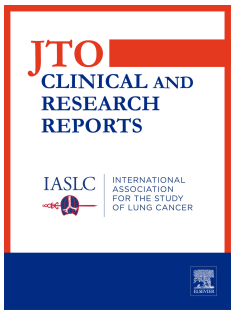

Exon20-mutated NSCLC: Extending the dataset to allow the recognition of potential causes.

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Letter to the editor JTO

Exon20-mutated NSCLC: Extending the dataset to allow the recognition of potential causes.

The consortium responsible for collecting data from 175 patients with EGFR exon 20-mutant non-small cell lung cancer (NSCLC), the European Exotic Registry (1), has added an important piece of information and for that we would like to congratulate the authors. To make this resource even more valuable, we would like to encourage the consortium to expand this important work beyond the identification of novel/better treatment approaches and to develop a plan to recognize causal factors associated with Exon 20 mutations (molecular archaeology). EGFR mutations, including those affecting Exon 20, are more frequent in non and never-smokers (2). The increasing incidence of lung cancers in non and never- smokers has been noticed in several parts of the world and it is a formidable challenge to identify its cause(s), and to try to translate them into public health measures. Asbestos and air pollution (PM2.5) are important causes of lung cancer in non and never-smokers and, also genetic susceptibility may contribute (3). Moreover, in contrast to multiple studies revealing carcinogenic synergy between smoking and asbestos exposure, little is known about the interaction between exposure to second-hand smoke and asbestos. Asbestos and PM2.5 exposures are found in occupational as well as in environmental settings and a recent study concluded that PM2.5 exposure and EGFR mutations are responsible for alveolar cell transformation in non and never-smokers (4). Considering that the average adult inhales about 10,000 L of air per day, even carcinogens present at relatively low concentrations may pose a risk factor. Healthy never-smokers, exposed to PM2.5 (at the same concentration found in polluted cities) for two hours, had an inflammatory response (IL-1beta) strong enough to drive alveolar cells into an activated state, ready to further transform into EGFR-mutant NSCLC (4).

It is also important to note that after the massive rise of asbestos consumption in the previous century, this group of minerals is now ubiquitously present in our man-made environment. This contamination may provide an explanation as to why the incidence of asbestos-related cancers fails to decline in most of the countries which have banned the use of asbestos and asbestos containing products (5). It may even be theorized, that small asbestos particles (length < 5 micrometer and considerably smaller than those asbestos fibres considered capable of inducing malignant mesothelioma) might become a part of PM2.5 pollution.

In order to attribute lung cancer to asbestos, air pollution, second-hand cigarette smoke or a combination of these carcinogens, occupational and

ideally also residential data should be collected and made available. Radiological signs of pleural plaques and pulmonary fibrosis have been accepted as indicative of asbestos exposure in the past and the list of occupations associated with asbestos exposure is considerable. Adding occupational, residential histories and radiological data to the EXOTIC database might well assist the consortium in getting closer to the cause(s) of Exon 20-mutated NSCLC.

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470 words, 5 authors, 5 references.

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