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PUBLICATION

Weekly paclitaxel/carboplatin and radiotherapy in inoperable squamous cell carcinoma of head & neck and lung

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Purpose: Treatment result in Patients with unresectable Head&Neck Cancer (H&NC) as well as Non Small Cell Lung Cancer (NSCLC) is not satisfying. We conducted a phase II trial to assess the efficacy and feasibility of weekly Paclitaxel (P) and Carboplatin (CP) in an outpatient setting.

Methods: From 02/96 to 11/97 35 patients with H&NC (25) and NSCLC (10) were treated with P: 90 mg/m² and CP: 150 mg/m² weekly × 6 with 2 weeks rest. Induction therapy with two cycles was followed by one cycle with simultaneous radiotherapy 2.0 Gy daily 5 times weekly for a total dose of 62–65 Gy. In this cycle the dose of P and CP was adapted to the mucositis, normally with >50% dose-reduction of both: P and CP.

Results: In Feb. 97 19/35 pts had completed therapy and were evaluated for toxicity and response.

We observed complete response in 3, partial response in 11, no change in 3 and progressive disease in 2 pts, overall response 14/19 (74%).

Toxicity: (Only grade 3 + 4) Alopecia: 19/19, haematotoxicity 3/19, mucositis 5/19, infections 3/19, diarrhoea 1 pt; during first cycle 1/19, second cycle 3/19 and third cycle (with radiotherapy) 7/19.

Conclusion: By preliminary evaluation treatment results and toxicity seem to be similar to other regimens with Cisplatin and 5 FU – by dose reduction to 33% in the third cycle toxicity become low and acceptable.

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PUBLICATION

Effects of radiation in radiotherapy treatments of laryngeal carcinoma: Clinical manifestations

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Purpose: The aim of our study is to evaluate the normal tissue reactions at irradiation and to establish the spectrum of radiotherapy results in laryngeal carcinoma.

Methods: We have analyzed the early and late irradiation reactions at 119 patients (T2-4No-1Mo) with laryngeal carcinoma, in distinct clinical dosimetric situation, in order to establish: the incidence of late oedema and fistula as a function of the field size, the incidence of pharyngo-cutaneous fistulae, the influence of age in the incidence of late injury, influence of the administration of prophylactic metronidazol, the reduction of normal tissue damage by increasing complexity of radiotherapy treatments.

Results: After a quantitative analyse of resulted data from the study we have made a description of the laryngeal carcinoma treatment morbidity and we have built a system for classification of normal tissue injury.

Conclusion: Because in clinical practice to obtain a therapeutic gain is necessary to reduce the risk of complication by taking into account the biological impact of the radiotherapy treatment we use with success the data given by this system of clinical manifestation of normal tissue damages after irradiation.

Breast cancer pathology and predictive factors

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ORAL

Prognostic Relevance of Microvessel Density (MVD) in primary human breast cancer and lymph node metastases

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The analysis of prognostic factors in breast cancer is of great importance for subsequent therapeutic approaches. Tumor angiogenesis is of high relevance in this context. We analyzed the MVD in 70 primary tumors (PT) (patient age: 33–85 yrs, mean 59.8 yrs) and 27 derived lymph node (LN) metastases using an immunohistological evaluation of CD31 expression. The results were correlated with other tumor/patient characteristics

of potential prognostic interest and clinical outcome (median follow-up: 34 months).

Compared to PT, LN metastases showed a much stronger expression of CD31 (median 11.1 vs. 5.3 MV/high power field (HPF), $p < 0.0001$) in general. However, MVD in LN and PT within one individual did not seem to be correlated with each other. In 8 of 10 T4 tumors, 5.3 MV/HPF were found. No other association between stage and CD31 expression was observed. A higher MVD was associated with higher serum levels of CA15-3 ($p = 0.028$). No correlation was found with age, alcohol intake, histology, grade, ploidy, LN involvement, serum CEA, and tumor expression of cathepsin D, c-erbB2, CD44s, CD44v6 and E-cadherin. After 36 months disease free survival (DFS) and overall survival (OS) of patients with <5.3 MV/HPF in PT were 90% and 93% resp. compared to 63% (DFS, $p = 0.015$) and 77% (OS, $p = 0.055$) for higher MVD. The CD31 expression in LN showed no correlation to OS or DFS.

In conclusion, assessment of MVD by histological determination of CD31 in PT has prognostic implications in breast cancer. In contrast, analysis of MVD in LN metastases does not provide prognosis related information.

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ORAL

Long-term prognostic impact of PAI-1 in primary breast cancer confirmed by six-year median follow-up

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We evaluated the prognostic impact of invasion markers uPA (urokinase-type plasminogen activator) and its inhibitor PAI-1 in primary breast cancer ($n = 316$) after a median follow-up of 77 (41–108) months. In a node-negative subgroup ($n = 100$), their prognostic strength was compared to that of new tumor biological factors S-phase (SPF), MIB1 (Ki-67), HER-2/neu, p53, and cathepsin D.

Levels of uPA and PAI-1 were determined in tumor tissue extracts by ELISA (American Diagnostica, CT), and that of cathepsin D by ELISA. SPF was determined flowcytometrically in paraffin sections. MIB1, p53, and HER-2/neu were assessed immunohistochemically in adjacent paraffin sections using APAAP technique. Optimized cutoff values were determined using isotonic regression.

In all patients, various factors showed significant impact on disease-free survival (DFS) in univariate analysis. However, in multivariate analysis, only lymph node status and PAI-1 remained significant. In the node-negative subset, uPA, PAI-1, and proliferation markers SPF and MIB1 had a significant impact on DFS. In multivariate analysis, only PAI-1 retained its significance. Statistical analysis performed after varying follow-up periods suggested time-dependency with PAI-1 as prognostic factor of delayed relapse, and uPA as indicator of early relapse.

In conclusion, PAI-1 remains a strong prognostic factor in breast cancer after a 6-year median follow-up. Its prognostic impact seems to indicate a time-dependent risk profile, which may help clinicians to individualize follow-up care, as well as provide a more profound insight into the dynamics of breast cancer metastasis.

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ORAL

p53 overexpression in node-negative breast cancer: Prognostic significance in a randomized study?

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Introduction: resistance to chemotherapy of breast cancer with p53 mutations has been reported. We have evaluated p53 alterations in 282 consecutive premenopausal patients with node-negative breast cancer who underwent primary surgery and were randomized either to CMF (Endoxan 400 mg/m²), Fluorouracil 400 mg/m² et Methotrexate 40 mg/m² or control arm from 1980 to 1989.

Methods: P53 alterations were analyzed by immunohistochemistry using DO7 MoAb, revealed by immunoperoxidase technique and quantitated in terme of percentage of positive cells.

Results: We observed a positive staining in 24% of the tumors. Among them, 10% had a positive staining in more than 75% of the cells. There was a highly significant association between the proportion of positive cells and histologic grade of the infiltrating ductal carcinomas ($p < 0.008$). However there was no association with age, tumor size, histological status, vascular