54P Investigation of the mechanisms of resistance to osimertinib in patients with T790M-associated NSCLC

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Background: Osimertinib (Osi) is a 3rd generation TKI that crosses the blood-brain barrier (BBB), which has been shown to be effective in both the second and first line of treatment in patients with NSCLC with an EGFR mutation. In use of Osi in patients with T790M associated progression during therapy with earlier TKIs, the median PFS was 10.1 months. The duration of treatment may vary significantly for each patient. The study of the mechanisms of resistance to 3rd generation TKIs is the subject of clinical studies, among the most common variants of resistance - the appearance of the gate-keeper mutation C797S - in 7% of cases.

Methods: It is prospective, single-center study we examined the appearance of resistance in patients receiving Osi treatment.The search for the C797S mutation was carried out using an original diagnostic platform based on real-time PCR, using the BioRad Real-Time CFX96 amplifier. Primers and fluorescent probes were synthesized by Applied Biosystems compony. The study included patients with progression during therapy with Osi. Before treatment, and then every 2 months until progression of the disease appease, blood sampling was performed to conduct a qualitative assessment of ctDNA (ex19del, L858R, T790M, C797S).

Results: From August 2016 to August 2019, in 12/22 patients, progression of the disease during the Osi. Emong them, 66.7% (7/12) are women, 33.3% (4/12) are men. The average age is 64.6 years (55-80). 1/12 smoked for over 30 years. The molecular genetic profile in 58.3% (7/12) of the patients is ex19del, 33.3% (4/12) of L858R, 8.4% (1/12) is a combination of rare mutations G719S + S768I. The median PFS during the Osi treatment was 9.6 months. (0.7 - 18.4).The analysis of ctDNA was performed in 11/12 patients: an activated mutation was detected in all cases, 1/12 recorded the mutation C796S (NGS), T790M and C797S (cis/ trans) were not detected.Histological material was taken from 4/12 patients, 2 of which showed the transformation of the tumor into small cell lung cancer.

Conclusions: The investigation of appearence the resistance mechanisms in the treatment with osimertinib did not reveal the EGFR C797S mutation, which may be associated with a small number of patients included in the study.Grant supported RUSSCO / RakFond 2018-01-YS-ECI.

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