Lipid profiles of TMC278 and efavirenz in treatment-naive, HIV-1-infected patients: pooled Week 48 data from the randomized, double-blind, Phase III ECHO and THRIVE trials

Jose Arribas,1 Jaime Andrade-Villanueva,2 Nick Bellos,3 Pedro Cahn,4 Christina Katlama,5 Jacob Lazarek,6 Kiat Ruxrungtham,7 David Wohl,8 Simon Vennevel,9 Katia Boven10

1Hospital Universitario La Paz, IDIAP, Madrid, Spain; 2Hospital Civil de Guadalajara, CUIC, Universidad de Guadalajara, Guadalajara, Mexico; 3Southwestern Infectious Disease Associates, Dallas, TX, USA; 4Hospital Juan A Fernández and Fundación Fuenpes, Buenos Aires, Argentina; 5Université Pierre et Marie Curie, Paris VI and Hôpital Pitié-Salpêtrière, Paris, France; 6Quest Clinical Research, San Francisco, CA, USA; 7HIV-NAT, Thai Red AIDS Research Centre and Chulalongkorn University, Bangkok, Thailand; 8The Center for AIDS Research, The University of North Carolina at Chapel Hill, NC, USA; 9TBVAC BBA, Beersel, Belgium; 10TBVAC Inc., Titusville, NJ, USA

Introduction

- TMC278 ([abacavir/lamivudine] ABC/3TC) (THRIVE).
- TMC278, an investigational NNRTI, had non-inferior efficacy to efavirenz (EFV) in treatment-naive patients in the Week 48 primary analysis of two Phase III, double-blind trials, ECHO (TMC278 C309, NCT00340464) and THRIVE (TMC278 C315, NCT00341215).
- The aim of the current analysis was to compare, under licensed conditions, abnormalities and changes in lipid parameters with TMC278 versus EFV over 48 weeks using pooled Phase IV data from the ECHO and THRIVE trials.

Methods

Study design

- ECHO and THRIVE are ongoing, global, Phase III, double-blind, double-dummy trials in treatment-naive, HIV-1-infected patients randomized to receive TMC278 25 mg or EFV 600 mg, plus zidovudine/didanosine/tenofovir (ZIDV/3TC/TFV) or an investigator-selected TDF/TDF/3TC/emtricitabine/tenofovir (A/ZT/C/T) or abacavir/lamivudine (ABC/3TC).

Study assessments and endpoints

- The use of lipid-lowering drugs at baseline or post-baseline was very low, therefore it was not taken into account in the analysis.
- Changes from baseline to fasting total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides were assessed over 48 weeks in the intent-to-treat (ITT) analysis.
- Baseline-corrected values for the proportion of patients with at least one lipid value outside (above or below) the National Cholesterol Education Program (NCEP) cut-off value at any time point were calculated. Cut-off values were total cholesterol: 200 mg/dL; LDL-C: 130 mg/dL; HDL-C: 40 mg/dL and triglycerides: 150 mg/dL.
- Treatment-emergent, lipid-related abnormalities were evaluated and graded according to Division of AIDS (DAIDS) criteria.

Results

Baseline characteristics

- Overall (N=1360), baseline patient demographics and disease characteristics were similar between groups (Table 1).

Baseline lipid parameters

- Baseline lipid parameters were similar between the TMC278 and EFV treatment groups (Table 2).

Changes in fasted lipid parameters from baseline to Week 48

- Changes in total cholesterol were similar between the two groups but lowest for the TMC278 group (2%; 15/686 patients) versus 4% (27/682 patients) in the EFV group (27/682 patients).
- There was no relevant difference between treatment groups in change in total-CHD risk in the TMC278 group (n=472) compared with 5% (n=459) in the EFV group (n=459) (Table 3).

Lipid-related, treatment-emergent abnormalities

- No relevant differences were observed between the two treatment groups (Table 4).
- There was no relevant difference between treatment groups in change in total-CHD risk in the TMC278 group (n=472) compared with 5% (n=459) in the EFV group (n=459) (Table 3).
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Conclusions

- TMC278 produced minimal changes in total cholesterol, LDL-C, triglycerides and HDL-C as compared with baseline 48 weeks of treatment. There was no relevant difference between treatment groups in change in total-CHD risk.
- The differences between treatment groups were more apparent in patients receiving TDF/TFC.

References