

ONCOLOGY KNOWLEDGE HUB · TEACHING SLIDES

Breast Cancer

A mini review for clinicians

For postgraduate residents, medical students and practising clinicians

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Learning objectives

- Recognise how breast cancer presents, and the traps that delay diagnosis
- Apply risk-based screening, including India's national programme
- Order the right workup: triple assessment, staging, biomarkers
- Choose surgery, axillary management and radiotherapy
- Match systemic therapy to subtype and setting (no doses)
- Plan survivorship care and reduce recurrence risk

Roadmap

- 1 Burden, biology and genetics
- 2 Presentation and common traps
- 3 Screening
- 4 Diagnosis and staging
- 5 Biomarkers
- 6 Local therapy: surgery and radiotherapy
- 7 Systemic therapy
- 8 Management algorithms
- 9 Survivorship
- 10 Evidence, cases and take-home messages

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Burden, biology and genetics

Breast cancer in India

- Most common cancer in Indian women: about 1.9 lakh new cases and nearly 1 lakh deaths (GLOBOCAN 2022)
- Presents about a decade younger than in Western series
- Large share present with locally advanced or metastatic disease
- Triple-negative disease is relatively more frequent (about a quarter in many series)
- Screening uptake is very low: under 1% of women aged 30–49 ever examined (NFHS-5)

Three working subtypes

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

HR+ / HER2- · ~70%

HER2+ · ~15%

TNBC · ~15%

HR+ / HER2-

Luminal A / B

- Most common; slower growth
- Late relapse (to 20+ years)
- Bone is the usual first site

**Endocrine backbone ± CDK4/6;
chemo by risk**

HER2+

HER2-enriched

- Aggressive if untreated
- Early relapse (years 1–3)
- Brain and visceral spread

**Anti-HER2 therapy at every
stage**

Triple-negative

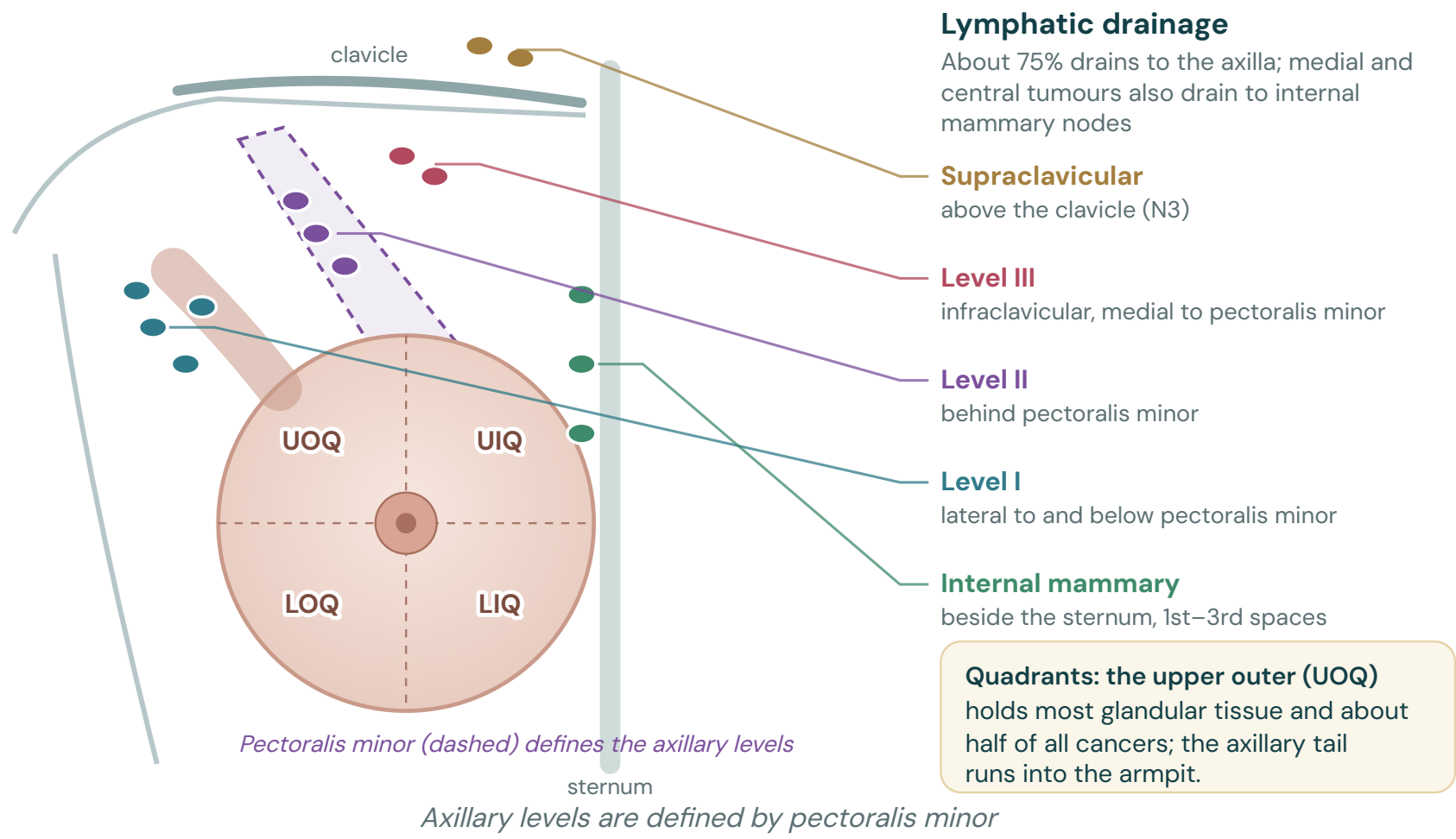
Mostly basal-like

- Younger; BRCA1-linked
- Relapse mostly by year 3–5
- Visceral and brain spread

**Chemo ± pembrolizumab; PARPi
if gBRCA; ADCs**

Each subtype has its own natural history and treatment backbone

Anatomy and lymphatic drainage



Risk factors

Risk factors

- Increasing age; female sex
- Family history; inherited variants (BRCA1/2, PALB2, TP53...)
- Early menarche, late first pregnancy, nulliparity, no breastfeeding
- Combined menopausal hormone therapy
- Obesity after menopause, alcohol, inactivity
- Dense breasts; atypia or LCIS; chest radiotherapy at a young age

Not risk factors

- Bras, deodorants, mobile phones
- Breast size
- Abortion, caffeine, hair dye
- Stress (not shown to cause breast cancer)
- Breast implants for cosmesis

Hereditary breast cancer: who to test

- About 5–10% of breast cancers are hereditary
- Test at least: diagnosis at ≤ 50 , TNBC at ≤ 60 , any man, bilateral cancer
- Strong family history of breast, ovarian, pancreatic or prostate cancer
- PARP-inhibitor eligibility (early high-risk or metastatic HER2-)
- ASCO-SSO extends testing to everyone diagnosed at ≤ 65
- A positive result changes surgery, systemic options and family care (cascade testing)

Genes and what they change

Gene	Breast pattern	What it changes
BRCA1	Young, triple-negative	PARP inhibitor, platinum; RRSO ~35–40
BRCA2	Often HR+; male breast cancer	As BRCA1; RRSO ~40–45
PALB2	High risk, often ER-	MRI from 30; PARP inhibitor option
TP53	Very young, often HER2+	Avoid radiotherapy where possible
CDH1	Lobular	Diffuse gastric cancer risk
CHEK2 / ATM	Moderate, ER+	Earlier screening; RRM not routine

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Presentation and common traps

How breast cancer presents

- A painless, hard, irregular lump: pain does not exclude cancer
- Skin dimpling, retraction, peau d'orange, ulceration
- Nipple inversion, unilateral eczema, spontaneous single-duct bloody discharge
- Axillary or supraclavicular node, arm swelling
- Rapid redness and swelling over $\geq \frac{1}{3}$ of the breast: inflammatory cancer
- First presentation with metastases: bone pain, breathlessness, jaundice, headache

Common traps (1)

Trap	Do instead
"Fibroadenoma" in a young woman	Triple assessment; biopsy suspicious or growing lumps
Non-resolving "mastitis"	Imaging + core and skin punch biopsy
Nipple eczema for months	Biopsy persistent one-sided changes (Paget)
"Mammogram normal"	10–15% of palpable cancers are occult: biopsy
FNAC benign or discordant	Core biopsy

Common traps (2)

Trap	Do instead
Lump in pregnancy called “milk”	Ultrasound and biopsy
Granulomatous / TB mastitis vs cancer	Tissue for histology and culture
Rapidly growing “fibroadenoma”	Think phyllodes: excise with margin
Axillary node, no breast lump	Occult breast primary: MRI, ER/PR/HER2, GATA3
Back pain in a survivor	Investigate: late relapse is common in HR+

Case snapshot: the “mastitis” that did not settle

- 38 years, 8 months postpartum, stopped breastfeeding 2 months ago
- 6 weeks of redness, warmth, swelling; two courses of antibiotics
- Peau d'orange over half the breast; matted axillary nodes
- Core + skin punch: dermal lymphatic invasion, HER2 3+
- Full staging → neoadjuvant chemo + HER2 therapy → modified radical mastectomy → PMRT
- Lesson: never a third antibiotic course without imaging and biopsy

3 Screening

Screening by risk

Risk group	Screening
Average (<15% lifetime)	Mammography every 1–2 y: shared decision 40–49, recommended 50–74, ≥75 if life expectancy ≥10 y
Moderate (15–20%)	As average; some start at 40 or 10 y before relative's diagnosis
High (>20%): BRCA, TP53, PALB2, chest RT 10–30	Annual MRI + mammography (BRCA: MRI from 25, mammography from 30)
India NP-NCD (all women 30–65)	Clinical breast examination every 5 years by trained health workers

The Indian evidence: Mumbai CBE trial (BMJ 2021)

- Cluster randomised trial, about 1.5 lakh women aged 35–64, 20 years of follow-up
- Clinical breast examination every 2 years by trained female health workers
- Significant downstaging of cancers at diagnosis
- Breast cancer mortality reduced by nearly 30% in women ≥ 50
- 15% reduction overall (not statistically significant)
- A practical model for low- and middle-income settings

Benefits and harms of screening

- Benefit: 15–20% relative reduction in breast cancer mortality at 40–69
- Smaller absolute benefit in the 40s
- False positives: about half of women over 10 years of annual screening (US data)
- Overdiagnosis: estimates vary widely; ~19% in one meta-analysis
- Use shared decision-making
- Screening is for women without symptoms; symptoms need diagnostic workup

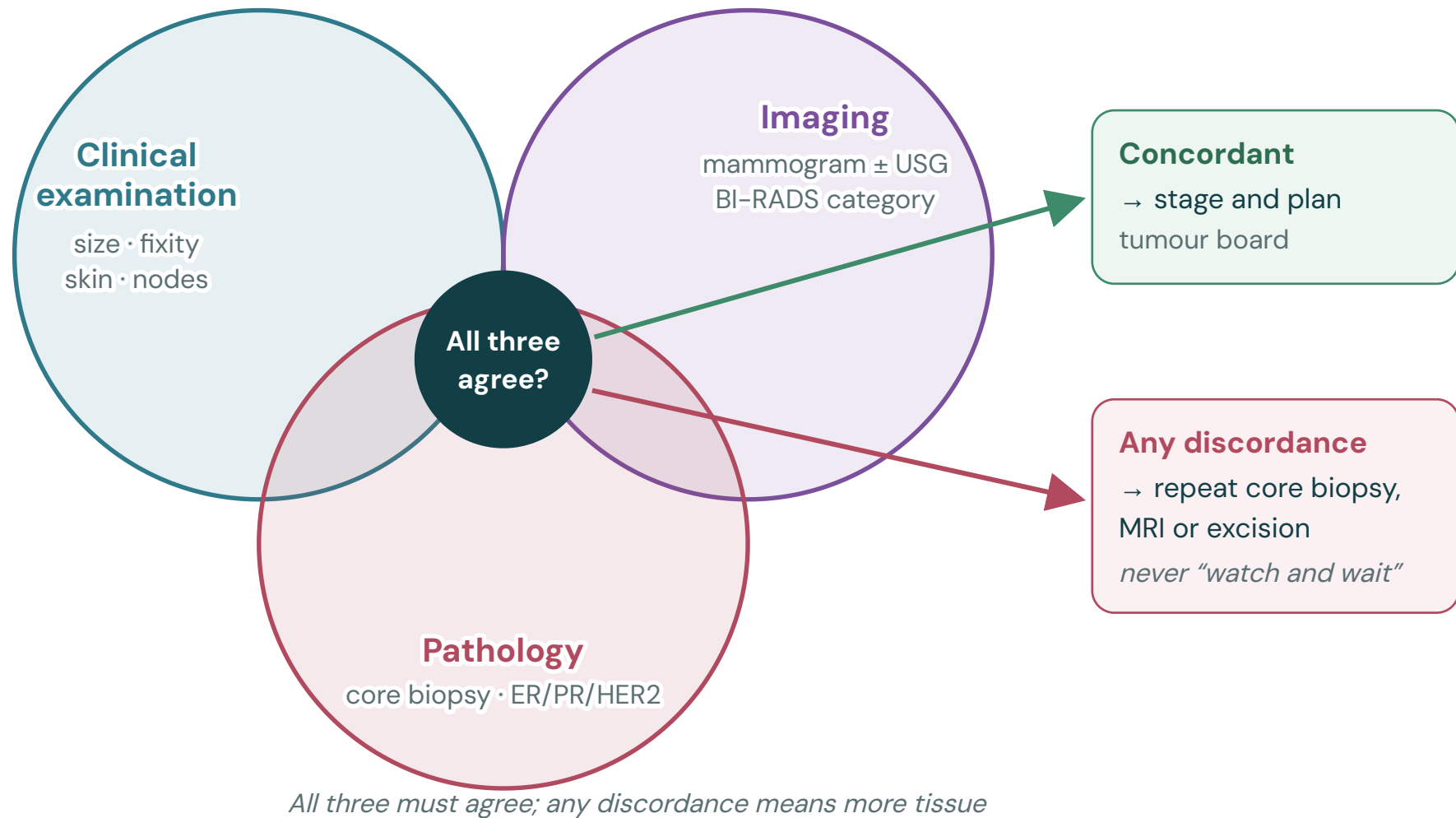
Tests that do NOT belong in screening

- Ultrasound alone: an adjunct for dense breasts or high risk only
- Thermography / heat scans: FDA warnings 2011 and 2023
- Tumour markers (CA 15-3, CEA)
- Whole-body PET-CT or CT
- Routine self-examination as a screening test: teach breast awareness instead
- Density alone does not change age- and risk-based screening

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Diagnosis and staging

Triple assessment



Imaging and biopsy

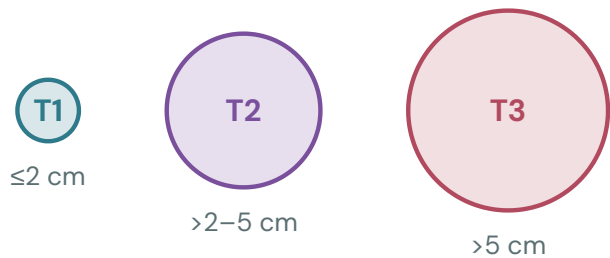
- Under 30: ultrasound first; 30–39: ultrasound or mammography; ≥ 40 : diagnostic mammography $\pm$ ultrasound
- Core needle biopsy before any surgery; open biopsy only if needle biopsy impossible
- Axillary ultrasound $\pm$ needle biopsy; clip the node before neoadjuvant therapy
- Clip the tumour before neoadjuvant therapy
- Breast MRI is not routine: no survival or local-control benefit; may increase mastectomy
- Inflammatory cancer: add a full-thickness skin punch biopsy

The pathology report: what you must see

- Histology (ductal NST, lobular, special types) and grade
- ER and PR with percentage (ER-low 1–10%)
- HER2 by IHC; ISH for IHC 2+ (ASCO/CAP)
- Ki-67 where used for risk decisions
- Lymphovascular invasion; margins; node count and size of metastases
- Post-neoadjuvant: residual cancer burden / ypTNM

TNM at a glance

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.
AJCC 8th edition, simplified

Who needs systemic staging?

- Clinical stage III
- Inflammatory breast cancer
- Symptoms or abnormal labs suggesting metastasis
- Not routine for asymptomatic stage I–II
- CT chest/abdomen/pelvis + bone scan, or PET–CT (upstages more patients)
- AJCC prognostic stage assumes effective treatment: it overstates outlook if therapy is not accessible

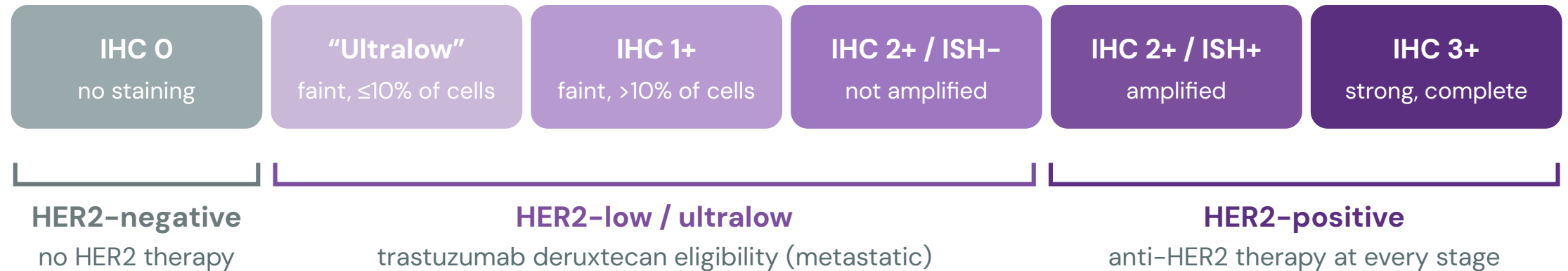
5 Biomarkers

Hormone receptors

- ER/PR $\geq 1\%$ → endocrine therapy
- ER-low (1–10%) often behaves like TNBC
- HER2 status should not withhold or select endocrine therapy
- Receptor status can change: re-biopsy the first metastasis
- PR loss and high Ki-67 signal more aggressive luminal disease

HER2 is a spectrum

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.

HER2-low and ultralow matter only for ADCs in metastatic disease

Genomic assays: sparing chemotherapy

- 21-gene recurrence score in HR+/HER2-, node-negative or 1–3 nodes
- TAILORx (NO): RS ≤ 25 above 50, or ≤ 15 at any age → no chemotherapy benefit
- RS 16–25 at ≤ 50 : chemotherapy or ovarian suppression
- RxPONDER (1–3 nodes): postmenopausal RS ≤ 25 → no chemotherapy benefit
- Premenopausal women benefited, possibly via ovarian suppression
- If unaffordable: decide on clinical risk and document the reasoning

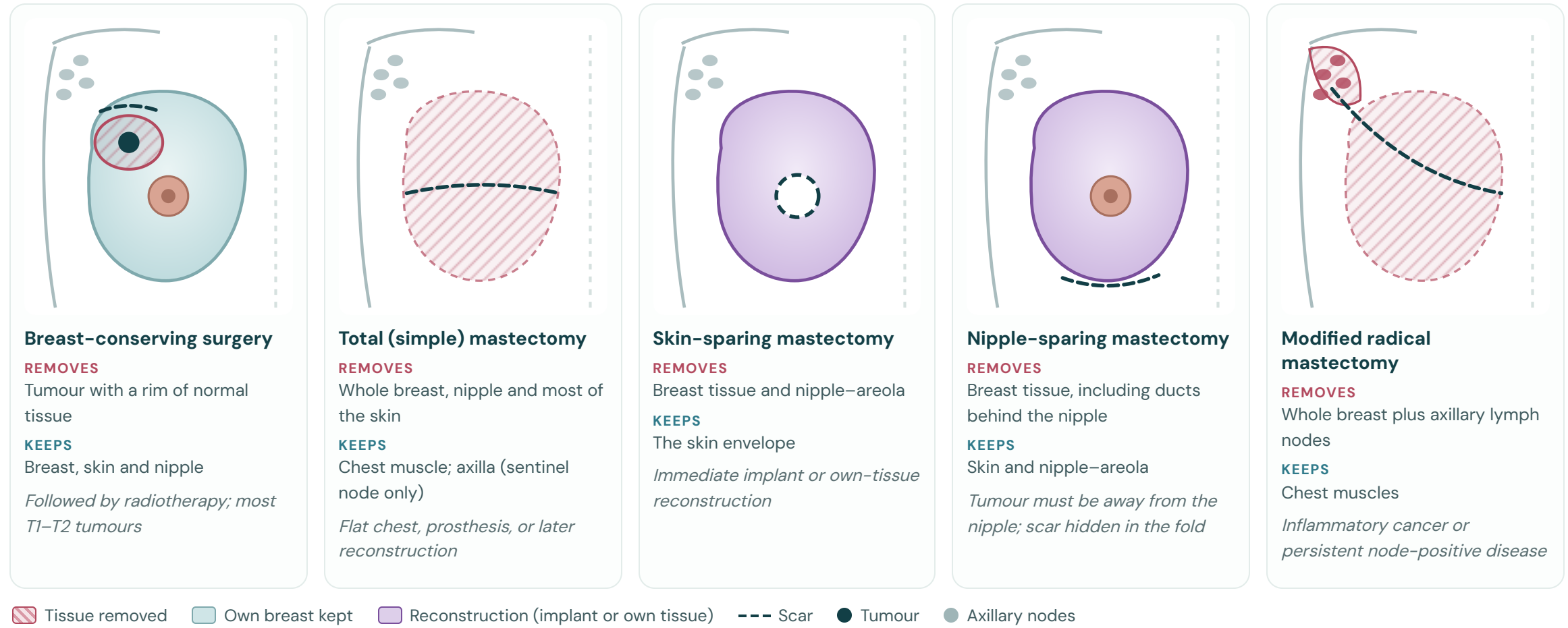
Biomarkers in metastatic disease

- ER/PR/HER2 on a metastatic biopsy
- ESR1 mutation (ctDNA after AI progression) → oral SERD
- PIK3CA / AKT1 / PTEN → capivasertib, alpelisib, inavolisib
- Germline BRCA (also PALB2) → PARP inhibitor
- PD-L1 CPS ≥ 10 (22C3) in TNBC → pembrolizumab
- HER2-low / ultralow → trastuzumab deruxtecan

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Local therapy

Types of breast surgery



Same survival with conservation and mastectomy for suitable patients

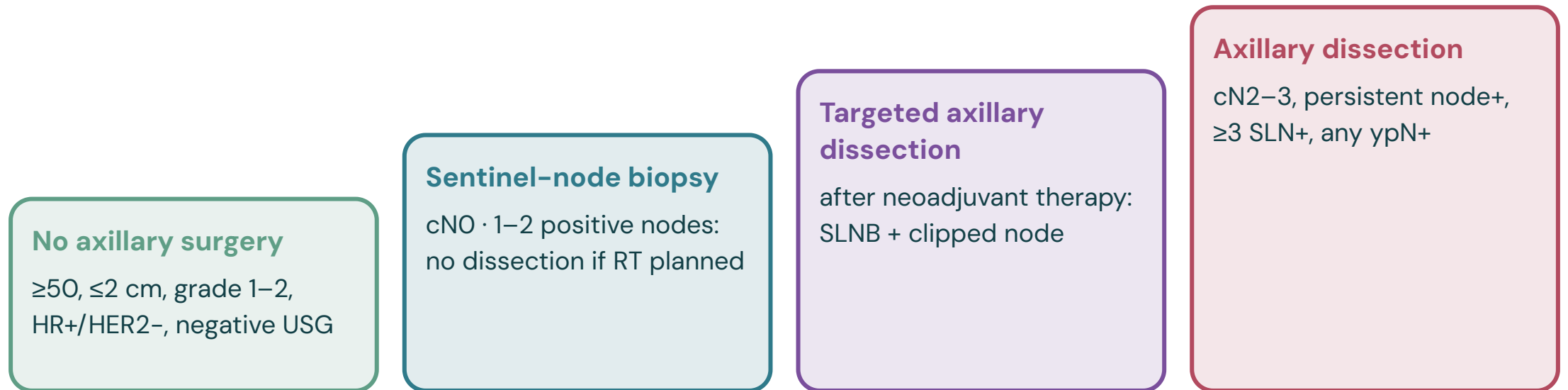
Breast conservation vs mastectomy

- Equal survival: NSABP B-06 and Milan, 20-year follow-up
- Conservation needs radiotherapy
- Not advised: multicentric disease, diffuse suspicious calcifications, persistently positive margins
- Not advised: prior chest radiotherapy, inflammatory cancer, radiotherapy not feasible
- Patient preference and genetics (BRCA) shape the choice
- India: conservation rates remain low outside major centres

Margins and reconstruction

- Invasive cancer: “no ink on tumour” is enough
- DCIS: 2 mm preferred
- Wider margins do not reduce recurrence
- Skin- and nipple-sparing mastectomy with immediate reconstruction when suitable
- Implant or autologous (DIEP, latissimus dorsi); radiotherapy raises implant complications
- Reconstruction is usually delayed in inflammatory cancer

The axillary ladder



Less surgery Lymphoedema risk: roughly 1 in 20 after sentinel-node biopsy → about 1 in 5 after full dissection **More surgery**

Climb only as far as the disease requires

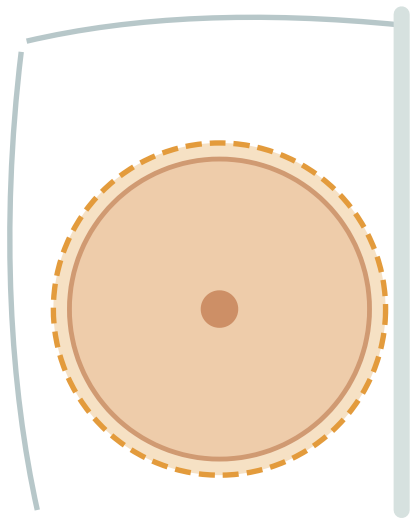
The axilla after neoadjuvant therapy

- cNO → sentinel-node biopsy after treatment
- cN1 → ycNO: dual-tracer sentinel node + clipped node (targeted axillary dissection)
- Any positive node at surgery (ypN+) → axillary dissection + nodal RT
- Initial cN2–3 → axillary dissection
- NSABP B-51: cN1 → ypNO, nodal RT did not reduce recurrence

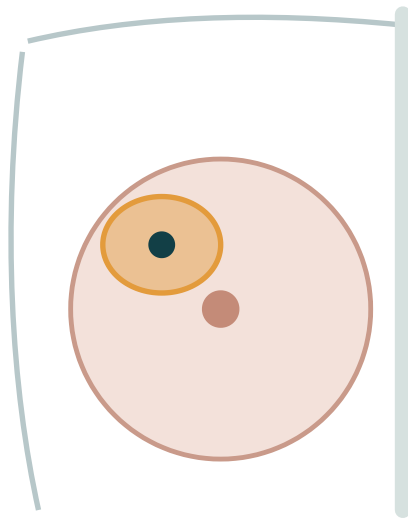
Radiotherapy: indications

- After breast conservation: almost always (halves local recurrence)
- May omit: ≥ 65 –70, small, node-negative, HR+, on endocrine therapy (PRIME II, CALGB 9343)
- After mastectomy: ≥ 4 nodes, T3–T4, positive margins; usually 1–3 nodes
- Regional nodal RT: node-positive or high-risk node-negative (MA.20, EORTC 22922)
- Boost: younger age, high grade, close margins
- Inflammatory cancer: always post-mastectomy radiotherapy

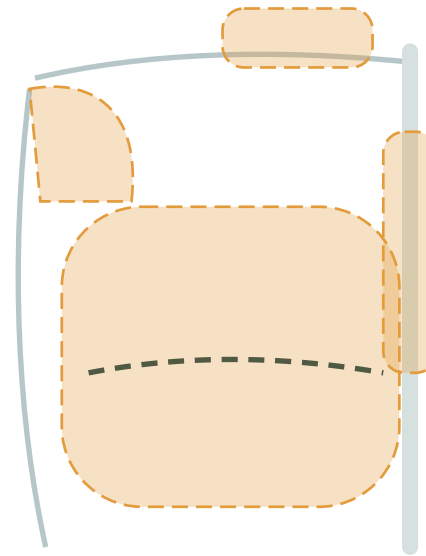
Radiotherapy fields



Whole breast
after breast conservation

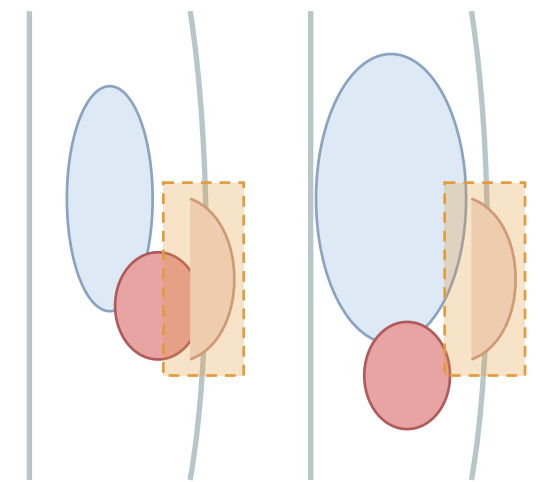


Partial breast
tumour bed + margin (low risk)



Chest wall + regional nodes
axillary · supraclavicular · IMN

**Left-sided cancers:
deep-inspiration breath-hold**

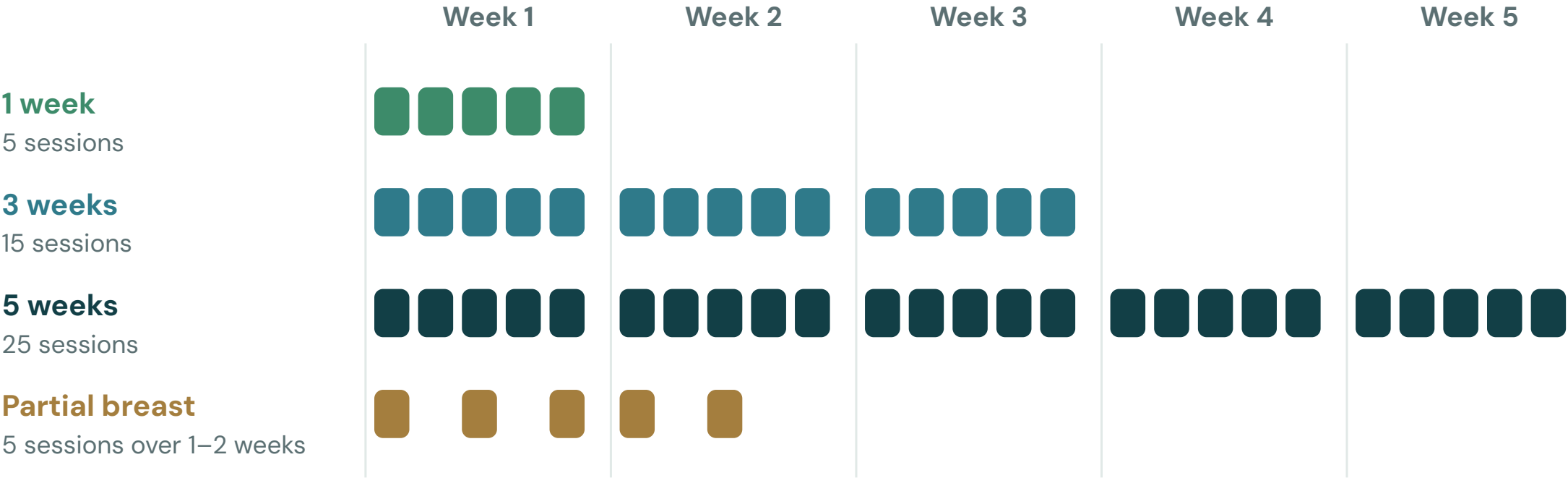


Free breathing **Breath-hold**
heart drops away from the field

 Radiation field (schematic)

Breath-hold keeps the heart out of the field for left-sided cancers

Radiotherapy schedules



Each block = one daily session (Mon–Fri). A tumour-bed boost adds a few sessions, or is integrated into the same course.

FAST-Forward: 1 week non-inferior to 3 weeks; HYPOR-Adjuvant (India) testing 1 week with nodes

Precision photons vs protons

Precision photon therapy (standard)

- 3D-conformal, IMRT/VMAT, image guidance
- Deep-inspiration breath-hold for left-sided cancers
- Low heart and lung dose for most patients
- Widely available

Protons (selected cases)

- No exit dose: lower heart/lung dose
- Left-sided + internal mammary nodes, difficult anatomy, re-irradiation
- Higher cost; very few Indian centres
- Randomised hard-outcome data still maturing (RADCOP)

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Systemic therapy

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Drug classes at a glance

Class	Main use
Endocrine (tamoxifen, AI, OFS, fulvestrant, oral SERDs)	All HR+ disease
CDK4/6 inhibitors	High-risk early HR+; first-line metastatic HR+
PI3K/AKT/mTOR inhibitors	HR+ metastatic by mutation
PARP inhibitors	gBRCA: high-risk early, metastatic
HER2-directed (trastuzumab, pertuzumab, T-DM1, T-DXd, tucatinib)	All HER2+; T-DXd also HER2-low
Pembrolizumab	Stage II–III TNBC; metastatic TNBC CPS ≥10
ADCs (sacituzumab, datopotamab)	Metastatic TNBC; pretreated HR+

Early HR+/HER2–

- Endocrine therapy for all: AI preferred after menopause
- At least 5 years; 7–10 years for stage II–III if tolerated
- Higher-risk premenopausal: ovarian suppression + AI or tamoxifen (SOFT/TEXT)
- Chemotherapy by clinical and genomic risk (dose-dense AC → T higher risk; TC lower risk)
- Start adjuvant chemotherapy within 4–6 weeks of surgery
- Residual HR+ disease after neoadjuvant chemo is expected: continue endocrine therapy

High-risk HR+: add-ons

- Abemaciclib 2 years (monarchE): IDFS and now OS benefit
- Ribociclib 3 years (NATALEE): broader stage II–III eligibility
- gBRCA carriers: olaparib 1 year (OlympiA), OS benefit
- Postmenopausal: adjuvant bisphosphonate (EBCTCG)
- Discuss toxicity (diarrhoea, neutropenia, liver tests) and cost

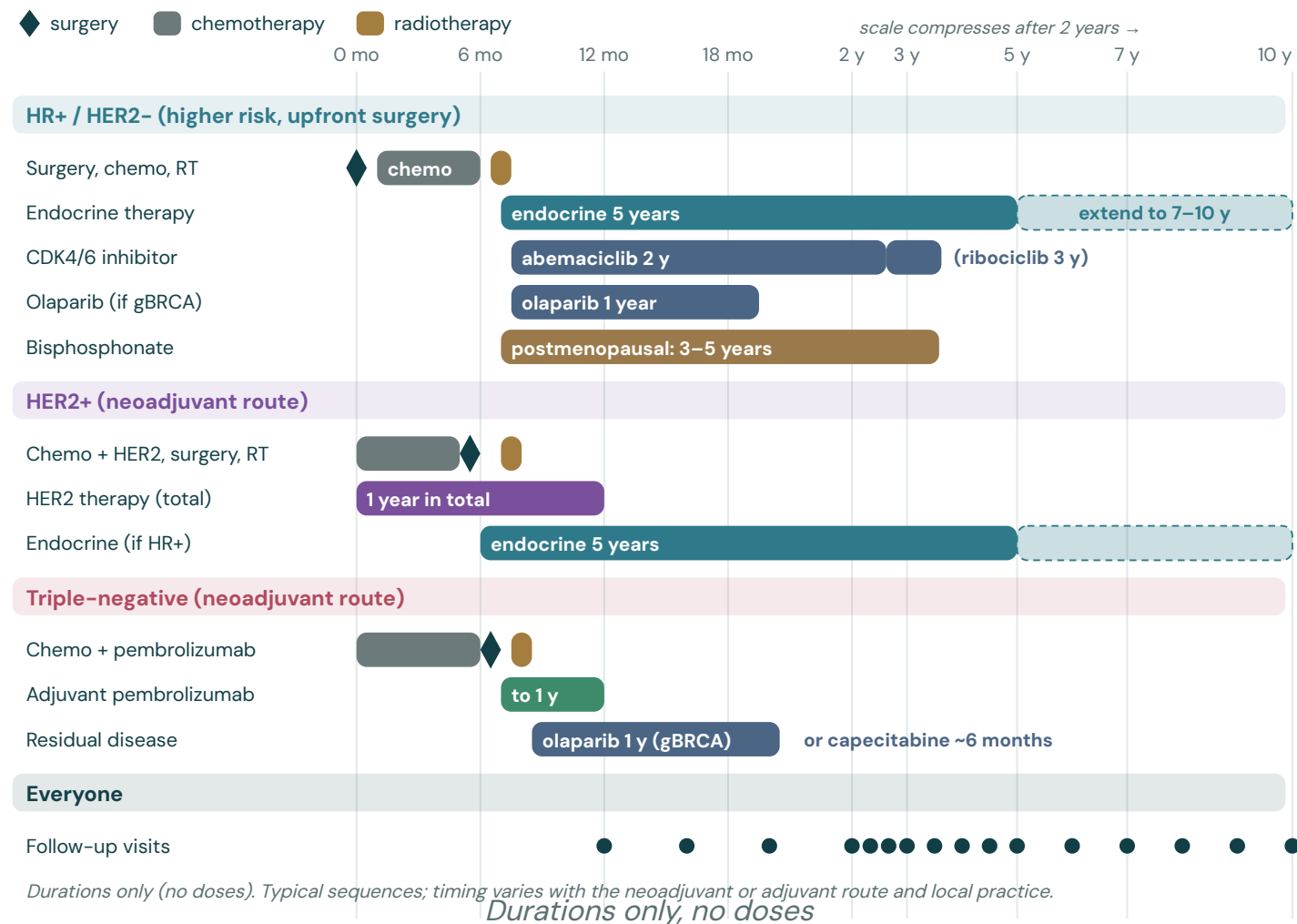
Early HER2-positive

- Chemotherapy + trastuzumab for ≥ 1 cm or node-positive; consider from 0.5 cm
- T1 N0 (<2 cm): weekly paclitaxel + trastuzumab (APT)
- cT2+ or N+: neoadjuvant taxane-carboplatin + trastuzumab + pertuzumab
- pCR → complete 1 year of HER2 therapy
- Residual in breast → T-DM1 (KATHERINE)
- Residual nodes / initially inoperable → trastuzumab deruxtecan (DESTINY-Breast05)

Early triple-negative

- Chemotherapy for >0.5 cm or node-positive
- Stage II–III: neoadjuvant chemo + pembrolizumab (KEYNOTE-522), regardless of PD-L1
- Overall survival improved (about 5 percentage points at 5 years)
- Residual disease: olaparib if gBRCA, otherwise capecitabine (CREATE-X)
- Watch for lasting immune toxicity (thyroid, adrenal)

The treatment calendar



Metastatic HR+/HER2–

- Re-biopsy; test ESR1, PIK3CA/AKT1/PTEN, gBRCA
- First line: AI or fulvestrant + CDK4/6 inhibitor (ribociclib OS benefit)
- Premenopausal: ovarian suppression
- Progression: oral SERD (ESR1), capivasertib (PI3K/AKT), everolimus
- Endocrine-refractory: T-DXd (HER2-low), sacituzumab, chemotherapy
- Chemotherapy first only for visceral crisis

Metastatic HER2-positive

- First line: taxane + trastuzumab + pertuzumab (CLEOPATRA OS benefit)
- Maintenance trastuzumab–pertuzumab (+ endocrine ± CDK4/6 if HR+)
- Alternative: T-DXd + pertuzumab, especially with brain metastases
- Second line or relapse <6 months after adjuvant: trastuzumab deruxtecan
- Later: T-DM1, tucatinib–capecitabine–trastuzumab (brain metastases)
- Echo monitoring throughout

Metastatic triple-negative

- PD-L1 CPS ≥ 10 : pembrolizumab + chemotherapy or + sacituzumab govitecan
- CPS < 10 : sacituzumab govitecan or datopotamab deruxtecan, or chemotherapy
- gBRCA with prior chemotherapy: PARP inhibitor
- HER2-low: trastuzumab deruxtecan
- Early palliative care

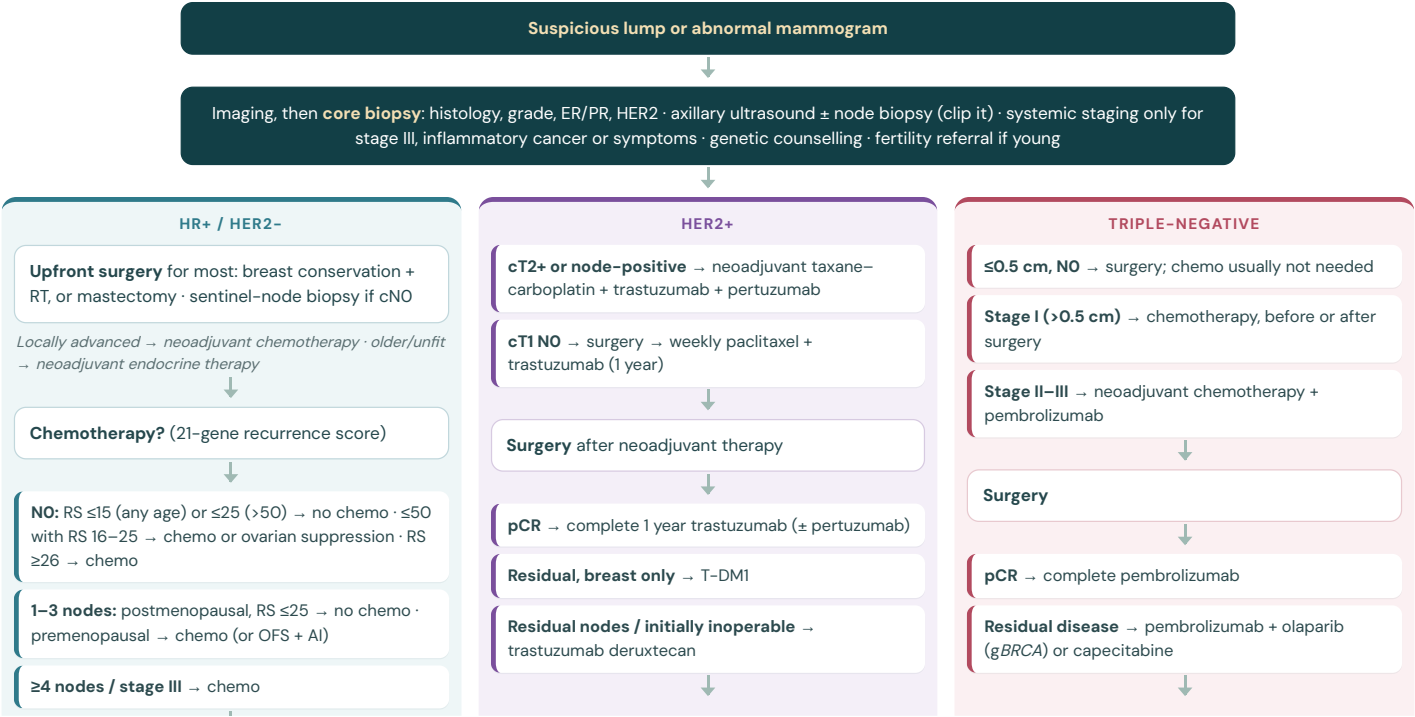
Emergencies not to miss

- Spinal cord compression: steroids, same-day whole-spine MRI, surgery/RT opinion
- Febrile neutropenia: antibiotics within the first hour
- Hypercalcaemia: fluids, bisphosphonate or denosumab
- Brain metastases: steroids, MRI, radiotherapy/surgery; HER2+ agents with CNS activity
- Pneumonitis on T-DXd or immunotherapy: stop drug, steroids

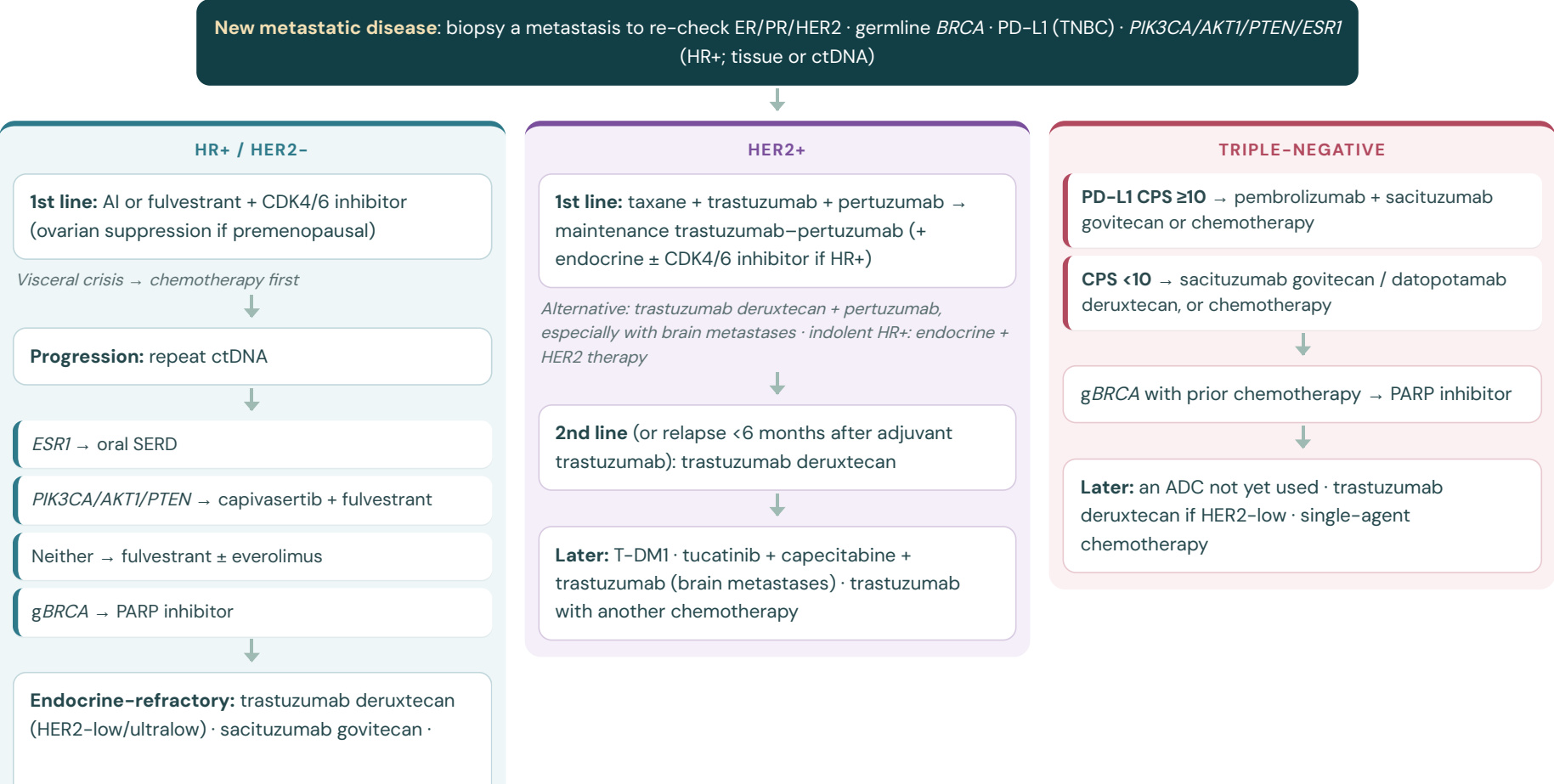
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Management algorithms

Algorithm 1: early breast cancer

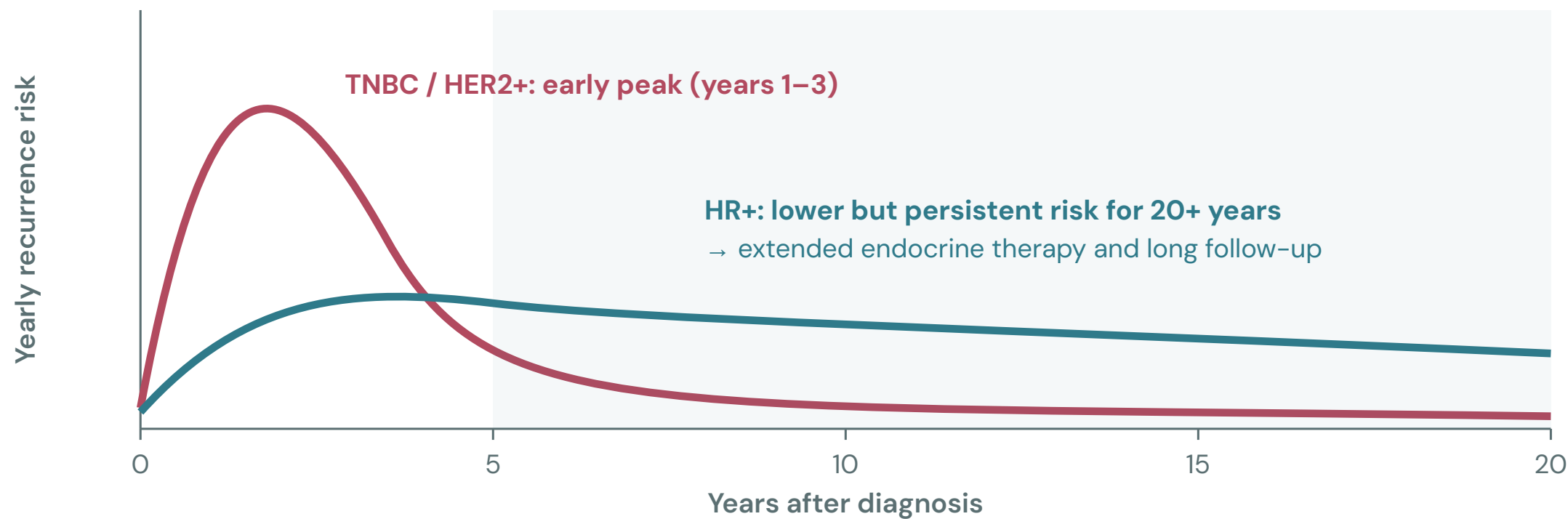


Algorithm 2: metastatic breast cancer



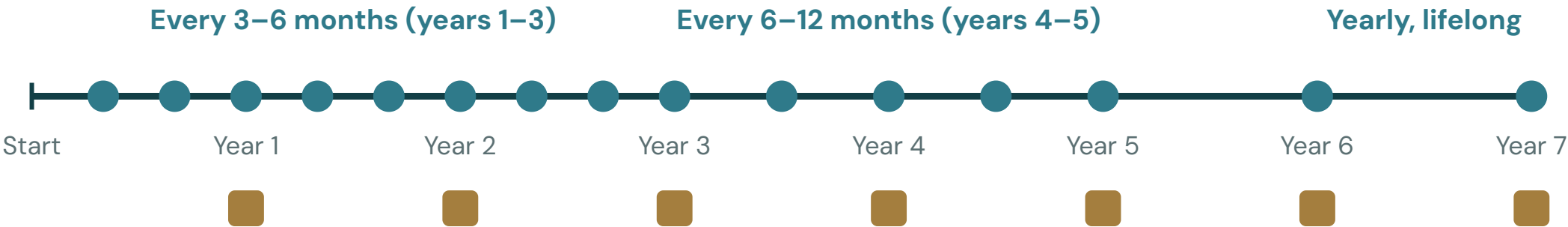
9 Survivorship

When relapses happen



Illustrative shape, not to scale

Follow-up rhythm



- Clinic visit: history, examination, adherence, side effects
- Mammogram, yearly (first one 6–12 months after radiotherapy)

Not routine when well: tumour markers, CT, PET, bone scan.
Add: bone density on an AI, gynaecology review on tamoxifen, cardiac risk care.

Symptoms, not scheduled scans, trigger investigations

Reducing recurrence

- Complete planned therapy; check endocrine adherence every visit
- Extended endocrine therapy for stage II–III
- Adjuvant bisphosphonate after menopause
- Targeted add-ons when eligible
- ≥ 150 min/week activity, healthy weight, minimal alcohol, no smoking
- No systemic HRT; avoid strong CYP2D6 inhibitors with tamoxifen

Late effects and quality of life

- Lymphoedema: baseline arm measurement, early referral
- Neuropathy (taxanes), cardiotoxicity (anthracyclines, trastuzumab)
- AI arthralgia and bone loss
- Menopausal symptoms and sexual health: non-hormonal first
- Fear of recurrence, depression, return to work
- Second cancers: endometrial (tamoxifen), myeloid (anthracyclines), angiosarcoma (RT)

Fertility, pregnancy and contraception

- Fertility referral before chemotherapy (oocyte or embryo freezing)
- GnRH agonists do not replace proven preservation methods
- Chemotherapy amenorrhoea is not menopause: use non-hormonal contraception
- Pregnancy after treatment does not appear to raise recurrence risk
- About 2 years is usual; POSITIVE trial supports a planned endocrine pause

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Evidence, cases and take-home messages

Landmark trials

Trial	Practice impact
TAILORx / RxPONDER	Genomic score spares chemotherapy for most HR+
KEYNOTE-522	Pembrolizumab in stage II–III TNBC; OS benefit
KATHERINE / DESTINY–Breast05	Response-adapted HER2 therapy after neoadjuvant
monarchE / NATALEE	CDK4/6 inhibitors in high-risk early HR+
ZO011 / AMAROS / SOUND / INSEMA	Less axillary surgery
FAST–Forward / HYPOR	One-week radiotherapy
Mumbai CBE trial	CBE screening reduces mortality ≥ 50 in India

Case: young woman, node-positive TNBC, BRCA1

- 34 y, cT2 N1, ER/PR/HER2 negative; mother had ovarian cancer
- Germline test → BRCA1; fertility referral in week 1
- Neoadjuvant chemo + pembrolizumab (KEYNOTE-522)
- Surgery choice discussed (bilateral mastectomy often chosen); targeted axillary dissection
- Residual disease → olaparib 1 year + continue pembrolizumab
- RRSO ~35–40, cascade testing

Case: screen-detected HR+, 1 positive sentinel node

- 58 y, pT1c N1a, ER 90%, HER2 1+, RS 18
- ZOO11 → no axillary dissection; whole-breast RT
- RxPONDER: postmenopausal RS ≤ 25 → no chemotherapy
- AI 7–10 years, bone density, bisphosphonate
- Ribociclib 3 years is an option (NATALEE); not monarchE-eligible

Case: HER2+, residual nodal disease

- 45 y premenopausal, cT2 N1, ER 40%, HER2 3+
- Neoadjuvant taxane–carboplatin + trastuzumab + pertuzumab
- ypT1b N1 → axillary dissection; trastuzumab deruxtecan (or T-DM1)
- Ovarian suppression + AI with HER2 therapy
- Whole breast + nodal RT; echo monitoring

Practice pearls for Indian clinics

- Biopsy first: excision before imaging and core biopsy is still common
- Read benefit in absolute terms; separate PFS from OS
- Biosimilar trastuzumab makes a full year of HER2 therapy feasible
- Discuss cost early so treatment is not abandoned midway
- Many new agents may not yet be approved or affordable in India: check access
- Teach breast awareness; refer high-risk families for genetics

Take-home messages

- Painless lump, non-resolving mastitis, one-sided nipple rash: biopsy
- Stage and biology (ER/PR/HER2, genomics, gBRCA) drive every decision
- De-escalate where evidence allows: axilla, radiotherapy, chemotherapy
- Neoadjuvant therapy lets response decide adjuvant treatment in HER2+ and TNBC
- HR+ disease needs long endocrine therapy and long follow-up
- Survivorship care is part of treatment

THANK YOU

Questions and discussion

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Full mini review, algorithms, MCQ bank and case vignettes: drharitha.co.in/professionals

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