Genotypic and phenotypic characterizing of HIV-1 isolates obtained from patients failing rilpivirine (RPV, TMC278) in the Phase III studies ECHO and THRIVE: 48 week analysis

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Introduction

- ECHO (TMC278-C20, NCT00440446) and THRIVE (TMC278-C21, NCT00732072) were 96-week, Phase III, randomized (1:1:1), double-blind, double-dummy trials in treatment-naive, HIV-1 infected adults.
- The trials compared RPV 25 mg qd (N = 668), an investigational NNRTI, and efavirenz (EFV) 600 mg qd (N = 668) both in combination with two NNRTIs (ECHO: TDF/FTC; THRIVE: Investigator’s choice of TDF/FTC (60%), ATR/3TC (30%), APV/3TC (10%)).

In the pooled Week 48 primary analysis, RPV 25 mg qd had inferior efficacy to EFV 600 mg qd (primary objective).

- Patients in the RPV group and 42% of patients in the EFV group achieved viral load (<50 c/mL) (difference in response: 2.2% [95% confidence interval (CI): 2.2%–2.2%]).

In intent-to-treat, time-to-loss of virologic response (ITT-TLOVR) analysis

- ECHOb and non-subtype B VFs did not exhibit specific patterns of NNRTI or N(t)RTI RAMs.

- Less common cross-resistance between RPV and other NNRTIs.

- Considering all of the available cell culture and clinical data, any of the following amino acids and substitutions, when present at baseline, and ≤grade 2 adverse events at least possibly related to treatment (in ≥5% and ≥11.5% in the BL VL > 100K c/mL subgroup were 77% (RPV; N’ = 318) vs 81% (RPV; N’ = 368) and 84% (EFV; N’ = 330) (difference: 6.6% [1.6%; 11.5%])

- One out of 107 patients in the BL VL > 100K c/mL group reported grade 3 or 4 adverse events.

Conclusions

- Number of NNRTI RAMs per VF compared between RPV and EFV.
- Proportion of VFs with NNRTI or N(t)RTI RAMs similar in B and non-B subtypes.
- Most common mutations were E138K/M184I.
- In the baseline viral load category with < 100K c/mL, fewer VFs with NNRTI or N(t)RTI RAMs.
- NNRTI RAMs: for the antiretrovirals in the treatment groups.

References


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