

imunomoduladoras do ART. **Conclusão:** Este estudo demonstra pela primeira vez os efeitos in vivo do ART em um modelo murino de SMD, evidenciando uma modulação imunológica significativa na medula óssea com redução de células imunossupressoras e aumento de células NK, além da diminuição da hematopoiese extramedular. Esses resultados reforçam o potencial terapêutico do ART para SMD.

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MOLECULAR CYTOGENETIC CHARACTERIZATION OF DER(7)T(1;7) IN MYELODYSPLASTIC SYNDROME: CLINICAL IMPLICATIONS

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Introduction: Myelodysplastic syndrome (MDS) represents a heterogeneous group of hematologic malignancies characterized by ineffective hematopoiesis, resulting in cytopenias and a high risk of progression to acute myeloid leukemia (AML). Approximately 50% of patients with MDS have chromosomal abnormalities, which are a prognostic marker. The most common chromosomal abnormalities in MDS include deletion of the long arm of chromosome 5 [del(5q)], alterations in chromosome 7 (deletion of the long arm of chromosome 7 [del(7q)]/monosomy 7), and trisomy 8. Alterations in chromosome 7 are associated with an unfavorable prognosis. The chromosomal abnormalities [-7/del(7q)] affect genes critical for cellular regulation, leading to dysfunctions in the development and maturation of blood cells. The unbalanced translocations der(7)t(1;7) has been considered by some studies as a variant of chromosome 7 alterations, presenting a prognosis similar to these alterations. However, according to the Revised International Prognostic Scoring System (IPSS-R), the der(7)t(1;7) presents an intermediate prognosis. **Objective:** To report cases of patients with MDS who presented the unbalanced translocations der(7)t(1;7) and their clinical outcomes. **Materials and methods:** This study included 4 patients of a total of 460 adult patients with MDS, between 2000-2023. Cytogenetic analyses were performed on bone marrow cells by G-banding and fluorescence in situ hybridization (FISH). **Results:** Chromosomal abnormalities were observed in 41% (190/460) of the patients. Of these patients, four had unbalanced translocations involving chromosomes 1 and 7. The patients were classified in advanced subtypes (MDS-AB1/AB2) and progressed to AML. Of these patients, three had der(7)t(1;7)(q10;q10) and one patient had a different breakpoint region [46,XY,der(7)t(1;7)(q21;q31)]. Not previously reported in the literature. **Discussion:** Although uncommon, unbalanced translocation involving the der(7)t(1;7)(q10;q10) breakpoints has been previously reported in approximately 0.6% to 2.6% of MDS cases. Some studies suggest that der(7)t(q10;p10) is associated with a more favorable prognosis compared with -7/del(7q), while others have not observed significant differences in prognosis between these cytogenetic alterations. In our study,

we observed that these chromosomal translocations were associated with advanced disease subtypes and progression to AML. **Conclusion:** Our study suggests that der(7)t(1;7) is associated with an unfavorable clinical outcome in adult patients with MDS. **Support:** Ministério da Saúde – INCA.

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ASSOCIATION BETWEEN EZH2 EXPRESSION PATTERN WITH KARYOTYPE AND EVOLUTION FROM MYELODYSPLASTIC NEOPLASM TO ACUTE MYELOID LEUKEMIA

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Introduction: Myelodysplastic Neoplasm (MDS) is a heterogeneous group of clonal hematopoietic stem cell diseases. MDS is characterized by the presence of bone marrow (BM) dysplasias, peripheral blood cytopenias and is frequently associated with progression to Acute Myeloid Leukemia (AML). MDS represents an ideal model to study the steps involved in leukemogenesis. Recent advances at the molecular level have provided new insights into the development of MDS and its progression to AML. The *Enhancer of Zeste Homolog 2* (EZH2) is a histone methyltransferase. It is the catalytic subunit of PCR2 for tri-methylation of histone 3 at lysine 27 (H3K27me) by SET domain in its C-terminus, which silences target genes involved in various biological functions as cell cycle, cell proliferation and differentiation. PcG proteins are important epigenetic regulators and critical factors of pluripotency and differentiation of stem cells as well as aberrant gene expression during the malignant transformation. Few studies have investigated the expression of EZH2 in MDS and the results are controversial. **Objective:** To analyze the expression pattern of the EZH2 gene in adult patients with MDS and its association with karyotype and progression to AML. **Materials and methods:** This study included 70 adult patients with MDS and 20 adult donors of bone marrow for hematopoietic stem cell transplantation (HSCT). Cytogenetic analyses were performed by G-banding and fluorescence in situ hybridization (FISH). Analysis of the expression pattern of the EZH2 gene was performed by real-time PCR. **Results:** Analysis of the relative expression levels of the EZH2 gene showed that patients had a higher expression when compared to controls ($p < 0.0005$). Abnormal karyotypes were observed in 49% of the cases analyzed (34/70). The association of relative expression levels of EZH2 between patients with normal karyotypes and abnormal karyotypes showed a higher relative expression. of EZH2 in patients with abnormal karyotypes ($p < 0.002$). Disease progression was observed in 44% of the patients (31/70). The patients who had leukemic evolution presented a relative expression pattern of EZH2 significantly higher compared to patients without progression ($p < 0.0001$). **Discussion:** Few studies have evaluated EZH2 expression in adult patients with MDS. However, these studies show controversial results. One study showed that EZH2 overexpression is associated

with poor prognosis. While the other showed that the low EZH2 expression is associated with alterations in chromosome 7 and disease progression. In our study, we observed that the EZH2 overexpression in adult patients with MDS was associated with abnormal karyotypes and leukemic evolution. **Conclusion:** Our study suggests that EZH2 overexpression is associated with the evolution from MDS to AML, being a possible prognostic biomarker. **Support:** Ministério da Saúde – INCA.

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IS FERRITIN A GOOD PREDICTOR OF SURVIVAL ACROSS ALL RISK LEVELS IN MYELODYSPLASTIC NEOPLASMS? INSIGHTS FROM A STRATIFIED COHORT STUDY

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Introduction: Myelodysplastic neoplasms (MDS) are a heterogeneous group of hematologic malignancies characterized by ineffective hematopoiesis. The Revised International Prognostic Scoring System (IPSS-R) is widely used to stratify MDS patients into different risk categories, guiding treatment decisions and predicting survival outcomes. Ferritin has been implicated in the pathophysiology of MDS. Elevated ferritin levels may reflect iron overload, inflammation, or both. However, the prognostic value of ferritin across different risk levels in MDS remains unclear. **Objective:** This study aims to evaluate the prognostic significance of ferritin in patients with MDS, stratified by IPSS-R risk categories. **Methods:** A retrospective cohort study at a single reference center reviewed patients diagnosed with MDS between 2004 and 2024. The study included patients with available clinical outcomes and ferritin values. Missing data for other variables were addressed using the classification and regression tree analysis (CART) Multiple imputation method, following confirmation of non-completely at random missingness through Little's test. Patients were stratified into two groups based on IPSS-R scores: 'high risk', comprising those categorized as 'High' or 'Very High', and 'low risk', encompassing all other IPSS-R categories. The CART method was utilized to determine the optimal ferritin cut-off for predicting overall survival, applying Martingale residuals from a univariate Cox model adjusted for ferritin. Kaplan-Meier curves were subsequently generated to assess survival rates at 1, 3, and 5 years post-diagnosis for patients below and above the ferritin cut-off, with comparisons conducted using log-rank tests. All statistical analyses were performed using R software, leveraging

the 'mice' package for imputation and the 'survfit' package for survival analysis. **Results:** A total of 143 patients with available ferritin values and clinical outcomes were included in the study. Using the CART method, an optimal ferritin cut-off of 888.5 was determined, classifying the cohorts into "High Ferritin" (32 patients) and "Low Ferritin" (111 patients). Kaplan-Meier 1, 3, and 5-year survival curves were constructed for both the 'high risk' (17 patients) and 'low risk' (126 patients) groups. Among the 'low risk' patients, those with low ferritin levels, compared to those with high ferritin levels, had significantly higher 3 (78.6% vs 44.3%, $p < 0.001$) and 5-year (57.3% vs. 34.8%, $p < 0.001$) survival rates, although no difference was seen in 1-year rates ($p = 0.45$). Within the 'high risk' group, no difference between the high and low ferritin groups was seen in 1, 3, or 5-year survival rates ($p = 0.26$, 0.066, and 0.066, respectively). **Discussion:** Ferritin, a marker of iron overload and inflammation, plays a role in the pathophysiology of MDS. Our study shows that ferritin levels predict long-term survival in low-risk MDS patients, consistent with previous studies, but are less predictive in high-risk patients. This suggests ferritin's impact may be overshadowed by other factors in high-risk MDS. **Conclusion:** Ferritin level at diagnosis is a good predictor of long-term survival for non-high risk MDS patients, but its efficacy in predicting outcomes for high-risk patients and general short-term survival is less evident.

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STRENGTHENING THE EVIDENCE: RAP1B GENE ASSOCIATION WITH SYNDROMIC THROMBOCYTOPENIA

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Introduction: Syndromic thrombocytopenia encompasses a heterogeneous group of disorders characterized by both quantitative and qualitative defects of platelets, often accompanied by other malformations. The clinical manifestations of patients vary in severity, but bleeding is considered the main complication, which can lead to the development of other disorders such as hematological malignancies. Recently, heterozygous, *de novo* variants in RAP1B have been reported in five cases of syndromic thrombocytopenia. Here, we report an additional case of syndromic thrombocytopenia associated with a rare *de novo* variant in RAP1B. **Case:** We present a case of a 2-year-old female patient with thrombocytopenia first observed at the age of 6 months. She has severe, persistent thrombocytopenia that is refractory to various therapies. The main phenotypic characteristics identified were hypertelorism, low ear implantation, and a broad forehead. Exome sequencing revealed a rare *de novo* heterozygous variant in the RAP1B gene (NM_001010942.3 c.178G>A p.