0114

TRISOMY 8 AS SOLE ANOMALY OR WITH OTHER CLONAL ABERRATIONS IN ACUTE MYELOID LEUKEMIA: IMPACT OF CLINICAL PRESENTATION AND TREATMENT OUTCOME

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Background. Trisomy 8 is the most frequent numerical aberration in acute myeloid leukemia (AML). It occurs either as the sole anomaly or together with other clonal chromosome aberrations. Only few data are available regarding their prognostic significance. *Aims.* In order to investigate whether accompanying chromosome anomalies influence the clinical outcome in patients with trisomy 8, we assess clinical and biological characteristics, and response to therapy, of an unselected group of patients with previously untreated AML, presenting with trisomy 8 either alone or with other clonal aberrations. *Methods.* One hundred and fifty-four cases (median age: 65 years) were diagnosed in our institution between 1981 and 2005 including 47 patients (31%) with trisomy 8 as the sole aberration, 107 patients (69%) with trisomy 8 associated with other cytogenetic abnormalities (13 with favorable risk, 54 with intermediate risk, and 40 with unfavorable risk cytogenetics). *Results.* Twenty-eight patients only received symptomatic therapy or died before any chemotherapy could be given. All other patients received induction treatment according to different protocols used during the period of study. Overall complete remission (CR) proportion was 48% (95% confidence interval (CI): 40 - 56%). Sixty-six patients achieved CR after one course of chemotherapy and 8 patients after salvage therapy. Median disease-free survival (DFS) of the entire cohort was 7.8 months (95% CI: 6.5-9.9 months) and median overall survival (OS) was 8.3 months (95% CI: 5.2 ‘ 9.8 months). In multivariate analysis, age more than 60 years and trisomy 8 associated with unfavorable chromosomal aberrations were of poor prognostic value for CR achievement. Age more than 60 years and antecedents of dysmyelopoiesis were of poor prognostic value for DFS and OS. Patients with trisomy 8 alone did not show a significant difference in terms of outcome as compared with those in whom trisomy 8 was associated to intermediate risk chromosomal aberrations. Patients with trisomy 8 in addition to favorable chromosome aberrations maintained a good clinical outcome, while those with trisomy 8 in addition to unfavorable karyotypes showed the worst prognosis. *Conclusions.* Trisomy 8 as a whole has poor survival, which is largely attribuable to worsened outcomes among patients whose trisomy 8 was associated with unfavorable cytogenetic abnormalities. A particular poor outcome was observed in patients presenting trisomy 8 with antecedents of myelodysplasia.

0115

ANALYSIS OF 1458 ACUTE MYELOID LEUKEMIA FROM THE ALERT PROJECT (ACUTE LEUKEMIA CLINICAL REGISTER) IN THE CZECH REPUBLIC IN 1996-2006

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Project ALERT was initiated 9 years ago as population registry for acute leukemias, based on the cooperation of large haematological centres in the Czech Republic. Although the primary aims were rather clinical than epidemiological, the growing database tends to become representative for the Czech population, at least in the category of intensively cured AML patients. The database is improved to provide patients parametric collection of data gathered in accord with the therapeutic protocols and is full-scale record of prognostic markers including cytogenetic maps. The now presented and analysed cohort consists of 1458 AML patients registered in ALERT from January 1996 to December 2005. Median age of the patients was 58 years (32-74 year 10-90% kvantil limit). 636 (44%) patients were ≥55y and 822 (56%) older than 55y. The patients were observed with median 2y (0-5.5 y 5-95% kvantil limit). 90.4% of younger group pats were treated by intensive induction (CR rate 76%, median OS 17 months, DFS 22m and OS of the patients that achieved CR was 47.5 m). No differences were found between different induction intensity regimens. In the older group out of 56% of patients that received induction treatment 53% pats achieved CR with median OS 9m (DFS 11.2 m and OS of the patients achieved CR was 20 m). Out of 435 younger pats 18.5% were treated with standard dose consolidation, 38% with intermediate or HDCH and 39% with SCT (31% Auto SCT, 20% MUD SCT and 49% sibling donor SCT). In the older group out of 254 patients treated with consolidation treatment 37% were treated with standard dose consolidation CH, 43% with ID or HDCH and 10% only with SCT. The differences for OS and DFS with different consolidation treatment regimens will be given. The analysis of prognostic significance of age confirmed age over 55 as poor prognostic factor. The cytogenetic results of 758 intensively treated patients were studied. These include 103 PML patients. More than 80% of these patients live in molecular CR. The stratification of cytogenetic data for very good prognosis (PML), good prognosis, standard prognosis and poor prognosis confirmed their prognostic significance for OS, but surprisingly there were not found prognostic differences for DFS between standard and good prognostic group. Very important result revealed the analysis of centers showing comparable therapeutic results in all centers treating AML in the Czech Republic, even if they do not use the same therapeutic protocols for the treatment of AML. More detailed data will be given in the presentation.

This presentation was prepared with support of Grant NR/8080-3.

0116

CLORETAZINE (VNP40101M) HAS SIGNIFICANT ACTIVITY AS INDUCTION THERAPY FOR ELDERLY PATIENTS WITH ACUTE MYELOID LEUKEMIA OR ADVANCED MYELODYSPLASTIC SYNDROME

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Background. The incidence of AML increases with age with a median age of 68 years at diagnosis. Elderly pts with AML are more likely to have adverse prognostic factors related to the biology of the disease (adverse cytogenetics, history of MDS or prior exposure to cytotoxic agents, increased expression of multi-drug resistance) and medical comorbidities. Little progress has been made in improving outcomes in older pts. Despite variations on the 7+3 regimen, most elderly pts do not receive cytotoxic chemotherapy; pts who are treated with current regimens have lower response rates and overall survival, as well as poorer tolerance of side effects, compared to younger pts. New agents are required to increase complete remission (CR) rate and duration with improved safety in this population. Cloretazine, is a novel alkylating agent that has shown significant anti-leukemia activity *in vitro* and *in vivo* models. *Aims.* A multi-center Phase II study was conducted to investigate activity and safety of Cloretazine, in pts ≥60 years old with newly diagnosed AML or high risk MDS. *Methods.* Cloretazine, was administered at 600 mg/m^2 as a single 30-60 min. IV infusion. Second induction was allowed for patients who showed improvement. Patients who achieved CR or CRp could receive a consolidation course of 400 mg/m^2.

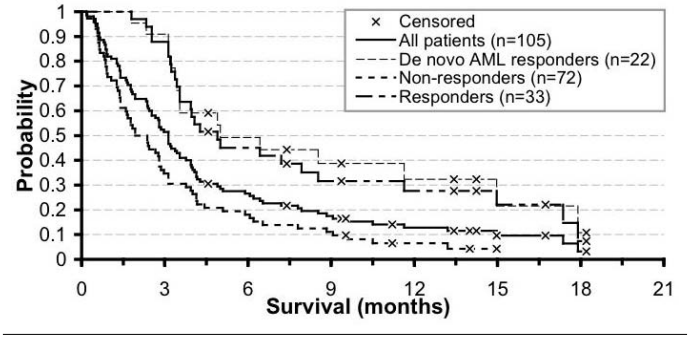

Figure 1.% Probability of Overall Survival.

Results. 105 pts were treated (median age 72, range 60-84), of whom 45 (43%) had *de novo* AML, 45 (43%) had secondary AML and 15 (14%) had high risk MDS. Twenty-eight pts achieved a CR and 5 pts a CRp for