THE ROLE OF P53 GENE IN LUNG CANCER WITH SPECIAL EMPHASIS ON HEREDITARY TYPES

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Lung cancer is the most common type of cancer affecting men and the fifth most frequent female cancer. The survival rate related to lung cancer is low, with the 5-year survival amounting to 10-13% in highly advanced countries. In Poland lung cancer survival does not exceed 5%.

The major causes of lung cancer incidence include tobacco smoking, environmental factors and genetic predisposition. The most frequent genetic modifications observed in lung cancer cells are mutations in the *myc*, *ras* and/or *erb1* genes.

The p53 gene has been located on the short arm of chromosome 17 and has been found to consist of 11 exons with the first one being non-coding. The analysis of its sequence in different species resulted in identifying five highly conservative regions, including exons 1, 4, 5, 7 and 8. The p53 has been classified as a suppresser gene.

The p53 protein is a nuclear phosphoprotein composed of 393 amino-acids. This protein is active in the two most important stages of the cellular cycle: during the transition between phases G_1 and S and between phases G_2 and M. The function of p53 can be described as ensuring the integrity of the genome by preventing replication of the damaged DNA and cell division. When the repair process fails, p53 triggers the apoptosis of cells. In addition to the regulatory function, p53 acts also as a transcription agent.

Mutations in p53 are responsible for 60% of cases of human lung cancer. The mutations are most often found in microcellular lung cancer (70%) and are less frequent in the cases of adenoid lung cancer (33%). The most common mutations related to lung cancers include: transversions of the G:C/A:T type, missense mutations, nonsense mutations and deletions. These mutations occur in as many as 100 various locations but the most characteristic ones for lung cancer are found in codon 157, 248 and 273. The hereditary mutations in p53 are associated with the Li-Fraumeni syndrome. This syndrome indicates a higher risk of developing different forms of cancer, including lung cancer. Genetic testing aimed at identifying the carriers of p53 mutations should be limited only to high-risk groups defined on the basis of a diagnostic pattern proposed by Lynch. In the families with one member affected by lung cancer the risk of developing lung cancer by first-degree relatives is four times higher compared to general population risk.

CONTINUOUS ACCELERATED IRRADIATION (CAIR) OF HEAD AND NECK CANCER - TREATMENT TECHNIQUE, TOXICITY AND 2-YEAR RESULTS

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Purpose

Evaluation of preliminary (2-year) treatment results of 7 days a week continuous accelerated irradiation (CAIR) in compare to convectional and concomitant radiotherapy.

Methods

One hundred and twenty eight patients with squamous cell carcinoma of oral cavity, oro- and hypopharynx and supraglottic larynx in stage T2-4 NO-1 MO were randomized between 3 groups: A (study-CAIR) - 51 pts, B (control-2) - 28 pts and treated by radiation therapy alone in 1994-96. In majority (81%) there were the patients in advanced clinical stage (T3+T4). Patient and tumour characteristic, radiation technique and volumes, total and fraction doses were exactly the same in 3 groups of patients. Only the overall treatment time was shorter by about 2 weeks in CAIR group comparing to control-1 because of the lack of weekend breaks. The overall treatment time in CAIR and control-2 group was exactly the same because in control-2 group the "CAIR weekend fractions" were given through the Tuesday and Fridays as a concomitant boost.