

refractory cytopenia of childhood (RCC) and high grade MDS (RAEB(t)) in this small cohort. However, some miRNAs are borderline and might hint towards interesting biological differences. One of them is miR-196b, lying within the HOXA gene cluster previously linked to childhood MDS.

### Conclusion

In this study, we showed the deregulation of miRNA expression in childhood MDS even in the absence of gross chromosomal rearrangements. Indeed, more than half of the patients have a normal karyotype. The study of the miRNome of childhood MDS is therefore promising to unravel pathogenetic mechanisms and to identify new therapeutic targets.

### P.32 The generation and activation of Myeloid-Derived Suppressor Cells in Multiple Myeloma

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Multiple Myeloma (MM) is an incurable malignancy of terminally differentiated plasma cells, which are predominantly localised in the bone marrow. The presence of an immunosuppressive bone marrow microenvironment and dysfunction of immune cells are both described in MM patients; however the mechanisms controlling this immunosuppression are not well defined. Recently, a heterogeneous population of immature myeloid cells, the so called myeloid-derived suppressor cells (MDSCs), were identified to be present and active in MM (*Van Valckenborgh et al, Leukaemia 2012, April 23*). MDSCs are thought to promote cancer progression by their T-cell suppressive capacity, however in MM little is known about the generation and activation of these MDSCs.

In this study we investigated the effects of the myeloma microenvironment on the total MDSC population using the 5T33MM mouse model. In a first instance, MDSCs (CD11b+) were isolated from the bone marrow of naive C57BL/KaLwRij mice and cultured in conditioned medium (CM) derived from 5T33MMvt cells. Increased viability and reduced apoptosis of MDSCs cultured in MM CM compared to control medium was observed. In literature GM-CSF is described as a major survival factor for MDSCs. The pro-survival effect induced by the MM CM could be abrogated by the use of a GM-CSF antibody. By Western Blot we also determined an increase in anti-apoptotic factors Mcl-1 and Bcl-xL, and an activation of the STAT3 pathway in the presence of CM. Furthermore, we cultured CD11b- cells in CM of 5T33MMvt cells up to 6 days and found a significant increase in the number of CD11b+ cells, indicating that MDSCs are generated in MM conditions. Importantly, MDSCs cultured or generated in MM CM have an increased T-cell suppressive capacity compared to control medium.

In conclusion, these data reveal MDSCs can be generated and activated in MM conditions *in vitro* by the presence of essential cytokines, including GM-CSF. Experiments on human material are currently performed to better understand the role and mechanisms of MDSCs in MM pathogenesis.

### P.33 Hematological and molecular responses in a case of refractory anemia with ring sideroblasts and thrombocytosis (RARS-T) treated by Lenalidomide

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RARS-T is a rare entity and is defined as an overlap syndrome with features of both myelodysplastic syndromes and BCR-ABL-negative

myeloproliferative neoplasm, including marked thrombocytosis associated with abnormal megakaryocytes. Recently, lenalidomide treatment resulted in hematological responses in 2 patients with RARS-T. We report a third case of RARS-T that was successfully treated by lenalidomide.

A 84-year-old woman consulted for unexplained normocytic anemia (Hb 7.7 g/dL) with marked thrombocytosis ( $1.515 \times 10^9/L$ ). Peripheral blood smear showed a left shift in neutrophils and Bone marrow cytology disclosed hypercellularity with presence of ringed sideroblasts who constituted 90% of erythroid precursors. Erythropoiesis was hyperplastic, with evidence of dyserythropoiesis. The granulocytic series showed signs of dysgranulopoiesis. The most prominent feature was the presence of atypical megakaryocytes of different sizes and shapes with hypolobated nuclei. Metaphase cytogenetics revealed the presence of 5q- in one mitosis, which could not be confirmed by FISH using a specific EGR1(5q31) probe. The presence of the JAK2-V617F mutation was estimated in 12.5-31% of JAK2 alleles. Based on these findings, RARS-T with a JAK2-V617F mutation was diagnosed. After transfusion of 4 units of red blood cells, she was started on lenalidomide 10 mg daily. Her platelet counts dropped  $281 \times 10^9/L$ , leukocytes normalized and she became transfusion-independent after four months of treatment. After ten months, atypical megakaryocytes and ringed sideroblasts had disappeared in new bone marrow cytology and the PCR for the JAK2-V617F mutation became negative. Lenalidomide treatment was continued, but later stopped after two years because of asthenia. During the active treatment period, the patient received only one RBC transfusion. The patient is currently followed without active treatment with normal platelet and leucocyte counts and a stable macrocytic anemia (Hb of 9.4 g/dL).

Some authors suggest to discard the RARS-T category since it is a rare disease with features and treatment options similar to ET. The described cases of RARS-T patients that were successfully treated with Lenalidomide suggest a distinct pathophysiology and a different therapeutic strategy for these patients

### P.34 Multiple Myeloma in the era of novel agents: a single center experience

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#### Introduction

The positive impact of the novel agents on the prognosis of multiple myeloma has been demonstrated in several phase III clinical trials. However, clinical trials may not reflect the real life situation because of selection bias.

#### Study aim

Our aim was to study overall survival in a consecutive cohort of patients exposed to novel agents.

#### Patient population and methods

A total of 63 consecutive symptomatic myeloma patients diagnosed and treated in the department of clinical hematology in UZ Brussel between January 1st 2007 and December 31st 2011, were included. Of these, 59 received at least one line of anti-myeloma treatment. Patient characteristics: M/F (46%/54%); ISS stage I (47%), II (31%) and III (22%); median age at diagnosis: 66 years; creatinine clearance  $<60 \text{ml/min}$  in 39%. Kaplan-Meier method was used for survival analysis, also performed separately for patients eligible or not for autologous stem cell transplantation (ASCT).

#### Results

First-line treatment was thalidomide-based in 44%, bortezomib-based in 46% and lenalidomide-based in 5% of cases. Only 19 (33%) patients were included in clinical trials. With a median