The impact of vitamin D on breast cancer treatment: literature review

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SUMMARY

Background: *Despite the progress in individualizing breast cancer therapy and achieving success in surgical and systemic treatment, the mortality remains high, which requires the search for new targets that can have a significant direct or indirect contribution to the development and prognosis of this disease. One such factor is vitamin D, which is deficient in most parts of the world, and its serum and receptor status have been extensively studied. Numerous studies have been published on the protective effects of vitamin D on breast cancer and other malignancies, risk of development, and treatment outcomes, in particular, increasing the sensitivity of tumors to systemic therapy, survival, and prognosis.*

Methods: *The authors analyzed and systematized research data on the predictive effect of vitamin D on the prognosis and course of breast cancer, the manifestation of its "non-classical" effects in preclinical and clinical studies, and assessed the possible practical application of the results obtained at the molecular-cellular level. The results allow us to use vitamin D as an important marker for monitoring the skeletal system's state during and after breast cancer treatment. In addition, vitamin D and its analogues in combination with other cytostatic drugs can help search for possible new therapeutic targets.*

Conclusion: *The presented results of vitamin D activity associated with the stages of carcinogenesis undoubtedly open up prospects for finding new possibilities for the treatment and prevention of breast cancer, creating prospects for further research to improve the prognosis and survival rates for such patients. The studied cytotoxic effects expand the field of clinical research on the "non-classical" properties of vitamin D and allow the integration of data on a potential antitumor agent for many malignant tumors.*

Keywords: *breast cancer, vitamin D, vitamin D levels, drug combination, efficacy*

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INTRODUCTION

Vitamin D (VD) is known for its classical effects on the regulation of bone metabolism. However, the non-classical effects attract broader scientific interest and serve as a field of constant research and clinical research. VD is one of the key antiproliferative and proapoptotic agents at different stages of carcinogenesis, inhibits angiogenesis, metastasis, invasion, and also stimulates cell differentiation (1-3). Vitamin D deficiency is observed in most of the world's population, and its serum and receptor status are widely studied as critical in many areas of medicine. Many studies have been conducted on the protective effect of vitamin D on breast cancer and other malignancies, the risk of development, and treatment outcomes, in particular increasing the response of tumors to systemic therapy, survival, and prognosis (4-7). The active circulating form of VD (calcitriol, also called 1,25-dihydroxyvitamin D3) suppresses cell proliferation by increasing the synthesis of cyclin-dependent kinase (CDK) inhibitors p21 and p27, inhibits mitogenic signaling by growth factors such as IGF1 and EGF (abbreviations for IGF and EGF), and modulates intracellular kinases (8, 9). Calcitriol induces apoptosis indirectly by inhibiting anti-apoptotic genes, such as BCL2, and promoting pro-apoptotic genes, such as BAX (Ref missing) Calcitriol inhibits the formation of the vascular endothelial growth factor (VEGF), tenascin C, α6 and β4 integrins, and induces E-cadherin, which in turn regulate the processes of invasion, angiogenesis and metastasis (10, 11). Calcitriol has been found to inhibit the expression of cyclooxygenase-2, thereby reducing the production of inflammatory prostaglandins. The published data were confirmed in vivo and in vitro and found that suppressing prostaglandin synthesis by calcitriol leads to decreased aromatase expression (5,12). There is evidence of the inhibitory effect of VD on ERα receptors and the indirect potential increase in tumor sensitivity to drug therapy. A suppressive effect of VD was discovered during the transcription in breast cancer cells, surrounding adipose tissue, and preadipocytes, which results in a decrease in aromatase expression (12, 13). Numerous data and scientific advances regarding the position of vitamin D and its metabolites in breast cancer carcinogenesis have led to the search for new combination antitumor regimens. VD and its analogues have recently begun to be rapidly introduced into preclinical studies aiming to improve a possible antitumor effect along with other therapeutic agents.

The place of vitamin D in the carcinogenesis of triple-negative breast cancer, which is identified by the absence of expression of estrogen and progesterone receptors and a limited number of therapeutic targets, deserves special attention. According to observational and prospective studies, the largest number of patients with this molecular subtype are observed with insufficient or deficient levels (14, 15). The data of preclinical studies on cell lines of triple-negative breast tumors indicated the presence of expression of vitamin D receptors (VDR) on their surface and that and the use of 1,25-dihydroxyvitamin D3 or its analogues can lead to suppression of the process of tumor invasion, which

leads to a decrease in metastatic potential (16-18). Also, in vivo studies showed that the effect of calcitriol on triple-negative tumors leads to the stimulation of ERα expression, which allows this effect to be interpreted as the action of a potential agent that induces and enhances the response to anti-estrogen therapy (19, 20).

The main effects of vitamin D in breast cancer pathogenesis are schematically shown in Figure 1.

Given the potential of vitamin D analogues to slow tumor progression by blocking various signaling pathways, numerous studies are currently exploring potential chemotherapy drugs or other compounds that could synergize with calcitriol analogues in combination therapies. This promising avenue of research is generating significant interest in the medical community. Preclinical studies indicate that vitamin D increases

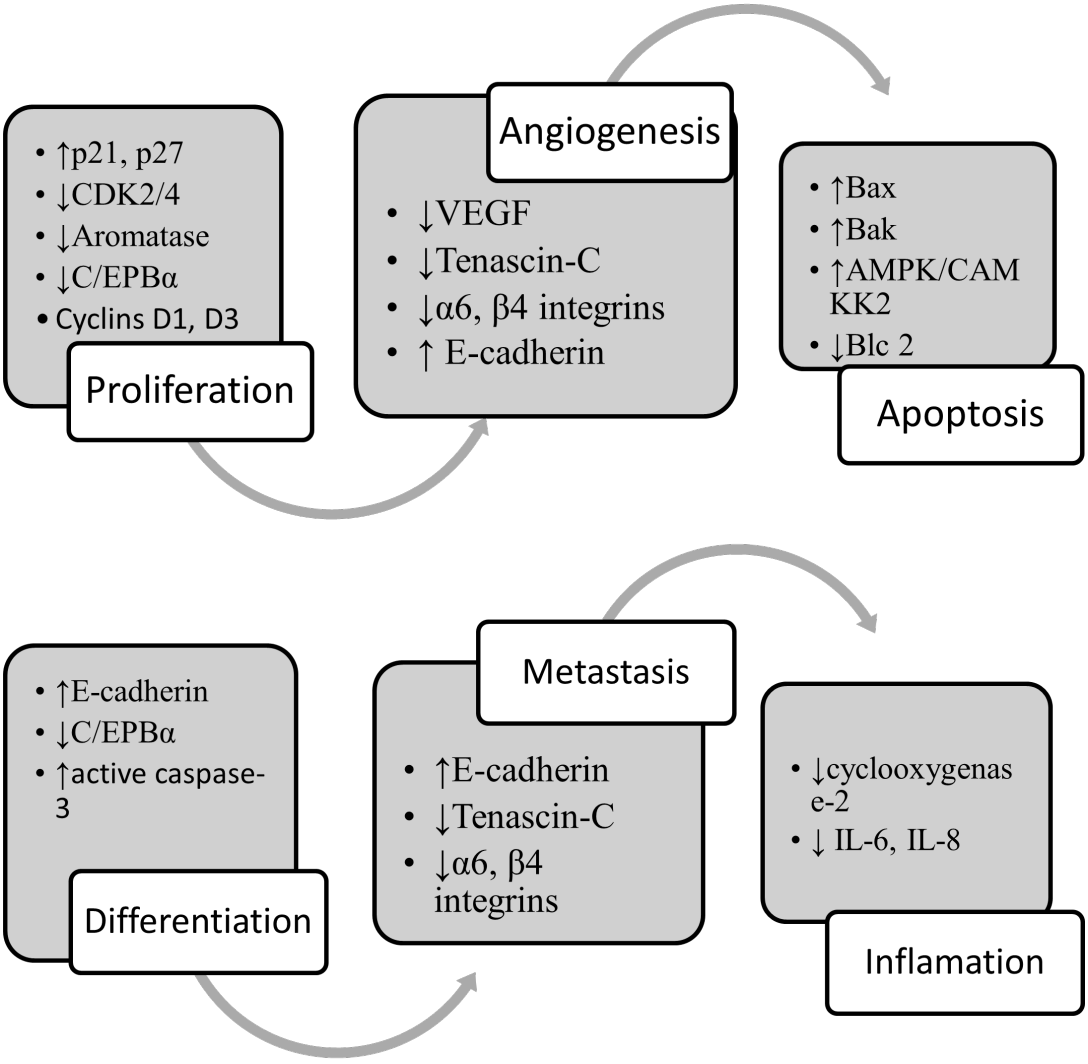

Figure 1. Vitamin D effects in breast cancer pathogenesis.

METHODS

This literature review aims to systematize existing studies that have examined the role of vitamin D in breast cancer treatment. It reviewed preclinical and clinical studies that reported the results of the use of calcitriol and its analogues in models of breast carcinoma and the latest published outcomes of intervention trials on the use of vitamin D during systemic therapy, both in neoadjuvant and adjuvant regimens.

The application of vitamin D and its analogues in combination with anticancer therapy for breast cancer (preclinical studies)

the sensitivity of breast tumors to hormone therapy. Swami S. et al. revealed a significant antiproliferative and cytostatic effect of calcitriol in combination with aromatase inhibitors in a study on a xenograft model of breast carcinoma in mice. It was also found that VD can cause effects similar to selective aromatase modulators, particularly in the form of a decrease in the expression of this enzyme in breast adipose cells, while simultaneously enlarging it in the bone marrow (21). The research by Filip-Psurska B. et al. similarly indicates a potentiation of the effect of aromatase inhibitors when using VD metabolites and their synthetic analogues in cell models of ER-PR-positive breast cancer

tumors (22). The opposite results are studies on the antitumor effect of VD in combination with tamoxifen. It has been established in vitro that using calcitriol does not enhance the anticarcinogenic effect of selective estrogen receptor modulators (23).

Segovia-Mendoza M. et al. studied the effect of a combination of VD and its analogues with tyrosine kinase inhibitors on breast cancer cell lines. The study was conducted on breast tumor cell lines producing EGFR and/or HER2. The antiproliferative efficacy profile of gefitinib in combination with calcitriol or its analogues (calcipotriol and EB1089) was initially discovered. In particular, it was found that all of the above biologically active substances can inhibit proliferation in a dose-dependent way, and the cumulative effectiveness was higher than when using each drug separately. Also, the authors studied the use of VD, its synthetic analogue EB1089, in combination with lapatinib and neratinib. It was found that the simultaneous use of all drug agents enhances the antiproliferative effect, inhibits the growth of cancer cells, the process of phosphorylation of the MAPK/ERK and PI3K/Akt signaling pathways, and also increases the expression of active caspase-3 (24, 25).

Achounna A. et al. continued to study the anticarcinogenic effect of calcitriol, in particular its analog EB1089, in combination with lapatinib and with the selective addition of antiestrogens (tamoxifen, fulvestrant) in HER2-positive breast tumors. A particularity of this study was that it was performed on both ER-positive/HER2-positive and ER-negative/HER2-positive breast cancer cell lines. The results revealed that EB1089 enhanced the inhibitory effect in two cell lines and restored the antiproliferative response to antiestrogens in ER-negative/HER2-positive cell lines. In addition, EB1089 alone and in combination modulated ERα protein expression and inhibited Akt phosphorylation (26).

Attia Y. et al. investigated the effect of vitamin D on carcinogenesis and resistance to paclitaxel. The expression levels of ALDH-1 (aldehyde dehydrogenase-1) and MDR-1 (multi-drug resistance gene) were determined as indicators to assess tumor resistance to a chemotherapeutic drug. The simultaneous use of calcitriol, paclitaxel, and curcumin in the MCF-7 breast carcinoma model in vitro showed a synergistic cytotoxic effect and increased antiproliferative activity. A decrease in MDR-1 and ALDH-1 gene expression was also observed. In vivo, concomitant triple therapy showed the smallest tumor size and lower levels of MDR-1 and ALDH-1. This study opens up new options for the potential application of VD and its metabolites as agents for overcoming resistance to chemotherapeutic drugs, particularly paclitaxel, and increasing tumor sensitivity to systemic therapy (27).

The results of the above studies are systematized in Table 1.

Table 1. The results of the study review examining the combined antitumor activity of vitamin D.

Research group	VD compound/ metabolites/ analogues	Study model	Combined compound	Effect
Filip-Psurska B. et al. (2021) (23)	VD metabolite (24R)-1.24-dihydroxycholecalciferol (PRI-2191) and its analogue 1.25(OH)2D3 (PRI-2205)	MCF-7	Anastrozole	The use of PRI-2191 and PRI-2205 in combination with anastrozole potentiates the inhibition of tumor growth due to the bilateral inhibition of aromatase synthesis and regulates ERα and VDR
Swami S. et al. (2011) (21)	Calcitriol (1.25(OH)2)	MCF-7	Aromatase inhibitors	Decreased aromatase expression and ERα
Yetkin D. et al.(2021) (23)	Calcitriol (1.25(OH)2)	MCF-7	Tamoxifen	The use of calcitriol in combination with tamoxifen does not enhance the antiproliferative and proapoptotic effects
Segovia-Mendoza M. et al.(2015) (24)	Calcitriol (1.25(OH)2) Synthetic analogues: Calcipotriol EB1089	SUM-229PE, SKBR3 and MBCDF	Gefitinib	The use of calcitriol (and its analogues) in combination with gefitinib enhances apoptosis and the antiproliferative effect
Segovia-Mendoza M. et al.(2017) (25)	Calcitriol (1.25(OH)2) Synthetic analogue: EB1089	SUM-229PE SK-BR-3, HCC1937 MDA-MB-231	Lapatinib Neratinib	The use of calcitriol and EB1089 in combination with lapatinib and neratinib enhances the antiproliferative effect, inhibits cell growth, phosphorylation of MAPK/ERK and PI3K/Akt, and increases the expression of active caspase
Achounna A. et al.(2024) (26)	EB1089	BT-474 (ER-positive/HER2-positive) SK-BR-3 (ER-negative/HER2-positive)	Lapatinib Antiestrogens	EB1089 enhances the inhibitory effect in BT-474 and SK-BR-3, restores the antiproliferative response to antiestrogens in SK-BR-3. EB1089 alone and in combination modulates ERα protein expression and inhibits Akt phosphorylation
Attia Y. et al.(2019) (27)	Calcitriol (1.25(OH)2)	MCF-7	Paclitaxel Curcumin	Triple therapy enhances the antiproliferative effect, inhibits tumor growth, and causes a decrease in the expression levels of the MDR-1 and ALDH-1 genes

THE USE OF VITAMIN D IN COMBINATION WITH ANTICANCER THERAPY FOR BREAST CANCER (CLINICAL EXPERIENCE)

Clinical and observational studies have described the use of vitamin D. Some studies have been carried out on the use of vitamin D in the preoperative regimen, as an adjuvant in combination with hormone therapy and chemotherapy, and on the significance of monitoring serum vitamin D status as an independent prognostic factor during treatment.

The NEOZOTAC trial highlighted the importance of measuring vitamin D levels before and after neoadjuvant treatment for breast cancer. Also, it highlighted the need to prevent its decline and the need for therapeutic adjustments. It was a randomized clinical trial involving 250 patients with non-metastatic breast cancer who received preoperative systemic treatment at 26 institutions in the Netherlands between 2010 and 2012, as well as a group of patients that included courses of systemic therapy and zoledronic acid. According to the study protocol, patients of the second group received vitamin D in the amount of 400 IU and calcium in a dosage of 500 mg. The initial level of vitamin D was obtained in 169 patients, and the level after completion of systemic therapy courses in 91 patients. Median baseline and final vitamin D levels were 58.0 nmol/L (±27.5) and 51.0 nmol/L (±28.4), respectively. In patients receiving systemic therapy alone, the median decrease in VD levels was 16 nmol/L ($p = 0.003$). No statistically significant reduction in VD levels was found in women receiving vitamin D and calcium supplementation. When conducting a multivariate analysis, there was no statistically significant effect of initial vitamin D on the frequency of pathologically complete regressions ($p = 0.92$, OR 1.00, 95% CI 0.97–1.03) or partial regressions of tumors ($p = 0.66$, OR 1.00, 95% (CI 0.97–1.02) (28).

Chartron E et al. reported the results of a bicentric phase II trial of high-dose vitamin D in patients with early breast cancer. The study included 44 patients undergoing adjuvant chemotherapy. To improve the blood levels of VD, patients received 100,000 IU VD orally every 3 weeks from day 1 of cycle 1 to day 1 of cycle 5. The number of patients achieving normalization of serum vitamin D levels on day 1 of cycle 6 (D1C6) was considered the primary endpoint. In turn, secondary endpoints determined safety, vitamin D and calcium levels at baseline and during chemotherapy. At D1C6, 21 patients achieved normalization of VD (47.7%, 95% CI: 33.0-62.8). After statistical analysis, the authors showed that high doses of VD increase the time to normalization of serum VD on D1C6. This result was achieved in 47% of patients. No clinical toxicity associated with VD has been reported. Asymptomatic grade 1 hypercalciuria was observed in 13 patients (29.5%). This led to the discontinuation of high doses of oral VD in 10 and was accompanied by a decrease in the concentration of VD in the blood serum. After data analysis, no initial clinical factor predicted VD normalization (29).

Bošković L. et al. emphasized the importance of vitamin D as a preventive factor for osteoporosis and the loss of bone density associated with aromatase inhibitors. This prospective study included 438 women with early breast cancer who received adjuvant endocrine therapy with nonsteroidal aromatase inhibitors (88.4% treated with anastrozole and 11.6% patients treated with letrozole). The median duration of endocrine therapy before inclusion in the study was 10.5 months. Densitometry was performed in 180 (41.1%) patients. Of the total cohort, 329 patients received vitamin D with or without calcium, and 54 patients received bisphosphonates. According to densitometry, osteoporosis was diagnosed in 24 patients (5.5%). It was also noted that patients who took vitamin D with calcium had a higher percentage of complaints about the skeletal system, compared to patients who did not take it (24.76% vs. 16.26%). This study highlights the importance of skeletal monitoring in breast cancer patients, especially during systemic treatment (30).

A study by Arul Vijaya Vani S. et al. (2016) showed the importance of vitamin D supplementation during endocrine therapy. This was a prospective study of 82 women taking letrozole for more than 2 months. All participants had baseline vitamin D levels measured. The deficient group (vitamin D level less than 10 ng/mL) received 4000 IU vitamin D3 and 1000 mg calcium per day for 6 weeks; the deficiency group (vitamin D 25 serum concentration ranged from 10 to 30 ng/ml) received 2000 IU vitamin D3 and 1000 mg calcium per day for 12 weeks; the sufficient group (serum 25(OH) vitamin D concentration greater than 30 ng/mL) was not observed without any supplementation for 12 weeks. After statistical analysis, a statistically significant difference was found in the duration of endocrine therapy, levels of calcium, parathyroid hormone, and alkaline phosphatase between the subgroups. Taking vitamin D3 and calcium has been found to increase calcium and phosphorus levels. The Health Assessment Questionnaire found that low serum concentrations of 25-hydroxy vitamin D were associated with more musculoskeletal symptoms. In conclusion, the authors recommend taking vitamin D3 and calcium at the concentrations described in the respective groups for patients receiving letrozole, as this may allow the correction of vitamin D levels and the improvement of letrozole-induced symptoms (31).

The results of the above studies are systematized in Table 2.

Table 2. Results of clinical studies examining vitamin D importance during systemic anticancer treatment.

Research group	Study group	Study design	Investigation	Outcomes
Charehbili A. et al. (2015) (28)	250 patients with non-metastatic breast cancer receiving preoperative systemic treatment	Randomized clinical tria	Measuring the initial level of vitamin D	No statistically significant effect of the initial vitamin D on the frequency of pathologically complete or partial regressions of tumors
Chartron E et al. (2021) (29)	44 patients receiving adjuvant chemotherapy	Bicentric phase II trial	Patients received 100,000 IU VD orally every 3 weeks from day 1 of cycle 1 to day 1 of cycle 5	High doses of VD increase the time to normalization of serum VD 47% of patients achieved normal blood level of VD on day1 of cycle 6
Bošković L. et al. (2017) (30)	438 patients with early breast cancer patients receiving adjuvant endocrine therapy (nonsteroidal aromatase inhibitors)	Prospective study	329 patients received vitamin D with or without calcium; 54 patients received bisphosphonates	Highlights the importance of skeletal monitoring in breast cancer patients during systemic treatment
Arul Vijaya Vani S. et al. (2016) (31)	82 women receiving adjuvant endocrine therapy for more than 2 months	Prospective study	Measuring the initial level of vitamin D: the deficient group received 4000 IU vitamin D3 and 1000 mg calcium per day for 6 weeks; the deficiency group received 2000 IU vitamin D3 and 1000 mg calcium per day for 12 weeks; the sufficient group was not observed without any supplementation for 12 weeks	The authors recommend taking vitamin D3 and calcium at the concentrations described in the respective groups for patients receiving letrozole

CONCLUSION

The results of these studies increase scientific interest in the potential prognostic and predictive role of vitamin D in the carcinogenesis, progression and treatment outcome of breast cancer. Although in vitro and in vivo studies suggest the potential anticarcinogenic effects of calcitriol in breast cancer, human studies may not always be conclusive as the vitamin D status, its pathophysiological pathways, and resulting prognostic/therapeutic positions are influenced by numerous factors that are not consistently implemented in clinical studies.

The regular monitoring of serum vitamin D levels is a crucial marker of skeletal health. While the use of vitamin D in chemotherapy is a subject of active research, its role in adjuvant endocrine therapy is well-established. Preventing vitamin D deficiency is of paramount importance, as there is statistically reliable evidence that vitamin D and calcium can alleviate symptoms induced by aromatase inhibitors. It is essential to measure vitamin D levels both at the beginning and during treatment to mitigate the risk of bone loss and fractures associated with the effects of calcitriol.

This analytical review of the literature, which included studies of various designs and samples, attempted to systematize the results obtained in recent years on the use of vitamin D in the treatment of breast cancer and assess the possibilities of implementing them in clinical practice.

REFERENCES

1. Feldman D, Krishnan AV, Swami S, Giovannucci E, Feldman BJ. The role of vitamin D in reducing cancer risk and progression. Nat Rev Cancer. 2014 May 14;(5):342-57. doi: 10.1038/nrc3691.
2. Bikle DD. Vitamin D metabolism, mechanism of action, and clinical applications. Chem Biol. 2014 Mar 20;21(3):319-29. doi: 10.1016/j.chembiol.2013.12.016.
3. Welsh J. Vitamin D and breast cancer: insights from animal models. Am J Clin Nutr. 2004; 80:1721S–1724S.
4. Haq A, Sofi N. Vitamin D and breast cancer: Indian perspective. Clin Nutr Exp. 2017;12:1–10.
5. Thabet RH, Gomaa AA, Matalqah LM, Shalaby EM. Vitamin D: an essential adjuvant therapeutic agent in breast cancer. J Int Med Res. 2022 Jul;50(7):3000605221113800. doi: 10.1177/03000605221113800.
6. Benarba B, Gouri A. Role of vitamin D in breast cancer prevention and therapy: recent findings. J Medicine. 2019;21;46–50.
7. Ismail A, El-Awady R, Mohamed G, Hussein M, Ramadan SS. Prognostic Significance of Serum Vitamin D Levels in Egyptian Females with Breast Cancer. Asian Pac J Cancer Prev. 2018 Feb 26;19(2):571-576. doi: 10.22034/APJCP.2018.19.2.571.
8. Flores O, Wang Z, Knudsen KE, Burnstein KL. Nuclear targeting of cyclin-dependent kinase 2 reveals essential roles of cyclin-dependent kinase 2 localization and cyclin E in vitamin D-mediated growth inhibition. Endocrinology. 2010;151:896–908.
9. Boyle BJ, Zhao XY, Cohen P, Feldman D. Insulin-like growth factor binding protein-3 mediates 1α, 25-dihydroxyvitamin d3 growth inhibition in the LNCaP prostate cancer cell line through p21/WAF1. J Urol. 2001;165:1319–1324.
10. Gonzalez-Sancho JM, Alvarez-Dolado M, Munoz A. 1,25-Dihydroxyvitamin D3 inhibits tenascin-C expression in mammary epithelial cells. FEBS Lett. 1998;426:225–228.
11. Fukuda R, Kelly B, Semenza GL. Vascular endothelial growth factor gene expression in colon cancer cells exposed to prostaglandin E2 is mediated by hypoxia-inducible factor 1. Cancer Res. 2003;63:2330–2334.
12. Krishnan AV, Swami S, Feldman D. Vitamin D, and breast cancer: inhibition of estrogen synthesis and signaling. J Steroid Biochem Mol Biol. 2010;121:343–348.
13. Negri M, Gentile A, de Angelis C, Montò T, Patalano R, Colao A, Pivonello R, et al C. Vitamin D-Induced Molecular Mechanisms to Potentiate Cancer Therapy and to Reverse Drug-Resistance in Cancer. Cells. Nutrients. 2020;12(6):1798. doi: 10.3390/nu12061798.
14. Rainville C, Khan Y, Tisman G. Triple negative breast cancer patients presenting with low serum vitamin D levels: a case series. Cases J. 2009;2:8390.
15. de Sousa Almeida-Filho B, De Luca Vespoli H, Pessoa EC, Machado M, Nahas-Neto J, Nahas EAP. Vitamin D deficiency is associated with poor breast cancer prognostic features in postmenopausal women. J Steroid Biochem Mol Biol. 2017 Nov;174:284-289.
16. Thakkar A, Wang B, Picon-Ruiz M, et al. Vitamin D and androgen receptor-targeted therapy for triple-negative breast cancer. Breast Cancer Res Treat. 2016;157:77–90.
17. Chiang KC, Yeh TS, Chen SC, et al. The vitamin D analog, MART-10, attenuates triple negative breast cancer cells metastatic potential. Int J Mol Sci. 2016;17:606.
18. LaPorta E, Welsh J. Modeling vitamin D actions in triple negative/basal-like breast cancer. J Steroid Biochem Mol Biol. 2014;144 Pt A:65–73.
19. Santos-Martínez, N, Díaz, L, Ordaz-Rosado D, et al. Calcitriol restores antiestrogen responsiveness in estrogen receptor negative breast cancer cells: A potential new therapeutic approach. BMC Cancer. 2014;14:230. doi: 10.1186/1471-2407-14-230.
20. Blasiak J, Pawlowska E, Chojnacki J, Szczepanska J, Fila M, Chojnacki C. Vitamin D in Triple-Negative and BRCA1-Deficient Breast Cancer-Implications for Pathogenesis and Therapy. Int J Mol Sci. 2020 May 23;21(10):3670. doi: 10.3390/ijms21103670.
21. Swami S, Krishnan AV, Wang JY, Jensen K, Peng L, Albertelli MA, Feldman D. Inhibitory effects of calcitriol on the growth of MCF-7 breast cancer xenografts in nude mice: selective modulation of aromatase expression in vivo. Horm Cancer. 2011 Jun;2(3):190-202. doi: 10.1007/s12672-011-0073-7.
22. Filip-Psurska B, Psurski M, Anisiewicz A, Libako P, Zbrojewicz E, Maciejewska M, et al. Vitamin D Compounds PRI-2191 and PRI-2205 Enhance Anastrozole Activity in Human Breast Cancer Models. Int J Mol Sci. 2021 Mar 9;22(5):2781. doi: 10.3390/ijms22052781.
23. Yetkin D, Balli E, Ayaz F. Antiproliferative activity of Tamoxifen, Vitamin D3 and their concomitant treatment. EXCLI J. 2021 Sep 21;20:1394-1406. doi: 10.17179/excli2021-3989.
24. Segovia-Mendoza M, Díaz L, González-González ME, Martínez-Reza I, García-Quiroz J, Prado-Garcia H, et al. Calcitriol and its analogues enhance the antiproliferative activity of gefitinib in breast cancer cells. J Steroid Biochem Mol Biol. 2015 Apr;148:122-31. doi: 10.1016/j.jsbmb.2014.12.006.
25. Segovia-Mendoza M, Díaz L, Prado-Garcia H, Reginato MJ, Larrea F, García-Becerra R. The addition of calcitriol or its synthetic analog EB1089 to lapatinib and neratinib treatment inhibits cell growth and promotes apoptosis in breast cancer cells. Am J Cancer Res. 2017 Jul 1;7(7):1486-1500.
26. Achounna AS, Ordaz-Rosado D, García-Quiroz J, Morales-Guadarrama G, Milo-Rocha E, Larrea F, et al. EB1089 Increases the Antiproliferative Response of Lapatinib in Combination with Antiestrogens in HER2-Positive Breast Cancer Cells. Int J Mol Sci. 2024 Mar 9; 25(6):3165. doi: 10.3390/ijms25063165.
27. Attia YM, El-Kersh DM, Ammar RA, Adel A, Khalil A, Walid H, et al. Inhibition of aldehyde dehydrogenase-1 and p-glycoprotein-mediated multidrug resistance by curcumin and vitamin D3 increases sensitivity to paclitaxel in breast cancer. Chem Biol Interact. 2020 Jan 5;315:108865. doi: 10.1016/j.cbi.2019.108865.
28. Charehbili A, Hamdy NA, Smit VT, Kessels L, van Bochove A, van Laarhoven HW, et al. Dutch Breast Cancer Research Group (BOOG). Vitamin D (25-0H D3) status and pathological response to neoadjuvant chemotherapy in stage II/III breast cancer: Data from the NEOZOTAC trial (BOOG 10-01). Breast. 2016 Feb;25:69-74. doi: 10.1016/j.breast.2015.10.005.
29. Chartron E, Firmin N, Touraine C, Chapelle A, Legouffe E, Rifai L, et al. A Phase II Multicenter Trial on High-Dose Vitamin D Supplementation for the Correction of Vitamin D Insufficiency in Patients with Breast Cancer Receiving Adjuvant Chemotherapy. Nutrients. 2021 Dec 10;13(12):4429. doi: 10.3390/nu13124429.
30. Bošković L, Gašparić M, Petković M, Gugić D, Lovasić IB, Soldić Ž, et al. Bone health and adherence to vitamin D and calcium therapy in early breast cancer patients on endocrine therapy with aromatase inhibitors. Breast. 2017 Feb;31:16-19. doi: 10.1016/j.breast.2016.10.018.
31. Arul Vijaya Vani S, Ananthanarayanan PH, Kadambari D, Harichandrakumar KT, Niranjjan R, Nandeesha H. Effects of vitamin D and calcium supplementation on side effects profile in patients of breast cancer treated with letrozole. Clin Chim Acta. 2016 Aug 1; 459:53-56. doi: 10.1016/j.cca.2016.05.020.