ASCO 2026 – NEURO-ONCOLOGY CLINICAL TRIALS

1. **DOC1021** (Dubodencel-Autologous dendritic cell-based therapy with tumor-derived mRNA; NCT04552886)

https://www.asco.org/abstracts-presentations/259151

This document reports pooled results from two clinical studies of DOC1021 (dubodencel), an autologous dendritic cell–based immunotherapy generated by loading with tumor-derived mRNA and tumor cell lysate for glioblastoma (GBM; NCT04552886). DOC1021 is designed to stimulate a broad anti-tumor immune response by presenting tumor-derived antigens and promoting CD8+ effector memory T-cell development, activating dendritic cells and targeting p38MAPK and MTORc1 signaling pathways.

The analysis included 25 patients with newly diagnosed or recurrent IDH-wildtype GBM who received DOC1021 after surgery and standard chemoradiation. Patients came from a Phase I trial and an expanded access protocol, with most receiving high-dose treatment. Importantly, the group included difficult-to-treat patients, such as those with subtotal resection or pre-treatment progression. The amplified mRNA and tumor lysate is administered bilaterally near deep cervical lymph node chains every other week for 3 doses with weekly pegylated-interferon.

Results suggest that DOC1021 plus standard of care was generally safe and feasible. Most adverse events were mild, such as flu-like symptoms and injection-site reactions, although one patient had grade 3 cerebral edema that resolved. Early survival observations were encouraging, with several newly diagnosed and recurrent patients still alive many months after surgery. Pseudoprogression was commonly observed. Immune monitoring also showed signs of biological activity, including increased CD4+ and CD8+ central memory T cells and higher CD127 expression (IL-7Rα) on circulating CD8+ T cells.

Overall, the findings support DOC1021 as a promising and well-tolerated immunotherapy approach in GBM, leading to an ongoing randomized Phase 2 trial comparing DOC1021 plus standard treatment versus standard treatment alone.

2. **DRI (INB-200)** (Autologous gamma delta (γδ) T cells; NCT04165941)

https://www.asco.org/abstracts-presentations/268244

This document describes updated results for patients with newly diagnosed GBM who failed chemotherapy and were placed on a novel immunotherapy for drug-resistant

patients (DRI). The treatment) combines MGMT-modified gamma-delta (γδ) T cells with temozolomide (TMZ) so the immune cells can survive chemotherapy and target residual tumor cells when the cancer may be most vulnerable.

In the study, 17 patients received temozolomide upregulating stress antigens that enable the γδ T cells to attack residual GBM cells, in 14 patients who received repeated doses while three received only a single dose. Their outcomes were compared with 10 contemporaneous patients who only received standard of care (SOC). The repeated-dose DRI group included patients with generally high-risk disease features, such as IDH-wildtype tumors, MGMT-unmethylated status, and a high rate of subtotal resection.

The treatment showed a manageable safety profile. There were no dose-limiting toxicities, cytokine release syndrome, ICANS, or treatment-related deaths. In terms of effectiveness, the median progression-free survival (PFS) for repeated-dose DRI patients was 13.0 months, compared with 6.6 months in the SOC control group, suggesting substantially longer disease control. Overall survival (OS) in the repeated-dose group was still increasing at 17.2+ months, compared with 13.2 months for controls. More than half of repeat-dose patients had **PFS** that exceeded their expected **overall survival** based on age and MGMT status. One patient has been progression-free for 4.6 years without additional maintenance therapy.

The document also reports encouraging biological evidence of immune activity. Manufactured cell products showed increased expression of genes linked to cytotoxicity and immune trafficking, while inflammatory cytokines associated with severe immune toxicity did not rise above baseline. Peripheral γδ T-cell and total T-cell levels improved with increasing dose frequency, and tumor biopsies from recurrent disease showed persistent γδ T-cell infiltration and necrosis long after treatment.

Overall, the study suggests that DRI is feasible, safe, and can improve outcomes in newly diagnosed GBM, supporting further clinical investigation.

3. **NeoVax** (Personalized Neoantigen Peptide Vaccine; NCT02287428)

https://www.asco.org/abstracts-presentations/267242

This document reports results from a phase I trial of NeoVax, a personalized neoantigen peptide vaccine, combined with pembrolizumab in patients with newly diagnosed GBM. The goal was to overcome the immunosuppressive tumor environment in GBM by generating patient-specific T cell responses against tumor mutations.

The study enrolled 39 patients, following gross total resection, of whom 37 began vaccination and 35 completed the priming series. Patients were divided into cohorts

based on MGMT methylation status and timing of pembrolizumab. Treatment was well tolerated, with no serious adverse events.

Results showed encouraging signs of both clinical activity and immune activation. Median overall survival was 36.9 months in *MGMT*-methylated patients and 19.0 months in *MGMT*-unmethylated patients, both higher than propensity score-matched historical controls.

The vaccine generated neoantigen-specific T cell responses in most patients, and those with detectable ex vivo immune responses had significantly better survival than non-responders. Tumor analyses also found vaccine-reactive T cell clones within post-vaccination tumors, along with increased populations of intratumoral T effector cells, suggesting that the immune response not only developed in the blood but also reached the tumor.

Overall, the findings suggest that NeoVax plus pembrolizumab is safe, immunogenic, and biologically active in newly diagnosed GBM, with improved survival, supporting further research into combination immunotherapy strategies.

4. LIPOCURC (Liposomal curcumin combined with SOC for nd-HGG; NCT05768919)

https://www.asco.org/abstracts-presentations/259142

This document describes a Phase I/II study of intravenous liposomal curcumin (LC) given with standard radiotherapy and temozolomide in patients with newly diagnosed high-grade glioma, most of whom had IDH-wildtype glioblastoma. Preclinical studies showed synergy between LC and chemoradiation. Curcumin modulates inflammatory, oxidative, and oncogenic pathways relevant to high-grade glioma (HGG), including kynurenine metabolism. The study aimed to identify the recommended Phase II dose, evaluate safety and feasibility, and look for early signs of efficacy.

A total of 25 patients were treated across planned dose levels of 300, 350, and 400 mg/m², although patients assigned to 400 mg/m² were ultimately treated at 350 mg/m² based on safety review. The trial found 350 mg/m² to be the recommended Phase II dose.

Two dose-limiting toxicities were reported at the highest planned dose level: grade 4 pancytopenia and grade 1 hemolysis. Overall, LC-related severe toxicities were limited, and there were no treatment-related deaths.

Early outcomes were encouraging. With a median follow-up of 12.9 months, median progression-free survival and overall survival have not yet been reached. Among

patients still being followed, 95% were alive at 6 months and 87% at 12 months after the first LC infusion.

Overall, the study suggests that liposomal curcumin can be safely combined with standard chemoradiation, with promising early signs of disease control in newly diagnosed GBM, supporting further testing in a larger Phase II/III trial.

5. **Rituximab-CARv3-TEAM-E** (The INCIPIENT Trial-CAR T cell Therapy-rGBM; NCT05660369)

https://www.asco.org/abstracts-presentations/259127

This document reports early results from the INCIPIENT first-in-human clinical trial of CARv3-TEAM-E, a novel CAR T-cell therapy for recurrent GBM. The therapy is designed to address tumor heterogeneity by targeting EGFRvIII while also secreting antibody molecules against wild-type EGFR.

A total of 13 patients received intraventricular CARv3-TEAM-E with different pre-treatment strategies: no lymphodepletion, lymphodepleting chemotherapy (LDC), or LDC plus rituximab (LDC+R). The treatment was feasible and well tolerated, with successful manufacturing for all patients and no dose-limiting toxicities.

A key finding was that patients who did not receive rituximab often developed anti-therapy antibodies, which appeared to limit CAR T-cell persistence after repeat dosing. Adding rituximab, however, prevented these antibody responses in all 3 treated patients and enabled persistence of CAR T cells in cerebrospinal fluid, including after reinfusion.

Early survival outcomes were also encouraging. As of December 15, 2025,10 of 13 patients were alive between 6 and 30 months after first infusion, and 7 remained alive beyond 14 months.

Overall, the study supports CARv3-TEAM-E as a promising, well-tolerated therapy for recurrent GBM; rituximab- preconditioning can improve repeat dosing by preventing anti-therapy immune responses.

6. **Bivalent EGFR-IL13Rα2 CAR T Cell Therapy in rGBM** (NCT05168423)

https://www.asco.org/abstracts-presentations/267261

This document reports updated follow-up from a study of bivalent CAR T cells targeting EGFR and IL13Rα2 in 18 patients with recurrent EGFR-amplified GBM. Patients

received a single intracerebroventricular dose of the therapy, and the analysis focused on longer-term survival, safety, and neurologic function.

With a median follow-up of 18.5 months, the treatment showed promising survival, with a median overall survival of 12.0 months and 3 patients surviving longer than 18 months. Safety remained encouraging over the longer follow-up period. Aside from one previously reported case of prolonged low-grade neurotoxicity, there were no prolonged, delayed, or unexpected toxicities, including no on-target off-tumor toxicity or secondary cancers.

Neurologic function, measured using the NANO scale, worsened briefly right after infusion but generally returned to baseline by day 4, and remained similar to baseline at 1 and 2 months after treatment. Patients who later received a second CAR T-cell dose at progression did not show the same early neurologic worsening seen after the first infusion.

Overall, the study suggests that intracerebroventricular CART-EGFR-IL13Rα2 is feasible, has no evident long-term safety signal so far, and shows encouraging survival in recurrent glioblastoma, supporting continued clinical development.

7. Randomized, Phase 2 Trial of $NanO_2$ in nd-GBM: RESTORE (NCT03862430)

https://www.asco.org/abstracts-presentations/259136

This document describes a blinded pooled safety analysis from the RESTORE trial, the first randomized, prospective, placebo-controlled study of $NanO_2$ in newly diagnosed GBM. $NanO_2$ is an oxygen-carrying fluorocarbon emulsion designed to reoxygenate hypoxic tumor tissue, with the aim of improving the effectiveness of standard radiation and temozolomide.

In the trial, patients received standard chemoradiation and were randomized 2:1 to receive either $NanO_2$ or placebo before each radiation treatment, along with supplemental oxygen. The study's main goal is to evaluate progression-free survival, with additional outcomes including overall survival, response rate, pseudoprogression, and patient-reported outcomes.

As of the December 29, 2025, data cutoff, 93 patients had been treated and enrollment was complete. Most patients remained on study, with 68 patients (73%) still receiving adjuvant therapy or in follow-up.

There were grade 3 or higher adverse events in 37% of patients and serious adverse events in 19%. The most common serious issues included pulmonary embolism, and

seizure; only three serious events were considered possibly or probably related to study drug, and no unexpected safety signals were identified.

Overall, the interim analysis suggests that $NanO_2$ can be combined with standard chemoradiation in newly diagnosed GBM, while final efficacy results remain pending as treatment assignment remains blinded.

8. **Phase II Trial of Chemoradiation plus FLUOXETINE for nd-Grade 4 Glioma** (Chinese Clinical Trial Registry -ChiCTR2400084456)

https://www.asco.org/abstracts-presentations/259209

This document describes a phase II, single-arm clinical trial evaluating fluoxetine in combination with radiotherapy and temozolomide for patients with newly diagnosed grade 4 glioma, including mostly GBM. The rationale is that fluoxetine, commonly used as an antidepressant, may also have anti-tumor activity in glioma and could improve outcomes when added to standard treatment.

This single-arm, single-center, prospective study enrolled 27 patients between May 2024 and November 2025, including 25 with GBM and 2 with grade 4 astrocytoma. Nearly half of patients showed depressive tendencies before treatment. As of the latest analysis, 17 patients had at least one year of follow-up or had progressed and were included in the preliminary efficacy analysis.

Early results were encouraging: the 1-year progression-free survival rate was 52.9%. The treatment combination also appeared to be generally well tolerated. The most common side effects were alopecia, nausea, insomnia, and seizures, and these were mostly mild (grade 1–2). Only one patient experienced a grade 3 adverse event, consisting of elevated liver enzymes.

Overall, the preliminary findings suggest that adding fluoxetine to standard chemoradiation for newly diagnosed grade 4 glioma is feasible, safe, and may improve progression-free survival, though longer follow-up and larger studies are needed to evaluate potential benefits.

9. Phase II Trial of Lucicebtide (ST101) plus Chemoradiation Phase 2 Trial for GBM (NCT04478279)

https://www.asco.org/abstracts-presentations/259158

This document describes early clinical results for lucicebtide (ST101), an experimental therapy, a peptide antagonist, targeting the transcription factor C/EBPß in patients with GBM. The investigators focused on both newly diagnosed GBM (ndGBM) and recurrent GBM (rGBM).

The rationale for the study is biologically important. Recurrent glioblastoma is often driven by a “mesenchymal-like” tumor state associated with aggressive growth, treatment resistance, and a highly immunosuppressive tumor microenvironment. A key regulator of both the mesenchymal tumor program and suppressive tumor-associated myeloid cells (TAMs) is the protein C/EBPß. Lucicebtide was designed as a first-in-class peptide antagonist to inhibit this pathway and potentially reverse both tumor aggressiveness and immune suppression.

The study enrolled 18 patients total: 9 with recurrent GBM and 9 with newly diagnosed GBM. Patients received several doses of lucicebtide before surgery, allowing investigators to directly analyze resected tumor tissue for evidence of drug penetration and biologic activity. After surgery, recurrent GBM patients continued lucicebtide alone until progression, while newly diagnosed patients received lucicebtide together with standard chemoradiation.

One of the most notable findings was that lucicebtide appeared to cross the blood-brain barrier successfully and accumulate within tumor tissue. Tissue analyses also demonstrated target engagement, meaning the drug appeared to inhibit the intended C/EBPß pathway within both tumor cells and immune cells in the tumor microenvironment.

In newly diagnosed GBM, progression-free survival (PFS) exceeded historical expectations, with most patients still progression-free beyond 21 months at the January 27, 2026 data cutoff. Median overall survival (mOS) had not yet been reached. The reported 18-month overall survival rate was 67%, and the 24-month survival rate was 44%. These results compare favorably with historic benchmarks from the landmark Stupp trials, which reported approximately 39–45% survival at 18 months and 26–31% at 24 months using standard therapy alone.

In recurrent GBM, lucicebtide produced a median progression-free survival of 4.0 months and a median overall survival of 12.3 months. Historically, recurrent GBM treated with chemotherapy alone often shows a median PFS of about 2 months and median overall survival between roughly 5.6 and 9.8 months. While cross-trial comparisons are inherently limited, these differences suggest potential clinical activity worthy of further investigation.

The mechanistic findings may be equally important as the survival data. Spatial transcriptomic analyses showed substantial suppression of the C/EBPß regulatory network in both tumor cells and macrophages. In addition, researchers observed increased infiltration of effector $CD8^+$ T cells and a higher M1/M2 macrophage ratio,

suggesting reprogramming away from an immunosuppressive environment and toward a more anti-tumor immune response.

The study concludes that lucicebtide was well tolerated both alone and in combination with standard chemoradiation. The data support continued clinical development of lucicebtide as a novel therapeutic strategy for GBM.

Limitations, however, include: i). The trial involved a relatively small number (n= 18 patients) divided into two groups (nd-GBM and rGBM). There is no randomized control arm, instead relying on comparisons with historical datasets. The immune correlates, however, are impressive with both clinical and biological efficacy signals, including a dramatic reduction in the mesencymal gene signature and a remodeling of the immune tumor microenvironment (TME).

Taken together, this study demonstrates that a novel brain penetrant, targeted molecule with favorable safety profile appears promising and will be evaluated in broader clinical trials. Lucicebtide could be part of a combination therapy to transform glioblastoma from an immunoresistant “cold” tumor to an immune permissive “hot” tumor.

10. Phase III Trial of Cesium-131 tile-based radiation therapy (TBRT, marketed as GammaTile®) (NCT04365374)

https://www.asco.org/abstracts-presentations/259084

The linked document describes the results of the Phase 3 ROADS randomized study of cesium-131 tile-based radiation therapy (TBRT, GammaTile®) compared with the current standard approach of postoperative stereotactic radiation therapy (SRT) for patients undergoing surgery to remove a newly diagnosed brain metastasis. Traditionally, radiation is delivered several days to weeks after surgery using SRT. In contrast, TBRT involves placing small collagen tiles containing cesium-131 radiation sources directly into the surgical cavity during the operation, allowing radiation treatment to begin immediately after tumor removal.

The trial enrolled 230 patients across 32 U.S. centers and randomized them to receive surgery followed by either SRT or TBRT. Patient and tumor characteristics were well balanced between the groups, and 204 patients were included in the final efficacy analysis. The median follow-up was approximately 13 months.

The key finding was improved local tumor control with GammaTile after surgery compared with stereotactic radiotherapy (SRT). GammaTile was associated with approximately 52% lower risk of tumor recurrence or death (a hazard ratio of 0.48) for surgical-bed recurrence-free survival, (statistically significant, p = 0.002).

Additionally, recurrence within the surgical cavity occurred in only 1.0% of patients treated with TBRT, compared with 11.9% of those treated with SRT, representing a

94% reduction in the risk of local recurrence (HR 0.06, p=0.007). Patients receiving TBRT also experienced significantly longer surgical bed recurrence-free survival, reflecting more durable local disease control. In the SRT group, the median time to surgical bed recurrence was 17.4 months and median recurrence-free survival was 10.9 months, whereas neither endpoint was reached in the TBRT group because so few local recurrences occurred during the study period.

The study also found a significant improvement in overall survival. At two years, an estimated 61.7% of patients treated with TBRT were alive, compared with 35.7% of patients treated with SRT. This translated to a 41% reduction in the risk of death during the study period (HR 0.59, p=0.032). While the study was not specifically designed to determine why survival improved, the investigators proposed that immediate radiation delivery and better local control may reduce interruptions in systemic cancer treatments such as immunotherapy, targeted therapy, or chemotherapy.

Another practical advantage of TBRT was the speed with which brain-directed treatment could be completed. The median time from surgery to completion of all planned cranial radiation treatments was just 1 day with TBRT, compared with 30 days with SRT. For many patients, this shorter treatment timeline could reduce travel, decrease treatment burden, and potentially allow earlier resumption of systemic therapy.

Safety outcomes were reassuring. Rates of radiation necrosis, a delayed complication in which irradiated brain tissue becomes damaged, were nearly identical between groups (7.8% with TBRT vs 6.9% with SRT). Serious treatment-related adverse events (grade 3 or higher) were also similar (18.1% with TBRT vs 19.3% with SRT), suggesting that the improved efficacy of TBRT did not come at the cost of increased toxicity.

One area that deserves ongoing monitoring is leptomeningeal disease (LMD), a form of cancer spread involving the lining of the brain and spinal cord. LMD occurred in 9.7% of patients treated with TBRT compared with 3.0% of those receiving SRT. However, this difference was not statistically significant (p=0.146), meaning the study could not confidently conclude that TBRT increased the risk. Furthermore, when considering the combined outcome of being alive and free from LMD at two years, patients treated with TBRT still appeared to fare better (57.7% vs 35.9%), although this difference also did not reach statistical significance.

Taken together, the ROADS trial provides some of the strongest evidence to date supporting the use of cesium-131 tile-based radiation after resection of a brain metastasis. Compared with standard postoperative SRT, TBRT produced markedly better local tumor control, significantly improved overall survival, and allowed completion of radiation treatment almost immediately after surgery, while maintaining a similar safety profile. Although longer follow-up will be important to confirm the durability of these findings and further clarify the leptomeningeal disease signal, the results suggest that TBRT may represent a meaningful advance in the management of patients with newly diagnosed, surgically resectable brain metastases.