پژوهشکده سرطان معتمد

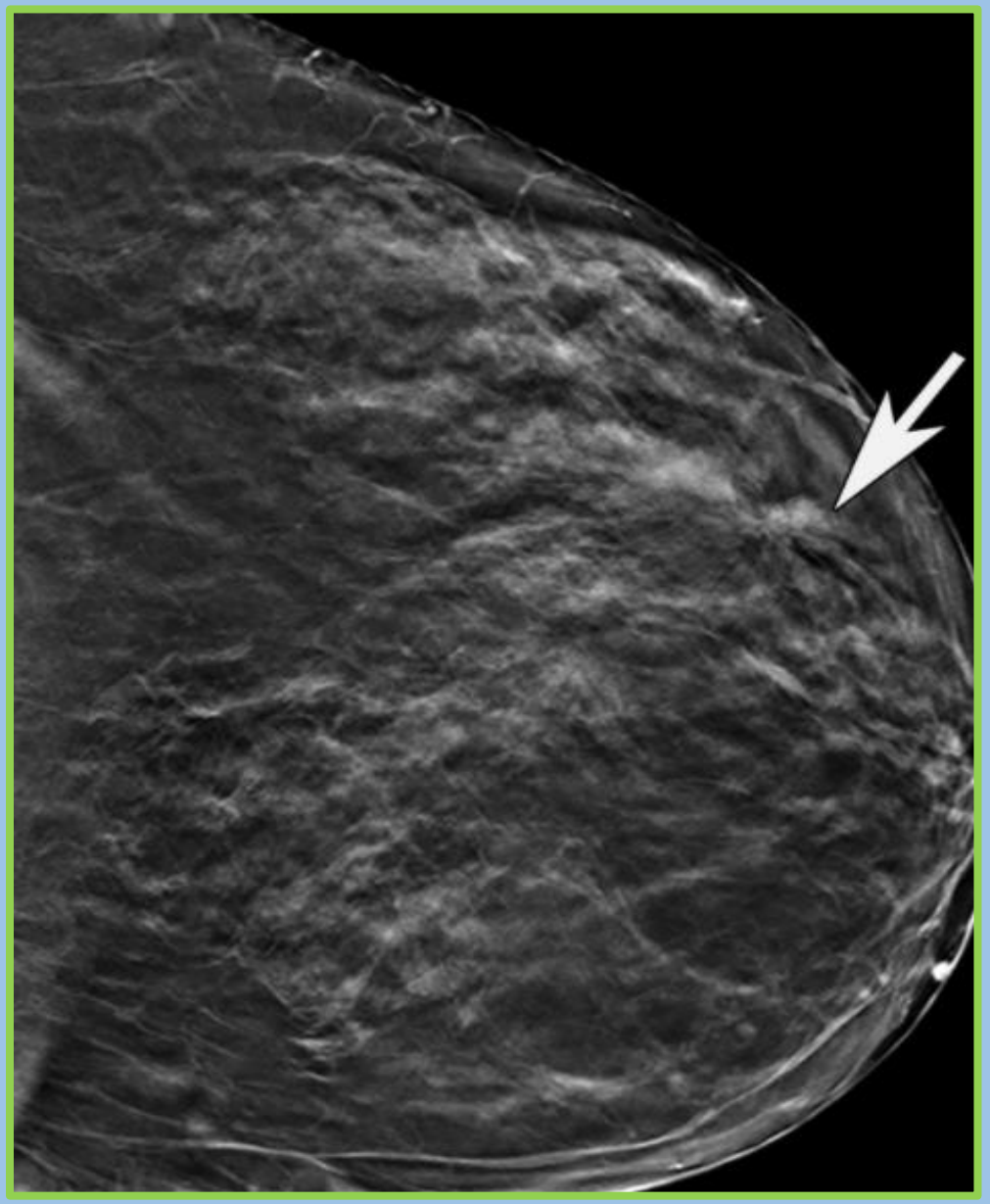
New options in Her2 positive Breast Cancer Treatment

Agenda

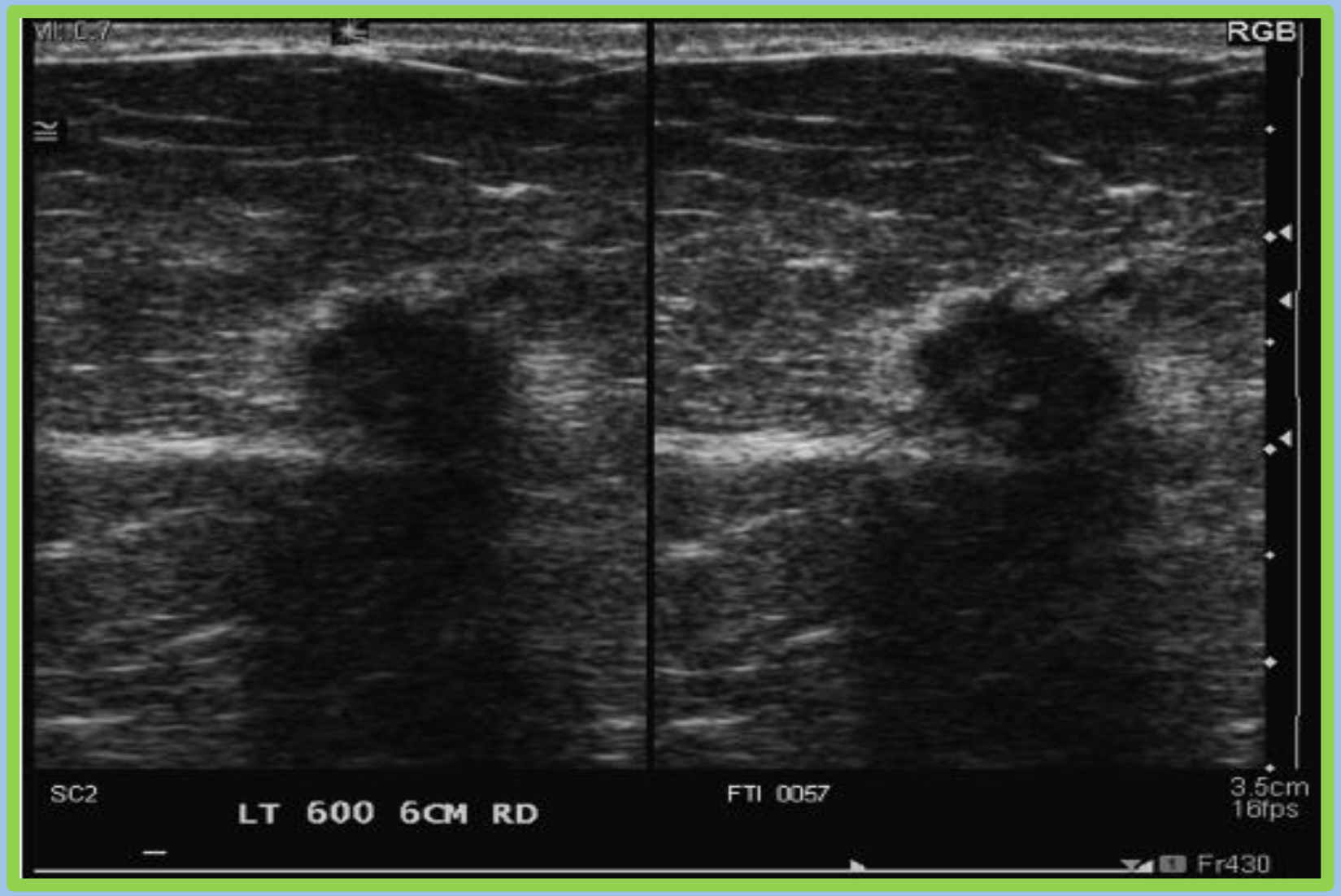
- Adjuvant therapy in HER-2 positive early breast cancer
  - ✓Low risk HER-2 positive
  - ✓High Risk HER-2 positive
- Extended adjuvant
- Neo-adjuvant
- Post neo-adjuvant
- First Distant recurrence
- Brain met

- 61-year-old patient
- Screen mammography:

✓There is small area of distortion in left lateral part.



US: Irregular hypo echoic mass in left breast 3 o clock is seen



- ✓ **CNB**: IDC, ER: 80%, PR: 30% and HER-2 neu by IHC was 2+ positive, Ki67: 20-25%
- ✓ had a lumpectomy and SLND
- ✓ Pathology showed an invasive ductal cancer, 2.1 cm, nodes were negative, grade 2 (T2N0M0)
- ✓ CISH : +

Next treatment :

- **Prefered regimen**
- **Anti Her2**
- **How long**

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SYSTEMIC ADJUVANT TREATMENT: HR-POSITIVE - HER2-POSITIVE DISEASE[d,q,y]

- Ductal/NST[t]
- Lobular
- Mixed
- Micropapillary

pT1, pT2, or pT3; and pN0 or pN1mi (≤2 mm axillary node metastasis)

- Tumor ≤0.5 cm
  - pN0 → Consider adjuvant endocrine therapy[z,aa] ± adjuvant chemotherapy[bb,cc] with trastuzumab[dd,ee] (category 2B)
  - pN1mi → Adjuvant endocrine therapy[z,aa] or Adjuvant chemotherapy[bb,cc] with trastuzumab[hh] and endocrine therapy[z,aa]
- Tumor 0.6–1.0 cm → Adjuvant chemotherapy[bb,cc] with trastuzumab[hh] and endocrine therapy[z,aa]
- Tumor >1 cm → Adjuvant chemotherapy[bb,cc] with trastuzumab (category 1) and endocrine therapy[z,aa]

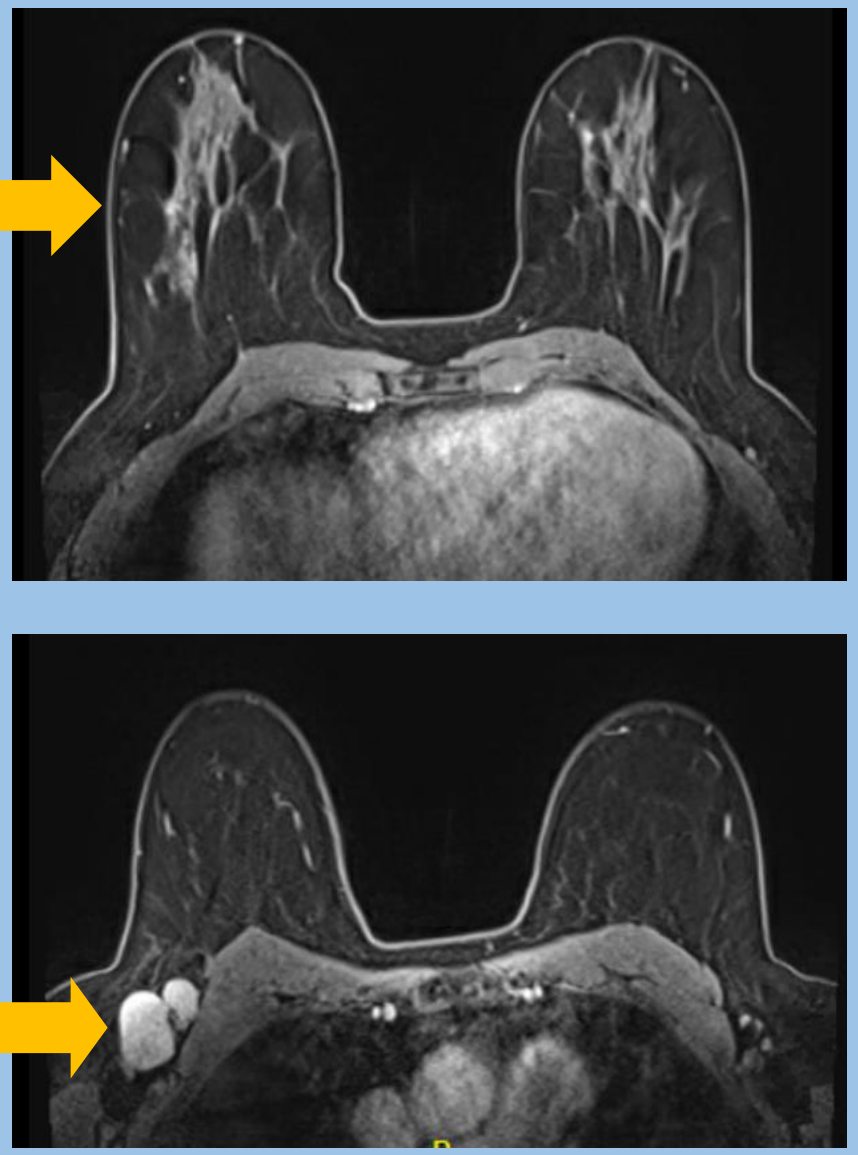
pN+ (≥1 ipsilateral metastases >2 mm) → Adjuvant chemotherapy[bb,cc] with trastuzumab[dd] (category 1) and endocrine therapy[z,aa,ff] or Adjuvant chemotherapy[bb,cc] with trastuzumab[dd] + pertuzumab and endocrine therapy[z,aa,ff]

- 33-year-old patient, palpable mass at her right axilla

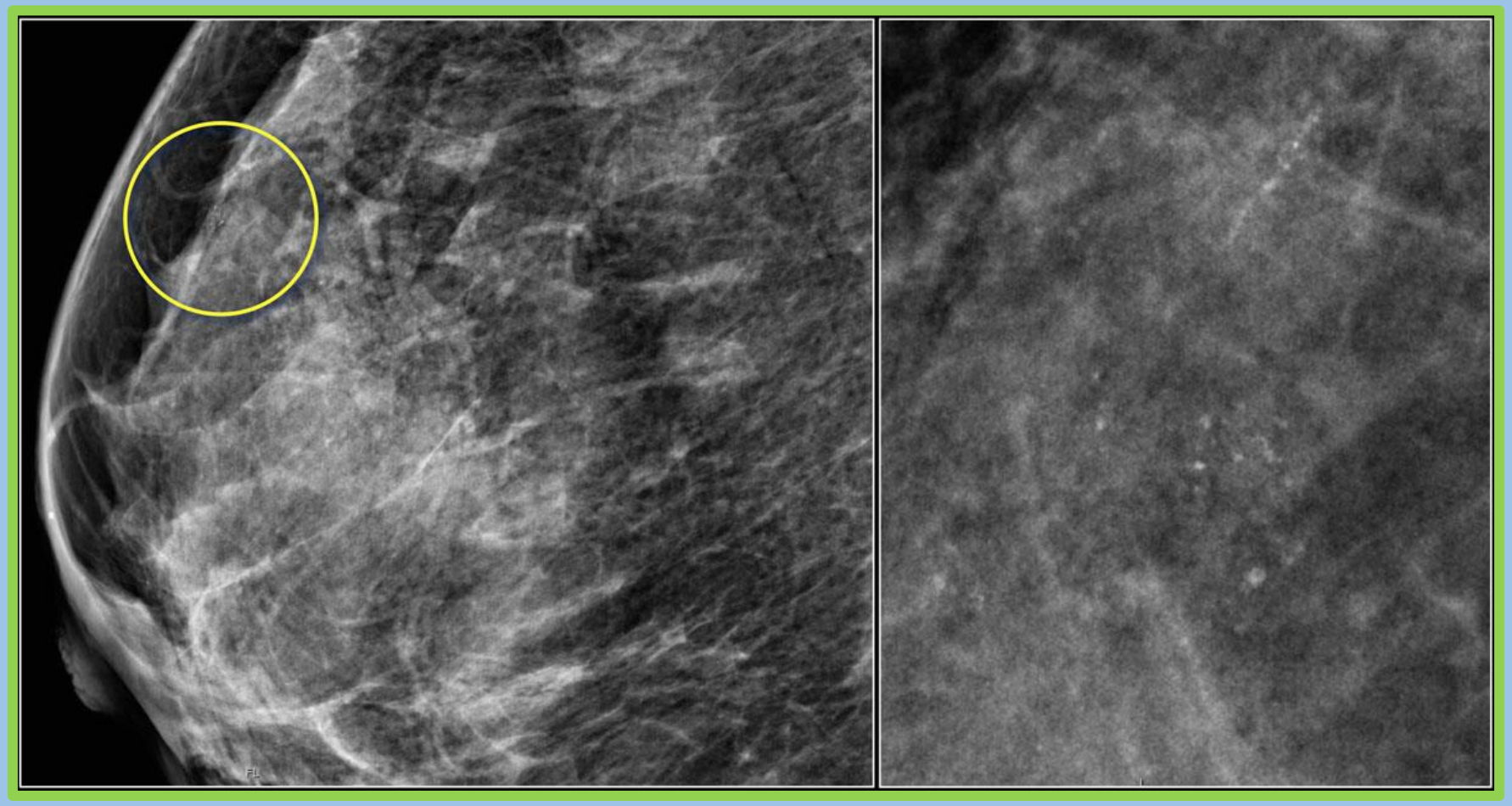
✓ US

✓ MRI

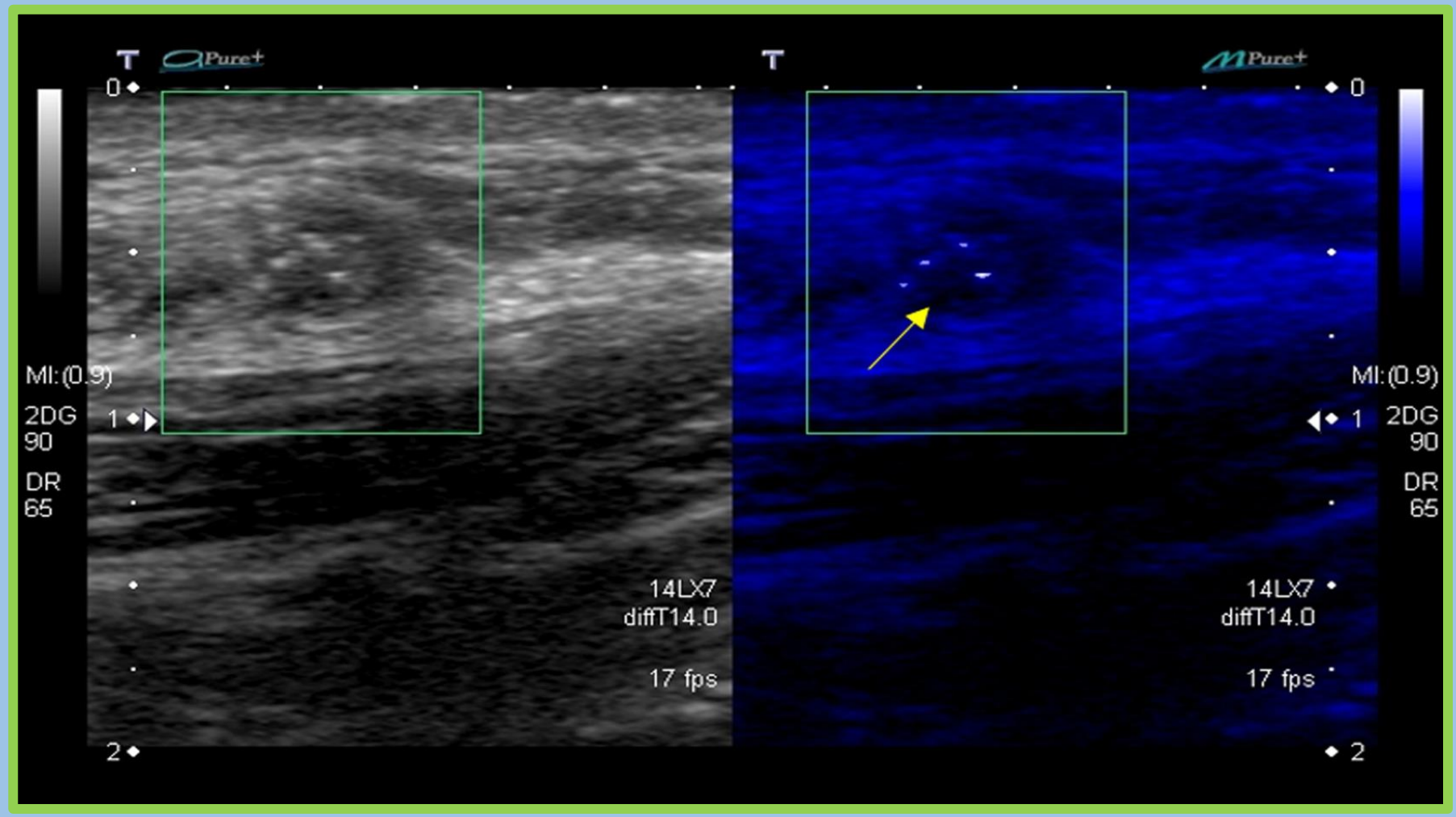
✓ Mammo



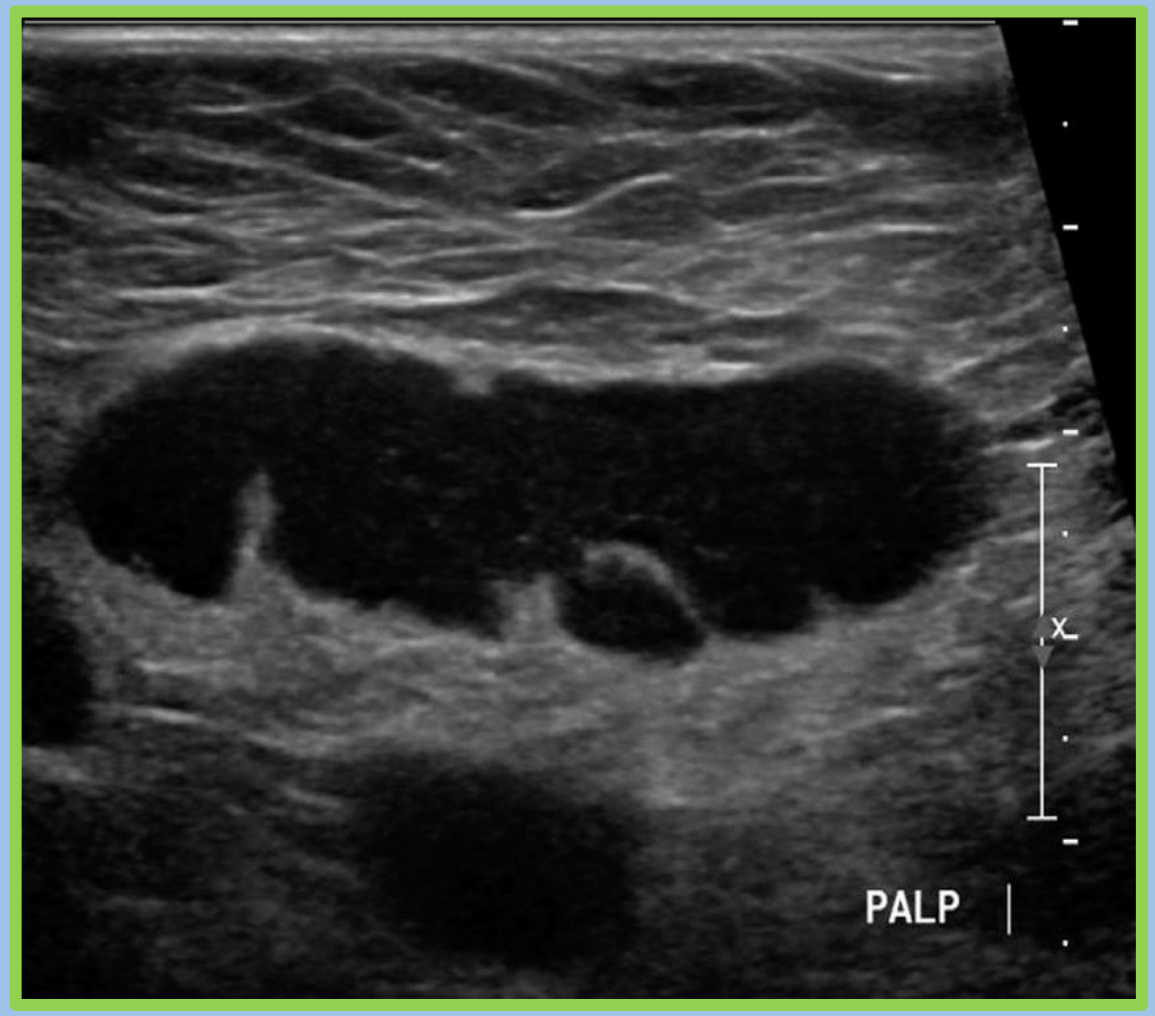
Mammography



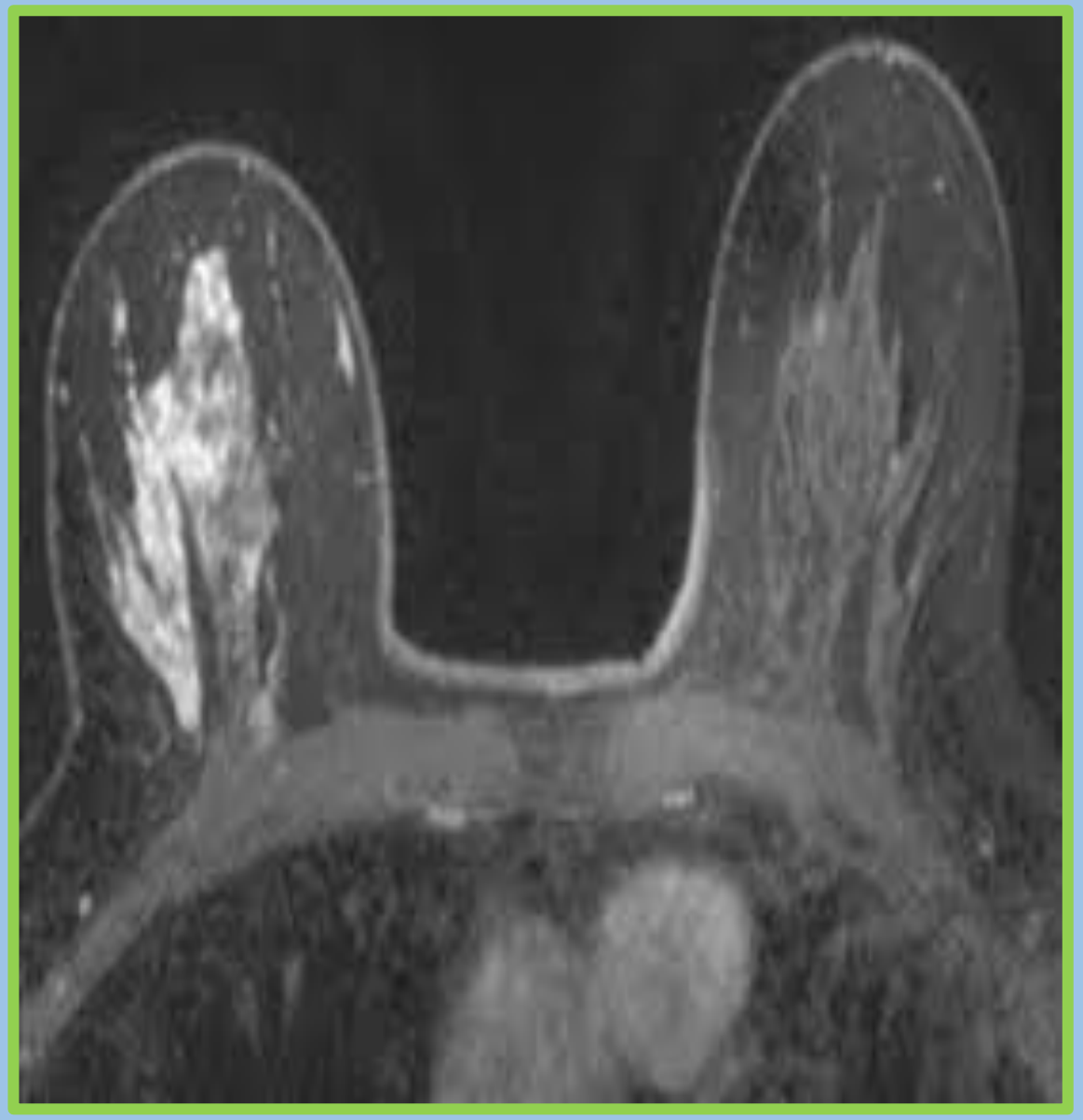
Breast Ultrasound



Axillary Ultrasound



Breast MRI



- Further work up and biopsy showed **invasive ductal cancer, grade 3**

- **ER: 40%, PR: 10%** and **HER-2 neu, IHC 3+ (positive)** , **ki67: 50%**

Who Should Be Considered for Preoperative Systemic Therapy for HER2-Positive EBC?

Patients with HER2+ EBC who have a tumor ≥ 2 cm (T2) diameter or who have node-positive disease regardless of hormone receptor status **should receive neoadjuvant chemotherapy with the addition of trastuzumab/pertuzumab**

Cardoso. Ann Oncol. 2019;30:1194. American Society of Breast Surgeons. Performance and practice guidelines for the use of neoadjuvant systemic therapy in the management of breast cancer. March 2, 2017.

- ✓ **Work ups**

  Fertility?

  Genetic tests?

- ✓ **Prefered regimen**

  Anthracyclin?

  Pertuzumab?

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PREOPERATIVE/ADJUVANT THERAPY REGIMENS[a,b,c,d,e]

HER2-Positive[l,m,n]

Preferred Regimens:

- Paclitaxel + trastuzumab[l,p]
- TCH (docetaxel/carboplatin/trastuzumab[l])
- TCHP (docetaxel/carboplatin/trastuzumab/pertuzumab[l])
- If no residual disease after preoperative therapy or no preoperative therapy: Complete up to one year of HER2-targeted therapy with trastuzumab[l] (category 1) ± pertuzumab.[q]
- If residual disease after preoperative therapy: Ado-trastuzumab emtansine (category 1) alone[r] If ado-trastuzumab emtansine discontinued for toxicity, then trastuzumab[l] (category 1) ± pertuzumab to complete one year of therapy.[q]

Useful in Certain Circumstances:

- Docetaxel + cyclophosphamide + trastuzumab[l]
- AC followed by T[h] + trastuzumab[l,o] (doxorubicin/cyclophosphamide followed by paclitaxel plus trastuzumab, various schedules)
- AC followed by T[h] + trastuzumab[l] + pertuzumab[o] (doxorubicin/cyclophosphamide followed by paclitaxel plus trastuzumab plus pertuzumab, various schedules)

Other Recommended Regimens:

- AC followed by docetaxel[h] + trastuzumab[l,o] (doxorubicin/cyclophosphamide followed by docetaxel + trastuzumab)
- AC followed by docetaxel[h] + trastuzumab[l] + pertuzumab[o] (doxorubicin/cyclophosphamide followed by docetaxel + trastuzumab + pertuzumab)

- **TCHP *6**
- **Clinical response**
- **Referred for surgery**
- **Surgery??**

- She had lumpectomy and node dissection
- 1 of 12 dissected LNs were involved by tumor.

Post-Neoadjuvant Therapy

- **TDM1 3.6mg/kg 14 courses**
  (major complications? Monitoring?)
- **Hormonal therapy?**
- **Follow up**

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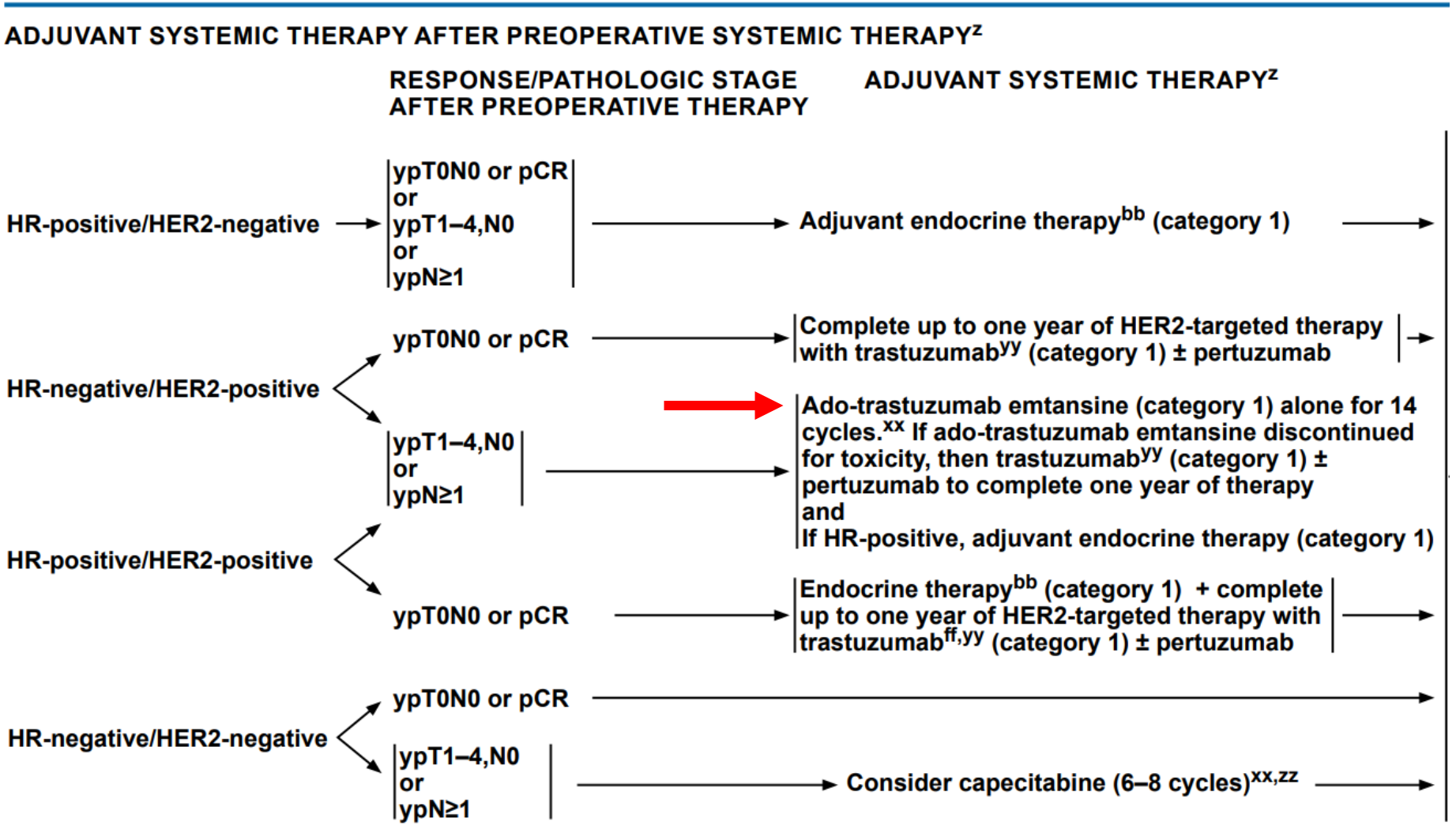

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SYSTEMIC ADJUVANT TREATMENT: HR-POSITIVE - HER2-POSITIVE DISEASE[d,q,y]

pT1, pT2, or pT3; → Tumor ≤0.5 cm → pN0 → Consider adjuvant endocrine therapy[z,aa] ± adjuvant chemotherapy[bb,cc] with trastuzumab[dd,ee] (category 2B)

Tumor ≤0.5 cm → pN1mi → Adjuvant endocrine therapy[z,aa] or

[ff] Consider extended adjuvant neratinib following adjuvant trastuzumab-containing therapy for patients with HR-positive, HER2-positive disease with a perceived high risk of recurrence. The benefit or toxicities associated with extended neratinib in patients who have received pertuzumab is unknown.

. Participation in clinical trials is especially encouraged.

ablation in premenopausal patients with HR-positive breast cancer is similar to that achieved with CMF alone. See Adjuvant Endocrine Therapy (BINV-K).

[bb] Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. Available data suggest that sequential or concurrent endocrine therapy with RT is acceptable. See Adjuvant Endocrine Therapy (BINV-K) and Preoperative/Adjuvant Therapy Regimens (BINV-L).

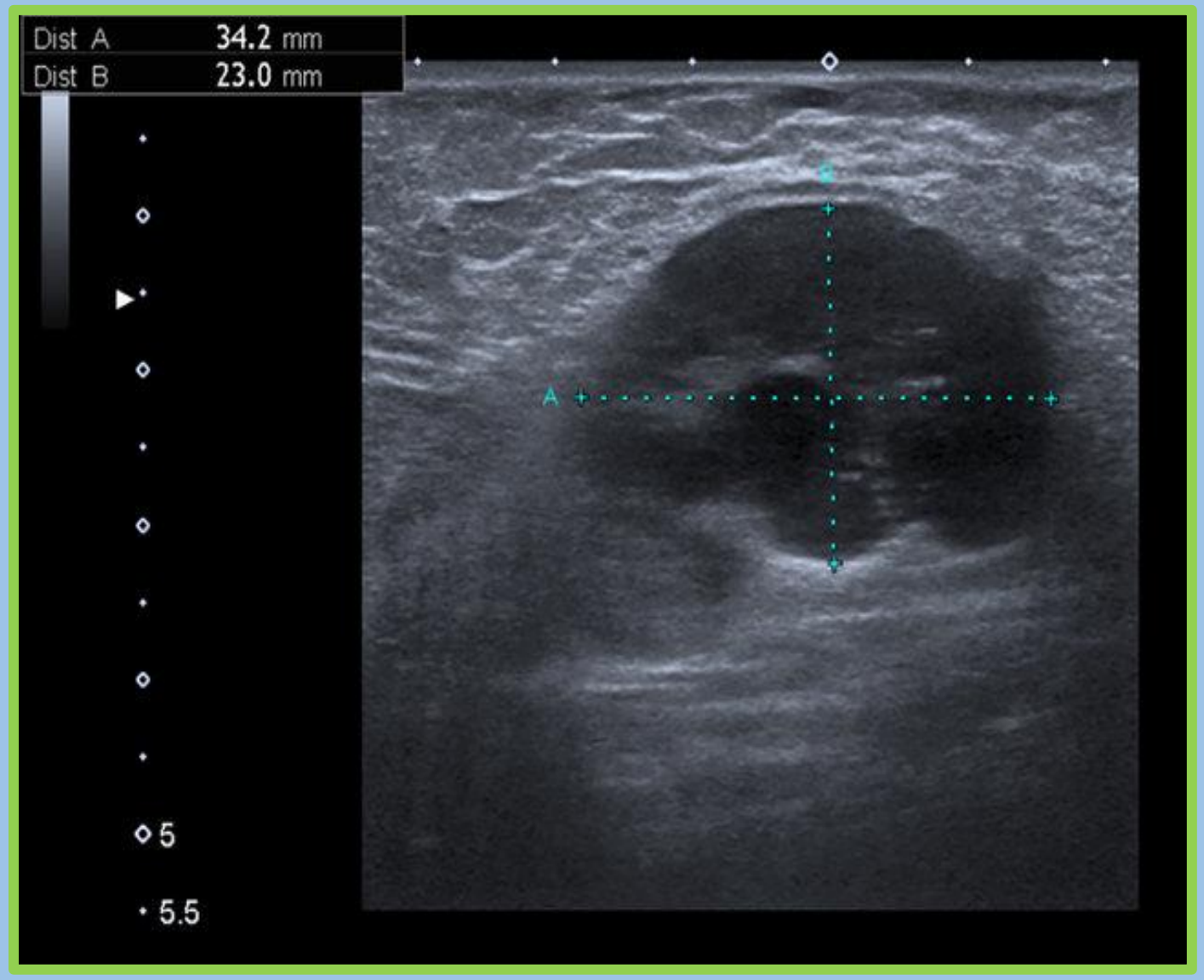
is less than 5% and endocrine therapy remains a viable option for systemic treatment.

[ff] Consider extended adjuvant neratinib following adjuvant trastuzumab-containing therapy for patients with HR-positive, HER2-positive disease with a perceived high risk of recurrence. The benefit or toxicities associated with extended neratinib in patients who have received pertuzumab is unknown.

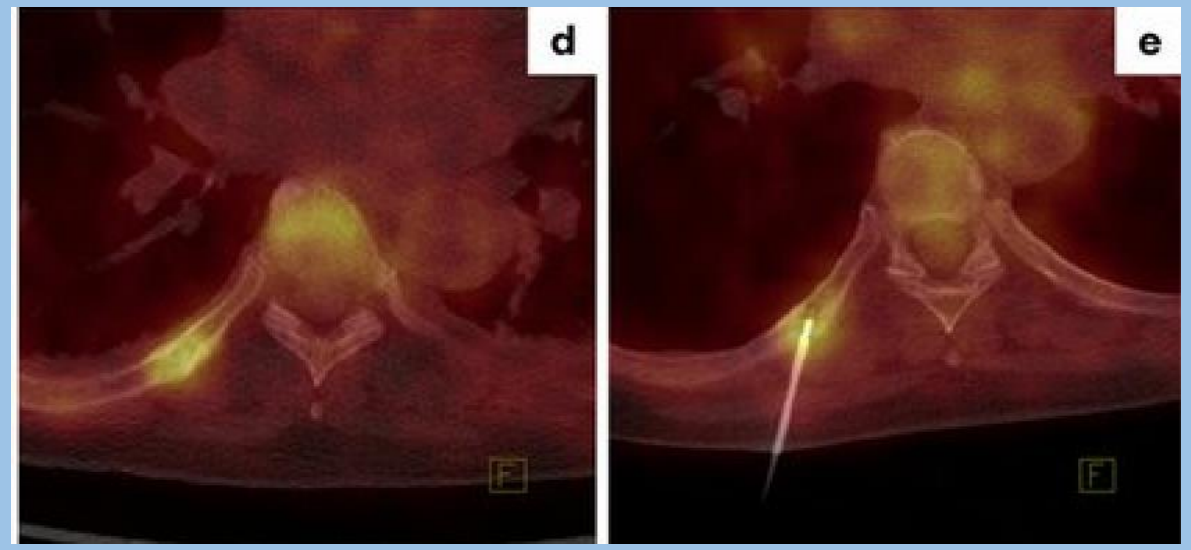
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

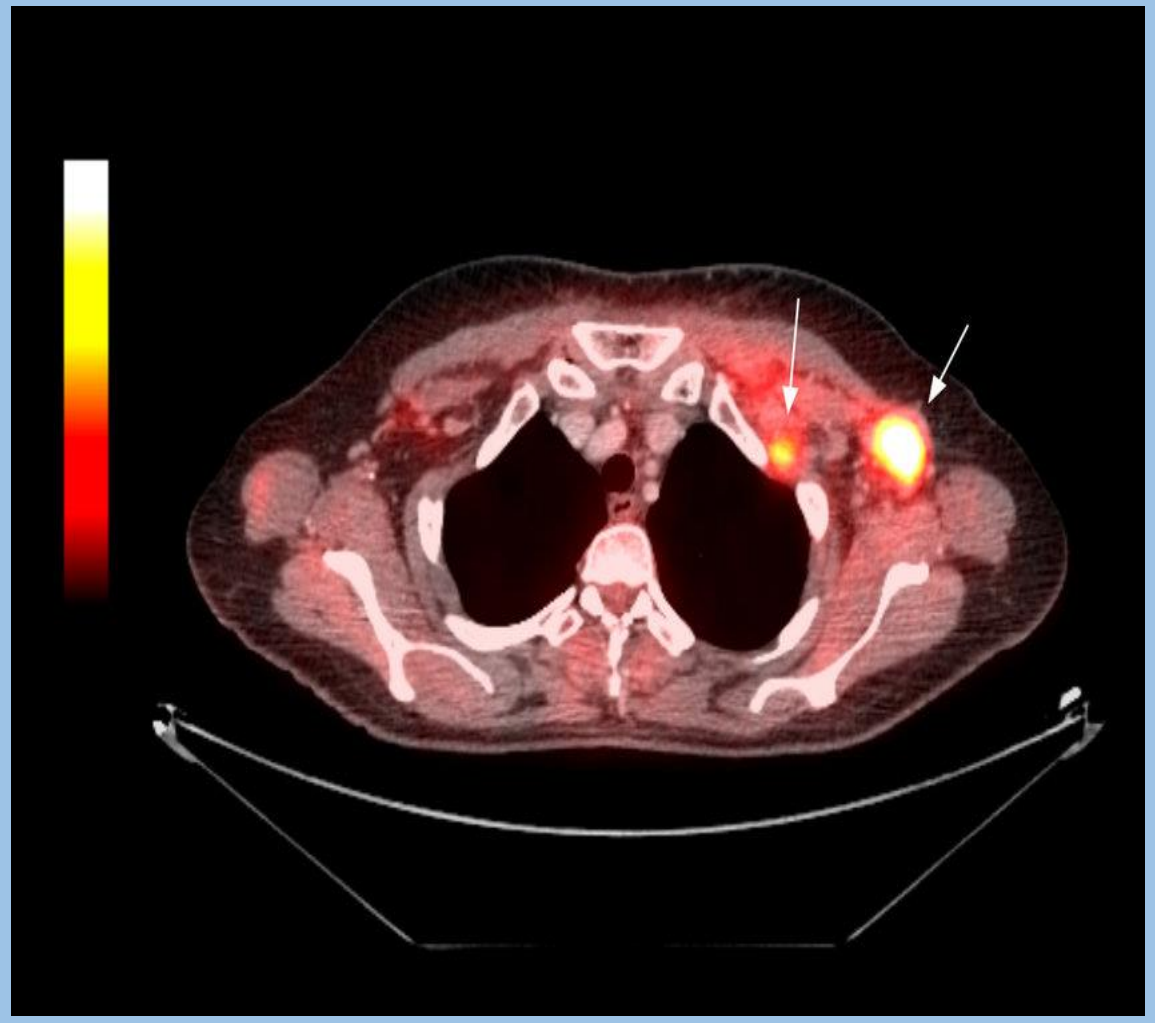
After 10 months:

- **Contralateral axillary mass**


Dist A 34.2 mm
Dist B 23.0 mm
A
5
5.5

Next Work ups?





- ✓ **PET CT**
- ✓ **Biopsy**

IDC; G:3; IHC: ER:30%, PR: neg, Her2: 3+

Next Step?

Next step

- ✓ Systemic therapy?
- ✓ Surgery?
- ✓ Bone modulating agents?

- **paclitaxel, trastuzumab, pertuzumab?**
- **TDM1?**

✓ **Do you think about local treatment?**

Surgery?
XRT?

Maintenance:

- **Trastuzumab +/- pertuzumab……..** (how long?)

  (she refused taking maintenance trastuzumab after 14 cycles)

- **Hormonal therapy**
  (OS + AI)

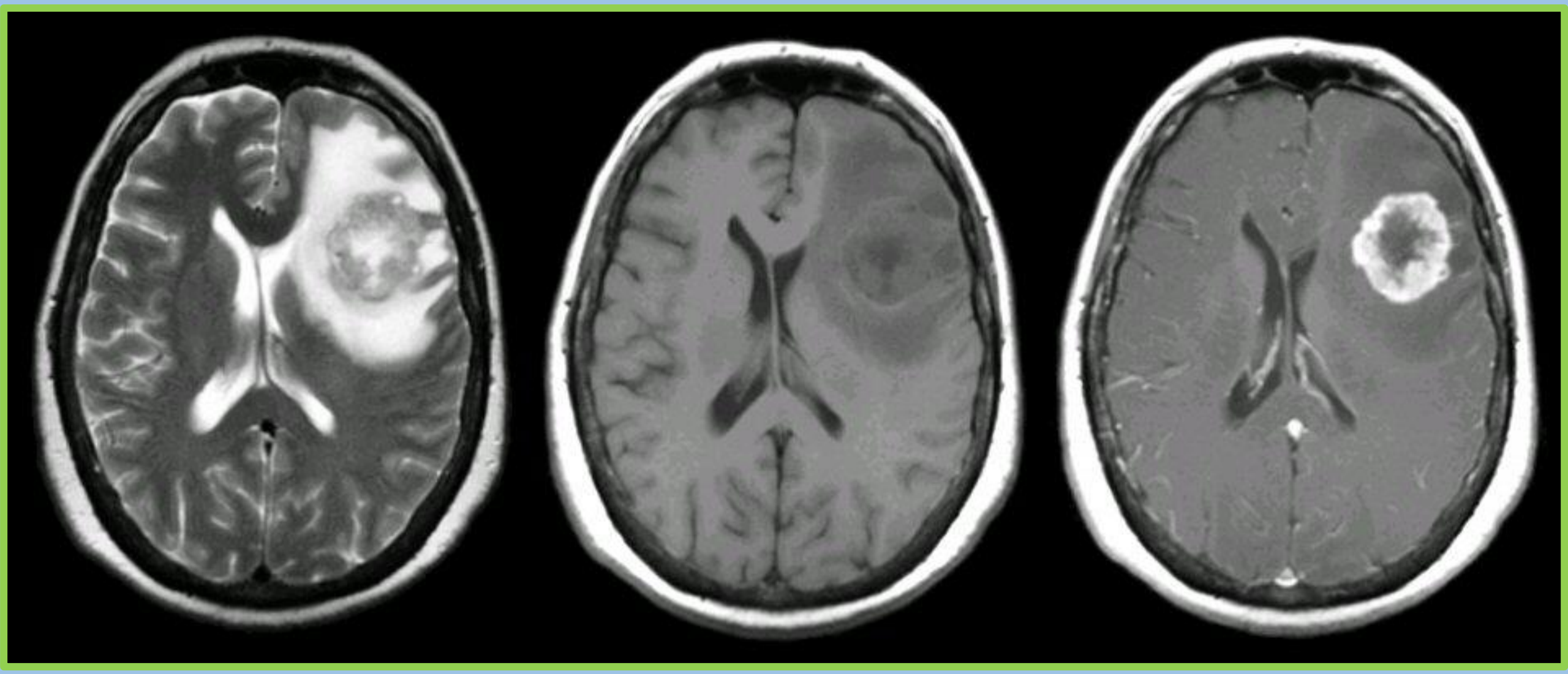
After 8 months:

- presented with headaches, difficulty expressing her words, and focal right sided seizures

T2

T1

T1 GAD



PET CT:

- ✓ **No other new abnormal finding**

Next Step?

- **Neurosurgical evacuation?**
- **SRS?**
- **Radiotherapy?**
  SRT Vs WBRT

- ✓ **Tucatinib, Trastuzumab, capecitabine?**
- ✓ **Hormon therapy?**

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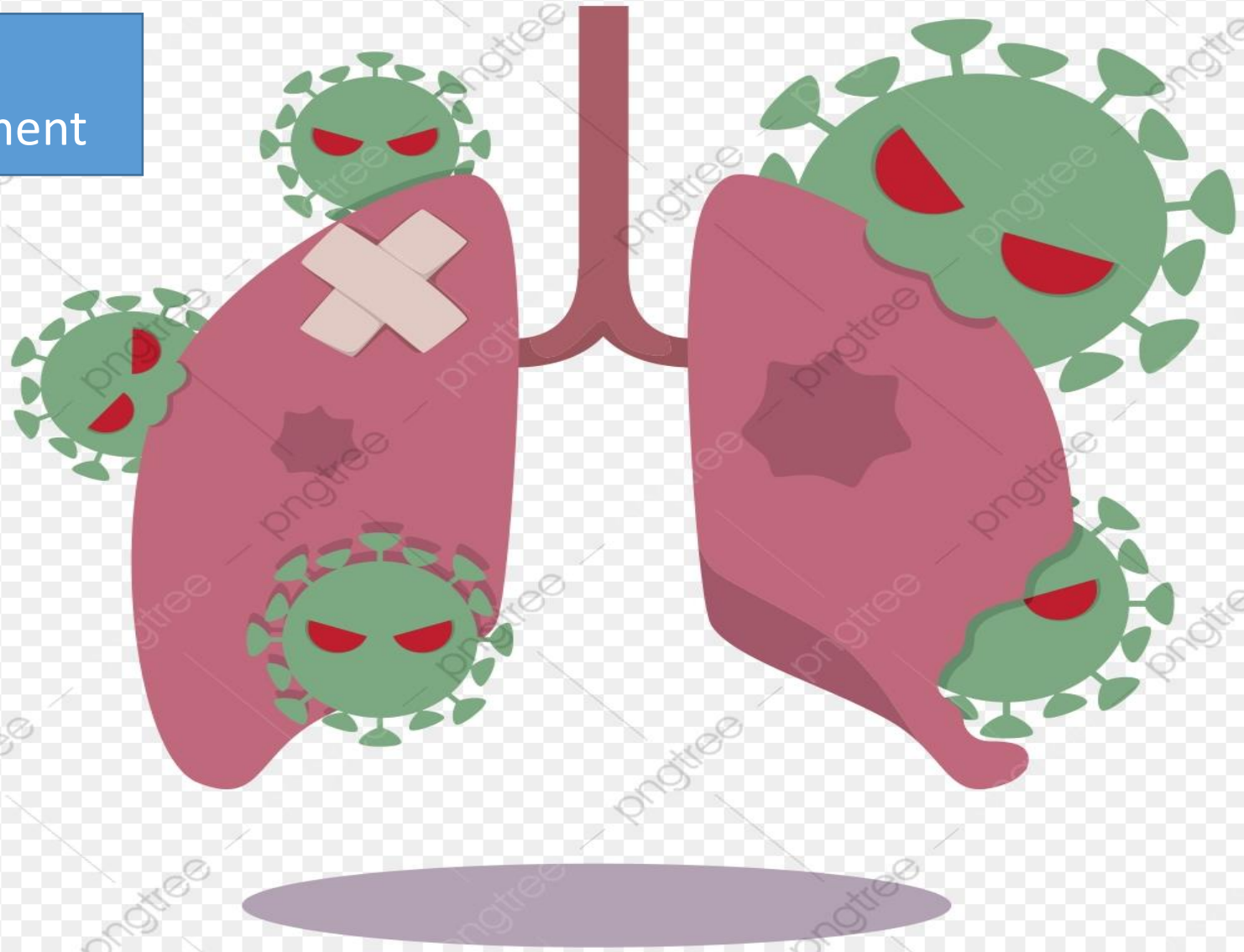
SYSTEMIC THERAPY REGIMENS FOR RECURRENT UNRESECTABLE (LOCAL OR REGIONAL) OR STAGE IV (M1) DISEASE[j]

HER2-Positive			
Setting	**Regimen**	**NCCN Category of Preference**	**NCCN Category of Evidence**
First line[k]	Pertuzumab + trastuzumab + docetaxel[l]	Preferred Regimen	1
	Pertuzumab + trastuzumab + paclitaxel[l]	Preferred Regimen	2A
Second line	Ado-trastuzumab emtansine (T-DM1)	Preferred Regimen	1
Third line and beyond	Tucatinib + trastuzumab + capecitabine[l,m,n]	Other Recommended Regimen	1
	Fam-trastuzumab deruxtecan-nxki[m,o,p]	Other Recommended Regimen	2A
	Trastuzumab + docetaxel or vinorelbine[l,q]	Other Recommended Regimen	2A
	Trastuzumab + paclitaxel ± carboplatin[l,q]	Other Recommended Regimen	2A
	Capecitabine + trastuzumab or lapatinib[l,q]	Other Recommended Regimen	2A
	Trastuzumab + lapatinib[l,q] (without cytotoxic therapy)	Other Recommended Regimen	2A
	Trastuzumab + other agents[l,q,r,s]	Other Recommended Regimen	2A
	Neratinib + capecitabine[q]	Other Recommended Regimen	2A
	Margetuximab-cmkb + chemotherapy[q] (capecitabine, eribulin, gemcitabine, or vinorelbine)	Other Recommended Regimen	2A
Additional targeted therapy options (See BINV-R)			

- **well controlled for 13 months**

  …. then

Finally …… expired
due to covid 19 lung involvement




Thank You

- For those with residual disease after neoadjuvant HER2-directed therapy, switch to T-DM1 in the adjuvant setting and continue for 14 cycles.
- Most of Her2 positive breast cancers are high grade (more than grade1).
- Lapatinib is not used in adjuvant setting.
- TDM1 is an anti her2 treatment consisting of the monoclonal Ab trastuzumab covalently linked to the cytotoxic agent.
- Thrombocytopenia is among the most important adverse effects of TDM1.
- In denovo metastatic disease (first line treatment) lapatinib- capecitabin has not been used.
- Neratinib targets Her1, Her2, Her4

- Anti-HER2-directed therapy can be continued for years in metastatic patients, without disease progression or cardiac toxicity.
- Evaluation of cardiac function during anti Her2 therapy is recommended in 3 months intervals.
- Local treatment in widespread metastatic breast cancer has not improved overall survival.
- Keytruda (pembrolizumab) is a PD1/PDL1 inhibitor drug. (not an anti Her2!)
- The preferred protocol for brain metastases in patients whom previously received other anti Her2 treatments is combination of Tucatinib, Trastuzumab, Capecitabin