

# MYC or BCL2 copy number aberration is a strong predictor of outcome in patients with diffuse large B-cell lymphoma

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## OBJECTIVES

Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma (NHL). Patients with DLBCL harboring *MYC* aberrations concurrent with *BCL2* or/and *BCL6* aberrations constitute a specific group with extremely poor outcome.

## METHODS

We retrospectively investigated the incidence and prognosis of *MYC*, *BCL2*, and *BCL6* aberrations with DLBCL patients in Chinese population. We applied fluorescence in situ hybridization and immunohistochemical analysis in 246 DLBCL patients.

## Graphs and tables

Table 1. Clinical features with *MYC*, *BCL2* and double CNA

Characteristics	MYC CNA <sup>+</sup>	MYC CNA <sup>-</sup>	P value	BCL2 CNA <sup>+</sup>	BCL2 CNA <sup>-</sup>	P value	MC/BC <sup>+</sup>	MC BC <sup>-</sup>	P value
No. of cases (%)	18 (22.2)	73 (77.8)	0.047	30 (46.2)	31 (53.8)	0.005	9 (77.3)	166 (22.7)	0.010
Age (years)	≤60 7 (38.0) ≥60 11 (61.1)	139 (62.0) 81 (37.3)		110 (66.3) 59 (33.7)	102 (58.3) 73 (41.7)		55 (31.1) 166		
Sex	Male 18 (77.8) Female 4 (22.2)	222 (90.4) 19 (9.6)		65 (35.0) 19 (30.6)	9 (44.4) 7 (33.3)		9 (44.4) 166	94 (56.6) 72 (43.4)	0.734
Stage	II 18 I-II 6 (33.3) III-IV 12 (66.7) I-II 6 (33.3)	213 (91.6) 103 (48.6)		63 (32.4) 33 (52.4)	168 (76.9) 76 (95.2)		9 (44.4) 55 (55.0)	84 (51.3) 75 (47.7)	0.738
LDH	Elevated 18 Normal 9 (50.0) 9 (50.0)	213 (91.6) 63 (33.3)		168 (76.9) 76 (95.2)	9 (44.4) 75 (47.7)		9 (44.4) 166	62 (39.0) 97 (61.0)	0.739
ECOG PS	≥2 18 <2 14 (77.8)	222 (90.4) 65 (35.0) 153 (73.8)		17 (36.0) 23 (33.1)	0.016 7 (77.3)		2 (22.2) 145 (87.3)	21 (12.7) 145 (87.3)	0.336
Extramedullary involvement	≥2 18 <2 14 (77.8)	213 (91.6) 63 (33.3) 168 (76.9)		170 (35.0) 168 (76.9)	9 (44.4) 75 (47.7)		9 (44.4) 166	62 (39.0) 97 (61.0)	1.000
IPF	18 3-5 0-2	213 (91.6) 63 (33.3) 168 (76.9)		101 (49.2) 135 (79.4)	0.016 7 (77.3)		2 (22.2) 145 (87.3)	31 (19.5) 138 (80.5)	
B symptoms	Positive 18 Negative 13 (72.2)	222 (91.6) 63 (33.3) 168 (76.9)		57 (31.0) 38 (38.5)	0.016 6 (66.7)		121 (61.1) 111 (66.9)	55 (31.1) 98 (53.0)	0.330
COO (Hem)	GCB Non-GCB 13 (72.2)	93 (41.9) 129 (58.0)		53 (24.9) 48 (73.8)	0.028 9 (33.7)		43 (21.0) 77 (77.3)	48 (44.0) 88 (53.0)	1.000

Abbreviations: CNA: copy number aberration; MC/BC<sup>+</sup>: *MYC* CNA concurrent with *BCL2* CNA; MC/BC<sup>-</sup>: negative for both *MYC* CNA and *BCL2* CNA; COO: cell of origin; ECOG PS: performance status of Eastern Cooperative Oncology Group; GCB: germinal-center B-cell type; IPF: International Prognostic Index; LDH: lactate dehydrogenase.

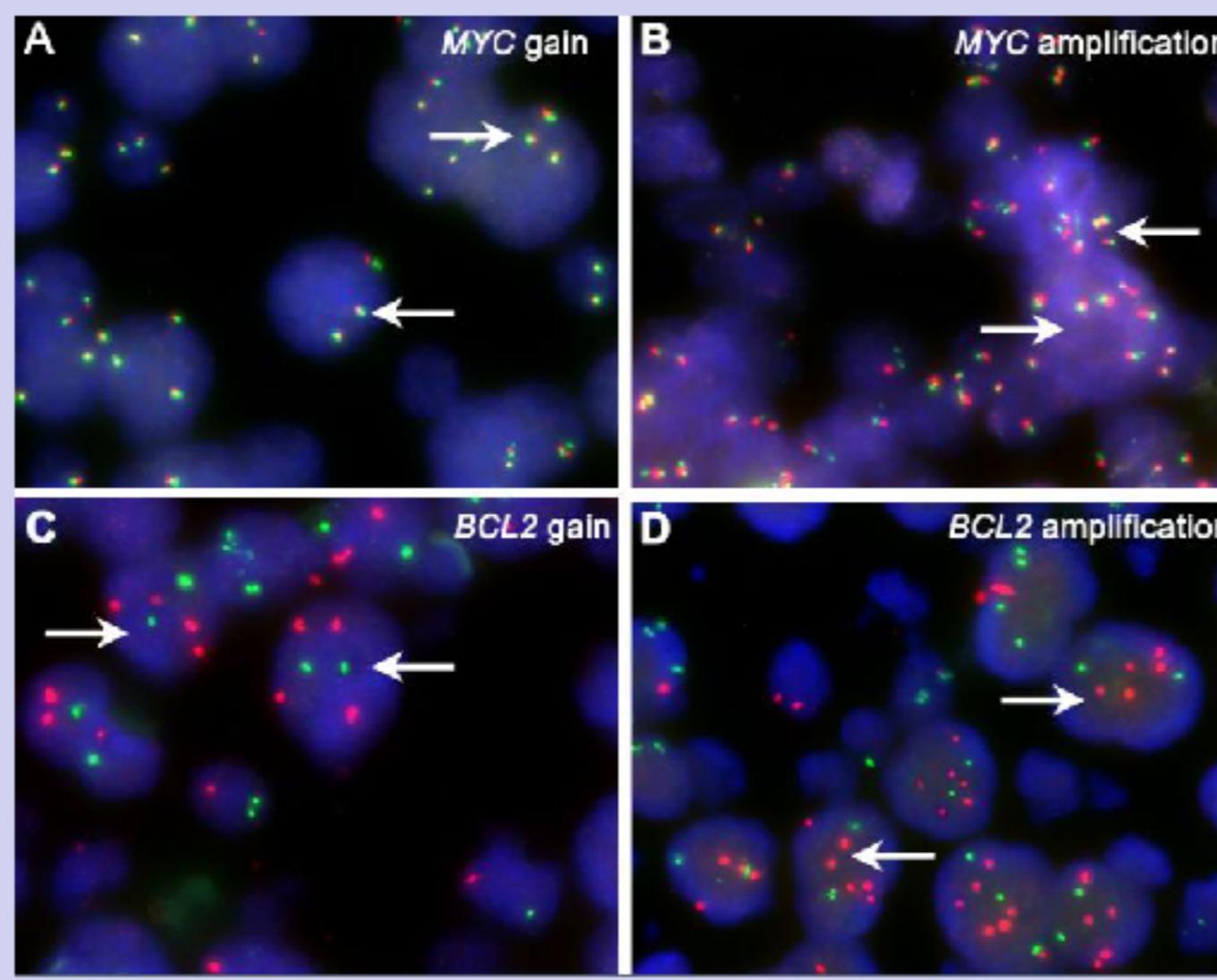


Figure 1. CNA of *MYC* and *BCL2*. White arrows show *MYC* and *BCL2* gain (A, C) and amplification (B, D).

Abbreviation: CNA: copy number aberration.

Table 2. Univariate and multivariate analysis with OS

Variables	HR	95% CI	P value	HR	95% CI	P value
ENI	2.064	1.387-3.071	0.0004	1.193	1.263-3.807	0.0053
LDH	1.945	1.363-2.777	0.0002	1.199	1.051-2.879	0.0286
Stage	1.556	1.098-2.013	0.0001	0.730	0.530-1.030	0.2320
IPF	2.010	1.374-3.399	0.0003	0.632	0.339-1.177	0.1482
ECOG PS <sup>+</sup>	1.842	1.195-2.341	0.0057	1.415	0.869-3.304	0.1610
Symptoms	1.781	1.235-2.324	0.0113	1.216	0.833-1.616	0.0818
MYC	1.411	1.044-1.775	0.0020	1.027	0.553-1.514	0.0010
<i>BCL2</i>	1.789	1.373-2.387	0.0020	0.666-1.383	0.9498	
Non-GCB	0.692	0.481-0.907	0.0479	0.943	0.651-1.020	0.0067
ECOG PS <sup>-</sup>	2.121	1.464-2.783	0.0005	0.790	0.530-1.050	0.0009
DHL	1.610	1.180-2.198	0.0027	1.466	0.992-1.151	0.0594
<i>MYC</i> CNA <sup>+</sup>	3.521	2.058-6.023	<0.0001	1.610	0.873-3.969	0.1271
<i>BCL2</i> CNA <sup>+</sup>	2.827	1.973-4.053	<0.0001	2.066	1.363-3.165	0.0008
MC/BC <sup>+</sup>	3.613	1.981-3.446	<0.0001	2.067	1.341-3.186	0.0010

Abbreviations: OS: overall survival; HR: hazard ratio; ENI: extranodal involvement; LDH: serum lactate dehydrogenase; IPF: International Prognostic Index; ECOG PS: performance status of Eastern Cooperative Oncology Group; +: positive; GCB: germinal-center B-cell; R: rearrangement; DHL: double hit lymphoma; CNA: copy number aberration; MC/BC<sup>+</sup>: double CNA of *MYC* and *BCL2*.

Table 3. Univariate and multivariate analysis with PFS

Variables	HR	95% CI	P value	HR	95% CI	P value
ENI	2.481	1.496-3.436	0.0004	1.983	1.366-3.399	0.0048
LDH	2.056	1.363-2.750	0.0001	0.793	0.530-1.050	0.0020
Stage	1.558	0.950-2.553	0.0077	0.674	0.251-1.399	0.3090
IPF	2.001	1.714-4.576	<0.0001	0.809	0.464-1.908	0.4379
ECOG PS <sup>+</sup>	1.821	1.235-2.412	0.0007	1.665	0.833-1.885	0.1180
ECOG PS <sup>-</sup>	2.121	1.464-2.783	<0.0001	0.790	0.530-1.050	0.0009
MYC	5.515	3.138-9.108	<0.0001	1.665	1.063-2.277	0.0003
<i>BCL2</i>	2.086	1.343-3.500	0.0054	0.934	0.454-2.443	0.4458
Non-GCB	0.665	0.415-1.066	0.0005	0.792	0.454-1.443	0.4458
ECOG PS <sup>-</sup>	4.715	2.873-7.739	<0.0001	7.527	2.338-24.031	0.0007
DHL	1.724	1.116-2.563	0.0070	1.595	1.005-2.534	0.0478
<i>MYC</i> CNA <sup>+</sup>	3.514	2.034-5.000	<0.0001	1.262	0.720-2.000	0.0008
<i>BCL2</i> CNA <sup>+</sup>	3.988	2.373-6.111	<0.0001	2.619	1.417-3.840	0.0003
MC/BC <sup>+</sup>	3.594	2.460-4.991	<0.0001	2.414	1.510-3.860	0.0011

Abbreviations: PFS: progression-free survival; HR: hazard ratio; ENI: extranodal involvement; LDH: serum lactate dehydrogenase; IPF: International Prognostic Index; ECOG PS: performance status of Eastern Cooperative Oncology Group; +: positive; GCB: germinal-center B-cell; R: rearrangement; DHL: double hit lymphoma; CNA: copy number aberration; MC/BC<sup>+</sup>: double CNA of *MYC* and *BCL2*.

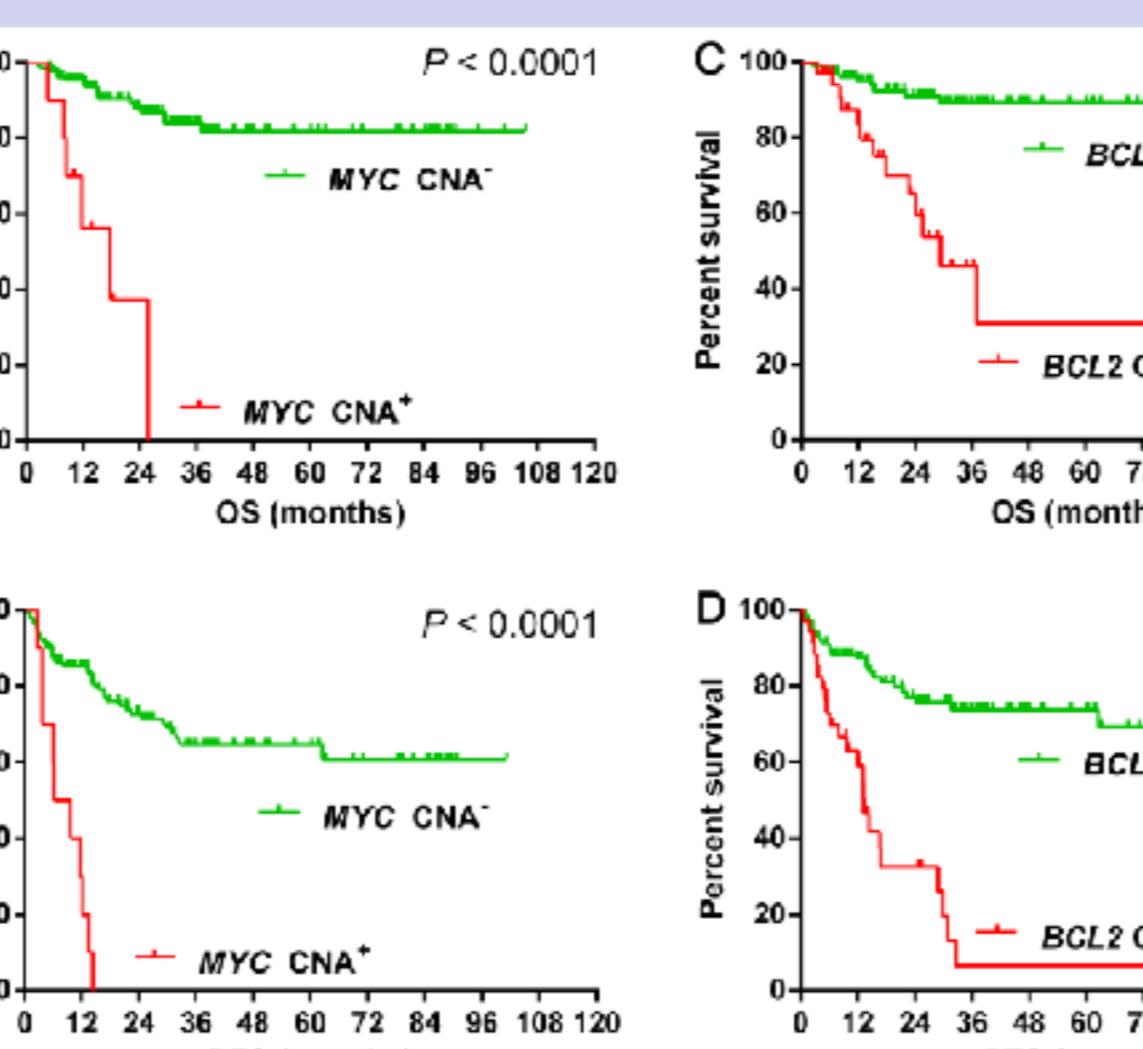


Figure 3. Overall survival and progression-free survival of cases grouped according to *MYC* CNA (A-B), *BCL2* CNA (C-D) and double CNA (E-F).

Abbreviations: CNA: copy number aberration; OS: Overall survival; PFS: progression-free survival; MC: *MYC* CNA; BC: *BCL2* CNA; MC+BC<sup>+</sup>: *MYC* CNA concurrent with *BCL2* CNA; MC+BC<sup>-</sup>: negative for both *MYC* CNA and *BCL2* CNA.

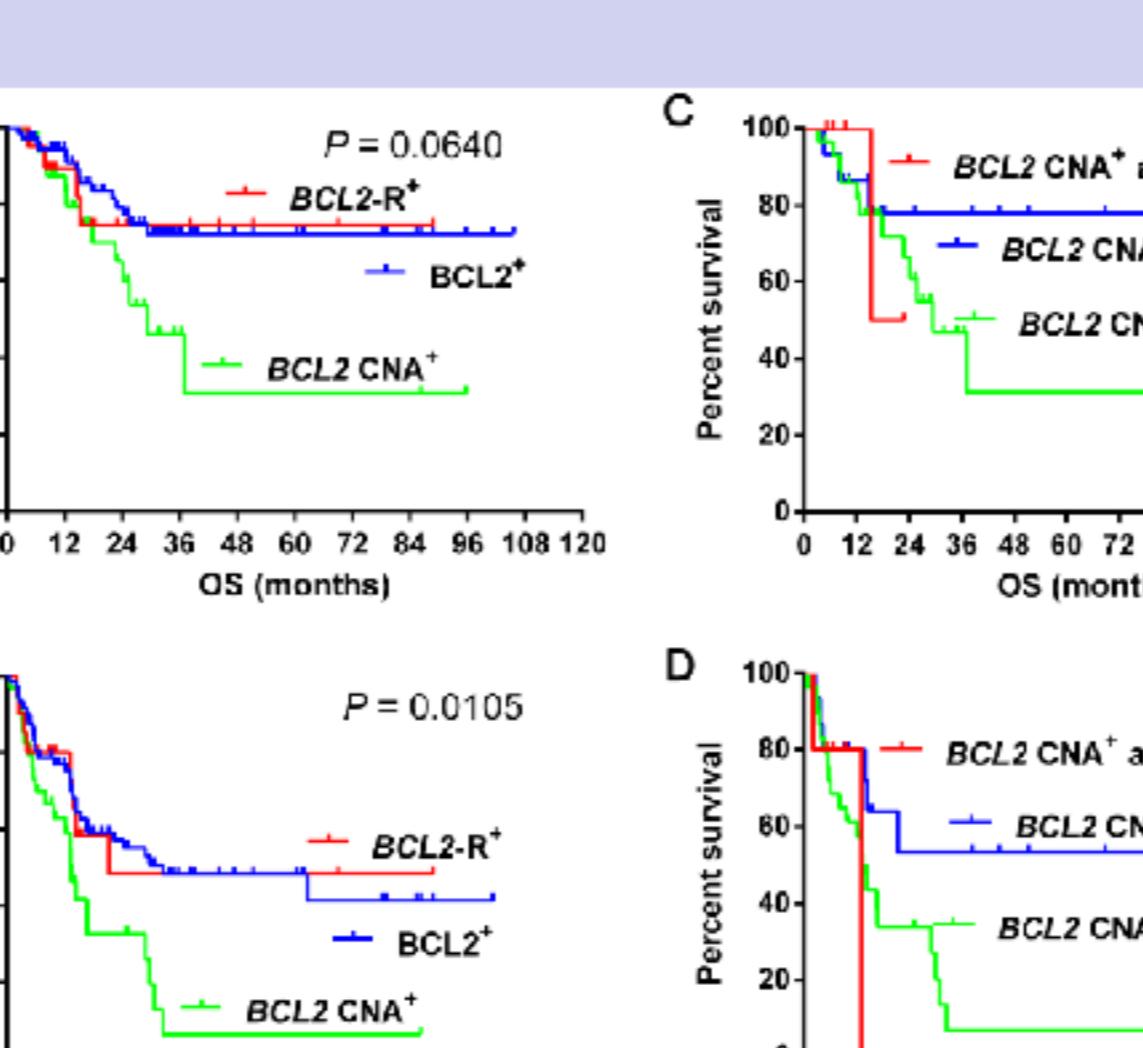


Figure 4. Overall survival and progression-free survival of cases grouped according to gain and amplification with *MYC* (A-B) and *BCL2* (C-D) in the R-CHOP-like group.

Abbreviations: OS: overall survival; PFS: progression-free survival.

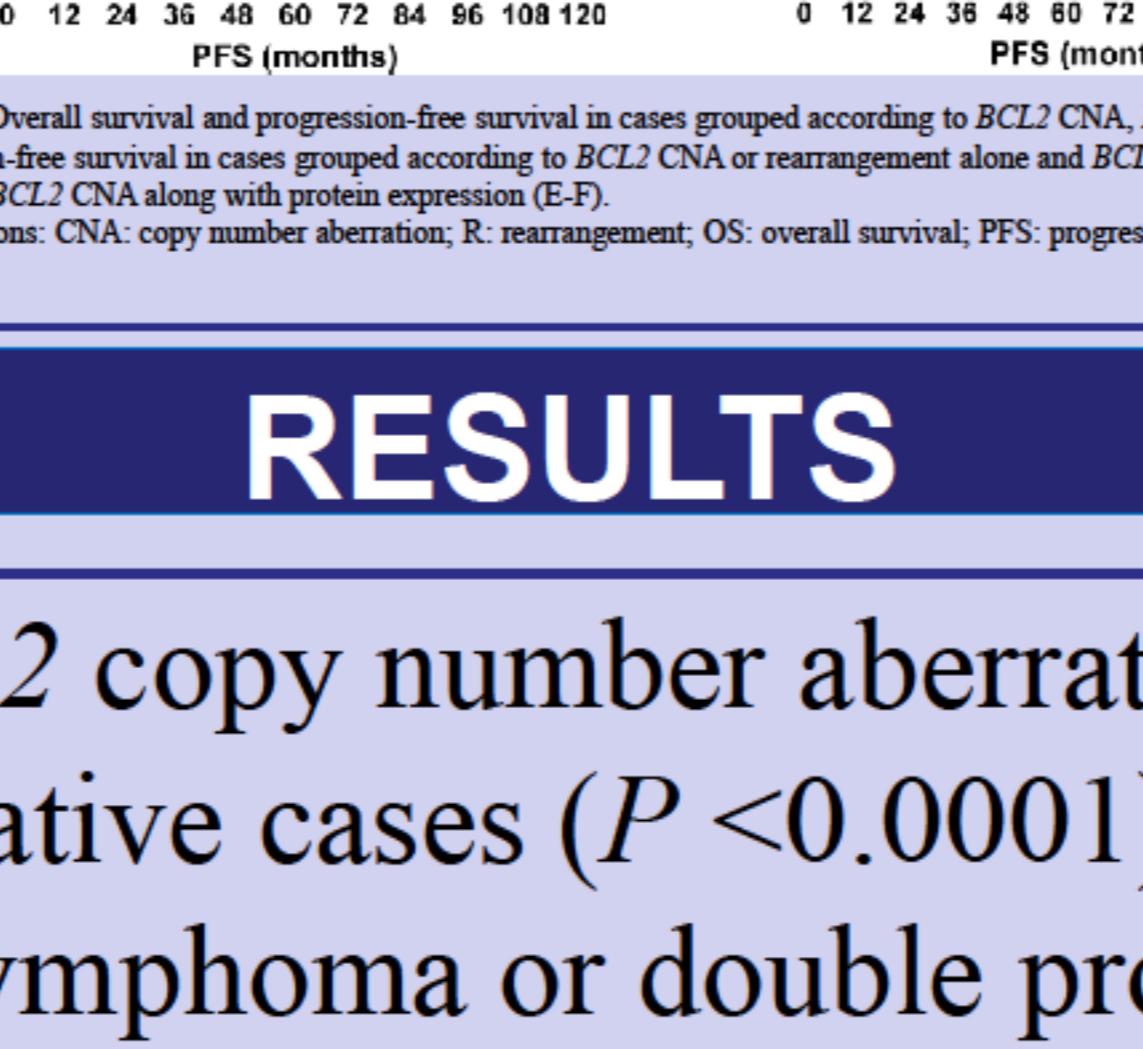


Figure 5. Overall survival and progression-free survival in cases grouped according to *MYC* CNA, *MYC* gene rearrangement and *MYC* expression (A-B). Overall survival and progression-free survival in cases grouped according to *MYC* CNA or rearrangement alone and *MYC* CNA along with expression (C-D) and *MYC* CNA or protein expression alone and *MYC* CNA along with protein expression (E-F).

Abbreviations: CNA: copy