curative treatment option. Although successful unrelated donor umbilical cord blood transplantations (UCBTs) have been reported, series of HLA-identical sibling donor UCBTs in JMML are not available.

Patients and Methods: From the European Working Group on Childhood MDS (EWOG MDS) registry 5 JMML patients who underwent a fully HLA matched sibling UCBT were identified.

Results: The median age at diagnosis was 18 months (range 15–30 months). None of the patients had clinical signs of NF1. In one case a PTPN11 mutation was found. In two other cases no mutation in RAS or PTPN11 was found. In one case no mutation analysis was performed, in four cases the conditioning regimen consisted of busulfan, cyclophosphamide and melphalan and in one case of cyclophosphamide, etoposide and total body irradiation. All patients engrafted slowly (ANC > 500 ul: median 33 days, range 10–35 days, platelets >20,000/ul: median 53 days, range 38–77 days). In 3 patients acute graft versus host disease was noticed (grade 1 and 2); no chronic graft versus host disease was reported. Two patients relapsed after the initial transplantation and underwent a second transplantation with marrow of the initial donor. One of them is in second complete remission and the other died after a second relapse. One patient developed increased donor chimerism from day 42 without any clinical sign of relapse. She was treated with DLI, 6-mercaptopurine and 13-cis retinoic acid respectively. She is still in complete remission 5 years after transplantation.

Conclusion: This EWOG series illustrates that, although this needs to be confirmed in larger series, transplantation with relatively immunologically naive cord blood stem cells from a HLA-matched sibling is feasible in selected cases of JMML.

C030 Long-term remission of post-transplant MDS/AML by adoptive transfer of allogeneic WT1-specific CD4+ and CD8+ T lymphocytes

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We treated a patient with post-transplant MDS/AML by adoptive transfer of Wilm's tumor 1 (WT1)-specific cytotoxic T lymphocytes (WT1-CTL). WT1-CTL were generated by stimulating donor T cells with dendritic cells transduced with recombinant adenovirus encoding truncated WT1 (ΔWT1) created by deletion of the N-terminal portion of full length WT1. ΔWT1-CTL was infused at a cumulative dose of $8x10^7$ cells/m^2 after fludarabine-based chemotherapy and DLI/stem cell support. Although GVHD developed on skin, mouth, and eye 2 months after CTL therapy, steroid therapy was effective. The patient remained in sustained remission for 37 months after ΔWT1-CTL therapy until disease relapsed again. The frequencies of ΔWT1-specific T cells gradually increased over one year and then decreased in peripheral blood. IFN-γ ELISPOT responses specific for ΔWT1 were detected in both $CD4^+$ and $CD8^+$ T cells at 2 years. Furthermore, IFN-γ secreting CD8+ T cells specific for peptides located within ΔWT1 were detected with higher frequencies compared to those for peptide within the deleted N-terminal portion of WT1. These results show that in vitro cultured ΔWT1-specific $CD4^+$ and $CD8^+$ cells can be expanded and function to overcome immune tolerance in a leukemic patient, eliciting long-lasting anti-leukemic immunity. These results raise the possibility that adoptive transfer of in vitro cultured leukemia-specific CTL can be successfully applied to treat hematological malignancies in an allogeneic setting.

C031 Maintenance treatment with 5-azacitidine for patients with high risk myelodysplastic syndrome (MDS) or acute myeloid leukemia following MDS (MDS-AML) in complete remission (CR) after induction chemotherapy

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Around 50% of patients with high-risk MDS or MDS-AML may enter CR after induction chemotherapy, but CR duration, as well as overall survival is usually short. To address this clinical problem the Nordic MDS Group designed a prospective multicenter phase II study, which assessed the clinical feasibility and utility of long-term maintenance treatment with azacitidine. Sixty patients with high-risk MDS (IPSS intermediate-2 or high) (n = 23) or AML following a previous known MDS (n = 37) were enrolled between 2004 and 2006. The mean age was 68 (54–83) and patients should not be eligible for stem cell transplantation. Induction treatment consisted of standard doses of daunorubicin and ara-C. Patients in CR received low dose azacitidine subcutaneously 5/28 days until relapse, unless unacceptable toxicity developed. Methylation status of the $P15^{ink4b}$ (*P15*), *E-cadherine* (*CDH*) and

Hypermethylated in Cancer 1 (*HIC*) gene was analyzed at study start, in CR and in some patients during follow up. Last follow up was on August 1 2008, 24 months after the last CR was reported. Twenty-four patients (40%) reached CR and 23 of these started maintenance treatment with azacitidine. The initial dose of azacitidine was 75 mg/m^2 but as four of the first five enrolled patients developed grade 4 cytopenia, the starting dose was lowered to 60 mg/m^2, and was allowed to be reduced to 45 or 30 mg/m^2 to avoid severe cytopenias. The mean dose of azacitidine was 54.3 mg/m^2. Azacitidine was well tolerated. In 52% of the cases no side effects at all were reported. The most commonly reported side effect was mild rashes at the injection site (35%). Twenty-two percent developed fever or some kind of infection, mostly mild. Myelosuppression (grade 1–3) was seen in 22% of the cases. As previously reported, the probability of reaching CR was negatively correlated to promoter hypermethylation of *CDH* ($p = 0.008$) and none of the 6 patients hypermethylated on all 3 genes reached CR ($p = 0.03$) and hence only four patients hypermethylated on other genes than *P15* received demethylating therapy. The median CR duration for the azacitidine treated group was 13.5 months (2–49+) and median survival time from time of inclusion in the study for the same group was 20 months (4–52+). Four of 23 patients (17%) had a CR exceeding 24 months (32–52+). The two patients hypermethylated on *CDH* pre-induction had CR durations of only 2 and 5 months respectively. By last follow up 3 patients were still in CR. Of 10 patients without any methylation pre-treatment, all but one maintained this pattern in CR. Of the nine patients with pre treatment methylation of at least one gene, only one remained hypermethylated in CR. This patient had a CR duration of only 5 months. One patient showed development of P15 hypermethylation in the bone marrow sampled at 12 months and relapsed at 15 months. These findings support previous reports on *P15* hypermethylation as a marker for minimal residual disease (MRD) and threatening relapse. In the whole group, survival was significantly shorter in patients with *CDH* methylation (3 vs. 9 months, $p = 0.005$), while pre-treatment p15 methylation status did not affect CR duration or overall survival. In conclusion, we show for the first time that maintenance treatment with azacitidine is feasible and associated with a median CR duration of 13.5 months, and very mild side effects. However azacitidine does not seem to prevent relapse in the majority of patients, including those with hypermethylation pre-treatment and/or in CR. Hypermethylation of multiple genes is a strong negative factor for survival, probability of CR, and CR duration. We observe a subset of patients, 17%, with a CR duration of >24 months; but no persistent pattern regarding cytogenetics, methylation or morphology could be identified in this group. The strong negative impact of *E-Cadherin* methylation, a gene involved in adhesion, warrants further investigation.

C032 Is allogeneic hematopoietic cell transplantation a reasonable therapeutic option for elderly (>60 years) patients with de novo myelodysplastic syndromes ?

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With the rare exception of patients, who achieve long lasting remissions with chemotherapy, allogeneic hematopoietic cell transplantation (HCT) is currently the only modality with proven curative potential for MDS patients (pts). However, given the heterogeneity of MDS, and the potential complications associated with HCT, it is often difficult to decide when and in whom to perform an allogeneic HCT. A survival advantage with early transplantation in patients with MDS classified as *intermediate-2* or *high risk* by IPSS criteria was demonstrated. However, this study was restricted to MDS patients below the age of 60 years. In fact, the results are therefore not a reflection of the "true" elderly MDS population who were, up to recently, not considered candidates for allogeneic HCT.

Therefore, this study tried to investigate the outcome of 89 elderly (median age 64 years [range 60–71]) *de novo* MDS patients receiving allogeneic HCT between 2000 and 2008. MDS categories prior to HCT were either RA ($n = 3$), RCMD ($n = 2$), RAEB-1/CMML-1 ($n = 18$), RAEB-2/CMML-2 ($n = 25$) or secondary AML out of MDS ($n = 41$). Almost all of the latter group had received at least one cycle of chemotherapy prior to HCT with 51% achieving a CR. Median time from MDS diagnosis to HCT was 10 months and HCT-comorbidity index (HCT-CI) ranged from 0 to 5 (median 1). The conditioning was of standard or reduced intensity in 30 and 59 pts, respectively and followed by donor cells from either related ($n = 29$) or unrelated ($n = 60$) donors. The graft versus host disease prophylaxis was cyclosporin A or tacrolimus based in all cases. With a median follow-up of 28 months the 3-year overall survival (OS) rate was 40% patients for all patients and was not different ($p = 0.5$) between related and unrelated donor based HCT. OS differed according to marrow blasts (median 8%, range 0–80) prior to Tx (<20%: 44% vs. $\geqslant$20%: 29%, $p = 0.04$). In contrast, grouping pts according to IPSS cytogenetic risk group revealed no statistically significant differences ($p = 0.5$). Of note was the observation that pts with HCT-CI of less or equal to 2 had a significant better OS compared to pts with more advanced co-morbidities (50 vs. 18%, $p = 0.003$). In a multivariate analysis only time from diagnosis to HCT ($p = 0.017$), HCT-CI ($p < .001$), and type of conditioning