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LETTER

Response to Miller et al: resistant mutations in CML and Ph(+) ALL – role of ponatinib

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Nathalie Bardy-Bouxin
Ewa Matczak
Geeta Devgan
Mabel Woloj
Mark Shapiro

Pfizer Oncology, Pfizer Inc., New York, NY, USA

Dear editor

Miller et al[1] recently reviewed the role of ponatinib in chronic myeloid leukemia (CML) and Philadelphia chromosome–positive acute lymphoblastic leukemia (Ph+ ALL), yet by the omission of an approved agent within the same class of drugs, provided an inaccurate summary of the current treatment landscape for CML. The authors discussed the evolution of tyrosine kinase inhibitor (TKI) treatment, beginning with imatinib approval in 2001, followed by the introduction of second- and third-generation TKIs, including dasatinib, nilotinib (both approved in the USA in 2010), and ponatinib (approved in the USA in December 2012). However, while citing all other approved TKIs, the authors did not discuss bosutinib (Bosulif®, Pfizer Inc., New York, NY, USA), a new second-generation TKI approved in the USA, in September 2012, for the treatment of patients with Ph+ CML who are resistant or intolerant to prior therapy, and in Europe, for Ph+ CML patients previously treated with one or more TKIs and for whom imatinib, nilotinib, and dasatinib are not appropriate choices. Bosutinib has manageable toxicity and acceptable tolerability; the most frequent adverse events observed are early-onset and generally low-grade gastrointestinal events, and with appropriate monitoring, the majority of patients are able to continue on therapy.[2]

Due to its potency[3,4] and toxicity profile distinct from other TKIs[2], bosutinib is an important option for CML therapy in the second-line and beyond. Mathisen et al recently reviewed the practical aspects of TKI selection for CML and highlighted bosutinib as a viable second- or third-line treatment option with an easy to manage toxicity profile.[5] In order to gain a more comprehensive understanding of the role of ponatinib in the CML treatment landscape, we strongly recommend reading the articles referenced here.

Disclosure

NB-B, EM, GD, MW, and MS are employees of Pfizer Inc. The authors report no other conflicts of interest in this work.

Correspondence: Mark Shapiro
Pfizer Oncology, Pfizer Inc.
10 Fawcett Street, Suite 203
Cambridge, MA 02138, USA
Email mark.shapiro1@pfizer.com

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Authors' response

Carol S Lim, Benjamin J Bruno, Geoff D Miller

Department of Pharmaceutics and Pharmaceutical Chemistry, College of Pharmacy, University of Utah, Salt Lake City, UT, USA

Correspondence: Carol S Lim
University of Utah, 30 South 2000 East,
Room 2916, Salt Lake City, UT 84112, USA
Tel +1 801 587 9711
Email carol.lim@pharm.utah.edu

Dear editor

We agree with Bardy-Bouxin et al that bosutinib is a legitimate treatment option "in the second-line and beyond." We are also well aware of the excellent references mentioned by this group, discussing bosutinib, and highlighting its "manageable toxicity and acceptable tolerability."

The purpose of this paper, however, was to highlight tyrosine kinase inhibitor (TKI)-resistant Bcr-Abl mutants in chronic myeloid leukemia (CML) and Ph+ ALL, and the evolution of TKIs to treat these mutant Bcr-Abl, culminating in the development of ponatinib. As bosutinib does not confer additional mutational coverage beyond dasatinib and nilotinib,1 it was not included in this paper. Bosutinib does not have efficacy against T315I,1,2 which was one of the driving forces for development of ponatinib.3,4 Omacetaxine is another agent that we did mention, because of its effectiveness (albeit non-specific) against T315I.4

The omission of bosutinib in this paper was not meant to imply it was not a useful agent with therapeutic benefit for certain CML patients.

Disclosure

The authors report no conflicts of interest in this work.

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