

Supplementary Table 1. Clinical trials of checkpoint inhibitors for the treatment of GBM.

Trial Number	Phase	Immune Checkpoint	Interventions	Status
1	III	PD-1	Drug: Nivolumab Drug: Temozolomide Radiation: Radiotherapy Other: Nivolumab Placebo	Active, not recruiting
2	III	PD-1	Drug: Nivolumab Drug: Temozolomide Radiation: Radiotherapy	Active, not recruiting
3	III	PD-1 CTLA-4	Biological: Nivolumab Biological: Bevacizumab Biological: Ipilimumab	Active, not recruiting
4	II III	CTLA-4 PD-1	Biological: Ipilimumab Biological: Nivolumab Radiation: Radiation Therapy Drug: Temozolomide	Recruiting
5	II	PD-1	Biological: PVSRIPO, Biological: Pembrolizumab	Recruiting
6	II	PD-1	Drug: Nivolumab, Drug: Bevacizumab	Recruiting
7	II	PD-L1	Biological: Avelumab	Active, not recruiting
8	II	PD-1	Biological: DNX-2401, Biological: Pembrolizumab	Active, not recruiting
9	II	PD-1	Biological: autologous dendritic cells pulsed with tumor lysate antigen Vaccine, Biological: Nivolumab,	Withdrawn
10	II	IDO	Drug: Indoximod, Radiation: Partial Radiation, Radiation: Full-dose Radiation, Drug: Temozolomide, Drug: Cyclophosphamide, Drug: Etoposide, Drug: Lomustine	Recruiting
11	II	PD-L1 CTLA-4	Biological: Durvalumab Procedure: Surgical Procedure Biological: Tremelimumab	Active, not recruiting
12	II	CTLA-4 PD-1	Biological: Ipilimumab Biological: Nivolumab	Recruiting
13	II	PD-1	Drug: Camrelizumab Radiation: radiation Drug: Temozolomide	Recruiting
14	II	Anti-GITR Anti-PD1	Drug: INCMGA00012 Drug: INCAGN01876 Drug: SRS Procedure: Brain surgery	Recruiting
15	II	PD-1	Drug: Nivolumab	Completed
16	II	PD-1	Drug: Pembrolizumab	Recruiting
17	II	PD-L1	Drug: Axitinib Drug: Avelumab	Completed
18	I II	PD-L1	Radiation: Hypofractionated stereotactic radiation therapy Drug: Durvalumab	Recruiting

19	NCT04077866	I II	B7-H3	Drug: Temozolomide, Biological: B7-H3 CAR-T	Recruiting
20	NCT03277638	I II	PD-1	Drug: Pembrolizumab at 7 days prior, Drug: Pembrolizumab at 14 days post, Drug: Pembrolizumab at 35 days post, Procedure: Laser Interstitial Thermotherapy	Recruiting
21	NCT03750071	I II	PD-L1	Biological: VXM01, Biological: Avelumab	Recruiting
22	NCT03491683	I II	PD-1	Biological: INO-5401, Biological: INO-9012, Biological: Cemiplimab, Radiation: Radiation Therapy, Drug: Temozolomide	Active, not recruiting
23	NCT04116658	I II	PD-1	Biological: Multiple dose of EO2401 in combination with nivolumab	Recruiting
24	NCT02052648	I II	IDO	Drug: Indoximod, Drug: Temozolomide, Drug: Bevacizumab, Radiation: Stereotactic Radiation	Completed
25	NCT03347097	Early I	PD-1	Drug: TIL Drug: PD1-TIL	Recruiting
26	NCT03707457	I	PD-1 GITR IDO1 CTLA-4	Drug: Nivolumab, Drug: Anti-GITR Monoclonal Antibody MK- 4166, Drug: IDO1 inhibitor INCB024360, Drug: Ipilimumab	Terminated
27	NCT03726515	I	PD-1	Biological: CART-EGFRvIII T cells Biological: Pembrolizumab	Active, not recruiting
28	NCT04003649	I	CTLA-4 PD-1	Biological: IL13Ralpha2-specific Hinge- optimized 4-1BB-co-stimulatory CAR/Truncated CD19-expressing Autologous TN/MEM Cells Biological: Ipilimumab Biological: Nivolumab	Recruiting
29	NCT03341806	I	PD-L1	Drug: Avelumab Combination Product: MRI-guided LITT therapy Biological: Dendritic Cell Tumor Cell Lysate Vaccine	Recruiting
30	NCT04201873	I	PD-1	Biological: Pembrolizumab Drug: Poly ICLC	Recruiting
31	NCT02311920	I	CTLA-4 PD-1	Biological: Ipilimumab Biological: Nivolumab Drug: Temozolomide	Active, not recruiting
32	NCT04606316	I	PD-1 CTLA-4	Drug: Nivolumab-Placebo Drug: Nivolumab Drug: Ipilimumab-Placebo Drug: Ipilimumab Procedure: Surgery	Recruiting
33	NCT03233152	I	CTLA-4 PD-1	Drug: Ipilimumab (YervoyTM, 50 mg/10 mL solution) Drug: Nivolumab (OpdivoTM, 40 mg/4mL solution)	Recruiting
34	NCT03961971	I	Tim-3 PD-1	Drug: MBG453	Recruiting

35	NCT02658981	I	LAG-3 PD-1 TNFRSF9/(C D137)	Biological: Anti-LAG-3 Monoclonal Antibody BMS 986016, Biological: Anti-PD-1, Biological: Anti-CD137	Active, not recruiting
36	NCT03493932	I	PD-1 LAG-3	Drug: Nivolumab, Drug: BMS-986016	Recruiting
37	NCT04656535	I	PD-1 TIGIT	Drug: AB122, Drug: AB154, Drug: Placebo	Not yet recruiting
38	NCT04385173	I	B7-H3	Drug: B7-H3 CAR-T, Drug: Temozolomide	Recruiting
39	NCT03576612	I	PD-1	Biological: AdV-tk, Drug: Valacyclovir, Radiation: Radiation, Drug: Temozolomide, Biological: Nivolumab,	Recruiting
40	NCT04047706	I	PD-1	Biological: IDO1 Inhibitor BMS-986205, Biological: Nivolumab, Radiation: Radiation Therapy, Drug: Temozolomide	Recruiting
41	NCT02502708	I	IDO	Drug: Indoximod, Drug: Temozolomide, Radiation: Conformal Radiation, Drug: Cyclophosphamide, Drug: Etoposide	Completed
42	NCT02852655	I	PD-1	Drug: Pembrolizumab (MK-3475)	Recruiting
43	NCT03422094	I	PD-1 CTLA-4	Biological: NeoVax, Biological: Nivolumab Biological: Ipilimumab, Procedure: Research blood draw, Procedure: Leukapheresis for research	Terminated
44	NCT02937844	I	PD-L1	Biological: Anti-PD-L1 CSR T cells, Drug: Cyclophosphamide, Drug: Fludarabine	Unknown status
45	NCT03661723	II	PD-1	Drug: Pembrolizumab Drug: Bevacizumab Radiation: Re-irradiation	Recruiting
46	NCT04118036	II	PD-1	Drug: Pembrolizumab Drug: Abemaciclib	Suspended
47	NCT03722342	I	PD-1	Drug: TTAC-0001 and pembrolizumab combination	Active, not recruiting
48	NCT03405792	II	PD-1	Drug: Temozolomide (TMZ) Device: Optune System Drug: Pembrolizumab	Recruiting
49	NCT02530502	I	PD-1	Other: Laboratory Biomarker Analysis Biological: Pembrolizumab Radiation: Radiation Therapy Drug: Temozolomide	Terminated
50	NCT02430363	I II	PD-1	Drug: MK – 3475 Biological: Suppressor of the PI3K/Akt pathways	Unknown status
51	NCT03018288	II	PD-1	Drug: Pembrolizumab Biological: HSPPC-96 Drug: Temozolomide Other: Placebo	Recruiting
52	NCT03347617	II	PD-1	Drug: Ferumoxytol Other: Laboratory Biomarker Analysis Procedure: Magnetic Resonance Imaging	Recruiting

Biological: Pembrolizumab					
53	NCT03665545	I II	PD-1	Drug: IMA950/Poly-ICLC and pembrolizumab	Recruiting
54	NCT04013672	II	PD-1	Drug: Pembrolizumab Drug: SurVaxM Drug: Sargramostim Drug: Montanide ISA 51	Recruiting
55	NCT02337491	II	PD-1	Drug: Pembrolizumab Drug: Bevacizumab	Completed
56	NCT02337686	II	PD-1	Other: Laboratory Biomarker Analysis Biological: Pembrolizumab Other: Pharmacological Study Procedure: Therapeutic Conventional Surgery	Active, not recruiting
57	NCT03426891	I	PD-1	Drug: Pembrolizumab Drug: Vorinostat Drug: Temozolomide Radiation: Radiotherapy	Recruiting
58	NCT03197506	II	PD-1	Radiation: External Beam Radiation Therapy Other: Laboratory Biomarker Analysis Biological: Pembrolizumab Radiation: Radiation Therapy Drug: Temozolomide Procedure: Therapeutic Conventional Surgery	Recruiting
59	NCT02287428	I	PD-1	Radiation: Radiation Therapy Biological: Personalized NeoAntigen Vaccine Drug: Pembrolizumab Drug: Temozolomide	Recruiting
60	NCT03311542		PD-1	Biological: pembrolizumab	No longer available
61	NCT03797326	II	PD-1	Biological: Pembrolizumab Drug: Lenvatinib	Recruiting
62	NCT01174121	II	PD-1	Biological: Young TIL Drug: Aldesleukin Drug: Cyclophosphamide Drug: Fludarabine Drug: Pembrolizumab (Keytruda)	Suspended
63	NCT04429542	I	PD-1	Drug: BCA101 Drug: Pembrolizumab	Recruiting
64	NCT03636477	I	PD-1	Biological: Ad-RTS-hIL-12 Drug: Veledimex Drug: Nivolumab	Active, not recruiting
65	NCT02648633	I	PD-1	Radiation: Stereotactic Radiosurgery Drug: Nivolumab Drug: Valproate	Terminated
66	NCT03430791	II	CTLA-4, PD-1	Drug: Nivolumab 240 mg IV Drug: Nivolumab 3 mg/kg Drug: Ipilimumab 1 mg/kg Device: NovoTTF200A (Optune)	Active, not recruiting
67	NCT03452579	II	PD-1	Drug: Nivolumab Drug: Standard Dose Bevacizumab Drug: Reduced Dose Bevacizumab	Active, not recruiting
68	NCT04195139	II	PD-1	Drug: Nivolumab Drug: Temozolomide	Recruiting
69	NCT03743662	II	PD-1	Radiation: Re-irradiation (RT)	Recruiting

				Drug: Bevacizumab Drug: Nivolumab Procedure: Re-resection	
70	NCT03367715	II	CTLA-4, PD-1	Drug: Nivolumab Drug: Ipilimumab Radiation: Radiation Therapy (RT)	Recruiting
71	NCT02529072	I	PD-1	Drug: nivolumab Biological: DC	Completed
72	NCT03718767	II	PD-1	Drug: Nivolumab	Recruiting
73	NCT02327078	I II	PD-1	Drug: Nivolumab (Phase 1) Drug: Epacadostat (Phase 1) Drug: Chemotherapy (Phase 1) Drug: Nivolumab (Phase 2) Drug: Epacadostat (Phase 2)	Completed
74	NCT04323046	I	CTLA-4 PD-1	Biological: Ipilimumab Biological: Nivolumab Drug: Placebo Administration Other: Quality-of-Life Assessment Other: Questionnaire Administration	Recruiting
75	NCT02335918	I II	PD-1	Drug: Combination of varlilumab and nivolumab	Completed
76	NCT03879512	I II	CTLA-4 PD-1	Drug: depletion of regulatory T cells Procedure: reoperation Biological: cancer vaccine Biological: checkpoint blockade Nivolumab/Ipilimumab	Recruiting
77	NCT03684811	I II	PD-1	Drug: FT-2102 Drug: Azacitidine Biological: Nivolumab Drug: Gemcitabine and Cisplatin	Active, not recruiting
78	NCT04704154	II	PD-1	Drug: Regorafenib, (Stivarga, BAY73-4506) Drug: Nivolumab (Opdivo)	Recruiting

Abbreviations: PD-1: programmed cell death protein 1, PD-L1: programmed death-ligand 1, CTLA-4: (Cytotoxic T-Lymphocyte Associated Protein 4, IDO: indoleamine 2,3-dioxygenase, Tim-3: T cell immunoglobulin and mucin-domain containing-3, TIGIT: T cell immunoreceptor with Ig and ITIM domain, LAG-3: lymphocyte activation gene-3, TNFRSF9: tumor necrosis factor receptor superfamily member 9

Supplementary Table 2: Completed clinical trials of oncolytic virotherapy for the treatment of GBM.

Virus	Strain	Features	Phase	Route	Trial Number
Adenovirus	Onyx-015	E1B-55kD deletion	I	-	-
	DNX-2401		I	IT	NCT00805376
	DNX-2401		I/II	Intracerebral infusion by CED	NCT01582516
	DNX-2401 + TMZ	Δ 24 deletion in E1A RGD-4C fiber modification	I	IT followed by oral TMZ	NCT01956734 (Spain)
	DNX-2401 + IFN γ		Ib	IT followed by IFN γ	NCT02197169 (TARGET-I)
Herpesvirus	G207	γ 34.5 and UL39 deletion	Ib/II	IT	NCT00028158
			I	IT followed by radiation	NCT00157703
	HSV 1716	γ 34.5 gene deletion	I	IT	(UK)
			I	IT	(UK)
			I	IT	(UK)
	G47 Δ	γ 34.5, UL39 and α 47 deletion. US11 expression under α 47 promoter	I/II	IT	UMIN00000266
			II	IT	UMIN000015995 (Japan)
Measles	MV-CEA	Attenuated expressing hCEA	I	Injection into resection cavity and/or IT	NCT00390299
Parvovirus	ParvOryx	Unmodified rat parvovirus	I/IIa	IT/IV followed by tumor resection	NCT01301430
Reovirus	REOLYSIN	Unmodified human reovirus (serotype 3)	I	IT	-
			I/II	IT	NCT00528684
			I	IV	EudraCT 2011-005635-10
Retrovirus	Toca 511 +Toca FC	Expressing CD gene	I	Injection into resection cavity	NCT01470794
			I	IT or IV	NCT01156584
			I	IV	NCT01985256

Abbreviations: RGD: arginine-glycine-aspartic acid, CED: convection-enhanced delivery, IT: intratumorally, TMZ: temozolomide, IFN γ : interferon gamma, CEA: carcinoembryonic antigen, IV: intravenously, CD: cytosine deaminase.

Supplementary Table 3: Currently active and/or recruiting clinical trials of oncolytic virotherapy for the treatment of GBM

Virus	Strain	Features	Phase	Route	Trial Number
Adenovirus	DNX-2401	Loaded onto allogeneic BM-hMSCs	I	IA	NCT03896568
	DNX2401+ pembrolizumab		II	IT	NCT02798406 (CAPTIVE)
	DNX-2440	DNX-2401 expressing OX40L	I	IT	NCT03714334
	NSC-CRAAd-S-pk7	E1A under survivin promoter Loaded onto NSCs	I	IT	NCT03072134
Herpesvirus	C134	γ 34.5 deletion IRS1 expression under control of an HCMV immediate early promoter	I	IT	NCT03657576
	G207 +/- 5 Gy radiation	Deletion of both copies of γ 34.5 gene Inactivating lacZ insertion in UL39 gene	I I II	IT IT IT	NCT02457845 NCT03911388 NCT04482933
	M032	Deletion of both copies of γ 34.5 gene Expressing human IL-12	I	IT	NCT02062827
	rQNestin34.5v2	γ 34.5 and UL39 deletion γ 34.5 expression under nestin promoter	I	IT +/- IV CPA	NCT03152318
				I/Ib Ib II	IT IT IT
Poliovirus	PVSRIPO	Attenuated poliovirus with IRES replaced by IRES from HRV2			
	PVSRIPO+ pembrolizumab		II	IT	NCT04479241 (LUMINOS-101)
Reovirus	REOLYSIN + rGM-CSF	Unmodified human reovirus (serotype 3)	I	IV	NCT02444546
Retrovirus	Toca 511 +Toca FC	Expressing CD gene	II/III	IT	NCT02414165
Vaccinia	TG6002 + 5-FC	Expressing FCU1 TK and RR gene deletion	I/II	IV	NCT03294486

Abbreviations: BM-hMSCs: bone-marrow human mesenchymal stem cells, IA: intra-arterial, IT: intratumorally, OX40L: OX40 ligand, NSCs: neural stem cells, IRS1: insulin receptor substrate 1, HCMV: human cytomegalovirus, UL39: ribonucleotide reductase large subunit, IL-12: interleukin 12, IV: intravenously, CPA: cyclophosphamide, IRES: internal ribosome entry site, HRV2: human rhinovirus type 2, rGM-CSF: recombinant granulocyte-macrophage colony-stimulating factor, CD: cytosine deaminase, 5-FC: 5-fluorocytosine, FCU1: fusion suicide gene 1, TK: thymidine kinase, RR: ribonucleotide reductase.

Supplementary Table 4: Currently active and/or recruiting clinical trials of CAR-T cell therapy for the treatment of GBM

	Target Antigen	Estimated Enrolment	Status	Phase	Trial Number
1	GD2		Withdrawn	II	NCT03252171
2	EphA2		Withdrawn	II	NCT02575261
3	EGFR		Unknown	I	NCT02331693
4	GD2		Withdrawn	II	NCT04406610
5	EGFRVIII, IL13R α 2, Her-2, EphA2, CD133, GD2	100 participants	Recruiting	I	NCT03423992
6	GD2	54 participants	Recruiting	I	NCT04196413
7	GD2-C7R	34 participants	Recruiting	I	NCT04099797
8	B7-H3	70 participants	Recruiting	I	NCT04185038
9	MUC1	20 participants	Unknown	II	NCT02617134
10	CD147	31 participants	Recruiting	I	NCT04045847
11	Chlorotoxin-Car T cells for MPP2 ⁺ Glioblastoma cells	36 participants	Recruiting	I	NCT04214392
12	EGFRVIII	18 participants	Completed	II	NCT01454596
13	EGFRVIII	3 participants	Terminated	I	NCT02664363
14	NKG2D	10 participants	Not yet recruiting	I	NCT04550663
15	EGFR	36 participants	Recruiting	I	NCT03638167
16	HER2	48 participants	Recruiting	I	NCT03500991
17	EGFRVIII, DR5, NY-ESO-1, Mesothelin	50 participants	Recruiting	II	NCT03941626
18	HER2		Withdrawn	II	NCT02713984
19	EGFRVIII	73 participants	Recruiting	II	NCT03638206
20	EGFRVIII	11 participants	Terminated	I	NCT02209376
21	IL13R α 2	92 participants	Recruiting	I	NCT02208362
22	EGFRVIII	24 participants	Suspended	I	NCT03283631
23	EGFRVIII	20 participants	Unknown	I	NCT02844062
24	NKG2D		Withdrawn	I	NCT04270461
25	HER2	42 participants	Recruiting	I	NCT03389230
26	IL13R α 2	30 participants	Recruiting	I	NCT04661384
27	IL13R α 2	60 participants	Recruiting	I	NCT04003649
28	EGFRVIII	7 participants	Completed	I	NCT03726515
29	PD-L1	20 participants	Unknown	I	NCT02937844
30	NKG2D	20 participants	Not yet recruiting		NCT0471799
31	B7-H3	40 participants	Recruiting	II	NCT04077866
32	B7-H3	12 participants	Recruiting	I	NCT04385173
33	HER2	16 participants	Completed	I	NCT01109095

Abbreviations: GD2: disialoganglioside, EphA2: erythropoietin-producing hepatocellular carcinoma A2, CLTX: chlorotoxin, NKG2DLs: natural killer group 2D ligands, CSPG4: chondroitin sulfate proteoglycan 4, CAIX: carbonic anhydrase IX, and integrin $\alpha\beta$ 3, EGFR: epidermal growth factor receptor, EGFRVIII: EGFR variant III, IL13R α 2: interleukin-13 receptor subunit alpha-2, Her-2: human epidermal growth factor receptor 2, MUC1: mucin 1, MMP2: multipotent progenitor 2, DR5: death receptor 5, NY-ESO-1: New York esophageal squamous cell carcinoma 1, PD-L1: programmed death-ligand 1