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	Screening Visit	Baseline Visit	Treatment phase						End of Therapy	Follow-up	End of Study	Unscheduled Visit
Time Points (accepted deviation)	within 5 days prior to visit 1	within 7 days prior to treatment start	MFA start Day 1	Day 7-10	Day 28 (±3)	Day 56 (±3) *	Start of Cycle 3 (±7) *	Start of Cycle 4-8 (±7)	EoT **	every 8 weeks (±3)	***	
Visit Number	0	1	2.1	OP	2.2	DLT	2.3	2.4 - 2.8	3	4.1 - 4.X	5	UV
Study eligibility												
Informed consent for trial participation	x											
Assessment of Inclusion / Exclusion criteria	x	x										
demographics, medical history	x											
Clinical examination												
Vital signs	x	x	x		x				x	x	x	x
Physical and neurological examination, and whole skin examination including adjacent transitional mucosal and oropharyngeal	x	x	x		x				x	x	x	x
Concomitant medication	x	x	x		x				x	x	x	x
Steroid need	x	x			x				x	x	x	x
Daily TMZ dose in the last 4 weeks					x				x			
Karnofsky score		x	x		x	x	x1		x	x		x
QoL: EORTC C30 and BN20		x	x			x	x1		x	x	x	
Further tumor therapy										x	x	x
MMSE		x							x			
Laboratory tests												
Pregnancy test (beta-HCG in serum)		x	x						x			
HIV, Hepatitis B and C serology		x										
Differential hematology		x	x						x	x		x
Chemistry2		x	x						x	x		x
CRP		x	x						x	x		x
Safety												
Evaluation of preexisting conditions in analogy to CTCAE V5		x										
(S)AE evaluation		x	x						x	x	x	x7
MRI and response assessment												
Gd-MRI		x3	x1							x		x8
Phase I												
DLT evaluation					x	x						
Phase II												
Randomization		x										
Accompanying scientific program												
Asservation of tumor material				x4								
Blood samples for PK			x5	x5		x	x	x1		x		
optional EEG or MEG analysis		x			x					x6		

* DLT visit will only be performed in Phase I. In Phase I visit 2.3 is only performed additionally, if the start of cycle 3 is prolonged for more than 3 days after the DLT visit. All patients in phase II have visit 2.3

** EoT: End of treatment is reached 3 days after last MFA intake (phase I and experimental arm of phase II) or on day 31 of the last TMZ cycle (standard arm of phase II)

*** End of study and of follow-up in the entire trial will be reached when BOTH of the following requirements are fulfilled: (1) at least 6 months after randomization of the last patient in phase II AND (2) at least 3 days after definite termination of MFA intake in the last patient receiving MFA therapy (i.e. all patients have concluded study-related MFA intake for more than 3 days)

[1] every 8 weeks: progression assessment, Karnofsky score and Quality of Life, blood samples

[2] Na, K, creatinine, ASAT, ALAT, bilirubin

[3] gadolinium-enhanced MRI obtained prior to inclusion/randomization can be used as baseline MRI if the interval between this MRI and start of study therapy is shorter than 21 days. In patients who have undergone re-resection prior to randomization (only possible in phase II) the MRI used as baseline MRI hast to be a postoperative MRI.

[4] Relapse tumor resection 7-10 days after initiation of study therapy, tissue asservation should take place 2-4h after last intake of MFA/TMZ : (1) fresh frozen, (2) 4% PFA, (3) FFPE tumor material for MFA/MFA metabolite level determination and for analysis of MFA-dependent tissue effects. The exact timepoint of last MFA intake prior to resection and the exact timepoint of asservation of the tumor material has to be

[5] Timepoints (to be documented): (a) 2h after first intake, (b) on the days between MFA start and resection daily blood sampling 2h after morning application of MFA (optional), (c) on the day of resection 5 blood samples at an interval of 2h (0h (prior to last preOP MFA dose) 2h, 4h, 6h, 8h later);

[6] only at the first follow-up visit after discontinuation of MFA

[7] only during ongoing MFA treatment + 3 days

[8] only if clinically indicated

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
0, 1, 2, DLT, 3, 4, 5, UV	**Vital signs**	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			
		Blood pressure systolic (mm/Hg)			
		Weight (kg)			
0, 1, 2, DLT, 3, 4, 5, UV	**Physical examination**	General condition		0=not examined 1=normal 2=pathologic	

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		General condition	Description of change		
		ENT		0=not examined 1=normal 2=pathologic	
		ENT	Description of change		
		Skin/ mucosa		0=not examined 1=normal 2=pathologic	
		Skin/ mucosa	Description of change		
		Lung/Thorax		0=not examined 1=normal 2=pathologic	
		Lung/Thorax	Description of change		

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		Abdomen		0=not examined 1=normal 2=pathologic	
		Abdomen	Description of change		
		Lymph nodes		0=not examined 1=normal 2=pathologic	
		Lymph nodes	Description of change		
		Cardiovascular system		0=not examined 1=normal 2=pathologic	
		Cardiovascular system	Description of change		
		Extremities		0=not examined 1=normal 2=pathologic	

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		Extremities	Description of change		
0, 1, 2, DLT, 3, 4, 5, UV	**Neurological examination**	Meningism	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		
		Oculomotor function	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		
		Consciousness and orientation	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		

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		Cranial nerves I-X12	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		
		visual acuity/ visual field	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		
		Speech	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		
		Motor function	Condition	1=normal 2=abnormal	

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			Description of change		
		Sensibility	Condition	1=normal 2=abnormal	
			Description of change		
		Coordination	Condition	1=normal 2=abnormal	
			Description of change		
		Other abnormalities	Description of change		
		Evaluation of the neurological examination	Comparison with baseline: clinical neurological progression present?	1=improved 2=stable 3=deteriorated	

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0, 1, 2, DLT, 3, 4, 5, UV	**Concomitant medication**	Does the Patient receive concomittant medication?	If "Yes", please document on the "Concomitant Medication" form.	1=Yes 2=No	
0, 1, 2.2 - 2.8, DLT, 3, 4, 5, UV	**Steroid need**	Which steroid was given?		1=Dexamethason (e.g. Fortecortin) 2=Prednisolon (e.g. Decortin H) 3=Prednison (e.g.. Decortin) 4=Methylprednisolon (e.g. Urbason) 5=other	
		If other steroid preparation, please indicate name in free text			
		Current dose	in mg		
		Maximum dose for the last 4 weeks	in mg		
2.2 - 2.8, DLT, 3	**Daily TMZ dose in the last course**	Daily dose in mg/m^2			Edit Check: Range 75-200 Dosisreduktion - Abgleich (S)Aes

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		Time interval (days)			Edit Check: Range 1-5
4, 5, UV	**Further tumor therapy**	Neurosurgical resection		1=Yes 2=No 3=NA	
		If Yes, please specify			
		Radiotherapy		1=Yes 2=No 3=NA	
		If Yes, please specify			
		Tumor directed e.g. medical therapy/ chemotherapy		1=Yes 2=No 3=NA	
		If Yes, please specify			

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1, 2.1, 2.2, DLT/ 2.3, 2.5, 2.7, 3, 4, UV	**Karnofsky score**	Index-Ergebnis		0-100%	
1, 2.1, DLT/ 2.3, 2.5, 2.7, 3, 4, 5, UV	**QoL: EORTC C30 and BN20**	EORTC C30 performed?		1=Yes 2=No 3=NA	Falls ja, Fragen einblenden
		EORTC BN20 performed?		1=Yes 2=No 3=NA	Falls ja, Fragen einblenden
1, 3	**MMSE**	Performed?		1=Yes 2=No 3=NA	
		Total score		0-30	
1, 2, OP, DLT, 3	**Pregnancy test (beta-HCG in serum)**	Pregnancy test done?	"Not applicable" for males or for females of non-childbearing potential.	1=Yes 2=No 3=NA	Edit Check Einschlusskriterien
		Date of blood sampling			

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		Result		1=positive 0=negative	
1	**HIV, Hepatitis B and C serology**	Date of blood sampling			
		HIV		1=positiv 0=negativ	Edit Check Einschlusskriterien
		Result Hep. B	if result is positive, report to local health department	1=positiv 0=negativ	Edit Check Einschlusskriterien
		Result Hep. C	if result is positive, report to local health department	1=positiv 0=negativ	Edit Check Einschlusskriterien
1, 2, OP, DLT, 3, 4, UV	**Differential hematology**	Date of blood sampling			
		Time of blood sampling			

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		Hemoglobin	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		Hemoglobin value	g/dL		
		Hematocrit	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		Hematocrit value	%		
		Leukocytes	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		Leukocytes value	G/L		
		Neutrophils (abs)	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	

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		Neutrophils (abs) value	G/L		
		Lymphocytes (abs)	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		Lymphocytes (abs) value	G/L		
		Platelets	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		Platelets value	G/L		
1, 2, OP, DLT, 3, 4, UV	**Chemistry**	Date of blood sampling			
		Time of blood sampling			

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		Sodium (Na)	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		Sodium (Na) value	mmol/L		
		Potassium (K)	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		Potassium (K) value	mmol/L		
		Creatinine	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		Creatinine value	mg/dL		
		ASAT	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	

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		ASAT value	U/L		
		ALAT	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		ALAT value	U/L		
		Total bilirubine	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	
		Total bilirubine value	mg/dL		
1, 2, OP, DLT, 3, 4, UV	**CRP**	Date of blood sampling			
		Result	if "3" is indicated: document on (S)AE sheet	1=normal 2=abnormal, clinically irrelevant 3=abnormal, clinically relevant 4=not done	

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		Value			
		Unit		1=g/dL 2=mg/L	
1, 2, OP, DLT, 3, 4, 5, UV	**(S)AE evaluation**	Has there been an AE/ SAE since the last visit?	If yes, please document on (S)AE sheet.	1=Yes 2=No 3=NA	
1, 2.1, DLT/2.3, 2.5, 2.7, 4, UV	**Gd-MRI**	Cranial MRI performed?		1=Yes 2=No 3=NA	
		If yes, date of MRI			
		Assessment of tumor response on MRI	RANO Criteria	1=Complete Response 2=Partial Response 3=Stable Disease 4=Progression	Editcheck Bewertung der neurologischen Untersuchung
		Clinical condition		1= Better 2=Worse 3=Same	

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		Steroid dose		1= Better 2=Worse 3=Same	
		Other causes for MRI results unlikely?		1=Yes 2=No 3=NA	
		If no, please describe:			
2.2, DLT	**DLT evaluation**	Have (S)Aes occurred since the last visit that meet the DLT definition?	DLT is determined in the first 2 courses of MFA (within 8 weeks/56 (+/-3) days after first study treatment administration) in subjects with a compliance rate of 90% (i.e. 50 days of treatment) and no overdose. If judged to be related to the administration of Meclofenamate, the following toxicities will be considered a DLT: - grade ≥4 hematotoxicity for >14 days in courses 1 and 2 - grade ≥3 for any other organ toxicity	1=Yes 2=No	Edit Check: Yes - DLT Meldung erfolgt?

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		If yes, please report on the DLT form			
2.1, OP	**Blood samples for PK**	Did the patient give his/her informed consent?		1=Yes 2=No	
		Blood sampling performed?		1=Yes 2=No	"entfällt" bei Verweigerung
		Time of collection			
		Time of Meclofenamate intake			
		Time of last meal before MFA intake			
		Time of meal following MFA intake			

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1, 2, OP, DLT, 4	**Blood samples biochemistry**	Did the patient give his/her informed consent?		1=Yes 2=No	
		Blood sampling performed?		1=Yes 2=No	"entfällt" bei Verweigerung
		Time of collection			
1, 2.2, 4.1	**EEG or MEG analysis**	Did the patient give his/her informed consent?	If performed, please upload to the UKB Cloud.	1=Yes 2=No	"entfällt" bei Verweigerung
		EEG or MEG performed?		1=EEG 0=MEG 2=No	

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen	
	Adverse Events (AMG)	Visit No.			fortlaufend	
		Event			fortlaufend	
		Onset			fortlaufend	
		Resolution			fortlaufend	
		Ongoing		1=Ja 0=Nein	fortlaufend	
		OUT		1=Resolved 2=Resolved with Sequelae 3=Ongoing at end of study 4=Death 5=unknown	fortlaufend	
		INT		1=mild 2=moderate 3=servere	fortlaufend	
		EXP		1=expected 2=unexpected	fortlaufend	
		THE		0=none 1=drug therapy (please specify on "comment") 2=other therapy (please specify on "comment")	fortlaufend	
		ACT		1=dose unchanged 2=drug 3=drug temorarily interrupted 4=drug withdrawn 5=dose increased 6=unknown	fortlaufend	
		SER		0=no 1=yes. If yes, please fill in SAE Report Form.	fortlaufend	

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		REL		1= not related 0= related	fortlaufend	
		Comment			fortlaufend	
		DLT	If judged to be related to the administration of Meclofenamate, the following toxicities will be considered a DLT: • grade ≥4 hematotoxicity for >14 days in courses 1 and 2 • grade ≥3 for any other organ toxicity	1= Yes 0= No	fortlaufend	

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen	
	Begleitmedikation					
		Wirkstoff				
		Dosis				
		Einheit				
		Applikationsform				
		Applikationsweg		1=oral 2=topisch 3=I.v. 4= respiratoirsch 5=subkutan 6=Transdemal 7=intraokular 8=intramuskulär 9=intraläsional 10=intraperitoneal 11=nasal 12=rektal 13=vaginal 14=andere (bitte spezifizieren)		
		Route	wenn andere, bitte spezifizieren			
		Indikation				
		Datum Start				
		Datum Stopp				
		andauernd				
		Gab es bis 3 Monate vor Screening irgendwelche Medikamente / Verfahren, die angewendet wurden um die Begleiterkrankung zu behandeln?		1=ja 2=nein		

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen	
	Medical History		MH Nummer			
		Diagnose Freitextfeld	Alle Vorerkrankungen innerhalb der letzten 3 Monate vor der Vorsorge, alle klinisch relevanten Vorerkrankungen (z.B. Malignome, Myokardinfarkt) und Begleiterkrankungen sollen hier dokumentiert werden			
		Start der Erkrankung Datumsfeld				
		Ende der Erkrankung Datumsfeld				
		andauernd				
		Wurden irgendwelche Medikamente / Verfahren zur Behandlung dieser Erkrankung innerhalb der letzten 3 Monate vor Screening angewendet?	*Bitte notieren Sie dies auf der Seite vorherige und begleitende Medikamente / Therapien.	1=*Ja 0=Nein		

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen	
Screening	**Informed consent for trial participation**	Was the patient informed?		1=Yes 2=No		
within 5 days prior to visit 1		Has the patient consented to the main study?		1=Yes 2=No		
		Date of the signed consent form (main study)				
		Did the subject consent to the transfer of biomaterials to the BioBank?		1=Yes 2=No		
		Date of signed consent form (BioBank)				
		Was a copy of the signed consent form given to the patient?		1=Yes 2=No		
		Has the patient been given a copy of the insurance conditions?		1=Yes 2=No		

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	Inclusion Criteria	1. First relapse after first-line therapy with radiotherapy (RT) and alkylating chemotherapy, > 3 months after last chemotherapy application and >6 months after end of RT. Drug therapy and/or radiotherapy for first relapse treatment not yet started.		1=Yes 2=No		
	Phase I and II	2. Tumor progression according to RANO criteria		1=Yes 2=No		
		3. Written informed consent		1=Yes 2=No		
		4. Cognitive state to understand rationale and necessity of study therapy and procedures		1=Yes 2=No		
		5. MGMT promotor-methylated (MGMTmeth), IDH wildtype glioblastoma (GBM) or gliosarcoma confirmed with histology of the primary resection		1=Yes 2=No		
		6. Age > 18 years		1=Yes 2=No		
		7. Karnofsky performance score (KPS) ≥60%;		1=Yes 2=No		

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		8. Life expectancy > 6 months		1=Yes 2=No		
		9. Adequate bone marrow reserve (WBC >3 G/nl, platelets >100 G/nl)		1=Yes 2=No		
		10. Adequate liver function (bilirubin <1.5 x ULN; ASAT /ALAT <3 x ULN, creatinine < 1.5 x ULN)		1=Yes 2=No		
		11. Patient compliance and geographic proximity that allow adequate follow up		1=Yes 2=No		
		12. Male and female patients with reproductive potential must use an approved contraceptive method during and for 3 months after the trial (Pearl index <1%)		1=Yes 2=No		
		13. Pre-menopausal female patients with childbearing potential: a negative serum pregnancy test (beta-HCG) must be obtained prior to treatment start		1=Yes 2=No		
	Additional criterion ONLY for Phase I:	14. Resection at first relapse not yet performed; according to the local treating neurosurgeon and the documented decision of local neurooncological tumor board, reresection of the tumor is clinically indicated and can be safely deferred until day 7-10 after initiation of MFA/TMZ therapy.		1=Yes 2=No		

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	Exclusion Criteria	1. Indication for hematotoxicity in first-line therapy not allowing TMZ starting dose 150 mg/m2/d		1=Yes 2=No		
	Phase I und II	2. Skin or liver toxicity >CTCAE5 grade 1 in first-line therapy		1=Yes 2=No		
		3. History of gastrointestinal bleeding or gastroduodenal ulcer, active gastritis		1=Yes 2=No		
		4. Asthma, urticaria or allergic-type skin reactions to NSAID		1=Yes 2=No		
		5. Prior malignancy other than glioma		1=Yes 2=No		
		6. Hypersensitivity or anaphylactic reaction to TMZ or NSAIDs		1=Yes 2=No		
		7. History of disease with poor prognosis		1=Yes 2=No		
		8. Severe coronary heart disease (esp. after CABG or MI), severe heart failure		1=Yes 2=No		

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		9. Known HIV infection, active hepatitis B or C		1=Yes 2=No		
		10. Breastfeeding or pregnant		1=Yes 2=No		
		11. Unable to undergo contrast-enhanced MRI (i.e. contrast allergy, implants, etc).		1=Yes 2=No		
		12. Treatment in another clinical trial with therapeutic medical intervention or use of any other investigational agent during the trial or within the 30 days before enrollment		1=Yes 2=No		
		13. Medication with a drug that is not allowed in conjunction with MFA intake and cannot be discontinued: i.e. lithium, methotrexate, etc.				
		14. Patients with active bleeding, diathesis or anticoagulants (low-dose thrombosis prophylaxis is permitted) or anti-platelet therapy. This restriction is due to a potentially increased risk of GI ulcers with subsequent bleeding under MFA therapy				

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		15. Patients with medically diagnosed hereditary Galactose Intolerance, complete lactase deficiency or confirmed Glucose-Galactose-Malabsortion				
		16. Medical History of gastrointestinal Resection of any kind that may potentially alter the absorption of the investigational study drug, according to investigators judgement		1=Yes 2=No		
		17. The presence of any other concomitant severe, progressive, or uncontrolled renal, hepatic, hematological, endocrine, pulmonary, cardiac, or psychiatric disease, or signs and symptoms thereof, that may affect the subjects participation in the study, according to investigators judgement		1=Yes 2=No		
	Demographics and medical history	Year of birth		JJJJ		
		Gender		1=weiblich 2=männlich		
		Height (cm)				
	Vital signs	Temperature(C°)				

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		Heart frequency (beats per min)				
		Blood pressure diastolic (mm/Hg)				
		Blood pressure systolic (mm/Hg)				
		Weight (kg)				
	Physical examination	General condition		0=not examined 1=normal 2=pathologic		
		General condition	Description of change			
		ENT		0=not examined 1=normal 2=pathologic		
		ENT	Description of change			

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		Skin/ mucosa		0=not examined 1=normal 2=pathologic		
		Skin/ mucosa	Description of change			
		Lung/Thorax		0=not examined 1=normal 2=pathologic		
		Lung/Thorax	Description of change			
		Abdomen		0=not examined 1=normal 2=pathologic		
		Abdomen	Description of change			
		Lymph nodes		0=not examined 1=normal 2=pathologic		
		Lymph nodes	Description of change			

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		Cardiovascular system		0=not examined 1=normal 2=pathologic		
		Cardiovascular system	Description of change			
		Extremities		0=not examined 1=normal 2=pathologic		
		Extremities	Description of change			
	Neurological examination	Meningism	Condition	0=not examined 1=normal 2=pathologic		
			Description of change			
		Oculomotor function	Condition	0=not examined 1=normal 2=pathologic		
			Description of change			

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		Consciousness and orientation	Condition	0=not examined 1=normal 2=pathologic		
			Description of change			
		Cranial nerves I-X12	Condition	0=not examined 1=normal 2=pathologic		
			Description of change			
		visual acuity/ visual field	Condition	0=not examined 1=normal 2=pathologic		
			Description of change			
		Speech	Condition	0=not examined 1=normal 2=pathologic		
			Description of change			

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		Motor function	Condition	1=normal 2=abnormal		
			Description of change			
		Sensibility	Condition	1=normal 2=abnormal		
			Description of change			
		Coordination	Condition	1=normal 2=abnormal		
			Description of change			
		Other abnormalities	Description of change			
		Evaluation of the neurological examination	Comparison with baseline: clinical neurological progression present?	1=improved 2=stable 3=deteriorated		

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	Concomitant medication	Does the Patient receive concomittant medication?	If "Yes", please document on the "Concomitant Medication" form.	1=Yes 2=No		
	Steroid need	Which steroid was given?		1=Dexamethason (e.g. Fortecortin) 2=Prednisolon (e.g. Decortin H) 3=Prednison (e.g.. Decortin)		
		If other steroid preparation, please indicate name in free text				
		Current dose	in mg			
		Maximum dose for the last 4 weeks	in mg			

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
Baseline	**Patient status**	Did the subject show up for the scheduled visit?		1=Yes 2=No	
		Is the subject still participating in the study?		1=Yes 2=No	
	Inclusion Criteria	1. First relapse after first-line therapy with radiotherapy (RT) and alkylating chemotherapy, > 3 months after last chemotherapy application and >6 months after end of RT. Drug therapy and/or radiotherapy for first relapse treatment not yet started.		1=Yes 2=No	
	Phase I and II	2. Tumor progression according to RANO criteria		1=Yes 2=No	

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		3. Written informed consent		1=Yes 2=No	
		4. Cognitive state to understand rationale and necessity of study therapy and procedures		1=Yes 2=No	
		5. MGMT promotor-methylated (MGMTmeth), IDH wildtype glioblastoma (GBM) or gliosarcoma confirmed with histology of the		1=Yes 2=No	
		6. Age > 18 years		1=Yes 2=No	
		7. Karnofsky performance score (KPS) ≥60%;		1=Yes 2=No	
		8. Life expectancy > 6 months		1=Yes 2=No	

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		9. Adequate bone marrow reserve (WBC >3 G/nl, platelets >100 G/nl)		1=Yes 2=No	
		10. Adequate liver function (bilirubin <1.5 x ULN; ASAT /ALAT <3 x ULN, creatinine < 1.5 x ULN)		1=Yes 2=No	
		11. Patient compliance and geographic proximity that allow adequate follow up		1=Yes 2=No	
		12. Male and female patients with reproductive potential must use an approved contraceptive method during and for 3 months after the trial (Pearl index <1%)		1=Yes 2=No	
		13. Pre-menopausal female patients with childbearing potential: a negative serum pregnancy test (beta-HCG) must be obtained		1=Yes 2=No	

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	Additional criterion ONLY for Phase I:	14. Resection at first relapse not yet performed; according to the local treating neurosurgeon and the documented decision of local neurooncological tumor board, reresection of the tumor is clinically indicated and can be		1=Yes 2=No	
	Exclusion Criteria	1. Indication for hematotoxicity in first-line therapy not allowing TMZ starting dose 150 mg/m2/d		1=Yes 2=No	
	Phase I und II	2. Skin or liver toxicity >CTCAE5 grade 1 in first-line therapy		1=Yes 2=No	
		3. History of gastrointestinal bleeding or gastroduodenal ulcer, active gastritis		1=Yes 2=No	
		4. Asthma, urticaria or allergic-type skin reactions to NSAID		1=Yes 2=No	
		5. Prior malignancy other than glioma		1=Yes 2=No	

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		6. Hypersensitivity or anaphylactic reaction to TMZ or NSAIDs		1=Yes 2=No	
		7. History of disease with poor prognosis		1=Yes 2=No	
		8. Severe coronary heart disease (esp. after CABG or MI), severe heart failure		1=Yes 2=No	
		9. Known HIV infection, active hepatitis B or C		1=Yes 2=No	
		10. Breastfeeding or pregnant		1=Yes 2=No	
		11. Unable to undergo contrast-enhanced MRI (i.e. contrast allergy, implants, etc).		1=Yes 2=No	

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		12. Treatment in another clinical trial with therapeutic medical intervention or use of any other investigational agent during the trial or within the 30 days before enrollment		1=Yes 2=No	
		13. Medication with a drug that is not allowed in conjunction with MFA intake and cannot be discontinued: i.e. lithium, methotrexate, etc.			
		14. Patients with active bleeding, diathesis or anticoagulants (low-dose thrombosis prophylaxis is permitted) or anti-platelet therapy. This restriction is due to a potentially increased risk of GI			
		15. Patients with medically diagnosed hereditary Galactose Intolerance, complete lactase deficiency or confirmed Glucose-Galactose-Malabsortion			
		16. Medical History of gastrointestinal Resection of any kind that may potentially alter the absorption of the investigational study		1=Yes 2=No	

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		17. The presence of any other concomitant severe, progressive, or uncontrolled renal, hepatic, hematological, endocrine, pulmonary, cardiac, or psychiatric disease, or signs and symptoms thereof, that may affect the subjects participation in the study		1=Yes 2=No	
	Vital signs	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			
		Blood pressure systolic (mm/Hg)			

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		Weight (kg)			
	Physical examination	General condition		0=not examined 1=normal 2=pathologic	

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
Visit 2.1	**Patient status**	Did the subject show up for the scheduled visit?		1=Yes 2=No	
		Is the subject still participating in the study?		1=Yes 2=No	
	Vital signs	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			

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		Blood pressure systolic (mm/Hg)			
		Weight (kg)			
	Physical examination	General condition		0=not examined 1=normal 2=pathologic	
		General condition	Description of change		
		ENT		0=not examined 1=normal 2=pathologic	
		ENT	Description of change		

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		Skin/ mucosa		0=not examined 1=normal 2=pathologic	
		Skin/ mucosa	Description of change		
		Lung/Thorax		0=not examined 1=normal 2=pathologic	
		Lung/Thorax	Description of change		
		Abdomen		0=not examined 1=normal 2=pathologic	
		Abdomen	Description of change		

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		Lymph nodes		0=not examined 1=normal 2=pathologic	
		Lymph nodes	Description of change		
		Cardiovascular system		0=not examined 1=normal 2=pathologic	
		Cardiovascular system	Description of change		
		Extremities		0=not examined 1=normal 2=pathologic	
		Extremities	Description of change		

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	Neurological examination	Meningism	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		
		Oculomotor function	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		
		Consciousness and orientation	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		

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		Cranial nerves I-X12	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		
		visual acuity/ visual field	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		
		Speech	Condition	0=not examined 1=normal 2=pathologic	
			Description of change		

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		Motor function	Condition	1=normal 2=abnormal	
			Description of change		
		Sensibility	Condition	1=normal 2=abnormal	
			Description of change		
		Coordination	Condition	1=normal 2=abnormal	
			Description of change		

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		Other abnormalities	Description of change		
		Evaluation of the neurological examination	Comparison with baseline: clinical neurological progression present?	1=improved 2=stable 3=deteriorated	
	Blood samples for PK	Did the patient give his/her informed consent?		1=Yes 2=No	
		Blood sampling performed?		1=Yes 2=No	"entfällt" bei Verweigerung
		Time of collection			
		Time of Meclofenamate intake			

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		Time of last meal before MFA intake			
		Time of meal following MFA intake			

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Visit	Modul	Variablenlabel	Begleittext	Format	Codeliste DB	Bemerkungen
Visit OP	**Patient status**	Did the subject show up for the scheduled visit?		Radio Button	1=Yes 2=No	
		Is the subject still participating in the study?		Radio Button	1=Yes 2=No	
	Blood samples for PK	Blood sampling performed?		DropDownList	1=Yes 2=No	"entfällt" bei Verweigerung
		Time of collection				
		Time of Meclofenamate intake				
		Time of last meal before MFA intake				

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		Time of meal following MFA intake				

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
Visit 2.2	**Patient status**	Did the subject show up for the scheduled visit?		1=Yes 2=No	
		Is the subject still participating in the study?		1=Yes 2=No	
	Vital signs	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			

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		Blood pressure systolic (mm/Hg)			
		Weight (kg)			
	Physical examination	General condition		0=not examined 1=normal 2=pathologic	

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Visit	Modul	Variablenlabel	Begleittext	Format	Codeliste DB	Bemerkungen
Visit DLT	**Patient status**	Did the subject show up for the scheduled visit?		Radio Button	1=Yes 2=No	
		Is the subject still participating in the study?		Radio Button	1=Yes 2=No	
	Vital signs	Temperature(C°)		2.1		
		Heart frequency (beats per min)		3.0		
		Blood pressure diastolic (mm/Hg)		3.0		
		Blood pressure systolic (mm/Hg)		3.0		

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		Weight (kg)		3.0		
	Physical examination	General condition		Dropdownliste	0=not examined 1=normal 2=pathologic	

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
Visit 2.3	**Patient status**	Did the subject show up for the scheduled visit?		1=Yes 2=No	
		Is the subject still participating in the study?		1=Yes 2=No	
	Vital signs	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			

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		Blood pressure systolic (mm/Hg)			
		Weight (kg)			
	Physical examination	General condition		0=not examined 1=normal 2=pathologic	

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
Visite 2.4 - 2.8	**Patient status**	Did the subject show up for the scheduled visit?		1=Yes 2=No	
		Is the subject still participating in the study?		1=Yes 2=No	
	Vital signs	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			

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		Blood pressure systolic (mm/Hg)			
		Weight (kg)			
	Physical examination	General condition		0=not examined 1=normal 2=pathologic	

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
Visit 3 End of treatment	**Patient status**	Did the subject show up for the scheduled visit?		1=Yes 2=No	
		Is the subject still participating in the study?		1=Yes 2=No	
	Vital signs	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			

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		Blood pressure systolic (mm/Hg)			
		Weight (kg)			
	Physical examination	General condition		0=not examined 1=normal 2=pathologic	

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
Visit 4.X Follow-up	**Patient status**	Did the subject show up for the scheduled visit?		1=Yes 2=No	
		Is the subject still participating in the study?		1=Yes 2=No	
	Vital signs	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			

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		Blood pressure systolic (mm/Hg)			
		Weight (kg)			
	Physical examination	General condition		0=not examined 1=normal 2=pathologic	

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
End of Study Visit V5	**Patient status**	Did the subject show up for the scheduled visit?		1=Yes 2=No	
		Is the subject still participating in the study?		1=Yes 2=No	
	Vital signs	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			

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		Blood pressure systolic (mm/Hg)			
		Weight (kg)			
	Physical examination	General condition		0=not examined 1=normal 2=pathologic	

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Visit	Modul	Variablenlabel	Begleittext	Codeliste DB	Bemerkungen
Unscheduled visit					
	Vital signs	Temperature(C°)			
		Heart frequency (beats per min)			
		Blood pressure diastolic (mm/Hg)			
		Blood pressure systolic (mm/Hg)			

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		Weight (kg)			
	Physical examination	General condition		0=not examined 1=normal 2=pathologic	
		General condition	Description of change		