diagnóstico fechado durante a internação. O Laboratório de Citometria de Fluxo realizou imunofenotipagem investigativa para leucemias com amostra de sangue periférico. Com isso, foi detectado 68% de blastos linfóides e marcadores compatíveis com Leucemia Linfoblástica Aguda de células B. Ainda nesse período, foi realizada entrevista e ficha social do paciente pelo Serviço Social. Constatou-se, que apesar de ter passado um mês internado em outra unidade, Tiê ainda não havia dado entrada em auxílio doença. O idoso e sua família apresentaram queixas sobre dificuldades financeiras. Foram orientados sobre a necessidade de requerimento deste benefício. Além do direito à saque do FGTS e PIS (devido à neoplasia maligna), e ainda do TFD – Tratamento Fora de Domicílio (município de origem do paciente deve se responsabilizar por seu deslocamento ao município da unidade em que faz tratamento). No geral, Tiê apresentou hemogramas com oscilações de hemoglobina, plaquetas e leucócitos de acordo com as transfusões realizadas. Por fim, Tiê recebeu alta hospitalar em 10/04 com parâmetros laboratoriais e hemodinâmicos aceitáveis. Retornou em 15/04 para realização de exames agendados no SPA relatando episódios diarreicos. Teve que permanecer internado e seguiu relatando dificuldades financeiras por não ter conseguido realizar o saque do FGTS e impasses no processo de auxílio-doença. **Conclusão:** A partir do acompanhamento de Tiê, foi possível concluir que o trabalho transdisciplinar é essencial para atenção integral ao paciente hematológico, visto que a doença envolve outros fatores além do físico. É necessário olhar para cada paciente como um todo, não só para suas condições clínicas; problemas financeiros podem acarretar em falta de fé, otimismo e persistência por parte do paciente. Além do tratamento da LLA que pode incluir quimioterapia, transfusão sanguínea, antibioticoterapia; o suporte familiar pode fazer a diferença. No caso descrito, Tiê possui quatro filhos que se revezavam para acompanhá-lo na internação e ainda contava com uma irmã que o ajudava na alimentação quando em casa. Isso o fez ficar mais confiante. Portanto, o presente estudo pode ajudar na motivação de profissionais da assistência a pacientes hematológicos a ter uma atuação integrada, visando o bem estar geral dos pacientes.

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HIGH FREQUENCY OF LEUKEMIC STEM CELLS IS ASSOCIATED WITH ADVERSE PROGNOSIS IN A BRAZILIAN COHORT OF ACUTE MYELOID LEUKEMIA WITH NORMAL KARYOTYPE

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Introduction: Normal karyotype in Acute Myeloid Leukemia (NK-AML) is present in 40-50% patients, commonly classified as intermediate-risk and for whom prognosis is less predictable. Other prognostic markers in NK-AML could refine disease assessment and therapeutic choices. Leukemic Stem Cells (LSCs) have been associated with initiation and persistence of AML. In this study, we aimed to assess the prognostic impact of the proportion of LSCs at diagnosis. **Methods:** Patients with de novo NK-AML (n = 54,19-71 years old) from 7 Brazilian centers enrolled in the International Consortium of Acute Leukemias Study–IC-AML2015 had bone marrow samples taken to assessment of FLT3 and NPM1 mutations, RUNX1/RUNX1T1 and CBFB-MYH11 rearrangements, karyotype analysis by classical cytogenetics and immunophenotyping by multiparametric flow cytometry. Data regarding ELN2017-based risk stratification (without TP53, ASXL1 and RUNX1) and overall survival (OS) were collected. Treatment comprised two cycles of induction, and consolidation with one or two cycles of chemotherapy and/or BM transplantation, according to clinical appraisal. LSCs were evaluated according to the percentage of CD34+/CD38low/CD123+ cells among total blast cells (from SSC versus CD45 gating population) and to their absolute numbers. Analyses were performed with SPSS (V.20), considering a p-value of 0.05. **Results:** Patients were classified in two groups (LSC<1%; LSC>1%). The presence of LSC>1% was associated with higher WBC (49.2 x 103/μL x 13.6 x 10^3/μL, p = 0.02), with combined NMP1 and FLT3-ITD mutations (88.9% of patients x 11.1%, p < 0,001) and with high FLT3-ITD allelic ratio (44.4% x 4.4%, p < 0,001). Complete remission rate 69% (n = 31) among the LSC<1% group, and 34% (n = 3) among the LSC>1% group. Within the whole cohort, those with LSC >1% (n = 9) had a mean OS of 6.3 months, while a 24.2 months OS was observed in patients of the LSC <1% group (n = 45). Among intermediate-risk patients, those with LSC >1% (n = 6) had a mean OS of 7.1 months, whereas the LSC <1% group (n = 25) had a 23.9 months OS. The logrank test demonstrated, however, equality of survival distributions

between the patients with LSC <1% or LSC >1% within the total cohort and within each risk group. **Discussion:** The increased understanding of AML pathogenesis has prompted interest in LSC as possible prognostic markers and therapeutic targets. In our cohort, higher percentages of LSCs (>1%) at diagnosis were associated with markers of inferior prognosis: higher leukocytosis, NPM1mutFLT3mut status and higher FLT3-ITD allelic ratio. In the group of intermediate-risk, those with LSC>1% presented a lower mean overall survival than that of the patients with LSC <1% at diagnosis. This finding is relevant for this group of patients, for which prognosis and therapy choices are not as well defined as for the low and high-risk patients. However, logrank test displayed equality of survival distributions between the two groups of LSC, which could have been due to the limited number of patients studied. **Conclusion:** Our results fortify the potential value of LSCs as an easily assessed prognostic factor at diagnosis that may be further evaluated along measurable residual disease time points and help on therapeutic decisions. **Funding:** FAPESP grant #2013/08135-2. GLJ: FAPESP grant #19/20215-8. AFOC: INCTC grant #88887.284979/2018-00. LOM: INCTC grant #88887.313021/2019-00. LLFP: FAPESP grant #2015/21866-1.

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IDENTIFICATION AND EVALUATION OF POTENTIAL STATHMIN 1 INHIBITORS IN ACUTE LEUKEMIA CELLULAR MODELS

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Objectives: Acute leukemia (AL) is characterized by exacerbated clonal proliferation of immature hematopoietic progenitors that accumulates in peripheral blood, bone marrow and extramedullary sites, impairs the normal blood production, and AL presents high relapse and mortality rates. Stathmin 1 (STMN1) is a highly expressed phosphoprotein in different types of cancer that regulates microtubule dynamics, relaying the integration of extra- and intracellular signals. In leukemia cells, STMN1 is overexpressed and induces cell proliferation and autonomous clonal growth being its role poor explored by pharmacological agents. The present study aimed to identify compounds that inhibit STMN1-mediated signaling and to evaluate their cellular and molecular effects. **Material and methods**: Cheminformatic tools were used to identify compounds similar to GDP366, the only STMN1 inhibitor reported. For the functional assays, acute lymphoblastic leukemia cells, Jurkat and Namalwa, and acute myeloid leukemia cells, NB4 and U937, were used. Cell viability was assessed by MTT, apoptosis by annexin V/7AAD labeling, cell cycle by propidium iodide labeling and flow cytometry (CF), clonogenicity by autonomous colony formation, and protein expression and phosphorylation by Western blot. Statistical analysis was performed by ANOVA test and Bonferroni post-test. A $p < 0.05$ was considered significant. **Results**: Cheminformatic analysis identified three compounds with high similarity to GDP366: AD80, GSK2606414, and GW768505A. In the initial drug screening, AD80 was more potent and effective that GSK2606414 and GW768505A in all leukemia cell lines tested, being it selected for further analysis. GPD336 was used as the reference compound. GDP366 and AD80 reduced cell viability in a dose- and time-dependent manner in leukemia cells ($p < 0.05$), being AD80 (IC_{50} for 72 hours ranged from 1.6 to 6.7 μM) more potent than GDP366 (6 to >50 μM). Both compounds induced apoptosis and G_2/M cell cycle arrest, and reduced autonomous clonal growth in a dose-dependent manner in all leukemia cells ($p < 0.05$). Namalwa cells were more resistant to the compounds compared to other leukemia cells. In the molecular scenario, GDP366 induces STMN1 phosphorylation (inactive form), and apoptosis (cleaved PARP1) and DNA damage markers (γH2AX) in Jurkat and NB4 cells. AD80 reduced STMN1 expression and also induces PARP1 cleavage and γH2AX expression. In addition, AD80, but not GDP366, effectively inhibits S6 Ribosomal Protein phosphorylation and Survivin (BIRC5) expression in both leukemia cell lines tested. **Discussion and conclusion:** GPD366 and AD80 inhibit STMN1 signaling and display antineoplastic effects in acute leukemia cellular models, reducing clonogenicity, survival, and cell cycle progression. AD80 was the most potent and effective compound identified in this context and presented an interesting multitarget activity in leukemia cells. **Funding:** Supported by CNPq and FAPESP (2017/24993-0, 2018/19372-9, 2018/15904-6, and 2015/17177-6).

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IMAGEAMENTO IN VIVO DE CAMUNDONGOS TRANSPLANTADOS COM LEUCEMIA PROMIELOCÍTICA AGUDA (PML-RARα)

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Objetivos: Nosso objetivo foi confirmar a eficiente padronização do modelo experimental de leucemia promielocítica aguda (LPA) em camundongos imunocompetentes BALB/c através da técnica de imageamento in vivo, e