AZACYTIDINE (A) ASSOCIATED WITH VITAMINS (B1, C, AND D) IN THE TREATMENT OF ACUTE MYELOID LEUKEMIA.

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Objective: To report the clinical evolution of AML with complex karyotype in an elderly individual using the AZAVIT-ABCDEF protocol. **Method:** Information was obtained through electronic medical record review (HSPE–IAMSPE-SP). **Introduction:** The cellular proliferation that occurs in AMLs requires significant energy access. Warburg described in 1956 that neoplastic cells, even in the presence of O2, utilize anaerobic metabolism. Improving the use of aerobic pathways with high doses of vitamins may favor the differentiation of hematopoietic cells. The AZAVIT-ABCDEF protocol (AZACYTIDINE 75 mg/m^2 subcutaneously for 7 days associated with high intravenous doses of Vitamins B1 (15-20 mg/kg every 12/12 hours), C (300 - 400 mg/kg intravenously every 12/12 hours), calcitriol 0.25 mcg orally every 6/6 hours, erythropoietin 10,000 IU subcutaneously once a day, and filgrastim 5-10 mcg/kg subcutaneously once a day) in a 28/28-day cycle. Between cycles, oral use includes Vitamin C 2 g every 8/8 hours, Benfotiamine 150 mg every 12/12 hours, Vitamin D 50,000 IU once a day until levels reach 80-100 ng/mL, and Famotidine 40 mg every 12/12 hours - (Plataforma Brasil CAAE: 53015421.0.0000.5463). After obtaining informed consent. **Case report:** Male 80-year-old in NOV/22 presented with anemic syndrome, Hb = 5.5 g/dL; Leukocytes = 3719/mm^3 (20/11/0/55/14); Platelets = 38,000/mm^3. Bone marrow: 30% blasts with phenotype: CD10, CD13, CD33, CD34, CD38, CD71, CD117, CD123, HLA-DR, and MPO. Karyotype: 45 XY add (3) (q21), del5, add(7) (p11.2), -9, der (12)t(1214) (p11.2q11.2), -14, +2mar [17] /46, XY [4]. FISH: Deletion of Chromosome 5 in 130/200 metaphases. He received 4 cycles of the protocol. Progressed with Hemogram: Hb = 14.1 g/dL; leukocytes = 13,670/mm^3 (neutrophils = 10,130) and platelets = 273,000/mm^3. Bone marrow: Hypercellular and normomaturative with negative minimal residual disease. Karyotype: 46, XY [20] and FISH: normal. As of August 2023, he is on the 8th cycle with stable hemogram. **Discussion:** Vitamins are closely linked to the Krebs cycle, not providing energy but releasing it through intense redox mechanisms. This may contribute to better epigenetic regulation of primitive hematopoietic cells. Genes linked to epigenetics: DNMT3A, TET2, ASXL1, IDH1, and IDH2 are frequently mutated in AML and are considered important for directly or indirectly leading to DNA methylation. Azacytidine: inhibits DNMT3A and promotes cell differentiation. Vitamin: An effective guardian of aerobic metabolism, serving as a cofactor for pyruvate dehydrogenase complex (PDHC), the enzyme allowing pyruvate to enter the Krebs cycle. It also acts on alpha-ketoglutarate metabolism, reducing 2-Hydroxyglutarate (2-HG) formation and DNA methylation. Vitamin C: Cofactor of TET2 gene in DNA demethylation. Vitamin D: Binds to VDR, which heterodimerizes with retinoid-X receptor (RXR) within the cell nucleus, serving as a transcription factor for numerous target genes. **Conclusions:** The patient exhibited an excellent response, and the AZAVIT-ABCDEF protocol should be studied in a prospective cohort to better define its role in treating AML in patients without performance status for intensive treatment. The main objective is to reduce transfusion dependence and extend survival in this population.

https://doi.org/10.1016/j.htct.2023.09.494

MYELOID ACUTE LEUKEMIA WITH INCREASED BASOPHILIC CELLS AND HISTAMINE RELEASE EPISODES

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Objective: Reporting a case of a patient with Acute Myeloid Leukemia (AML) and increased basophils and episodes of histamine release. **Methods:** Data collection in HSPE's digital system. **Case report:** A 58-year-old woman, addicted, ex-smoker and ex-alcoholic complaining of fatigue, headache, visual scotomas and loss of 30 kgs who on physical examination showed dyspnea, splenomegaly and signs of retinal leukostasis. Hemoglobin 6.4 g/dL, leukocytes 312,870/mm^3 (5% blasts) and platelets 186,000/mm^3, LDH 4,317 U/L and uric acid 15 mg/dL. Myelogram: 21% blasts, some with metachromatic granules and 9% basophils. Normal karyotype and FISH. There was no description of basophils in immunophenotyping (IPP). It was not possible to measure serum tryptase and the PCR for BCR-ABL was negative. She had hydroxyurea and 1 session of leukapheresis. Ten days after discontinuation of the antimetabolite due to leukopenia, the patient presented with hypotension and dyspnea, responsive to volume expansion, corticosteroid therapy and broad-spectrum antibiotic therapy. Without performance status for an intensive chemotherapy regimen due to chronic obstructive pulmonary disease and karnofsky= 60%, the AZAVIT-ABCDEF protocol (azacitidine associated with erythropoietin, filgrastim with high doses of vitamins B1, C and D3) was chosen, after signing a consent form - CAAE 53015421000005463. She was discharged and returned in 15 days with leukocytosis. Cytoreduction with hydroxyurea was reinitiated. A new medullary evaluation and IPP with a panel to study basophils showed increased immature basophils. There was a drop in leucometry and 5 days after its suspension, in the absence of neutropenia, she presented with dyspnea, cough, desaturation and hypotension, responsive to volume resuscitation, corticotherapy and diphenhydramine. There was no infectious focus and cultures were negative. After this second episode, the patient is on continuously use of H1 and H2 antihistamines. She is still undergoing treatment for AML, however, the protocol has been changed for azacitidine and venetoclax, for 7 days every 28 days, due to the increase in blasts in peripheral blood. She has had 2 cycles and is now in complete remission.

Discussion: However, the protocol was changed to azacitidine and venetoclax, for 7 days every 28 days, due to the increase in peripheral blood blasts, she received 2 cycles and is in complete remission. The basophilic AML classification is not standardized and the WHO classification does not specify the number of basophils. Valent et al classified basophilic leukemia in the presence of 40% of basophils, being acute if it has more than 20% of blasts. The reported case, despite not having a number of basophils above 40%, presented a typical picture of histamine release. Distinguishing the basophilic blast is difficult even with toluidine blue staining. **Conclusion:** basophils store histamine in their granules and its degranulation can lead to serious conditions with increased vascular permeability, increased complement and release of other inflammatory cytokines. There is little information about the prognosis and survival of this subtype of AML, the patient in question has a current survival of 9 months. It is important to think about this entity when the morphology and immunophenotyping are suggestive for the treatment of histamine release to be adequate, a serious and potentially fatal situation.

https://doi.org/10.1016/j.htct.2023.09.495

CLINICAL CHARACTERISTICS, COMPLICATIONS AND OUTCOME OF PATIENTS RECEIVING VENETOCLAX-BASED REGIMENS IN BRAZIL: A REAL-WORLD STUDY

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Introduction: The combination of venetoclax with hypomethylating agents (VEM-HM) is considered standard of care for unfit or elderly patients with acute myeloid leukemia (AML). However, in the real world, venetoclax-based regimens have been used also to treat fit patients with AML, relapsed/refractory AML, and myelodysplastic syndromes (MDS). **Objective:** To describe the early results of a multicentric study that evaluated patients with AML or MDS treated with venetoclax-based regimens in Brazil. **Methods:** In this retrospective study, we evaluated clinical characteristics, complications and outcome of the first cycle of venetoclax-based regimens in the treatment of patients with AML and MDS. **Results:** A total of 64 patients were analyzed, 58% were male and the median age was 64 years (range 19-82). Most patients had AML (88%) with high risk disease (64%), and the main indication for venetoclax use was unfit patient (51%). VEN-HM was the most common regimen used (74%), while intensive chemotherapy regimens plus venetoclax was given in 10 patients. The most common symptoms were nausea (45%) and diarrhea (39%). Mucositis occurred in all patients receiving intensive chemotherapy vs. 20% in patients receiving VEN-HM ($p < 0.001$). Antifungal prophylaxis was used in 67.5% of patients, and micafungin was the most frequent agent (70%). Antibacterial and antiviral prophylaxis was used in 53% each. Febrile neutropenia occurred in 82% of patients, with 47% classified as fever of unknown origin, 15% bacteremia, 22% clinically documented and 15% microbiologically documented infection. Proven or probable invasive fungal disease (IFD) was diagnosed in 1 of 10 (10%) patients receiving intensive chemotherapy and 3 of 43 (7.0%) receiving VEN-HM: aspergillosis in 1, fusariosis in 2 and invasive candidiasis in 1. At the end of the first cycle, 52% of patients had complete response (CR) or complete response with incomplete hematologic recovery (CRi) and 34% were considered refractory. CR + CRi was 57.5% in patients receiving VEN-HM and 30% in patients receiving intensive regimens. Death occurred in 6% of patients. **Discussion:** This is the first real-world study in Brazil evaluating the use o venetoclax-based regimens in patients with AML or MDS. These preliminary results show that a) antibacterial, antifungal and antiviral prophylaxis are a common practice; b) most clinicians chose an echinocandin, probabily to avoid venetoclax dose reduction; c) The 52% CR + CRi rate after the first cycle is similar to the rates observed in the randomized trial.

https://doi.org/10.1016/j.htct.2023.09.496

DESENVOLVIMENTO DE TESTE DIAGNÓSTICO PARA LEUCEMIA LINFOBLÁSTICA AGUDA POR SEQUENCIAMENTO DE NOVA GERAÇÃO

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Objetivos: Desenvolver e validar um teste genético para análise de mutações somáticas relacionadas a leucemia linfoblástica aguda (LLA) e assim dispor de uma abordagem molecular de investigação genética por meio de