INTERIM ANALYSIS OF THE IELSG-19 RANDOMISED STUDY OF CHLORAMBUCIL ALONE VERSUS CHLORAMBUCIL PLUS RITUXIMAB VERSUS RITUXIMAB ALONE IN EXTRANODAL MARGINAL ZONE LYMPHOMAS OF MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT LYMPHOMA)

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The available clinical information on MALT lymphoma is mostly based on retrospective series. In 2003 the International Extranodal Lymphoma Study Group launched the IELSG-19 study to compare Chlorambucil alone versus the combination of Chlorambucil and Rituximab. Because of the excellent initial recruitment, a third arm with Rituximab alone was later introduced. The study is still ongoing and at the end of July 2009, 403 patients (pts) of the 450 planned have entered. The Italian Lymphoma Intergroup and the French GELA group were the main contributors to this study together with Cancer Research UK, the Catalan Hematology Group and the Oncology Institute of Southern Switzerland. All the MALT lymphoma pts with localized disease at any extranodal site who do not respond or are not suitable to local therapy, the H.pylori-negative gastric lymphomas or those who failed antibiotic therapy are eligible, as well as those with disseminated or multifocal MALT lymphoma. Histology review of all cases is underway. A planned interim analysis was performed in April 2009 on the first 320 pts, 169 men (53%) and 151 women (47%); 292 pts (91%) had no previous treatment. The treatment was completed in in 86% of the 320 analysed pts, in 64% without dose changes or time delay. The primary MALT lymphoma site was the stomach in 138 pts (43%);182 pts (57%) had a non-gastric presentation. The most common non-gastric sites were the lungs (N=42, 13%), the ocular adnexa (N=32; 10%), the intestine (N=29; 9%), the salivary glands (N=26; 8%), and the skin (N=21; 7%). In 95 pts (30%) the lymphoma involved more than 1 extranodal site. Lymph node involvement was present in 118 pts (37%); 181 pts (58%) had localized disease (Ann Arbor stage I-II) while 129 (42%) had advanced stage. The ECOG performance status was 0 in 230 pts (74%). According to the international prognostic index (IPI) 190 pts (59%) had a low risk, 68 (21%) a low-intermediate risk , 54 (17%) an intermediate-high risk, and only 8 (2.5%) a high risk score. B-symptoms were present in 33 pts (11%) and LDH levels were higher than normal in 31 (10%). The median age is 61 year (range, 26-81). At a median follow-up of 40 months, overall survival (OS), progression-free survival (PFS) and event-free survival (EFS) are 96%, 88%, and 62%, respectively. Among the main clinical characteristics, the presence of B-symptoms, elevated LDH, more than one extranodal site, advanced stage, poorer performance and unfavourable IPI scores were significantly (p<0.05) associated with shorter OS, PFS and EFS. The presence of lymph nodal involvement was significantly associated with shorter PFS and EFS but did not affect the OS. Patient younger than 60 years had longer OS and PFS but age had no effect on the EFS. Differently from previous series, there were no differences in outcome between pts with gastric and non-gastric localization; this finding is likely due to the fact that H. pylori-positive gastric MALT lymphoma pts still responding to antibiotics were excluded from the study. This is by far the largest prospective study ever conducted in MALT lymphomas; further analyses are in progress.