

Azacitidine benefits patients with myelodysplastic syndromes

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Data presented at the 14th Congress of the European Society of Hematology demonstrate that treatment with azacitidine (Vidaza®) significantly extends overall survival and helps patients with myelodysplastic syndromes (MDS) become or remain red blood cell transfusion independent. Patients who benefited included those with higher-risk MDS or acute myeloid leukaemia (AML) with 20-30% blasts, as defined by the World Health Organization (WHO).

“The presentations at EHA this year continue to support the clinical benefit associated with Vidaza in MDS, including significantly extended overall survival, and add to the data from the international AZA-001 survival study published in The Lancet Oncology earlier this year,” said Jean-Pierre Bizzari, Group Head of Global Oncology/Hematology of Celgene. “Additionally, they reinforce the significant and durable transfusion independence provided by Vidaza, which is associated with improved overall survival in this difficult to treat group of diseases.”

Azacitidine (AZA) improves overall survival in WHO acute myeloid leukaemia (AML) in elderly patients with low bone marrow blast counts

A sub-analysis of the AZA-001 survival trial sought to confirm and further elucidate a positive overall survival trend shown by a subset of patients in an earlier phase III study (CALGB 9221) comparing VIDAZA against best supportive care in patients with WHO-defined AML with blasts <30%.

Patients with higher-risk MDS classifications (FAB: RAEB, RAEB-t, CMML and IPSS: Int-2 or High) were enrolled and randomised either to azacitidine therapy or conventional care regimens (CCR: best supportive care, low dose ara-C or intensive chemotherapy).

Of 358 patients, 113 (32%) met WHO AML criteria (median 23% marrow blasts). Subsequently, 55 were randomised to azacitidine and 58 to CCR. Of the 58 CCR patients, 47 percent were treated with best supportive care, 34 percent with low-dose ara-C and 19 percent with intense chemotherapy.

In the study, at two years, 50 percent of patients in the azacitidine group were alive compared to 16 percent of those in the CCR group ($p=0.0007$). The median overall survival was 24.5 and 16.0 months in the azacitidine and CCR groups, respectively, ($HR=0.47$ [95%CI: 0.28-0.79], $p=0.004$).

“As shown with higher-risk MDS patients in the AZA-001 study, patients with WHO-defined AML treated with VIDAZA also demonstrate an improved overall survival rate compared to conventional care regimens,” said Prof. Valeria Santini of Policlinico di Careggi, in Florence, Italy. “This also supports the trend shown in the CALGB 9221 study.”

The impact of azacitidine and decitabine (hypomethylating agents) in myelodysplastic syndromes: A systematic review and meta-analysis

In an effort to perform a systematic review of randomised controlled trials of azacitidine and decitabine versus best supportive care in the absence of a direct comparative trial, a comprehensive literature search was conducted for randomised controlled trials published prior to July 2008 and meeting abstracts from

the American Society of Clinical Oncology, American Society of Hematology and European Hematology Association between 2006 and 2008.

Four randomized controlled trials assessing the efficacy of hypomethylating agents for the treatment of MDS were found. Two comparing azacitidine to supportive care, and two comparing decitabine versus supportive care. Meta-analysis of randomised controlled trials comparing hypomethylating agents versus supportive care showed significantly better overall survival, event-free survival and response rate in favor of the hypomethylating agents without a significant increase in treatment-related mortality. Comparison of azacitidine versus supportive care also showed a significant advantage in overall survival and event-free survival without significant risk of treatment-related mortality. Comparison of decitabine versus supportive care showed significantly better event-free survival and response rate with decitabine but no difference in overall survival and treatment-related mortality.

Evaluation of azacitidine versus decitabine showed significantly better overall survival favoring azacitidine but similar event-free survival, response rate and treatment-related mortality.

“The results of this study demonstrate that patients treated with hypomethylating agents show significant improvement in survival and response. In our indirect comparison, however, VIDAZA had superior overall survival without a significant increase in treatment-related mortality,” said Dr. Ambuj Kumar of the H. Lee Moffitt Cancer Center in Tampa, Florida, USA.

Effect of azacitidine (AZA) on transfusion independence (TI) and overall survival (OS) in patients with higher-risk myelodysplastic syndromes

A second analysis of the AZA-001 survival trial sought to examine overall survival in higher-risk MDS patients relative to their transfusion status – as red blood cell (RBC) transfusion requirements have been shown to correlate with overall survival in these patients.

In the analysis, 179 patients with higher-risk MDS and WHO-defined AML were randomised to azacitidine and evaluated for RBC or platelet transfusion independence, which was defined as a transfusion-free period of ≥ 56 consecutive days.

In the azacitidine group, 50 of 111 RBC transfusion-dependent patients (45%, 95% CI: 35.6, 54.8) achieved RBC-transfusion independence and 16 of 38 patients with platelet transfusion dependence (42%) achieved platelet-transfusion independence.

Additionally, patients who were transfusion independent at some point during treatment regardless of their baseline transfusion status had a longer duration of azacitidine therapy and longer overall survival. A median overall survival was not reached for patients who were either RBC- or platelet-transfusion dependent at baseline and achieved transfusion independence during azacitidine treatment.

“Through this study, we were able to confirm that patients who became or remained transfusion independent as a result of azacitidine therapy had longer treatment duration and a prolonged overall survival compared to transfusion-dependent patients,” said Dr. John Seymour of the Peter MacCallum Cancer Centre in East Melbourne, Australia.

Source: Celgene International Sàrl

Watch Prof Pierre Fenaux discussing Vidaza and MDS on ecancer tv