VIA MEDICA

CASE REPORT

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Long-term overall survival in a patient with non-small cell lung cancer with *KRAS* mutation

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ABSTRACT

The prognosis of patients with metastatic non-small cell lung cancer depends not only on the general condition and stage of the disease but also on the treatment method. Management of lung cancer in stage 4, usually requires a multidisciplinary approach. Frequently in the treatment process, we combine local and systemic treatment. By detecting new therapeutic targets, we can incorporate new elements of therapy. In the described case, the treatment sequence: chemotherapy, immunotherapy, targeted treatment combined with symptomatic local treatment resulted in prolonged survival time and maintaining a good quality of life. The new molecule sotorasib is a drug targeting the G12C mutation in the Kirsten rat sarcoma virus (KRAS) gene approved by the FDA and EMA.
Key words: non-small-cell lung cancer, *KRAS* mutation, sotorasib

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Case report

A 62-year-old male patient with a history of long-term smoking (a pack a day for 25 years, had not smoked for 10 years) was referred for treatment and further diagnostics due to increasing exercise dyspnea. The patient had symptoms of progressive superior vena cava syndrome. Chest X-ray showed a tumor at the apex of the right lung (Fig. 1). Computed tomography confirmed pressure on the mediastinal structures, including the superior vein. To reduce the symptoms, before the diagnosis, the patient was secured by implanting a stent into the narrowed superior vein (Fig. 2). His symptoms decreased. Urgent diagnosis of the neoplastic lesion was performed. In January 2019, adenocarcinoma was diagnosed by bronchoscopy with ultrasound (EBUS). Molecular tests performed at this stage did not reveal any driver mutations that would allow targeted treatment. Genetic alterations in the EGFR,

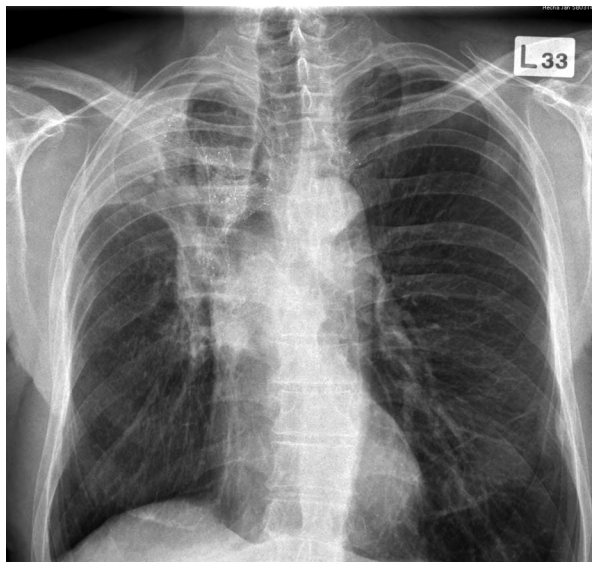

Figure 1. Tumor at the apex of the right lung (chest X-ray)

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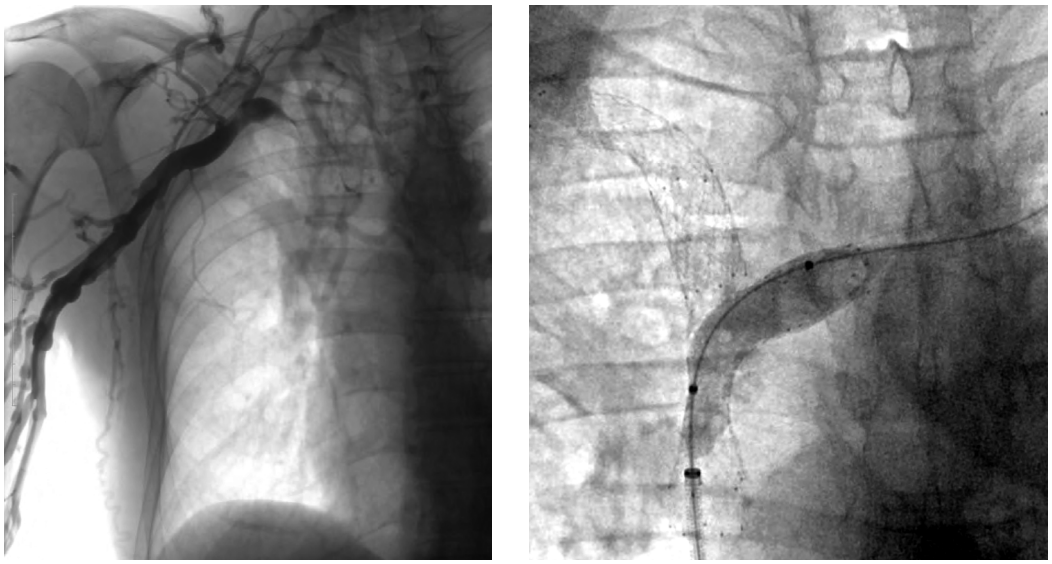

Figure 2. Effective treatment of symptoms by implanting a stent into the narrowed superior vein

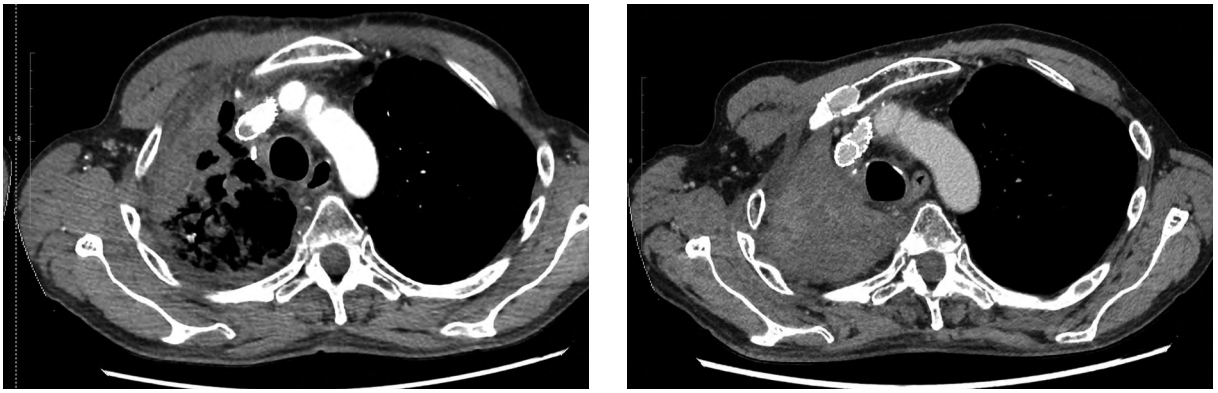

Figure 3. Progression in the lungs after 10 months of treatment with atezolizumab

ALK, ROS-1 genes were excluded. Expression of PD-L1 (programmed death protein ligand-1) was present on 10% of the tumor cells. In 2019, it was not possible to include the patient in the treatment combined with pembrolizumab due to the lack of reimbursement. The patient received chemotherapy in the cisplatin + pemetrexed regimen. After two cycles, a good response to treatment was obtained. Unfortunately, in the evaluation after 4 cycles, there was a progression of tumor in the chest. Additionally, the patient reported double vision. Magnetic resonance imaging (MRI) revealed a pathological mass in the right eye socket. The patient was scheduled for radiotherapy (30 Gy) of the lesion in the eyeball. After radiotherapy, in September 2019, the second line of systemic treatment was started. The patient received immunotherapy. After 10 months of successful treatment with atezolizumab, a progression was observed in the lungs (Fig. 3) and the central nervous system (Fig. 4). Based on recent reports, the patient was ordered a G12C mutation test in the KRAS gene. After obtaining a positive result, the treatment with sotorasib was started, and the disease stabilized. The patient received treatment for over a year with very good tolerance. Optimal sequential treatment, including molecularly targeted therapy and symptomatic local therapy, allowed the patient to achieve long-term survival (Fig. 5).

Discussion

The US Food and Drug Administration granted accelerated approval to sotorasib for treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a G12C mutation in the KRAS gene who have received at least one prior systemic

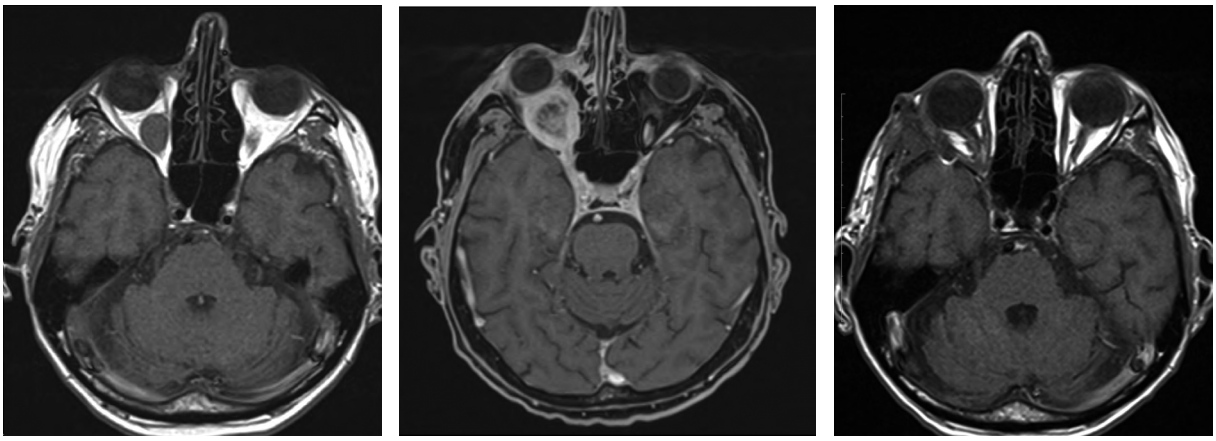

Figure 4. Metastatic lesion in the eye socket after surgery, radiotherapy and completion of immunotherapy

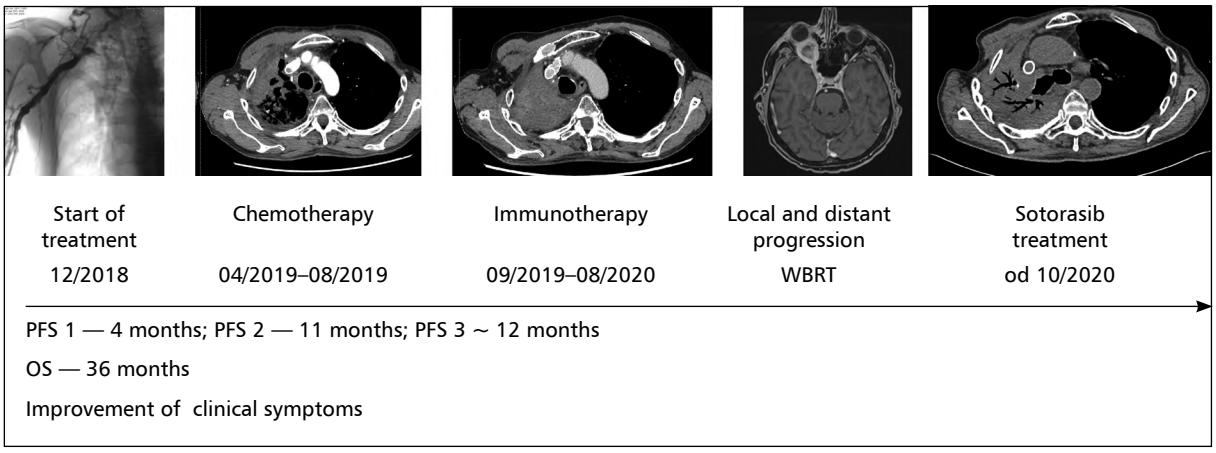

Figure 5. Summary of treatment; WBRT — whole brain radiotherapy; PFS — progression-free survival; OS — overall survival

therapy. The registration was based on the results of the CodeBreaK 100 multi-center, single-arm, open-label clinical study (NCT03600883), which enrolled patients with locally advanced or metastatic NSCLC with the G12C mutation in the KRAS gene. The drug effectiveness was assessed in 124 patients whose disease had progressed after at least one prior systemic therapy. Patients received sotorasib 960 mg daily orally until disease progression or unacceptable toxicity. The main efficacy endpoints were objective response rate (ORR) according to RECIST 1.1 and duration of response (DOR). The ORR was 36% (95% CI: 28%, 45%) with a median duration of response of 10 months. The most common adverse reactions (≥ 20%) were diarrhea, musculoskeletal pain, nausea, fatigue, hepatotoxicity, and cough. Laboratory abnormalities, such as decreased lymphocyte counts, decreased hemoglobin levels, and increased liver enzymes, were also observed. The recommended dose of sotorasib is 960 mg orally once daily with or without food. It is the first registered targeted therapy in the indication of patients with solid tumors with a mutation in the KRAS gene [1].

KRAS mutations occur in 20–30% of adenocarcinoma patients, especially tobacco users (5% of non-smoking patients may also have KRAS mutations). These mutations are more common in males and Caucasian patients rather than females and Asians. Since mutations in the KRAS gene exclude the presence of other genetic abnormalities, the examination of the KRAS gene may have some value in qualifying for other genetic tests [2]. Sotorasib is the first drug conditionally approved in the European Union for the treatment of adults with advanced non-small cell lung cancer (NSCLC) with KRAS G12C mutation and who have progressed after at least one prior line of systemic therapy. Adagrasib and combinations of these drugs including immunotherapy, are also available in clinical

trials. It is also being assessed whether drugs targeting the G12C mutation in the KRAS gene will be effective in the first-line setting [3].

Conflict of interest

Author declare no conflict of interest.

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