Clinical Relevant Oncogenic Drivers in Advanced Adenocarcinoma Discloses New Therapeutic Targets in Negative EGFR:ALK:KRAS Patients

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Conclusion: HC-based MPS changed therapeutic strategy in close to half of the patients with lung cancer, and was associated with high overall response rate, which may translate into a survival benefit.

Keywords: massive parallel sequencing, Driver Mutations, Targeted therapy, Immunotherapy

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Clinical Relevant Oncogenic Drivers in Advanced Adenocarcinoma Discloses New Therapeutic Targets in Negative EGFR/ALK/KRAS Patients

Topic: Biomarkers

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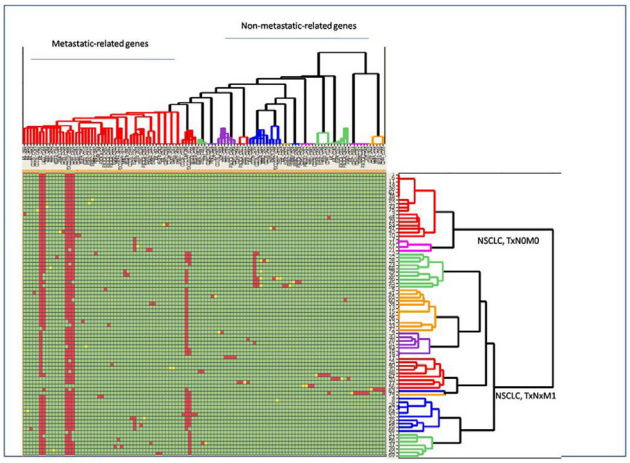
Background: The mutation profile in the Brazilian population with advanced lung adenocarcinoma remains largely unexplored and also their relationship to many other genes. Next Generation Sequencing(NGS) allows higher sensitivity and multiplexing for several genes for translational research.

Methods: 80 lung adenocarcinoma patients were collected. DNA concentration and quality was determined by Qubit2.0fluorometer and Agilent2100Bioanalyzer. Genomic libraries were constructed using the TruSeq®Custom Amplicon v1.5) comprising 764 amplicons of 38genes on the Illumina-MiSeq®sequencing plataform.

Results: The 7362 genetic mutation were observed with 78% of single-nuclotide variants (SNVs) and 22% insertions and deletions. The majority of the SNVs were located in inter-genic regions or introns. *EGFR* were mutated in 21 (6%) of patients with 19 (57%) of mean expression. The most frequent *EGFR*-mutation was exon 19deletions, followed by L858R amino acid substitution in exon 21. *KRAS* was mutated in 26 (4%) of patients. ALK rearrangement was detected in 6 patients (4.8%). The stop gained mutation was present in *PIK3CA*, *TP53*, *AXL*, *EGFR*, *RAB25*, *CDH1*, *CD276* and *TGFB1*. The AXL receptor tyrosine kinase gene showed 11 missense-mutations, of which 7 are considered possibly damaging (Polyphen)/deleterious(SIFT)(74/79) and 14 intronSNVs(49/80). CD44 showed 50 variants, however most of them have an undetermined significance. The clustering analysis demonstrated that a select group of AXL-related gene alterations was highlighted (Fig 1).



Conclusion: The results suggest that genomic variants in lung adenocarcinoma tissues are complex and show that NGS is an effective way to detect novel mutations in lung cancer. 58% of patients wild type by standard testing for EGFR/KRAS/ALK have genomic changes identifiable by CGP that suggest benefit from target therapy. The AXL and CD44 genes remain a relatively unexplored target, thus we intend to increase the available data for the true translational potential of target AXL and CD44 therapy in lung cancer. CGP used when standard molecular testing for adenocarcinoma is negative can reveal additional avenues of benefit from targeted therapy.

Keywords: non-small cell lung cancer, advanced lung cancer, mutations, next generation sequencing

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EGFR FISH as Potential Predictor of Necitumumab Benefit with Chemotherapy in Squamous NSCLC: Subgroup Analyses from SQUIRE

Topic: Biomarkers

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