

**CXCL13 levels are elevated in patients with Waldenström macroglobulinemia, and are predictive of major response to ibrutinib**

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### **Supplementary methods section for cytokine testing**

The following 24 cytokines were analyzed including soluble CD27 as a known biomarker in WM:  
TNF- $\alpha$ , IL6, IFNG, CXCL10, IL10, CCL2, IL8, IL1 $\beta$ , IL7, IL1RA, CCL3, CCL4, IL4,  
IL2, GMCSF, IL2RA, CXCL9, IL12, IL15, IL13, CCL11, CXCL12, CXCL13, sCD27.

All samples were kept at -80°C until analysis, and evaluated in duplicate.

We used magnetic multiplex enzyme-linked immunosorbent assays (R&D Systems Inc., Minneapolis, MN).

Luminex XMAP Technology MAGPIX System version 4.2 was used for reading plates.

xPONENT software was used to analyze data.

Supplementary data on four patients that went off study within the first year of the trial.

Case Number	CXCR4 status	TIME ON IBR (Months)	On/off IBR at the time of sampling	CXCL13 level (pg/ml)	Clinical status
1	CXWT	baseline	off	1150	baseline
1	CXWT	1	on	708	Partial response
1	CXWT	9	on	4590	Progressive disease; off study
2	CXWT	baseline	off	129	baseline
2	CXWT	1	on	134	Stable Disease
2	CXWT	4	on	176	Stable disease; Off study due to progressive complications of systemic AL amyloidosis
3	CXMUT (NS)	baseline	off	389344	baseline
3	CXMUT (NS)	7	on	5026	Partial response
3	CXMUT (NS)	9	off	389344	Off study due to toxicities, then progressive disease shortly after that (last sample was taken after stopping the drug)
4	CXMUT (NS)	baseline	off	198	baseline
4	CXMUT (NS)	1	on	59	Minor response
4	CXMUT (NS)	4	on	62	Minor response Off study due to toxicities

CXWT= CXCR4 wildtype  
 CXMUT= CXCR4 mutated  
 NS= nonsense mutation  
 All 4 cases carried the MYD88L265P mutation  
 IBR- ibrutinib