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## Follicular Lymphoma grade 3B. A separate entity?

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# Appendix

Supplementary clinical data, treatment results and additional immunohistochemistry data of FL3B cases.

The patients included in this study are all adults and were diagnosed as FL3B at time of the obtained biopsy. Patients were classified using clinical data and treatment data for both primary and secondary FL3B. The clinical data from 28 patients with the primary and secondary diagnosis FL3B are summarised in Table A1. From 2 patients was no clinical data available and in 2 cases it concerns a sequential biopsy.

The treatment data includes details of treatment in 18 patients with the primary diagnosis FL3B (Table A2a). Ten patients were diagnosed with NHL and treated before the biopsy was obtained on which the diagnosis FL3B was based and of which the cytogenetic results were obtained (Table A2b).

In addition, we investigated our panel of 30 cases with special emphasis on BCL6, CD10 and MUM1/IRF4 expression and the 3 different subgroups with I: a 3q27 abberation and no t(14;18), II: a subgroup with none of these abberations and III: a t(14;18) without a 3q27 abberation. (Table A3)

Table A1: Clinical Data from 28 patients with the diagnosis FL3B.

		N=28	%
Age	Median:	57.6	
	Range:	29-85	
Sex	Male:	17	61%
	Female:	11	39%
B-symptoms	Yes:	4	13%
Clinical stage	I-IA:	5	18%
	II:	8	28%
	III-IV:	15	54%
WHO performance score	1-2:	7	25%
	3-4:	0	0%
BM involvement	Yes:	7	25%
E-localisation <sup>1</sup>	Yes:	9	32%
Bulky mass <sup>2</sup>	Yes:	7	25%
LDH >> <sup>3</sup>	Yes:	10	36%
IP-index	0-1:	16	57%
	2-3:	12	43%
	4-5:	0	0%
Survival	First diagnosis - > last follow up:	Median Range	5.6 years 7months-25 years

<sup>1</sup> other than BM<sup>2</sup> > 10 cm<sup>3</sup> normal = < 400

Supplementary data of FL3B cases

Table A2a: Cytogenetic grouping and treatment results of 18 patients with the primary diagnosis FL3B.

Subgroup	Case	primary diagnosis	Primary therapy	Response	No of relapses	Subtype	OS
I <sup>a</sup>	2	FL3B	6xCHOP + XRT	PR	? → ?	GC	??
I	25	FL3B	12xCHOP-like	CR	1 → DOC	GC	14 months
I	29	FL3B	XRT 3500Gy	CR	0 → A	GC?	> 4.5 years
II	9	FL3B	Excision lymphnode	CR	1 → A (NED)	GC	> 3years
II	12	Rec.na prim.FL3B	6xCHOP, 5xCEP	CR	2 → A (NED)	GC	> 9 years
II	8	FL3B	6xCHOP	CR	0 → A (NED)	ABC	> 9 years
II	15	FL3B	4xCHOP	PD	1 → DOD	ABC	1.5 years
II	16	FL3B	1xCHOP,4xCOP,1xCHOP, 1xCHOP	PR	1 → AWD	GC	> 8 years
II	18	FL3B	7xCHOP,1xmini-BEAM	PD	0 → DOD	GC	7 months
II	19	FL3B	4xCHOP,1xDHAP,1xmini-BEAM	NR/PD	0 → DOD	GC	9 months
II	32	FL3B	XRT 40Gy (2 months)	CR	0 → A (NED)	??	> 4 years
III	10	FL3B	5xCP	PR	1 → DOC	GC	2 years
III	11	FL3B	3xCHOP,1xXRT 30Gy	CR	0 → A (NED)	GC	> 7 years
III	13	FL3B	6xCHOP	CR	3 → A (NED)	GC	> 6 years
III	20	FL3B	8xCHOP	CR	0 → A (NED)	GC	> 7 years
III	21	FL3B	6xCHOP/MTX,after 17 months x8	CR	3 → DOD	??	4.5 years
III	26	FL3B	12xVACOP-B ,XRT2500Gy,+other	PR/CR	1 → DOD	GC	4 years
III	27	FL3B	12xVACOP-B + XRT250Gy	CR	0 → A (NED)	GC	> 8 years

I: t(14;18) negative and 3q27 positive, II: t(14;18) and 3q27 negative, III: t(14;18) positive and 3q27 negative, <sup>a</sup> : incomplete data; A: Alive, D: Dead, AWD: alive with disease, DOD: dead of disease, DOC: dead of other cause, NED: no evidence of disease. GC: Germinal Center like lymphoma, ABC: Activated B-Cell lymphoma, CR: complete response, PR: partial response, PD: partial disease, NR: no response, OS: overall survival

Appendix

Table A2b: Cytogenetic grouping of 10 patients with an antecedent NHL diagnosis, treatment results and time to diagnosis FL3B.

subgroup	Case	Antecedent diagnosis	Primary Therapy	Response	Time to FL3B	Therapy after transformation	Response	No of relapses	Subtype	OS
I	17	FL1,2	MVPP,chl.amb,CHOP,DHAP,XRT	CR/PR	10; 6;5;2 years 17 months	6xLPP	PR	5 → DOD	GC	25 years
I	4	DLBCL	XRT + 6xCOP	CR	9 years	3xCHOP/MTX + 5xCHOP/MTX	PR	2 → DOD	ABC	12 years
I	6	FL3B?	Leukeran/plasmapheresis	PR	4 years	3xCHOP	PR	2 → DOD	ABC	5 years
I	30	FL1,2	Prednisolone (10wks)	PR	5 years	No therapy	CR	1 → A (NED)	GC	> 14 years
II	1	IBL./DLBCL	7xCHOP	CR	10 months	6xMOPP/APOV	CR	2 → AWD	ABC	2 years
II	5	DLBCL	XRT+6xCOP,6xCHOP	CR	12,5 years	4xpromaceMOPP,ABMT, leukeran	PR	2 → DOD	ABC	13 years
III	7	FL1,2	8x fludarabine	PR	20 months	1xCHOP,MACOP-B	PR/PD	2 → DOD	??	2 years
III	14	FL1,2	9xLeukeran,10xCOP,7xMOPP, 2xCHOP	PD/NR	8 years	DHAP/VIM/DHAP	??	2 → DOD	GC	9 years
III	28	FL1,2	14x(Cyclo+BCNU+Vinc.+predn.	CR	17 years	6xCHOP-like + XRT3500Gy	CR	2 → DOC	??	22 years
III	31	FL1,2	No therapy	??	2 years	6xCNOP	PR	2 → DOD	GC	5,5 years

I: t(14;18) negative and 3q27 positive, II: t(14;18) and 3q27 negative, III: t(14;18) positive and 3q27 negative

A: Alive, D: Dead, AWD: alive with disease, DOD: dead of disease, DOC: dead of other cause, NED: no evidence of disease.

GC: Germinal Center like B-cell lymphoma, ABC: Activated B-Cell lymphoma, CR: complete response, PR: partial response, PD: partial disease, NR: no response, OS: overall survival

Table A3: Expression data of FL3B cases for BCL6, CD10 and MUM1

Case nr	Bcl6	CD10	MUM1 combination paraffin and frozen tissue	subtype	Primary diagnosis
	<b>I: → 3q27 break no t(14;18)</b>				
2	+	+	-	GC	FL3B
6	+	-	+	ABC	FL3B →FL3B?
17	+	-	-	GC	FL1,2 →FL3B
22**	+	ND	ND		FL3B
25	+/-	+	-	GC	FL3B
29	+	-	- ?	GC?	FL3B
30	+	-	-	CG	FL1,2 →FL3B
4	+	-	+	ABC	DLBCL →FL3B
	<b>II: → no 3q27 break no t(14;18)</b>				
1	+	-	+	ABC	IBL →FL3B
5	+	-	+	ABC	DLBCL →FL3B
8	+	-	+	ABC	FL3B
15**	+	-	+	ABC	FL3B
16	+	-	-	GC	FL3B
18	+	+	-	GC	FL3B
19	+	+	-	GC	FL3B
24	++	-	- ?	GC?	no data
32	+	-			FL3B
9	+	-	-	GC	FL3B
12	+	+	+	GC	FL3B
	<b>III: → t(14;18) no 3q27 break</b>				
7	+	ND	ND		FL1,2 →FL3B
10	+	+	-	GC	FL3B
11	+	-	ND	GC	FL3B
13	+	+	-	GC	FL3B
14	+	+	-	GC	FL1,2 →FL3B
20	+	-	-	GC	FL3B
21	ND	ND	ND		FL3B
26	ND	+	ND	GC	FL3B
27	ND	+	-	GC	FL3B
28	ND	-	-		FL1,2 →FL3B
31	+	+	ND	GC	FL1,2 →FL3B

GC: Germinal Center like B-cell lymphoma, ABC: Activated B-Cell lymphoma

ND: not done, ^ 3q27 pos. with Southern Blot hybridization; \*\* cases with a sequential biopsy.