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Proinflammatory macrophage activation by the polysialic acid-Siglec-16 axis is linked to increased survival of glioblastoma patients

Supplementary Tables S1-S14

Supplementary Table S1.

Demographic and clinical parameters of GB patient cohorts

	MHH cohort n = 70	UMG cohort n = 100
Age at primary resection [years]		
Median	60	65
Range	32 - 85	25 - 80
Overall survival [months]		
Median	10	13
Range	0 - 76	1 - 55
Sex: female/male (ratio)	31 / 39 (1 : 1.26)	43 / 57 (1 : 1.33)
Extent of resection: n (%)		
Gross total resection	37 (54%)	75 (75%)
Sub-total resection	25 (36%)	24 (24%)
Biopsy	8 (11%)	1 (1%)
IDH1/2 **mutation: n (%)**	not determined	3 (3%)
MGMT **gene promoter methylation: n (%)**	not determined	35 (35%)
Therapeutic intervention after surgery: n (%)		
Combined radio- and chemotherapy [a]	45 (64%)	100 (100%)
Radiotherapy	18 (26%)	0 (0%)
No adjuvant therapy	7 (10%)	0 (0%)

[a] MHH: temozolomide, UMG: temozolomide, nimustine, or carmustine

Supplementary Table S2.

Characteristics of the two cohorts of n = 70 (MHH) and n = 100 (UMG) GB patients stratified for the presence of a functional *SIGLEC16* allele (**A**) or for the occurrence of polySia on tumor cells (**B**)

A. Comparison of *SIGLEC16*-positive and -negative GB patients

		SIGLEC16 P/P	*SIGLEC16 +/P*	Statistics	
Distribution n (%)	MHH	45 (64%)	25 (36%)	*P* = 0.116 (MHH versus UMG)	Fisher's exact test
	UMG	51 (51%)	49 (49%)		
	MHH+UMG	96 (56%)	74 (44%)		
Age [years][a] median ± SD (range)	MHH	58 ± 12 (35-80)	61 ± 13 (32-85)	*P* = 0.481	Mann-Whitney test
	UMG	66 ± 10 (37-80)	64 ± 13 (25-78)	*P* = 0.294	
Sex female /male (ratio)	MHH	23 / 22 (1 : 0.96)	8 / 17 (1 : 2.13)	*P* = 0.140	Fisher's exact test
	UMG	21 / 30 (1 : 1.43)	22 / 27 (1 : 1.23)	*P* = 0.840	
Gross total resection n (%)[c]	MHH	23 (51%)	14 (56 %)	*P* = 0.804	Fisher's exact test
	UMG	34 (66%)	41 (84%)	*P* = 0.065	
Chemotherapy[b] n (%)[c]	MHH	28 (62%)	17 (68 %)	*P* = 0.795	Fisher's exact test
	UMG	51 (100%)	49 (100%)	*P* > 0.999	
MGMT promotor methylated[d] n (%)[c]	UMG	16 (31%)	19 (39%)	*P* =0.530	Fisher's exact test
Cases with polySia-positive tumor cells n (%)[c]	MHH	38 (84%)	22 (88%)	*P* > 0.999	Fisher's exact test
	UMG	39 (77%)	43 (88%)	*P* = 0.194	
	MHH+UMG	76 (79%)	65 (88%)	*P* = 0.154	

[a] Age at primary resection
[b] MHH: temozolomide, UMG: temozolomide, nimustine, or carmustine
[c] % of all *SIGLEC16 P/P* or *SIGLEC16 +/P* (A) and polySia-positive or –negative cases (B), respectively
[d] For MHH cohort not determined

Supplementary Table S2 (continued).

B. Comparison of GB patients with polySia-positive and -negative tumor cells

		polySia-positive tumor cells	no polySia-positive tumor cells	Statistics	
Distribution n (%)	MHH	60 (86%)	10 (14%)	P = 0.675 (MHH versus UMG)	Fisher's exact test
	UMG	82 (82%)	18 (18%)		
	MHH+UMG	142 (84%)	28 (16%)		
Age [years] [a] median ± SD (range)	MHH	59.5 ± 13 (32-85)	60 ± 11 (43-78)	P = 0.682	Mann-Whitney test
	UMG	65.5 ± 12 (25-80)	64.5 ± 11 (37-79)	P = 0.861	
Sex female /male (ratio)	MHH	25 / 34 (1 : 1.36)	6 / 5 (1 : 0.83)	P = 0.520	Fisher's exact test
	UMG	35 / 47 (1 : 1.34)	8 / 10 (1 : 1.25)	P > 0.999	
Gross total resection n (%) [c]	MHH	32 (53%)	5 (50 %)	P > 0.999	Fisher's exact test
	UMG	62 (75%)	13 (72%)	P = 0.769	
Chemotherapy [b] n (%) [c]	MHH	40 (68 %)	5 (46 %)	P = 0.183	Fisher's exact test
	UMG	82 (100%)	18 (100%)	P > 0.999	
MGMT promotor methylated [d] n (%) [c]	UMG	28 (34%)	7 (39%)	P = 0.787	Fisher's exact test
SIGLEC16 [+/P] cases n (%) [c]	MHH	22 (37%)	3 (30%)	P > 0.999	Fisher's exact test
	UMG	43 (52%)	6 (33%)	P = 0.194	
	MHH+UMG	65 (46%)	9 (32%)	P = 0.154	

[a] Age at primary resection
[b] MHH: temozolomide, UMG: temozolomide, nimustine, or carmustine
[c] % of all *SIGLEC16* [P/P] or *SIGLEC16* [+/P] (A) and polySia-positive or –negative cases (B), respectively
[d] For MHH cohort not determined

Supplementary Table S3.

Cox proportional hazards regression analysis of covariates for *SIGLEC16* and polySia status in relation to OS (MHH and UMG cohorts combined)

Variable (see Table 1C)	Covariates	HR [a] (95% CI)	*P*
SIGLEC16	cohort	1.15 (0.80 – 1.67)	P = 0.46
	Age at resection	1.02 (1.01 – 1.03)	***P* = 0.005** [b]
	Sex	1.27 (0.92 – 1.74)	*P* = 0.14
	Gross total resection	0.90 (0.63 – 1.30)	*P* = 0.56
	Chemotherapy	0.29 (0.17 – 0.56)	***P* < 0.0001**
polySia	cohort	1.06 (0.74 – 1.55)	*P* = 0.75
	Age at resection	1.02 (1.01 – 1.04)	***P* = 0.002**
	Sex	1.37 (1.00 – 1.87)	*P* = 0.050
	Gross total resection	0.76 (0.54 – 1.09)	*P* = 0.13
	Chemotherapy	0.37 (0.22 – 0.64)	***P* = 0.0003**
SIGLEC16 / polySia double-positive	cohort	1.11 (0.78 – 1.62)	*P* = 0.57
	Age at resection	1.02 (1.01 – 1.03)	***P* = 0.008**
	Sex	1.27 (0.92 – 1.74)	*P* = 0.15
	Gross total resection	0.88 (0.62 – 1.26)	*P* = 0.46
	Chemotherapy	0.32 (0.19 – 0.55)	***P* < 0.0001**

[a] Abbreviations: HR, hazard ratio; CI, confidence interval

[b] *P*-values < 0.05 are shown in bold

Supplementary Table S4.

Median age of GB cases stratified for *SIGLEC16* genotype and polySia on tumor cells

	Median age [years] [a] ± SD (range), n		
	SIGLEC16 P/P	*SIGLEC16 +/P*	**Mann-Whitney test**
MHH	58.0 ± 12.4 (35-80), 45	61.0 ± 13.0 (32-85), 25	*P* = 0.48
UMG	66.0 ± 10.1 (37-80), 51	64.0 ± 12.7 (25-78), 49	*P* = 0.29
MHH+UMG	62.5 ± 11.6 (35-80), 96	64.0 ± 12.7 (25-85), 74	*P* = 0.89
	Negative for polySia on tumor cells	**Positive for polySia on tumor cells**	
MHH	60.0 ± 11.0 (43-78), 10	59.5 ± 12.9 (32-85), 60	*P* = 0.68
UMG	64.5 ± 10.9 (37-79), 18	65.5 ± 11.7 (25-80), 82	*P* = 0.86
MHH+UMG	63.5 ± 10.8 (37-79), 28	63.0 ± 12.3 (25-85), 142	*P* = 0.87

		Median age [years] [a] ± SD (range), n	
		SIGLEC16 P/P	*SIGLEC16 +/P*
polySia-negative	MHH	56.0 ± 12.0 (43-78), 7	70.0 ± 8.1 (57-72), 3
	UMG	66.0 ± 12.4 (37-79), 12	63.5 ± 8.0 (54-78), 6
	MHH+UMG	63.0 ± 12.1 (37-79), 19	64.0 ± 7.6 (54-78), 9
polySia-positive	MHH	58.5 ± 12.6 (35-80), 38	60.5 ± 13.5 (32-85), 22
	UMG	66.0 ± 9.4 (46-80), 39	65.0 ± 13.2 (25-78), 43
	MHH+UMG	62.0 ± 11.5 (35-80), 77	64.0 ± 13.2 (25-85), 65
Statistics		**Kruskal-Wallis test**	**Dunn's post test**
	MHH	*P* = 0.74	*P* > 0.999 for all group comparisons
	UMG	*P* = 0.70	
	MHH+UMG	*P* = 0.91	

[a] Age at primary resection

Supplementary Table S5.

OS analysis of GB cases receiving (A) or not receiving gross total resection (B) stratified for *SIGLEC16* genotype and polySia on tumor cells (MHH and UMG cohorts combined)

A. Gross total resection (n=112)

GB status	n	median OS [months]	statistics (log-rank test)	
SIGLEC16[P/P]	57	9	P = 0.0003	
SIGLEC16[+/P]	55	15		
polySia-negative	18	8	P = 0.031	
polySia-positive	94	13		
SIGLEC16[P/P] polySia[−]	11	9	P = 0.0009	P = 0.0005 [a] q = 0.002
SIGLEC16[+/P] polySia[−]	7	5		
SIGLEC16[P/P] polySia[+]	46	9		P = 0.0009 q = 0.002
SIGLEC16[+/P] polySia[+]	48	15.5		

[a] Differences with *P* < 0.05 and respective FDR adjusted *q* values are shown

B. Subtotal resection or biopsy (n=58) [a]

GB status	n	median OS [months]	statistics (log-rank test)	
SIGLEC16[P/P]	38 [a]	10	P = 0.151	
SIGLEC16[+/P]	19	10		
polySia-negative	10 [a]	5.5	P = 0.060	
polySia-positive	47	10		
SIGLEC16[P/P] polySia[−]	8	4	P = 0.015	P = 0.004 [b] q = 0.019
SIGLEC16[+/P] polySia[−]	2	16.5		
SIGLEC16[P/P] polySia[+]	30 [a]	11.5		P = 0.017 q = 0.045
SIGLEC16[+/P] polySia[+]	17	10		

[a] One value censored because OS was zero

[b] Differences with *P* < 0.05 and respective FDR adjusted *q* values are shown

Supplementary Table S6.

OS analysis of GB cases receiving (A) or not receiving chemotherapy (B) stratified for *SIGLEC16* genotype and polySia on tumor cells (MHH cohort only)

A. Combined radio- and chemotherapy (n=45)

GB status	n	median OS [months]	statistics (log-rank test)
SIGLEC16 [P/P]	28	11	P = 0.010
SIGLEC16 [+/P]	17	15	
polySia-negative	4	7	P = 0.005
polySia-positive	41	13	
SIGLEC16 [P/P] polySia [−]	3	7	P = 0.003
SIGLEC16 [+/P] polySia [−]	1	7	
SIGLEC16 [P/P] polySia [+]	25	11	
SIGLEC16 [+/P] polySia [+]	16	16	

P = 0.0006 [a] q = 0.002
P = 0.006 q = 0.010
P = 0.012 q = 0.013

[a] Differences with $P < 0.05$ and respective FDR adjusted q values are shown

B. Radiotherapy or no adjuvant therapy (n=25) [a]

GB status	n	median OS [months]	statistics (log-rank test)
SIGLEC16 [P/P]	16 [a]	4	P = 0.059
SIGLEC16 [+/P]	8	7.5	
polySia-negative	6	4.5	P = 0.63
polySia-positive	18 [a]	4	
SIGLEC16 [P/P] polySia [−]	4	4.5	P = 0.27
SIGLEC16 [+/P] polySia [−]	2	9	
SIGLEC16 [P/P] polySia [+]	12 [a]	4	
SIGLEC16 [+/P] polySia [+]	6	7.5	

[a] One value censored because OS was zero

Supplementary Table S7.

OS analysis of GB cases receiving gross total resection and chemotherapy stratified for *SIGLEC16* genotype and polySia on tumor cells (MHH and UMG cohorts combined, n=101)

GB status	n	median OS [months]	statistics (log-rank test)	
SIGLEC16 $^{P/P}$	49	11	*P* = 0.002	
SIGLEC16 $^{+/P}$	52	15		
polySia-negative	15	9	*P* = 0.020	
polySia-positive	86	14		
SIGLEC16 $^{P/P}$ polySia $^-$	10	10	*P* = 0.003	*P* = 0.001 [a] / *q* = 0.006
SIGLEC16 $^{+/P}$ polySia $^-$	5	5		
SIGLEC16 $^{P/P}$ polySia $^+$	39	12		*P* = 0.004 / *q* = 0.007
SIGLEC16 $^{+/P}$ polySia $^+$	47	16		

[a] Differences with *P* < 0.05 and respective FDR adjusted *q* values are shown

Supplementary Table S8.

OS analysis of IDH-wildtype GB cases (UMG cohort) stratified for *SIGLEC16* genotype and polySia on tumor cells

GB status	n	median OS [months]	statistics (log-rank test)	
SIGLEC16 $^{P/P}$	49	12	*P* = 0.014	
SIGLEC16 $^{+/P}$	48	14.5		
polySia-negative	17	11	*P* = 0.136	
polySia-positive	80	13		
SIGLEC16 $^{P/P}$ polySia $^-$	11	11	*P* = 0.031	*P* = 0.005 [a] / *q* = 0.024
SIGLEC16 $^{+/P}$ polySia $^-$	6	9.5		
SIGLEC16 $^{P/P}$ polySia $^+$	38	12		*P* = 0.048 / *q* = 0.125
SIGLEC16 $^{+/P}$ polySia $^+$	42	15		

[a] Differences with *P* < 0.05 and respective FDR adjusted *q* values are shown

Supplementary Table S9.

OS analysis of UMG cohort stratified for *MGMT* gene promoter methylation and *SIGLEC16* genotype, polySia on tumor cells, CD163 and CD74 status

GB status	n	median OS [months]	statistics (log-rank test)	
MGMT unmethylated SIGLEC16 [P/P]	35	12		*P* = 0.012 [a] *q* = 0.024
MGMT unmethylated SIGLEC16 [+/P]	30	13	*P* = 0.033	
MGMT methylated SIGLEC16 [P/P]	16	7		*P* = 0.010 *q* = 0.024
MGMT methylated SIGLEC16 [+/P]	19	19		
MGMT unmethylated polySia [−]	11	11		
MGMT unmethylated polySia [+]	54	13	*P* = 0.366	
MGMT methylated polySia [−]	7	9		
MGMT methylated polySia [+]	28	13.5		
MGMT unmethylated CD163 [high]	48	12.5		
MGMT unmethylated CD163 [low]	17	12	*P* = 0.227	
MGMT methylated CD163 [high]	22	12		
MGMT methylated CD163 [low]	13	20		
MGMT unmethylated CD74 [low]	40	11		
MGMT unmethylated CD74 [high]	25	14	*P* = 0.242	
MGMT methylated CD74 [low]	20	12.5		
MGMT methylated CD74 [high]	15	18		

[a] Differences with *P* < 0.05 and respective FDR adjusted *q* values are shown

Supplementary Table S10.

Characteristics of the two cohorts of n = 70 (MHH) and n = 100 (UMG) GB patients stratified for CD74^{low} and CD74^{high}

		CD74^{low}	CD74^{high}	Statistics	
Distribution n (%)	MHH [f]	56 (82%)	12 (18%)	P = 0.002 (MHH versus UMG)	Fisher's exact test
	UMG	60 (60%)	40 (40%)		
	MHH+UMG	116 (69%)	52 (31%)		
Age [years] [a] median ± SD (range)	MHH	60 ± 13 (35-85)	56 ± 12.5 (32-69)	P = 0.357	Mann-Whitney test
	UMG	63 ± 11.5 (32-80)	64 ± 11.5 (25-18)	P = 0.427	
Sex female /male (ratio)	MHH	27 / 29 (1 : 1.07)	3 / 9 (1: 3)	P = 0.204	Fisher's exact test
	UMG	23 / 37 (1 : 1.61)	20 / 20 (1 : 1)	P = 0.304	
Gross total resection n (%) [c]	MHH	29 (52%)	7 (58%)	P = 0.761	Fisher's exact test
	UMG	44 (73%)	31 (78%)	P = 0.814	
Chemotherapy [b] n (%) [c]	MHH	37 (66%)	8 (67%)	P > 0.999	Fisher's exact test
	UMG	60 (100%)	40 (100%)	P > 0.999	
MGMT promotor methylated [d] n (%) [c]	UMG	20 (33%)	15 (38%)	P = 0.675	Fisher's exact test
SIGLEC16 $^{+/P}$ cases n (%) [c]	MHH	17 (30%)	7 (58%)	P = 0.096	Fisher's exact test
	UMG	27 (45%)	22 (55%)	P = 0.41	
	MHH+UMG	44 (38%)	29 (56%)	**P = 0.042** [e]	
SIGLEC16 $^{+/P}$ with polySia-positive tumor cells n (%) [c]	MHH	15 (27%)	6 (50%)	P = 0.168	Fisher's exact test
	UMG	24 (40%)	19 (47%)	P = 0.54	
	MHH+UMG	39 (34)	25 (48%)	**P = 0.028**	

[a] Age at primary resection
[b] MHH: temozolomide, UMG: temozolomide, nimustine, or carmustine
[c] % of all CD74^{low} or CD74^{high}, respectively
[d] For MHH cohort not determined
[e] *P*-values < 0.05 are shown in bold
[f] For two specimen of the MHH cohort, the available FFPE tissue did not suffice for CD74/IBA1 immunostaining

Supplementary Table S11. Median age at resection of GB cases stratified for CD163 to CD68 (A) or CD74 to IBA1 ratios (B) alone or in combination with the *SIGLEC16* genotype

A. CD163 — Median age [years] [a] ± SD (range), n

	CD163^{high}	CD163^{low}	Mann-Whitney test
MHH	59.0 ± 13.3 (32-85), 42	60.0 ± 11.6 (35-76), 28	*P* = 0.72
UMG	65.0 ± 10.5 (35-79), 70	66.5 ± 13.8 (25-80), 30	*P* = 0.51
MHH+UMG	63.0 ± 11.7 (32-85), 112	64.0 ± 12.9 (25-88), 58	*P* = 0.92

Median age [years] [a] ± SD (range), n

		SIGLEC16 [P/P]	*SIGLEC16 [+/P]*
CD163^{high}	MHH	58.0 ± 12.8 (40-80), 32	65.0 ± 15.1 (32-85), 10
	UMG	66.0 ± 10.0 (37-79), 41	64.0 ± 11.2 (35-78), 29
	MHH+UMG	62.0 ± 11.5 (37-80), 73	64.0 ± 12.1 (32-85), 39
CD163^{low}	MHH	60.0 ± 11.9 (35-74), 13	60.0 ± 11.8 (43-76), 15
	UMG	72.0 ± 11.0 (49-80), 10	66.5 ± 14.9 (25-78), 20
	MHH+UMG	63.0 ± 12.1 (35-80), 23	64.0 ± 13.4 (25-78), 35

Statistics		**Kruskal-Wallis test**	**Dunn's post test**
	MHH	*P* = 0.76	*P* > 0.999 for all group comparisons
	UMG	*P* = 0.63	
	MHH+UMG	*P* = 0.92	

B. CD74 — Median age [years] [a] ± SD (range), n [b]

	CD74^{low}	CD74^{high}	Mann-Whitney test
MHH	59.8 ± 12.6 (35-85), 56	56.3 ± 12.5 (32-69), 12	*P* = 0.36
UMG	62.7 ± 11.5 (32-80), 60	64.3 ± 11.5 (25-18), 40	*P* = 0.43
MHH+UMG	61.3 ± 12.1 (32-85), 116	62.4 ± 12.1 (25-78), 52	*P* = 0.44

Median age [years] [a] ± SD (range), n

		SIGLEC16 [P/P]	*SIGLEC16 [+/P]*
CD74^{low}	MHH	59.1 ± 12.6 (35-80), 39	61.7 ± 12.7 (43-85), 17
	UMG	63.9 ± 10.5 (37-80), 33	61.2 ± 12.7 (32-78), 27
	MHH+UMG	61.3 ± 11.9 (35-80), 72	61.4 ± 12.6 (32-85), 44
CD74^{high}	MHH	55.8 ± 12.3 (43-69), 5	56.6 ± 13.7 (32-69), 7
	UMG	66.6 ± 9.4 (45-77), 18	62.4 ± 12.9 (25-78), 22
	MHH+UMG	64.3 ± 10.8 (43-77), 23	61.0 ± 12.6 (32-85), 29

Statistics		**Kruskal-Wallis test**	**Dunn's post test**
	MHH	*P* = 0.67	*P* > 0.90 for all group comparisons
	UMG	*P* = 0.54	
	MHH+UMG	*P* = 0.92	

[a] Age at primary resection

[b] For two specimen of the MHH cohort, the available FFPE tissue did not suffice for CD74/IBA1 immunostaining

Supplementary Table S12. OS analysis of GB cases receiving (A) or not receiving gross total resection (B) stratified for CD163 to CD68 or CD74 to IBA1 ratios alone or in combination with the *SIGLEC16* genotype (MHH and UMG cohorts combined)

A. Gross total resection (n=112)

GB status	n	median OS [months]	statistics (log-rank test)	
CD163^{high}	74	12	P = 0.001	
CD163^{low}	38	15		
CD163^{high} *SIGLEC16*[P/P]	43	8	P = 0.0001	P = 0.005 [a] / q = 0.010
CD163^{high} *SIGLEC16*[+/P]	30	14		
CD163^{low} *SIGLEC16*[P/P]	14	12		P < 0.0001 / q < 0.0004
CD163^{low} *SIGLEC16*[+/P]	25	16		
CD74^{low}	73 [b]	12	P = 0.006	
CD74^{high}	38	15.5		
CD74^{low} *SIGLEC16*[P/P]	43	9	P = 0.0003	P < 0.0001 [a] / q < 0.0003
CD74^{low} *SIGLEC16*[+/P]	30	13		P = 0.0088 / q = 0.0092
CD74^{high} *SIGLEC16*[P/P]	14	9.5		P = 0.0007 / q = 0.0011
CD74^{high} *SIGLEC16*[+/P]	24	17.5		

B. Subtotal resection or biopsy (n=58) [a]

GB status	n	median OS [months]	statistics (log-rank test)
CD163^{high}	37 [a]	10	P = 0.53
CD163^{low}	20	10.5	
CD163^{high} *SIGLEC16*[P/P]	29 [c]	11	P = 0.55
CD163^{high} *SIGLEC16*[+/P]	9	10	
CD163^{low} *SIGLEC16*[P/P]	9	7	
CD163^{low} *SIGLEC16*[+/P]	10	13	
CD74^{low}	42 [c]	10	P = 0.26
CD74^{high}	14	12	
CD74^{low} *SIGLEC16*[P/P]	28 [c]	9.5	P = 0.37
CD74^{low} *SIGLEC16*[+/P]	14	10	
CD74^{high} *SIGLEC16*[P/P]	9	12	
CD74^{high} *SIGLEC16*[+/P]	5	10	

[a] Differences with P < 0.05 and respective FDR adjusted q values are shown
[b] For two specimen of the MHH cohort, the available FFPE tissue did not suffice for CD74/IBA1 immunostaining.
[c] One value censored because OS was zero

Supplementary Table S13. OS analysis of GB cases receiving (A) or not receiving chemotherapy (B) stratified for CD163 to CD68 or CD74 to IBA1 ratios alone or in combination with the *SIGLEC16* genotype (MHH cohort only)

A. Combined radio- and chemotherapy (n=45)

GB status	n	median OS [months]	statistics (log-rank test)	
CD163^{high}	23	10	*P* = 0.009	
CD163^{low}	22	15		
CD163^{high} *SIGLEC16* [P/P]	19	10	*P* = 0.020	*P* = 0.003 [a] *q* = 0.013
CD163^{high} *SIGLEC16* [+/P]	4	10		*P* = 0.034 *q* = 0.010
CD163^{low} *SIGLEC16* [P/P]	9	12		*P* = 0.047 *q* = 0.082
CD163^{low} *SIGLEC16* [+/P]	13	17		
CD74^{low}	37	12	*P* = 0.036	
CD74^{high}	8	14.5		
CD74^{low} *SIGLEC16* [P/P]	24	11	*P* = 0.002	*P* = 0.002 [a] *q* = 0.005
CD74^{low} *SIGLEC16* [+/P]	13	14		*P* = 0.006 *q* = 0.005
CD74^{high} *SIGLEC16* [P/P]	4	10.5		*P* = 0.007 *q* = 0.005
CD74^{high} *SIGLEC16* [+/P]	4	51		

[a] Differences with *P* < 0.05 and respective FDR adjusted *q* values are shown

B. Radiotherapy or no adjuvant therapy (n=25) [a]

GB status	n	median OS [months]	statistics (log-rank test)
CD163^{high}	18 [a]	4	*P* = 0.33
CD163^{low}	6	4.5	
CD163^{high} *SIGLEC16* [P/P]	12 [a]	4	*P* = 0.19
CD163^{high} *SIGLEC16* [+/P]	6	9	
CD163^{low} *SIGLEC16* [P/P]	4	4.5	
CD163^{low} *SIGLEC16* [+/P]	2	5	
CD74^{low}	18 [a, b]	4	*P* = 0.71
CD74^{high}	4	3.5	
CD74^{low} *SIGLEC16* [P/P]	14 [a]	4	*P* = 0.12
CD74^{low} *SIGLEC16* [+/P]	4	9	
CD74^{high} *SIGLEC16* [P/P]	1	3	
CD74^{high} *SIGLEC16* [+/P]	3	4	

[a] One value censored because OS was zero
[b] For two specimen of the MHH cohort, the available FFPE tissue did not suffice for CD74/IBA1 immunostaining

Supplementary Table S14.

OS analysis of GB cases receiving both gross total resection and chemotherapy stratified for CD163 to CD68 or CD74 to IBA1 ratios alone or in combination with the *SIGLEC16* genotype (MHH and UMG cohorts combined, n=101)

GB status	n	median OS [months]	statistics (log-rank test)	
CD163^{high}	65	13	*P* = 0.002	
CD163^{low}	36	15		
CD163^{high} *SIGLEC16 [P/P]*	36	11	*P* = 0.0008	*P* = 0.0002[a] *q* = 0.001
CD163^{high} *SIGLEC16 [+/P]*	28	14		
CD163^{low} *SIGLEC16 [P/P]*	13	13		
CD163^{low} *SIGLEC16 [+/P]*	24	17		
CD74^{low}	65	12	*P* = 0.009	
CD74^{high}	36	16		
CD74^{low} *SIGLEC16 [P/P]*	36	11.5	*P* = 0.0009	*P* = 0.0002[a] *q* = 0.0006
CD74^{low} *SIGLEC16 [+/P]*	29	13		*P* = 0.0013 *q* = 0.0020
CD74^{high} *SIGLEC16 [P/P]*	13	11		*P* = 0.0061 *q* = 0.0064
CD74^{high} *SIGLEC16 [+/P]*	23	18		

[a] Differences with *P* < 0.05 and respective FDR adjusted *q* values are shown