24 week Efficacy and Safety of Efavirenz- and Dolutegravir-based antiretroviral Therapy with isoniazid and rifapentine for Tuberculosis Preventive Therapy (1 HP and 3HP) in Thai people living with HIV

Anchalee Avihingsanon[1,2], S. Jirajariyavet[3], P. Treebupachatsakul[4], T.P.N. Ayuthaya[5], S. Gatechompol[1,2], J. Sophonphan[1], P. Danpornprasert[6], W. Imsanguan[7], J. Visuthranukul[8], S. Wiwatrojanagul[9], V. Klinbuayaem[10], P.Noopetch,[11], C. Fujitnirun[12], P. Panarat[13], N. Saetiew[14], S. Mekviwattanawong[15], H.M.S. Lwin[1], W.M. Han[1,2], S.J Kerr[1,16,17], G. Suwanpimolkul[2,18], P. Chetchotisakd[19]

[1] HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok, Thailand, [2] Center of Excellence in Tuberculosis, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [3] Infectious Disease Taksin Hospital, Bangkok, Thailand, [4] Infectious Disease Buddhachinaraj Phitsanulok Hospital, Phitsanulok, Thailand, [5] Health Center 28 (Krung Thon Buri), Krung Thon Buri, Thailand, [6] Klang Hospital, Bangkok,Thailand, [7] Infectious Disease Chiangrai Prachanukroh Hospital, Chiang Rai, Thailand, [8] Police General Hospital, Department of Medicine, Bangkok, Thailand, [9] Maharat Nakhon Ratchasima Hospital,Department of Medicine, Nakhon Ratchasima, Thailand, [10] Sanpatong Hospital, Chiangmai, Thailand, [11] Hatyai Hospital, Department of Medicine, Songkla, Thailand, [12] Bhumibol Adulyadej Hospital,Department of Medicine, Bangkok, Thailand, [13] Queen Savang Vadhana Memorial Hospital, Department of Medicine, Chonburi, Thailand, [14] Sisaket Hospital, Department of Medicine, Sisaket, Thailand,[15] Pranangklao Hospital, Department of Medicine, Nonthaburi, Thailand, [16] Biostatistics Excellence Centre, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [17] The Kirby Institute, University of New South Wales, Sydney, Australia, [18] Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, [19] Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Background

- There is limited data to inform evidence-based co-administration of DTG/TDF/3TC (TLD) with daily isoniazid and rifapentine for 1 month (1HP) or weekly HP for 3 months (3HP) for TB preventive therapy (TPT) among people living with HIV (PLWH), particularly from Asia
- In March 2022, the A5372 study reported there was lower oral clearance and higher dolutegravir (DTG) concentrations among PLWH, especially Asian participants[1]
- Radiant TB demonstrated similar efficacy of DTG 50 mg vs DTG 50 mg BID in HIV/TB patients on rifampicin from South Africa[2]

Methods

- A randomized control trial of 1 HP vs 3 HP for TPT among PLWH was conducted in 15 HIV clinics in Thailand
- For ART: EFV/TDF/FTC was used until March 2022, after that, TLD was allowed
- ALT was monitored at weeks 0, 1, 12 then every 24 weeks. CD4 and creatinine were measured at week 0, and every 24 weeks thereafter
- HIV-1 RNA was measured at 24, 48, 96 and 144 weeks
- We report here the 24 weeks efficacy of TLD with 1 HP or 3 HP

Results

- Of 1257 participants analyzed, 854 (68%) were taking EFV/TDF/FTC and 403 (32%) were taking TLD; 629 (50%) participants received 1HP for TPT
- Baseline characteristics, safety and efficacy of ART are presented in Table 1
- Median ART duration prior to TPT was 3.2 (IQR:0.8-38.5) months; the majority of participants started TPT within 6 months of ART initiation (56%), especially in the TLD group (84%)
- At week 24, the percent with HIV VL ≤50 copies/mL was high in both EFV/TDF/FTC (92.2% 1HP and 91% 3HP) and TLD (92.8% 1HP and 94.7% 3HP) groups (Figure 1B)
- Participants with elevated grade 2 ALT were mostly asymptomatic and self-limited, occurring in 9.2% of participants on EFV/TDF/FTC (6.9% of 1 HP and 2.9% 3HP) and 7.3% among those on TLD (5.7% of 1 HP and 1.6% 3HP)
- ALT elevated grade 3 or 4 during TPT occurred 2.5% in participants on EFV/TDF/FTC (1.9% of 1 HP and 0.6% 3HP) and 2.5% among those on TLD (2.4% of 1 HP and 2.5% 3HP)
- Hypersensitivity reactions during TPT was 0.1% among those on EFV/TDF/FTC (0% of 1 HP and 0.2% 3HP) and 1% in participants on TLD (1.1% of 1 HP and 0.9% 3HP)

Figure 1. (A) CD4 week 24 change from baseline, (B) viral suppression at week 24, and (C) ALT grading.

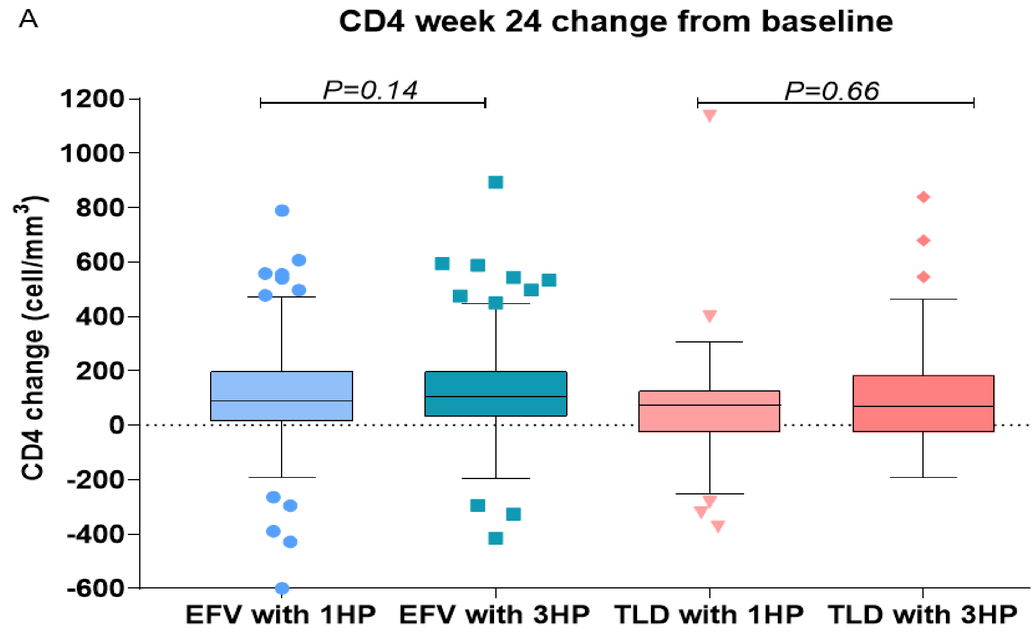

Table 1. Baseline characteristics of participants (at TPT start).

Baseline	Total (N=1257)	EFV/TDF/FTC		TLD	
		1HP (N=444)	3HP (N=410)	1HP (N=185)	3HP (N=218)
Age (years)	31 (25-41)	30 (25-40)	30 (25-39)	33 (27-44)	33 (25-42)
Male	1052 (83.7)	385 (86.7)	358 (87.3)	141 (76.2)	168 (77.1)
Weight (kg)	62.5 (55.3-72)	62 (55.5-71)	62.5 (55-71.3)	64.1 (57.1-72.9)	62.7 (55.1-73)
BMI (kg/m^2)	21.9 (19.8-24.5)	22.8 (20.8-25.4)	22.5 (20.4-24.7)	21.9 (19.9-24.5)	22.0 (19.8-24.6)
ART Duration (months)	3.2 (0.8-38.5)	2.1 (0.7-19.3)	1.9 (0.6-13.4)	10.9 (1.7-121)	16.0 (1.4-117)
< 6 months	701 (55.8)	283 (63.7)	260 (63.4)	67 (36.2)	91 (41.7)
≥ 6 months	556 (44.2)	161 (36.3)	150 (36.6)	118 (63.8)	127 (58.3)
CD4 cell count	353 (228-539)	315.5 (220-456)	314 (204-470)	507 (325-694)	445 (300-633)

Data are presented as median (p25-p75) or n (%)

Conclusion

Similar efficacy and safety was observed for PLWH 24 weeks after receiving dolutegravir and efavirenz based ART, co-administered with 1HP or 3HP, suggesting once daily DTG doses were appropriate with 1HP or 3 HP, especially among a Southeast Asian population

Acknowledgement:
We express our sincere gratitude to the participants of the LTBI project for their invaluable contributions to this research. We also extend our appreciation to the entire team of professionals involved in this study.

References:
1 Podany A CROI 2022 Feb 11-16, virtual meeting abstract 78; 2 Griesel R et al Lancet HIV May 23, 2023

Presented at IAS 2023, the 12th IAS Conference on HIV Science

IAS 2023 23–26 July