WRHI052

The WRHI052 trial is designed to generate evidence to replace the current standard of care second-line HIV treatment LPV/r with a lower-dose DRV/r, when both used in combination with 2 nucleoside reverse transcriptase inhibitors (NRTIs). The population of people failing EFV-based first-line treatment is expected to grow and second-line regimens in low and middle income countries rely on protease inhibitors (PIs), like LPV, since they are very robust. However, PIs are expensive, have high toxicity, and are not co-formulated. DRV/r is a next-generation PI with fewer side effects and a higher resistance barrier, but at current dosages it is an even more expensive option than other PIs. There is evidence that lower dosages of DRV could have similar effectiveness and be less costly than the currently used PIs.

DRUG ABBREVIATIONS

LPV/r	lopinavir + ritonavir
DRV/r	darunavir + ritonavir
EFV	efavirenz
DTG	dolutegravir
TDF	tenofovir disoproxil fumarate
3TC	lamivudine

Study Design & Methods

WRHI052 is a phase 3b trial that intends to demonstrate that DRV/r 400 mg/100 mg is equivalent or better compared to LPV/r 800 mg/200 mg daily in second-line HIV treatment of stable patients already on LPV/r that are 18 years or older. The trial will take place at one site in South Africa.

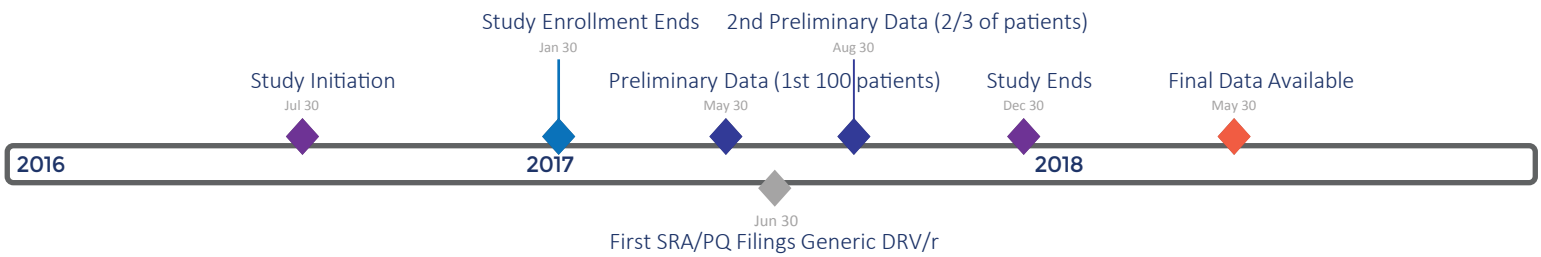
Inclusion criteria: Age ≥18 years, on LPV/r-based regimen for ≥ 6 months with no history of other PIs, plasma HIV-1 RNA(VL) < 50 copies/mL.

Exclusion criteria: On antiretrovirals (ARVs) other than NRTIs and LPV/r, history of PI resistance, on TB treatment, pregnant or breastfeeding. Those who become pregnant during the trial may elect to stay in and have their DRV increased to 800 mg.

~300 male and female patients with HIV-1 will be randomly assigned in an equal ratio to the two treatment arms, either switching to DRV/r regimen or staying on the LPV/r regimen, with approximately 150 participants per group.

Primary Outcome: Proportion of patients in regimen with undetectable plasma HIV-1 RNA levels (< 50 copies/mL) at week 48
Secondary Outcomes: Week 48 viral suppression, CD4 count changes, tolerability, overall safety, and efficacy of each

Trial Timeline



Key Collaborations

WRHI052 is co-funded by USAID and the Medicines and Research Council of South Africa, and led by the Wits Reproductive Health and HIV Institute (Wits RHI). WRHI052 received ethics and regulatory approvals from the Human Research Ethics Committee and the Medicines Control Council, and is overseen by the National Institutes of Health (NIH) Multinational Data and Safety Monitoring Board, and a Scientific Advisory Committee (SAC).

Key Considerations

The WRHI052 SAC — in collaboration with the AIDS Clinical Trials Group, USAID, and NIH — have actively coordinated efforts to provide the evidence needed to support recommendation of lower dose DRV/r. This regimen has additional advantages as second-line treatment: considered in combination with DTG, DRV/r would have no cross-resistance to an EFV/TDF/3TC first- line.

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