imal bone marrow involvement. This study was purposed to demonstrate the usefulness of immunohistochemistry to reveal minimal bone marrow involvement of blastic plasmacytoid dendritic cell neoplasm. *Design and Methods.* 8 patients who were diagnosed as blastic plasmacytoid dendritic cell neoplasm from June 2000 to September 2008 were investigated. Except 2 patients who didn't receive bone marrow study, immunohistochemistry of CD4, CD56 and CD123 were done on biopsy or clot section to confirm minimal bone marrow involvement. *Results.* On initial morphologic diagnosis, bone marrow involvement was found in only 1 patient of 6 who received bone marrow biopsy. But Immunochemistry revealed minimal bone marrow involvement of 5 patients (CD123:5/5, CD56:2/3, CD4:2/3) whose bone marrow had been morphologically normal. *Conclusions.* Minimal bone marrow involvement of blastic plasmacytoid dendritic cell neoplasm can be precisely detected by immunohistochemistry. So we recommend CD4, CD56 and CD123 immunohistochemistry for the patients with blastic plasmacytoid dendritic cell neoplasm even though initial bone marrow study shows normal morphology.

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### COMPARISON OF SECONADRY ACUTE MYELOID LEUKEMIA WITH *DE NOVO* AML: CLINICAL FEATURES AND TREATMENT OUTCOME

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*Background.* Secondary acute myeloid leukemia (AML) includes AML in patients who were exposed to chemo- and/or radiotherapy previously (t-AML) or AML evolving from myelodysplasia or myeloproliferative disorder (m-AML). Aims: We intended to investigate the clinical features at diagnosis and the therapeutic outcomes of t-AML and m-AML, comparing with those of *de novo* AML (d-AML). *Design and Methods.* Between June 1989 and July 2008, 886 consecutive patients with newly diagnosed AML in Asan Medical Center, Seoul, Korea were included in our retrospective analysis. Patients were classified into the three groups of d-AML (n=816, 92.1%), m-AML (n=46, 5.2%) and t-AML (n=24, 2.7%). The data of clinico-pathologic findings and clinical outcomes were retrieved from the Asan Medical Center Leukemia Registry. *Results.* Median number of peripheral blast count at diagnosis was lower in patients with m-AML ($1.41x10^9$/uL) and t-AML ($2.09x10^9$/uL) than patients with d-AML ($6.15x10^9$/uL) ($p$=0.01). Proportion of blasts in bone marrow nucleated cells was also significantly different among the three groups (66.4%, 43.6%, and 55.0% for d-AML, m-AML and t-AML respectively; $p$<0.001). More than 80% of patients in each group received induction chemotherapy. The complete remission (CR) rate after remission induction chemotherapy in patients with m-AML was significant lower than those with d-AML and t-AML [11/38 (28.9%) vs 560/720 (77.9%) and 13/20 (65.0%), respectively, $p$<0.001]. The 5-year actuarial overall survival (5-OS) rate in t-AML and m-AML patients was lower than d-AML patients (9.8% and 12.8% vs. 32.1%, respectively; $p$<0.001). But we observed no statistically significant difference in disease free survival (DFS) and event free survival (EFS) among the three groups. More patients with t-AML tended to die of non-relapse causes than those with m-AML after the first CR achievement [4/13 (30.7%) vs 4/38 (10.5%)]. HCT was performed for 184 (22.5%) of 816 patients with d-AML, 12 (26.1%) of 46 patients with m-AML, and 3 (12.5%) of 26 patients with t-AML. All of the 4 patients whose HCT was the initial therapy for m-AML did not relapse but 1 died of non-relapse cause, whereas 3 (37.5%) of the 8 patients whose HCT followed remission induction chemotherapy for m-AML, relapsed and died. For t-AML, three patients undertaken HCT in the first complete remission state followed by remission induction chemotherapy but 2 (66.6%) of 3 patients relapsed after transplantation, and all subsequently died. *Conclusions.* Our results suggest that prompt HCT may be more preferable therapeutic option particularly for patients with m-AML. To improve the overall outcome of patients with t-AML, novel therapeutic strategies are needed.

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### THE ADDITION OF BORTEZOMIB TO INDUCTION THERAPY OF REFRACTORY ADULTORY AML, PRELIMINARY RESULTS

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*Background.* Proteasome inhibition, the block of angiogenesis, modification of the NF-κ-B system seems to be a important target in refractory acute myeloid leukemia (AML). *in vitro* data clearly support, that bortezomib possesses antiproliferative and pro-apoptotic effects in different AML cell-lines, moreover bortezomib was able to improve anthracyclin and possibly ARA-C sensitivity in different AML cell-lines. More recently, a Phase I trial showed bortezomib monotherapy efficient (only in few percents) in childhood refractory acute leukemia. Aims We have tried bortezomib containing first or second line combinations in 35 (18 female, 17 male, mean age 59.76 years) patients with refractory or poor risk AML, in a retrospective fashion, analysing responses and safety.. *Design and Methods.* The combinations were as follows: HAM or Flag-Ida, combined with bortezomib 1,3 mg pro sqm, day 0 and seven). The following groups were considered as refractory or poor risk AML: 1.*De novo* AML, 2nd line: Lack of remission to first line standard treatment ("3+7"), n=4 (Velcade- Flag-Ida treatment) 2. *De novo* AML 1st line: bilineal or biphenotypic (flow-cytometry) n=3 (Velcade-Flag-Ida treatment) 3.De novo AML with complex karyotype or with flt-3 mutation, n=13, 1st line (Velcade-Flag-Ida n=10, Velcade-HAM protocol, n=3) 4.Secondary AML or AML with evidence of previous MDS, n=15, 1st line: (Velcade-Flag-Ida n=10, Velcade-HAM n=5) Results Complete remission (CR) 16/35, partial remission (PR) 10/35, no remission 8/35, progression during treatment: 1/35. CR had been achieved in all patients of group, and group 2 (biphenotypic, bilineal). The CR rate was quite appreciable in group 3, i.e. 9/13 (complex karyotype or normal karyotype with FLt-3 mutation) - the response rate was excellent with flt-3 mutated cases). In group 4. (MDS, secondary AML) the results were less impressive. There were no differences according to protocol (Flag-Ida or HAM). Allogeneous stem cell transplantation could have been performed in 1st CR in two patients (one from group 1. and another from group 2.) One of them died due to relapse, the other one is in CR since then. The combinations seem to be relatively safe. Induction related death rate was low (1 MDS/AML patient, thrombocytopenic bleed). 9 other patients had severe neutropenic sepsis (2 with fatal outcome). Pulmonary syndrome, which may follow Velcade+ARA-C had not been documented. Other adverse events did not differ from the pattern observed with standard induction therapies. The addition of bortezomib to induction therpay might imrpove responsiveness in different cohorts of refractory AML, without significant additional risk.

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### THERAPEUTIC REGIMENS INCLUDING CLOFARABINE IN ADULT PATIENTS WITH RELAPSE OR REFRACTORY ACUTE LEUKEMIA

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*Background.* Clofarabine is a new generation purine nucleoside antimetabolite effective in the treatment of Relapse or Refractory Acute Leukemias either in children and in adults. *Aims.* The aim of our study was to demonstrate the effectiveness and the tolerability of a treatment regimen including Clofarabine or Clofarabine plus Cytarabine in adults with AML and ALL refractory to standard treatment. *Design and Methods.* In 2008 at the Department of Hematology of the University of Pise (Italy) we treated 11 adults with refractory leukemias with chemotherapy regimens Clofarabine based. Patients' diagnosis were as follows: 7 with AML and 4 with ALL. Of them, 4 patients were treated with Clofarabine as second-line therapy, 6 patients as third-line therapy and 1 patient as fourth-line therapy. Clofarabine based regimens were as follows: -Cycle A - 7 patients (4 AML, 3 ALL): Clofarabine 20 mg/mq days 1-5; -Cycle B - 3 patients (AML): Clofarabine 40 mg/mq days 1-5, Cytarabine 1 gr/mq days 1-5. Cycle A and B were repeated every 3 to 5 weeks based on response to the previous one (CR, PR or non-response) and were started when hematopoiesis was fully recovered. Patients were allowed to receive a maximum of 2 cycles of induction therapy or until a CR, CR with incomplete platelet recovery (CRp) or partial response (PR) was achieved. A CR required normalization of the marrow (5% blasts) and peripheral counts with no circulating blast cells, a neutrophil count ≥$1x10^9$/L and platelet counts ≥$100x10^9$/L. A PR consisted of a blood count recovery as for CR, but with persistence of 5% to 25% marrow blasts. A CRp had criteria similar to a CR, but without recovery of platelets ≥$100x10^9$/L. 6 patients received just one cycle of therapy and 5 patients received two cycles. During the treatment, transient liver dysfunctions were common in most patients. Myelotoxicity was grade III-IV in all patients; neurotoxicity never occurred. Mucosytis grade III-IV occured in 3 patients and also bacterial sepsis in 3 patients (colonized before the treatment). *Results.* Our results have shown an overall response rate (CR+PR) to Clofarabine higher than 70%: 8 out of