RCT OF DOLUTEGRAVIR VS EFAVIRENZ-BASED THERAPY INITIATED IN LATE PREGNANCY: DOLPHIN-2

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Background:
ART initiation late in pregnancy is associated with failure to achieve viral suppression by delivery and increased MTCT.

Methods:
DolPHIN-2 (NCT03249181) is an open label trial, randomising (1:1) pregnant women from Uganda and South Africa initiating ART from 28w gestation to dolutegravir (DTG) vs efavirenz (EFV) plus 2NRTIs. Viral load (VL) was measured at baseline, 1w and 4w after initiation, then at 36w gestation and delivery, and 6w post-partum (PP). The primary endpoint was VL<50 cps/mL at delivery (measured up to 14d PP) for efficacy, and occurrence of drug toxicity in mothers and infants. Here we report on all primary trial endpoints through delivery.

Results:
All 268 mothers randomised were included in safety, and 237 (122 DTG, 115 EFV) in efficacy analyses by ITT. At enrolment there were no differences between DTG vs EFV in median gestation (31w), VL (log10 4.4 vs 4.5 cps/mL), CD4 count (464 vs 412 cells/µL) or other characteristics. The median duration of ART at delivery was 52 vs 59 days (range 0 – 133 days). VL<50 cps/mL at delivery was significantly higher with DTG (90/122, 74%) vs EFV (49/115, 43%); adjusted risk ratio (RR) and 95% CI, 1.66 (1.32-2.09) (Figure). This trend was consistent across subgroups of baseline VL; CD4 cell count; gestation at initiation; and other characteristics. VL<1000 cps/mL at delivery was also more likely in women on DTG vs EFV (93% vs 83%); RR, 1.11 (1.00-1.23). DTG was well-tolerated in pregnancy with no differences with EFV in frequency or organ class of severe adverse events. There were no significant differences between DTG and EFV arms in median gestational age at delivery (39.9w for both arms), or births at <34w (4.76% vs 5.13%) and <37w (16.67% vs 15.38%) gestation respectively. There were 4 stillbirths (aetiological factors under investigation), all in the DTG arm. Of 270 live births, congenital anomalies (excluding umbilical hernias and birthmarks) were reported in 17 infants (DTG 8, EFV 9) up to 6w of age; no neural tube defects were observed. There were 7 infant deaths (DTG 4, EFV 3). Three cases of MTCT were detected at birth, all from the DTG arm, and considered likely to be in-utero transmissions.

Conclusion:
DTG is well-tolerated and achieves more rapid virological suppression before delivery compared to EFV when initiated in late pregnancy. Late presentation in pregnancy is associated with poor outcomes despite ART and regardless of arm.