Pharmacokinetics and Efficacy of Dolutegravir Dispersible Tablets in Thai Children - Living with HIV Weighing 6 to below 20 kg (DTGkids)

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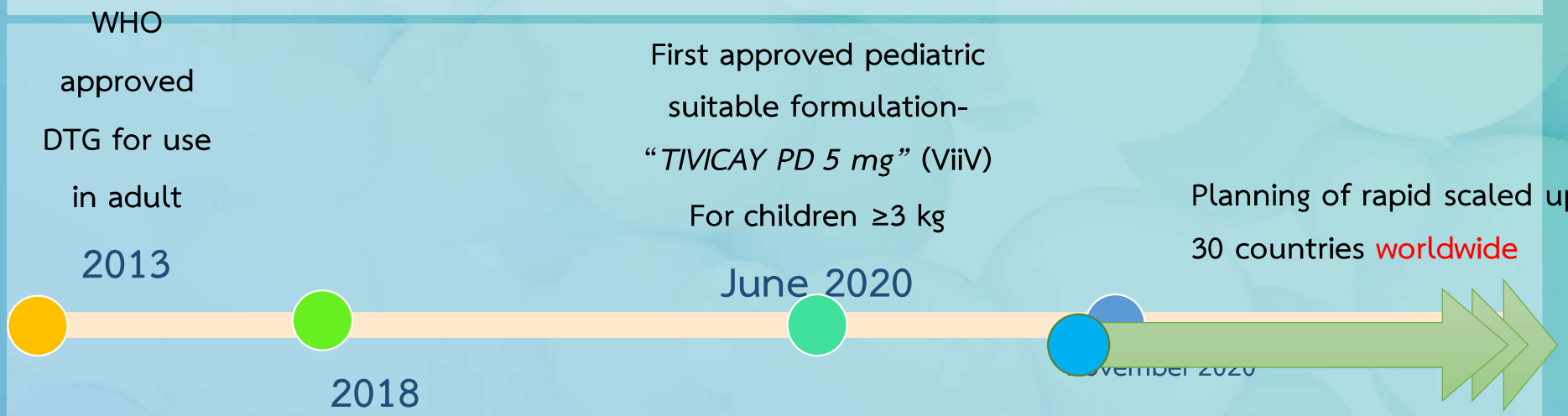
Background and Rationale

- Dolutegravir (DTG) based ART is a preferred regimen due to its excellent antiviral efficacy, high genetic barrier to resistance, less S/E, and once-daily dosing regimen thus facilitating better drug compliance.
- DTG was recommended as first-line ART for children and adults worldwide



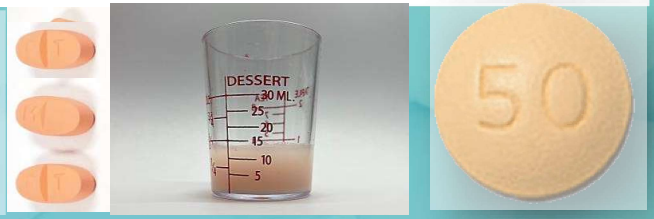
DTG pharmacokinetic properties

Trough Concentration (C_{trough} or C_{24h}) = parameter for predicting antiviral efficacy of DTG at steady state (Adult C_{trough} = 0.83 mg/L)

EC90 = concentration at which 90% of the maximl viral load reduction was obtained in a 10-day monotherapy study (0.32 mg/L)

Film-Coated Tablet (FCT) vs Dispersible tablet :

- DT has 60-80% greater bioavailability than FCT.
- Recommended DT cannot be directly compared to those using FCT



Pharmacokinetic study (PK) of DTG in children: ≥20 kg

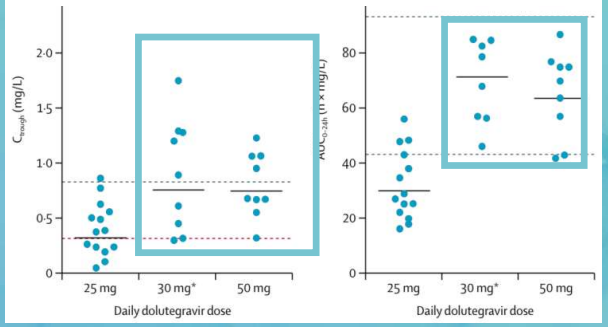
DTG formulation for children weight ≥20 kg

- Children weighing ≥20 kg can take either once daily

50 mg FCT ⟷ 30 mg DT

Both dose and preparation provided similar PK and comparable efficacy to adults.

Individual DTG C_{trough}, AUC_{0-24h} in children weighing 20 to <25 kg



Bollen PDJ, et al. The Lancet HIV 2020;7:e533-e44.

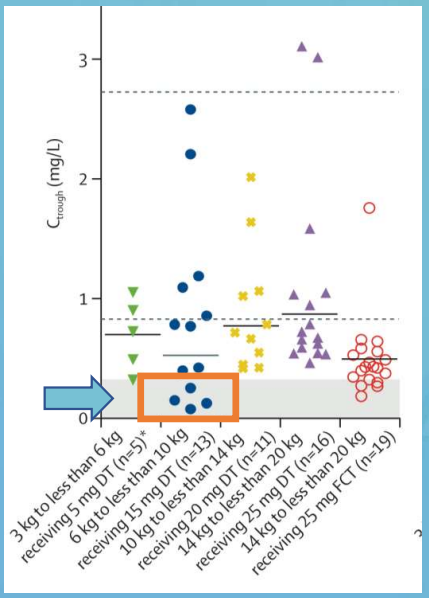
Background and Rationale

FDA recommended doses DTG-DT for children age ≥ 4 wk and BW 3 to < 20 kg

BW (kg)	3 to <6	6 to <10	10 to <14	14 to <20
DTG DT (mg)*	5	15	20	25

DTG DT pharmacokinetics studies in CLHIV weight 3 to < 20 kg

- The ODYSSEY substudy
- IMPAACT P1093



The ODYSSEY trial DTG PK

The smallest weight band (WB 6 to <10 kg): DTG DT 15 mg once daily

- GM trough concentration (C_{24h}) was 36% lower than adult reference (0.53 vs 0.83 mg/L) 31% did not achieve EC90 of 0.32 mg/L

Rationale of this study

- To add the knowledge of the pharmacokinetic profile of generic formulation of DTG dispersible tablet which will be widely accessible in Thailand and Worldwide.
- PK profiles would be within the reference PK ranges

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Study objectives

- Primary objective was to evaluate the steady-state pharmacokinetics parameter (PK) and efficacy of generic DTG DT
    - $C_{trough\ or}\ C_{24h}$ (trough concentration) * *
    - $AUC_{0\text{-}24h}$
    - C_{max}
- Secondary objectives were to evaluate efficacy and safety endpoint
    - Proportion of participants with HIV VL <200 copies/mL
    - Incidence of serious and severe adverse events (grade 3 or more) associated with DTG.