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Efficacy and safety of TMC278 in treatment-naïve, HIV-infected patients: week 96 data from TMC278-C204

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Background

NNRTIs are very effective antiretrovirals, but new NNRTIs with improved tolerability are needed.

Methods

A randomised Phase IIb study assessed the investigational next-generation NNRTI, TMC278, 25, 75 and 150 mg QD blinded up to 96 weeks and an open-label control, efavirenz (EFV) 600 mg QD in 368 treatment-naïve patients (33% females). All patients received AZT/3TC (76%) or TDF/FTC (24%).

Summary of results

No differences in efficacy were observed across TMC278 arms or vs. EFV at week 96. The potent antiviral efficacy of TMC278 at week 48 was sustained to week 96. Mean increase from baseline in CD4 cell count was higher at week 96 vs. 48. (Table 1.)

At week 96 vs. week 48, there were few TMC278 dose-related effects, and no change in types nor notable increase in incidence of AEs. All rashes were grade 1 or 2, except one case of grade 3 rash (TMC278 75 mg arm, dapsone-related). Rashes resolved with continued dosing (median duration: all TMC278 17 vs. EFV 15 days). Incidences of grade 3 or 4 nervous system AEs (no discontinuations; all TMC278: 0.7% vs. EFV: 1.1%) and psychiatric AEs (1.8% vs. 1.1%) were low. Psychiatric AEs led to discontinuation in 0.4% vs. 2.2% of patients.

Conclusion

Over 96 weeks, TMC278 demonstrated a high, sustained virological response rate and was generally well tolerated with lower incidences of rash, nervous system and psychiatric AEs, and less lipid increases than EFV.

Table 1:

Parameter	Wk	TMC278 25 mg qd (n = 93)	TMC278 75 mg qd (n = 95)	TMC278 150 mg qd (n = 91)	TMC278 All (n = 279)	EFV 600 mg gd (n = 89)[1]
VL <50 cps/mL (ITT-TLOVR algorithm), % (95% CI)	48	80(71–88)	80(72–88)	77(68–86)	79(74–84)	81(73–89)
	96	76(68–85)	72(62–81)	71(62–81)	73(68–78)	71(61–80)
Mean (SE) increase from baseline in CD4 cell count, cells/mm^3	48	122(12)	145(15)	143(15)	137(8)	127(11)
	96	146(12)	172(16)	159(16)	159(9)	160(13)
AE incidence at Wk 96 (%)						
Any AE		90	97	92	93	93
AEs leading to discontinuation		9	12	14	12	9
Any grade 3 or 4 AEs		30	25	26	27	21
Any serious AEs		13	14	10	12	15
Grade 3 or 4 lab abnormalities		33	22	24	27	24
AEs of interest* †						
Any Rash		5	10	13	9‡	21
Nervous system AEs		32	32	30	31‡	48
Headache		17	23	19	20	16
Dizziness		13	10	10	11‡	30
Somnolence		3	3	4	4§	11
Psychiatric AEs		17	17	14	16	21
Insomnia		8	6	7	7	6
Depression		7	6	3	5	7
Abnormal dreams/nightmares		1	6	0	3	11
Mean (SD) changes from baseline in lipids (mg/dL)						
Total cholesterol (TC)		10(28)	8(35)	9(29)	9(31)‡	34(31
LDL-C		5(25)	5(30)	3(25)	5(27)‡	18(28)
HDL-C		6(10)	7(11)	6(12)	6(11)‡	11(12)
Ratio TC/HDL-C		-0.4(1.3)	-0.5(1.1)	-0.3(1.0)	-0.4(1.1)	0.1(0.9)
Triglycerides		-8(75)	-15(79)	-7(90)	-10(81)‡	29(87)

1N = 88 for CD4; *Regardless of causality, occurring in ≥ 5% in any group; †well-described AEs for current NNRTIs; §p < 0.05, ‡p < 0.01 vs EFV; Fisher Exact test (AEs); non-parametric Wilcoxon rank-sum test (lipids)