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Case Report

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The Use of Selpercatinib in Recurrent Medullary Thyroid Carcinoma with the RET p.C630R Mutation: A Clinical Case

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Abstract. Medullary thyroid carcinoma (MTC) is a rare malignant tumor arising from parafollicular C cells and accounts for 1–5% of all thyroid cancers. Somatic RET mutations occur in 40–50% of sporadic cases and represent targets for selective RET inhibitors. Selpercatinib (RETIVO, Eli Lilly), approved by the FDA in 2020 and the EMA in 2021, is currently not registered in Kazakhstan. This study describes its successful use in a 74-year-old patient with recurrent MTC, cervical lymph node and lung metastases, vandetanib intolerance, and a confirmed RET p.C630R mutation. Diagnostic evaluation included histology, immunohistochemistry, next-generation sequencing (NGS), contrast-enhanced CT, MRI, ¹⁸F-FDG PET/CT, and laboratory monitoring of calcitonin, carcinoembryonic antigen, thyroid hormones, and liver and kidney function. NGS identified an activating RET p.C630R mutation with an allele frequency of 21.14%. Vandetanib was discontinued because of Quincke's edema, drug-induced liver injury, and Stevens–Johnson syndrome. Selpercatinib was subsequently administered at a dose of 160 mg/day. After three months, PET/CT performed on March 4, 2026, showed no evidence of local recurrence and an approximately twofold decrease in the metabolic activity of the pulmonary lesions. Calcitonin levels remained stable near the upper limit of normal (16.0–16.3 pg/mL). No adverse events requiring treatment discontinuation were reported, while liver and kidney function remained normal. This case demonstrates the efficacy and favorable tolerability of selpercatinib in RET-positive MTC following intolerance to a first-generation multikinase inhibitor and supports its registration and improved accessibility in Kazakhstan.

Keywords: medullary thyroid cancer, RET mutation, selpercatinib, targeted therapy, Next-Generation Sequencing (NGS), vandetanib, clinical case.

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Introduction

Medullary thyroid cancer (MCT) is a rare malignant neoplasm that develops from parafollicular C-cells of the thyroid gland that produce calcitonin. According to world statistics, breast cancer accounts for 1 to 5% of all malignant thyroid tumors [1, 2]. Despite its relatively low prevalence, this disease is characterized by a tendency to early regional and long-term metastasis, insensitivity to traditional radioiodine therapy, and a more unfavorable prognosis compared to differentiated forms of thyroid cancer [3-5].

Mutations in the proto-oncogene RET (during RE-arranged during Transfer), which encodes a receptor tyrosine kinase, play a key role in the pathogenesis of MTS. Somatic RET mutations are detected in approximately 40-50% of sporadic cases, whereas in hereditary forms (MEN2A, MEN2B, familial MRCC), germinal RET mutations are detected in 95-98% of cases [6, 7]. Activating RET mutations lead to constitutive activation of tyrosine kinase signaling and stimulate pathological C-cell proliferation [8-11].

For a long time, systemic treatment of unresectable, recurrent, and metastatic breast cancer was limited to multikinase inhibitors-vandetanib (approved by the FDA in 2011) and cabozantinib (approved by the FDA in 2012). Both drugs selectively block several tyrosine kinase targets (RET, VEGFR, EGFR, etc.), which leads to a high frequency of adverse events, including severe hepatotoxicity, Stevens-Johnson syndrome, angioedema, diarrhea, and prolongation of the QTc interval [12-14].

A fundamentally new stage in the treatment of RET-positive tumors began with the introduction of highly selective RET inhibitors. Selpercatinib (RECEVMO, Eli Lilly) is a first – in-class highly selective ATP-competitive RET inhibitor approved by the FDA in May 2020 and the EMA in 2021 for the treatment of patients with advanced or metastatic RET-altered breast cancer and RET-positive non-small cell lung cancer [15, 16]. The mechanism of action is based on highly selective inhibition of both wild-type RET kinase and its clinically significant mutant forms, with significantly less effect on other kinases compared to multikinase inhibitors [17-22].

This problem is of particular importance in the context of Kazakhstan cancer practice: despite a strong international evidence base (LIBRETTO-001 study), selpercatinib is currently not registered in the Republic of Kazakhstan and is not included in the Kazakhstan National Formula (KNF). This clinical case demonstrates the feasibility and validity of its use in a patient with recurrent medullary carcinoma, vandetanib intolerance, and confirmed mutation RET p.C630R.

Materials and methods

Objective

To describe a clinical case of successful use of selpercatinib in a patient with recurrent medullary thyroid carcinoma, vandetanib intolerance and confirmed mutation RET p. C630R.

A clinical case of patient N., 74 years old, with a diagnosis of medullary thyroid carcinoma, relapse, and metastases to the lymph nodes of the neck is presented.

The following methods were used to verify the diagnosis and evaluate the effectiveness of treatment:

morphological and immunohistochemical (IHC) studies: expression of TTF-1, Thyroglobulin, Chromogranin, Synaptophysin (block 7750/24. 6, conclusion #51061240);

* molecular genetic testing (NGS): genome-wide sequencing of tumor DNA (sample #14062789-DNA) with analysis of >100 genes, including RET, NF1 BRAF, EGFR, KRAS, NRAS, PIK3CA, TP53, as well as determination of copy number variations and chimeric mergers (performed in the Hospital of the Medical Center of the UDP RK);

* radiation methods: CT of the soft tissues of the neck with intravenous contrast (17.02.2025; 23.09.2025), CT of the OGK and OBP (23.09.2025), MRI neck with contrast (21.02.2025), PET/CT with 1FF-FDG (06.05.2025 and 04.03.2026) [23];

laboratory monitoring: UAC, biochemical analysis of blood (ALT, AST, bilirubin, creatinine, urea, phosphorus, calcium, alkaline phosphatase, GGTP, CRP, electrolytes), calcitonin and CEA in dynamics, thyroid hormones (TSH, sv. T3, sv. T4, thyroglobulin, calcitonin), vitamin D, coagulogram [24];

functional methods: ECG, echocardiography, EGDS, consultations with a cardiologist, nephrologist, endocrinologist, gastroenterologist, dermatologist;

Status assessment: ECOG scale, Karnowski scale [25].

The patient's personal data is depersonalized in accordance with the requirements of the Helsinki Declaration of the World Medical Association: the name is replaced with the initial "N."; only the age is indicated; IIN, full name, and other identifiers are not given in the text [26, 27].

Results

A clinical case

Patient information: Patient N., 74 years old (born in 1951), is observed in the cancer center with a diagnosis of: thyroid cancer T3N0M0, stage III; medullary carcinoma of the thyroid gland, relapse, metastases to the lymph nodes of the neck on the right.

Concomitant diseases: chronic kidney disease C2 stage (GFR 78.0 ml / min according to CKD-EPI) in the outcome of paraneoplastic nephropathy; arterial hypertension II stage; postoperative hypothyroidism in the stage of drug-induced euthyroidism; metabolic-associated fatty liver disease (steatohepatitis F2 according to Metavir); erosive antral gastritis.

Anamnesis and medical history: patient N., 74 years old, has been registered at the dispensary since 2003. In 2003, a planned thyroidectomy was performed for thyroid cancer; in the postoperative period, remote radiation therapy (SOD 40 Gy) was performed. During the following years, the patient was under the supervision of an endocrinologist and oncologist and received hormone replacement therapy with levothyroxine (Eutirox 87.5 mcg / day).

In November 2024, a planned examination revealed a lump in the projection of the thyroid gland bed. Fine needle aspiration biopsy (NAB) on 01.11.2024 (cytological study No. 52/3-52/7): the cytological picture corresponds to medullary carcinoma (Bethesda VI). At the meeting of the multidisciplinary group (MDG) on 19.10.2024, surgical treatment was recommended.

On November 21, 2024, the operation was performed: removal of a recurrent thyroid tumor; cervical lymph node dissection (zones II-VI) on the right, tracheostomy.

Postoperative immunohistochemical study (block 7750/24. 6, conclusion No. 51061240): the morphological picture and immunophenotype of metastatic lymph nodes correspond to medullary thyroid carcinoma (Table 1).

Table 1

Results of postoperative immunohistochemical study in a patient

Marker	Result
TTF-1	Positive
Thyroglobulin	Negative
Chromogranin	Positive
Synaptophysin	Positive

Results of radiation diagnostic methods

CT scan of the soft tissues of the neck with contrast (17.02.2025): thyroid gland bed without features. Cervical lymph nodes: IIa on the right – up to 7.6 mm, I on the left – up to 8.6 mm. Conclusion: CT scan shows a picture of undetected cervical lymphadenopathy.

MRI of the cervical region with contrast (21.02.2025): no pathological foci were detected in the projection of the thyroid gland bed. Local thickening in the projection of the false vocal cord on the left (inflammatory genesis?). Moderate lymphadenopathy of submandibular and cervical lymph nodes. Conclusion: MR-signs of soft tissue infiltration of the supraclavicular region, possible local defect of the tracheal wall at the Th1 level.

CT OGK with contrast (23.09.2025): in S6 of the left lung – areas of frosted glass with indistinct contours. Mediastinal lymph nodes are not enlarged. Conclusion: CT image of frosted-glass areas of the lower lobe of the left lung.

CT scan of OBP with contrast (23.09.2025): the liver is not enlarged; the parenchymal structure is uniform. The pancreas is a heterogeneous structure. In the sinuses of both kidneys – cysts (on the right up to 18 × 15 mm, on the left up to 12×10 mm). Conclusion: CT scan of parapelvic cysts of both kidneys.

CT scan of the neck with contrast (23.09.2025): cervical lymph nodes: IIa on the right – 7×6 mm, IIa on the left – 8×6 mm. Conclusion: stable CT picture of undetected cervical lymphadenopathy (in comparison with CT from 17.02.2025).

- PET / CT with 1FF-FDG (04.03.2026): in comparison with PET/CT from 06.05.2025: * relapse in the thyroid gland bed with increased metabolic activity is not detected;
- There were no signs of regional metastatic lesions with high metabolic activity.

- the area of consolidation of the pulmonary parenchyma of the lower lobe of the left lung – a decrease in volume, a decrease in metabolic activity by 2 times (data for inflammatory changes);

- in the middle lobe of the right lung – the formation of fibrous changes with resorption of high metabolic activity.

Laboratory data in dynamics are shown in Tables 2-4.

Table 2

Dynamics of blood biochemical parameters

Indicator	Norm	11.11.2025	03.12.2025	03.04.2026
ALT, Units/ l	up to 41	32.40	19.86	12.16
AST, Units/ l	up to 40	16.00	21.99	18.29
General. bilirubin, µmol/l	22.2	19,21	16,35	17,63
Creatinine, µmol/l	45-97	-	73,43	74,12
Urea, mmol/l	2,3-8,3	-	of 5.26	5.25 in
Glucose, mmol/l	3,05-6,38	4,74	-	a 4.53
Cholesterol, mmol/l	to 5.2	7,50	-	6,50 ↑
alkaline phosphatase, IU/l	to 105	147 ↑	110,28 ↑	121,23 ↑
GGT, U/l	up to 38	153 ↑	49,35	of 35.77
CRP, mg/l	up to 5	-	7,76 ↑	8,98 ↑
Phosphorus, mmol/l	0,81-1,45	-	1,55 ↑	1.55 V ↑
Calcium, mmol/l	2,15-2,55	-	2,23	2,18

Table 3

Dynamics of calcitonin and thyroid hormones

Indicator	Norm	03.12.2025	03.04.2026
Calcitonin, pg/ ml	up to 11.5 (women)	16.0 ↑	16.3 ↑
TSH, mIU/l	0,3-4,0	0,08	0,71
St. John the BaptistT4, pmol/ l	10,5-22,5	15,94	16,84
St. John the BaptistT3, pg/ ml	2,2-4,2	3,26	3,18
Thyroglobulin, ng/ ml	0,01-54,9	-	0,30
AntiTH, IU / ml	0-100-10.	-	5
Vitamin D, ng/ ml	30-100	34.43	32.0

Table 4

UAC from 03.04.2026

Indicator	Norm	Result
Hemoglobin (HGB), g/l	112-140	150 ↑
Red blood cells (RBC), ×10 ¹² /L	3.93-5.0	4.95
Hematocrit (HCT), %	34.1-44.9	46.6 ↑
MCV, fl	79.0-92.2	94.2 ↑
White blood cells (WBC), ×10 ⁹ /L	3.98-10.0	4.77
Platelets (PLT), ×10 ⁹ /l	180-369	194
ESR (according to Westergren), mm / h	2-30	17

Molecular Genetic Research (NGS)

In April 2025, genome-wide sequencing of tumor DNA (sample No. 14062789-DNA) was performed. The panel covered more than 100 genes, including analysis of point mutations, copy number variations, and chimeric mergers (RET, NTRK1 / 2 / 3, FGFR1/2/3, ALK, ROS1), as well as full exon coverage of TP53, BRCA1/2, ATM, PTEN, and CDKN2A (Table 5).

Table 5

Clinically significant molecular changes (NGS)

Mutation	Type	Allelic Frequency	Localization	Database
RET Database p. C630R (c. 1888T>C)	Missense	21,14%	chr10:43609936	COSMIC ID COSM964
NF1 p.P678Qfs*10 (c.2033_2034delCGinsA)	Frameshift	4,29%	chr17:29553484	-

The RET mutation p. C630R is an activating missense mutation of exon 11 localized in the extracellular cysteine-rich domain of the RET receptor. According to international recommendations (NCCN, ESMO, FDA, EMA), this mutation is an indication for the appointment of highly selective RET inhibitors.

Previous treatment: vandetanib

Based on the decision of the multidisciplinary group (MDG) and the clinical protocol of the Ministry of Health of the Republic of Kazakhstan (Protocol No. 189 dated 08.09.2023), targeted therapy with vandetanib 300 mg/day was started on 04.06.2025. During treatment, severe adverse events developed:

- toxic-allergic dermatitis / Stevens-Johnson syndrome (inpatient treatment at the allergological center of GKB No. 1, 20.10.2025-29.10.2025);
- Quincke's edema of unclear origin (recorded twice);
- drug-induced liver damage (cytolysis: ALT 32.40 U/ L, ALP 147 U/ L, GGTP 153 U/L);
- pruritus of the skin, pasty extremities.

Vandetanib therapy was discontinued on 01.10.2025 due to life-threatening toxicity.

Prescribing and monitoring selpercatinib therapy

Based on the decision of the MDG on 06.10.2025, taking into account:

1. verified diagnosis of recurrent medullary thyroid carcinoma;
2. NGS results: mutation RET p. C630R (AF 21.14%);
3. vandetanib intolerance вандетаниба (Stevens-Johnson syndrome, hepatotoxicity, angioedema);
4. international recommendations of the FDA and EMA;

The patient was prescribed selpercatinib (Recevmo) 160 mg /day (2 tablets of 40 mg 2 times a day, daily, regardless of food intake).

Objective assessment at the time of initiation of therapy:

- ECOG – 1; Karnowski scale - 80%;
- Blood pressure 130/80 mm Hg, heart rate 76 beats / min;
- UAC – within the normal range.
- ECG: sinus rhythm, heart rate 83 beats / min, incomplete blockage of the right bundle branch;
- Echocardiography: EF according to Simpson 64%, heart cavities are not dilated, SDLA is 16 mm Hg, no pathology was detected.
- Concomitant therapy with selpercatinib:
- Ursosan 750 mg /day (hepatoprotector);
- Nephroles 5 mg x 2 times a day (nephroprotection);
- Adsorbix 1 capsule 3 times a day before meals;
- Eutirox 87.5 mcg daily in the morning;
- Alfacalcidol 1 mcg /day;
- Rosuvastatin 10 mg /day (lipid-lowering therapy).

Monitoring and treatment outcomes during selpercatinib therapy

After 3 months of using selpercatinib (April 2026), the following results were obtained:

• Liver function: ALT 12.16 U/l (normal), AST 18.29 U/L (normal), total bilirubin 17.63 mmol/l (normal). Normalization of transaminases compared to the period of vandetanib toxicity is a strong indicator of selpercatinib's safety.

• Renal function: creatinine 74.12 mmol / l, urea 5.25 mmol/L-without worsening the initial CKD C2.

• Calcitonin: 16.3 pg/ ml-stabilization at a level close to the upper limit of normal (the norm is up to 11.5 pg/ ml for women). Previously, calcitonin levels were not documented before the start of therapy (until 2003); an increase was recorded from 07.03.2025 (1.13 pg/ml after

surgery) to 03.12.2025 (16.0 pg/ml), indicating continued growth of the RET-positive clone, which stabilized on the background of selpercatinib.

- PET / CT (04.03.2026): positive dynamics relative to the study from 06.05.2025 – no recurrence in the thyroid gland bed, a twofold decrease in the metabolic activity of pulmonary changes.

- Adverse events: skin toxicity, hepatotoxicity or nephrotoxicity, QTc prolongation during selpercatinib administration were not recorded. The ECOG status remains at level 1.

The timeline of the clinical case is shown in Table 6.

Table 6

Chronology of the clinical case of patient N., 74 years old

Date	Event
2003	Thyroidectomy for thyroid cancer; DLT (SOD 40 Gy). Start taking levothyroxine.
October-November 2024	TAB: medullary carcinoma (Bethesda VI). MDG: the operation is shown.
21.11.2024	Removal of recurrent thyroid tumor + cervical lymph dissection (zones II-VI) on the right + tracheostomy.
November 2024	IHC No. 51061240: medullary thyroid carcinoma (TTF-1+, Chromogranin+, Synaptophysin+, Thyroglobulin-).
17.02.2025	CT scan of the neck: undetected cervical lymphadenopathy.
02/21/2025	MRI of the neck: no recurrence in the thyroid gland bed; soft tissue infiltration of the supraclavicular region.
March 2025	MDG: targeted therapy with vandetanib 300 mg/day was prescribed.
April 2025	NGS (sample # 14062789-DNA): mutation <i>RET</i> p.C630R (AF 21.14%), <i>NF1</i> frameshift (AF 4.29%).
06.05.2025	PET/CT with 1FF-FDG (baseline study for dynamics).
04.06.2025	Start of vandetanib therapy of vandetanib therapy.
September 2025	CT of the neck, OGK, OBP: stable picture; frosted glass in S6 of the left lung. EGDS: erosive gastritis.
October 2025	Development of severe toxicity: Stevens-Johnson syndrome, angioedema, drug-induced hepatitis. Hospitalization in an allergy center (20.10-29.10.2025).
01.10.2025	Discontinuation of vandetanib due to life-threatening toxicity.
06.10.2025	MDG: decision on the appointment of selpercatinib 160 mg /day.
October 2025	Start of selpercatinib therapy селперкатинибом (RECEVMO) 160 mg / day.
19.12.2025	Consultation of a gastroenterologist: CKD steatohepatitis F2, giardiasis. Ursosan, and rosuvastatin were prescribed.
03.12.2025	Control biochemistry: normalization of ALT (19.86), AST (21.99); calcitonin 16.0 pg/ ml ↑.
17. 02. 2026	Nephrologist's consultation: CKD C2 (GFR 78.0 ml / min). Nephroprotective therapy.
02.02.2026	Cardiologist's consultation: no coronary pathology was detected.

04.03.2026	PET/CT with 1FF-FDG: positive dynamics – no recurrence in the thyroid bed, a 2-fold decrease in the metabolic activity of pulmonary foci.
03.04.2026	Control tests: ALT 12.16, AST 18.29 (normal); calcitonin 16.3 pg/ ml; UAC is normal.
06.05.2026	Scheduled follow-up examination (PET/CT, biochemistry, calcitonin).

Discussion

Molecular and genetic characteristics of the case. The RET mutation p. C630R (c. 1888T>C) is an activating missense mutation of exon 11 localized in the cysteine-rich extracellular domain of the RET receptor. Substitution of cysteine for arginine at position 630 breaks intramolecular disulfide bonds, which leads to the formation of abnormal intermolecular disulfide bridges, constitutive ligand-independent dimerization, and permanent activation of the RET receptor [28]. The allele mutation rate of 21.14% indicates a significant contribution of the RET-positive clone to the tumor cell population.

The C630R mutation is rare compared to the most common codon 634 mutations (C634R/W/Y/F/S/G), but the mechanism of action is similar to them: both groups are associated with MEN2A syndrome and constitutive RET activation [29]. According to LIBRETTO-001, selpercatinib shows clinically significant activity against a wide range of RET mutations, including cysteine-rich domain mutations (exons 10-11) [30].

Additionally, the NF1 mutation p.P678Qfs*10 with an allelic frequency of 4.29% can potentially activate the MAPK pathway and indicates tumor heterogeneity. Currently, there is no specific therapy for NF1-mutated medullary thyroid cancer in international protocols; however, this fact should be taken into account in further follow-up.

Limitations of first-generation multikinase inhibitors

Vandetanib, the first approved drug for the systemic treatment of medullary thyroid cancer, is a multikinase inhibitor that blocks RET, VEGFR, and EGFR. The ZETA clinical trial showed a significant increase in progression-free survival compared to placebo (median PFS 30.5 vs 19.3 months). However, the non-selectivity of exposure causes a wide and often severe range of adverse events.

In this case, the toxicity of vandetanib became life-threatening: Stevens-Johnson syndrome, double angioedema, and drug-induced hepatitis were recorded. All three complications are considered undesirable events of ≥ 3 degrees of severity on the CTCAE scale and are absolute indications for drug withdrawal. It should be emphasized that this patient had predisposing factors – previously documented allergy (to garlic) and hypothyroidism as a predictor of impaired immune response.

Efficacy and safety profile of selpercatinib

Selpercatinib was developed as a highly selective ATP-competitive RET kinase inhibitor. Due to the unique structure of the molecule optimized to overcome the steric barriers of the active site, the drug has a 100-fold higher selectivity for RET compared to multikinase inhibitors [30].

Key efficacy data were obtained in the LIBRETTO-001 (NCT03157128) study [15, 16].

- In previously treated patients with medullary thyroid cancer: objective response (OR) – 69%, median response time – 22.3 months.
- In patients without previous systemic treatment: OR-73%.

- Median progression-free survival-not achieved with a median follow-up of 20.3 months. Acquired resistance to selective RET inhibition can develop through RET solvent-front mutations and should be considered during long-term follow-up [31].

- The incidence of grade 3 adverse events is significantly lower than with vandetanib: increased ALT/AST in 5-9% of patients (usually grade 1-2), hypertension in 12%, and QTc prolongation in 1.7%.

In the presented clinical case, after 3 months of therapy, the following was recorded: no recurrence by PET/CT, a twofold decrease in the metabolic activity of pulmonary foci, normalization of transaminases (ALT 12.16 U/l, AST 18.29 U/L), stabilization of calcitonin at the level of 16.3 pg/ml. Tolerability of the drug was good – no adverse events requiring dose reduction or discontinuation were recorded.

It is also important to take into account the laboratory context: a number of indicators against the background of previous vandetanib toxicity remained unchanged (ALP 121.23 U/l ↑, CRP 8.98 mg/l ↑, cholesterol 6.50 mmol/l ↑). The increase in alkaline phosphatase is most likely due to the initial metabolic-associated fatty liver disease (F2 fibrosis) and is not associated with the progression of the underlying disease. Hypercholesterolemia is corrected by rosuvastatin. A moderate increase in CRP may reflect the inflammatory component of residual pulmonary changes.

Monitoring of target organ function during therapy

In accordance with the data of expert consultations, the patient was diagnosed with concomitant conditions that require multidisciplinary management against the background of long-term targeted therapy:

- Nephrology (19.02.2026): chronic kidney disease (CKD) C2 (GFR 78.0 ml / min/1.73 m²), chronic pyelonephritis in the acute stage. A nephroprotective diet is recommended (protein restriction to 120-140 g /day, water regime of 1.2-1.5 l/day), nephroles and adsorbix are prescribed нефролес и адсорбикс.

- Cardiology (02.02.2026): no coronary pathology was detected; echocardiography – EF 64%, LVL type I, no effusion. ECG – incomplete block of the right bundle branch leg. ECG monitoring once every 3 months.

- Endocrinology: postoperative hypothyroidism in the stage of drug-induced euthyroidism (TSH 0.71 mIU/l, T₄ sv. 16.84 pmol/L). Vitamin D – 32.0 ng/ ml (within the normal range), continue monitoring.

- Gastroenterology (19.12.2025): metabolic-associated fatty liver disease (steatohepatitis, fibrosis F2), giardiasis-treated. Continue with ursodeoxycholic acid (ursosan), rosuvastatin.

Conclusion

1. Molecular genetic testing (NGS) is a mandatory component of the diagnosis of medullary thyroid cancer. Detection of the RET mutation p. C630R in the allelic frequency of 21.14% determined the validity of prescribing a highly selective RET inhibitor.

2. Multikinase inhibitors (vandetanib, cabozantinib) remain an important treatment tool, but their non-selectivity causes severe toxicity in a significant part of patients. Stevens-Johnson syndrome, Quincke's edema, and drug-induced hepatitis are life-threatening adverse events and are absolute indications for discontinuation of therapy.

3. Selpercatinib provides a high objective response (69-73% according to LIBRETTO-001) with a significantly more favorable tolerability profile. The dynamics of clinical and laboratory parameters confirms its effectiveness and safety.

4. Comprehensive management involving a nephrologist, cardiologist, endocrinologist, and gastroenterologist is a mandatory component of the treatment of elderly patients with orphan cancer.

5. It is necessary to register selpercatinib in the Republic of Kazakhstan and ensure patients' access to targeted therapy.

Author Contributions

A.M, A.Zh. - concept and supervision of the work; A.B., U.K. - project administration; A.Zh., A.K. - investigation; A.Zh., A.B. - interpretation and discussion of the results; A.Zh., D.B., A.M - writing and editing the text of the article.

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Conflict of interest

The authors declare no conflict of interest.

Compliance with ethical standards

All procedures performed in this study involving a human participant were in accordance with the ethical standards of the national research ethics committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed voluntary consent was obtained from the patient for participation and for the publication of clinical data and accompanying diagnostic images. All patient data were anonymized to ensure confidentiality and protect the patient's privacy.

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Селперкатинибті RET р. С630R мутациясы бар қалқанша безінің қайталанатын медулярлық карциномасында қолдану: клиникалық жағдай

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Аңдатпа. Қалқанша бездің медулярлық карциномасы (ҚБМК) — қалқанша без обырының барлық жағдайларының 1–5%-ын құрайтын парафолликулярлық С-жасушалардан дамиды сирек кездесетін қатерлі ісік. RET генінің соматикалық мутациялары спорадиялық жағдайлардың 40–50%-ында кездеседі және RET селективті тежегіштері үшін нысана болып табылады. 2020 жылы АҚШ-тың Азық-түлік және дәрі-дәрмек сапасын бақылау басқармасы (FDA), ал 2021 жылы Еуропалық дәрілік заттар агенттігі (EMA) мақұлдаған селперкатиниб (RETIVO, Eli Lilly) қазіргі уақытта Қазақстанда тіркелмеген. Бұл зерттеуде қайталанған ҚБМК, мойын лимфа түйіндері мен өкпеге метастаздары, вандетанибке төзімсіздігі және расталған RET р.С630R мутациясы бар 74 жастағы пациентте селперкатинибтің сәтті қолданылуы сипатталған. Диагностикалық тексеруге гистологиялық және иммуногистохимиялық зерттеулер, жаңа буын секвенирлеуі (NGS), контрастылы компьютерлік томография (КТ), магниттік-резонанстық томография (МРТ), ¹⁸F-FDG қолданылған позитрондық-эмиссиялық және компьютерлік томография (ПЭТ/КТ), сондай-ақ кальцитонин, карциноэмбриондық антиген, қалқанша без гормондары деңгейлерін және бауыр мен бүйрек қызметін зертханалық бақылау кірді. Жаңа буын секвенирлеуі (NGS) аллельдік жиілігі 21,14% болатын белсендіруші RET р.С630R мутациясын анықтады. Квинке ісінуінің, дәрілік препараттан туындаған бауыр зақымдануының және Стивенс–Джонсон синдромының дамуына байланысты вандетаниб қабылдау тоқтатылды. Кейіннен тәулігіне 160 мг дозада селперкатиниб тағайындалды. Үш айдан кейін, 2026 жылғы 4 наурызда жүргізілген ПЭТ/КТ жергілікті рецидив белгілерін анықтамады және өкпедегі ошақтардың метаболизмдік белсенділігінің шамамен екі есе төмендегенін көрсетті.

Кальцитонин деңгейі қалыптың жоғарғы шегіне жақын тұрақты деңгейде сақталды (16,0–16,3 пг/мл). Емдеуді тоқтатуды талап ететін жағымсыз әсерлер тіркелген жоқ, ал бауыр мен бүйрек қызметінің көрсеткіштері қалыпты деңгейде қалды. Бұл клиникалық жағдай бірінші буындағы мультикиназалық тежегішке төзімсіздік болғаннан кейін RET-позитивті қалқанша бездің медулярлық карциномасын емдеуде селперкатинибтің тиімділігі мен жақсы көтерімділігін көрсетеді, сондай-ақ оны Қазақстанда тіркеудің және пациенттер үшін қолжетімділігін арттырудың орындылығын растайды.

Түйін сөздер: қалқанша безінің медулярлық қатерлі ісігі, рет мутациясы, селперкатиниб, мақсатты терапия, жаңа буын секвенциясы (NGS), вандетаниб, клиникалық жағдай

Применение Селперкатиниба при рецидивирующей медулярной карциноме щитовидной железы с мутацией RET p.C630R: клинический случай

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Аннотация. Медулярная карцинома щитовидной железы (МКЩЖ) — редкая злокачественная опухоль парафолликулярных С-клеток, составляющая 1–5% от всех случаев рака щитовидной железы. Соматические мутации RET встречаются в 40–50% спорадических случаев и являются мишенями для селективных ингибиторов RET. Селперкатиниб (RETEVMO, Eli Lilly), одобренный FDA в 2020 году и ЕМА в 2021 году, в настоящее время не зарегистрирован в Казахстане. В данном исследовании описывается его успешное применение у 74-летнего пациента с рецидивирующей МКЩЖ, метастазами в шейные лимфатические узлы и легкие, непереносимостью вандетаниба и подтвержденной мутацией RET p.C630R. Диагностическое обследование включало гистологию, иммуногистохимию, секвенирование нового поколения (NGS), контрастную КТ, МРТ, ПЭТ/КТ с ¹⁸F-FDG, а также лабораторный мониторинг кальцитонина, карциноэмбрионального антигена, гормонов щитовидной железы, функции печени и почек. Секвенирование нового поколения (NGS) выявило активирующую мутацию RET p.C630R с частотой аллеля 21,14%. Прием вандетаниба был прекращен из-за отека Квинке, лекарственно-индуцированного поражения печени и синдрома Стивенса-Джонсона. Впоследствии был назначен селперкатиниб в дозе 160 мг/сутки. Через три месяца ПЭТ/КТ, выполненная 4 марта 2026 года, не выявила признаков местного рецидива и показала приблизительно двукратное снижение метаболической активности легочных очагов. Уровень кальцитонина оставался стабильным, близким к верхней границе нормы (16,0–16,3 пг/мл). Не было зарегистрировано побочных эффектов, требующих прекращения лечения, а функции печени и почек оставались в норме. Этот случай демонстрирует эффективность и благоприятную переносимость селперкатиниба при RET-позитивной медулярной карциноме щитовидной железы после непереносимости ингибитора мультикиназ первого поколения и подтверждает целесообразность его регистрации и улучшения.

Ключевые слова: медулярный рак щитовидной железы, мутация RET, селперкатиниб, таргетная терапия, секвенирование нового поколения (NGS), вандетаниб, клинический случай.

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