921 PUBLICATION

Stereotactic external beam radiotherapy of brain metastases – Clinical results of a prospective study

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Purpose: The aim of this study is to analyze the clinical results of the treatment with linac radiosurgery in patients with brain metastases, especially concerning the neurological follow up and the radiological tumor control.

Method: 40 patients with brain metastases (solitary, two or three lesions) were treated with stereotactic radiosurgery using an adapted linearaccelerator. The median radiosurgery dose was 20 Gy. The patients were investigated 6 weeks and every 3 month after therapy, until to death. The neurological status, the Barthel Index and the Karnofsky Index (KI) were prospective quantified.

Results: In 22 patients one lesion and in 18 patients two lesions were treated. Only 5 patients had no extracerebral tumor manifestations. The most important selection criteria was a KI lower than 70%. The rate of the local tumor control was 90%. The median survival time was about 11.5 month, (range 1–18 month). The neurological status and the Barthel and Karnofsky Index showed a very good palliative effect after therapy. Only in 5 patients a whole brain irradiation with 30 Gy in 10 fractions was performed 4 to 12 month after stereotactical irradiation, because of occurrence of new metastases.

Conclusions: Stereotactic linac radiosurgery of brain metastases is a therapy with very good palliative results and high local control rates even in patients presenting two metastases. The best method to analyze the neurological follow up is quantifying the neurological status. The whole brain irradiation is only in the situation of multiple metastases indicated.

922 PUBLICATION

Chemotherapy of relapsing glioblastoma multiforme IV (GBM IV) with fotemustine (F) and dacarbacine (D)

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Purpose: In several recent phase II studies, the median duration of survival of patients (pts) with anaplastic gliomas in first relapse is 27.5 weeks (17–44 weeks). The aim of this study was to evaluate efficacity and toxicity of the regimen F + D in pts with GBM IV in first relapse.

Patients: 21 pts (16 male, 5 female) aged 33–66 years, median 45 years, who had received adjuvant irradiation, were treated with F (100 mg/m^2) and D (200 mg/m^2), given intravenously every 3 weeks at blood leucocyte count $\geq$3,000/μl and platelet count $\geq$100,000/μl. 13 of the pts had received adjuvant chemotherapy, mostly Lomustine. The first 4 pts received a monotherapy with F 100 mg/m^2 (days 1, 8, 15, on recommendation of the company Servier). Due to hematotoxicity of WHO grade 4 during the first cycle in all pts, this monotherapy was replaced by F + D.

Results: A total of 91 cycles are evaluable. Hematotoxicity was the predominant side effect: leucopenia and thrombocytopenia of WHO grade $\geq$3 occurred in 4 and 5 pts respectively. Nausea/vomiting was not observed under support with serotonin-antagonists. At study evaluation 10 pts are still alive. The median survival is not reached at 29+ weeks (3–14 months).

Conclusion: F+D had acceptable efficacity and toxicity and did not affect negatively the quality of life in relapsed GBM IV pts.

Gynaecological cancers II

923 ORAL

Radiation enhancement of Gemcitabine® in three human cervical cancer cell lines

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Purpose: Cervical Cancer is commonly treated with surgery or radiation. Concomitant chemoradiotherapy is a possibility to improve radiation. We studied the radiosensitisizing effect of Gemcitabine (dFdC) in an in-vitro model.

Methods: We used 3 human cervical cancer cell lines: SiHa, CaSki and Hela. We compared survival of untreated cells to cells treated with non-cytotoxic concentrations of dFdC (1, 10, 25, 50 nM) for 24 h following irradiation (RT) with 2, 4, 6, 8 Gy. ATP bioluminesce assay was performed to measure the surviving fraction. Mean inactivation dose (D), enhancement ratio (ER) and the concomitant effect were calculated. Data analysis with t-test and analysis of variance were performed.

Results: We determined maximal non-cytotoxic drug-concentrations: SiHa (50 nM), CaSki (25 nM), Hela (50 nM). dFdC showed in all three cell lines a significant enhancement effect of RT: SiHa (50 nM; ER = 3.6), CaSki (25 nM; ER = 1.6), Hela (25 nM; ER = 1.5). The observed enhancement effect of dFdC was mainly additive only SiHa showed synergism.

Conclusions: These findings demonstrate that dFdC enhances the radiation effect of human cervical cancer cell lines in vitro. dFdC should be considered for further clinical investigation.

924 ORAL

DNA in-situ hybridisation for the detection of apoptosis specific DNA fragments (Frag-EL) in routine endometrial curettage specimens

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Purpose: Cell apoptosis conserves energy invested into epithelium of endometrium. Detectable in extracted DNA by the presence of electrophoretic "ladder" patterns, the relationship between apoptosis and endometrial cycle stage may now be studied using apoptosis specific DNAfragment in-situ labelling, suitable for routinely processed samples and non-radioactive labelling (Frag-EL). We assessed the applicability of Frag-EL to routinely sampled and fixed/processed endometrial curettage tissue samples.

Methods: 10 Consecutive routine endometrial curettage samples without, 10 with hyperplasia and 2 cases of endometrial carcinoma were used. Samples were routinely fixed and processed to 10 μm paraffin sections. With commercially available probes (Frag-EL, CalBiochem, USA) in-situ labelling was carried out using appropriate positive and negative controls for DAB-dependent peroxidase end labelling. All samples were assessed for evenness of staining, and for distribution of apoptotic activity over stroma, epithelial lining of uterine cavity and of glands separately, using a 4 point semiquantiative grading system (0, +/–, +, ++).

Results: Apoptotic activity was present in the stroma of all specimens and in all tissue components is higher than would be expected based on classic appearance of apoptotic nuclei. Apoptosis in stroma and epithelial components can easily be assessed separately and varies with cycle stage. Apoptosis in hyperplastic lesions appears reduced whereas in cancer this may possibly be increased.

Conclusions: DNA-in-situ hybridisation based detection of apoptotic cells in clinical endometrial tissue samples is routinely possible. The results warrant application of this method for the understanding of both ovulatory cycle, pre-neoplastic, transformation related, and malignant endometrial pathology.