SUMMARY

Chronic lymphocytic leukemia is accumulative disease which occur due to defect in programmed cell death (Apoptosis).

CLL . characteeized by accumulation of lymphocytes in peripheral blood, Lymph node, spleen, liver and bone marrow .

CLL . is more common in old age more than 50 years old, and in males more than in females. Mostly patients with CLL paste without any symptoms and the disease discovered accidentally with routine laboratory investigations. Were CBC revealed presence of leukocytosis more than 100.1000 and lymphocytosis more than 15% With disease progression patients complaining of easily fatigability, palpitation, tachycardia, Lymph node enlargement, atosplenomegaly and, purperic eruptions.

CLL was classified according to Rai staging as follows:

Stage 0 : Leukocytosis and lymphoctosis.
Stage 1 : lymphoctosis + Lymph node enlargement.
Stage 2 : lymphoctosis + (LN + spleen + liver) enlargement.
Stage 3 : lymphoctosis + LN + spleen + liver + Anemia.
Stage4 :lymphoctosis + LN + spleen + liver + Anemia + Thombocytopenia.

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.

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.

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.