Prospective blinded evaluation predicting efficacy of adjuvant cisplatinum and vinorelbine by a multigene assay after radical surgery in non-small cell lung cancer

Background

This study evaluated the predictive effect of a mRNA-based Drug Response Predictor DRP[®] in the adjuvant setting of non-small cell lung cancer (NSCLC). We apply a mathematical method combining *in vitro* sensitivity with gene expression patterns in tumors [1]. The cisplatinum DRP[®] has previously been tested in three independent datasets [2].

Methods

RNA was isolated from formalin-fixed paraffin embedded tumor tissue obtained after radical surgical resection in 95 consecutive stage Ib-IIIb NSCLC patients of different histotypes. Adjuvant chemotherapy was four courses of i.v. cisplatinum and vinorelbine. Affymetrix HG-133_Plus_2 microarray method was applied. Multigene biomarker profiles for cisplatinum and vinorelbine were evaluated blinded on the samples.
Primary endpoint was overall survival (OS).

Results

Baseline demographics are representative of a NSCLC population. Follow-up time was in median 76.6 months (range 3.5-7 years) after surgery.

Statistical analysis suggested that time-dependent analysis of OS was warranted. Using a time dependent Cox model stratifying at 3 years, the hazard ratio (HR) for OS up to 3 years was 0.50 (95% CI: 0.30-0.84, p=0.008) and the HR for cancer-specific death was 0.46 (95% CI: 0.27-0.78, p=0.004). Results for multivariable analyses for OS are shown in the table. The DRP[®] remained significant in the multivariable analysis for each endpoint.

Conclusions

The DRP[®] for the combined cisplatinum and vinorelbine adjuvant treatment of resectable NSCLC offers definite prediction of effect of the two drugs since it is significant within 36 months after surgery.

[1] Knudsen et al PLoS ONE 2014 9(2): e87415.

[2] ASCO **Abstract 2015** e18502.

Covariate		Hazard ratio (95 % CI)	P-value
DRP < 36 months		0.49 (0.28-0.86)	0.013
DRP ≥ 36 months		1.26 (0.76-2.10)	0.38
Stage	II vs I	3.20 (1.46-7.02)	0.004
	III vs I	4.08 (1.72-9.70)	0.001
Age/10 year difference		1.52 (0.99-2.33)	0.053
Gender	M vs F	1.04 (0.53-2.03)	0.92
Histology[*]	ASCC	0.22 (0.05-0.98)	0.047
	Other	1.48 (0.48-4.55)	0.49
	SCC	0.37 (0.12-1.14)	0.08

*Vs. adenocarcinoma. ASCC = adenosquamous cell carcinoma, SCC = squamous cell carcinoma.