

Supplementary table 5: Detailed analysis of the predictive accuracy for patient survival based on two different models using the Harrel's C index. Model 1 contains all biological parameters (IDH1 mutation, 1p19q LOH, MGMT promoter methylation) and histology (diagnosis AOA or AOD). This model is tested either without (model 1a) or with (model 1b) CIMP as a factor. Model 2 contains all biological factors (IDH1 mutation, 1p/19q LOH, MGMT methylation), clinical factors (age and performance status) and histology. This model is also tested either without (model 2a) or with (model 2b) CIMP as a factor. Final models are also presented in supplementary table 4.

Harrel's C index comparison

	Model 1	Model 2
without CIMP	0.672	0.738
with CIMP	0.713	0.751

Model 1: Multivariate analysis

Model 1a: Multivariate analysis

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
IDH1 mut	1	-1.15204	0.40521	8.0831	0.0045	0.316	0.143	0.699
1p19qLOH	1	-0.73626	0.42489	3.0026	0.0831	0.479	0.208	1.101
MGMT meth	1	0.04679	0.37182	0.0158	0.8999	1.048	0.506	2.172
AOA diagnosis	1	0.03066	0.40988	0.0056	0.9404	1.031	0.462	2.303

Model 1b: Multivariate analysis

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
IDH1 mut	1	-0.78273	0.5327	2.159	0.1417	0.457	0.161	1.299
1p19q LOH	1	-0.44785	0.50538	0.7853	0.3755	0.639	0.237	1.721
MGMT meth	1	0.17074	0.38324	0.1985	0.6559	1.186	0.56	2.514
AOA diagnosis	1	-0.01435	0.42132	0.0012	0.9728	0.986	0.432	2.251
CIMP	1	-0.63562	0.62001	1.051	0.3053	0.53	0.157	1.785

Model 1: Forward stepwise analysis to select for independent variables

Model 1a

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
IDH1 mut	1	-1.12126	0.33711	11.0632	0.0009	0.326	0.168	0.631
1p19qLOH	1	-0.73383	0.40225	3.328	0.0681	0.48	0.218	1.056

Model 1b

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
CIMP	1	-1.27729	0.32908	15.0652	0.0001	0.279	0.146	0.531

CIMP is the only factor selected for in this model.

Model 1: Frequency of selection for individual parameters after bootstrapping (1000 iterations)

Model 1a

Variable	Inclusion (#)	Inclusion (%)	Pos. incl. (#)	Pos. incl. (%)	Neg. incl. (#)	Neg. incl. (%)
IDH1 mutation	903	90.3	0	0	903	90.3
1p/19q LOH	550	55	1	0.1	549	54.9
MGMT	192	19.2	51	5.1	141	14.1
AOA diagnosis	285	28.5	217	21.7	68	6.8

Model 1b

Variable	Inclusion (#)	Inclusion (%)	Pos. incl. (#)	Pos. incl. (%)	Neg. incl. (#)	Neg. incl. (%)
IDH1 mutation	458	45.8	21	2.1	437	43.7
1p/19q LOH	197	19.7	10	1	187	18.7
MGMT	173	17.3	120	12	53	5.3
AOA diagnosis	284	28.4	206	20.6	78	7.8
CIMP	692	69.2	9	0.9	683	68.3

Model 1: Top 10 models based on 1000 bootstraps

Model 1a

Model ranking	IDH1 mut	1p/19q LOH	MGMT meth	AOA diagnosis	Frequency Count	Frequency %
1	1	1	0	0	309	30.9
2	1	0	0	0	248	24.8
3	1	0	0	1	108	10.8
4	1	1	0	1	96	9.6
5	1	1	1	0	54	5.4
6	1	0	1	1	43	4.3
7	0	1	0	0	35	3.5
8	1	0	1	0	24	2.4
9	0	0	1	0	23	2.3
10	0	1	1	0	21	2.1

1 denotes selected for in the respective model

Model 1b

Model ranking	IDH1 mut	1p/19q LOH	MGMT meth	AOA diagnosis	CIMP	Frequency Count	Frequency %
1	0	0	0	0	1	291	29.2
2	0	0	0	1	1	117	11.7
3	1	0	0	0	0	112	11.2
4	1	0	0	0	1	77	7.7
5	1	1	0	0	0	72	7.2
6	0	0	1	0	1	51	5.1
7	1	0	0	1	0	48	4.8
8	0	0	1	1	1	28	2.8
9	1	0	0	1	1	25	2.5
10	0	1	0	0	1	23	2.3

1 denotes selected for in the respective model

Model 1: Final model

Model 1a

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter		Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
		Estimate	Standard Error					
IDH1 mut	1	-1.07224	0.32767	10.7078	0.0011	0.342	0.18	0.651
1p19qLOH	1	-0.76673	0.40112	3.6536	0.0559	0.465	0.212	1.02

Model 1b

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter		Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
		Estimate	Standard Error					
CIMP	1	-1.46169	0.31732	21.2192	<.0001	0.232	0.124	0.432

Harrel's C index comparison

	Model 1	Model 2
without CIMP	0.672	0.738
with CIMP	0.713	0.751

Model 2: Multivariate analysis

Model 2a without CIMP

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter	Standard	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
		Estimate	Error					
Performance Status	1	0.74332	0.23043	10.4061	0.0013	2.103	1.339	3.303
Age >50	1	1.2662	0.38637	10.7398	0.001	3.547	1.664	7.565
IDH1 mut	1	-1.94528	0.50354	14.9244	0.0001	0.143	0.053	0.384
1p19q LOH	1	-0.6575	0.44417	2.1912	0.1388	0.518	0.217	1.237
MGMT meth	1	0.12483	0.37511	0.1108	0.7393	1.133	0.543	2.363
AOA diagnosis	1	0.52644	0.45595	1.3331	0.2482	1.693	0.693	4.137

Model 2b with CIMP:

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter	Standard	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
		Estimate	Error					
Performance Status	1	0.76092	0.23295	10.6697	0.0011	2.14	1.356	3.379
Age >50	1	1.2135	0.39251	9.558	0.002	3.365	1.559	7.263
IDH1 mut	1	-1.64276	0.65104	6.3669	0.0116	0.193	0.054	0.693
1p19q LOH	1	-0.45413	0.52509	0.748	0.3871	0.635	0.227	1.777
MGMT meth	1	0.20201	0.3853	0.2749	0.6001	1.224	0.575	2.604
AOA diagnosis	1	0.48659	0.46725	1.0845	0.2977	1.627	0.651	4.065
CIMP	1	-0.47552	0.65645	0.5247	0.4688	0.622	0.172	2.25

Model 2: Forward stepwise analysis to select for independent variables

Model 2a without CIMP

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter	Standard	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
		Estimate	Error					
Performance Status	1	0.70536	0.2267	9.6813	0.0019	2.025	1.298	3.157
Age >50	1	1.14852	0.36705	9.7911	0.0018	3.154	1.536	6.475
IDH1 mut	1	-1.68217	0.40343	17.3861	<.0001	0.186	0.084	0.41
1p19q LOH	1	-0.7955	0.41825	3.6175	0.0572	0.451	0.199	1.025

Model 2b with CIMP

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter	Standard	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
		Estimate	Error					
Performance Status	1	0.62881	0.21905	8.2404	0.0041	1.875	1.221	2.881
Age >50	1	1.22771	0.37475	10.7324	0.0011	3.413	1.638	7.115
IDH1 mut	1	-1.85629	0.40594	20.9106	<.0001	0.156	0.071	0.346

Model 2: Frequency of selection for individual parameters after bootstrapping (1000 iterations)

Model 2a without CIMP

Variable	Inclusion (#)	Inclusion (%)	Pos. incl. (#)	Pos. incl. (%)	Neg. incl. (#)	Neg. incl. (%)
Performance Status	940	94	940	94	0	0
Age >50	928	92.8	928	92.8	0	0
IDH1 mut	976	97.6	0	0	976	97.6
1p/19q LOH	500	50	1	0.1	499	49.9
MGMT meth	215	21.5	95	9.5	120	12
AOA diagnosis	437	43.7	424	42.4	13	1.3

Model 2: Top 10 models based on 1000 bootstraps

Model 2a without CIMP

Model ranking	Performance Status	Age >50	IDH1 mut	1p/19q LOH	MGMT meth	AOA diagnosis	Frequency Count	Frequency %
1	1	1	1	1	0	0	256	25.6
2	1	1	1	0	0	1	219	21.9
3	1	1	1	0	0	0	146	14.6
4	1	1	1	1	0	1	88	8.8
5	1	1	1	0	1	1	71	7.1
6	1	1	1	1	1	0	44	4.4
7	1	1	1	1	1	1	32	3.2
8	1	0	1	1	0	0	27	2.7
9	1	1	1	0	1	0	15	1.5
10	0	1	1	0	0	0	13	1.3

Model 2: Final model

Model 2a without CIMP

Analysis of Maximum Likelihood Estimates								
Parameter	DF	Parameter	Standard	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
		Estimate	Error				Lower	Upper
Performance Status	1	0.60539	0.22101	7.5034	0.0062	1.832	1.188	2.825
Age >50	1	1.08093	0.35503	9.2698	0.0023	2.947	1.47	5.911
IDH1 mut	1	-1.60217	0.39014	16.865	<.0001	0.201	0.094	0.433
1p19q LOH	1	-0.77594	0.41146	3.5563	0.0593	0.46	0.205	1.031