**Supplementary Table S1. Detailed Study Design of Clinical Studies Implementing Molecular Targeted Therapies in Glioma**

| Study Author | Year | Tumor Details | Molecular target | Intervention | Patient Age(s)* | N | Study Design | Quality Rating |
|---|---|---|---|---|---|---|---|---|
| **Protein Kinase Pathways** | | | | | | | | |
| Berzero et al | 2021 | BRAF-V600 Mutant Gliomas | RAF + MEK | Vemurafenib, Dabrafenib, Cobimetinib, Trametinib | Median age 36 | 28 | Retrospective Cohort | Level IV |
| Butowski et al | 2010 | Newly diagnosed GBM or GS with a biopsy or resection 5 weeks prior to treatment | Protein kinase C-beta + PI3K/AKT pathway | Enzastaurin + TMZ | > 18 | 12 | Phase I Trial | Level IV |
| Chinnaiyan et al | 2013 | Newly diagnosed GBM | mTOR | Everolimus + TMZ + RT | Median age 57.6 | 35 | Phase I/II Trial | Level IV |
| Drobysheva et al | 2017 | Pilocytic astrocytomas | BRAF + MAPK | Dabrafenib +/- Trametinib | 15-Jan | 5 | Case Series | Level VI |
| Franceschi et al | 2012 | Histologically documented GBM and IDH-mutant Glioma | Src kinase | Dasatinib | Median age 54.8 | 26 | Phase I/II Trial | Level IV |
| Fusco et al | 2021 | 3/4 cases IDH-wt and BRAFV600E, 1/4 cases IDH1 mutant and BRAFV600E | BRAF + MEK | Dabrafenib + Trametinib | 23.5 ± 6.40 | 4 | Case Series | Level IV |
| Hottinger et al | 2019 | BRAF-mutated glioma | MAPK + ERK | Dabrafenib + Trametinib | Median ages 31 and 40 | 2 | Case Report | Level VI |
| Johanns et al | 2018 | IDH-wt GBM | BRAF + MEK | Dabrafenib + Trametinib | 28 + 24 | 2 | Case Series | Level VI |
| Kaley et al | 2018 | GBM, anaplastic astrocytoma, pleomorphic xanthoastrocytoma, anaplastic ganglioma, pilocytic astrocytoma, HGG | BRAF | Vemurafenib | 18-81 | 24 | Phase II Trial | Level IV |
| Kanemaru et al | 2019 | GBM with BRAF V600E, TERT, and CDKN2A mutations | BRAF + MEK | Dabrafenib + Trametinib | Median age 57 | 1 | Case Report | Level VI |
| Kebir et al | 201 | 5 IDH-wt GBM; | Multitarget | Regorafenib | 18–69 | 6 | Retrospectiv | Level |

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|---|---|---|---|---|---|---|---|---|
| | 9 | 1 IDH-mutant | kinase | | | | e Cohort | IV |
| Kleinschmidt-DeMasters et al | 2015 | 19 IDH-wt GBM; 1 IDH-mutant Astrocytoma | BRAF V600E kinase | Vemurafenib | 10–82 | 20 | Retrospective Cohort | Level IV |
| Lapointe et al | 2020 | 14 IDH-wt; 1 IDH-mutant | mTORC1/2 | Vistusertib | Median age 66 | 15 | Phase I Trial | Level IV |
| Lee et al | 2012 | Histology confirmed GBM | Multitarget kinase + mTOR | Sorafenib + Temsirolimus | Median age 50 | 31 | Phase I/II Trial | Level IV |
| Lombardi et al | 2019 | Histology confirmed GBM | Multitarget kinase + mTOR | Regorafenib | 54.8–58.9 | 119 | Phase II Trial | Level II |
| Mason et al | 2012 | Newly diagnosed, histologically confirmed GBM | mTOR1 | Everolimus + TMZ | >18 | 103 | Phase I Trial | Level IV |
| Migliorini et al | 2017 | Pleomorphic xanthoastrocytoma | BRAF + MEK | Dabrafenib + Trametinib | Median age 32 | 1 | Case report | Level VI |
| Rosenberg et al | 2022 | HGG, GBM, anaplastic gangioglioma, diffuse midline glioma, high-grade neuroepithelial tumor, anaplastic astrocytoma, anaplastic astroblastoma | BRAF; BRAF + MEK | Vemurafenib/Dabrafenib (BRAF) + Trametinib (MEK) | 2.3-21.4 | 19 | Multi-institutional Retrospective Analysis | Level IV |
| Sanai et al | 2018 | 1st recurrence GBM | Wee1K | AZD1775 | Median age 59 | 20 | Phase 0 Trial | Level VI |
| Schiff et al | 2015 | 25 recurrent GBM; 1 Astrocytoma | MET + VEGFR2 | Cabozatinib | 56.5 | 26 | Phase I trial | Level IV |
| Shah et al | 2007 | Various gliomas | PDGFR | Imatinib + Hydroxyurea | Median age 47 | 16 | Retrospective Review | Level IV |
| Shi et al | 2019 | BRAF V600E IDH-wt, 1p19q co-deletion Glioma | BRAF V600E | Vemurafenib and Everolimus | Median age 22 | 1 | Case Report | Level VI |
| Werner et al | 2022 | Grade III and IV treatment-refractory gliomas | Multitarget kinase | Regorafenib | Median age 54 | 30 | Phase II Trial | Level IV |
| Wick et al | 2019 | IDH-wt, MGMT-negative GBM | ALK mTOR MDM2 SHH CDK4/6 | Alectinib Temsirolimus Idasanutlin Vismodegib Palbociclib | Still Recruiting Patients | | Open-label, Multicenter, Phase I/IIa Trial | Level II |

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|---|---|---|---|---|---|---|---|---|
| Yau et al | 2020 | Grade I Unresectable BRAF V600E ganglioglioma | BRAF + MEK | Vemurafenib and Cobimetinib | Median age 32 | 1 | Case Report | Level VI |
| Zustovich et al | 2013 | Histologically confirmed GBM | Multitarget kinase | Sorafenib | Median age 60 | 43 | Phase II Trial | Level IV |
| **Microenvironmental Targets (angiogenesis, cell-cell adhesion, iron/cation regulation)** | | | | | | | | |
| Badruddoja et al | 2017 | Recurrent GBM | VEGF | Bevacizumab + TMZ | 55.00 ± 14.81 years | 26 | Phase II Trial | Level II |
| Brown et al | 2016 | GBM with prior resection, radio, chemo, and TMZ | VEGFR + EGFR | Cediranib + Gefitinib/placebo | 30-71 | 38 | Phase II Trial | Level IV |
| Clarke et al | 2014 | Newly diagnosed, surgically confirmed GBM or gliosarcoma, with study treatment starting 3–5 wk after open surgery or 2–5 wk after biopsy | VEGF + tyrosine kinase | Bevacizumab + Erlotinib | Median age 54 | 59 | Phase II Trial | Level IV |
| D'Alessandris et al | 2013 | Recurrent GBM | VEGF + EGFRvIII | Bevacizumab + Erlotinib | 30-77 | 10 | Prospective Trial | Level IV |
| Desjardins et al | 2012 | Histologically documented GBM | VEGF | Bevacizumab | Median age 56 | 32 | Phase II Trial | Level IV |
| Hasselbalch et al | 2010 | Grade IV astrocytoma/GBM | EGFR, VEGF, topoisomerase I | Cetuximab + Bevacizumab + Irinotecan | 50.5–57.9 | 61 | Phase II Trial | Level IV |
| Lassen et al | 2015 | Recurrent GBM | Placental growth factor (PlGF) + VEGF | RO5323441 + Bevacizumab | 58 | 22 | Phase Ib Trial | Level II |
| Lu et al | 2014 | GBM and anaplastic astrocytoma | VEGF | Bevacizumab + TMZ | Not Provided | 15 | Clinical Trial | Level IV |
| Prados et al | 2009 | Newly diagnosed GBM or gliosarcoma | EGFR | Erlotinib + TMZ + RT | Median age 55 | 65 | Phase II Trial | Level IV |
| Vaccaro et al | 2014 | Recurrent gliomas of various types | VEGF | Bevacizumab | Median age 38 | 26 | Phase I Trial | Level IV |
| Vredenburgh et al | 2012 | Newly diagnosed GBM | VEGF | Bevacizumab + RT + TMZ | 56.2 | 125 | Phase I Trial | Level IV |

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|---|---|---|---|---|---|---|---|---|
| Wang et al | 2014 | GBM | EGFR | Nimotuzumab, TMZ and RT | Median age 50 | 26 | Phase I Trial | Level IV |
| Wang et al | 2017 | Recurrent gliomas | VEGFR2 | Apatinib + Irinotecan | Median age 49 | 10 | Pilot Study | Level IV |
| Weller et al | 2017 | EGFRvIII GBM | EGFR | TMZ +/- Rindopepimut | Median ages 58,59 | 338 | Phase III Trial | Level II |
| Wick et al | 2020 | GBM or oligodendroma | TGF B | TMZ+RT +/- Galunisertib | 58.4 | 33 | Phase II Trial | Level II |
| **Immunotherapy Pathways** | | | | | | | | |
| Anghileri et al | 2021 | Lynch Syndrome recurrent GBM | PD1 | Nivolumab | Median age 33 | 1 | Case Report | Level VI |
| Nayak et al | 2021 | Recurrent GBM (bevac naive) | PD1 + VEGF | Pembrolizumab + Bevacizumab | Median age 53 | 80 | Phase II Trial | Level IV |
| Reardon et al | 2020 | Recurrent GBM treated with TMZ and radiation originally | PD1 | Nivolumab | 55.5 | 184 | Phase III Trial | Level II |
| **Cell Cycle/Apoptosis/Transcription Pathways** | | | | | | | | |
| Brachman et al | 2015 | Newly diagnosed, supratentorial, histologically confirmed GBM or gliosarcoma | Thioredoxin reductase + ribonucleotide reductase | Motexafin Gadolinium + TMZ + RT | Not Provided | Phase 1 21; Phase 2 92 | Phase I/II Trial | Level II |
| Kubicek et al | 2009 | 17 GBM, 1 anaplastic oligodendroglioma, 1 astrocytoma | 26S Proteasome | Bortezomib | Median age 52 | 23 | Phase I Trial | Level IV |
| Lin et al | 2020 | Spinal astrocytoma | CDK4 | Palbociclib | Median age 38 | 1 | Case Report | Level VI |
| **Other** | | | | | | | | |
| Desjardins et al | 2011 | GBM, WHO grade IV | Farnesyl transferase | SCH 66336 | Median age 51 | 36 | Phase I Trial | Level IV |
| Geletneky et al | 2017 | GBM | Protein NS1 | Rat H-1 parvovirus (H-1PV) | 57.8 +/- 10.6 | 18 | Phase I/IIa Trial | Level IV |
| Hashimoto et al | 2015 | GBM confirmed by pathological review and IDH-wt status | WT1 (Wilms Tumor 1) | WT1 peptide vaccination + TMZ | Median age 49 | 7 | Phase I Trial | Level IV |
| Patel et al | 2012 | Grade III and IV glioma | ER | Tamoxifen + TMZ + RT | Median age 51 | 17 | Phase I Trial | Level IV |
| Sauter et al | 2022 | Primary inoperable or recurrent GBM | CSF1R, ABL, cKIT, PDGFR | Imatinib | 63,52 (median for each arm) | 51 | Phase II Trial | Level IV |

Abbreviation: RCT, randomized control trial; DIPG, diffuse intrinsic pontine glioma; EGFR, epidermal growth factor receptor; GBM, glioblastoma multiforme; PFS, progression-free survival; PT, patient; RR, response rate; VEGFR, vascular endothelial growth factor; CDK, cyclin-dependent kinase; EGFR,

epidermal growth factor receptor; GBM, glioblastoma multiforme; HGG, high grade glioma; IDH, isocitrate dehydrogenase; PDGFR, platelet-derived growth factor receptor; TMZ, temozolomide; VEGFR, vascular endothelial growth factor receptor; WHO, World Health Organization
*Age variables include the provided averages or range from each respective paper, unless otherwise stated as a median age

**Supplementary Table S2. Detailed Study Design of Laboratory Studies Implementing Molecular Targeted Therapies in Glioma**

| Study Author | Year | Tumor Sample | Molecular target | Intervention | Design | 3D Culture | Study Subject | Modality |
|---|---|---|---|---|---|---|---|---|
| **Protein Kinase Pathways** | | | | | | | | |
| Aldea et al | 2014 | Patient Samples | mTOR + RAF | Metformin + Sorafenib | in vitro | Yes | Human cell line | small molecule |
| Aoki et al | 2013 | C6 | Ras | Nobiletin | in vivo | No | Rat cell line | citrus flavonoid |
| Arcella et al. | 2013 | U87 | mTOR | Rapamycin | in vivo and ex vivo | No | Human cell line | macrolide |
| Ariey-Bonnet et al. | 2020 | U87, U87vIII, T98, U251 | MAPK14 | Benzimidazole | in vitro and in silico | Yes | Human cell line | anthelmintic small molecule |
| Balkhi et al | 2016 | C6 | Multitarget kinases | Caffeic Acid Phenethyl Ester (CAPE) + Dasatinib | in vitro | No | Rat cell line | small molecule |
| Barbarisi et al. | 2018 | T98, A172 | CD44 | Quercetin, Temozolomide | in vitro | No | Human cell line | nanocarriers |
| Benezra et al | 2012 | murine GBM | Multitarget kinases | Dasatanib | in vitro and in vivo | No | Mouse cell line | small molecule |
| Camorani et al. | 2015 | U87vIII | EGFRvIII | CL4 aptamer with EGFR TKIs | in vitro | No | Human cell line | aptamer |
| Chen et al. | 2019 | U87, U118, A172, LN18 | CD163 pathway (CK2, kinase) | TBB (4,5,6,7-tetrabromo-1H-benzotriazole) | in vitro and in vivo | Yes | Human cell line | small molecule |
| Cheng et al. | 2022 | LN229, T98, A172 | CTSC (Cysteine cathepsin C) | Piperlongumine, Scopoletin | in vitro | No | Human cell line | small molecule |
| Ciesielski et al | 2018 | U87 and T98G | Src-kinase + tubulin polymerization inhibitory activity | KX2-361 | in vivo | No | Mice | small molecule |
| Cloninger et al | 2011 | U87 and LN229 | SAPK2/p38 + mTORC1 | SB203580 + Rapamycin | in vitro and in vivo | No | Mice | small molecule |

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|---|---|---|---|---|---|---|---|---|
| Combs et al | 2007 | U87, LN229, LN18, NCH 82, and NCH 89 | EGFR | Cetuximab | in vitro | No | Human cell line | Monoclonal antibody |
| Dasgupta et al | 2015 | AM-38 and DBTRG05 MG | BRAF V600E | PLX4720 + RT | in vitro and in vivo | No | Human cell line | small molecule |
| Dantas-Barbosa et al. | 2015 | U87, U118, ependymoma, IGRG121 glioma | NOTCH, FBXW7 downregulation | γ-secretase inhibitor RO4929097 | in vitro and in vivo | No | Human cell lines | small molecule |
| Davare et al. | 2018 | U118, Ba/F3, NIH3T3 | ROS1 | Lorlatinib | in vitro and in vivo | Yes | Human cell line | small molecule |
| Di Stefano et al. | 2015 | GIC-1123 | FGFR kinase | JNJ-42756493 | in vitro and in vivo | Yes | GIC | small molecule |
| Dominguez et al. | 2013 | U87, U251, patient samples | DGKalpha | R59022, R59949 | in vitro and in vivo | No | Human cell line, Rat | kinase inhibitor and siRNA |
| Du et al | 2012 | BT325 and U251 | Raf/MEK/ERK signaling pathway | Sorafenib + Vitamin K | in vitro | No | Human cell line | small molecule |
| Emlet et al. | 2014 | patient samples | EGFRvIII + CD133 | EGFRvIII, CD133 AB | in vivo | Yes | Human tumor cell line, mice | bispecific antibody |
| Farrell et al | 2017 | U87 | MET | WO2010/019899A1, PF04217903, Crizotinib | in vivo | No | Mice and Human cell line | small molecule |
| Feng et al. | 2010 | C6 rat glioma (IDH-wt) | PI3K/Akt; JNK; ERK | Tamoxifen | in vitro | No | Rat cell line | estrogen receptor inhibitor |
| Glassman et al | 2021 | A172, A1207, U87MG, U178MG, U251MG, U373MG, SK-MG4, SK-MG5, SK-MG15, TC620, C6 rat cell line | MAPK kinase | U0126 | in vitro | No | Human and rat cell lines | small molecule |
| Goker et al | 2020 | T98G | ALK | AZD3463 + TMZ | in vitro | No | Human cell line | small molecule |
| Golubovskaya et al | 2013 | U87 | FAK | Y15 | in vitro and in vivo | No | Human cell line | small molecule |

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|---|---|---|---|---|---|---|---|---|
| Grossauer et al. | 2016 | BRAFV600E, Glioma cells | BRAF/MEK | Dabrafenib, Trametinib | in vitro and in vivo | No | Mouse cell line | small molecule inhibitors |
| Gursel et al. | 2011 | Mouse and human astrocytomas | PI3K/Akt | PI103 | in vivo | No | Human and mouse glioma cell lines transplanted into mice | kinase inhibitor |
| He et al | 2016 | U251 and U87 | MEK2 | MEK2 antibody | in vitro and in vivo | No | Human cell line | Antibody |
| Hjelmeland et al | 2007 | U87 and U373 | Raf + TOR | LBT613 + Everolimus | in vitro and in vivo | No | Mice and Human cell line | small molecule |
| Hong et al | 2014 | Patient Samples | Aurora-A kinase | Alisertib | in vitro | Yes | Human cell line | small molecule |
| Jiang et al. | 2018 | U87, U251 | EGFR/EGFRvIII | EGFR/EGFRvIII CAR T cells | in vitro and in vivo | No | Human cell line | chimeric antigen receptor T cells |
| Jin et al. | 2013 | U87, U251 | Notch + AKT | MRK003, MK-2206 | in vitro | No | Human cell line | kinase inhibitor |
| Joel et al. | 2015 | GICs from T08 | PBK/TOPK | HI-TOPK-032 | in vitro and in vivo | Yes | Patient derived GIC cultures, T08 cells into mice | small molecule |
| Joshi et al | 2012 | GBM oncosphere line 020913 | Multitarget kinases | Gefitinib, Erlotinib, Sunitinib | in vitro and in vivo | Yes | Mice and Human cell line | small molecule |
| Ju et al | 2016 | U87 | COX-2 | Celecoxib | in vitro and in vivo | Yes | Mice and Human cell line | small molecule |
| Junca et al. | 2017 | patient samples | ALK, ROS1, MET | Crizotinib | in vitro | Yes | Human tumor cells | small molecule |
| Jung et al. | 2014 | U87, U251 | FOXO3A | Z-ajoene | in vitro | Yes | Human cell line | garlic derived molecule |
| Kawauchi et al | 2021 | U87, LN229, and GSC23 | ALK | Alectinib + Ceritinib | in vitro and in vivo | Yes | Mice and Human cell line | small molecule |
| Kim et al | 2012 | U87 and Patient Samples | Phosphoinositide 3-kinase/AKT and Ras/Raf | 5-Bromo-3-(3-hydroxyprop-1-ynyl)-2H-pyran-2-one (BHP) | in vitro and in vivo | Yes | Mice and Human cell line | small molecule |
| Koul et al. | 2005 | U87, U251, LN229, | Integrin-linked kinase | QLT0276 | in vitro | No | Human cell line | kinase inhibitor |

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|---|---|---|---|---|---|---|---|---|
| | | SNB19, U373, D54 | | | | | | |
| Koul et al. | 2010 | U87 | PI3K/AKT | PX-866 | in vitro and in vivo | No | Human tumor cell lines and mouse xenografts | kinase inhibitor |
| Liu et al. | 2011 | U251 | basic Fibroblast Growth Factor (bFGF) - STAT3 pathway | Anti bFGF siRNA | in vitro | No | Human cell line | siRNA |
| Liu et al. | 2014 | U87 | EGFR & PI3K/AKT | G19 | in vitro and in vivo | No | Human cell line | oligosaccharide |
| Liu et al | 2014 | T98G, A172 and U87 | AMPK | Compound C | in vitro | Yes | Human cell line | small molecule |
| Luchman et al | 2014 | Patient sample | mTOR1/2 | AZD8055 | In vitro and in Vivo | Yes | Human cell line and mice | small molecule |
| Ma et al. | 2015 | U87, U251 | STAT3 | Tetrandrine | in vivo | No | Human cell line and tumor cells | alkaloid |
| Matsuda et al | 2012 | U87, T98G, patient samples | JNK | SP600125 | In vitro and in Vivo | Yes | Human cell line and mice | small molecule |
| Maxwell et al | 2021 | BT40 | mTOR1/2 + MEK | TAK228 + Trametinib | In vivo | No | Mice | small molecule |
| Nicolaides et al | 2011 | AM38 | BRAF | PLX4720 | In vivo | No | Mice | small molecule |
| Paternot et al | 2009 | T98G, U87MG, U138MG | mTOR1 + MEK1/2 | Rapamycin + PD184352 | In vitro | No | Human cell line | small molecule |
| Peng et al. | 2013 | U87, CHG5 | RACK1-PKC | siRNA | in vitro and in vivo | No | Human cell and tumor lines | siRNA |
| Pezuk et al | 2013 | U251, U138, U87, T98G, U343 and MO59K | PLK1 | BI2536 + TMZ | in vitro | No | Human cell line | small molecule |
| Phillips et al. | 2016 | A431, U87 | EGFR | ABT-414 | in vitro and in vivo | No | Human cell line | antibody-small molecule fusion |
| Premkumar et al | 2010 | U87, T98G, U373, LN229 and | IGF1R + Src | NVP-AEW541 + Dasatinib | | No | Human cell line | small molecule |

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|---|---|---|---|---|---|---|---|---|
| | | A172 | | | | | | |
| Qin et al. | 2014 | U87, U138, U373 | EMP2 | Anti-EMP2 antibodies, Anti-EMP2 IgG1 | in vitro and in vivo | No | Human cell line | antibody |
| Raub et al | 2015 | U87 | CDK4 + CDK6 | Abemaciclib or Palbociclib + TMZ | In vitro and in vivo | No | Human cell line and rats | small molecule |
| Salphati et al. | 2012 | U87, GS2, GBM10 | PI3k | GNE-317 | in vitro and in vivo | Yes | Human cell line in mice | kinase inhibitor |
| Sathornsumetee et al | 2006 | U87MG, T98G, and U373MG | BRAF, CRAF, VEGFR | AAL881 | In vitro and in vivo | No | Human cell line and mice | small molecule |
| See et al | 2012 | 19 different GBM lines | MEK + PI3K/mTOR | Vemurafenib + PI103 | In vitro and in vivo | No | Human cell lines | small molecule |
| Selvasaravanan et al | 2020 | U87GM and A172 | MEK or PI3K | Trametinib + Pictilisib | In vitro | Yes | Human cell lines | small molecule |
| Shingu et al | 2015 | U87MG, LNZ308, LN428 | MEK, EGFR, PI3K | Various small molecule inhibitors | in vitro | Yes | Human cell lines | small molecule |
| Siegelin et al | 2010 | U87, U251, LN229 | BRAF | Sorafenib | In vitro and in vivo | No | Human cell lines and mice | small molecule |
| Signore et al. | 2014 | U87, T98 | PDK1 + CHK1 | UCN-01 | in vitro and in vivo | No | Human cell line | staurosporin derivative |
| Spino et al | 2019 | Patient sample | DLL3 | Rovalpituzumab tesirine | In vitro | Yes | Human cell lines | Monoclonal antibody |
| Thanasupawat et al | 2017 | U87 and U251 | FGFR | Dovitinib | In vitro and in vivo | No | Human cell lines and mice | small molecule |
| Thompson et al | 2018 | Patient sample | Various | Various antibodies + kinase inhibitors + chemo drugs | In vivo | No | Mice | Small molecule and MAB |
| Tsigelny et al | 2017 | U87 and patient sample | OLIG2 | SKOG102 | In vitro and in vivo | Yes | Human cell lines | small molecule |
| van den Heufel | 2017 | E98 | MET | Compound A | In vitro and in vivo | Yes | Human cell lines and mice | small molecule |
| Wang et al | 2013 | U87, U251, and patient samples | MEK1 | miR-181b + TMZ | In vitro | No | Human cell lines | miRNA |
| Wang et al. | 2014 | U87, U251 | RAS | miR-143 | in vitro and in vivo | No | Human cell line and tumor cells | miRNA |

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|---|---|---|---|---|---|---|---|---|
| Wang et al. | 2019 | Glioma stem cells from patient xenografts | EGFR or PI3K w/ DHODH | Lapatinib (EGFR) + BKM120 (PI3K) + Teriflunomide | in vitro and in vivo | No | Human cell line | small molecule |
| Wichmann et al. | 2015 | U251, LN229 | EGFR + HER2 | siRNAs + therapeutic antibodies (EGFR: Cetuximab; HER2: Trastuzumab) | in vitro | No | Human cell lines | siRNA, small molecule |
| Yan et al | 2017 | DF1-virus laden cells | CSF-1R + cKIT + RTKs | PLX3397 + Vatalanib + Dovitinib | In vivo | No | Mice | Small molecule |
| Yang et al | 2008 | F98 | EGFR | Boronated EGFR MAB + Cetuximab | In vitro and in vivo | No | Rats | Small molecule and MAB |
| Yao et al. | 2015 | AM38, DBTRG-05MG, NMC-G1 | EGFR + BRAF | BRAF(V600E) inhibitor PLX4720 | in vitro and in vivo | No | Human cell lines, orthotopic mouse model | small molecule |
| Zavalhia et al | 2014 | Patient sample | cKIT | Imatinib | ex vivo | No | Human tumors | Small molecules |
| Zhang et al. | 2015 | U87 | mGluR1 | siRNA ,Riluzole , BAY36-7620 | in vitro and in vivo | No | U87, U87 orthotopic mouse model | siRNA, small molecule |
| Zhang et al. | 2016 | patient samples | HER2 | HER2 specific NK cells | in vitro and in vivo | Yes | Human tumor cells and cell lines | modified cells |
| Zhang et al | 2017 | AM-38, DBTRG-05MG, NMC-G1 | BRAF V600E + MEK | PLX4032 + GDC0973 | In vivo | No | Mice | Small molecule |
| **Cell Cycle/Apoptosis/Transcription Pathways** | | | | | | | | |
| Bychov et al. | 2020 | U251, A172 | ASIC1a containing channels | Mambalgin-2 | in vitro | Yes | Human cell line | venom derivative |
| Chen et al. | 2013 | U251, SHG44 | S100A9 (a heterodimer for calprotectin) | shRNA | in vivo and ex vivo | Yes | Human cell lines in mice and tumor cells | shRNA in virus |
| Chen et al. | 2019 | U87, U118 | IGFBP3 | IGFBP3 siRNA | in vitro and in vivo | No | Human cell line | siRNA |
| Grinshtein et al. | 2016 | patient samples | HDAC/EZH2 | Compound 26/unc1999 | in vitro and in vivo | Yes | Human cell line | small molecules |

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|---|---|---|---|---|---|---|---|---|
| Festa et al. | 2011 | patient samples | BAG3 | BAG3 siRNA | in vitro and in vivo | No | Rats with human transplants | siRNA |
| Ge et al. | 2013 | U87 | miR-27a (FOXO3a) | AntagomiR-27a | in vitro and in vivo | No | Human cell line | miRNA inhibitor |
| Genoud et al | 2021 | SB28 and GL261 | Tumor checkpoint controller targeting microtubules | BAL101553 | in vivo and ex vivo | No | Mouse cell line | small molecule |
| Gu et al. | 2015 | U87, SHG44, CHG5, U251 | PAK5 | PAK5 shRNA | in vitro and in vivo | No | human cell line and tumor cells | shRNA |
| Guo et al | 2011 | U87 | DR4/5 | TRAIL + Doxorubicin | in vitro and in vivo | No | Human cell line | small molecule |
| Hamada et al. | 2022 | HEK293T | CDK 4/6 + PDGFRα | Lenvatinb, Crernolanib, Abemaciclib, Palbociclib | in vitro | Yes | Human cell line | small molecules |
| Joshi et al. | 2017 | U87, D54 | Procaspase-3 | PAC-1 (*activating molecule) | in vitro and in vivo | Yes | Human and rat tumor cells | small molecule |
| Kalluri et al. | 2017 | GSCs from gliomas | Phospholipase C | D609 | in vitro | Yes | Human tumor cells | small molecule |
| Kaneta et al. | 2013 | U1242 | NEK9 | NEK9-siRNA | in vitro | No | Human cell line | siRNA |
| Kong et al. | 2018 | U87, T98 | BMI1 | PTC-209 | in vivo and in vitro | Yes | Human cell line | small molecule |
| Lamour et al. | 2015 | U87 | Osteopontin | shRNA | in vitro and in vivo | Yes | GICs, orthotopic mouse model | shRNA |
| Lee et al. | 2012 | SF188, U251 | Polo-like kinase 1 (PLK1) | BI2536 | in vitro and in vivo | Yes | Human cell line in mice | competitive kinase inhibitor |
| Lescarbeau et al. | 2016 | patient samples | Wee1K | MK-1775 | in vitro and in vivo | No | Human tumor cells | small molecule |
| Li et al. | 2012 | U87, U251 | p53/MDM2 | D-PMIBeta | in vitro and in vivo | No | Human cell line in mice | palmylated D-peptide |
| Lian et al. | 2013 | SHG44, U251, U87 | miR-23a (APAF1) | Anti-miR-23a | ex vivo | No | Human tumor | miRNA inhibitor |
| Liu et al | 2019 | U87, U251, U118, | EGFR | AZD9291 | in vitro and in | Yes | Human cell line | small molecule |

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|---|---|---|---|---|---|---|---|---|
| | | LN229, T98G and LN18 | | | vivo | | | |
| Mao et al. | 2013 | U87, SNB19, SNB44, SNB75, U118, U563, A172, SNB19 | STK17A | Anti-STK17A shRNA | in vitro | No | Human cell line | shRNA |
| Merlino et al. | 2018 | U87 | MDM2/4 + α5β1/αvβ3 | Compound 9 | in vitro | No | Human cell line | peptidomimetic |
| Michaud et al. | 2010 | patient samples | CDK4/6 | PD-0332991 | in vitro and in vivo | No | Human tumor cell lines and mouse xenografts | kinase inhibitor |
| Niu et al. | 2015 | U87, A172, SHG44, U251 | FOXM1 | Plumbagin | in vitro an in vivo | No | Human cell lines, human cell lines in mice | natural compound |
| Nonnenmacher et al. | 2015 | TiC35 in mice | XIAP + BCL-2 | RIST (Rapamycin, Irinotecan, Sunitinib, Temozolomide) + the variant aRIST (alternative to Rapamycin, GDC-0941 | in vitro | No | Human cell lines and primary cultured patient material, orthotopic mouse model | small molecule |
| Patyka et al. | 2016 | U87, T98, A172, U138 LN18 | MGMT | PRIMA-1MET | in vitro | Yes | Human cell lines | small molecule |
| Punganuru et al. | 2020 | U87 | MDM2 | SP-141 | in vitro and in vivo | No | Human cell line | small molecule |
| Sasame et al. | 2022 | 293T | HSP90 | BIIB021, 17-AAG (HSP90 inhibitor) + BRAFi + MEKi | in vitro and in vivo | Yes | Human cell line | siRNA |
| Tasaki et al. | 2016 | Grade II-IV Gliomas | HGFR aka MET | Crizotinib | in vitro and in vivo | Yes | Human tumor cells | small molecule |
| Tchoghandjian et al. | 2016 | patient samples | IAPs | GDC-0152 | in vitro and in vivo | Yes | Human tumor cells | small molecule |
| Vengoji et al | 2019 | U87 | EGFR | Afatinib + TMZ | In vitro and in | Yes | Human cell lines and mice | small molecule |

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| | | | | | vivo | | | |
| Wang et al. | 2011 | U87 | Survivin | Survivin-siRNA/Transferrin receptor conjugate | in vitro and in vivo | No | Human cell line and rats | siRNA |
| Wang et al. | 2019 | U87 | EZH2 | EZH2si-DMC | in vitro and in vivo | Yes | Human cell line | siRNA |
| Wang et al | 2019 | Glioma stem cells | Carbamoyl-phosphate synthetase 2 (CAD) | Teriflunomide | In vitro and in vivo | Yes | Human cell line and mice | siRNA |
| Xu et al. | 2017 | A172, T98, HEK293T, MDA-MB-231, T-47D, U87, U138, U251, U343 | BCL6 | RI-BPI | in vitro and in vivo | No | Human cell lines | peptide |
| Xu et al. | 2020 | U87, U251, GSC267 | CUL7 | miR-3940-5p | in vitro and in vivo | Yes | Human cell line | microRNA |
| Yang et al | 2006 | F98 | EGFRvIII | L8A4 | in vitro and in vivo | No | Rat cell line | Monoclonal antibody |
| Zhang et al. | 2011 | T98G, LN229 | eEF2-kinase | eEF2-siRNA | in vitro | No | Human cell line | siRNA |
| Zhao et al. | 2015 | U87, U251, SHG44 | ID2 | Anti-ID2 siRNA | in vitro | No | human cell line | siRNA |
| Zhong et al. | 2018 | U87, U251, LN18, T98, SHG-44, U373, HUVEC, hepatocyte (HL7702) | CDK + Aurora (dual inhibitor) | JNJ-7706621 | in vitro | No | Human cell line | small molecule |
| **Microenvironmental Targets (angiogenesis, cell-cell adhesion, iron/cation regulation)** | | | | | | | | |
| Abdul Rahim et al. | 2017 | patient samples | ATG9A | Bevacizumab +/- Chloroquine | in vivo and ex vivo | Yes | Human tumor cells | monoclonal antibody with small molecule |
| Angara et al | 2017 | U251 | 20-HETE | HET0016 | in vivo | No | Rats | Small molecule |
| Blanco et al. | 2014 | U87vIII | Phosphatidylserine | SAPc-DOPS | in vitro and in vivo | No | human cell line | lysosomal protein |
| Blank et al. | 2001 | C6 rat glioblastoma | Endothelial pigpen protein | Aptamer III.1 | in vitro | No | Mouse tissue samples | aptamer |
| Chen et al. | 2013 | U87, C6 | NRP-1 | NRP-1 Mab | in vitro and in vivo | No | Human and rat cell line in mice | monoclonal antibody |
| Fleurence et | 2016 | patient | O-acetyl GD2 | Anti-GD2 | in vitro | Yes | Human | monoclonal |

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| al. | | samples | ganglioside | antibody | and in vivo | | tumor cells and cell lines | antibody |
| Franco et al. | 2018 | U87 | TFAM | Melatonin | in vitro | No | human cell line | hormone |
| Grossman et al | 2013 | U87 | Pan-VEGF | Cediranib + TMZ | in vivo | No | Rats | small molecule |
| He et al. | 2018 | NSCG cells | LTβR | LIGHT-VTP | in vitro and in vivo | No | human cell line | cytokine/vascular targeting peptide |
| Huang et al. | 2021 | U87, LN18, U118 | TRPV4 | Cannabidiol | in vitro and in vivo | Yes | Human cell line | phytocannabinoid |
| Huveldt et al. | 2013 | GBM10 | VEGF + Src Family kinases | Bevacizumab, Dasatinib | in vivo | No | Human cell line transplanted into mice | monoclonal antibody with small molecule |
| Jaszberenyi et al. | 2013 | U87 | Growth-Hormone Releasing Hormone | MIA-604, MIA-690 | in vitro and in vivo | No | Human cell line in mice | Hormone analog |
| Ji et al. | 2013 | patient samples, U251 | Nrf2 | siRNA | in vivo and ex vivo | No | Human cell line in mice and human tumor cells | siRNA |
| Kuan et al. | 2010 | patient samples | MRP3 | Anti-MRP antibody | in vitro and ex vivo | No | Patient samples and human cell line | monoclonal antibody |
| Lu et al. | 2015 | U87, MGG4 GSC-derived, 005 GSC-derived | VEGFR | TKI VEGF inhibitor | in vitro and in vivo | Yes | Human and murine cell lines | small molecule |
| Mojarad-Jabali et al. | 2022 | GL261 (IDH-wt) | TfR (transferrin receptor) | T12, B6, T7 (TfR-targeting peptides) | in vitro and in vivo | No | Murine cell line | small molecules |
| Mostafavi et al. | 2015 | U87, 1321N1 | CX43 + miR21 | B2 cAMP agonist | in vitro | No | Human cell lines | small molecule |
| Nandhu et al. | 2018 | U251 | Fibulin-3 | | in vitro and in vivo | Yes | Human cell line | monoclonal antibody |
| Nawashiro et al. | 2006 | C6, patient samples | LAT1 | BCH | in vivo and ex vivo | No | Patient samples and rat cell lines | small molecule |
| Pall et al. | 2019 | U251, U87 | NHE9 | Gold nanoparticle-enabled | in vitro | No | Human cell line | nanoparticle |

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| | | | | photothermal therapy (NEPTT) | | | | |
| Phillips et al. | 2019 | DIPG-VI, GBM-0401 | Lanosterol synthase | MI-2 (menin inhibitor) | in vitro | No | Human cell line | small molecule |
| Renfrow et al. | 2020 | patient samples | HIF2α | PT2385 | in vitro and in vivo | No | Human cell line | small molecule |
| Saw et al. | 2021 | U87, U251, U373, MCF7, PC3, B16F10, B16F1 | EDB-FN (extra domain B of fibronectin) | Docetaxel-loaded EDB-FN specific micelles | in vitro and in vivo | Yes | Human cell line | targeted micelle with taxane |
| Takano et al | 2003 | U87MG and U251MG | VEGF | Anti-VEGF AB + Nimustine | In vitro and in vivo | No | Human cell line and mice | MAB |
| Tyrinova et al. | 2018 | Grade III-IV gliomas | tmTNFa | Recombinant IL2 or dsDNA | ex vivo | No | Patient samples | interleukin or double-stranded DNA |
| Watanabe et al. | 2020 | U251 | CTL1 (choline transporter-like protein 1) | Amb4269951 | in vitro and in vivo | No | Human cell line | small molecule |
| Xia et al. | 2022 | U251, U87 | VEGFR2 | Apatinib | in vitro and in vivo | No | Human cell line | small molecule |
| Xiong et al. | 2019 | MCF7, HL60, MCF7 | Calmodulin, EGFR, Aromatase | W-13, Gefitinib, Exemestane | in silico | No | miRNA expression profiling in GBM were obtained from the Gene Expression Omnibus (GEO) database | small molecule |
| Xu et al. | 2019 | U87, LN229 | ITGA9 | miR-148a | in vitro and in vivo | No | Human cell line | miRNA |
| **Immunotherapy Pathways** | | | | | | | | |
| Baehr et al. | 2017 | U87, LN229, U251, LN308 | STING ( stimulator of interferon gene) | ASA404 | in vitro and in vivo | No | Human cell line | small molecule |
| Goswami et al. | 2020 | GL261 | CD73 | Anti-CD73 | in vitro and in vivo | No | Murine cell line | monoclonal antibody |
| Merrill et al. | 2004 | G3 anaplastic | CD155 receptor | PVS-RIPO | in vitro | No | Patient samples | recombinant virus |

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| | | astrocytoma, G4 GBM | | | | | | |
| Schleicher et al. | 2011 | GL261 | ATX + LPA receptors | siRNA | in vitro and in vivo | No | Human cell lines and mice | siRNA |
| Xu et al | 2015 | U87 | EMMPRIN | Icaritin | in vitro | No | Human cell line | small molecule |
| Zanotto-Filho et al. | 2011 | C6 rat and U138, U87, U373 | NFkB | BAY117082, MG132 | in vitro | No | Rat and human cell lines | small molecule |
| Zhang et al. | 2009 | U87, U251, human astrocytoma cells | Formyl Peptide Receptor (FPR) | F2 procyanidins | in vitro | No | Human cell line | Oligomer |
| **Other Pathways/Targets** | | | | | | | | |
| Barone et al. | 2014 | U87 | CXCR4 + VEGF | POL555, mcr89 | in vitro and in vivo | Yes | Human cell line | protein epitope mimetic & antibody |
| Caruana et al. | 2017 | T98, U87, A172 | Site-1 protease | PF-429242 | in vitro | No | Human cell lines | small molecule |
| Chen et al. | 2013 | C6 | CXCR4 | Tetramethylpyrazine | in vitro | No | Rat cell line | small molecule |
| Chen et al. | 2021 | U251, U87, SHG44, A172 | miR-106a-5p | Circ-ITCH | in vitro and in vivo | No | Patient samples and human cell lines | circRNA |
| Colen et al. | 2011 | U87 | Lactate (monocarboxylate) transporters | α-cyano-4-hydroxycinnamic acid | in vitro and in vivo | No | Human cell lines, rat | lactate transporter inhibitor |
| Harford-Wright et al. | 2017 | U87, LN229 | Apelin G-protein coupled receptor | MM54, MM193 | in vitro and in vivo | Yes | Human tumor cells | small molecule |
| Ishiwata et al. | 2011 | patient samples, A172 GBM, KG-1-C glioma | Nestin | Anti-Nestin IgG | in vitro and ex vivo | Yes | Human cell line and patient samples | Immunoglobulin |
| Jiang et al. | 2021 | Gliomas from GSE31095 and GSE109857 from the NCBI Gene Expression Comprehensive database | EEF1A1 + RPL11 | Puromycin, Doxorubicin, Daunorubicin, Mitoxantrone | ex vivo | No | Patient samples | Small molecules |
| Kim et al. | 2018 | U87, T98, LN18 | MALAT1 | siRNA, Temozolomide | in vitro and in vivo | Yes | Human cell line | siRNA |

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| Kim et al. | 2019 | U87, U373 | IDH1R132H | AGI-5198 (in combo with HDACi) | in vitro | No | Human cell line | small molecule |
| Li et al. | 2018 | U251, U87, non-glioma human tumor cells | hnRNP A1/B2 | β-Asarone | in vitro | No | Human tumor cells | plant product |
| Liu et al. | 2016 | U251, SHG-44 | CRM1 | S109 | in vitro and in vivo | No | Patient samples and human cell line | small molecule |
| Loskutov et al. | 2018 | patient samples | LPAR1/3 | Ki16425 | in vivo and in vitro | Yes | Human tumor cells | small molecule |
| Luwor et al. | 2019 | U87, U251 | Dynamin 2 | Dynole 34-2, CyDyn 4-36 | in vitro and in vivo | Yes | Human cell lines | |
| Miyazaki et al. | 2012 | 8 human GBM cell lines | c-Myb | Telomestatin | in vitro and in vivo | Yes | Human cell lines | hydrophobic agent |
| Peng et al. | 2019 | U373, U87, U251 | miR-25 | miR-25 inhibitor | in vitro | No | Human cell line | miRNA |
| Piunti et al. | 2017 | SF8628, SF7761, SU-DIPG-IV, pcGBM2, SF9402, SF9427 | PRC2 + BET bromodomain proteins | JQ1, I-BET | in vitro and in vivo | No | Human cell lines | small molecule |
| Preukschas et al. | 2012 | G55T2, U87, U251 | eIF-5A, DHS, DOHH (both eIF-5A activators) | GC7 | in vitro | No | Human cell line | small molecule |
| Saito et al | 2004 | U87 | TRAILR | Recombinant TRAIL + TMZ | In vitro and in vivo | No | Human cell line and rats | Recombinant human protein |
| Saito et al. | 2014 | U87, U251, KNS81, T98G, SF126, KALS-1 | EFTUD1 | EFTUD1 shRNA | in vitro and in vivo | No | Human cell line and patient samples | shRNA |
| Sanzey et al. | 2015 | U87, U251, T98 | PFK1 | Clotrimazole | in vitro and in vivo | Yes | Patient samples | small molecule |
| Saunders et al. | 2021 | GBM39, GBM43 | YAP1 (yes-associated protein 1) | NSC682769 | in vitro and in vivo | No | Human cell line | small molecule |
| Shulepko et al. | 2020 | U251, A172 | α7 nAChR | rSLURP-1 | in vitro | No | Human cell line | recombinant analogue of human protein |
| Song et al. | 2019 | U87, U251, | A1CF + | shRNA | in vitro | No | Human | shRNA |

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| | | HEK293T | FAM224A | | and in vivo | | cell line | |
| Spino et al. | 2019 | U87, MGG18, MGG152, MGG119 | DLL3 (Notch ligand) | Rova-T ( Rovalpituzum ab tesirine) | in vitro | Yes | Human cell line | antibody–drug conjugate (ADC) |
| Tu et al. | 2017 | U87, A172, U251, C6 | smoothened | GDC-0449 | in vitro and in vivo | No | Human and murine cell lines | small molecule |
| Venere et al. | 2015 | patient samples | KIF11 | Ispinesib | in vitro and in vivo | Yes | patient samples | small molecule |
| von Spreckelsen et al. | 2021 | GBM6 | Brevican | Anti-deglycosylated brevican peptide | in vitro and in vivo | No | Human cell line | peptide |
| Wu et al. | 2011 | U251, T98, A172 | miR-128 | Ginsenoside Rh2 | in vitro | No | Human cell line | small molecule |
| Yan et al. | 2013 | U87, SF295 | 14-3-3 | siRNA | in vitro | No | Human cell line | |
| Zhang et al. | 2021 | U87 | IDH1R132H | WM17 | in vitro | No | Human cell line | small molecule |
| Zhang et al. | 2022 | U87, U251, A172, LN229, U118, P3 | Fat mass + obesity associated protein (FTO) | SPI1 inhibitor DB2313 | in vitro and in vivo | Yes | Human cell line | microRNA |

Abbreviations: CDK, cyclin-dependent kinase; EGFR, epidermal growth factor receptor; GBM, glioblastoma multiforme; HIF, hypoxia-induced factor; IDH, isocitrate dehydrogenase; miR(NA), micro ribonucleic acid; PDGFR, platelet-derived growth factor receptor; siRNA, small interfering ribonucleic acid; TKI, tyrosine kinase inhibitor; TMZ, temozolomide; TNF, tumor necrosis factor; VEGFR, vascular endothelial growth factor receptor; oligodendroglioma, IDH-mutant/p19q co-deleted Glioma; 20-HETE, 20-hydroxy eicosatetraenoic acid; HGF, hepatocyte growth factor; TRAIL, Tumor necrosis factor-related apoptosis-inducing ligand; ALK, anaplastic lymphoma kinase; ROCK, Rho-associated protein kinase

**Supplementary Table S3. Detailed Study Design of Ongoing Clinical Trials on ClinicalTrials.gov Implementing Molecular Targeted Therapies in Glioma**

| Title | Sponsor/ Collaborator | Funding | Phase | Status | Results (if applicable) |
|---|---|---|---|---|---|
| **Protein Kinase Pathways** | | | | | |
| Imatinib Mesylate in Treating Patients With Recurrent Malignant Glioma or Meningioma | Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins\| NCI | NIH | Phase 1\| Phase 2 | Completed | Six-month progression-free survival was 3% for glioblastoma multiforme and 10% for anaplastic glioma patients. CYP3A4 inducers, such as enzyme-inducing antiepileptic drugs, substantially decreased plasma exposure of imatinib |
| Gefitinib in Treating Patients With Newly Diagnosed Glioblastoma Multiforme | National Cancer Institute (NCI) | NIH | Phase 2 | Completed | |
| CCI-779 in Treating | National Cancer Institute | NIH | Phase | Complet | |

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| Patients With Recurrent Glioblastoma Multiforme | (NCI) | | 2 | ed | |
| Gefitinib in Treating Patients With Recurrent or Progressive CNS Tumors | Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins\|National Cancer Institute (NCI) | NIH | Phase 2 | Completed | |
| Erlotinib in Treating Patients With Solid Tumors and Liver or Kidney Dysfunction | National Cancer Institute (NCI) | NIH | Phase 1 | Completed | |
| Gefitinib and Radiation Therapy in Treating Patients With Glioblastoma Multiforme | National Cancer Institute (NCI)\|NRG Oncology | NIH | Phase 1\| Phase 2 | Completed | |
| Imatinib Mesylate in Treating Patients With Gliomas | European Organisation for Research and Treatment of Cancer - EORTC | Other | Phase 2 | Completed | |
| Erlotinib in Treating Patients With Recurrent Malignant Glioma or Recurrent or Progressive Meningioma | National Cancer Institute (NCI) | NIH | Phase 1\| Phase 2 | Completed | MTD was 650 mg |
| Erlotinib and Temozolomide With Radiation Therapy in Treating Patients With Glioblastoma Multiforme or Other Brain Tumors | National Cancer Institute (NCI) | NIH | Phase 2 | Completed | |
| A Phase II Exploratory, Multicentre, Open-label, Non-comparative Study of ZD1839 (Iressa) and Radiotherapy in the Treatment of Patients With Glioblastoma Multiforme | AstraZeneca | Industry | Phase 2 | Completed | |
| Imatinib Mesylate in Treating Patients With Recurrent Brain Tumor | Alliance for Clinical Trials in Oncology\|National Cancer Institute (NCI) | NIH | Phase 1\| Phase 2 | Completed | PFS rates were between 25 and 33.5% depending on EIACs and number of previous regimens |
| Everolimus and Gefitinib in Treating Patients With Progressive Glioblastoma Multiforme or | Memorial Sloan Kettering Cancer Center\|National Cancer Institute (NCI) | NIH | Phase 1\| Phase 2 | Completed | Primary outcome was overall objective response. Partial response in 2/43 patients at highest dose of 70mg everolimus. Remaining patients had stable disease or |

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| Progressive Metastatic Prostate Cancer | | | | | progression of disease. |
| Erlotinib Compared With Temozolomide or Carmustine in Treating Patients With Recurrent Glioblastoma Multiforme | European Organisation for Research and Treatment of Cancer - EORTC | Other | Phase 2 | Completed | |
| Sorafenib in Treating Patients With Recurrent or Progressive Malignant Glioma | National Cancer Institute (NCI) | NIH | Phase 1 | Completed | |
| Lapatinib in Treating Patients With Recurrent Glioblastoma Multiforme | National Cancer Institute (NCI)\|NCIC Clinical Trials Group | NIH | Phase 1 \|Phase 2 | Completed | |
| GW572016 to Treat Recurrent Malignant Brain Tumors | National Cancer Institute (NCI)\|National Institutes of Health Clinical Center (CC) | NIH | Phase 2 | Completed | |
| Ph I Gleevec in Combo w RAD001 + Hydroxyurea for Pts w Recurrent MG | Annick Desjardins\|Novartis Pharmaceuticals\|Duke University | Industry | Phase 1 | Completed | |
| Phase II Imatinib + Hydroxyurea in Treatment of Patients With Recurrent/Progressive Grade II Low-Grade Glioma (LGG) | Duke University\|Novartis Pharmaceuticals | Industry | Phase 2 | Completed | Astrocytomas had43.8% PFS and oligodendromas had 34.4% PFS at 12 months |
| Oral Tarceva Study for Recurrent/Residual Glioblastoma Multiforme and Anaplastic Astrocytoma | Northwell Health\|Genentech, Inc. | Industry | Phase 1\|Phase 2 | Completed | Coexpression of EGFR and PTEN is related to response to EGFR inhibitors |
| Sorafenib Tosylate and Temsirolimus in Treating Patients With Recurrent Glioblastoma | National Cancer Institute (NCI) | NIH | Phase 1\|Phase 2 | Completed | Limited activity of sorafenib and temsirolimus in this dose and schedule was observed with considerable grade 3+ toxicity. |
| Sorafenib Combined With Erlotinib, Tipifarnib, or Temsirolimus in Treating Patients With Recurrent Glioblastoma Multiforme or | National Cancer Institute (NCI) | NIH | Phase 1\|Phase 2 | Completed | Sorafenib + erlotinib had 42.1%, Sorafenib + temsirolimus had 55.6% 12-mo survival, Sorafenib + tipifarnib combo was too toxic |

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| Gliosarcoma | | | | | |
| Temsirolimus, Temozolomide, and Radiation Therapy in Treating Patients With Newly Diagnosed Glioblastoma Multiforme | National Cancer Institute (NCI) | NIH | Phase 1 | Completed | |
| Tumor Tissue Analysis in Patients Receiving Imatinib Mesylate for Malignant Glioma | Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins\|National Cancer Institute (NCI) | NIH | Phase 1 | Completed | |
| Erlotinib and Sorafenib in Treating Patients With Progressive or Recurrent Glioblastoma Multiforme | National Cancer Institute (NCI) | NIH | Phase 2 | Completed | 14% PFS with no adverse effects reported |
| Dasatinib in Treating Patients With Recurrent Glioblastoma Multiforme or Gliosarcoma | National Cancer Institute (NCI)\|Radiation Therapy Oncology Group\|NRG Oncology | NIH | Phase 2 | Completed | Dasatinib is safe but ineffective in recurrent GBM |
| A Phase II Trial of Sutent (Sunitinib; SU011248) for Recurrent Anaplastic Astrocytoma and Glioblastoma | H. Lee Moffitt Cancer Center and Research Institute\|Pfizer | Industry | Phase 2 | Completed | 4/30 patients had 6 month PFS after sunitinib treatment |
| Ph II Erlotinib + Sirolimus for Pts w Recurrent Malignant Glioma Multiforme | Duke University\|Genentech, Inc.\|OSI Pharmaceuticals | Industry | Phase 2 | Completed | 3.1% PFS6, with median PFS 6.9 weeks |
| Radiation Therapy and Temozolomide Followed by Temozolomide Plus Sorafenib for Glioblastoma Multiforme | SCRI Development Innovations, LLC\|Bayer | Industry | Phase 2 | Completed | Addition of sorafenib showed no benefit over the standard therapy |
| Sunitinib Tumor Levels in Patients Not on Enzyme-Inducing Anti-Epileptic Drugs Undergoing Debulking Surgery for Recurrent Glioblastoma | Massachusetts General Hospital\|Brigham and Women's Hospital\|Dana-Farber Cancer Institute\|Pfizer | Industry | Early Phase 1 | Completed | |
| Sunitinib in Treating | National Cancer Institute | NIH | Phase | Complet | 1/21 patients with PFS at 6 |

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| Patients With Recurrent Malignant Gliomas | (NCI) | | 2 | ed | months |
| Ph. 2 Sorafenib + Protracted Temozolomide in Recurrent GBM | Duke University\|Bayer\|Schering-Plough | Industry | Phase 2 | Completed | Sorafenib + TMZ is safe but ineffective in recurrent GBM |
| Ph I Dasatinib + Erlotinib in Recurrent MG | Duke University\|Bristol-Myers Squibb\|Genentech, Inc. | Industry | Phase 1 | Completed | |
| Ph I SU011248 + Irinotecan in Treatment of Pts w MG | Duke University\|Pfizer | Industry | Phase 1 | Completed | |
| BIBW 2992 (Afatinib) With or Without Daily Temozolomide in the Treatment of Patients With Recurrent Malignant Glioma | Boehringer Ingelheim | Industry | Phase 2 | Completed | Afatinib is more effective than TMZ alone as monotherapy, though not as combination with TMZ |
| A Study of Temsirolimus and Bevacizumab in Recurrent Glioblastoma Multiforme | Rigshospitalet, Denmark\|University of Copenhagen\|Wyeth is now a wholly owned subsidiary of Pfizer\|Roche, Copenhagen | Industry | Phase 2 | Completed | Temsirolimus can be safely administered in combination with bevacizumab. This study failed to detect activity of such a combination in patients with progressive GBM beyond bevacizumab therapy. |
| Everolimus in Treating Patients With Recurrent Low-Grade Glioma | Susan Chang\|Novartis\|University of California, San Francisco | Industry | Phase 2 | Completed | Primary outcome was progression free survival at 6 months. 39/47 patients with grade II glioma met 6 month PFS. 6/11 patients with Grade III/IV glioma met 6 month PFS. |
| Sorafenib in Newly Diagnosed High Grade Glioma | University Hospital, Geneva\|Bayer | Industry | Phase 1 | Completed | |
| Everolimus, Temozolomide, and Radiation Therapy in Treating Patients With Newly Diagnosed Glioblastoma | Alliance for Clinical Trials in Oncology\|National Cancer Institute (NCI) | NIH | Phase 1\|Phase 2 | Completed | 64% of patients achieved PFS12 |
| Study of Sunitinib Before and During Radiotherapy in Newly Diagnosed Biopsy-only Glioblastoma Patients | | Other | Phase 2 | Completed | |
| Dasatinib or | Alliance for Clinical Trials | NIH\|Indus | Phase | Complet | The addition of dasatinib to |

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| Placebo, Radiation Therapy, and Temozolomide in Treating Patients With Newly Diagnosed Glioblastoma Multiforme | in Oncology\|National Cancer Institute (NCI)\|Bristol-Myers Squibb | try | 1\|Phase 2 | ed | conventional therapy did not confer any survival benefit |
| Open Label Trial to Explore Safety of Combining Afatinib (BIBW 2992) and Radiotherapy With or Without Temozolomide in Newly Diagnosed Glioblastoma Multiform | Boehringer Ingelheim | Industry | Phase 1 | Completed | MTD of afatinib was 30 mg for RT + TMZ, and 40mg for RT alone |
| Radiation Therapy and Temsirolimus or Temozolomide in Treating Patients With Newly Diagnosed Glioblastoma | European Organisation for Research and Treatment of Cancer - EORTC\|Pfizer | Industry | Phase 2 | Completed | |
| Temsirolimus and Perifosine in Treating Patients With Recurrent or Progressive Malignant Glioma | National Cancer Institute (NCI) | NIH | Phase 1\|Phase 2 | Completed | MTD of temsirolimus was 115mg/wk |
| A Study in Subjects With Recurrent Malignant Glioma | Eisai Inc. | Industry | Phase 2 | Completed | Primary outcome was 6 month PFS. Participants with recurrent Grade 4 malignant glioma (ie, glioblastoma [GBM]) who were bevacizumab-naive; received bevacizumab - 11% PFS. Participants with recurrent Grade 4 malignant glioma (ie, glioblastoma [GBM]) who were bevacizumab-naive; received lenvatinib capsules - 21.2% PFS. Participants with recurrent Grade 3 malignant glioma who were bevacizumab-naive; received lenvatinib - 8% PFS. Participants with recurrent GBM who had disease progression following prior bevacizumab treatment; received lenvatinib - 7.6% PFS. |
| Bafetinib in | City of Hope Medical | NIH | Phase | Complet | |

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| Treating Patients With Recurrent High-Grade Glioma or Brain Metastases | Center\|National Cancer Institute (NCI) | | 1 | ed | |
| Everolimus, Temozolomide, and Radiation Therapy in Treating Patients With Newly Diagnosed Glioblastoma Multiforme | Radiation Therapy Oncology Group\|National Cancer Institute (NCI)\|NRG Oncology | NIH | Phase 1\|Phase 2 | Completed | Combining everolimus with conventional chemoradiation leads to increased treatment-related toxicities and does not improve PFS in patients with newly diagnosed glioblastoma. Although the median survival time in patients receiving everolimus was comparable to contemporary studies, it was inferior to the control in this randomized study. |
| EGFR Inhibition Using Weekly Erlotinib for Recurrent Malignant Gliomas | Andrew B Lassman, MD\|Genentech, Inc.\|OSI Pharmaceuticals\|Columbia University | Industry | Phase 1 | Completed | |
| AZD8055 for Adults With Recurrent Gliomas | National Cancer Institute (NCI)\|National Institutes of Health Clinical Center (CC) | NIH | Phase 1 | Completed | |
| Phase I-II Everolimus and Sorafenib in Recurrent High-Grade Gliomas | National Cancer Institute (NCI)\|National Institutes of Health Clinical Center (CC) | NIH | Phase 1\|Phase 2 | Completed | Median survival was 7.75 mo in BEV-naive GBM, 4.77 mo in BEV-treated GBM, and 11.97 mo in anaplastic astrocytoma |
| Lapatinib With Temozolomide and Regional Radiation Therapy for Patients With Newly-Diagnosed Glioblastoma Multiforme | Jonsson Comprehensive Cancer Center\|GlaxoSmithKline\|Novartis | Industry | Phase 2 | Active, not recruiting | Pulse high-dose lapatinib in addition to standard therapy for newly-diagnosed GBM is a tolerable and safe regimen, but higher rates of lymphopenia should be noted. |
| Sorafenib, Valproic Acid, and Sildenafil in Treating Patients With Recurrent High-Grade Glioma | Virginia Commonwealth University\|National Cancer Institute (NCI) | NIH | Phase 2 | Active, not recruiting | Primary outcome number of patients with 6 month PFS was 8/47. 25/47 did not meet 6 month PFS. 14/47 were not evaluable. |
| Lapatinib Ditosylate Before Surgery in Treating Patients With Recurrent High-Grade Glioma | National Cancer Institute (NCI) | NIH | Phase 1 | Active, not recruiting | |
| Study to Evaluate Safety and Activity of Crizotinib With Temozolomide and Radiotherapy in Newly Diagnosed Glioblastoma | | Industry | Phase 1 | Completed | |

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| Perifosine and Torisel (Temsirolimus) for Recurrent/Progressive Malignant Gliomas | Andrew B Lassman, MD\|Pfizer\|AEterna Zentaris\|Columbia University | Industry | Phase 1 | Completed | |
| Study of LY2228820 With Radiotherapy Plus Concomitant TMZ in the Treatment of Newly Diagnosed Glioblastoma | Centre Jean Perrin\|National Cancer Institute, France\|ARC Foundation for Cancer Research | Other | Phase 1\|Phase 2 | Completed | |
| Study of Tesevatinib Monotherapy in Patients With Recurrent Glioblastoma | Kadmon Corporation, LLC | Industry | Phase 2 | Completed | 22.5% overall PFS6, with 25% in EGFR amplified and 18.2% in EGFRvIII gliomas |
| Dabrafenib and/or Trametinib Rollover Study | Novartis Pharmaceuticals\|Novartis | Industry | Phase 4 | Recruiting | |
| Ruxolitinib With Radiation and Temozolomide for Grade III Gliomas and Glioblastoma | Case Comprehensive Cancer Center | Other | Phase 1 | Active, not recruiting | |
| A Trial of Ipatasertib in Combination With Atezolizumab | Institute of Cancer Research, United Kingdom\|Hoffmann-La Roche | Industry | Phase 1\|Phase 2 | Recruiting | |
| 18F-FDG PET and Osimertinib in Evaluating Glucose Utilization in Patients With EGFR Activated Recurrent Glioblastoma | Jonsson Comprehensive Cancer Center\|AstraZeneca | Industry | Phase 2 | Active, not recruiting | Treated patients exhibited a reduced glycolytic flux as indicated by reduction in 18F-FDG PET uptake (-3% change in SUV), tumor acidity (-19% change in MTRasym@3ppm) on pH-weighted CEST MRI, and glycolytic index (GI) (-25% change) in EGFR amplified recurrent GBM within 24 hours of treatment. |
| 9-ING-41 in Patients With Advanced Cancers | Actuate Therapeutics Inc. | Industry | Phase 2 | Recruiting | |
| Nedisertib and Radiation Therapy, Followed by Temozolomide for the Treatment of Patients With Newly Diagnosed MGMT Unmethylated Glioblastoma or Gliosarcoma | M.D. Anderson Cancer Center\|National Cancer Institute (NCI) | NIH | Phase 1 | Recruiting | |

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| Tofacitinib in Recurrent GBM Patients | University of Texas Southwestern Medical Center\|Pfizer | Industry | Phase 3 | Recruiting | |
| DETERMINE Trial Treatment Arm 5: Vemurafenib in Combination With Cobimetinib in Adult Patients With BRAF Positive Cancers. | Cancer Research UK\|University of Manchester\|University of Birmingham\|Royal Marsden NHS Foundation Trust\|Hoffmann-La Roche | Industry | Phase 2\|Phase 3 | Recruiting | |
| Superselective Intra-arterial Cerebral Infusion of Temsirolimus in HGG | Nader Sanai\|Barrow Neurological Institute\|Ivy Brain Tumor Center\|St. Joseph's Hospital and Medical Center, Phoenix | Other | Early Phase 1 | Recruiting | |
| **Microenvironmental Targets (angiogenesis, cell-cell adhesion, iron/cation regulation)** | | | | | |
| Gefitinib Plus Temozolomide in Treating Patients With Malignant Primary Glioma | Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins\|National Cancer Institute (NCI) | NIH | Phase 1 | Completed | For patients on anti-epileptic drugs, the MTD of gefitinib was 1,000 mg/day in combination with temozolomide. Dose-limiting toxicity (DLT) was due to diarrhea, nausea and vomiting. For patients not on anti-epileptic drugs, the MTD was 250 mg/day in combination with temozolomide. The DLT was due to increases in liver transaminases. |
| Safety and Efficacy Study of Tarceva, Temodar, and Radiation Therapy in Patients With Newly Diagnosed Brain Tumors | University of California, San Francisco\|Genentech, Inc. | Industry | Phase 2 | Completed | Median survival was 19mo, median PFS was 8.2 mo |
| Erlotinib and Temsirolimus in Treating Patients With Recurrent Malignant Glioma | National Cancer Institute (NCI) | NIH | Phase 1\|Phase 2 | Completed | 1/12 patients treated with maximally tolerated dose with partial response at 8 weeks |
| Temozolomide and Radiation Therapy With or Without Vatalanib in Treating Patients With Newly Diagnosed Glioblastoma Multiforme | European Organisation for Research and Treatment of Cancer - EORTC | Other | Phase 1\|Phase 2 | Completed | |
| Imatinib Mesylate, Vatalanib, and Hydroxyurea in | Duke University\|National Cancer Institute (NCI) | NIH | Phase 1 | Completed | |

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| Treating Patients With Recurrent or Relapsed Malignant Glioma | | | | | |
| Cetuximab, Bevacizumab and Irinotecan for Patients With Malignant Glioblastomas | Rigshospitalet, Denmark\|Aalborg University Hospital\|Odense University Hospital | Other | Phase 2 | Completed | |
| PTK787/ZK 222584 in Combination With Temozolomide and Radiation in Patients With Glioblastoma Taking Enzyme-Inducing Anti-Epileptic Drugs | Massachusetts General Hospital\|Dana-Farber Cancer Institute\|Novartis | Industry | Phase 1 | Completed | 13/19 patients evaluable for a radiographic response, 2 had a partial response and 9 had stable disease. Vatalanib significantly increased PlGF and sVEGFR1 in plasma circulation and decreased sVEGFR2 and sTie2. Plasma collagen IV increased significantly by day 50 of treatment. Vatalanib was well tolerated. |
| Pazopanib In Combination With Lapatinib In Adult Patients With Relapsed Malignant Glioma | GlaxoSmithKline | Industry | Phase 2 | Completed | Pazopanib and lapatinib can be given safely at single-drug doses |
| Phase (Ph) II Bevacizumab + Erlotinib for Patients (Pts) With Recurrent Malignant Glioma (MG) | Duke University\|Genentech, Inc. | Industry | Phase 2 | Completed | Bevacizumab plus erlotinib was adequately tolerated in recurrent MG patients. However, this regimen was associated with similar PFS benefit and radiographic response when compared with other historical bevacizumab-containing regimens. |
| Bevacizumab and Cediranib Maleate in Treating Patients With Metastatic or Unresectable Solid Tumor, Lymphoma, Intracranial Glioblastoma, Gliosarcoma or Anaplastic Astrocytoma | National Cancer Institute (NCI) | NIH | Phase 1 | Completed | |
| Study of Bevacizumab Plus Temodar and Tarceva in Patients With Glioblastoma or Gliosarcoma | University of California, San Francisco | Other | Phase 2 | Completed | Median overall survival was 19.8 months |

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| Ph I Zactima + Imatinib Mesylate & Hydroxyurea for Pts w Recurrent Malignant Glioma | Annick Desjardins\|Novartis Pharmaceuticals\|AstraZeneca\|Duke University | Industry | Phase 1 | Completed | |
| Cediranib, Temozolomide, and Radiation Therapy in Treating Patients With Newly Diagnosed Glioblastoma | National Cancer Institute (NCI) | NIH | Phase 1\|Phase 2 | Completed | |
| Bevacizumab and Sorafenib in Treating Patients With Recurrent Glioblastoma Multiforme | Alliance for Clinical Trials in Oncology\|National Cancer Institute (NCI) | NIH | Phase 2 | Completed | Primary outcome 6 month PFS. 26.3% PFS in sorafenib 400 mg and 5 mg/kg bevacizumab group. 17.1% PFS in sorafenib 200 mg and 5mg/kg bevacizumab group. |
| RT, Temozolomide, and Bevacizumab Followed by Bevacizumab/Everolimus in First-line Treatment of GBM | SCRI Development Innovations, LLC\|Genentech, Inc.\|Novartis | Industry | Phase 2 | Completed | This combination therapy regimen is safe and shows improved efficacy vs TMZ+RT |
| Afatinib (BIBW 2992) QTcF Trial in Patients With Relapsed or Refractory Solid Tumours | Boehringer Ingelheim | Industry | Phase 2 | Completed | Objective response in 1/60 patients. PFS in 10.6/53 patients. Mean QTcF change -0.3 for 49 participants. |
| Bevacizumab and Erlotinib After Radiation Therapy and Temozolomide in Treating Patients With Newly Diagnosed Glioblastoma Multiforme or Gliosarcoma | Northwestern University\|M.D. Anderson Cancer Center | Other | Phase 2 | Completed | 32/46 reached PFS12, and 4 achieved complete responses with average overall survival of 13.2 mo and 4 still alive at time of publication |
| Dasatinib and Bevacizumab in Treating Patients With Recurrent or Progressive High-Grade Glioma or Glioblastoma Multiforme | Alliance for Clinical Trials in Oncology\|National Cancer Institute (NCI) | NIH | Phase 2 | Completed | PFS6 was 29% in patients on BEV + dasatinib vs 18% for BEV alone |
| Temozolomide and Radiation Therapy With or Without Cediranib Maleate in Treating Patients With Newly Diagnosed | National Cancer Institute (NCI)\|NRG Oncology\|Radiation Therapy Oncology Group | NIH | Phase 2 | Completed | Cediranib added to conventional therapy significantly increased the PFS6 rate in this GBM cohort |

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| Glioblastoma | | | | | |
| Cediranib Maleate and Cilengitide in Treating Patients With Progressive or Recurrent Glioblastoma | National Cancer Institute (NCI) | NIH | Phase 1 | Completed | |
| Gamma-Secretase Inhibitor RO4929097 and Cediranib Maleate in Treating Patients With Advanced Solid Tumors | National Cancer Institute (NCI) | NIH | Phase 1 | Completed | |
| A Study of Avastin (Bevacizumab) and Irinotecan Versus Temozolomide Radiochemistry in Patients With Glioblastoma | Hoffmann-La Roche | Industry | Phase 2 | Completed | 79.31% bevacizumab and irinotecan with progression free survival at 6 months. 42.95% temozolomide with progression free survival at 6 months. |
| BIBF 1120 in Recurrent Glioblastoma Multiforme | Ulrik Lassen\|Boehringer Ingelheim\|University of Copenhagen\|Rigshospitalet, Denmark | Industry | Phase 2 | Completed | |
| BIBF 1120 for Recurrent High-Grade Gliomas | Patrick Y. Wen, MD\|Boehringer Ingelheim\|Wake Forest University Health Sciences\|University of Virginia\|Massachusetts General Hospital\|The Cleveland Clinic\|Dana-Farber Cancer Institute | Industry | Phase 2 | Completed | No patients achieved PFS6 |
| CAR T Cell Receptor Immunotherapy Targeting EGFRvIII for Patients With Malignant Gliomas Expressing EGFRvIII | National Cancer Institute (NCI)\|National Institutes of Health Clinical Center (CC) | NIH | Phase 1\|Phase 2 | Completed | 2/13 participants with treatment related adverse events (primary outcome). |
| Tivozanib for Recurrent Glioblastoma | Massachusetts General Hospital\|National Comprehensive Cancer Network | Other | Phase 2 | Completed | 10% PFS6 |
| A Randomized Phase II Clinical Trial on the Efficacy of Axitinib as a Monotherapy or in Combination With Lomustine for the Treatment of Patients With | Bart Neyns\|Pfizer\|Universitair Ziekenhuis Brussel | Industry | Phase 2 | Completed | |

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| Recurrent Glioblastoma | | | | | |
| Apatinib in Recurrent or Refractory Intracranial Central Nervous System Malignant Tumors | Rongjie Tao\|Shandong Cancer Hospital and Institute | Other | Phase 2 | Completed | |
| Safety Study of Afatinib for Brain Cancer | Santosh Kesari\|Boehringer Ingelheim\|Saint John's Cancer Institute | Industry | Phase 1 | Completed | In total, 26 patients were screened and 24 were enrolled (median age 60, 78% male, 87.5% Caucasian, glioblastoma N=16, chordoma N=3, brain metastases N=2, meningioma N=1, anaplastic mixed oligoastrocytoma N=1). Patients had received a median of 2.5 prior treatments. Diarrhea (75%), rash (75%), nausea/vomiting (37.5%), fatigue (29.2%), anorexia (25%), and limb edema (16.7%) were the most common side effects. There were no CTCAE defined grade 4 toxicities. Grade 3 side effects infrequently occurred in the highest dosing cohort. These results demonstrate that pulsatile Afatinib at a dose of 280mg every 7 days is safe and tolerable for patients with brain involving cancers. |
| Clinical Trial on the Combination of Avelumab and Axitinib for the Treatment of Patients With Recurrent Glioblastoma | Universitair Ziekenhuis Brussel | Other | Phase 2 | Completed | |
| Prediction of Therapeutic Response of Apatinib in Recurrent Gliomas | The First Affiliated Hospital of Zhengzhou University | Other | | Recruiting | |
| Ketoconazole Before Surgery in Treating Patients With Recurrent Glioma or Breast Cancer Brain | Wake Forest University Health Sciences\|National Cancer Institute (NCI) | NIH | Early Phase 1 | Recruiting | |

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| Metastases | | | | | |
| Anlotinib Combined With STUPP for MGMT Nonmethylated Glioblastoma | Second Affiliated Hospital, School of Medicine, Zhejiang University | Other | Phase 2 | Recruiting | |
| **Cell Cycle/Apoptosis/Transcription Pathways** | | | | | |
| Study of the Poly (ADP-ribose) Polymerase-1 (PARP-1) Inhibitor BSI-201 in Patients With Newly Diagnosed Malignant Glioma | Sanofi | Industry | Phase 1\|Phase 2 | Completed | |
| Virus DNX2401 and Temozolomide in Recurrent Glioblastoma | Clinica Universidad de Navarra, Universidad de Navarra\|DNAtrix, Inc. | Industry | Phase 1 | Completed | |
| Trial of Ponatinib in Patients With Bevacizumab-Refractory Glioblastoma | Dana-Farber Cancer Institute | Other | Phase 2 | Completed | No patients achieved PFS3 |
| Safety and Efficacy of PD0332991 (Palbociclib), a Cyclin-dependent Kinase 4 and 6 Inhibitor, in Patients With Oligodendroglioma or Recurrent Oligoastrocytoma Anaplastic With the Activity of the Protein RB Preserved | | Industry | Phase 2 | Completed | |
| Zotiraciclib (TG02) Plus Dose-Dense or Metronomic Temozolomide Followed by Randomized Phase II Trial of Zotiraciclib (TG02) Plus Temozolomide Versus Temozolomide Alone in Adults With Recurrent Anaplastic Astrocytoma and Glioblastoma | National Cancer Institute (NCI)\|National Institutes of Health Clinical Center (CC) | NIH | Phase 1\|Phase 2 | Completed | MTD was 250mg/d and PFS4 was 40% |
| Phase I/IIa Study of | Centre Francois | Other | Phase | Recruiti | |

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| Concomitant Radiotherapy With Olaparib and Temozolomide in Unresectable High Grade Gliomas Patients | Baclesse\|National Cancer Institute, France | | 1\|Phase 2 | ng | |
| A Phase 0 /II Study of Ribociclib (LEE011) in Combination With Everolimus in Preoperative Recurrent High-Grade Glioma Patients Scheduled for Resection | St. Joseph's Hospital and Medical Center, Phoenix\|Ivy Brain Tumor Center\|Barrow Neurological Institute | Other | Early Phase 1 | Completed | Ribociclib exhibited good CNS penetration, and target modulation was indicated by inhibition of RB phosphorylation and tumor proliferation. Six of 12 patients were enrolled into the pharmacokinetic/pharmacodynamic-guided expansion cohort and demonstrated a median PFS of 9.7 weeks |
| BGB-290 and Temozolomide in Treating Isocitrate Dehydrogenase (IDH)1/2-Mutant Grade I-IV Gliomas | University of California, San Francisco\|BeiGene USA, Inc.\|Pacific Pediatric Neuro-Oncology Consortium | Industry | Phase 1 | Recruiting | |
| Anticancer Therapeutic Vaccination Using Telomerase-derived Universal Cancer Peptides in Glioblastoma | Centre Hospitalier Universitaire de Besancon | Other | Phase 2 | Recruiting | |
| B7-H3 CAR-T for Recurrent or Refractory Glioblastoma | Second Affiliated Hospital, School of Medicine, Zhejiang University\|Ningbo Yinzhou People's Hospital\|Huizhou Municipal Central Hospital\|BoYuan RunSheng Pharma (Hangzhou) Co., Ltd. | Other | Phase 1\|Phase 2 | Recruiting | |
| **Immunotherapy Pathways** | | | | | |
| A Dose Escalation and Cohort Expansion Study of Anti-CD27 (Varlilumab) and Anti-PD-1 (Nivolumab) in Advanced Refractory Solid Tumors | Celldex Therapeutics\|Bristol-Myers Squibb | Industry | Phase 1\|Phase 2 | Completed | GBM overall survival at 12 months was 40.9% Varlilumab and nivolumab were well tolerated, without significant toxicity beyond that expected for each agent alone. Clinical activity was observed in patients that are typically refractory to anti-PD-1 therapy, however, overall was not greater than expected for nivolumab monotherapy. |
| Ipilimumab and/or | National Cancer Institute | NIH | Phase | Complet | IPI and NIVO are safe and |

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| Nivolumab in Combination With Temozolomide in Treating Patients With Newly Diagnosed Glioblastoma or Gliosarcoma | (NCI)\|NRG Oncology | | 1 | ed | tolerable with similar toxicity profiles noted with other cancers when given with adjuavant TMZ for newly diagnosed GBM. |
| Study of Cabiralizumab in Combination With Nivolumab in Patients With Selected Advanced Cancers | Five Prime Therapeutics, Inc.\|Bristol-Myers Squibb | Industry | Phase 1 | Completed | 99.6% participants received 4 mg/kg cabiralizumab IV and 3 mg/kg nivolumab IV Q2W experienced adverse events. 52.1% participants in this group experienced severe adverse events. |
| Intra-tumoral Ipilimumab Plus Intravenous Nivolumab Following the Resection of Recurrent Glioblastoma | Universitair Ziekenhuis Brussel | Other | Phase 1 | Recruiting | |
| Nivolumab for Recurrent or Progressive IDH Mutant Gliomas | Fabio Iwamoto, MD\|Bristol-Myers Squibb\|Columbia University | Industry | Phase 2 | Active, not recruiting | |
| Efficacy and Safety of Pembrolizumab (MK-3475) Plus Lenvatinib (E7080/MK-7902) in Previously Treated Participants With Select Solid Tumors (MK-7902-005/E7080-G000-224/LEAP-005) | Merck Sharp & Dohme LLC\|Eisai Inc. | Industry | Phase 2 | Active, not recruiting | |
| Efficacy of Nivolumab for Recurrent IDH Mutated High-Grade Gliomas | | Industry | Phase 2 | Completed | At 24 weeks, 11/39 patients without disease free progression. Median PFS and OS were 1.84 (CI95% [1.81 ; 5.89]) and 14.7 months (CI95% [9.18; NR]), respectively. No patient definitively stopped Nivolumab due to side effects; the safety profile was consistent with prior studies of Nivolumab in gliomas and other cancers. |
| Trial of Anti-Tim-3 in Combination With Anti-PD-1 and SRS in Recurrent | Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins\|Novartis | Industry | Phase 1 | Active, not recruiting | |

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| GBM | Pharmaceuticals | | | | |
| Neoadjuvant Carilizumab and Apatinib for Recurrent High-Grade Glioma | Sun Yat-sen University | Other | Phase 2 | Recruiting | |
| Ivosidenib (AG-120) With Nivolumab in IDH1 Mutant Tumors | Jason J. Luke, MD\|Agios PharmaceuticalsInc.\|Bristol-Myers Squibb\|University of Pittsburgh | Industry | Phase 2 | Recruiting | |
| **Other** | | | | | |
| A Phase 2b Clinical Study With a Combination Immunotherapy in Newly Diagnosed Patients With Glioblastoma | Imvax | Industry | Phase 2 | Recruiting | IGV-001 |