Supplementary Table S1: Kinetics of imaging and plasma biomarkers (pg/ml) – that are mechanistically related to tumor vascular normalization – after cediranib treatment in the recurrent GBM patients. Data are shown as medians and interquartile ranges (in square brackets) measured pre-treatment (Pre-Tx) and 1 day post-treatment.

Biomarker	Pre-Tx	Day 1
K^{trans} (MRI[1])	0.095* [0.062 – 0.155] (N=30)	0.033 [0.017 – 0.044] (N=29)
P-value[2]	N/A	<0.0001
CBV small vessels (MRI)	0.7* [0.5 – 0.8] (N=30)	0.6 [0.5 – 0.7] (N=29)
P-value	N/A	<0.0001
Vessel caliber (MRI)	7.29 [6.15 – 7.95] (N=30)	6.64 [5.80 – 7.56] (N=30)
P-value	N/A	0.0098
ADC (MRI)	1287 [1218 – 1406] (N=30)	1289 [1206 – 1361] (N=30)
P-value	N/A	<0.0001
FLAIR (MRI)	126 [96 – 162] (N=30)	144 [93 – 170] (N=30)
P-value	N/A	0.90
v_e (MRI)	0.095 [0.042 – 0.209] (N=29)	0.054 [0.030 – 0.110] (N=27)
P-value	N/A	0.06
Plasma Ang1 (ELISA)	2658 [1496,4674] (N=28)	1778 [1298,6359] (N=28)
P-value	N/A	0.92
Plasma Ang2 (ELISA)	1532 [1229,1858] (N=31)	1485 [1161, 1923] (N=31)
P-value	N/A	0.23
Plasma MMP-2 (ELISA)	1378 [855,1937] (N=25)	1157 [809,1507] (N=25)
P-value	N/A	0.0020
Plasma Collagen IV (ELISA)	0.17 [0.16 – 0.18] (N=30)	0.16 [0.13 – 0.17] (N=30)
P-value	N/A	0.0041

[1]Double baseline MRI scans were performed and reported previously in a subset of patients (Batchelor et al, Cancer Cell 2007). The mean K^{trans} on the other baseline was 0.098 and the mean CBV on the other baseline was 0.68, indicating good reproducibility.

[2]P-values are from the paired exact Wilcoxon test.

Supplementary Table S2: Multivariable models of association between log-transformed changes at day 1 after cediranib treatment in K^{trans}, collagen IV, and microvascular CBV with radiographic progression of disease and mortality in patients with recurrent GBM. Data are shown as hazard ratios with 95% confidence intervals (in square brackets).

Biomarker	Progression	Mortality
log(Ktrans.ch)	2.5 [1.4,4.4] P=0.0015	2.3 [1.3,4.0] P=0.0039
log(ColIV.ch)	0.00077 [0.000011,0.056] P=0.0010	0.14 [0.0033,6.2] P=0.3115
log(CBV.ch)	0.073 [0.0024,2.2] P=0.1326	0.0071 [0.00021,0.23] P=0.0056

Abbreviations: log(ktrans.ch): ratio of day 1 to baseline K^{trans} (log-transformed); log(coliv.ch): ratio of day 1 to baseline Collagen IV (log-transformed); log(cbvs.ch): ratio of day 1 to baseline cerebral blood volume (log-transformed).

Supplementary Table S3: Multivariable models of association between RPA class, log-transformed baseline CE-T1 volume, and changes at day 1 after cediranib treatment in K^{trans}, collagen IV, and microvascular CBV with radiographic progression of disease and mortality in patients with recurrent GBM. Data are shown as hazard ratios with 95% confidence intervals (in square brackets).

Biomarker	Progression	Mortality
RPA	0.58 [0.29,1.1] P=0.1179	1.5 [0.80,2.8] P=0.2067
CE-T1v	0.69 [0.34,1.4] P=0.3056	0.79 [0.41,1.5] P=0.4689
log(Ktrans.ch)	3.5 [1.7,7.4] P=0.0008	2.4 [1.3,4.5] P=0.0059
log(ColIV.ch)	0.00068 [0.0000091,0.051] 0.0009	0.082 [0.0018,3.6] P=0.1962
log(CBV.ch)	0.014 [0.00032,0.66] P=0.0295	0.0040 [0.000063,0.25] P=0.0089

Abbreviations: RPA: recursive partitioning analysis; log(CE-T1v) enhancing tumor volume at baseline (log-transformed); log(ktrans.ch): ratio of day 1 to baseline K^{trans} (log-transformed); log(coliv.ch): ratio of day 1 to baseline Collagen IV (log-transformed); log(cbvs.ch): ratio of day 1 to baseline cerebral blood volume (log-transformed).

Supplementary Table S4: The residual deviance table for six-month progression-free survival of disease for three parameters

	Df	Deviance Resid.	Df	Resid. Dev	P(>|Chi|)
NULL			28	134.393	
log(ktrans.ch)	1	6.855	27	127.538	0.009
log(coliv.ch)	1	9.347	26	118.191	0.002
log(cbvs.ch)	1	2.193	25	115.998	0.139

Abbreviations: Df: degrees of freedom (associated with added variable, and of the model, respectively); Deviance Resid: deviance residual contributed by the added variable; Resid. Dev: residual deviance of the model or partial log likelihood; P(>|Chi|): P-value from the likelihood ratio test; NULL: model with no covariates; log(ktrans.ch): ratio of day 1 to baseline Ktrans (log-transformed); log(coliv.ch): ratio of day 1 to baseline Collagen IV (log-transformed); log(cbvs.ch): ratio of day 1 to baseline cerebral blood volume (log-transformed).

Supplementary Table S5: The residual deviance table for overall survival for three parameters

	Df	Deviance Resid.	Df	Resid. Dev	P(>|Chi|)
NULL			28	134.393	
log(ktrans.ch)	1	6.142	27	128.251	0.013
log(coliv.ch)	1	0.002	26	128.249	0.961
log(cbvs.ch)	1	7.137	25	121.112	0.008

Abbreviations: Df: degrees of freedom (associated with added variable, and of the model, respectively); Deviance Resid: deviance residual contributed by the added variable; Resid. Dev: residual deviance of the model or partial log likelihood; P(>|Chi|): P-value from the likelihood ratio test; NULL: model with no covariates; log(ktrans.ch): ratio of day 1 to baseline Ktrans (log-transformed); log(coliv.ch): ratio of day 1 to baseline Collagen IV (log-transformed); log(cbvs.ch): ratio of day 1 to baseline cerebral blood volume (log-transformed).

Supplementary Table S6: The residual deviance table for six-month progression-free survival for five parameters

	Df	Deviance Resid.	Df	Resid. Dev	P(>|Chi|)
NULL			28	134.393	
RPA class	1	0.987	27	133.407	0.321
log(CE-T1v)	1	0.209	26	133.198	0.648
log(ktrans.ch)	1	8.030	25	125.168	0.005
log(coliv.ch)	1	8.156	24	117.011	0.004
log(cbvs.ch)	1	4.546	23	112.466	0.033

Abbreviations: Df: degrees of freedom (associated with added variable, and of the model, respectively); Deviance Resid: deviance residual contributed by the added variable; Resid. Dev: residual deviance of the model or partial log likelihood; P(>|Chi|): P-value from the likelihood ratio test; NULL: model with no covariates; RPA: recursive partitioning analysis; log(CE-T1v): enhancing tumor volume at baseline (log-transformed); log(ktrans.ch): ratio of day 1 to baseline K^{trans} (log-transformed); log(coliv.ch): ratio of day 1 to baseline Collagen IV (log-transformed); log(cbvs.ch): ratio of day 1 to baseline cerebral blood volume (log-transformed).

Supplementary Table S7: The residual deviance table for overall survival for five parameters

	Df	Deviance Resid.	Df	Resid. Dev	P(>|Chi|)
NULL			28	134.393	
RPA class	1	0.987	27	133.406	0.159
log(CE-T1v)	1	0.209	26	131.544	0.353
log(ktrans.ch)	1	6.142	27	125.914	0.018
log(coliv.ch)	1	0.002	26	125.574	0.560
log(cbvs.ch)	1	7.137	25	119.027	0.011

Abbreviations: Df: degrees of freedom (associated with added variable, and of the model, respectively); Deviance Resid: deviance residual contributed by the added variable; Resid. Dev: residual deviance of the model or partial log likelihood; P(>|Chi|): P-value from the likelihood ratio test; NULL: model with no covariates; RPA: recursive partitioning analysis; log(CE-T1v): enhancing tumor volume at baseline (log-transformed); log(ktrans.ch): ratio of day 1 to baseline K^{trans} (log-transformed); log(coliv.ch): ratio of day 1 to baseline Collagen IV (log-transformed); log(cbvs.ch): ratio of day 1 to baseline cerebral blood volume (log-transformed).

Supplementary Figure Legend

Supplementary Figure S1: Kaplan-Meier estimate of the progression-free survival function after cediranib treatment in recurrent glioblastoma patients (n=31). The figures show regression lines with 95% predictive confidence intervals.

Supplementary Figure S2: Kaplan-Meier estimate of the overall survival function after cediranib treatment in recurrent glioblastoma patients (n=31). The figures show regression lines with 95% predictive confidence intervals.

Supplementary Figure S3: Univariate analyses for correlation between parameters related to vascular normalization and survival outcomes. The ratio of K^{trans} values measured at day 1 and baseline are significantly correlated with progression-free survival (PFS) at 3, 4.5, and 6 months (**a**) and overall survival (OS) at 6, 9, and 12 months (**b**) after treatment onset. The extent of circulating collagen IV change at day 1 is significantly correlated with PFS at 3, 4.5, and 6 months (**c**), and the extent of microvessel CBV change at day 1 is significantly correlated with OS at 6, 9, and 12 months (**d**).

Supplementary Figure S4: Plots depicting association (hazard ratios with 95% confidence intervals obtained in a multivariable Cox regression) between changes in K^{trans}, CBV, collagen IV, CE-T1 tumor enhancement volume and RPA (recursive partitioning analysis) class and survival outcomes. (**a**) Correlations with progression-free survival (PFS) at six months. (**b**) Correlations with overall survival OS at one year.