DOLUTEGRAVIR-BASED ART IS SUPERIOR TO NNRTI/PI-BASED ART IN INFANTS, CHILDREN AND ADOLESCENTS

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Background: ODYSSEY is an international randomised non-inferiority trial evaluating dolutegravir (DTG) + 2NRTIs versus standard-of-care (SOC) in children starting first or second-line ART.

Methods: Children weighing ≥14kg were enrolled to the main trial 09/16-06/18, children 3-<14kg were enrolled later 07/18-08/19. The primary outcome is a Kaplan-Meier(K-M) estimated proportion of treatment failure defined as confirmed viral load(VL) ≥400c/mL after week 36, no virological response by 24 weeks with ART switch, death or new/recurrent WHO4/severe WHO3 event by 96 weeks. Main trial data were analysed first. Data on children <14kg were analysed with a Bayesian approach, using information from those ≥14kg as a prior distribution (weight 78%).

Results: 707 children ≥14kg were randomised (Uganda 47%, Zimbabwe 21%, South Africa 20%, Thailand 9%, Europe 4%); 350 DTG (most took adult 50mg film-coated tablets following results of nested PK studies), 357 SOC. Median age 12 years; weight 31kg. 311 children started first-line (92% EFV in SOC); 396 second-line (98% boosted PIs in SOC). 47 (K-M estimate, 14%) DTG vs 75(22%) SOC had treatment failure by 96 weeks; difference (95% CI) -8%(-14, -3); p=0.004. 85% failures were virological. Treatment effects were similar on first and second-line (heterogeneity p=0.16). 85 children <14kg were randomised (all in Africa); 42 DTG, 43 SOC (DTG given as 5mg dispersible tablets dosed using WHO weightbands). Median (range) age 1.4 years (0.1,5.9); weight 8kg (3,13). 85% children started first-line. In SOC 74% took LPVr. 11 (K-M estimate 29%) DTG vs 21(48%) SOC had treatment failure by 96 weeks. In the Bayesian analysis, the estimated difference (95% CI) was -11%(-19, -2); p=0.02. A standalone analysis of the <14kg cohort and a pooled analysis of both cohorts also showed superior efficacy for DTG. Proportions of children with SAEs or grade ≥3 events were similar between arms. At 96 weeks total cholesterol was lower on DTG (difference (DTG-SOC) -15mg/dL(-19,-11), p<0.001 in ≥14kg; -26(-42,-9), p=0.003 in <14kg. In children ≥14kg, weight, height, BMI increased marginally more in DTG than SOC (differences between arms 1kg, 0.8cm, 0.3kg/m^2 respectively at 96 weeks).

Conclusions: DTG-based ART was superior to SOC based on treatment failure by 96 weeks in infants/children/adolescents starting first or second-line. There were no safety concerns on DTG. Results strongly support treatment guidelines recommending DTG-based regimens for children.