Clinical utility of a protein-based oncopanel in patients with end-stage head and neck cancer

Johannes Doescher*, Stephanie E Weissinger, Stefan S Schönsteiner, Catharina Lisson, Lars Bullinger, Thomas FE Barth, Frank Leithäuser, Urs Mueller-Richter, Simon Laban, Thomas K Hoffmann, Peter Möller, Jochen K Lennerz, & Patrick J Schuler

1Department of Otorhinolaryngology, Head & Neck Surgery, University of Ulm, Germany
2Institute of Pathology, University of Ulm, Germany
3Department of Internal Medicine III, University of Ulm, Germany
4Department of Radiology, University of Ulm, Germany
5Department of Internal Medicine, Division of Hematology, Oncology & Tumor Immunology, Charité University Medicine, Berlin, Germany
6Department of Oral & Maxillofacial Plastic Surgery, University of Würzburg, Germany
7Center for Integrated Diagnostics, Massachusetts General Hospital/Harvard Medical School, Boston, MA, USA

*Author for correspondence: Tel.: +49 731 500 59501; Fax: +49 731 500 59502; johannes.doescher@uniklinik-ulm.de

‡Authors contributed equally

Aim: In a prospective clinical initiative, we selected heavily pretreated head and neck carcinoma patients and assessed the clinical utility of a protein-based oncopanel for identification of potential targetable markers. Patients & methods: Tumor samples of 45 patients were evaluated using a 12-marker immuno-histochemistry panel. The primary end point was the prevalence of potentially actionable markers. Results: At least one expressed marker in each case could be identified. We noted a high prevalence of EGFR (80%, 39/45) and MET (57.4%, 28/45). Three patients received oncopanel-based therapy with variable results. Conclusion: Despite the limited number of treated subjects, oncopanel analysis in end-stage head and neck cancer is operationally and technically feasible. Combination with targeted next generation sequencing might provide additional therapy options.

Head and neck carcinoma represent 4% of all newly diagnosed malignancies and standard of care is, whenever possible, complete surgical resection. In advanced tumor stages, surgery is followed by either radiation or combined chemoradiation [1]. For recurrent and metastatic tumors, first-line palliative therapy follows the EXTREME regimen, if the patient’s condition is adequate [2]. Treatment for platinum-refractory tumors is not standardized and includes monotherapy with cetuximab, docetaxel or methotrexate. In 2017, the programmed death 1 (PD-1) inhibitor nivolumab has received a labeling extension for patients with head and neck squamous cell carcinoma (HNSCC) after platinum failure. The approval study showed a 2-months survival benefit with nivolumab when compared with treatment of investigators choice [3]. However, the objective response rate of 13% leaves a high percentage of patients without tumor reduction and indicates that alternative regimens in palliative head and neck cancer patients are urgently needed.

One option to identify possible therapeutic targets is the analysis of the genetic tumor landscape in head and neck cancers [4]. While genotyping strategies are under development [5,6], identification of relevant numbers of targets requires comprehensive next-generation sequencing efforts (including bioinformatics expertise), which is not available in all clinical settings. Given that proteins are the carriers of biological function and ultimately serve as target structures for many of the drugs, target analysis can also be performed at the protein level. We refer to this approach as oncopanel [7], and best to our knowledge, this approach has not been systematically applied in a prospective setting.
Here, we assessed the clinical utility of a protein-based oncopanel for identification of potential targetable markers in the setting of recurrent or metastatic head and neck cancer. The selected targets are based on availability of clinically validated protein markers in our setting. Demonstration of clinical feasibility would suggest a straightforward approach to establish molecularly informed decision-making when alternative systemic regimens are limited.

Materials & methods

Study design

The attending head and neck oncologist identified patients and the inclusion criteria were: patients with recurrent or metastatic head and neck cancer in a palliative setting with lack of conventional treatment options, with an Eastern Cooperative Oncology Group performance status (ECOG) 0-2, and willingness to receive further treatment. Oncopanel analysis was contingent upon tissue availability and if no recent biopsy was available, a new tumor biopsy was performed. The interdisciplinary head and neck tumor board at the University Medical Center reviewed oncopanel results. If a patient was identified as a candidate for targeted therapy, selection of the specific drug was matched to the oncopanel signature. Cost-coverage was tailored to the patient's insurance contract. The study was IRB approved and patients signed an informed consent before any kind of treatment.

Oncopanel

The oncopanel assessed expression of ten proteins from May 2014 to July 2016 and has been supplemented with PD-1 and PD-L1 since August 2016 (= 12 markers). In total, 45 patients were analyzed, 24 of them with the 10-marker panel and another 21 with the 12-marker panel. Staining was performed on the Dako Omnis platform (Dako, Glostrup, Denmark) as previously published [7]. Briefly, we used formalin-fixed paraffin-embedded tissues and antibody details are provided in Supplementary Table 1. Cases were considered positive if more than 10% of tumor cells showed immunopositivity in the appropriate cellular compartment (Supplementary Table 1). Representative histological images are displayed in Figure 1. Repeat oncopanel testing was performed in four patients (Table 2).

Literature review

We performed a literature search for the terms ‘head and neck’ AND ‘precision oncology’ for the specific question of biomarker-driven therapy of head and neck carcinoma. A total of 316 publications were reviewed and 14 of them analyzed. Two of the authors selected relevant publications (Table 3).

Statistics

We defined the primary end point as the prevalence of actionable markers. Secondary end points were: the technical ability to apply the oncopanel routinely in clinical practice; any additional diagnostic value; the oncopanel signature at different time points (re-biopsy); the number of patients placed on targeted therapy as well as; their radiographic
Table 2. Changes in marker expression over time in cases which had multiple oncopanel analyses.

<table>
<thead>
<tr>
<th>Case A (HNSCC)</th>
<th>Timepoint 1</th>
<th>Timepoint 2</th>
<th>Timepoint 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR, MET</td>
<td>EGFR, PDGF</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Case B (SNUC)</td>
<td>EGFR, HER2</td>
<td>EGFR, PDGF</td>
<td>–</td>
</tr>
<tr>
<td>EGFR, HER2, KIT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case C (sarcoma)</td>
<td>EGFR, FLI1†</td>
<td>EGFR, FLI1</td>
<td></td>
</tr>
<tr>
<td>EGFR, FLI1, PDGF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case D (salivary duct CA)</td>
<td>EGFR, HER2</td>
<td>HER2</td>
<td>–</td>
</tr>
</tbody>
</table>

† Friend leukemia integration 1 transcription factor.

CA: Carcinoma; HNSCC: Head and neck squamous cell carcinoma; SNUC: Sinonasal undifferentiated carcinoma.

Table 3. Studies with molecularly matched targeted therapies for head and neck cancer.

<table>
<thead>
<tr>
<th>Study (year) [ref.]</th>
<th>Method of analysis</th>
<th>Patients analyzed</th>
<th>Patients treated (%)</th>
<th>HNC patients treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Von Hoff (2010) [23]</td>
<td>IHC, FISH, MA</td>
<td>86</td>
<td>66 (77%)</td>
<td>3</td>
</tr>
<tr>
<td>Schwaederle (2016) [25]</td>
<td>NGS</td>
<td>347</td>
<td>87 (25%)</td>
<td>6</td>
</tr>
<tr>
<td>Chau (2016) [26]</td>
<td>Targeted NGS</td>
<td>213</td>
<td>8 (4%)</td>
<td>8</td>
</tr>
<tr>
<td>Massard (2017) [27]</td>
<td>NGS, CGH, RNAseq</td>
<td>843</td>
<td>199 (24%)</td>
<td>15</td>
</tr>
<tr>
<td>Tredan (2017) [28]</td>
<td>TES, CGH</td>
<td>1826</td>
<td>101 (6%)</td>
<td>n/a†</td>
</tr>
<tr>
<td>Rack (2019) [29]</td>
<td>Targeted NGS</td>
<td>101</td>
<td>3 (3%)</td>
<td>3</td>
</tr>
<tr>
<td>Present study</td>
<td>IHC</td>
<td>45</td>
<td>3 (7%)</td>
<td>3</td>
</tr>
</tbody>
</table>

† Subgroup analysis not yet available.

CGH: Comparative genomic hybridization; FISH: Fluorescence in situ hybridization; IHC: Immunohistochemistry; MA: Oligonucleotide microarray gene expression assay; NGS: Next generation sequencing; RNAseq: RNA sequencing; TES: Targeted exon sequencing.

Results

Considerations of oncopanel testing in clinical routine

We established oncopanel testing for patients with recurrent or metastatic head and neck carcinoma. All attending head and neck oncologists were able to order oncopanel testing from May 2014 to May 2018. In total, 59 patients were eligible for oncopanel testing (Figure 2A); however, after discussion with the patients, 14 patients refused testing. Although not formally assessed, rapid tumor progress and unwillingness for additional treatment were common reasons. The pertinent clinicopathologic features of the remaining 45 patients (median age: 59 years; range: 23–90) are provided in Table 1. We did not restrict testing to a specific subset of tumors by anatomic location or histologic subtype. Review of Table 1 illustrates the heterogeneous spectrum of encountered cases. Oncopanel testing was performed on archived material or fresh tumor biopsies as described above. Oncopanel results were discussed in our interdisciplinary tumor board at the Comprehensive Cancer Center Ulm. We presented on average 1 oncopanel testing eligible patient per month (range: 0–3) to the board whereas a total of 331 patients with recurrent or metastatic head and neck cancer were presented at the same time (average of 1–2 patients per week).

The oncopanel identifies potentially actionable markers

The oncopanel results are shown in Figure 2B. Briefly, in the initial 24 patients the oncopanel consisted of ten markers (n = 24 × 10 = 240 data points) and we extended the oncopanel in August 2016 by adding PD-1/PD-L1 (n = 21 additional patients × 12 = 252 data points). This led to a total of 492 data points in 45 cases. The overall technical failure rate was 0.8% (n = 4/492; empty fields in Figure 2B). The overall fraction of immunopositive tumor across all markers was 23% (n = 112/488) with an average number of expressed markers of 2.4 per case. The range of immunopositive markers per case was 1–5, and each case showed immunopositivity for at least one response. The marker distribution was plotted using R (www.r-project.org) and for statistical calculations we used SPSS v23 (IBM, NY, USA) and Excel v16.10 (Microsoft, WA, USA); statistical significance was defined as p < 0.05.
Figure 2. Oncopanel testing in clinical practice. (A) The CONSORT diagram displays the study course. Eligibility criteria: no conventional treatment options, ECOG 0-2, patient’s wish for further treatment, availability of tissue for testing. From 331 palliative cases, 59 cases were selected for oncopanel analysis (selection rate: 18%). A total of 14 out of 59 eligible patients were either too weak for a new biopsy or withdrew consent for further treatment after tumor board decision (dropout rate: 24%). Three cases of the total 45 tested patients were treated according to oncopanel results (oncopanel directed treatment rate: ∼7%). (B) Landscape of marker expression (rows) per case (columns). Co-expression status of EGFR/MET/PDGFR served to group patients into four groups. Treated cases are indicated. Marker expression of case #4 was of diagnostic value because it revealed a late metastasis at an unusual site as of prostatic origin.
Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency (n = 45)</th>
<th>Percent</th>
<th>Number of markers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Entity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Squamous cell carcinoma</td>
<td>30</td>
<td>66.7</td>
<td>2.2</td>
</tr>
<tr>
<td>- Adenoid cystic carcinoma</td>
<td>7</td>
<td>15.6</td>
<td>3.1</td>
</tr>
<tr>
<td>- Sinonasal undifferentiated carcinoma</td>
<td>2</td>
<td>4.4</td>
<td>3.0</td>
</tr>
<tr>
<td>- Adenocarcinoma (prostate)</td>
<td>1</td>
<td>2.2</td>
<td>2.0</td>
</tr>
<tr>
<td>- Thyroid carcinoma</td>
<td>1</td>
<td>2.2</td>
<td>1.0</td>
</tr>
<tr>
<td>- Mucosal melanoma</td>
<td>1</td>
<td>2.2</td>
<td>3.0</td>
</tr>
<tr>
<td>- Merkel cell carcinoma</td>
<td>1</td>
<td>2.2</td>
<td>2.0</td>
</tr>
<tr>
<td>- Synovial sarcoma</td>
<td>1</td>
<td>2.2</td>
<td>2.0</td>
</tr>
<tr>
<td>- Salivary duct carcinoma</td>
<td>1</td>
<td>2.2</td>
<td>4.0</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Oral cavity</td>
<td>10</td>
<td>22.2</td>
<td>2.4</td>
</tr>
<tr>
<td>- Oropharynx</td>
<td>9</td>
<td>20.0</td>
<td>2.3</td>
</tr>
<tr>
<td>- Tongue base</td>
<td>7</td>
<td>15.6</td>
<td>2.4</td>
</tr>
<tr>
<td>- Paranasal sinus/lacrimal duct</td>
<td>6</td>
<td>13.3</td>
<td>2.2</td>
</tr>
<tr>
<td>- Skin</td>
<td>4</td>
<td>8.9</td>
<td>2.5</td>
</tr>
<tr>
<td>- Salivary glands</td>
<td>3</td>
<td>6.7</td>
<td>3.7</td>
</tr>
<tr>
<td>- Larynx/hypopharynx</td>
<td>5</td>
<td>11.1</td>
<td>2.4</td>
</tr>
<tr>
<td>- Thyroid</td>
<td>1</td>
<td>2.2</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Primary or adjuvant therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Surgery only</td>
<td>3</td>
<td>6.7</td>
<td>2.3</td>
</tr>
<tr>
<td>- Chemoradiotherapy</td>
<td>23</td>
<td>51.1</td>
<td>2.4</td>
</tr>
<tr>
<td>- Radiotherapy</td>
<td>19</td>
<td>42.2</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Previous palliative therapies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 0</td>
<td>12</td>
<td>26.7</td>
<td>2.2</td>
</tr>
<tr>
<td>- 1</td>
<td>18</td>
<td>40.0</td>
<td>2.7</td>
</tr>
<tr>
<td>- 2</td>
<td>7</td>
<td>15.6</td>
<td>2.9</td>
</tr>
<tr>
<td>- 3 and more</td>
<td>8</td>
<td>18.2</td>
<td>1.9</td>
</tr>
</tbody>
</table>

1 Simultaneously expressed potential protein targets per case (average number).

The most commonly expressed marker was the EGFR (80% of the cases), followed by MET (57.4%) and the PDGFR (32.8%). According to these main markers, cases clustered in three groups: positive for EGFR only (n = 10), positive for EGFR and MET (n = 16), positive for EGFR, MET and PDGFR (n = 9). Interestingly, the fraction of PD-1 and PD-L1 positivity in our series was low with only one tumor showing moderately intense staining in 5–10% of tumor infiltrating lymphocytes for both markers (tumor cells were negative). The patient had no measurable disease after resection of pulmonary metastasis. The significantly lower rate of PD-1/PD-L1 positivity, when compared with prior studies [3,8], is probably related to the combination of histotypes in our series (Table 1). Of note, in 13.3% of the cases, single PD-L1 positive cells were observed, although the fraction of immunopositive cells was below 1%. The other tested markers were mainly expressed in the group negative for EGFR, MET and PDGFR. In four cases, oncopanel analysis was performed repeatedly after tumor progress (Table 2) and we observed both a gain and loss of marker expression (Table 2). These alterations over time illustrate the heterogeneity of head and cancer and that repeated testing may identify new targets.

Given the prognostic and therapeutic relevance in locally advanced head and neck cancers [9,10], we had included assessment of the androgen receptor expression status in the oncopanel. Despite the high prevalence of expression in other studies [11,12], we rarely detected androgen receptor expression – and when first encountered in a 71-year-old male patient (case X_21), chart review – and subsequent workup clarified a metachronous metastasis of a previously known and treated prostate cancer. A consultation with the local uro-oncology team redirected care and the patient was treated with radiotherapy. Albeit unintentional, this case illustrates additional diagnostic value – namely clarifying that this was a metastasis to an unusual site rather than a new primary; akin to employing protein panels in the setting of cancer of unknown primary [13].

Three oncopanel patients received molecularly matched therapies

One secondary end point of the study was the number of patients receiving oncopanel-directed molecularly matched targeted treatment. Three of 45 tested patients (~7%) received oncopanel-matched therapies and the objective radiologic responses included two patients with progressive disease (cases X.3 and X.53) and one patient with a regional complete response (case X.58).
Figure 3. Objective response documentation. CT-imaging of the patient treated with trastuzumab, showing regional complete response of a pulmonary metastasis (A & B). CT-imaging of the patient treated with crizotinib before (C) and 3 months after therapy start (D). Comparison of maximum length and volume before and after treatment shows progressive disease (E). CT: Computed tomography.

Case X.3
The first patient was a 31-year-old male who initially presented with a keratinizing squamous cell carcinoma of the tongue (pT1N1cM0). After primary surgery and adjuvant radiation, the tumor recurred 6 months later and the patient underwent two systemic treatments. The first one consisted of induction chemotherapy with docetaxel, cisplatin and 5-flourouracil (TPF-regimen) followed by incomplete (R1) surgical resection. The patient had another recurrence after 7 months and received radiation combined with cetuximab. Due to persistent tumor burden, an oncopanel analysis was performed and showed strong MET expression in the tumor cells. After review in the tumor board, the patient was treated with 250 mg crizotinib twice daily p.o. for 140 days (4 months) until disease-related death. Volumetric reconstruction at day 104 on crizotinib indicated 80% tumor growth (Figure 3 C–E). However, the post-therapeutic CT scan showed pronounced central tumor necrosis.

Case X.53
The second patient was a 57-year-old male patient who initially presented with a nonkeratinizing squamous cell carcinoma of the floor of the mouth (pT4a cN2bM0). Primary treatment with chemoradiotherapy (CRT) resulted in complete remission. However, after 1 year the tumor relapsed and the patient received three different palliative treatments including: the TPF-regimen, re-radiation combined with cetuximab and methotrexate. Oncopanel
analysis was performed on a re-biopsy of the tumor after the second-line treatment with re-radiation. Tumor cells showed strong expression of PDGFR and due to a lack of therapeutic alternatives, the patient was treated with the tyrosine kinase inhibitor imatinib (400 mg daily p.o. for the first 28 days, followed by 400 mg twice daily). After 1 month (35 days), therapy was discontinued due to tumor progression and the patient received monotherapy with gemcitabine. The patient died 3 months later.

Case X

The third patient, a 62-year-old woman, presented with a sinonasal undifferentiated carcinoma, staged clinically as cT4bN2M0. Due to infiltration of the frontal dura and clivus, chemoradiotherapy was performed and resulted in a partial response. One year later, the tumor progressed with a single pulmonary metastasis and the patient was treated with cisplatin and 5-flourouracil. Due to complications (i.e., intractable mucositis), the chemotherapy had to be discontinued. Oncopanel analysis showed high expression of the HER2 and KIT in the tumor cells. After review by the interdisciplinary tumor board, the patient received a combination of trastuzumab (6 mg/kg, q3w) and docetaxel (30 mg/m², qw) [14]. Hereunder, the local tumor burden was stable, and the pulmonary metastasis vanished (regional complete response cM1 to cM0, Figure 3A & B). While the local tumor burden remained stable in control imaging 3- and 6-months after therapy, the therapy had to be stopped due to development of pneumonitis – a rare side effect of trastuzumab [15]. The patient received a total of 9 cycles trastuzumab and 10 cycles docetaxel (total of 161 and 203 days respectively).

Discussion

We report our experience with protein-based oncopanel testing in patients with end-stage head and neck cancer. We show that it is possible to prospectively test tumor samples and employ the oncopanel for treatment selection. Specifically, we have implemented oncopanel testing for eligible patients that make up approximately 18% of all head and neck cancer patients at our institution. We were able to place three (∼7%) of the tested patients on targeted therapy and objective radiographic responses underscore clinical utility. Our data on clinical utilization and radiographic response characterization supports continued assessment of oncopanel testing in clinical practice.

Options for palliative head and neck cancer patients are limited. Current recommendations mainly emphasize platinum-based systemic therapies; however, guidelines are primarily addressing patients with excellent performance (ECOG 0-1) [16]. Other agents show only limited efficacy due to tumor heterogeneity (e.g., of genetic alterations) which further increases with tumor progress [17,18]. Tumor progression results in severe functional impairments and a poor prognosis [19]. Once platinum-based therapies fail, there are fewer effective therapy options, yet, patients with tumor progress and their treating teams seek additional treatment. The oncopanel represents another tool to gain insights into the molecular composition of end-stage tumors that can be expanded to include other immuno-oncologically relevant targets.

Individualization of treatment strategies for end-stage cancer patients is one of the mainstays of precision oncology. Robust diagnostic, prognostic and predictive biomarkers are urgently needed. Currently, genotyping strategies represent the predominant approach for treatment stratification in clinical trials and clinical practice [6,20–22]. This emphasis is likely related to the stability of DNA and in our literature review (Table 3) on molecular matched therapies in head and neck cancer, we confirmed a heavy emphasis of genotyping strategies. The rate of matched therapies within the screened cohorts ranged from 3 to 77% [23–30]. Genotyping strategies require comprehensive panels to capture the small subsets of potentially relevant aberrations. Consecutively, comprehensive genotyping requires next-generation sequencing technology. These techniques come at a price – not only in equipment – but also in terms of expertise and a highly skilled bioinformatics team. Moreover, these programs are currently largely restricted to tertiary care and academic medical centers. While commercial solutions are growing, unfortunately, most community settings will not have access to these types of programs. However, even if such programs are in place, payors consider the current evidence as not sufficient to justify comprehensive genotyping in end-stage head and neck cancer – and more importantly, expert panels do not mention genotyping in the workup of head and neck cancers [16,31]. In contrast, recent trials (Keynote-040, Keynote-048) demonstrated a pronounced benefit from pembrolizumab in PD-L1 overexpressing tumor patients. Thus PD-L1 testing is recommended [32] and we consider this a shift to more comprehensive assessments (i.e., integrated diagnostics). Similarly, the functional consequences of cancer-specific, somatic genetic variants manifest at the protein level. Moreover, proteins represent the biological target structure of most (targeted) cancer therapies [6]. While integrated characterization at the genetic and protein level is preferred at the discovery stage (e.g., TCGA initiative, cBioPortal, etc.), from a turnaround time, financial
and clinical perspective, we argue that the oncopanel approach may represent a feasible alternative when genetic programs are not available. Though the oncopanel could consist of many additional markers, we outline one approach that can harness the regional/local-available immunohistochemical procedures.

Despite the high dropout rate of patients and the limited number of patients who received treatment, we consider our preliminary targeted treatment data informative. Based on their tumor expression status of MET, PDGFR and HER2, we treated three patients with crizotinib, imatinib and trastuzumab, respectively.

High EGFR expression in HNSCC, as in our cohort, is reported to be apparent in 80–100% of tumor tissue [33], although the success of EGFR-targeted therapy, for example, cetuximab, is not dependent on EGFR expression levels [34]. MET overexpression in about 60% of cases was not surprising [35] and there exist several effective therapeutic strategies in other tumors (e.g., crizotinib in non-small-cell lung cancer with MET amplification) [36,37]. In our cohort, one patient (X-3) was treated with crizotinib and experienced progression within 4 months of therapy. While we noted radiographic evidence of central tumor necrosis, it remains unclear whether this was caused by treatment or central hypoxia. High PDGFR expression was found in about 35% of our cases, which is consistent with a variable, but high expression rate in reports on HNSCC [38]. The multikinase inhibitor imatinib has been shown to be effective in vitro, but failed end points in a Phase II study [39–41]. At last, patient X-58 was treated with trastuzumab and had a partial complete response (i.e., disappearance of pulmonary metastasis). While literature findings on HER2 expression in head and neck cancer is controversial [42], overexpression of HER2 in cell lines followed by treatment with lapatinib is effective in vitro and in vivo [43].

Compared with the reviewed studies (Table 3) our rate of 7% of tested patients having received targeted therapy is rather low. However, this is likely related to many end-stage patients in our study design. Therefore, we currently aim to expand the oncopanel by additional markers (immuno-oncology, BRAF- and IDH-mutation-specific antibodies, etc.) and to refine scoring algorithms (e.g., CPS for PD-L1 testing). It is clear that the complex network between tumor, immune system and oncologic intervention has to be better elucidated in order to develop more efficient multimodality treatments. We are fully aware that the total number of cases in our study is low. Furthermore, the inclusion of patients across histotypes is unusual; however, these patients reflect our daily clinical practice and indicate the target group with a definite need for additional treatment options. The data indicate that our approach is generally feasible, and we continue to employ the oncopanel in our routine clinical practice for advanced and heavily pretreated patients. Continued testing will increase the total number of patients and contribute to assess overall clinical utility.

Conclusion
Oncopanel analysis is an option for palliative patients having received several lines of conventional treatment including checkpoint inhibition. The presented concept can help to identify possible targets and is in line with emerging field of precision oncology. However, the present study is only providing a small contribution to the field. A lot more data will be needed to move individualized cancer treatment toward a clear demonstration of clinical validity and utility. Based on our current experience, patients progress quickly and run out of options. Thus, we suggest to perform oncopanel testing early in the disease course.

Future perspective
With many emerging precision oncology studies, we will have more data that demonstrate feasibility of individualized treatment approaches. However, at the moment several hurdles have to be overcome. First, head and neck carcinomas as a cancer type is under-represented in many studies. At the 2019 annual meeting of the American Society of Clinical Oncology, one clinical study on salivary gland carcinomas has been presented, and it is to be hoped that this trend will continue. Second, in head and neck cancer there are hardly any established predictive biomarkers and the response rates are not promising. At last, genetic analysis is costly.

The present study attempts to alleviate the financial burden by repurposing a cost-effective and widely established method (i.e., immunohistochemistry). In light of the promising results for PD-L1 antibody testing and continued cost-pressures in healthcare, we anticipate that adoption of protein-based testing will continue – and possibly supplement DNA-based testing strategies.
Summary points

- Head and neck carcinoma are difficult to treat in very advanced stages.
- Measuring protein expression is a feasible method to detect therapeutic targets.
- A total of 45 patients suffering of different entities could be analyzed.
- Tumors were stained for a panel of 12 targetable proteins.
- Each patient had at least one marker at high expression.
- Three patients could be treated following the panel results.
- One of three accordingly treated patients had a regional complete response.
- The panel has to be refined in order to comprise more targetable markers.

Author contributions

JK Lennerz designed research; TKH Hoffmann and PJ Schuler selected patients; F Leithäuser, TFE Barth, P Möller and J Doescher analyzed results; L Bullinger, SS Schönsteiner, S Laban and J Doescher treated patients; J Doescher, JK Lennerz and PJ Schuler wrote the paper; all authors edited the paper.

Conflict of interest

The authors declare no conflict of interest.

Financial & competing interests disclosure

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

Patients signed an informed consent about off-label treatment. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References


