Supplemental material

Supplemental tables

Supplemental Table 1. Primer and probe sequences

	Name	Sequence
FCGR2A R131H rs1801274	Forward PCR primer	CATATATTGCCTATAAGAGAATGCT
	Reverse PCR primer	CCTGACTACCTATTACCTGGGA
FCGR2B I232T rs1050501	Floto et al. 2005[1] forward primer	AAGGGGAGCCCTTCCCTCTGTT
	Floto et al. 2005[1] reverse primer	CATCACCCACCATGTCTCAC
	Custom TaqMan forward primer	GATGGGGATCATTGTGGCTGT
	Custom TaqMan reverse primer	AGGCCACTACAGCAGCAACAAT
	Custom TaqMan 232I probe	ACTGGGATTGCTGTAGC
	Custom TaqMan 232T probe	ACTGGGACTGCTGTAGC
	Alternative *FCGR2B*-specific sequencing forward primer	CTGCCTGCTCACAAATGTA
	Alternative *FCGR2B*-specific sequencing reverse primer	CACTGCTCTCCCCAAGAC
FCGR3A F158V rs396991	Forward PCR primer	CCTCTAATAGGGCAATTCATCATT
	Reverse PCR and sequencing primer	AGATGTGGCTTCTGCTCCTG
	Forward sequencing primer	TGCTCTGCATAAGGTCACATATT

FCGR, Fc gamma receptor; PCR, polymerase chain reaction.

Supplemental Table 2. Fc gamma receptor (FcγR) genotype prevalence by ethnicity in (A) patients with follicular lymphoma (FL) in the GALLIUM trial and (B) patients with diffuse large B-cell lymphoma (DLBCL) in the GOYA trial.

A

Covariate	Subgroup	Asian, No. (%)	White, No. (%)	Other, No. (%)	*P*-value
FCGR2A	R131R	23 (12.5)	200 (21.6)	8 (22.9)	<.0001
	R131H	73 (39.7)	459 (49.6)	15 (42.9)	
	H131H	88 (47.8)	266 (28.8)	12 (34.3)	
FCGR2B	I232I	88 (68.2)	712 (79.2)	23 (67.6)	.008
	I232T	35 (27.1)	174 (19.4)	11 (32.4)	
	T232T	6 (4.7)	13 (1.4)	0 (0.0)	
FCGR3A	F158F	92 (50.0)	373 (40.3)	14 (40.0)	0.2
	F158V	72 (39.1)	432 (46.7)	17 (48.6)	
	V158V	20 (10.9)	120 (13.0)	4 (11.4)	

B

Covariate	Subgroup	Asian, No. (%)	White, No. (%)	Other, No. (%)	*P*-value
FCGR2A	R131R	102 (35.1)	175 (60.1)	14 (4.8)	.0002
	R131H	181 (30.4)	393 (66.1)	21 (3.5)	
	H131H	177 (41.2)	249 (57.9)	4 (0.9)	
FCGR2B	I232I	145 (58.0)	597 (75.4)	31 (81.6)	<.0001
	I232T	93 (37.2)	182 (23.0)	7 (18.4)	
	T232T	12 (4.8)	13 (1.6)	0 (0)	
FCGR3A	F158F	245 (53.7)	324 (39.6)	22 (56.4)	<.0001

	F158V	176 (38.6)	382 (46.7)	16 (41.0)
	V158V	35 (7.7)	112 (13.7)	1 (2.6)

FCGR, Fc gamma receptor.

Supplemental Table 3. Fc gamma receptor (FcγR) genotype prevalence by cell of origin (COO; activated B-cell [ABC] and germinal center B-cell [GCB]) in patients with diffuse large B-cell lymphoma (DLBCL) in the GOYA trial.

		COO (ABC, GCB)		
Covariate	Subgroup	GCB, No. (%)	ABC, No. (%)	*P*-value*
FCGR2A	R131R	99 (19.08)	39 (16.53)	.6590
	R131H	232 (44.7)	112 (47.46)	
	H131H	188 (36.22)	85 (36.02)	
FCGR2B	I232I	362 (72.69)	166 (71.86)	.9429
	I232T	124 (24.9)	59 (25.54)	
	T232T	12 (2.41)	6 (2.6)	
FCGR3A	F158F	221 (42.5)	115 (48.73)	.2732
	F158V	241 (46.35)	99 (41.95)	
	V158V	58 (11.15)	22 (9.32)	

*The *P*-value was calculated using the Fisher's exact test.

FCGR, Fc gamma receptor.

Supplemental Table 4. Univariate survival analysis of the impact of single nucleotide polymorphism genotype on progression-free survival in patients with diffuse large B-cell lymphoma (DLBCL) in the GOYA trial for each treatment arm (obinutuzumab [G] and rituximab [R]) stratified by cell of origin (COO; activated B-cell [ABC] and germinal center B-cell [GCB]).

COO	Biomarker	Effect	Treatment	Total (No.)	Subgroup (No.)	HR	95% CI lower	95% CI upper	*P*-value	Adj. *P*-value
GCB	*FCGR2A*	R131H vs R131R	R	252	97 vs 56	0.63	0.35	1.13	.1190	.6270
GCB	*FCGR2A*	H131H vs R131R	R	252	99 vs 56	0.63	0.35	1.13	.1183	.6270
GCB	*FCGR2A*	R131H vs R131R	G	267	135 vs 43	1.08	0.53	2.20	.8255	.9427
GCB	*FCGR2A*	H131H vs R131R	G	267	89 vs 43	1.16	0.55	2.44	.6949	.8778
ABC	*FCGR2A*	R131H vs R131R	R	115	52 vs 15	1.13	0.42	3.02	.8136	.9427
ABC	*FCGR2A*	H131H vs R131R	R	115	48 vs 15	1.85	0.71	4.86	.2111	.6270
ABC	*FCGR2A*	R131H vs R131R	G	121	60 vs 24	1.59	0.72	3.52	.2521	.6270
ABC	*FCGR2A*	H131H vs R131R	G	121	37 vs 24	1.54	0.66	3.61	.3180	.6270
GCB	*FCGR2B*	I232T vs I232I	R	244	63 vs 175	0.68	0.38	1.22	.1967	.6270
GCB	*FCGR2B*	T232T vs I232I	R	244	6 vs 175	1.85	0.58	5.92	.3011	.6270
GCB	*FCGR2B*	I232T vs I232I	G	254	61 vs 187	1.21	0.69	2.12	.4960	.7440
GCB	*FCGR2B*	T232T vs I232I	G	254	6 vs 187	0.00	0.00	Inf	.9949	.9949
ABC	*FCGR2B*	I232T vs I232I	R	114	26 vs 86	1.16	0.60	2.25	.6531	.8708
ABC	*FCGR2B*	T232T vs I232I	R	114	2 vs 86	6.91	1.61	29.64	.0093	.2240
ABC	*FCGR2B*	I232T vs I232I	G	117	33 vs 80	1.45	0.79	2.67	.2275	.6270
ABC	*FCGR2B*	T232T vs I232I	G	117	4 vs 80	2.12	0.50	8.90	.3055	.6270
GCB	*FCGR3A*	F158V vs F158F	R	252	127 vs 98	1.28	0.78	2.12	.3319	.6270
GCB	*FCGR3A*	V158V vs F158F	R	252	27 vs 98	1.06	0.46	2.45	.8963	.9427
GCB	*FCGR3A*	F158V vs F158F	G	268	114 vs 123	1.27	0.76	2.11	.3658	.6270
GCB	*FCGR3A*	V158V vs F158F	G	268	31 vs 123	0.73	0.30	1.79	.4950	.7440
ABC	*FCGR3A*	F158V vs F158F	R	115	47 vs 55	0.56	0.29	1.09	.0882	.6270
ABC	*FCGR3A*	V158V vs F158F	R	115	13 vs 55	1.45	0.66	3.20	.3555	.6270
ABC	*FCGR3A*	F158V vs F158F	G	121	52 vs 60	1.04	0.58	1.84	.9034	.9427

ABC	*FCGR3A*	V158V vs F158F	G	121	9 vs 60	0.76	0.23	2.52	.6508	.8708

Adj, adjusted; CI, confidence interval; *FCGR*, Fc gamma receptor; HR, hazard ratio.

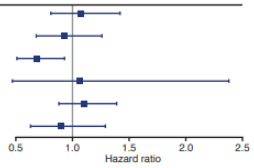
Supplemental figures

Supplemental Figure 1. Forest plot representing the (A) univariate and (B and C) multivariate survival analyses of the impact of single nucleotide polymorphism genotype on progression-free survival (PFS) in patients with follicular lymphoma (FL) in the GALLIUM trial.

Cox regression (univariate analysis): pooled treatment arms (obinutuzumab and rituximab)

A

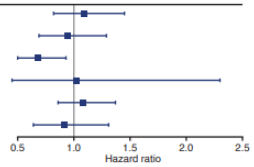
Biomarker	Effect	Total (N)	Subgroup (n)	HR	95% CI	*P*–value	Adj. *P*-value
FCGR2A	R131H vs R131R	1144	547 vs 231	1.07	(0.81-1.42)	.6265	.7661
FCGR2A	H131H vs R131R	1144	366 vs 231	0.93	(0.68-1.26)	.6384	.7661
FCGR2B	I232T vs I232I	1062	220 vs 823	0.69	(0.51-0.93)	.0136	.0819
FCGR2B	T232T vs I232I	1062	19 vs 823	1.06	(0.47-2.38)	.8906	.8906
FCGR3A	F158V vs F158F	1144	521 vs 479	1.10	(0.88-1.39)	.4050	.7661
FCGR3A	V158V vs F158F	1144	144 vs 479	0.90	(0.63-1.29)	.5823	.7661



Cox regression (multivariate analysis): pooled treatment arms (obinutuzumab and rituximab)

B

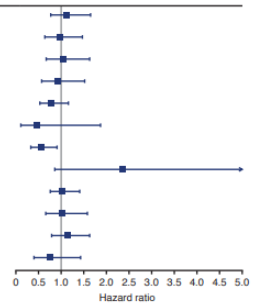
Biomarker	Effect	Total (N)	Subgroup (n)	HR	95% CI	*P*-value	Adj. *P*-value
FCGR2A	R131H vs R131R	1110	529 vs 224	1.09	(0.82-1.45)	.5613	.8438
FCGR2A	H131H vs R131R	1110	357 vs 224	0.94	(0.69-1.29)	.7032	.8438
FCGR2B	I232T vs I232I	1033	213 vs 801	0.68	(0.50-0.93)	.0146	.0877
FCGR2B	T232T vs I232I	1033	19 vs 801	1.02	(0.45-2.30)	.9602	.9602
FCGR3A	F158V vs F158F	1110	497 vs 470	1.08	(0.86-1.37)	.5114	.8438
FCGR3A	V158V vs F158F	1110	143 vs 470	0.92	(0.64-1.31)	.6288	.8438



Cox regression (multivariate analysis) for each treatment arm (obinutuzumab and rituximab)

C

Biomarker	Effect	Treatment	Total (N)	Subgroup (n)	HR	95% CI	*P*-value	Adj. *P*-value
FCGR2A	R131H vs R131R	R	557	264 vs 113	1.13	(0.77-1.65)	.5447	.9143
FCGR2A	H131H vs R131R	R	557	180 vs 113	0.97	(0.64-1.47)	.8980	.9143
FCGR2A	R131H vs R131R	G	553	265 vs 111	1.05	(0.67-1.63)	.8315	.9143
FCGR2A	H131H vs R131R	G	553	177 vs 111	0.93	(0.57-1.52)	.7796	.9143
FCGR2B	I232T vs I232I	R	518	110 vs 398	0.79	(0.53-1.16)	.2216	.8414
FCGR2B	T232T vs I232I	R	518	10 vs 398	0.46	(0.11-1.87)	.2805	.8414
FCGR2B	I232T vs I232I	G	515	103 vs 403	0.55	(0.33-0.91)	.0196	.2357
FCGR2B	T232T vs I232I	G	515	9 vs 403	2.37	(0.86-6.54)	.0972	.5830
FCGR3A	F158V vs F158F	R	557	229 vs 252	1.03	(0.76-1.41)	.8353	.9143
FCGR3A	V158V vs F158F	R	557	76 vs 252	1.02	(0.66-1.58)	.9143	.9143
FCGR3A	F158V vs F158F	G	553	268 vs 218	1.14	(0.79-1.63)	.4777	.9143
FCGR3A	V158V vs F158F	G	553	67 vs 218	0.76	(0.40-1.43)	.3904	.9143



Time to event was defined by PFS (days). All analyses were adjusted and unstratified. Variables for the univariate analysis included biomarker and treatment arm. Variables for the multivariate analysis included biomarker, treatment arm (pooled analysis only), FLIPI and chemotherapy. No interaction terms were included. *P*-value (for hypothesis testing of whether the biomarker effect was equal to zero) was calculated using the Wald test. Adjusted *P*-values were corrected for multiple comparisons using the Benjamini and Hochberg method.

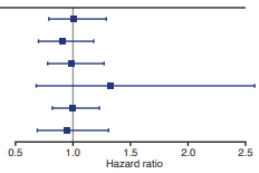
Adj, adjusted; CI, confidence interval; *FCGR*, Fc gamma receptor; HR, hazard ratio.

Supplemental Figure 2. Forest plot representing the (A) univariate and (B and C) multivariate survival analyses of the impact of single nucleotide polymorphism genotype on progression-free survival (PFS) in patients with diffuse large B-cell lymphoma (DLBCL) in the GOYA trial.

Cox regression (univariate analysis): pooled treatment arms (obinutuzumab and rituximab)

A

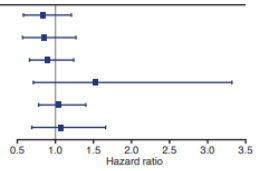
Biomarker	Effect	Total (N)	Subgroup (n)	HR	95% CI	*P*-value	Adj. *P*-value
FCGR2A	R131H vs R131R	1316	595 vs 291	1.01	(0.79-1.29)	.9606	.9951
FCGR2A	H131H vs R131R	1316	430 vs 291	0.91	(0.70-1.18)	.4669	.9951
FCGR2B	I232T vs I232I	1080	282 vs 773	0.99	(0.78-1.27)	.9590	.9951
FCGR2B	T232T vs I232I	1080	25 vs 773	1.33	(0.68-2.58)	.4058	.9951
FCGR3A	F158V vs F158F	1313	574 vs 591	1.00	(0.82-1.23)	.9951	.9951
FCGR3A	V158V vs F158F	1313	148 vs 591	0.95	(0.69-1.31)	.7499	.9951



Cox regression (multivariate analysis): pooled treatment arms (obinutuzumab and rituximab)

B

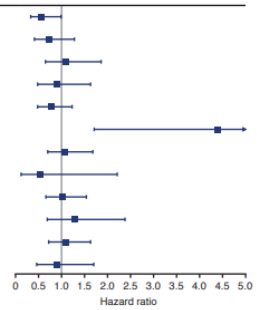
Biomarker	Effect	Total (N)	Subgroup (n)	HR	95% CI	*P*-value	Adj. *P*-value
FCGR2A	R131H vs R131R	689	313 vs 122	0.84	(0.58-1.21)	.3527	.7736
FCGR2A	H131H vs R131R	689	254 vs 122	0.85	(0.57-1.27)	.4163	.7736
FCGR2B	I232T vs I232I	668	175 vs 477	0.90	(0.66-1.24)	.5157	.7736
FCGR2B	T232T vs I232I	668	16 vs 477	1.53	(0.71-3.32)	.2808	.7736
FCGR3A	F158V vs F158F	689	313 vs 297	1.04	(0.78-1.40)	.7726	.7741
FCGR3A	V158V vs F158F	689	79 vs 297	1.07	(0.69-1.66)	.7741	.7741



Cox regression (multivariate analysis) for each treatment arm (obinutuzumab and rituximab)

C

Biomarker	Effect	Treatment	Total (N)	Subgroup (n)	HR	95% CI	*P*-value	Adj. *P*-value
FCGR2A	R131H vs R131R	R	336	136 vs 61	0.57	(0.33-0.99)	.0469	.2815
FCGR2A	H131H vs R131R	R	336	139 vs 61	0.73	(0.41-1.28)	.2715	.8002
FCGR2A	R131H vs R131R	G	353	177 vs 61	1.10	(0.65-1.86)	.7161	.8002
FCGR2A	H131H vs R131R	G	353	115 vs 61	0.89	(0.48-1.63)	.7002	.8002
FCGR2B	I232T vs I232I	R	328	90 vs 232	0.77	(0.48-1.23)	.2694	.8002
FCGR2B	T232T vs I232I	R	328	6 vs 232	4.40	(1.71-11.32)	.0021	.0254
FCGR2B	I232T vs I232I	G	340	85 vs 245	1.08	(0.70-1.68)	.7336	.8002
FCGR2B	T232T vs I232I	G	340	10 vs 245	0.53	(0.12-2.21)	.3789	.8002
FCGR3A	F158V vs F158F	R	336	164 vs 134	1.01	(0.66-1.54)	.9790	.9790
FCGR3A	V158V vs F158F	R	336	38 vs 134	1.28	(0.69-2.38)	.4272	.8002
FCGR3A	F158V vs F158F	G	353	149 vs 163	1.09	(0.72-1.63)	.6922	.8002
FCGR3A	V158V vs F158F	G	353	41 vs 163	0.89	(0.46-1.70)	.7210	.8002



Time to event was defined by PFS (days). All analyses were adjusted and unstratified. Variables for the univariate analysis included biomarker and treatment arm. Variables for the multivariate analysis included biomarker, treatment arm (pooled analysis only), geographic region, number of chemotherapy cycles, IPI categories, COO and BCL2 by IHC. No interaction terms were included. *P*-value (for hypothesis testing of whether the biomarker effect was equal to zero) was calculated using the Wald test. Adjusted *P*-values were corrected for multiple comparisons using the Benjamini and Hochberg method.

Adj, adjusted; CI, confidence interval; *FCGR*, Fc gamma receptor; HR, hazard ratio.

References

1. Floto RA, Clatworthy MR, Heilbronn KR, et al. Loss of function of a lupus-associated FcgammaRIIb polymorphism through exclusion from lipid rafts. *Nat Med*. 2005;11(10):1056-1058.