Background: According to the WHO/EORTC classification, primary cutaneous diffuse large B-cell lymphomas are divided into three types; namely in primary cutaneous follicle center lymphoma, primary cutaneous diffuse large B-cell lymphoma of leg type and primary cutaneous diffuse large B-cell lymphoma of other type. The third type pools cases of primary cutaneous diffuse large B-cell lymphoma that are rare and do not belong to the types of primary cutaneous follicle center lymphoma or primary cutaneous diffuse large B-cell lymphoma of leg type. This classification is based on a combination of clinical, histological and immunohistochemical criteria. Primary cutaneous follicle center lymphoma are is associated with an excellent prognosis and are is in most cases localized in the head and neck regions or on the trunk. Primary cutaneous diffuse large B-cell lymphoma of leg type shows an intermediate course and are is mostly found in the legs. Thus, the WHO/EORTC classification for cutaneous lymphomas includes distinct diseases entities, with well-defined clinical and histological criteria.

Question: The goal of our study was to show whether diffuse large B-cell lymphoma of primary cutaneous follicle center lymphoma (cFCL) type also occurs in extranodal non-cutaneous localisation and if it has similar clinical characteristics as primary cutaneous follicle center lymphoma.

Methods: We identified among 1500 non-Hodgkin's Lymphomas during the period from 1992 to 2004 109 cases of extranodal non-cutaneous diffuse large B-cell lymphomas (DLBCL). Thymus, spleen, gastrointestinal tract, patients with known immunosuppression or immunodeficiency and cases with known lymph node involvement by biopsy were excluded. These 109 cases were reviewed, upon which 17 cases with insufficient material, 30 patients with a previous diagnosis of low grade lymphoma or nodal large B-cell lymphoma, and 16 patients with Burkitt lymphoma, blastoid mantel cell lymphoma, follicular lymphoma or other lymphoma were excluded. Clinical information was obtained from the patients' hospital records. Survival information was obtained from the cancer registry of the Canton of Zurich. Ten patients had advanced stage disease, seven were HIV positive, one was EBV positive, and no clinical information or follow-up data was available for four patients. These patients were also excluded. The remaining 24 cases were evaluated by morphology and immunohistochemistry. According to criteria of the WHO/EORTC classification of cutaneous lymphomas, according to which primary cutaneous diffuse large B-cell lymphoma is divided into primary cutaneous follicle center lymphoma and primary cutaneous diffuse large B-cell lymphoma of leg type, we assigned the 24 cases with the aid of morphology and an immunohistochemical score/algorithm to either cutaneous follicle centre lymphoma type (cFCL; large centrocytoid, Bcl-6 +, Irf-4-, Bcl-2 -, CD10-), transformed follicular lymphoma type (tFL; large centrocytoid, Bcl-6+, Irf-4-, Bcl-2+, CD10+) or to other type ("large centrocytoid and centroblastic", "centroblastic and immunoblastic" or "immunoblastic", Bcl6+/-, Irf-4+, Bcl2+/-, CD10-/+).

Results: Among the 24 cases, we found nine lymphomas with pure large centrocytoid (cc) morphology, and 15 lymphomas with either "centrocytoid and centroblastic" (cc,cb), or "centroblastic and

immunoblasitic " (cb,ib) morphology. Six of the cases with centrocytoid morphology fulfilled the immunohistochemical criteria for diffuse large B-cell lymphoma of cFCL-type in extranodal localisation other than the skin. The remaining three cases were transformed follicular lymphomas (tFL) of nodal type. The 15 lymphomas with centroblastic or immunoblastic morphology were classified as diffuse large B-cell lymphoma of other type. The nine pure centrocytoid lymphomas did not express Irf-4 and were always positive for Bcl-6. Lymphomas with centroblastic or immunoplastic morphology expressed mostly Irf-4 (12/15 cases) and were frequently positive for Bcl-6 (9/15 cases). All nine cases of extranodal non-cutaneous diffuse large B-cell lymphoma with purely centrocytoid nuclear morphology were stage IE. Most of the remaining 15 other cases of diffuse large B-cell lymphoma were already stage II (11/15 cases). Extranodal non-cutaneous DLBCL stage I and II showed a good prognosis overall. Five of 24 patients died of lymphoma (25%). No significant differences in disease specific survival between the different groups were found, but there was a tendency toward longer survival in lymphomas with centrocytoid morphology.

Conclusion: To summarise, the findings suggest that the criteria to divide primary cutaneous diffuse large B-cell lymphoma into primary cutaneous follicle center lymphoma and primary cutaneous diffuse large B-cell lymphoma of leg type can as well be used to differentiate cFCL from other types in extranodal non-cutaneous localisation. The results further suggest that DLBCL that have been identified in the skin as distinct clinico-pathological entities can also occur in non-cutaneous extranodal localisations**.**