Society for Neuro-Oncology's 29th Annual Scientific Meeting and Education Day 2024

Highlights from select abstracts of interest - a patient's perspective

HIGH GRADE GLIOMA / GLIOBLASTOMA – TRIALS FOR NEWLY DIAGNOSED

CTNI-18 Results from a phase 1 study of sonodynamic therapy with whole hemispheric low intensity non-ablative ultrasound in patients with recurrent high grade glioma

New York - This trial combined low-intensity diffuse ultrasound across the entire brain hemisphere with oral 5-aminolevulinic acid (5-ALA) in 12 patients across three cohorts, with escalating treatment durations. The treatments were delivered monthly for ≥four sessions, and a treatment duration of 120 minutes was established after dose escalation. Per the SNO abstract, there was a significant increase in overall survival (mOS of 14.0+ months, with final median OS not yet achieved); a later press release reported extended median overall survival (OS) to 15.7 months and progression-free survival (PFS) to 5.5 months. This is particularly impressive given that two patients were enrolled after multiple recurrences and seven patients had multifocal or multicentric disease. The therapy was well-tolerated, with no severe side effects or toxicities limiting treatment duration. A larger Phase 2b randomized trial is planned for 2025 to further test the treatment's safety and effectiveness in newly diagnosed glioblastoma patients.

CTIM-10 Phase 1 Trial of Personalized Neoantigen Vaccines In Combination With Standard Care To Treat Glioblastoma

New York - This was a Phase 1 trial of 12 newly diagnosed glioblastoma patients treated with a personalized neoantigen vaccine alongside standard of care, including tumor treating fields. All 12 (100%) were progression-free at six months. Eight of the 12 (67%) survived to 2 years, and seven (58%) continued on to 3-year survival. However, one patient experienced serious adverse events which ultimately led to brain demyelination and death. These are remarkable survival outcomes, although we need a better understanding of the one serious adverse event.

CTNI-31 AI-guided personalized precision radiation therapy with targeted dose escalation for newly diagnosed glioblastoma: a matched-control study

UPenn – This study used AI-guided personalized precision radiation therapy (PPRT) with targeted dose escalation in patients with newly diagnosed glioblastoma. The PPRT group received personalized radiation dose escalation to 75 Gy in 30 fractions guided by AI-based predictive modeling of recurrence, along with temozolomide chemotherapy. The control group received standard-of-care chemoradiotherapy, 60 Gy in 30 fractions. Median overall survival was 24.3 months in the PPRT group versus 17.5 months in the control group. Excluding two patients with leptomeningeal disease and bone marrow metastasis, median survival was 35.4 months in the PPRT group. These results show the potential of personalized precision radiation therapy, with focused dose escalation, in improving outcomes for GBM patients.

CTNI-50. Clinical Efficacy And PK/PD Response In a Phase 0/2 Study of Niraparib Plus Radiotherapy For Newly-Diagnosed, MGMT-Unmethylated Glioblastoma

Ivy Brain Tumor Center (Arizona) - We reported previously on these positive results (median overall survival 20.3 months) in a Brain Blast newsletter (see here).

CTNI-25 Tumor Treating Fields (TTFields) therapy with chemoradiation, followed by maintenance TTFields therapy/temozolomide (TMZ), in newly diagnosed glioblastoma (ndGBM). Results of phase II clinical study.

Germany - This was a randomized trial comparing the efficacy and safety of starting TTFields therapy alongside radiotherapy and temozolomide versus the standard practice of starting TTFields one month after chemoradiation. Patients in the investigational arm (concomitant TTFields) had a one-year progression-free survival (PFS) rate of 36% versus 19% in the control group. Although median overall survival (OS) did not significantly differ between groups, patients with high TTFields usage exhibited a markedly improved two-year OS rate of 78% compared to 34% in the control group. These findings suggest that starting TTFields at the time of chemoradiation may improve outcomes for newly diagnosed GBM patients. There is a larger ongoing study (TRIDENT trial) which will shed more light on this topic in coming years.

CTIM-16. Safety and Preliminary Efficacy of AZD1390 + Radiation Therapy For Glioblastoma

Ivy Brain Tumor Center (Arizona) - AZD1390 is a new drug designed to enhance radiation therapy for GBM. In a Phase 1 study, 115 patients were treated with escalating doses of AZD1390 during radiation. The study included 75 patients with recurrent GBM (35 Gy of radiation over 10 fractions in 2 weeks) and 40 with newly diagnosed, MGMT-unmethylated GBM (60 Gy over 30 fractions in 6 weeks). AZD1390 doses ranged from 10–900 mg/day, given once daily during radiation; patients also received 2 additional weeks of adjuvant AZD1390 post-radiation. Common side effects were fatigue (51.3%), nausea (39.1%), and headache (38.3%). More serious adverse events occurred in 18/115 patients, and 15/115 patients discontinued the drug to adverse events. The highest doses safely tolerated were 400 mg for recurrent GBM and 300 mg for newly diagnosed GBM. Although this study was aimed at evaluating safety, preliminary efficacy results showed a median overall survival of 12.7 months for recurrent GBM patients, with survival data for newly diagnosed patients still being analyzed. Following these results, AZD1390 will be added as a treatment arm in the larger GBM AGILE trial to further assess efficacy.

CTNI-78. PNOC008: A Pilot Trial Testing The Clinical Benefit of Using Molecular Profiling To Determine An Individualized Treatment Plan In Children And Young Adults With Newly Diagnosed High-Grade Glioma (Excluding Diffuse Intrinsic Pontine Glioma)

Multicenter - Fifty-five patients (median age 11 years) were enrolled, and comprehensive molecular profiling of tumor tissue was used to create personalized treatment plans combining up to four FDA-approved drugs. For the 44 patients who followed the recommended treatment, median overall survival (mOS) from enrollment was 26.5 months for localized, hemispheric HGG and 23.6 months for non-DIPG DMG. Notably, H3G34-mutant patients (n=10) had a mOS of 30 months. The treatment combinations, often including alkylators with targeted therapies, were generally well-tolerated.

CTIM-14 Early safety data from a randomized, multicenter, double-blind, phase 2b study of IGV-001, an autologous cell immunotherapy, versus placebo, in newly diagnosed glioblastoma (ndGBM)

(see also CTIM-11. Long-term Survivors From a Phase 1B Study of IGV-001 in Patients with Newly Diagnosed Glioblastoma)

Multicenter - Imvax's vaccine, called IGV-001, consists of a patient's own GBM tumor cells combined with an antisense oligonucleotide. The combination is irradiated and then administered via biodiffusion chambers which are implanted in the patient's abdomen for 24-48 hours. A Phase 1b study showed IGV-001 was well-tolerated and had promising efficacy signals, including improved progression-free survival (PFS), overall survival (OS), and radiographic tumor response. Notably, 15.2% of subjects survived 5 years

or more. The ongoing Phase 2b placebo-controlled study has completed enrollment with 99 subjects, and early safety data from 95 implanted subjects showed no emerging risks, with no treatment discontinuations due to adverse events. Updated PFS results from this Phase 2b trial are expected in 2025 and will provide more robust evidence for IGV-001's safety and efficacy.

DNAR-10 Phase I clinical trial of peposertib plus radiotherapy in adults with newly-diagnosed MGMT-unmethylated glioblastoma

MD Anderson (Houston) - Peposertib is a small molecule inhibitor, given orally in combination with radiotherapy. This trial for newly diagnosed MGMT-unmethylated GBM enrolled 21 patients and established a maximum tolerated dose (MTD) of 300mg per RT fraction day. Results showed median progression-free survival (PFS) of 10.8 months and a median overall survival (OS) of 22.9 months, with one dose-limiting toxicity (grade 3 radiation necrosis at the MTD). Advanced tumor analysis showed the treatment changed the tumor environment; it caused cancer cells to become more mature and inflamed, and increased the presence of immune cells called macrophages, particularly those that promote inflammation.

CTIM-27 DOC1021 cell-based vaccination as adjuvant therapy for glioblastoma: phase I clinical trial analysis

Texas and New Jersey - DOC1021 is a dendritic cell vaccine that combines autologous tumor lysate and mRNA. This Phase I trial evaluated DOC1021 in newly diagnosed GBM patients, administering it near deep cervical lymph nodes after chemoradiation. The study included 16 GBM patients, and all but one had unmethylated MGMT promoter. DOC1021 showed a favorable safety profile with mainly mild side effects. Post-vaccination analysis revealed increased CD8+ T-cell tumor infiltration and expansion of memory T-cell populations in blood. Importantly, median survival for the MGMT unmethylated cohort has not been reached but is significantly higher than historical controls.

CTIM-09 INB-200: Fully Enrolled Phase 1 Study of Gene-Modified Autologous Gamma-Delta (γδ) T Cells in Newly Diagnosed Glioblastoma Multiforme (GBM) Patients Receiving Maintenance Temozolomide (TMZ)

University of Alabama - IN8bio is developing a drug called DeltEx drug resistant immunotherapy (DRI), with TMZ-resistant γδ T cells engineered to express MGMT. The treatment is administered into the resection cavity along with IV TMZ on Day 1 of each of the 6 Stupp maintenance TMZ cycles. The Phase 1 trial evaluated DRI in adult newly diagnosed grade 4 glioma patients, with cohorts receiving 1, 3, or 6 doses of DRI cells during Stupp maintenance cycles. A total of 23 patients were enrolled but only 13 received treatment. Results showed no dose-limiting toxicities. 83% of subjects exceeded the median 7-month PFS of the Stupp regimen alone, with manageable toxicity and an encouraging trend in PFS. One patient with IDH mutant tumor remained progression-free for >35 months. Long-term follow-up for PFS and OS is ongoing.

CTNI-27. Systemic Delivery of Low Energy Radiofrequency Electromagnetic Fields for the Treatment of Patients With Primary Brain Tumors

Brazil - The AutEMsys device emits low-energy amplitude modulated systemic electromagnetic fields (EMF) at patient-specific frequencies. In a prospective compassionate access program for adult GBM patients, patients underwent a 90-minute session of EMF exposure therapy repeated every 2 weeks until progression, deterioration in QOL or death. 31 participants enrolled, including 29 with GBM and 2 with DMG. 14 patients received EMF+chemoradiotherapy followed by EMF+maintenance TMZ (mTMZ), and 17 patients received EMF+mTMZ (post chemoradiotherapy). Survival time was measured from the start

of mTMZ to date of the last follow-up. Median overall survival (mOS) for all 31 patients was 26 months. Specifically for 21 patients with unmethylated MGMT, mOS was 25.0 months. The addition of AutEMsys with chemoRT+mTMZ demonstrated an improved role functioning in 79% of patients, with 25% of these with >10-point score. These findings warrant further prospective investigation and validation in a multicenter clinical trial.

CTNI-86 The RESECT study: a French multicenter randomized phase-III study comparing 5-ALA fluorescence-guided surgery versus white-light conventional microsurgery for the resection of newly-diagnosed glioblastomas

France (multicenter) - This Phase III trial compared 5-aminolevulinic acid (5-ALA) fluorescence-guided surgery to conventional white-light microsurgery for glioblastoma resection. The study found significantly higher gross total resection (GTR) rates with 5-ALA (76.8%) compared to the conventional surgery group (47.8%). As expected, multivariate analysis showed that GTR was an independent predictor of progression free survival PFS and overall survival (OS). Although 5-ALA fluorescence-guided adds an extra cost (€2,732.36) to surgery, it was deemed cost-effective.

CTNI-64. Trial In Progress: DIET2TREAT -- A Randomized Multicenter Phase 2 Trial of a Ketogenic Diet Vs Standard Dietary Guidance In Combination With Standard-of-Care Treatment For Patients With Newly Diagnosed Glioblastoma

Multicenter – Target enrollment for this trial is 170 patients over 5 years. As of December 2024, the trial is open for enrollment at three centers in California, and will be opening soon at Duke and the Medical College of Wisconsin. 13 patients have been randomized to date. Participants will follow their assigned diet for 18 weeks, starting alongside standard chemoradiation treatment.

LTBK-02. Evaluation of Paxalisib in GBM AGILE Phase 3 Registration Platform Trial For Newly Diagnosed and Recurrent Glioblastoma

Multicenter – The GBM AGILE trial enrolled over 150 patients into the paxalisib investigational arm between December 2020 and May 2022. However, the treatment did not meet the necessary thresholds for progression to stage 2 of the trial, and final analysis revealed that paxalisib did not demonstrate a significant survival benefit compared to standard treatment, with median overall survival of 14.77 months for the paxalisib group versus 13.84 months for controls in newly diagnosed patients, and 8.58 months versus 10.06 months in recurrent GBM.

HIGH GRADE GLIOMA / GLIOBLASTOMA – TRIALS FOR RECURRENCE

CTNI-05. A Prospective Study of Tumor-Treating Fields Combined With Systemic Therapy In Recurrent Glioblastoma

China - Tumor-treating Fields (TTFields) were combined with physician's choice systemic therapy for 40 recurrent GBM patients in China. Most patients started TTFields soon after their first recurrence diagnosis. The treatment showed promising results, with 87.2% of patients surviving at least 6 months, and a median overall survival of 20.2 months. The median progression-free survival was 8.5 months - significantly better than historical data for chemotherapy alone.

CTNI-19. Mycophenolate Mofetil Targets Glioblastoma De-Novo Purine Metabolism To Overcome Chemoradiation Resistance In Newly Diagnosed And Recurrent Glioblastoma

Univ of Michigan - This phase 0/1 trial investigated mycophenolate mofetil (MMF) in combination with standard chemoradiation. MMF works by inhibiting an enzyme which is crucial for de novo purine synthesis; by blocking this process, MMF selectively targets cancer cells and inhibits proliferation. In this study, MMF had generally good tolerability in both newly diagnosed and recurrent GBM patients. In recurrent patients, median overall survival (mOS) was 16.1 months for MGMT-methylated and 6.1 months for unmethylated tumors. For newly diagnosed patients, mOS was 27.2 months for MGMT-methylated and 14.2 months for unmethylated tumors. This trial established a recommended phase 2 dose of 1500mg twice daily.

CTIM-01 Outcomes and immune responses after peptide vaccination targeting human cytomegalovirus antigen pp65 in children and young adults with recurrent high-grade glioma and medulloblastoma: results of a Phase 1 trial

Duke - This trial tested a new peptide vaccine called PEP-CMV in 38 children and young adults with recurrent medulloblastoma and high-grade glioma. The vaccine targets a protein called pp65, which is found in these brain tumors but not in normal brain tissue. Patients received temozolomide, followed by PEP-CMV vaccine every two weeks for three doses, then monthly. The vaccine was generally well-tolerated, with mostly mild side effects. After 12 months, 26.6% of patients were still alive, which is promising for this group of heavily pre-treated patients with recurrent brain tumors. Following these results, a Phase 2 trial for PEP-CMV opened recently.

CTNI-49 Precision Medicine Clinical Trial for Adult Patients with Recurrent Glioblastoma

UCSF - Researchers used individualized treatment regimens for 30 recurrent GBM patients who underwent surgery and genomic profiling; they used combinations of up to 4 FDA-approved drugs, including one cytotoxic agent, based on molecular tumor board recommendations. The most common regimen was lomustine, afatinib, and abemaciclib (23% of patients). Results showed modest efficacy with a 9-month overall survival (OS-9) of 70% and 6-month progression-free survival (PFS-6) of 27%. Median OS was 11.6 months, and median PFS was 3.7 months. While these outcomes are not markedly better than historical data, the study shows the feasibility and safety of implementing personalized multi-drug approaches for rGBM.

CTIM-13. D2C7-IT In Combination With An FC-Engineered Anti-HumanCD40 Monoclonal Antibody (2141-V11) Administered Intratumorally Via Convection-Enhanced Delivery (CED) Followed By Cervical Perilymphatic Injections (CPLIS) of 2141-V11 In Patients With Recurrent Glioblastoma (RGBM)

Duke – A previous phase I trial established safety and recommended dosing for the combination of D2C7-IT, an antibody-toxin conjugate, and the anti-CD40 agent 2141-V11 administered via convection enhanced delivery (CED). This follow-up Phase I trial is now testing the safety and efficacy the CED treatment plus cervical perilymphatic injections (CPLIs) of 2141-V11. Eighteen patients with recurrent GBM were treated, and as of May 2024, 83% remained alive (survival ranging from 3.3 to 14.8 months post-treatment). Patients received a median of 8 CPLIs of 2141-V11. The treatment exhibited an acceptable safety profile, with no grade 4 or 5 adverse events reported; however, there were some grade 3 adverse events, including hydrocephalus and seizures.

CTIM-28. Neoadjuvant Anti-PD1 Immunotherapy for Surgically Accessible Recurrent Glioblastoma: Clinical and Molecular Outcomes of a Stage 2 Single-Arm Expansion Cohort

Multicenter - Researchers analyzed tumor tissue from 25 patients with recurrent glioblastoma who received neoadjuvant pembrolizumab (i.e., patients received the drug prior to surgical resection for

recurrence). The analysis showed a unique molecular signature associated with the treatment, characterized by decreased cell cycle-related gene expression, along with increased expression of T-cell and interferon-related genes. Nevertheless, the study found no significant improvement in overall or progression-free survival compared to historical controls, with median values of 6.8 months and 2.5 months, respectively. These results indicate there is a pharmacodynamic effect of anti-PD1 therapy, but it's not enough on its own to translate to a survival benefit.

HIGH GRADE GLIOMA / GLIOBLASTOMA – GENERAL

CTIM-36. In-Situ Vaccination of Biopsy-Only GBM Tumors by Tumor Treating Fields Plus Anti-PD-1 Immunotherapy Results in Robust Antigen-Specific T Cell Selection and Expansion, High Response Rate, and Significantly Extended Survival

University of Florida – Initial results from the 2-the-Top study combining Tumor Treating Fields (TTFields) and pembrolizumab in newly diagnosed GBM were shared at the 2023 SNO conference, but more in-depth analysis has revealed that patients with bulky, biopsy-only tumors achieved a more robust in-situ vaccination effect, enhanced anti-tumor immunity, and longer survival compared with those with maximally reduced tumors. The biopsy-only tumors had significantly improved progression-free survival (27.2 vs 9.6 months), overall survival (31.6 vs 18.8 months), and response rates (66.6% vs 25%) compared to those with maximally resected tumors. Molecular testing showed that TTFields activated a type 1 interferon immune response, leading to T cell activation and expansion. Investigators also observed potential mechanisms of resistance in recurrent tumors, including suppression of the PD-1/PD-L1 axis and upregulation of alternative immune checkpoints.

PATH-30 Clinical outcomes and predictive biomarkers for IDH-wildtype glioblastomas developing hypermutation following temozolomide treatment

UCSF - Researchers comprehensively evaluated paired initial and recurrent GBM tumors from 106 patients in order to understand the occurrence and implications of temozolomide-induced hypermutation (TMZ-HM). Seven patients (7%) developed hypermutation at first recurrence, while an additional five patients (5%) developed hypermutation at a subsequent recurrence. Interestingly, in contrast to IDH-mutant gliomas where TMZ-HM is associated with poor prognosis, patients with IDH-wildtype GBM who developed TMZ-HM had significantly longer overall survival from both initial surgery (67.9 vs. 20.3 months) and from time of recurrence after development of hypermutation (30.9 vs. 9.5 months). Specific hypermethylation patterns in the MGMT and KCNQ1DN genes were identified as potential biomarkers for predicting which patients might benefit from extended temozolomide.

CTIM-12. A Retrospective Analysis on the Safety, Efficacy and Immunogenicity of 203 Glioblastoma Patients Treated With Personalized Therapeutic Cancer Vaccines (PTCV)

Cegat (Germany) – This was a retrospective analysis of 203 GBM patients treated with personalized vaccines derived from individual tumor mutations. The vaccines were generally well-tolerated, with mostly Grade 1 and 2 adverse events. Injection site reactions were common (67%), and seven patients developed Grade 3 allergic or anaphylactic reactions after multiple vaccinations. Importantly, 97% of patients developed vaccine-induced T-cell responses, with 71% showing both CD4+ and CD8+ T-cell responses. Median overall survival (OS) for the entire cohort was 26 months. Primary GBM patients without recurrence before vaccination had a median OS of 41 months (MGMT hypermethylated) or 23 months (MGMT non-hypermethylated). These results align with and expand upon the recently published paper by the Cegat team.

BIOS-05 Peptide-based Vaccines Versus Dendritic Cell-Based Vaccine Therapies for Patients with Glioblastoma: A Network Meta-Analysis of Controlled Clinical Trials

Literature meta-analysis - Researchers used clinical literature to compare the efficacy of dendritic cell vaccines (DCV) versus peptide vaccines in extending overall survival (OS) for GBM patients. The analysis included 5 studies with 451 patients receiving investigational vaccines and 445 control patients (control = standard of care [SOC] or Placebo + SOC). They found that adding DCV to standard treatment significantly improved survival rates compared to standard treatment alone. Peptide vaccines also showed some benefit, but not as much as DCV. The results suggest that DCV may be more effective than peptide vaccines in helping glioblastoma patients live longer. However, the researchers note that more studies are needed to confirm these findings.

DDEL-08. Megadose Boswellia Serrata Causes Significant Decrease In Cerebral Edema With Minimal Toxicity In Brain Tumor Patients

Case reports - Boswellia serrata has been shown to reduce cerebral edema following radiation in brain tumors by Kirste et al in a prospective, randomized, placebo-controlled trial. The Kirste et al study used a dose of 4,200mg/day, and it was well tolerated. In this case report, 2 patients inadvertently took doses 10x that which was used in the Kirste study. Both patients obtained significant reduction in cerebral edema and enhancing disease on MRI. The dose of 42,000mg/day was tolerated well, with only mild dysphonia in one patient. The optimal dosing of Boswellia serrata for brain tumor patients should be studied further.

CTNI-41. Long-Term Survival and Patterns of Progression in Patients With Newly Diagnosed Glioblastoma Treated With Or Without Tumor Treating Fields (TTFields) In A Real-World Setting

Wisconsin - This real-world study of 210 GBM patients confirms the survival benefit of TTFields observed in previous trials. Patients who received TTFields in addition to standard therapy (n=110) showed significantly improved overall survival compared to those who did not (n=100), with median overall survival (OS) of 21.6 vs 17.7 months. Median progression-free survival was also longer in the TTFields group (12.1 vs 9.6 months). Notably, 5-year OS rates were 17% for TTFields users vs 11% for non-users. The study also found a higher rate of non-local progression in TTFields-treated patients (28% vs 15%), consistent with previous trial findings.

DNAR-03. Oncomagnetic Treatment Kills Glioma Cells By Inhibiting Mitochondrial Electron Transport And By Inducing Oxidative Stress And DNA Damage

Texas - The Oncomagnet is an investigational device that uses spinning oscillating magnetic fields (sOMF) to target cancer cells. Compassionate use of the device in 7 end-stage GBM patients showed promising initial results, reducing tumor volumes by >30% within 4-8 weeks. In mouse models, the device also decreased tumor size and increased survival. The device's mechanism involves inhibiting mitochondrial ETC complex-I, increasing reactive oxygen species, and causing DNA damage in GBM cells while sparing normal cells. In vitro studies demonstrated cell cycle arrest and reduced colony formation in GBM cells.

BIOM-24 Glioblastoma DNA alterations and rapid early progression after surgery

University of Miami - Rapid early progression (REP) in glioblastoma is where tumors quickly regrow after surgery but before radiation therapy begins. Researchers examined genetic changes in tumors from 100 patients to understand what might contribute to REP. The key finding was that alterations in the EGFR gene are strongly linked to rapid regrowth. This discovery is important because it suggests that patients whose tumors show EGFR changes might benefit from starting adjuvant therapies sooner after surgery.

DIPG / DMG

CTIM-02. PIONEERING QUAD-TARGETING CAR T CELL THERAPY IN PEDIATRIC CNS TUMORS – ANALYSIS FROM THE INITIAL PATIENTS TREATED ON THE FIRST-IN-HUMAN PHASE 1 TRIAL BRAINCHILD-04

Seattle Children's - This trial is investigating a new CAR T cell therapy that targets four different proteins simultaneously—B7-H3, EGFR, HER2, and IL-13Ralpha2—aiming to address tumor heterogeneity. Preliminary results show that 15 patients have been enrolled (6 with DMG, 5 with DIPG, and 4 with other CNS tumors), with 7 patients infused and 8 awaiting infusion. A total of 33 intracranial CAR T doses have been delivered, and the most common adverse events reported include grade 1-2 fever, grade 1-3 headache, and grade 1-2 nausea/vomiting. Importantly, there have been no dose-limiting toxicities, cytokine release syndrome, or immune effector cell-associated neurotoxicity observed. All treated patients are alive, with a median follow-up of 93 days (range: 14-198 days) post-infusion, and CAR T cells were detected in 14 out of 24 CSF samples analyzed after infusion. The trial is ongoing to further assess the anti-tumor activity of this therapy.

NCOG-07 Safety of ONC201 treatment in patients with previously treated H3 K27M-mutant glioma: results from ONC028, an ongoing compassionate use program

Multicenter EAP - The ONC028 compassionate use program provides ONC201 (dordaviprone), an investigational targeted therapy, to patients with previously treated H3 K27M-mutant gliomas. In this program, 422 patients have enrolled, including 191 adults and 231 children. Any causality grade ≥3 adverse events were reported in 47.4% patients (n=200), but only 4.5% patients (n=19) had treatment-related grade ≥3 adverse events. The investigators conclude ONC201 is well-tolerated and offers a potential treatment option for patients who are ineligible for ongoing clinical trials.

CTNI-74. Sonodynamic Therapy (SDT) Using Intravenous 5-AMINOLEVULINIC ACID With Non-Ablative Focused Ultrasound For The Treatment of Diffuse Intrinsic Pontine Gliomas In Pediatrics: Initial Safety And Outcomes The Multicenter SDT-201 Trial

Multicenter - This study (NCT05123534) has been suspended due to lack of funding, but the initial outcomes are promising. Twelve patients with DIPG (age range 3-23) were treated from August 2022-April 2024. There were 2 partial responses, and 9 patients had stable or improved baseline symptoms (Lansky Status), including improved mobility and double vision. There were no dose-limiting toxicities. Ten patients are alive a median of 11 months after diagnosis; 2 have deceased; 4 have discontinued treatment.

CTIM-17. Individualized Multimodal Immunotherapy (IMI) for Adults With Diffuse Midline Glioma or Diffuse Hemispheric Glioma

IOZK - This retrospective study examined four adult DMG patients treated with Integrative Multimodal Immunotherapy (IMI). Of the four, three demonstrated extended survival beyond typical DMG prognosis, with one patient still stable at 30 months. Treatment approaches varied but included radiochemotherapy, immunotherapies like IO-Vac® dendritic cell vaccines, maintenance immunotherapy (e.g. oncolytic viral injections, modulated electrohyperthermia), and checkpoint inhibitors. While the sample size is extremely small, this analysis suggests IMI might contribute to improved survival and warrants further investigation in DMG patients.

LOW GRADE GLIOMA

CTNI-47 A phase 1, randomized, perioperative trial of vorasidenib and ivosidenib in IDH1-mutant diffuse glioma: updated results

Multicenter - Vorasidenib (VOR) and ivosidenib (IVO) were compared in a study of grade 2/3 non-enhancing mIDH1 mutant gliomas. Patients received treatment for 4 weeks pre-surgery, with the option to continue post-surgery. By September 2023, 46% of VOR and 20% of IVO patients remained on treatment. Median post-operative treatment duration was 44.7 months for VOR and 23.9 months for IVO. VOR showed a median PFS of 41.4 months and 46% objective response rate, while IVO had 38.6 months PFS and 27% response rate. These results demonstrate prolonged response in non-enhancing gliomas and align with the Phase 3 INDIGO study, where VOR showed PFS benefit with manageable safety compared to placebo. (See also here for updated efficacy results from an additional 6 months of follow-up in the INDIGO trial.)

HIGH GRADE MENINGIOMA

DDDR-49. Repurposing of the Anti-Viral Drug Ribavirin as a Potential Meningioma Therapeutic

UCLA - The antiviral drug ribavirin significantly inhibited growth and proliferation of meningioma cells in laboratory settings. In mouse models, ribavirin treatment improved median survival from 41 days in control groups to 67 days in treated mice. These findings suggest that ribavirin may be a therapeutic adjuvant option for meningioma treatment, and it should be further investigated for its mechanisms and potential clinical applications.

BIOMARKERS / IMPORTANCE OF MOLECULAR TESTING

BIOM-01. CDKN2A Homozygous Deletion Has Stronger Prognostic Power Than IDH Mutation in CNS WHO Grade 4 Gliomas

Korea - Researchers at one center retrospectively reviewed medical records and pathology slides of 142 GBM patients treated over a 15-year period, and they updated diagnoses according to the newer 2021 World Health Organization classifications. The study found that 23.9% of previously diagnosed GBMs were reclassified as IDH-mutant astrocytomas, while 76.1% remained IDH-wildtype GBMs. Among the reclassified patients, 56% had CDKN2A deletions, which were shown to significantly impact overall survival (OS). Specifically, the mean OS varied by group: 15.70 months for IDH-wildtype with CDKN2A deletion, 19.37 months for IDH-mutant with CDKN2A deletion, 22.63 months for IDH-wildtype without CDKN2A deletion, and 33.38 months for IDH-mutant without CDKN2A deletion. Multivariate analysis indicated that both IDH mutation status and CDKN2A deletion are critical prognostic factors, suggesting that CDKN2A deletion has a strong negative impact on outcomes in CNS WHO grade 4 gliomas, even among those with IDH mutations.

BIOM-05. Fusion Transcriptome Landscape In Glioblastoma

CARIS Life Sciences - Most targeted therapies used to date in brain cancer focus on DNA gene mutations. However, RNA fusion transcripts may also provide viable therapeutic targets. A genomic testing company used their large database to determine the prevalence of fusion transcripts in GBMs. A total of 4,392 GBMs were tested with NextGen sequencing (NGS), and pathogenic fusions were found in 428 (9.7%). The most prevalent were FGFR3:TACC3 (n=134), PTPRZ1:Met (n=31; ST7:MET N), EGFR:SETP14 (N=21), NTRK2 (N=27), PDGFRA (N=23), ROS1 (N=14) and BRAF (N=10). The broad spectrum of observed fusions

underscores the need for new clinical trial designs that can efficiently match and enroll appropriate patients for potential targeted agents.