CLINICAL PRACTICE GUIDELINE FOR THE INITIAL MANAGEMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA

- **Title:** Clinical Practice Guideline for the initial management of acute lymphoblastic leukemia
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Abstract: This paper abstracts the Clinical Practice Guideline for the initial management of acute lymphoblastic leukemia (ALL) in EsSalud. A guideline task force (GTF) was formed with specialized physicians and methodologists. The GTF proposed 8 clinical questions to be answered in this Clinical practice guideline (CPG). Systematic searches of preview reviews were performed and when it was necessary, primary studies from PubMed and CENTRAL during 2019 were reviewed. The evidence was selected aiming to answer each proposed question. Certainty of evidence was evaluated using Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology. In periodical work sessions, the group used GRADE methodology for reviewing the evidence and formulating recommendations, good clinical practice items and the flowchart of evaluation and management. This CPG approached 8 clinical questions, divided into four topics: diagnosis, general measures, chemotherapeutic management of ALL, and transplantation. Based on these questions; 5 recommendations (3 strong recommendations and 2 weak recommendations), 20 good clinical practice items and three flowcharts were formulated.

- **Key words:** Acute lymphoblastic leukemia; Practice Guideline; GRADE Approach; Evidence-Based Medicine.
- **PICO questions for CPG:**

CHOOSING THE MANAGEMENT PROTOCOL		
Question 1: In children (1 to 14 years old) with acute lymphoblastic leukemia, what management protocol should be used?		
POPULATION	**INTERVENTION / COMPARATOR**	**OUTCOME(S)**
Children with ALL	Management protocols in pediatrics	• Event-free survival • Global survival • All-cause mortality at 3 years of follow-up and the longest follow-up period.

		• Complete remission post-induction • Relapse rate. • Mortality not related to relapse. • Complete remission
Question 2: In adolescents and young adults (15 to 35 years old) with acute lymphoblastic leukemia, what management protocol should be used?		
POPULATION	**INTERVENTION / COMPARATOR**	**OUTCOME(S)**
Adolescents and young adults with ALL	Management protocols (inspired by pediatric regimen vs adult regimen)	• Event-free survival • Global survival • All-cause mortality at 3 years of follow-up and the longest follow-up period. • Complete remission post-induction • Relapse rate. • Mortality not related to relapse. • Complete remission
Question 3: In adults (36 to 60 years old) and elders (61 to more years old) with acute lymphoblastic leukemia, what management protocol should be used?		
POPULATION	**INTERVENTION / COMPARATOR**	**OUTCOME(S)**
Adults and /or elders with ALL	Management protocols (inspired by pediatric regimen vs adult regimen)	• Event-free survival • Global survival • All-cause mortality at 3 years of follow-up and the longest follow-up period.

		• Complete remission post-induction • Relapse rate. • Mortality not related to relapse. • Complete remission

EVALUATION PRIOR TO CHEMOTHERAPY MANAGEMENT			
Question 4: In patients with acute lymphoblastic leukemia, when should the first lumbar puncture be performed to diagnose central nervous system involvement and prophylaxis?			
POPULATION	**INTERVENTION**	**COMPARATOR**	**OUTCOME(S)**
People with ALL	First lumbar puncture concomitant with the initiation of systemic chemotherapy	First lumbar puncture days after the initiation of systemic chemotherapy	• Mortality • Disease-free survival • Quality of life • CNS involvement

MANAGEMENT DURING THE EARLY CONSOLIDATION PHASE			
Question 5: In patients with acute lymphoblastic leukemia with intermediate or high risk who are in early consolidation phase with ALL IC-BFM 2009 protocol, which IB protocol should be used: high intensity or standard intensity protocol?			
POPULATION	**INTERVENTION**	**COMPARATOR**	**OUTCOME(S)**
Patients with ALL	High intensity B protocol	Standard intensity B protocol	• Event-free survival • Global survival • Disease-free survival • Toxicity after therapy

MANAGEMENT DURING THE EARLY CONSOLIDATION PHASE		
Question 6: In patients with B-lineage acute lymphoblastic leukemia with intermediate risk who are in early consolidation phase with ALL IC-BFM 2009 protocol, what dose of methotrexate should be administered?		
POPULATION	**INTERVENTION / COMPARATOR**	**OUTCOME(S)**
Patients with B-lineage acute	Different doses of methotrexate	• Mortality

lymphoblastic leukemia with intermediate risk		• Disease-free survival • Quality of life • Adverse effects

MANAGEMENT OF PHILADELPHIA CHROMOSOME-POSITIVE PATIENTS			
Question 7: In patients with Philadelphia chromosome-positive acute lymphoblastic leukemia (PH+), should tyrosine kinase inhibitor (TKI) Imatinib be administered?			
POPULATION	**INTERVENTION**	**COMPARATOR**	**OUTCOME(S)**
Patients with ALL	Administer TKI	Not administer TKI	• Mortality • Disease-free survival • Quality of life • Adverse effects

MANAGEMENT BY HEMATOPOIETIC PROGENITOR CELL TRANSPLANTATION			
Question 8: In patients with ALL in complete remission who are candidates for hematopoietic stem cell transplantation, in whom related donor HLA-identical allogeneic transplantation, should unrelated donor HLA-identical allogeneic transplantation or HLA-haploidentical transplantation be used?			
POPULATION	**INTERVENTION**	**COMPARATOR**	**OUTCOME(S)**
Patients with ALL	Haploidentical transplantation	Allogeneic transplantation	• Relapse • Event-free survival • Global survival • Disease-free survival • Acute and chronic graft-versus-host disease