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