ARV Therapies and Therapeutic Strategies

INDEPENDENT REPORTING ON EACS 2017

COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

TWICE DAILY ADMINISTRATION OF TENOFOVIR ALAFENAMIDE IN COMBINATION WITH RIFAMPIN: POTENTIAL FOR TENOFOVIR ALAFENAMIDE USE IN HIV-TB COINFECTION

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Abstract PS13/4

TWICE DAILY ADMINISTRATION OF TENOFOVIR ALAFENAMIDE IN COMBINATION WITH RIFAMPIN: POTENTIAL FOR TENOFOVIR ALAFENAMIDE USE IN HIV-TB COINFECTION

- TAF is a substrate of human drug transporters
- RIF is commonly used in a multi-drug regimen for TB
- RIF is potent inducer and associated with DDI

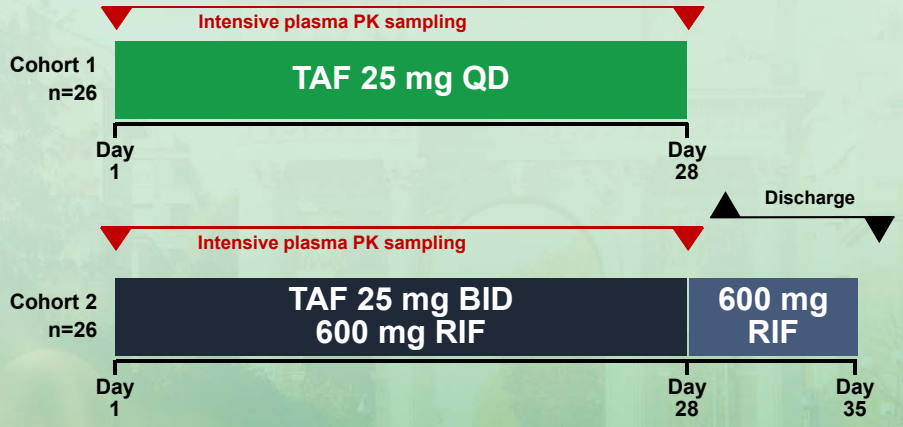
DDI Mechanism		TAF	RIF
Drug transporters	P-gp/BCRP	Substrate	Inducer
	OATP1B1/1B3	Substrate	Inducer

To evaluate the PK of TAF, TFV-DP, and plasma TFV, following co-administration of TAF BID with RIF 600 mg OD vs TAF OD

Custodio K, et al; 16th EACS, Milan, Italy, October 25-27, 2017; Abst. PS13/4.

STUDY DESIGN

- Phase 1, open-label, parallel-design, multiple-dose, single center study in healthy subjects



TAF QD administered as Bictegravir/Emtricitabine/TAF QD; TAF BID administered as Bictegravir/Emtricitabine/TAF BID

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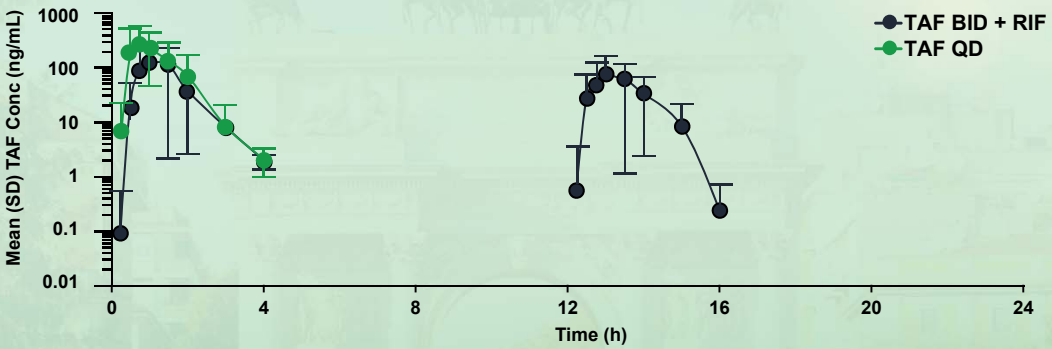
RESULTS: TAF PLASMA PK = 15% REDUCTION



TAF PK Mean (%CV)	TAF QD n=26 (ref)	TAF BID + RIF n=26 (test)	GLSM Ratio 90% CI
AUC_{0-24} (ng•h/mL)	345 (52)	290 (48)	85.8 (69.7, 106)
C_{max} (ng/mL)	471 (72)	207 (64)	44.1 (33.2, 58.7)

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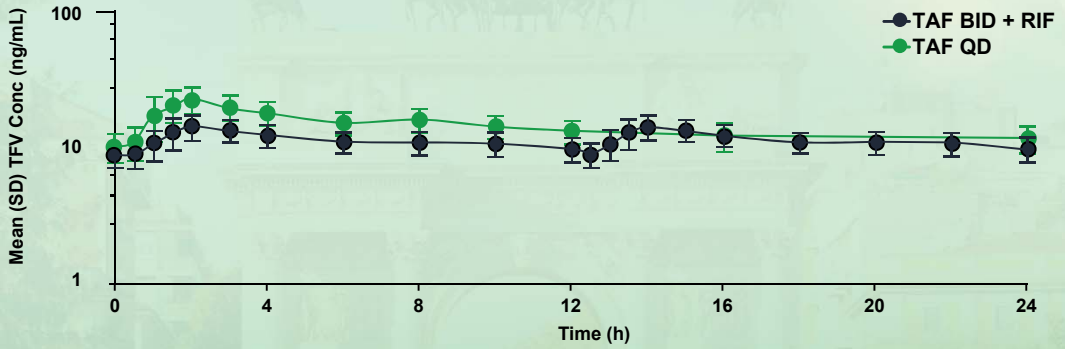
RESULTS: PLASMA TFV PK = 30% REDUCTION



TAF PK Mean (%CV)	TAF QD n=26 (ref)	TAF BID + RIF n=26 (test)	GLSM Ratio 90% CI
AUC_{0-24} (ng•h/mL)	348 (20)	277 (19)	79.9 (73.1, 87.3)

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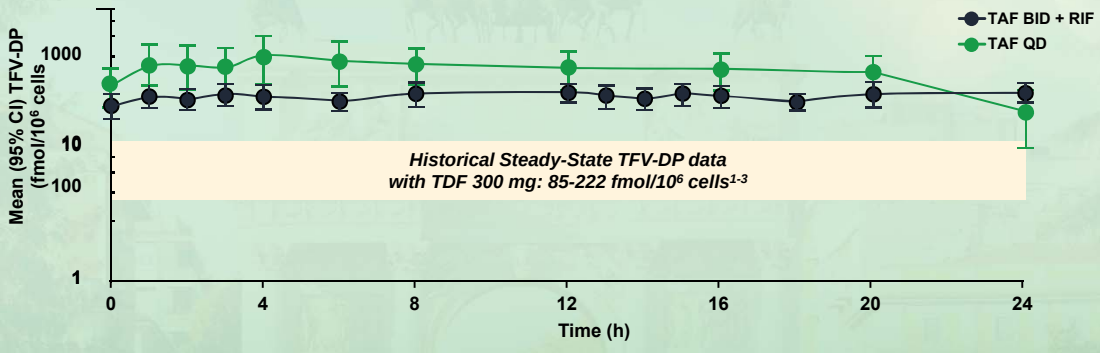
RESULTS: TFV-DP PK = 24% REDUCTION



TFV-DP PK	GLSM Ratio (90% CI)
AUC_{0-24} (fmol•h/10^6 cells)	76.3 (58.7, 99.2)

Conclusions: TAF plus RIF was well tolerated
No Grade 3 / 4 AEs or lab changes
PD evaluations in patients with TB and HIV needed

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