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Supplementary information

Exploring the landscape of targetable alterations in patients with glioblastoma

In the format provided by the authors and unedited

Table 1 supplement: Selected ongoing trials of targeted therapies for glioblastomas

Targeted therapies						
Target	**Frequency of alteration**	**Therapeutic agent**	**Therapeutic modality**	**Phase**	**Glioblastoma setting**	**NCT ID**
EGFR	Altered in >50% of glioblastomas through focal amplfications, fusions and mutations. EGFR vIII found in ~11% of cases	EGFR-IL13Ra2 CAR-T	Bivalent CAR-T (EGFR + IL13Rα2)	I	EGFR-amplified recurrent glioblastoma	NCT05168423
EGFR	Altered in >50% of glioblastomas through focal amplfications, fusions and mutations. EGFR vIII found in ~11% of cases	ERAS-801	CNS-penetrant EGFR inhibitor	I	Recurrent EGFR-altered glioblastoma	NCT05222802
EGFR	Altered in >50% of glioblastomas through focal amplfications, fusions and mutations. EGFR vIII found in ~11% of cases	BDTX-1535 (Silevertinib)	CNS-penetrant EGFR inhibitor	I	Recurrent EGFR-altered glioblastoma	NCT05256290
EGFR	Altered in >50% of glioblastomas through focal amplfications, fusions and mutations. EGFR vIII found in ~11% of cases	Verteporfin	YAP/TAZ-TEAD inhibitor, YAP/TAZ regulates transcription of EGFR	I/II	Recurrent EGFR-altered glioblastoma	NCT04590664
EGFR	Altered in >50% of glioblastomas through focal amplfications, fusions and mutations. EGFR vIII found in ~11% of cases	Intra-arterial Cetuximab	EGFR antibody	I/II	Newly diagnosed EGFR-altered glioblastoma	NCT02861898

EGFR	Altered in >50% of glioblastomas through focal amplfications, fusions and mutations. EGFR vIII found in ~11% of cases	ABBV-637 or ABBV-155 with ERAS 801	EGFR inhibitors and B7-H3 inhibitor	I	Recurrent EGFR-altered glioblastoma	NCT06934889
EGFRvIII	Altered in >50% of glioblastomas through focal amplfications, fusions and mutations. EGFR vIII found in ~11% of cases	CARv3-TEAM-E T cells		I	Newly diagnosed and recuurent glioblastoma	NCT05660369
EGFR	Altered in >50% of glioblastomas through focal amplfications, fusions and mutations. EGFR vIII found in ~11% of cases	EGFR-IL13Ra2 CAR-T	Bivalent CAR-T (EGFR + IL13Rα2); different dosing strategies	I	EGFR-amplified recurrent glioblastoma	NCT07209241
EGFR	Altered in >50% of glioblastomas through focal amplfications, fusions and mutations. EGFR vIII found in ~11% of cases	E-SYNC CAR-T	Anti-EGFRvIII synNotch receptor–induced CAR-T	I	EGFRvIII+ tumors	NCT06186401
FGFR-TACC fusions and FGFR mutations	FGFR-TACC fusions in ~3% of glioblastomas, mutations in 1-3% of cases	Erdafitinib	FGFR inhibitor	II	FGFR-TACC fusion positive recurrent/progressive glioma	NCT05859334
FGFR-TACC fusions and FGFR mutations	FGFR-TACC fusions in ~3% of glioblastomas, mutations in 1-3% of cases	Infigratinib	FGFR inhibitor	0	Recurrent high grade glioma with FGFR alterations	NCT04424966
ALK, ROS, MET, RET, NTRK	Rare fusions in glioblastoma, more common in pediatric gliomas	Selpercatinib	RET inhibitor	I/II	RET fusion-positive solid tumors	NCT03157128

BRAF V600E	BRAF V600 mutatons ~2% of glioblastomas, rare fusions	Encorafenib + binimetinib	BRAF + MEK inhibitors	II	Recurrent primary brain tumors with BRAF V600 mutations	NCT03973918
BRAF aletered	BRAF V600 mutatons ~2% of glioblastomas, rare fusions	Plixorafenib	BRAF inhibitor	II	Recurrent gliomas and other cancers	NCT05503797
MTAP deletions	~40-50% co-deleted with *CDKN2A*	TNG908	PRMT5 inhibitor	I/II	MTAP-deleted solid tumors	NCT05275478
MTAP deletions	~40-50% co-deleted with *CDKN2A*	AMG 193	PRMT5 inhibitor	I	Advanced MTAP-deleted solid tumors (basket)	NCT05094336
MTAP deletions	~40-50% co-deleted with *CDKN2A*	BMS-986504	PRMT5 inhibitor	0/I	MTAP deleted recurrent glioblastoma	NCT06883747
MTAP deletions	~40-50% co-deleted with *CDKN2A*	BGB 58067	PRMT5 inhibitor	I	MTAP deleted recurrent tumor	NCT06589596
MTAP deletions	~40-50% co-deleted with *CDKN2A*	Bay 3713372	PRMT5 inhibitor		MTAP deleted recurrent tumor	NCT06914128
MTAP deletions	~40-50% co-deleted with *CDKN2A*	MRTX1719	PRMT5 inhibitor	I	Advanced MTAP-deleted solid tumors (basket)	NCT05245500
High TMB, MMR deficiency, POLE/POLD1 mutations	De novo TMB-H in 2% of cases, post-treatment MMR deficiency in 7-12% of cases	Pembrolizumab	Anti–PD-1 (pembrolizumab)	II	MMR-deficient solid tumors	NCT02359565
MDM2	Wild-type TP53 in ~60% of glioblastomas	Navtemadlin (KRT-232 / AMG 232)	MDM2 inhibitor	I	Newly diagnosed or recurrent glioblastoma	NCT03107780
DLL3	Overexpressed in a subset of glioblastomas	DLL3 CAR-T	DLL3-directed CAR-T	Early phase	Brain tumors expressing DLL3	NCT07180927
DLL3	Overexpressed in a subset of glioblastomas	Tarlatamab	DLL3xCD3 bispecific T-cell engager	II	Recurrent/refractory oligodendroglioma or astrocytoma	NCT06776250

DLL3	Overexpressed in a subset of glioblastomas	Rovalpituzumab tesirine	DLL3 antibody–drug conjugate	I/II	DLL3+ tumors including glioblastoma	NCT02709889
Epigenetic modifiers	Epigenetic dysregulation is common in glioblastoma	Vorinostat + TMZ + radiation	HDAC inhibitor	I/II	Newly diagnosed glioblastoma	NCT00731731
DDR-targeting agents						
Target		**Therapeutic agent**	**Treatment paradigm**	**Phase**	**Glioblastoma setting**	**NCT ID**
PARP		Veliparib	TMZ+veliparib (40mg po bid)	I/II (RCT)	Recurrent (BEV-naïve and BEV-refractory)	NCT01026493
		Olaparib	Cediranib/olaparib (200mg po twice daily) vs. BEV	II (RCT)	Recurrent	NCT02974621
			Ceralasertib (ATR inhibitor) +/- olaparib or durvalumab	II	Recurrent	NCT03682289
			TMZ/pembrolizumab/olaparib (BID dosing) vs. TMZ/pembrolizumab -> surgery	WOO/II	Recurrent	NCT05188508
		Niraparib	Initial: Niraparib (300/200mg QD) -> surgery Expansion: RT/niraparib-> niraparib	0/II	Newly diagnosed	NCT04221503
		AZD9574	AZD9574 + TMZ	I	Recurrent	NCT05417594
		NMS-03305293	NMS-03305293 + TMZ	I/II	Recurrent	NCT04910022
Wee1		Debio 0123	Debio 0123 +TMZ in current glioblastoma and with RT and TMZ in newlydiagnosed glioblastoma	I	Newly diagnosed	NCT05765812

ATM		AZD1390	AZD1390 + RT	I	Recurrent and newly diagnosed glioblastoma	NCT05182905
		AZD1390	AZD1390 + RT	II/III	Newly diagnosed glioblastoma	NCT03970447
		WSD0628	WSD0628 + RT	0/I	Recurrent glioblastoma	NCT05917145
Cancer neuroscience-targeting agents						
Therapeutic agent			**Treatment paradigm**	**Phase**	**Glioblastoma setting**	**NCT ID**
Perampanel			AMPA receptor inhibitor	II	Resectable recurrent glioblastoma	PerSurge
Troriluzole			Glutamate modulator	II/III	Resectable recurrent glioblastoma	NCT03970447 NCT06552260
INCB7839			ADAM 10 and 17 inhibitor	I	Recurrent high grade glioma	NCT04295759
Meclonenamate			Dysregulation of glioblastoma communicating networks	I/II	MGMT methylated glioblastoma at first relapse	MecMeth
Gabapentin, sulfasalazine, memantine			Glutamate inhibitors	I/II	Newly diagnosed glioblastoma	NCT05664464
Antibody-drug conjugates						
Therapeutic agent			**Mechanism**	**Phase**	**Glioblastoma setting**	**NCT ID**
M3554			Anti-GD2	I	Recurrent glioblastoma	NCT06641908
LCB84			Anti-TROP2	II	Recurrent glioblastoma	NCT05941507
ABBV-637, ABBV-155			Anti-EGFR, Anti-B7H3	I	Newly diagnosed and recurrent glioblastoma	NCT06934889
Theranostics						
Therapeutic agent		**Molecular target**	**Modality**	**Phase**	**Glioblastoma setting**	**NCT ID**
[^{177}Lu]Lu-DOTA-TATE		Somatostatin Receptor 2	β-emitter	I	Newly diagnosed and recurrent glioblastoma	NCT05109728
[^{177}Lu]Lu-NeoB		Gastrin-releasing	β-emitter	I	Newly diagnosed	NCT05739942

		peptide receptor			and recurrent glioblastoma	
[^{177}Lu]Lu-PSMA		PSMA	β-emitter	I	Recurrent glioblastoma	NCT05644080
[^{225}Ac]Ac-DOTA-Substance P		NK-1 (Substance-P) receptor	α-emitter	I	Recurrent glioblastoma	NCT06975332