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

Abstract Number:

174

Authors:

Anna Turkova[1], for the ODYSSEY/PENTA-20 Trial Team

Institutions:

[1]MRC Clinical Trial Unit at UCL, London, UK

Background:

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

Methods:

The primary outcome is a Kaplan-Meier estimated proportion of treatment failure defined as confirmed viral load (VL) ≥400c/mL after week 36, lack of virological response by 24 weeks with ART switch, death or new/recurrent WHO4/severe WHO3 event by 96 weeks. Non-inferiority margin is 10% (12% for first-/second-line subgroups).

Results:

707 children ≥14kg were randomised (Uganda 47%, Zimbabwe 21%, South Africa 20%, Thailand 9%, Europe 4%); 350 to DTG; 357 to SOC. Median (range) age was 12.2 years (2.9-18); weight 31kg (14-85); 51% male. 311 children started first-line (92% efavirenz among SOC); 396 second-line (72% lopinavir/ritonavir, 25% atazanavir/ritonavir among SOC). Median follow-up was 142 weeks; 687 (97%) reached the primary endpoint or were seen on/after 96 weeks. 48 (14%) DTG vs 75 (22%) SOC had treatment failure by 96 weeks; difference (95% CI) −7.7% (-13.2, -2.3); p=0.006. 40 vs 67 were virological failures and 8 vs 8 were WHO3/4 events/death. Treatment effects were similar in first- and second-line, with no evidence of heterogeneity (p=0.20; fig). 13 (4%) children randomised to DTG changed regimen during follow-up vs 32 (9%) SOC (excluding NRTI changes and changes for growth, simplification, guideline change, stock-out) (p=0.004); 2 vs 21 changes were for treatment failure. At 48 and 96 weeks, proportion with cross-sectional VL<50c/mL and change in CD4 count from baseline were similar between arms. There were 65 SAEs (35 children) in DTG versus 46 (42) in SOC (p=0.45), including 2 vs. 3 deaths; 119 (73 children) grade ≥3 adverse events in DTG vs 135 (88) in SOC (p=0.23). At week 96, mean change in total cholesterol from baseline was -5 mg/dL (95% CI -8,-2) in DTG versus 10 mg/dL (7,13) in SOC (difference (DTG-SOC) -15 (-19,-11); p<0.001). Weight, height and BMI increased marginally more in DTG than SOC (differences (SE) between arms 1kg (0.4), 0.7cm (0.3), 0.3kg/m2 (0.1) respectively at 96 weeks).

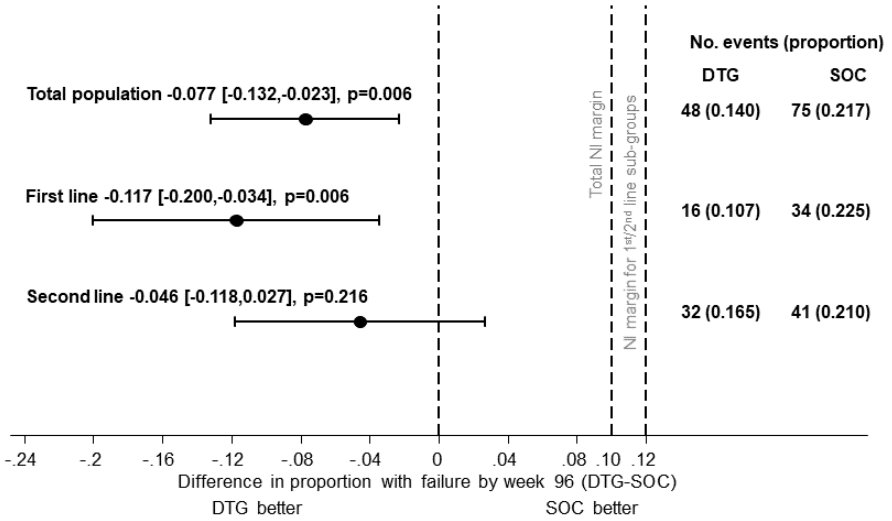
Conclusion:

DTG-based ART was superior to SOC based on treatment failure by 96 weeks in children/adolescents starting first- or second-line. There were no safety concerns on DTG. These results support WHO guidelines which recommend DTG-based regimens as preferred ART for children ≥14kg starting first- or second-line ART, allowing harmonisation with adult treatment programmes.

Clinical:

(Q) HIV, SARS-CoV-2, or Both in Infants, Children, and Adolescents

Fig. Difference in proportion with clinical or virological failure by 96 weeks (DTG-SOC)



Test for heterogeneity of treatment effect by first-/second-line: p=0.201

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