

Case Report: Precision-Guided Integrative Oncology in a Patient with Stage IV Bilateral Breast Cancer with Bone Metastases and Prior Dual Hematological Malignancies

Introduction

The management of metastatic breast cancer in patients with a complex oncologic history requires a nuanced approach, integrating standard-of-care modalities with molecularly guided, low-toxicity, and immune-supportive strategies. This report presents the case of a woman in her 60s, who successfully underwent personalized, integrative cancer therapy for stage IV bilateral breast cancer, following prior treatment for **Hodgkin's disease** and **non-Hodgkin's lymphoma**.

Clinical Background

The patient had a history of:

- **Hodgkin's disease** in her 20s, treated with **chest and mediastinal radiation**
- **Non-Hodgkin's lymphoma** in her 40s, managed with **high-dose chemotherapy** followed by **autologous bone marrow transplant**

In early 2025, she presented with bilateral breast lesions. Core needle biopsy confirmed:

- **Right breast:** Infiltrating ductal carcinoma (ER++, PR++, HER2-negative)
- **Left breast:** One sample showed infiltrating lobular carcinoma, though other biopsies were inconclusive

PET-CT demonstrated multiple vertebral metastases, classifying the disease as **Stage IV**.

Treatment Challenges

1. Prior chest irradiation limited surgical options.
2. Post-BMT status contraindicated full-dose chemotherapy due to secondary hematologic malignancy risk.
3. Bilateral presentation with skeletal spread required a multimodal, low-toxicity, molecularly informed treatment strategy.

Molecular and Functional Profiling (RGCC Onconomics Plus, 20-Jan-2025)

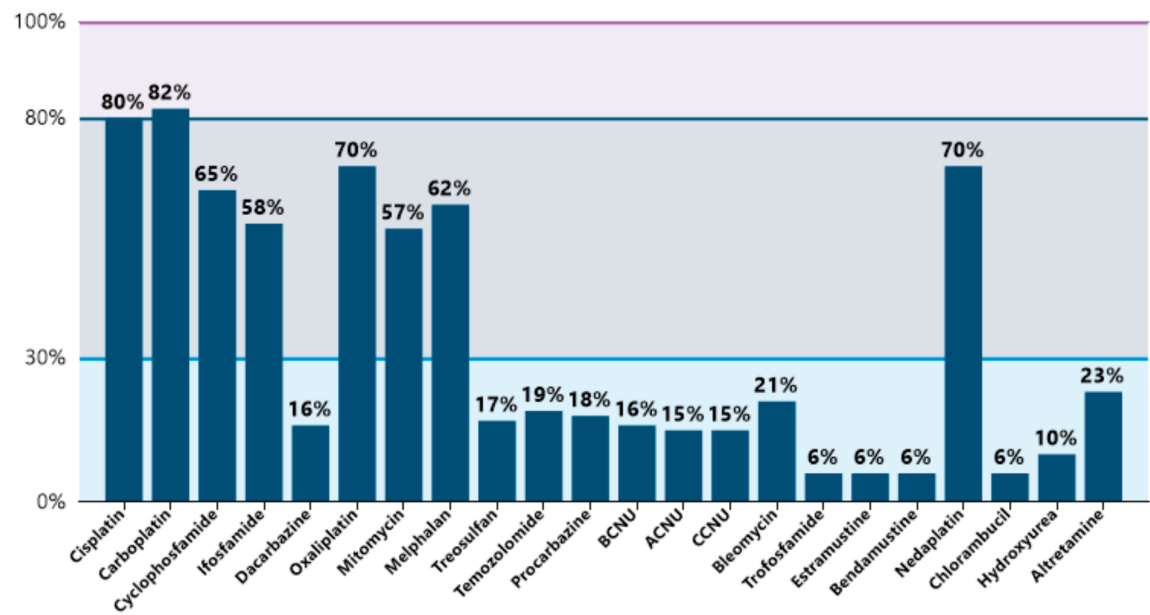
A comprehensive CTC-based functional and transcriptomic analysis revealed the following:

Chemosensitivity

- **High Sensitivity:**
 - Alkylating agents: **Carboplatin, Cisplatin**
 - Taxanes: **Paclitaxel, Docetaxel**
 - Nucleoside analogue: **Capecitabine**

Alkylating Agents

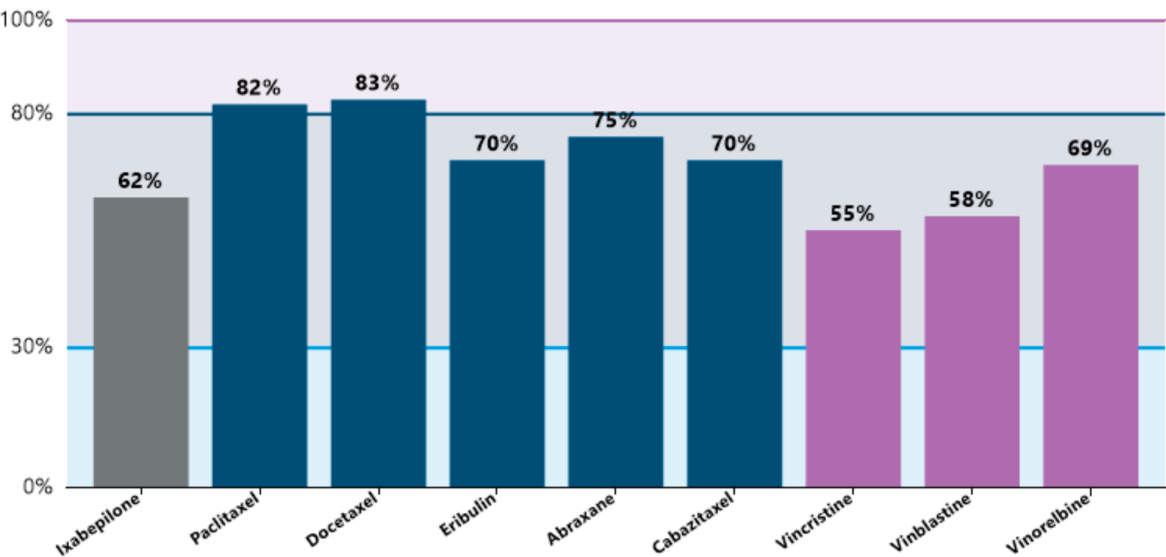
High sensitivity: Carboplatin



Epothilones & Nucleus Spindle Stabilizer I & II

High sensitivity: Paclitaxel, Docetaxel

Epothilones
Nucleus Spindle Stabilizer I
Nucleus Spindle Stabilizer II



- **Partial Sensitivity:** Etoposides, 5-FU, Vinca alkaloids

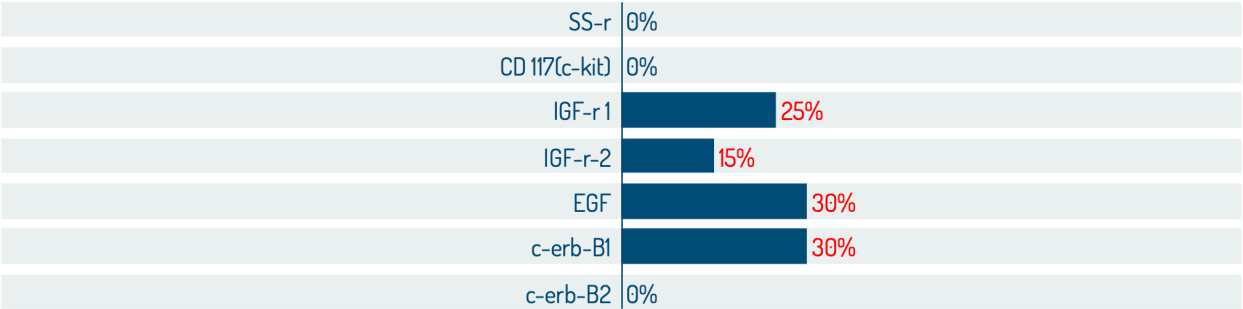
Gene Expression and Tumor Drivers

Marker	Implication	Expression
VEGF, PDGF, ANG1/2	Angiogenesis	High (10–35%)
c-erb-B1, EGF	EGFR pathway activation	30% ↑
IGF-r1/2	Metabolic driver	25–15% ↑
mTOR	Downstream of ER/PR pathway	35% ↑
COX2	Inflammatory microenvironment	15% ↑
PTEN	Tumor suppressor loss	30% loss
CDK4/6, p53	Cell cycle deregulation	40–55% ↑
MMP	Invasion and migration	55% ↑
HSPs (-30%)	Sensitivity to hyperthermia/radiation	Decreased
MDR1 (ABCB1)	Drug resistance	Overexpressed

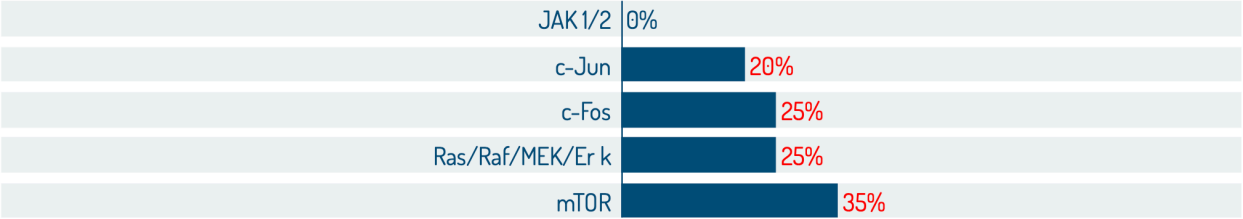
Transcriptomic Highlights

- Dominant driver: **ER/PR → mTOR axis**
- Epigenetic dysregulation: **HDAC overactivity**
- Resistance pathways: **ABC transporter overexpression (MDR1)**

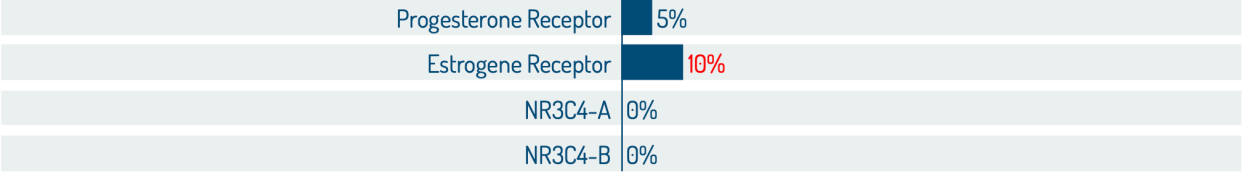
Growth Factor Receptor



Signal Transduction Pathway



Hormone Receptors



Treatment Strategy

Chemotherapy (Low-Toxicity)

- **Paclitaxel (low doses weekly)**
- **Carboplatin (low dose weekly)**
Regimen was adapted for post-BMT status to reduce marrow toxicity.

Integrative and Targeted Therapies

Agent(s)	Target Pathway	Justification
Ivermectin, Quercetin	MDR1	Downregulate drug resistance proteins
Resveratrol, Metformin	IGF1, mTOR	Block tumor metabolism and proliferation
Curcumin, EGCG, AKBA	COX-2, VEGF, MMP	Anti-inflammatory and anti-angiogenic
Berberine	EGFR, hTERT	Inhibits telomerase and cell growth
Valproic Acid	HDAC	Epigenetic reprogramming
Low Dose Naltrexone (LDN)	Immune checkpoint reset	Immune modulation
Oxaloacetate (Benagene)	Metabolic reprogramming	Starves cancer cells of glycolytic fuel
High-dose IV Vitamin C	Redox modulation	Cytotoxic in high concentrations
IV Artesunate (120 mg)	Oxidative stress induction	Pro-apoptotic effect in CTC-sensitive tumors

All interventions were aligned with RGCC recommendations and supervised for safety and response.

Therapeutic Response

PET/CT Scan (Post 6 Weeks)

- **Resolution of osseous metastases**
- **Marked reduction in metabolic activity** and size of primary tumors

Surgical Intervention

Procedure: Bilateral nipple-sparing, robot-assisted partial mastectomy with sentinel lymph node biopsy using the **Da Vinci Surgical System**

Given the patient’s history of prior chest irradiation and bone marrow transplant, traditional open or radical surgeries posed significant risk of morbidity, disfigurement, and delayed healing. A **robotic**

surgical approach was therefore selected to ensure **maximum oncologic precision with minimal tissue trauma**.

Technological Integration:

- **Da Vinci Robotic Platform:** Enabled fine dissection and deep field visualization with tremor-free control, critical for preserving the skin envelope and neurovascular structures in irradiated tissue.
- **Firefly™ Near-Infrared Fluorescence Imaging:** Guided **real-time identification of tumor boundaries and perfusion zones**, ensuring maximal tumor resection while sparing healthy breast tissue.
- **Intraoperative Frozen Section Pathology:** Allowed immediate confirmation of margin status and complete tumor excision.



Outcomes:

- **Right breast:** Approximately 2 cm necrotic tumor removed with **clear margins**; no viable tumor identified
- **Left breast:** Showed **benign fibrocystic tissue** with small foci of **ductal carcinoma in situ (DCIS)**
- **Right axilla: Sentinel lymph node biopsy (5 nodes):** All negative for metastasis

Postoperative Benefits:

- **No external scarring** on the chest wall due to the hidden axillary access ports
- **Preservation of breast contour and nipple-areolar complex**
- **Rapid recovery and early discharge** without significant postoperative pain or complications
- **Cosmetically and functionally superior outcome** compared to conventional breast surgeries

Significance of Robotic Surgery in This Case

This case highlights the **transformational potential of robotic breast surgery**, particularly in complex scenarios where prior treatment has compromised tissue integrity. Robotic assistance enabled:

- Oncologic clearance without compromising cosmetic outcomes
- Avoidance of extensive dissection and secondary complications

- Precise resection in fibrotic or radiated fields where human tactile feedback is insufficient

In high-risk, recurrent, or previously treated cancers, robotic breast surgery emerges not merely as an alternative—but as a **standard-setting advancement in surgical oncology**.

Current Status & Maintenance

- **Disease status:** No radiological or histological evidence of active disease
- **Maintenance:**
 - **Hormonal therapy** (Tamoxifen) based on ER+/PR+ status
 - **Transcriptomically guided nutraceuticals** continued

Discussion

This case exemplifies the power of **real-time molecular diagnostics** in managing high-risk, heavily pre-treated metastatic breast cancer. Despite the patient's prior hematological cancers and treatment constraints, the integrative precision strategy achieved:

- Rapid regression of bone metastases
- Complete histological clearance of primary tumors
- Organ preservation with minimal morbidity via robotic surgery

Key drivers—**mTOR, IGF, VEGF, MDR1, COX2, HDAC**—were successfully addressed through multimodal interventions spanning chemotherapy, targeted therapy, and natural compounds.

Conclusion

A patient with **Stage IV bilateral breast cancer**, compounded by **two previous hematologic malignancies**, achieved **complete response** through a carefully tailored **precision-integrative treatment strategy**. This case underscores the feasibility and efficacy of combining **CTC-based molecular diagnostics, adaptive chemotherapy, off-label repositioned agents, and robotic surgical precision** in overcoming complex, high-risk cancer presentations.