

ONCOLOGY KNOWLEDGE HUB · FOR HEALTH PROFESSIONALS

Breast Cancer

A mini review for clinicians

For postgraduate residents (medical and surgical oncology, radiation oncology, general surgery, medicine, obstetrics & gynaecology), practising clinicians and medical students

Dr. Haritha Chiramana

MD (Internal Medicine), DM (Medical Oncology)

Senior Medical Oncologist & Hemato-Oncologist

C.R. Reddy Cancer Center, C.R. Reddy Superspeciality Hospital

17/406, Old Post Office Road, near Leela Mahal Road, Nellore, Andhra Pradesh 524003

Phone 0861 232 5344 · WhatsApp +91 79896 42272

info@drharitha.co.in · drharitha.co.in

Dr. Haritha teaches oncology to postgraduates and medical students. Colleges and departments may write to info@drharitha.co.in for teaching sessions.

CONTENTS

01 At a glance

02 Clinical presentation, common traps & genetic causes

03 Screening, workup & staging essentials

04 Biomarkers that change treatment

05 Local therapy: surgery & radiotherapy

06 Systemic therapy: indications & options

07 Management algorithms

08 Survivorship, follow-up & reducing recurrence

09 Landmark trials

10 Practice pearls & pitfalls

11 Case vignettes: lines of management

12 References & guidelines

Cite as: Chiramana H. Breast Cancer: a mini review for clinicians. Oncology Knowledge Hub [Internet]. Nellore (India): drharitha.co.in; 2026 [updated 2026 Oct 10]. Available from: <https://drharitha.co.in/professionals/breast-cancer> · Free for education with attribution (CC BY-NC-ND 4.0).

Updated 10 October 2026. Educational summary written in our own words from current guidelines and primary trials; no drug doses; not advice for an individual patient. Verify current guidelines and Indian regulatory approvals before treatment decisions. Patients and families: please see the patient guides at drharitha.co.in.

Breast Cancer

HR+/HER2- · HER2+ · TNBC · Key points for clinicians · Last updated 9 October 2026

01 At a glance

- The most common cancer in Indian women: about 1.9 lakh new cases and nearly 1 lakh deaths in 2022 (GLOBOCAN).
- Indian patients present about a decade younger than in Western series, often with locally advanced disease; triple-negative disease is relatively more frequent.
- Roughly three in four breast cancers are hormone-receptor positive and about one in seven is HER2-positive. **Stage** and **biology** drive almost every decision.
- Recurrence timing differs by subtype: HER2+ and TNBC relapse mostly within 5 years (with more visceral and brain spread); HR+ disease can recur 20 years or more later.

Approximate share (global series). Triple-negative is higher, about 25%, in Indian series.

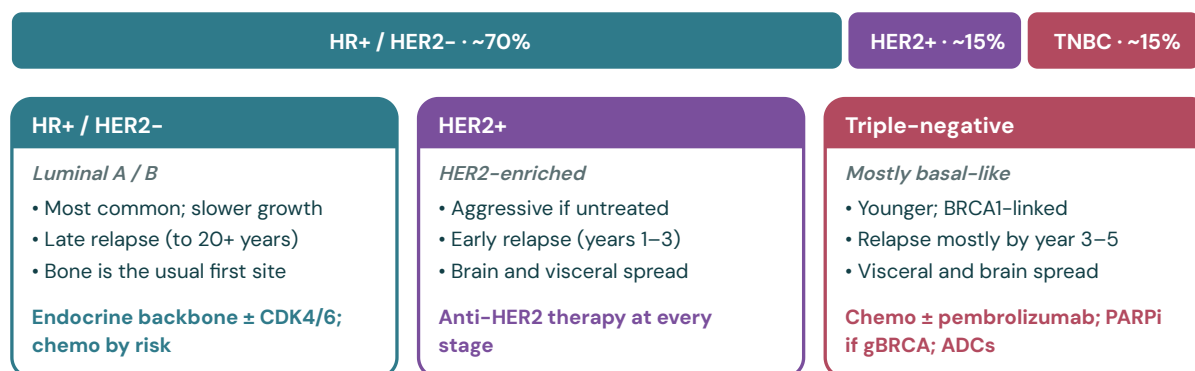


Figure 1. The three working subtypes. Each one has its own natural history and treatment backbone.

02 Clinical presentation, common traps & genetic causes

How breast cancer presents

- A **painless**, hard, irregular lump is the commonest presentation. Pain does not exclude cancer.
- Skin changes (dimpling, retraction, peau d'orange, ulceration) and nipple changes (new inversion, unilateral eczema, or spontaneous single-duct bloody or clear discharge).
- An axillary or supraclavicular node, or arm swelling, sometimes with no palpable breast lump.
- Diffuse redness, warmth and swelling over a third or more of the breast, developing within weeks: think **inflammatory cancer**.
- First presentation with metastases: persistent bone pain, breathlessness or effusion, jaundice, headache, or back pain with leg weakness (cord compression).

Common traps

Trap	What to do instead
"Painless and mobile in a young woman, so a fibroadenoma"	Triple assessment. Biopsy any solid lump with suspicious imaging, growth, or risk factors; never rely on age or feel alone.
Non-resolving "mastitis" or "abscess" in a woman who is not breastfeeding	Image early. If it is not settling after one course of antibiotics, take a core and skin punch biopsy (inflammatory cancer).
Unilateral nipple eczema treated with creams for months	Biopsy persistent one-sided nipple changes (Paget disease).
"Mammogram normal, so no cancer"	About 10–15% of palpable cancers are invisible on mammography (dense breasts, lobular type). A clinically suspicious lump needs biopsy regardless.
FNAC reported benign, or discordant with imaging	Core biopsy. FNAC cannot separate in situ from invasive disease and gives no receptor status.
Lump in pregnancy or lactation called a galactocele or "milk lump"	Ultrasound and biopsy. Pregnancy-associated cancer is often diagnosed late.
Granulomatous or tuberculous mastitis versus cancer (both common in India)	They mimic each other clinically and on imaging: obtain tissue for histology and culture before treating.
A rapidly growing "fibroadenoma"	Consider phyllodes tumour: core biopsy, then excision with a margin.
Adenocarcinoma in an axillary node, no breast lump	Treat as occult breast cancer until proven otherwise: mammography, ultrasound and MRI; ER/PR/HER2 and GATA3 on the node.
Male breast lump assumed to be gynaecomastia	Eccentric, hard, fixed or nipple-involving masses need biopsy.
New back pain or cough in a survivor called "age-related"	Investigate. HR+ cancers can recur 10–20 years later.
GI, peritoneal or ovarian mass in a woman with past lobular cancer	Think metastatic lobular cancer (ER, GATA3 on biopsy) before treating as a new GI or ovarian primary.

Genetic causes

About 5–10% of breast cancers arise from an inherited pathogenic variant; the share is higher in young women, TNBC and men.

Gene	Breast cancer pattern	Other risks	What it changes
<i>BRCA1</i>	Young onset, often triple-negative	Ovarian/tubal	PARP inhibitor and platinum options; contralateral risk-reducing mastectomy; salpingo-oophorectomy around 35–40
<i>BRCA2</i>	Often HR+; male breast cancer	Ovarian, pancreatic, prostate, melanoma	As for <i>BRCA1</i> ; salpingo-oophorectomy around 40–45
<i>PALB2</i>	High risk, more often ER-negative	Pancreatic; small ovarian risk	MRI screening from 30; discuss risk-reducing mastectomy; PARP inhibitor option
<i>TP53</i> (Li-Fraumeni)	Very young onset (often <35), frequently HER2+	Sarcoma, brain, adrenal, leukaemia	Avoid radiotherapy where possible (mastectomy favoured); whole-body surveillance
<i>PTEN</i> (Cowden)	High lifetime risk	Thyroid, endometrial, kidney	Multisystem surveillance
<i>CDH1</i>	Lobular breast cancer	Diffuse gastric cancer	Gastric surveillance or gastrectomy discussion
<i>STK11</i> (Peutz-Jeghers)	Raised risk	GI, pancreatic, gynaecological	GI surveillance
<i>CHEK2, ATM</i>	Moderate risk, mostly ER+	Variable	Earlier mammography ± MRI; risk-reducing mastectomy not routinely advised
<i>RAD51C/D, BARD1</i>	Moderate risk, often ER-negative	Ovarian (<i>RAD51C/D</i>)	Salpingo-oophorectomy around 45–50 (<i>RAD51C/D</i>)

- **Who to test** (at minimum): diagnosis at ≤50, TNBC at ≤60, any male, bilateral cancer, Ashkenazi ancestry, close relatives with breast, ovarian, pancreatic or prostate cancer, or PARP-inhibitor eligibility. ASCO-SSO extends testing to all patients diagnosed at ≤65.
- A positive result changes surgery, systemic options, contralateral and ovarian risk management, and **cascade testing** of parents, siblings and children (sons too).
- Variants of uncertain significance are common on panels: manage on family history, not on the variant.

SHARE WITH PATIENTS: WARNING SIGNS THAT GET MISSED

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[A red, swollen breast is just an infection?](#)

[A nipple rash is just eczema?](#)

[A lump while breastfeeding is just milk?](#)

[No pain, no breast cancer?](#)

[Every breast lump means cancer?](#)

[Better to remove the lump first and test later?](#)

[Biopsy spreads cancer?](#)

03 Screening, workup & staging essentials

Screening and early detection (asymptomatic women)

Risk group	Who	Screening	Notes
Average ($<15\%$ lifetime risk)	Most women, including most with no or a distant family history	Mammography (digital $\pm$ tomosynthesis) every 1–2 years: shared decision at 40–49; recommended at 50–74; at ≥ 75 only if life expectancy is ≥ 10 years	Absolute benefit is smallest in the 40s. Annual rather than 2-yearly screening adds more false positives than benefit.
Moderate (15–20%)	A first-degree relative with breast cancer, no known variant	As for average risk; some start at 40, or about 10 years before the relative's age at diagnosis	Evidence for supplemental ultrasound or MRI is inconclusive, and costs are out of pocket.
High ($>20\%$)	<i>BRCA1/2, PALB2, TP53, PTEN</i> carriers; chest radiotherapy at age 10–30; atypia or LCIS (guidelines differ on MRI here: decide on overall calculated risk); untested first-degree relatives of carriers	Annual MRI plus mammography, with start age by gene (for <i>BRCA</i> carriers, typically MRI from 25 and mammography from 30)	MRI is more sensitive but less specific; a survival benefit is not proven in randomised trials. Use ultrasound if MRI is not possible.
Indian public programme	All women aged 30–65	Clinical breast examination every 5 years by trained health workers at Ayushman Arogya Mandirs (NP-NCD)	Uptake is very low (under 1% of women aged 30–49 in NFHS-5). In the Mumbai cluster trial ^[1] , 2-yearly CBE downstaged cancers and cut breast cancer deaths by nearly 30% at ≥ 50 (15%, non-significant, overall).

- **Benefit and harms:** randomised trials show a 15–20% relative fall in breast cancer mortality at ages 40–69 ([UK Independent Panel](#)^[2], [USPSTF 2024](#)^[3]). The harms are false positives (about half of women have at least one over 10 years of annual screening, in US data) and overdiagnosis (estimates vary widely; around 19% in one meta-analysis). Discuss both: shared decision-making.
- **Tests that do not belong in screening:**
 - Ultrasound alone: an adjunct for dense breasts or high risk, not a primary screening test.
 - Thermography or heat scans: poor accuracy; the FDA warns they do not replace mammography.
 - Tumour markers, whole-body PET-CT or CT.
 - Routine self-examination as a screening test: no mortality benefit in trials, and more benign biopsies. Teach breast awareness instead.
- **Dense breasts** raise risk and lower mammographic sensitivity, but density alone does not change age- and risk-based screening. Tomosynthesis helps; consider supplemental imaging individually.
- **Risk tools:** Tyrer-Cuzick (IBIS), BCRAT (Gail) and CanRisk/BOADICEA. All were built on Western populations, so calibration in Indian women is uncertain.
- **Special situations:** no screening mammography of the mastectomy side (examine it), but continue screening the other breast; no screening mammography in pregnancy (use ultrasound for symptoms); stop when life expectancy is under 10 years.

- **Practical approach in Indian clinics:** breast-awareness education for all women; CBE from 30 (through the programme or opportunistically); mammography from 40 where available and affordable, prioritising 50–69; early referral of high-risk families for genetics and MRI.
- **Screening is not diagnosis:** any symptom (lump, skin or nipple change, nipple discharge, axillary node) needs triple assessment, below, however recent the last normal mammogram.

SHARE WITH PATIENTS: SCREENING QUESTIONS

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

A breast ultrasound is as good as a mammogram for screening?

Normal mammogram, safe for life?

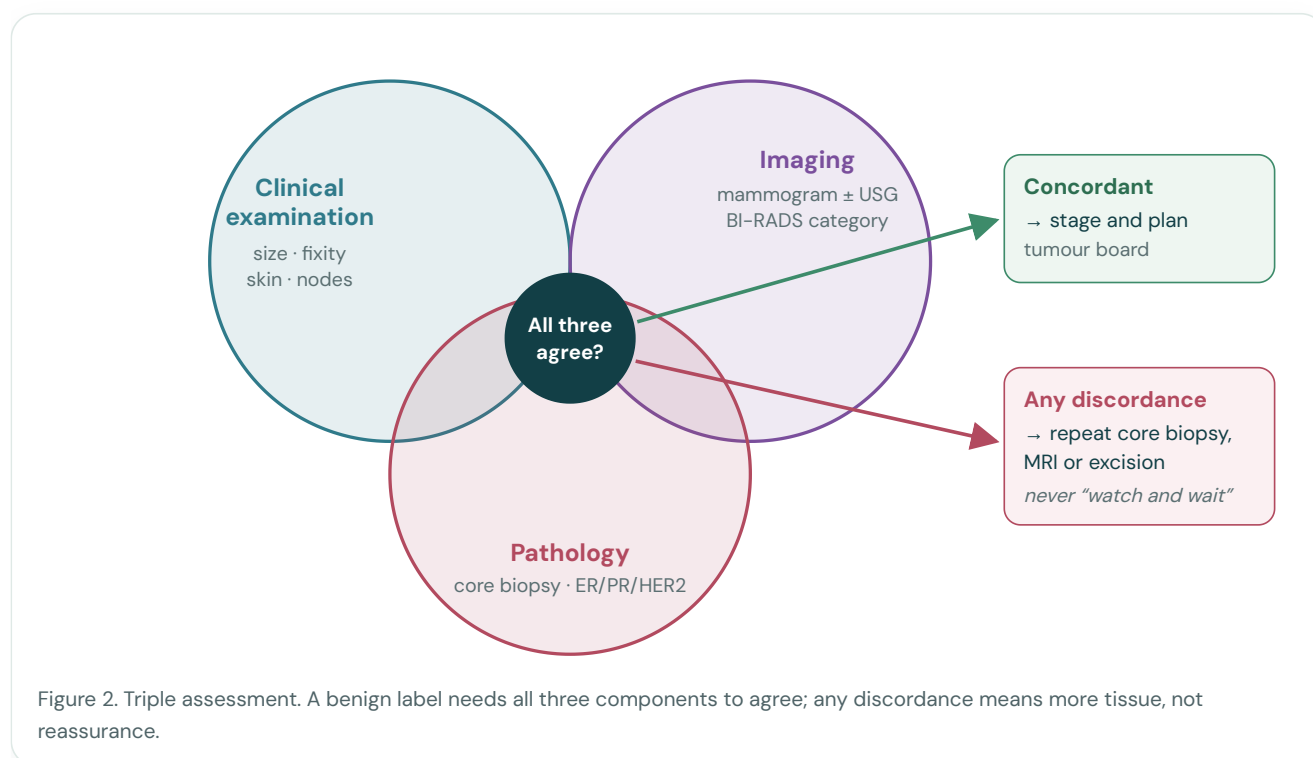
Mammogram radiation is dangerous?

Examining my own breasts every month is enough; I don't need a check-up?

A thermal (heat) scan can replace a mammogram?

More screening tests always mean better cancer prevention?

Diagnosis and staging



- **Image first, then core biopsy.** Diagnostic mammography from age 40 (ultrasound first under 30; either at 30–39). A clinically suspicious lump needs biopsy even if imaging is normal. Open surgical biopsy only if needle biopsy is not possible.
- Breast MRI is not routine: it finds more disease but has not improved survival or local control, and can increase mastectomy rates and delay treatment.
- Pathology: histology, grade, ER and PR (with percentage), and HER2 by IHC with ISH for IHC 2+ (ASCO/CAP). Lobular cancers (5–10%) are more often multicentric or bilateral, relapse late, and spread to unusual sites (peritoneum, GI tract, meninges).

- Axilla: examine every patient. Ultrasound with needle biopsy of any abnormal node, and always before neoadjuvant therapy; clip the biopsied node.
- **Systemic staging** only for clinical stage III, inflammatory cancer, or symptoms or abnormal labs (CT chest/abdomen/pelvis + bone scan, or PET-CT, which upstages more patients). Not for asymptomatic stage I–II.
- Inflammatory cancer also needs a full-thickness skin biopsy (dermal lymphatic invasion).
- Stage with AJCC 8th edition: clinical (cTNM), pathological (pTNM) and post-neoadjuvant (ypTNM). The prognostic stage assumes effective treatment (anti-HER2 therapy, endocrine therapy); when a patient cannot access it, the stage overstates her outlook.
- Genetic counselling and testing criteria: see section O2.
- Before gonadotoxic therapy, refer young women for fertility preservation (embryo or oocyte freezing). GnRH agonists are not a substitute for proven methods.

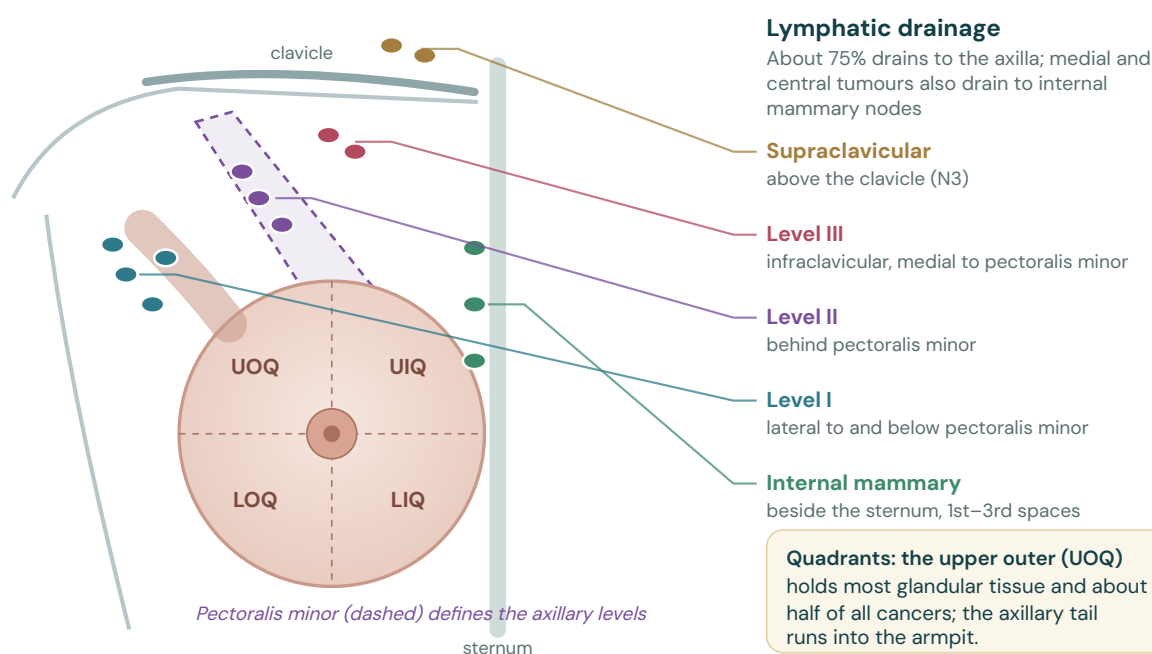


Figure 3. Breast anatomy and lymphatic drainage (patient's right breast, front view). Axillary levels are defined by their relation to pectoralis minor; these stations underpin sentinel-node biopsy, axillary dissection, nodal radiotherapy and N staging.

T: primary tumour (circles drawn to scale)**T4: any size, with**

T4a chest-wall invasion (not pectoralis alone)
 T4b skin ulceration, satellite nodules or oedema
 T4c both a and b
 T4d inflammatory carcinoma

N: regional nodes (clinical)

N1 Movable ipsilateral level I–II axillary nodes

N2 Fixed or matted level I–II nodes, or internal mammary nodes without axillary nodes

N3 Level III (infraclavicular) nodes; or internal mammary plus axillary; or supraclavicular nodes

M1: distant metastasis (bone, liver, lung, brain, distant nodes). Pathological N (pN) counts positive nodes: pN1 1–3, pN2 4–9, pN3 ≥10.

Anatomic stage groups (simplified)

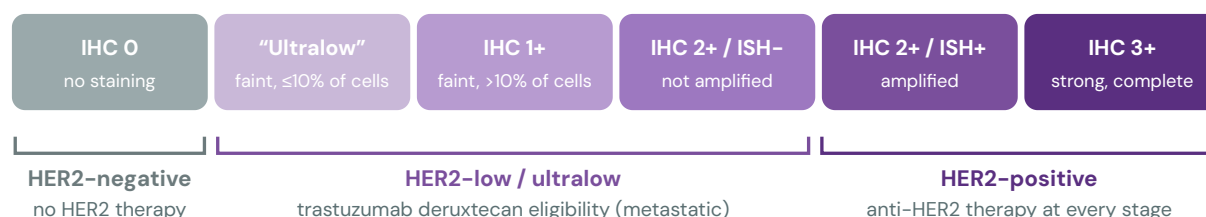
AJCC 8th edition prognostic stage also uses grade, ER, PR and HER2, and the recurrence score for small HR+ node-negative tumours. Use it whenever these biomarkers are known.

Figure 4. TNM staging at a glance (AJCC 8th edition, simplified). Size is drawn to scale; T4 depends on skin or chest-wall involvement, not size.

04 Biomarkers that change treatment

- **ER/PR $\geq 1\%$** → endocrine therapy. ER-low (1–10%) often behaves like TNBC.
- **HER2-positive** (IHC 3+, or ISH ratio ≥ 2.0 with ≥ 4 copies/cell) → HER2-directed therapy at every stage. HER2 status should not be used to withhold or choose endocrine therapy.
- **HER2-low** (IHC 1+ or 2+/ISH-) and **ultralow** (faint staining in $\leq 10\%$ of cells) → trastuzumab deruxtecan eligibility in metastatic disease. IHC 0 versus 1+ is poorly reproducible, so ask for a careful re-read when it matters.
- **21-gene recurrence score** (HR+/HER2-, node-negative or 1–3 nodes) → whether chemotherapy adds benefit (see section 06 and Algorithm 2).
- **Germline *BRCA1/2*** → adjuvant olaparib in high-risk HER2- disease; PARP inhibitor in metastatic disease (also reasonable for germline *PALB2* or somatic *BRCA* mutations).
- ***PIK3CA/AKT1/PTEN* and *ESR1*** (HR+ metastatic; test tissue and/or ctDNA, and repeat ctDNA at progression for *ESR1*) → PI3K/AKT-pathway inhibitors or oral SERDs (see section 06 and Algorithm 2).
- **PD-L1 CPS ≥ 10** (22C3; metastatic TNBC) → pembrolizumab in first line. Early TNBC uses pembrolizumab regardless of PD-L1.
- **Re-biopsy the first metastasis.** Receptor status changes in a meaningful minority (HER2 discordance 2–25%).

Increasing HER2 protein expression →



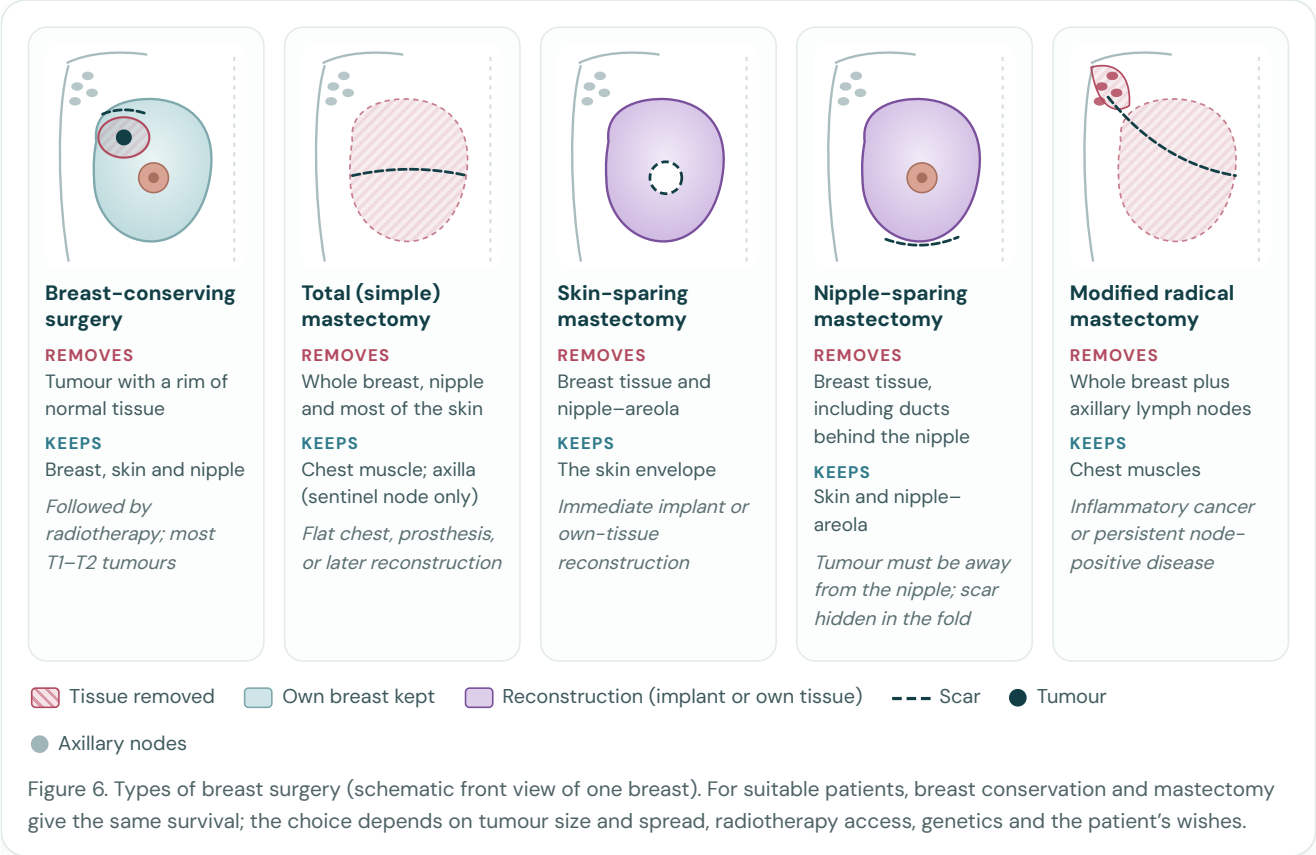
IHC 0 versus 1+ is poorly reproducible between pathologists.

When it decides treatment, ask for a careful re-read, or re-test the metastasis.

Figure 5. HER2 is a spectrum. ASCO/CAP scoring defines HER2-positive; the newer "low" and "ultralow" groups matter only for antibody–drug conjugates in metastatic disease.

05 Local therapy: surgery & radiotherapy

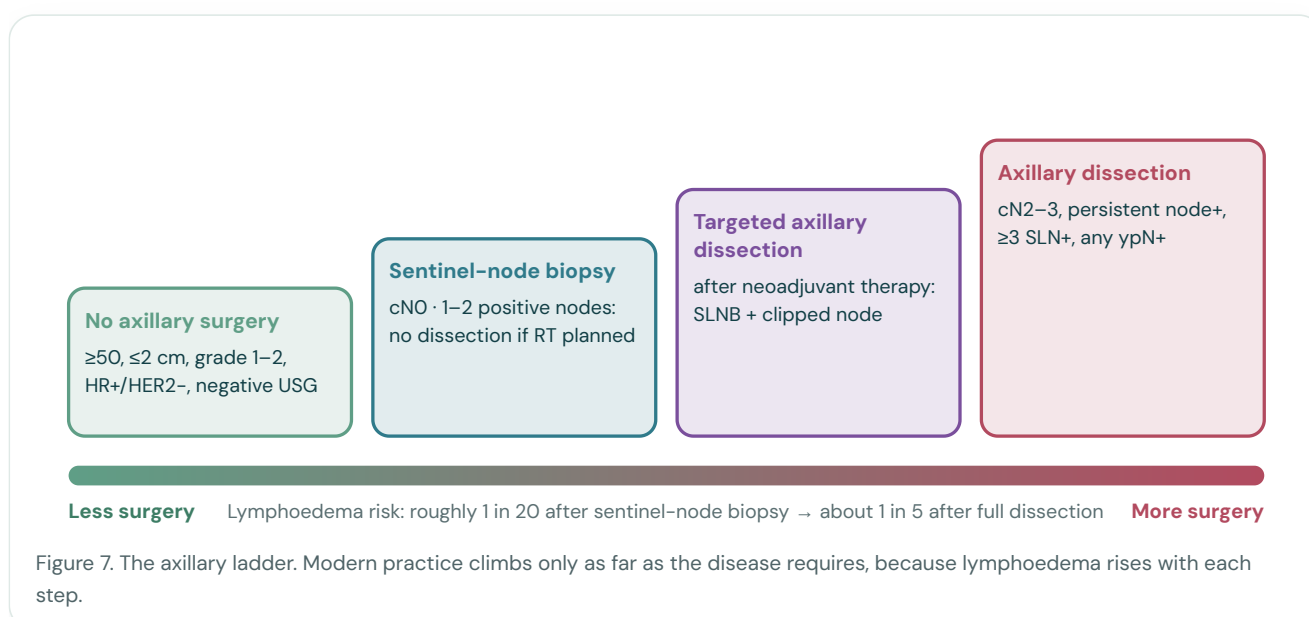
Surgery: types, pros and cons



Procedure	Best suited to	Advantages	Disadvantages
Breast-conserving surgery (wide local excision ± oncoplastic techniques) + radiotherapy	Most T1–T2 tumours, and many after neoadjuvant downstaging	Survival equal to mastectomy (NSABP B-06 ^[4] ; Milan trial ^[5]); better body image; shorter recovery	Needs radiotherapy; re-excision for margins in a minority; lifelong surveillance of the treated breast
Total (simple) mastectomy	Multicentric disease, diffuse calcifications, large tumour-to-breast ratio, radiotherapy unavailable or contraindicated, patient choice	May avoid radiotherapy in low-risk disease; single procedure	Loss of the breast; prosthesis or reconstruction needed; no survival advantage
Skin- or nipple-sparing mastectomy with immediate reconstruction	Early disease or risk-reducing surgery; nipple-sparing only when the tumour is away from the nipple	Best cosmetic result with mastectomy; one operation	Longer surgery, flap or implant complications; needs oncoplastic or plastic expertise; radiotherapy raises implant complication rates
Modified radical mastectomy (mastectomy + axillary dissection)	Inflammatory cancer; persistent node-positive disease	Maximal local clearance	Highest lymphoedema and shoulder morbidity

Procedure	Best suited to	Advantages	Disadvantages
Reconstruction: implant or autologous (DIEP, latissimus dorsi), immediate or delayed	Any patient who wants it, if fit	Body image and quality of life	Additional surgery; autologous needs microsurgical skill; timing interacts with radiotherapy

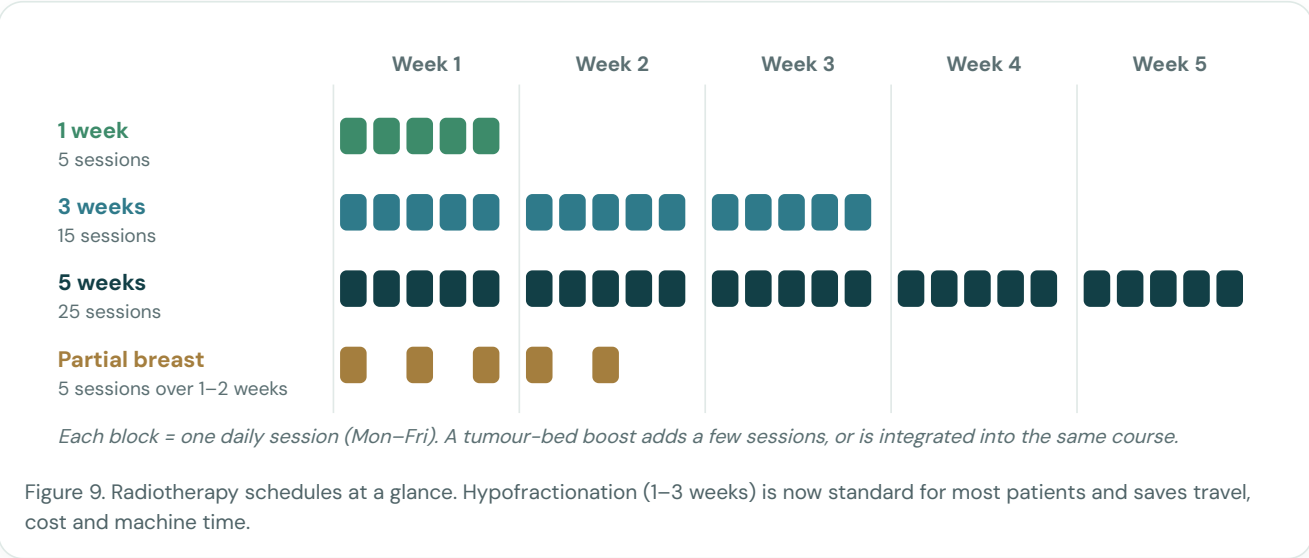
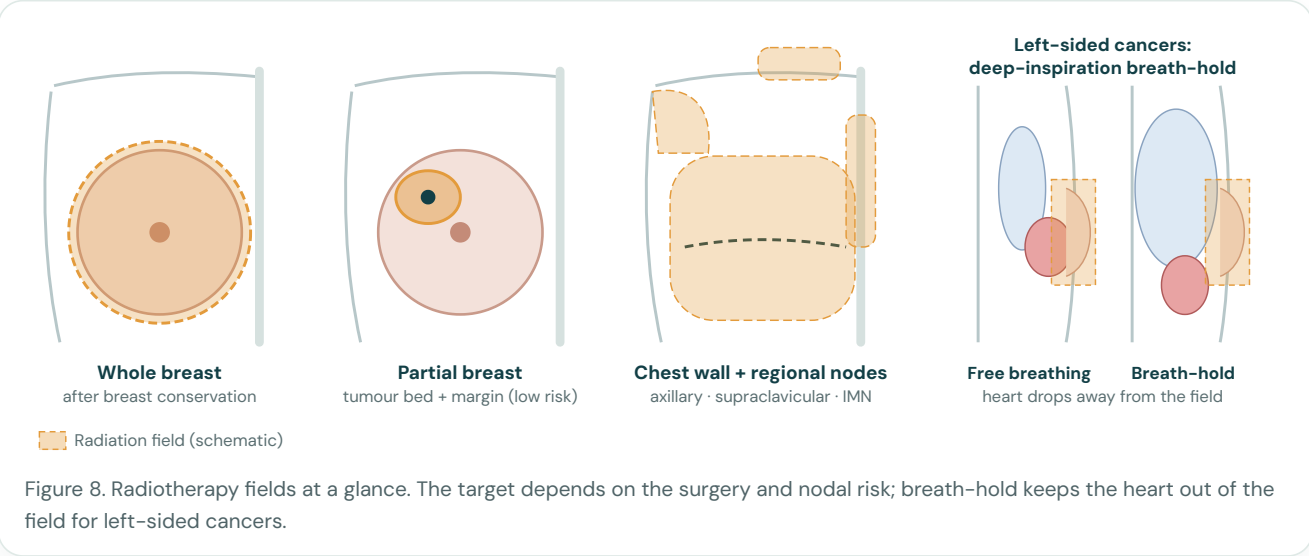
- **Margins:** “no ink on tumour” is adequate for invasive cancer after breast conservation; 2 mm for DCIS. Wider margins do not lower recurrence.
- **Breast conservation is not advised** for multicentric disease, diffuse suspicious calcifications, persistently positive margins, prior chest radiotherapy, inflammatory cancer, or when radiotherapy is not possible.
- **Axilla**, from least to most surgery:
 - No axillary surgery: selected women ≥ 50 with ≤ 2 cm, grade 1–2, HR+/HER2– cancer and a negative axillary ultrasound ([SOUND](#)^[6], [INSEMA](#)^[7]).
 - Sentinel-node biopsy for cNO. With 1–2 positive sentinel nodes and planned whole-breast or chest-wall radiotherapy, no dissection ([ACOSOG Z0011](#)^[8], [AMAROS](#)^[9]).
 - After neoadjuvant therapy: sentinel-node biopsy (dual tracer) plus removal of the clipped node (targeted axillary dissection).
 - Axillary dissection: cN2–3, persistent node-positive disease, ≥ 3 positive sentinel nodes, any positive node after neoadjuvant therapy.
- **Lymphoedema risk** is far lower with sentinel-node biopsy than with axillary dissection.



Radiotherapy: when, how, and how long

- **After breast conservation:** almost always, which halves local recurrence and lowers breast cancer death ([EBCTCG radiotherapy meta-analysis](#)^[10]). It may be omitted in women ≥ 65 –70 with small, node-negative, HR+ cancers who will take endocrine therapy ([PRIME II](#)^[11], [CALGB 9343](#)^[12]).
- **After mastectomy:** for ≥ 4 positive nodes, T3–T4 or positive margins; usually for 1–3 positive nodes ([EBCTCG](#)^[13]).
- **Regional nodal radiotherapy** for node-positive or high-risk node-negative disease ([MA.20](#)^[14], [EORTC 22922](#)^[15]).

- **After neoadjuvant therapy:** decide on the initial stage and the response. In cN1 disease that became ypNO, nodal radiotherapy did not reduce recurrence ([NSABP B-51^{\[16\]}](#)).
- **Boost** to the tumour bed for younger women, high grade or close margins: either sequential (extra sessions) or simultaneous integrated within the same course.
- **Timing:** after chemotherapy, or within about 8 weeks of surgery if no chemotherapy is given. Endocrine and HER2 therapy can run alongside.



Schedule	Sessions	Typical use	Evidence
1 week	5 daily sessions	Whole breast after breast conservation; chest wall without reconstruction; partial breast in low-risk disease. Nodal use is supported by quality-of-life data, with disease-control results awaited.	FAST-Forward^[17] · IMPORT LOW^[18] · HYPORT-Adjuvant (India)^[19]
3 weeks	15–16 sessions	Current standard for breast, chest wall and regional nodes, including after reconstruction in most centres	START-B (START^[20]) · Ontario trial^[21]
5 weeks	25 sessions	Now selective: some implant reconstructions, complex anatomy or re-irradiation, and certain proton or trial protocols	Conventional fractionation; largely replaced by hypofractionation (ASTRO, ESTRO guidance)

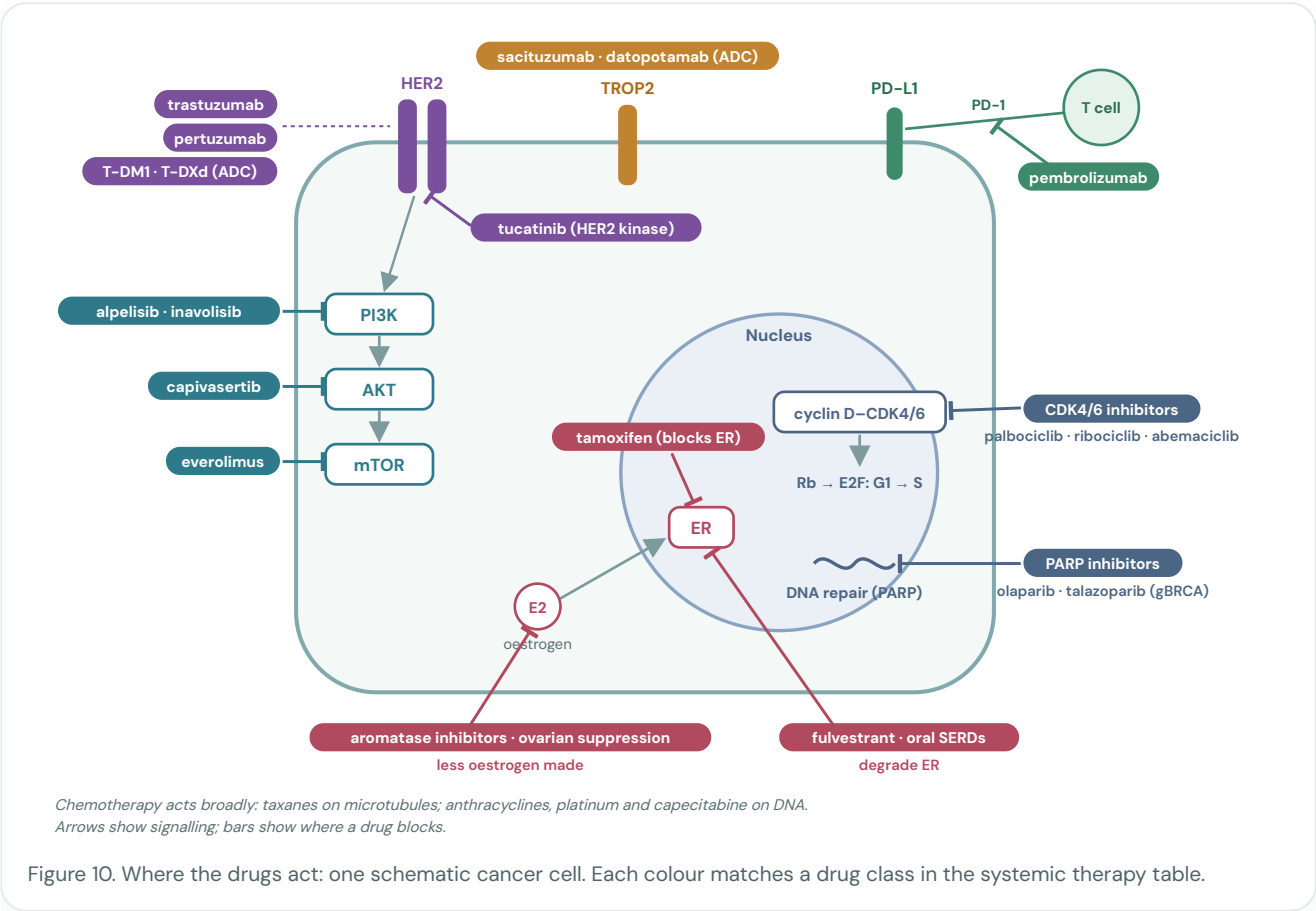
Schedule	Sessions	Typical use	Evidence
Partial breast	5 sessions over 1–2 weeks	Low-risk: older age, small, node-negative, HR+, clear margins, not lobular-extensive	IMPORT LOW^[18] · Florence trial^[22]

Precision photon radiotherapy versus protons

- **Precision photon techniques** (3D-conformal tangents, IMRT/VMAT, image guidance, and **deep-inspiration breath-hold** for left-sided cancers) keep heart and lung doses low for the vast majority of patients. This is the standard.
- **Proton therapy** has no exit dose, so it can lower heart and lung dose further. Consider it when photons cannot meet heart or lung limits: left-sided cancers needing internal mammary nodal treatment, unfavourable chest anatomy, bilateral treatment, re-irradiation, or young patients with high cardiac risk.
- Limits of protons: higher cost, availability at very few Indian centres, more skin reaction and reconstruction complications in some series. Randomised evidence on hard outcomes (for example [RADCOMP^{\[23\]}](#)) is still maturing.
- Inflammatory cancer always receives post-mastectomy radiotherapy, even after complete response.

o6 Systemic therapy: indications & options

No doses are given here. Options are matched to the evidence; each trial name links to the PubMed record of its primary publication.



Drug classes and where they are used

Class	Options	Indication / setting	Key evidence
Endocrine therapy	Tamoxifen; aromatase inhibitors (letrozole, anastrozole, exemestane); ovarian suppression (GnRH agonist or oophorectomy); fulvestrant; oral SERDs (elacestrant and newer agents)	All HR+ disease: adjuvant 5–10 years; metastatic backbone	EBCTCG tamoxifen ^[24] · EBCTCG aromatase inhibitors ^[25] · SOFT/TEXT ^[26] · EMERALD ^[27]
CDK4/6 inhibitors	Abemaciclib, ribociclib, palbociclib	High-risk early HR+ (abemaciclib, ribociclib); first-line metastatic HR+	monarchE ^[28] · NATALEE ^[29] · MONALEESA-2/3/7 ^[30] · MONARCH 3 ^[31] · PALOMA-2 ^[32]
PI3K/AKT/mTOR inhibitors	Capivasertib, alpelisib, inavolisib; everolimus	HR+ metastatic, by <i>PIK3CA</i> / <i>AKT1</i> / <i>PTEN</i> status	CAPItello-291 ^[33] · SOLAR-1 ^[34] · INAVO120 ^[35] · BOLERO-2 ^[36]
PARP inhibitors	Olaparib, talazoparib	<i>gBRCA</i> : high-risk early HER2– (olaparib, 1 year); metastatic HER2–	OlympiA ^[37] · OlympiAD ^[38] · EMBRACA ^[39]

Class	Options	Indication / setting	Key evidence
HER2-directed	Trastuzumab (and biosimilars), pertuzumab, T-DM1, trastuzumab deruxtecan, tucatinib	All HER2+ settings; trastuzumab deruxtecan also for HER2-low/ultralow metastatic	HERA ^[40] · APHINITY ^[41] · KATHERINE ^[42] · DESTINY-Breast05 ^[43] · CLEOPATRA ^[44] · DESTINY-Breast03 ^[45] · HER2CLIMB ^[46] · DESTINY-Breast04 ^[47] · DESTINY-Breast06 ^[48]
Immunotherapy	Pembrolizumab	Stage II–III TNBC (neoadjuvant and adjuvant); metastatic TNBC with PD-L1 CPS ≥10	KEYNOTE-522 ^[49] · KEYNOTE-355 ^[50]
Other antibody–drug conjugates	Sacituzumab govitecan, datopotamab deruxtecan	Metastatic TNBC (first line or later); pretreated HR+ metastatic	ASCENT ^[51] · ASCENT-04 ^[52] · TROPICS-02 ^[53] · TROPION-Breast01 ^[54]
Chemotherapy	Anthracyclines, taxanes, cyclophosphamide, platinum, capecitabine; eribulin, vinorelbine, gemcitabine later	Neoadjuvant or adjuvant for higher-risk disease; post-neoadjuvant capecitabine in TNBC; metastatic after targeted options	EBCTCG chemotherapy ^[55] · Dose-dense EBCTCG ^[56] · CREATE-X ^[57]
Bone-modifying agents	Zoledronic acid and other bisphosphonates; denosumab	Adjuvant in postmenopausal women; bone metastases; AI-related bone loss	EBCTCG bisphosphonates ^[58]

Indications by setting

Setting	HR+ / HER2–	HER2+	Triple-negative
Neoadjuvant	Locally advanced or to enable breast conservation: chemotherapy; neoadjuvant endocrine therapy for older or unfit patients	cT2+ or node-positive: taxane–carboplatin (or anthracycline-based) chemotherapy + trastuzumab + pertuzumab (TRAIN-2 ^[59] , NeoSphere ^[60])	Stage II–III: carboplatin–paclitaxel then anthracycline–cyclophosphamide, with pembrolizumab (KEYNOTE-522)
Adjuvant (upfront surgery)	Endocrine therapy for all; chemotherapy by recurrence score and clinical risk (TAILORx ^[61] , RxPONDER ^[62]); dose-dense AC then paclitaxel for higher risk, TC for lower risk or ≥65	T1NO (<2 cm): weekly paclitaxel + trastuzumab (APT ^[63]); larger or node-positive: chemotherapy + trastuzumab ± pertuzumab, 1 year in total	>0.5 cm or node-positive: anthracycline–taxane chemotherapy (TC for lower risk)
After neoadjuvant therapy	Endocrine therapy ± CDK4/6 inhibitor; capecitabine not used for HR+ residual disease	pCR: complete 1 year of trastuzumab ± pertuzumab; residual in the breast: T-DM1; residual nodes or initially inoperable: trastuzumab deruxtecan	Continue pembrolizumab; residual disease: olaparib (gBRCA) or capecitabine
High-risk add-ons	Abemaciclib (2 years) or ribociclib (3 years); ovarian suppression if premenopausal; olaparib if gBRCA; bisphosphonate if postmenopausal	Extended neratinib is an option for HR+/HER2+ high risk (ExteNET ^[64])	Olaparib if gBRCA (OlympiaA)

Setting	HR+ / HER2-	HER2+	Triple-negative
Metastatic	Endocrine + CDK4/6 inhibitor; then by <i>ESR1</i> /PI3K pathway/ <i>gBRCA</i> ; then ADCs and chemotherapy (see Algorithm 2)	Taxane + trastuzumab + pertuzumab, then trastuzumab deruxtecan, then T-DM1 or tucatinib-based therapy	PD-L1 CPS ≥ 10 : pembrolizumab + sacituzumab or chemotherapy; otherwise an ADC or chemotherapy; PARP inhibitor if <i>gBRCA</i>

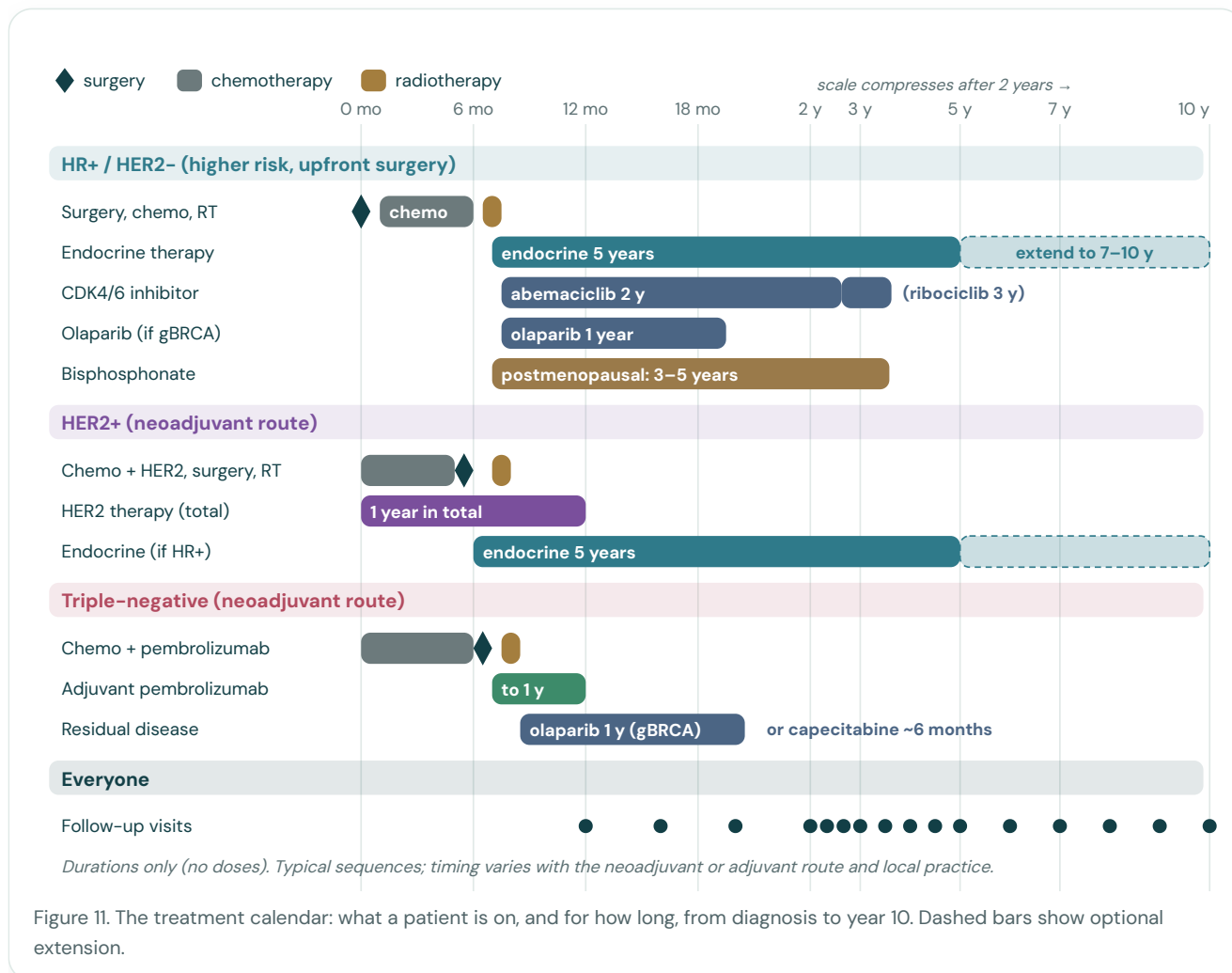


Figure 11. The treatment calendar: what a patient is on, and for how long, from diagnosis to year 10. Dashed bars show optional extension.

- **Durations** (not doses): endocrine therapy 5 years minimum (7–10 for stage II–III); HER2 therapy 1 year; abemaciclib 2 years; ribociclib 3 years; olaparib 1 year. Start adjuvant chemotherapy within 4–6 weeks of surgery.
- **Older patients:** base decisions on fitness and life expectancy, not age (use geriatric assessment and toxicity tools); non-anthracycline regimens are usually preferred.
- **Monitoring:** echocardiography during HER2 therapy; check lung symptoms on trastuzumab deruxtecan (interstitial lung disease); immune-related effects (including late endocrine effects) with pembrolizumab; diarrhoea, neutropenia and liver tests with CDK4/6 inhibitors.

07 Management algorithms

These decision paths pull together sections O2–O6: presentation, workup, biomarkers, local and systemic therapy. Follow the colour of the subtype.

ALGORITHM 1

Early (non-metastatic) breast cancer

Suspicious lump or abnormal mammogram

Imaging, then **core biopsy**: histology, grade, ER/PR, HER2 · axillary ultrasound ± node biopsy (clip it) · systemic staging only for stage III, inflammatory cancer or symptoms · genetic counselling · fertility referral if young

HR+ / HER2-

Upfront surgery for most:
breast conservation + RT, or
mastectomy · sentinel-node
biopsy if cNO

*Locally advanced → neoadjuvant
chemotherapy · older/unfit →
neoadjuvant endocrine therapy*

Chemotherapy? (21-gene
recurrence score)

NO: RS ≤15 (any age) or ≤25 (>50)
→ no chemo · ≤50 with RS 16–25
→ chemo or ovarian suppression
· RS ≥26 → chemo

1–3 nodes: postmenopausal, RS
≤25 → no chemo ·
premenopausal → chemo (or
OFS + AI)

≥4 nodes / stage III → chemo

Endocrine therapy 5–10 years:
AI if postmenopausal · OFS +
AI/tamoxifen for higher-risk
premenopausal

High risk → + abemaciclib or
ribociclib · gBRCA → olaparib ·
postmenopausal →
bisphosphonate

HER2+

cT2+ or node-positive →
neoadjuvant taxane–carboplatin
+ trastuzumab + pertuzumab

cT1 NO → surgery → weekly
paclitaxel + trastuzumab (1 year)

Surgery after neoadjuvant
therapy

pCR → complete 1 year
trastuzumab (± pertuzumab)

Residual, breast only → T-DM1

**Residual nodes / initially
inoperable** → trastuzumab
deruxtecan

HR+ → add endocrine therapy ·
echo monitoring throughout

TRIPLE-NEGATIVE

≤0.5 cm, NO → surgery; chemo
usually not needed

Stage I (>0.5 cm) →
chemotherapy, before or after
surgery

Stage II–III → neoadjuvant
chemotherapy + pembrolizumab

Surgery

pCR → complete pembrolizumab

Residual disease →
pembrolizumab + olaparib
(gBRCA) or capecitabine

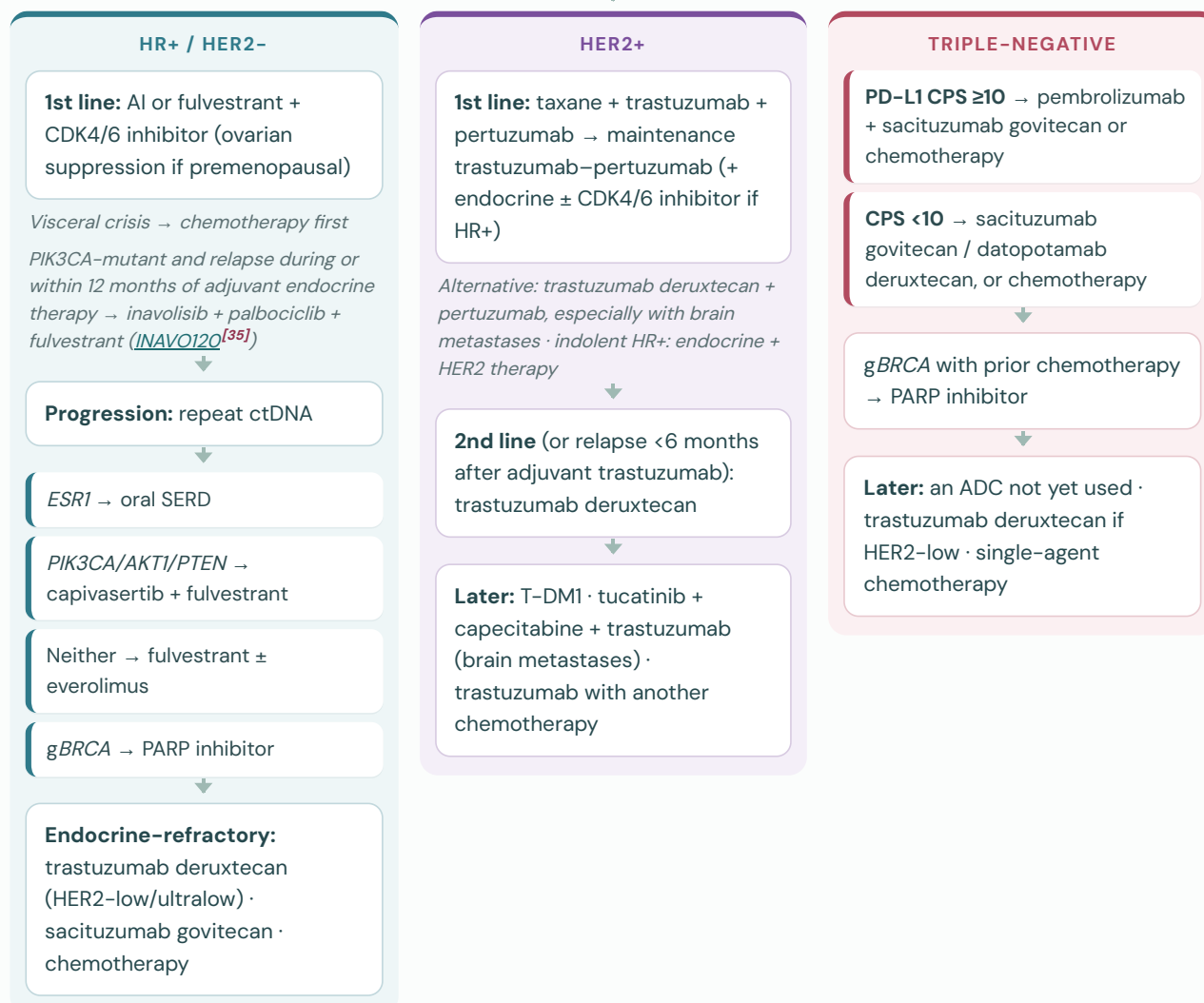
Germline testing for all TNBC up
to age 60 (ASCO-SSO: ≤65)

All patients: radiotherapy after breast conservation; post-mastectomy radiotherapy for high-risk disease · inflammatory cancer → neoadjuvant chemotherapy, modified radical mastectomy, radiotherapy.

ALGORITHM 2

Metastatic breast cancer

New metastatic disease: biopsy a metastasis to re-check ER/PR/HER2 · germline *BRCA* · PD-L1 (TNBC) · *PIK3CA/AKT1/PTEN/ESR1* (HR+; tissue or ctDNA)



All patients: bone-modifying agent for bone metastases · palliative care from the start · local therapy (radiotherapy, surgery) for symptoms or emergencies · check drug access and cost in India early.

o8 Survivorship, follow-up & reducing recurrence

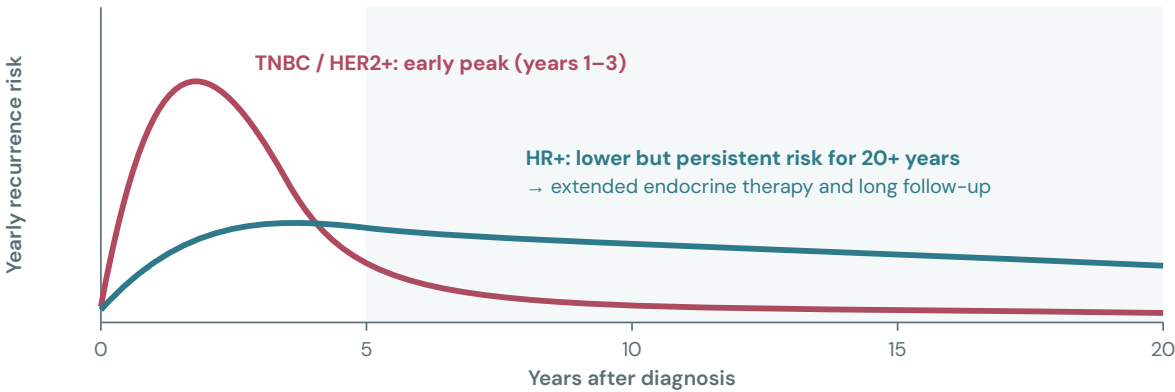


Figure 12. When relapses happen (illustrative shape, not to scale). Follow-up intensity and education should match the subtype.

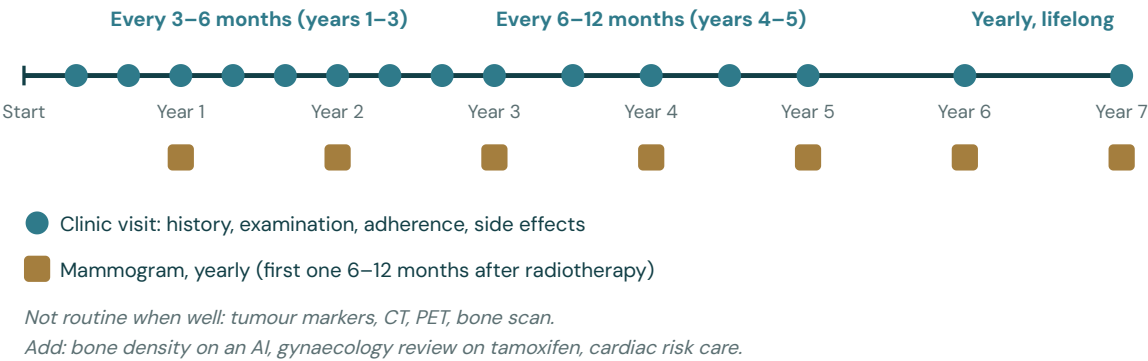


Figure 13. A simple follow-up rhythm (ASCO/ACS). Symptoms, not scheduled scans, trigger investigations.

Follow-up protocol (ASCO/ACS survivorship guidance)

What	How often	Notes
History and examination	Every 3–6 months for years 1–3; every 6–12 months for years 4–5; then yearly	Include breast, chest wall, nodes, arm; review symptoms, adherence and side effects
Mammography	Yearly (first one 6–12 months after radiotherapy if breast conserved)	Contralateral breast after mastectomy; no routine imaging of a reconstructed breast
Breast MRI	Only for high-risk survivors	Gene carriers, chest radiotherapy before 30, or dense breasts with other risk after discussion
Blood tests, tumour markers, CT, PET or bone scan	Not in asymptomatic patients	Randomised trials of intensive surveillance showed no survival benefit (GIVIO^[65] ; Rosselli Del Turco^[66]); investigate symptoms promptly instead
Bone density	Baseline and every 1–2 years on aromatase inhibitors or ovarian suppression	Calcium, vitamin D, exercise; bisphosphonate or denosumab if bone loss
Gynaecological review	Yearly on tamoxifen	Report any vaginal bleeding; routine endometrial ultrasound is not needed

What	How often	Notes
Cardiovascular risk	Yearly	After anthracyclines, trastuzumab or left-sided radiotherapy: control blood pressure, lipids, diabetes and weight; echo if symptoms
Genetic counselling	Once, if not already done	Cascade testing of relatives when a variant is found

Reducing the risk of recurrence

- **Complete the planned treatment.** Endocrine non-adherence is common (a large minority stop early) and is linked to more recurrences. Ask about it at every visit and manage side effects actively (joint pain, hot flushes, vaginal dryness).
- **Extended endocrine therapy** (7–10 years) for stage II–III disease if tolerated.
- **Adjuvant bisphosphonate** in postmenopausal women reduces bone recurrence and breast cancer death (EBCTCG).
- **Targeted add-ons** for eligible high-risk patients: CDK4/6 inhibitor, olaparib (gBRCA), or post-neoadjuvant T-DM1, trastuzumab deruxtecan or capecitabine.
- **Lifestyle** (associated with lower recurrence and mortality): at least 150 minutes a week of moderate activity plus strength work, healthy weight, minimal alcohol, and no smoking. Randomised outcome trials are ongoing (for example [BWEL](#) ^[67]).
- **Avoid systemic hormone replacement.** Treat hot flushes non-hormonally; avoid strong CYP2D6 inhibitors (paroxetine, fluoxetine) with tamoxifen, using venlafaxine or gabapentin instead.
- Gene carriers: discuss contralateral risk-reducing mastectomy and salpingo-oophorectomy at the recommended ages.
- **Teach red-flag symptoms** to report promptly: a new lump or swelling, persistent bone pain, cough or breathlessness, abdominal pain or jaundice, headache or neurological symptoms, unexplained weight loss.

Late effects and quality of life

- **Lymphoedema:** measure both arms before surgery, screen high-risk patients, and refer early for compression and physiotherapy. New swelling years later needs a search for recurrence.
- **Other late effects:**
 - Taxane neuropathy: duloxetine may help.
 - Cardiotoxicity, fatigue and cognitive complaints: exclude anaemia, thyroid disease, depression and poor sleep first.
 - Weight gain.
- **Menopause and sexual health:** non-hormonal lubricants and moisturisers first; ask routinely.
- **Fertility and pregnancy:** chemotherapy-related amenorrhoea is not menopause, so use non-hormonal contraception (a copper IUD). Pregnancy does not appear to raise recurrence risk; about 2 years from diagnosis is usual, and the [POSITIVE](#) ^[68] study supports a planned endocrine pause.
- **Second cancers** (rare, but recognise them):
 - Endometrial cancer on tamoxifen.
 - Myeloid neoplasms after anthracyclines.
 - Angiosarcoma of the irradiated breast.

- Contralateral breast cancer.
- **Psychological:** fear of recurrence, depression, and return to work; offer counselling and peer support.
- Give every patient a **treatment summary and survivorship care plan**, and share care with the family physician.

SHARE WITH PATIENTS: AFTER TREATMENT

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[Once I feel fine, I can stop the hormone tablets?](#)

[Breast cancer, once treated, never comes back?](#)

[After breast cancer, no children?](#)

[Chemo means losing your hair forever?](#)

[Breast cancer is a death sentence?](#)

09 Landmark trials

- **TAILORx**^[61] and **RxPONDER**^[62]: can the 21-gene score spare chemotherapy in HR+/HER2- disease? Yes for most postmenopausal women (node-negative, or 1–3 nodes with a score ≤ 25); younger women with intermediate scores still gained. → Chemotherapy is now selective; menopausal status shapes the call.
- **monarchE**^[28]: does 2 years of abemaciclib help high-risk node-positive HR+ disease? Invasive disease-free survival improved (7-year 77% vs 71%), with a small overall survival gain (86.8% vs 85.0%). → An option for high-risk patients; weigh the diarrhoea and cost.
- **KATHERINE**^[42] and **DESTINY-Breast05**^[43]: what should follow residual HER2+ disease after neoadjuvant therapy? T-DM1 beat trastuzumab, including for survival. Trastuzumab deruxtecan then beat T-DM1 in residual node-positive or initially inoperable disease (3-year invasive disease-free survival 92% vs 84%), with more lung toxicity (about 10%). → Response-adapted adjuvant therapy.
- **KEYNOTE-522**^[49]: adding pembrolizumab to neoadjuvant chemotherapy in stage II–III TNBC raised pCR and improved event-free and overall survival (about 5 percentage points at 5 years). → New standard; monitor for lasting immune toxicity.
- **DESTINY-Breast04**^[47]: trastuzumab deruxtecan versus chemotherapy in pretreated HER2-low metastatic disease improved both PFS and OS. → Created the HER2-low category; watch for interstitial lung disease.

10 Practice pearls & pitfalls

- Lumps excised before imaging and core biopsy remain common in India. This compromises staging, neoadjuvant options and breast conservation: biopsy first.
- Read benefit in **absolute** terms, and separate PFS from overall survival when weighing cost and toxicity.
- Without an affordable genomic test, decide on clinicopathological risk (age, grade, size, nodes, Ki-67) and record the reasoning. Biosimilar trastuzumab makes a full year of HER2 therapy feasible; discuss cost early so treatment is not abandoned midway.
- Chemotherapy-induced amenorrhoea is not menopause: confirm before switching to an aromatase inhibitor, and advise non-hormonal contraception. Use G-CSF with docetaxel-containing or dose-dense regimens.
- Many newer agents (oral SERDs, capivasertib, inavolisib, newer ADCs) may not be approved or affordable in India yet. Check access early and prioritise options with proven overall-survival benefit.
- Male breast cancer: always offer genetic testing. Tamoxifen is preferred for adjuvant endocrine therapy; if an AI is used, add a GnRH agonist.

11 Case vignettes: lines of management

Seven cases, written for postgraduates and practising clinicians. Read the presentation, decide on stage, workup and plan, then open the line of management. No doses are given; durations follow the evidence.

CASE 1 Triple-negative · early

Young woman, node-positive TNBC, family history of ovarian cancer

34 years

cT2 N1 (stage IIB)

ER O · PR O · HER2 O

gBRCA1+

A 34-year-old woman with no children has a painless 3 cm lump in the right breast for 6 weeks. Her mother had ovarian cancer at 48. On examination there is a 3.2 cm mass and a mobile 1.5 cm axillary node.

Before you open the answer: what is the stage, what must be done before treatment, and what is the plan?

1

WORKUP

Bilateral mammography and ultrasound. Core biopsy: invasive ductal carcinoma, grade 3, ER O, PR O, HER2 IHC O, Ki-67 70%. Ultrasound-guided biopsy of the node: positive. Clip both the tumour and the node before any treatment. Staging scans are optional at cT2N1; many centres image before neoadjuvant therapy, and here they were clear.

2

BEFORE TREATMENT

Germline testing (TNBC under 60 plus family history): pathogenic *BRCA1* variant. Urgent fertility referral for oocyte or embryo freezing (about 2 weeks; it does not meaningfully delay treatment). Baseline echo, thyroid and adrenal function before immunotherapy.

3

SYSTEMIC FIRST

Stage II TNBC: neoadjuvant chemotherapy with pembrolizumab (carboplatin–paclitaxel, then anthracycline–cyclophosphamide), as in KEYNOTE–522.

4

SURGERY

Discuss the options openly. Breast conservation is oncologically safe, but as a *BRCA1* carrier her risk of new cancers in both breasts is high, so many women choose bilateral mastectomy with reconstruction. Axilla: if the node becomes clinically negative, sentinel-node biopsy with dual tracer plus removal of the clipped node; any residual nodal disease means axillary dissection.

5

AFTER SURGERY

pCR: complete a year of pembrolizumab. Residual disease: continue pembrolizumab and add olaparib for 1 year (gBRCA, OlympiA). Capecitabine is the alternative without a *BRCA* variant.

6

RADIOTHERAPY

Always after breast conservation; after mastectomy, decide on initial stage and response. If the node becomes ypN0, nodal radiotherapy may be omitted (NSABP B–51).

7

LONG TERM

Risk-reducing salpingo-oophorectomy around 35–40 once her family is complete; MRI plus mammography of any remaining breast tissue; cascade testing of sisters and other relatives; non-hormonal contraception; a pregnancy discussion after about 2 years; watch for late immune effects (thyroid, adrenal).

TEACHING POINTS

- Every TNBC diagnosed at 60 or younger needs germline testing; the result changes surgery, adjuvant therapy and her family's care.
- Fertility referral must happen in the first week, before chemotherapy starts.
- Response to neoadjuvant therapy decides adjuvant treatment, which is why stage II–III TNBC is treated systemically first.

See: Sections 02 (genetics), 05, 06 · Algorithm 1 · [KEYNOTE-522](#)^[49], [OlympiA](#)^[37], [NSABP B-51](#)^[16]

CASE 2 HR+ / HER2- · early**Screen-detected cancer with one positive sentinel node**

58 years, postmenopausal

pT1c N1a (stage IIA)

ER 90% · PR 60% · HER2 1+

Recurrence score 18

A 58-year-old postmenopausal woman has a 1.6 cm spiculated mass on her first screening mammogram. Nothing is palpable, and axillary ultrasound is normal.

Before you open the answer: what is the stage, what must be done before treatment, and what is the plan?

1**WORKUP**

Core biopsy: invasive ductal carcinoma, grade 2, ER 90%, PR 60%, HER2 IHC 1+ (HER2-low has no role in early disease). cT1c N0, stage I: no staging scans.

2**SURGERY FIRST**

Clip-guided breast-conserving surgery with sentinel-node biopsy: 1.6 cm, margins clear, 1 of 2 sentinel nodes with a 3 mm macrometastasis.

3**AXILLA**

Meets ACOSOG Z0011 criteria (cT1–2, 1–2 positive sentinel nodes, breast conservation with whole-breast radiotherapy): no axillary dissection.

4**CHEMOTHERAPY?**

21-gene recurrence score 18. Postmenopausal with 1–3 nodes and a score ≤25: no chemotherapy benefit (RxPONDER). Omit chemotherapy.

5**ENDOCRINE AND ADD-ONS**

Aromatase inhibitor, with a baseline bone density scan. Stage II, so plan 7–10 years if tolerated. Ribociclib for 3 years is an option (NATALEE eligibility includes node-positive stage II); discuss the modest absolute gain against liver tests, ECG checks and cost. She does not meet monarchE criteria for abemaciclib. Adjuvant bisphosphonate (postmenopausal).

6**RADIOTHERAPY**

Whole-breast radiotherapy, 1–3 weeks of hypofractionation; nodal radiotherapy is a centre-level decision with 1 positive node.

7**FOLLOW-UP**

Yearly mammography; ask about adherence and joint pain at every visit; repeat bone density every 1–2 years.

TEACHING POINTS

- One or two positive sentinel nodes no longer mean axillary dissection for most patients.
- Menopausal status changes how the recurrence score is read in node-positive disease.
- If a genomic test is unaffordable, decide on clinical risk (grade, size, nodes, Ki-67) and record the reasoning.

See: Sections 05, 06 · Algorithm 1 · [ACOSOG Z0011](#)^[8], [RxPONDER](#)^[62], [NATALEE](#)^[29]

CASE 3 HER2+ · early**HER2-positive, node-positive, residual disease after neoadjuvant therapy**

45 years, premenopausal

cT2 N1 → ypT1b N1

ER 40% · PR 10% · HER2 3+

LVEF 62%

A 45-year-old premenopausal woman has a 2.8 cm lump and a palpable axillary node.

Before you open the answer: what is the stage, what must be done before treatment, and what is the plan?

1**WORKUP**

Core biopsy: invasive ductal carcinoma, grade 3, ER 40%, PR 10%, HER2 IHC 3+. Node biopsy positive and clipped. cT2 N1, stage IIB. Baseline echocardiogram: LVEF 62%.

2**SYSTEMIC FIRST**

Neoadjuvant taxane–carboplatin with trastuzumab and pertuzumab: anthracycline-free (TRAIN-2), with biosimilar trastuzumab to contain cost. Echo every 3 months.

3**SURGERY**

Partial response. Breast-conserving surgery with targeted axillary dissection: 0.8 cm residual invasive cancer and 1 of 3 nodes positive (ypN1). Residual nodal disease: complete axillary dissection.

4**ADJUVANT HER2 THERAPY**

Residual nodal disease: trastuzumab deruxtecan is preferred (DESTINY-Breast05, 3-year invasive DFS 92% vs 84% against T-DM1). Warn about and screen for interstitial lung disease. T-DM1 (KATHERINE) remains acceptable where access or cost decides. Total HER2 therapy: about 1 year.

5**ENDOCRINE**

Higher-risk premenopausal HR+ disease: ovarian suppression with an aromatase inhibitor (SOFT/TEXT), started after chemotherapy and given alongside HER2 therapy, for 5–10 years.

6**RADIOTHERAPY**

Whole breast plus regional nodes, given alongside HER2 therapy.

7**FOLLOW-UP**

Cardiac monitoring until HER2 therapy ends; bone density on ovarian suppression; non-hormonal contraception; genetic testing (diagnosed at ≤50).

TEACHING POINTS

- HER2+ tumours from cT2 or node-positive go to neoadjuvant therapy so that the adjuvant drug can be matched to the response.
- Never give pertuzumab–trastuzumab together with an anthracycline.
- HR+/HER2+ disease needs both pathways treated: HER2 therapy and endocrine therapy.

See: Sections O4, O6 · Algorithm 1 · [TRAIN-2](#)^[59], [DESTINY-Breast05](#)^[43], [KATHERINE](#)^[42], [SOFT/TEXT](#)^[26]

CASE 4 Trap · inflammatory cancer**The “mastitis” that did not settle**

38 years, 8 months postpartum

cT4d N2 (stage III)

ER 0 · PR 0 · HER2 3+

2 courses of antibiotics

A 38-year-old stopped breastfeeding 2 months ago. For 6 weeks her right breast has been red, swollen and warm despite two courses of antibiotics from a local clinic. She has no fever. Erythema covers more than half the breast with peau d'orange; there is no discrete lump; the axillary nodes are matted.

Before you open the answer: what is the stage, what must be done before treatment, and what is the plan?

1

RECOGNISE

Rapid-onset erythema and oedema over a third or more of the breast, lasting under 6 months, in a woman who is not breastfeeding and not responding to antibiotics: treat it as inflammatory breast cancer until proven otherwise.

2

WORKUP

Mammography and ultrasound: skin thickening and an ill-defined mass. Core biopsy plus full-thickness skin punch: invasive carcinoma with dermal lymphatic invasion; ER O, PR O, HER2 3+. Full staging (CT chest/abdomen/pelvis + bone scan, or PET-CT) is mandatory: no distant metastases. cT4d N2.

3

SYSTEMIC FIRST

Neoadjuvant chemotherapy with trastuzumab and pertuzumab: taxane–carboplatin (as in Case 3), or anthracycline–cyclophosphamide first and then a taxane, with trastuzumab and pertuzumab given only with the taxane. Genetic testing (≤ 50) and a fertility discussion before starting.

4

SURGERY

Modified radical mastectomy, whatever the response: no breast conservation and no sentinel-node biopsy in inflammatory cancer. Reconstruction is usually delayed.

5

AFTER SURGERY

HER2 therapy guided by response: pCR, complete 1 year of trastuzumab–pertuzumab; residual disease, trastuzumab deruxtecan (or T-DM1).

6

RADIOTHERAPY

Post-mastectomy radiotherapy to the chest wall and regional nodes, even after a pathological complete response.

TEACHING POINTS

- Non-resolving “mastitis” in a non-lactating woman needs imaging and a biopsy, not a third antibiotic.
- Inflammatory cancer is always trimodality: systemic therapy, then mastectomy with dissection, then radiotherapy.
- Inflammatory cancer always needs full systemic staging, whatever the size of the breast findings.

See: Sections 02 (traps), 03, 05 · Algorithm 1 · [IBC international consensus](#)^[69]

CASE 5 HR+ / HER2- · metastatic**Back pain and a breast lump: de novo metastatic disease**

66 years

Stage IV, bone only

ER 95% · PR 50% · HER2 O

No visceral crisis

A 66-year-old has had back pain for 6 months and a 4 cm left breast mass with skin tethering. MRI spine shows multiple vertebral metastases without cord compression; CT shows bone-only disease.

Before you open the answer: what is the stage, what must be done before treatment, and what is the plan?

1

WORKUP

Core biopsy of the breast mass, and ideally of one bone lesion: invasive ductal carcinoma, ER 95%, PR 50%, HER2 IHC O. Ask the pathologist to distinguish HER2 O from “ultralow”. Offer germline testing (PARP-inhibitor relevance), and test *PIK3CA/ESR1* on tissue or ctDNA where available.

2

FIRST LINE

Aromatase inhibitor plus a CDK4/6 inhibitor (ribociclib has shown an overall survival benefit, MONALEESA-2). Chemotherapy first is reserved for visceral crisis.

3

BONE CARE

Dental check, then zoledronic acid or denosumab, with calcium and vitamin D. Assess spinal stability; palliative radiotherapy (often a single session) for painful lesions.

4

PRIMARY TUMOUR

Surgery on an asymptomatic primary has not improved survival; treat locally only for symptoms such as fungation or bleeding.

5 MONITORING

Symptoms, examination, tumour markers if raised at baseline, and imaging every 2–3 months initially.

6 AT PROGRESSION (26 MONTHS)

Repeat ctDNA: *ESR1* mutation → oral SERD (elacestrant). *PIK3CA/AKT1/PTEN* → capivasertib with fulvestrant. Later: trastuzumab deruxtecan if HER2-ultralow or low, sacituzumab govitecan, then chemotherapy.

7 THROUGHOUT

Early palliative care; goals-of-care discussion; check drug access and cost in India before each line.

TEACHING POINTS

- Bone-only HR+ disease can be controlled for years with endocrine-based therapy.
- Re-read HER2: "O" versus "ultralow" now opens a treatment line.
- Biomarkers at progression, not only at diagnosis, decide the second line.

See: Sections O4, O6 · Algorithm 2 · [MONALEESA-2](#)^[30], [EMERALD](#)^[27], [CAPitello-291](#)^[33]

CASE 6 Trap · survivorship emergency**New back pain three years after TNBC**

48 years

Previous stage II TNBC

3 weeks of back pain

New leg weakness

A 48-year-old was treated 3 years ago for stage II TNBC (neoadjuvant chemotherapy, breast conservation, radiotherapy, capecitabine for residual disease). She now has 3 weeks of thoracic back pain, worse at night, and 2 days of mild leg weakness.

Before you open the answer: what is the stage, what must be done before treatment, and what is the plan?

1 RECOGNISE

Night pain plus a new neurological deficit in a cancer survivor is metastatic spinal cord compression until proven otherwise. This is an emergency, not "age-related back pain".

2 SAME DAY

Dexamethasone; urgent whole-spine MRI: T8 metastasis with epidural compression. Same-day spinal surgery and radiation oncology opinion: decompression plus radiotherapy if she is fit and the spine is unstable, otherwise radiotherapy.

3 RE-STAGE AND RE-BIOPSY

CT chest/abdomen/pelvis. Biopsy an accessible metastasis to confirm the subtype and check HER2 (HER2-low?), PD-L1 (22C3 CPS) and germline *BRCA* if not already done.

4 FIRST LINE

PD-L1 CPS ≥10: pembrolizumab with sacituzumab govitecan, or with chemotherapy. CPS <10: sacituzumab govitecan or datopotamab deruxtecan, or chemotherapy. *gBRCA*: a PARP inhibitor is an option.

5 SUPPORT

Bone-modifying agent, rehabilitation, early palliative care, and psychological support for her and her family.

TEACHING POINTS

- TNBC relapses mostly in years 1–3, often in viscera, brain and spine; survivors should know the red flags.
- Hours matter in cord compression: neurological outcome depends on function at the start of treatment.
- Always re-biopsy the first relapse: biomarkers now decide first-line therapy.

See: Sections O2 (traps), O8 (red flags) · Algorithm 2 · [KEYNOTE-355](#)^[50], [ASCENT](#)^[51]

CASE 7 HR+ / HER2- · older patient**A small, low-risk cancer at 76**

76 years

cT1c NO (stage IA)

ER 95% · HER2 O · grade 1

Hypertension, diabetes, mild CKD

A 76-year-old with treated hypertension, diabetes and mild kidney disease lives independently. She has a 1.2 cm grade 1, ER-positive, HER2-negative cancer; clinical examination and axillary ultrasound are normal.

Before you open the answer: what is the stage, what must be done before treatment, and what is the plan?

1 ASSESS THE PERSON

Geriatric assessment (function, comorbidity, cognition, life expectancy, priorities). She is fit, with an estimated life expectancy of more than 10 years. Decide on fitness, not age.

2 SURGERY

Breast-conserving surgery. Sentinel-node biopsy can be omitted: older, small HR+ cancer, clinically and sonographically node-negative, and the result would not change treatment (SOUND, INSEMA).

3 RADIOTHERAPY

Can be omitted if she takes endocrine therapy: local recurrence is higher but survival is the same (PRIME II). If she prefers the lower recurrence risk, a 1-week whole-breast or partial-breast course is a gentle alternative.

4 SYSTEMIC

Aromatase inhibitor for 5 years, with bone density and fracture-risk care; tamoxifen if it is not tolerated. No chemotherapy.

5 FOLLOW-UP

Yearly clinical review; mammography while it would still change management; reassess goals as her health changes.

TEACHING POINTS

- De-escalation (no sentinel node, sometimes no radiotherapy) spares morbidity without costing survival in carefully chosen older women.
- Endocrine therapy is the treatment that matters most in this group; protect adherence and bone health.

See: Sections 05, 06 · [PRIME II](#)^[1], [SOUND](#)^[6], [INSEMA](#)^[7]

12 References & guidelines

- NCCN Clinical Practice Guidelines in Oncology: Breast Cancer (current version); ESMO and ASCO guidelines for metastatic breast cancer.
- ESMO Clinical Practice Guidelines: early breast cancer; metastatic breast cancer (living guideline).
- ASCO/CAP guideline on HER2 testing (2018 focused update); ASCO-SSO guideline on germline testing in breast cancer.
- AJCC Cancer Staging Manual, 8th edition. ICMR consensus document for the management of breast cancer.
- ASTRO guideline on whole-breast radiotherapy fractionation; ESTRO-ACROP guidance on breast radiotherapy.
- ASCO/ACS breast cancer survivorship care guideline; ASCO guideline on surveillance after primary treatment.
- NCCN Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic and Prostate.
- Each trial name above links to the PubMed record of its primary publication.

Core trials cited on this page (69)

Journal, year, volume and first page; each links to its PubMed record (exact journal, volume and page match).

NUMBERED IN ORDER OF FIRST CITATION IN THE TEXT

1. **Mumbai CBE trial:** Mittra I, Mishra GA, Dikshit RP, et al. Effect of screening by clinical breast examination on breast cancer incidence and mortality after 20 years: prospective, cluster randomised controlled trial in Mumbai. *BMJ* 2021;372:n256. [PubMed](#)
Screening
2. **UK Independent Panel:** Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. *Lancet* 2012;380:1778. [PubMed](#) **Screening**
3. **USPSTF 2024:** US Preventive Services Task Force; Nicholson WK, Silverstein M, et al. Screening for breast cancer: US Preventive Services Task Force recommendation statement. *JAMA* 2024;331:1918. [PubMed](#) **Screening**
4. **NSABP B-06:** Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;347:1233. [PubMed](#)
Surgery and the axilla
5. **Milan I:** Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002;347:1227. [PubMed](#) **Surgery and the axilla**
6. **SOUND:** Gentilini OD, Botteri E, Sangalli C, et al. Sentinel lymph node biopsy vs no axillary surgery in patients with small breast cancer and negative results on ultrasonography of axillary lymph nodes. *JAMA Oncol* 2023;9:1557. [PubMed](#) **Surgery and the axilla**
7. **INSEMA:** Reimer T, Stachs A, Veselinovic K, et al. Axillary surgery in breast cancer: primary results of the INSEMA trial. *N Engl J Med* 2025;392:1051. [PubMed](#) **Surgery and the axilla**
8. **ACOSOG Z0011:** Giuliano AE, Ballman KV, McCall L, et al. Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis. *JAMA* 2017;318:918. [PubMed](#)
Surgery and the axilla
9. **AMAROS:** Bartels SAL, Donker M, Poncet C, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer: 10-year results of the EORTC 10981-22023 AMAROS trial. *J Clin Oncol* 2023;41:2159. [PubMed](#) **Surgery and the axilla**
10. **EBCTCG radiotherapy meta-analysis:** Early Breast Cancer Trialists' Collaborative Group (EBCTCG); Darby S, et al. Effect of radiotherapy after breast-conserving surgery: meta-analysis of individual patient data. *Lancet* 2011;378:1707. [PubMed](#)
Radiotherapy
11. **PRIME II:** Kunkler IH, Williams LJ, Jack WJL, et al. Breast-conserving surgery with or without irradiation in early breast cancer. *N Engl J Med* 2023;388:585. [PubMed](#) **Radiotherapy**
12. **CALGB 9343:** Hughes KS, et al. Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer (CALGB 9343). *J Clin Oncol* 2013;31:2382. [PubMed](#) **Radiotherapy**
13. **EBCTCG:** EBCTCG; McGale P, et al. Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality. *Lancet* 2014;383:2127. [PubMed](#) **Radiotherapy**

14. **MA.20:** Whelan TJ, Olivetto IA, Parulekar WR, et al. Regional nodal irradiation in early-stage breast cancer. *N Engl J Med* 2015;373:307. [PubMed](#) [Radiotherapy](#)
15. **EORTC 22922:** Poortmans PM, Collette S, Kirkove C, et al. Internal mammary and medial supraclavicular irradiation in breast cancer. *N Engl J Med* 2015;373:317. [PubMed](#) [Radiotherapy](#)
16. **NSABP B-51:** Mamounas EP, Bandos H, White JR, et al. Omitting regional nodal irradiation after response to neoadjuvant chemotherapy. *N Engl J Med* 2025;392:2113. [PubMed](#) [Radiotherapy](#)
17. **FAST-Forward:** Murray Brunt A, Haviland JS, Wheatley DA, et al. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results. *Lancet* 2020;395:1613. [PubMed](#) [Radiotherapy](#)
18. **IMPORT LOW:** Coles CE, Griffin CL, Kirby AM, et al. Partial-breast radiotherapy after breast conservation surgery for patients with early breast cancer (UK IMPORT LOW trial): 5-year results. *Lancet* 2017;390:1048. [PubMed](#) [Radiotherapy](#)
19. **HYPORT-Adjuvant (India):** Chatterjee S, Chakraborty S; HYPORT Adjuvant Author Group. Hypofractionated radiation therapy comparing a standard radiotherapy schedule (over 3 weeks) with a novel 1-week schedule in adjuvant breast cancer (HYPORT-Adjuvant): study protocol for a multicentre, randomized phase III trial. *Trials* 2020;21:819. Quality-of-life results with nodal radiotherapy reported in *Radiother Oncol* 2026; efficacy results awaited. [PubMed](#) [Radiotherapy](#)
20. **START:** Haviland JS, Owen JR, Dewar JA, et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. *Lancet Oncol* 2013;14:1086. [PubMed](#) [Radiotherapy](#)
21. **Ontario trial:** Whelan TJ, et al. Long-term results of hypofractionated radiation therapy for breast cancer. *N Engl J Med* 2010;362:513. [PubMed](#) [Radiotherapy](#)
22. **Florence trial:** Meattini I, et al. Accelerated partial-breast irradiation compared with whole-breast irradiation for early breast cancer (Florence trial). *J Clin Oncol* 2020;38:4175. [PubMed](#) [Radiotherapy](#)
23. **RADCOMP:** Bekelman JE, Lu H, Pugh S, et al. Pragmatic randomised clinical trial of proton versus photon therapy for patients with non-metastatic breast cancer: the RadComp Consortium trial protocol. *BMJ Open* 2019;9:e025556 (NCT02603341). Cardiac and cancer-control results awaited. [PubMed](#) [Radiotherapy](#)
24. **EBCTCG tamoxifen:** EBCTCG; Davies C, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen. *Lancet* 2011;378:771. [PubMed](#) [Early disease: systemic therapy](#)
25. **EBCTCG aromatase inhibitors:** EBCTCG. Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. *Lancet* 2015;386:1341. [PubMed](#) [Early disease: systemic therapy](#)
26. **SOFT/TEXT:** Francis PA, Pagani O, Fleming GF, et al. Tailoring adjuvant endocrine therapy for premenopausal breast cancer. *N Engl J Med* 2018;379:122. [PubMed](#) [Early disease: systemic therapy](#)
27. **EMERALD:** Bidard FC, Kaklamani VG, Neven P, et al. Elacestrant versus standard endocrine therapy for ER-positive, HER2-negative advanced breast cancer: results from the randomized phase III EMERALD trial. *J Clin Oncol* 2022;40:3246. [PubMed](#) [Metastatic disease](#)
28. **monarchE:** Johnston SRD, Harbeck N, Hegg R, et al. Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2-, node-positive, high-risk, early breast cancer (monarchE). *J Clin Oncol* 2020;38:3987. [PubMed](#) [Early disease: systemic therapy](#)
29. **NATALEE:** Slamon D, Lipatov O, Nowecki Z, et al. Ribociclib plus endocrine therapy in early breast cancer. *N Engl J Med* 2024;390:1080. [PubMed](#) [Early disease: systemic therapy](#)
30. **MONALEESA-2:** Hortobagyi GN, Stemmer SM, Burris HA, et al. Overall survival with ribociclib plus letrozole in advanced breast cancer. *N Engl J Med* 2022;386:942. [PubMed](#) [Metastatic disease](#)
31. **MONARCH 3:** Goetz MP, et al. MONARCH 3: abemaciclib as initial therapy for advanced breast cancer. *J Clin Oncol* 2017;35:3638. [PubMed](#) [Metastatic disease](#)
32. **PALOMA-2:** Finn RS, et al. Palbociclib and letrozole in advanced breast cancer. *N Engl J Med* 2016;375:1925. [PubMed](#) [Metastatic disease](#)
33. **CAPitello-291:** Turner NC, Oliveira M, Howell SJ, et al. Capivasertib in hormone receptor-positive advanced breast cancer. *N Engl J Med* 2023;388:2058. [PubMed](#) [Metastatic disease](#)
34. **SOLAR-1:** André F, et al. Alpelisib for PIK3CA-mutated, hormone receptor-positive advanced breast cancer. *N Engl J Med* 2019;380:1929. [PubMed](#) [Metastatic disease](#)
35. **INAVO120:** Turner NC, et al. Inavolisib-based therapy in PIK3CA-mutated advanced breast cancer. *N Engl J Med* 2024;391:1584. [PubMed](#) [Metastatic disease](#)
36. **BOLERO-2:** Baselga J, et al. Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. *N Engl J Med* 2012;366:520. [PubMed](#) [Metastatic disease](#)
37. **OlympiA:** Tutt ANJ, Garber JE, Kaufman B, et al. Adjuvant olaparib for patients with BRCA1- or BRCA2-mutated breast cancer. *N Engl J Med* 2021;384:2394. [PubMed](#) [Early disease: systemic therapy](#)

38. **OlympiAD:** Robson M, Im SA, Senkus E, et al. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. *N Engl J Med* 2017;377:523. [PubMed](#) **Metastatic disease**
39. **EMBRACA:** Litton JK, et al. Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. *N Engl J Med* 2018;379:753. [PubMed](#) **Metastatic disease**
40. **HERA:** Piccart-Gebhart MJ, et al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. *N Engl J Med* 2005;353:1659. [PubMed](#) **Early disease: systemic therapy**
41. **APHINITY:** von Minckwitz G, Procter M, de Azambuja E, et al. Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. *N Engl J Med* 2017;377:122. [PubMed](#) **Early disease: systemic therapy**
42. **KATHERINE:** von Minckwitz G, Huang CS, Mano MS, et al. Trastuzumab emtansine for residual invasive HER2-positive breast cancer. *N Engl J Med* 2019;380:617. Overall survival: Geyer CE Jr, et al. *N Engl J Med* 2025;392:249. [PubMed](#) **Early disease: systemic therapy**
43. **DESTINY-Breast05:** Loibl S, Park YH, Shao Z, et al. Trastuzumab deruxtecan in residual HER2-positive early breast cancer. *N Engl J Med* 2026;394:845. [PubMed](#) **Early disease: systemic therapy**
44. **CLEOPATRA:** Swain SM, Baselga J, Kim SB, et al. Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. *N Engl J Med* 2015;372:724. [PubMed](#) **Metastatic disease**
45. **DESTINY-Breast03:** Cortés J, Kim SB, Chung WP, et al. Trastuzumab deruxtecan versus trastuzumab emtansine for breast cancer. *N Engl J Med* 2022;386:1143. [PubMed](#) **Metastatic disease**
46. **HER2CLIMB:** Murthy RK, Loi S, Okines A, et al. Tucatinib, trastuzumab, and capecitabine for HER2-positive metastatic breast cancer. *N Engl J Med* 2020;382:597. [PubMed](#) **Metastatic disease**
47. **DESTINY-Breast04:** Modi S, Jacot W, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer. *N Engl J Med* 2022;387:9. [PubMed](#) **Metastatic disease**
48. **DESTINY-Breast06:** Bardia A, et al. Trastuzumab deruxtecan after endocrine therapy in metastatic breast cancer. *N Engl J Med* 2024;391:2110. [PubMed](#) **Metastatic disease**
49. **KEYNOTE-522 (pCR/EFS):** Schmid P, Cortes J, Pusztai L, et al. Pembrolizumab for early triple-negative breast cancer. *N Engl J Med* 2020;382:810. [PubMed](#) **Early disease: systemic therapy**
50. **KEYNOTE-355:** Cortes J, Rugo HS, Cescon DW, et al. Pembrolizumab plus chemotherapy in advanced triple-negative breast cancer. *N Engl J Med* 2022;387:217. [PubMed](#) **Metastatic disease**
51. **ASCENT:** Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med* 2021;384:1529. [PubMed](#) **Metastatic disease**
52. **ASCENT-04:** Tolaney SM, et al. Sacituzumab govitecan plus pembrolizumab for advanced triple-negative breast cancer. *N Engl J Med* 2026;394:354. [PubMed](#) **Metastatic disease**
53. **TROPICS-02:** Rugo HS, et al. Sacituzumab govitecan in hormone receptor-positive/HER2-negative metastatic breast cancer. *J Clin Oncol* 2022;40:3365. [PubMed](#) **Metastatic disease**
54. **TROPION-Breast01:** Bardia A, et al. Datopotamab deruxtecan versus chemotherapy in previously treated inoperable/metastatic HR+/HER2- breast cancer (TROPION-Breast01). *J Clin Oncol* 2025;43:285. [PubMed](#) **Metastatic disease**
55. **EBCTCG chemotherapy:** EBCTCG; Peto R, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100 000 women in 123 randomised trials. *Lancet* 2012;379:432. [PubMed](#) **Early disease: systemic therapy**
56. **Dose-dense EBCTCG:** EBCTCG. Increasing the dose intensity of chemotherapy by more frequent administration or sequential scheduling: a patient-level meta-analysis of 37 298 women with early breast cancer in 26 randomised trials. *Lancet* 2019;393:1440. [PubMed](#) **Early disease: systemic therapy**
57. **CREATE-X:** Masuda N, Lee SJ, Ohtani S, et al. Adjuvant capecitabine for breast cancer after preoperative chemotherapy. *N Engl J Med* 2017;376:2147. [PubMed](#) **Early disease: systemic therapy**
58. **EBCTCG bisphosphonates:** Early Breast Cancer Trialists' Collaborative Group. Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials. *Lancet* 2015;386:1353. [PubMed](#) **Survivorship**
59. **TRAIN-2:** van Ramshorst MS, et al. Neoadjuvant chemotherapy with or without anthracyclines in the presence of dual HER2 blockade for HER2-positive breast cancer (TRAIN-2). *Lancet Oncol* 2018;19:1630. [PubMed](#) **Early disease: systemic therapy**
60. **NeoSphere:** Gianni L, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere). *Lancet Oncol* 2012;13:25. [PubMed](#) **Early disease: systemic therapy**
61. **TAILORx:** Sparano JA, Gray RJ, Makower DF, et al. Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. *N Engl J Med* 2018;379:111. [PubMed](#) **Early disease: systemic therapy**
62. **RxPONDER:** Kalinsky K, Barlow WE, Gralow JR, et al. 21-gene assay to inform chemotherapy benefit in node-positive breast cancer. *N Engl J Med* 2021;385:2336. [PubMed](#) **Early disease: systemic therapy**

63. **APT:** Tolaney SM, Barry WT, Dang CT, et al. Adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer. *N Engl J Med* 2015;372:134. [PubMed](#) **Early disease: systemic therapy**
64. **ExteNET:** Chan A, et al. Neratinib after trastuzumab-based adjuvant therapy in patients with HER2-positive breast cancer (ExteNET). *Lancet Oncol* 2016;17:367. [PubMed](#) **Early disease: systemic therapy**
65. **GIVIO:** The GIVIO Investigators. Impact of follow-up testing on survival and health-related quality of life in breast cancer patients: a multicenter randomized controlled trial. *JAMA* 1994;271:1587. [PubMed](#) **Survivorship**
66. **Rosselli Del Turco:** Rosselli Del Turco M, et al. Intensive diagnostic follow-up after treatment of primary breast cancer: a randomized trial. *JAMA* 1994;271:1593. [PubMed](#) **Survivorship**
67. **BWEL:** Breast Cancer Weight Loss (BWEL) trial, Alliance A011401: telephone-based weight-loss programme versus usual care in overweight women with stage II–III breast cancer (NCT02750826). Weight-loss results reported; invasive disease-free survival results awaited. [PubMed](#) **Survivorship**
68. **POSITIVE:** Partridge AH, Niman SM, Ruggeri M, et al. Interrupting endocrine therapy to attempt pregnancy after breast cancer. *N Engl J Med* 2023;388:1645. [PubMed](#) **Survivorship**
69. **IBC international consensus:** Dawood S, et al. International expert panel on inflammatory breast cancer: consensus statement for standardized diagnosis and treatment. *Ann Oncol* 2011;22:515. [PubMed](#) **Guidelines and consensus**

FURTHER READING (NOT CITED IN THE TEXT ABOVE)

- **KEYNOTE-522 (OS):** Schmid P, Cortes J, Dent R, et al. Overall survival with pembrolizumab in early-stage triple-negative breast cancer. *N Engl J Med* 2024;391:1981. [PubMed](#) **Early disease: systemic therapy**

Last updated 9 October 2026. Key points only, written in our own words; no dosing or individual patient advice.

Educational summary for health professionals. Verify current primary literature, guidelines, regulatory approvals in India and individual patient factors before making treatment decisions.