

PP215 Differential efficacy of tyrosine kinase inhibitors (TKIs) according to the type of EGFR activating mutations and agents in non-small cell lung cancer (NSCLC): A real-world study

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Background: Both 1st and 2nd-generation (gen) EGFR-TKIs are recommended in advanced NSCLC with EGFR activating mutations. However, there are few data about the difference in the efficacy of EGFR-TKIs according to type of EGFR mutations and agents.

Methods: This retrospective real-world study evaluated the outcome and clinicopathologic characteristics including the type of EGFR activating mutations in 214 advanced NSCLC patients (pts) treated with 1st or 2nd-gen (afatinib) EGFR TKIs as first-line therapy.

Results: The median progression-free survival (PFS) and overall-survival (OS) of all pts were 12 months (M) and 26M, respectively. In univariate analysis, pts with exon 19 deletion (del) (n=130) tended to have a longer median OS compared to those with L858R mutation (n=84) (30 vs. 22 M, p=0.071), without difference in PFS (p=0.472). Pts treated with afatinib (n=56) had a tendency of longer median OS compared to those treated with 1st gen TKIs (gefitinib: 142, erlotinib: 16) (30 vs. 24 M, p=0.068). In pts with exon 19 del, there was no significant difference in median PFS (p=0.868) and OS (p=0.361) between pts treated with afatinib and those with 1st gen TKIs, while a trend in better PFS (14 vs. 10 M, p=0.071) was observed in pts receiving afatinib without difference in OS (p=0.160) in L858R mutation. Exon 19 del was independently associated with favorable OS (p=0.040), while age >70 years (p=0.026), ECOG performance status ≥ 2 (p=0.005), and primary metastatic disease (p=0.003) were independent prognostic factors of poor OS.

Conclusions: The EGFR exon 19 del was associated with favorable outcome in advanced NSCLC pts receiving first-line TKIs, regardless of the type of agents. The mutation subtypes should be considered when selecting TKIs for pts with EGFR activating mutations.

Keywords: EGFR, Lung Cancer, Tyrosine Kinase Inhibitor

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PP217 Dynamics of disease progression during treatment with osimertinib in patients with EGFR T790M-positive non-small cell lung cancer

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Background: Despite the remarkable efficacy of osimertinib in epidermal growth factor receptor (EGFR) T790M-positive non-small cell lung cancer (NSCLC), the development of resistance is inevitable. We aimed to analyze the disease progression pattern during osimertinib treatment to identify potential treatment strategies.

Methods: We retrospectively identified patients with advanced NSCLC who began osimertinib treatment after progression on previous EGFR-TKI between June 2014 and November 2018. Patient characteristics, efficacy outcomes, radiological sites of metastases, and treatment modalities before and after osimertinib were analyzed.

Results: Eighty-four patients were included. On osimertinib initiation, bone (50.0%) and brain (41.9%) were the most common single metastatic sites, whereas thoracic involvement (73.3%) was more frequent than bone (27.4%) or brain (20.2%) metastasis during disease progression on osimertinib. Oligo-progressive disease (PD) and central nervous system (CNS)-sanctuary PD were observed in 15 (17.9%) and 3 (3.6%) patients, respectively. Most patients without brain metastasis (BM) at the initiation of osimertinib administration remained BM-free (46/49, 93.9%), and 60% of patients (21/35) with pre-existing BM showed intracranial disease control despite extracranial PD. The mechanism of resistance to osimertinib was explored in 23 patients (27.4%), and T790M-loss was observed in 13 patients (56.5%); these 13 patients had worse survival outcomes than patients without T790M-loss (progression-free survival 6.1 months vs. 13.9 months, P=0.04, overall survival 44.9 months vs. not reached, P=0.03).

Conclusions: PD during osimertinib treatment preferentially occurred in the thorax and pre-existing sites. Extracranial PD prevailed over intracranial PD regardless of baseline BM and prior brain radiation. These results support the intracranial efficacy of osimertinib and may guide treatment strategies for EGFR-mutated NSCLC with BM.

Keywords: NSCLC, EGFR, Osimertinib

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PP223 Single-cell RNA sequencing in metastatic lung cancer uncovers the efficacy of PD-1/PD-L1 inhibitors on immune cell population

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Background: Programmed cell death protein and its ligand (PD-1 / PD-L1) inhibitors are approved for the treatment of metastatic non-small cell lung cancer. It is well known that in cancer, PD-L1 is highly expressed hence cancer cell can evade the host immunity in tumor microenvironment (TME). Although PD-1 / PD-L1 inhibitors have been clinically utilized, the biological factors determining treatment outcome remain convoluted. An in-depth investigation of cellular heterogeneity – including both cell subtypes and states will provide foundational evidence for clinicians and researchers to improve PD-1 / PD-L1 immunotherapeutic practice. Unlike bulk RNA-seq, scRNA-seq enables researchers to properly decipher and analyze the complex cellular heterogeneity. Thus, clustering cells by its cell type makes it possible to reflect unique features of gene expression in each cluster.

Methods: scRNA-seq from 674,609 cells populating early, late, metastatic stage lung cancer and the normal lung tissues from 100 subjects, as well as samples from patients in advanced metastatic stages with differing biopsy sites were analyzed. Single-cell tools: SCANPY, SCVI, AZIMUTH, PYSCENIC, DEG. Each of these tools was used to analysis: Clustering, Annotation, Trajectory, Cell-cell interaction.

Results: Specific transcription factors (TF) are up-regulated in progressive-disease samples. - In T lymphocyte, TF "NR2F6" proposed as an alternative cancer immune checkpoint is up-regulated and notably expended in exhausted CD8+ T cell. - In Macrophage, TF "FOXA1" known to have relation with progression and therapy resistance is up-regulated. Plasma proportion extension is widely observed in most diseases' samples. Likewise NSCLC data show prominently high population of Plasma cell. In Plasma cell, TF activities show difference before and after treatment. - TF "E2Fs" known to associated with the development of cancer. E2Fs are high in pre-treatment sample and relatively low in post-treatment samples. - TFs "GRHL2", "Six1" known to suppress tumor metastasis via regulation of transcriptional activity are up-regulated in post-treatment samples.

Conclusions: Through robust bioinformatic analyses, immune cell represented differential population composition and each cell type show different transcription factor expression according to treatment or responder status. This single-cell analysis potentially reveals pathways targeted by immunotherapy and discover possible therapeutic targets.

Keywords: Single-Cell, Immunotherapy, Non-Small Cell Lung Cancer

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PP225 Real-world data of ramucirumab plus docetaxel compared with docetaxel after immune-checkpoint inhibitors in stage IV non-small cell lung cancer patients

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Background: Non-small cell lung cancer (NSCLC) is a leading cause of cancer death worldwide. Ramucirumab plus docetaxel became one of the available options for subsequent treatment in NSCLC after REVEL study. In addition, immune-checkpoint inhibitors (ICIs) became standard of treatment for NSCLC. Combining ICIs with anti-vascular endothelial growth factor blockade is one of many tries to overcome the resistance. We present our real-world data of ramucirumab plus docetaxel compared with docetaxel after ICIs in stage IV NSCLC patients.

Methods: We retrospectively collected clinicopathologic data of NSCLC patients who were treated with ramucirumab plus docetaxel or docetaxel for second to fourth line of treatment after ICIs from 1st January 2019 to 31th October 2021 in Samsung Medical Center. After patients with EGFR, ALK or ROS1 mutations were excluded, 38 patients in ramucirumab/docetaxel group and 183 patients in docetaxel group were included in the analysis. Primary endpoint was progression-free survival (PFS), and secondary endpoints were overall survival (OS) and overall response rate (ORR).

Results: Variables of age, treatment line were significantly different between two groups. Ramucirumab/docetaxel showed significantly better PFS than docetaxel alone after ICIs (p = 0.012) in this analysis. Hazard ratio was 0.59 (95% confidence interval 0.37 – 0.96). Median PFS was 6 months in ramucirumab/docetaxel group, and 2 months in docetaxel group. In multivariable analysis for PFS with cox proportional hazard regression, only treatment group and histology showed significant differences. Ramucirumab/docetaxel group had a significantly better response than docetaxel group (p = 0.019). 14 (36.8%) and 47 (25.7%) in ramucirumab/docetaxel group and docetaxel group each achieved partial response. Only one patient who were treated with docetaxel showed complete response among all patients. 18 (47.4%) patients in ramucirumab/docetaxel group and 68 (37.2%) patients in docetaxel group showed stable disease as a best response. However, there was no significant benefit regarding