**8704** ORAL

**Adjuvant whole brain radiotherapy versus observation after radiosurgery or surgical resection of 1−3 cerebral metastases - results of the EORTC 22952−26001 study**

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**Background:** The role of prophylactic whole brain radiotherapy (WBRT) after either surgery (S) or radiosurgery (RS) of brain metastases is still debated. The EORTC conducted a phase III trial to define the role of adjuvant WBRT after local treatment (S or RS) of a limited number of brain metastases in solid tumors with stable systemic disease. It was hypothetized that WBRT would increase the duration of functional independence by reducing the number of intracranial relapses.
**Material and Methods:** Pts eligible for RS had 1−3 metastases of solid tumors (SCLC excluded) $\leqslant$3.5 cm in diameter ($\leqslant$2.5 cm for 2−3 lesions) located outside the brain stem. For S, a complete resection of the metastatic lesions was mandatory. Only pts with absent or stable systemic disease or with asymptomatic primary tumors and in good condition (WHO PS 0−2) were allowed. Pts were randomized to receive either WBRT or observation (OBS). Primary endpoint was survival with functional independence measured by the survival time with WHO PS $\leqslant$ 2. Secondary endpoints were time to intracranial progression, neurologic deaths and overall survival. Analysis is by intent-to-treat (Logrank, two-sided $\alpha = 0.05$).
**Results:** From 1996 - 2007, 359 pts were recruited, 353 were eligible. Median survival time with WHO PS $\leqslant$ 2 was 10.0 months (95% CI 8.1−11.7) in the OBS arm and 9.5 months (95% CI 7.8−11.9) in the WBRT arm ($p>0.5$). It was only significantly influenced by initial WHO PS and initial systemic disease status ($p < 0.01$). Overall survival was 10.9 months in the OBS and 10.7 months in the WBRT arm ($p>0.5$). Cumulative incidence of intracranial progression at 6 and 24 months was 39.7% (95% CI 32.5−46.8) and 54.2% (95% CI 46.9−61.5) of the OBS pts, but only 15.2% (95% CI 9.9−20.4) and 31.2% (95% CI 24.4−38.0) of the WBRT pts. Both relapses at sites treated initially with S or RS (incidence at 24 months 31.3% vs 16.4%) and at new intracranial sites (32.4 vs 17.6%) were significantly reduced ($p < 0.0001$). Intracranial progression was a cause of the death in 77/179 pts (43%) of the OBS group and in 45/180 pts (25%) of the WBRT group. Median progression-free survival was 3.4 months (95% CI: 3.1−3.9) in the OBS arm and 4.6 months (95% CI: 3.9−6.1) in the WBRT arm ($p < 0.002$).
**Conclusions:** After radiosurgery or surgery of a limited number of brain metastases, adjuvant whole brain radiotherapy does not prolong the time period of functional independence and overall survival time. Adjuvant whole brain radiotherapy significantly reduces the risk of neurologic death and prolongs progression-free survival.

**8705** ORAL

**Change in MGMT methylation status between first surgery for newly diagnosed glioblastoma and second surgery for recurrence: clinical implications**

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**Background:** *MGMT* promoter methylation status is a prognostic factor in newly diagnosed glioblastoma patients. However, it is not yet clear whether, and if so how, *MGMT* methylation status may change; nor is it known whether the prognostic role of this epigenetic feature is retained during the disease course.
**Methods:** A retrospective analysis was made using a database of 614 glioblastoma patients treated prospectively from 01/2000 to 08/2008. We evaluated only patients who met the following inclusion criteria: age $\geqslant$18; PS 0−2; histological diagnosis of glioblastoma at both first and second surgery for recurrence; postoperative treatment consisting of: a) radiotherapy (RT) followed by adjuvant temozolomide (TMZ) until 2005, and b) TMZ concurrent with and adjuvant to RT after 2005; a time interval $\geqslant$3 months between first and second surgery.
**Results:** *MGMT* status was evaluated at first and second surgery in all 44 patients (M:F 32:12, median age: 49 years, range: 27−67 years). In 38 patients (86.4%) *MGMT* promoter status was assessable at both first and second surgery. *MGMT* methylation status, changed in 37% of second surgery samples and more frequently in methylated than in unmethylated pts (61.5% vs 24%, $p = 0.03$). The median survival was significantly influenced only by *MGMT* methylation status determined at first surgery ($p = 0.04$).
**Conclusion:** Significant changes in *MGMT* methylation status during the course of GBM occur more frequently in *MGMT* methylated than unmethylated cases. *MGMT* methylation status determined at first surgery appears to be of prognostic value, however it is not predictive of outcome following second surgery.

**8706** ORAL

**Aggressive management of adult high risk patients with medulloblastoma (MB): 12 years experience at the Instituto Nacional de Enfermedades Neoplásicas, Lima, Peru**

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**Background:** To describe the clinical outcome of adult high risk patients with MB aggressively treated with sequential postoperative external beam radiation therapy (EBRT) and chemotherapy (CHT).
**Materials and Methods:** We retrospectively collected data from all consecutive adult ($\geqslant$16y) patients treated at our institution for MB from January 1993 to December 2004. High risk patients (according to Chang's Classification) had incomplete surgical resection ($\geqslant$1.5 $cm^2$ residual) and/or metastases outside the posterior fossa. EBRT delivered 36 Gy at the craniospinal axial level and a boost to 55 Gy in the posterior fossa. CHT consisted mostly of the association of an alkylating agent and a vinca alkaloid for 6 cycles. Survival was calculated from the time of surgery.
**Results:** Data were retrieved from 78 patients. Median age was 23y (16−51 range). Male/female ratio was 1.2 (43/35). Sixty-four (82%) patients had PS $\leqslant$2. Thirty-three (42%) histologies were desmoplastic. Thirty-seven (47%) patients were classified as high risk: 9 were aggressively treated with both EBRT and CHT, 17 with EBRT alone and 11 received no adjuvant treatment. The groups were homogeneous for clinical pathological characteristics. The association of EBRT followed by CHT yielded a median survival time and a 5y survival rate of 76.9 months (mo) and 75%, respectively. The outcome figures of these patients were significantly better than those of high risk patients not receiving both postoperative treatments (21.2 mo and 6%, RR = 0.19, $p = 0.008$), and comparable to those of patients with standard risk (95.3 mo and 77%, RR = 1.11, $p = 0.867$). Treatment toxicity was mostly mild to moderate and no toxic death was reported.
**Conclusions:** In our experience, despite the poor prognosis, adult high risk patients with medulloblastoma can display survival outcome comparable to standard risk patients, when treated aggressively. Thus, our findings suggest that, sequential EBRT and CHT are safe and should be proposed, whenever possible, to high risk medulloblastoma patients.

**8707** ORAL

**Clinical assessment of corticosteroid use and neurocognitive function in patients with glioblastoma at first or second relapse treated with bevacizumab in the BRAIN study**

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**Background:** Patients (pts) with glioblastoma (GBM) can suffer from symptomatic peritumoral edema requiring corticosteroids (CS) and experience neurocognitive decline. We assessed CS use and neurocognitive function (NCF) of pts with recurrent GBM who participated in the BRAIN study (ClinicalTrials.gov NCT00345163).
**Material and Methods:** BRAIN, a Phase II, open label, multicenter, randomized, noncomparative trial, evaluated efficacy and safety of