months (7–34). Median doses to the whole brain and the spine were 35 Gy. 29 patients had a boost radiotherapy to the posterior fossa (median dose 20 Gy; 8.0–25 Gy). 21 patients were treated with a standard chemotherapy. Patients were analyzed for the pattern of failure and ototoxicity during the primary treatment.

Results: After treatment of the primary pattern relapse was locally in the posterior fossa in 4 patients. Craniospinal dissemination was found in 2 patients. Hearing toxicity in the combined treatment arm was significantly higher.

Conclusion: Survival after local relapse is poor. The toxicity of the combined modality treatment is significant. 3-D conformal boost treatment should be considered to increase dose to the target and reduce the dose in non-target tissues.

917 POSTER

Phase II trial of topotecan (T) as a continuous intravenous infusion in patients (PTS) with high grade gliomas

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Purpose: A Phase II study is currently being conducted to evaluate single agent T as treatment for recurrent progressive high grade gliomas.

Methods: Topotecan is administered as a continuous IV infusion every 28 days, with a starting dose of 0.4 mg/m^2 per day. Pts being treated with a stable dose of dexamethasone (dex) may enter the study, but initiation of dex therapy or increase in dose is not permitted during the study. Twenty-nine pts (20 M, 9 F) have been enrolled and treated at two centers. Twenty-four pts received prior chemotherapy. Lesions measured by CT or MRI scan are assessed after every 2 courses.

Results: Fifty-one courses have been administered at the starting dose level, 7 courses at an increased dose level and 6 courses at a reduced dose level. Twenty-six pts are evaluable for efficacy. There have been 3 (11.5%) pts with documented objective responses, 4 (15.4%) pts with stable disease, and 16 (61.5%) with progressive disease. Three pts are ongoing and too early to evaluate. A total of 62 courses of T in 26 pts are evaluable for toxicity. Documented severe toxicities (pts with NCI Grade 3/4) have been: granulocytopenia 3 (11.5%), infection 2 (7.7%), anemia 2, nausea or vomiting 2, thrombocytopenia 1 (3.8%), leukopenia 1, fever 1 and diarrhea 1.

Conclusion: Continuous IV infusion with T is a well tolerated regimen with activity in recurrent high grade gliomas. Evaluation of topotecan in combination with other agents or with radiotherapy is warranted. Development of an oral formulation of topotecan may facilitate further evaluation for this indication. (Supported by SmithKline Beecham.)

918 POSTER

Modifying the Gill-Thomas-Cosman (GTC) head frame to expand the range of fractionated stereotactic radiosurgery (FSR)

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Current relocatable head frames limit the range of FSR. Described is a modification to the GTC head frame which enables stereotactic radiosurgery to be directed to tumors below the base of skull to areas of head and neck and cervical sites while maintaining the accuracy of the original head frame.

The original GTC head frame has two fixation points; anteriorly a custom dental Height of the occipital plate is adjustable in its vertical plane, however the dental piece is fixed. Treatment of head and neck and cervical spine tumors is accomplished by modifying the dental apparatus. Bracket extensions of 3 cm and 8 cm have been engineered to which the dental tray is secured thereby allowing the head frame to be lowered to encompass these regions. The depth helmet is also modified.

The accuracy and reproducibility was performed on the Rando Phantom. Each extension was tested 20 times; for each test 18 depth helmet positions were measured. Standard deviation of the modified head frame ranged 0.05 to 0.35 mm (mean 0.20) and 0.13 to 0.34 mm (mean 0.24) for the original GTC head frame.

The accuracy and reproducibility of the original frame is maintained. This modification facilitates treatment to sites involving the head and neck and cervical area. Ability to localize previously inaccessible sites while maintaining the accuracy and advantages of the non-invasive head frame should stimulate interest in innovative therapy.

919 PUBLICATION

Liposomal daunorubicin in children with brain tumors

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Purpose: Liposomes can be used as carrier for anthracyclines to pass the blood-brain barrier for chemotherapy of malignant central nervous tissue tumors. In this phase-II study the efficacy of liposomal entrapped daunorubicin (DNX) is studied in children with progressive or recurrent brain tumor.

Method: 14 children with progressive growing or recurrent malignant brain tumor received every 4 weeks DNX (60 mg/m^2 in D5 as one-hour infusion), upto a cumulative dose of 600 mg/m^2. Every 3 months the tumor process was evaluated by CT-scan or MRI. Toxicity was evaluated weekly according to the WHO-grading system.

Results: Six children died during the treatment due to rapid progression of the tumor. In 5 children the tumor reduced in size with 10–40%. In 3 children cysts had to be drained after the 6th 7th and 10th course respectively. and biopsies have been taken from the tumorregion. All 3 biopsies showed inactive tumor remnants without signs of malignancy.

Toxicity: The toxicity of DNX is mild (grade 1–3 hematologic toxicity, grade 1–2 hair loss). In all children the contractibility of the left ventricle (Sf) showed a transient decrease. In 5 of the children the Sf decreased to 20–30%. In one child the Sf decreased to 16%.

Conclusion: Malignant brain tumors in children response to liposomal daunorubicin, but in slowly progressive growing tumors only. The toxicity, including cardiotoxicity, is mild and transient.

920 PUBLICATION

Intraarterial chemotherapy (IACH) in patients with advanced primary central nervous system malignancies (APCNM)

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Purpose: The intraarterial chemotherapy gives the possibility to elevate the concentration of cytotoxic drugs in the tumor mass and to obtain better results of the local therapy.

Methods: In the period from 06.1993 to 11.1996 11 patients (pts) with primary central nervous system tumors was enrolled to the study due to unsuccessful radiotherapy, systemic chemotherapy treatment or surgery techniques that could not be used because of the advancement of disease (2 pts) with tumors of "butterfly" type. Patients were atheterized with caniula through the femoral artery. Then dependently on the tumor localization the appriopriate brain arteries were microcatheterized. The BCNU was dissolved in 5% glucose solution (vol.50 ml) and subsequently administered in the range of doses 160–180 mg/m^2. After the third course of such a treatment the BCNU doses to the values of 120–140 mg/m^2 have been reduced. The maximum tolerated dose (MTD) was completed to the value of 600 mg/m^2. The drug was injected with constant infusion (10 ml/min.) in order to avoid the "stream effect". Courses were repeated every 6–8 weeks.

Results: The response to the IACH by the mean of the axial computed tomography 24 hours before, 24 hours and 3 weeks after were evaluated. In the evaluated patients side effects like: pyrexia (2 pts), sensory aphasia (1 pts), headaches (3 pts), transient blindness (1 pts), hemiparesis (1 pts), enlargement of oedemal zone around the tumor in ACT (1 pts), narrow of the artery after microcatheterization (1 pts). The results of the therapy are following: CR-0, PR + SD-8, PD-3. From this studied group 9 (87.3%) died of the APCNM, and 2 (12.7%) are alive. The time of survival was 5.4 months (range 0.5–29.6).

Conclusion: Intraarterial BCNU chth with the highly selective microcatheterization of brain arteries in patients with advanced CNS malignancies can be useful when other therapeutic procedures cannot be applied.