

UR:20.3), and median overall survival was not reached (R: not reached, UR:32.8).

Conclusions: Modified neoadjuvant TPF followed by CT/RT has demonstrated satisfactory activity and favourable tolerance in LAHNC, with encouraging organ preservation rate.

8521

POSTER

Treatment-related toxicities in patients with squamous cell carcinoma of the head and neck (SCCHN)

M. Ulcickas Yood¹, P. Feng Wang², Z. Zhao², S. Hensley Alford³, S. Oliveria¹, K. Wells³, S. Phillips¹, H. Ali⁴, C. O'Malley². ¹EpiSource LLC, NIA, Hamden, USA; ²Amgen, Global Epidemiology, Thousand Oaks, USA; ³Henry Ford Health System, Biostatistics and Research Epidemiology, Detroit, USA; ⁴Henry Ford Medical Group, Oncology, Detroit, USA

Background: Little information is published from real-world clinical practice on treatment-related toxicities among patients with squamous cell carcinoma of the head and neck (SCCHN). Although randomized clinical trials report treatment-related toxicities, the treatment patterns and patient populations in clinical practice are more heterogeneous than those in clinical trials.

Materials and Methods: We used a population-based tumor registry at a large, US health system, to identify all cases of stage III or IV SCCHN diagnosed from 2000 to 2006. We identified the incidence/severity of acute and late toxicities associated with SCCHN treatment from detailed medical record review of health system encounters, including physician notes. Acute and late toxicities were evaluated using Common Terminology Criteria for Adverse Events (CTCAE3) criteria and Radiation Therapy Oncology Group/ European Organization for Research and Treatment of Cancer (RTOG/EORTC) late radiation morbidity scoring scheme, respectively. The incidence and severity of toxicities are presented by treatment. Detailed analyses according to tumor stage and location, grade, and acute versus late events were examined.

Results: We identified 195 patients with SCCHN: 104 patients (53%) received chemotherapy (chemo) + radiation therapy (RT); 87 (45%) received RT only; four patients (2%) received chemotherapy only or other/no treatment.

Table 1. Adverse Events of Interest (grade 2–4) by Treatment Received (N = 191*)

Adverse Events	Total (n = 191) n (%)	Chemo+RT (n = 104) n (%)	RT only (n = 87) n (%)
Gastrointestinal	160 (83.8)	89 (85.6)	71 (81.6)
Xerostomia	61 (31.9)	41 (39.4)	20 (23.0)
Dysphagia	70 (36.6)	44 (42.3)	26 (29.9)
Dermatology	91 (47.6)	54 (51.9)	37 (42.5)
Pulmonary	74 (38.79)	41 (39.4)	33 (37.9)
Aspiration pneumonia	62 (32.5)	37 (35.6)	25 (28.7)
Dehydration	43 (22.5)	29 (27.9)	14 (16.1)
Subcutaneous tissue	30 (15.7)	18 (17.3)	12 (13.8)
Infection	29 (15.2)	21 (20.2)	8 (9.2)
Renal/Genitourinary	19 (9.9)	14 (13.5)	5 (5.7)
Auditory	16 (8.4)	12 (11.5)	4 (4.6)
Bone	4 (2.1)	3 (2.9)	1 (1.1)

*Four patients received chemotherapy only or other/no treatment

Conclusions: Findings from this study reveal that treatment-related toxicity in patients with advanced SCCHN is common. The addition of chemotherapy to radiation is associated with increased risk treatment-related toxicities. These data provide real-world incidence rates of toxicity as observed in clinical practice.

8522

POSTER

Particle therapy for mucosal malignant melanoma of the head and neck: a retrospective study

D. Miyawaki¹, M. Murakami², Y. Demizu², M. Mima², K. Terashima², T. Arimura², Y. Niwa², R. Sasaki¹, K. Sugimura³, Y. Hishikawa². ¹Kobe University Graduate School of Medicine, Radiation Oncology, Kobe, Japan; ²Hyogo Ion Beam Medical Center, Radiology, Tatsuno, Japan; ³Kobe University Graduate School of Medicine, Radiology, Kobe, Japan

Background: Mucosal malignant melanoma (MMM) of the head and neck is resistant to conventional photon (X-ray or gamma-ray) radiotherapy. Particle therapy including proton therapy and carbon-ion therapy may be useful for the treatment of MMM because of its ability to deliver high dose to tumors while minimizing the dose to risk organs. Moreover, carbon-ion is supposed to be effective against MMM according to the results of biologic experiments. The purpose of this study was to assess the efficacy and toxicity of particle radiotherapy for MMM of the head and neck at Hyogo Ion Beam Medical Center retrospectively.

Materials and Methods: Between February 2002 and April 2008, 73 patients with MMM of the head and neck were treated with particle therapy. Forty seven of 73 patients had no treatment before the particle therapy, whereas 25 had undergone surgery and/or chemotherapy, and 1 surgery and photon radiotherapy. Fifty two patients received proton therapy and 21 patients received carbon-ion therapy. The total dose of proton therapy was ranging from 65 to 70.2 GyE (median, 65 GyE) in 26–28 fractions and the total dose of carbon ion therapy was ranging from 57.6–64 GyE (median, 57.6 GyE) in 16 fixed fractions. Primary tumor sites were nasal cavity in 43, maxillary sinus in 9, ethmoid sinus in 7, palate in 5, and others in 9. Overall and progression-free survivals, and local control were evaluated using the Kaplan-Meier method. Acute and late morbidities were assessed based on the Common Terminology Criteria for Adverse Events (CTCAE) v3.0. The median follow-up was 19 months (range, 5–62 months).

Results: The 2-year overall survival and progression-free survival rates were 62% and 28%, respectively. Six patients experienced local recurrence and the 2-year local control rate was 82%. Thirty three patients experienced distant metastases (lymph node, bone, lung, etc.). Within 1 year, 35 patients (48%) developed distant metastases. Grade 3 acute reactions were observed in 21 patients (mucositis in 17, dermatitis in 2, and otitis media in 2); however, no patients discontinued the treatment. Grade 4 late adverse effect was observed in 1 patient (visual loss).

Conclusions: Particle radiotherapy showed favorable outcome for local control of MMM of the head and neck. As for distant metastasis, however, even the patients with early stage MMM (T1–2) developed multiple metastases even though the primary tumors are controlled. The current multidrug chemotherapy has limited effects on distantly recurrent patients and good treatment to address this problem is awaited.

8523

POSTER

Pretreatment fluorodeoxyglucose positron emission tomography as predictive factor for the outcome of head and neck cancer patients

A. Farrag¹, G. Ceulemans², M. Voordeckers³, H. Everaert², G. Storme³. ¹Assiut University Hospital, Clinical Oncology, Assiut, Egypt; ²UZ Brussel, Department of Nuclear Medicine, Brussels, Belgium; ³UZ Brussel, Department of Radiation oncology, Brussels, Belgium

Background: The aim of this study was to determine if fluorodeoxyglucose positron emission tomography (FDG-PET) uptake assessment before treatment can be used as an additional predictive factor for outcome in head and neck cancer patients receiving radiotherapy by helical tomotherapy (Hi-Art Tomotherapy®) ± chemotherapy.

Methods and Materials: Between June 2005 and March 2008, 58 patients with a biopsy proven head and neck cancer (HNC) were treated with radiotherapy at the UZ Brussel. All patients underwent a baseline FDG-PET before treatment. The maximum standardized uptake value (SUV_{max}) within the lesion was considered as a semi-quantitative measure representing the most metabolic active part of the tumor.

Results: The Median SUV_{max} = 7.92. SUV_{max} for patients who died was significantly higher than living patients (9.16 vs. 7.32, respectively, p=0.037). The median SUV_{max} was chosen as a cutoff value to categorize the patients into 2 separate groups with low and high SUV_{max}. 3-years Overall survival (OS) was 80% vs. 54% (p=0.009) and disease free survival (DFS) was 83% vs. 41% (p=0.018) for low and high SUV_{max} groups, respectively. Multivariate analysis also confirmed these observations. In multivariate analysis, included the SUV_{max}, Karnofsky performance status, AJCC stage and chemotherapy use, SUV_{max} was the only factor which showed significant difference in outcome. The 3-y OS (p=0.015), and DFS (p=0.027) were in favor of the low SUV_{max} group.

Conclusion: PET-FDG scan before treatment is a good predictor of outcome in HNC patients. Future work on a larger number of patients is warranted to determine SUV_{max} cut off value which could be used for early identification of patients with poor treatment outcome for perhaps other therapeutic approaches.

8524

POSTER

Expression of BRAK/CXCL14 is associated with antitumor efficacy of gefitinib in head and neck squamous cell carcinoma

R. Hata¹, S. Ozawa², Y. Kato¹, S. Ito¹, R. Komori³, N. Shiiki⁴, K. Tsukinoki⁴, Y. Maehata⁵, E. Kubota². ¹Kanagawa Dental College, Biochemistry and Molecular Biology, Yokosuka, Japan; ²Kanagawa Dental College, Oral and Maxillofacial Surgery, Yokosuka, Japan; ³Kanagawa Dental College, Pediatric Dentistry, Yokosuka, Japan; ⁴Kanagawa Dental College, Pathology, Yokosuka, Japan; ⁵Kanagawa Dental College, Pharmacology, Yokosuka, Japan

Background: The clinical efficacy of gefitinib (ZD1839, Iressa), which is an inhibitor specific for the epidermal growth factor (EGF) receptor

tyrosine kinase, has been demonstrated in non-small cell lung carcinoma patients with EGF receptor mutations, and so these mutations are a useful marker(s) to find responders to this drug. However recent studies showed that the EGF receptor gene mutation is rare in squamous cell carcinomas of the esophagus and head and neck regions. In the present study we investigated the relationship between BRAK expression and gefitinib efficacy for tumor suppression.

Material and Methods: HNSCC cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) containing 10% fetal bovine serum. Nearly confluent cells were cultured overnight in serum-free DMEM. After starvation, they were incubated with or without EGF (10 ng/ml) and/or gefitinib (1 μ M). HSC-3 cells were subcutaneously injected into athymic nude mice. Tumor cell-xenografted mice were daily administered gefitinib (50 mg/kg) orally. In some experiments, tumor cells were introduced BRAK ShRNA expressing vector to knockdown BRAK mRNA expression and established stable transformants.

Results: Gefitinib attenuated the effect of EGF, or even stimulated BRAK mRNA expression of HNSCC cells *in vitro*. Oral administration of gefitinib significantly ($P < 0.001$) reduced tumor growth of xenografts in female athymic nude mice accompanied by increased in BRAK expression specifically in tumor tissue. Introduction of BRAK ShRNA vector reduced both the expression of BRAK in the cells and the antitumor efficacy of gefitinib *in vivo*.

Conclusions: Our results indicate that oral administration of gefitinib reduced tumor size, at least in part, through elevation of BRAK expression. Thus, the use of gefitinib for treatment of patients with HNSCC in whom there is an inducing effect of the drug on the BRAK expression in cancer cells in culture may be advantageous. Furthermore, BRAK may be a promising molecule for gene therapy of HNSCC.

This work was performed in collaboration with Drs. Takahide Taguchi, Yukari Imagawa-Ishiguro and Mamoru Tsukuda, Department of Biology and Function in the Head and Neck, Yokohama City University Graduate School of Medicine.

8525

POSTER

Prediction of pathological response of preoperative 5-fluorouracil-based chemotherapy for oral cancer

M. Nakazawa¹, R. Takabatake¹, T. Meshii¹, S. Iwai¹, I. Kato¹, K. Amino², N. Takeuchi³. ¹Osaka University Dental Hospital, Oral & Maxillofacial Surgery, Osaka, Japan; ²Nishinomiya Central Municipal Hospital, Oral & Maxillofacial Surgery, Nishinomiya, Japan; ³Matsubara Tokushuikai Hospital, Oral & Maxillofacial Surgery, Matsubara, Japan

Background: The response of chemotherapy is individually different in patients with oral squamous cell carcinoma (OSCC). Prediction of chemotherapy response is very important to select adequate therapy for every patient. We retrospectively investigated the relationship between chemotherapy response and expression of biomarkers in OSCC patients who received 5-fluorouracil (5-FU) based chemotherapy and following radical surgery. The aim of this study is to make the formula which predicts chemotherapy sensitivity using some biomarkers.

Material and Methods: Retrospective analysis of biomarker expressions in biopsy specimen was performed immunohistochemically in 95 OSCC patients. These received 5-FU based chemotherapy such as TS-1@cisplatin, UFT@cisplatin, etc. We use 17 biomarkers including dihydropyrimidine dehydrogenase (DPD), thymidylate synthase, EGFR, cyclinD1, Ki-67, c-Met, MMP-1, MMP-2, MMP-9, TIMP-1, TIMP-2, Bax, Bcl-2, CD25, Foxp-3, Caveolin-1. The expression of these biomarkers were evaluated by staining intensity or percentage of positive cells. Pathological effects were evaluated in surgical specimens. We compared these 2 factors and selected significant biomarkers which had association with chemotherapy response. Statistical analysis was performed using Spearman's correlation coefficient test and logistic regression model.

Results: There was a statistically significant relation between the expression of five biomarkers (DPD, VEGF, MMP-2, Ki-67 and Bcl-2) and the pathological response for 5-FU based chemotherapy. The formula which predicts chemotherapy sensitivity was made by logistic regression model consisted of above five markers. We applied this formula to another 14 OSCC patients for verifying its accuracy. In consequence, the accuracy rate was 85.7%.

Conclusions: The expression of DPD, VEGF, MMP-2, Ki-67 and Bcl-2 were independent predictor for sensitivity of 5-FU based chemotherapy. The combination of these biomarkers was useful for predicting chemotherapy response. The formula was applicable for OSCC patients before chemotherapy and realized high accuracy to predict chemotherapy response.

8526

POSTER

The tumour volume for F-18 fluorodeoxyglucose predicts for response to treatment and progression free survival biomarker in head and neck cancer

Y.M. Seol¹, Y.J. Choi¹, M.G. Song¹, B.R. Gwon¹, J.S. Chung¹, G.J. Cho¹. ¹Pusan National University Hospital, Internal Medicine, Busan, South Korea

Purpose: To evaluate the prognostic value of metabolic tumor volume measured on 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) imaging and other clinical factors in patients treated for locally advanced head-and-neck cancer (HNC) at a single institution.

Materials and Methods: Between June 2005 and August 2008, fifty nine patients with HNC who underwent pretreatment FDG-PET studies received neoadjuvant chemotherapy and radiation therapy. Metabolically active tumor regions were delineated on pretreatment PET scans by a fixed SUV of 2.5. We evaluated the relationship of 18F-fluorodeoxyglucose-PET maximum standardized uptake value (SUV) and metabolic tumor volume (MTV) with response to treatment, progression-free survival (PFS) and overall survival (OS).

Results: The average SUVmax was 8.9 (range, 1.4–78.0) and the mean MTV was 23.5 cm³ (range, 1.2–170.8) for all patients. Higher MTV was associated with an increased risk of lymph node metastasis at diagnosis ($p = 0.028$) and response to treatment ($p = 0.026$). A Cox proportional-hazards model for progression free survival from head and neck cancer was used to evaluate sex, age, organ, stage, T-stage, lymph node metastasis, MTV, and SUVmax and neoadjuvant chemotherapy type. The results indicated that MTV was the only significant independent factor ($p = 0.021$).

A higher MTV of 9.3 cm³ (median MTV) was significantly associated with an increased hazard of recurrence (2.19-fold, $p = 0.007$). We did not find a significant relationship of maximum SUV, stage, or other clinical factors with response to treatment or PFS or OS.

Conclusions: Metabolic tumor volume is an adverse predictive factor for treatment response and disease progression in HNC. MTV is a direct measure of tumor burden and is a potentially valuable tool for risk stratification and guiding treatment in future studies.

8527

POSTER

A phase II trial of erlotinib after gemcitabine plus platinum-based chemotherapy in patients (pts) with recurrent and/or metastatic nasopharyngeal carcinoma (NPC)

B. You¹, C. Le Tourneau¹, E.X. Chen¹, S.F. Chin¹, L. Wang¹, A. Jarvi¹, R.R. Bharadwaj¹, S. Kamel-Reid¹, B. Perez-Ordóñez¹, L.L. Siu¹. ¹Princess Margaret Hospital, Drug Development Program, Toronto Ontario, Canada

Background: Although chemotherapy with a platinum compound and gemcitabine (G) is effective in recurrent and/or metastatic NPC, the outcome remains poor with time-to-progression (TTP) <1 year. The epidermal growth factor receptor (EGFR), expressed in 85% NPC, is associated with poor prognosis. We conducted a phase II study to determine the efficacy of the EGFR tyrosine kinase inhibitor erlotinib, given as maintenance therapy, following cisplatin (C) or carboplatin (Ca) + G in pts with recurrent and/or metastatic NPC.

Methods: Pts were treated with up to 6 cycles of chemotherapy (G 1000 mg/m² day 1 and 8, C 70 mg/m² day 1 or Ca AUC=5 day 1 if contraindication to C) every 3 week. Pts were switched to erlotinib 150 mg PO daily Q4W after 6 chemotherapy cycles, or before if they progressed on chemotherapy. Primary endpoint was TTP in non progressive disease (PD) pts after 6 chemotherapy cycles and treated with maintenance erlotinib. EBV DNA plasma levels were measured using qRT-PCR.

Results: Of 20 pts, 1 pt never started chemotherapy. Median follow-up was 5.8 months. Pts characteristics were: M:F=13:7, asian:non-asian = 14:6, median age 56 [range 32–72], PS 0:1 = 10:10, locoregional recurrent:metastatic = 6:14. With G, 8/20 pts (40%) and 12/20 (60%) were treated with C and Ca, respectively. After 96 chemotherapy cycles, the most frequent grade 3/4 adverse events (AE) were neutropenia (63%), thrombocytopenia (47%) and anemia (21%). Of the 19 pts evaluable for response to chemotherapy, 7 pts had a PR (35%), 11 SD (58%) and 1 PD (6%). Of them, 15 pts received 36 cycles of erlotinib (median = 2, range = 0–6). The most frequent grade 3 AE related to erlotinib were lymphopenia (26%), acneiform rash (20%), hand-foot syndrome (13%), neutropenia (13%) and fatigue (7%). No grade 4 toxicity was observed. Of 11 pts evaluable for response to erlotinib, all progressed except 3 pts (27%) with stable disease for 3, 4 and 7 months. Median TTP was 6.3 months for all 17 evaluable pts, and 6.9 months for 13 pts with no PD after 6 chemotherapy cycles. One-year overall survival was 80% for all pts. No correlation between EBV DNA plasma levels or kinetics and clinical outcome was detected.

Conclusions: Maintenance or 2nd line therapy with erlotinib post-chemotherapy is not effective in recurrent and/or metastatic NPC. Historical