DolPHIN-1: Randomised controlled trial of dolutegravir (DTG)- versus efavirenz (EFV)-based therapy in mothers initiating antiretroviral treatment in late pregnancy

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Background: ART initiation in the 3rd trimester of pregnancy is associated with failure to achieve viral suppression (VS) by delivery and increased transmission of HIV. We randomised 60 treatment naive pregnant women at 28-36w gestation in Uganda and South Africa 1:1 to receive EFV or DTG+2NRTIs. The primary endpoint was pharmacokinetics (PK) of DTG in women and breastfed infants; secondary endpoints included VS.

Methods: To comply with national guidelines, EFV+2NRTI was initiated on referral, with subjects randomized to DTG switched within 7 days. Viral load (VL) was collected at every visit; intensive maternal PK sampling (0-24h) was performed at 14 days on DTG, and 2 weeks post-partum, with paired sampling between maternal plasma and cord blood, breastmilk and infant plasma. All infants were exclusively breastfed.

Results: There was no significant pre-ART differences between DTG (n=29) and EFV (n=31) arms in maternal age, gestation at treatment initiation (30.8w), weight, obstetric history, VL (log 4 copies) and CD4 count (394 cells/mm\(^3\)). Third trimester DTG exposures were low with C\textsubscript{trough} at or below target (MEC 324ng/mL) in 9/28 (32\%) mothers. DTG transfer across the placenta (122\%) and in breast milk (3\%) coupled with delayed elimination resulted in significant infant exposures potentially persisting during breast-feeding. Both regimens were well-tolerated. A total of 10 SAEs were reported in 5 mothers and 3 infants, with no significant differences between arms.

Superior VS was observed with DTG (Table 1) at the 2w post-partum visit (P=0.005). However, VL>1000 copies/mL near delivery was still observed with both DTG (3.7\%) and EFV (7.4\%). No HIV transmissions were observed.

Conclusions: HIV RNA suppression < 50 copies/mL was more rapid with DTG (despite low DTG exposures when started in the third trimester) which may translate to improved PMTCT for ART initiation in late pregnancy. The impact of significant infant DTG exposures related to intrauterine transfer, continued breastfeeding and delayed elimination is being evaluated in the DolPHIN-2 study.

More information