UNIVERSITY OF MEDICINE AND PHARMACY
"CAROL DAVILA" BUCHAREST
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MEDICINE-HEMATOLOGY

ACUTE LEUKEMIA IN PATIENTS WITH A HISTORY OF NEOPLASIA
PARTICULAR ELEMENTS

ABSTRACT OF THE DOCTORAL THESIS

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Achieving complete remission following the diagnosis of oncohematological neoplastic pathology is the goal of each clinician, but the patient's exposure to chemotherapy and/or radiotherapy can have long-term consequences, such as the development of acute leukemia.

Secondary acute leukemia is a heterogeneous hematopectic pathology that occurs in patients with a history of hematology including myeloproliferative neoplasms, myelodysplastic syndrome or following exposure to chemotherapy and radiotherapy agents.

Considerable progress has been made following the identification of molecular abnormalities, recurrent chromosomal abnormalities and cytogenetic mutations, offering the possibility of classifying acute leukemias into different subgroups, depending on their response to current therapy. The major contribution is also due to the identification of targeted therapies and new therapeutic agents such as FLT3, IDH2 and BCL2 inhibitors, however the mortality rate remained high, especially in patients over 60 years of age [1,2]. With the identification of these cytogenetic changes and the mechanisms of production, the hope of the emergence of targeted therapies increases, especially in patients with acute leukemia, whose evolution is rapidly progressive towards exitus.

In 2022, the revision of the classification of acute myeloblastic leukemia took place by the World Health Organization working group [3] (the main change consists in the waiver of the percentage of myelogenous leukemia, which was previously over 20% in patients with AML with defined genetic abnormalities except for BCR ABL, CEBPA), the European LeukemiaNet[4] group that classifies acute myelogenous leukemia according to cytogenetic risk in favorable risk, intermediate and unfavorable (currently the FLT3 ITD+ mutation presents intermediate cytogenetic risk, AML with MDS related genetic mutations (MDS related) are classified as adverse risk, the CEBPA mutation with in-frame mutations affecting the bZIP region are classified in the favorable risk group, the unfavorable risk group includes recurrent cytogenetic abnormalities such as t(3q26.3,V) involving the MECOM gene or t(8,16)(p11, p13) associated with the KAT6A CREBBP fusion gene.

Immunophenotypic examination is the technique of measuring the expression of specific proteins in a cell population by coupling specific antibodies with fluorescent compounds; it is a type of flow cytometry test, the principle of which is to determine the presence or absence of markers on the cell surface[5]; another essential role is related to the evaluation of the response to treatment and the highlighting of minimal residual disease (MRD) [6]. The importance of this technique is crucial in the diagnosis of acute leukemia for both the certainty and differential diagnosis, highlighting the cell line. It should be noted that in acute leukemia there may be aberrant cells from an immunophenotypic point of view, thus identifying acute leukemia with mixed phenotype. This technique may suggest the existence of genetic abnormalities [7,8,9]. Hematopoietic cells exhibit immunophenotypic markers or specific antigenic expressions on their surface. The antigens identified by immunophenotyping in acute myeloid leukemia are classified as follows: myeloid precursors (CD34, CD117, HLA-DR), myeloid markers (cMPO, CD33, Cd13), mature myeloid markers (CD14, CD36, CD64), megakaryocytic markers (CD41, CD36, CD61) and erythrocyte markers (CD235, CD71 and Cd36) [4,7,10,11]. Leukaemia cells can sometimes exhibit certain expressions that are not normally present on the surface of the cells of that line, called aberrant phenotypes. They can be divided into four categories:1. linear infidelity, translated by the co-expression of lymphoid markers in myeloid cells 2. linear asynchrony where there are unexpected markers for maturation stage 3. Overexperience 4. the lack of expression of a marker [12,13]. Aberrant phenotypes are classified as negative prognostic factors [14], being associated with cytogenetic abnormalities [15]. **Linear infidelity** consists of the presence of particular immunophenotypic elements, in which a lymphoid marker can co-express on the surface of myeloid line cells, e.g. CD7, CD56, CD2, CD3, CD19 [13]. **The overexpression of** myeloid markers is another form of aberrant expression, with prognostic value in the pathology of acute myeloblastic leukemia (CD123). There are certain correlations between the presence of these aberrant phenotypes and the prognosis of acute myeloblastic leukemia, along with the presence of certain molecular markers (such as FLT3 ITD).

Acute myeloblastic leukemia can occur as a secondary form (sAML) following another malignant hematological disorder such as myelodysplastic syndrome, myeloproliferative neoplasms (polycythemia vera, essential thrombocythemia, myeloid metaplasia with myelofibrosis, chronic granulocytic leukemia), aplastic or postcytotoxic anemia, as a result of exposure to chemotherapy agents and/or radiotherapy [16-18].

Secondary acute myeloid leukemia is a hematological pathology with a poor prognosis, with a median overall survival of 4.7 months and an event-free survival of 2.9 months [19]. It mainly affects older people, with the median age being 67 years old, and about a third of patients are over 75 years old. The common mutations that lead to the evolution of secondary acute myelogenous leukemia are located in the components of the spylosome, such as SRSF2, epipetic modifiers such as TET2, IDH1/2, ASXL1 and EZH2, or TP53 which has a role in maintaining genomic integrity, these mutations being acquired in addition to the mutations that lead to the development of myelodysplastic syndrome or myeloproliferative neoplasms [20]. The moment of transformation into secondary acute leukemia is difficult to estimate, depending on the patient's genetic predisposition, age at the onset of the first disease, the therapeutic line administered for the first disease, the cumulative dose of chemotherapy, the dose of radiotherapy.

Postcytotoxic acute myeloid leukemia (pCT AML) or therapy-related leukemia (t-AML) is defined as a form of acute myeloid leukemia resulting from cytotoxic treatment, ionizing radiation therapy, or immunosuppressive therapy for an unrelated pathology [21]. The development of t AML is preceded by therapeutic administration for solid tumors, hematological pathologies (e.g., Hodgkin's disease, non-Hodgkin's lymphoma, and multiple myeloma), or autoimmune diseases (e.g., rheumatoid arthritis) [22,23].

Breast cancer is the most common primary solid malignancy preceding t-AML, followed by hematological pathology, non-Hodgkin's lymphoma [24]. The frequency of t-AML cases in patients diagnosed and treated for breast cancer and non-Hodgkin's malignant lymphoma, respectively, was 4.6 and 5.85 times higher than expected in the general population of patients diagnosed with a malignancy and treated with chemotherapy [25]. Of all cases of acute myeloblastic leukemia, it has been estimated that postcytotoxic AML accounts for 7-8% [24]. It is believed that with the increase in the overall survival rate of oncohematological patients, their incidence will also increase [25].

Initially, t-AML was thought to occur due to DNA damage by cytotoxic therapy; however, current evidence suggests several mechanisms, which are not mutually exclusive, that lead to the pathogenesis of postcytotoxic AML [26,27]. These are represented by: (1) direct induction of a fusion oncogene by chromosomal translocation; (2) induction of genome instability; (3) chemotherapy or radiation-induced lesions of the bone marrow creating a pro-

inflammatory, proleukemic environment; and (4) selection of hematopoietic cell clones resistant to pre-existing treatment [26,27]. Postcytotoxic secondary acute myeloid leukemias are commonly associated with prior exposure to drugs targeting topoisomerase II, such as etoposide and doxorubicin. These drugs work by inhibiting topoisomerase II enzymes, which normally induce double-stranded DNA breaks [28,29]. The inhibitors block topoisomerase II in a DNA cleavage complex, preventing the re-ligation of DNA strands and leading to the accumulation of DNA breaks [30,31]. These persistent breaks can trigger chromosomal translocations, especially in the MLL gene at chromosomal band 11q23 [32]. This leads to oncogenic fusion proteins that disrupt genes involved in hematopoiesis, such as Hox genes, contributing to leukemogenesis [33].

Locked topoisomerase II cleavage complexes are responsible for initiating DNA breaks, which can lead to chromosomal aberrations when repair mechanisms fail [34,35]. As a result, chromosomal translocations 11q23 are frequently observed in acute postcytotoxic myeloblastic leukemia, especially in those treated with etoposide or doxorubicin, suggesting that topoisomerase II-mediated ruptures are the origin of these secondary leukemias [36,37]. Postcytotoxic AML induced by alkylating agents such as bendamustine, cyclophosphamide, melphalan, chlorambucil, nitrozourea, and platinum compounding agents such as cisplatin and carboplatin produce monosomy for chromosome 5 or 7, or loss of chromosome arms 5q or 7q [27, 38]. Alkylating agents produce covalent changes in DNA, causing crosslinking of DNA, double-stranded breaks, mutations and cytotoxicity. Platinum compounding agents have a weaker association with postcytotoxicAML [39,40]. The probability of causing the development of a therapy-associated disease varies with regard to alkylating agents (melphalan>cyclophosphamide) [41,42], with a dose-response relationship between the amount of alkylating agent received and the risk of developing the disease [43]. Pedersen-Bjergaard J et al. proposed eight pathways of transformation into acute postcytotoxic myelogenous leukemia. Tumor protein 53 (TP53) is a tumor suppressor gene located on the surface of chromosome 17p13.1; it controls apoptosis (programmed cell death), aging, cell cycle arrest, and DNA restoration [44]. TP53 is the most common gene in patients with t-AML, with up to 70% of them having the gene [45,46,47]. In the literature, two main DNA-binding positions have been highlighted that show the maximum frequency of alteration in cancer, these being R273 and R248 [48,49]; other DNA binding points include remnants K120, A276, C277, R280 and D281, which are mainly present in the vicinity of R273

[50]. TP53 mutations are linked to an increased risk of leukemic transformation, show resistance to chemotherapy treatment, and low overall survival rate 51,52,53].

Rates of progression to sAML for myeloproliferative diseases vary by subtype: on average 15% of patients with myelofibrosis, 8.35% of patients with polycythemia vera, and 1.85% of patients with essential thrombocythemia within ten years [54]. In the case of patients with myelodysplastic syndrome, one third progresses to sAML, being characterized by pancytopenia due to apoptosis (programmed cell death) of hematopoietic progenitor cells [55,56].

The purpose of the paper is to highlight certain particular elements with a possible starting point for targeted therapies, to improve the evolution of the pathology, by increasing the hope of survival, and, why not, to achieve complete remission. Despite all the progress made in the classification of acute myeloblastic leukemia on the cytogenetic and molecular risk group, currently, the therapies discovered and approved are not sufficient to achieve complete remission; Thus, this hematological pathology represents an incurable disease, with a low survival duration. The usefulness of continuing research on the discovery of new immunological therapies using monoclonal antibodies, through various mechanisms of action is increased.

The paper aims to study a prospective batch of patients diagnosed with acute leukemia between 2015 and 2024 February, following the approval of the Ethics Committee of the Bucharest University Emergency Hospital and the Colentina Clinical Hospital Bucharest, after the patient's signature of the informed consent. The people included in the study met the criteria for inclusion in the study, I mention that no patient was analyzed without the consent granted.

During the COVID-19 global pandemic, Colentina Clinical Hospital was a support hospital, so it was impossible to enroll patients from that period, as they did not meet the enrollment criteria.

A total of 107 patients diagnosed with acute leukemia were analyzed, distributed as follows: acute myeloblastic leukemia de novo LAMdn (41), secondary acute myeloblastic leukemia after MDS (23) and after myeloproliferaative disorders (patients with chronic granulocytic leukemia were excluded) (6), acute postcytotoxic myeloblastic leukemia (secondary to chemotherapy and/or radiotherapy treatment for solid cancer or hematopathy) (32) and secondary acute lymphoblastic leukemia (5). The study protocol

consisted of the patient's identification data (initials, age, sex, general data, date of diagnosis of the first neoplasia, date of diagnosis with acute leukemia), comorbidities, pathological personal history, the classification of acute leukemia was performed according to the FAB classification, ELN, blood count values, evaluation of the percentage of peripheral and molecular blasts, coagulation tests, biochemical samples, immunophenotypic examination, cytogenetic analysis, molecular examination analysis, results obtained through funding by the National Oncology Program Subprogram for immunophenotypic, cytogenetic and biomolecular diagnosis of acute leukemias. Following the analysis of the 107 patients, we presented the results in two studies:

1. Acute myeloblastic leukemia secondary to MDS and MPD

2. Acute postcytotoxic leukemia (onset in patients with a history of chemotherapy and/or radiotherapy).

STUDY I Secondary acute myeloblastic leukemia after myelodysplastic syndrome, chronic post-myeloproliferative syndrome A number of 23 patients with secondary acute myeloblastic leukemia after MDS and 6 patients after MPD (patients with chronic granulocytic leukemia were excluded) (6) were analyzed in the study along with 41 patients with acute myeloblastic leukemia de novo.

Study II Acute Postcytotoxic Leukemia (Post-Exposure Chemotherapy/Radiation Therapy)

In the study group we analyzed patients with acute postcytotoxic myeloblastic leukemia (secondary to chemotherapy and/or radiotherapy treatment for solid cancer or malignant hematopathy) we followed 31 patients with various oncohematological conditions, namely:

- Breast cancer (16)
- Prostate Adenocarcinoma (2)
- Uterine Neoplasm (3)
- Chronic lymphocytic leukemia (2)
- DLBCL (2)
- Hodgkin Lymphoma (2)
- Follicular Lymphoma (1)

- Thyroid cancer (1)
- Osteosarcoma (1)
- Waldenstrom Disease (1)
- Mediastinal Cancer (1)

In this study I would just like to mention the cytotoxic impact on the patient and the possibility of secondary acute lymphoblastic leukemia (5) with prostate adenoma, breast cancer, pancreatic cancer and chronic lymphocytic leukemia.

An increased share of patients with breast cancer in the studied group is observed, breast cancer being the most common cause of acute postcytotoxic myeloid leukemia, despite the increased frequency, the mortality rate of patients with breast cancer is low (15%), the diagnosis can be made from the first imaging changes, the adjuvant therapy used leads to a prolonged survival rate, It is estimated that one patient out of 20 breast cancer patients will develop another neoplasm after 10 years, representing a 22% relative risk for secondary acute myeloid leukemia.

Conclusions

- Secondary acute leukemia is a pathology with high mortality rate
- **The latency period** was longer in patients with acute postcytotoxic leukemia compared to those diagnosed with secondary acute leukemia
- **The survival of patients** with secondary acute leukemia is influenced by the presence of lifestyle peculiarities - smoking, increases in body mass index, but also by the presence of cardiovascular comorbidities, diabetes.
- **The survival** of patients with secondary acute leukemia compared to de novo acute leukemia is short, both due to the increased frequency of unfavorable risk cytogenetic changes, and due to the impossibility of administering intensive chemotherapy secondary to old age or the presence of comorbidities. The causes of death on the entire group were either by disease progression, or by severe sepsis or other causes
- The value of monocytes correlates with the percentage of bone marrow blades in LAMs, with a positive index, resulting in a directly proportional correlation, with a statistical p value of 0.0204.
- The correlation between lecucocytes and the percentage of bone marrow blasts was

performed in patients with secondary acute myeloid leukemia, resulting that there is a directly proportional correlation because the index is positive, with a p-value with statistical significance of 0.0083.

- LDH is a potent biochemical marker associated with a negative prognosis, in the analyzed group, patients with de novo AML and CD56+ AMLs had a median value of increased LDH 579.5 and 420, respectively, compared to those with median pCT AML of 240.5 with a statistically significant p value of 0.029241.
- There appears to be a correlation between leukocyte count and LDH value in patients with secondary acute leukemia with a statistical p-value of 0.0003.
- It seems that there is a directly proportional correlation between ICD and death, with a positive index, with a statistical p-value of 0.0006**.**
- The FAB distribution of CD7+ patients detects an increased incidence in AML patients. According to the ELN classification, 7 patients with CD7+ had an unfavorable risk, 4 had an intermediate risk and 2 had a favorable risk, and 5 had a normal karyotype (in 4 of the patients with CD7+, cytogenetic and molecular examination was not evaluated.
- CD7 is positive in 22 patients from the followed group - 11 patients with dnAML, 5 with sAML and 6 with pCT AML. According to Bahia and collaborators, the presence of this marker leads to an aggressive form of the pathology [55], in the studied group of the 22 CD7+ patients, 14 patients died, one of whom had early mortality (less than one month).
- **CD56+** was found in 14 patients in the analyzed group (6 with dnAML and 4 cases each in sAML and pCT AML), with death occurring in 71.4% (10 cases).
- In a study conducted by Iriyama mentioned that CD56 positive is associated with leukocytosis at diagnosis [58]. In our group, only those with de novo AML and sAML presented leukocytosis at diagnosis, those with leukocyte pCTAML presenting a median leukocyte value of 3350/mmc, with a $p>0.05$ value (0.1366).
- In the group studied, CD56+ is associated with FLT3+ in 3 cases
- **CD123+** was detected in 43 patients from the analyzed group - 28 cases with dsAML, 7 cases of sAML and 8 patients with pCT AML ($p=0.09$).
- According to the literature [32,33] CD123+ is frequently associated with the FLT3 positive mutation, in our group we found this association in 5 patients (4 patients with dn AML and 1 patient with pCT AML).

- The death rate for secondary acute myeloid leukemia (s AML and Pct AML) with CD123+ was above 85% (85.1% and 87.5%, respectively) compared to de novo acute myelogenous leukemia (35.7%), resulting in the negative impact on secondary acute leukemias.
- The median duration of survival in CD123+ dnAML was 15 months, compared to sAML with a duration of 5.5 months and pCT AML with a mean survival duration of 3 months, with a statistically significant p-value of 0.012381.
- **CD117+** (c-KIT, receptor tyrosine kinase, is expressed on the surface of the hematopoietic stem cell, showing an important role in cell survival, proliferation and differentiation, being expressed in most cases of AML, in our group it is present in 58 patients - in 33 cases of de novo AML, 12 patients with LAMs and 13 with postcytotoxic AML.
- Of the 58 CD117+ patients, the FLT3+ mutation was found in 8 patients.
- In CD117+ patients, it is confirmed that dnAL patients have a longer survival period (median 12 months) than those with LAMs (median 5.5 months) and LAMpCT (median 3 months).
- Out of the entire batch of 107 cases, 74 patients were investigated with cytogenetic and molecular examination, thus 25 did not present changes, 5 patients presented favorable risk, with a median age of 66 years, 23 patients presented intermediate risk with a median age of 56 years, and 21 patients were classified as unfavorable risk, with a median of 66 years, presenting a p-value with statistical significance equal to **0.032608**
- The death occurred in the case of patients in the entire group according to the risk group according to the ELN classification is distributed as follows: 16 cases with normal karyotype with a median age of 72.5 years, 3 cases with favorable risk factors with a median of 76.5 years, 13 cases with intermediate risk factors with a median of 58 years and 15 cases with unfavorable risk factors with a median of 67 years, with a statistically significant p = **0.0106**.
- Of the 47 deceased patients, 8 had early mortality (3 with intermediate risk and 5 with unfavorable cytogenetic risk).
- Early mortality death less than 1 month after diagnosis, was detected in 8 patients with pCT AML with a median age of 59 years, which demonstrates that the unfavorable

evolution is also frequent in young patients, under 60 years of age.

- Of the 13 patients who died early (less than 1 month), 6 patients had undergone radiotherapy sessions in the past (p=0.1734).
- 13 patients were FLT3+, 8 de novo AML patients, 3 patients sAML and 2 postcytotoxic AML patients
- The complex karyotype is defined by the presence of more than 3 clonal chromosomal abnormalities, it was observed in 16 patients from the entire group, with an unfavorable prognosis, only 3 patients being alive; thus, 4 patients with complex karyotype with dnAML, 4 patients with sAML and 5 patients with pCT AML, aged between 59 and 81 years, died.
- Breast cancer is the most common oncological cause of developing secondary acute myeloblastic leukemia; Despite the increased frequency, the mortality rate of patients with breast cancer is low (15%), the diagnosis can be suspected from the first changes detected by imaging, the adjuvant therapy used leads to a prolonged survival rate [7], it is estimated that out of 20 patients with breast cancer one patient will develop another neoplasia after 10 years, representing a relative risk of 22% for secondary acute myeloid leukemia [8,9,10]. In most cases, they develop secondary acute myeloblastic leukemia, but they can also develop secondary acute lymphoblastic leukemia, less common cases [13,14], a case being also present in the subgroup studied.
- The median bone marrow infiltrate with blasts is 70% in breast cancer patients, compared to that of patients with post-myelodysplastic syndrome AML of 41%, with a statistical p value of 0.0197
- The latency period of patients with breast cancer was 35 months (median, with a minimum value of 7 months and a maximum of 124 months), compared to the latency period of those with acute myeloblastic leukemia after myelodysplastic syndrome 11 months (median, with a minimum of 1 month and a maximum of 60 months, with a statistical p of 0.0015.
- According to the ELN Classification, 2 patients present normal karyotype, 1 patient with favorable risk (patient who at diagnosis had marked leukocytosis (293,000/mmc) with major bone marrow blast inflation, 6 patients with intermediate risk and 2 patients with unfavorable risk.

- Only one patient had the FLT3-positive mutation and one patient had a complex karyotype (compared to the 7 patients with de novo AML).
- The treatment of these patients for acute leukemia was represented by intensive chemotherapy - 9 cases, hypomethylating agent with azacitidine 7 cases and 1 patient with BCL2 inhibitor (Venetoclax), only one patient underwent hematopoietic stem cell transplantation, two patients had achieved complete remission but died from infections at the last course of consolidation of complete remission.
- Death occurred in 15 patients, with a median survival value after diagnosis of acute leukemia of only 3 months (minimum 1 month, maximum 18 months).
- Early mortality (less than one month) occurred in 5 patients out of 17 patients wiht breast cancer
- SARSCOV2 infection

  During the period of the study, worldwide we faced the emergence of Coronavirus infection, during the pandemic Colentina Hospital was called a support hospital, patients with COVID-infected hematological pathology were admitted to our clinic. From the studied group, 4 patients with secondary acute leukemia were diagnosed with COVID infection, of which 3 died with acute respiratory failure, so the small number of cases with Covid infection did not allow an analysis on the degree of risk.COVID-19 infection was a feared complication in the evolution of patients with secondary and cytotoxic acute leukemia, but also for those with de novo acute leukemia because they frequently associated sepsis and worsening respiratory failure with admission to intensive care, the unfavorable evolution being much more frequently noted compared to patients with other oncohematological conditions. Intensive chemotherapy and aplasia were aggravating factors, with the use of deacetylase inhibitors giving a better prognosis to patients with AML and COVID-19. The results obtained by us require evaluation in a larger batch of patients and analysis during the COVID-19 follow-up period
- In order to achieve complete remission of this patient profile, I believe that the treatment regimens should be personalized according to genetic mutations.
- The case of the patient with breast cancer and multiple myeloma in the past, plus acute promyelocytic leukemia, who is alive (28 months from the diagnosis of acute leukemia until February 2024 when the data entry ended) reinforces the need to discover new

therapies targeted at cytogenetic and molecular changes, even monoclonal antibody therapies.

- New therapies have been approved in recent years for patients with acute myeloid leukemia such as Gentuzumab Ozogamicin an antiCD33 monoclonal antibody, for secondary acute myeloblastic leukemia CPX351 which is a liposomal formula containing daunorunicin and cytarabine, Midostaurin an inhibitor of fms like tyrosine kinase and inhibitors of IDH1 isocitrate dehydrogenase-1, along with the anti-BCL2 inhibitor Venetoclax which is used together with Azacitidine – to decrease the risk of infection tries to decrease the duration of administration of Venetoclax to 7 days, resulting in the 7+7 cure.
- I believe that the results obtained on the relatively small group of patients did not have an impact on the statistical significance, but they can be taken into observation for future in-depth studies with the enrollment of a larger number of patients and observation for a longer period, possibly the creation of a national or local registry (Bucharest).
- Clinical trials are taking place with antiCD123, antiCD70, antiCD56 monoclonal antibody molecules
- I believe that it would be useful to preserve a sample for the diagnosis of patients with secondary acute myeloblastic leukemia for future cytogenetic and molecular tests, thus increasing the number of patients with this hematological picture.
- For the best possible therapeutic response, immunophenotypic, cytogenetic and molecular evaluation is the first step in treating these patients, by administering personalized therapy.

PUBLISHED ARTICLES

- A comparative approach to classifications in the diagnosis of acute myeloblastic leukemia with reference to cytogenetetic, myelodisplasiz elements and mutations of the TP53 gene-WHO, ICC,ELN 2022- **Omer Meilin** , Andreescu Mihaela , Popov Viola-Maria , Ana Maria VlădăreanuRevista oncohematolog year XVIII no 66 (1) march 2024 10.26416/OnHe.66.1.2024.9389

https://tstmh20.medichub.ro/reviste-de-specialitate/oncolog-hematolog-ro/a-comparative-approach-to-classifications-in-the-diagnosis-of-acute-myeloblastic-leukemia-with-reference-to-cytogenetic-myelodysplastic-elements-and-mutations-of-the-tp53-gene-who-icc-eln-2022-id-9389-cmsid-68

- Evaluation of the impact of Covid-19 infection on the evolution and prognosis of patients with acute leukaemia -**Meilin Omer**, Ana M. Vladareanu, Viola M. Popov, Mihaela Andreescu, Lelia Iliescu, Horia Bumbea, Serban DragosloveanuRevista Română de Medicina de Laborator,vol 29 nr 4, oct 2021; 29(4):377-85. DOI:10.2478/rrlm-2021-0032

https://www.rrml.ro/articole/articol.php?year=2021&vol=4&poz=3#

Abstract

- ACUTE LEUKEMIA PARTICULARITIES IN PATIENTS WITH A HISTORY OF BREAST CANCER- **Meilin Omer**, Ana Maria Vladareanu, Mihaela Andreescu, Viola Maria Popov, Ion Dumitru, Lidia Felicia Mihai, Florina-Oana Patrinoiu, Mihaela Popescu, Dan Soare, Aurora Arghir, Ana Iova, Horia Bumbea(Abstract release date: 05/14/24) EHA Library. Omer M. 06/13/2024; 421286; PB2531
- Particularities of Evolution in Acute Leukemia Patients With a History of Neoplasms Retrospective Analysis- **Meilin Omer**, Viola Maria Popov MD , Mihaela Andreescu, Horia Bumbea, Oana Patrinoiu, Mihaela Popescu , Felicia Mihai , Geanina Ofiteru, Aurora Arghir, Dan Soare, Ion Dumitru, Ana Maria Vladareanu Clinical Lymphoma Myeloma and Leukemia Volume 24, Supplement 1, September 2024, Pages S319-S320 https://doi.org/10.1016/S2152-2650(24)01211-4

Submitted in response

- ASH 2024-Evaluation of Prognostic Factors Involved in the Evolution of Secondary Acute Leukemia Patients
- 16th International Congress on Myeloproliferative Neoplasms-The assessment of the particularities of secondary acute leukemia in patients with chronic myeloproliferative neoplasms or myelodysplastic syndromes

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