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RANDOMIZED TRIAL OF RALTEGRAVIR-ART VS EFAVIRENZ-ART WHEN INITIATED DURING PREGNANCY

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Background:
There are no randomized trial data comparing the efficacy and safety of antiretroviral therapy (ART) containing an integrase inhibitor with efavirenz (EFV) when initiated during pregnancy.

Methods:
NICHD P1081 is a Phase IV multicenter, randomized open-label trial comparing HIV virologic response (plasma HIV viral load <200 copies/ml near delivery), tolerability (remaining on study drug through delivery), and safety (maternal and infant adverse event (AE) ≥grade 3) of ART when initiated during pregnancy. ART-naïve pregnant women with HIV were randomized to raltegravir (RAL)-or EFV-based ART through delivery. Enrollment began in Sept 2013 for women 28 to <37 weeks (wks) gestation (gest), was expanded to 20 to <37 wks gest after 22% were enrolled, and was completed in Feb 2018. Women and their infants were followed through 24 wks post-delivery. The randomization and primary statistical comparisons were stratified by gestage at entry.

Results:
408 pregnant women (206 RAL arm, 202 EFV arm) were enrolled at 19 sites in South America (n=210), Africa (n=144), Thailand (n=47) and the US (n=7), 205 (50%) at 20 to <28 wks and 203 (50%) at 28 to <37 wks. In the primary efficacy subgroup (n=307 with no HIV genotypic resistance to study ART at entry), a larger proportion of women in the RAL arm vs. EFV arm had delivery viral load <200 copies/mL (94% vs. 84%; p=.001), mainly among those enrolled at ≥28 wks gest (interaction p=.04); results were similar after including women with HIV genotypic resistance to study ART at entry (n=362, Table, interaction p=.06). Viral load decline was greater in RAL arm at study wks 2, 4 and 6 (Wilcoxon p<.05). Both regimens were well tolerated (Table). A larger proportion of RAL arm women achieved a rapid, sustained viral load reduction while staying on study drug until delivery, mainly by achieving a rapid viral load decline by study wk 2 (Table). There were no significant differences in occurrence of AE ≥grade 3 among women or infants, stillbirth, or preterm birth (Table). One RAL infant and 4 EFV infants were HIV infected (Fisher exact p>.05).

Conclusion:
Both regimens were well tolerated in women initiating ART during pregnancy. Viral load reduction with RAL-ART was faster leading to more women with delivery viral load <200 copies/mL. These data from the first large randomized trial comparing an integrase inhibitor with EFV-ART initiated during pregnancy support the use of RAL-ART during pregnancy, especially for women starting ART late in gestation.