major complications were recorded: a bilateral blindness 2 years following the administration of 55 Gy (2 Gy per fraction) in a 14 year-old girl; a bitemporal glioblastoma 9 years following the administration of 50 Gy in a 1 year-old girl. All patients required GH and thyroid hormone replacements and the endocrinological condition deteriorated in 12. Severe psychological disturbances recorded in 11. RT administered to a dose of 45–55 Gy provide an excellent and durable local control when administered early in the course of disease.

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A PHASE III MULTI-INSTITUTIONAL RANDOMISED TRIAL OF LONIDAMINE (L) AND POST-OPERATIVE RADIOTHERAPY (RT) IN SUPRATENTORIAL MALIGNANT GLIOMA

D. Bardelli, F. Bertoni[1], B. Caraffini[2], F. Cazzaniga[3], D. Cosentino[1], B. Morrica[2], L. Pompei[4], A. Richetti, E. Sarti[4], F. Terraneo[1]

Radiotherapy Departments of [1]Brescia, [2]Cremona, [3]Como, [4]Bergamo, Varese, Italy

Lonidamine, an indazole carboxylic acid derivative, was reported in Phase II/III trials to have efficacy as radiopotentiator in malignant glioma.

Between October 1990 and August 1994, 191 pts. with supratentorial malignant glioma were randomly allocated to treatment with RT or RT + L, following surgical resection. Prior to randomisation patients were stratified according to age. One patient was ineligible and excluded from the study (not malignant glioma).

Patients (pts) in arm A (98 pts) received RT alone (50 Gy whole brain plus 14 Gy coned-down boost to the tumour volume, 2 Gy/day for 5 days a week), those in arm B (92 pts) received RT + L (150 mg 3 times daily for 1 year starting from 3 days before irradiation). The groups were comparable in median age, performance status, TNM classes, sex, residual tumour size after surgery and histologic grade. Median follow up was 49 weeks. Intention to treat analysis failed to demonstrate significance difference in the survival rates and shapes of the survival curves between the two treatment arms.

Cumulative survival at 12 and 24 months calculated by the Kaplan-Meier method were 50% ± 5% and 13.4% ± 4% for arm A, 49% ± 5% and 13.4% ± 4% for arm B. ($P > 0.4$). The Cox proportional hazards model confirmed the prognostic variables of age ($P < 0.002$), Karnofsky performance status ($P < 0.02$) and histologic grade ($P < 0.03$). No subgroup examined demonstrated a survival or response advantage for the combination arm. Both acute and late radiation reactions were similar in the two groups. This trial fails to substantiate therapeutic synergy of RT + Lonidamine with this dosage and schedule in the postoperative radiotherapy of malignant glioma.

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RADIOTHERAPY FOR GRADE II GLIOMAS

L. Stalpers, G. Bauman, P. Sneed, K. Lamborn, W. Wara, M. Prados, C. Wilson, D. Larson

Department of Radiation Oncology, Neurosurgery and Neuro-Oncology, University of California, San Francisco, CA 94143, U.S.A.

From 1980–1991, 164 patients with a WHO-grade II astrocytoma received radiotherapy following surgery at UCSF. All patients had CT or MRI for diagnosis and/or treatment planning. Radiation doses were above 50 Gy in most patients, usually 54 Gy or 59.4 Gy. The 5- and 10-year overall survival rates were 79% and 67%, respectively; the median survival was 12.9 years. In the multivariate analysis, KPS, histology and duration of symptoms were significant. Age, location, surgical extent, or radiation dose were not significant. The 5-year survival rates for patients with KPS $\leq$ 70 and KPS > 70 were 60% and 87%, respectively. The 5-year survival rates for the different histologies were 95% for (mixed) oligodendroglial, 78% for ordinary, and 57% for gemistocytic astrocytomas. The 5-year survival rates for patients with a duration of symptoms $\leq$2 months versus >2 months were 65% and 83%. Progression free survival rates at 2-, 5- and 10-years were 77%, 68% and 50% respectively. In predicting progression free survival, only KPS was significant. Histology was important in predicting the survival following progression, with a 5-year survival of 83% in recurrent (mixed) oligodendroglial versus 33% in recurrent ordinary astrocytoma.

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HIGH-DOSE CHEMOTHERAPY (HDC) FOLLOWED BY AUTOLOGOUS BONE MARROW TRANSPLANTATION (ABMT) IN PLACE OF CRANIOSPINAL IRRADIATION (RXT) IN YOUNG CHILDREN TREATED FOR MEDULLOBLASTOMA (MB)?

O. Hartmann, D. Valteau-Couanet, S. Dupuis, F. Doz, J.C. Gentet, F. Méchinaud, E. Bouffet, E. Benhamou, C. Kalifa

French Society of Pediatric Oncology (SFOP), IGR, Villejuif, France

Cranio-spinal RxT is the standard prophylaxy in MB but, because of its late effects, children under 3 years of age are currently treated with conventional chemotherapy in order to delete or even avoid RxT. Among these patients treated without RxT in the SFOP study, 20 relapsed under conventional chemotherapy and entered a study of HDC followed by ABMT. Their median age at diagnosis was 23 m (R5-71) and the relapse occurred at a median time of 6.3 m (±5 m) after initiation of chemotherapy. A complete surgery of local relapse was performed in 4/20 and these patients were not evaluable for response. Sixteen out of twenty had measurable disease at primary site (9 pts) at metastatic sites (3 pts) or both (4 pts). Conditioning regimen consisted of combination Busulfan 600 mg/m^2 over 4 days and Thiotepa 900 mg/m^2 over 3 days. After recovery of aplasia, pts with local relapse received local RxT limited to posterior fossa. Among the 16 pts with measurable disease, following HDC, 6 CR, 6 PR, 3 NR, 1 NE were observed (Response rate 75%). For the 20 pts, EFS is 60% with a median follow up of 9 m post BMT (R3-65). Nine pts with localized relapse are alive NED without craniospinal RxT. Toxicity was high but manageable. One complication related death occurred 1 m post BMT. In conclusion: with a 75% response rate, this HDC proved to be very efficient in relapsed MB. A longer follow up is necessary to demonstrate whether, after local relapse, HDC could replace craniospinal RxT as prophylaxis of CNS metastases.

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DOSIMETRIC CONSIDERATIONS IN THE OUTCOME OF MEDULLOBLASTOMA

J. Michalski, J. Simpson, H. Fagundes, P. Thomas

Washington University School of Medicine, St. Louis, MO, U.S.A.

Seventy-three patients aged 2 to 48 years were treated for medulloblastoma (MB). Chang staging was: 7% T1, 42% T2, 16% T3a, 27% T3b, 8% T4. Thirty-three percent of patients had spinal axis (SAX) staging. Median radiation doses were posterior fossa (PF) 52 Gy, whole brain (WB) 40 Gy, and SAX 35 Gy. Fraction sizes ranged 0.5–3 Gy (median 1.7 Gy WB, 1.7 Gy SAX, 1.8 Gy PF).

The 5-year overall and disease-free survival are 67% and 59%, respectively. PF control was better for patients receiving >50 Gy to the PF (86% vs 42%, $P = 0.0007$). PF dose >50 Gy gave improved actuarial and disease-free survival. PF control was improved when patients were treated with fraction $\geq$1.7 Gy/day to the brain and spine (84% vs 51%, $P = 0.0006$). When PF was controlled, neuroaxis control was better if >30 Gy to the SAX (97% vs 71%, $P = 0.05$). WB dose did not have an impact on neuroaxis control, but few patients received $\leq$30 Gy WB. Incidence of extra-CNS metastases is 13% and 20% at 5 and 10 years, respectively. Patients with continuous PF and neuroaxis control have an extra-CNS relapse rate of 10%.

Our data confirm a dose response >50 Gy for PF control in MB. SAX dose of >30 Gy is necessary for neuroaxis control. Fraction size >1.7 Gy appears to improve local control. Ten percent of patients develop extra-CNS metastases despite CNS control.

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LOW EXPRESSION OF PLASMINOGEN ACTIVATOR INHIBITOR (PAI) TYPE I (PAI1) AND HIGH LEVEL OF PAI TYPE 2 (PAI2) ARE ASSOCIATED TO A BETTER OUTCOME IN GLIOMAS

O. Chinot[1,2], S. Romain[1], F. Grisoli[2], N. Graziani[2], X. Muracciole[1], P.M. Martin[1], L. Ouafik[1]

[1]Laboratoire de Cancérologie Expérimentale, CJF INSERM 93-11, Faculté de Médecine Nord, Bd P. Dramard. 13916 Marseille Cedex 20, France

[2]Service de Neurochirurgie. CHU Timone, Bd Jean Moulin, 13385 Marseille, Cedex 5, France

Urokinase-type plasminogen activator (uPA) and PAI1, are involved in invasive phenotype of several tumors, and have been recently described in malignant gliomas. Expression and tissular localization of PAI2, as well as the clinical relevance of these proteases, need however to be investigated. In the present study, 42 patients with glioma were analyzed for expression of uPA, PAI1, and PAI2 (oligodendrocytoma (n = 2), glioma