INTRODUCTION

Leukemia is the most common type of blood malignancies. Histologically, they can be differentiate into mylogenous and lymphocytic. Chronic lymphocytic leukemia (CLL) is a monoclonal disorder characterized by a progressive accumulation of functionally incompetent lymphocytes. It is the most common form of leukemia found in adults in Western countries. It considered an incurable, generally indolent lymphoproliferative neoplasm, in which therapy is usually reserved for patients with symptoms and/or cytopenias. **(Cazzola and malcovati, 2005)**

Major advances have been made in understanding of the biology and opportunities for treatment of chronic lymphocytic leukemia in recent times. Newer treatment regimens incorporating purine nucleoside analogs have increased the rate of successful remission induction in chronic lymphocytic leukemia patients. Moreover, recent combination chemoimmunotherapy regimens have produced more frequent complete molecular remissions, and early evidence seems to suggest that this could result in prolonged duration of responses, although this association remains to be clearly demonstrated. In the future a significant improvement of clinical benefits in chronic lymphocytic leukemia will be obtained through the administration of combination of monoclonal antibodies combined with chemotherapy in different modalities **(Malcovati et al., 2005).**

This recent advances in understanding the biology of chronic lymphocytic leukemia (CLL) indicate that there are 2 variants arising at different stages of B-cell differentiation. This variance is reflected by the mutational status of the immunoglobulin variable region (IgV) genes. In addition, by using fluorescence in situ hybridization technique, genomic aberrations can be diagnosed in up to 80% of cases. Both the IgV mutation status and the pattern of genomic aberrations have a high predictive value for disease progression and survival in patients with CLL. Therefore, therapeutic approaches are currently being reassessed with emphasis on prognostic factor-directed therapy. **(Kim et al., 2006).**

This development is accompanied by promising new treatment options. The most convincing results were reported for a single-agent therapy using the purine analog fludarabine. In pretreated patients the overall response rates range from 50% to 60%. Approximately 80% of untreated patients respond with a complete remission (CR) rate of 35%. Randomized trials demonstrated that fludarabine induces higher responses and more durable remissions compared with chlorambucil; cyclophosphamide, hydroxydaunomycin, Oncovin (vincristine), and prednisone (CHOP); or cyclophosphamide, Adriamycin (doxorubicin), and prednisone (CAP). However, the most relevant clinical end point, overall survival, was not substantially different. **(Kattamis et al., 2006).**

Despite encouraging results with fludarabine or fludarabine combinations, all patients ultimately relapse. Relapse is most probably a result of residual tumor cells. Studies using minimal residual disease (MRD) assays with lower sensitivity reported some MRD-negative cases after fludarabine therapy.

In contrast, a more recent study comprising 16 newly diagnosed cases of CLL documented that all patients in CR had polymerase chain reaction (PCR)-detectable residual tumor cells. Thus, most likely all patients with CLL treated with conventional chemotherapy have residual tumor cells. Because a true CR is the major therapeutic goal in CLL, there is a need for new therapeutic approaches with different mechanism of action. **(Rofail et al., 2006).**

Monoclonal antibodies such as rituximab (anti-CD20) have attracted substantial interest as a new class of effective reagents in the treatment of malignant lymphoma. Rituximab is a chimeric-humanized monoclonal antibody that has given response rates of 50% in relapsed or refractory low-grade non-Hodgkin lymphoma (NHL). Treatment results with single-agent rituximab in patients with CLL using conventional doses were inferior compared with follicular lymphoma. This result might, at least in part, be due to the lower density of CD20 antigen expression on CLL cells. Pharmacokinetic studies revealed a substantially lower pretreatment plasma level of rituximab in patients with CLL compared with those with other low-grade lymphoma. Patients with higher numbers of circulating $CD20^{+}$ tumor cells were more likely to experience severe side effects related to a massive release of cytokines. Severe acute reactions were generally more common during initial infusion. These side effects can be controlled by a "stepped-up" dosing of rituximab or the addition of steroids. **(Alessandrino et al., 2002).**