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Low-Dose Decitabine Vs Best Supportive Care In Older Patients With AML and Low Blast Counts: Results Of a Subgroup Analysis Of The Randomized Phase III Study 06011 Of The EORTC Leukemia Cooperative Group and German MDS Study Group

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Abstract

Introduction Decitabine has been approved for the treatment of myelodysplastic syndromes (MDS) in the United States and acute myeloid leukemia (AML) in older patients in Europe. The definitions of MDS and AML differ between the FAB and WHO classification, mainly with regards to patients with 20 to 30% blasts in blood or bone marrow having MDS according to the FAB classification (i.e. refractory anemia with excess blasts [RAEB] or RAEB in transformation), but AML according to the WHO. In the phase III trial 06011, we compared low-dose decitabine with best supportive care (BSC) in patients ≥60 years with MDS according to the FAB classification (Lübbert et al., J Clin Oncol. 2011;29:1987-96). Here, we examine trial 06011 for the efficacy and safety of decitabine in patients with AML according to WHO and low proliferation, i.e., blast counts of 20 to 30%.

Patients and Methods Patients were randomly assigned to receive decitabine or BSC. Decitabine 15 mg/m^2 was given intravenously over 4 hours every 8 hours for 3 consecutive days in 6-week cycles, with a maximum of 8 cycles. Results were evaluated every 2nd cycle. In case of complete remission (CR) at least 2 further courses were administered. Primary endpoint was overall survival (OS). Response rates (CR; PR, partial remission; HI, hematologic

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improvement; PD, progressive disease), progression-free survival (PFS; time from random assignment to PD, relapse or death), AML-free survival (AMLFS; time from random assignment to AML according to FAB [>30% bone marrow blasts] or death), and toxicity were secondary endpoints.

Results Applying the WHO criteria to the 233 patients enrolled onto the trial, 164 had MDS and 50 had AML with blast counts of 20 to 30%. The remaining 19 patients were excluded from the present analyses. They comprised 14 patients with chronic myelomonocytic leukemia, 2 with AML and ≥40% blasts, and 3 with no blast counts available.

Among the AML patients, 27 were in the decitabine and 23 in the BSC arm. In both arms, the median age was 70 years. Of the patients in the decitabine arm, 59% received 3 or more treatment cycles. Response rates in the decitabine and the BSC arm were as follows: CR, 11% vs 0%; PR, 11% vs 0%; HI, 11% vs 0%; and PD, 37% vs 74%. Compared with the patients receiving BSC, those receiving decitabine had longer PFS (P=0.008; **Table 1**). However, this did not translate into a significantly improved AMLFS or OS of the decitabine treated patients, although median OS was 9.8 months, compared to 5.9 months among patients receiving BSC only (**Table 1**). With regard to toxicity differences between the decitabine and BSC arms, grade 1-2 nausea was observed in 46% vs 14% and grade 3-4 febrile neutropenia in 19% vs 0%.

Among the MDS patients, those receiving decitabine (n=78) had a longer PFS (P=0.07) but similar AMLFS and OS compared to the patients receiving BSC only (n=86; **Table 1**). The impact of decitabine on PFS, AMLFS and OS did not significantly differ between the AML and MDS patients (**Table 1**). Response rates among the MDS patients in the decitabine and BSC arms were as follows: CR, 14% vs 0%; PR, 4% vs 0%; HI, 18% vs 2%; and PD, 23% vs 66%.

Conclusions Our data point to the clinically relevant efficacy of decitabine given in the 3-day schedule among patients with AML and low blast counts, particularly by delaying progression or relapse. No impact of decitabine, compared to BSC or low-dose cytarabine, on OS in older patients with AML and 20 to 30% marrow blasts (median, 8.0 vs 6.1 months) has been previously also reported by Kantarjian et al. (J Clin Oncol. 2012;30:2670-7). In that study, decitabine was given with 20 mg/m^2/day on 5 days every 4 weeks; PFS was not presented. The prolonged PFS that we observe may be used for example as non-intensive bridge to allogeneic stem cell transplantation after reduced-toxicity conditioning. Due to the post-hoc nature of our analyses and the relatively small patient numbers, further studies appear warranted to fully establish the benefit of decitabine in AML patients with low blast counts.

Table 1 View inline | View popup

Disclosures: Rüter: *Boehringer-Ingelheim:* Employment. **Platzbecker:** *Celgene:* Honoraria, Research Funding; *Novartis:* Honoraria, Research Funding. **Giagounidis:** *Celgene:* Consultancy, Honoraria. **Selleslag:** *Celgene:* Consultancy; *Novartis:* Consultancy; *Amgen:* Consultancy. **Baron:** *Genzyme:* Honoraria.

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