BACKGROUND: The benefit of adding chemotherapy to radiotherapy (RT) in newly diagnosed anaplastic glioma without 1p/19q co-deletion is unknown. The CATNON trial investigated the impact of adjuvant and/or concurrent chemoradiotherapy with temozolomide (TMZ) in these tumors. METHODS: Eligible were patients with newly diagnosed WHO grade III glioma without 1p/19q co-deletion, ≥ 18 years, and WHO performance status (PS) 0–2. All patients received RT 54 Gy and TMZ 150 mg/m² + 5-FU in a 2 x 2 factorial design (NCT01156584). Primary end-point was overall survival (OS). RESULTS: Between Dec 2007 and Aug 2015 748 patients were randomized. On Oct 6, 2015 the interim analysis was conducted based on 221 events (median follow-up: 27 months). The analysis showed a HR reduction for OS of 0.645 (95% CI 0.450, 0.926; p = 0.0014) after adjuvant TMZ (arms iii and iv), TMZ status could be determined in 74% of patients, and was found methylated in 42% of them. TMZ methylation was prognostic for OS (HR 0.54, 95% CI 0.38, 0.77; p = 0.001). TMZ did not predict overall outcome with or without TMZ. For progression free survival (PFS), the risk adjusted HR of adjuvant TMZ was 0.586 (95% CI 0.472, 0.727; p = 0.0001).

ACTR-05. PHASE II STUDY OF TEMOZOLOMIDE PLUS ABT-414 METHOTREXATE AS PRECURSOR DRUG CONJUGATE IN MALIGNANT GLIOMA: KYOTO NEURO-ONCOLOGY GROUP (KNONG) Tomokazu Aoki1, Yoshihiko Arakawa2, Tetsuya Ueba3, Masashi Oda4, Nishida5, Yukinori Akiyama1, Tetsuya Tsukahara4, Koichi Iwaki5, Nobuhiko Mikuni5 and Susumu Miyamoto5, 1Kyoto Medical Center, Kyoto, Japan; 2Kyoto University, Kyoto, Japan; 3Department of Neurosurgery, Kyoto University, Kyoto, Japan; 4Department of Neurology, Kyoto University Hospital, Kyoto, Japan; 5Kyoto Medical College, Kyoto, Japan, 6Himeji Medical Center, Himeji, Japan; 7Kitano Hospital, Osaka, Japan; 8Sapporo Medical College, Sapporo, Japan

OBJECTIVE: The aim of this phase II study was to examine the efficacy and toxicity profile of TMZ plus nimustine (ACNU), which is one of nitrosoureas for malignant glioma. METHODS: Patients who had received a standard radiotherapy with one or two previous chemo-regimens were enrolled in this phase II study. The maximum-tolerated dose (MTD) by TMZ (150 mg/m²/day) (Day1-5) plus various doses of ACNU (30, 40, 44.5 mg/m²/day) (Day15) per week was defined on a standard 3+3 design. In phase II including the cohort 3 (MTD) of phase I, these therapeutic activity and safety of this regimen were evaluated. RESULTS: Forty-nine patients were enrolled. Their median age was 50 years-old. Eighty percent of patients (39/49 cases) had a KPS of 70–100. These histologies were 73% (36 cases) glioblastoma, 22% (11 cases) anaplastic astrocytoma, 4% (2 cases) anaplastic oligodendroglioma. In phase I, 15 patients were treated at four cohorts by TMZ plus ACNU. MTD was TMZ (150 mg/m²) plus ACNU (40 mg/m²). In phase II, 40 patients were treated at the dose of cohort 3 (MTD). Thirty-five percent of patients (14 of 40) experienced grade 3 or 4 toxicity, mainly hematologic toxicity. The overall response rate (ORR) was 11% (4/37). Eighty-six percent (25/29) showed progression. Progression free survival (PFS) at 6 and 12 month were 24% (95%CI, 12–35%) and 8% (95%CI, 4–15%). Median PFS was 13 months (95%CI, 9.2–17.2months). Overall survival (OS) and Median OS were 11.8 months (95%CI, 6.8–24months) and 8% (95%CI, 3–15%). CONCLUSION: This phase II study showed a moderate toxicity in hematology and may have a promising efficacy in OS, without inferiority in PFS, comparing with other regimens.

ACTR-07. EFFICACY OF A NOVEL ANTIBODY-DRUG CONJUATE (ADC) ABT-414, AS MONOTHERAPY IN EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) AMPLIFIED (EGFRa) RECURRENT Glioblastoma (rGBM) Martin van den Bent1, Hai Gan2, Andrew Lassman3, Priya Kumthekar4, Ryan Merrell5, Nicholas Butowsk6, Zarmie Lwani5, Tom Mikkelsen5, Louis Nabors5, Kyriakos Paspalopoulos5, Marta Penal-Prado6, John Simes5, Tobias Wall bert7, Andrew Scott8, Erica Gomez9, Ho-Jin Lee10, Lisa Roberte Rapp9, Hao Xiong11, Earle Bain12, Kyle Hollien12, David Maag12 and David Readson13, 1Erasmus MC Cancer Institute, Rotterdam, Netherlands; 2Olivia Newton-John Cancer Research Institute, Melbourne, Australia, 3Columbia University Medical Center, New York, NY, USA, 4Northwestern University Feinberg School of Medicine, Chicago, IL, USA, 5Northshore University Health System, Evanston, IL, USA, 6Department of Neurological Surgery, University of California, San Francisco, San Francisco, CA, USA, 7Royal Brisbane & Women’s Hospital, Queensland, Australia, 8Department of Neurology and Neurosurgery, Henry Ford Hospital, Detroit, MI, USA, 9University of Alabama at Birmingham, Birmingham, AL, USA, 10South Texas Accelerated Research Therapeutics (START), San Antonio, TX, USA, 11University of Texas Southwestern Medical, Dallas, TX, USA, 12NHMRC Clinical Trials Centre, Sydney, Australia, 13Henry Ford Health System, Detroit, MI, USA, 14Austin Health and Olivia Newton-John Cancer Research Institute, Melbourne, Australia, 15ABBvie, North Chicago, IL, USA, 16Department of Neurooncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

BACKGROUND: Patients (pts) with rGBM have a poor prognosis. EGFRa is present in ~30% of GBMs. ABT-414 is an ADC that releases a potent toxin, monomethyl auristatin F (MMAF), inside cells with EGFRa. Here we report the safety and efficacy of ABT-414 monotherapy in newly diagnosed GBM. METHODS: ABT-414 (16 mg/m²) was given intra-arterially every 3 weeks for >= 5 cycles or until progression. One 1.5 mg/m² dose was given intra-arterially on Day 1 and 5 of each cycle. A total of 16 cycles were given. A planned interim analysis was foreseen after 219 events (41%). In the event of tumor progression, patients were referred to i. RT alone; ii. RT with concurrent daily 75 mg/m² TMZ; iii. RT with concurrent and 12 cycles of adjuvant TMZ. RESULTS: Between Dec 2007 and Aug 2015 748 patients were randomized. On Oct 6, 2015 the interim analysis was conducted based on 221 events (median follow-up: 27 months). The analysis showed a HR reduction for OS of 0.645 (95% CI 0.450, 0.926; p = 0.0014) after adjuvant TMZ (arms iii and iv), TMZ status could be determined in 74% of patients, and was found methylated in 42% of them. TMZ methylation was prognostic for OS (HR 0.54, 95% CI 0.38, 0.77; p = 0.001). TMZ did not predict overall outcome with or without TMZ. For progression free survival (PFS), the risk adjusted HR of adjuvant TMZ was 0.586 (95% CI 0.472, 0.727; p = 0.0001).

ACTR-06. THE TOCA 7 STUDY: PHASE 1B STUDY OF TOCA 511, A LIVE GAMMA RETROVIRUS, AND TOCA FC, AN EXTENDED-RELEASE FORMULATION OF 5-FUROCYTOXINE COMBINED WITH STANDARD OF CARE IN NEWLY DIAGNOSED HIGH GRADE GLIOMA (NCT02598011) Michael Vogelbaum1, Adam Lassman2, Ian Lee3, Linda Lau4, Adam Sonabend5, Tobias Walbert5, Luqang Yang6, Asha Das7 and Timothy Butowski8, 1Cleveland Clinic Foundation, Cleveland Clinic Neuro-Oncology Center, Cleveland, OH, USA, 2Columbia University Medical Center, New York, NY, USA, 3Henry Ford Health System, Detroit, MI, USA, 4UCAL Neurosurgery, Los Angeles, CA, USA, 5Tocagen Inc., San Diego, CA, USA, 6University of California, Los Angeles, Los Angeles, CA, USA

Toca 511 (vogonavirus amiretrovirus), a live gamma retrovirus, encodes the transgene cytosine deaminase (CD). Toca 511 selectively infects, persists and spreads in actively proliferating cancer cells. Subsequent oral administration of the extended-release antifungal drug 5-fluorocytosine (Toca FC) results in production of 5-fluorouracil (5-FU), via the CD enzyme, within infected cells and myeloid derived suppressor cell (MDSC) subsets, which activates the immune system against cancer, leading to durable antitumor immune responses in animal models. This sequence of events is amplified with multiple cycles of 5-fluorocytosine. Clinical data from 2 ongoing phase 1 trials (NCT01156584, NCT01470794) in recurrent high grade glioma (HGG) are consistent with this mechanism of action, and show a favorable safety profile and extended survival compared to historical controls. Standard of care for newly diagnosed HGG includes maximum safe extent resection and chemoradiation with temozolomide (TMZ). A Phase Ib/II study, treating newly diagnosed HGG patients with Toca 511 and Toca FC added to standard of care (SOC), will examine safety and overall survival (OS) compared to historical controls. Based on the high unmet need for effective therapies and the additive preclinical efficacy demonstrated with Toca FC, establishing this as a multi-center, open-label study will enroll approximately 24 subjects with newly diagnosed HGG prior to tissue diagnosis or definitive initial surgical resection. Subjects will be treated with Toca 511 and dose escalation of Toca FC added to SOC. The primary objective is to establish the recommended Phase 2 dose of Toca FC and secondary objectives are to evaluate the safety, tolerability and preliminary efficacy as measured by OS and progression-free survival. Evidence for immunologic mechanisms of disease control and molecular profiling of regressed tumor will be evaluated to identify potential biomarkers for treatment-related response.