

Table SI. Demographics and clinical characteristics of each patient.

Patient no.	Sex	Age at first surgery, years	Histology	IDH mutation	MGMTp met	Other treatment	Age at start of FTM, years	FTM			survival after FTM start, months	Survival after FTM end, months	Comorbidity
								First reason for interruption	Duration of therapy, months	Survival from diagnosis, months			
1	F	58	GBM	0	1	None	59	AE	2.3	11	4	2	None
2	M	42	GBM	0	1	4 surgeries	44	NA	6.8	39	15	8	None
3	M	71	GBM	0	1	None	72	NA	7.4	17	10	2	None
4	M	38	Grade IV astrocytoma IDH mut	1	0	CK	40	PD	2.5	22	4	1	None
5	M	48	GBM	0	1	None	49	NA	7.1	72	48	41	None
6	F	51	GBM	0	NK	CK	54	NA	7.8	65	24	16	None
7	F	47	GBM	0	1	None	49	AE	0.7	23	5	4	Osteoporosis
8	M	34	GBM	0	1	None	35	PD	6.3	24	11	5	None
9	M	44	GBM	0	0	None	46	PD	1.9	31	5	3	None
10	M	61	GBM	0	1	CK	62	PD	3.8	19	5	2	None
11	F	23	GBM	0	0	None	23	AE	5.6	15	14	8	None
12	F	65	GBM	0	0	2 surgeries	66	PD	3.5	21	10	6	None
13	M	41	GBM	0	NK	3 surgeries	45	PD	6.4	62	16	10	None

14	F	48	Grade IV astrocytoma IDH mut	1	NK	None	48	Therapy changed due to no peripheral venous thrombosis	5.4	24	17	12	None
15	M	44	GBM	0	NK	CK	45	PD	0.9	19	4	3	HBP
16	F	56	GBM	0	1	2 surgeries + CK	61	AE	0.9	65	4	3	None
17	M	55	GBM	0	1	2 surgeries + CK	57	PD	2.1	27	4	2	Breast benign nodule
18	M	47	GBM	0	0	2 surgeries	51	PD, AE	1.5	61	12	10	None
19	M	69	GBM	0	1	None	71	PD	4.1	29	9	5	HBP, ADD

ADD; anxiety-depressive disorder; AVNRT, atrial-ventricular nodal reentrant tachycardia; GBM, glioblastoma; CK, cyber-knife; FTM, fotemustine; IDH mut, isocitrate dehydrogenase mutated (0, no; 1, yes); NK, not known; MGMTp met, O<sup>6</sup>-methylguanine-DNA methyltransferase promoter methylation (1, methylated; 0, unmethylated); HBP, high blood pressure; NA, not applicable (indicating the case completed the FTM schedule as planned according to the Addeo schedule); PD, Progressive Disease; AE, adverse event; M, male; F, female.

Table SII. Treatment details and related AEs.

Patient no.	FTM induction		FTM maintenance		Presence	AEscausing FTM interruption AE type (1, hematological; 2,aspartate aminotransferase increase; 3, lung embolism)
	Cycles, n	Dose (R, regular; M, modified)	Cycles, n	Dose (R, regular; M, modified)		
1	4	M <sup>a</sup>	0	NA	Y	1 (leucopenia), 3
2	5	R	5	R	N	NA
3	5	R	4	M <sup>b</sup>	Y	1 (leucopenia)
4	4	R	0	NA	N	NA
5	5	R	5	R	N	NA
6	5	R	5	R	N	NA
7	3	R	0	NA	Y	1 (leucopenia)
8	5	R	3	R	N	NA
9	5	R	0	NA	N	NA
10	5	R	1	R	N	NA
11	5	R	3	R	Y	2
12	5	M <sup>a</sup>	0	NA	N	1 (leucopenia)
13	5	R	3	R	N	NA
14	5	R	3	R	N	NA
15	3	R	0	NA	N	NA
16	3	R	0	NA	Y	1 (leucopenia)
17	5	R	0	NA	N	NA
18	4	R	0	NA	Y	1 (leucopenia, thrombocytopenia)
19	4	M <sup>b</sup>	0	NA	Y	1 (thrombocytopenia)

AE, adverse event; FTM schedule modification: <sup>a</sup>Postponed FTM dose; <sup>b</sup>FTM dose reduction. FTM, fotemustine; Y, yes; N, no; NA, not applicable.

Table SIII. Volume and ADC values at baseline and follow-up, and relative percentage change.

Patient no.	Baseline		Follow-up		Difference vol, %	Difference ADC, %	Classification according to RANO criteria
	Volume CET, mm <sup>3</sup>	ADC <sup>10</sup> , x10 <sup>-3</sup> mm <sup>2</sup> /sec	Volume CET, mm <sup>3</sup>	ADC <sup>10</sup> , x10 <sup>-3</sup> mm <sup>2</sup> /sec			
1	15227	0.888	13724	0.832	-10	-6	SD
2	0	1.197	4354	1.241	NA <sup>a</sup>	4	PD
3	1844	1.008	2556	1.412	39	40	PD
4	6459	0.036	9271	0.698	44	1843	PD
5	0	0.998	288	0.766	NA <sup>a</sup>	-23	PD
6	2216	0.824	294	1.061	-87	29	PR
7	30380	0.852	13280	0.929	-56	9	PR
8	8858	1.091	59680	1.196	574	10	PD
9	689	1.060	85760	0.973	12347	-8	PD
10	3878	0.875	4557	1.215	18	39	SD
11	76	1.276	735	1.106	867	-13	PD
12	46	0.891	25	1.271	-46	43	SD
13	1206	1.164	7130	1.152	491	-1	PD
14	27169	0.250	9539	0.264	-65	6	PR
15	920	1.111	19670	0.926	2038	-17	PD
16	21120	1.093	9934	0.759	-53	-31	PR
17	22721	1.131	54713	1.041	141	-8	PD
18	11110	0.991	9178	0.989	-17	0	SD
19	846	1.182	60450	0.915	7045	-23	PD

<sup>a</sup>Since the baseline volume was 0, the percentage change in volume was not computable. ADC<sup>10</sup>, tenth percentile of Apparent Diffusion Coefficient; CET, Contrast-Enhancing Tumors; vol, volume; NA, not available. RANO, Response Assessment in Neuro-Oncology (26); PD, progressive disease; SD, stable disease; PR, partial response.

Table SIV. Comparison of radiological changes and disease control rate after FTM treatment according to MGMTp methylation status.

Characteristic	MGMTp methylated (n=10)	MGMTp unmethylated (n=5)	P-value
CET volume difference, %			
median	+28%	+43%	0.622
IQR	-21% to +249%	-17% to +867%	
range	-56% to +7045%	-46% to +12347%	
ADC <sup>10</sup> difference, %			
median	-1%	0%	0.513
IQR	-19% to +9%	-8% to +43%	
range	-31% to +40%	-13% to 1843%	
RANO classification, n. of patients			
PR	6	3	-
SD	2	2	
PR	2	0	
DCR, %	40%	40%	-

P-values were computed with Mann-Whitney test. CET, Contrast-Enhancing Tumor; IQR, interquartile range; ADC<sup>10</sup>, 10th percentile of apparent diffusion coefficient; MGMTp, O(6)-methylguanine-DNA methyltransferase promotor; RANO, Response Assessment in Neuro-Oncology; PD, Progressive Disease; SD, Stable Disease; PR, Partial Response; DCR, Disease Control Rate.