NSCLC, metastatic

ERMETIC-2 PROJECT: IMPACT OF SYSTEMATIC EGFR AND KRAS MUTATION EVALUATION BY ALTERNATIVE TESTING METHODS ON PROGRESSION-FREE (PFS) AND OVERALL SURVIVAL (OS) IN PATIENTS WITH ADVANCED NON–SMALL-CELL LUNG CANCER (NSCLC) TREATED BY ERLOTINIB (E) IN THE IFCT ERMETIC COHORT

M. Beau-Faller1, M. Texier2, H. Blons3, N. Richard4, F. Escande5, I. Bieche6, S. Lizard7, F. De Fraipont8, F. Morin9, G. Zalcman10, J. Pignon2, J. Cadranel11

1Laboratoire de Biochimie et de Biologie Moléculaire, Hôpitaux Universitaires de Strasbourg et INSERM U682 Hôpital de Hautepierre, Strasbourg, FRANCE
2Biostatistics, Gustave Roussy, Villejuif, FRANCE
3UMR-S775, Université Paris Descartes, Paris, FRANCE
4Laboratoire de Génétique Moléculaire, CHU, Caen, FRANCE
5Pôle de Biologie Pathologie Génétique, CHRU, Lille, FRANCE
6Laboratoire d’oncogénétique, Institut Curie, Paris, FRANCE
7Unité de Biologie Moléculaire, Centre Georges François Leclerc, Dijon, FRANCE
8Laboratoire de Génétique, CHU, Grenoble, FRANCE
9IFCT (Intergroupe Francophone de Cancérologie Thoracique), Paris, FRANCE
10Service de Pneumologie, C.H.U. de Caen, Caen, FRANCE
11Service de Pneumologie, APHP, CancerEst, Tenon University Hospital, Paris, FRANCE

Aim: ERMETIC is a French (IFCT) prospective study of EGFR and KRAS mutation evaluation by sequencing in patients with advanced NSCLC treated by E. The aim of the ERMETIC-2 project was to determine the prognostic impact of using alternative molecular techniques in the available tumor samples of the ERMETIC cohort.

Methods: 239 patients (pts) with tumors were available for re-analyze by previously described alternative techniques (J Mol Diag 2014). Multivariate Cox model with performance status, histology, smoking status and initial number of metastatic sites was used for prognostic analysis.

Results: Population included 59% of adenocarcinoma, 37% of women and 19% of non-smokers. Overall mutation rate is 46%: 31 EGFR mutations (13%) and 78 KRAS mutations (33%); 40 new mutations compared to previous study were found: 9 EGFR and 31 KRAS. In the ERMETIC 2 cohort, OS and PFS remained significantly (global test p < 0.01) better for EGFR mutated (hazard ratio [HR] 0.57 [95%CI: 0.33-1.00] and 0.47 [0.28-0.78] respectively) and worse for KRAS mutated (HR 1.35 [0.97-1.88] and 1.16 respectively [0.85-1.59]) compared to wild-type (WT) NSCLC. No prognostic significant difference was found in the 177 pts common to both cohorts between pts with KRAS mutation in both cohorts (n= 28) and those with new (n= 31) mutations. In the 228 pts with several techniques, KRAS mutations detected by less sensitive technique (n= 42) have a lower OS compared to WT than those detected only by the best sensitive technique (n= 34), but are not significantly different: 1.63 (1.09-2.44) and 1.08 (0.69-1.69); results between techniques were similar for PFS. Among the KRAS mutated group, no prognostic difference was found comparing mutations in codon 12 (67 pts) and 13 (8 pts), or transitions (24 pts) and transversions (51 pts).

Conclusions: 1. KRAS but not EGFR mutations were detected in higher proportion by alternative molecular techniques compared to sequencing. 2. KRAS mutations identified by more sensitive technique did not identify a group of patients with a different prognostic.

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