

## Follicular lymphoma (FL)

### Clinics and Pathology

Phenotype / cell stem origin	Pan-B antigens test positive. The immunophenotypic profile is CD10+, CD5-, slg+ and the cell of origin is a germinal centre B-cell that has encountered the antigen.
Epidemiology	This lymphoma accounts for 30-40% of all lymphomas occurring in the adult population in western countries. Its peak incidence is in the fifth and sixth decade.
Clinics	<p>The patients most often present widespread disease at diagnosis, with nodal and extranodal (bone marrow) involvement. Peripheral blood involvement is detectable by light microscopy in approximately 10% of the cases, but the majority of cases can be shown to have circulating malignant cells by sensitive molecular genetic methods.</p> <p>The disease usually runs an indolent course. Grade 3 FL may be characterized by earlier relapse, especially if treated with regimens not including an anthracycline drug.</p>
Pathology	The lymphoma is composed of a mixture of centrocytes and centroblasts with a follicular and diffuse pattern. Lymphoma grading by the number of large cells/centroblasts is recommended: three grades are recognized with increasing number of centroblasts.
Treatment	Depending on age and stage at presentation it may vary from a "watch and wait" policy in initial stages to multiagent chemotherapy in advanced stages. Immunotherapy using chimeric anti-CD20 monoclonal antibody has an important role in combination with chemotherapy. Radioimmunotherapy has an important role in relapsed or refractory patients.
Evolution	The majority of patients cannot be cured by chemotherapy and eventually relapse. Histologic switch into high grade lymphoma may occur. A positive impact on long term disease free survival and overall survival is likely to derive from the introduction of monoclonal antibodies in association with multiagent chemotherapy.
Prognosis	Approximately 60% of the patients presenting with limited disease are alive at 10 years. Patients in stages III and IV were reported to have a median survival in the 8-12 years range

### Cytogenetics

Cytogenetics Morphological Seventy-80% of the cases carry the [t\(14;18\)\(q32;q21\)](#) as the primary chromosome anomaly. Rare variant translocation [t\(2;18\)\(p11;q21\)](#) and [t\(18;22\)\(q21;q11\)](#) were described. Approximately 15% of the cases show a 3q27 break. half of which include the [t\(3;14\)\(a27:a32\)](#) and the

	variant translocations <a href="#">t(3;22)(q27;q11)</a> and <a href="#">t(2;3)(p11;q27)</a>
Cytogenetics	The incidence of 6q21 deletion and 17p13/p53 deletion (see below) by interphase FISH analysis may be around 60% and 20%, respectively
Molecular	
Additional anomalies	<p>Secondary chromosome changes are both numerical and structural. Trisomy 7, <a href="#">+8</a>; <a href="#">+12</a>, <a href="#">+3</a>, <a href="#">+18</a>, +X each occur in 10-20% of the cases. There is an association between +7 and the presence of a large cell component, but no numerical anomaly has an independent impact on prognosis.</p> <p><a href="#">Deletions of 6q23-26</a> occur at a 25-30% incidence; <a href="#">17p anomalies</a> are present in approximately 10% of the cases. The presence of these anomalies may have a correlation with disease transformation and it was associated with an inferior prognosis.</p> <p>Rarely, histologic switch into a high grade lymphoma may be associated with the development of an additional <a href="#">t(8;14)(q24;q32)</a>. The clinical course in these cases is aggressive</p> <p>The incidence of 6q21 deletion and 17p13/p53 deletion by interphase FISH analysis may be around 60% and 20%, respectively.</p> <p>Other anomalies include 1p36 deletion in 10-12% of the cases, probably centered around the p73 gene; 10q22-24 deletions in 10-13% of the cases and 9p21 deletions/ <a href="#">p16</a> deletions, associated with histologic transformation</p>

## Result of the chromosomal anomaly

<b>Fusion Protein</b>	No fusion protein. The <a href="#">t(14;18)</a> brings about the juxtaposition of <a href="#">BCL-2</a> with the <a href="#">lg heavy chain</a> joining segment, with consequent marked overexpression of the BCL2 protein product. The majority of breakpoints on 18q22 fall into two regions: the major breakpoint region (60-70% of the cases) and the minor cluster region (20-25% of the cases).
Description	In those cases with 3q27/BCL6 involvement the breakpoints on 3q27 are usually located in a different region with respect to high grade diffuse large cell lymphoma. This region is located 245 and 285 kb 5' of <a href="#">BCL6</a> (alternative breakpoint cluster region)
Oncogenesis	BCL-2 overexpression prevents cell to die by apoptosis. BCL-2 forms heterodimers with BAX and the relative proportion of BCL-2 to BAX determines the functional activity of BCL-2. In vitro, BCL-2 constitutive expression has a definite role in sustaining cell growth, whereas in vivo, BCL-2 transgenes induce a pattern of polyclonal proliferation of mature B-cells.

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