In Brief: Midostaurin (Rydapt) for AML and Advanced Systemic Mastocytosis

Important Copyright Message

FORWARDING OR COPYING IS A VIOLATION OF U.S. AND INTERNATIONAL COPYRIGHT LAWS

The Medical Letter, Inc. publications are protected by U.S. and international copyright laws. Forwarding, copying or any distribution of this material is prohibited.

Sharing a password with a non-subscriber or otherwise making the contents of this site available to third parties is strictly prohibited.

By accessing and reading the attached content I agree to comply with U.S. and international copyright laws and these terms and conditions of The Medical Letter, Inc.

For further information click: Subscriptions, Site Licenses, Reprints or call customer service at: 800-211-2769
IN BRIEF

**Midostaurin (Rydapt) for AML and Advanced Systemic Mastocytosis**

The FDA has approved the oral multikinase inhibitor midostaurin (Rydapt – Novartis) for first-line treatment, in addition to standard chemotherapy, of adults with FLT3 (fms-like tyrosine kinase 3) mutation-positive acute myeloid leukemia (AML). About 30% of patients with AML have FLT3 mutations. Midostaurin is also approved as a single agent for treatment of adults with aggressive systemic mastocytosis, systemic mastocytosis with associated hematological neoplasm, or mast-cell leukemia. In mastocytosis, midostaurin targets mutant c-KIT, not FLT3.

In a randomized, double-blind trial, 717 adults 18-59 years old with newly diagnosed FLT3-mutated AML were treated with midostaurin (50 mg twice daily on days 8–21 of each 28-day cycle) or placebo in addition to standard chemotherapy (induction therapy with cytarabine and daunorubicin and consolidation therapy with high-dose cytarabine), followed by up to 12 additional maintenance cycles of midostaurin or placebo. More than half of the patients (57%) stopped treatment and underwent hematopoietic stem-cell transplantation during the trial. Median event-free survival was 8.2 months with midostaurin compared to 3.0 months with placebo, a significant difference. Median overall survival after a median follow-up of 59 months was significantly longer with midostaurin than with placebo (hazard ratio 0.78). The 4-year overall survival rate was 51.4% with midostaurin and 44.3% with placebo. Common adverse effects reported in the midostaurin plus chemotherapy group at a rate at least 2% higher than in the placebo plus chemotherapy arm included febrile neutropenia (83% vs 81%), nausea (83% vs 70%), vomiting (61% vs 53%), and mucositis (66% vs 62%). There were no differences between the two groups in the rates of severe (≥grade 3) adverse events.

A single-arm, phase 2 study of midostaurin (100 mg twice daily in 4-week continuous cycles) included 89 adults with advanced systemic mastocytosis (16 had mast-cell leukemia) and evidence of organ damage. The overall response rate was 60%, and 45% of patients had a major response (complete resolution of at least one type of mastocytosis-related organ damage). The median duration of response was 24.1 months. Treatment with midostaurin also decreased splenomegaly and bone marrow mast-cell burden. Median progression-free survival was 14.1 months and median overall survival was 28.7 months (9.4 months in patients with mast-cell leukemia). The most common adverse effects of midostaurin were nausea, vomiting, and diarrhea. New or worsening grade 3 or 4 neutropenia, anemia, and thrombocytopenia occurred in >20% of patients.2

Rydapt is available in 25-mg capsules. For patients with AML, a 4-week treatment cycle (50 mg twice daily on days 8–21) costs $7495. For patients with advanced systemic mastocytosis, 4 weeks of treatment at 100 mg twice daily costs $29,980.3

3. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource®Monthly. July 5, 2017. Reprinted with permission by First Databank, Inc. All rights reserved. ©2017. www.fdbhealth.com/policies/drug-pricing-policy.