STUDY 200: Study Evaluating Bosutinib in Philadelphia Chromosome Positive Leukemia

| INTRODUCTION | • Chronic myeloid leukemia (CML), one of the four main types of leukemia, is a slow-growing blood cancer that starts in the blood-forming cells of bone marrow, the soft inner part of some bones. Once these cells are affected by leukemia, they do not go through their normal process of maturing.  
  
  • An abnormal chromosome, the Philadelphia chromosome, is a hallmark of CML. The Philadelphia chromosome initiates a series of events leading to the development of Bcr-Abl, a tyrosine kinase that causes CML cells to reproduce rapidly.  
  
  • Therapies such as imatinib, dasatinib and nilotinib target the inhibition of the Abl tyrosine kinase.  
  
  • The Src family of nonreceptor tyrosine kinases has been identified as potential mediators of Bcr-Abl-induced leukemogenesis.  
  
  • Bosutinib is an investigational orally available dual Src and Abl kinase inhibitor with minimal inhibitory activity against c-kit and PDGFR. |
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| SELECTED ELIGIBILITY CRITERIA | • Selected Inclusion Criteria:  
  o Ph+ CML or Ph+ ALL patients who are primarily refractory to full-dose imatinib (600 mg), have disease progression/relapse while on full-dose imatinib, or are intolerant of any dose of imatinib.  
  o At least three months post stem cell transplantation.  
  • Selected Exclusion Criteria:  
  o Subjects with Ph+, and Bcr-Abl negative CML  
  o Overt leptomeningeal leukemia  
  o Subjects without evidence of leukemia in bone marrow |
| NUMBER OF PATIENTS | • The trial enrolled 571 patients from research sites in the United States and ex-U.S. This study is currently ongoing, but is closed to enrollment. |
| RESULTS | • Initial results from a cohort of Study 200 that consists of more than 100 patients with chronic phase Ph+ CML who have failed prior imatinib therapy and were resistant or intolerant to dasatinib or resistant to nilotinib were previously presented at the American Society of Hematology 2010 annual meeting. |


