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CHARACTERISTICS AND TRENDS OF CLINICAL TRIALS ON LEUKEMIA TREATMENTS: ANALYSIS OF THE PERUVIAN CLINICAL TRIAL REGISTRY (1995–2024)

CARACTERÍSTICAS Y TENDENCIAS DE LOS ENSAYOS CLÍNICOS SOBRE TRATAMIENTOS EN LEUCEMIAS: ANÁLISIS DEL REGISTRO PERUANO DE ENSAYOS CLÍNICOS (1995-2024)

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ABSTRACT

Introduction: To describe the characteristics and trends of clinical trials (CTs) on leukemia registered in the Peruvian Clinical Trial Registry (REPEC, by its Spanish acronym), a descriptive study was conducted on CTs registered between 1995 and July 2024. The REPEC database was searched using the term "leukemia." Included were CTs involving patients with acute or chronic leukemias, regardless of disease stage or prior treatment. Variables analyzed included type of leukemia, trial phase, type of product, sponsor, international registration, type of outcome, and methodological characteristics. Out of 2,058 CTs identified, 30 (1.5%) were related to leukemia; of these, 70% were chronic and 76% were myeloid. Fifty-seven percent were phase II trials. Fifty percent were sponsored by the pharmaceutical industry, primarily international companies. Eighty percent were open-label studies. Fifty-three percent reported progression-free survival as a surrogate endpoint. In Peru, leukemia clinical trials prioritize chronic forms and early phases, with few clinically relevant outcomes.

Keywords: Clinical trial; Leukemia; Leukemia, Leukemia; Myeloid; Chronic-phase. (Source: MESH-NLM)

RESUMEN

Introducción: Con el objetivo de describir las características y tendencias de los ensayos clínicos (EC) sobre leucemias registrados en el Registro Peruano de Ensayos Clínicos (REPEC), se realizó un estudio descriptivo de EC registrados entre 1995 y julio de 2024. La búsqueda en REPEC utilizó el término "leucemia". Se incluyeron EC en pacientes con leucemias agudas o crónicas, sin restricción por estadio o tratamiento previo. Las variables fueron tipo de leucemia, fase del EC, tipo de producto, patrocinador, registro internacional, tipo de desenlace y características metodológicas. De 2 058 EC identificados, 30 (1,5%) correspondieron a leucemias; de éstas, 70% fueron crónicas y 76%, mieloide. El 57% estuvo en fase II. El 50% fue patrocinado por la industria farmacéutica, principalmente extranjera. El 80% fueron abiertos. El 53% reportó sobrevida libre de progresión como desenlace subrogado. En Perú, los EC en leucemias priorizan formas crónicas y fases tempranas, con pocos desenlaces clínicamente relevantes.

Palabras clave: Ensayo clínico; Leucemia; Leucemia mieloide de fase crónica. (Fuente: DeCS- BIREME)

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INTRODUCTION

Clinical trials (CTs) have emerged as a fundamental pillar in the fight against cancer, serving as a crucial platform for evaluating effective therapeutic and palliative strategies [1]. The global incidence of acute leukemias ranges from one to five cases per 100,000 inhabitants[2]; in Peru, nearly 1,700 cases of hematologic malignancies were reported in children between 2006 and 2011 [3]. Within this context, leukemias represent a heterogeneous group of malignant neoplasms characterized by clinical manifestations such as anemia, thrombocytopenia, bone pain, bleeding, infections, hepatosplenomegaly, among others, resulting from blast infiltration in the bone marrow[4].

This disease is defined by clonal proliferation of hematopoietic cells that arises when blood cells generated in the bone marrow undergo alterations and begin to multiply uncontrollably [5]. Additionally, clonal proliferation of various subsets of lymphocytes in their early stages—from B cells to T cells—can give rise to both acute and chronic leukemias. These conditions challenge our current understanding and demand adaptive therapeutic approaches [6]. In recent decades, traditional CTs focused exclusively on histology and cytotoxic chemotherapy have transitioned toward more dynamic evaluations, driven by biomarkers and molecular therapies, offering new perspectives in cancer treatment[7]. In this context, a recent study in the Peruvian oncology field reported a sustained increase in CT frequency, with particular emphasis on phases II and III[8]. However, the absence of specific evaluations of CTs in the field of leukemias was noted.

To date, no comprehensive evaluation of the status of CTs on leukemias in Peru has been conducted, according to the available data in the Peruvian Clinical Trial Registry (REPEC, by its Spanish acronym). Therefore, the objective of this study was to describe the characteristics and trends of CTs on leukemias registered in REPEC, with the aim of contributing to the strengthening of clinical research in the country.

METHODS

A descriptive study was conducted on CTs related to leukemias registered in REPEC and submitted to the General Office for Research and Technological Transfer of the Instituto Nacional de Salud for review and approval between 1995 and July 2024. Access to REPEC was open and was carried out through the portal https://ensayosclinicos-repec.ins.gob.pe.

The REPEC website was accessed, and using the advanced search option, a filter was applied with the keyword "leukemia" to identify CTs containing this term in the title or in the body of the registration form. CTs involving patients diagnosed with acute or chronic leukemia, regardless of clinical stage or prior treatment, were included. CTs whose records were not accessible through REPEC were excluded.

The main variables were the disease under study, type of leukemia (acute or chronic), and clinical outcome. Additional variables related to the CTs were also analyzed, such as sponsor (national or international), sponsor type (cooperative groups [research networks, scientific societies, civil associations, foundations, and research organizations], pharmaceutical industry [companies, labs], national institutes of health [Peruvian or foreign], and universities [public or private, national or international]), year of registration, trial status (authorized or unauthorized), registration in international databases (ClinicalTrials.gov or WHO Universal Trial Number [UTN]), phase (I, II, III, or IV), design approach (superiority, equivalence, non-inferiority, or dose-response), type of randomization (blocks or other), type of blinding (single, double, triple, or open-label), allocation model (single-arm, parallel groups, crossover, or factorial), product type (pharmaceutical or other), product characteristics (biological or chemical), immunochemotherapy (yes or no), comparator (standard treatment, no treatment, or placebo), treatment duration, follow-up duration, recruitment status, number of participating research

centers globally and nationally, and number of ethics committees approving the study. Outcomes were classified as clinically relevant or surrogate. A database was created in Microsoft Excel version 2016 using a template specifically designed for this study, considering the variables of interest. A list of CT titles was obtained, each with a hyperlink redirecting to the corresponding registration record, which could be downloaded.

If relevant data were missing from the registration form, the protocol registered in the corresponding international database was consulted. Frequencies and percentages were presented for qualitative variables, and summary measures (mean and standard deviation or median and interquartile range) were reported based on the results of normality tests (Kolmogorov–Smirnov test with Lilliefors significance correction). Data were processed using the R programming language (version 4.3.1) in the graphical interface RStudio (version 2024.04.2+764). This analysis was conducted using a publicly accessible database; therefore, approval by a research ethics committee was not required. It was a secondary analysis, and the data did not include any information that could identify research subjects.

RESULTS

As of the last search date, a total of 2,058 CTs were identified in REPEC. Of these, 31 (1.5%) corresponded to CTs conducted in patients with leukemias. One study was excluded for not meeting the inclusion criteria, resulting in a final total of 30 CTs included in the analysis (Figure 1).

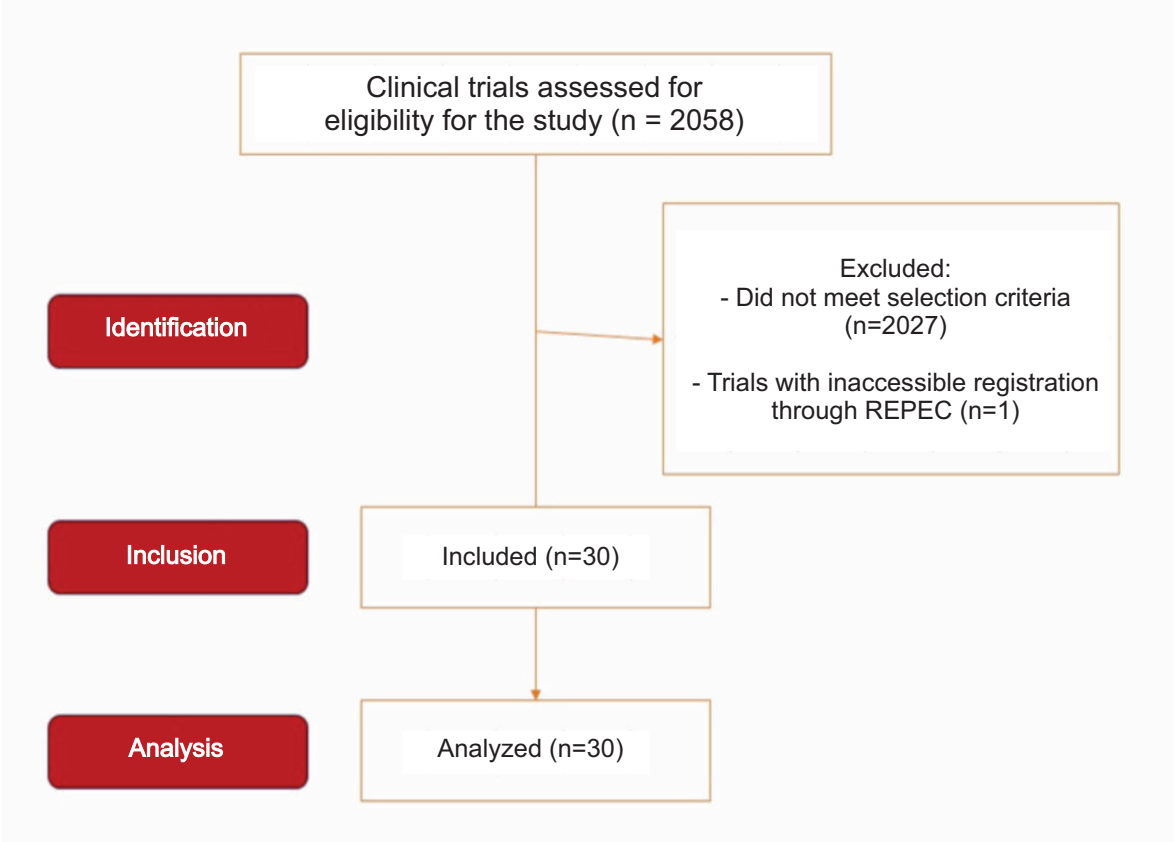

Figure 1. Flow diagram for clinical trial selection.

The most common type of leukemia was chronic leukemia, representing 70% (n=21) of the total; within this group, 76% (n=16) corresponded to myeloid leukemia. Regarding the type of investigational product, 40% (n=12) of the CTs evaluated biological products, while 60% (n=18) studied non-biological products.

In terms of sponsorship type, 50% (n=15) of the CTs were sponsored by the pharmaceutical industry, 10% (n=3) by companies or corporations, 3% (n=1) by cooperative groups, and in 37% (n=11), this information was not reported. Regarding the sponsor's origin, 50% (n=15) were foreign, 10% (n=3) national, and 40% R(n=12) did not specify this information.

Most CTs were authorized (97%, n=29), while 3% (n=1) were not. egarding international registration, 47% (n=14) were not registered in ClinicalTrials.gov, and 13% (n=4) were registered only in the WHO UTN database. With respect to study phase, 57% (n=17) were phase 2, 40% (n=12) phase 3, and only 3% (n=1) phase 4.

The most common methodological design was superiority (47%, n=14), followed by dose-response (23%, n=7); 30% (n=9) of CTs did not report this information. All studies (100%, n=30) did not specify the type of randomization. Regarding blinding, 80% (n=24) were open-label studies, and 20% (n=6) were double-blind (Table 1).

Table 1. Characteristics of leukemia-related clinical trials registered in REPEC (1995–2024).

Variable	Category	Frequency, n=30 (%)
Sponsor origin	Foreign	15 (50.0)
	National	3 (10.0)
	Not reported	12 (40.0)
Type of sponsor	Pharmaceutical industry	15 (50.0)
	Company/Corporation	3 (10.0)
	Cooperative group	1 (3.3)
	Not reported	11 (36.7)
Trial status	Authorized	29 (96.7)
	Not authorized	1 (3.3)
Number of centers in Peru	1 center	15 (50.0)
	2 centers	8 (26.7)
	3 centers	0 (0.0)
	4 centers	1 (3.3)
	Not reported	6 (20.0)
Study phase	Phase 1	0 (0.0)
	Phase 2	17 (56.7)
	Phase 3	12 (40.0)
	Phase 4	1 (3.3)
Methodological design	Superiority	14 (46.7)
	Dose-response	7 (23.3)
	Not reported	9 (30.0)

The follow-up period ranged from 0 to 96 months. Figure 2 shows the distribution of leukemia CTs according to the year of registration, with the highest number recorded between 2005 and 2009. In the past five years, only two CTs were registered.

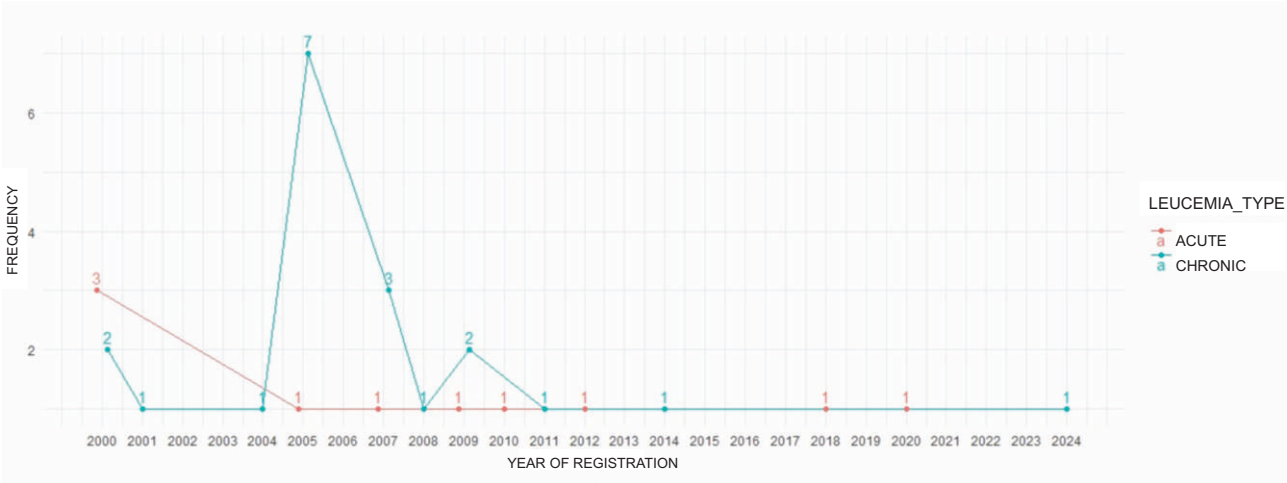

Figure 2. Trend of clinical trial registrations by leukemia type.
LMost of the outcomes evaluated were surrogate endpoints, with progression-free survival being the most frequently reported (53%, n=16). In a considerable proportion of the reviewed records, the primary outcome was not clearly stated.

DISCUSSION

The analysis of clinical trials on leukemias registered in REPEC provides relevant findings that contribute to understanding the characteristics and trends of clinical research in this area in Peru. One of the most notable findings is the predominance of CTs on chronic leukemias over acute leukemias. This pattern not only reflects the national context but also aligns with certain international trends in oncology research[9].

The predominance of studies on chronic leukemias observed in REPEC is consistent with the global literature, which reports that these types of leukemias are more frequent in certain populations, especially adults [9]. In particular, studies from the Surveillance, Epidemiology, and End Results (SEER) Program in the United States show that chronic myeloid leukemia (CML) is more common than acute leukemias in adults [9]. His may be partly explained by the slow progression of chronic leukemias [10], which allows for prolonged follow-up of therapies. In contrast, acute leukemias have a faster progression and require aggressive therapeutic interventions [11], which may hinder their evaluation in traditional CT designs. Regarding CT phases, the finding that most are in phases 2 and 3 aligns with international reports [12,13]. These phases are essential for establishing the efficacy and safety of new therapeutic interventions and are often prioritized in oncology treatment development[13]. However, the high proportion of CTs sponsored by the pharmaceutical industry, mostly of foreign origin, highlights a significant dependence on external funding for the development of clinical research in oncology in Peru [14].

This situation presents both challenges and opportunities in terms of scientific autonomy and the strengthening of national research capacity. A particularly relevant aspect is the type of outcomes evaluated in CTs. By definition, an outcome represents a clinical, medical, or surgical event used to measure the effectiveness and safety of an intervention [15].

Its selection should be based on the nature of the study and the research question being addressed [15]. In this analysis, a predominance of surrogate endpoints was observed, with progression-free survival being the most commonly reported. This choice may be influenced by the leukemia subtype, as in the context of chronic leukemias, due to their longer clinical course[10], progression-free survival may be more appropriate than overall survival. Progression-free survival has been widely validated as a surrogate for overall survival in hematologic malignancies, including acute myeloid leukemia and lymphomas [16-18]. Recent studies have shown a significant correlation between both parameters, even in the context of innovative therapeutic strategies such as immunochemotherapy, reinforcing its usefulness as a predictive indicator in the evaluation of new interventions[16].

However, this trend may also reflect a lack of focus on clinically relevant outcomes such as quality of life or mortality—fundamental aspects for evaluating the real impact of interventions on patients. A previous study analyzing oncology CTs registered in REPEC over a 25-year period reported that 23.5% corresponded to oncology studies[8]. In contrast, in this analysis, CTs on leukemias represented only 1.5% of the total, suggesting a low proportion of studies focused on this disease. This finding highlights the need to promote clinical research on leukemias in the country. Among the strengths of this study is the thorough review of available records in REPEC. The continuous and open access to the database allowed for an advanced and detailed search, facilitating the analysis of trends and characteristics of leukemia CTs. This description significantly contributes to the understanding of the current landscape of clinical research in this field within the Peruvian context. However, several important limitations were identified. One of the main issues was the lack of complete data in several registration forms. The absence of critical information, such as outcome type or methodological details, may affect the validity of the analysis and limit the interpretation of results. This deficiency underscores the need to improve the quality of CT registration, promoting more rigorous and standardized documentation.

The findings of this study have relevant implications for clinical research in Peru. The predominance of CTs in chronic leukemias and the frequent use of surrogate outcomes highlight the need to strengthen registration standards, encourage the inclusion of clinically significant outcomes, and improve the documentation of studies in REPEC. Likewise, there is a clear need to encourage research on acute leukemias, which remain underrepresented among the registered CTs[19,20].

CONCLUSION

In conclusion, the analysis of leukemia CTs in REPEC reveals a predominance of studies focused on chronic leukemias. However, significant gaps in registration and data quality were also identified, underscoring the need to improve documentation systems, promote patient-centered outcomes, and expand clinical research to include other leukemia subtypes. These efforts are essential to strengthen the available evidence and contribute to the development of better therapeutic strategies within the national context.

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