Follicular lymphoma (FL) 3B patients have an increased risk of an aggressive subtype at first event compared to those with FL1-3A treated with frontline R-CHOP

Patrizia Mondello[1], Alexandra Smith[2], Brian K. Link[3], Andrew L. Feldman[4], Thomas M. Habermann[1], Yucai Wang[1], Ivana N. Micallef[1], Patrick B. Johnston[1], Grzegorz S. Nowakowski[1], James R. Cerhan[2], Matthew J. Maurer[2], Stephen M Ansell[1]

[1]Division of Hematology, Mayo Clinic, Rochester, MN, USA; [2]Division of of Quantitative Health Sciences, Mayo Clinic, Rochester, MN, USA; [3]Division of Hematology, Oncology and Bone Marrow Transplantation, University of Iowa, Iowa City, Iowa; [4]Division of Hematopathology, Mayo Clinic, Rochester, MN, USA

Background and Objective

FL3B presents a distinctly adverse prognosis compared to the lower-grade FL. Accumulating evidence suggests that FL3B resembles diffuse large B-cell lymphoma (DLBCL) rather than FL1-3A. Accordingly, R-CHOP is the mainstay therapy for FL3B but fails to cure half of patients (pts), suggesting a biological dichotomy with clinical implication. However, it is unclear whether composite FL3B with DLBCL (FL3Bc) rather than uniform FL3B (FL3Bu) might be responsible for a worse prognosis. Hence, we aimed to compare the outcomes of R-CHOP-treated FL1-3B pts and clarify the phenotypic distinction of FL3B subpopulations.

Patient Characteristics

	Grade I-II (N=122)	Grade IIIA (N=114)	Grade IIIB (N=31)	Grade IIIB + DLBCL (N=36)	p-value
Age					0.678
Median	58.5	60	64	61	
<60	69 (56.6%)	58 (50.9%)	14 (45.2%)	17 (47.2%)	
>60	53 (43.4%)	56 (49.1%)	17 (54.8%)	19 (52.8%)	
Gender					0.139
Female	43 (38.1%)	52 (45.6%)	8 (25.8%)	17 (50.0%)	
Male	70 (61.9%)	62 (54.4%)	23 (74.2%)	17 (50.0%)	
LDH					**0.012**
abnormal	54 (50.0%)	28 (28.3%)	10 (38.5%)	15 (48.4%)	
BM involvement	52 (49.1%)	37 (35.6%)	6 (25.9%)	7 (21.2%)	**0.010**
Hb <12	24 (22.0%)	13 (12.6%)	8 (28.6%)	9 (26.5%)	0.111
Stage					0.425
I-II	29 (23.8%)	33 (29.7%)	10 (33.3%)	13 (36.1%)	
III-IV	93 (76.2%)	78 (70.3%)	20 (66.7%)	23 (63.9%)	
Num Extranodal group					0.917
< 1	112 (91.8%)	105 (92.9%)	28 (90.3%)	34 (94.4%)	
>1	10 (8.2%)	8 (7.1%)	3 (9.7%)	2 (5.6%)	
FLIPI					0.625
Low	35 (28.7%)	47 (41.2%)	12 (40.0%)	13 (36.1%)	
Low Intermediate	33 (27.0%)	31 (27.2%)	6 (20.0%)	10 (27.8%)	
High Intermediate	38 (31.1%)	27 (23.7%)	7 (23.3%)	9 (25.0%)	
High	16 (13.1%)	9 (7.9%)	5 (16.7%)	4 (11.1%)	
EFS24					**0.026**
Achieved	74 (67.3%)	90 (82.6%)	25 (86.2%)	21 (70.0%)	
Failed	36 (32.7%)	19 (17.4%)	4 (13.8%)	9 (30.0%)	
EFS					0.157
Median (months)	89.6	165.7	160.5	NA	
OS					0.771
Median (months)	NA	NA	160.5	194.3	

FL3A-B had a superior EFS compared to FL1-2, but similar OS

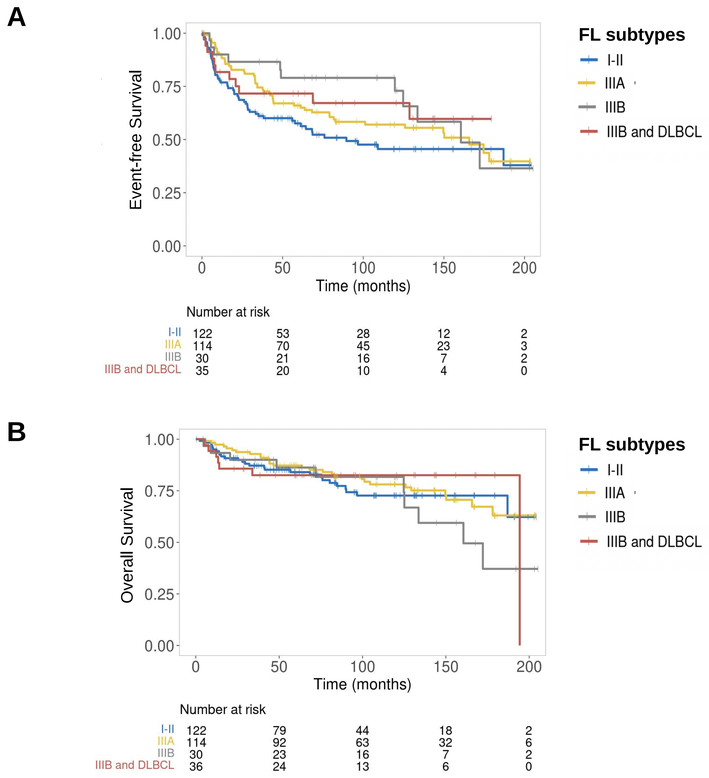


Figure 1. Kaplan-Meier curves representing event-free survival (**A**) and overall survival (**B**) in patients with FL I-II (blue), IIIA (yellow), IIIB (gray) and IIIB mixed with DLBCL (red).

FL1-3A had indolent disease at first event while aggressive disease was the most common subtype in patients with FL3B

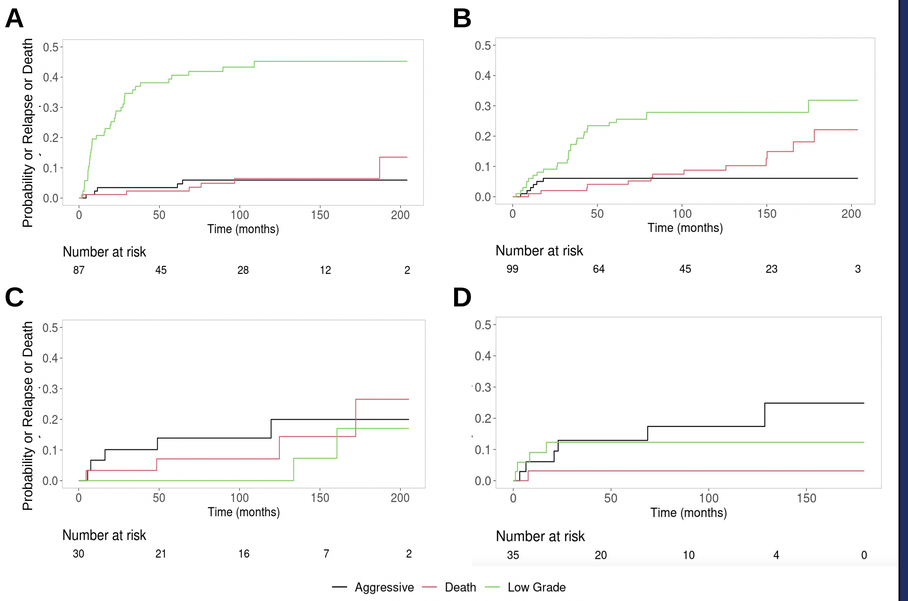


Figure 2. Cumulative incidence of relapse and transformation by FL grade: I-II (**A**), IIIA (**B**), IIIB (**C**), IIIB mixed with DLBCL (**D**).

Conclusions

FL3B pts treated with R-CHOP have improved EFS but are more likely to present an aggressive subtype at progression compared to pts with FL1-2 and FL3A treated with R-CHOP. Larger studies are warranted.

Acknowledgments

This work was supported by ASCO-YIA 3392116949 and LRF #818463 grants.