**8502** ORAL

**Phase II Study of RAD001 Monotherapy in Patients With Unresectable Adenoid Cystic Carcinoma**

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**Background:** To examine the efficacy and toxicity of RAD001 when used as a treatment in patients with progressing unresectable adenoid cystic carcinoma.
**Methods:** Patients with histologically confirmed adenoid cystic carcinoma, with at least one measurable lesion were eligible for the study. Other eligibility criteria included; documented disease progression according to RECIST criteria within12 months prior to the entry, not amenable to curative-intent treatment, ECOG PS 0 or 1, and adequate organ function. RAD001 was given at a dose of 10 mg daily every 4 weeks. Response was assessed according to RECIST (v 1.0) every 8 weeks. Primary end-point was 4-month progression-free survival rate (PFSR). Hypothesis was that 4m-PFSR would be improved from 50% to 65%.
**Results:** A total of 34 patients were enrolled. Thirty one patients were evaluable for response. Partial response was not achieved. Twenty seven patients (87.1%) had stable disease and 4 patients (12.9%) showed disease progression. Overall disease control rate was 87.1%. Fifteen patients (48.4%) showed tumour shrinkage within SD. Pre-treatment and post-treatment (after 8 weeks) PET was available in 18 patients. All these 18 patients showed SD on RECIST criteria. Among them, 8 patients showed early PR metabolic response (>25% reduction from baseline SUVmax) and 9 patients showed SD metabolic response and one patient showed PD metabolic response (>25% increase from baseline SUVmax). The PFS was 11.7 months (95% CI, 8.1–15.2 months) and 4-month PFSR was 65%. Mean treatment duration was 6.4 months (range 0.4–23.2 months).
The most common AEs (all grades) were: stomatitis (82%), anemia (67%), asthenia (36%), leucopenia (33%). The major Gr 3/4 toxicities were: asthenia (6%), infection (6%), leucopenia (3%). Dose adjustment was done in 8 patients (24%).
**Conclusions:** RAD001 showed promising efficacy and good tolerability in unresectable adenoid cystic carcinoma.
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**8503** ORAL

**A Prospective Study Evaluating the Influence of Smoking on Effective Hemoglobin Level and Outcome in Patients With Squamous Cell Carcinoma of the Head and Neck**

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**Background:** Patients with head and neck cancer and a high hemoglobin level have been shown to respond better to irradiation compared to patients with low hemoglobin. The hemoglobin level is, however, a crude indicator of the amount of oxygen available to the tissue and may be influenced by a number of factors, smoking being of major importance.
The aim of the present study was to examine the effect of smoking on available oxygen to tumours and the effect on outcome in head and neck cancer patients treated with radiotherapy.
**Material and Methods:** A total of 233 patients with squamous cell carcinoma of the larynx, pharynx and oral cavity completed questionnaires on smoking habits and venous blood samples were collected prior to treatment to determine the amount of total hemoglobin, carboxy-hemoglobin, p50 and tumour unloading capacity. Patients were treated with primary curative radiotherapy 62−68 Gy/, 2 Gy/fx, 5 fx/week. All but 12 patients had a history of smoking, 36 were long term quitters, 23 recent quitters, 54 smokers and 108 heavy smokers (>1 pack/day).
**Results:** The amount of carboxy-hemoglobin increased with increasing smoking habits. There was no relationship between total hemoglobin and carboxy-hemoglobin, but effective hemoglobin and carboxy-hemoglobin was linearly correlated. Thus, the oxygen utilization in a tumour in a heavy smoking patient was found to be on average 20% lower than in non-smoking patients.
Actuarial 5-year univariate analysis showed that the heavy smoking patients had a significant reduced probability of loco-regional control (45% vs 65%, p = 0.002), disease-specific (56% vs 78%, p = 0.002) and overall survival (39% vs 66%, p = 0.0003) compared to non-smoking patients. In a multivariate analyses stratifying by site, the independent prognostic factors were found to be heavy smoking, T and N classification, age and gender, however moderate smoking did not influence the outcome after radiotherapy.
**Conclusion:** The effect of smoking on radiotherapy outcome in head and neck cancer patients can be explained by a reduced tumour oxygen supply caused by the increased carboxy hemoglobin concentration. The data strongly advocate that smoking should be avoided in order to improve the therapeutic efficacy of radiotherapy.
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**8504** ORAL

**Tumoural MRNa Profile of Angiogenesis/hypoxia Effectors in Patients With Operable Squamous Cancer of the Larynx**

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**Background:** Tumour hypoxia and angiogenesis have been implicated in disease progression providing the basis for targeted anti-angiogenic therapeutic interventions. The aim of the present study was to explore the prognostic impact of angiogenesis and hypoxia related mRNA expression in patients with localized squamous laryngeal cancer.
**Patients and Methods:** We retrospectively analysed mRNA levels of Vascular Endothelial Growth Factor (VEGF)-A, -B, -C and the relevant receptors VEGFR 1, 2, 3 as well as the Hypoxia-Inducible Factor 1a (HIF1a) by means of quantitative real-time polymerase chain-reaction that was performed on RNA samples extracted from formalin-fixed paraffin-embedded squamous laryngeal carcinomas of patients with localized disease. We performed distributional and receiver-operating curve analyses that revealed the median mRNA relative expression value as the cut-off for VEGF-A, -B, -C, -R2 and HIF1A, and the 32nd and the 80st percentiles for VEGF-R1 and -R3 respectively. We studied their correlation with clinicopathologic parameters, relapse and death.

Table 1. Multivariate analysis

| | HR | 95% CI | Wald-p |
|---|---|---|---|
| **Disease-free survival** | | | |
| Node-positive | 2.75 | 1.66–4.55 | <0.001 |
| Supraglottic localisation | 0.62 | 0.41–0.94 | 0.023 |
| Total laryngectomy | 0.64 | 0.39–1.05 | 0.076 |
| High tumoural VEGFR1 mRNA | 2.00 | 1.22–3.28 | 0.006 |
| **Overall survival** | | | |
| Node-positive | 2.67 | 1.60–4.45 | <0.001 |
| High tumoural VEGFA mRNA | 0.69 | 0.45–1.04 | 0.080 |
| High tumoural VEGFC mRNA | 1.49 | 0.98–2.26 | 0.061 |
| High tumoural VEGFR1 mRNA | 1.93 | 1.13–3.29 | 0.015 |
| High tumoural VEGFR3 mRNA | 1.56 | 0.96–2.53 | 0.073 |

**Results:** Clinical and mRNA expression data were available for 229 patients, mostly males (95%), smokers (86%) with locally advanced (T3/4 in 79%) node-negative (82.5%) glottic or supraglottic (89.5%) squamous carcinoma of the larynx were managed with total laryngectomy (85%) in the ENT Department, Papageorgiou Hospital from 1988 until 2008. At a median follow-up of 70 months, 34% of these patients had relapsed and 42% had died, resulting in median relapse-free survival (RFS) of 87.3 months (95% CI 69.5–105.2) and in median overall survival (OS) of 100.3 months (95% CI 82.6–118). We observed significant correlations between mRNA levels of VEGFR 1, 2, 3 with each other, the respective ligands and HIF1A. Significant associations were seen between high VEGFA, high VEGFR1 and advanced T stage (T3/4, p = 0.005 and p = 0.014 respectively), low VEGFB and alcohol abuse (p = 0.001), low VEGFC and supraglottic primary (p = 0.001). Relapse was significantly associated with high tumoural VEGFR1 mRNA (hazard ratio, HR 1.93, 95% CI 1.19–3.15,