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Combined neoadjuvant radiotherapy and endocrine therapy enables radical surgery in locally advanced breast cancer: A clinical case

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Abstract
Introduction: Locally advanced breast cancer (LABC) presents significant therapeutic challenges, often requiring multimodal treatment to achieve locoregional control and surgical resectability. Neoadjuvant endocrine therapy combined with CDK4/6 inhibition and neoadjuvant radiotherapy (NART) has emerged as a potential strategy for tumor downstaging in selected hormone receptor-positive cases.
Case: We report the case of a 61-year-old woman presenting with a long-standing, ulcerated, bleeding right breast mass, associated with weight loss and anemia. Imaging and biopsy confirmed a locally advanced ER+/HER2-low invasive carcinoma, staged cT4bN3M0. Initial management consisted of endocrine therapy with anastrozole and abemaciclib, which achieved marked clinical and radiological tumor regression over 10 months. Given the favorable response and absence of distant metastasis, NART was administered to the right breast and regional lymph nodes. Post-RT imaging demonstrated no vascular invasion, allowing for curative-intent surgery.
An adapted Halsted mastectomy with partial pectoralis excision, axillary dissection, and immediate chest wall reconstruction using a pedicled TRAM flap and V-Y advancement flap was performed. Postoperatively, partial flap necrosis required five additional reconstructive procedures. Final pathology revealed Grade 2 NST carcinoma, ER 100%, PR 5%, HER2-low, pT4bN1M0, with R0 resection. Despite postoperative complications, the patient achieved excellent local control and satisfactory functional and aesthetic results. She remains under regular follow-up, with good upper-limb mobility, no lymphedema, and improved quality of life.
Conclusion: This case demonstrates that combined neoadjuvant endocrine therapy, CDK4/6 inhibition, and NART can successfully downstage selected LABC cases, enabling radical surgical resection with curative intent. NART played a pivotal role in achieving R0 margins and facilitating immediate reconstruction. Further studies are needed to define optimal patient selection and refine multimodal treatment sequencing in LABC.

Keywords: Locally advanced breast cancer, neoadjuvant radiotherapy, radical surgical resection

Introduction
Locally Advanced Breast Cancer (LABC) represents a relatively uncommon yet clinically significant presentation. In Europe, approximately 4% of patients with breast cancer are diagnosed with LABC [1, 2]. Under the 8th edition of the American Joint Committee on Cancer (AJCC), a breast cancer will be considered locally advanced when it has locally or regionally aggressive features but remains non-metastatic and is most frequently classified within stages IIIB and IIIC, although certain clinical guidelines and practitioners also extend the definition to include selected stage IIIA cases.
LABC is associated with a distinctly poorer prognosis compared to early-stage breast cancer, largely owing to the elevated risk of locoregional progression and distant dissemination [1, 3]. Consequently, accurate disease staging is of paramount importance, fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) is increasingly recognized as the standard of care due to its superior diagnostic accuracy and ability to detect metastatic disease [2].
The criteria for determining tumor resectability in LABC have evolved considerably, particularly with the advent of neoadjuvant systemic therapies. Although no universal definition of irresectability exists, several clinical features are widely considered.

These include tumor fixation to the periosteum or intercostal muscles, inability to achieve complete gross resection due to invasion of critical structures such as the brachial plexus, axillary vessels, or ribs, skin nodules extending toward or beyond the inframammary fold or sternum, and presentations consistent with *"cancer en cuirasse"* [1]. In operable locally advanced breast cancer (LABC), radical surgery may be required to obtain R0 margins. Radical mastectomy entails *en bloc* removal of the breast, nipple-areolar complex, overlying skin, pectoralis muscles, and level I-II axillary nodes, although this procedure is now rarely performed due to similar oncologic outcomes and lower morbidity with less extensive approaches. Modified radical mastectomy, which preserves the pectoralis major muscle, is therefore preferred (4-6).

Systemic therapy remains the cornerstone of initial treatment in LABC. Neoadjuvant chemotherapy (NACT) is most frequently employed, either alone or in combination with HER2-targeted therapies in HER2-positive disease. For patients with inoperable tumors, neoadjuvant radiotherapy (NART) has emerged as a valuable modality for tumor downstaging, frequently enabling surgical resection with clear margins (R0), while R1 and R2 margins indicate microscopic and macroscopic residual tumor, respectively [7]. Importantly, the therapeutic effect of NART appears to be independent of intrinsic tumor subtype, with pathological response (pR) rates exceeding 90% being associated with improved overall survival (OS) outcomes [1]. Both clinical (cR) and pathological responses serve as important surrogate markers for long-term survival and play a critical role in guiding subsequent therapeutic decisions [3].

The integration of NART into multimodal strategies is an area of growing interest. Beyond facilitating surgical resection, NART may enable single-stage surgery, combining mastectomy with immediate autologous reconstruction without increasing perioperative complication rates compared to conventional treatment sequencing. Additional potential benefits include enhanced downstaging of the primary tumor, shortened overall treatment duration, elimination of prolonged intervals with breast tissue deficits, and improvements in patient's quality of life [8].

Despite notable progress in systemic treatments and multimodal strategies, LABC continues to pose a considerable therapeutic challenge. Its' management requires a multidisciplinary decision-making, integrating systemic therapy, surgery, and radiotherapy, often in complex sequences tailored to the disease burden and individual patient characteristics. [3].

Materials and Methods

Clinical case of 61 years old woman with locally advanced breast cancer submitted to endocrine therapy combined with neoadjuvant radiotherapy enabling surgical resection with curative intent.

Results

A 61-year-old woman, a daily smoker with no relevant oncologic family history, presented with a neglected, ulcerated and bleeding right breast mass, accompanied by marked weight loss and anemia. She reported a 15-year history of a growing right breast lesion with intermittent bleeding for the last 4-5 years, without prior medical evaluation. On examination, she had a 30 cm friable exophytic mass in the upper outer quadrant of the right breast, without axillary or supraclavicular lymphadenopathies. The left breast and axillae were unremarkable (Figure 1).

Fig 1: Right breast tumor

Core-Biopsy revealed invasive carcinoma no special type (NST), Grade 2, ER 100%, PR 5%, HER2-low (1+), without lymphovascular invasion. Initial management included imaging for staging, systemic evaluation and initiation of hormonal therapy (anastrozole and abemaciclib), along with local malignant wound care once every week at the hospital.

CT imaging suggested possible pectoral muscles' invasion and suspicious internal mammary and retro-pectoral lymphadenopathies as showned in Figure 2. Bone scintigraphy showed no metastases. PET-CT confirmed extensive right breast involvement with regional lymphadenopathy but no distant metastases (M0). Axillary biopsy on the contralateral side confirmed node-negative disease (N0) after a suspicious node was identified on the CT scan. There were no other lesions on the left breast.

So, the patient had a locally advanced, ulcerated, ER+/HER2-low (luminal B-like), ki67 below 10, breast cancer (cT4bN3M0). On multidisciplinary group reunion was decided systemic therapy with endocrine therapy (Anastrozole) and CDK4/6 inhibitors (Abemaciclib) for 10 cycles. The patient showed excellent response to the therapy 10 months after the initial assessment, as shown in Figure 3, leading to the decision to do neoadjuvant radiotherapy with possibility of a curative resection.

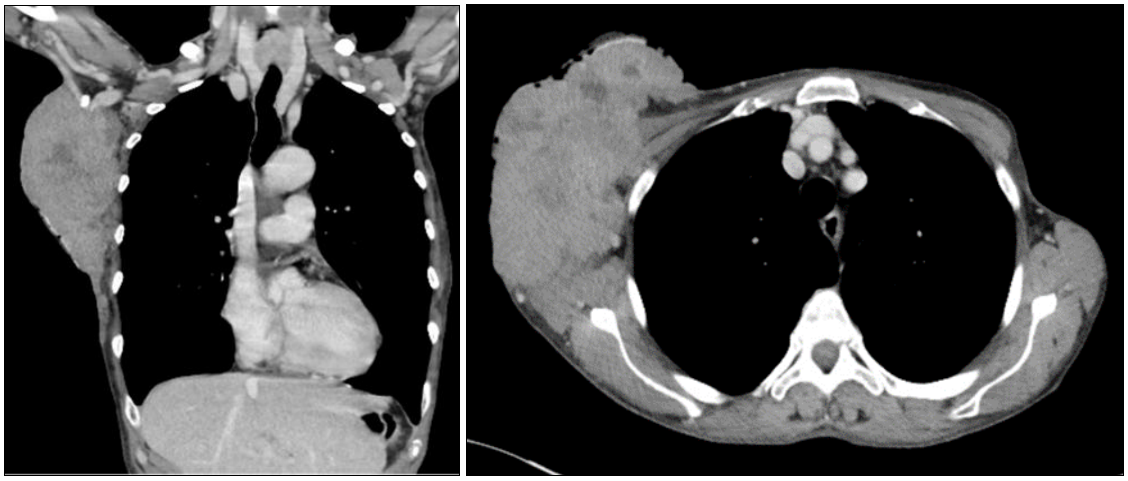

Fig 2: CT imaging before radiotherapy: a) coronal view; b) axial view

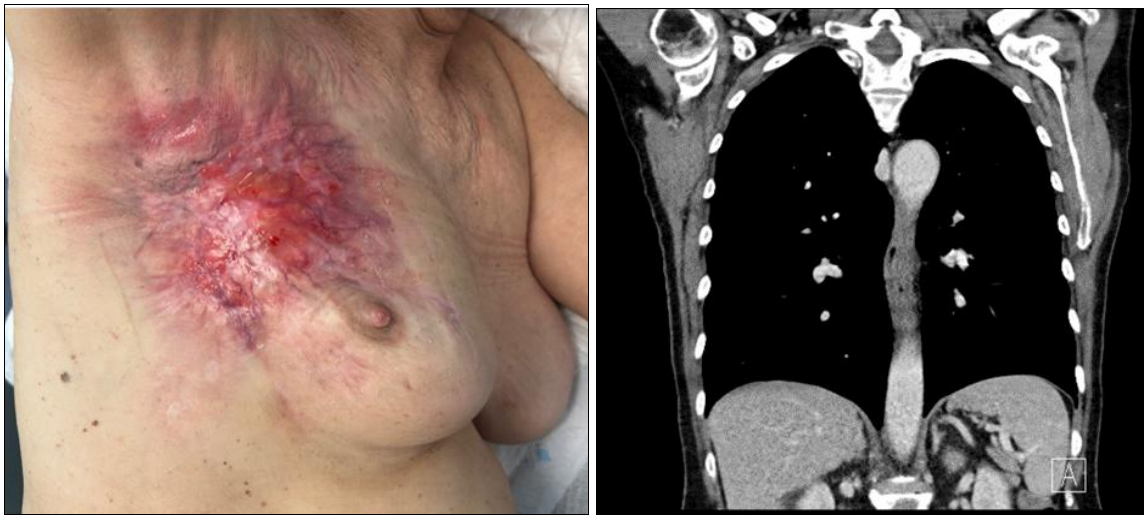

Fig 3: Right breast tumor after endocrine therapy in: a) patients' photo; b) CT imaging coronal view

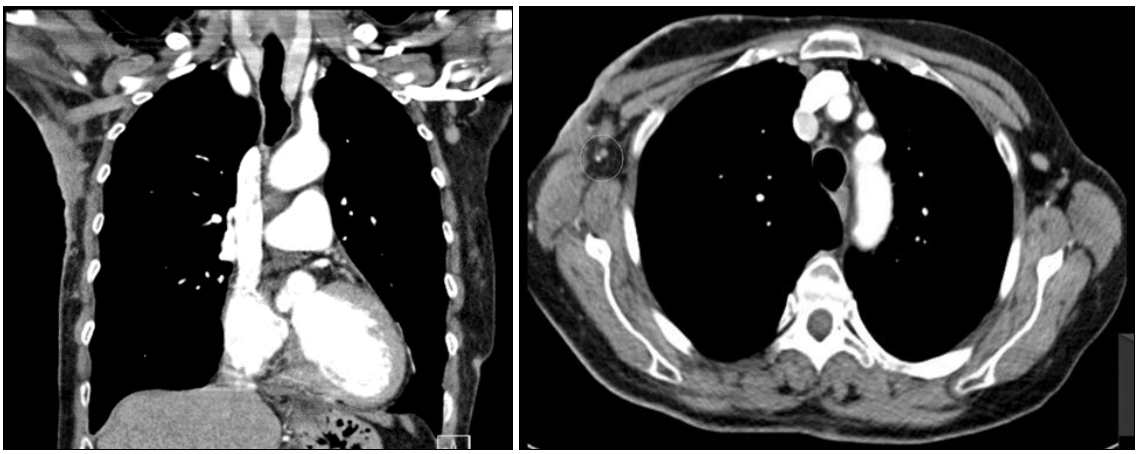

Fig 4: CT imaging after radiotherapy: a) coronal view; b) axial view, showing no vascular invasion

Surgery was postponed in favor of neoadjuvant radiotherapy (RT) to the right breast and regional lymph nodes (full axilla, supraclavicular and internal mammary chain) to a total dose of 40Gy, in 15 fractions, with simultaneous integrated boost till 48Gy to all PET-positive volumes. Treatment was planned in DIBH (deep-inspiration breath hold) with VMAT (volumetric modulated arc therapy). The aim was to optimize resection margins and reduce surgical morbidity. Post-RT imaging ruled out vascular invasion (Figure 4).

The patient signed an informed consent after being informed about the surgical risks such as lymphedema, sensory/motor deficits and vascular complications. The patient was proposed for surgery 14 months after the beginning of endocrine therapy.

Fig 5: Pre-operative preparation

Abemaciclib was discontinued two weeks prior. Eight weeks post-RT, the patient underwent an adapted Halsted mastectomy with partial pectoralis excision, axillary dissection and immediate chest wall reconstruction using a pedicled TRAM flap and a V-Y advancement flap complemented with a prolene mesh.

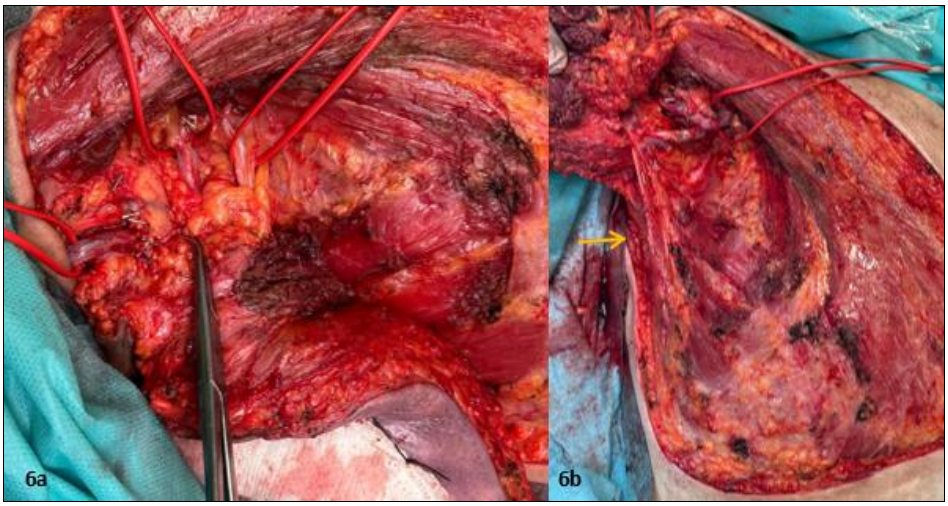

Fig 6: Tumor isolation with axillary artery and vein involved by it in figure 6a and already isolated in 6b. Toracodorsdal bundle (blue arrow) is also present in figure 6b

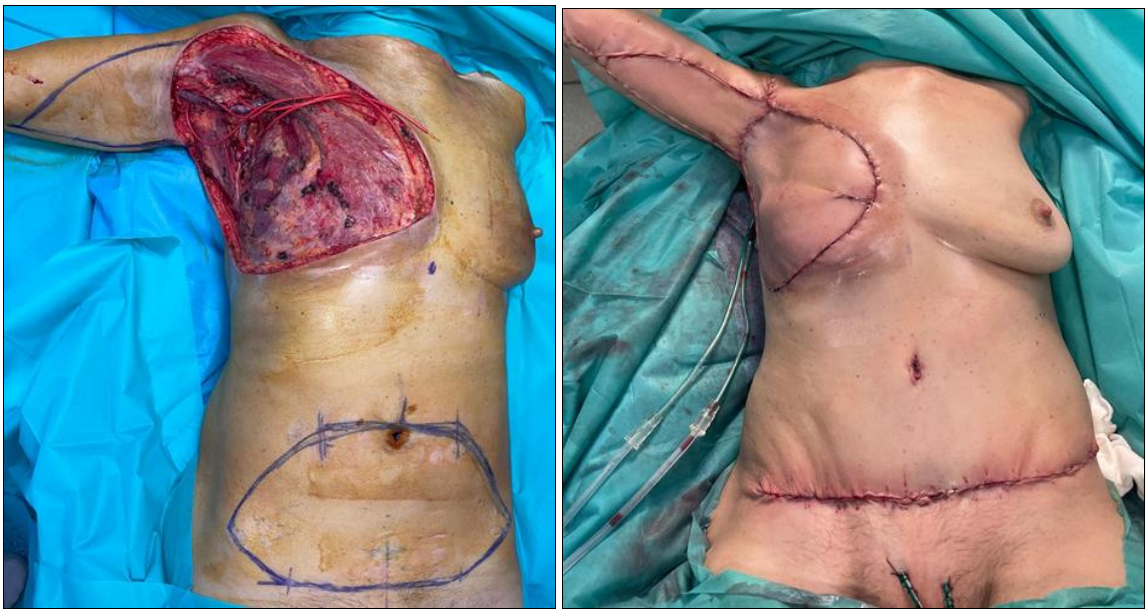

Fig 7: Immediate reconstruction with TRAM flap

Postoperatively, she developed partial flap necrosis requiring five additional surgical interventions leading to 115 days of hospitalization. Final histopathology report confirmed Grade 2 NST invasive carcinoma (ER 100%, PR 5%, HER2 1+), no lymphovascular invasion, with pT4bN1M0 staging and R0 resection.

Fig 8: Mastectomy with partial pectoralis excision

She remains under close follow-up for ongoing recovery and long-term management with clinical evaluations every three months. She has no evidence of lymphedema, maintains good arm mobility with continued physiotherapy and reports satisfaction with the aesthetic outcome and an improvement in overall quality of life.

Fig 9: 8 months postoperatively

Discussion

Notably, LABC has rarely been investigated as an independent clinical entity. Historically, patients with this condition have been enrolled in either palliative or neoadjuvant clinical trials [2]. This lack of focused investigation has limited the generation of disease-specific evidence and highlights the need to consider LABC as a distinct biological and clinical subset [9].

Neoadjuvant chemotherapy (NAC) remains the most employed systemic strategy in LABC, aimed at tumor downstaging and reduction of mastectomy rates [9]. Hormonal therapy combined with CDK4/6 inhibitors is preferred as neoadjuvant therapy instead of chemotherapy in locally advanced, HR-positive, HER2-negative breast tumors who exhibit high endocrine sensitivity [10-11]. Usually in patients that have significant comorbidities or wish to avoid the toxicity associated with cytotoxic chemotherapy. This approach is particularly considered in patients with indolent tumor biology and frailty like in this case for whom chemotherapy risks outweigh potential benefits [12-13].

Since the patient had no distant disease and with curative intents, the patient was proposed for preoperative neoadjuvant radiotherapy (NART). NART remains relatively understudied, although current evidence suggests it can reduce tumor volume and induce fibrosis, potentially decreasing intraoperative tumor spread and improving surgical precision, local control, and patient-reported quality of life [14]. Current evidence indicates that NART can result in meaningful tumor shrinkage and increase rates of pathological complete response (pCR), which is closely related to R0 resection. Systematic review data show pCR rates after neoadjuvant chemoradiotherapy ranging from 12% to 53% in locally advanced breast cancer, with locoregional recurrence rates between 3% and 10%. NART may also improve patient satisfaction and reduce complication rates compared to adjuvant radiotherapy, especially in the context of immediate breast reconstruction, with lower rates of flap failure and implant loss. However, the incidence of grade 3 skin toxicity and mastectomy skin necrosis remains a consideration [15].

The attending physicians expect a final Residual tumour (R) Classification by the pathologist. This classification describes the presence or absence of residual tumour after treatment, the effects of therapy, influences further therapeutic procedure, and is a strong prognostic predictor [7]. Achieving R0 status is a critical goal in breast cancer surgery, as it is associated with improved local control and long-term survival [16]. R0 resection rates after neoadjuvant radiotherapy in breast cancer are typically above 90%, and pathological complete response rates range from 12% to 53%, with higher rates observed in HER2-positive and triple-negative subtypes and with combined chemoradiotherapy. Factors influencing pCR include tumor subtype, stage, and interval between radiotherapy and surgery [15, 17].

Immediate breast reconstruction (IBR) or wall chest reconstruction is recognized as oncologically safe with survival outcomes comparable to delayed reconstruction. In addition to oncologic safety, IBR offers advantages in aesthetics, psychological well-being, social functioning and may reduce the total number of surgical procedures (18-20). The main challenge lies in reconstruction timing when radiotherapy is required. Post-IBR radiation may compromise cosmetic and oncologic outcomes, increasing the risks of capsular contracture, fibrosis, asymmetry, wound-healing complications and technical limitations in radiotherapy planning (21-23). Delayed reconstruction avoids these issues but prolongs treatment and recovery. The reverse sequence (RS) approach-systemic therapy, preoperative irradiation, mastectomy and immediate reconstruction-has emerged as an alternative, with available data indicating no increase in postoperative morbidity in appropriately selected patients [9, 19].

Preoperative radiotherapy in breast cancer is not yet recommended for routine clinical use outside of research settings but is recognized by European Society for Radiotherapy and Oncology (ESTRO) as a promising strategy warranting further investigation, particularly for locally advanced and high-risk cases where it may improve surgical and oncologic outcomes [24]. In the present case, NART played a pivotal role in achieving local control of the disease and allowing an R0 resection. Moreover, a satisfactory aesthetic result was obtained despite flap necrosis, further underscoring the potential value of incorporating NART into multimodal treatment pathways for patients with LABC. Dedicated studies are essential to optimize diagnostic approaches, refine therapeutic sequencing and improve long-term oncological outcomes.

Conclusion

This case highlights the complex management of an extensive neglected breast cancer, requiring coordinated multimodal treatment with neoadjuvant endocrine and radiation therapy, extensive radical surgery and multiple reconstructive interventions. It underscores the importance of multidisciplinary decision-making and flexibility in surgical planning in the setting of advanced disease. Despite the tumor's extensive local invasion, systemic control was achieved and curative-intent surgery with reconstruction was successfully performed. NART allowed a single-stage surgical intervention with a curative.

Conflict of Interest

Not available

Financial Support

Not available

References

1. Sousa C, Cruz M, Neto A, Pereira K, Peixoto M, Bastos J, *et al*. Neoadjuvant radiotherapy in the approach of locally advanced breast cancer. ESMO Open. 2020 Mar;4(Suppl 2):e000640. DOI: 10.1136/esmoopen-2019-000640.
2. Aebi S, Karlsson P, Wapnir IL. Locally advanced breast cancer. Breast. 2022 Mar;62 Suppl 1:S58-S62. DOI: 10.1016/j.breast.2021.12.011. EPUB 2021 Dec 15.
3. Kountourakis P, Missitzis I, Doufexis D, Zobolas V, Pissakas G, Arnogiannaki N, *et al*. Neoadjuvant sequential epirubicin and docetaxel followed by surgery-radiotherapy and post-operative docetaxel or gemcitabine/vinorelbine combination based on primary response: A multimodality approach for locally advanced breast cancer. J Cancer Res Clin Oncol. 2011 Feb;137(2):221-8. DOI: 10.1007/s00432-010-0878-8. Epub 2010 Apr 13.
4. Halsted CP, Benson JR, Jatoi I. A historical account of breast cancer surgery: Beware of local recurrence but be not radical. Future Oncol. 2014;10(9):1649-57. DOI: 10.2217/fon.14.98.
5. Jatoi I, Benson JR, Toi M. De-escalation of axillary surgery in early breast cancer. Lancet Oncol. 2016;17(10):e430-e441. DOI: 10.1016/S1470-2045(16)30311-4.
6. Hermann RE, Steiger E. Modified radical mastectomy. Surg Clin North Am. 1978;58(4):743-54. DOI: 10.1016/S0039-6109(16)41586-0.
7. Sunitsch S, Fischer P, Pregartner G, Regitnig P. The misunderstanding of the R classification: A survey amongst medical specialties treating breast cancer. Virchows Arch. 2024;485(3):479-90. DOI: 10.1007/s00428-024-03876-8.
8. Chidley P, Foroudi F, Tacey M, Khor R, Yeh J, Bevington E, *et al*. Neoadjuvant radiotherapy for locally advanced and high-risk breast cancer. J Med Imaging Radiat Oncol. 2021 Jun;65(3):345-53. DOI: 10.1111/1754-9485.13180. EPUB 2021 Apr 5.
9. Maire M, Debled M, Petit A, Fournier M, Macgrogan G, Thueux QN, *et al*. Neoadjuvant chemotherapy and radiotherapy for locally advanced breast cancer: Safety and efficacy of reverse sequence compared to standard technique? Eur J Surg Oncol. 2022 Aug;48(8):1699-705. DOI: 10.1016/j.ejso.2022.04.022. Epub 2022 Apr 29.
10. Morrison L, Loibl S, Turner NC. The CDK4/6 inhibitor revolution: A game-changing era for breast cancer treatment. Nat Rev Clin Oncol. 2023. DOI: 10.1038/s41571-023-00840-4.
11. O'Sullivan CC, Clarke R, Goetz MP, Robertson J. Cyclin-dependent kinase 4/6 inhibitors for treatment of hormone receptor–positive, ERBB2-negative breast cancer: A review. JAMA Oncol. 2023;9(9):1273-82. DOI: 10.1001/jamaoncol.2023.2000.
12. Jackson EB, Chia SKL. Sequencing of endocrine and targeted therapies in hormone-sensitive, human epidermal growth factor receptor 2-negative advanced breast cancer. J Clin Oncol. 2023;41(24):3976-83. DOI: 10.1200/JCO.23.00759.

13. Zhang M, Song J, Guo S, Jin F, Zheng A. Adjuvant and neoadjuvant therapy with cyclin-dependent kinase 4 and 6 inhibitors in hormone receptor-positive, human epidermal growth factor receptor 2-negative early breast cancer: A systematic review and meta-analysis. Endocr Relat Cancer. 2023;30(8):e220365. DOI: 10.1530/ERC-22-0365.
14. Kong X, Song J, Gao P, Gao R, Zhang L, Fang Y, *et al*. Revolutionizing the battle against locally advanced breast cancer: A comprehensive insight into neoadjuvant radiotherapy. Med Res Rev. 2021;41(5):2724-57. DOI: 10.1002/med.21998.
15. Nelissen SH, Afat YDA, Bongard HJGv D, *et al*. Neoadjuvant radiotherapy and immediate breast reconstruction: A systematic review of literature of the last decade. Radiother Oncol. 2025;209:110991. DOI: 10.1016/j.radonc.2025.110991.
16. Yau C, Osdoit M, Noordaa VDM, *et al*. Residual cancer burden after neoadjuvant chemotherapy and long-term survival outcomes in breast cancer: a multicentre pooled analysis of 5161 patients. Lancet Oncol. 2022;23(1):149-60. DOI: 10.1016/S1470-2045(21)00589-1.
17. Haussmann J, Budach W, Krämling NC, *et al*. Factors influencing pathological complete response and tumor regression in neoadjuvant radiotherapy and chemotherapy for high-risk breast cancer. Radiat Oncol. 2024;19(1):99. DOI: 10.1186/s13014-024-02450-5.
18. Downes KJ, Glatt BS, Kanchwala SK, *et al*. Skin-sparing mastectomy and immediate reconstruction is an acceptable treatment option for patients with high-risk breast carcinoma. Cancer. 2005;103(5):906-13. DOI: 10.1002/cncr.20851.
19. Monrigal E, Dauplat J, Gimbergues P, *et al*. Mastectomy with immediate breast reconstruction after neoadjuvant chemotherapy and radiation therapy. A new option for patients with operable invasive breast cancer. Results of a 20 years single institution study. Eur J Surg Oncol. 2011;37(10):864-70. DOI: 10.1016/j.ejso.2011.07.009.
20. Zhong T, Hu J, Bagher S, *et al*. A comparison of psychological response, body image, sexuality, and quality of life between immediate and delayed autologous tissue breast reconstruction: A prospective long-term outcome study. Plast Reconstr Surg. 2016;138(4):772-80.
DOI: 10.1097/PRS.0000000000002536.
21. Motwani SB, Strom EA, Schechter NR, *et al*. The impact of immediate breast reconstruction on the technical delivery of postmastectomy radiotherapy. Int J Radiat Oncol Biol Phys. 2006;66(1):76-82. DOI: 10.1016/j.ijrobp.2006.03.040.
22. Kronowitz SJ, Robb GL. Breast reconstruction with postmastectomy radiation therapy: Current issues. Plast Reconstr Surg. 2004;114(4):950-60. DOI: 10.1097/01.prs.0000133200.99826.7f.
23. Chidley P, Foroudi F, Tacey M, Khor R, Yeh J, Bevington E, *et al*. Neoadjuvant radiotherapy for locally advanced and high-risk breast cancer. J Med Imaging Radiat Oncol. 2021 Jun;65(3):345-53. DOI: 10.1111/1754-9485.13180. Epub 2021 Apr 5.
24. Zamagni A, Montero Luis A, Mjaaland I, *et al*. ESTRO recommendations on preoperative radiation therapy in breast cancer: Current and future perspectives-endorsed by ASTRO. Radiother Oncol. 2026;214:111236. DOI: 10.1016/j.radonc.2025.111236.

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