4−10, median 7). Most pts presented with massive T recurrence (6 pts). Massive T and N recurrence in 2 pts. All the pts completed the treatment as scheduled. One case of G III skin toxicity inside the irradiated field occurred. Systemic skin rush occurred in 5 pts (G1 in four and G2 in one). No other relevant side effects occurred. At the end of the treatment, all pts showed a dramatic improvement in clinical conditions: complete control of pain without analgesics was achieved in 5 pts, while the remaining had VAS value between 1 and 2 with analgesics. CT scan demonstrated objective responses in three pts and SD in 2.
Conclusions: R-RT with C-mab and carboplatin results in clear improvement of clinical status and in some objective responses in this very heavily pretreated pts population. Toxicity was moderate and did not required treatment interruptions. This compassionate experience supports the development of clinical trials.

8580 POSTER

Social support service impact to the anxiety and depression of oral cavity cancer patients in Taiwan

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Purpose: To understand the impact of social support service to anxiety and depression of oral cavity cancer patients
Material and Methods: Oral cavity cancer patients who will receive radical surgery treatment are invited to take part in three arms randomized trial. Group A included basic social support program, group B included basic and previous treated cancer survivor volunteer visit and share, group C include frequent social worker visit except group B service. All patients are evaluated the anxiety and depression status by Hospital Anxiety and Depression Scale(HADS) and social support questionnaire included emotion, information, evaluation and solid support domains. Patients are evaluated at three time point: T1, pre-surgery; T2, 10−14 days after surgery (discharge from ICU) and T3, discharge from hospital.
Result: One hundred and thirty four oral cavity cancer patients are included in this study after informed consent. Median age is 47 and 98% are male. Seventy one percents of patients married. Most patients are blue-collar workers and have economic duty for the family. All patients receive radical surgery, 43% of them received adjuvant chemoradiotherapy and 24% received adjuvant radiotherapy. All patients are definite anxiety and depression at T1 (mean: 16.3), T2 (mean: 16.2) and T3 (13.8). The change is significant between T3 and others. Patients in C group have significantly better HADS improvement compared to group A and B but no difference between group A and B. There is no significant difference in social support domain among different patients group except patients feel more social support from family than medical personnel at T1 and patients with religion belief can appreciate more support from medical personnel.
Conclusion: All oral cavity cancer patients will have anxiety and depression condition from admission to discharge. Combined more intensive social support care can significantly improve patient anxiety and depression condition during admission. Further study is needed to know what change after discharge and long term condition.

8581 POSTER

Single centre experience in the use of induction TPF (docetaxel, cisplatin, 5FU) in locally advanced head and neck squamous cell carcinoma (LAHNC)

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Background: Induction TPF followed by radiotherapy (RT) or concurrent chemoradiotherapy (CTRT) has been shown to give improved overall survival compared to PF (cisplatin, 5FU) in LAHNC. This is a retrospective review of the experience of a single centre in the use of TPF in a non trial setting.
Materials and Methods: We reviewed 98 patients with stage 4 LAHNC treated between Mar 2006 and Feb 2009 with a modified version of the TPF regime used in TAX 324 (T and P 75 mg/m^2, both d1, F 750 mg/m^2/d, d2−5) q 3 wks. We aimed to deliver 3 cycles of TPF.
Results: Median age was 56 (35−74). 10 patients started treatment at a lower dose due to various co-morbidities. The first 7 patients did not receive antibiotic prophylaxis, 1 (14%) developed febrile neutropenia (FN). 49 patients received routine prophylaxis with ciprofloxacin 500 mg bd d5−15, of these 16 (33%) developed FN; 42 patients received both GCSF and ciprofloxacin routine prophylaxis, and 6 (14%) developed FN. 7 patients had minor cardiac events, 2 of which were associated with raised Trop T. There were 2 treatment related death during induction chemotherapy (CT). 16 patients had dose reduction due to toxicities. 93 patients proceeded to radical RT with concurrent cisplatin (56), carboplatin (17), capecitabine (2), cetuximab (7) or without concurrent CT (11). 1 patient received palliative RT. 1 patient underwent surgical management, 1 patient refused further treatment. Following induction CT, 94 patients were evaluable, 70 (74.5%) had PR, 9 (9.6%) had CR and 15 (16%) had SD.
Conclusion: TPF is deliverable in a non trial setting with manageable toxicities. Response rates were comparable to TAX 324 (84% versus 72%) with a higher proportion of patients proceeding to definitive RT or CTRT (96% versus 79%). Patients with both GCSF and antibiotic prophylaxis have lower risk of FN.

8582 POSTER

Radiosensitivity of neck metastases from squamous cell carcinoma of the head and neck assessed by immunocytochemical profiling of fine-needle aspiration biopsy cell specimens

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Background: To assess radiosensitivity of neck metastases of squamous cell carcinoma of the head and neck (SCCHN) by immunocytochemical profiling of fine-needle aspiration biopsy (FNAB) cell specimens.
Methods: Immunocytochemical reactions (localization, percentage and intensity of positive cells) to p53, cyclin D1, stefin A and Ki-67 was determined in FNAB cell samples of neck metastases from 21 patients treated with concomitant chemoradiotherapy with mitomycin C and cisplatin. Immunoreactivity was graded according to the percentage of positively stained cells (p53, cyclin D1, stefin A: <10% vs. $\geqslant$10%; Ki-67: <20% vs. $\geqslant$20%) and correlated to clinical characteristics and response to therapy.
Results: Six (28.6%), eight (38.1%) and 15 (71.4%) FNAB cell samples were classified as p53, cyclin D1 and stefin A positive, respectively. Ki-67 staining positivity ranged between 0−80% (median 10%). Threshold value of 20% classified nine (42.9%) FNAB samples as Ki-67 positive. Statistically significant predictors of favorable nodal response to chemoradiations were p53 ($P = 0.025$) and cyclin D1 ($P = 0.048$) negativity and Ki-67 positivity ($P = 0.045$). Neck mestastasis recurrence correlated only with Ki-67 immunoreactivity (no vs. yes: negative 4 vs. 8, positive 8 vs. 1, $P = 0.024$). Favorable profile of the tandem cyclin D1 and Ki-67 (one or both of the two) further improved the predicitive strength of these markers: it was associated with less advanced cN-stage ($P = 0.045$), complete nodal clearance after therapy ($P = 0.004$), absence of regional recurrence (0.006), and favorable survival status ($P = 0.045$). Its clinical repercussion was tested for two outcomes, i.e. regional response at 8−12 weeks post-therapy and regional disease reappearance: the the sensitivity, specificity and positive predictive value were 93.8%, 80%, 93.8% and 100%, 55.6%, 75%, respectively. Combination of all three markers (favorable immunocytochemical profile of $\geqslant$2 of them) did not add to their predictive value.
Conclusion: FNAB is non-invasive, simple and cheap procedure, which could serve simultaneously for diagnostic purposes and for radiosensitivity testing. Immunocytochemical determination of the tandem cyclin D1 and Ki-67 in FNAB cell samples from neck metastases of SCC of the head and neck seems to be valuable marker for predicting regional response to radiotherapy and might assist when deciding on appropriate primary therapy.

Central nervous system

Oral presentations (Tue, 22 Sep, 09:00−10:45) Central nervous system

8700 ORAL

Subclinical systemic disease and relapse pattern in primary central nervous system lymphoma (PCNSL)

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Background: An unresolved question is why some PCNSL spread systemically while most others do not. It was postulated that extracerebral relapse of PCNSL may represent a sequel of initial occult systemic disease rather than true extracerebral spread.

Materials and Methods: We examined bone marrow and peripheral blood specimens of 47 patients with newly diagnosed and relapsed PCNSL using PCR for the presence of clonally rearranged IgH genes. The applied IgH PCR method was developed by a European Concerted Action (BIOMED-2). To all samples (50 ng DNA), 3 different FR primer sets (FR1, FR2 and FR3) were applied in conjunction with a JH consensus primer (JH22). Baseline routine staging procedures showed no evidence of systemic lymphoma manifestations in all patients.
Results: In two patients, bone marrow aspirates and/or blood samples showed the same dominant PCR products as in the tumor biopsy specimen, indicating the presence of the same tumor cell population in the CNS as well as in extracerebral sites. Three additional patients had dominant amplificates detected in blood or bone marrow different from the brain tumor specimens that might represent the second rearranged allele of the tumor cell population. To date, one patient has relapsed systemically in the gastrointestinal tract. In this patient, the same clonal IgH rearrangement could be demonstrated in CNS, blood and the systemic relapse.
Conclusions: Extracerebral disease not detectable by routine staging may be present in PCNSL patients. This finding may have an impact on the understanding of PCNSL pathogenesis and the extent of staging and treatment. Patients with subclinical systemic disease may present with unusual sites of systemic relapse.

8701 ORAL

Replication and excretion of parvovirus H-1 in a rat model on oncolytic virotherapy of glioma

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The rodent parvovirus H-1 (H-1PV) is non pathogenic for its natural host but was shown to exhibit anti-tumor activity. H-1PV can infect human cells with a selective cytotoxicity for transformed cells while being innocuous for normal cells. Therefore this virus is currently being assessed for its possible use as an oncolytic agent for virotherapy of glioma, notably since human glioma cells in culture were found susceptible to the killing effect of H-1PV. In a rat model with gliomas established from RG-2 cells, treatment with H-1PV resulted in complete remission of advanced tumors without any side effects.
In preparation of a clinical trial of virotherapy with H-1PV, we analyzed replication of virus in tissue (brain tissue and glioma) in the above rat model, as well as excretion of virus from infected animals.
We could demonstrate synthesis of infectious progeny virus in glioma bearing brain tissue of animals infected with H-1PV intratumorally (intracranially), but not in brains of infected animals that were not bearing tumors. In tumor brains, the titer of virus was 100- to 1000-fold increased within 2 days after infection compared with brains of control animals. This shows virus replication being restricted to tumor tissue.
To address the issue of virus excretion/shedding, body fluids and excretions from animals infected with H-1PV by intracranial or i.v. routes, were assessed by quantitative PCR and infectivity assay for the presence of virus, 14 days after infection. Paralleling results with other animal parvoviruses, infectious virus was demonstrated most frequently in urine samples.
The data demonstrate that therapeutically injected H-1PV is able to replicate in tumor cells, thereby increasing viral amounts may render oncolytic activity more efficient. If confirmed in humans, virus shedding from urine may reduce concern of contamination of personnel in a clinical trial with H-1PV.

8702 ORAL

Methionine PET of (pseudo) tumour progression after stereotactic radiotherapy/ radiosurgery of brain tumours; differential diagnosis of radiation necrosis and tumour recurrence

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Background: Following radiosurgery/stereotactic radiotherapy (SRS/SRT) of primary and secondary brain tumours, differentiation between radionecrosis and recurrent tumour in case of increasing abnormalities on MRI may be difficult. The purpose of this study was to determine the added value of Methionine PET (MET-PET) to MRI in the differentiation between radionecrosis and recurrent tumour and to assess the prognostic value with regard to clinical outcome.
Material and Methods: Scheduled MRI follow up of 12 patients after SRS/SRT(glioblastoma n = 2 meningioma n = 2 and metastases n = 9) showed increase in gadolinium (GADO) high signal areas outside the original tumour area. MET-PET was performed at the time of radiological progression and was co-registered with the MRI at the time of progression and the MR before progression in BRAIN LAB IPlan image 4.1®. The area of progression was determined by subtracting the GADO+ area of the tumour at SRS/SRT at baseline from the GADO+ area at progression. Maximal standard uptake value of MET-PET of this area, original tumour area and SUV max of the contralateral normal hemisphere were calculated. Ratios of SUVmax of the progression area or original tumour area over SUVmax of the normal brain were calculated (SUVpa/nb and SUVot/nb, respectively). Two groups of patients were defined depending on clinical outcome after (pseudo) tumour progression.
Results: Clinical outcome was defined as good (n = 5) if patients remained alive, neurologically stable after MET-PET and additional follow up scans showed regression or no further progression. Outcome was defined as poor (n = 7) if patients showed progressive neurological decline, died (n = 5), showed progressive changes extending into distant normal brain on MRI (n = 1), or showed vital tumour at craniotomy (n = 1). In good outcome patients, the mean SUVpa/nb was 0.95 (min 0.68 max 1.1) versus 1.34 (min 0.90 max 1.68) in poor outcome patients. SUVot/nb were 1.18 (0.60−1.78) and 1.24 (0.52−1.77) in good and poor outcome respectively. SUVpa/nb correlated significantly (Pearson −0.65 p = 0.02) with outcome whereas SUVot/nb did not (Pearson −0.080 p = 0.80).
Conclusions: Low MET-PET SUVmax of progression area after SRS/SRT was correlated with good outcome and likely represents radionecrosis whereas high MET-PET SUV max of the area of progression associated with poor outcome and likely represents true tumour progression.

8703 ORAL

Clinical effect of hypo-fractionated high-dose irradiation on local control of glioblastoma owing to the status of MGMT promotor methylation

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Backgrounds: Our hypo-fratctionated high-dose irradiation (HdI; 68 Gy/8F) showed excellent local control and, with prophylactic intrathecal chemotherapy, significant survival benefit in glioblastoma (GBM) pts. However, it also increased the risk of radiation-induced brain damage in long survivors. MGMT is a DNA repair protein which plays an important role in resistance to anti-cancer treatments. This protein is induced by cytological stresses including irradiation, but its expression level is depending upon the status of MGMT promotor methylation (MGMT-met). The aim of this study is to clarify the significance of MGMT-met as a predictor of radioresistance of GBM and possibility to select pts who really require HdI.
Materials and Method: Histologically confirmed 106 GBMs were enrolled. Among these pts, 56 pts were treated by HdI and 50 were by conventional radiotherapy (cRT; 60 Gy/30F). The status of MGMT-met was determined by methylation specific PCR. Pts were classified into four groups owing to the status of MGMT-met and chemotherapeutic regimens as follows: Group A pts (n = 34) were MGMT-met(+) treated by PAV (procarbazine, nimustine, vincristine); Group B (n = 37) were MGMT-met(−) treated by PAV; Group C (n = 13) were MGMT-met(+) treated by TMZ (temozolomide); and Group D (n = 22) were MGMT-me(−) treated by TMZ. The progression-free survival time (PFS) of pts were compared between HdI and cRT in each groups.
Results: The PFS of pts treated by HdI was significantly longer than those by cRT in both the MGMT-met(+) (p = 0.001) and (−) pts (p = 0.0004), indicating that we can not determine the necessity of HdI by the status of MGMT-met alone. Pts treated by HdI showed significantly longer PFS in Group A (p = 0.003), B (p = 0.047), D (p = 0.0006) but not in Group C (p = 0.141). These results demonstrated that MGMT-met is a predictor of efficacy of TMZ but not PAV, even though PAV also includes alkylating agents. In MGMT-met(−) cases, concurrent effect of HdI and TMZ was observed. The superiority of HdI to cRT was not observed in MGMT-me(+) pts treated by TMZ, and decreased dose of irradiation might preserve the QOL of these pts while keeping the same effect on local control.
Conclusions: HdI was effective regardless of the status of MGMT-met. However, TMZ showed significant effect on MGMT-met(+) GBMs and decreased dose irradiation with TMZ for these pts might be recommended to keep their QOL.