The treatment of acute myeloid leukemia with mitoxantrone, etoposide and low-dose cytarabine in elderly patients – a report of Polish Acute Leukemia Group (PALG) phase II study

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The common dilemma in the treatment of elderly patients with acute myeloid leukemia (AML) is whether to use intensive myelosuppressive therapy with higher risk of treatment related mortality (TRM), but a chance for complete remission (CR), or to treat less intensively in order to prolong survival time with a better quality of life. The aim of this prospective, phase II study was to assess the efficacy and toxicity of low dose combination induction treatment consisted of cytarabine at a dose of 10 mg/m² every 12 h s.c. for 7 days, VP-16 at a dose of 100 mg/day p.o. for 7 days and mitoxantrone at a dose of 6 mg/m² i.v daily on days 1–3. Two induction courses were planned. In the group of 44 patients 12 (27%) achieved CR, 4 (9%) patients were in PR and there were 9 (20%) early deaths (ED). Age, performance status, preceding myelodysplastic syndrome, karyotype, WBC and % of blasts in bone marrow were not significant prognostic factors for CR probability. The following factors appeared to be related to a shorter duration of survival time from the start of treatment: age >70 (p<0.03), poor performance status (p<0.03), and % of BM blasts 50 (p<0.05). We conclude that, despite promising results in the pilot study the efficacy of this induction treatment is not better than the efficacy of other regimens. The hematological toxicity of this treatment seems to be comparable with “3+7“ regimen.

Key words: Acute myeloid leukemia, elderly, low dose therapy.

More than 50% of newly diagnosed patients with acute myeloid leukemia (AML) are over 60 years of age. To the important advances in the treatment of AML and improved overall survival contribute mainly the patients below this age. The treatment results of AML in the elderly are significantly worse comparing with the younger group of patients. The complete remission (CR) rate is 28–58%, TRM 11–48% and overall survival (OS) 1.5–9 months in patients over 60 years of age [1]. The CR rate is about 50% with standard induction treatment consisting of anthracycline and arabinoside cytosine. However, TRM is higher than 20% and OS is below 12 months in some reports [1, 10, 12, 13]. More intensive chemotherapy in patients above the age of 60 has increased TRM significantly without any improvement in the treatment results [10]. The reasons for that are possibly different biology of the disease (adverse cytogenuous, higher multidrug resistance gene (MDR) expression, antecedent hematological disorders (AHD), as well as factors concerning individual (impaired renal excretion, oligoclonal hematopoiesis, concomitant disorders) [10, 15].

Optimization of induction therapy specific for elderly patients with AML appears of considerable clinical relevance. Only 10% of elderly AML patients are qualified to prospective, multicenter, randomized trials assessing the efficacy of intensive, antileukemic chemotherapy [10]. Most