Safety and efficacy of Dolutegravir and EFV400 for pregnant and breastfeeding women: a randomized non-inferiority clinical trial

The project

PREGART is a multi-national clinical trial aimed to identify the optimal treatment regimen to prevent mother to child transmission of HIV. It will be carried out over a period of 60 months, enrolling nearly 1830 HIV infected pregnant and breastfeeding mothers in Ethiopia and Uganda.
PREGART project is funded by European and Developing Countries Clinical Trials Partnership (EDCTP). The study is conducted by four European and African partner organizations: Hawassa University (HU) - Ethiopia (coordinator), Makerere University - Uganda, Karolinska Institutet - Sweden, Istituto Superiore di Sanità - Italy.

Current treatment and hypothesis of intervention

According to WHO guidelines, HIV can be suppressed by combination ART consisting of 3 or more antiretroviral drugs (ARV), also during pregnancy and breastfeeding.
In WHO guidelines use of Tenofovir (TDF), Lamivudine (3TC) and standard dose of Efavirenz 600mg/day (EFV600) has been recommended as first line drugs for pregnant mothers.
Though systematic reviews and meta-analysis guarantee the safety of EFV, recent studies indicated a higher toxicity risk of the 600 mg/day dose of EFV in adults, including pregnant women. Recently WHO revised the HIV treatment guideline to include TDF and 3TC with a lower dose of EVF 400mg/day (EFV400) or Delutegravir (DTG) as first line ART regimen for adults, but pregnant and breastfeeding women are excluded from this recommendation because of lack of safety and efficacy data..
According to WHO, lack of these data remains a priority research gap.

The trial

The study consists of a multicenter, interventional, double blind, parallel assignment, and controlled three-arm non-inferiority randomized clinical trial.
HIV infected pregnant and breastfeeding women will be enrolled during their 2nd (12-24 weeks) trimester of pregnancy and will be randomly assigned to one of the three arms. The Arm 1, in which women will be treated with the current standard ART regimen (EFV 600 mg/day, TDF, 3TC), will serve as a control to compare safety and efficacy of different ART regimens. In the Arm 2 and Arm 3, Delutegravir and EFV 400 mg/day will be administered instead of EFV600 respectively.
The specific objectives of the project are:

1. to show that the combination TDF, 3TC, DTG is non-inferior to current standard ART regimen for pregnant and breastfeeding women;
2. to show that the combination TDF, 3TC, EFV400 is non-inferior to current standard ART regimen for pregnant and breastfeeding women;
3. To compare safety and efficacy of the first ART alternative with the second one.

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