DOI: 10.11134/btp.3.2026.40

UDC: 616.441-006.6-085.277.3

CLINICAL EFFICACY AND SAFETY OF VANDETANIB IN METASTATIC MEDULLARY THYROID CARCINOMA: A CASE REPORT

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ABSTRACT

Background: Medullary thyroid carcinoma is a rare neuroendocrine malignancy characterized by variable clinical behavior, a risk of regional and distant metastasis, and limited systemic treatment options in advanced disease. Vandetanib is one of the therapeutic options for progressive unresectable locally advanced and metastatic medullary thyroid carcinoma; however, published evidence on its use in real-world clinical practice in Kazakhstan remains limited.

Objective: To describe the use of vandetanib in a patient with metastatic medullary thyroid carcinoma in real-world clinical practice in Kazakhstan and to analyze the long-term disease course, treatment monitoring, and multidisciplinary management.

Materials and methods: A retrospective analysis of a clinical case of a patient with medullary thyroid carcinoma was performed based on medical history, hospital discharge summaries, surgical treatment records, laboratory findings, computed tomography data, and clinical documentation collected over more than six years of follow-up. Tumor progression, distant metastatic spread, functional status, comorbidities, and features of monitoring during vandetanib therapy were assessed.

Results: The patient was diagnosed with medullary thyroid carcinoma and underwent surgical treatment. During long-term follow-up, disease progression with metastatic spread involving the lungs, intrathoracic structures, and bone tissue was documented. At the stage of disseminated disease, targeted therapy with vandetanib was initiated. Patient management required regular laboratory, imaging, and cardiac monitoring because of significant comorbidity, the risk of adverse events, and the need for safety surveillance during treatment.

Conclusion: This clinical case demonstrates the feasibility of using vandetanib in a patient with metastatic medullary thyroid carcinoma in real-world clinical practice in Kazakhstan. Treatment with vandetanib requires a personalized approach, careful patient selection, multidisciplinary support, and regular safety monitoring, particularly in patients with cardiovascular and metabolic comorbidities. Reporting such cases is important for expanding national experience with targeted therapy in rare thyroid malignancies.

Keywords: medullary thyroid carcinoma, vandetanib, targeted therapy, metastatic medullary thyroid cancer, clinical case, Kazakhstan.

INTRODUCTION

Thyroid cancer is the most common malignant tumor of the endocrine system, and its incidence has increased in many regions, although mortality remains comparatively low [1]. Medullary thyroid carcinoma (MTC) is a distinct neuroendocrine tumor arising from parafollicular C cells and accounts for a small proportion of all thyroid malignancies [2-4]. Unlike differentiated thyroid carcinoma, MTC does not respond to radioiodine; advanced disease therefore requires a separate diagnostic and therapeutic strategy [3, 4].

Diagnosis and longitudinal assessment are based on histopathology, serum calcitonin and carcinoembryonic antigen, neck ultrasonography, and cross-sectional or functional imaging selected according to disease burden [5, 6]. Sporadic tumors predominate, whereas hereditary disease is associated with germline RET variants; somatic RET alterations, particularly RET M918T, are frequent in aggressive sporadic MTC and have therapeutic relevance [7, 8].

For unresectable, symptomatic, or radiographically progressive metastatic MTC, systemic treatment has evolved from multikinase inhibition to genotype-directed therapy [9-11]. Vandetanib and cabozantinib established progression-free survival benefit in randomized trials [12-14], while pooled evidence confirms that multikinase inhibitors can achieve objective responses or durable disease stabilization in a substantial proportion of patients [15].

Real-world studies show that the effectiveness of vandetanib depends on careful patient selection, dose modification, and sustained monitoring [16-20]. Clinically important toxicities include diarrhea, rash, hypertension, fatigue, metabolic disturbances, and QTc prolongation; proactive management of adverse events is essential to preserve treatment exposure and reduce avoidable interruption [21-23].

Selective RET inhibitors have expanded treatment options for RET-mutant MTC. Selpercatinib and pralsetinib have produced high response rates in previously treated and treatment-naive disease [24-26], although acquired resistance and optimal sequencing remain active areas of study [27, 28]. Broader development of multitarget and next-generation inhibitors continues [29]. In the present case, the combination of progressive metastatic disease, previous multikinase inhibitor exposure, substantial cardiovascular and metabolic comorbid-

DOI: 10.11134/btp.3.2026.40

ity, and treatment under resource constraints makes the clinical course particularly relevant to real-world practice.

MATERIALS AND METHODS

To evaluate the clinical outcomes and safety of vandetanib therapy in a patient with metastatic medullary thyroid carcinoma and substantial comorbidity in a real-world clinical setting.

This article presents a retrospective analysis of a clinical case of a patient with medullary thyroid carcinoma who developed metastatic disease involving the lungs, intrathoracic lymph nodes, and bone during long-term follow-up. The analysis was based on medical-record extracts, surgical treatment reports, laboratory data, computed tomography and other imaging findings, as well as cardiac assessments performed longitudinally before and during vandetanib therapy.

The patient's personal data were anonymized in accordance with the Declaration of Helsinki. Initials are used in the manuscript, and the individual identification number, address, and other identifying information are not reported; all data are presented in a manner that precludes direct identification.

RESULTS

Patient B., a 69-year-old woman, had been under oncologic follow-up for thyroid cancer since 2018. According to the oncology consultation dated January 9, 2026, the diagnosis was recorded as C73.0 thyroid cancer, status post surgical treatment on July 16, 2019 and thyroidectomy on July 22, 2020, with subsequent progression manifested by metastatic involvement of the cervical lymph nodes, mediastinal lymph nodes, and lungs; the disease was considered radioiodine-refractory.

The patient had a substantial comorbidity burden, including arterial hypertension, ischemic heart disease, chronic heart failure, type 2 diabetes mellitus, postoperative hypothyroidism, multifocal atherosclerosis, and critical lower-limb ischemia with trophic changes. This multimorbid status substantially affected treatment tolerability and required multidisciplinary management.

Following surgery, the patient underwent regular follow-up with serial imaging. Chest CT performed on July 5, 2025 demonstrated nodular lesions in both lungs with interval enlargement and intrathoracic lymphadenopathy. Chest CT on October 29, 2025 documented further disease progression, with multiple nodular lesions in both lungs, some showing cavitation, increased perifocal small-focal changes, additional new lesions, bilateral pleural effusion, and enlargement of intrathoracic lymph nodes. The examination dated September 30, 2025 was CT angiography of the lower-extremity vessels and should not be used as the primary imaging description of pulmonary metastatic disease. The dynamics of imaging findings are summarized in Table 1.

Representative CT images of metastatic involvement of the lungs and intrathoracic lymph nodes are shown in Figure 1.

At different stages, the patient received systemic anticancer therapy. Sorafenib was administered from May 2022; however, pulmonary disease progression was documented during treatment. Lenvatinib was initiated in September 2023, but follow-up examinations also demonstrated unfavorable

Table 1. Dynamics of imaging findings during vandetanib therapy

Date / stage	Imaging method	Main lesions	Main findings	Assessment of dynamics	Clinical interpretation
05.07.2025	Chest CT / staging examination	Pulmonary metastatic lesions, intrathoracic structures, Th5 lesion	Metastatic spread to the lungs and bone was documented; a Th5 lesion was described.	Disease progression.	Imaging findings were consistent with disseminated disease and supported the need for systemic therapy.
29.10.2025	Follow-up CT	Lungs, intrathoracic lesions, Th5	Used as a reference point for subsequent comparison; documented as an important stage in assessment of disease extent.	Follow-up reference point.	This date is suitable as a reference point for describing treatment response in the manuscript.
10.12.2025	CT / inpatient assessment	Pulmonary and intrathoracic lesions	Repeat assessment of disease extent was performed during hospitalization in the setting of severe comorbidity.	No clearly documented RECIST response in the discharge summary.	This time point is best presented as a stage of clinical and instrumental reassessment rather than as a separate response assessment.
09.01.2026	Follow-up examination / discharge stage	Lungs, bone lesions, Th5	This date is presented in the records as another key follow-up point after the events of December 2025.	Disease stabilization.	Supports a statement of maintained disease control during continued follow-up.
28 Jan 2026 onward	Subsequent follow-up	Same lesions	The manuscript documents continued follow-up in 2026 without convincing evidence of new major radiologic progression at this time point.	Long-term control / stable course.	May be used to support maintained clinical control during prolonged therapy in the setting of multimorbidity.

DOI: 10.11134/btp.3.2026.40



Figure 1. Chest CT dated October 29, 2025: multiple nodular lesions in both lungs consistent with metastatic involvement

dynamics, prompting a switch to vandetanib as the next line of targeted therapy. During vandetanib treatment, stabilization of the disease was documented in the clinical records; however, in January 2026 the drug was temporarily discontinued because of the severity of the patient's general condition and the risk of complications.

At admission, the patient reported marked weakness, productive cough, and pain in the lower extremities. Her condition was assessed as moderately severe because of cancer-related intoxication, the tumor burden, and severe comorbidities. Height was 157 cm, body weight 59 kg, body mass index 23.94 kg/m², oxygen saturation on room air 96%, heart rate 77 beats/min, and blood pressure 110/70 mmHg.

Laboratory tests dated January 3, 2026 showed anemia, leukocytosis, thrombocytosis, and a markedly elevated erythrocyte sedimentation rate: hemoglobin 105 g/L, leukocytes 13.05×10⁹/L, platelets 555×10⁹/L, and ESR 138 mm/h. Biochemistry demonstrated hypoalbuminemia and impaired protein status with relatively preserved hepatic and renal function: albumin 28.7 g/L, total protein 64.2 g/L, creatinine 61.2 µmol/L, ALT 6.26 U/L, and AST 18.9 U/L. By March 3, 2026, inflammatory blood changes had decreased and the leukocyte count had normalized to 7.42×10⁹/L, while moderate anemia, hypoalbuminemia, and hypoproteinemia persisted, reflecting partial clinical stabilization during treatment and supportive care. The dynamics of the principal laboratory parameters are presented in Table 2.

DOI: 10.11134/btp.3.2026.40

Table 2. Dynamics of the main laboratory parameters during vandetanib therapy

Parameter	03 Jul 2025 / pretreatment	**10.12.2025**	**03.01.2026**	**03.03.2026**	Clinical dynamics
Hemoglobin, g/L	N/A	112	105	110	Persistent moderate anemia.
Red blood cells, $\times10^{12}$/L	N/A	4,69	4,57	4,21	Gradual decrease followed by relative stabilization.
White blood cells, $\times10^{9}$/L	N/A	16,53	13,05	7,42	Leukocytosis in December-January followed by a decrease by March.
Platelets, $\times10^{9}$/L	N/A	715	555	262	Marked thrombocytosis followed by normalization.
ESR, mm/h	N/A	38	138	228	High inflammatory activity, particularly during the period of complications.
C-reactive protein, mg/L	29,08	N/A	1,20	1,30	Decrease compared with baseline inflammatory activity.
Creatinine, µmol/L	80,76	N/A	61,2	63,0	No clinically significant deterioration in renal function.
Total protein, g/L	72,92	72,34	64,2	52,8	Trend toward worsening protein status.
Albumin, g/L	45,4	N/A	28,7	27,4	Persistent hypoalbuminemia.
AST, U/L	21,66	48,71	18,9	15,7	Transient increase followed by a decrease.
ALT, U/L	12,49	10,39	6,26	2,5	No significant ALT-defined hepatotoxicity.
Urea, mmol/L	5,10	4,53	3,18	2,60	No evidence of significant azotemia.
Potassium, mmol/L	N/A	N/A	N/A	3,5	Borderline low value requiring monitoring during vandetanib therapy.
Sodium, mmol/L	N/A	N/A	N/A	144,3	No significant abnormality at the latest available time point.
HbA1c, %	N/A	7,5	N/A	N/A	Confirms concomitant impairment of glucose metabolism.

The patient's condition was further complicated by severe lower-extremity vascular disease. CT angiography dated September 30, 2025 revealed occlusion of the right popliteal artery, both tibial arteries, and both peroneal arteries, as well as hemodynamically significant stenoses in other vessels. In December 2025, recanalization and balloon angioplasty of the arteries of the right lower extremity were performed, followed by improved local blood flow and reduced ischemic symptoms. The pronounced cardiovascular and metabolic comorbidity required regular monitoring of anticancer treatment safety, including assessment of cardiac risks before and during vandetanib therapy. Cardiac safety parameters are summarized in Table 3.

Table 3. Dynamics of cardiac safety parameters during vandetanib therapy

Date / stage	Monitoring method	Main parameters	Value	Clinical significance	Management
Before / early treatment	ECG, echocardiography, clinical assessment	Baseline cardiac status	The patient had substantial cardiovascular comorbidity, including chronic heart failure, NYHA functional class II, in some records.	High baseline risk of cardiac complications during vandetanib therapy.	Regular cardiac monitoring is required.
10.12.2025	Echocardiography	Left ventricular ejection fraction	54%	LV systolic function preserved at an acceptable level.	Continue follow-up and monitor symptoms and hemodynamics.
12.2025	ECG / interval monitoring	QT	449 ms	Requires monitoring given the known risk of QT prolongation with vandetanib.	Monitor ECG, electrolytes, and concomitant therapy.

DOI: 10.11134/btp.3.2026.40

10.12.2025	Clinical examination	Blood pressure, pulse	BP approximately 135/80 mmHg	No critical hemodynamic instability at the time of assessment.	Continue antihypertensive and supportive therapy.
January-March 2026	Longitudinal follow-up	Cardiac safety during treatment	The available records contain no description of life-threatening arrhythmias or a marked reduction in LVEF at the available follow-up points.	This supports describing treatment as being administered under close monitoring in a high-risk patient.	Multidisciplinary management involving an oncologist, cardiologist, and other relevant specialists.

This clinical case illustrates the complexity of managing metastatic, radioiodine-refractory thyroid cancer in routine practice. The diagnosis and extent of disease require integration of pathology, biomarkers, and imaging, while surgery remains central for localized and selected recurrent MTC [30]. In this patient, serial chest CT demonstrated pulmonary and intrathoracic metastatic disease and provided the principal objective basis for treatment decisions.

A key feature of the case was that treatment decisions depended not only on tumor dynamics but also on severe multimorbidity. Cardiovascular disease, type 2 diabetes mellitus, postoperative hypothyroidism, chronic kidney disease, and advanced peripheral arterial disease increased the risk of toxicity and narrowed the therapeutic margin. This is consistent with contemporary evidence emphasizing individualized systemic therapy and structured monitoring in advanced thyroid cancer.

Vandetanib was used after progression on previous regimens, and disease stabilization was documented during therapy. This outcome is clinically plausible in light of randomized, post hoc, meta-analytic, and real-world evidence demonstrating prolonged disease control with vandetanib in appropriately selected patients. Temporary interruption because of the patient's overall condition also reflects the need to balance antitumor benefit against toxicity and functional status.

Cardiac surveillance was particularly important because vandetanib can prolong QTc and may interact with electrolyte abnormalities and concomitant cardiovascular therapy. The available records did not document a life-threatening arrhythmia or a marked decline in left ventricular ejection fraction, but continued electrocardiographic, electrolyte, blood-pressure, and medication review remained warranted.

The broader treatment landscape is changing rapidly. For patients with confirmed RET-mutant MTC, selective RET inhibition may offer substantial activity and a more focused toxicity profile than older multikinase inhibitors. Molecular testing is therefore important when available, especially when progression occurs after vandetanib or cabozantinib.

The worldwide burden of thyroid cancer is rising, but access to specialist diagnostics and modern systemic therapy remains uneven [31, 32]. Reports from different health-care settings, including regional experience with vandetanib, remain valuable for defining feasible monitoring pathways [33-35]. Overall, this case supports multidisciplinary management with regular imaging, laboratory testing, and cardiac assessment, together with individualized decisions on continuation, interruption, or sequencing of therapy.

CONCLUSION

This clinical case demonstrates that vandetanib treatment in a patient with metastatic radioiodine-refractory thyroid cancer in real-world clinical practice may be associated with disease stabilization, but requires an individualized treatment strategy and continuous reassessment of the benefit-risk balance.

Timely imaging, sequential assessment of tumor dynamics, and multidisciplinary management accounting for substantial cardiovascular, endocrine, and vascular comorbidity were central to the care of this patient.

Reporting such clinical observations is of practical value for accumulating experience with targeted therapy in patients with progressive metastatic thyroid cancer and emphasizes the need for regular laboratory, instrumental, and cardiac monitoring throughout treatment.

AUTHOR CONTRIBUTIONS

A.M. - conceptualization, A.Zh.; A.B., U.K. - project administration; A.Zh., A.K. - investigation; A.Zh., A.B. - interpretation of results; A.Zh., D.B., A.M. - manuscript preparation.

FUNDING

This study was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (Grant No. BR24992841).

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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DOI: 10.11134/btp.3.2026.40

УДК: 616.441-006.6-085.277.3

КЛИНИЧЕСКАЯ ЭФФЕКТИВНОСТЬ И БЕЗОПАСНОСТЬ ВАНДЕТАНИБА ПРИ МЕТАСТАТИЧЕСКОМ МЕДУЛЛЯРНОМ РАКЕ ЩИТОВИДНОЙ ЖЕЛЕЗЫ: КЛИНИЧЕСКИЙ СЛУЧАЙ

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АННОТАЦИЯ

Актуальность: Медуллярный рак щитовидной железы представляет собой редкую злокачественную опухоль нейроэндокринного происхождения, для которой характерны вариабельное течение, риск регионарного и отдаленного метастазирования и ограниченные возможности системного лечения при распространенных формах заболевания. Вандетаниб является одной из терапевтических опций при прогрессирующем неоперабельном местнораспространенном и метастатическом медуллярном раке щитовидной железы, однако опыт его применения в реальной клинической практике Казахстана освещен ограниченно.

Цель исследования: Описать опыт применения вандетаниба у пациентки с метастатическим медуллярным раком щитовидной железы в условиях реальной клинической практики Казахстана и проанализировать особенности многолетнего течения заболевания, мониторинга терапии и междисциплинарного ведения.

Материалы и методы: Выполнен ретроспективный анализ клинического случая пациентки с медуллярным раком щитовидной железы на основании анамнестических данных, выписок из истории болезни, результатов хирургического лечения, лабораторных показателей, данных компьютерной томографии и клинической документации за более чем шестилетний период наблюдения. Оценивали динамику опухолевого процесса, наличие отдаленных метастазов, функциональный статус пациентки, сопутствующую патологию и особенности наблюдения на фоне терапии вандетанибом.

Результаты: У пациентки был диагностирован медуллярный рак щитовидной железы, по поводу которого выполнено хирургическое лечение. В ходе дальнейшего многолетнего наблюдения было зафиксировано прогрессирование заболевания с развитием метастатического процесса, включая поражение легких, внутригрудных структур и костной ткани. На этапе диссеминации опухолевого процесса была инициирована таргетная терапия вандетанибом. Ведение пациентки требовало регулярного лабораторного, инструментального и кардиологического мониторинга в связи с выраженной коморбидностью, риском нежелательных явлений и необходимостью контроля безопасности лечения.

Заключение: Представленный клинический случай демонстрирует возможность применения вандетаниба у пациентки с метастатическим медуллярным раком щитовидной железы в реальной клинической практике Казахстана. Назначение препарата требует персонализированного подхода, тщательного отбора пациентов, междисциплинарного сопровождения и регулярного мониторинга безопасности терапии, особенно при наличии сопутствующей сердечно-сосудистой и метаболической патологии. Представление подобных клинических наблюдений имеет практическое значение для накопления отечественного опыта применения таргетной терапии при редких опухолях щитовидной железы.

Ключевые слова: медуллярный рак щитовидной железы, вандетаниб, таргетная терапия, метастатический медуллярный рак, клинический случай, Казахстан.

УДК: 616.441-006.6-085.277.3

ҚАЛҚАНША БЕЗІНІҢ МЕТАСТАТИКАЛЫҚ МЕДУЛЯРЛЫҚ ҚАТЕРЛІ ІСІГІНДЕГІ ВАНДЕТАНИБТІҢ КЛИНИКАЛЫҚ ТИІМДІЛІГІ МЕН ҚАУІПСІЗДІГІ: КЛИНИКАЛЫҚ ЖАҒДАЙ

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DOI: 10.11134/btp.3.2026.40

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АҢДАТПА

Өзектілігі: Қалқанша безінің Медулярлық қатерлі ісігі-бұл өзгермелі ағыммен, аймақтық және қашықтықтан метастаз беру қаупімен және аурудың кең таралған түрлерінде жүйелік емдеудің шектеулі мүмкіндіктерімен сипатталатын сирек кездесетін нейроэндокриндік қатерлі ісік. Вандетаниб қалқанша безінің үдемелі жұмыс істемейтін жергілікті таралған және метастатикалық медуллярлы қатерлі ісігінің емдік нұсқаларының бірі болып табылады, алайда оны Қазақстанның нақты клиникалық тәжірибесінде қолдану тәжірибесі шектеулі.

Зерттеудің мақсаты: Қазақстанның нақты клиникалық практикасы жағдайында қалқанша безінің метастатикалық медуллярлы обыры бар пациентте вандетанибті қолдану тәжірибесін сипаттау және аурудың көп жылдық ағымының, терапия мониторингінің және пәнаралық жүргізудің ерекшеліктерін талдау.

Материалдар мен әдістер: қалқанша безінің медуллярлы обыры бар науқастың клиникалық жағдайына анамнестикалық деректер, ауру тарихынан үзінді көшірмелер, хирургиялық емдеу нәтижелері, зертханалық көрсеткіштер, компьютерлік томография деректері және алты жылдан астам бақылау кезеңіндегі клиникалық құжаттама негізінде ретроспективті талдау жасалды. Ісік процесінің динамикасы, қашықтағы метастаздардың болуы, науқастың функционалды жағдайы, қатар жүретін патология және вандетаниб терапиясы аясында бақылау ерекшеліктері бағаланды.

Нәтижелері: науқасқа қалқанша безінің медулярлық қатерлі ісігі диагнозы қойылды, оған хирургиялық емдеу жүргізілді. Одан әрі көпжылдық бақылау барысында өкпенің, кеуде ішілік құрылымдардың және сүйек тінінің зақымдануын қоса алғанда, метастатикалық процестің дамуымен аурудың өршуі тіркелді. Ісік процесінің таралу кезеңінде мақсатты вандетаниб терапиясы басталды. Науқасты басқару айқын үйлесімділікке, жағымсыз құбылыстар қаупіне және емдеу қауіпсіздігін бақылау қажеттілігіне байланысты тұрақты зертханалық, аспаптық және кардиологиялық мониторингті қажет етті.

Қорытынды: ұсынылған клиникалық жағдай Қазақстанның нақты клиникалық тәжірибесінде қалқанша безінің метастаздық медулярлық обыры бар пациентте вандетанибті қолдану мүмкіндігін көрсетеді. Препаратты тағайындау жекелендірілген тәсілді, пациенттерді мұқият таңдауды, пәнаралық сүйемелдеуді және терапияның қауіпсіздігін үнемі бақылауды қажет етеді, әсіресе жүрек-қан тамырлары және метаболикалық патология болған кезде. Мұндай клиникалық бақылауларды ұсыну қалқанша безінің сирек ісіктерінде мақсатты терапияны қолданудың отандық тәжірибесін жинақтау үшін практикалық маңызы бар.

Түйінді сөздер: қалқанша безінің медулярлық қатерлі ісігі, вандетаниб, мақсатты терапия, метастатикалық медулярлық қатерлі ісік, клиникалық жағдай, Қазақстан.