



Eighth International Congress on Drug Therapy in HIV Infection

Glasgow, UK - 12-16 November 2006

[PL5.2] TMC125 IN COMBINATION WITH OTHER MEDICATIONS: SUMMARY OF DRUG-DRUG INTERACTION STUDIES

Int Cong Drug Therapy HIV 2006 Nov 12-16;8:Abstract No. PL5.2

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PURPOSE OF THE STUDY: TMC125 is a next generation NNRTI with potent activity against both wild-type and NNRTI resistant HIV-1. *In vitro* TMC125 is a substrate and inducer of CYP3A4 and a substrate and inhibitor of CYP2C. A summary of the pharmacokinetic (PK) interactions between TMC125 co-administered with other medications commonly used in HIV-infected patients is presented.

METHODS: PK studies were conducted at steady-state. Two-way interaction studies were conducted with TMC125 and didanosine (ddI), tenofovir (TDF), the ritonavir (rtv)-boosted PIs darunavir (DRV), fosamprenavir (FPV) and tipranavir (TPV). The 1-way effect of omeprazole (OME) and ranitidine (RAN) on TMC125, and the 1-way effect of TMC125 on lopinavir (LPV) with saquinavir (SQV), methadone (MET) and sildenafil (SIL) were also studied.

SUMMARY OF RESULTS: TMC125 increases exposure to FPV 69% and decreases exposure to SIL 57% and N-desmethyl-SIL by 41%. TMC125 had no significant effect on ddI, DRV, LPV, MET, SQV, TDF or TPV. TPV/rtv decreased TMC125 exposure by 76%. No relevant changes on TMC125 were observed when combined with ddI, TDF, FPV/rtv or RAN. TMC125 exposure decreased 37% and increased by 41% in combination with DRV/r and OME, respectively - these changes are not considered clinically relevant. TMC125 PK were comparable to historical controls when co-administered with LPV/SQV/rtv, MET, or SIL.

CONCLUSIONS: TMC125 can be combined with most of the drugs studied without dosage adjustment. Dose adjustments may be required for FPV and SIL. It is not recommended to combine TMC125 with TPV/rtv. Drug interactions between TMC125 and medications commonly used in HIV

therapy are well characterized and manageable.

Plenary Session: Oral Papers

2006-11-12

PL5.2

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