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Oral Abstract Session
THLBB2 - Late Breaker Track B - 2

THLBB206 - Pooled week 48 efficacy and safety results from ECHO and THRIVE, two double-blind, randomised, phase III trials comparing TMC278 versus efavirenz in treatment-naïve, HIV-1-infected patients

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Background: Pooled 48-week primary analysis results of two Phase III trials with TMC278, ECHO (TMC278-C209, NCT00540449) and THRIVE (TMC278-C215, NCT00543725), are presented.
Methods: These international trials include treatment-naïve adult patients receiving (1:1) TMC278 25mg qd or efavirenz 600mg qd, plus either tenofovir disoproxil fumarate (TDF)/emtricitabine (ECHO) or TDF/emtricitabine, lamivudine/zidovudine or abacavir/lamivudine (THRIVE). The primary objective was to demonstrate non-inferiority of TMC278 to efavirenz in confirmed virologic response (viral load [VL] < 50 copies/mL ITT-TLOVR algorithm) at Week 48.
Results: A total of 1368 patients were randomised and treated. Median baseline VL was 5.00 $\log_{10}$ copies/mL and median CD4 256 cells/mm^3. TMC278 showed non-inferior efficacy versus efavirenz (Table). The virologic failure rate was 9.0% in the TMC278 group and 4.8% in the efavirenz group. There were lower incidences with TMC278 of adverse events (AEs) leading to discontinuation, and grade 2-4 AEs at least possibly related to treatment, rash, dizziness and abnormal dreams/nightmare (Table). Grade 3/4 laboratory abnormalities for cholesterol (0.1% vs. 2.5%), LDL-cholesterol (0.7% vs. 4.1%) and triglycerides (0.3% vs. 2.2%) were lower with TMC278 versus efavirenz, respectively (p≤0.001). There was no difference in QTc interval between groups.

	TMC278 25mg qd (n=686)	Efavirenz 600mg qd (n=682)	Difference between groups
Efficacy (Week 48 outcomes)			
VL <50 copies/mL (ITT-TLOVR), n (%) [95% CI]*	578 (84.3)	561 (82.3)	2.0 [-2.0,6.0]
ECHO	287/346 (82.9)	285/344 (82.8)	0.1 [-5.5,5.7]
THRIVE	291/340 (85.6)	276/338 (81.7)	3.9 [-1.7;9.5]
VL <50 copies/mL (per-protocol, ITT-TLOVR), n (%) [95% CI]	569/669 (85.1)	548/662 (82.8)	2.3 [-1.7,6.2]
Virologic failures,† n (%)	62 (9.0)	33 (4.8)	ND
Discontinued due to AE/death, n (%)	15 (2.2)	49 (7.2)	ND
Discontinued for other reasons, n (%)	31 (4.5)	39 (5.7)	ND
Mean [95% CI] increase from baseline in CD4 count (NC=F‡), cells/mm^3	192 [181,203]	176 [165,188]	NS
Resistance**			
Failures (regardless of discontinuation reason) n (%)	72 (10.5)	39 (5.7)	p=0.0014
Failures developing NNRTI mutations§, n	39/62¶	15/28¶	ND
Failures developing IAS-USA NRTI mutations, n	42/62¶	9/28¶	ND
Most frequent NNRTI and NRTI mutations	E138K, M184I	K103N, M184V	
Safety**			
Grade 2–4 AE at least possibly related to treatment, n (%)	109 (15.9)	212 (31.1)	p<0.0001#
Serious AEs, n (%)	45 (6.6)	55 (8.1)	NS
AEs leading to discontinuation, n (%)	23 (3.4)	52 (7.6)	p=0.0005
AEs of interest at least possibly related to treatment¥, n (%)			
Psychiatric Abnormal dreams/nightmare	102 (14.9) 56 (8.2)	155 (22.7) 87 (12.8)	p=0.0002# p=0.0061#
Neurological events of interest Dizziness	117 (17.1) 55 (8.0)	258 (37.8) 179 (26.2)	p<0.0001# p<0.0001#
Rash (any type)	21 (3.1)	93 (13.6)	p<0.0001#

ITT-TLOVR = intent-to-treat-time-to-loss of virologic response; CI=confidence interval; ND = not determined as not predefined; NS=non-significant; *Based on normal approximation; **p-value for Fisher's Exact test; †Rebound or never suppressed; ‡NC=F = non completer = failure: missing values after discontinuation imputed with change=0; Last observation carried forward otherwise; §Extended NNRTI resistance-associated mutation list; ¶62/72 and 28/39 of these patients had resistance data; #Predefined analysis for these AEs; ¥Observed in ≥10% of patients in the combined TMC278 group or efavirenz group and excluding laboratory abnormalities reported as an AE

patients had resistance data; ‡Predefined analysis for these AEs; §Observed in ≥10% of patients in the combined TMC278 group or efavirenz group and excluding laboratory abnormalities reported as an AE

[Table]

Conclusions: Response rates were among the highest observed in recent treatment-naïve trials. TMC278 demonstrated non-inferior efficacy versus efavirenz, when administered with NRTIs. The virologic failure rate was higher with TMC278. Incidences of AEs leading to discontinuation, grade 2-4 AEs at least possibly related to treatment, rash, dizziness and abnormal dreams/nightmare, and grade 3/4 laboratory abnormalities for lipids were significantly lower with TMC278.
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Abstract Details

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Session	Late Breaker Track B (2/2)
Date	22.07.2010
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