to the ipsilateral neck only failed in the contralateral neck while 2/108 (2%) of those treated with bilateral techniques failed in the contralateral neck. The neck failure rate for patients with N0/N1 disease treated with bilateral techniques that included the posterior neck was 4/29(14%). When posterior neck treatment was omitted the failure rate was 18/65(28%) with 10/18(56%) of these failures in zone V. No patients failed in the lower neck (zone IV).

Conclusions: Local control rates for patients with SCSP in this series were unsatisfactory and support our contemporary practice of more intensive radiotherapy dose schedules than those administered during this study era. Patterns of lymph node failure confirm the need for bilateral neck treatment that also includes the posterior neck zones. Treatment to zone IV in the lower neck appears unnecessary in N0 patients.

135 POSTER

The effect of STI 571 on deoxycytidine kinase activity in head and neck squamous cell carcinoma in vitro: clinical implications

I. Bruce[1,3], T.H. Ward[1], J.J. Homer[2,3], N.J. Slevin[2]. [1]*Paterson Institute for Cancer Research, Drug Development, Manchester, United Kingdom;* [2]*Christie Hospital, Clinical Oncology, Manchester, United Kingdom;* [3]*Manchester Royal Infirmary, Otolaryngology, Manchester, United Kingdom*

The biological agent STI 571 is a 2-phenyl aminopyrimidine derivative that was designed to be effective against CML via inhibition of bcr-abl tyrosine kinase. The drug is known to inhibit 2 further tyrosine kinases to date, namely PDGFR and c-kit. Recently the authors have demonstrated gleevec to have a growth inhibitory effect on Head and Neck Squamous Cell Carcinomas (HNSCCs). Combinations of STI 571 with other routinely used chemotherapeutic agents were assessed using a 2 dimensional 96 well assay and the results were displayed using a 3-D model. STI 571 was found to display significant antagonism when used in combination with gemcitabine across a panel of 6 HNSCCs. Gemcitabine requires phosphorylation by deoxycytidine kinase prior to incorporation into DNA and RNA. The authors hypothesised that the basis of this observed antagonism might be deoxycytidine kinase inhibition. A deoxycytidine kinase assay using [3H] deoxycytidine was used to assess activity. Deoxycytidine phoshorylation by thymidine kinase was obviated by the addition of thymidine too the reaction mixture. Enzyme activity was recorded and a correlation was seen between activity and gemcitabine toxicity. Further testing demonstrated a dose dependant inhibition of deoxycytidine kinase activity by STI 571. This study highlights in deoxycytidine kinase a new potential target for STI 571 inhibition. This suggests that STI 571 has a more widespread action on kinase pathways than as yet understood. Future clinical usage of STI 571 in HNSCCs will almost certainly lead to resistance and if the mechanism involves upregulation of deoxycytidine kinase the possibility of collateral sensitivity to gemcitabine should be considered.

136 POSTER

Phase II trial of Docetaxel (D) and Cisplatin (C) combination in locally advanced undifferentiated carcinoma of nasopharyngeal type (UCNT)

M. Yamouni[1], Y. Beldjillali[1], I. Lahfa[1], K.A. Benhadji[1], B. Larbaoui[1], M. Brahimi[2], M. Ait-Said[2], L. Djellali[1], K. Bouzid[3]. [1]*CHU Oran, Department of Medical Oncology, Oran, Algeria;* [2]*Aventis Pharma, Algiers, Algeria;* [3]*EHS Pierre & Marie CURIE Center, Department of Medical Oncology, Algiers, Algeria*

Aim of the study: To asses the antitumoral efficacy and the toxicity of neoadjuvant DC in patients (pts) with locally advanced UCNT (WHO type 3).

Patients & Methods: Previously untreated pts with histologically diagnosed locally advanced UCNT (Stage IVA and IVB TNM/UICC 1997) were enrolled between august 2001 and august 2002 in this phase II study. Pts received D 75 mg/m 2 and C 75 mg/m2 both on day 1. Cycles repeated every 21 days. Every pt received three cycles in a neoadjuvant setting. Before radiotherapy (4 to 6 weeks after the third cycle of DC), pts were evaluated by clinical examination, nasofibroscopy with biopsy and CT scan of nasopharynx.

Results: All pts were evaluable for efficacy and toxicity. There are 65 pts (46 male, 19 female) with a median age of 41 years (range 18 69) and a performance status (WHO) of 0-1 in 61 pts, 2 in 4 pts. Fourteen pts had stage IVA and 51 pts had stage IVB. Response rates for the 65 pts were: complete pathologic response 44%, partial response 46%, stable disease 7% and progression 3%. The overall response rate (ORR) was 90%. After 195 cycles, grade 3 & 4 toxicity (WHO) were: neutropenia (15.5%), febrile neutropenia (3%), anemia (1.5%), nausea and vomiting (23%), diarrhea (7%), mucositis (1%), reversible alopecia (71%). Two pts had oncolysis.

Conclusion: DC is an effective regimen with an acceptable safety profile in locally advanced UCNT.

137 POSTER

Advanced tumors of the skull base. Diagnostic, clinical and therapeutic features.

A.M. Mudunov[1], E.G. Matyakin[1], O.M. Meluzova[2]. [1]*Blokhin's Cancer Research Centre, Upper Aerodigestive Tract Tumors, Moscow, Russian Federation;* [2]*Blokhin's Cancer Research Centre, X-Ray Diagnostic Methods, Moscow, Russian Federation*

Introduction: tumors of the skull base are one of the most difficult nosological forms among others in head and neck due to the complex topography, absence of clear clinical picture and therapeutic tactic, difficulties of surgical intervention owing to the combined lesion of several anatomic zones and consequently low survival rate and disease-free follow-up.

Material and methods: 320 patients with various tumors of the skull base were treated at our clinic for the period within 1980-2003. 146(45.6%) pts out of them with various malignant tumors of paranasal sinuses and nose cavity (including 12(3.7%) with esthesioneuroblastoma), 167(52.2%) with the soft-tissue tumors of parapharyngeal localization, 4(1/2%) primary tumors of the orbit, 3(1%) advanced skin cancer spreading into the skull base. Cure tactic depended on histologic type, tumor spreading and localization. Main diagnostic procedures were CT, MRI scanning, ultrasound, in some cases angyography, endoscopy, aspiration biopsy and postoperative histology.

Results: 18 (5.6%) pts mainly with mesenchymal tumors and primary skull base cancer had chemoradiotherapy as the first step procedure with subsequent surgery. 36 (11.2%) pts had palliative chemoradiotherapy with 27.7% complete clinical response. Combined treatment modality (radiotherapy + surgery) performed in 48 (15%) cases of epithelial cancers. 44 (13.7%) pts had palliative radiotherapy with 6.8% complete clinical response. 223 patients had an operation. Extended surgery performed in 71 (31.8%) cases with combined resections of maxilla at one or both sites, orbit, ethmoidal cells, walls of frontal and sphenoid sinuses, dura mater. 27 (8.4%) pts had intracranial tumor spreading into anterior, middle and/or posterior cranial fossa. In these cases combined craniofacial approach performed for radical surgery with subsequent plastic reconstruction of the dura defect by pericranial or myofascial flap. Liquorrhea developed in 2 (7.4%) cases. An external neck approach was quiet enough for total removal of parapharyngeal tumors (160 pts) located basically in the limits of infratemporal fossa. 27 (8.4%) pts with advanced primary tumors had different treatment failures such as local recurrence or distant metastasis.

Conclusions: preoperative chemoradiotherapy in advanced non-epithelial tumors of the skull base allows to achieve significant regress of the primary site and to increase resectability. Application of CT and MRI allows in most cases detect correct diagnosis, especially in benign tumors, estimate tumor spreading and connections to the main anatomic formations of the head and neck (blood vessels, nervous branches, brain and spinal cord), plane further surgery volume and adequate cure. Intracranial tumor spreading required combined craniofacial approach with the purpose for radical surgery.

138 POSTER

Tumors of maxilla defeating the orbit.

U.T. Holtaev, R.I. Azizyan. *Blokhin's Cancer Research Centre, Upper Aerodigestive Tract Tumors, Moscow, Russian Federation*

Introduction: Anatomic feature of accessory nasal sinuses and their correlation with walls of orbit are actual problem of tumor pathology of orbit.

Material and methods: 286 patients with tumor of maxilla have been treated in department of Upper Aerodigestive tract tumors at the N.N.Blokhin's Cancer research center RAMS during 1980-2002 years. Defeat of orbit was observed in 80(28%) patients. Different morphological forms of cancer have been identified in 47 cases: squamous cell cancer in 30(63,8%) patients, transepithelial cancer 6(12,8%), adenocystic cancer 9(19,2%), adenocarcinoma 2(4,2%). In other cases we observed following tumors: sarcoma in 13 patiehts, esthezyoneuroblastoma-10, melanoma-2, benign tumors and pseudotumors of orbit - 7 patients.33 patients have been treated by combined method, 10 by complex, 1 by surgery, 18 by chemoradiotherapy, 13 by only radiotherapy, 5 by palliative chemotherapy.

Results: Operative intervention have been performed in 44 patients. Resection of maxilla with ecsenteration of orbit have been done in 27(61%) patients. Different volum of resections of maxilla with preserving of eyeball have been performed in 17(39%) patients. Resections of the lower wall of the orbit with simultaneous plastic reconstruction (Kyonig type) using m.temporalis have been done in 7 patients.

Conclusions: Above mentions allows to considers, that study of clinical course and elaborate new approach to combined and complex of treatment patients with malignant tumors of accessory nasal sinuses with defeating orbit are actual problem

139 POSTER

The impact of prognostic factors and treatment on the outcome of anaplastic carcinoma of thyroid.

A. Mahmud[1], J. Tonita, G. Kaban, C. MacDonald, R. Alvi, A. Kirby. [1] *Allan Blair Cancer Centre, Radiation Oncology, Regina, Canada;* [2] *Saskatchewan Cancer Agency, Epidemiology, Regina;* [3] *College of Medicine, Surgery, Regina;* [4] *College of Medicine, Health Sciences, Saskatoon;* [5] *Saskatchewan Cancer Agency, Epidemiology, Saskatoon;* [6] *Pasqua Hospital, Pathology, Regina*

Background: To assess the outcome of anaplastic carcinoma of thyroid and analyse the treatment and/or other factors influencing the prognosis.

Materials and Methods: Cases of anaplastic carcinoma of thyroid were identified from the population based Saskatchewan cancer registry.A detailed chart review was conducted.For the cases with a suvival of more than or equal to two years, pathological material was reviewed, where possible.Survival was calculated using Kaplan Meier method and log rank test to compare the groups.

Results: 21 out of 107 cases, initially identified were excluded. The reasons included a coding error, diagnsis at autopsy, based on a pathology review or absence of histological documentation Observed one, two and five year survival was 23%, 12% and 7% respectively. The difference in survival between the sexes was not statistically significant. However after 2 years, females had a slightly better survival trend. Patients with small cell morphology had a better survival versus large cell in 50 evaluable cases (p=0.0271).There was a survival advantage for the patients who underwent a surgical procedure compared to to the group that underwent biopsy alone(p=0.0011). Patients with total thyroidectomy fared better versus lobectomy.An advantage was seen for the patients who received radiation therapy (p=0.0563).A better survival was observed among the patients receiving the higher dose (>4000 cGy) compared to those with the lower dose (<4000 cGy), (p=0.0337). The patients having surgery alone or surgery in combination with radiation therapy fared better than radiation therapy alone (p=0.0051).

Conclusion: Prospective trials of a rare disease entity such as anaplastic thyroid ca. are extremely difficult. Retrospective reviews like this can help in improving the therapeutic approach. It is recommended based on this observational data to combine a higher dose of radiation therapy with total thyroidectomy, where possible, when managing the anaplastic carcinoma of thyroid.

140 POSTER

Prognostic factors of overall survival for patients with recurrent head and neck cancer: a retrospective study.

L. Chaigneau[1], T. Nguyen[1], U. Stein[1], E. Guardiola[1], A. Danzon[2], P. Bontemps[3], X. Pivot[1]. [1] *CHU Minjoz, Medical Oncology, Besançon, France;* [2] *CHU Minjoz, Doubs Cancer Registry, Besançon, france;* [3] *CHU Minjoz, Radiotherapy, Besançon, france*

Background: The aim of the present study was to determine the clinical prognostic factors for overall survival from recurrence (OSR) in patients with recurrent head and neck squamous cell carcinoma.

Material and methods: Using data recorded in the Doubs Cancer Registry between 1983 and 1998, 309 patients were analysed. The major characteristics were: primary tumor size T1-2 49.8%, primary nodal involvement 63.8%, exposure to radiotherapy during treatment of primary tumor 88.7%, performans status at recurrence date PS0-1 27.8%, local-regional relapse 75.4% and distant recurrence 24.6%. The median disease free survival (DFS) was 10.2 months (range: 1.2 - 157).

Results: The median OSR was 6.6 months (range: 0.1 - 158). The univariate analysis identified as pronostic factors for OSR duration the following parameters: size of primary tumor (T1-2 versus T3-4: $p < 6$ months versus > 6 months: $p = 0,01$), performans status (≥ 2 versus < 2: $p = 0,0001$) at the relapse and type of relapse (loco-regional versus metastatic recurrence: $p = 0,004$). In the multivariate analysis, size of primary tumor ($p = 0.002$), primary lymph nodes involvement ($p = 0.04$), DFS ($p = 0.01$), performans status at the relapse ($p = 0.001$) and type of relapse ($p = 0.007$) remaind significant pronostic factor for the OSR duration.

Conclusion: These prognosis factors are relevant to understand the results of phase II and to encure a fairer comparative evaluation during randomized studies.

141 POSTER

A phase II feasibility study of concurrent radiotherapy and gemcitabine for patients with cancer of the head and neck.

J. Van Den Brande[1], M. Rasschaert[1], D. Van den Weyngaert[2], C. Van Laer[3], J. Dyck[1], P. Wilmes[1], B. Pauwels[1], J.B. Vermorken[1]. [1] *University Hospital Antwerp, Medical Oncology, Edegem, Belgium;* [2] *Middelheim Hospital, Radiotherapy, Antwerp, Belgium;* [3] *University Hospital Antwerp, Otolaryngology, Edegem, Belgium*

Background: Gemcitabine (G) has excellent radiosensitizing properties, shown both in preclinical and clinical studies. In addition the drug is active in squamous cell head and neck (HN) cancer. Purpose of the study:1) to study the feasibility of weekly G concomitantly with radiotherapy (RT) in patiens (pts) with tumours in the HN site, 2) to study the safety profile, 3) to assess the antitumour activity of the combination.

Methods: based on previous experiences in phase I studies (Eisbrüch et al. ASCO 1997, 1998) we started in 12.98 with a weekly dose of 100mg/m^2 (given i.v. over 30 min). Eligible were pts with locally advanced tumors of the HN (recurrent (rec) or primary) not amenable to curative surgery (S) with adequate bone marrow, renal and hepatic function and in acceptable condition (Performance status (PS): 0,1,2), who gave consent. Prior use of RT or CT was permitted if discontinued > 4 weeks. Response evaluation (eval) was done according to WHO, toxicity to NCI-CTC.

Results: so far 31 pts entered the study, median age 59 yrs (range 44-80yrs), PS 1 (0-2). Tumor sites: pharynx 21, larynx 4, thyroid 2, oral cavity 1, paranasal sinus 1, primary unknown (TuN3M0)1, melanoma 1. Apart from the Tu and melanoma tumor stages were: 1 stage II (rec), 5 stage III (1 rec), 23 stage IV (3rec). Four pts were not evaluable for resp: 1 was not eval., 2 stopped early (1 unrelated death, 1 refusal), 1 had primary surgery. The median RT dose was 70 Gy (range 50-84.75), the median number of G cycles was 7 (range 2-8). 29 pts were evaluable for toxicity. Five pts were not eval. for pharyngitis, because of preexisting toxicity. Grade (gr.) 3 hematologic toxicity was rare: 2 pts gr. 3 leukopenia and 1 gr. 3 thrombocytopenia. Severe (gr.3/4) mucositis was seen in 83%, dermatitis in 61%, dysphagia in 75%, pain in 18%. Most (77%) pts received tube feeding, prior or during therapy. Response evaluation: 3/3 rec. disease pts responded (1CR) and all of primary disease pts did (10 CR).

Conclusion: RT + G is toxic, but tolerable and highly active.

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Phase II study of imatinib mesylate in salivary gland adenoid cystic carcinoma

E. Winquist[1], E. Lamont[2], S. Hotte[1], M. MacKenzie[1], S. Brown[1], A. Murgo[3], L. Siu[1]. [1] *Princess Margaret Hospital Phase II Consortium, Toronto, Canada;* [2] *University of Chicago, Chicago, USA;* [3] *Cancer Therapy Evaluation Program, Rockville, USA*

Background: The goal was to assess the antitumor activity of imatinib in adenoid cystic carcinoma of the salivary gland (ACC) expressing *c-kit*. ACC accounts for 22% of malignant salivary gland tumors, arises most commonly from the minor salivary glands & often recurs after local therapy. Pulmonary metastases are present in 40% of pts. The clinical course is often indolent & typical survival is 73% at 5 yrs, 45% at 10 yrs & 35% at 15 yrs. The response rate & duration to conventional cytotoxic agents is sub-optimal. A high level of *c-kit* expression has been identified in 90% of ACCs (Holst 1999). Imatinib specifically inhibits autophosphorylation of the *bcr-abl*, PDGFR-*beta* & *c-kit* tyrosine kinases & inhibits the growth of ACC cell lines *in vitro* (Ward 2002).

Materials and methods: In a single-arm 2-stage phase II clinical trial, adult pts with histologically documented unresectable or metastatic ACC measurable by RECIST criteria & with immunohistochemical expression of *c-kit* were treated with imatinib 400 mg PO bid repeated every 4 weeks. Doses were reduced for gr 3-4 or intolerable gr 2 toxicity. Response was assessed every 8 weeks.

Results: Fourteen pts have received 30 cycles of therapy (9 female & 5 male). Median age is 50 years (range, 31-69). Median ECOG PS 1 (range, 0-2). Twelve pts had lung metastases. Eleven had prior radiotherapy &