Their pharmacokinetic (pk) behavior could be dependent not only on PTX excipient (polyethoxylated castor oil) interference, but even on different i.v. administration intervals between the two drugs. This study evaluated any possible administration interval-dependent pk interaction, when PLD infusion started 0, 1, 3, 12 or 24 h after PTX infusion end.
Materials and Methods: 30 patients, affected by recurrent cisplatin pre-treated squamous cellhead/neck cancer, were randomized to receive PTX 80 mg/m^2 q1w and PLD 12.5 mg/m^2 q2w at administration intervals of 0, 1, 3, 12 or 24 h. Pk parameters were evaluated during the first course by non-compartmental analysis, while statistical analysis was performed by non-parametric Kruskal Wallis test
Results: median pk parameters are reported in the table. The PTX pk profile is strongly affected by PLD administration. PTX total exposure is highly reduced, with a consequent increase in Cl_{tot}: this alteration is totally due to K_{el} modifications. On the other side, no statistically significant interactions affected PLD pk parameters. Some in vitro experiments indicate that PLD is able to partially absorb PTX, driving to PTX plasmatic concentration reduction, when PLD is administered at 0−1h interval.

Parameter	PTX						PLD					
	Administration interval					p	Administration interval					p
	0 h	1 h	3 h	12 h	24 h		0 h	1 h	3 h	12 h	24 h	
C_{max} (mg/l)	0.26	0.40	0.76	0.61	0.41	0.042	5.11	6.71	6.08	6.92	6.86	0.121
AUC_{tot} (mg/l*h)	0.87	1.57	4.67	4.29	3.36	0.005	676.4	606.8	749.6	723.8	739.6	0.515
K_{el} (h^{-1})	0.39	0.26	0.19	0.02	0.11	0.003	0.007	0.008	0.007	0.008	0.007	0.613
Cl_{tot} (l/h)	153.2	92.5	28.7	32.2	41.7	0.005	0.031	0.036	0.029	0.030	0.029	0.681

Conclusions: PLD liposomal components seem to be able to entrap PTX, therefore reducing PTX plasmatic concentrations: so, it is very important to choose the ideal administration interval. In order to avoid pk interaction, the i.v. administration interval between PTX and PLD had to be 3 h at least. For shorter interval, patients could be underexposed to PTX, with lesser clinical efficacy.

5523 POSTER

Risk of distant metastases after postoperative radiation therapy for locally advanced laryngeal cancer

A. Idasiak, S. Blamek, R. Suwinski. *M. Sklodowska-Curie Memorial Institute, Radiotherapy department, Gliwice, Poland*

Background: Laryngeal cancer is the most common head and neck malignancy. Postoperative radiotherapy in advanced laryngeal cancer reduces risk of local and regional recurrences. An improvement in local and regional control achieved by combined therapy results that distant metastases become an increasingly common case of treatment failure.
Objective: The aim of the study is to evaluate the risk of development distant metastases for patients with laryngeal cancer after postoperative radiotherapy. The particular aim of the study is:
1. To estimate the prognostic factors for the risk of distant metastases.
2. To construct theoretic algorithm of the relationship between clinical and pathological parameters and risk of distant metastases.

Material and Methods: Medical records of 267 patients (23 women, 244 men) with laryngeal cancer treated between 1997–2002 were analyzed. The age ranged from 37 to 78 (median 58). All patients had locally advanced squamous cell laryngeal cancer treated with surgery and postoperative radiotherapy. Locally advanced tumors (T3, T4) constituted 205 cases (77%). There were 62 (23%) patients in stage T1 and T2. Enlarged lymph nodes were found in 155 cases.
The survival plots were estimated using the Kaplan-Meier method. A multivariate Cox proportional hazard model and logistic regression model was used to evaluated influence of the following variables on MFS and the ultimate risk of metastases: age, sex, localization, TN stage, HGB before and at the end radiotherapy, total radiation dose, dose per fraction, overall treatment time, interval surgery-radiation time, pathological margins and positive nodes in surgical specimen. The effective doubling time of tumor clonogens has been estimated for local recurrences and distant metastases.
Results: The crude incidence of distant metastases was 12% (33/267 pts). One year, 3-year, 5-year actuarial metastases free survival were 95%, 85% and 84% respectively.
The Cox regression analysis revealed two variables, which had significant and independent influence on metastases-free survival: localization of cancer (glottic vs. supraglottic) and number of positive lymph nodes at pathological staging. The lungs and bones were the most common sites of metastases (58% and 33% respectively), whereas metastases to liver (6%) and brain (3%) were rare. The effective clonogen doubling time for loco-regional recurrence and distant metastases were estimated as 12.5 day and 16−32 days respectively.
Conclusion: Distant metastases rate is comparable with percentage of local treatment failure and in the presented group of patients was 12% vs. 16%. Number of positive lymph nodes in pathological specimen and site of primary cancer (glottic vs. supraglottic) significantly and independently predict a risk of distant metastases in combined modality treatment for laryngeal cancer.

5524 POSTER

Primary tumor volume predicts locoregional control and survival after concurrent chemoradiation with daily low dose cisplatin for advanced stage head and neck carcinoma

F. Hoebers[1], F. Pameijer[2], J. de Bois[1], W. Heemsbergen[1], A. Balm[3], J. Schornagel[4], C. Rasch[1]. *[1]The Netherlands Cancer Institute, Radiotherapy Department, Amsterdam, The Netherlands; [2]The Netherlands Cancer Institute, Radiology Department, Amsterdam, The Netherlands; [3]The Netherlands Cancer Institute, Department of Head and Neck Oncology and Surgery, Amsterdam, The Netherlands; [4]The Netherlands Cancer Institute, Department of Medical Oncology, Amsterdam, The Netherlands*

Background: To evaluate the prognostic value of tumor volume in patients with advanced HNSCC treated with concurrent cisplatin-chemoradiation.
Material and Methods: 46 patients were treated with radiotherapy (35×2 Gy) and cisplatin (6 mg/m^2 i.v. daily). Tumor sites were: oropharynx 72%, oral cavity 22%, hypopharynx 2%, and larynx 1%. Baseline primary tumor volume was recorded from diagnostic MRI-scan. In uni- and multivariate analysis, the prognostic impact of patient-, tumor-, and treatment-related factors was investigated, including primary tumor volume, for locoregional control and disease free survival.
Results: Mean follow up was 40 months (range 23−69) for patients alive at last follow-up. Mean tumor volume was 28 cm^3 (median 23, range 3–112). Oral cavity tumors were statistically significantly larger than oropharyngeal tumors (41 vs. 24 cm^3, p = 0.05). Tumor volume and T-stage were positively correlated: T3-tumors had a mean tumor volume of 19 cm^3, whereas the volume of T4-tumors was 40 cm^3 (p = 0.003). Locoregional (LR) control at 3 years was 72% for all patients. Disease free survival (DFS) was 36%. The LR control rate at 3-years was 81% for patients with tumor-volumes = median (p = 0.036). Oropharyngeal tumors had significantly better 3-year LR control rates compared to oral cavity tumors: 75% vs. 44% (p = 0.013). T3-tumors had significantly better 3-year LR control rates compared to T4-tumors: 78% vs. 44% (p = 0.033). In multivariate analysis, primary tumor site and larger tumor volumes were factors significantly associated with decreased LR control and DFS. T-stage was associated with LR control, but not DFS (Table).
Conclusions: In advanced HNSCC treated with concurrent chemoradiation, primary tumor volume is significantly associated with LR control and DFS and should therefore be incorporated in the staging system as a tool to guide treatment and predict outcome.

Variable	UV analysis, HR (95% CI)	p-value	MV analysis, HR (95% CI)	p-value
Disease free survival				
Site (oral cavity vs rest)	0.5 (0.2−1.0)	0.05	0.4 (0.2−1.0)	0.05
T-stage	1.4 (0.8−2.3)	0.2	-	
Tumor volume	1.02 (1.00−1.03)	0.01	1.02 (1.00−1.03)	0.05
Locoregional control				
Site (oral cavity vs rest)	0.3 (0.1−1.0)	0.04	0.2 (0.1−0.8)	0.02
T-stage	3.6 (1.2−10.7)	0.02	-	
Tumor volume	1.03 (1.00−1.04)	0.005	1.02 (1.00−1.05)	0.04
Level IV involvement yes/no	3.1 (1.0−10.0)	0.06	2.0 (0.4−9.9)	0.4
ASA (Co-morbidity score, 1−3)	2.1 (0.9−6.35)	0.02	1.6 (0.7−3.7)	0.2

5525 POSTER

Retropharyngeal nodal metastasis is related to a higher rate of distant metastasis in patients with nasopharyngeal cancer – results from a single centre retrospective study

I.W.K. Tham[1], S.P. Yap[1], J. Tuan[1], S.W. Hee[2], J. Wee[1]. *[1]National Cancer Centre, Department of Radiation Oncology, Singapore, Singapore; [2]National Cancer Centre, Department of Clinical Trials & Epidemiological Sciences, Singapore, Singapore*

Background: There is currently no consensus on how Retropharyngeal Lymph Nodes (RLN) in Nasopharyngeal Cancer (NPC) should be “staged”. A recent study showed a borderline significant difference of distant metastasis-free survival (DMFS) rates between patients with or without