

Figure 1: Study of OS according to the period of diagnosis (group 1: diagnosis from 2005 to 2012 vs group 2: diagnosis from 2013 to 2018).

The median follow-up for patients diagnosed from 2005 to 2012 is 60 months (range: 0.5 – 146) and for patients diagnosed from 2013 to 2018 is 19 months (0.2- 63).

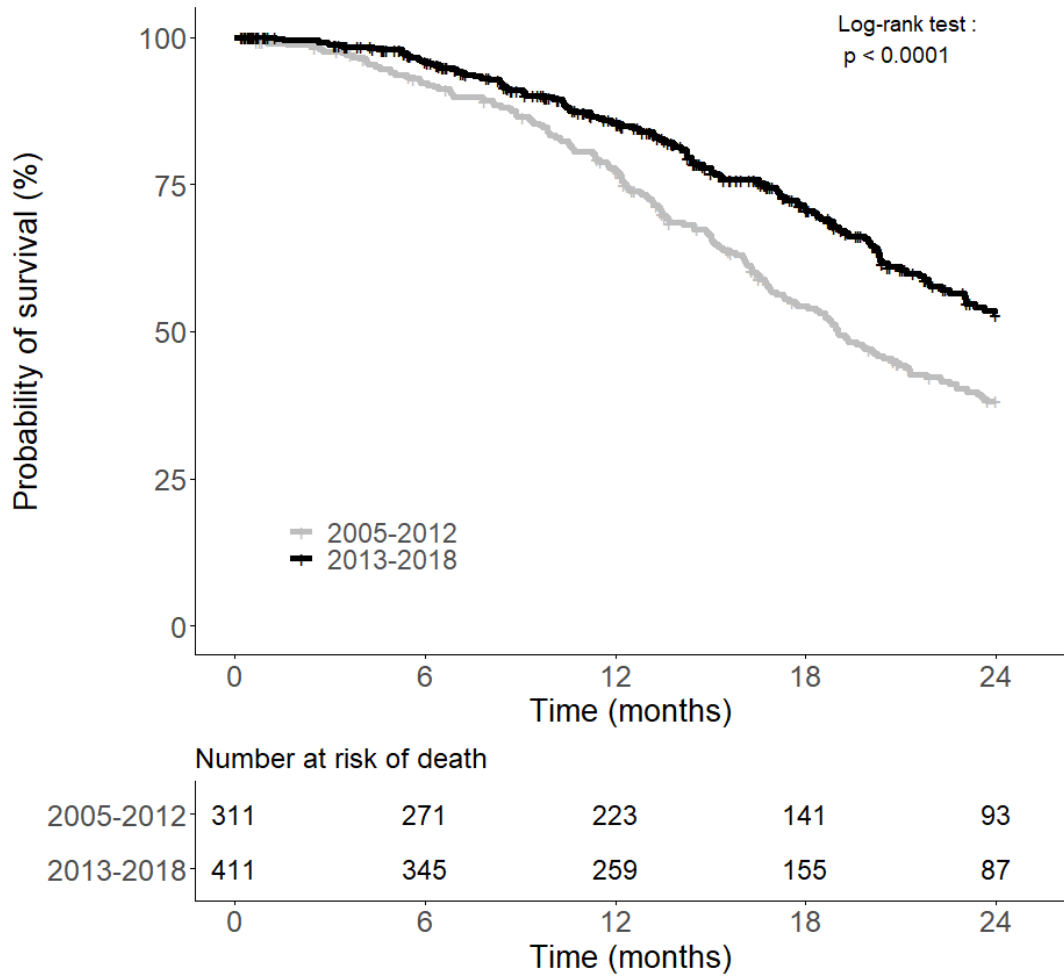


Figure 2: Study of OS according to the period of diagnosis (follow-up time truncated at 24 months)

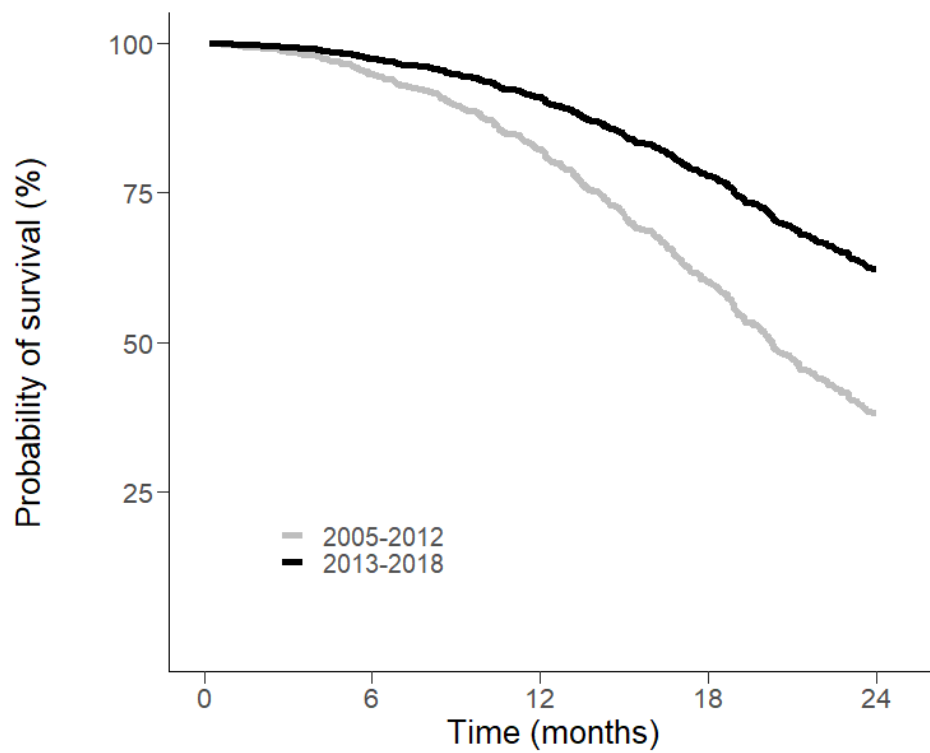


Figure 3: OS according to the period of diagnosis after adjusting on other prognostic factors (age, KPS score, *MGMT* promoter methylation status, surgery at relapse and the extent of resection at initial diagnosis) using multivariate Cox model presented in Table 3

		2005-2012 n = 311	2013-2018 n = 411	Total n = 722	p
<b>Age; mean (sd)</b>		55.24 (9.71)	56.04 (10.02)	55.7 (9.89)	0.1189
<b>KPS score</b>	70	45 (14.47%)	57 (13.87%)	102 (14.13%)	0.9118
	80	110 (35.37%)	138 (33.58%)	248 (34.35%)	
	90	137 (44.05%)	187 (45.5%)	324 (44.88%)	
	100	19 (6.11%)	29 (7.06%)	48 (6.65%)	
<b>MGMT promoter status</b>	Unmethylated	66 (53.23%)	54 (58.06%)	120 (55.3%)	0.4780
	Methylated	58 (46.77%)	39 (41.94%)	97 (44.7%)	
	Missing data	187	318	505	
<b>Initial surgery</b>	Biopsy	72 (24%)	134 (34.53%)	206 (29.94%)	0.0001
	Complete resection	88 (29.33%)	63 (16.24%)	151 (21.95%)	
	Partial resection	140 (46.67%)	191 (49.23%)	331 (48.11%)	
	Missing data	11	23	34	
<b>Surgery at relapse</b>		56 (18.01%)	48 (11.86%)	104 (14.4%)	0.0165
<b>Surgery at relapse before 24 months</b>		39 (12.54%)	37 (9%)	76 (10.53%)	0.1251
<b>Number of lines of treatment; mean (sd)</b>		2.48 (1.26)	2.19 (1.15)	2.31 (1.21)	0.0019
<b>Bevacizumab</b>		170 (54.66%)	237 (57.66%)	407 (56.37%)	0.4206

Table 1: Demographics and clinical characteristics of the GBM patients divided into treatment groups: 2005-2012 vs 2013-2018

		<b>aHR</b>	<b>CI 95%</b>	<b>p</b>
<b>Age (+5 years)</b>		1.01	[ 1.00 ; 1.02 ]	0.064
<b>KPS score (+10%)</b>		0.72	[ 0.62 ; 0.83 ]	<0.001
<b>MGMT promoter status</b>	<i>Unmethylated</i>	1.00	-	<0.001
(missing n=505)	<i>Methylated</i>	0.36	[ 0.24 ; 0.55 ]	
<b>Period of diagnosis</b>	2005-2012	1.00	-	<0.001
	2013-2018	0.64	[ 0.51 ; 0.81 ]	
<b>Surgery at relapse</b>	No	1.00	-	0.579
	Yes	0.90	[ 0.62 ; 1.31 ]	
	Biopsy	1.00	-	
<b>Initial surgery</b>	Complete resection	0.50	[ 0.36 ; 0.70 ]	<0.001
	Partial resection	0.61	[ 0.47 ; 0.81 ]	

Table 2: Univariate Cox analysis of factors affecting OS, when treating the missing data of *MGMT* promoter methylation status and initial surgery by multiple imputations

		aHR	CI 95%	p
<b>Age (+5 years)</b>		1.11	[ 1.03 ; 1.20 ]	0.026
<b>KPS score (+10%)</b>		0.71	[ 0.60 ; 0.84 ]	<0.001
<b>MGMT promoter status</b>	Unmethylated	1.00	-	<0.001
	Methylated	0.27	[ 0.15 ; 0.45 ]	
<b>Period of diagnosis</b>	2005-2012	1.00	-	<0.001
	2013-2018	0.49	[ 0.36 ; 0.67 ]	
<b>Surgery at relapse</b>	No	1.00	-	0.465
	Yes	1.16	[ 0.78 ; 1.72 ]	
	Biopsy	1.00	-	
<b>Initial surgery</b>	Complete resection	0.40	[ 0.25 ; 0.62 ]	<0.001
	Partial resection	0.60	[ 0.43 ; 0.83 ]	

Table 3: Multivariate Cox analysis of factors affecting OS. Missing values of *MGMT* promoter status were handled by multiple imputations. Time of treatment was considered as a dichotomous variable (2005-2012 vs 2013-2018)

		aHR	CI 95%	p
<b>Age (+5 years)</b>		1.11	[ 1.03 ; 1.20]	0.015
<b>KPS score (+10%)</b>		0.71	[ 0.60 ; 0.84 ]	<0.001
<b>MGMT promoter status</b>	Unmethylated	1.00	-	<0.001
	Methylated	0.28	[ 0.16 ; 0.48 ]	
<b>Year of diagnosis (+3 years)</b>		0.76	[ 0.67 ; 0.86 ]	<0.001
<b>Surgery at relapse</b>	No	1.00	-	0.244
	Yes	1.26	[ 0.85 ; 1.87 ]	
	Biopsy	1.00	-	
<b>Initial surgery</b>	Complete resection	0.39	[ 0.25 ; 0.60 ]	<0.001
	Partial resection	0.58	[ 0.42 ; 0.80 ]	

Table 4: Multivariate Cox analysis of factors affecting OS, when treating the missing data of *MGMT* promoter methylation status by multiple imputations and considering the time of treatment as a quantitative variable