IMPORTANCE OF EVALUATION OF CYTOGENETIC AND MOLECULAR MARKERS IN ACUTE MYELOID LEUKEMIA.

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Acute myeloid leukemia (AML) is a heterogeneous disease in clinical presentation, outcome and therapeutic response. Cytogenetic and molecular characteristics are important prognostic indicators allowing identifying distinct subtypes of AML, prognostic stratification and risk-adapted treatment.

We present our experience during the 3 years when we treated 245 patients with AML of which we could genetically characterize 48 cases (26 females, 22 males) with a median age of 52 years.

Cytogenetic analysis was performed by GTG banding on cultures of marrow cells treated with colcemid. Molecular analysis used RT-PCR performed on ABI 9700 platform in order to identify the following fusion genes: E2A-PBX1, TEL-AML1, AML1-ETO, PML-RARα, MLL-AF4, CBFC-MYH11, BCR-ABL, SIL-TAL, and MLL-AF9as well as mutations in Flt3, NPM1, WT1 genes.

Fourteen patients were older than 60 years. In 12 we performed cytogenetic analysis showing 5 cases with complex karyotype, 2 normal karyotypes, 1 case of del(21), del (9), 11q- and t(3;15) respectively as well as 2 unevaluable karyotypes.. These anomalies were associated with a high incidence of secondary AMLs (10/14) and with a low remission (CR) rate (5/14).

Out of the 35 patients younger than 60 years, 25 were evaluated by cytogenetics showing a high incidence of favorable cytogenetic changes: 6 anomalies of chromosome 16 (5 inv (16) and 1 t (16; 16)), 3 t (15; 17), 3 cases of t (8; 21) of which 2 with additional abnormalities, 7 normal karyotypes and 1 case 0f 7q-, -y,-3 and respectively -8 associated with +18. In 25 cases molecular analysis was performed showing alterations in 21 patients: 6 cases with AML/ETO, 3 PML/RAR, 7 Flt3 mutations (2 associated with NPM1 mutation) as well as 1 case of isolated mutation of NPM1 and respectively WT1. CR rate was of 28/35. All cases with t (15; 17) and PML/RAR as well all cases with t (8; 21) and/or AML/ETO achieved CR. Out of the 7 cases with Flt3 mutations only 4 achieved CR including the 2 cases with associated NPM1 mutations.

In our experience, genetic characteristics correlate with other prognostic markers such as age and secondary leukemia; "favorable" genetic anomalies were associated with a high CR rate; association of t (8; 21) with additional abnormalities did not influence CR rate.

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