0.36; p = 0.001), radiotherapy (HR: 0.17; p < 0.0001) and ASCT (HR: 0.03; p = 0.001). In the multivariate analysis, factors associated with better 2-year OS were: LDH < 480 U/L (HR: 0.40; p = 0.005) and ASCT (HR: 0.47; p = 0.003). LDH < 480 U/L (HR: 0.45; p = 0.01) and ASCT (HR: 0.07; p = 0.01) were also associated with higher 2-year PFS in our cohort. **Conclusion:** This is the largest real-life Latin American nPTCL cohort published to date. Patients with nPTCL have poor survival and high rate of chemo-resistance. In our cohort, adding etoposide to the CHOP regimen showed no survival benefit and was associated with high toxicity. Normal values of LDH and consolidation with ASCT were independent factors associated with better outcomes in Brazilian patients with nPTCL.

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IMMUNE SENESCENCE-RELATED GENE EXPRESSION PROFILE IN CD4+ T-LYMPHOCYTES OF HTLV-1 ASYMPTOMATIC CARRIERS AND PATIENTS WITH ADULT T-CELL LEUKEMIA/LYMPHOMA (ATLL): A BRAZILIAN PRELIMINARY STUDY

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Introduction: ATLL is a rare and aggressive neoplasm caused by the human T-lymphotropic virus type 1 (HTLV-1). It is estimated that at least 5-10 million people carry HTLV-1 and 2-5% out of them will develop ATLL. Our group demonstrated an increase of cells in G0/G1 phase of cell cycle and aneuploidy in CD4+ T-cells in HTLV-1 asymptomatic carriers. These findings may reflect an adverse intracellular environment, caused by genetic stress due to viral particles inserted into host DNA. Intracellular mechanisms aiming to control and prevent replication of cells carrying genetic aberrations in genes involved in cell cycle regulation, DNA repair and apoptosis could be activated to hold cell division while DNA damage is repaired. Based on this hypothesis, delay of cell cycle in G0/G1 may be a step in the process of oncogenesis. Herein, we did a pilot study in order to analyze the pattern of expression of a set of genes involved in cell cycle control and senescence in CD4+ T-lymphocytes of HTLV-1 infected individuals searching for additional genetic abnormalities in this setting. **Methods:** Peripheral blood samples were tested obtained from five HTLV-1 asymptomatic carriers and four ATLL patients. T-CD4+ cells were isolated in magnetic column followed by RNA extraction. Subsequently, it was converted into cDNA for the assays of the qRT-PCR in microplates of 96 wells customized with 44 senescence related genes. A pool of five samples from healthy individuals (control group) was used as a calibrator. RNA transcription was measured using *7500 Fast real time PCR system* (*Applied Biosystems*) and data were collected by the *7500 software v2.0.5* (*Applied Biosystems*). The expression levels of the target genes were calculated using the Livak and Schmittgen (2001) method. The mRNA expression was normalized using the β-glucuronidase (*GUSB*) gene (*Applied Biosystems*, cod. Hs99999908_m1) and those genes with expression ≥ 2x or ≤ 2x in comparison to control group were considered as differentially expressed and were chosen to be validated in a secondary cohort of thirty HTLV-1 infected individuals. **Results:** In HTLV-1 asymptomatic carriers the median age was 55 years (37-62 years) and 20% (1/5) of them were males, in ATLL patients: 45 years (38-66 years) and 100% (4/4) were females, while the control group had median age of 43 years (22-62 years) and 60% (3/5) were males. Among the ATLL group, 50% (2/4) were classified as *smoldering*, 25% (1/4) were acute and 25% (1/4) were lymphomatous, according to Shimoyama classification. *COL3A1*, *SPARC* and *TWIST1* genes were overexpressed and *CDKN1A*, *ID1*, *IFNG* and *TERT* were suppressed in HTLV-1 asymptomatic carriers when compared to healthy controls. HTLV-1 infected and ATLL patients showed *TWIST1* and *COL3A1* genes overexpressed and *IFNG*, *CDKN1A* and *TERT* repressed. The *ALDH1*, *FN1*, *NOX4* and *COL1A1* genes did not amplified. **Conclusion:** These preliminaries results showed for the first time that HTLV-1 asymptomatic carriers present a set of genes differentially expressed in T-CD4+ cells, especially *SPARC*, *TWIST1*, *COL3A1*, *CDNK1A* and *IFNG*. These results will be confirmed in a validation cohort. We expected that this data shed some light on the comprehension of the cell microenvironment of the T-CD4+ lymphocyte in HTLV-1 asymptomatic carriers. Furthermore, we will be able to understand potential mechanisms associated with leukemogenesis in chronic infection by this virus, explaining eventual progression to ATLL.

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INCIDÊNCIA E CARACTERIZAÇÃO CLÍNICA E MORFOLÓGICA DAS NEOPLASIAS LINFOPROLIFERATIVAS MALIGNAS EM PACIENTES COM TRANSMISSÃO VERTICAL DE HIV NO RIO DE JANEIRO NA ERA PÓS TERAPIA ANTIRRETROVIRAL COMBINADA (CART): UM ESTUDO MULTICÊNTRICO

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A terapia antirretroviral combinada (cART) tornou a infecção pelo HIV uma doença crônica. Na população pediátrica, mais de 95% das infecções ocorrem por transmissão vertical (TV). O CDC inclui alguns linfomas na categoria de doenças definidoras de AIDS. Crianças e adolescentes infectados pelo HIV apresentam risco 60 a 200 vezes maior de desenvolver malignidades, principalmente Linfomas não-Hodgkin (LNH). Antes da disseminação da cART, a incidência de malignidades em crianças e adolescentes infectados variou muito entre

estudos. Porém, em países desenvolvidos, ainda é 8 vezes maior se comparado a pacientes não infectados. A incidência de neoplasias definidoras de AIDS, como os LNH, diminuiu em 60% na era cART (após anos 2000). No Brasil, dados sobre incidência de NLM nessa população são escassos e pouco se sabe sobre o impacto do uso da cART na sobrevida de crianças e adolescentes infectados e o desenvolvimento dessas neoplasias. O objetivo do estudo foi avaliar a incidência de neoplasias linfoproliferativas malignas (NLM) em pacientes de 0 a 20 anos incompletos, com TV de HIV, que iniciaram acompanhamento em 6 hospitais de referência para HIV/AIDS no Rio de Janeiro de 01/01/1995 a 01/01/2018, e estudar sua sobrevida. Trata-se de um estudo observacional, de coorte retrospectiva de pacientes pediátricos portadores de HIV por TV. Foram estudados 1.307 pacientes com TV de HIV, com 27 linfomas encontrados no total. A coorte foi dividida em 3 eras – *Early* cART, *Midle* cART e *Pós* cART (pontos de corte: 1995-1999, 2000-2003 e 2004-2018). Quanto à densidade de incidência de linfomas, o valor foi de 1,83 a cada 1.000 pessoas-ano para o estudo global, bem como de 2,71 a cada 1.000 pessoas-ano no período *Early*, 2,63 na era *Midle* e 0,37 na era *Pós*. Foi encontrada uma probabilidade cumulativa de evento total de 3,1% em 23 anos de acompanhamento. Entre as eras, a mesma foi de 5,1% na era *Early*, de 4,0% na era *Midle* e de 0,7% na era *Pós*, com p(logrank) valor de 0,005. O tempo de acompanhamento mediano foi de 12,83 anos para a coorte *Early*, 13,50 anos para a *Midle* e de 11,63 anos para a coorte *Pós*, sendo o total de 12,63 anos. A Hazard Ratio (HR) entre as Eras *Midle* e *Early* foi de 0,956 (IC = 0,436 – 2,095; p = 0,910), entre as Eras *Pos* e *Early* foi de 0,131 (IC = 0,030 – 0,580; p = 0,007) e, entre as eras *Pos* e *Midle* foi de 0,135 (IC = 0,030 – 0,601; p = 0,009). Tais achados confirmam a eficácia da cART na redução da incidência de neoplasias relacionadas à imunossupressão pelo HIV. Além disso, a proporção de tipos de linfomas encontrados está de acordo com a literatura. Embora o Brasil tenha um programa para redução de TV de HIV, o número de crianças e adolescentes infectados ainda é elevado. Dessa forma, esse estudo trouxe resultados robustos e inéditos para o entendimento do espectro de NLM nessa população.

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INDUCTION R2 FOLLOWED BY MAINTENANCE IN PATIENTS WITH RELAPSED/REFRACTORY MANTLE CELL LYMPHOMA: INTERIM ANALYSIS FROM THE PHASE 3B MAGNIFY STUDY

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Objectives: The combination of lenalidomide + rituximab (R^2) has shown complementary clinical activity and is a tolerable regimen in both untreated and relapsed or refractory (R/R) indolent non-Hodgkin lymphoma (NHL), as well as mantle cell lymphoma (MCL), an uncommon but aggressive form of NHL. The MAGNIFY phase 3 trial previously reported an ORR of 54% in patients with R/R MCL (Sharman J, et al. *Hematol Oncol*. 2019). Presented here are updated analyses from this trial. **Materials and methods:** MAGNIFY is a multicenter, phase 3b trial (NCT01996865) in patients with R/R follicular lymphoma (FL) grades 1–3b, transformed FL, marginal zone lymphoma, and MCL. Lenalidomide 20 mg on d 1–21 of a 28-d cycle + rituximab 375 mg/m^2/wk cycle 1 and then every 8 wk starting with cycle 3 (R^2) is given for 12 cycles followed by 1:1 randomization in patients with stable disease, partial response, or complete response/complete response unconfirmed (CR/CRu) to R^2 vs rituximab maintenance for 18 mo. The primary end point is progression-free survival (PFS) by 1999 International Working Group (IWG) criteria. Secondary end points include safety, CR rate, duration of response (DOR), duration of CR (DOCR), time-to-response (TTR), time-to-next antilymphoma therapy, and overall survival. This analysis evaluates the interim primary endpoint of overall response rate (ORR) by 1999 IWG criteria and safety of R^2 induction in patients with MCL in the induction intention-to-treat population. **Results:** As of August 28, 2020, 73 patients with MCL were enrolled (median age, 70.0 y [range, 51–88]); 89% had stage III/IV disease, and 41% had bulky disease (> 7 cm or > 3 cm ×3 lymph nodes). All patients had received prior rituximab-containing therapy, with 25 (34%) rituximab refractory (progression ≤ 6 mo after last rituximab dose). Seven patients (10%) had received prior ibrutinib. Median follow-up was 31.7 mo for patients still alive. ORR was 51%, with 34% CR rate (CR + CRu). Response rates were similar in patients refractory to rituximab (ORR = 48%, CR/CRu = 32%) and patients not refractory to rituximab (ORR = 52%, CR/CRu = 35%). Median DOR was 31.6 mo; median DOCR was not reached; median TTR was 2.8 mo, and median PFS was 28.0 mo, with 1-year PFS rate of 57%. The most common treatment emergent adverse events (TEAEs) of any grade were neutropenia (51%), fatigue (44%), diarrhea (32%), constipation (28%), cough (28%), dyspnea (26%), and nausea (26%). Grade 3/4 neutropenia was 46%; all other grade 3/4 TEAEs were ≤ 11%. **Discussion:** R^2 is an active and tolerated regimen with durable responses among patients with R/R MCL and mostly naive to Bruton tyrosine kinase inhibitor therapy. **Conclusions:** These results suggest that R^2 should be considered as a therapeutic option for patients with R/R MCL.

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