Oral Presentations (Sun, 25 Sep, 09:00−10:55)
Central Nervous System

8700 ORAL

Hearing Preservation After Low Dose Radiosurgery for Acoustic Neuroma Depends Upon Initial Hearing and Time

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Background: To assess long term outcomes and factors determining hearing preservation after low dose linac radiosurgery (RS) for acoustic neuroma (AN) at the Royal Adelaide Hospital.
Material and Methods: Data were collected prospectively in a dedicated RS clinic. Between 1994 and 2010, 102 patients had RS for AN. Their median age was 60 (range 19−83), 54% were male and the median tumour size was 22 mm (range 11−40 mm). Five patients had neurofibromatosis type 2, six sporadic cases had relapsed after surgery, and the remaining 91 sporadic cases had primary RS. Treatment was planned on a Fisher-Leibinger system until Feb 2009, thereafter on a BrainLAB System. A dose of 12 or 14 Gy was prescribed to the 70−90% isodose envelope encompassing the gross tumour volume. Sustained changes $\geqslant$ 2 mm in any diameter were deemed significant, and useful hearing was defined as inter-aural pure tone average (PTA) $\leqslant$ 50 dB. Possible prognostic factors for hearing retention were tested by dividing the patients at reasonable cutpoints specified before examining the hearing data viz: age (60 years), maximum tumour diameter (20 mm), initial PTA (20 dB), dose (12 vs 14 Gy).
Results: Eighty-four of the 91 sporadic primary RS cases were evaluable for tumour control (at least one post-treatment MRI). Their median follow-up was 65 mo (range 10–184 mo). Eighty-two of the 84 tumours (97.6%) remained stable (30) or decreased (52), the remaining two requiring salvage surgery for progression at 5.8 and 9.8 years. Also, one of the post-operative cases required surgery at 2.1 years after RS. Fifty of the 91 primary RS patients had initially useful hearing. Their median age was 56 (range 21−76), median initial PTA 16 dB (range −11 to +45 dB) and median tumour diameter 21 mm (range 10−33 mm). Four received 14 Gy, the rest 12 Gy. After RS, 31 patients lost useful hearing (crude preservation rate 19/50 = 38%). The Kaplan–Meier estimated preservation rate at 5 years was 50% (95% CI 36−64%) but by 10 years, this had fallen to 23% (95% CI 12−41%). On univariate analysis, the only significant factor of the four variables tested was initial PTA ($P < 0.0001$). The estimated risk of hearing loss after RS for patients with initial PTA $\geqslant$ 20 dB was 5.0 (95% CI 2.2–11.2) times that with PTA <20 dB.
Conclusions: Tumour control was excellent (99/102 = 97% freedom from surgical salvage). Hearing preservation was strongly dependent on initial PTA, but there was a steady fall-off in hearing out to about 10 years.

8701 ORAL

TEMOFRAC − a Phase II Trial − Concurrent 3-times Daily Ultrafractionated Radiation Therapy and Temozolomide for Newly Inoperable Glioblastoma

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Background: Ultrafractionation radiation therapy consists in irradiating cells or tumours several times daily, delivering low doses at which hyperradiosensitivity occur. We recently reported the efficiency of ultrafractionation radiotherapy regimen in newly inoperable glioblastoma. We are now conducting a phase II clinical trial to determine the effect of a concurrent ultrafractionation regimen and temozolomide for inoperable glioblastoma patients.
Methods: A prospective, multicenter, phase II study has opened for accrual in February 2008. Patients over 18 years of age who are able to give informed consent and have histologically proven, newly inoperable diagnosed and supratentorial glioblastoma are eligible. Three doses of 0.75 Gy spaced by at least four hours are delivered daily, five days a week for six consecutive weeks for a total of 67.5 Gy, and concomitant chemotherapy consisted of temozolomide given at dose of 75 mg/m^2, 7 days per week during the ultrafractionated radiotherapy. After a 4-week break, chemotherapy is resumed up to 6 cycles of adjuvant temozolomide every 28 days, according to the standard 5-day regimen. Tolerance and toxicity is the primary endpoints; survival and progression- free survival are secondary endpoints.
Results: To date 36 patients have been enrolled in this study, 24 men and 12 women, median age 62, median Karnofsky performance status was 80. The concomitant ultrafractionated radiotherapy − temozolomide was been well tolerated; no acute grade 3 and/or 4 CNS toxicity has been observed. Complete response were reported in 3 patients, and stabilisation or minor responses in 8 patients. Two patients progressed during the radiation therapy, and two patients died of pulmonary embolism. Median survival from initial diagnosis was not yet reached. Half of the patients have survived for more than one year.
Conclusions: TEMOFRAC regimen is safe and well tolerated. It may prolong the survival of patients with glioblastoma. Updated definitive results will be presented at the meeting.

8702 ORAL

A Phase II, Multicenter, Clinical Trial to Evaluate the Efficacy and Safety of Bevacizumab Alone in Japanese Patients With Recurrent Malignant Glioma

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Background: Glioblastoma (GBM) is the most aggressive malignant primary brain tumour. There are no standard therapies established for recurrent malignant glioma, and survival is poor. Bevacizumab (Bev) is a humanized monoclonal antibody that inhibits vascular endothelial growth factor (VEGF). In phase II trial of patients with recurrent GBM (rGBM) in the United States, Bev alone or in combination with irinotecan has shown efficacy as measured by objective response rate and 6-month progression free survival (PFS6). This open-label, multicenter, phase II trial evaluated the efficacy and safety of Bev alone for Japanese patients with recurrent malignant glioma.
Material and Methods: Thirty-two patients (include at least 28 rGBM patients) were planned to be assigned to receive Bev alone (10 mg/kg, q2wks) continued to disease progression. The primary endpoint was PFS6 for rGBM patients as determined by an independent radiology facility (IRF), with secondary endpoints of PFS, objective response rate determined by the IRF (ORR), overall survival (OS), and safety for all patients. The threshold value of PFS6 was set at 15% and an anticipated value of PFS6 was set at 35% (80% power and one-sided significance level of 0.05).
Results: From August 2009 to July 2010, 31 patients were enrolled: 29 with rGBM and 2 with WHO Grade III glioma, 17 with 1st relapse and 12 with 2nd relapse. For patients with rGBM, the PFS6 was 33.9% (90% CI, 19.2 to 48.5%); median PFS was 3.3 months (95% CI, 3.0 to 12.8 months); ORR was 27.6% (95% CI, 12.7 to 47.2%); and median OS was 10.5 months. Of all patients, 41.9% experienced adverse events of grade $\geqslant$3, the most common of which was hypertension (9.7%). Intracranial hemorrhage (grade 1) was noted in one patient (3.2%). However, no new safety signals for Bev were detected in any of the rGBM and WHO Grade III glioma patients. Adverse events led to Bev discontinuation in only two patients (intracranial hemorrhage and neutropenia), and Bev was well-tolerated.
Conclusions: Bev was efficacious and well-tolerated in this trial. Therefore, Bev seems to provide significant clinical benefit for Japanese patients with recurrent malignant glioma.