Abstract

Precisation prediction of therapeutic response to cancer immunotherapy

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Introduction and aims: Over the last few years, anticancer immunotherapy has increasingly become an important agent in treatment of oncologic patients.

The aim of this thesis was to assess the clinical parameters and to find any biological markers that would predict efficacy of pembrolizumab and nivolumab.

Methods: The research was based on retrospective data analysis of patients treated with pembrolizumab or nivolumab during 2015–2020 at Oncology Clinic of General Uviersity Hospital in Prague. The patients were divided into responder or non-responder groups based on their treatment response. Subsequently the analysis of clinical parameters, adverse events, panel gene sequencing of tumor DNA and RNA was performed. Finally, the obtained data were tested to find any correlations between biological markers and the treatment outcomes by the descriptive statistic method.

Results: The data of 70 patients (60 % men, between 42–86 years old) were analysed. The most frequent patient profile was man in age 70–79 years with non-small cell lung cancer diagnosis. In parallel to oncologic conditions, the patients were suffering from two and more diseases (74 %) of which arterial hypertensis was the most frequent (51 %). Immune-related adverse events were found in 14 % of patients. The analysis identified 44 % of patients as checkpoint therapy responders. Valid gene panel sequencing was performed in 17 % of the cases. The responders exhibited more pathogen variants of genes (minimum 2, median 4) than non-responders (median 2.5). Variants of these genes (total 13) were found exclusively in non-responders: APC, ARID2, BRAF, CDH2, CDK12, DPYD, ERBB4, H3F3A, KEAP1, KRAS, MTOR, NTRK3, PMS2. For responders, the exclusive 4 variants of mutations were found in genes GRM3, GHF, MLL2 and NOTCH2.

Conclusin: The clinical parameters of the patients did not show significant abnormalities and several potentially predictive variants for treatment with checkpoint inhibitors were found in both groups. Furthermore, larger groups of patients should be assessed to confirm the results on basis of statistical significance.