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# [Case Study] Targeting the Warburg Effect with the Glucose Mutation Theory: A Case Study of a 35-Year-Old Female Treated for Stage II Triple-Positive Metastatic Breast Cancer Involving Lymph Nodes Using Glucosodiene Over a 20-Day Period.

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**Funding:** No specific funding was received for this work.

**Potential competing interests:** No potential competing interests to declare.

## Abstract

Triple-positive breast cancer, characterized by the overexpression of estrogen receptors (ER+), progesterone receptors (PR+), and human epidermal growth factor receptor 2 (HER2+), poses a formidable challenge in oncology. This subtype, known for its aggressive nature and metastatic potential, requires a comprehensive therapeutic strategy. Current approaches, predominantly involving targeted therapies, face challenges, necessitating the exploration of alternative interventions. The emergence of Glucosodiene, rooted in Maher Akl's theory on glucose mutation, introduces a promising avenue for treatment. This innovative drug demonstrates efficacy in targeting the Warburg effect prevalent in tumors dependent on anaerobic glucose metabolism. A case study involving a 35-year-old woman with stage II triple-positive breast cancer showcases Glucosodiene's impact, revealing a complete absence of active lesions post-treatment. The results indicate its potential as a primary or secondary therapy, complementing traditional treatment protocols. Glucosodiene's mechanism of action positions it as a versatile and impactful option in the realm of

cancer therapeutics, offering hope in the pursuit of improved patient outcomes. **The trial is registered under [clinicaltrials.gov](https://clinicaltrials.gov) number NCT05957939.**

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**Keywords:** Triple- positive breast cancer, Lymph nodes metastasis, HER2-positive breast cancer, Glucose Mutation Theory, Glucosodiene.

## 1. Background

Triple-positive breast cancer, characterized by the overexpression of estrogen receptors (ER+), progesterone receptors (PR+), and human epidermal growth factor receptor 2 (HER2+), represents a formidable challenge in oncology. The positive HER2 status in this subtype accentuates the aggressive nature of the disease, elevating its potential for rapid progression and metastasis. The amplification of HER2, a proto-oncogene, intensifies the signal transduction pathways, fostering uncontrolled cell growth and proliferation. One pivotal aspect of concern is the propensity of triple-positive breast cancer to invade the lymph nodes, significantly amplifying the risk of distant metastasis. The intricate interplay between HER2 overexpression and lymph node involvement underscores the intricate pathophysiology of this malignancy, necessitating comprehensive diagnostic and therapeutic strategies.<sup>[1][2][3]</sup> Addressing the therapeutic landscape, current modalities predominantly focus on targeted therapies, such as anti-HER2 agents like trastuzumab and pertuzumab. These drugs aim to impede HER2-mediated signaling cascades, hindering tumor progression. Despite the remarkable advancements, challenges persist, with treatment limitations and the emergence of resistance posing formidable

hurdles.<sup>[4]</sup> The complexity of triple-positive breast cancer demands a multifaceted approach, integrating chemotherapy, endocrine therapy for ER and PR components, and HER2-targeted agents.<sup>[5]</sup>

Moreover, the limitations of existing treatments become evident in the face of resistance mechanisms, necessitating ongoing research into novel therapeutic avenues. The quest for more effective interventions against triple-positive breast cancer remains an imperative in the relentless pursuit of improving patient outcomes and mitigating the morbidity associated with this intricate malignancy.<sup>[6]</sup> Maher Akl's theory on glucose mutation has laid the foundation for the development of Glucosodiene, offering a ray of hope amidst the formidable challenges. This innovative drug exhibits great promise in targeting the Warburg effect prevalent in tumors dependent on anaerobic glucose metabolism.<sup>[7]</sup> Notably, positive outcomes have been documented, exemplified by a case study involving a patient with metastatic triple-negative breast cancer affecting the bones. Within a concise 15-day treatment period, Glucosodiene demonstrated remarkable efficacy, leading to significant improvements.<sup>[8]</sup>

Given the positive clinical observations in the context of metastatic triple-negative breast cancer in bones, Glucosodiene's impact prompts exploration into its effects on various breast cancer subtypes. In this study, the effectiveness of Glucosodiene is meticulously documented in the case of a 35-year-old woman battling stage II triple-positive breast cancer with lymph node involvement. Despite undergoing chemotherapy with a combination of Carboplatin and Taxol, the results revealed a complete absence of active lesions in the body. The affirmative response observed in this triple-positive breast cancer case, during a comparable timeframe to the previous case of TNBC, underscores Glucosodiene's potential to target all recognized breast cancer receptors effectively. This promising compound could serve as a primary, secondary, complementary, or salvage therapy, particularly in cases where traditional treatments falter. Its mechanism of action, targeting the Warburg effect within the tumor, positions Glucosodiene as a versatile and impactful option in the realm of cancer therapeutics.<sup>[9]</sup>

## 2. Patient information

The patient, a 35-year-old woman of mixed Caucasian and Arab descent, has been diagnosed with an intricate case of stage II triple-positive breast cancer. The malignancy exhibits lymph node metastasis, underscoring its advanced nature. This case signifies a complex manifestation of triple-positive breast cancer in a relatively young patient, emphasizing the advanced stage and aggressive nature of the malignancy.

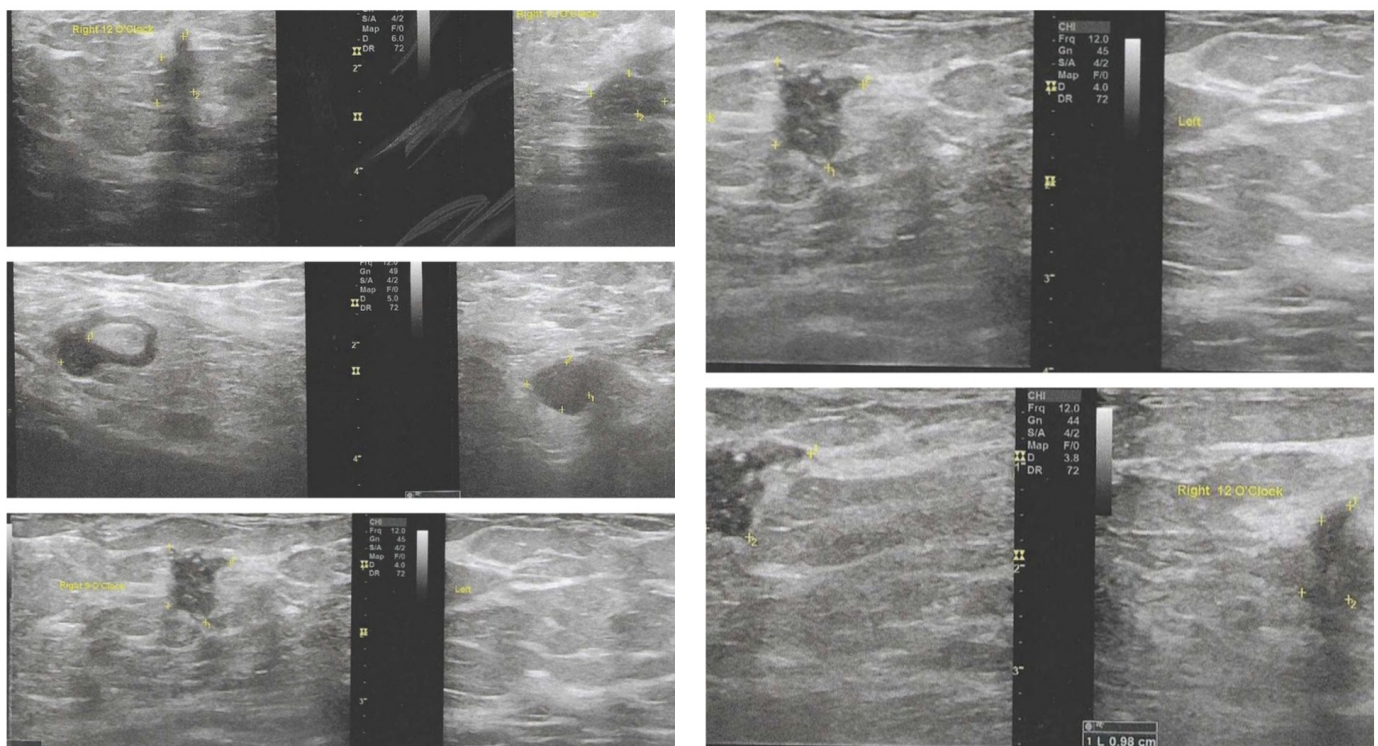
### 2.1. *Clinical findings timeline*

In the intricate case of a 35-year-old woman devoid of prior oncological history, the clinical findings unfold a compelling narrative. During her routine monthly breast self-examination, a palpable mass of significant proportions was detected in the right axillary region. This sizable lump was accompanied by an electric-like pricking sensation localized to the lymph node areas, introducing a distinctive neuropathic element to the clinical presentation. Concurrently, observable changes in breast morphology manifested, including breast sagging, constriction of the areolar halo, and atrophy at the forefront of

the nipple.

**On November 12, 2023**, initiating a meticulous evaluation through Bilateral Digital Soft Tissue Mammography and High-Resolution Breast Sonography. The findings reveal scattered glandular condensations with an ACR density classification of B, accompanied by multiple clusters of suspicious microcalcifications. Calcified spiculated lesions in the right Upper Outer Quadrant (UOQ) were detected, measuring 13x11mm at 9 o'clock, and an ill-defined 12x9mm lesion at 12 o'clock. The left breast exhibits normal findings (BIRADS 1), while the right side indicates suspicious lesions (BIRADS 4C), warranting additional investigations through dynamic contrast MRI and US-guided core needle tissue sampling with subsequent histopathology.

BIRADS classification delineates risk levels, with 0% risk for BIRADS 1 and 2, 2% for BIRADS 3, and 50% for BIRADS 4. The left breast falls into BIRADS 1, signifying a normal study, while the right side is categorized as BIRADS 4C, implying probable malignancy and necessitating further investigations. The characteristics of the lesions and lymph nodes suggest potential infiltration. Left axillary lymph nodes exhibit non-specific features. [Figure 1]



**Figure 1.** In-depth assessment commenced with Bilateral Digital Soft Tissue Mammography and High-Resolution Breast Sonography, meticulously revealing diffuse glandular condensations typified by an ACR density classification of B. Concurrently, numerous clusters of suspicious microcalcifications manifested, with calcified spiculated lesions in the right Upper Outer Quadrant (UOQ) measuring 13x11mm at 9 o'clock and an ill-defined 12x9mm lesion at 12 o'clock. The left breast presents unremarkable findings (BIRADS 1), contrasting with the right side denoted by suspicious lesions (BIRADS 4C). The BIRADS classification system stratifies risk, associating 0% risk with BIRADS 1 and 2, 2% with BIRADS 3, and 50% with BIRADS 4. The left breast aligns with BIRADS 1, indicative of a normative study, while the right side merits a classification of BIRADS 4C, suggesting potential malignancy and necessitating additional scrutiny. Notably, the lesion characteristics, coupled with lymph node observations, intimate possible infiltration. The left axillary lymph nodes exhibit non-specific features.

**On November 27, 2023**, a High Field Dynamic MRI of Both Breasts was conducted, employing various techniques such as axial T2 (plate 1), axial STIR (plate 2), sagittal post-contrast 3D TFE of the right breast (plate 3), sagittal post-contrast 3D TFE of the left breast (plate 4), dynamic multiphase post-contrast study done in 8 minutes with MIP reconstruction (plate 5), and time intensity curves (plate 6).

The findings indicate bilateral glandular condensation with homogeneous glandular enhancement.

In the right breast Upper Outer Quadrant (UOQ), a partially ill-defined non-mass lesion measuring about 2x1.5 cm is observed.

The lesion exhibits low signal in T2 and STIR, and the kinetic data suggests a suspicious pattern with rapid rise followed by a plateau (Type 2 curves). Two small suspicious enhancing nodules are detected in the UOQ midline, located at the 12:00 position peripheral and midzonal, measuring 8x7 mm and 12x10 mm in diameter.

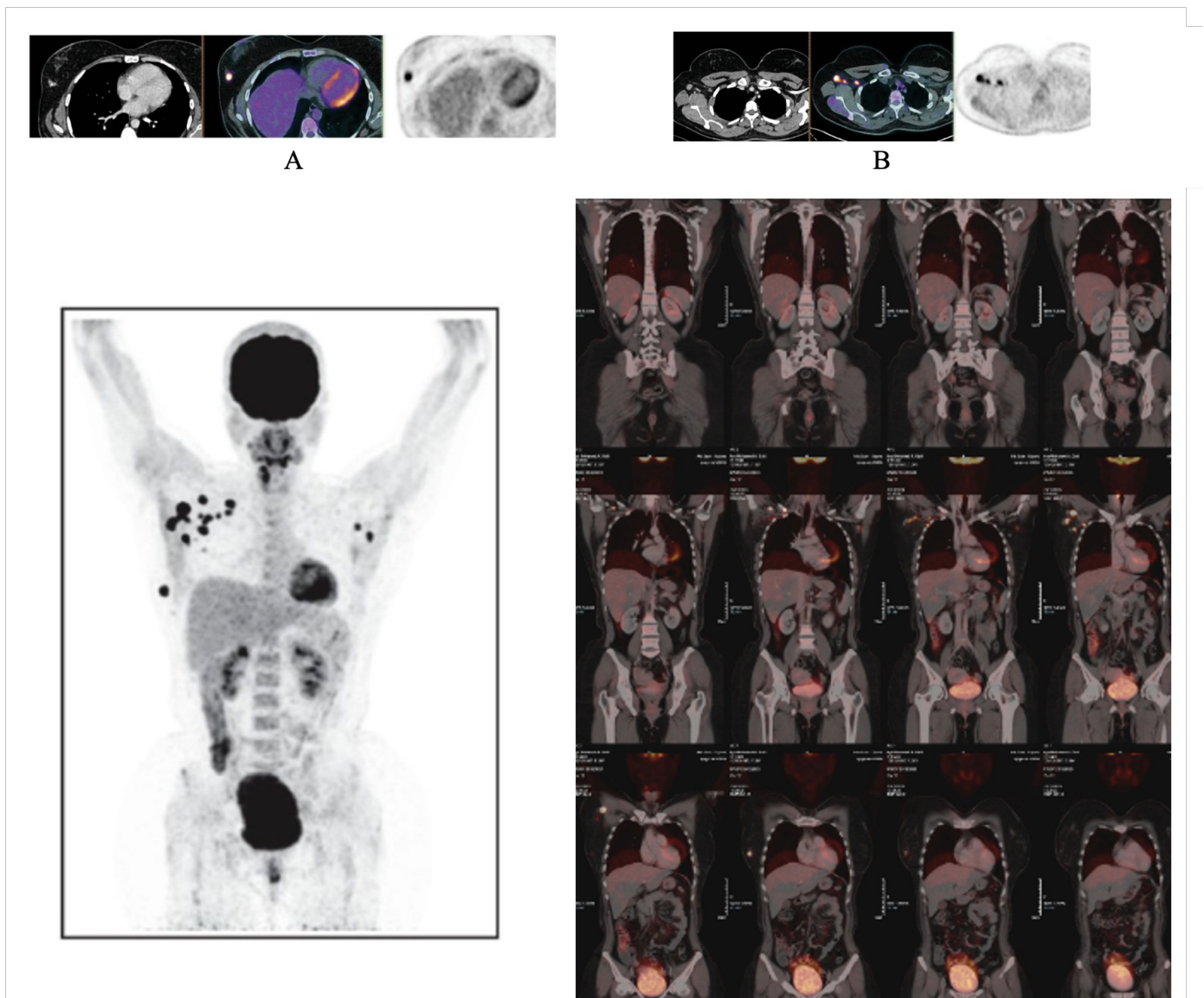
These lesions also display low signal in T2 and STIR with suspicious kinetics (Type 2 plateau curves). Associated mild diffuse skin thickening and edema are noted. Pathologically enlarged right axillary lymph nodes are observed, showing a globular appearance, with the largest measuring 2.5 cm in diameter. No masses or architectural distortion is found in the left breast, and the skin thickness and contour are normal. Multiple likely non-specific left axillary lymphadenopathy is identified. The right breast UOQ exhibits highly suspicious multifocal lesions with skin changes and ipsilateral lymphadenopathy, categorized as BIRADS 5 based on morphological and kinetic data. A micro biopsy is recommended. Conversely, the left breast study is deemed normal, categorized as BIRADS 1.

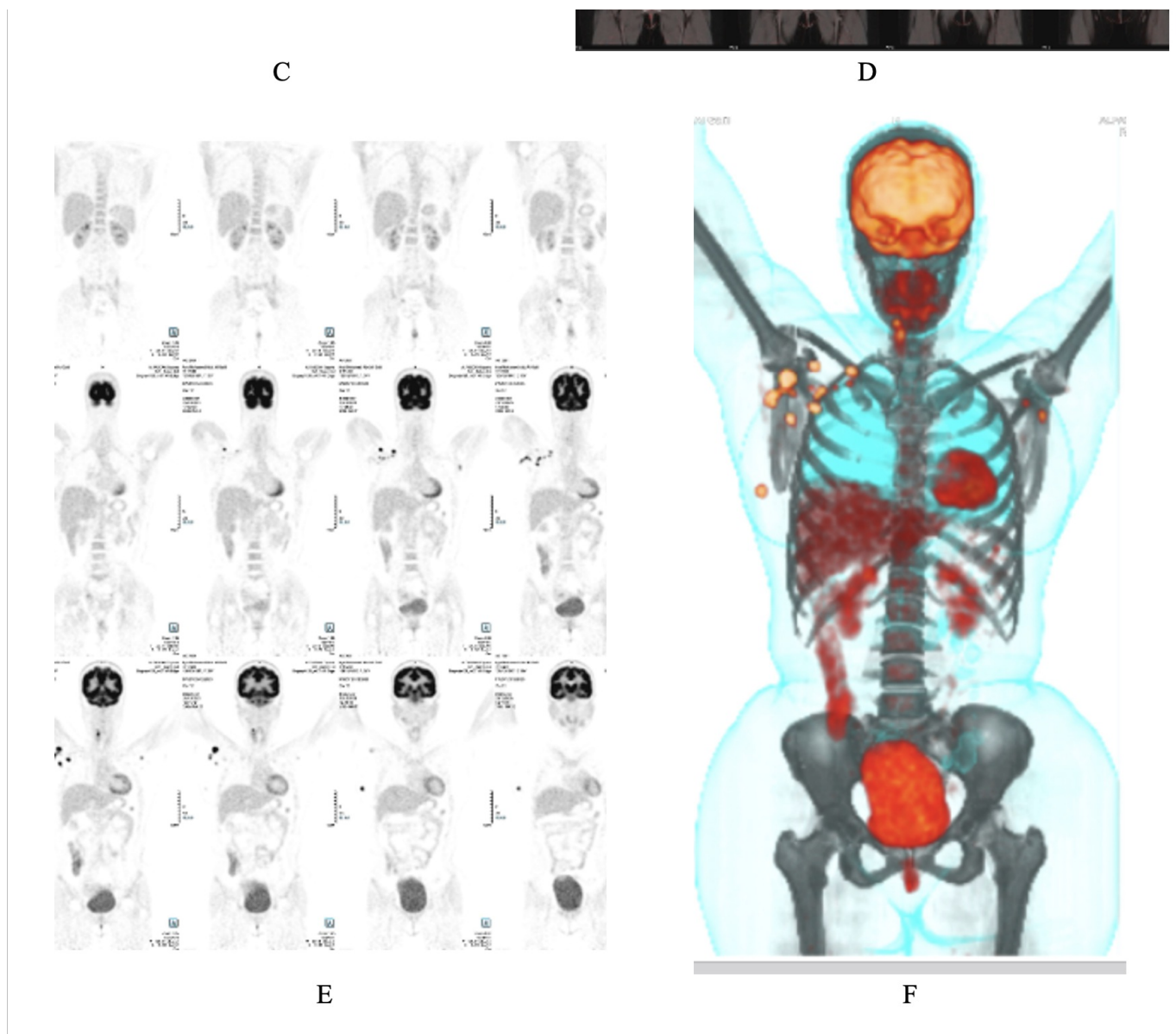
**On December 9, 2023**, a comprehensive evaluation encompassing micro biopsy and immunohistochemical analyses was conducted, shedding light on the intricate details of the diagnostic process. Four specimens were meticulously assessed, originating from two masses situated at 12 o'clock and 9 o'clock in the right breast. Each mass provided multiple grayish-white tissue cores, measuring 0.8 cm. The ensemble included four unstained films and a syringe containing hemorrhagic material (0.2x0.2 cm). Under microscopic scrutiny, distinct characteristics emerged in the two specimens. Specimen (1) manifested irregular groups of malignant ductal cells, displaying moderate nuclear pleomorphism, hyperchromasia, attempts at tubular formation, scattered mitotic figures, moderate desmoplasia, peritumoral lymphocytic infiltrate (5%), focal necrosis, and an intraductal component (5%) with a comedo pattern. In contrast, specimen (2) exhibited infiltrated breast tissue with irregular groups of malignant ductal cells, moderate nuclear pleomorphism, hyperchromasia, poor attempts at tubular formation, predominantly arranged strands and cords, scattered mitotic figures, and moderate desmoplasia, devoid of necrosis or intraductal components. Cytological examination of films and cell block brought to the forefront red blood cells and hyperchromatic cells within eosinophilic proteinaceous material. The cell block revealed malignant epithelial cells with moderate nuclear anaplasia surrounded by mature lymphocytes. Immunohistochemistry analysis underscored positive staining for estrogen receptors (35% and 15% in Block 1 and Block 2, respectively), progesterone receptors (45% and 15% in Block 1 and Block 2, respectively), Her2 positivity with a score of 3+, and Ki67 proliferation indices of 30% and 20% in Block 1 and Block 2, respectively.

**On December 23, 2023**, a F-FDG PET/CT examination was conducted for a female patient with a history of pathologically

confirmed infiltrating duct carcinoma grade IIa in the right breast. The examination protocol encompassed a whole-body PET/CT study and a diagnostic multislice CT examination. PET/CT findings: Within the right breast, an FDG-avid enhancing nodular lesion in the LOQ exhibited an SUVmax of 14.4 with associated calcification. Additional smaller nodular lesions and soft tissue thickening in the UOQ showed an SUVmax of 3.0 over a 1.2 cm nodule, with no evidence of skin or chest wall invasion.

FDG-avid lymph nodes were identified in the right axillary levels 1, II, and III, with an SUVmax of 25.3. An infraclavicular lymph node displayed an SUVmax of 15.9. Left axillary levels I and II lymph nodes exhibited an SUVmax of 7.9. Increased FDG activity was noted in the cervical right level II lymph node. Pulmonary and bone assessments revealed no FDG-avid lesions. The liver displayed mild fatty changes with a likely cyst in segment V. No FDG-avid lesions were found in the left breast. The right thyroid exhibited an FDG-avid nodule with an SUVmax of 10.6. Brain imaging revealed no FDG-avid lesions. Low-grade FDG activity was identified in subcutaneous fat stranding in the chest, abdomen, pelvis, and back, requiring clinical correlation. Similarly, low-grade FDG activity related to the endometrium and adnexae was noted, likely functional. [Figure 2]





**Figure 2.** Conducting a comprehensive F-FDG PET/CT examination for a female with a confirmed history of grade IIa infiltrating duct carcinoma in the right breast yielded intricate findings. Noteworthy discoveries include an FDG-avid nodular lesion in the LOQ of the right breast, exhibiting a high SUVmax of 14.4, along with associated calcification. Additionally, smaller nodular lesions and soft tissue thickening in the UOQ displayed an SUVmax of 3.0 over a 1.2 cm nodule, with no signs of skin or chest wall invasion. The right axillary levels 1, II, and III contained FDG-avid lymph nodes with a significant SUVmax of 25.3, and an infraclavicular lymph node exhibited an SUVmax of 15.9. Conversely, left axillary levels I and II lymph nodes had a lower SUVmax of 7.9. Pulmonary and bone assessments revealed no FDG-avid lesions. The liver displayed mild fatty changes, along with a probable cyst in segment V, without FDG-avid lesions. The left breast showed no abnormal FDG uptake.

**On January 1, 2024**, a treatment protocol was established for the patient, encompassing traditional chemotherapy administered by oncologists. The regimen consisted of alternating sessions of carboplatin and taxol at reduced doses on a weekly basis, spanning four months. Subsequently, the patient will undergo a complete mastectomy, including the breast and axillary regions.

**On January 12, 2024**, she opted for Glucosodiene treatment due to the lack of perceived improvements, the tumor's increasing size, and a rapid deterioration in overall health, as evident in the image before Glucosodiene treatment. During

the initial preparation phase, 24 to 48 hours before Glucosodiene treatment, the patient strictly adhered to a specialized diet, eliminating all sources of glucose, sugars, and carbohydrates. The nutritional plan emphasized a balanced intake of animal and plant proteins, legumes, and various vegetables. Throughout the 20-day treatment period, fruits, sugars, and starchy foods were strictly avoided.

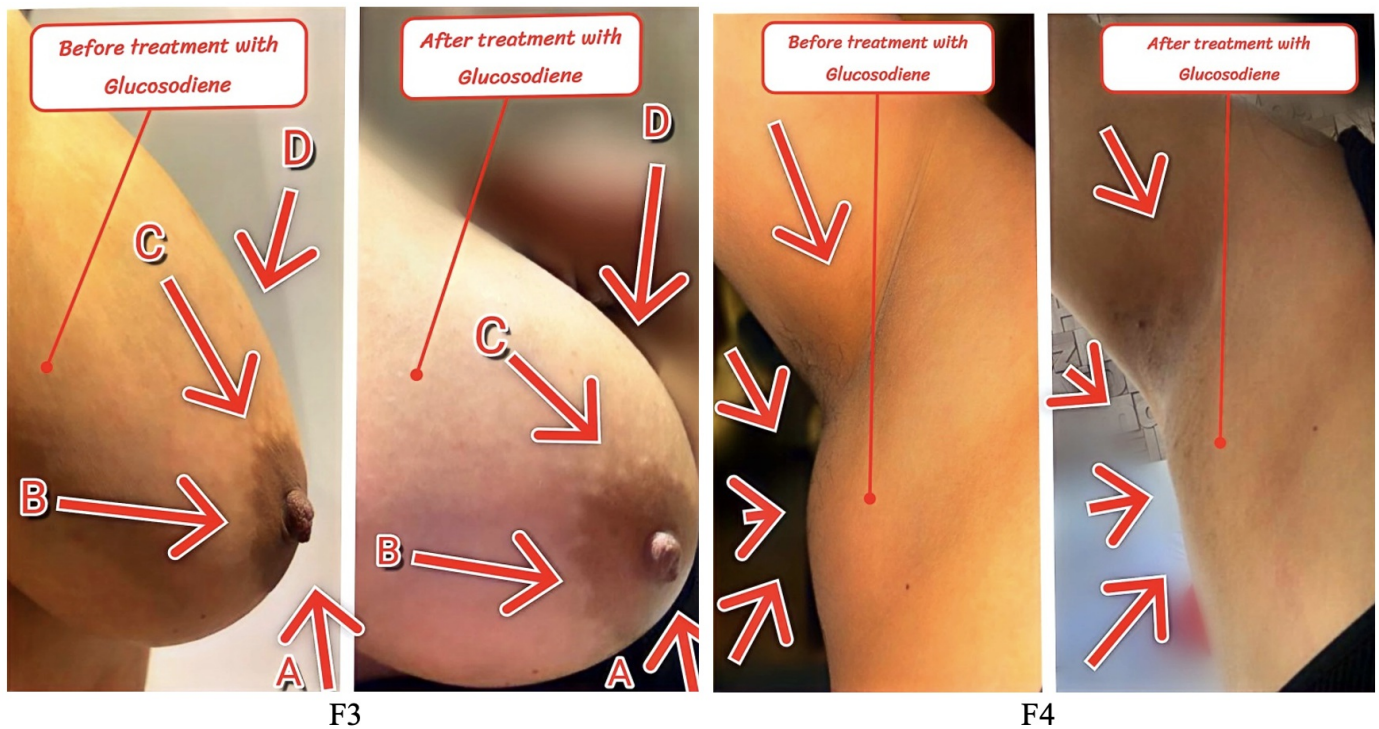
To ensure optimal digestion, a daily blend of yogurt and chia seeds was incorporated, promoting the activation of beneficial probiotics and facilitating smooth bowel movements. Chia seeds, a potent source of fiber, contributed to overall digestive well-being, and healthy fats were sourced from olive oil and assorted nuts, enhancing the nutritional composition of meals.

The patient followed the same Glucosodiene protocol reported and documented in the initial case, involving the administration of 100 ml of Glucosodiene orally once daily for a limited duration of 20 days. Importantly, the patient continued traditional chemotherapy during the Glucosodiene treatment, receiving alternating doses of carboplatin and paclitaxel weekly to maintain a comprehensive therapeutic approach. During the Glucosodiene treatment course, the patient received only one dose of carboplatin and one of taxol, both at reduced concentrations.

### 3. Results

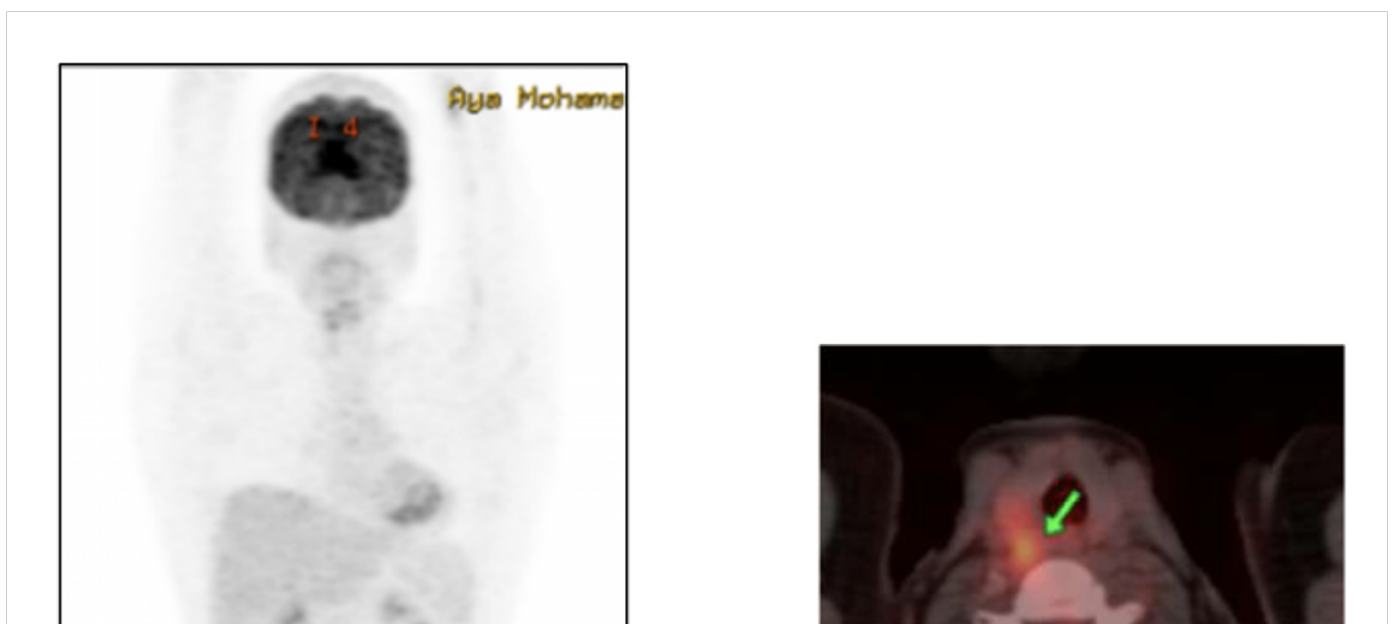
Following the administration of Glucosodiene orally at a daily dose of 100 ml for 20 consecutive days, notable changes were observed in the breast and axillary regions. Starting from the fifth day, vital indicators of breast and axillary appearance began to manifest. These indicators included the restoration of the breast to its natural form before and after Glucosodiene treatment, as illustrated in the figures <sup>[Figure 3, 4]</sup>. Upon the disappearance of the tumor and the restoration of breast vitality, a subsequent PET scan was conducted on February 3, 2024. The results indicated the following: No metabolically active cervical or supra-clavicular lymph nodes were noted in the head and neck region. The brain exhibited normal FDG bio-distribution with physiologic FDG uptake in the oropharynx, salivary glands, and larynx. An FDG-avid hypodense nodule in the right thyroid lobe was identified. In the chest, minimal diffuse skin thickening in the right breast was observed, along with scattered insignificantly avid ill-defined glandular tissue. No metabolically active lesions were found in the left breast. Bilateral non-FDG-avid axillary lymph nodes were noted. Moving to the abdomen and pelvis, no evidence of hepatic or splenic FDG-avid focal lesions was found. No metabolically active pelvi-abdominal lymph nodes or FDG-avid adrenal or peritoneal nodules were observed. Lastly, in the musculoskeletal system, no metabolically active sclerotic or lytic osseous deposits were found, and focal FDG avidity within the muscles of the left forearm, likely due to strain, was noted. In conclusion, the PET/CT study demonstrated positive outcomes, showcasing the effectiveness of Glucosodiene in inducing favorable changes in the breast and axillary regions, along with the absence of metabolically active lesions in various anatomical sites. The restoration of breast vitality and the absence of active lesions in follow-up imaging suggest a positive response to the treatment protocol. <sup>[Figure 5]</sup>

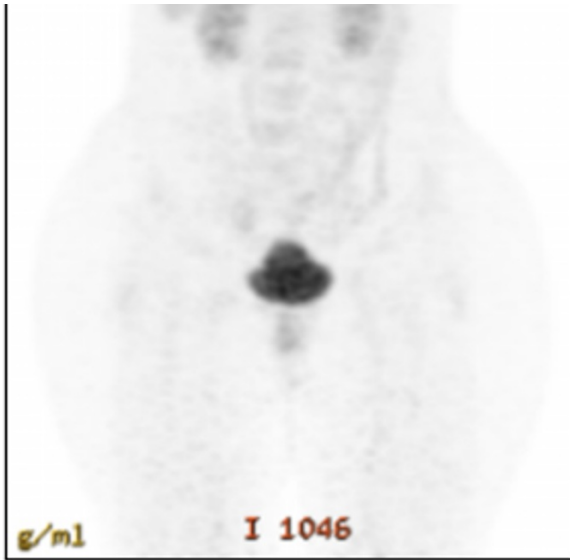




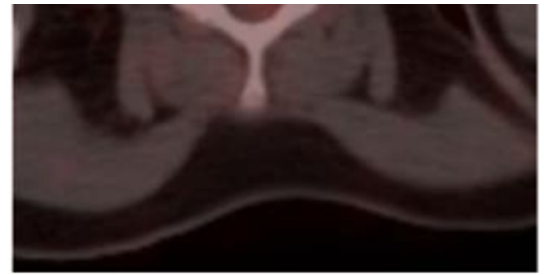
**Figure 3. (left)** The figure depicts notable differences before and after treatment according to the indicated letters. Symbol (A) denotes the retraction of the nipple before treatment, contrasting with its erect appearance after the intervention. Symbol (B) signifies the constriction followed by dilation of the areolar area, while symbol (C) illustrates the atrophy of the areola specifically in the upper part of the breast before and after treatment. Conversely, symbol (D) conveys the ptosis of the breast before and after treatment. Hence, all improvements can be summarized by the fact that the breast image before commencing direct Glucosodiene treatment closely resembled the general visual indicators of breast cancer, whereas post-treatment, the breast exhibits a markedly natural and vibrant appearance.

**Figure 4. (right)** The figure highlights the notable differences before and after treatment for a case of metastatic triple-positive breast cancer involving lymph node metastasis at stage two, as classified by pathological reports and PET scan imaging. The tumor and lymph node swelling were visibly prominent, and the tumor size could be discerned by the naked eye throughout the treatment phases. The initial reduction in tumor growth began on the fifth day and continued until complete tumor regression by the twentieth day, indicative of tumor lysis syndrome, demonstrating the effectiveness of Glucosodiene treatment.

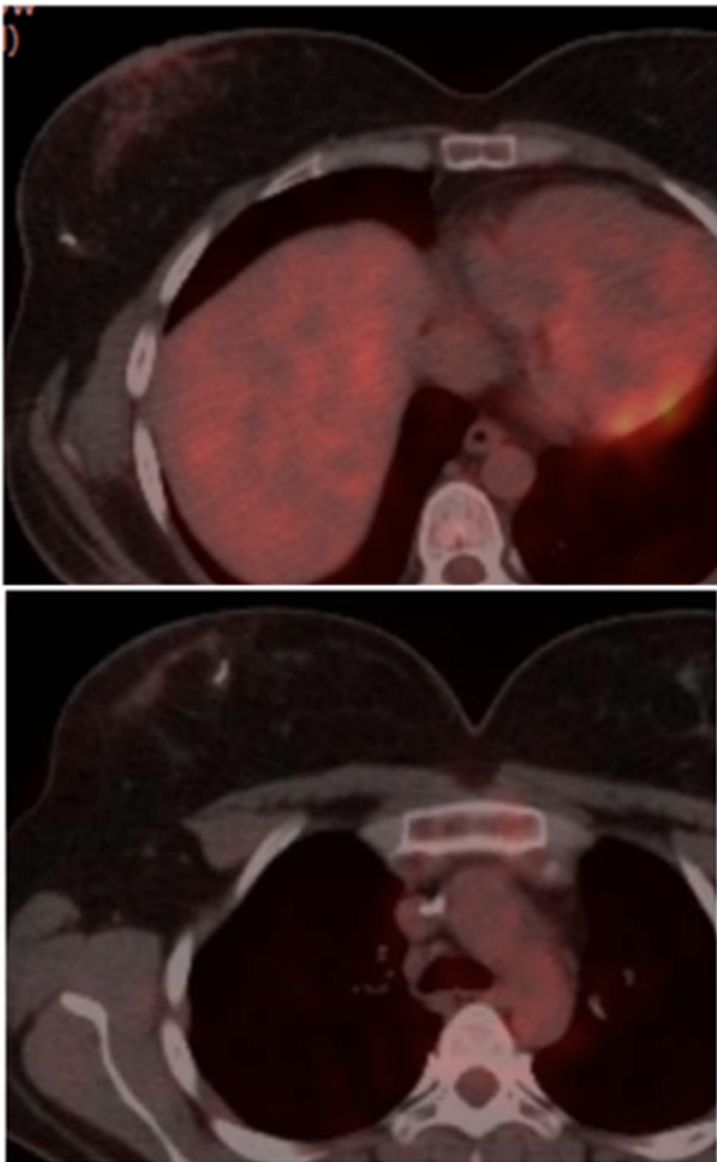




A



B



C

**Figure 5.** Following tumor disappearance and breast vitality restoration, a subsequent PET scan indicated positive outcomes. Notably, no metabolically active cervical or supra-clavicular lymph nodes were detected, and the brain exhibited normal FDG bio-distribution. An FDG-avid hypodense nodule was identified in the right thyroid lobe. In the chest, minimal diffuse skin thickening in the right breast and insignificantly avid ill-defined glandular tissue were observed. No metabolically active lesions were found in the left breast, and axillary lymph nodes were non-FDG avid bilaterally. Moving to the abdomen and pelvis, no hepatic or splenic FDG avid focal lesions were found. There was an absence of metabolically active pelvi-abdominal lymph nodes, as well as FDG avid adrenal or peritoneal nodules. In the musculoskeletal system, no metabolically active sclerotic or lytic osseous deposits were present. Focal FDG avidity within the muscles of the left forearm, likely due to strain, was noted. The PET/CT study demonstrated the effectiveness of Glucosodiene, with the absence of active lesions in follow-up imaging suggesting a positive response to the treatment protocol.

## 4. Discussion

The emergence of Glucosodiene in a case report, substantiated as an independent pharmaceutical agent, has been employed in the treatment of metastatic Triple-Negative Breast Cancer (TNBC) to the bones within a 15-day therapeutic cycle.

The confirmation from the PET scan examination, in this case, compared to previous assessments, unequivocally supports Glucosodiene's role as a primary therapeutic agent. It has demonstrated the remarkable ability to cause the complete disappearance of all active foci in the bones within the specified treatment period. In the specific case under discussion, exploring its impact on Triple-Positive Breast Cancer, Glucosodiene has functioned as a drug that coexists safely with the mentioned chemotherapies (modified Carboplatin and Taxol). It accompanied the Glucosodiene treatment cycle with a dose of Carboplatin and a dose of Taxol, affirming the safety profile of Glucosodiene in conjunction with traditional treatments. Its alkaline nature potentially enhances the effectiveness of chemotherapy, focusing on the Warburg effect and the metabolic activity of tumors. The findings underline that Glucosodiene, when administered safely with reduced doses of Carboplatin and Taxol, effectively causes the disappearance of active tumor sites in the bones. This positions Glucosodiene as a companion drug for targeting tumors reliant on the Warburg effect. The evidence suggests that it could serve as a primary or secondary treatment modality, complementing traditional treatment protocols. Glucosodiene's documented impact on halting tumor activity within an approximate 20-day duration strengthens its potential as an adjunctive pharmaceutical, integrating seamlessly with conventional treatment protocols.

## 5. Conclusion

This manuscript delves into the complexities of triple-positive breast cancer, emphasizing the challenges posed by overexpressed estrogen receptors (ER+), progesterone receptors (PR+), and human epidermal growth factor receptor 2 (HER2+). Current therapies, including targeted agents like trastuzumab and pertuzumab, show progress but face persistent obstacles. The introduction of Glucosodiene, rooted in Maher Akl's glucose mutation theory, presents a promising therapeutic avenue. The case study highlights Glucosodiene's efficacy against triple-positive breast cancer, showcasing positive outcomes within a 20-day treatment. Its impact on diverse breast cancer subtypes positions it as a

versatile option alongside traditional treatments. Glucosodiene, coexisting safely with chemotherapy, emerges as a companion drug enhancing treatment effectiveness.

The manuscript contributes valuable insights, emphasizing Glucosodiene's potential as a primary or secondary modality in targeting tumors relying on the Warburg effect. This research underscores the ongoing quest for more effective interventions against triple-positive breast cancer, offering a breakthrough in cancer therapeutics.

## Statements and Declarations

**Informed consent:** Before taking this case, information was given to the patient, and informed consent was obtained from the patient for follow-up and consent to share the investigations, figures, and any required data.

**Funding information:** The authors received no financial support for the research and publication of this article.

**Competing interest declaration:** The authors declare that there are no conflicts of interest.

**Ethical approval statement or statement of informed consent for case studies:** This case was conducted in accordance with the Declaration of Helsinki and meets the CARE guidelines. Informed consent was obtained from the patient for follow-up, including permission for publication of all photographs, lab, and images herein. **Trial registration details:** **NCT05957939**

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