CROI 2025 / Abstract 202

202 - Randomized Trial of Long-Acting Cabotegravir and Rilpivirine in Africa (CARES): Week 96 Results

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Session Name
Late-Breaking Antiviral Therapy: It Doesn't Get Any Hotter Than This!

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Key Terms
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Category
Late-Breaking Abstract Submission

SubCategory
(G) Antiviral Therapy: Pre-Clinical Data, Randomized Trials, Efficacy, and Effectiveness Studies in HIV or SARS-CoV-2 or MPXV in Adults

Background
Evidence is required to support use of long-acting injectable therapy (LA) in Africa, where demographic factors, viral subtypes, prior treatment, archived drug resistance, and approaches to treatment delivery and monitoring differ from resource-rich settings. We previously reported non-inferior efficacy of LA versus oral antiretroviral therapy (ART) at 48 weeks, but longer-term data are needed to assess durability in program settings.

Methods
This randomized, multicentre, open-label trial evaluated efficacy, safety, and tolerability of switching from oral ART to LA. Adults with HIV-1, stable on first-line oral ART (TDF +3TC/FTC+EFV/NVP/DTG) with screening VL <50 copies/ml were enrolled at 8 African sites. Main exclusion criteria were past virologic failure, current pregnancy and HBV co-infection. Participants were randomized (1:1) to continue oral ART (OT group) or switch to cabotegravir (CAB)+rilpivirine (RPV) intramuscular injections every 8 weeks (LA group). VL was monitored every 24 weeks. Main outcome is % participants with VL <50 copies/ml at week 96 (FDA snapshot; non-inferiority margin 10%). Confirmed virologic failure (CVF, secondary outcome) was defined as 2 consecutive VL ≥200 copies/ml. Subtype and resistance mutations were determined at baseline in all (archived DNA, retrospective), and at CVF (real-time, RNA).

Conclusion
At 96 weeks, CAB and RPV LA showed high efficacy, non-inferior to oral ART when used in the public health approach with sparse VL monitoring and without real-time baseline resistance testing. CVF and acquired resistance was uncommon. LA was effective with an acceptable safety profile and may be considered for use in treatment programs in sub-Saharan Africa.

Results
512 participants were enrolled (median age 42y; 58% female; 92% on DTG-based ART; 74% with prior NNRTI exposure; 8% baseline archived RPV resistance mutations [in sequences without APOBEC mutations]; 57% viral subtype A1; 21% baseline BMI ≥30kg/m2). Seven withdrew (3 LA, 4 OT group) and two died (1LA, 1OT) by week 96. At 96 weeks, 247/255 (96.9%) in LA and 250/257 (97.3%) in OT group had VL<50 copies/mL (difference -0.4%; 95%CI -3.1 to 2.0%); demonstrating non-inferiority (Table). Four participants (1.6%) in LA group and none in OT group had CVF by week 96; 3 resuppressed on TDF/3TC/DTG. Adverse events of grade ≥3 severity occurred in 41 (16%) in LA and 22 (9%) in OT group; only one treatment-related adverse event in the LA group led to treatment discontinuation (injection-site abscess).