SSAT062 (Low-dose EFV)

SSAT062 is designed to evaluate the pharmacokinetics (PK) of EFV 400mg in the presence of RIF and INH treatment for HIV co-infection with tuberculosis (TB). Providing the evidence needed to recommend EFV 400 mg instead of EFV 600 mg in combination with TDF/3TC or FTC as preferred first line antiretroviral regimens for HIV in countries where TB co-infections are common. Despite anticipation that EFV 400 mg may be eventually further replaced by DTG in many low income countries, investigating EFV 400 mg still has important added value, including 3 year projected cost savings of $336M. DTG trials must also address use in TB and pregnancy before it can replace EFV, therefore if DTG does not work or new toxicities arise EFV is likely the only agent available for broad use. Recent forecasting also suggests that while EFV use will decrease, it will remain a significant portion (50%) of first-line therapy for adults through 2023. Finally, middle income countries may not be able to realize the full potential of DTG savings due to drug patents, making lower-dose EFV the best alternative.

DRUG ABBREVIATIONS

EFV	efavirenz
RIF	rifampicin
INH	isoniazid
TDF	tenofovir disoproxil fumarate
3TC	lamivudine
FTC	emtricitabine
DTG	dolutegravir

Study Design & Methods

SSAT062 is a sequential 2 stage phase 1 study in males and females 18 years or older with a CD4 count > 100 cell/mm^3. Stage 1 is 98/99 (± 1) days of treatment and will take place in the UK, and stage 2 in Uganda will be 28 (± 7) days.

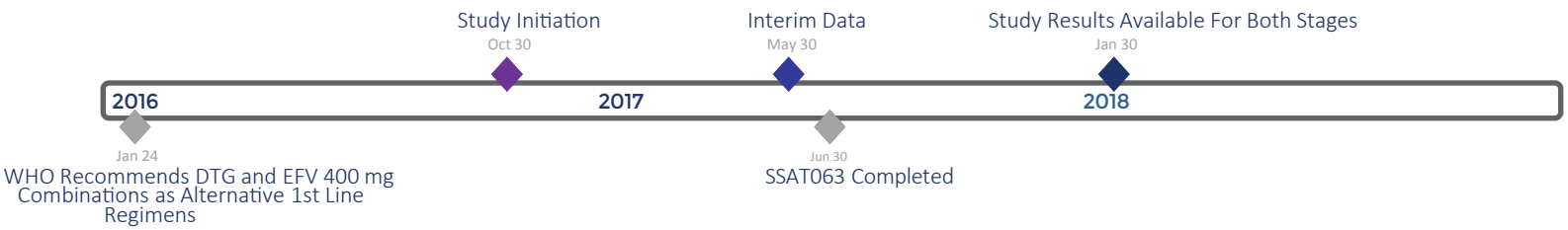
Stage 1: PK evaluation in 25 HIV-positive participants without TB infection on established EFV 600 mg-based ART switched to EFV 400 mg plus RIF and INH for 12 weeks (2 weeks after reduced EFV dose).

Stage 2: PK evaluation in 10 participants with HIV and TB co-infection on established EFV 600 mg-based antiretroviral treatment switched to EFV 400 mg plus RIF and INH for 28 weeks (2 weeks after reduced EFV dose)

Primary Outcome: Evaluate the steady-state PK of EFV 400 mg once daily during co-administration with RIF and INH

Secondary Outcomes: Assess the safety and tolerability of regimen, investigate association between genetic polymorphisms in drug disposition genes and drug exposure

Trial Timeline



Key Collaborations

SSAT062 is funded by USAID, through PEPFAR, and is being implemented by St. Stephen's AIDS Trust. SSAT062 received ethics and regulatory approvals from the United Kingdom Medicines and Health Products Regulatory Agency 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 SSAT062 SAC — in collaboration with the AIDS Clinical Trials Group, USAID, and NIH — have actively coordinated efforts to provide the PK evidence needed to support EFV 400 mg in TB co-infected patients after the ENCORE1 trial previously demonstrated EFV 400 mg was equivalent to EFV 600 mg. Mylan has independently funded a PK trial of EFV 400 mg in pregnant women (SSAT063). Together these PK studies are the final pieces needed for EFV 400 mg to be recommended in the preferred first-line antiretroviral regimen.

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