

treated from January 1980 to December 1989 at Ankara Oncology Hospital. Locoregional recurrence occurred in 187 (18%) of these patients within a mean disease-free period of 15 months. Age, sex, anatomical location, size of lesion, lymph node status at diagnosis, stage according to TNM classification, histopathologic differentiation, prior therapy, treatment modality, lesions arising from scar tissue (scar carcinoma), concomitant premalignant tumor of the skin, development of secondary non-melanotic skin carcinoma and second malignancy were used as variables which could be correlated with locoregional recurrent disease. No correlation was found between development of recurrence and prior treatment, second non melanoma skin cancer, second malignancy, premalignant skin tumor, sex or regional lymph node dissection. Although univariate analysis demonstrated that location, size, lymph node status, stage, histologic differentiation, scar carcinoma and treatment modality were associated with an increased risk of locoregional recurrence, it was found out that stage of the disease ($P < 0.001$), treatment modality ($P < 0.01$), tumor arising from scar tissue ($P < 0.01$) and histologic differentiation ($P < 0.05$) were statistically significant as risk factors of recurrence when a multivariate analysis was applied.

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POSTER

CHEMOTHERAPY (CT) WITH RADIOTHERAPY (RT): LARYNX PRESERVATION STRATEGY IN CERVICAL SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS (CSCCE)

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In order to evaluate a new strategy to increase long term survival avoiding laryngoesophagectomy (LE), from 5/1985 to 12/1993, 37 pts with CSCCE were treated with combined CT (CDDP 100 mg/sqm, day 1, FU 1000 mg/m²q, day 1-4 in 96 h infusion) every 4 week for 4-5 courses and RT (split course in 27 pts: 30 Gy days 1-19, 20 Gy days 67-78; continuous in 10 pts: 60 Gy). LE was limited to pts with resectable residual disease at the end of the treatment program or local relapse after initial CR. Characteristics of pts were: median age 62 yrs, range 46-78, stage I: 4 pts, stage II: 13 pts, stage III: 20 pts (resectable 9/20). Response was documented in 33 of 34 evaluable pts (97%) with CR in 24 pts (71%). Three cases were not evaluable: fistula, toxic death and severe myelosuppression. As of January 1995, 13 pts are alive with a total 5 yrs survival of 32%. Relapses were observed in 21/34 responsive pts (local 14, distant 7). Salvage LE was performed in 6/14 local relapsed pts; 2 pts are alive at 41 and 15 mos.; two others progressed after 24 mos from LE; while the remaining pts deceased within 3 mos. All pts with stage I disease are alive and disease-free at 5 yrs, while no difference was detected between stage II (24%) and III (18%). Mortality due to toxicity of CT plus RT was 3% (1/37). In conclusion, combined CT plus RT provides at least the same expected long-term results as primary surgery but preserves the larynx in nearly one third of cases. Surgery could be advocated only in event of local relapse after failure of combined CT plus RT.

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POSTER

P53 SERUM ANTIBODIES IN HEAD AND NECK SCC

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Purpose: To determine whether a correlation existed between the presence of serum antibodies against p53 protein (SAAp53) and clinical and pathological features in a series of 80 consecutive patients with HNSCC. **Methods:** The presence of SAAp53 was studied by ELISA, and p53 gene expression in tumor samples by immunohistochemistry. **Results:** At diagnosis, 18.7% of the patients had SAAp53. Over-expression of the p53 protein was found in 54% of the tumor samples. All the patients with SAAp53 also exhibited overexpression of the p53 gene on the corresponding tumor sample ($P < 0.001$). In a univariate analysis, T stage ($P < 0.001$), nodal involvement ($P = 0.03$), the performance status (WHO ≥ 2) ($P = 0.06$), and the presence of SAAp53 ($P < 0.0001$) were significantly associated with a decrease in disease-free and overall survival, when stratified on the type of treatment. In a multivariate analysis, only T stage ($P < 0.05$) and SAAp53 ($P < 0.001$) remained significantly associated with a decrease in disease-free and overall survival. The DFS rate at 2 years was 62% when no SAAp53 were detectable, compared to 12% when SAAp53 were detectable. **Conclusion:** SAAp53 was strongly associated with clinical outcome.

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POSTER

RADIOTHERAPY FOR PRIMARY CARCINOMA OF THE CERVICAL TRACHEA: A REPORT OF 30 CASES

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Primary carcinoma of the cervical trachea is a rare malignancy whose treatment is not clearly defined. This work describes the experience of three radiation oncology centers over 30 years.

Thirty patients (pts): 27 male, 3 female, median age 61 years, presenting with carcinoma of the cervical trachea (squamous cell in 27) have been treated by irradiation, as a definitive treatment in 26 pts, median dose 60 Gy (35-70 Gy), and postoperatively in 4 pts, median dose 58 Gy. The radiation response was assessable in 19 pts: 9 complete responses (2 for a dose lower than 60 Gy vs 7 for a dose of 60 Gy or more). The 5-year overall survival rate is 29% after definitive irradiation for a dose of 60 Gy or more compared to 0% for a lower dose, and 25% after post-operative irradiation. These results raise the question of further dose escalation, using endotracheal brachytherapy and/or conformal therapy, within prospective collaborative studies.

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POSTER

5 FLUOROURACIL (FU) BLEOMYCIN (B), EPIRUBICIN (E), CISPLATIN (P) IN LOCALLY ADVANCED (LA), RECURRENT AND/OR METASTATIC (REC/MTS) UNDIFFERENTIATED CARCINOMA NASOPHARYNGEAL TYPE (UCNT) PRELIMINARY ACTIVITY/TOXICITY REPORT

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Based on accumulated efficacy and tolerance experiences (JCO 91, ASCO 91-92), in 01/92 we started a new Ph I-II study in LA and REC/MTS UCNT, combining four known active agents in UCNT. **Protocol:** FU 700 mg/m²/d CIV d1-4, B 10 mg IV d1 + 12 mg/m²/d CIV d1-4, E 70 mg/m²/d d1, P 100 mg/m²/d d5 (d1 = d21). As 3/95, 33 patients (pts) were enrolled, 23 M/10 F, mean age 50 years (15-71). **PS (WHO):** 0-1: 31, 2-3: 2, 16 pts with LA disease (T3-T4: 56%, N2-N3: 100%) (UICC-AJCC87), 8 with isolated locoregional REC, 5 MTS alone and 4 bath. **Tumor sites:** 12 nasopharynx (NP), 6 bone, 3 liver, 2 extraregional nodes (ERN), 3 lung. All REC/MTS pts were pretreated, 6 RT alone, 11 pts CT + RT, 10 of them Platinum based. **Toxicity (WHO):** 111 cycles (c) and 33 pts evaluable, Gr3-4: mucositis 20c, in 7/8 pts preirradiated locoregionally, PNN 45c (22 pts), mean duration of neutropenia brief 3 days (1-7), Hemoglobin 9c (7 pts), platelets 15c (8 pts), febrile neutropenia 10c (7 pts), Gr3 nausea-vom: 5c (3 pts), Gr2 skin 4 pts, lung 3 pts, oto 2 pts, 1 death pulmonary fibrosis, 5-FU reversible cardiomyopathy 1 pt. **Response (Res) (WHO) in LA disease (Group 1: G1) 16 pts evaluable after CT (1 CR, 14 PR, 1 NC) (ORR 94%) and 14 pts after RT (13 CR, 1 PD) (2 pts too early). In REC/MTS disease (G2) 16 evaluable (1 refusal), 4 CR and 8 PR, 35 D, 1 PD (ORR 75%). Res by site: CR liver 2/3, bone 1/6, ERN 2/2, lung 2/3, NP 4/12. In G2 median Res duration 10 m (CR = 6 + - 26+, PR = 5 + - 19). With median followup (FUP) of 16 m (4-39): G1: 11 NED (7 + - 25+), 2 AWD (13+, 22+), 1 DOD at 5 m and 2 still on treatment. G2: 4 still responding free of progression (12 + - 34+), 4 AWD (20 + - 34+). This regimen shows high CR in visceral sites, with good Res duration in the palliative setting and good activity as induction chemotherapy. A larger accrual is needed with increased FUP before comparing it with our current standard of B, E, P. (E. Cvitkovic et al., ASCO 94.)**

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POSTER

"GLUTATHIONE SYSTEM" AND CHEMORESPONSE TO 5-FLUOROURACIL AND CISPLATINE IN HEAD AND NECK SQUAMOUS CELL CARCINOMA: A PILOT STUDY

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The relationship between the glutathione system and the chemoresponse to neo-adjuvant chemotherapy (CT) commonly used (cisplatin/5-fluorouracil: CDDP/5-FU) in head and neck squamous carcinoma (HNSCC). We assayed in the total blood of 38 patients (pt) the glutathione

system before treatment (BT) and after 3 courses of CT. Objective response based on clinical examination (CE) and CT-Scan was achieved in 19/38 patients. The regression stage (RS) based on tumors histology obtained surgically ($n = 28$) after 3 courses of chemotherapy was achieved in 8/28 patients. Total glutathione (GSH), glutathione-S-transferase (GST) activity and GST- π content were assayed on cytosols of total blood. For each cycle and each pt, GST activity and GSH content were investigated by spectrophotometric assays, GST- π by Western blot. According to CE and RS, our results showed difference between non responders (NR) and objective responders pt (R) only for GST activity. The difference was significant after one course of CT [according to CE for NR (5 ± 2 nmoles/min/mg) and R (4 ± 2 nmoles/min/mg) ($P < 0.05$), according to RS for NR (5 ± 2 nmoles/min/mg) and R (3 ± 1 nmoles/min/mg) ($P < 0.01$)]. No difference were detected for GSH and for GST- π . These preliminary results suggest that GST activity plays a role in the chemoresponse of HNSCC pts. Patients with decreased GST activity may be more chemosensitive than others. Indeed, it is too early to detect some correlation between disease free and overall survival.

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403 POSTER TIME INTERVALS VERSUS PROGNOSIS IN COMBINED TREATMENT OF SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK

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The present study investigated whether clinical outcome correlated with the length of different time intervals associated with combined treatment of 186 cases of primary cancer of the oral cavity. Unexpectedly it was found that patients with short time to start of treatment had significantly worse prognosis than patients with longer time to treatment. Median survival was 27 months in the first group as compared to 77 months in the other. Further analysis revealed that in the group with short time to first treatment, significantly fewer patients received radiotherapy (RT), time intervals between surgery and RT was longer and the overall treatment time tended to be longer. From our study we conclude that a standardized combined treatment regime with careful planning of time intervals once the treatment has started, is more important to the outcome than variations in the duration of the time interval between first diagnosis and start of treatment. Patients with pre op RT had better prognosis than patients treated with post op RT. Chemotherapy did not have effect on patient survival.

404 POSTER INTERSTITIAL BRACHYTHERAPY FOR ORAL CAVITY CARCINOMA: SEARCH OF THE FACTORS RESPONSIBLE FOR LATE COMPLICATIONS

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In order to identify the factors responsible for late postradiological necrosis (l.n.) a retrospective analysis of 100 pts with a squamous cell carcinoma of the oral cavity treated with Ir-192 interstitial brachytherapy (BRT) between 1967 and 1992 has been performed. M/F ratio was 73/27, median age was 57 yrs (range 21–82). There were 82 oral tongue, 9 floor of mouth and 9 cheek mucosa pts. TNM stage was: T1-13, T2-50, T3-37, N0-65, N1-31, N2-4. Pts received 60–75 Gy (m.69.2). Linear activity of Ir-192 wires was 0.75–2.68 mCi/cm (m. 1.46). Dose rate (d.r.) range was 25–114 cGy/t (m. 57) and time of treatment was 53–280 hrs (m. 134). Overall 3-year survival was equal to 61%. At first clinical control, 2 mos after BRT, 95 pts obtained local CR. However, only 86 pts were disease-free (9 were N+). In the group of disease-free pts probability of 3-year disease-free interval was 55.8%. Severe (grade 2&3) soft tissue and bone l.n. occurred in 28 pts and 8 pts respectively. In 89% of cases l.n. was observed during the first 18 mos after BRT. Probability of 3-year l.n.-free interval was 71.5%. In the univariate analysis of the time to appearance of l.n. the following factors were considered: T-localization, age, sex, T-stage, total dose and d.r. Only the effect of the T-localization has been found to be statistically significant ($P = 0.0004$).

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POSTER

ADENOMATOUS GOITER AND THYROID GLAND CANCER

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Probability of cancer /Ca/ detection in the tissue of adenomatous goiter /A.g./ determines the way of treatment. 3591 patients with goiter have been operated in our department during 50 years (1945–1995). The share of A.g. has reached 68%. Of 595 patients with A.g. who have been treated over the last 20 years 178 (29.9%) presented with Ca in the tissue of recidives Ca was detected in 60% cases. The histological structure of our data: follicular Ca—45.7%, papillary Ca—19.7%, mixed form—30.8%, low differentiated—3.8%. We consider adenomatous and recurrent goiter as a group of risk. The principles of a surgical operation: extrafascial resection of thyroid gland, obligatory revision of the regional lymphoccollector, neck-dissection in the cases of metastatic damage of lymphatic knots. Patients with T3-4, N1, G3-4 receive gamma-therapy. We use no cytostatics. All patients after operation need thyroindinum or triiodthyroninum.

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POSTER

CARCINOMA OF THE NASAL CAVITY AND PARANASAL SINUSES: A RETROSPECTIVE STUDY OF 169 PATIENTS

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In the period 1963–1992, a total of 169 consecutive patients with carcinoma of the nasal cavity and paranasal sinuses were treated at our institution. The histological types included squamous cell carcinoma (75%), adenocarcinoma (22%), and undifferentiated carcinoma (3%). All adenocarcinomas were located in the nasal cavity and generally associated with occupational exposure to sawdust. Eleven percent of all patients had positive neck nodes at the time of diagnosis. A combined radiotherapeutic-surgical approach was used throughout the entire period. Twenty patients had no or only palliative treatment. The overall actuarial ten-year loco-regional tumor control was 37% and the corrected survival 36%. The failure pattern was 80% in T-position, 28% in N-position and 18% distant metastasis. Univariate analysis showed a significantly worse prognosis for high T-stage, nodal involvement, maxillary sinus tumors, low histological differentiation, and high age. In the Cox proportional hazards model, the strongest prognostic parameters were T-stage and differentiation. T-staging of maxillary sinus tumors according to Lederman (1970) was more prognostic than the AJC/UICC staging system. Finally, the present data revealed that the overall treatment results have not improved over the last three decades despite refinements in diagnostic and therapeutic capabilities.

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POSTER

CURE RATE AFTER LONG-TERM FOLLOW-UP IN HEAD AND NECK CANCER

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Between 1973 and 1993, 1355 consecutive head & neck cancer patients were diagnosed and treated with a multidisciplinary approach, and followed until death or until 10 years with no event of disease. Primary patients incidence site were 615 in supraglottis; 280, oral cavity; 254, glottis; 126, hypopharynx; 33, oropharynx, and 47, nasopharynx. Local relapse rate was 20% and node-regional relapse rate other 15%. Distant metastases were observed in 6% of patients, mainly arising from nasopharynx (23%), followed by hypopharynx (11%). Main organ involved was lung (50%).

Median follow-up was 10 years (range 4 months to 15 years). Cancer cure was observed after 5 years in glottis, supraglottis, mouth and nasopharynx cancer and after 2 $\frac{1}{2}$ years in oropharynx and hypopharynx. Highest cure rate was 80% in glottis, followed by 70% in supraglottis, 45% in mouth, 30% in nasopharynx, 25% in oropharynx, and 20% in hypopharynx.

Second primary was observed in 7% and a third primary in 0.6% of the patients. Only in 7 patients the second or third primary was seen after 5 year of follow-up.

In head & neck cancer, curability is observed after 5 years from definitive therapy in glottis, supraglottis, mouth and nasopharynx, and earlier