TMC125 in Treatment-Experienced Patients: An Update

Poster 53-7

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Abstract

The clinical utility of a newly approved NNRTI is limited by essentially complete cross-resistance within the class. After development of resistance to one NNRTI, patients generally respond poorly to other NNRTIs. Treatment-naive patients are ineligible for clinical trials since active NNRTI resistance is expected to be present in at least two-thirds of patients. To assess the clinical utility of TMC125, a novel NNRTI, we conducted a phase IIb study in treatment-experienced patients with NNRTI resistance. Treatment-naive patients were also included.

Methods

- 250 mg TMC125 (PEG 4,000) or 900 mg TMC125 was dosed at 200 mg bid, utilizing a new formulation that provides a 12-hour drug concentration.

- Lopinavir/r and Clarithromycin

- Co-administration not recommended

- NRTIs ± ENF

- Selection of NRTI(s) ± ENF

- Clarithromycin is not recommended for the treatment of Mycobacterium avium complex or M. abscessus.

- Fosaprepavir/r: dose adjustment of fosaprepavir/r might be considered when combined with TMC125; no dose adjustment is necessary for TMC125

Conclusions

- TMC125 is a novel-generation NNRTI with potent in vitro activity against all NNRTI-resistant clinical isolates.

- TMC125 is the first NNRTI to demonstrate significant and durable efficacy in treatment-experienced patients with NNRTI resistance.

- A phase II randomized, active-controlled, open-label exploratory trial in PI-naive patients (Figure 6) showed a significant and durable decrease in HIV-1 RNA levels in the TMC125 arm.

- The mean change from baseline in VL at 12 months was significantly greater for TMC125 than for placebo, as shown in Figure 4.

- A significant difference in viral load was observed between the TMC125 groups.

- Analysis of response by baseline resistance showed that activity was retained in the presence of multiple NNRTI mutations where currently approved NNRTIs are not expected to be active.

- No statistical difference in virologic response was observed between the TMC125 groups.

- The combination of high-level NRTI and NNRTI resistance adversely impacted the virologic response.

References