Comprehensive molecular and phenotypic profiling of end-stage IV cancer identifies treatable targets and improves survival in individual patients

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BACKGROUND

Comprehensive profiling of patients’ tumor tissue in cases of end-stage IV cancer of different tumor sites was conducted to identify mutations, proteins and activated cancer pathways potentially eligible for targeted therapies. Data evaluation included test results, clinical data, clinical trials and longitudinal follow-up data.

METHODS

Rapid tissue collection and processing was conducted under highly standardized conditions (scheme time <20 min) to preserve the expression profile in tissue as it appears in the human body. Samples that passed the quality control (tumor content ≥50%) were analyzed using the following techniques: immunohistochemistry (IHC), next-generation sequencing (NGS) and single western charge-based assays (NanoPro 1000 system). Expression of the major receptor proteins and phosphorylation of the signaling proteins ERK1/2, MEK1/2 and AKT of the MAP kinase pathway and the PI3K/Akt/PI3K pathway were measured to infer targets on the (phospho) proteomic level. On the genomic level DNA sequencing of “hotspot” regions covering 50 oncoproteins and tumor suppressor genes was conducted using the Ion-AmpliSeq™ Cancer Hotspot Panel v2.

RESULTS

Analyses of 83 patients were performed. 28 patients met the determined evaluation criteria. These patients were divided into two groups. In one group (n = 14) targets for available therapeutics could be identified and patients were treated accordingly. In the other group (n = 14) targets could not be found or were not regarded as useful by the oncologics. These patients were treated with conventional, palliative therapies. The 6-month follow-up revealed a better outcome when patients were treated according to an identified target. 90% of patients responded to targeted treatment. 14% of patients had a complete remission (CR), 14% had a stable disease (SD) and another 21% had a partial remission (PR), 30% progressed under targeted therapy and 14% died. In contrast, only 21% responded under conventional, palliative therapy by showing a stable disease, 60% of patients progressed (PD) and 24% died. No complete or partial remission was observed in patients treated by conventional approaches.

OVERVIEW OF FOLLOW-UP AND TREATMENT RESPONSE

Figure 1: Kaplan-Meier survival curve. The red line indicates survival probability of the 14 evaluated patients who were initially treated according to a specific molecular target. The blue line belongs to the 14 patients who initially received no molecular target.

CONCLUSION

A comprehensive molecular and phenotypic tumor characterization can identify in individual patients - suffering from highly advanced cancer - targeted therapies that impact cancer growth and lead in single cases even to a complete remission.