margin 6%). Safety, tolerability and confirmed virologic failure (CVF) were secondary endpoints.

Results:
566/629 participants who initiated induction therapy were randomly assigned to the LA or CAR arm (283/arm). The median age was 34 yr (11% ≥50 yr); 22% were female and 74% were white. At the induction phase start, median CD4 count was 444 cells/mm³ (7% <200 cells/mm³), median VL was 4.49 log10 c/mL (20% ≥100,000 c/mL). Six participants in the LA arm (2.1%) and 7 in the CAR arm (2.5%) had HIV-1 RNA ≥50 c/mL at W48, meeting noninferiority criteria for the primary endpoint (Table) and for the key secondary endpoint of HIV-1 RNA <50 c/mL (LA 93.6% vs CAR 93.3%). Four LA recipients (1.4%) had CVF; 3 had mutations in the NNRTI + INSTI domains (K101K/E/Q + G140R, E138K + Q148R, and E138E/A/K/T + Q148R, respectively) and 1 was not tested (PO only). The CAR arm had 3 CVFs with no INSTI resistance. Adverse events (AE) leading to withdrawal and serious AE were infrequent in both arms. The most common drug-related AE was injection site reactions (ISRs; 82% of participants in the LA arm); frequency decreased over time. 99% of ISRs were Grade 1 or 2; the median duration was 3 days. Of 263 LA participants completing HIVTSQc at W48, 99% were more satisfied with CAB+RPV compared with their prior daily oral CAR.

Conclusion:
The regimen of monthly injections of CAB+RPV was noninferior to DTG/ABC/3TC at W48. The LA regimen was generally well tolerated with few CVFs. Overall, these results demonstrated the therapeutic potential of CAB+RPV injections, following short initial induction with oral DTG/ABC/3TC to achieve viral suppression.