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IS OUR SELECTION OF NSCLC (NON-SMALL CELL LUNG CANCER) PATIENTS FOR EPIDERMAL GROWTH FACTOR RECEPTOR-TARGETED ASSESSMENT TOO NARROW?

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Purpose: Assessment of EGFR mutation status is currently the most successful and widely used potentially prognostic and predictive tool in the selection of NSCLC patients to personalized therapy with TKIs. In this prospective, epidemiological study, men and women in various stages of NSCLC were sequentially tested for EGFR mutation status. **Patients and Methods:** Between 09/2009 and 08/2010, 598 patients diagnosed at Helios Klinikum Berlin Zehlendorf (HKBZ) and 193 patients from other centers (control group) in various stages of NSCLC participated in this study. Tumor samples were formalin treated, paraffin embedded and DNA was isolated after microdissection. Samples were evaluated for EGFR mutations on Exon 18, 19, and 21 by Pyrosequencing (PS) and BioFilmChipHybridization (CHIP). In addition, a LightCycler Assay - based on Real-Time PCR - was performed for Exon 19. All detected mutations were tested by Sanger sequencing. **Results:** 791 tumor patients, 598 from HKBZ comprised of 239 women (39.9%) and 359 men (60.1%) and 193 from other centers (control group) comprised of 85 women (44.0%) and 108 men (56.0%) were evaluable. In the HKBZ group median age was fairly consistent: women 66.06y (range, 25-89y) and men 66.46y (range 40-100y). In the control group median age during the first six-month period was for women 60.55y (range 40-82y) and men 66.14y (range 43-84y); in the second six-month period the median age shifted to women 62.67y (range 40-85y) and men 65.67y (range 40-84y). 49.5% of all diagnosed tumors in the HKBZ group were adenocarcinomas, 26.4% squamous cell carcinomas, and 23.9% large cell carcinomas. In the control group there were 59.1% adenocarcinomas, 6.2% squamous cell carcinomas, and 34.7% large cell carcinomas. In the HKBZ group EGFR mutations were detected in 23 women (15.65%) and 5 men (3.33 %) with adenocarcinomas and in 1 woman (2.04%) and 3 men (3.19%) with large cell carcinomas. In the control group in the first 6 months, EGFR mutations were found in 3 women (9.68 %) and 2 men (5.88%) with adenocarcinomas. But in the second 6-month period EGFR-mutations were detected in 10 women (17.24%) and 3 men (2.6%) with adenocarcinomas and in 2 more patients with large cell carcinomas (8%). The median age of EGFR mutation-positive patients were 69.06y (HKBZ) vs. 56.67y (control group) in the first 6 months, and 69.31y (HKBZ) vs. 65.47y (control group) after 12 months. Smoking history was not always available, but at least 9 of 23 EGFR mutation-positive women from HKBZ were smokers. **Conclusion**: EGFR mutation analysis is the most efficient prognostic tool for identifying a cohort of patients most likely to respond to personalized therapy with TKIs. Our results indicate that limiting assessment of EGFR mutation status to a particular clinical phenotype (young, female with a smoking history and adencarcinoma) is too narrow and likely overlooks other NSCLC patients with EGFR mutations.