

Supplementary Information

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author names: Taketo Ezaki

affiliation and e-mail address of the corresponding author:

Toshihide Tanaka, MD, PhD

Department of Neurosurgery, Jikei University School of Medicine

3-25-8 Nishi-Shinbashi, Minato-ku, Tokyo 105-8461, Japan

TEL: +81-3-3433-1111 (ext. 3461); FAX: +81-3-3459-6412

E-mail: ttanaka@jikei.ac.jp

Supplement Table 1

Characteristics of patients stratified by responsiveness of Bev

Characteristic	timing for obtaining of samples during Bev therapy		
	naïve Bev (n=25)	effective Bev (n=15)	refractory Bev (n=14)
Age: Median (years old) [range],yr	55 [29-79]	68 [48-80]	52 [29-77]
Male (n)	18	9	8
Female (n)	7	6	6
no. cycles of neo-adjuvant Bev	0	1 Time, 11 2 Times, 1 3 Times, 3	
Interval between last Bev to surgery/autopsy (days) [range]		23 [15-51]	33 [5-208]
no. cycles of Bev: median [range]	3 [1-24]	9 [0-28]	
no. cycles of TMZ: median [range]	12 [1-28]	8 [1-24]	
<i>IDH-1</i> wild status: (n)	23	14	
Methylation status of promoter region of <i>MGMT</i> (n)	6	2	
MRI pattern of recurrence			
cT1-Flare up (n)	6	8	
T2 diffuse / T2 circumscribed (n)	10	6	
non-responder (n)	4	0	

no: Number

Bev: Bevacizumab

TMZ: Temozolomide

IDH: isocitrate dehydrogenase

MGMT: O6-methylguanine-DNA methyltransferase

Supplement Table2

Characteristics of genetic status, content of chemotherapy, and number of angiogenic factors positive cells

	Case	age/sex	genetic status		no. cycles of Bev/TMZ			MRI pattern of recurrence	number of angiogenic factors positive cell in tumor vessels				
			IDH-1 status	MGMT status	no. cycles of neo-adjutant Bev	no. cycles of Bev	no. cycles of TMZ		ANGPT1	ANGPT2	FGF2	EFNA2	PLGF
Naïve Bev	N1 N1-Rs	29/F	WT	N/A		19	3	non-responder	3	0	0	2	0
	N2 N2-Rs	67/M	WT	N/A		21	19	T2 circumscribed	0	0	0	6	11
	N3 N3-Rs	51/F	WT	N/A		18	16	cT1 flare-up	1	0	0	0	0
	N4 N4-Rs	50/F	WT	N/A		14	20	non-responder	13	16	14	0	8
	N5 N5-Rs	52/F	WT	N/A		9	16	T2 diffuse	8	30	0	0	0
	N6 N6-Rs	73/M	WT	N/A		13	26	T2 diffuse	0	12	6	5	0
	N7 N7-Rs	52/M	WT	N/A		20	41	T2 diffuse	3	28	35	0	8
	N8 N8-Rs	33/F	WT	N/A		27	4	non-responder	0	8	0	5	10
	N9 N9-Rs	41/M	WT	N/A		26	26	T2 diffuse	4	21	21	1	4
	N10 N10-Rs	51/M	WT	N/A		9	15	T2 circumscribed	0	0	5	6	0
	N11 N11-Rs	56/M	WT	N/A		28	21	cT1 flare-up	3	18	6	0	0
	N12	36/M	R132H mut	Met		0	7	non-responder	0	2	0	0	0
	N13	51/M	WT	Met		2	2	N/A	0	0	4	0	5
	N14	77/M	WT	Met		3	13	N/A	5	0	33	0	0
	N15	44/M	WT	Unmet		19	6	T2 circumscribed	8	7	6	0	0
	N16	72/M	WT	Unmet		0	11	cT1 flare-up	10	12	7	6	5
	N17	57/M	WT	Met		0	0	cT1 flare-up	0	18	6	0	9
	N18	64/F	WT	Unmet		0	11	cT1 flare-up	1	0	0	0	0
	N19	55/M	WT	Unmet		N/A	14	T2 diffuse	10	8	44	2	0
	N20	66/M	WT	Unmet		0	5	T2 circumscribed	6	7	8	20	6
	N21	79/M	WT	Met		0	12	N/A	6	7	21	0	0
	N22	59/M	WT	Unmet		0	1	cT1 flare-up	0	0	2	4	0
	N23	48/M	WT	Unmet		11	11	N/A	0	7	2	0	0
	N24	56/M	WT	Met		0	6	N/A	8	10	22	20	0
	N25	71/F	WT	Unmet		0	14	N/A	4	6	0	0	0
	Case	age/sex	genetic status		no. cycles of Bev/TMZ			MRI pattern of recurrence	number of angiogenic factors positive cell in tumor vessels				
			IDH-1 status	MGMT status	no. cycles of neo-adjutant Bev	no. cycles of Bev	no. cycles of TMZ		Ang1	Ang2	bFGF	EphrinA2	PIGF
Effective Bev	E1	48/M	R132H mut	Met	3	3	3	cT1 flare-up	1	7	0	12	0
	E2 E2-Rs	51/M	WT	Unmet	2	2	2	cT1 flare-up	0	11	9	9	21
	E3 E3-Rs	55/M	WT	N/A	1	18	38	T2 diffuse	8	20	14	10	4
	E4	68/M	WT	N/A	1	1	0	T2 diffuse	6	22	12	15	8
	E5 E5-Rs	77/F	WT	N/A	1	9	17	T2 circumscribed	0	0	6	11	18
	E6	68/M	WT	N/A	1	24	35	cT1 flare-up	0	30	40	5	48
	E7	53/F	WT	N/A	1	9	24	T2 diffuse	0	0	6	11	18
	E8	72/M	WT	N/A	1	2	4	cT1 flare-up	2	6	5	0	0
	E9	72/M	WT	N/A	1	1	1	cT1 flare-up	7	26	3	4	53
	E10	61/F	WT	Met	3	3	3	cT1 flare-up	0	0	0	7	5
	E11	76/F	WT	Unmet	3	3	3	cT1 flare-up	0	9	7	0	27
	E12	80/F	WT	N/A	1	8	24	T2 diffuse	0	16	25	0	3
	E13	58/F	WT	Unmet	1	3	8	cT1-flare-up	2	10	0	6	0
	E14	69/M	WT	Unmet	1	12	8	cT1 flare-up	3	9	42	3	4
	E15	50/M	WT	N/A	1	8	12	cT1 flare-up	3	8	17	8	0

ANGPT; angiopoietin, Bev; bevacizumab, E; effective Bev, EFNA2; Ephrin A2, F; female, FGF2; basic fibroblast growth factor., IDH; isocitrate dehydrogenase, M; male, Met; Methylation of promoter region of MGMT, MGMT; methyl guanine methyltransferase, N; naïve Bev, N/A; not analyzed, PLGF; placenta growth factor, Ra; sample in refractory Bev obtained from autopsy, Rs; sample in refractory Bev obtained from salvage surgery, TMZ; temozolomide, Unmet; Unmethylation of promoter region of MGMT, WT; wild type