Lung cancer is the most common type of cancer in the world with over 1.5 million new cases per year. Within this devastating disease, squamous cell carcinomas account for approximately 25% in the group of non-small-cell lung cancers (NSCLC). Smoking is the main cause for lung cancer as 85% of patients were exposed to this risk factor (1).

In the last decades the research focus regarding classification of cancers developed from pure histomorphological features to the inclusion of molecular subtyping of genetic aberrations. This led to new treatment strategies using small molecule inhibitors or specific antibodies in cancers of different organ sites with major advances in tumors of the lung. For example epidermal growth factor receptor (EGFR) inhibitors such as gefitinib and erlotinib (2) and anaplastic lymphoma kinase (ALK) inhibitor (crizotinib) (3) are already being used for specific lung cancer therapies. However, new treatment options are desperately needed to improve overall survival and life quality of patients.

In 2010 Weiss et al. were the first to describe frequent fibroblast growth factor receptor 1 (FGFR1) amplification in squamous cell cancer (SCC) of the lung. The FGFR1 amplification was detected in an unbiased approach using SNP (Single Nucleotide Polymorphisms) arrays on a large cohort of patients with SCC of the lung (n=155) and was validated in an independent cohort (n=153) by fluorescence in-situ hybridization (FISH) with a frequency of 22%. Weiss et al. were also able to show growth inhibition of FGFR1 amplified cell lines in vitro and in vivo using the FGFR inhibitor PD173074 (4). The FGFR1 amplification rate described by Weiss et al. for SCC of the lung was confirmed by Dutt et al. shortly afterwards (5). In a follow-up study, we detected the occurrence of FGFR1 amplification not only at a similar frequency in primary SCCs of the lung but also in the corresponding regional lymph node metastases of FGFR1 amplified primary tumors, suggesting a clonal event in tumor progression.

Our findings provide a rationale for treating patients with advanced disease with FGFR small molecule inhibitors and suggest that biopsy of the metastases would be adequate for determining the FGFR1 status of the primary tumor and vice versa (6). Of interest, Weiss et al. and we observed an association between inhalative tobacco consumption and FGFR1 amplification status (4,6).
of the lung as described by Kim et al., but also in SCC of the head and neck region. In a current study, we set out to further elucidate the importance of FGFR1 not only as a prognostic biomarker but also as a target for therapy in patients with SCC of the head and neck region. We characterized SCC cell lines of the head and neck region according to their FGFR1 copy number, mRNA and protein expression status and subsequently tested their sensitivity towards the small molecule FGFR inhibitor BGJ398. We found FGFR1 gene amplification neither correlating with mRNA nor with protein expression. Interestingly, sensitivity to BGJ398 was only observed in those cell lines harboring high protein and mRNA levels (manuscript under review).

In another publication, Freier et al. described a FGFR1 amplification frequency of 17.4% in oral SCC (n=92), but could not find an association between FGFR1 copy number and protein overexpression (9). In lung cancer, Pros et al. also specified the association between FGFR1 amplification and overexpression as inconclusive (10). In contrast, Kim et al. observed a high correlation between FGFR1 amplification by FISH and FGFR1 mRNA levels as well as protein expression by immunohistochemistry in SCC of the lung (7). Thus, we suppose that there is still a need to define the best predictive biomarker to select patients who will profit most from a FGFR1 targeted therapy. As emphasized, this could be gene copy number, mRNA expression as well as protein expression or mutational status of cancers.

Beyond serving as a targetable prognostic biomarker, Kim et al. noted FGFR1 amplification in SCC of the lung to be a predictor of sensitivity towards chemotherapy (7). This indicates that certain patients might also benefit from a combined treatment with conventional chemotherapy.

Taken together, the study by Kim et al. confirmed and extended the FGFR1 amplification frequency in SCC of the lung to East Asian patients. Furthermore, they demonstrated an association of FGFR1 amplification with smoking habits and provided evidence that this particular genomic aberration is not only a prognostic biomarker but does also have predictive implications on the success of a chemotherapy in lung cancer patients (7).

The success story of the discovery of FGFR1 amplification as a targetable genomic alteration in SCC of the lung and head and neck region and the quick entrance of small molecule FGFR inhibitors into first clinical trials highlights genomic profiling as a promising approach to detect so far unknown aberrations in the genomes of cancer cells. These might not only serve as a predictive
or prognostic marker, but could also be a target in tumor therapy.

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