

W38: Real Life Outcome of Lymphoplasmacytic Lymphoma and Splenic Marginal Zone Lymphoma: an Analysis From the NF10 Project, an International, Prospective, Observational Study of the Fondazione Italiana Linfomi

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Background: Lymphoplasmacytic Lymphoma (LPL) and Splenic Marginal Zone Lymphoma (SMZL) are low-grade B cell lymphomas that share some clinical features at presentation and generally shows an indolent course.

Aim of the study: The NF10 Project was started in 2010 by the Fondazione Italiana Linfomi (FIL) as a prospective registry specifically conceived to investigate the prognosis of Indolent Non-Follicular B-Cell Lymphomas (INFL). We present an analysis of the registered LPL and SMZL, focusing on clinical aspects, pattern of care and outcome.

Methods: The registration of clinical, laboratory data along with treatment and outcome details of consecutive adult pts with newly diagnosed INFL is active at a dedicated website. All patients with a histologic confirmed diagnosis of INFL, including LPL and MZL, were eligible with no exclusion criteria. So far, the study has been activated in 65 centres in Europe and South America.

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Results: Between July 2010 and March 2018, 1.144 INFL cases have been registered. LPL were 208 (28%) and MZLs were 544: 213 SMZL (28%), 268 EMZL (36%), 63 NMZL (9%). Comparison of clinical features between LPL and SMZL is summarized in Table 1: in SMZL LDH and β_2 -microglobulin > UNL and platelets < $80 \times 10^9/L$ were more frequent in comparison to LPL. HCV prevalence was similar in 2 diseases (5% in SMZL and 6% in LPL). Regarding treatment, immediate systemic treatment was planned in 98 SMZL pts (46%) and in 95 LPL pts (46%). The median time to first treatment for not planned treated was 14 months (13 for SMZL and 14 for LPL). R-bendamustine was employed in 18% of LPL and 27% of SMZL; combination of R with alkylating agent in 39% of LPL and 9% of SMZL.

The median follow-up was 36 months (range 1-87). 5y-OS was 81% (95 CI 66-88%) for SMZL and 86% (95 CI 78-91%) for LPL. Lymphoma progression was the cause of death for 48% of events in SMZL and for 30% of LPL; death due to second primary malignancies was 12% for SMZL and 15% for LPL.

5y-OS was 79% for pts who were immediately treated after diagnosis, 74% for those who started treatment after initial observation and was 96 % for pts never treated ($p = 0.002$).

The 5y OS for LPL treated and not treated were 80% and 97%, respectively ($p=0.029$).

5y-PFS was 56% (95 CI 43-68%) for SMZL and 65% (95 CI 52-75%) for LPL.

In univariate analysis factors associated with a shorter PFS were; ECOG >1, hemoglobin < 9.5 g/dl, platelets < $80 \times 10^9/L$, absolute lymphocyte count < $1 \times 10^9/L$, albumin < 3.5 g/dl, lymph node size > 6 cm and planned chemotherapy. In multivariate analysis factors associated with a shorter PFS were; ECOG >1, hemoglobin < 9.5 g/dl, absolute lymphocyte count < $1 \times 10^9/L$.

Conclusions: We provide an analysis of initial characteristics, treatment and outcome of a large series of pts with LPL and SMZL. The NF10 study, through a prospective collection of a large series of consecutive patients with INFL will contribute to a better characterization of this heterogeneous group of lymphomas and to the identification of more accurate prognostic models.

Table 1 – Clinical features of patients with splenic marginal zone lymphoma and lymphoplasmacytic lymphoma

Parameter [n. of pts]	SMZL, n (%)	LPL, n (%)	Total, n (%)	p-value
Age > 60 y [419]	148 (70)	152 (73)	300 (72)	0.449
Male [421]	114 (54)	119 (57)	233 (55)	0.493
Female [421]	99 (46)	89 (43)	188 (45)	
ECOG >1 [418]	13 (6)	16 (8)	29 (7)	0.567
B symptoms [419]	42 (20)	13 (6)	55 (13)	
Stage III-IV [394]	203 (98)	180 (97)	383 (97)	0.762
BM involvement [412]	198 (96)	195 (95)	393 (95)	0.819
Hemoglobin < 9.5 g/dL [417]	41 (19)	43 (21)	84 (20)	0.715
LDH > ULN [395]	94 (46)	192 (27)	143 (36)	<0.001
β_2 -microglobulin > ULN [353]	136 (76)	112 (64)	248 (70)	0.020
Lymph node size > 6 cm [387]	8 (4)	8 (4)	16 (4)	1.000
Albumin \leq 3.5 g/dL [299]	29 (21)	31 (19)	60 (20)	0.667
Platelets < 80 x 10 ⁹ /L [416]	31 (15)	14 (7)	45 (11)	0.011
Serum MC [416]	45 (21)	163 (79)	208 (50)	<0.001
ALC < 1 x 10 ⁹ /L [405]	35 (17)	18 (9)	53 (13)	0.019
HCV positivity [401]	10 (5)	11 (6)	21 (5)	0.823
HBV positivity [389]	46 (23)	28 (15)	74 (19)	0.071