

Cardiovascular safety of novel non-small cell lung cancer oncotherapy in a patient treated with novel generations of tyrosine kinase inhibitors

Bezpieczeństwo kardiologiczne nowoczesnego leczenia onkologicznego niedrobnokomórkowego raka płuc u pacjenta leczonego inhibitorami kinazy tyrozynowej nowej generacji

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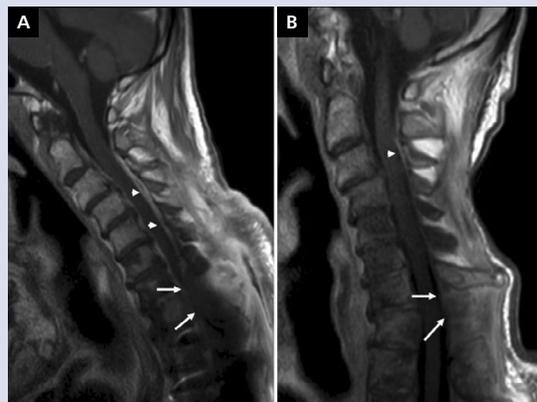


Figure 1. A. Non-small cell lung cancer metastases to the spine, which occurred during the therapy with afatinib; B. Regression of the metastatic changes in the spine after the therapy with osimertinib

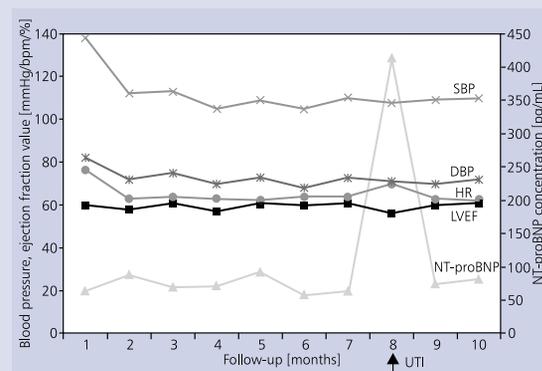


Figure 2. Changes in the cardiac parameters during treatment with tyrosine kinase inhibitors; DBP — diastolic blood pressure; HR — heart rate; LVEF — left ventricular ejection fraction; NT-proBNP — N-terminal-pro B-type natriuretic peptide; SBP — systolic blood pressure; UTI — urinary tract infection

Lung cancer is one of the cancer types associated with the fastest progression and the worst prognosis. A 64-year-old never-smoker was diagnosed with lung cancer in 2015. A chest computed tomography (CT) showed metastases to the chest lymph nodes. The patient had bronchoscopy and lymph node biopsy performed. Histological examination and molecular testing revealed the tumour to be non-small cell lung cancer (NSCLC) with *EGFR*-positive genotype. Prior to the diagnosis the patient was diagnosed with only hypercholesterolaemia and was treated with rosuvastatin (20 mg/d). Before cancer treatment was introduced, the patient was evaluated by a cardiologist. Echocardiography showed left ventricular ejection fraction of 60%, without structural abnormalities. N-terminal-pro B-type natriuretic peptide (NT-proBNP) level was 21 pg/mL. Because of the planned treatment cardioprotection was initiated with nebivolol 2.5 mg/d and ramipril 2.5 mg/d, and because of vitamin D deficiency the patient received vitamin D supplementation of 2000 IU/day. Treatment with afatinib 40 mg, a second-generation tyrosine kinase inhibitor (TKI) active against *EGFR* positive NSCLC, was started. The patient remained in partial response, progression free, and had no adverse effects of the treatment per a period of 13 months. After this time the patient developed paraesthesia and gradual lower limb paralysis. Spine magnetic resonance imaging showed metastases to the spine with compression of the spinal cord (Fig. 1A). Progression of the disease was associated with resistance to afatinib. Surgical removal was performed and a new tumour specimen revealed p.T790M mutation. Treatment was switched to next-generation TKI — osimertinib 80 mg with an initial response and disease regression, both in the spine and lungs (Fig. 1B). The patient was free from progression for 11 months, but then a control CT showed enlargement of the initial tumour and new metastases in the liver. At this time a decision was made to switch to a first-generation TKI, gefitinib 250 mg/d, with this approach being successful in preliminary studies and case reports. During the whole treatment with TKI and rosuvastatin 20 mg/d, nebivolol 2.5 mg/d and ramipril 2.5 mg/d, serial measurements of cardiac parameters were performed every three months (Fig. 2). They showed no deterioration of cardiac function during the treatment and observed a transient rise in the NT-proBNP concentration was associated only with a severe urinary tract infection. Currently, the patient is under observation during gefitinib treatment. TKIs are a new drug class with growing potential in the treatment of lung cancer. Initial results show that they may be associated with the occurrence of left ventricular dysfunction or heart failure caused by TKI, particularly in cancer patients with pre-existing cardiovascular risk factors. The present study shows that early pharmacological cardioprotection may be beneficial also in patients treated with innovative oncotherapy.

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