Efficacy and Safety of Ponatinib in CP-CML Patients by Number of Prior Tyrosine Kinase Inhibitors: 4-Year Follow-up of the Phase 2 PACE Trial

INTRODUCTION

- Approximately 60% of patients with chronic myeloid leukemia (CML) who receive a second-generation tyrosine kinase inhibitor (TKI) after experiencing failure with imatinib discontinue treatment because of disease progression or adverse events (AEs)
- The long-term prognosis is generally poor for patients who receive another second-generation TKI after failure of a previous second-generation TKI
- Ponatinib is a potent oral TKI approved for use in adult patients with refractory CML or who have progressed at least twice on previous TKIs
- The PACE trial was a phase 2, open-label trial of ponatinib in patients with CML who had received 1, 2, or 3 previous TKIs
- The primary endpoint was major cytogenetic response (MCyR) by 1 month post-ponatinib initiation

OBJECTIVE

- To assess the longitudinal efficacy and safety of ponatinib in CP-CML patients who had received 1, 2, or 3 prior TKIs at enrollment

METHODS

- The PACE trial design has been described previously
- Primary endpoints were major cytogenetic response (MCyR) by 1 month post-ponatinib initiation and major molecular response (MMR) by 5 months post-ponatinib initiation
- Secondary endpoints included minor molecular response (MR2), ≤1% BCR-ABL1 transcripts, and molecular response (MR) at 5 months
- The PACE trial provided ponatinib 30 mg once daily for an initial period of 12 months
- The trial included 318 patients with CML, of whom 161 patients had received 1, 2, or 3 prior TKIs
- The study was designed to compare the efficacy and safety of ponatinib in patients who had received 1, 2, or 3 prior TKIs
- The study was terminated early due to adverse events (AEs)
- The study was conducted in Italy and the United States

RESULTS

- Among patients who had received 1, 2, or 3 prior TKIs, the proportion of patients with a current response of MMR or better was higher with fewer TKIs; only 1 patient who had received 4 prior TKIs continued to receive ponatinib
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- Median and median time from diagnosis to first dose of ponatinib increased with number of prior TKIs
- Among patients who had received only 1 prior TKI who had the T315I mutation, which qualified them for the PACE trial
- Most patients (60%) had CCyR at study entry
- The authors would like to thank the patients, their families, and their caregivers; the PACE investigators and their team members at each study site; and colleagues from ARIAD Pharmaceuticals, Inc., MolecularMD, and the CML trial of ponatinib in Philadelphia chromosome–positive leukemias. The authors would like to thank the patients, their families, and their caregivers; the PACE investigators and their team members at each study site; and colleagues from ARIAD Pharmaceuticals, Inc., MolecularMD, and the CML

OBJECTIVE

- To assess patient characteristics, longitudinal efficacy and safety among CP-CML patients in the phase 2 PACE trial (NCT02070404) according to the number of TKIs received prior to study entry, with a median follow-up of 4 years

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