



DTG/TAF/FTC DTG/TDF/FTC EFV/TDF/FTC

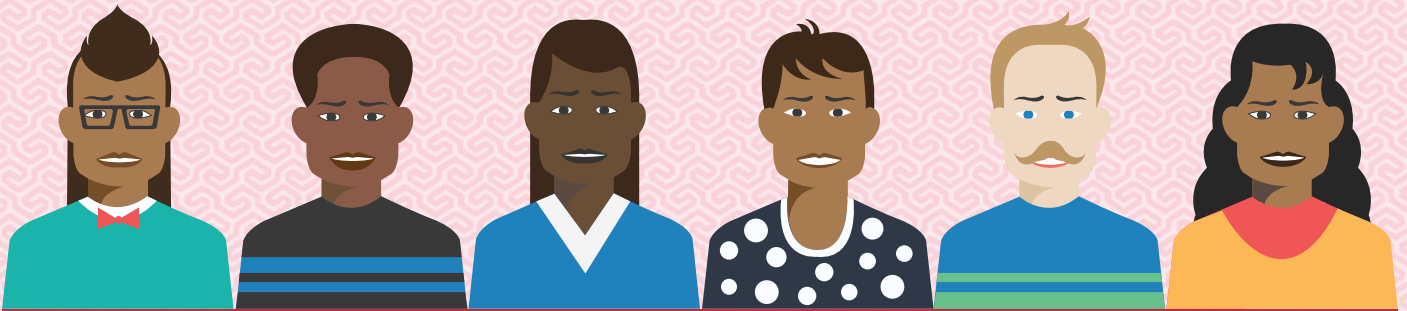
# THE ADVANCE STUDY

ADVANCE CLINICAL TRIAL, SOUTH AFRICA



## FREQUENTLY ASKED QUESTIONS

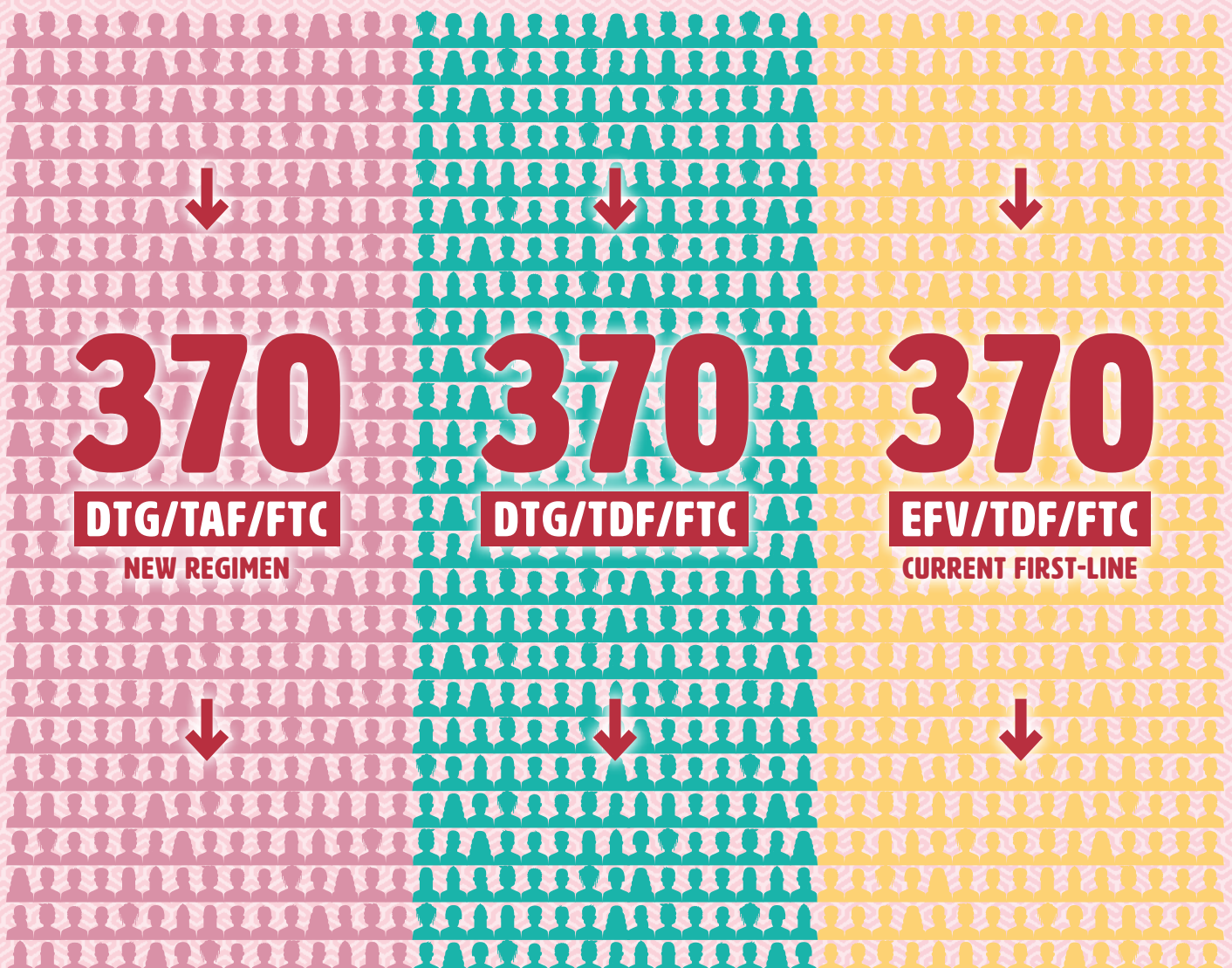
# THE ADVANCE STUDY



**1,100 HIV+ TREATMENT-NAIVE PARTICIPANTS**

+ PARTICIPANTS MUST: • be at least 12 years old • weigh at least 40kg • have a viral load >500 copies/mL  
+ Participants between the ages of 12 and 18 will be recruited and analysed separately

**RANDOMISED 1:1:1 INTO THREE GROUPS**



**370**

**DTG/TAF/FTC**

**NEW REGIMEN**

**370**

**DTG/TDF/FTC**

**370**

**EFV/TDF/FTC**

**CURRENT FIRST-LINE**

**PRIMARY OUTCOME: PROPORTION OF PARTICIPANTS IN EACH GROUP WITH A VIRAL LOAD <50 COPIES/ML AT 48 WEEKS**



## WHAT IS THE ADVANCE STUDY?

ADVANCE is a clinical trial designed to help change the current first-line HIV treatment (efavirenz/ tenofovir disoproxil fumarate/emtricitabine or EFV/TDF/ FTC) in South Africa and other low- and middle-income countries (LMICs).

## WHAT IS THE NEW REGIMEN?

The regimen that is being tested is dolutegravir/tenofovir alafenamide/emtricitabine (DTG/TAF/FTC). There is also a third arm in the trial with DTG/TDF/FTC.



## WHAT IS DOLUTEGRAVIR?

- DTG is an integrase inhibitor. When HIV infects a cell, it combines its genetic code into the cell's own code – this is called integration. DTG blocks integration, so HIV can't make more copies of itself.
- DTG is more effective, and has less side effects than EFV. But, it has not been used widely in LMICs.



## WHAT IS TENOFOVIR ALAFENAMIDE?

TAF is a nucleotide analogue and new version of tenofovir. It has a much lower dose than TDF (original version of tenofovir).

## DO THESE NEW DRUGS HAVE SIDE EFFECTS?

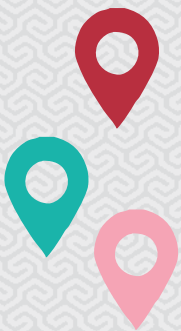
- There were less central nervous system (CNS) side effects with DTG than EFV in its registrational studies (conducted by the originator company to gain approval in the US and EU).
- There was an increased risk of insomnia but no increase in risk for other CNS side effects.
- More severe CNS side effects, including depression and feelings of wanting to commit suicide, have been very rare with DTG.
- Immune Reconstitution Inflammatory Syndrome (IRIS) happens mostly among people with low CD4 cell count starting first-line ART. As integrase inhibitors suppress viral load faster than other ARV classes, IRIS could be more likely in people taking them with low CD4. There have been some reports of an increased risk.
- TAF appears to be less likely to cause kidney damage and thinning bones than TDF.
- All ADVANCE participants will be monitored for potential side effects. Participants with low CD4 counts will be strictly monitored for IRIS.



## IF DOLUTEGRAVIR AND TAF ARE ALREADY BEING USED IN HIGH-INCOME COUNTRIES, WHY DO WE NEED A STUDY FOR LMICs?

- When new medicines are developed the clinical trials usually have few women and non-white participants. Pregnant women and people co-infected with TB are not included.
- Women of child-bearing age and people with HIV/TB make up large numbers of people with HIV in LMICs. We need to understand more about using new medicines in these groups.
- Other studies will also give us more information about using regimens with DTG and TAF in pregnancy and TB coinfection.





## HOW ARE THE REGIMENS COMPARED?

- ADVANCE is a non-inferiority study. This type of trial aims to show that a new treatment is not worse than the comparator or control (in this case EFV/TDF/FTC, the current first-line) by more than a small pre-specified amount.
- 1110 participants will be randomised in a 1:1:1 ratio to the three treatment groups. This means the participants will be split randomly and equally among the three treatment groups.
- The primary outcome (the most important outcome) is the proportion of participants with undetectable viral load less than 50 copies/mL at 48 weeks – compared by group.
- Secondary outcomes include: the proportion of participants with undetectable viral load less than 50 copies/mL at 96 weeks, CD4 count changes, tolerability (do people get any adverse effects or side effects), safety and efficacy of each regimen.

## WHO CAN JOIN THE STUDY?

Treatment naïve HIV positive people aged 12 years or more and weighing at least 40 kg with viral load of at least 500 copies/mL. Treatment naïve means they have never taken HIV treatment before.

## WHO CAN'T JOIN THE STUDY?

- People who have previously received 30 days or more of any ART or any ART within the last 6 months, pregnant women and people with TB coinfection or are on TB treatment.
- But women who become pregnant or people that develop TB while on the study can stay on it. People needing TB treatment will have their ART regimens adjusted.

## WHEN DOES THE STUDY START?

ADVANCE has started and is enrolling participants.

## WHEN WILL WE GET THE RESULTS?

The 48 week results will be available in 2018 and the final results in 2020.

## WHERE DOES THE STUDY TAKE PLACE?

There are three sites:

- **Wits RHI Yeoville Clinic**, 35 Bedford Street, corner Dunbar Street, Yeoville, Johannesburg – participants aged 19 and older.
- **Charlotte Maxeke Johannesburg Academic Hospital**, HIV/AIDS Adult Clinic, Area 556, Jubilee Road, Johannesburg – participants aged 19 and older.
- **Wits RHI Shandukani**, 2nd Floor, Hillbrow Health Precinct, corner Klein and Esselen Streets, Hillbrow, Johannesburg – only for adolescents (aged 12–18) and pregnant women

## WILL PARTICIPANTS IN THE ADVANCE STUDY

## BE REIMBURSED FOR STUDY VISITS?

Yes. The study team will discuss the reimbursement with them and let them know the amount.