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**Supplementary information**

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**Advances in local therapy for glioblastoma  
– taking the fight to the tumour**

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**Supplementary Tables | Current active trials regarding local therapy for glioblastoma**

**Supplementary Table 1 | Intraoperative treatment modalities**

Category	Treatment	Study type	Glioma type	Number of patients	Estimated study completion date	ClinicalTrials.gov identifier
Localized thermotherapy	LITT + chemoradiation	Phase I	Primary GBM	45	December 2020	NCT02970448
	LITT+ hypo-fractionated RT	Phase I	Recurrent GBM	32	February 2023	NCT04181684
	LITT + lomustine	Phase II	Recurrent GBM or AA	32	November 2021	NCT03022578
	LITT+ pre- and post-operative pembrolizumab	Phase I/II	Recurrent GBM	34	January 2021	NCT03277638
	LITT + avelumab	Phase I	Recurrent GBM	30	February 2021	NCT03341806
	LITT + hypofractionated RT	Phase I	Primary GBM	32	December 2025	NCT04699773
	MR-guided LITT	Phase I	Primary GBM	20	December 2021	NCT04596930
Photodynamic therapy	Per-operative PDT with Gliolan	Phase I	Primary GBM	10	May 2021	NCT03048240
	Biopsy followed by stereotactic PDT with Gliolan	Phase II	Recurrent GBM	106	July 2025	NCT04469699
	Stereotactic PDT with Gliolan and PD-L 506	Phase II	Primary, IDHwt GBM	20	February 2026	NCT03897491
	Intraoperative PDT + Gliolan	Phase II	Primary GBM	21	September 2024	NCT04391062
	Interstitial PDT with PDL506	Phase II	Primary IDHwt GBM	20	November 2026	NCT03897491
Focused ultrasound	Sonodynamic therapy with ExAblate system and 5-ALA	Phase I	GBM	5	December 2022	NCT04845919
	RT with FUS	Phase I	Recurrent GBM	8	January 2023	NCT04988750

**Supplementary Table 2 | Local delivery of chemotherapeutic agents**

Category	Treatment	Study type	Glioma type	Number of patients	Estimated study completion date	ClinicalTrials.gov identifier
Convection-enhanced delivery	Intratumoral topotecan via CED after biopsy	Phase I	Recurrent WHO grade III or IV glioma	5	April 2022	NCT03927274
	Irinotecan liposome injection via CED	Phase I	Paediatric DIPG, post-RT	19	September 2021	NCT03086616
	MTX110 (panobinostat nanoparticle formulation) via CED	Phase I	Paediatric primary diffuse midline glioma	9	February 2024	NCT04264143
	MTX110 (panobinostat nanoparticle formulation) via CED	Phase I/II	DIPG post-RT	24	March 2025	NCT03566199
	CED delivery of liposomal irinotecan	Phase I	Recurrent HGG	30	January 2022	NCT02022644
Intra-arterial delivery	Superselective intra-arterial cerebral infusion of cetuximab and/or bevacizumab	Phase I/II	Recurrent glioma, age <22 years	30	January 2025	NCT01884740
	Superselective intra-arterial cerebral infusion of cetuximab combined with hypofractionated RT	Phase II	Recurrent HGG	37	May 2022	NCT02800486
	Superselective intra-arterial cerebral infusion of TMZ	Phase I	Primary GBM and AA	30	December 2020	NCT01180816
	Superselective intra-arterial cerebral infusion of cetuximab	Phase I/II	Primary GBM	33	June 2021	NCT02861898
	Repeated superselective intra-arterial cerebral infusion of bevacizumab	Phase I	GBM	30	June 2022	NCT02285959

	Repeated superselective intra-arterial cerebral infusion of bevacizumab	Phase I/II	Primary GBM	25	January 2020	NCT01811498
	Repeated superselective intra-arterial cerebral infusion of bevacizumab	Phase I/II	Recurrent GBM and AA	54	October 2021	NCT01269853
	Intra-arterial carboplatin + RT	Phase II	Recurrent GBM	35	July 2021	NCT03672721
Localized chemotherapy	SI-053 (TMZ) as a powder in resection cavity	Phase I	Primary GBM	27	May 2023	NCT04967690
	Cerebraca wafer + TMZ	Phase I/II	Recurrent GBM	36	December 2022	NCT03234595

**Supplementary Table 3 | Localized immunotherapy**

Category	Treatment	Study type	Glioma type	Number of patients	Estimated study completion date	ClinicalTrials.gov identifier
Oncolytic viral therapy	Injection of D2C7-IT (immunotoxin) via CED	Phase I	Recurrent HGG	115	December 2022	NCT02303678
	Injection of D2C7-IT (immunotoxin) via CED with systemic Atezolizumab	Phase I	Recurrent GBM	18	January 2025	NCT04160494
	HSV G207 + single dose of RT	Phase II	Pediatric recurrent HGG	30	October 2025	NCT04482933
	HSV G207 + single dose of RT	Phase I	Recurrent cerebellar brain tumours	15	September 2024	NCT03911388
	HSV G207 + single dose of RT	Phase I	Paediatric recurrent supratentorial brain tumours	12	March 2022	NCT02457845
	Single dose of rQNestin34.5v.2 (HSV1 virus) + cyclophosphamide	Phase I	Recurrent GBM	108	July 2022	NCT03152318
	PVSRIPO delivered via CED	Phase I	Paediatric recurrent HGG	12	March 2022	NCT03043391
	PVSRIPO delivered via CED	Phase II	Recurrent HGG	122	December 2023	NCT02986178
	PVSRIPO delivered via CED	Phase I	Recurrent GBM	61	June 2021	NCT01491893
	Single injection of PVSRIPO with pembrolizumab	Phase II	Recurrent GBM	30	March 2023	NCT04479241
	Intratumoral injection of genetically engineered HSV-1 expressing IL-12	Phase II	Recurrent HGG	36	September 2023	NCT02062827

	Intra-arterial injection of Mesenchymal stem cells loaded with oncolytic adenovirus DNX-2401	Phase I	Recurrent HGG	36	February 2020	NCT03896568
	Intratumoral injection of DNX-2401 combined with pembrolizumab	Phase II	Recurrent GBM or gliosarcoma	49	June 2021	NCT02798406
	Intratumoral injection of DNX-2440	Phase I	Recurrent GBM	24	October 2022	NCT03714334
Viral gene therapy	Intra tumoral HSV-tk, RT and TMZ	Phase I/II	Primary GBM	62	December 2025	NCT03603405
	Intra tumoral HSV-tk, Valacyclovir, RT, TMZ	Phase I/II	Recurrent GBM	62	December 2025	NCT03596086
	AdV-tk + valacyclovir + RT	Phase I	Paediatric brain tumors	12	December 2021	NCT00634231
	Intra tumoral Ad-RTS-hIL-12 with Veledimex in combination with Nivolumab	Phase I	Recurrent GBM	21	December 2021	NCT03636477
	Intra tumoral Ad-RTS-hIL-12 with Veledimex in combination with cemiplimab	Phase II	Recurrent GBM	36	August 2022	NCT04006119
	Intra tumoral Ad-RTS-hIL-12 with Veledimex	Phase I	Recurrent GBM	36	June 2021	NCT03679754
	Intra tumoral Ad-RTS-hIL-12 with Veledimex	Phase I	Recurrent HGG	48	December 2019	NCT02026271
	Intra tumoral Ad-RTS-hIL-12 with Veledimex	Phase I/II	Paediatric brain tumours, DIPG	45	December 2024	NCT03330197
	Intra tumoral Ipilimumab + Intravenous Nivolumab following resection	Phase I	Recurrent GBM	6	November 2023	NCT03233152

Cytokine and antibody therapy	Injection of 124I-omburtamab via CED	Phase I	DIPG post-RT	64	December 2020	NCT01502917
	Injection of OS2966 (anti-CD29) via CED	Phase I	Recurrent HGG	24	July 2023	NCT04608812
	Injection of anti-CD40 antibody (2141-V11) via CED	Phase I	Recurrent HGG	30	December 2025	NCT04547777
	Injection of D2C7-IT via CED + atezolizumab	Phase I	Recurrent GBM	18	January 2026	NCT04160494
	Injection human recombinant bone morphogenetic protein 4 via CED	Phase I	Recurrent GBM	15	March 2021	NCT02869243

**Supplementary Table 4 | Local radiotherapy**

<b>Category</b>	<b>Treatment</b>	<b>Study type</b>	<b>Glioma type</b>	<b>Number of patients</b>	<b>Estimated study completion date</b>	<b>ClinicalTrials.gov identifier</b>
Brachytherapy	<sup>186</sup> Re nanoliposomes delivered via CED	Phase I/II	Recurrent glioma	55	January 2025	NCT01906385
	<sup>125</sup> I brachytherapy and TMZ versus standard of care	Phase I	Primary GBM	84	August 2023	NCT04856852
	Intraoperative radiotherapy	Phase I	Recurrent GBM	5	December 2024	NCT04763031
	Intraoperative radiotherapy and bevacizumab	Phase II	Recurrent GBM	100	December 2026	NCT04681677
	Intraoperative radiotherapy in addition to TMZ	Phase III	Primary GBM	314	March 2024	NCT02685605



**Supplementary Table 5 | Cell therapy**

Category	Treatment	Study type	Glioma type	Number of patients	Estimated study completion date	ClinicalTrials.gov identifier
Neural stem cells	Injection of genetically modified NSCs, flucytosine and leucovorin	Phase I	Recurrent HGG	18	June 2019	NCT02015819
	NSCs with oncolytic adenovirus (NSC-CRAAd-Survivin-pk7)	Phase I	Primary GBM	13	December 2021	NCT03072134
	Injection of c-expressing allogeneic NSCs and irinotecan hydrochloride	Phase I	Recurrent HGG	53	July 2021	NCT02192359
T cell therapy	Intraventricular and intratumoral injection of B7-H3 CAR-T cells	Phase I	Recurrent GBM	12	July 2022	NCT04385173
	Intraventricular and intratumoral injection of B7-H3 CAR-T cells	Phase I/II	Recurrent GBM	40	July 2024	NCT04077866
	Intratumoral IL13R $\alpha$ 2-targeted CAR-T cells with checkpoint inhibition	Phase I	Recurrent GBM	60	December 2022	NCT04003649
	Intracavity CD147-CAR-T cells via Ommaya reservoir	Phase I	Recurrent GBM	31	May 2022	NCT04045847
	Intracavitary $\gamma\delta$ T cell therapy + TMZ	Phase I	Primary GBM	12	January 2023	NCT04165941
	Intratumoral/cavitary HER2(EQ)BBZ/CD19t T cell injection	Phase 1	Recurrent HGG	42	June 2021	NCT03389230
	Intraventricular injection of IL13R $\alpha$ 2-CAR-T cells	Phase I	Leptomeningeal GBM,	30	December 2022	NCT04661384

			ependymoma or medulloblastoma			
	Intratumoral injection of IL13(EQ)BBzeta/CD19t+ TCM-enriched T cells	Phase I	Recurrent GBM	92	January 2022	NCT02208362
	Intraventricular NKG2D CAR-T via Ommaya reservoir	Phase I	Recurrent GBM	20	December 2023	NCT04717999
NK cell therapy	Intracavitary injection of NK-92/5.28.z cells	Phase I	Recurrent HER2-positive GBM	30	December 2022	NCT03383978
	NK cells (CYNK-001) via Ommaya reservoir	Phase I	Recurrent GBM	30	February 2024	NCT04489420
	Repeated intra tumoral engineered NK cells containing deleted TGFβR2 and NR3C1	Phase I	Recurrent GBM	25	January 2024	NCT04991870

5-ALA: 5-aminolevulinic acid, AA: anaplastic astrocytoma, CAR: chimaeric antigen receptor, CED, convection-enhanced delivery, DIPG: diffuse intrinsic pontine glioma, FUS: focused ultrasound, GBM: glioblastoma, HGG: high-grade glioma, IDHwt: isocitrate dehydrogenase wild type, LITT: laser interstitial thermal therapy, MR: magnetic resonance, NK: natural-killer, NSC: neural stem cell, PDT: photodynamic therapy, PVSRIPO: recombinant non-pathogenic polio-rhinovirus chimera, RT: radiotherapy, TMZ: temozolomide.