mean onset of response in all patients was 2.9 cycles (range = 1–14), with a mean response duration of 12.1 cycles (range = 2–112). Onset of response and response duration did not differ between any groups. For patients with abnormal cytogenetics, 10 of 25 evaluable patients (40%) demonstrated a normal karyotype on follow-up marrow testing. An IWG response was seen in 7 of these 10 patients (70%). Treatment was well tolerated in all groups. The most common side effects were nausea, vomiting, diarrhea, and cytopenia.

Conclusion: Results of this study demonstrate similar response rates, duration of response and tolerability in MDS patients irrespective of karyotype. There does not appear to be a material difference in response to AZA between MDS patients with and without cytogenetic abnormalities or in those with simple versus complex karyotype. Moreover, complete cytogenetic responses can be seen with this agent.

P151 Azacitidine in combination with EPO + G-CSF and valproic acid rapidly determines hematological improvement in pretreated non responsive IPSS INT-1 MDS patients

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The DNMTinhibitor azacitidine has been approved by FDA for treatment of patients with myelodysplastic syndromes (MDS) of all IPSS risk scores. In Europe approval will be subject to results obtained in the ongoing phase III study involving only INT-2 and high risk MDS patients. In fact, a large number of MDS patients with lower IPSS score could be advantageously treated with azacitidine alone or combined with other agents, but data focused on this specific subset of patients are lacking. We evaluated whether azacitidine, in combination with growth factors and the histone deacetylase (HDAC) inhibitor valproic acid (VPA) could determine hematological response in pretreated, refractory MDS patients with IPSS score INT-1. We treated 6 patients with azacitidine 50 mg/m^2/day for five days every 28 days, plus erythropoietin (hrEPO) 40.000 U twice weekly, granulocyte colony stimulating factor (hrG-CSF) 300 ug, once weekly and VPA 600–1200 mg/day. These patients were not eligible for treatment with DNMTinhibitors in any of the ongoing trials and all of them had undergone previous treatment with EPO plus G-CSF for more than 24 weeks, without any hematological response. Five out of six had been treated also with thalidomide 100mg/day, but no response was observed, due to intolerance to treatment and subsequent early drop out. All patients were RBC transfusion dependent, 3/6 both for RBC and platelets. Mean age was 60.8 (35–78). None of the patients had more than 6% bone marrow blasts and only 1/6 had a complex karyotype. Because of the heavy burden of transfusions and deteriorating general conditions, we started treatment. Courses were very well tolerated, with only nausea grade 1–2; in particular, the slow escalation in VPA doses prevented CNS side effect. VPA blood concentrations were kept within neurological therapeutic range. At present, patients received 3–6 courses of therapy, and all showed hematological improvement after only 2 courses. In particular, RBC and platelet transfusion independence was achieved for 5/6 patients, with also general reversal of neutropenia. In one patient, starting with platelets counts below 10×10^9/L and regularly transfused weekly, platelet number was within normal range after 2 cycles of therapy. Hemoglobin levels were in all patients above 9 g/dL, but in none achieved normalization. Only one patient after 4 courses is still transfusion dependent, although with a significantly lower requirement. In conclusion, combination treatment with low dose-azacitidine, growth factors and HDACi VPA was safe and well tolerated, and was extremely effective in inducing rapid hematological improvement in the entire small cohort of pretreated, resistant INT-1 risk MDS patients analyzed.

P152 G-CSF increases hematological response and survival among patients with myelodysplasia treated with azacitidine

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Introduction: In a previous publication we demonstrated that the addition of G-CSF to azacitidine (AZA) improved overall hematological response rate (OHR), as well as erythroid and platelet response in patients with myelodysplastic syndrome (MDS). Here we report further analysis of response onset, response duration, and overall survival (OS).

Methods: We identified 86 MDS patients treated at our institution who received an average of 10.8 cycles of AZA. Forty-nine (49) of these patients also received either erythropoietin (Epo), G-CSF or both during the course of their AZA treatment, while 37 did not receive hematopoietic growth factors. These 2 groups did not differ significantly either in number of cycles of AZA received ($p = 0.500$), FAB MDS subtype ($p = 0.347$) or IPSS score ($p = 0.970$). In the groups receiving growth factors, G-CSF was given for an average of 3.5 cycles and Epo for an average of 6 cycles. Hematological responses were tabulated by International Working Group criteria and compared using chi-square statistics. Survival was calculated from first treatment with AZA and compared using Mann-Whitney U tests as data was not normally distributed.