SUPPLEMENTAL MATERIAL

Supplemental Table 1. Demographic characteristics of patients, oral dose, response to treatment, and previous lines of treatment.

	Age at Diagnosis	Sex	Condition	Dose (p.o., mg/day)	Response	Previous lines of chemo (#)	Treatment: Start Date - End Date	Pt enroll date/ PD
1	60	M	MESOTHELIOMA	500	No	1	CBDCA: Feb-Mar13 Ptx: Feb-Mar13 RT: Apr-May13	Jun13 PD 2 cycles
2	67	M	MESOTHELIOMA	500	SD[1]	2	RT: 12-14 Nov 2012 Ptx+CBDCA: 22Nov12-04Jan13	Jul13/ wd after 10m
3	70	F	GBM	500	No	2	RT + TMZ: Nov11-Jan12 (PD 3 cycles) Ltine: Mar-May13 (PD 2 m)	Jul13/ PD 1Cycle
4	19	M	GBM	1,000	No	4	RT+TMZ: Nov11-Jan12 Bzmab: Feb-Oct12 (PD 8 m) Bzmab+Ican: Nov12-Apr13 (PD 5m) Bmab: May-Jun13 (PD 1 m)	Aug13/ PD 1Cycle
5	51	M	GBM	1,000	PR[2]	2	RT+TMZ: Apr-Aug12 (PD 3 cycles) Pzine+Ltine+Vcine: Nov-Feb13 (PD 4 m)	Sep13 No PD on target lesion Wd in Jun16
6	65	M	GBM	1,000	No	5	RT+TMZ: Sept-Dec2007 RT: Nov-Dec10 TMZ: Aug11-Feb12 (PD 6m) G028070: Apr-Oct12 (CT, PD 6m) 16F-MC-JJCA: Jan-Jul13 (CT, PD 5m)	Sep13 PD 2 cycles
7	61	F	PANCREAS ADK	1,000	SD	2	Gem: Feb-Jul13	Sep13 PD 2 cycles
8	58	M	GBM	2,000	No	2	RT+TMZ: Nov12-Jan13 (PD 2m) Bzmab: Jan-May13 (PD 4m)	Nov13 PD 2 cycles
9	58	M	GBM	2,000	SD	1	RT+TMZ: May-Jul13 TMZ: Aug-Oct13 (PD 2m)	Nov13 PD 1 cycle
10	60	F	SMALL CELL LUNG	2,000	No	4	CBDCA: May- Jun13 Etoposide IV: May- Jun13 Etoposide Oral: May- Jun13 Topotecan: Jul-Aug13	Dec13 PD 1 cycle
11	63	F	ENDOMETRIAL ADK	4,000	No	5	CBDCA: May-Sep12 Pcxel: May-Sep12 CDDP: May-Sep12 Adriamycin: May-Sep12	Feb14 PD

							Tamoxifen: Feb-May13	2 cycles
12	50	M	RECTAL ADK	4,000	No	8	Oxaliplatin R1: Jun-Aug12 Cap R1: Jun-Aug12 Ican R1: Dec12-April13 5-FU R2: Dec12-Apr13 OXDP: Jun13 5-FU R3: Jun13 BAL101553: Dec13 Bzmab R2: Dec12-Apr13	Mar14 PD 2 cycles
13	68	F	METASTASIC RECTAL ADK	4,000	NA	3	Cap: UNK-Sep12 Xelox: UNK12-May13 5-FU+levin+IRT+Bzmad: May-Dec13	replaced
14	46	F	GLIOMA	4,000	No	1	RT+TMZ: Oct-Nov13 TMZ: Dec13-Apr14 (PD 3m)	Jun14 PD 1 cycle
15	50	F	COLON ADK	8,000	No	5	Folfox: 08 Folfiri+cxmab:uk10-Apr11 Folfiri+cxmab: Sep11-UK Cxmab: Apr-Sep11 Bzmab: Apr-UK13	Aug14 PD 2 cycle
16	44	F	URACHAL ADK	8,000	No	12	CDDP: Aug-Oct10 5-FU: Aug-Oct10 OXDP: Apr-May12 5-FU: Apr-May12 CBDCA: Jul-Nov12 5-FU: Jan13 Fol ac: Jan13 OXDP: Jan13 Fol ac: Jan-Aug13 5-FU: Jan-Aug14 OXDP: Jan-Aug13	Aug14 PD 2 cycle
17	61	M	METASTASIC SIGMOID COLON ADK	8,000	No	9	5-FU: Apr12-Mar13 Ican: Apr12-Mar13 Fol ac: Apr12-Mar13 Bzmab: May12-Mar13 OXDP	Sep14 PD 2 cycle
18	45	F	METASTASIC RECTAL (KRAS WT)	12,000	No	6	Cap: UNK-Dec12 Folfox CT: UNK-Oct12 Folfori+cxmab: Mar-Sep13 Folfox : Dec13-Mar14 Folfox: Jun-Aug14 Bzmab: Jun-Aug14 RT: UNK-Dec12 RT: Dec13	Oct2014 PD 2 cycles
19	36	M	GBM	12,000	NA	4	TMZ: Nov11-Jan12 TMZ: Feb-Jul12 TMZ: Apr-May14 IRT: Aug-Sep14 Bzmab: Aug-Sep1 RT: Nov11-Jan12	replaced
20	63	F	GBM	12,000	SD	2	RT+TMZ: Jul-Sep13 TMZ: Oct13-Mar14 (PD 5m) TMZ: Jul-Oct14 (PD 3m)	Dec14 PD 1 cycle
21	66	M	COLON ADK	12,000	No	11	Cap: UNK-UNK05 OXPD: UNK-UNK05 IRT: Jan-Apr08 Cxmab: Jan-Apr08 Cap: Nov-UNK12 IRT: Nov-UNK12 Fol ac: Jan13 5-FU: Jan13 IRT:Jan13 IRT: Mar13 Cap:Mar13 RT: Mar-Mai11	Dec14 PD 1 cycle

							RT:Aug-Sep13	
22	65	M	OLIGOASTROCYTOMA	12,000	NA	2	TMZ: Oct13-Feb14 Bzmab: Feb-Dec14 RT: Oct-Dec13	replaced
23	57	M	GBM	12,000	SD	2	RT+TMZ: May-Jun13 TMZ: Jul-Dec13 (PD 6m) PCV: May-Nov14 (PD 6m)	Feb15 No PD Wd new lesion
24	67	M	ASTROCYTOMA	12,000	SD	3	RT: Mar-May13 TMZ: May-Nov13 (PD 5m) Ican+Bzmab: Jul14-Jan15 (PD 6m)	Feb15 PD 2 cycle
25	76	M	METASTASIC RECTO-SIGMOID JUNCTION ADK	12,000	No	12	IRT: Jan-Jun09 Fol ac: Jan-Jun09 5-FU: Jan-Jul09 IRT: Oct10-Jan11 Fol ac: Oct10-Jan11 5-FU: Oct10-Jan11 IRT: Feb-Apr11 Cap: Feb-Apr11 Bzmab: Dec11-Dec13 OXPD: Dec11-May12 Cap: Dec11-Oct12 Czmib: May-Sep14	Feb15 PD 2 cycle
26	39	F	G3 GLIOMA	16,000	SD	2	RT:09 PVC: Oct12-Jan13 TMZ: Jul-Sp14 (PD 2m)	Apr15 No PD Wd
27	57	F	ASTROCYTOMA	16,000	No	2	RT+TMZ: Apr-May12 TMZ: Jun-Nov12 TMZ: Mar-Apr14	Apr15 PD 2 cycle
28	73	M	PLEURAL MESOTHELIOMA	16,000	NA	4	CBDCA: Jun-Aug14 Ptx: Jun-Aug14 GSK2256098: Nov14-Jan15 Trnib: Nov14-Jan15 RT: Sep14	replaced
29	65	F	CHONDROSARCOMA OF THE UTERUS	16,000	No	4	DOX: Oct-Dec12 Imide: Feb-Apr14 Pnib: Jun14-Mar15 Trdin: Apr-May15	Jul15 PD 1 cycle
30	50	F	ENDOMETRIAL ADK	16,000	No	7	CBCDA: Nov12-Mar13 Taxol: Nov12-Mar13 MA: Aug-Oct13 AZ108 CT: Feb-Aug14 MLN1117 CT: Feb15 CBCDA: Apr-May15 Pcxel: Apr-May15	Aug15 PD 3 cycle
31	71	M	METASTASIC LUNG ADK	16,000	SD	3	CBCDA: Feb-Mar14 Ptx: Feb-Mar14 Dcxel: Sep-Nov14 RT: Aug14	Aug15 PD 3 cycle
32	25	M	ANAPLASTIC ASTROCYTOMA	16,000	No	4	RT: Mar14 TMZ: Apr-Oct14 Ican: Jul15 Bzmab: Jul-Sep15	Oct15 PD 2 cycles
33	42	F	GBM	12,000	No	3	RT+TMZ: Mar-Apr14 TMZ: May-Jul14	Dec15

							PVC: Aug-Mar15 CCNU: Apr-Sep15	PD <1 cycle
34	52	M	GBM	12,000	No	1	RT: Jun-Jul15 TMZ: Aug-Oct15	Dec15 Wd
35	57	M	GLIOMA	12,000	NA	1		
36	38	M	OLIGODENDROG LIOMA	12,000	SD	2	PCV: Feb-Sep11 PCV: Mar-Jul14 RT+TMZ: Feb-Mar14 TMZ: Apr-Sep14	Dec15 PD 9 cycles
37	68	M	GBM	12,000	No	4	RT: Jan-Apr13 TMZ: Apr-Oct13 TMZ: Jan-Jul15 Fine: Aug-Sep15 Bzmab: Oct15	Dec15 PD < 1m
38	48	M	GBM	12,000	SD	2	RT+TMZ: Apr-May15 PCV: Jul-Nov15	Jan16 PD 7cycles
39	56	M	GBM	12,000	No	6	RT+TMZ: May-Jun13 BKM120: May13 TMZ: Jul-Dec13 Gliadel: Oct14 Bzmab: Feb-Nov15 Ltine: Feb-Nov15	Jan16 PD 1m
40	49	M	GLIOSARCOMA	12,000	No	6	RT+TMZ: Aug-Oct13 TMZ: Oct13-Apr14 Bzmab: Oct13-Mar15 Ltine+Bzmab: Apr15 (CT) Ican+Bzmab: May15 (CT) CBDCA: Oct-Dec15	Jan16 PD 1 cycle
41	53	F	GLIOMATOSIS CEREBRI	12,000	No	2	RT+TMZ: Jul14 TMZ: Sep14-Aug15 PVC: Oct-Dec15	Feb16 PD 1 cycle
42	63	F	GBM	12,000	NA	2	TMZ: Oct-Nov14 TMZ: Oct15 RT: Oct-Nov14	replaced
43	50	M	GBM	12,000	NA	5	TMZ: Mar-Oct14 IRT: Dec14-Sep15 Bzmab: Dec14-Sep15 Fine: Oct-Nov11 TMZ: Dec15-Feb16 RT: Mar-Apr14	replaced
44	50	F	GBM	12,000	No	1	RT+TMZ: Mar-Apr15	Apr16 PD 1 cycle
45	75	M	METASTASIC COLORECTAL ADK	12,000	No	4	5-FU: Nov04-Jul05 Cap: Aug-Sep13 Bzmab: Aug13 Rtxed: Nov11-Aug14 RT: Oct-Nov15	Dec15 PD 3 cycle
46	75	F	COLON ADK	12,000	SD	7	Fol ac.+5-FU+Oxpt: Feb-uk13 Cxmab: Feb13-Feb14 Fol ac. +5-FU+Icam: Fb14-Nov15	Dec15 Wd new lesion

47	73	M	RECTUM ADK	12,000	No	8	Fol ac: Dec14-May15 5-FU: Dec14-May15 IRT: Dec14-May15 Fol ac: May-Aug15 5-FU: May-Aug15 OXDP: May-Aug15 R06895882: Oct-Nov15 Ozmab: Oct15 RT: Jun15	Dec15 PD 2 cycle
48	68	F	COLORECTAL CARCINOMA	12,000	No	6	Folfox: Nov10-Jun11 Bzmab: Nov10-Jun11 IRT: UNK/UNK-Jul14 Abrept: UNK/UNK-Jul14 Folfox: Nov14-Mar15 Rfnib: Jul-Nov15	Jan16 PD 2 cycle
49	55	M	DISTAL BILE DUCT ADK	12,000	SD	3	Ptx: Aug-Sep15 Nmab: Oct-Dec15 CDDP: Aug-Sep15	Jan16 Wd new lesion
50	78	M	METASTASIC SCC OF OESOPHAGUS	12,000	NA	3	Ebcin: Dec14-Feb15 OXDP: Dec14-Jun15 Bzmab: Dec14-Jun15 RT: Oct15	replaced
51	74	M	METASTASIC RECTAL ADK	12,000	No	6	Cap+OXDP: May-Jul12 Bzmab: Sept-Oct13 IRT+ 5-FU: Sep-Nov13 IRT+5FU+Fol ac: UNK13-UNK14 IRT+5FU+Fol ac: Jun14-May15 Folfox: Sept-Oct15 RT: Jun-Jul12	Feb16 PD 2 cycle
52	67	F	RECTUM	12,000	No	14	Fol ac: Jul-Oct13 5-FU: Jul-Oct13 OXDP: Jul-Oct13 5-FU: Oct13-Mar14 IRT: Oct13-Mar14 Cxmab: OCt13-Mar14 5-FU: Aug14-May15 IRT: Aug14-May15 Cxmab: Aug14-May15 5-FU: Apr-Jun15 Fol ac: Jun-Nov15 5-FU: Jun-Nov15 OXPD: Jun-Nov15 Abrecpt: Jun-Nov15 RT Apr-Jun14	Feb16 PD 3 cycle
53	67	F	GALLBLADDER ADK	12,000	No	4	Gem: Jan-Jun14 Cap: Dec14-May15 Gem+CDDP: Jun-Sep15 Aktinh: Dec15-Jan16	Feb16 PD 3 cycle
54	74	M	CAECUM ADK	12,000	No	5	Folfiri: Jun-Oct15 Rfnib: Nov15-Jan16 OXPD: Nov14-Mar15 Cap: Nov14-Mar15 Bzmab: Nov14-Mar15	Mar16 PD 2 cycle
	57.6 yr	32M/ 22F						

Abbreviations: NA=not applicable, PR=partial response, SD=stable disease, wd=withdrawal, pt=patient

Supplemental Table 2. Molecular Markers of glioma patients

	Age at Diagnosis	Sex	Condition	Molecular Specification	
				Markers Malignant Glioma	Result
3	70	F	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	wt
				BRAF mutation	No
				PTEN mutation	Yes
				EGFR amplification	No
				EGFR mutation	No
				MAPK13 alteration	NA
				KRAS alteration	No
				MET (N3755)	Yes
				PIK3CA (R115L)	Yes
				PIK3CA (E542K)	Yes
				TP53 (K132N)	Yes

4	19	M	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
5	51	M	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	No
				PTEN mutation	No
				EGFR amplification	No
				EGFR mutation	No
				MAPK13 alteration	NA
				KRAS alteration	NA
				ATM (T17691),	Yes
				FBXW7 (R484K)	Yes
6	65	M	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
8	58	M	GBM	MGMT promoter methylation status	Un-
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK

				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
9	58	M	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	wt
				BRAF mutation	No
				PTEN mutation	Yes
				EGFR amplification	No
				EGFR mutation	No
				MAPK13 alteration	NA
				KRAS alteration	No
14	46	F	Glioma	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	wt
				BRAF mutation	No
				PTEN mutation	Yes
				EGFR amplification	No
				EGFR mutation	No
				MAPK13 alteration	NA
				KRAS alteration	No
19	36	M	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	No
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
20	63	F	GBM	MGMT promoter methylation status	UNK

				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	No
				EGFR amplification	UNK
				EGFR mutation	No
				MAPK13 alteration	NA
				KRAS alteration	NA
22	65	M	Oligoastro-cytoma (glioma)	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	wt
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
				P53 amplification	Yes
23	57	M	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
24	67	M	Astrocytoma	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK

				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
				PGFA mutation,	Yes
				P53 mutation	Yes
				WT-1 mutation	Yes
26	39	F	G3 glioma	MGMT promoter methylation status	Met
				1p19 co-deletion	No
				IDH 1/2 mutation	Mut
				BRAF mutation	No
				PTEN mutation	No
				EGFR amplification	No
				EGFR mutation	No
				MAPK13 alteration	No
				KRAS alteration	No
27	57	F	Astrocytoma	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	No
				PTEN mutation	No
				EGFR amplification	No
				EGFR mutation	No
				MAPK13 alteration	No
				KRAS alteration	No
32	25	M	Anaplastic Astrocytoma	MGMT promoter methylation status	Met
				1p19 co-deletion	UNK
				IDH 1/2 mutation	wt
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA

				P53 amplification	Yes
33	42	F	GBM	MGMT promoter methylation status	Un-
				1p19 co-deletion	No
				IDH 1/2 mutation	wt
				BRAF mutation	No
				PTEN mutation	No
				EGFR amplification	No
				EGFR mutation	No
				MAPK13 alteration	NA
				KRAS alteration	NA
34	52	F	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	wt
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	Yes
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
35	57	M	Glioma	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
36	38	M	Oligodendro-glioma	MGMT promoter methylation status	UNK
				1p19 co-deletion	Yes
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	No

				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
37	68	M	GBM	MGMT promoter methylation status	Un-
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
38	48	M	GBM	MGMT promoter methylation status	Un-
				1p19 co-deletion	No
				IDH 1/2 mutation	wt
				BRAF mutation	No
				PTEN mutation	Yes
				EGFR amplification	No
				EGFR mutation	No
				MAPK13 alteration	NA
				KRAS alteration	No
				BLM (K323R)	Yes
				RAD51B (Y180C)	Yes
39	56	F	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	wt
				BRAF mutation	UNK
				PTEN mutation	Yes
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA

40	49	M	Gliosarcoma	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	Yes
				EGFR mutation	Yes
				MAPK13 alteration	NA
				KRAS alteration	NA
41	53	F	Gliomatosis cerebri	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	UNK
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
42	63	F	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	wt
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK
				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
43	50	M	GBM	MGMT promoter methylation status	UNK
				1p19 co-deletion	UNK
				IDH 1/2 mutation	wt
				BRAF mutation	UNK
				PTEN mutation	UNK
				EGFR amplification	UNK

				EGFR mutation	UNK
				MAPK13 alteration	NA
				KRAS alteration	NA
44	50	F	GBM	MGMT promoter methylation status	Un-
				1p19 co-deletion	No
				IDH 1/2 mutation	UNK
				BRAF mutation	No
				PTEN mutation	No
				EGFR amplification	No
				EGFR mutation	No
				MAPK13 alteration	NA
				KRAS alteration	No
				ATRX (1360fs*6)	Yes
				RB1 (E926G)	Yes
				RET (M1109T)	Yes
				TP53 (C1765;R273C)	Yes

Abreviations: UNK: unknow; NA: No available; Wt: wildtype; Un-: unmethylated; Met: metilated; Mut: mutated

Supplemental Table 3. Best overall response and duration of response in glioma patients with stable disease or partial response by RANO criteria

Treatment Cohort (per day)	Patient Age (years)	Diagnosis	Treatment Duration	Best Overall Response	Estimated Duration of Response
1,000mg	51	Glioblastoma	C48D8	PR	33 months
2,000mg	58	Glioblastoma	C1D15	SD	1 month
12,000mg (dose escalation)	63	Glioblastoma	C9D8	SD	6 months
	57	Glioblastoma	C9D8	SD	6 months
	67	Astrocytoma	C4D1	SD	2 months
16,000mg	39	Grade 3 glioma	C2D1	SD	1 month
12,000mg (glioma expanded safety cohort)	68	Glioblastoma	C1D8	SD	8 months
12,000mg (glioma expanded safety cohort)	56	Glioblastoma	C2D8	SD	7 months
Clinical benefit rate				PR or SD>6months	5/21 (23.8%)
				PR or SD < 6 months	8/21 (38.1%)

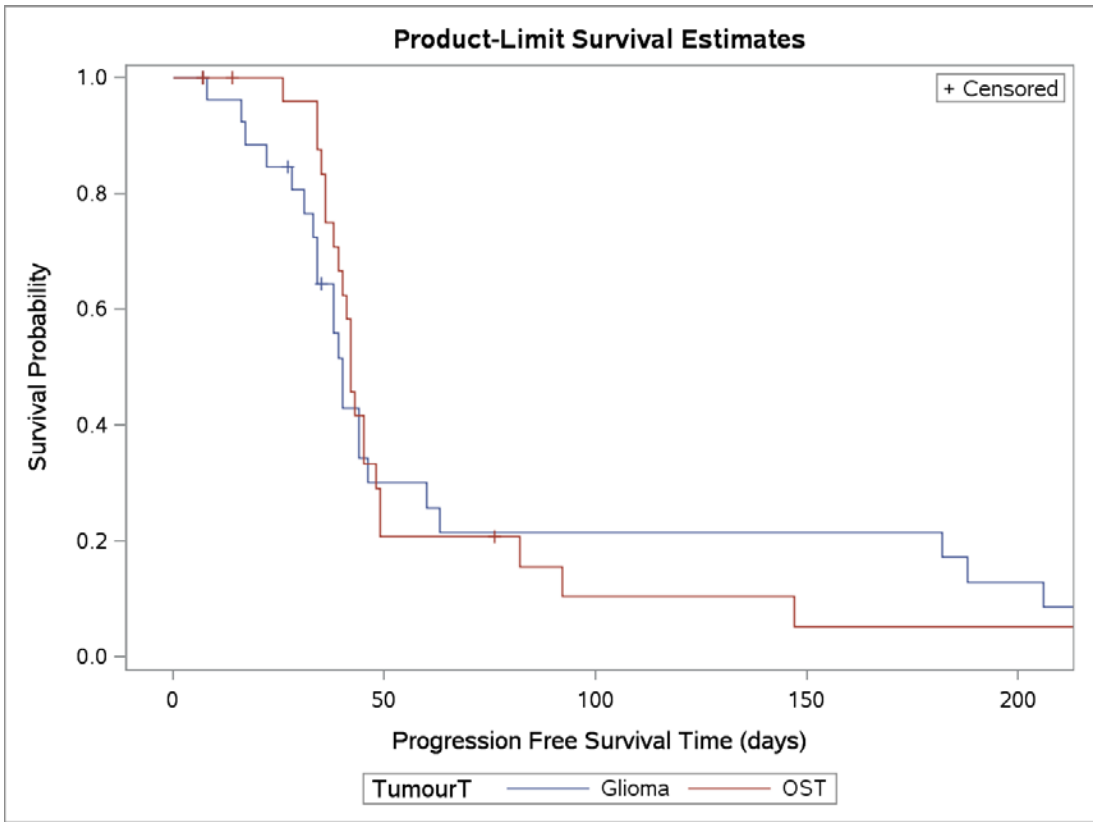
Abbreviations: PR=partial response, SD=stable disease

Supplemental Table 4.

Tumour Type	Study Population	PFS Overall			PFS at 6 months N (%)	PFS <6months N (%)
		Evaluable N (%)	Censored N (%)	Median PFS (days) (95%CI)		
Glioma	ITT (N=27)	24 (88.9%)	3 (11.1%)	40 (34.0-46.0)	5 (18.5%)	19 (81.5%)
	PPS (N=14)	14 (100%)	0	44 (39.0-188.0)	5 (35.7%)	9 (64.3%)
Other solid tumours	ITT (N=27)	23 (85.2%)	4 (19.2%)	42 (39.0-48.0)	1 (3.7%)	22 (96.3%)
	PPS (N=19)	18 (94.7%)	1 (5.3%)	42 (36.0-49.0)	1 (5.3%)	17 (94.7%)

Abbreviations: PFS=progression free survival, ITT=intention to treat, PPT=per protocol

Supplemental Figure 1. Kaplan-Meier Plot of Progression Free Survival (ITT Population). Data from Supplemental table 4.



Supplemental text 1. Full eligibility criteria

Inclusion Criteria

- Able and willing to give written informed consent
- Male or female patients ≥18 years of age
- With histologically- or cytologically-confirmed advanced solid malignancy that is refractory to standard-of-care treatment, or for which there is no standard therapy
- If this is glioma:

- Grade III / Grade IV malignant glioma recurring or progressing after first or second line standard of care treatment and
- True progressive disease, confirmed according to the RANO criteria

- A life-expectancy of at least 12 weeks
- ECOG performance status of 0–2
- Able to swallow and ingest oral medication
- Able to undergo adequate tumor imaging, via CT or MRI scans, to evaluate disease evolution
- Availability of paraffin-embedded archival material for possible genomic evaluation
- Hematology values at screening/baseline: hemoglobin ≥90 g/L (9 g/dL) or 5.6 mmol/L, absolute neutrophil count ≥1.5 x 10^9/L, platelets ≥100 x 10^9/L
- Coagulation values at screening/baseline: International Normalized Ratio (INR) ≤1.5, partial thromboplastin time (PTT) ≤2 x upper limit of normal (ULN)

- Liver function test values at screening/baseline: total bilirubin ≤1.5 × ULN – unless explained by a genetic syndrome such as Gilberts; alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤2.5 × ULN
- Renal function test value at screening/baseline: serum creatinine ≤1.5 x ULN
- No history of corrected QT interval (QTc) prolongation, and a normal QTc interval at screening/baseline (QTc ≤450 msec)
- Female patients (or male patient whose partner is) of non-childbearing potential (defined as >2 years after last menstruation or surgically sterile), female patients of childbearing potential with a negative serum pregnancy test within 7 days prior to the first dose of 2-OHOA, or within 14 days followed by a confirmatory negative urine pregnancy test within 7 days prior to first dose of 2-OHOA, and using (or if male and not surgically sterile, whose partner is using) effective, non-hormonal means of contraception (non-hormonal intrauterine contraceptive device, barrier method of contraception in conjunction with spermicidal gel)

For patients with solid tumors other than glioma:

- The presence of lesions suitable for biopsy (mandatory for non-glioma patients enrolled in the expanded safety cohort and highly desirable for non-glioma patients enrolled in the dose escalation phase)

Exclusion Criteria

- Known hypersensitivity to any component of the study drug
- Use of any other investigational drug in the 30 days prior to the first dose of 2-OHOA

- Anti-cancer therapy within 4 weeks prior to the first dose of 2-OHOA (6 weeks for mitomycin and nitrosureas and 2 weeks for palliative radiotherapy)
- Any NCI CTCAE >Grade 1 toxicities from prior chemotherapy or radiotherapy that could impact on safety outcome assessment
- Any surgery within 14 days prior to the first dose of 2-OHOA
- Known recent >Grade 1 intracranial or intratumoral hemorrhage either by CT or MRI scan. Patients with resolving hemorrhage changes, punctuate hemorrhage or hemosiderin may enter the study
- Significant or uncontrolled cardiovascular disease, including New York Heart Association Class 3-4 heart failure, a left ventricular ejection fraction which is clinically significantly abnormal as measured by 2 dimensional (2D) echocardiogram or Multi Gated Acquisition (MUGA) scan, unstable angina or myocardial infarction within the preceding 6 months
- Known impairment of gastrointestinal function that could alter the absorption of study drug (e.g. active Crohn's disease, malabsorption syndrome or states, unresolved diarrhea, small bowel resection or gastric by-pass surgery)
- A history of uncontrolled hyperlipidemia and/or the need for concurrent lipid-lowering therapy
- Concurrent severe and/or uncontrolled other medical diseases (e.g. uncontrolled diabetes mellitus, active uncontrolled infection) that could compromise participation in the study
- Need for warfarin, phenytoin or sulphonylureas (glibenclamide, glimepiride, glipizide, glyburide or nateglanide)

- Females who are pregnant or breastfeeding
- Any serious and/or unstable pre-existing medical, psychiatric or other condition which in the Investigator's opinion could interfere with subject safety, obtaining written informed consent, or compliance with the study protocol

Supplemental text 2. Dose escalation and Dose Limiting Toxicities (DLTs) criteria and definitions.

A DLT was defined by the occurrence of any of the following toxicities defined in the National Cancer (NCI) Common Terminology Criteria for AEs (CTCAE) Version 4.03 and which were considered by the Investigator to be related to 2-OHOA:

- ⩾Grade 3 febrile neutropenia (absolute neutrophil count <1.0 x 10^9/L with a sustained temperature of ≥38ºC for more than 1 hour) or Grade 4 neutropenia (absolute neutrophil count <0.5 x 10^9/L) for more than 7 consecutive days
- ≥Grade 3 thrombocytopenia (platelet count 25 to <50 x 10^9/L) with bleeding or Grade 4 thrombocytopenia (platelet count <25 x 10^9/L)
- ≥Grade 3 non-hematological toxicity of any duration, *except:*

- Grade 3 or 4 nausea/vomiting or diarrhea was considered a DLT only if it persisted despite optimal medical management
- Alopecia was not considered a DLT
- Reversible temporary laboratory changes without clinical symptoms or relevance (discussed individually upon occurrence by the active Investigators and the Medical Monitor)
    - Any other toxicity occurring at any time during the study that in the view of the active Investigators and the Medical Monitor represented a clinically significant hazard to the patient
    - Any other toxicity that prevented the patient from taking at least 80% of doses during cycle 1