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CLINICAL CASE REPORTS

EXPERIENCE OF PEMETREXED IN MAINTENANCE THERAPY FOR METASTATIC LUNG ADENOCARCINOMA

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ABSTRACT

Lung cancer is among the most common malignant diseases in Russia. In 80–90%, its morphological type is non-small cell lung cancer. Stage IV primary advanced lung cancer is diagnosed in 41% of patients. Median overall survival in stage IV patients receiving chemotherapy is 7–12 months. Treatment for stage IV lung adenocarcinoma is based on predictive and prognostic factors. Chemotherapy, chemoimmunotherapy or immunotherapy is recommended in the absence of driver mutations in the EGFR (exons 19 and 21) and BRAF genes, ALK and ROS1 translocations. Platinum-based regimens are preferred as the first-line chemotherapy. Stabilization, partial or complete response after 4–6 chemotherapy cycles allow for maintenance therapy with pemetrexed to increase progression-free survival and overall survival.

Purpose of the study. Using a real clinical case, to confirm the efficacy of pemetrexed in the treatment for stage IV lung adenocarcinoma in the second-line therapy in combination with platinum-based agents and in a maintenance therapy.

A clinical case of a patient with central cancer of the lower lobe of the right lung St IV (cT3N2M1) is presented; the first treatment stage involved 3 cycles of the first-line polychemotherapy (paclitaxel 175 mg/m² intravenously on day 1, carboplatin AUC 5 intravenously on day 1, every 3 weeks), and 6 cycles of the second-line polychemotherapy (pemetrexed 500 mg/m^2 intravenously on day 1, cisplatin 75 mg/m² intravenously on day 1 of the 21-day cycle). Stabilization of the disease was achieves, and 20 cycles of maintenance therapy with pemetrexed followed; the achieved effect persisted and was confirmed by spiral X-ray computed tomography every 3 months. The objective effect of anticancer therapy was assessed according to the RECIST 1.1 criteria. It took 20 months from the beginning of the second-line anticancer medical therapy to progression, and 16 months from the start of maintenance pemetrexed to progression. The safety profile was satisfactory, and the ECOG performance status 0 maintained. Only one adverse effect, degree I general weakness, was noted, which did not have a negative impact on the patient's quality of life.

Keywords:
non-small cell lung cancer, adenocarcinoma, pemetrexed, maintenance therapy, adverse effects, disease stabilization.

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КЛИНИЧЕСКОЕ НАБЛЮДЕНИЕ

ОПЫТ ИСПОЛЬЗОВАНИЯ ПЕМЕТРЕКСЕДА В ПОДДЕРЖИВАЮЩЕЙ ТЕРАПИИ МЕТАСТАТИЧЕСКОЙ АДЕНОКАРЦИНОМЫ ЛЕГКОГО

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РЕЗЮМЕ

Лидирующие позиции в структуре онкологической заболеваемости населения России занимает рак легкого. В 80–90% случаев встречается немелкоклеточный морфологический вариант. Первично генерализованный рак легкого IV стадии выявляется у 41% больных. Медиана общей выживаемости при проведении химиотерапии пациентам с IV стадией составляет 7–12 месяцев. Лечение аденокарциномы легкого IV стадии назначают с учетом предиктивных и прогностических факторов. При отсутствии драйверных мутаций в генах EGFR (рецептор эпидермального фактора роста) (19 и 21 экзоны), BRAF, транслокаций ALK (киназа анапластической лимфомы), ROS1 рекомендуется назначение химиотерапии, химиоиммунотерапии или иммунотерапии. В качестве химиотерапии первой линии предпочтительнее использовать комбинации на основе платины. При стабилизации, частичном или полном ответе после 4–6 курсов химиотерапии возможно проведение поддерживающей терапии пеметрекседом с целью увеличения выживаемости без прогрессирования, общей выживаемости.
Цель исследования. На случае из реальной клинической практики подтвердить эффективность применения пеметрекседа в лечении аденокарциномы легкого St IV во второй линии терапии в комбинации с препаратами платины в поддерживающем режиме.
Представлено клиническое наблюдение пациентки с центральным раком нижней доли правого легкого St IV (cT3N2M1), на первом этапе лечения которой было проведено 3 курса полихимиотерапии 1 линии (паклитаксел 175 мг/м² внутривенно капельно в 1-й день, карбоплатин AUC (площадь под фармакокинетической кривой) 5 внутривенно капельно в 1-й день, каждые 3 недели), 6 курсов полихимиотерапии 2 линии (пеметрексед 500 мг/м² внутривенно капельно в 1-й день, цисплатин 75 мг/м² внутривенно капельно в 1-й день 21 дневного цикла). В связи с достигнутой стабилизацией заболевания далее проведено 20 циклов поддерживающей терапии пеметрекседом, на протяжении которых достигнутый эффект сохранялся и подтверждался рентгенологически при выполнении спиральной рентгеновской компьютерной томографии каждые 3 месяца. Оценка объективного эффекта противоопухолевой лекарственной терапии проводилась согласно критериям Response evaluation criteria in solid tumours (RECIST) 1.1. От начала 2 линии противоопухолевой лекарственной терапии до прогрессирования прошло 20 месяцев, а от начала введения пеметрекседа в поддерживающем режиме до прогрессирования – 16 месяцев. Профиль безопасности был удовлетворительным, сохранялся статус ECOG 0. Отмечено только одно нежелательное явление – общая слабость I степени, что не оказывало отрицательного влияния на качество жизни пациентки.

Ключевые слова:
немелкоклеточный рак легкого, аденокарцинома, пеметрексед, поддерживающая терапия, нежелательные явления, стабилизация заболевания.

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Lung cancer occupies a leading position in the structure of cancer incidence in the Russian population. In 2018, malignant diseases of the lung, trachea and bronchi were first diagnosed in 51,573 people. At the same time, the proportion of patients with stage IV from the number of patients with a first-time diagnosis of a malignant neoplasm was 41% [1]. Non-small cell morphological variant of lung cancer occurs in 80–90% of all cases [2]. According to the clinical recommendations of the Ministry of Health of the Russian Federation for stage IV lung adenocarcinoma, treatment is prescribed taking into account predictive and prognostic factors. Thus, when activating mutations of the EGFR gene (exons 19 and 21) or translocations of ALK, ROS1, and BRAF mutations are detected, targeted therapy is recommended. In the absence of driver mutations in these genes, chemotherapy, chemoimmunotherapy or immunotherapy is recommended, the purpose of which depends on a number of clinical and laboratory parameters, in some cases taking into account the level of PD-L1 expression by tumor cells [3, 4]. As a first-line chemotherapy, it is preferable to use platinum-based combinations [5, 6]. The median overall survival during chemotherapy in patients with locally advanced (III b) and metastatic (IV) stages is 7–12 months [6–8]. One of the chemotherapeutic options is to use a combination of pemetrexed 500 mg/m^2 intravenously drip on day 1 with cisplatin 75 mg/m^2 or carboplatin AUC 5 intravenously drip on day 1 every 3 weeks. With stabilization, partial or complete response after 4–6 courses of treatment, maintenance therapy with pemetrexed is recommended. Maintenance therapy is prescribed to increase progression-free survival, overall survival, while the number of side effects should be minimal and not have a significant negative impact on the quality of life of patients. Maintenance therapy is performed until progression or unacceptable toxicity. Conducting maintenance therapy immediately after line 1 therapy may lead to an increase in the number of patients who may benefit clinically from additional lines of therapy [9]. It is important that pemetrexed therapy has a low incidence of side effects and controlled toxicity [10].

The efficiency of maintenance therapy with pemetrexed in patients with late-stage non-small cell lung cancer (NSCLC) was confirmed in a double-blind randomized controlled trial of phase III PARAMOUNT. This study involved patients with late-stage non-squamous cell NSCLC aged 18 years and older, with at least one measurable tumor site, and with an Eastern Cooperative Oncology Group (ECOG) score of 0–1, who had not previously received systemic chemotherapy for lung cancer. The study included two phases: the induction phase without randomization and the maintenance phase with randomization. Before randomization, patients (939 people) underwent 4 cycles of therapy with pemetrexed (500 mg/m^2) and cisplatin (75 mg/m^2), which were administered intravenously by drip on the 1st day of the 21-day cycle. Further, patients without signs of disease progression (539 people) were randomized into two groups (in a ratio of 2:1). In group 1, consisting of 359 people, patients received maintenance therapy with pemetrexed (500 mg/m^2 on day 1 of each 21-day cycle) and optimal symptomatic therapy (OST), in group 2 (180 people)-placebo (on day 1 of each 21-day cycle) and OST. Maintenance therapy was carried out until the disease progressed or unacceptable toxicity, and it was discontinued at the decision of the patient or doctor. From 1 to 19 cycles of maintenance therapy with pemetrexed were performed (an average of 4.9). More than 6 cycles of pemetrexed were received by 23% of patients (84 people out of 359 patients in the pemetrexed group). The main criterion for effectiveness in this study was progression-free survival. The objective effect frequency, quality of life, use of medical resources, adverse events, and overall survival (S) were additionally studied. Median progression-free survival, calculated from the date of randomization, was 4.1 months (95% CI 3.2–4.6) in the pemetrexed group and 2.8 months (95% CI 2.6–3.1) in the placebo group. Grade III–IV hematological adverse events, possibly related to treatment, were more common in the pemetrexed group (33 [9%] of 359 patients) compared to the placebo group (1 [< 1%] of 180 patients; p<0.0001), the same trend was observed for non–hematological adverse events of grade III–V (32 [9%] of 359 patients in the pemetrexed group; 8 [4%] of 180 patients in the placebo group; p=0.080). In each group, one fatal outcome was recorded, possibly related to treatment. The most common grade III–IV adverse events in the pemetrexed group were anemia

(16 [4%] of 359 patients), neutropenia (13 [4%]), and fatigue (15 [4%]). In the placebo group, the above adverse events were less common: anemia (1 [< 1%] of 180 patients), neutropenia (0), and fatigue (1 [< 1%]). The most common serious adverse events were anemia (8 [2%] of 359 patients in the pemetrexed group vs 0 in the placebo group) and febrile neutropenia (5 [1%] vs 0). At the same time, 19 (5%) patients from the pemetrexed group and 6 (3%) patients from the placebo group aborted participation in the study due to adverse events associated with treatment [11].

The efficiency of pemetrexed in maintenance therapy in late-stage NSCLC after induction chemotherapy with pemetrexed-free duplets was evaluated in a multicenter, randomized, double-blind phase III trial [12]. This study included patients with squamous and non-squamous cell histological tumor types, who were randomized in a 2:1 ratio after completing 4 cycles of induction chemotherapy with duplets based on platinum derivatives and not containing pemetrexed in the absence of progression. A total of 663 patients were randomized, 441 of them received maintenance therapy with pemetrexed (500 mg/m^2) in combination with optimal symptomatic therapy, and 222 patients received placebo in combination with optimal symptomatic therapy on day 1 of the 21-day cycle. The main criterion for effectiveness was progression-free survival (PFS), which was determined from the date of randomization. Secondary end points were overall survival (OS), the frequency of the objective effect, safety. The use of pemetrexed as maintenance therapy resulted in a statistically significant increase in the median progression-free survival (4.3 months; 95% CI 4.1–4.7) compared to placebo (2.6 months; 95% CI 1.7–2.8). A more significant advantage in IBD was demonstrated in patients with the non-squamous cell histological subtype-IBD: HR 0.47; 95% CI 0.37–0.6; p<0.001; 4.4 months for the pemetrexed group and 1.8 months for the placebo group. In the pemetrexed group, the incidence of treatment – related adverse events of grade III–IV was significantly higher (16%; n=70) than in the placebo group (4%; n=9, p<0.0001). No deaths from treatment-related toxicity were observed in any of the groups.

In the publications we found, maintenance therapy with pemetrexed was carried out from 1 to 19 cycles (an average of 4.9), after which treatment was discontinued due to progression or unacceptable toxicity. We found it interesting to publish a clinical case in which a patient with stage IV NSCLC underwent 20 cycles of antitumor drug therapy with pemetrexed after platinum and pemetrexed chemotherapy in a supportive mode.

In patient S., born in 1955, during a routine examination on a chest X-ray, pathological changes were found in the right lung. In this regard, in April 2018, she turned to the clinical and diagnostic department of the Federal State Budgetary Institution of the National Research Center of Oncology of the Ministry of Health of Russia. According to the spiral X-ray computed tomography of the chest organs (05.04.2018), metastatic foci were found in the lung tissue on both sides, larger on the right from 0.5 cm to 1 cm. Pulmonary fibrosis. Peripheral tumor of the lower lobe of the right lung 4.2 x 4.6 cm (target focus) with centralization and damage to the segmental bronchus, sprouting into the pleura paravertebral at the level of the 9th thoracic vertebra. In the upper mediastinum, lymph nodes up to 1.7 cm, retrocaval up to 1.7 cm, bifurcation up to 2.3 cm, aortic window up to 2.3 cm, bronchopulmonary on the right up to 2.3 cm, on the left up to 1.1 cm. (fig. 1).

On 10.04.2018, a fibrobronchoscopy was performed, which revealed a peribronchial, mainly submucosal tumor of the right lung with the involvement of the lower lobe, intermediate, and upper lobe bronchi. A biopsy was performed and a histological conclusion was obtained: "a fragment of the bronchial mucosa with diffuse infiltration from large cells suspected of tumor cells, an immunohistochemical study (IHC) is necessary to clarify the diagnosis." According to the IHC data, the morphological picture and immunophenotype most closely correspond to low-grade lung adenocarcinoma, a solid variant with invasion of the bronchial wall. A molecular genetic analysis was performed. When studying the obtained sample of deoxyribonucleic acid (DNA), no mutations were found in the EGFR gene, and no rearrangement was detected in the ALK and ROS-1 genes.

According to spiral X-ray computed tomography of the brain, abdominal cavity and pelvis (11.04.2018), no foci of pathological density in the brain substance were detected, in the lower parts of the lungs on the

right, multiple metastatic foci up to 1 cm, the density of the liver parenchyma is uniform.

The patient complained of discomfort in the chest on the right (in the lower parts), bad habits and occupational hazards did not have. A clinical diagnosis was made: central cancer of the lower lobe of the right lung, metastases to the lymph nodes of the root and mediastinum, metastases to the lungs on both sides of St IV (cT3N2M1), clinical group 2. Concomitant diseases (I 11) hypertension stage 2, risk 2, NC 0, (I 83.9) varicose veins of the lower extremities. Since May 2018, 3 courses of 1-line polychemotherapy have been carried out according to the scheme: paclitaxel 175 mg/m^2 intravenously drip on day 1, carboplatin AUC 5 intravenously drip on day 1, every 3 weeks. When performing a control spiral X-ray computed tomography (SRCT) of the chest, abdominal cavity and pelvis (27.07.2018) in the lung tissue on the right, a centralized peripheral tumor of the lower lobe of 5.6 x 4.9 cm on both sides, multiple metastatic foci up to 1.2 cm, hypoventilation, pulmonitis of the lower lobe on the right. The lumen of the lower lobe bronchus on the right is narrowed. Retrocaval lymph nodes 2 cm, aortic window 1.5 cm, right root up to 2.2 cm, upper mediastinum on the right 1.4 cm. The density of the liver parenchyma is uniform. Uterus 5 x 4.5 cm, appendages on the left with a liquid structure 4 x 2.4 cm. (fig. 2).

According to the RECIST criteria marked by the growth of targeted lesion in 21%, in this connection, the decision of the medical Council of National Medical Research Centre for Oncology of the Ministry of Health of Russia recommended a change of line chemotherapy and conduct of chemotherapy line 2 on the scheme, pemetrexed 500 mg/m^2 intravenously 1 day, cisplatin 75 mg/m^2 intravenously 1 day 21-day cycle. The above scheme of antitumor drug therapy was started in August 2018. After 3 cycles of polychemotherapy, SRCT of the brain, neck, chest, abdominal cavity and pelvis was performed (10.10.2018) in the lungs, multiple metastatic foci on both sides up to 0.4 cm. The central tumor of the right lung is 6.6 x 4.5 cm with a lesion of the lower lobe, middle lobe and intermediate bronchi. Retrocaval lymph nodes 1.5 cm, aortic window 1.8 cm, bifurcation 2.1 cm, right root up to 1.4 cm. The density of the liver parenchyma is uniform. The concretion of the gallbladder is 1.6 cm, the wall is not thickened. The retroperitoneal lymph nodes are not enlarged. There are no foci of abnormal density in the substance of the brain (fig. 3).

The growth of the target focus was revealed by 17%, according to the RECIST criteria, the tumor process was stabilized, antitumor drug therapy was continued according to the previous scheme (pemetrexed 500 mg/m^2 intravenously drip on day 1, cisplatin

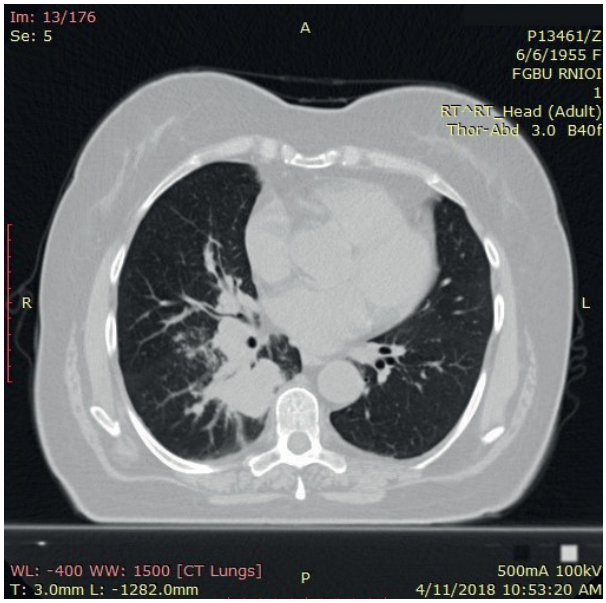

Fig. 1. SRCT of the chest organs before the start of antitumor drug therapy.

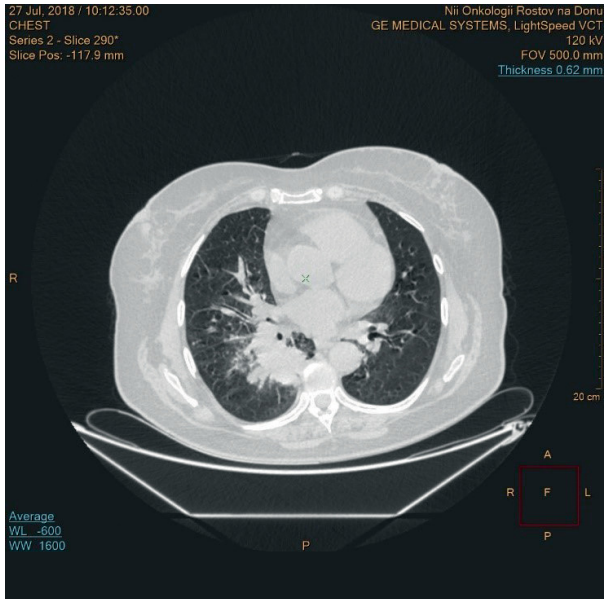

Fig. 2. SRCT of the chest organs before starting line 2 chemotherapy with pemetrexed and cisplatin.

75 mg/m^2 intravenously drip on day 1 of the 21-day cycle) up to 6 courses. Further, SRCT of the brain and chest organs was performed (17.12.2018) – no foci of abnormal density in the brain substance were detected. In the lung tissue on both sides, there are multiple metastatic foci up to 1 cm. Hypoventilation of the lower lobe on the right. On the right, a central tumor with a lesion of the lower lobe bronchus of 4.5 x 4.4 cm with a non-uniform structure. The lymph nodes of the aortic window are 1.3 cm. The tumor process remains stable according to the RECIST criteria. In connection with the above, according to the clinical recommendations of the Association of Oncologists of Russia, the Ministry of Health of Russia has continued to administer pemetrexed 500 mg/m^2 intravenously on the 1st day of the 21-day cycle as a maintenance therapy since December 2018. Every 3 months, SRCT of the brain, chest, abdominal and pelvic organs was monitored, which still maintained the stabilization of the tumor process. 20 cycles of maintenance therapy were performed. During the entire period of antitumor drug therapy, only general weakness of the first degree was observed among the adverse events, which did not affect the quality of life, social activity and the conduct of antitumor drug therapy.

At the next control examination of the SRCT of the brain, neck, chest, abdominal cavity and pelvis (28.04.2020), no foci of pathological density in the brain substance were detected. The right eyeball is enlarged in relation to the left to 2.9 x 2.7 cm, the left eyeball 2.3 x 2.3 cm. In the lung tissue on both sides, there are multiple metastatic foci up to 1.5 cm, an increase compared to the previous study in December 2019. On the right, a centralized peripheral tumor of the lower lobe is 4.7 x 3.3 cm, an increase compared to the previous study in December 2019. On both sides of the pleura there are multiple metastatic foci up to 0.5 cm. The density of the liver parenchyma is uniform, local areas of decrease or increase in density are not observed. In the bones of the skeleton without focal changes. The uterus is 5 x 4 cm, the appendages on the left with a liquid structure up to 3.2 x 3 cm, on the right are not visualized (fig. 4).

Taking into account the appearance of previously undetected metastatic foci in the pleura, the progression of the disease was revealed. Atezolizumab 1200 mg intravenously once every 21 days was chosen as the next line of antitumor drug therapy. Since May 2020, immunotherapy has been started (continues to the present). From the beginning of the third line of antitumor drug therapy to the submission of the article to the journal, 6 months have passed (the effect of stabilization remains).

This clinical observation is interesting for the long period of maintenance therapy with pemetrexed,

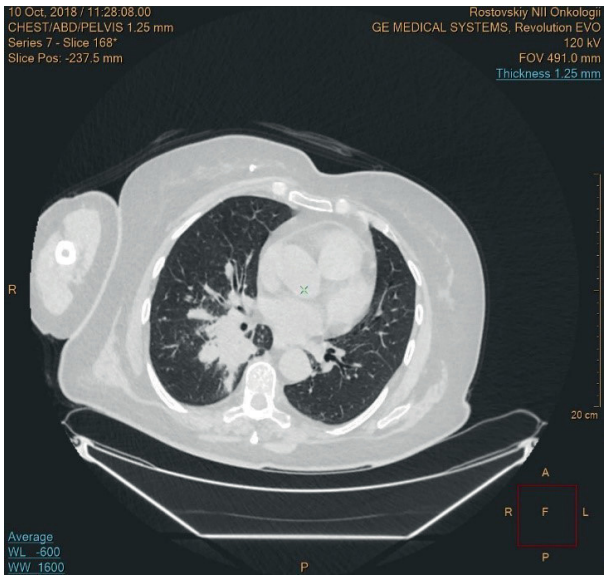

Fig. 3. SRCT of the chest organs after 3 courses of 2-line chemotherapy (pemetrexed, cisplatin).

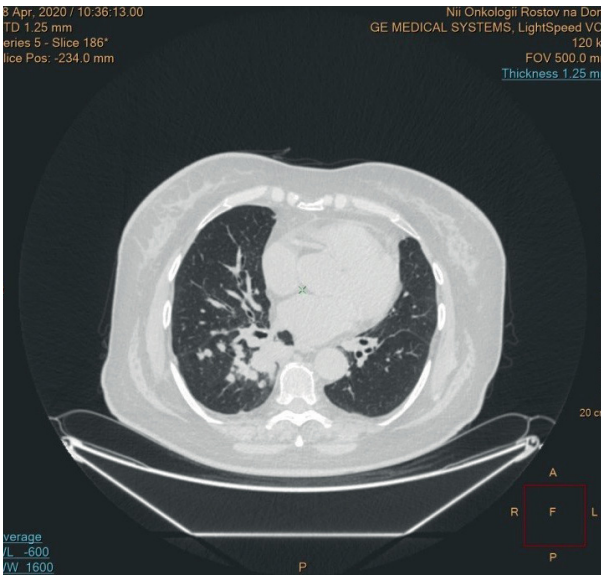

Fig. 4. SRCT of the chest organs (tumor progression after 20 cycles of maintenance therapy with pemetrexed).

the continued long-term stabilization of the disease against this background, and the absence of toxicity.

As mentioned earlier, in the double-blind randomized controlled trial of phase III PARAMOUNT, only 23% of patients received more than 6 cycles of pemetrexed in the maintenance mode, while the maximum number of cycles was 19. Our patient underwent 20 cycles of pemetrexed maintenance therapy, which exceeds the number of cycles described in the literature. According to our clinical observation, 20 months passed from the beginning of the 2 – line antitumor drug therapy to the progression, and 16 months passed from the beginning of the administration of pemetrexed in the maintenance mode to the progression. In the PARAMOUNT phase III study, the median IBD from the date of randomization was 4.1 months, and from the start of induction therapy was 6.9 months.

The long-term preservation of the stabilization effect, despite the primary metastatic tumor process, the ECOG 0 status, allowed the use of the immunotherapy option during the progression. At the time of our patient's diagnosis (April 2018), immunotherapy drugs in the treatment of NSCLC were not yet widely used. So, atezolizumab was registered in Russia only on 18.01.2018 (and in the clinical and statistical group (CSG) appeared only in 2019). At the time of the beginning of treatment of our patient, the only registered immuno-oncological drug for the treatment of metastatic NSCLC in Russia was pembrolizumab (registration date 18.11.2016). Today, indications for the use of immunotherapy in monotherapy and in combination with chemotherapy are expanding. A regimen of antitumor drug therapy with pembrolizumab in combination with pemetrexed and cisplatin/carboplatin was introduced, followed by the transition to the maintenance regimen of pemetrexed+pembrolizumab, which opens up new prospects for the treatment of patients with non-small cell non-small cell lung cancer without activating mutations.

CONCLUSIONS

The presented clinical case demonstrates the possibility of long-term disease control in a patient with metastatic lung adenocarcinoma without activating mutations in the EGFR, BRAF, ALK, ROS1 genes when using a combination of platinum and pemetrexed drugs with further maintenance therapy with pemetrexed.

Authors contribution:

Vladimirova L.Yu. – research concept and design, scientific editing, data analysis and interpretation.

Storozhakova A.E. – research concept and design, scientific editing, data analysis and interpretation.

Kalabanova E.A. – collection, analysis and interpretation of data, writing of the text, material processing, preparation of a bibliography, preparation of the article.

Meshcheryakov P.N. – preparation of illustrations.

Oskin S.V. – preparation of illustrations.

Kabanov S.N. – design of the bibliography.

Samaneva N.Yu. – technical editing.

Svetitskaya Ya.V. – design of the bibliography.

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References

1. The state of cancer care in Russia in 2018. Edited by A.D.Kaprin, V.V.Starinsky, G.V.Petrova. M.: P.A.Hertsen Moscow Oncology Research Institute – Branch of the National Medical Research Radiological Centre, 2019, 236 p. (In Russian).

2. Azzoli CG, Temin S, Aliff T, Baker S, Brahmer J, Johnson DH, et al. 2011 Focused Update of 2009 American Society of Clinical Oncology Clinical Practice Guideline Update on Chemotherapy for Stage IV Non-Small-Cell Lung Cancer. J Clin Oncol. 2011 Oct 1;29(28):3825–3831. https://doi.org/10.1200/JCO.2010.34.2774

3. Laktionov KK, Artamonova EV, Breder VV, Gorbunova VA, Moiseenko FV, Reutova EV, et al. Practical recommendations for the drug treatment of non-small cell lung cancer. Malignant tumors: Practical recommendations of RUSSCO 2019;9(3s2):32–48. https://doi.org/10.18027/2224-5057-2019-9-3s2-32-48

4. Vladimirova LYu, Kit OI, Sholokhova EA. The role of histological and molecular analysis in the choice of treatment for late-stage non-small cell lung cancer. Pharmateca. 2012;(8(241)):9–22. (In Russian).

5. D'Addario G, Früh M, Reck M, Baumann P, Klepetko W, Felip E, et al. Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2010 May;21(S5):v116–119. https://doi.org/10.1093/annonc/mdq189

6. Azzoli CG, Baker S, Temin S, Pao W, Aliff T, Brahmer J, et al. American Society of Clinical Oncology Clinical Practice Guideline update on chemotherapy for stage IV non-small-cell lung cancer. J Clin Oncol. 2009 Dec 20;27(36):6251–6266. https://doi.org/10.1200/JCO.2009.23.5622

7. Wakelee H, Belani CP. Optimizing first-line treatment options for patients with advanced NSCLC. Oncologist. 2005;10(S3):1–10. https://doi.org/10.1634/theoncologist.10-90003-1

8. Sandler A. Bevacizumab in non-small cell lung cancer. Clin Cancer Res. 2007 Aug 1;13(15 Pt 2):s4613– 4616. https://doi.org/10.1158/1078-0432.CCR-07-0647

9. Kit OI, Vladimirova LYu, Sholokhova EA. Efficacy and safety of pemetrexed maintenance therapy in advanced non-small-cell lung cancer: a review of phase III studies. Modern oncology. 2013;15(1):8–13. (In Russian).

10. Vladimirova LYu, Storozhakova AE, Kabanov SN, Kalabanova EA. Results of treatment of patients with locally advanced and metastatic non-squamous cell non-small-cell lung carcinoma with pemetrexed (by own experience). Siberian journal of oncology. 2016;15(1):26-30. (In Russian). https://doi.org/10.21294/1814-4861-2016-15-1-26-30

11. Paz-Ares L, de Marinis F, Dediu M, Thomas M, Pujol J-L, Bidoli P, et al. Maintenance therapy with pemetrexed plus best supportive care versus placebo plus best supportive care after induction therapy with pemetrexed plus cisplatin for advanced non-squamous non-small-cell lung cancer (PARAMOUNT): a double-blind, phase 3, randomised controlled trial. Lancet Oncol. 2012 Mar;13(3):247–255. https://doi.org/10.1016/S1470-2045(12)70063-3

12. Ciuleanu T, Brodowicz T, Zielinski C, Kim JH, Krzakowski M, Laack E, et al. Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care for non-small-cell lung cancer: a randomised, double-blind, phase 3 study. Lancet. 2009 Oct 24;374(9699):1432–1440. https://doi.org/10.1016/S0140-6736(09)61497-5

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