lymph node metastasis, primary tumor size larger than 2 cm, and estrogen and/or progesterone receptor negativity in the primary tumor the effect of the CCND1 genotype on metastasis-free survival time was estimated.
Results: The age of the patients at the time of diagnosis was between 28 and 84 years, with a mean age of 57 ± 11 years. Median metastasis-free survival time was 120 months (95%CI: 106–134). In the subgroup of 302 patients with stage III-IV breast cancer, 250 (82.8%) patients developed metastases in the time between diagnosis and study entry, whereas 52 (17.2%) patients remained free of metastases. The CCND1 870_AA genotype was found more frequently among patients without metastases (44.2%) than among those with metastases (24.8%; chi^2 test, p = 0.005). In a logistic regression model including age at diagnosis and estrogen and/or progesterone receptor negativity in the primary tumor as potential confounders, the 870_AA genotype was still significantly associated with metastasis risk (odds ratio 0.43, 95%CI: 0.23–0.83; p = 0.010).
Conclusions: Our data support the hypothesis that the CCND1 870 G > A polymorphism is associated with metastasis-free survival time in patients with breast cancer.

163 ORAL

Association of the A870G cyclin D1 gene polymorphism with genetic susceptibility to nasopharyngeal carcinoma

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Background: Nasopharyngeal cancer (NPC) is a human malignancy consistently associated with EBV. However, the etiology of NPC is complex and multifactorial, and exposure to non-viral carcinogens and genetic predisposititon are other crucial etiological factors. Cyclin D1 (CCND1) is a key regulator of the G1/S phase of the cell cycle and its altered activity is associated with the development of several human cancers, including Squamous Cell Carcinoma of the Head and Neck.
Material and methods: We analysed the A870G *CCND1* polymorphism by PCR-RFLP in 281 individuals including, 94 cases with NPC and 187 healthy individuals.
Results: Our results indicate that individuals carrying two G-alleles have a 2.17-fold increase in the risk for the development of NPC (OR = 2.17, 95%CI: 1.19–3.98, *P* = 0.016). Age-adjusted logistic regression analysis confirmed the association between the presence of the GG *CCND1* genotype and increased genetic susceptibility for the development of NPC (aOR = 2.14, 95%CI: 1.14–4.04, *P* = 0.018). Multivariate logistic regression analysis of the GG *CCND1* genotype (aOR = 2.06), male gender (aOR = 2.66) and age at diagnosis (aOR = 2.02) demonstrate an independent association between the *CCND1* GG genotype and the development of the undifferentiated histological type of nasopharyngeal carcinoma (UCNT). The proportion of cervical cancer cases attributable to the GG *CCND1* genotype was 14.76%.

Table 1: Multivariate analysis of the GG *CCND1* genotype, gender and age at diagnosis regarding the susceptibility to undifferentiated histological type of nasopharyngeal carcinoma (UCNT)

	*P**	aOR*	95%CI*
GG genotype	0.039	2.06	1.04–4.09
Age ⩾ 50	0.019	2.02	1.12–3.62
Male gender	0.002	2.66	1.45–4.86

**P*, aOR and 95%CI using logistic regression analysis.

Our data suggest that A870G CCND1 polymorphism is associated with the susceptibility to NPC and supports evidence for a site-specific prevalence of genetic alterations. These results may be important in the definition of a biological predictive profile for the development of NPC.

164 ORAL

Increased risk of cervical cancer associated with cyclin D1 gene A870G polymorphism

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Background: Human papillomavirus (HPV) play the major role in the etiology of cervical cancer. However, a complex correlation between viral and cellular genes is necessary for cell cycle control deregulation in the progression to invasive cervical cancer (ICC). Cyclin D1 is an important positive regulator of the G1/S phase of the cell cycle.
Material and methods: We analysed the A870G *CCND1* polymorphism by PCR-RFLP in the genomic DNA isolated from peripheral blood of 246 women including, 50 cases with high-grade squamous intraepithelial lesions of the cervix (HSIL), 93 with ICC and 103 healthy women. Statistical analysis was performed using the computer software SPSS for Windows (version 11.5). Chi-square analysis was used to compare categorical variables and a 5% level of significance was used in the analysis. The odds ratio (OR) and its 95% confidence interval (CI) were calculated as a measurement of the association between *CCND1* genotypes and cervical cancer risk. Logistic regression analysis was used to calculate the adjusted OR (aOR) and 95%CI for the influence of *CCND1* genotypes in the risk of cervical cancer, with adjustment for age. We estimated the cumulative probabilities for developing cervical cancer (cumulative hazard function plots) by the Kaplan-Meier methodology.
Results: The GG genotype was associated with a significantly higher risk of ICC (OR = 3.20, 95%IC 1.55–7.41, *P* = 0.001). Furthermore, our results indicate a 3.7 higher risk for the development of HSIL in women carrying the GG *CCND1* genotype (OR = 3.67, 95%CI 1.45–9.31, *P* = 0.007). Age-adjusted logistic regression analysis confirmed the association between the presence of the GG *CCND1* genotype and increased genetic susceptibility for the development of cervical cancer. The proportion of cervical cancer cases attributable to the GG *CCND1* genotype was 17.26%. Furthermore, our results suggest that GG genotype of *CCND1* A870G polymorphism is associated with an earlier onset of cervical cancer (log rank test: *P* = 0.015) (Figure 1).

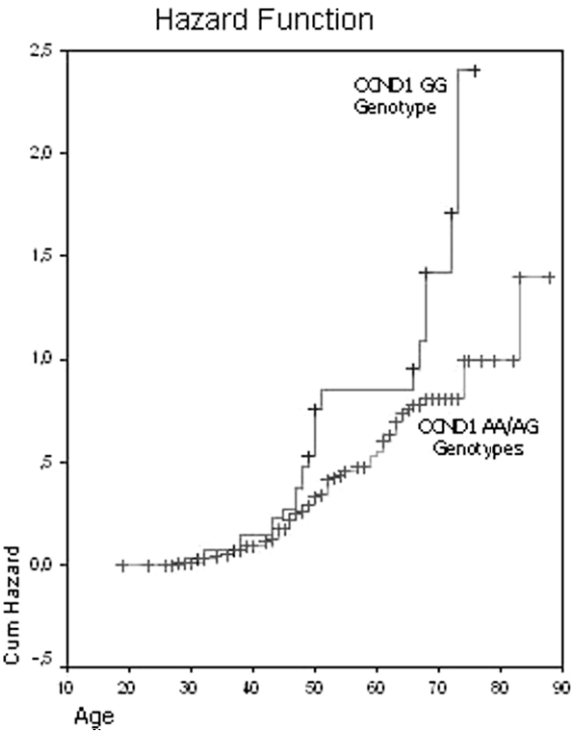

Fig. 1: Association of the A870G *CCND1* polymorphism and age of onset of cervical cancer. Cumulative hazard function plots by the Kaplan-Meier methodology and log rank test (*P* = 0.015).