Supplementary material

Title

Survival of diffuse astrocytic glioma, *IDH1/2*-wildtype, with molecular features of glioblastoma, WHO grade IV:

a confirmation of the cIMPACT-NOW.

Authors

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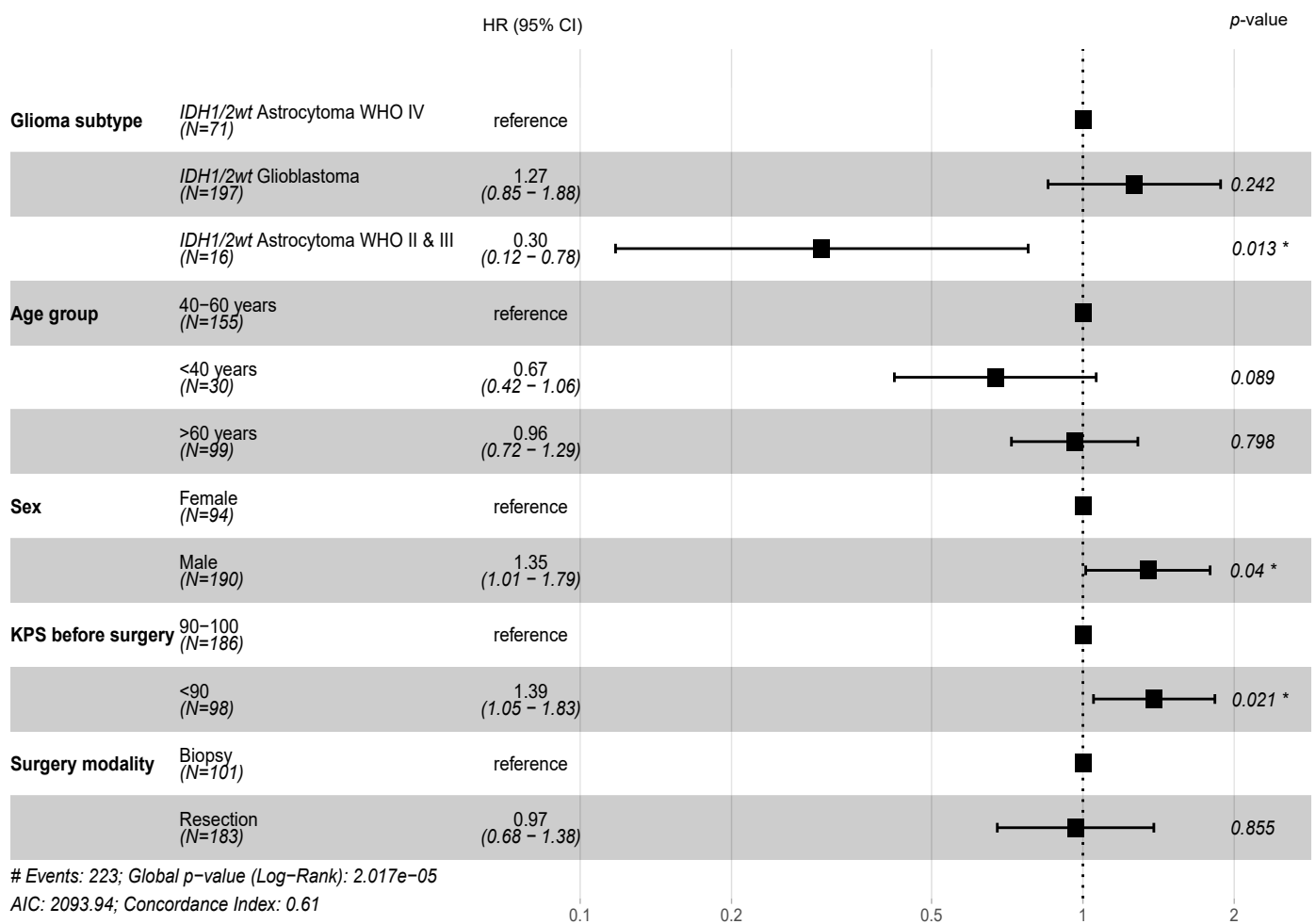J.B. Taphoorn, Pim J. French, Martin J. van den Bent

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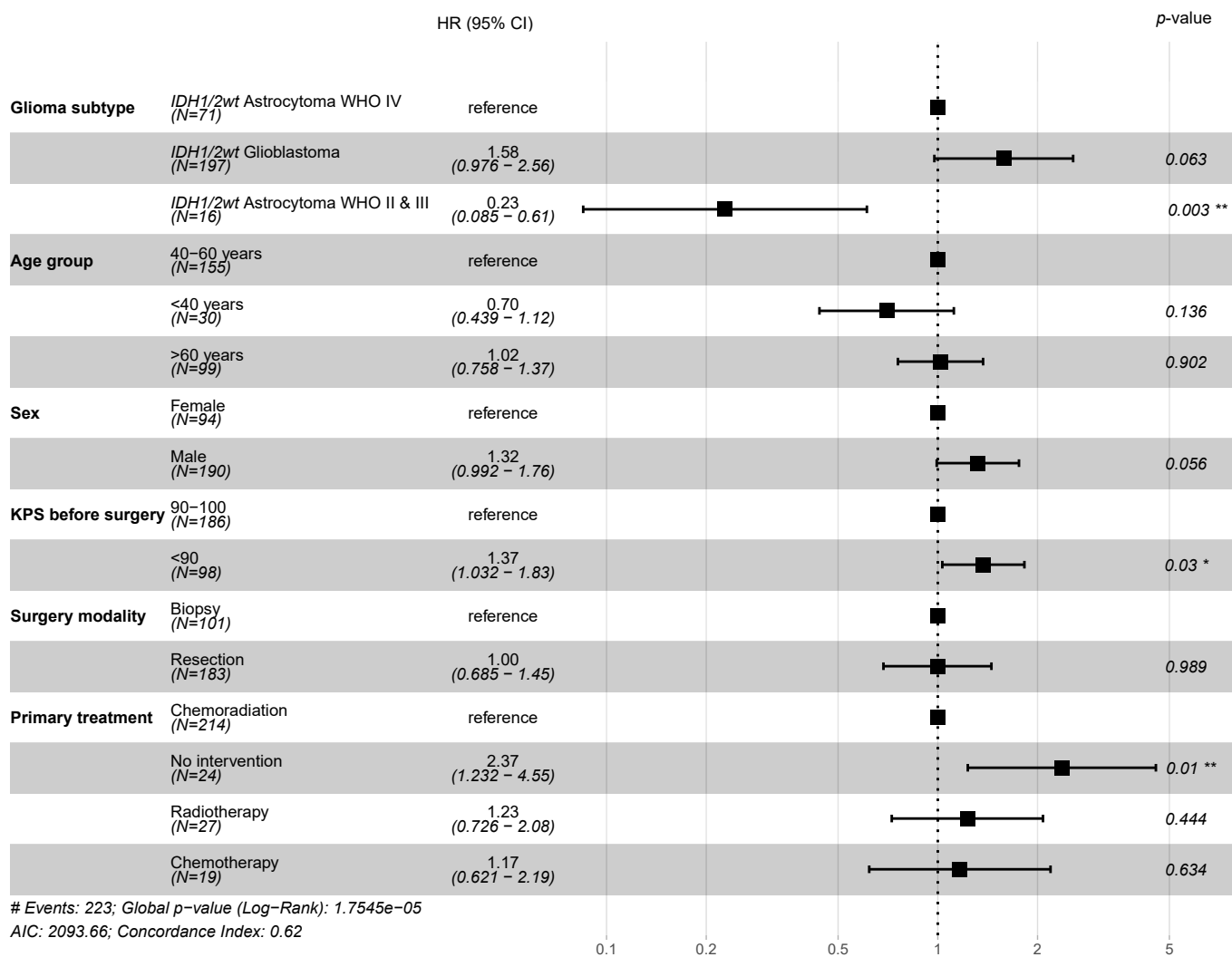Email address: c.tesileanu@erasmusmc.nl

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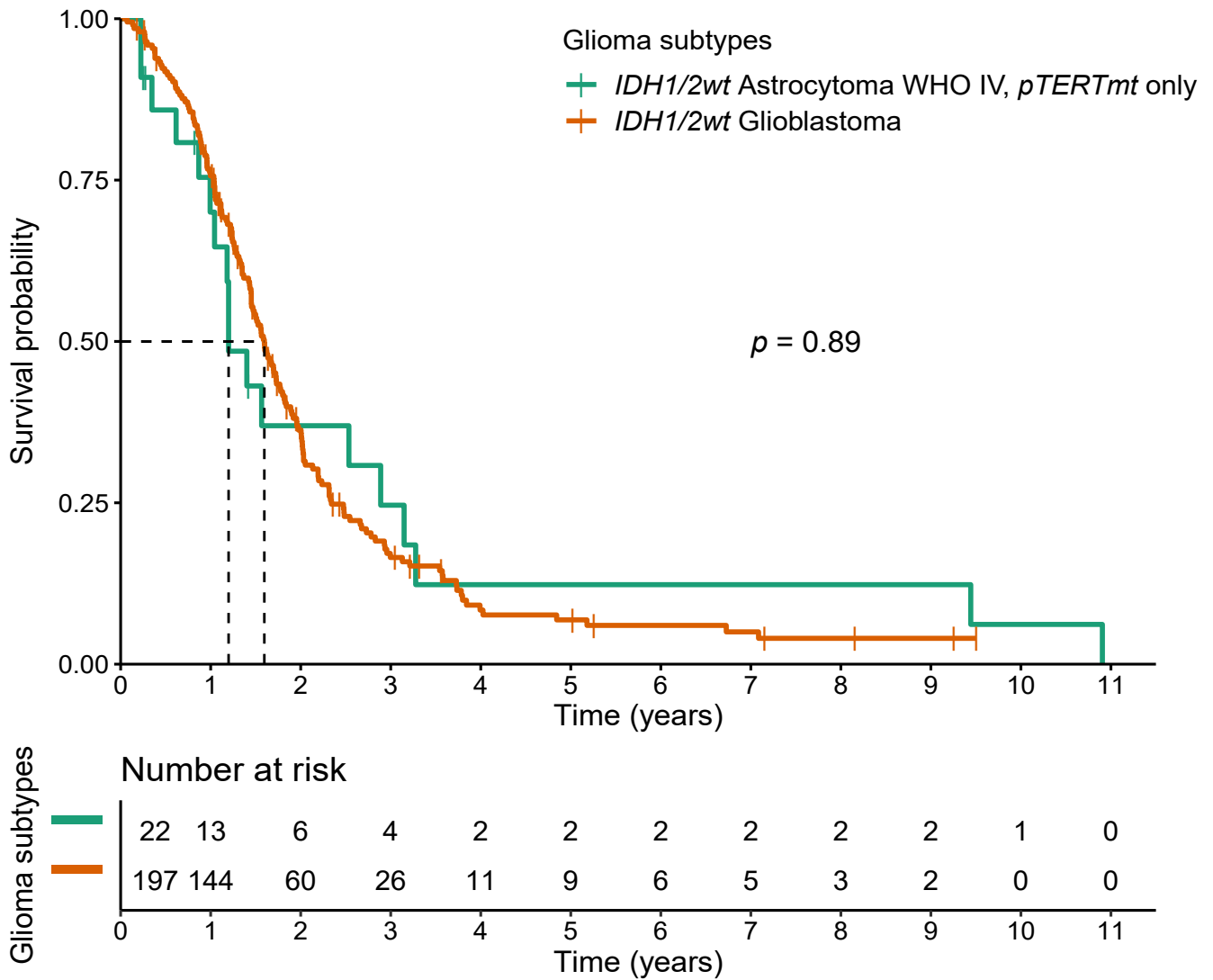| Characteristics	HR	95% CI	p
Glioma subtype			<0.001
IDH1/2wt Astrocytoma WHO IV	reference		
IDH1/2wt Astrocytoma WHO II & III	0.23	0.09-0.58	
IDH1/2wt Glioblastoma	1.19	0.87-1.63	
Age			0.070
40-60 years	reference		
<40 years	0.62	0.39-0.97	
>60 years	1.02	0.77-1.36	
Sex			0.050
Female	reference		
Male	1.33	1.00-1.76	
KPS before surgery			0.002
90-100	reference		
≤ 80	1.54	1.17-2.02	
Surgery modality			0.500
Biopsy	reference		
Resection	1.10	0.83-1.46	

Supplementary Table 1 The univariate analysis of OS for all *IDH1/2wt* gliomas taking into account the known prognostic factors for gliomas. The *p*-values of the likelihood ratio test are listed comparing the HR to the reference.

		HR (95% CI)		p-value
Glioma subtype	*IDH1/2wt* Astrocytoma WHO IV (N=71)	reference		
	IDH1/2wt Glioblastoma (N=197)	1.27 (0.85 − 1.88)		0.242
	IDH1/2wt Astrocytoma WHO II & III (N=16)	0.30 (0.12 − 0.78)		0.013 *
Age group	40−60 years (N=155)	reference		
	<40 years (N=30)	0.67 (0.42 − 1.06)		0.089
	>60 years (N=99)	0.96 (0.72 − 1.29)		0.798
Sex	Female (N=94)	reference		
	Male (N=190)	1.35 (1.01 − 1.79)		0.04 *
KPS before surgery	90−100 (N=186)	reference		
	<90 (N=98)	1.39 (1.05 − 1.83)		0.021 *
Surgery modality	Biopsy (N=101)	reference		
	Resection (N=183)	0.97 (0.68 − 1.38)		0.855

Events: 223; Global p−value (Log−Rank): 2.017e−05
AIC: 2093.94; Concordance Index: 0.61

Supplementary Figure 1 Forest plot with hazard ratios of the multivariable analysis of OS for all *IDH1/2wt* gliomas taking into account age, sex, KPS before surgery and surgery modality.

		HR (95% CI)		p-value
Glioma subtype	*IDH1/2wt* Astrocytoma WHO IV *(N=71)*	reference		
	IDH1/2wt Glioblastoma *(N=197)*	1.58 (0.976 − 2.56)		*0.063*
	IDH1/2wt Astrocytoma WHO II & III *(N=16)*	0.23 (0.085 − 0.61)		*0.003 ***
Age group	40−60 years *(N=155)*	reference		
	<40 years *(N=30)*	0.70 (0.439 − 1.12)		*0.136*
	>60 years *(N=99)*	1.02 (0.758 − 1.37)		*0.902*
Sex	Female *(N=94)*	reference		
	Male *(N=190)*	1.32 (0.992 − 1.76)		*0.056*
KPS before surgery	90−100 *(N=186)*	reference		
	<90 *(N=98)*	1.37 (1.032 − 1.83)		*0.03 **
Surgery modality	Biopsy *(N=101)*	reference		
	Resection *(N=183)*	1.00 (0.685 − 1.45)		*0.989*
Primary treatment	Chemoradiation *(N=214)*	reference		
	No intervention *(N=24)*	2.37 (1.232 − 4.55)		*0.01 ***
	Radiotherapy *(N=27)*	1.23 (0.726 − 2.08)		*0.444*
	Chemotherapy *(N=19)*	1.17 (0.621 − 2.19)		*0.634*

 # Events: 223; Global p−value (Log−Rank): 1.7545e−05
AIC: 2093.66; Concordance Index: 0.62
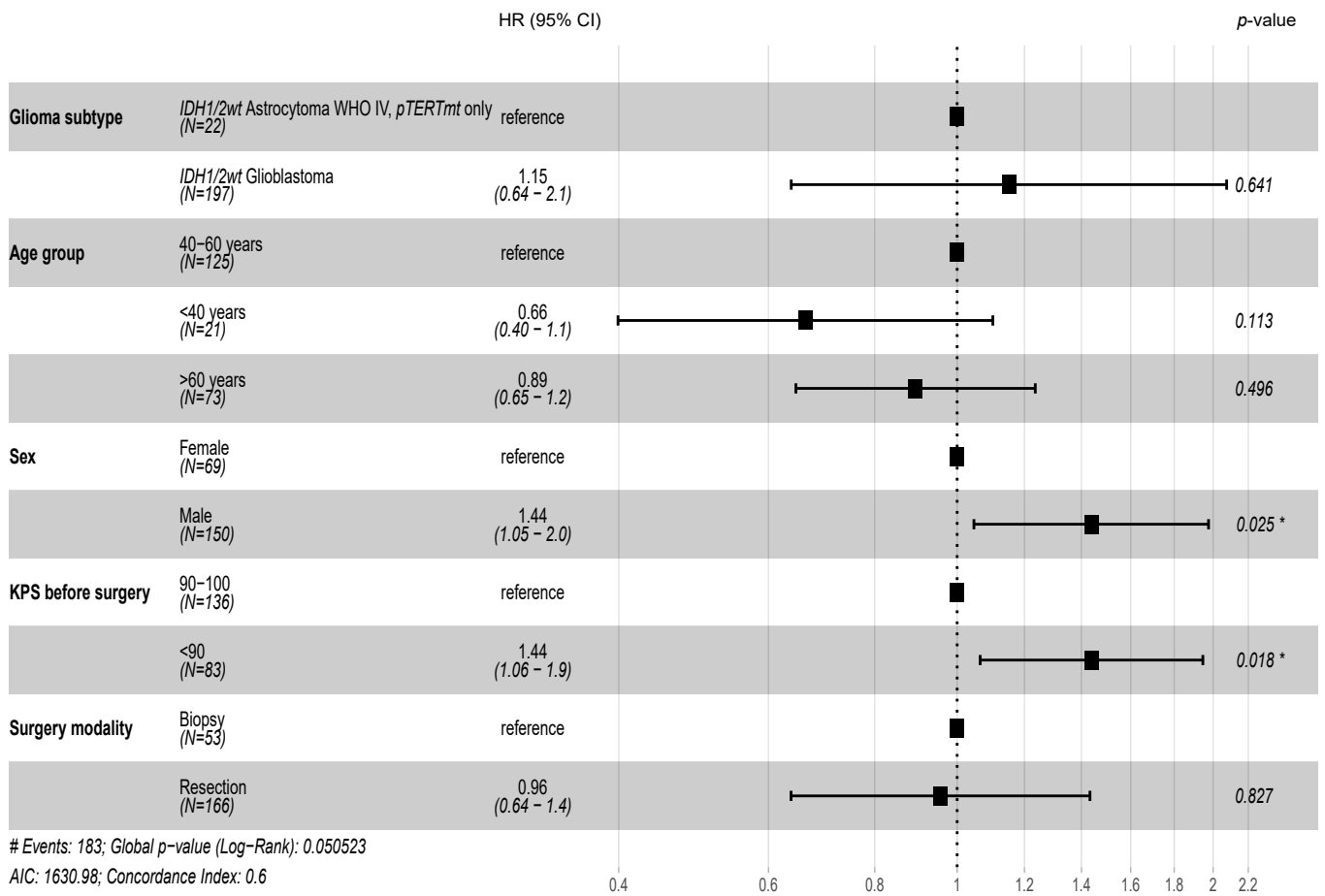
0.1   0.2   0.5   1   2   5

Supplementary Figure 2 Forest plot with hazard ratios of the multivariable analysis of OS for all *IDH1/2wt*

gliomas taking into account age, sex, KPS before surgery, surgery modality and primary treatment after surgery.
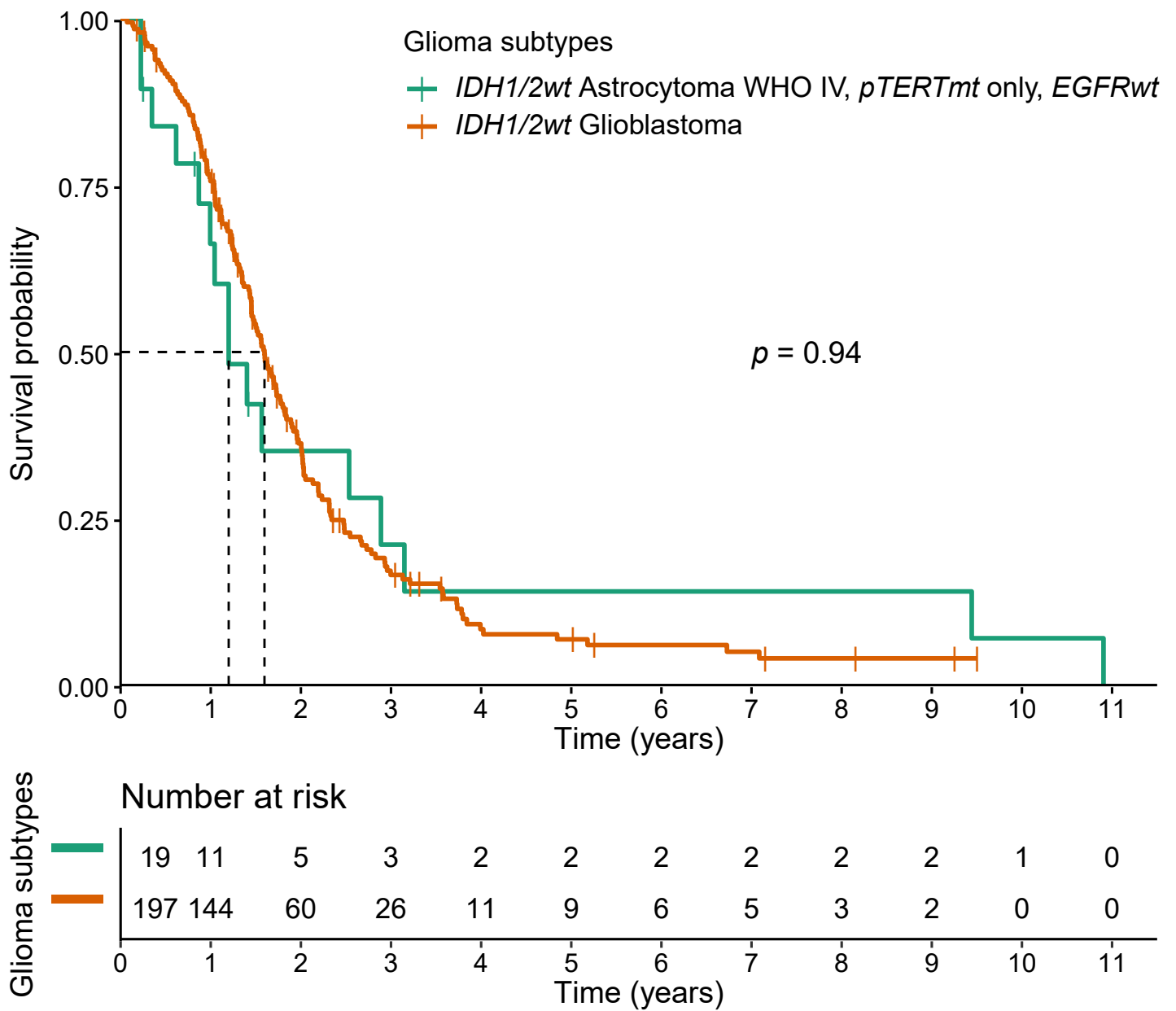
Supplementary Figure 3 Kaplan-Meier curves of the OS of the *IDH1/2wt* astrocytomas WHO IV, *pTERTmt* only and the *IDH1/2wt* glioblastomas. The dashed line represents the median OS.

Characteristics	HR	95% CI	p
Glioma subtype			0.900
IDH1/2wt Astrocytoma WHO IV, pTERTmt only	reference		
IDH1/2wt Glioblastoma	1.04	0.63-1.72	
Age			0.400
40-60 years	reference		
<40 years	0.70	0.43-1.16	
>60 years	0.93	0.68-1.28	
Sex			0.040
Female	reference		
Male	1.40	1.02-1.92	
KPS before surgery			0.030
90-100	reference		
≤80	1.40	1.04-1.89	
Surgery modality			0.800
Biopsy	reference		
Resection	0.96	0.67-1.36	

Supplementary Table 2 The univariate analysis of OS for the *IDH1/2wt* astrocytomas WHO IV, *pTERTmt* only and the *IDH1/2wt* glioblastomas taking into account the known prognostic factors for gliomas. The *p*-values of the likelihood ratio test are listed comparing the HR to the reference.

		HR (95% CI)		p-value
Glioma subtype	IDH1/2wt Astrocytoma WHO IV, pTERTmt only (N=22)	reference		
	IDH1/2wt Glioblastoma (N=197)	1.15 (0.64 − 2.1)		0.641
Age group	40−60 years (N=125)	reference		
	<40 years (N=21)	0.66 (0.40 − 1.1)		0.113
	>60 years (N=73)	0.89 (0.65 − 1.2)		0.496
Sex	Female (N=69)	reference		
	Male (N=150)	1.44 (1.05 − 2.0)		0.025 *
KPS before surgery	90−100 (N=136)	reference		
	<90 (N=83)	1.44 (1.06 − 1.9)		0.018 *
Surgery modality	Biopsy (N=53)	reference		
	Resection (N=166)	0.96 (0.64 − 1.4)		0.827

\# Events: 183; Global p-value (Log−Rank): 0.050523

AIC: 1630.98; Concordance Index: 0.6

0.4 0.6 0.8 1 1.2 1.4 1.6 1.8 2 2.2

Supplementary Figure 4 Forest plot with hazard ratios of the multivariable analysis of OS for the *IDH1/2wt* astrocytomas WHO IV, *pTERTmt* only and the *IDH1/2wt* glioblastomas taking into account age, sex, KPS before surgery and surgery modality.

Supplementary Figure 5 Kaplan-Meier curves of the OS of the *IDH1/2wt* glioblastomas and the *IDH1/2wt*

astrocytomas WHO IV, *pTERTmt* only excluding the *EGFRmt*. The dashed line represents the median OS.