

Chronic Myeloid Leukemia: New Targeted Therapies

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Abstract

Chronic myelogenous leukemia (CML) is a progressive and often fatal hematopoietic neoplasm. The Bcr-Abl tyrosine kinase inhibitor imatinib mesylate represented a major therapeutic advance over conventional CML therapy, with more than 90% of patients obtaining complete hematologic response, and 70% 80% of patients achieving a complete cytogenetic response. Resistance to imatinib represents a clinical challenge and, is often a result of point mutations causing a conformation change in Bcr-Abl, which impair imatinib binding. Novel targeted agents designed to overcome imatinib resistance, include dasatinib (a potent dual Src and Bcr-Abl inhibitor), nilotinib (a selective potent Bcr-Abl inhibitor), bosutinib and INNO406 (both Src-Abl inhibitors), and others. Other approaches are exploring combination therapy, with agents affecting different oncogenic pathways, and immune modulation. Herein, we review some of these targeted therapies, particularly those for which clinical data are already available.

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