ADVANCE

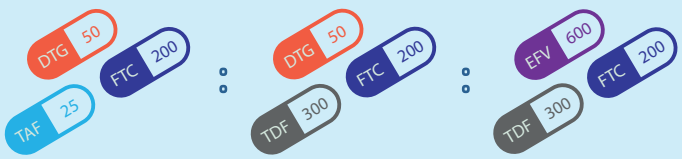
ADVANCE is designed to generate evidence to replace the current standard of care first-line HIV treatment (TDF/EFV/FTC or 3TC) with a fixed-dose, DTG/TAF-based regimen in low and middle income countries (LMIC). DTG and TAF have demonstrated increased robustness, and safety, in addition to better patient tolerability and reduced costs. A switch to a DTG/TAF-based regimen could enable South Africa to treat everyone by 2019 with its current antiretroviral (ART) budget, suggesting the power of this regimen to enable LMIC to meet the increasing treatment demands under "treat all" and to achieve UNAIDS 90-90-90 targets.

DRUG ABBREVIATIONS

TDF	tenofovir disoproxil fumarate
EFV	efavirenz
FTC	emtricitabine
3TC	lamivudine
DTG	dolutegravir
TAF	tenofovir alafenamide fumarate
RIF	rifampicin

Study Design & Methods

The ADVANCE trial intends to demonstrate that DTG/TAF/FTC is equivalent or better compared to DTG/TDF/FTC or EFV/TDF/FTC in first-line HIV treatment of patients 12 years old or older. The trial will take place at two to three sites in South Africa.



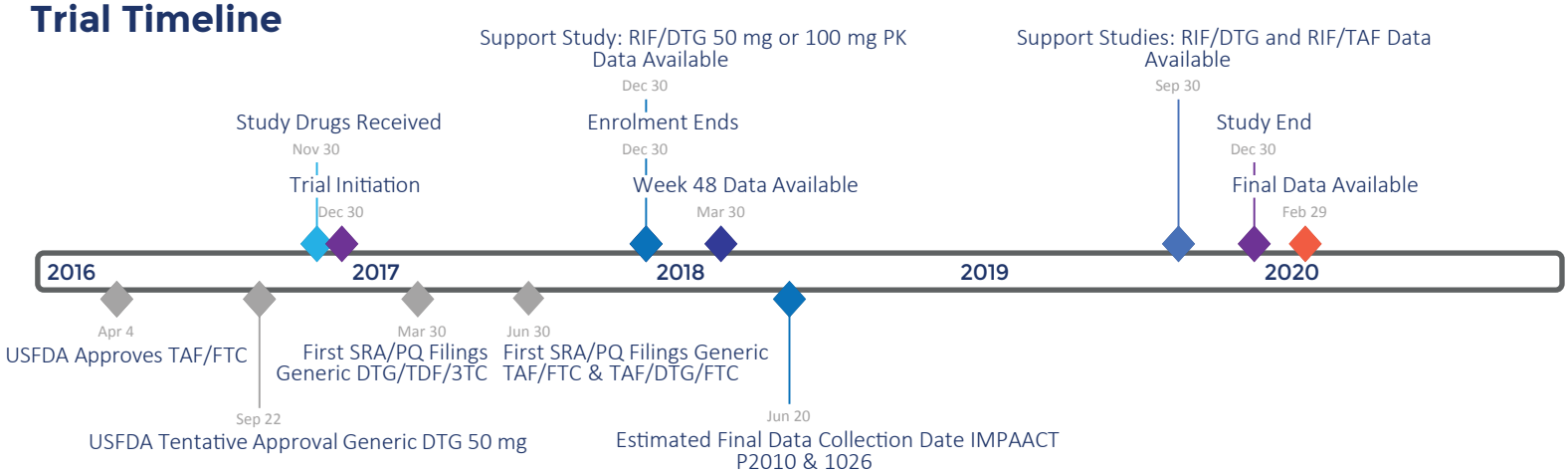
Inclusion criteria: Age ≥12 years and ≥40 kg, HIV-1 positive, plasma HIV-1 RNA(VL) ≥500 copies/ml and CrCl> 60 mL/min.

Exclusion criteria: Received >30 days of any ART or any ART within last 6 months, pregnancy, tuberculosis (TB) co-infection or are on TB therapy. Those that become pregnant, or develop TB while on the trial will be able to remain in the study, with dose/regimen adjustments.

~1110 male and female patients with HIV will be randomly assigned in an equal ratio to the three treatment groups. 12-18 year old patients will be recruited and analyzed separately from those who are 18 years or older, for a total maximum of 370 in each trial arm. The trial is open-label.

Primary Outcome: Proportion of patients in regimen with undetectable plasma HIV-1 RNA levels (<50 copies/mL) at week 48
Secondary Outcomes: Week 96 viral suppression, CD4 count changes, tolerability, overall safety, and efficacy of each regimen

Trial Timeline



Key Collaborations

ADVANCE is co-funded by USAID, through PEPFAR, and UNITAID, and led by the Wits Reproductive Health and HIV Institute (Wits RHI). ViiV and Gilead are donating the study drugs. ADVANCE 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 ADVANCE SAC — in collaboration with the AIDS Clinical Trials Group, USAID, and NIH— have actively coordinated efforts to eliminate duplication while ensuring comprehensive evidence on the safety of new ART regimens is available in: pregnant women (IMPAACT 1026 and IMPAACT P2010), adolescents and TB/HIV co-infection (ADVANCE Support Studies on DTG/TAF/RIF). Provision of this evidence is essential for facilitating WHO's recommendation of DTG/TAF/XTC as the preferred primary first-line treatment.

REFERENCES

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4. Venter FWD, et al. *Cutting the cost of antiretroviral therapy using newer, safer drugs.* South African Medical Journal. In Press.
5. Venter FWD, et al. *Transforming first line antiretroviral therapy with tenofovir alafenamide and dolutegravir: what do we need to do?* Draft.
6. Study Protocols (Confidential): WRHI060/ADVANCE, WRHI052, SSAT062, NAMSAL/ANRS 12313