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Child Health Research

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No age-related difference in dolutegravir metabolic glucuronidation ratio in children between 3 months and 18 years old in the ODYSSEY trial

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Background

- Dolutegravir (DTG)-based ART is preferred for children living with HIV.
- DTG exposure in children is lower and more variable compared to adults based on mg/kg dose.
- DTG is mainly metabolized by UGT1A1 into its inactive metabolite DTG glucuronide (DTG-gluc).
- This study aimed to assess whether DTG-gluc/DTG molar metabolic ratio (DTG-MR) in children changes with age and causes differences in DTG pharmacokinetics compared to adults.



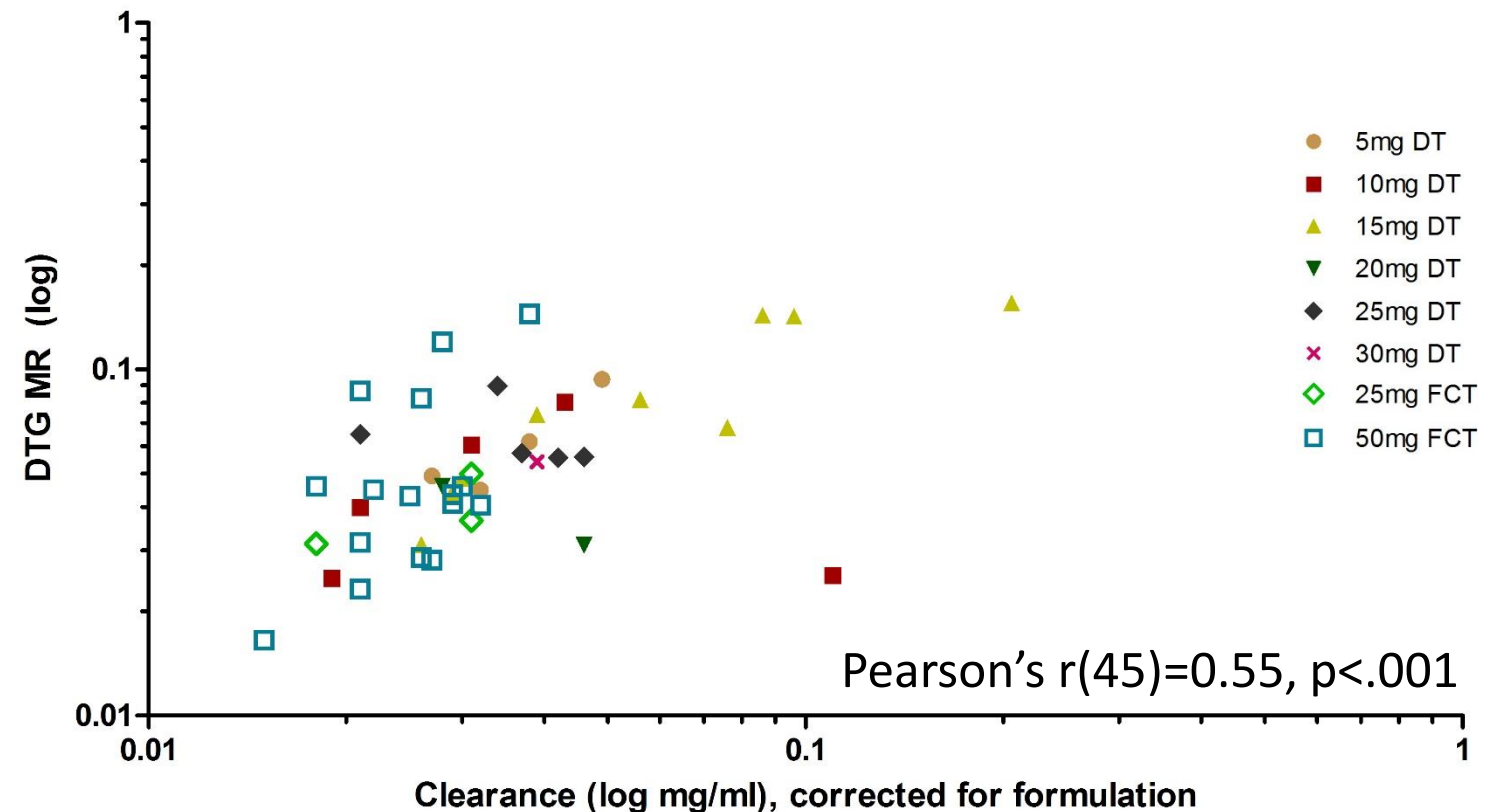
Methods

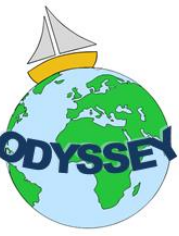
- Subjects included in this study were selected from ODYSSEY PK substudies.
- DTG and DTG-gluc concentrations were measured with a validated UPLC-MS/MS assay.
- Geometric mean (GM) DTG-MR was determined using 3 plasma samples per PK curve (t=2, 6 and 24h).
- Pearson's correlation coefficient was used on log-transformed data to assess the relationships between DTG-MR and DTG oral clearance/kg (corrected for higher bioavailability of DT, using factor of 1.8), and DTG-MR and age (not log-transformed).

Results

- 45 children (age 3 months – 18 years) included
- DTG-MR positively correlates with clearance
- No relation between DTG-MR and age
- GM DTG-MR in children was 0.052(66%)

DTG metabolic glucuronidation ratio by DTG Clearance





Conclusions

- DTG-MR is likely to contribute to high variability of DTG exposure seen in children.
- DTG-MR in children was similar to adult values and did not change with age.
- Further studies are needed to assess the role other factors contributing to differences in DTG exposure in children.

Thank you

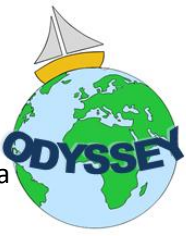
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- ODYSSEY investigators
- Trial Management Team
- Trial Steering Committee
- Data Monitoring Committee
- Endpoint Review Committee
- Penta (sponsor)
- ViiV Healthcare (funder)
- Mylan



Smarter Studies
Global Impact
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