1. **An Emergent Change in Epidemiologic and Microbiological Characteristics of Bloodstream Infections in Adults With Febrile Neutropenia Resulting From Chemotherapy for Acute Leukemia and Lymphoma at Reference Centers in Chile, Ecuador, and Peru**

   Un cambio emergente en las características epidemiológicas y microbiológicas de las infecciones del torrente sanguíneo en adultos con neutropenia febril resultante de la quimioterapia para la leucemia aguda y el linfoma en centros de referencia de Chile, Ecuador y Perú

   INVESTIGADORES: Ricardo Rabagliati, Grace Salazar, Giancarlo Pérez-Lazo, Maria Paz Iturrieta, Diana Portillo, Carmen Soria-Segarra, María José Ojeda, Jimena Flores, Margarita Galarza, Roxana Sandoval-Ahumada, Pablo Cartes Aguilera, Lady Dimitrakis, Fabiola Avelga Reinoso, Patricia Garcia.

   LINK: https://pubmed.ncbi.nlm.nih.gov/38444817/

   REVISTA: Open Forum Infect Dis. 2024 Feb 1;11(3):ofae052. doi: 10.1093/ofid/ofae052. eCollection 2024 Mar.

   ASTRACTO: Background: Febrile neutropenia is a life-threatening condition commonly observed in patients with hematologic malignancies. The aim of this article is to provide updated knowledge about bloodstream infections in febrile neutropenia episodes within the Andean region of Latin America. Method: This retrospective study was based in 6 hospitals in Chile, Ecuador, and Peru and included adult patients with acute leukemia or lymphoma and febrile neutropenia between January 2019 and December 2020. Results: Of the 416 febrile neutropenia episodes, 38.7% had a bloodstream infection, 86% of which were caused by gram-negative rods, with Klebsiella pneumoniae, Escherichia coli, and Pseudomonas aeruginosa being the most frequently identified bacteria. K pneumoniae isolates were more frequently resistant than E coli to cefotaxime (65% vs 39.6%), piperacillin-tazobactam (56.7% vs 27.1%), and imipenem (35% vs 2.1%) and were more frequently multidrug resistant (61.7% vs 12.5%). Among P aeruginosa, 26.7% were resistant to ceftazidime, piperacillin-tazobactam, and imipenem, and 23.3% were multidrug resistant. Overall 30-day mortality was 19.8%, being higher with vs without a bloodstream infection (26.7% vs 15.3%, P = .005). Fever duration was also significantly longer, as well as periods of neutropenia and length of hospital stay for patients with bloodstream infection. Additionally, the 30-day mortality rate was higher for episodes with inappropriate vs appropriate empirical antibiotic therapy (41.2% vs 26.6%, P = .139). Conclusions: Considering the high rates of bacteria-resistant infection and 30-day mortality, it is imperative to establish strategies that reduce the frequency of bloodstream infections, increasing early identification of patients at higher risks of multidrug bacteria resistance, and updating existing empirical antibiotic recommendations.

2. **Impact of Concurrent Genomic Alterations on Clinical Outcomes in Patients With ALK-Rearranged NSCLC**

   Impacto de las alteraciones genómicas concurrentes en los resultados clínicos en pacientes con NSCLC reordenado con ALK

   INVESTIGADORES: Luis Lara-Mejía, Andres F Cardona, Luis Mas, Claudio Martin, Suraj Samtani, Luis Corrales, Graciela Cruz-Rico, Jordi Remon, Marco Galvez-Nino, Rossana

Ruiz, Eduardo Rios-Garcia, Fernanda Tejada, Natalia Lozano-Vazquez, Rafael Rosell, Oscar Arrieta.

LINK: https://pubmed.ncbi.nlm.nih.gov/37572870/

REVISTA: J Thorac Oncol. 2024 Jan;19(1):119-129. doi: 10.1016/j.jtho.2023.08.007. Epub 2023 Aug 10.

ASTRACTO: Introduction: ALK tyrosine kinase inhibitors have exhibited promising activity against advanced ALK-rearranged NSCLC. However, co-occurring genetic alterations, such as CDKN2A/B or TP53, may negatively affect the efficacy of targeted therapies. Methods: From December 2017 to December 2022, this study cohort analyzed next-generation sequencing data of 116 patients with metastatic ALK-rearranged NSCLC from five Latin American cancer centers. Clinicopathologic and molecular features were associated with clinical outcomes and risk of brain metastasis (BrM) in patients with and without concurrent somatic alterations. Results: All patients (N = 116) received a second-generation ALK tyrosine kinase inhibitor, and alectinib was selected in 87.2% of cases. Coalterations occurred in 62% of the cases; the most frequent were TP53 mutations (27%) and CDKN2A/B loss (18%). The loss of CDKN2A/B was associated with an increased risk of BrM, with a cumulative incidence of 33.3% versus 7.4% in the non-coaltered subgroup. Compared with patients without coalterations, patients with concurrent CDKN2A/B loss (n = 21) had a shorter median progression-free survival (10.2 versus 34.2 mo, $p < 0.001$) and overall survival (26.2 versus 80.7 mo, $p < 0.001$). In the multivariate analysis, co-occurring CDKN2A/B loss was associated with poorer progression-free survival and OS despite the presence of other somatic coalterations, TP53 mutations, BrM, and Eastern Cooperative Oncology Group Performance Status. Conclusions: This study confirmed the worse prognostic value, which depicted co-occurring alterations in patients with ALK rearrangement. CDKN2A/B loss was substantially associated with worse outcomes and a higher risk of brain metastases. The evidence presented in our study may help select patients with ALK-positive tumors suitable for treatment escalation and closer brain follow-up.

3. **Real-World Outcomes of Adolescents and Young Adults with Diffuse Large B-Cell Lymphoma: A Multicenter Retrospective Cohort Study**

   Resultados en el mundo real de adolescentes y adultos jóvenes con linfoma difuso de células B grandes: un estudio de cohorte retrospectivo multicéntrico

   INVESTIGADORES: Denisse Castro-Uriol, Ligia Rios, Daniel Enriquez-Vera, Jacqueline Montoya, Thanya Runciman, Sandra Alarcón, Arturo Zapata, Eddy Hernández, Esmeralda León, Luis Malpica, Bryan Valcarcel.

   LINK: https://pubmed.ncbi.nlm.nih.gov/37843922/

   REVISTA: Multicenter Study J Adolesc Young Adult Oncol. 2024 Apr;13(2):323-330. doi: 10.1089/jayao.2023.0095. Epub 2023 Oct 16.

   ASTRACTO: Purpose: Patients with diffuse large B-cell lymphoma (DLBCL) are typically treated with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). However, a standard of care for managing adolescents and young adults (AYAs) with DLBCL is lacking. We examine treatment approaches and outcomes of this population. Methods: We included 90 AYAs (15-39 years) diagnosed with DLBCL between 2008 and 2018 in three tertiary centers in Peru. Overall response rates (ORR) were available for all patients. Overall survival (OS) and progression-free survival (PFS) rates were estimated using the Kaplan-Meier method. Results: The median age at diagnosis

was 33 years, 57% were males, 57% had good performance status (Lansky/Karnofsky ≥90), and 61% were diagnosed with early-stage disease (Ann Arbor stages I-II). R-CHOP (n = 69, 77%) was the most frequently used first-line regimen, with an ORR of 91%. With a median follow-up of 83 months, the 5-year OS and PFS among all patients were 79% and 67%, respectively. Among the patients who received R-CHOP, the 5-year OS and PFS were 77% and 66%, respectively. Of the 29 (32%) patients with relapsed/refractory (R/R) disease, 83% received second-line treatment and only 14% underwent consolidation therapy with autologous transplantation. The 3-year OS for R/R DLBCL was 36%. Conclusion: Our data show that AYAs with DLBCL who received conventional therapy had comparable outcomes to those observed in studies conducted among the adult population. However, the prognosis for AYAs with R/R disease was dismal, indicating the unmet need for developing and increasing access to novel treatment modalities in AYAs.

4. **Clinical networking results in continuous improvement of the outcome of patients with acute promyelocytic leukemia**

La creación de redes clínicas da como resultado una mejora continua del resultado de los pacientes con leucemia promielocítica aguda

INVESTIGADORES: Luisa Corrêa de Araujo Koury, Haesook T Kim, Maria Soledad Undurraga, Juan Ramon Navarro-Cabrera, Victor Salinas, Pablo Muxi, Raul A M Melo, Ana Beatriz F Gloria, Katia B B Pagnano, Elenaide C Nunes, Rosane Isabel Bittencourt, Ninoska Rojas, Shirley Milenca Quintana Truyenque, Ana Ilda Ayala-Lugo Dr, Ana Carolina Oliver, Lorena Lobo de Figueiredo-Pontes, Fabiola Traina, Frederico Moreira, Evandro M Fagundes, Bruno Kosa L Duarte, Analí Pamela Mora-Alferez, Percy Ortiz, Jose Luis Untama, Martin S Tallman, Raul C Ribeiro, Arnold Ganser, Richard James Dillon, Peter J M Valk, Miguel A Sanz, Bob Löwenberg, Nancy Berliner, Eduardo M Rego.

LINK: https://pubmed.ncbi.nlm.nih.gov/38805638/

REVISTA: Blood. 2024 May 28:blood.2024023890. doi: 10.1182/blood.2024023890. Online ahead of print.

ASTRACTO: The introduction of all-trans retinoic acid (ATRA) combined with anthracyclines has significantly improved the outcomes for patients with acute promyelocytic leukemia (APL), and this strategy remains the standard of care in countries where arsenic trioxide is not affordable. However, data from national registries and real-world databases indicate that low- and middle-income countries (LMIC) still face disappointing results, mainly due to high induction mortality and suboptimal management of complications. The American Society of Hematology established the International Consortium on Acute Leukemias (ICAL) to address this challenge through international clinical networking. Here, we present the findings from the ICAPL study involving 806 patients with APL recruited in Brazil, Chile, Paraguay, Peru, and Uruguay. The induction mortality rate has decreased to 14.6% compared to the pre-ICAL rate of 32%. Multivariable logistic regression analysis revealed as factors associated with induction death: age ≥ 40 years, ECOG = 3, high-risk status based on the PETHEMA/GIMEMA classification, albumin level ≤ 3.5 g/dL, bcr3 PML/RARA isoform, the interval between presenting symptoms to diagnosis exceeding 48 hours, and the occurrence of central nervous system and pulmonary bleeding. With a median follow-up of 53 months, the estimated 4-year overall survival (OS) rate is 81%, the 4-year disease-free survival (DFS) rate is 80%, and the 4-year cumulative incidence of relapse (CIR) rate is 15%. These results parallel those observed in studies conducted in high-

income countries, highlighting the long-term effectiveness of developing clinical networks to improve clinical care and infrastructure in LMIC.

5. **Geographic EBV variants confound disease-specific variant interpretation and predict variable immune therapy responses**

Las variantes geográficas del VEB confunden la interpretación de las variantes específicas de la enfermedad y predicen respuestas variables a la terapia inmunitaria

INVESTIGADORES: Edward L Briercheck, Shashidhar Ravishankar, Elshafa Hassan Ahmed, Cesar Camilo Carias Alvarado, Juan Carlos Barrios Menéndez, Oscar Silva, Elizabeth Solórzano-Ortiz, Marcos Mauricio Siliezar Tala, Philip A Stevenson, Yuexin Xu, Anthony Wilder Wohns, Daniel Enriquez-Vera, Carlos Barrionuevo, Shan-Chi Yu, Aharon G Freud, Christoph Weigel, Christopher C Oakes, David M Weinstock, Haley L Klimaszewski, Apollinaire Ngankeu, Nora Mutalima, Gabriela Samayoa-Reyes, Robert Newton Prof, Rosemary Rochford, Fabiola Valvert, Yasodha Natkunam, Andrei Shustov, Robert A Baiocchi, Edus H Warren.

LINK: https://pubmed.ncbi.nlm.nih.gov/38815238/

REVISTA: Blood Adv. 2024 May 30:bloodadvances.2023012461. doi: 10.1182/bloodadvances.2023012461. Online ahead of print.

ASTRACTO: Epstein-Barr virus (EBV) is a potent carcinogen linked to hematologic and solid malignancies, causing significant global morbidity and mortality. Therapy using allogeneic EBV-specific lymphocytes shows promise in certain populations, but the impact of EBV genome variation on these strategies remains unexplored. To address this, we sequenced 217 EBV genomes, including hematologic malignancies from Guatemala, Peru, Malawi, and Taiwan, and analyzed them alongside 1,307 publicly available EBV genomes from cancer, non-malignant diseases, and healthy individuals across Africa, Asia, Europe, North America, and South America. These included the first NK/T-cell lymphoma (NKTCL) EBV genomes reported outside East Asia. Our findings indicate that previously proposed EBV genome variants specific to certain cancer types are more closely tied to geographic origin than cancer histology. This included variants previously reported to be specific to NKTCL but were prevalent in EBV genomes from other cancer types and healthy individuals in East Asia. After controlling for geographic region, we did identify multiple NKTCL-specific variants associated with a 7.8- to 21.9- fold increased risk. We also observed frequent variations in EBV genomes affecting peptide sequences previously reported to bind common MHC alleles. Finally, we found several non-synonymous variants spanning the coding sequences of current vaccine targets BALF4, BKRF2, BLLF1, BXLF2, BZLF1, and BZLF2. These results highlight the need to consider geographic variation in EBV genomes when devising strategies for exploiting adaptive immune responses against EBV-related cancers, ensuring greater global effectiveness and equity in prevention and treatment.

1. **Distinctive genomic features of human T-lymphotropic virus type 1-related adult T-cell leukemia-lymphoma in Western populations**
   Características genómicas distintivas de la leucemia-linfoma de células T adultas relacionada con el virus linfotrópico de células T humano tipo 1 en poblaciones occidentales

   INVESTIGADORES: Caroline S Myers, Eli Williams, Carlos Barrionuevo Cornejo, Georgios Pongas, Ngoc L Toomey, Jose A Sanches, Maxime Battistella, Samuel Mo, Melissa Pulitzer, Cristopher A Moskaluk, Govind Bhagat, Kenneth Ofori, Jonathan J Davick, Octavio Servitje, Denis Miyashiro, Fina Climent, Kimberley Ringbloom, Daniela Duenas, Calvin Law, Sandro Casavilca Zambrano, Luis Malpica, Brady E Beltran, Denisse Castro, Luciana Barreto, Carlos Brites, Jennifer R Chapman, Jaehyuk Choi, Alejandro A Gru, Juan C Ramos.
   LINK: https://pubmed.ncbi.nlm.nih.gov/39113648/
   REVISTA: Haematologica. 2024 Aug 8. doi: 10.3324/haematol.2024.285233. Online ahead of print.
   ABSTRACTO: Adult T-cell leukemia-lymphoma (ATLL) is an aggressive Human T-cell Leukemia Virus Type 1 (HTLV-1)-driven malignancy. Although Western hemisphere (Afro-Caribbean and South American) patients face worse prognoses, our understanding of ATLL molecular drivers derives mostly from Japanese studies. We performed multi-omic analyses to elucidate the genomic landscape of ATLL in Western cohorts. Recurrent deletion and/or damaging mutations involving FOXO3, ANKRD11, DGKZ, and PTPN6 implicate these genes as potential tumor suppressors. RNA-seq, published functional data and in vitro assays support the roles of ANKRD11 and FOXO3 as regulators of T-cell proliferation and apoptosis in ATLL, respectively. Survival data suggest ANKRD11 mutation may confer a worse prognosis. Japanese and Western cohorts, in addition to acute and lymphomatous subtypes, demonstrated distinct molecular patterns. GATA3 deletion was associated with unfavorable chronic cases. IRF4 and CARD11 mutations frequently emerged in relapses after interferon therapy. Our findings reveal novel putative ATLL driver genes and clinically relevant differences between Japanese and Western ATLL patients.

2. **The Latin-American Experience in POEMS Syndrome: A Study of the GELAMM (Grupo de Estudio Latinoamericano de Mieloma Múltiple)**
   La experiencia latinoamericana en el síndrome POEMS: un estudio del GELAMM (Grupo de Estudio Latinoamericano de Mieloma Múltiple)

   INVESTIGADORES: Moisés Manuel Gallardo-Pérez, Paola Negrete-Rodríguez, Morie A Gertz, Camila Peña, Eloisa Riva, Virginia Gilli, Gloritza Rodríguez, César Samánez, Joaquín Ferreira, Sergio Portiño, Jacqueline Montaña, Pilar León, Yaima Gutiérrez, Caroline Del-Castanhel, Cristian Seehaus, Maria Eugenia Funes, Rodrigo Meneces-Bustillo, Patricio Duarte, Claudia Shanley, Giannini Elvira, Paola Ochoa, Hernán López-Vidal, Humberto Martinez-Cordero, Jule Vasquez, Alana von-Glasenapp, Javiera Donoso, Jose Luis Viñuela, Guillermo J Ruiz-Delgado, Guillermo J Ruiz-Argüelles.
   LINK: https://pubmed.ncbi.nlm.nih.gov/39128463/
   REVISTA: Acta Haematol. 2024 Aug 10:1-9. doi: 10.1159/000540890. Online ahead of print.

ABSTRACTO: Introduction: POEMS syndrome is a rare paraneoplastic syndrome caused by an underlying plasma cell disorder. The acronym refers to the following features: polyradiculoneuropathy, organomegaly, endocrinopathy, monoclonal paraproteinemia, and skin changes. Methods: The study was conducted at 24 hematological centers across 8 Latin-American countries. The study included a total of 46 patients {median age was 52 years (interquartile range [IQR]: 42-61.5), 30 males and 16 females} fulfilling the POEMS syndrome criteria diagnosed over a period of 12 years (January 1, 2011, through July 31, 2023). Epidemiological and clinical data were collected in an ad hoc database sent to the members of GELAMM, as well as the Kolmogorov-Smirnov test and Kaplan-Meier estimates. Results: All patients had polyneuropathy and monoclonal gammopathy; 89% had bone marrow plasma cell infiltration, 33% had sclerotic bone lesions. Only 10 patients underwent vascular endothelial growth factor (VEGF) testing in plasma samples. The paraproteinemia was IgG λ in 32% and IgA λ in 30%. 59% patients presented with cutaneous changes, mainly hyperpigmentation, 54% had organomegaly, and 74% endocrinopathy. The median interval from symptom onset to diagnosis was 7.7 months (IQR: 4.0-12.6). 69% of patients received a single line of treatment. The median follow-up period was 25 months (IQR: 9.37-52.0) and the 2-year overall survival rate was 100%. All patients who underwent transplantation (43%) are alive, with a median follow-up of 45.62 months (IQR: 15.46-70). Conclusion: This study investigates POEMS syndrome in Latin America and presents an initial overview of the disease in the region. VEGF usage is recommended for accurate diagnosis, but only 7 hematology centers in the region used it. Survival rate in Latin America is comparable with those observed internationally.

3. **Early death and intracranial hemorrhage prediction in acute promyelocytic leukemia: validation of a risk score in a chemotherapy plus ATRA cohort from an international consortium**

   Predicción de muerte temprana y hemorragia intracraneal en leucemia promielocítica aguda: validación de un puntaje de riesgo en una cohorte de quimioterapia más ATRA de un consorcio internacional

   INVESTIGADORES: Wellington F Silva, Haesook T Kim, Maria S Undurraga, Juan R Navarro-Cabrera, Victor Salinas, Pablo Muxi, Raul A M Melo, Ana Beatriz F Gloria, Katia B B Pagnano, Elenaide C Nunes, Rosane Isabel Bittencourt, Ninoska Rojas, Shirley M Q Truyenque, Ana Ilda Ayala-Lugo, Ana Carolina Oliver, Lorena L Figueiredo-Pontes, Fabiola Traina, Frederico Moreira, Evandro M Fagundes, Bruno K L Duarte, Analí Pamela Mora-Alferez, Percy Ortiz, Jose Luis Untama, Martin S Tallman, Raul C Ribeiro, Arnold Ganser, Richard James Dillon, Peter J M Valk, Miguel A Sanz, Bob Löwenberg, Nancy Berliner, Eduardo M Rego.

   LINK: https://pubmed.ncbi.nlm.nih.gov/39479861/

   REVISTA: Haematologica. 2024 Oct 31. doi: 10.3324/haematol.2024.286338. Online ahead of print.