ACTR-01. THE ROLE OF CLINICAL CHARACTERISTICS IN LOW GRADE GLIOMAS PATIENTS IN THE ERA OF MOLECULAR BIOMARKERS: A STUDY FROM GRUPPO ITALIANO COOPERATIVO DI NEURO-ONCOLOGIA (GICNO)
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BACKGROUND: Outcome of low-grade gliomas (LGG) is highly variable and depends on clinical factors, molecular features, and treatments. Molecular characterization of LGG has improved in recent years and is now essential for diagnosis and treatment of these diseases. Clinical factors, such as age and the extent of surgery, were considered prognostic for decades, but now their role is less clear. METHODS: We retrospectively evaluated all adult LGG patients from our data warehouse who received surgery and had sufficient tissue to assess biomarkers characterization. IDH1/2 mutation, MGMT methylation and 1p/19 coding were detected by an Illumina platform and a custom array. RESULTS: 204 consecutive LGG were included. Median follow up was 78.6 months. The mean age was 40 (range: 18-72). 111 patients (54.4%) were <40 years of age; 27 patients (13.2%) underwent biopsy, 123 patients (60.3%) partial resection, 54 patients (26.5%) complete resection. Twenty-eight patients (13.7%) were considered low risk according to RTOG (<40 years with complete resection). IDH1/2 mutation was found in 82.8% of patients. 1p19q coding was found in 46.4% of patients, MGMT methylation in 65.2% of patients. Median survival was 211.0 months (95% CI:190.4-231.6) in low risk patients, and 145.3 months (95% CI: 135.1-155.6) in high risk patients (P<0.001). Median survival for patients with IDH1/2 mutation was 164.0 months (95%CI:112.1-215.9) and 77.1 months in patients IDH1/2 wild type (95%CI:115.4-138.9; P<0.001). Multivariate analysis showed that low risk according to RTOG (P=0.006), IDH1/2 mutation (P<0.001) and 1p19q coding (P=0.035) were significantly correlated with overall survival. MGMT methylation was not significant. CONCLUSIONS: The management of LGG is complex. Both molecular profiling and clinical risk assessment are necessary for the decision making process in these rare tumors.

ACTR-02. AN MULTIVARIATE ANALYSIS FOR PROGNOSTIC SURVIVAL OF 121 ELDERLY PATIENTS WITH NEWLY DIAGNOSED GLOBLASTOMA
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OBJECTIVE: To verify the role and impact of extent of resection on elderly patients with newly diagnosed GBM for survival. METHODS: The medical data like gender, age, symptom, symptom duration, preoperative Karnofsky performance status (KPS), preoperative Charlson comorbidity index21, preoperative Performance status of ECOG (PS), preoperative American Society of Anesthesiologists index (ASA), preoperative comorbid disease, tumor location, tumor size, extent of resection (EOR), adjuvant therapy, interval of adjuvant-treatment administration after operation and immunohistochemistry, duration for anesthesia and surgery, and volume of bleeding of 121 patients aged ≥65 years treated between 2007 January to 2015 June was systematically collected. RESULTS: The mean survival for 121 patients (2 excluded) was 15.30 months. Age (P<0.001), KPS (P<0.001), IDH mutation (P<0.001), extent of resection (P<0.001), Stupp schedule (P<0.001) was significantly different between groups. COX hazard models identified KPS (HR 1.977 [95% CI 1.118–3.312]; P>0.001), Extent of resection(HR 0.97 [95% CI 0.93–0.99]; P<0.0003) and Stupp schedule or not (HR 0.483 [95% CI 0.292–0.717]; P<0.001) were independent predictors of survival. CONCLUSION: We consider that the elderly patients with newly diagnosed GBM can also benefit from extending resection and Stupp schedule. Patients with bad performance status, low preoperative KPS couldn't achieve more OS benefit though extending resection, but still achieved increased OS compared to patients who under partial resection. Age is not a significant prognostic factor for survival in elderly patients.

ACTR-03. SAFETY AND FEASIBILITY OF RAPID RITUXIMAB INFUSIONS IN PATIENTS WITH PRIMARY CNS LYMPHOMA
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OBJECTIVES: To establish the safety and feasibility of rapidly infusing rituximab over 90 minutes in patients with primary CNS lymphoma. METHODS: We reviewed all patients with CNS lymphoma who received rapid rituximab infusions from January 2016 to June 2016. Pilot inclusion criteria include age ≥18 years, tolerated ≥1 previous rituximab infusions at standard rate without reaction, and did not receive concurrent chemotherapy infusion. Concomitant corticosteroids to control disease related neurologic symptoms were allowed. The primary endpoint was incidence of infusion reactions. RESULTS: Five out of nine patients screened for rapid rituximab infusion met criteria and a total of 21 infusions were administered. Patients had a median age of 61 years (range 45–63 years) and 4 were female. All patients received rituximab doses over 90 minutes for diagnosis of primary CNS lymphoma. Pre-medication consisted of acetaminophen and diphenhydramine. Prior to first rapid infusion, four patients received one standard infusion and one patient had received three. None of the five patients experienced a reaction during any rapid infusion. Two patients were on dexamethasone 2mg daily during their first rapid infusion. Steroids were not administered with any other infusion. CONCLUSION: Rapid administration of rituximab was safe and feasible for patients with primary CNS lymphoma.
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 chemotherapy 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 59.4 Gy in and in a 2 x 2 factorial design were randomized to receive TMZ or not in each study arm. Primary endpoints were overall survival (OS). 748 patients and 334 events were needed to detect a HR reduction of 0.775 for both concurrent and adjuvant TMZ. An interim analysis was foreseen after 219 events (41%), and required a p value of 0.0084 for rejecting the null hypothesis of no OS difference. 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, MGMT status could be determined in 74% of patients, and was found methylated in 42% of them. MGMT methylation was prognostic for OS (HR 0.38, 95% CI 0.18, 0.79; p = 0.0048), but did not predict disease progression or OS in adjuvant 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).

ACRT-05. PHASE II STUDY OF TEMOZOLOMIDE PLUS NIMUSTINE CHEMOTHERAPY FOR RECURRENT MALIGNANT GLIOMAS: KYOTO UNIVERSITY NEURO-ONCOLOGY GROUP

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OBJECTIVE: The aim of this phase II trial was to examine the efficacy and toxicity profile of TMZ plus nimustine (ACNU), which is one of nitrosoureas for malignant gliomas. METHODS: Patients who had received a standard radiotherapy with or two previous chemo-regimens were enrolled on the phase II study. In phase I, the maximum-tolerated dose (MTD) by TMZ (150mg/m2/day) (Day 1–5) plus various doses of ACNU (30, 35, 40, 45mg/m2/day) (Day 15) per 4 weeks 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 (%) (22 cases) anaplastic astrocytoma, 4% (2 cases) anaplastic oligodendroglioma. In phase II, 15 patients were treated at four cohorts by TMZ plus ACNU. MTD was TMZ (150/mg/m2) plus ACNU (40mg/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 toxicities, mainly hematologic. The overall response rate was 11% (4/37). Sixty-eight percent (25/37) had stable disease. Twenty-two percent (8/37) had progressive disease. The 12 month PFS and OS were 78% (95%CI, 67–89%) and 49% (95%CI, 33–57%). Median PFS and OS were 24% (95%CI, 12–35%) and 8% (95%CI, 4–15%). Median PFS and OS were not reached (95%CI, 0–12 months). The risk adjusted HR of adjuvant TMZ was 0.586 (95% CI 0.472, 0.727; p < 0.0001).

ACRT-07. EFFICACY OF A NOVEL ANTIBODY-DRUG CONJUGATE (ADC) ABT-414, AS MONOTHERAPY IN EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) AMPLIFIED (EGFRamp) RECURRENT GLIOBLASTOMA (rGBM)

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BACKGROUND: Patients (pts) with rGBM have a poor prognosis. EGFRFlap is present in ~30% of GBMs. ABT-414 is an ADC that releases a potent toxin, monomethyl auristatin F (MMAF), inside cells infected with a tumor. 5-FU kills cancer cells and myeloid derived suppressor cells (MDSCs). The combination of 5-FU and a monoclonal antibody to EGFR, ABT-414, is being developed as a novel anticancer agent for EGFRamp GBMs. METHODS: M12-356 (NCT01800695) is an open-label, Phase 1 study of ABT-414, alone or with TMZ, vs. TMZ or lomustine, is underway in patients with rGBM. RESULTS: As of March 1, 2016, 60 pts with EGFRamp, rGBM underwent treatment. Median age was 58 years (range, 35–80). Pts received pt 1 (43% each) or pt 3 (13%) prior therapies. The most common treatment emergent adverse events (TEAEs) (220% pts) included blurred vision (56%), headache, fatigue (30% each), eye pain and photophobia (28% each). Grade 3/4 TEAEs (13% each) were keratitis (13% each), dry eye, ulcerative keratitis and reduced visual acuity (3% each). The best RANO responses of 56 pts with complete data were: 3 (5%) partial responses, 24 (43%) stable diseases and 29 (52%) progressive diseases. The median duration of study and RPTD was 3 months. The median duration of effusions in the first 36 pts was 4.4 months (range, 1–5.6). The 6-month progression-free survival (PFS) estimate was 25.3% [95% CI 14.8, 37.2]. CONCLUSIONS: ABT-414 monotherapy displayed frequent but mostly grade 1/2 ocular events. An encouraging RPTD benefit (25%) was observed in the overall population where 56% had ≥2 prior therapies. A global randomized trial of ABT-414, alone or with TMZ, vs. TMZ or lomustine, is underway in EGFRFlap, rGBM (NCT02343406).