The DCCC Brain Tumor Center

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Prediction of distant recurrence in glioblastoma patients treated with standard therapy

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Background

Migratory growth is a hallmark of glioblastoma (GBM) and is a major factor in therapeutic failure.

Hypothesis: Biomarkers that predict distant recurrence (migratory growth) can be used to personalize the treatment of GBM patients

Related Abstracts:

Abstract #: BIOM-39, Fougner VN et al.

Abstract #: CTNI-32, Fougner VN et al.

Method

Patients

Two prospective cohorts of consecutive, non-selected GBM IDHwt patients treated with standard therapy between 2005-2016 (cohort 1) and 2016-2021 (cohort 2) at Rigshospitalet, Copenhagen were included.

Patterns of recurrence

Distant recurrence = new tumor lesion outside the radiotherapy (RT) field (Figure 1).

Statistics

Cox regression analysis was used to model the association with time to distant recurrence.

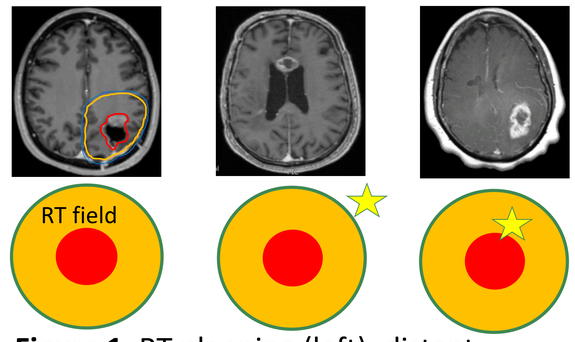


Figure 1. RT planning (left); distant recurrence (middle); local recurrence (right)

Aim

Identify clinical and molecular factors associated with distance recurrence of glioblastoma

Results

Figure 2. Overall survival and pattern of recurrence

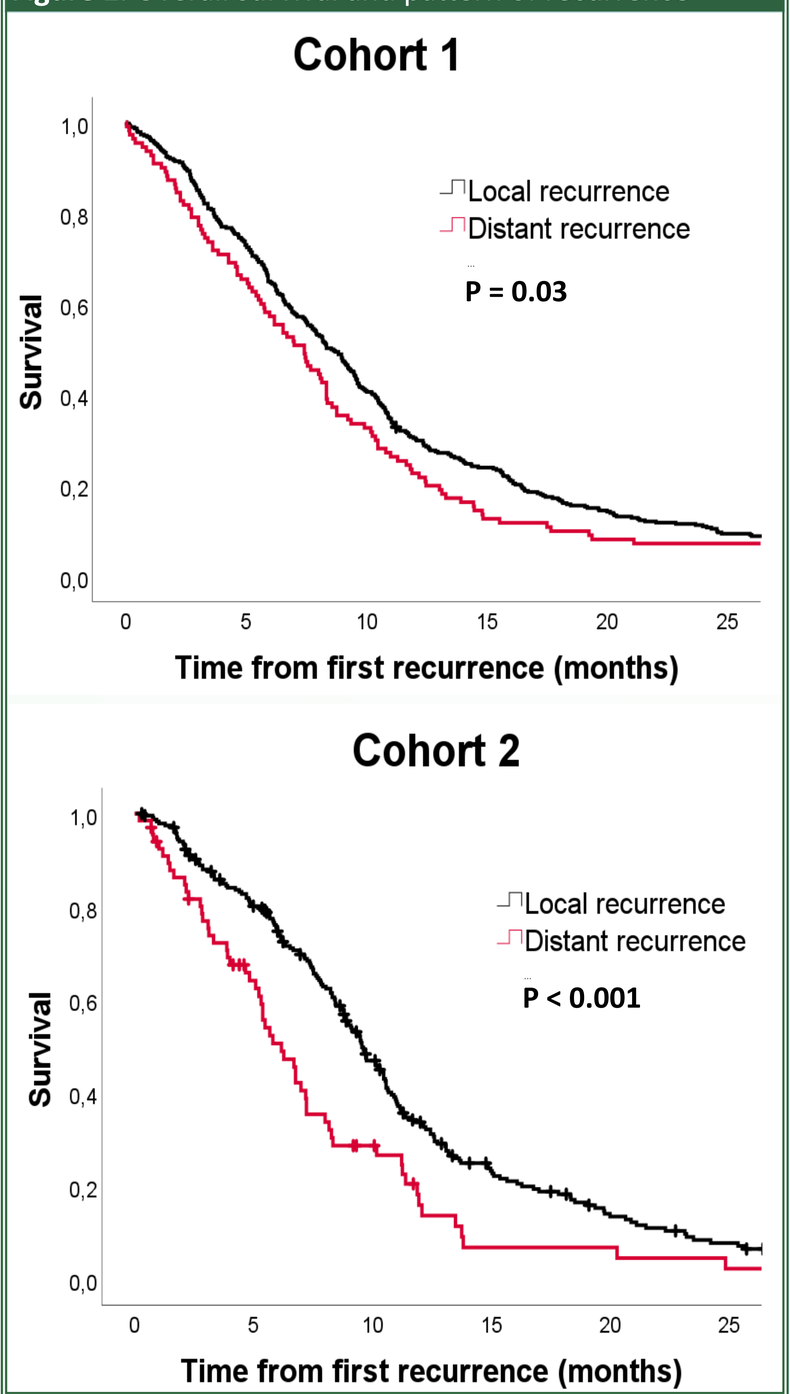


Table 1. Patient characteristics

	Cohort 1 n = 628	Cohort 2 n = 395	p-value
Median age, years (range)	60 (22-79)	59 (17-77)	0.13
Gender, Male, n (%)	393 (66)	220 (62)	0.27
PS, n (%)			
0	364 (62)	209 (60)	0.56
1	192 (32)	124 (35)	
2	35 (6)	17 (5)	
Multifocal, n (%)	75 (13)	45 (13)	0.94
Steroid use, n (%)	354 (60)	161 (46)	<0.001
Resection, n (%)			
Biopsy	83 (14)	65 (19)	0.07
Resection	507 (86)	287 (81)	
MGMT methylated, n (%)	260 (53)	148 (42)	<0.001
Positive P53, n (%)	379 (75)	215 (68)	0.02
Positive EGFR, n (%)	417 (82)	NR	-
Distant recurrence pattern, n (%)	110 (23)	67 (22)	0.82
Median PFS (95% CI)	7.1 (6.5-7.6)	7.5 (6.8-8.2)	0.28
Median OS (95% CI)	15.1 (14.1-16.1)	17.2 (15.8-18.6)	0.01
Resection at recurrence	228 (41)	114 (34)	0.04
Second line treatment	316 (54)	241 (74)	<0.001

Table 2. Selected biomarkers associated with distant recurrence (Univariate)

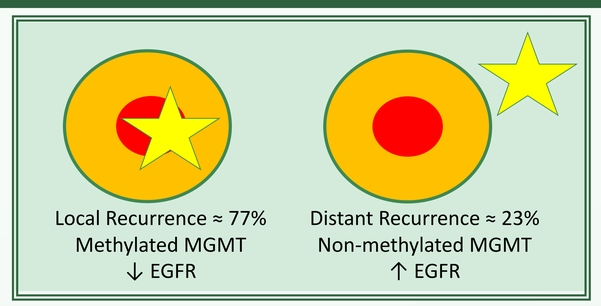
	Cohort 1: HR (95% CI)	Cohort 2: HR (95% CI)
Age (10-years increase)	1.02 (0.86-1.22) *P* = 0.80	0.93 (0.75-1.15) *P* = 0.51
Multifocal	1.48 (0.79-2.78) *P* = 0.22	1.69 (0.80-3.57) *P* = 0.17
Subependymal localisation	NR	0.78 (0.46-1.31) *P* = 0.35
Non-methylated MGMT	2.03 (1.35-3.05) ***P* <0.001**	2.21 (1.30-3.74) ***P* = 0.003**
P53 expression	0.71 (0.46-1.10) *P* = 0.13	0.54 (0.32-0.91) *P* = 0.02
EGFR expression	1.96 (1.02-3.78) ***P* = 0.04**	NR

Table 3. Biomarkers associated with time to distant recurrence (Multivariate)

	Cohort 1: HR (95% CI)	Cohort 2: HR (95% CI)
Age (10-years increase)	0.87 (0.70-1.09) *P* = 0.23	1.06 (0.85-1.33) *P* = 0.61
Performance status 1-2 vs. 0	1.38 (0.86-2.21) *P* = 0.18	0.95 (0.55-1.66) *P* = 0.86
Multifocal disease	1.08 (0.51-2.27) *P* = 0.84	2.05 (0.94-4.46) *P* = 0.07
Corticosteroid use	1.55 (0.97-2.48) *P* = 0.07	0.89 (0.52-1.52) *P* = 0.66
Biopsy	1.50 (0.78-2.90) *P* = 0.22	1.71 (0.85-3.46) *P* = 0.13
Non-methylated MGMT	2.48 (1.60-3.85) ***P* < 0.001**	2.70 (1.52-4.80) ***P* < 0.001**
EGFR expression	4.84 (2.03-11.58) ***P* < 0.001**	NR

Conclusion

- Distant recurrence occurs in ≈20% of patients
- Distant recurrence predicts poor prognosis
- Clinical factors did not predict distant recurrence
- EGFR and MGMT were associated with distant recurrence



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