Conclusions: The small group of pts renders presentation of univocal conclusions impossible. The treatment of pts with AG gives worse results than in the cases of AF and AP. Cht did not better results.

1282 POSTER

Whole brain irradiation versus limited fields in the treatment of high-grade malignant gliomas

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Purpose: Delineation of the target volume is a controversial issue in radiation treatment of high grade malignant gliomas. Our purpose was to verify if the choice of different volumes in radiation treatment influence the overall survival (OS). The effect of age, performance status, extent of surgery and histology was analysed for prognostic importance.

Methods: From January 1995 to June 2000, 75 patients (pts) with histologically confirmed malignant astrocitomas were treated. No patient was lost for follow-up. The total dose of 50-60 Gy was applied with 6Mv or Co60 teletherapy device, in one day fraccion of 1.8-2 Gy. The entire brain was irradiated in 40 pts (52%). In 11 pts (19%), the entire brain was first irradiated, and in a second phase the total doses were achived with reduced fields. Twenty four pts (29%) were treated with reduced fields directed to the treatment volume encompassing the contrast-enhancing lesion with a 2 cm margin based on preoperative MRI and CT. Survival was calculated using the Kaplan-Meier method. Significance of the differences was analysed with Log Rank test. The significance level was $p < 0,05$.

Results: Median survival was 9 months (range 2-68 months). There were 45 males (60%) and 30 females (40%), with a median age of 62 years (range 23-77 years). The pts were classified in three groups of age: <45, 45-65 and > 65 years. The OS for these groups were 21, 9 and 8 months (p= 0,0003). The median WHO performance status score was 2. Twelve pts had a score 0 (16%), 31 a score 1 (41%), 20 a score 2 (27%), 7 a score 3 (9%) and 5 a score 4 (7%). The OS for these groups were 25, 11, 6, 7 and 6 months (p=0,0003). Histology consisted of anaplastic astrocytoma (AA) in 12 (16%) and glioblastoma multiforme (GBM) in 63 (84%). The OS for AA was 15 months and for GBM 9 months (p=0,03). Eighteen (24%) pts underwent biopsy, 21 (48%) gross total resection, and 36 (48%) subtotal resection. The OS for these groups were 9, 10 and 9 months (p=0,28). The OS for pts who irradiated the entire brain was 7 months, while for those that irradiated the entire brain plus a boost was 11 months. The OS for pts who were treated with limited fields was 16 months (p= 0,0006).

Conclusion: In our series, age, performance status and histological subtype proved to be important prognostic factors. In high-grade gliomas there is no benefit in the irradiation of the entire brain. The best results are for pts who were treated with limited fields of irradiation.

1283 POSTER

Concomitant radiation therapy and temozolomide (TMZ) in the treatment of multiform glioblastoma and anaplastic astrocytoma: a pilot study

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TMZ has demonstrated efficacy against recurrent malignant gliomas (MG). We evaluated the tolerance of TMZ associated with radiation therapy (RT) in post surgery treatment of incompletely resected MG. From September 1998 to Dicember 2000, we treated 18 patients (15 glioblastomas, 3 anaplastic astrocytomas) with incomplete resection after surgery and an average residual disease of 3.25 cm (range 2-5 cm). Mean age was 58.6 (range 37-73 years); 7 patients were > 65 years. TMZ was given with a weekly schedule (150 mg/m2 daily for 5 days, repeated every 28 days for three times). TMZ was administered at the beginning of the fourth week of RT (dose 30 Gy) in 7 patients (Group A) and at the first day of RT in 11 patients (Group B). The average total dose was 65.6 Gy (range 54-70) with standard schedule. 3-D planning was performed for all patients with customized shielding and multiple coplanar beams arranged to include Planning Target Volume within the 95% isodose line. Two patients in group A completed RT but not the planned dose of TMZ: 1 due to progression after one cycle of TMZ and 1 due to kidney failure after two cycles. Two patients in Group B developed grade IV leuko-thrombocytopenia after two cycles of TMZ (RT 54 and 60 Gy). Of the latter, one died and one finished planned RT with some delay, obtaining partial remission. All 4 patients were older than 65 years. In the other patients, no toxicity was observed. Out the 16 patients that completed treatment an MRI/CT showed: 4 progressions, 5 stable diseases, 5 partial responses and 2 complete response (1 multiform glioblasoma and 1 anaplastic astrocytoma). To date, 9/18 patients are alive with a mean follow up of 16 months (range 8-21) from surgery. A overall survival analysis with Kaplan-Meier method showed a 35% at 24 months.

Conclusion: Concomitant RT and TMZ is feasible and well tolerated (compliance 70%) in MG patients with incomplete surgical resection. We had a tolerance problem in the patients older than 65 years.

1284 POSTER

Simultaneous radio-chemotherapy of malignant gliomas with topotecan

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Purpose: Because of the pronounced radioresistance of glioblastoma multiforme (GBM) the prognosis of this disease remains poor. Therefore, we investigated the impact of an additional simultaneous chemotherapy with the topoisomerase-I-inhibitor topotecan (TTC) on the quality of life and toxicity of radiotherapy.

Materials & Methods: In this multicenter trial patients with histologically proven GBM underwent a simultaneous radio-chemotherapy. Including pilot phase 60 patients, 41 male and 19 female, were treated. Age ranged from 26 to 76 years, the mean was 57 yrs. Conventionally fractionated conformal radiotherapy was performed with daily doses of 2.0 Gy to a total dose of 60 Gy. One hour prior to irradiation 0.5 mg (absolute dose) of TTC were administered intravenously resulting in a cumulative dose of 15 mg. Hematologic and non-hematologic toxicity and survival time were recorded. Quality of life was assessed by Karnofsky performance scale (KPS) and Spitzer-index (SI).

Results: Median administered dose of radiation was 60 Gy (32.4-76 Gy). Median cumulative TTC dose was 15 mg (5-19 mg). Grade-III toxicity was found in 6 cases (2x hematologic, 2x motoric disorder, 1x infection, 1x nausea) and grade-IV toxicity in 3 cases (1x esophagitis, 1x motoric disorder, 1x mental disorder). Two patients died of septic disease most likely caused by steroid induced immunosuppression. Mean KPS and SI initially, at the end of therapy and 6 wks after therapy showed values of 87%, 81% and 80% and 19 pts, 18 pts and 19 pts, respectively. The differences were all not significant. Median survival time was 13.5 months. This was slightly longer than a historical collective with a median survival of 10 months.

Conclusion: This multimodal approach for patients with GBM is well tolerated. Quality of life remains preserved and outpatient treatment is possible.

1285 POSTER

A phase II trial of topotecan and radiation therapy for CNS-metastases of patients with solid tumors

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Once the diagnosis of CNS-metastases in patients with solid tumors is etasblished, the prognosis is poor and there is a need for new concepts in therapy.

This is an interim-analysis of 68 patients with CNS-metastases due to solid tumors (14 SCLC, 36 NSCLC, 6 breast, 2 unknown) treated with a simultaneous therapy of topotecan and whole brain radiation (20 x 2 Gy, 20 x 0.4 mg/m* topotecan as short infusion within 2 h to radiation therapy) in a phase II clinical trial. At this time 54 patients finished the therapy, 14 patients are still in course, 45 patients are evaluable for toxicities and survival, 36 patients are available for evaluation of remission. Hematologic toxicity: anemia grade 3 one, grade 4 one; neutropenia grade 3 two, grade 4 one; thrombopenia grade 3 three, grade 4 two. Non-hematologic toxicity: sensorium grade 3 five; stomatitis grade 3 two; infection grade 3 one, grade 4 four. Infection occurred only in the beginning of the study if dexamethason was given at dosages > 12 mg daily. Remission: out of 36 at this time

evaluable patients 6 CR, 22 PR, 5 SD and 3 PD occurred. Follow up: out of 54 patients 4 died within therapy, 6 patients died within 2 month after completion of therapy. At least 39 patients are alive three, 15 after six, 4 after nine and 2 after 12 month of completion the therapy.

Conclusion: Combined radio-chemotherapy with topotecan as mentioned above is a very effective and tolerable regimen. Patients on therapy with high doses of dexamethason should not receive this regimen.

Symptom management & quality of life

1286 POSTER

Comparing the efficacy of fixed vs. weight-based dosing of epoetin alfa in anemic cancer patients receiving platinum-based chemotherapy

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Purpose: Epoetin alfa has been shown to be effective and safe in decreasing transfusion requirements and improving hemoglobin (Hb) and quality of life (QOL) in anemic cancer patients (pts) receiving chemotherapy (CT).(1-3) A fixed dose of epoetin alfa (EPREX/ERYPO, Ortho Biotech/Janssen-Cilag) vs. weight-based dosing may offer a more convenient option to physicians for anemia management.

Methods: An open-label, randomized (1:1), 12-week trial was conducted to compare the effects of fixed (10,000 IU) vs. weight-based (150 IU/kg) dosing of epoetin alfa three times weekly (tiw) subcutaneously (sc) in anemic cancer pts receiving platinum-based CT. The primary efficacy endpoint was freedom from transfusion during Days 29-84.

Results: Of 546 pts enrolled, 510 fulfilled the protocol entry criteria. Mean age was 61 years. Tumor types included primarily lung (34%) and ovarian (22%), and most pts had advanced disease (stage III, 32%; Stage IV, 53%). During the 3 months before trial entry, 11.0% of pts had received one or more transfusions. During Days 29-84, 85.5% (CI95 82-89) were transfusion-independent as calculated by the lifetable method, with no statistically significant difference between the two groups (P>.3). Overall, 83% of pts in the 10,000 IU fixed dose arm were transfusion-independent vs. 86% pts receiving 7-9,000 IU and 85% pts receiving 11-15,000 IU in the weight-based arm. Of the 449 pts with baseline and final Hb levels, mean Hb increased 2.0 g/dL from 9.7 g/dL at baseline to a final Hb of 11.7 g/dL (CI95 11.4-11.9) in both groups. Of 315 pts who had both baseline and final LASA/CLAS QOL scores, the average of the three scores (Energy Level, Ability to Do Daily Activities, and Overall QOL) increased from 47 (±23) to 56 (±25) mm (mean±SD). In addition, QOL improvements correlated with Hb increases (P<.01, multiple linear regression), as well as to CT response, and were similar in both groups.

Conclusion: Both fixed (10,000 IU) and weight-based (150 IU/kg) dosing of epoetin alfa showed similar efficacy in maintaining transfusion independence, increasing Hb, and improving QOL scores. These findings, along with previously reported results of a large, open-label, community-based study,2 favor use of the more convenient fixed dose of 10,000 IU tiw sc in anemic cancer pts receiving CT.

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1287 POSTER

Effect of treatment of tumor patients with epoetin alfa on hemoglobin levels and exhaustion

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This German multicenter study assessed the efficacy of epoetin alfa to improve hemoglobin levels and exhaustion in tumor patients (pts). From Nov. 1998 until Dec. 2000, 701 pts were enrolled to receive epoetin alfa 10.000 IU t.i.w. for 8-18 weeks during chemotherapy and/or radiotherapy. At this time data from 578 pts are evaluable for intent-to-treat analysis, 405 (70.1%) females and 173 (29.9%) males with a median age of 61 (23-85)years. 535 pts (92.6%)were treated because of solid tumors and 43 (7.4%)because of hematological malignancies. The most frequent tumors were breast cancer (174 pts,30.1%), ovarian cancer (100 pts,17.3%), lung cancer (81 pts,14%), and colorectal cancer (57 pts, 9.9%). All pts were treated with chemotherapy, 94 received additional radiotherapy. Platinum was administered in 193 pts (33.4%). Exhaustion was measured as part of a standardized quality of life (QoL) questionnaire recording scores for separate aspects like social activities, mood, interest and exhaustion. QoL data were inquired from the physician, the patient, and a nurse.

Results: The mean number of epoetin alfa applications was 31 ± 14, the mean treatment duration with epoetin alfa was 12 ± 6 weeks. Complete tumor response was found in 97 pts (17%), partial response in 122 (21%), no change in 73 (13%), and progressive disease in 99(17%). 75 pts (13%) were not evaluable. 148 pts received blood transfusions with a median of 3 units (1-14). Hemoglobin levels increased from 10.1 ± 1 g/dl to 11.9 ± 2 g/dl during epoetin alfa treatment. This improvement was statistical significant (p<0.0001)in the total sample and in all tumor response groups. Changes in QoL were reflected above all in the reduction of exhaustion; according to the physician, exhaustion decreased significantly from 7.3 ± 1.2 to 4.8 ± 2.9 points on an 11-point rating scale (0-10) in the total sample. The increase of hemoglobin was strongly correlated with improvement of the exhaustion score (0.39,p<0.0001).

Conclusion: In patients with solid tumors as well as various hematological malignancies the treatment with epoetin alfa is accompanied by a significant increase of Hb-levels resulting in an improvement of exhaustion. The definition of subgroups with good or bad risk factors for epoetin alfa response is under exploration.

1288 POSTER

Review of the health related quality of life associated with irinotecan and 5FU/FA in the treatment of advanced metastatic colorectal cancer in the UK

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Background: Colorectal cancer (CRC) is the third most common form of cancer in the UK, with approximately 30,000 new cases and over 17,000 deaths registered annually. Whilst recent new chemotherapies have been shown to extend life, there are still questions concerning their impact on quality of life (HRQoL).

Objective: This study aims to review the published evidence on the HRQoL implications of irinotecan in the treatment of advanced CRC.

Methods: A systematic literature search was undertaken (cut-off date 25/10/00) to identify the HRQoL implications of irinotecan in Phase II and Phase III studies, within UK licensed indications, in advanced CRC. Databases included BIOSIS, EMBASE, Alert, HealthSTAR, CancerLit, MEDLINE, NEED, DARE, DEC reports, Cochrane Library, and ASCO/ESMO proceedings.

Results: Four Phase III clinical trials utilising irinotecan where identified, all of which used the EORTC QLQ-C30 to assess HRQoL. Two studies were conducted in the first line setting using irinotecan and 5-fluouracil/folinic acid (5FU/FA). Douillard et al, 2000 showed a significant delay in the time to definitive deterioration in HRQoL from baseline with irinotecan + 5FU/FA. Saltz et al, 2000 found no significant differences in global health status. However, univariate analyses showed smaller mean increases in severity of symptoms in the irinotecan plus 5-FU/FA group for fatigue, anorexia and pain but a smaller decrease from baseline in role functioning.

In the second line setting two studies were also identified, one which compared irinotecan to 5FU/FA and one which compared irinotecan to best supportive care (BSC). Rougier et al, 1998 showed significant differences in favour of 5FU/FA for nausea/vomiting and diarrhea. Median pain-free survival was 10.3 months for the irinotecan group compared with 8.5 months for the 5FU/FA group. In Cunningham et al, 1998 univariate analyses were significantly in favour of the irinotecan for cognitive functioning, global health status, pain, dyspnoea, appetite loss and financial impact. The diarrhea score was significantly better in the BSC group.

Conclusion:. The published evidence supports the fact that in the first line setting irinotecan plus 5FU/FA prolongs life in advanced CRC patients without compromising quality of life. Analysis also suggested that as second-line treatment in advanced CRC, the side effects of irinotecan monotherapy are favorably balanced by a reduction in tumour-related events.