AB008. OA01.08: Thymic carcinoma: preliminary data of next generation sequencing analysis

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Background: The genomic events leading to thymic carcinoma (TC) development are largely unknown, although a series of cases were investigated by the Cancer Genome Atlas (TCGA) study and by different groups interested in thymic carcinogenesis. Although the mutational burden in TC was found to be low in the limited series investigated by the TCGA study, a next generation sequencing (NGS) mutational analysis of other cases could allow the identification of further genomic alterations. This would provide biological data with relevant prognostic/predictive value. We aim to explore by NGS the genomic asset of a series of TC.

Methods: Ten TC cases were examined, derived from biopsies/surgical specimens and one matched peritumoral thymic sample. In one case a lung metastatic nodule was available. Six epidermoid carcinomas, 3 undifferentiated carcinomas and one lymphoepithelioma-like carcinoma were investigated. The percentage of neoplastic cells was not <70–80% of total cells. The DNA was extracted using the QIAcube and QIAamp DNA FFPE Tissue Kit (Qiagen, Valencia, CA) from microdissected 5 µm formalin-fixed, paraffin-embedded (FFPE) tissue sections. By the NGS platform Ion S5 (Thermofisher) the Ion AmpliSeq™ Cancer Hotspot Panel v2 was used; this panel is designed to amplify 207 amplicons covering over 2,800 COSMIC mutations from 50 oncogenes and tumor suppressor genes. Libraries from Ion AmpliSeq Cancer Hotspot Panel v2 were prepared and sequenced by Ion Chef and S5 system. Data analysis was conducted by using the dedicated Ion Reporter Software.

Results: The NGS sequencing identified in 7/10 cases the variant (SNP) c.1416A>T p.Q472H of the "Kinase insert Domain Receptor" gene (KDR) (coding for VEGFR2). In one out of three cases a KIT mutation (c.1900C>T; p.R634W) (ex. 13), already reported in TC, was identified, and in four cases p53 mutations occurring in different sites were identified. One case harboured a KRAS mutation (c.35G>T; p.) (ex. 2). The AKT1 (also termed protein kinase B) (PKBα) variant c.49G>A p.E17K was observed in one case.

Conclusions: The Ion AmpliSeq™ Cancer Hotspot Panel applied contained part of the common mutations found by the TCGA study in TC. The preliminary data allowed to identify several genomic alterations. The KDR variant Q472H represents a described Single Nucleotide Polymorphism (SNP) which was reported to be correlated with longer OS in patients with thymic tumor. The reported p53 mutations are described in the international database of Cancer genomics study Cbioportal as causing a protein loss of function in different cancer types. Moreover, we found in one case the variant E17K of AKT1, previously reported as a deleterious variant in various cancer types, possibly associated to aberrant AKT activation. This mutation has been proved to be targetable by the pan-AKT inhibitor AZD5363. The KIT identified variant R634W, exon 13, could be considered relevant for target therapy with Sorafenib multikinase inhibitor as described. The reported mutations have been found in thymic epithelial tumors or in lymphoid neoplasias and need to be better characterized and validated by pre-designed TaqMan Genotyping Assays Real Time PCR. Our purpose is to contribute to dissect the molecular pathways underlying TC pathogenesis.

Keywords: Next generation sequencing (NGS); target therapy; thymic carcinoma; genomics

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