

VIDAZA(R) Receives Expanded FDA Approval to Include Overall Survival in Higher-Risk MDS

First and only drug to significantly extend survival for patients with higher-risk MDS

First drug approved by FDA for treatment of all MDS risk categories

First drug to achieve a transfusion independence rate of greater than 40 percent across all MDS risk categories

First MDS drug approved with multiple routes of administration (SC and IV)

SUMMIT, N.J.--(BUSINESS WIRE)--Aug. 21, 2008--Celgene Corporation (Nasdaq:CELG) today announced VIDAZA (azacitidine) received expanded U.S. Food and Drug Administration (FDA) approval to reflect new overall survival achieved in the AZA-001 survival study of patients with higher-risk myelodysplastic syndromes (MDS). This expanded indication supplements the 2004 FDA authorization of VIDAZA as the first therapy approved in the U.S. for the treatment of patients with all five French American British (FAB) subtypes of MDS. VIDAZA is also the first and only drug to show a statistically significant and clinically meaningful extension of survival in higher-risk MDS patients.

"The overall survival detailed in the expanded FDA approval of VIDAZA is extremely important for patients with higher-risk MDS, a group with limited options and median survival of about 15 months with classical treatments," said Pierre Fenaux, M.D., Ph.D. of the Universite of Paris and lead investigator of the AZA-011 survival trial.

"VIDAZA, however, is also effective across a broad range of MDS subgroups, including WHO-classified AML patients, the largest subgroup in our study."

The approval is based upon the significant improvement in overall survival achieved in the VIDAZA survival trial (AZA-001), the largest, international randomized Phase III controlled study ever conducted in higher-risk MDS. The median overall survival for patients treated with VIDAZA in the study was 24.5 months compared to 15 months for conventional care regimens (CCR), demonstrating a survival benefit of over 9 additional months with a stratified log-rank p-value of 0.0001. The hazard ratio describing this treatment effect was 0.58 (95 percent confidence interval of 0.43 to 0.77).

The extension of survival was seen across the relevant patient subgroups including those greater than 65 years, as well as poorer prognostic groups such as those with World Health Organization (WHO) classified acute myelogenous leukemia (AML), which formed 31 percent of the enrolled patients, and patients with poor risk cytogenetics. In the trial, the two-year survival rate for patients with higher-risk MDS treated with VIDAZA was almost doubled with 50.8 percent compared to 26.2 percent for CCR. Patients treated with VIDAZA received treatment for a median of nine cycles.

"The clinical data from this randomized Phase III controlled study demonstrated that patients with higher-risk MDS treated with VIDAZA benefit from a significant survival advantage, a critical measure of a drug's effectiveness," said Lewis Silverman, M.D., of the Mount Sinai Medical Center in New York City. Dr. Silverman was the lead author and Principal Investigator for the original VIDAZA approval study (CALGB 9221) and an author and investigator of the international AZA-001 survival trial. "Additionally, the efficacy and safety profile of VIDAZA allows for long-term therapy in patients with higher-risk MDS, underscoring the ability to treat until disease progression for optimal survival benefit."

In the AZA-001 study, the most commonly occurring adverse reactions for patients with higher-risk MDS receiving VIDAZA were thrombocytopenia (69.7%), neutropenia (65.7%) and anemia (51.4%).

"This decision by the FDA reflects the unprecedented survival advantage demonstrated by VIDAZA in patients with higher risk MDS," said Mohamad A. Hussein, M.D., Global Head, Medical Affairs, Hematology of Celgene, formerly of the H. Lee Moffitt Cancer Center and Research Institute. "VIDAZA is another example of Celgene developing novel therapies for critical blood diseases that are enabling patients to live for years, rather than weeks and months. Today's decision strengthens our Company's ability to deliver VIDAZA and our other therapies to patients in need around the world."

IMPORTANT SAFETY INFORMATION

VIDAZA is contraindicated in patients with a known hypersensitivity to azacitidine or mannitol and in patients with advanced malignant hepatic tumors.

In Study 1 (a randomized, open-label, controlled trial carried out in 53 U.S. sites compared the safety and efficacy of subcutaneous VIDAZA plus supportive care with supportive care alone ("observation") in patients with any of the five FAB subtypes of myelodysplastic syndromes (MDS)) and Study 2 (a multi-center, open-label, single-arm study of 72 patients with RAEB, RAEB-T, CMMoL, or AML), the most commonly occurring adverse reactions by SC route were nausea (70.5%), anemia (69.5%), thrombocytopenia (65.5%), vomiting (54.1%), pyrexia (51.8%), leukopenia (48.2%), diarrhea (36.4%), injection site erythema (35.0%), constipation (33.6%), neutropenia (32.3%), and ecchymosis (30.5%) Other adverse reactions included dizziness (18.6%), chest pain (16.4%), febrile neutropenia (16.4%), myalgia (15.9%), injection site reaction (13.6%), and malaise (10.9%). In Study 3, the most common adverse reactions by IV route also included petechiae (45.8%), weakness (35.4%), rigors (35.4%), and hypokalemia (31.3%).

In Study 4 (the AZA-001 survival trial), the most commonly occurring adverse reactions were thrombocytopenia (69.7%), neutropenia (65.7%), anemia (51.4%), constipation (50.3%), nausea (48.0%), injection site erythema (42.9%), and pyrexia (30.3%). The most commonly occurring Grade 3/4 adverse reactions were neutropenia (61.1%), thrombocytopenia (58.3%), leukopenia (14.9%), anemia (13.7%) and febrile neutropenia (12.6%).

Because treatment with VIDAZA is associated with anemia, neutropenia and thrombocytopenia, complete blood counts should be performed as needed to monitor response and toxicity, but at a minimum, prior to each dosing cycle.

Because azacitidine is potentially hepatotoxic in patients with severe preexisting hepatic impairment, caution is needed in patients with liver disease. In addition, azacitidine and its metabolites are substantially excreted by the kidneys and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function.

VIDAZA may cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be apprised of the potential hazard to the fetus. Men should be advised not to father a child while receiving VIDAZA.

Nursing mothers discontinue nursing or the drug, taking into consideration the importance of the drug to the mother.

SOURCE: Celgene Corporation

<http://www.fda.gov/cder/foi/label/2008/050794s011lbl.pdf>