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The effects of continued azacitidine treatment cycles on response in higher risk patients with myelodysplastic syndromes: an update

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Abstract

The international, phase III, multi-centre AZA-001 trial demonstrated azacitidine (AZA) is the first treatment to significantly extend overall survival (OS) in higher risk myelodysplastic syndromes (MDS) patients (Fenaux (2007) *Blood* **110** 817). The current treatment paradigm, which is based on a relationship between complete remission (CR) and survival, is increasingly being questioned (Cheson (2006) *Blood* **108** 419). Results of AZA-001 show CR is sufficient but not necessary to prolong OS (List (2008) *Clin Oncol* **26** 7006). Indeed, the AZA CR rate in AZA-001 was modest (17%), while partial remission (PR, 12%) and haematological improvement (HI, 49%) were also predictive of prolonged survival. This analysis was conducted to assess the median number of AZA treatment cycles associated with achievement of first response, as measured by IWG 2000-defined CR, PR or HI (major + minor). The number of treatment cycles from first response to best response was also measured.

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Methods

Patients (pts) with higher risk MDS (FAB: RAEB, RAEB-T, or CMML and IPSS: Int-2 or High) were included. Pts were randomized to AZA (75 mg/m^2/d SC x 7d q 28d) or to a conventional care regimen (CCR). AZA treatment was continued up to disease progression (or unacceptable toxicity), regardless of haematological response. Erythropoiesis stimulating agents were not allowed.

Results

In all, 358 pts were randomized (179 to AZA and 179 to CCR). Of the 179 AZA pts, 91 (51%) achieved a CR, PR or HI. For the 91 pts who achieved an IWG response, the median number of cycles to first response was three (range: 1–22), 81% of pts achieved a first response by six cycles, and 90% achieved a first response by nine cycles. For 57% of responders (*n*=52), their first response was their best response; the remaining 43% (*n*=39) had an improvement in their response status at a median of approximately four additional treatment cycles (range 1–11 treatment cycles) after their first response.

Conclusions

While many pts achieving a haematological response with AZA do so in early treatment cycles, continued AZA dosing can further improve pt responses. In the AZA-001 study, a significant OS benefit was observed compared with CCR. In this study, AZA pts received a median of nine treatment cycles (range 1–39). For those achieving a response of HI or better, 90% did so by nine cycles; more than 40% of responders later achieved an improved response. In the absence of unacceptable toxicity or disease progression, continued AZA treatment is appropriate and may maximize patient benefit.

Conflicting interests

Silverman: Celgene: Speakers Bureau. *Fenaux:* Celgene: Consultancy, Honoraria, Research Funding; Ortho Biotech: Consultancy, Honoraria, Research Funding; Roche: Consultancy, Honoraria, Research Funding; Amgen: Consultancy, Honoraria, Research Funding; Cephalon: Consultancy, Honoraria, Research Funding; GSK: Consultancy, Honoraria, Research Funding; MSD: Consultancy, Honoraria, Research Funding. *Mufti:* Celgene: Honoraria, Speakers Bureau; Amgen: Honoraria, Speakers Bureau. *Santini:* Celgene: Honoraria; Novartis: Honoraria; J&J: Honoraria. *Hellström-Lindberg:* Celgene: Consultancy, Research Funding. *Gattermann:* Celgene: Research Funding, Speakers Bureau. *Sanz:* Celgene: Membership on an entity's Board of Directors or advisory committees. *List:* Celgene: Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau. *Gore:* Celgene: Consultancy, Equity Ownership, Research Funding. *Seymour:* Celgene: Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding, Speakers Bureau. *Backstrom:* Celgene: Employment. *McKenzie:* Celgene: Employment. *Beach:* Celgene: Employment.