non-hematologic toxicities included oral mucositis and diarrhea. No treatment–related cardiotoxicity or cerebellar toxicity was observed. Median overall survival duration was 4 months (range 1-30); at 10 months, the survival rate was 32%. Median relapse free survival duration was 8 months (range 4.5-29). In conclusion, our data support the use of GO in combination with conventional salvage chemotherapy in this very high risk category of patients and suggest that, for responders, allo-HSCT is feasible.

P027

A SIMPLE PROGNOSTIC SCORING SYSTEM FOR NEWLY DIAGNOSED ACUTE LEUKAEMIA PATIENTS WITH NORMAL KARYOTYPE: A RETROSPECTIVE ANALYSIS ON 420 CASES

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Background. Cytogenetics is the most important prognostic factor for acute myeloid leukaemia (AML), enabling to categorize AML patients in three risk categories: favourable, intermediate and unfavourable. The post-induction therapeutic strategy, including or not allogeneic-SCT, is not well established in patients with NK, who account for at least the 40-50% of cases and show an extremely variable long term survival, ranging from 20-70%. *Aims*. The aim of the study is to provide a simple prognostic scoring system, to better define the disease-risk in AML patients with NK and to optimally address the issue of post-induction therapy. *Methods.* We retrospectively analyzed 420 AML patients with NK (NK-AML) consecutively treated from 1990 to 2005. Induction regimen was Fludarabine-based in 281 patients (67%) and ICE/DCE in 139 cases. After the first consolidation, patients were addressed to intensification therapy including allogeneic-SCT if aged less then 45 yrs, with a HLA compatible donor and at least one other high risk feature (WBC over $30x10^9$/L, secondary AML, non response to the first induction therapy, multidrug-resistance Pgp over-expression and presence of Flt3-ITD). An allogeneic-SCT was performed in 71/418 cases (17%). By univariate analysis age at least 55 yrs, Pgp positive phenotype and secondary AML significantly affected the CR rate. Moreover, age at least 55 yrs, FAB subtype, secondary AML, WBC count over $16x10^9$/L and no response to the first induction cycle significantly affected disease free survival (DFS) and overall survival (OS). By multivariate analysis, only Pgp over-expression significantly affected the CR rate, whereas age at least 55 yrs, WBC count aver $16x10^9$/L, secondary AML and no response to induction significantly affected the DFS and OS. Univariate and multivariate analysis were conducted using the logistic regression model for CR rates and the Cox proportional hazard model for survival. A numerical score was derived from the regression coefficients of each independent prognostic variable and was 1 for WBC count over $16x10^9$/L, age at least 55 yrs and secondary AML and 2 for no response to the first induction regimen. The prognostic score for each patient was then calculated by totalling up the score of each independent variable. *Results.* The allo-transplanted patients were censored at the time of SCT. Patients could be stratified in low (score = 0), intermediate (score = 1) and high risk group (score at least 2), with a median DFS of 115, 11 and 8, respectively ($p<0.0001$). Similarly, the median OS was 120, 24 and 8 in low, intermediate and high risk group, respectively ($p=0.0001$). *Conclusions*. These preliminary retrospective data suggest that common available clinical variables may still represent a valid approach for determining a prognostic stratification for NK-AML patients.

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P028

P2 RECEPTORS ARE EXPRESSED ON ACUTE MYELOBLASTIC LEUKEMIA CELLS AND THEIR STIMULATION MODULATES LEUKEMIA CELLS FUNCTION

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Extracellular nucleotides ATP and UTP are emerging as ubiquitous molecules involved in a wide variety of biological responses and their biological effects are mediated by specific plasma membrane receptors, P2 receptors (P2R). Previously, we showed that extracellular nucleotides stimulate the proliferation and engraftment potential of normal human hematopoietic stem cells. In this study, we assessed whether P2R are expressed on acute myeloblastic leukemia (AML) cells and whether their engagement modulates leukemic cell functions. By RT-PCR we found in AML the mRNA expression of P2X1, P2X3, P2X4, P2X5, P2X6, P2X7, P2Y1, P2Y2, P2Y4 receptors. The expression of P2X7, P2X4, P2Y1 was confirmed at the protein level. Stimulation of AML cells by extracellular nucleotides (ATP, UTP, BzATP) induced intracellular Ca^{2+} concentration increases. Furthermore we identified a number of genes significantly modulated by ATP treatment. Gene expression profiling revealed that leukemic cells stimulated with ATP underwent a down-regulation of genes involved in cell proliferation and migration whereas those involved in cell cycle inhibition were strongly up-regulated. At the functional level, the clonogenic efficiency of leukemic blasts was significantly inhibited by the addition of ATP and, to a higher extent, by the stable analogs INS415 and INS973. We also observed a pronounced inhibitory effect of triphosphate nucleotides on blast spontaneous migration and in response to CXCL12. To assess the activity of nucleotides on AML cell migration in vivo, NOD/SCID/Gamma-Null mice were sublethally irradiated and intravenously injected with human AML cells incubated with nucleotides or their analogues. Xenotransplant experiments demonstrated that the homing and the engraftment capacity of human AML cells to murine bone marrow was significantly inhibited by pre-treatment with ATP, UTP and INS415 and INS973 analogues. Thus, our data show that purinergic signaling modulates leukemic cells in a opposite way than normal cells. Characterization of P2R expression and function in leukemia may help the better understading of the mechanism of neoplastic transformation and tumor progression.

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WILMS' TUMOR 1 (WT1) MUTATIONS IN NORMAL KARYOTYPE ACUTE MYELOID LEUKEMIA

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Introduction. Acute myeloid leukemia (AML) is a heterogeneous disease characterized by different recurrent chromosomal aberrations that determine the current risk-group classification. In adult AML approximately 40-50% of cases at diagnosis cannot be characterized by karyotypic aberrations. Several molecular aberrations have been identified in this subgroup, such as internal tandem duplications of the FLT3 gene (FLT3/ITD), mutations in NPM1 and CEBPα. The WT1 gene is known to be overexpressed in myeloid leukemias, and is therefore utilized as a marker for minimal residual disease detection. The gene encodes for a zinc-finger transcription factor involved in the regulation of growth and differentiation. Recently WT1 mutations have been identified in ~10% of adult AML with normal karyotype (NK-AML), and their association with unfavourable prognosis is controversial. To determine the role of WT1 aberrations in our patients , we searched for these aberrations in a well-characterized cohort of adult *de novo* AML patients Results and conclusion: Pre-treatment samples from all patients were studied by