GS Conference

June 21st , 2016

Presenter: R1蘇鈺文

Supervisor:常傳訓主任

Case profile

- Chart number: xxxxxxx
- Name: OOO
- Age: 51 years old
- Gender: female
- Marital: Married
- Hospitalization date: 2016/05/30~06/06

Chief complaint

- Left breast extensive tumor with bleeding for days.

Present illness

- Left breast palpable mass half year ago
- Left breast extensive tumor with bleeding and left chest wall skin multiple satellite lesions for days.
- Left breast locally advanced cancer suspected. Further left breast cancer staging was indicated. She was admitted for further evaluation.

Past & Personal history

- Past history: History of hepatitis B infection
- GYN history: G1P1, premenopause, no HRT use
- Allergy: NKA

- Tobacco: 0.5PPD for 30 years and quit for 1 year
- Alcohol drinking: No
- Betel nuts: No

- Family history: Aunt has cervical cancer

Left breast extensive tumor with bleeding, with left axillary enlarged lymphadenopathies, Left chest wall skin multiple satellite lesions.

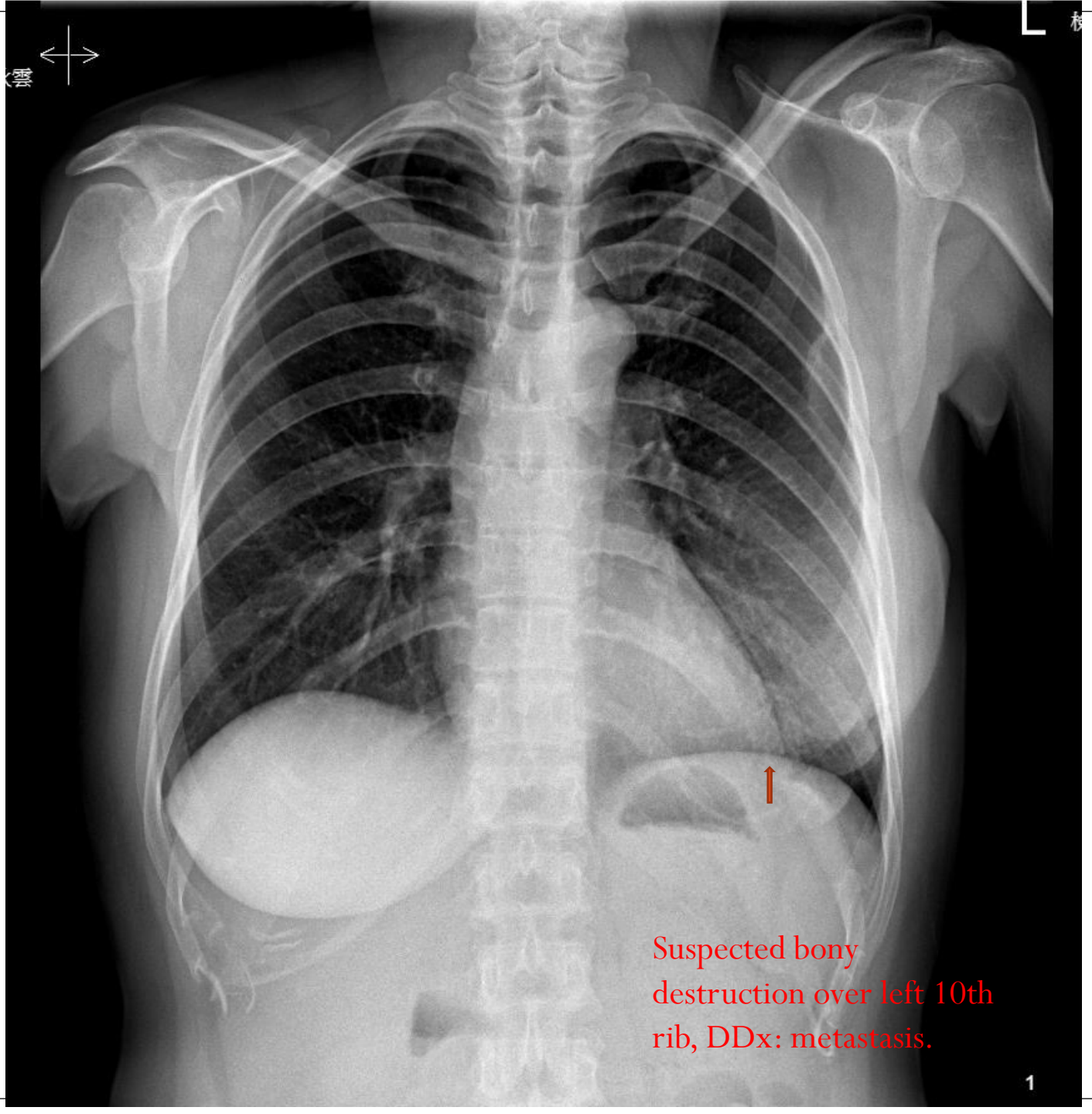
Laboratory data

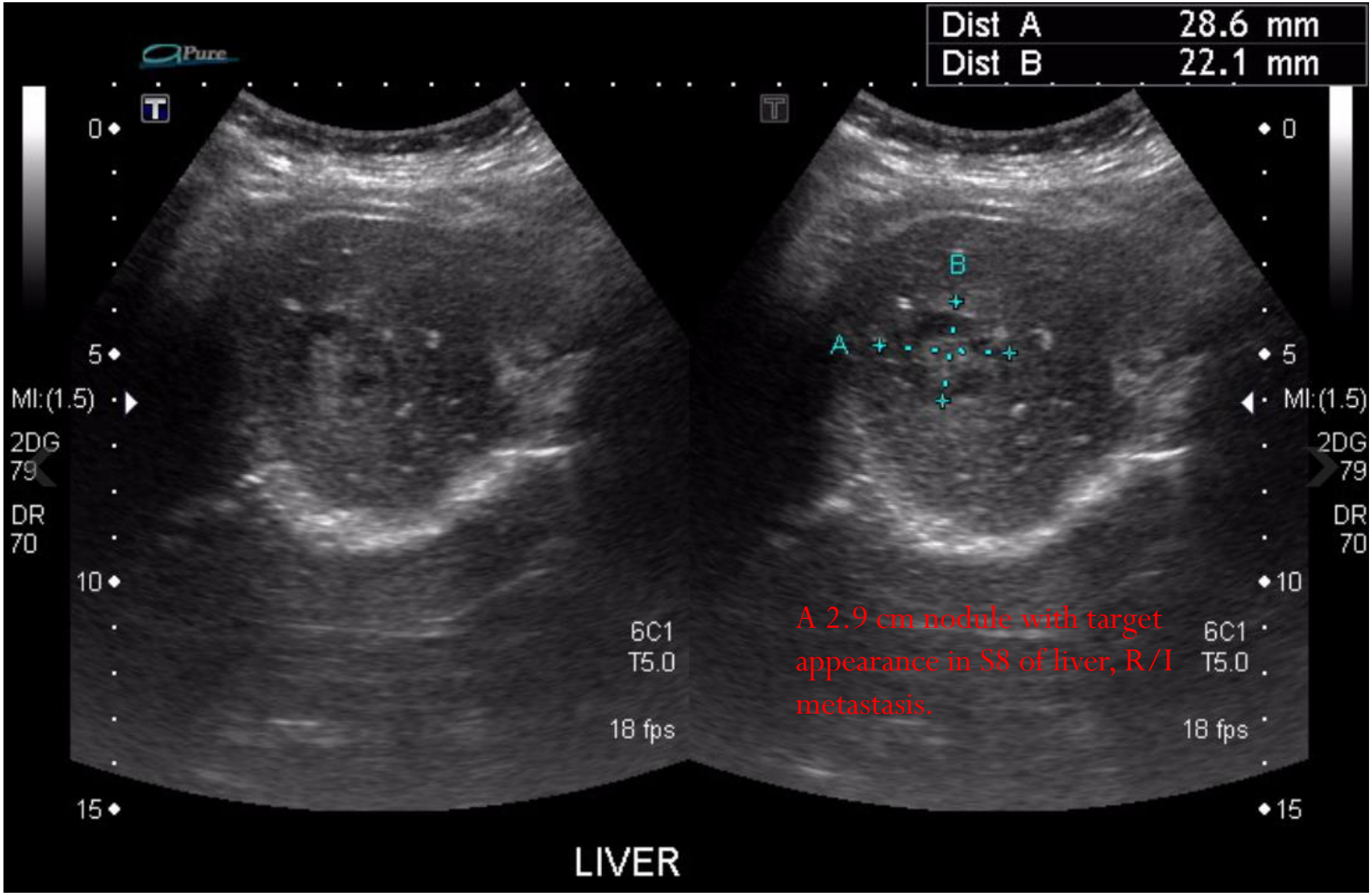
項目名稱	檢驗報告	單位	正常值(Low)	正常值(High)
CBC				
WBC	8.5	10^3/uL	4.000	10.000
RBC	3.66	10^6/uL	3.700	5.500
HGB	10.6	g/dL	11.300	15.300
HCT	32.4	%	33.000	47.000
MCV	88.5	fL	80.000	100.000
MCH	29.0	pg	25.000	34.000
MCHC	32.7	g/dL	30.000	36.000
PLT	398	10^3/uL	130.000	400.000
DIFF				
NEUT%	77.3	%	40.000	75.000
LYMPH%	14.8	%	20.000	45.000
MONO%	6.3	%	2.000	10.000
EO%	1.5	%	1.000	6.000
BASO%	0.1	%	0.000	1.000

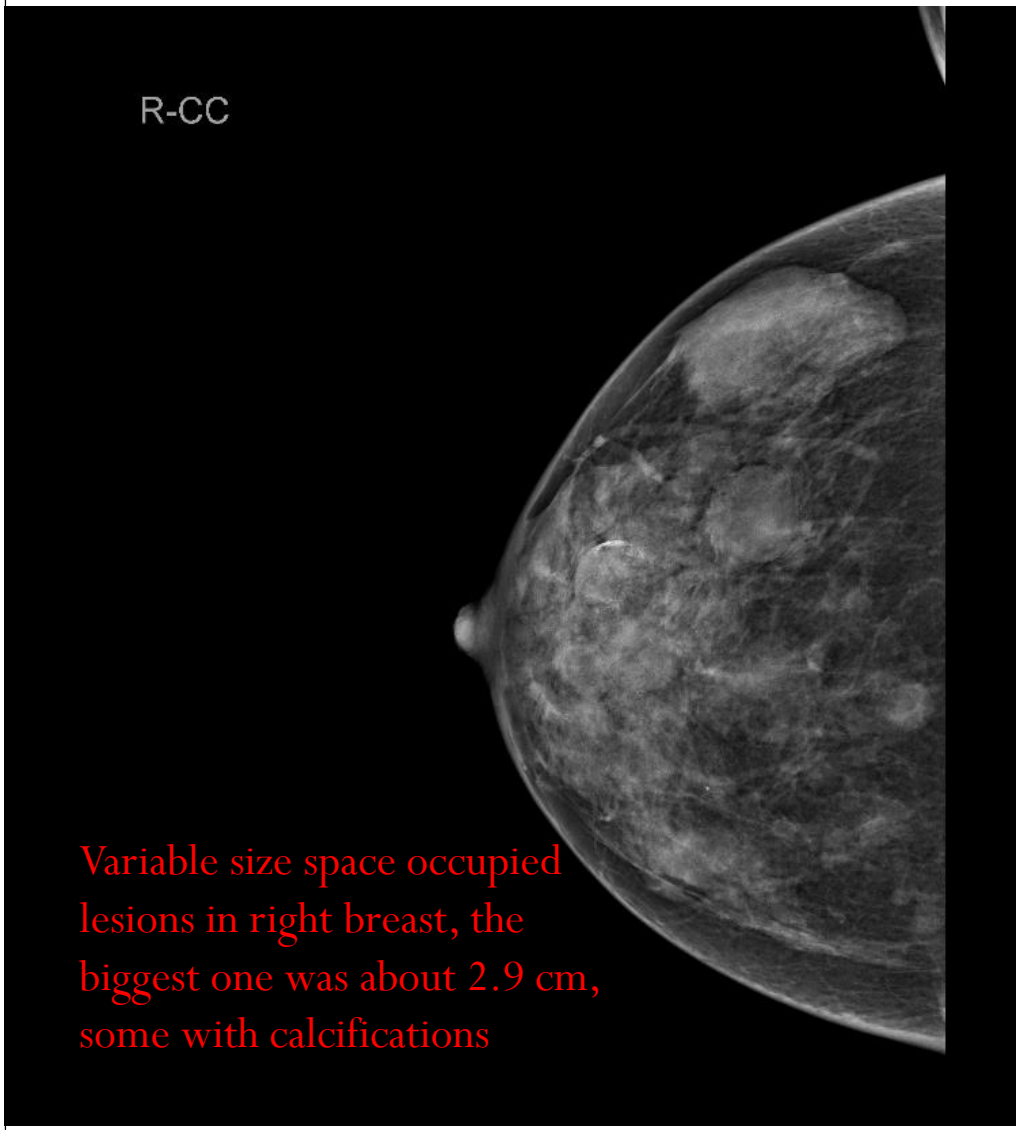
項目名稱	檢驗報告	單位	正常值(Low)	正常值(High)
Glucose AC	98	mg/dL	70.000	110.000
BUN	10.1	mg/dL	8.000	20.000
Creatinine	0.61	mg/dL	0.440	1.270
eGFR	110		0.000	99999.000
Uric acid	5.3	mg/dL	2.600	8.000
AST	69	IU/L	5.000	50.000
ALT	21	IU/L	5.000	50.000
Alkalinphosohatase	124	IU/L	38.000	126.000
Triglyceride	138	mg/dL	50.000	200.000
Cholesterol, Total	149	mg/dL	0.000	200.000
Na	139	mmol/L	136.000	144.000
K	4.2	mmol/L	3.600	5.100
Cl	103	mmol/L	101.000	111.000

項目名稱	檢驗報告	單位	正常值(Low)	正常值(High)
CEA	27.1	ng/mL	0.000	6.500
CA153	22.1	U/mL	0.000	25.000

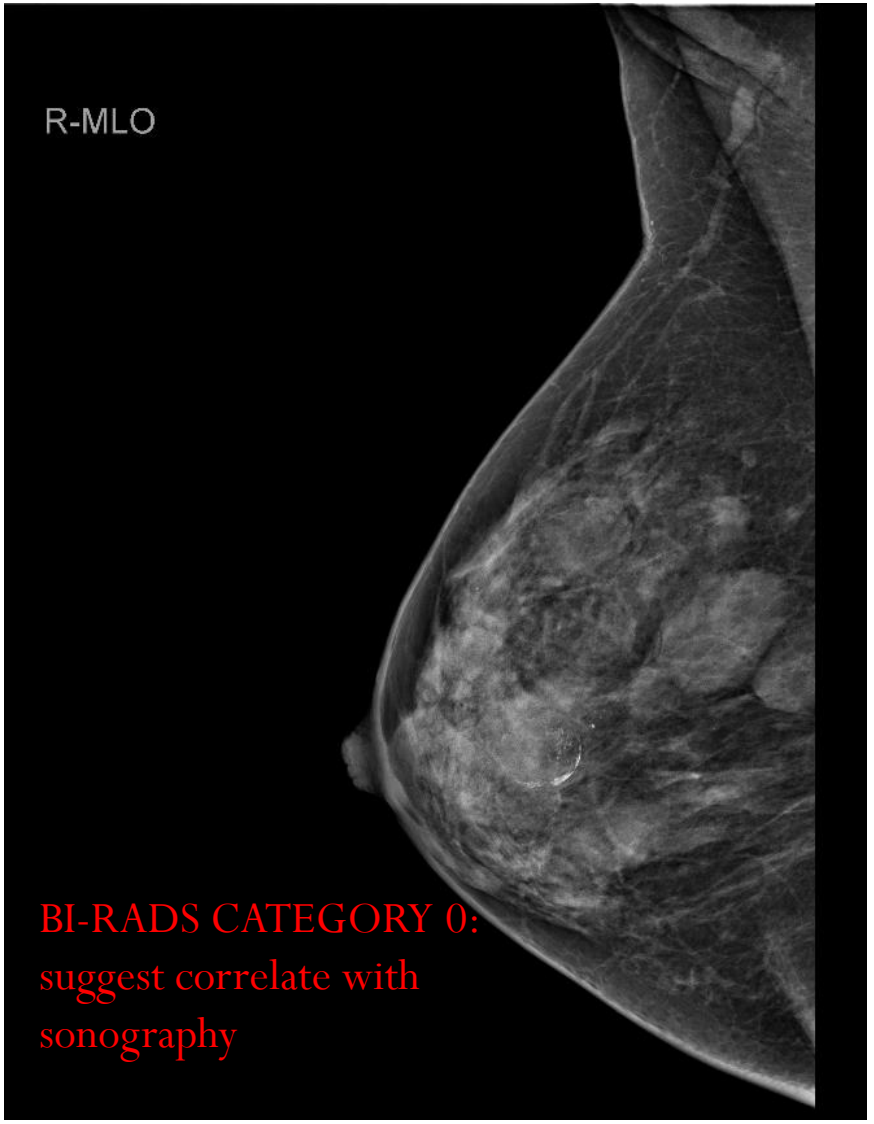
項目名稱	判斷	結果值	單位
HBsAg		0.020	IU/mL
備註：(Non-Reactive)			
Anti-HBs	*	17.4	mIU/mL
備註：(Reactive)			
Anti-HBc	*	10.21	S/CO
備註：(Reactive)			
Anti-HCV		0.06	S/CO
備註：(Non-Reactive)			


Suspected bony destruction over left 10th rib, DDx: metastasis.

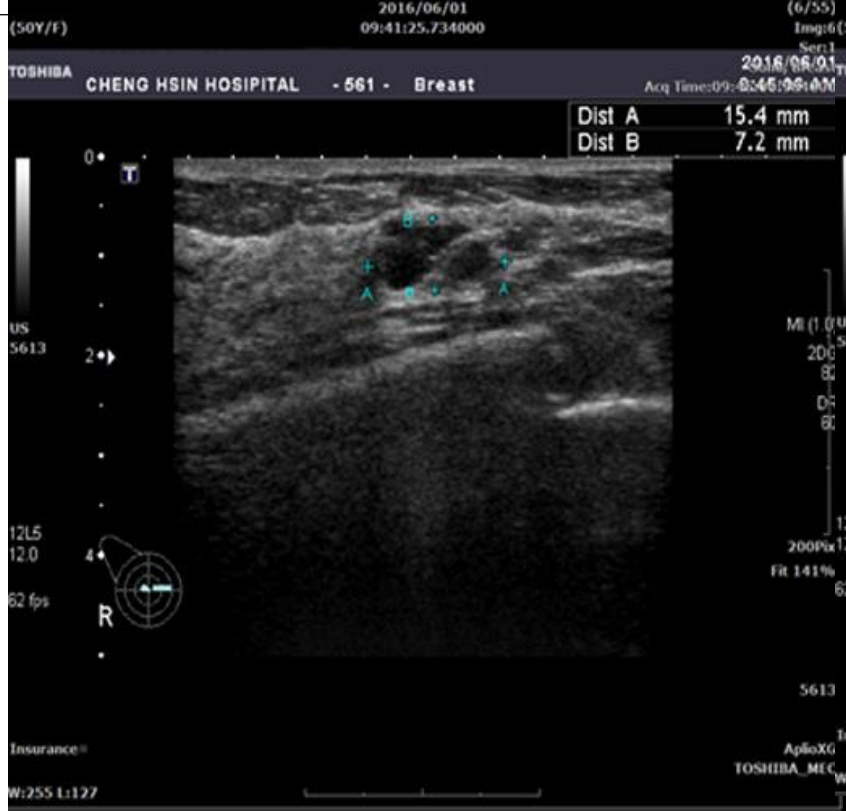

Dist A 28.6 mm
Dist B 22.1 mm
B
A
MI:(1.5)
2DG
79
DR
70
6C1
T5.0
18 fps
A 2.9 cm nodule with target appearance in S8 of liver, R/I metastasis.
LIVER

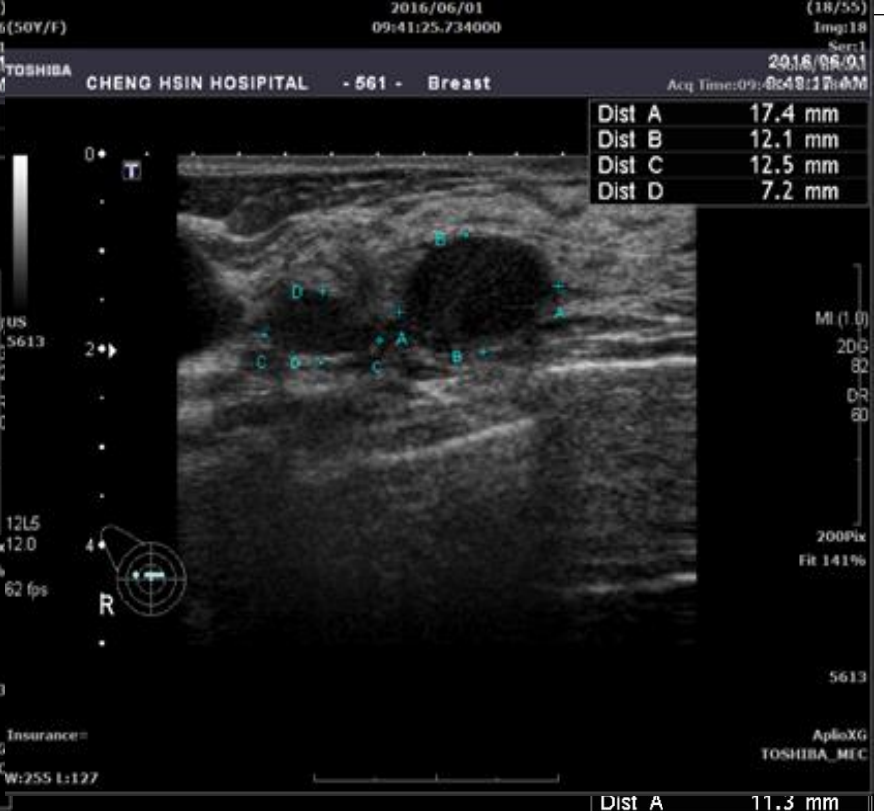


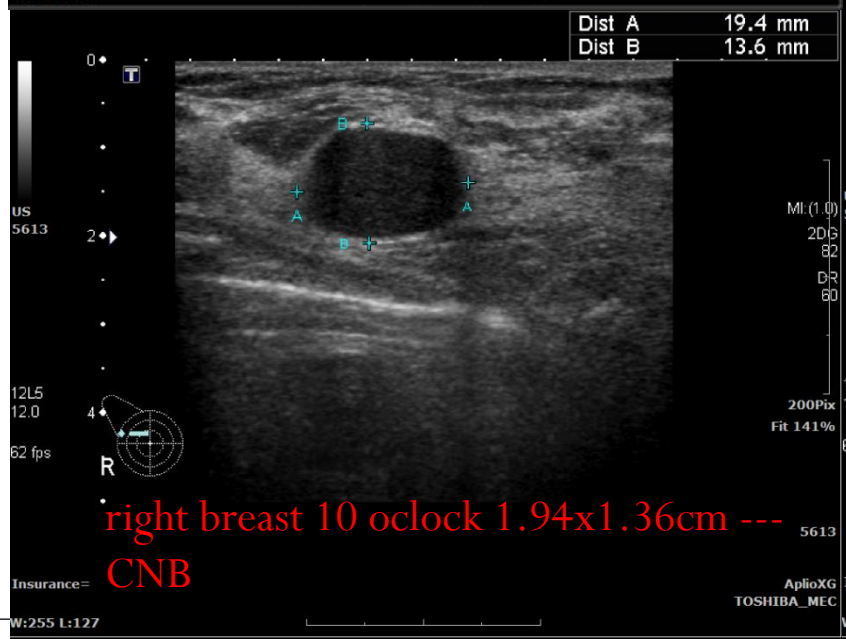
Variable size space occupied lesions in right breast, the biggest one was about 2.9 cm, some with calcifications



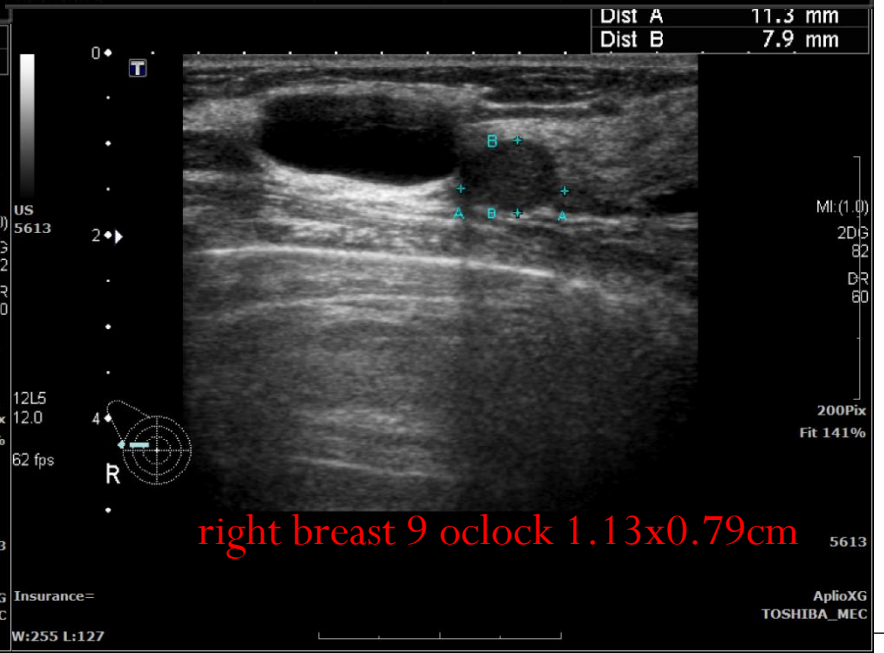
BI-RADS CATEGORY 0: suggest correlate with sonography



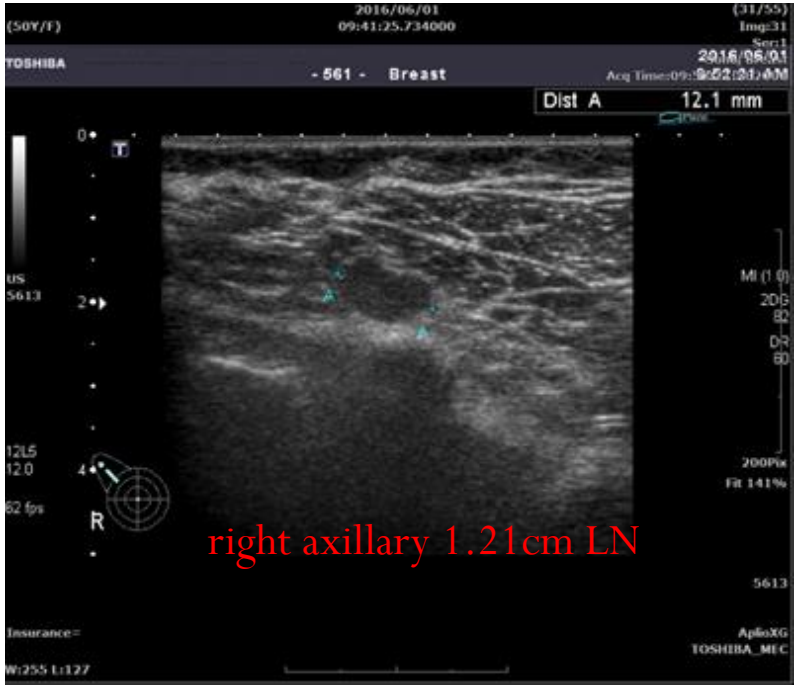




right breast 10 oclock 1.94x1.36cm --- CNB



right breast 9 oclock 1.13x0.79cm


2016/06/01
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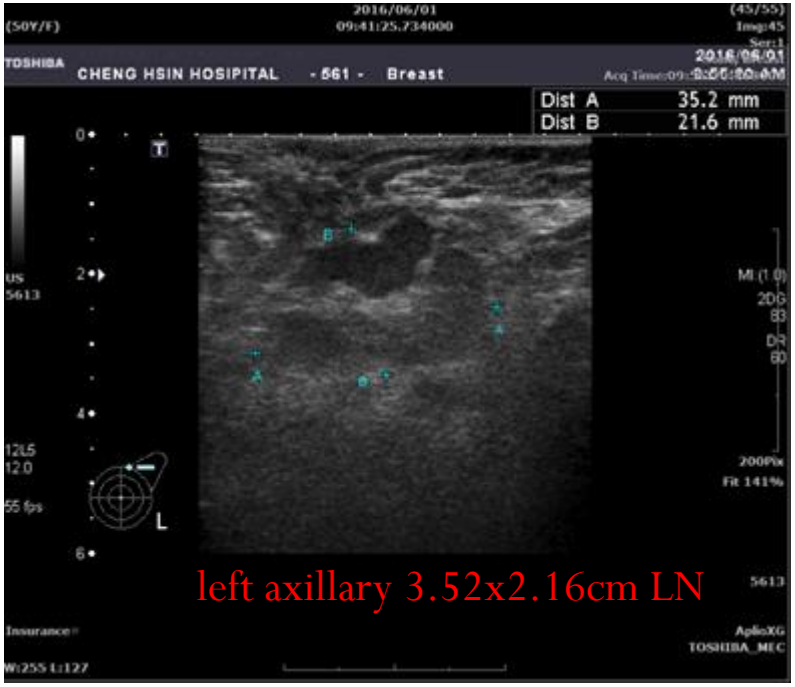
TOSHIBA
- 561 - Breast
Dist A 12.1 mm
right axillary 1.21cm LN


2016/06/01
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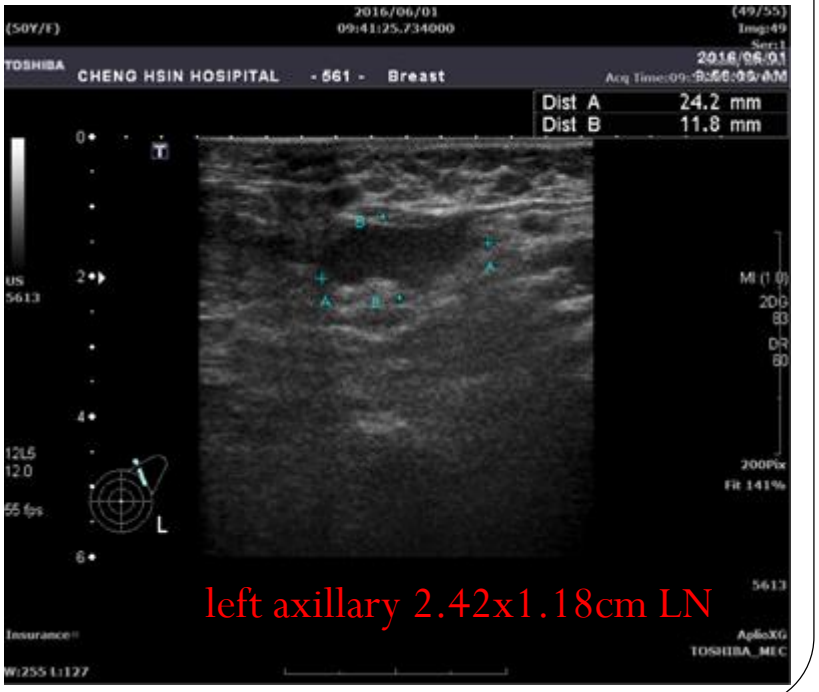
TOSHIBA
CHENG HSIN HOSPITAL - 561 - Breast
Dist A 35.2 mm
Dist B 21.6 mm
left axillary 3.52x2.16cm LN


2016/06/01
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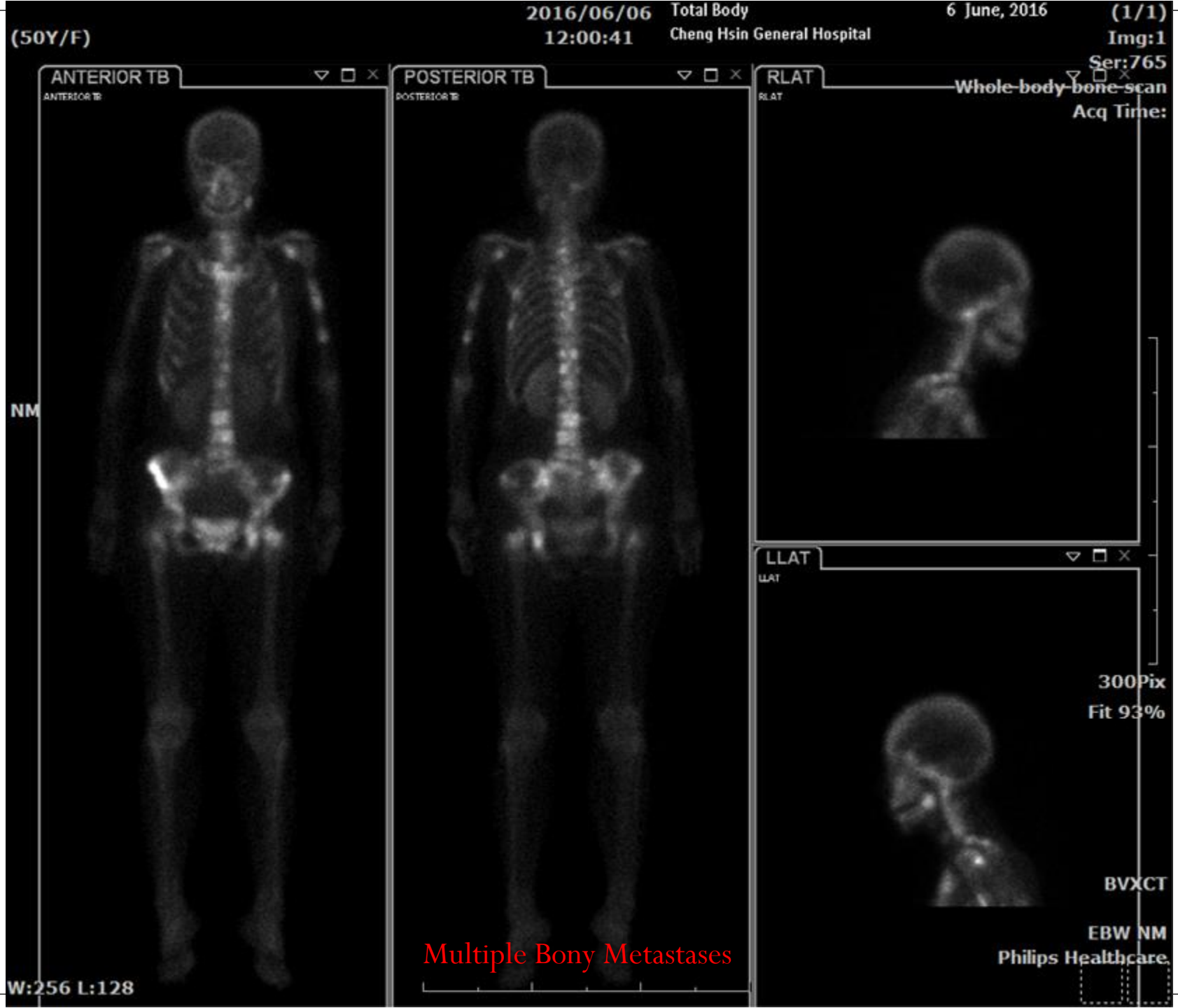
TOSHIBA
CHENG HSIN HOSPITAL - 561 - Breast
Dist A 24.2 mm
Dist B 11.8 mm
left axillary 2.42x1.18cm LN

Breast sono

- Some hypoechoic nodules in right breasts, the biggest one was about 1.9 cm, mild increased AP diameter.
- There was wound over the left breast, left cannot be well evaluated. Thickening of cutaneous and subcutaneous layer with a huge hypoechoic space occupied lesion noted, C/W breast ca.
- Some anchogenic cysts in right breast.
- Lymph nodes in bilateral axilla, prominant parenchyma. R/I metastases.

- 2016/06/03 sono-guided core needle biopsy.
  (1.94x1.83x1.36cm), right breast 10 o'clock.
  Cytology: Cystic fluid only


(50Y/F)
2016/06/06
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Total Body
Cheng Hsin General Hospital
6 June, 2016
(1/1)
Img:1
Ser:765
Whole-body-bone-scan
Acq Time:
ANTERIOR TB
POSTERIOR TB
RLAT
LLAT
NM
300Pix
Fit 93%
BVXCT
EBW NM
Philips Healthcare
W:256 L:128
Multiple Bony Metastases

Diagnosis

- Left breast locally advanced cancer with left chest wall skin multiple satellite lesions, cT4cN1M1, stage 4, premenopause with liver, multiple bony metastases

06/02 Operation

- Right chest wall Port-A implantation
- Left chest wall skin lesion excision, left axillary lymph nodes biopsies

06/02 Pathology (Skin & Lymph Node)

- Metastatic carcinoma
- Weakly to moderately immunoreactive to ER (40-50%)
- PR (-), Her-2-neu (-)

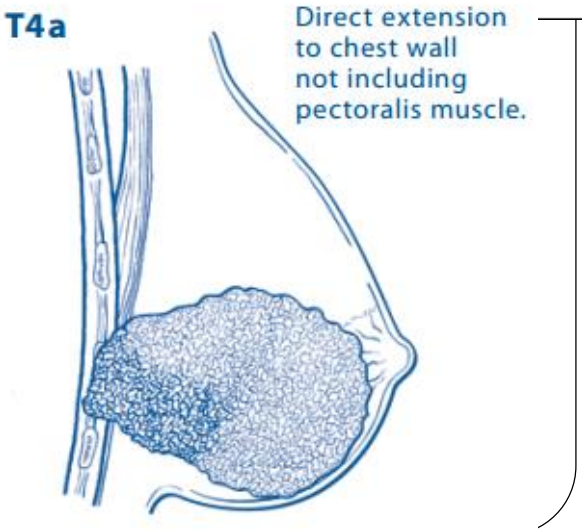
Follow up

- 06/09~06/14: bilateral salpingo-oophorectomy
- 06/14: Femara 2.5mg 1# QD PO

Tumor node metastases (TNM) staging system for carcinoma of the breast

Primary tumor (T)*¶Δ	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
T1	Tumor ≤20 mm in greatest dimension
T1mi	Tumor ≤1 mm in greatest dimension
T1a	Tumor >1 mm but ≤5 mm in greatest dimension
T1b	Tumor >5 mm but ≤10 mm in greatest dimension
T1c	Tumor >10 mm but ≤20 mm in greatest dimension
T2	Tumor >20 mm but ≤50 mm in greatest dimension
T3	Tumor >50 mm in greatest dimension
T4◇	Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules)
T4a	Extension to the chest wall, not including only pectoralis muscle adherence/invasion
T4b	Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma
T4c	Both T4a and T4b
T4d	Inflammatory carcinoma§

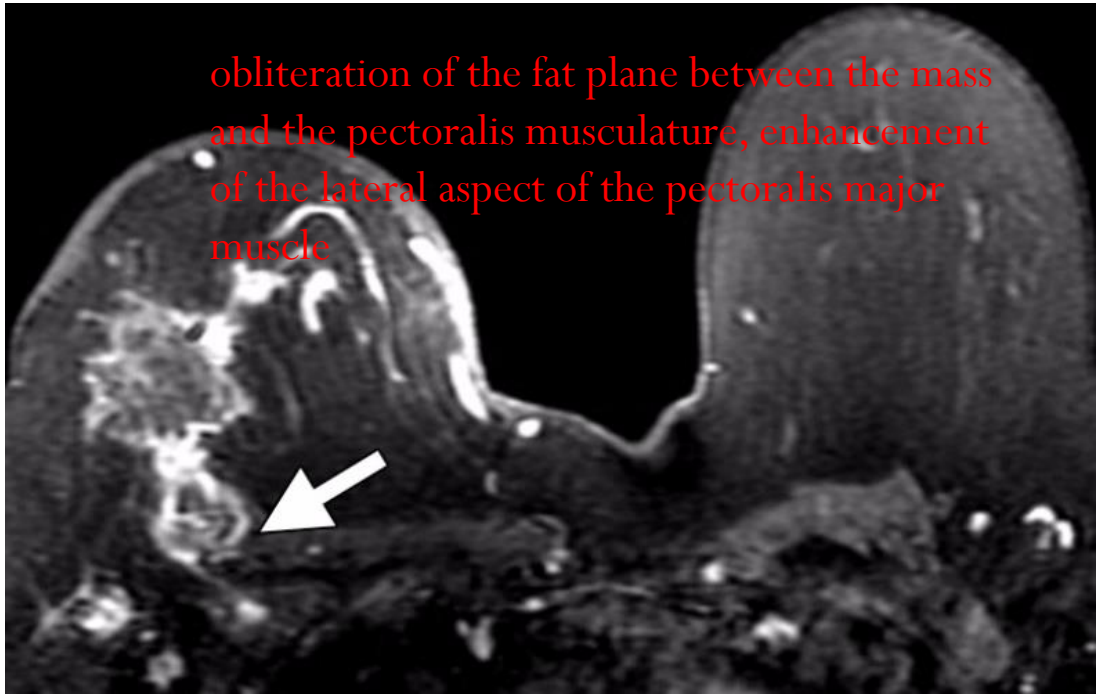
ribs, intercostal muscles, serratus anterior muscle

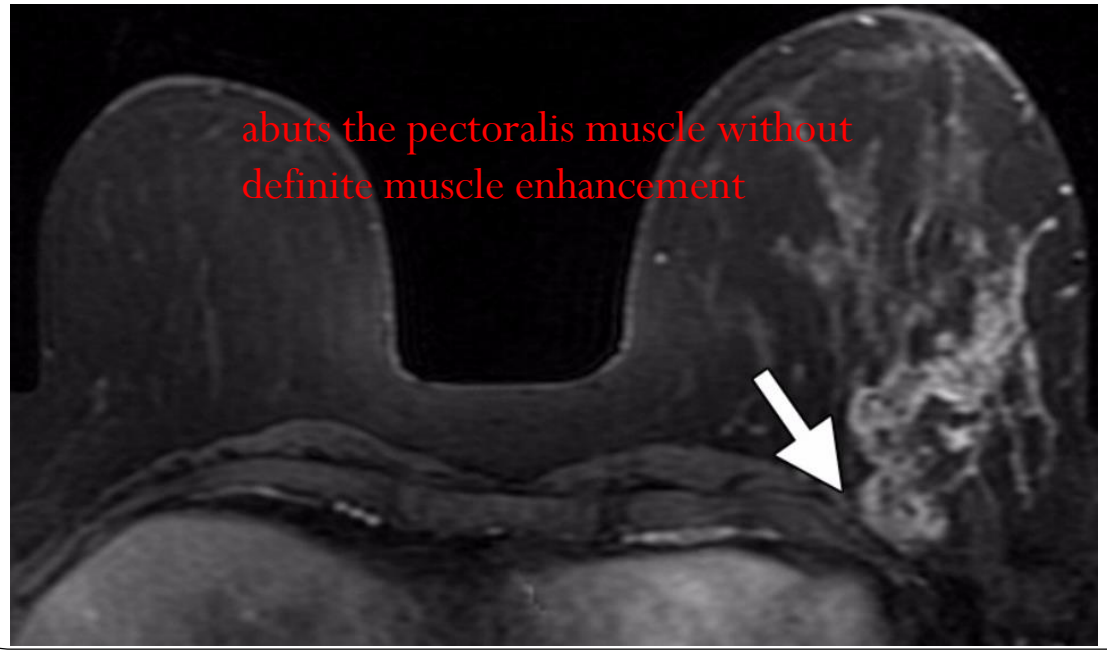


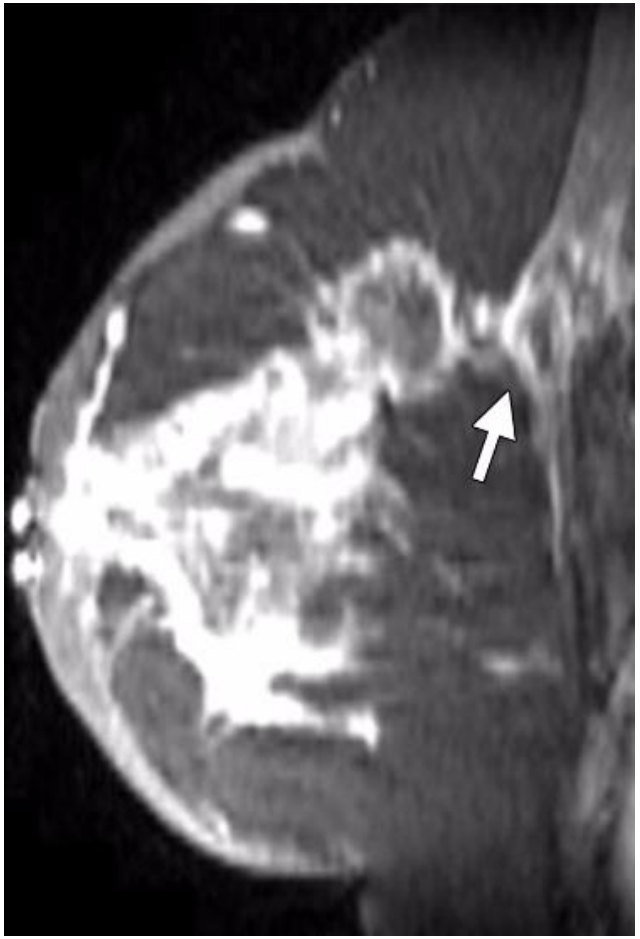
Radiologist's Role in Breast Cancer Staging: Providing Key Information for Clinicians

March-April 2014
Volume 34, Issue 2

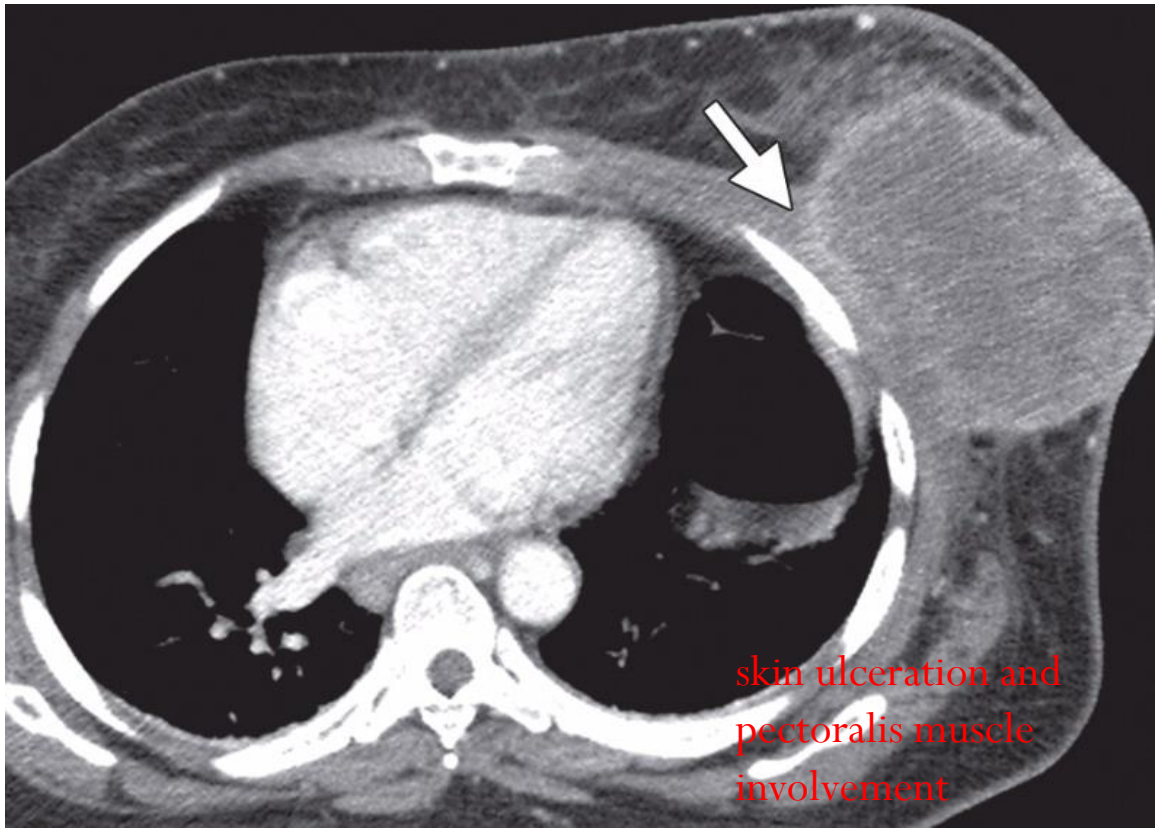
- Contrast-enhanced breast MR imaging is the best imaging modality for determining chest wall involvement.







Contrast-enhanced fat-saturated T1-weighted MR images


skin ulceration and
pectoralis muscle
involvement

Surg Clin N Am 87 (2007) 379–398

Management of Patients with Locally Advanced Breast Cancer

Marie Catherine Lee, MD[a],
Lisa A. Newman, MD, MPH, FACS[b,*]

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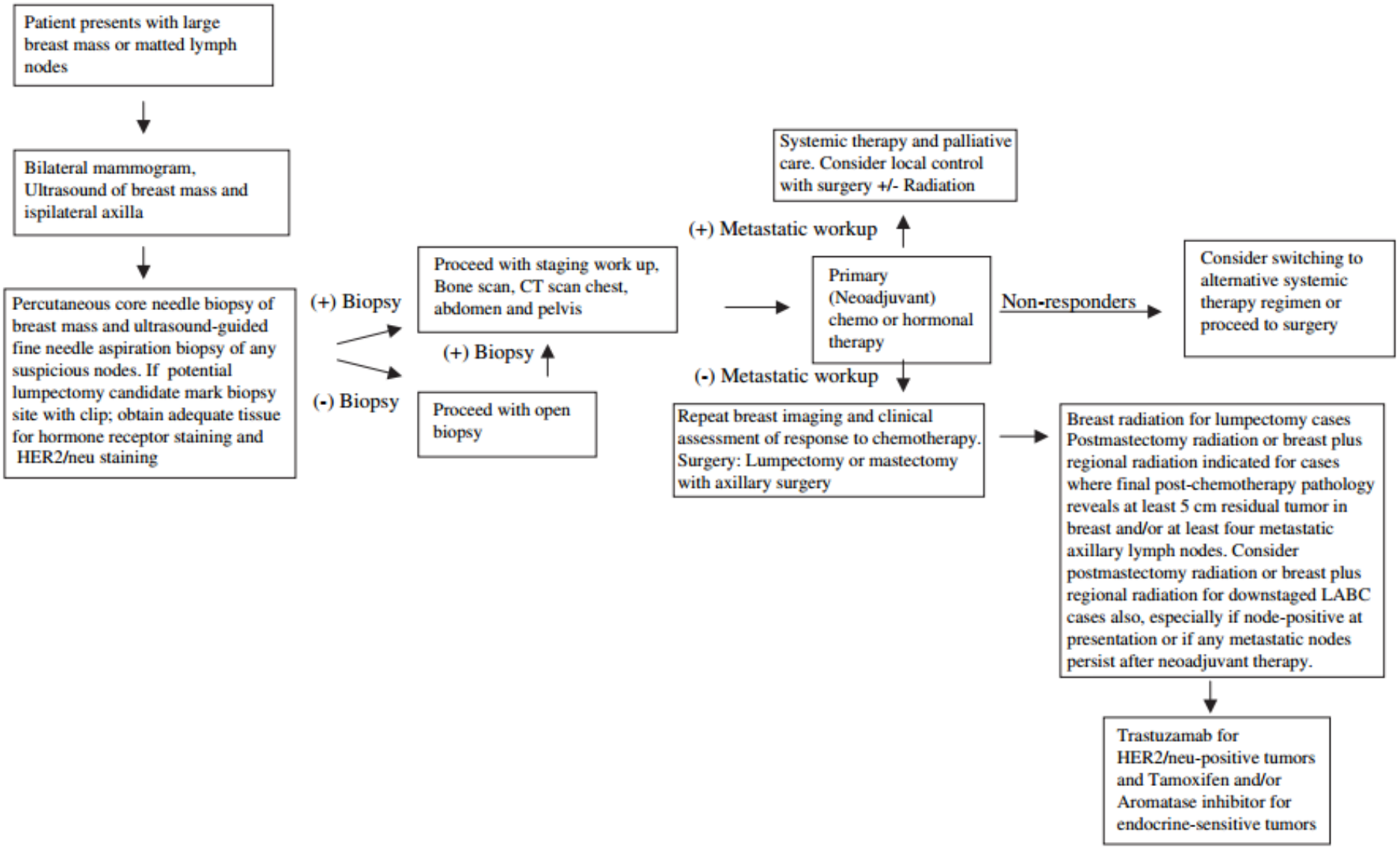
[b]*University of Michigan Comprehensive Cancer Center, Breast Care Center, 1500 East Medical Center Drive, Ann Arbor, MI 48167, USA*


Patient presents with large breast mass or matted lymph nodes
Bilateral mammogram, Ultrasound of breast mass and ispilateral axilla
Percutaneous core needle biopsy of breast mass and ultrasound-guided fine needle aspiration biopsy of any suspicious nodes. If potential lumpectomy candidate mark biopsy site with clip; obtain adequate tissue for hormone receptor staining and HER2/neu staining
(+) Biopsy
(-) Biopsy
Proceed with staging work up, Bone scan, CT scan chest, abdomen and pelvis
(+) Biopsy
Proceed with open biopsy
Systemic therapy and palliative care. Consider local control with surgery +/- Radiation
(+) Metastatic workup
Primary (Neoadjuvant) chemo or hormonal therapy
Non-responders
Consider switching to alternative systemic therapy regimen or proceed to surgery
(-) Metastatic workup
Repeat breast imaging and clinical assessment of response to chemotherapy. Surgery: Lumpectomy or mastectomy with axillary surgery
Breast radiation for lumpectomy cases Postmastectomy radiation or breast plus regional radiation indicated for cases where final post-chemotherapy pathology reveals at least 5 cm residual tumor in breast and/or at least four metastatic axillary lymph nodes. Consider postmastectomy radiation or breast plus regional radiation for downstaged LABC cases also, especially if node-positive at presentation or if any metastatic nodes persist after neoadjuvant therapy.
Trastuzamab for HER2/neu-positive tumors and Tamoxifen and/or Aromatase inhibitor for endocrine-sensitive tumors

JOURNAL OF CLINICAL ONCOLOGY May 23, 2016

Endocrine Therapy for Hormone Receptor–Positive Metastatic Breast Cancer: American Society of Clinical Oncology Guideline

Hope S. Rugo, R. Bryan Rumble, Erin Macrae, Debra L. Barton, Hannah Klein Connolly, Maura N. Dickler, Lesley Fallowfield, Barbara Fowble, James N. Ingle, Mohammad Jahanzeb, Stephen R.D. Johnston, Larissa A. Korde, James L. Khatcheressian, Rita S. Mehta, Hyman B. Muss, and Harold J. Burstein

METHODS

- MEDLINE (OVID: 2008 through week 4 of April 2014)
- Cochrane Library databases (to Issue 3 of March 2013)
- San Antonio Breast Cancer Symposium (2011 to 2014) and ASCO abstracts (2012 to 2014)
- keywords "advanced" and "metastatic"

- 7 systematic reviews with meta-analyses, 29 individual trial reports met the inclusion criteria

Table 1. Main Findings From Systematic Review (all included meta-analyses)

Study	Evidence Base	Main Findings
Endocrine *v* chemotherapy		
Wilcken[8]	Six trials including 692 patients with MBC (for OS comparison)	No significant difference in OS was detected (hazard ratio, 0.94; 95% CI, 0.79 to 1.12; $P = .5$), with nonsignificant heterogeneity detected
	Compared single-agent endocrine treatment with single-agent chemotherapy	Significant benefit in response rates (eight trials involving 817 women) for chemotherapy over endocrine therapy was detected (RR, 1.25; 95% CI, 1.01 to 1.54; ***P* = .04**)
		Authors conclude that standard first-line treatment for patients with MBC should be endocrine therapy rather than chemotherapy, except in presence of rapidly progressing disease
Single-agent *v* single-agent hormone therapies		
Chi[30]	23 trials including 7,242 patients (patients with advanced breast cancer were subset of total population)	Toremifene was associated with more vaginal bleeding (OR, 0.45; 95% CI, 0.26 to 0.80; ***P* < .05**) and greater decrease in serum triglyceride levels (SMD, −1.15; 95% CI, −1.90 to −0.39; ***P* < .05**) than tamoxifen
	Compared toremifene and tamoxifen	no differences between the two Evidence suggests toremifene could be an alternative to tamoxifen for patients with advanced breast cancer
Cope[31]	11 RCTs including 5,808 postmenopausal women with advanced breast cancer after endocrine therapy failure	Fulvestrant 500 mg was superior to fulvestrant 250 mg, megestrolacetate, and anastrozole for PFS (***P* < .05**)
	Compared fulvestrant 500 mg, fulvestrant 250 mg, fulvestrant 250 mg loading dose, anastrozole 1 mg, megestrol acetate, letrozole 2.5 mg, letrozole 0.5 mg, and exemestane	
Xu[32]	Six RCTs including 2,560 postmenopausal patients with HR-positive advanced breast cancer	AIs were superior to tamoxifen alone for response (ORR; OR, 1.56; 95% CI, 1.17 to 2.07; ***P* < .05**) and CBR (OR, 1.70; 95% CI, 1.24 to 2.33; ***P* < .05**)
	Compared AIs *v* tamoxifen	

Single-agent *v* combination endocrine therapies		
Tan[33]	Two RCTs including patients with HR-positive advanced breast cancer (total patients, NR) Compared fulvestrant + AI *v* AI alone (both studied anastrozole in combination with fulvestrant)	None of the comparisons for PFS, OS, or response showed statistically significant difference
Valachis[34]	Four RCTs including 2,125 patients with HR-positive advanced breast cancer Compared fulvestrant + AIs *v* tamoxifen	No difference detected between fulvestrant + AIs and tamoxifen for OS, TTP, CBR, or ORR Hormonal agents other than fulvestrant were associated with great likelihood of joint disorders (***P* < .05**)
Endocrine therapy ± mTOR inhibitors		
Bachelot[35]	Six RCTs (total patients, NR) All patients had HR-positive, HER2-negative advanced breast cancer Included studies identified by systematic literature review (sources: Cochrane Library, National Horizon Scanning Centre, and NICE Web sites) Comparisons were: everolimus + exemestane or everolimus + tamoxifen *v* fulvestrant	Everolimus + exemestane was superior to fulvestrant 250 mg and fulvestrant 500 mg for PFS and TTP (hazard ratio, 0.47; 95% CI, 0.38 to 0.58; ***P* < .05** and hazard ratio, 0.59; 95% CI, 0.45 to 0.77; ***P* < .05**, respectively) Analysis suggests that everolimus + exemestane is superior to fulvestrant 250 mg and 500 mg for PFS and TTP in patients with HR-positive, HER2-negative breast cancer with disease progression after endocrine therapy; however, there are no RCTs currently available providing direct comparison

Source	Intervention or Comparison	Treatment Line	No. of Patients Evaluated	Survival (months)		CBR (%)*	Time to Initiation of Chemotherapy
				OS	PFS or TTP		
Single-agent *v* single-agent hormone therapies							
Phase II							
Llombart-Cussac[23]; SBCG 2001/03	Exemestane	First	47	Median, 19.9	Median TTP, 6.1	59.6	NR
	Anastrozole		50	48.3	12.1	68	NR
P				NS	NS		
Robertson[14,15]; FIRST	Fulvestrant	First	102	Median, 54.1 (n = 86)	Median TTP, 23.4	72.5	NR
	Anastrozole		103	48.4 (n = 84)	13.1	67.0	NR
P				**.041**	**.01**	.386 (primary end point)	
Ohno[24]; FINDER-1	Fulvestrant (250 mg/month)	Second	45	NR	Median TTP, 6.0	42.2	NR
	Fulvestrant (250 mg + 500 mg on day 0, 250 mg on days 14 and 28, and monthly thereafter)		51	NR	7.5	54.9	NR
	Fulvestrant (500 mg per month + 500 mg on day 14 of month 1)		47	NR	6.0	46.8	NR
Pritchard[25]; FINDER-2	Fulvestrant (250 mg per month)	Second	47	NR	Median TTP, 3.1	31.9	NR
	Fulvestrant (250 mg + 500 mg on day 0, 250 mg on days 14 and 28, and monthly thereafter)		50	NR	6.1	47.1	NR
	Fulvestrant (500 mg per month + 500 mg on day 14 of month 1)		46	NR	6.0	47.8	NR
Phase III							
Di Leo[21,36]; CONFIRM	Fulvestrant 250 mg	Second	374	**Median, 22.03**	**Median PFS, 5.5**	39.6	NR
	Fulvestrant 500 mg		362	**26.4**	**6.5**	45.6	NR
P				**< .05**	**< .05**	NS	
Iwata[22]	Exemestane	First	147	Median, not reached	Median, 13.8 (range, 10.8-16.5)	75 (range, 66.7-82.1)	NR
	Anastrozole		145	60.1	11.1(range, 10.8-16.6)	77.3 (range, 69.1-84.3)	NR
P				NS	NS		
Xu[26]	Fulvestrant	Second	121	NR	Median TTP, 3.6	48.2	NR
	Anastrozole		113	NR	5.2	36.1	NR
P					NS		
Chia[20]; EFECT	Fulvestrant	Second	351	NR	Median PFS, 3.7	32.2	NR
	Exemestane		342	NR	3.7	31.5	NR
P					NS	NS	
Paridaens[37]	Exemestane	First	182	1 year, 86%; Median, 37.2	1-year PFS, 41.7%; Median, 9.9	NR	NR
	Tamoxifen		189	82%; 43.3	31.2%; 5.8	NR	NR
P				NS	NS		

Source	Intervention or Comparison	Treatment Line	No. of Patients Evaluated	Survival (months)		CBR (%)*	Time to Initiation of Chemotherapy
				OS	PFS or TTP		
Single-agent *v* combination endocrine therapies							
Phase II							
Johnston[38]; SoFEA	Fulvestrant + placebo	Second	231	19.4 (A *v* B)	4.8 (A *v* B)	NR	NR
	Fulvestrant + anastrozole		243	Median, 20.2	Median PFS, 4.4	NR	NR
P				NS	NS		
	Exemestane		249	21.6 (B *v* C)	3.4 (B *v* C)	NR	NR
P				NS	NS		
Phase III							
Bergh[13]; FACT	Anastrozole alone	First	256	38.2	10.2	NR	NR
	Fulvestrant + anastrozole		258	Median, 37.8	Median TTP, 10.8	NR	NR
P				NS	NS		
Mehta[12]; SWOG 0226	Anastrozole alone → fulvestrant	First	345	**Median, 41.3**	**PFS, 13.5**	70	NR
	Anastrozole + fulvestrant		349	**47.7**	**15**	73	NR
P				**.05**	**.05**		
Endocrine therapy ± HER2-targeted therapies							
Phase II							
Johnston[39]; MINT	Placebo	First	121	90%	14.0	NR	NR
	Anastrozole + AZD8931 20 mg		118	83%	10.9	NR	NR
	Anastrozole + AZD8931 40 mg		120	87%	13.8	NR	NR
P				NS	NS		
Phase III							
Burstein[40]; CALGB 40302	Fulvestrant + placebo	First	145	Median, 26.4	Median, 3.8	NR	NR
	Fulvestrant + lapatinib		146	30	4.7	NR	NR
P				NS	NS		
Huober[41]; eLEcTRA	Letrozole alone	First	31	NR	3.3	39	NR
	Letrozole + tratuzumab		26	NR	TTP, 14.1	65	NR
P				NS	NS	.06	
Schwarzberg[42] Johnston[5]	Letrozole + placebo	First	108	Median, 32.3	**Median PFS, 3.0**	**29**	NR
	Letrozole + lapatinib		111	33.3	**8.2**	**48**	NR
P				NS	**< .05**	**< .05**	
Kaufman[6]; TAnDEM	Anastrozole alone	First	104	Median, 23.9	**PFS, 2.4 (range, 2-4.6)**	**27.9 (range, 19.5-37.5)**	NR
	Trastuzumab + anastrozole		103	28.5	**4.8 (range, 3.7-7.0)**	**42.7 (range, 33-52.9)**	NR
P				NS	**< .05**	**< .05**	

no difference

no benefit

Source	Intervention or Comparison	Treatment Line	No. of Patients Evaluated	Survival (months)		CBR (%)*	Time to Initiation of Chemotherapy
				OS	PFS or TTP		
Endocrine therapy ± mTOR inhibitors							
Phase II							
Bachelot[43]; GINECO	Tamoxifen	First	57	**Median not yet reached**	**Median TTP, 4.5**	**42**	NR
	Tamoxifen + everolimus		54	**32.9**	**8.6**	**61**	NR
P				**< .05**	**< .05**	**< .05**	
Phase III							
Wolff[44]; HORIZON	Letrozole + placebo	First	555	NR	Median, 9.0	NR	NR
	Letrozole + temsirolimus		555	Median, NR	8.9	NR	NR
P				NS	NS		
Piccart[45] Yardley[50] Baselga[4]; BOLERO-2	Exemestane + placebo	Second	239	26.2	**Median PFS, 3.2**	**25.5**	NR
	Everolimus + exemestane		485	31.0	**7.4**	**50.5**	NR
P				.14	**< .05**	**< .05**	
Endocrine therapy ± CDK 4/6 inhibitor							
Phase II							
Finn[7]; PALOMA-1	Letrozole alone	First	81	33.3	10.2	58	NR
	Letrozole + palbociclib		84	37.5	20.2	81	NR
P				.42	**< .001**	**< .001**	
Turner[17]; PALOMA-3	Fulvestrant + placebo	≥ Second	171	NR	3.8	19	NR
	Fulvestrant + palbociclib		347	NR	9.2	34	NR
P					**< .001**	**< .001**	
Endocrine therapy ± novel agents							
Endocrine therapy ± RET, VEGFR, and EGFR TKI							
Phase II							
Clemons[46]; OCOG-Zamboney	Fulvestrant + placebo	First	68	69.1%	4.8	NR	NR
	Fulvestrant + vandetanib		61	73.7%	6	NR	NR
P				NS	NS		
Endocrine therapy ± IGFR antibody							
Phase II							
Robertson[47]	Placebo + fulvestrant or exemestane	Second	50	Not reached	5.7	NR	NR
	Ganitumab + fulvestrant or exemestane		106	22.2 months	Median PFS, 3.9	NR	NR
P				**.025** (favors placebo)	NS		
Endocrine therapy ± VEGF antibody							
Phase III							
Martin[48]; LEA	Letrozole or fulvestrant	First	184	51.8	14.4	67.4	NR
	Letrozole or fulvestrant + bevacizumab		190	52.1	19.3	76.8	NR
P				NS	NS	**.041**	
Dickler[49]; CALGB 40503	Letrozole	First	170	44	16	62	NR
	Letrozole + bevacizumab		173	47	20	80	NR
P				NS	**.016**	**.005**	

Source	Intervention or Comparison	Treatment Line	No. of Patients Evaluated	Survival (months)		CBR (%)*	Time to Initiation of Chemotherapy
				OS	PFS or TTP		
Endocrine therapy ± HDAC inhibitor							
Phase II							
Yardley[50]; ENCORE	Exemestane + placebo	Second	66	**Median PFS, 19.8**	Median, 2.3	25.8	NR
	Exemestane + entinostat		64	**28.1**	4.3	28.1	NR
P				**< .05**	NS	NS	
Endocrine therapy ± pan-PI3K inhibitor							
Phase II							
Krop[51]	Fulvestrant + placebo	Second	79	NR	5.1	6.3 (ORR)	NR
	Fulvestrant + pictilisib		89	NR	6.6	7.9	NR
P					NS		
Phase III							
Baselga[52]	Fulvestrant + placebo	Second	571	NR	**5.0 (range, 4.0-5.2)**	7.7 months (ORR)	NR
	Fulvestrant + buparlisib		576	NR	**6.9 (range, 6.8-7.8)**	11.8 months	NR
P					**< .001**		

Adverse Events

- Single-agent versus combination endocrine therapies
  - anastrozole alone or fulvestrant with anastrozole, Bergh et alnoted significantly more hot flashes associated with the combination arm (24.6% v 13.8%; P ,.05).
- Endocrine therapy with or without HER2-targeted therapies
  - Fulvestrant with lapatinib or fulvestrant alone, Burstein et al reported significantly higher grade 3 adverse effects associated with the combination arm (19% v 5%; P ,.05)
- Endocrine therapy with or without mTOR inhibitors
  - Baselga et al reported significantly higher grade 3 stomatitis(8%v,1%), fatigue (4% v 1%), pneumonitis (3% v 0%), and hyperglycemia (5% v , 1%) and Rugo et al reported a higher discontinuation rate because of adverse events in those receiving everolimus compared with placebo in combination with exemestane (9% v 3%).

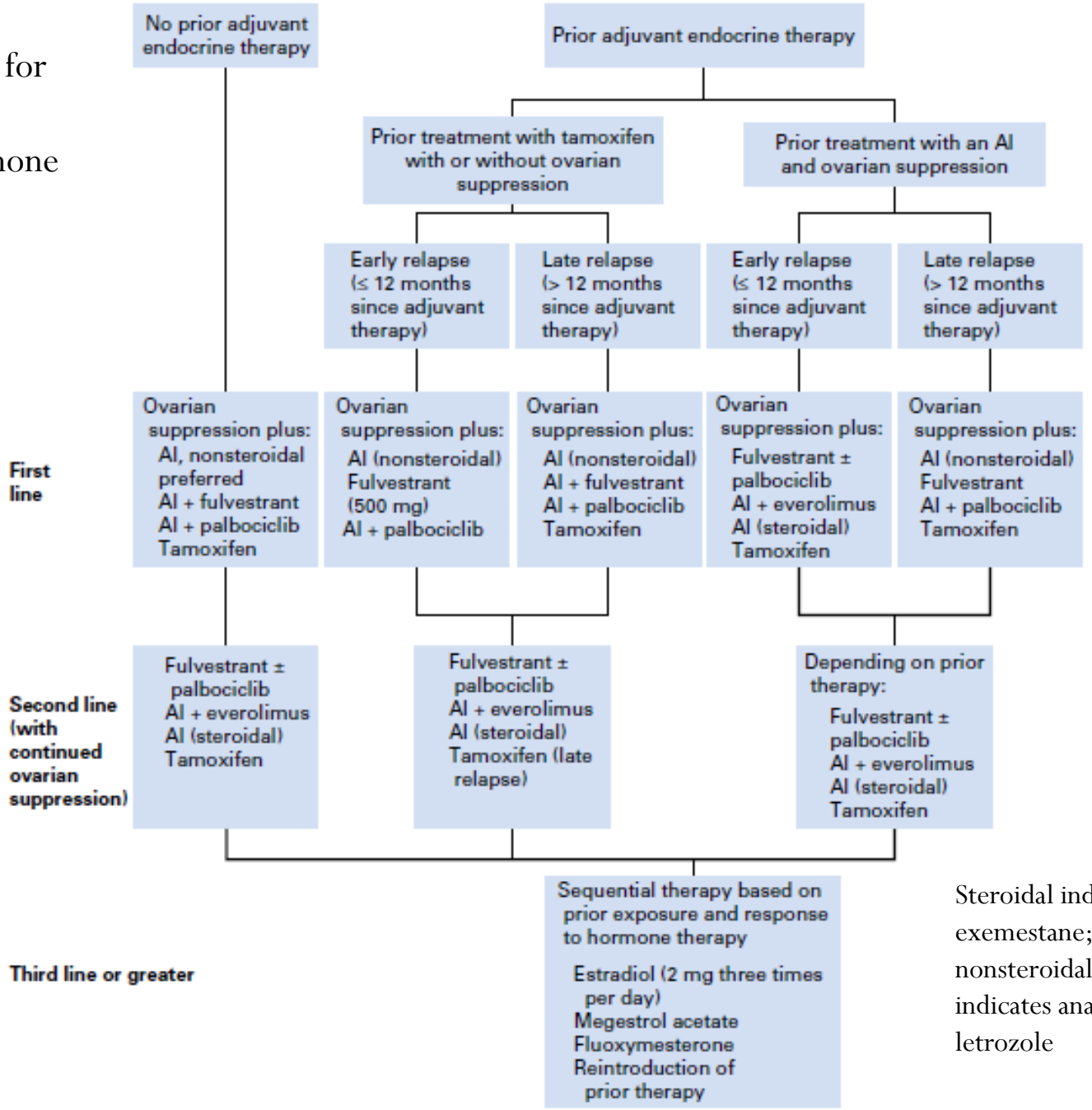
Adverse Events

- Endocrine therapy with or without CDK 4/6 inhibitors
  - Turner et al reported significantly higher grade 3 to 4 neutropenia (62% v 0.6%), without an increase in febrile neutropenia, in patients receiving palbociclib in combination with letrozole compared with those receiving placebo and letrozole.
- Endocrine therapy plus a pan-PI3K inhibitor
  - Baselga et al reported significantly higher grade 3 to 4 rash (7.9% v 0%), liver enzyme elevation (AST, 18% v 2.8%; ALT, 25.5% v 1.1%), hyperglycemia (15.4% v 0.2%), anxiety (5.4% v 0.9%), and depression (4.4% v 0.4%) in patients receiving buparlisib in combination with fulvestrant compared with those receiving placebo and fulvestrant.

Premenopausal women with HR-positive MBC

- Should be offered ovarian suppression or ablation in combination with hormone therapy.
- Ovarian suppression with either GnRH agonists or ablation with oophorectomy seems to achieve similar results in MBC.

Hormone therapy for premenopausal women with hormone receptor–positive metastatic breast cancer

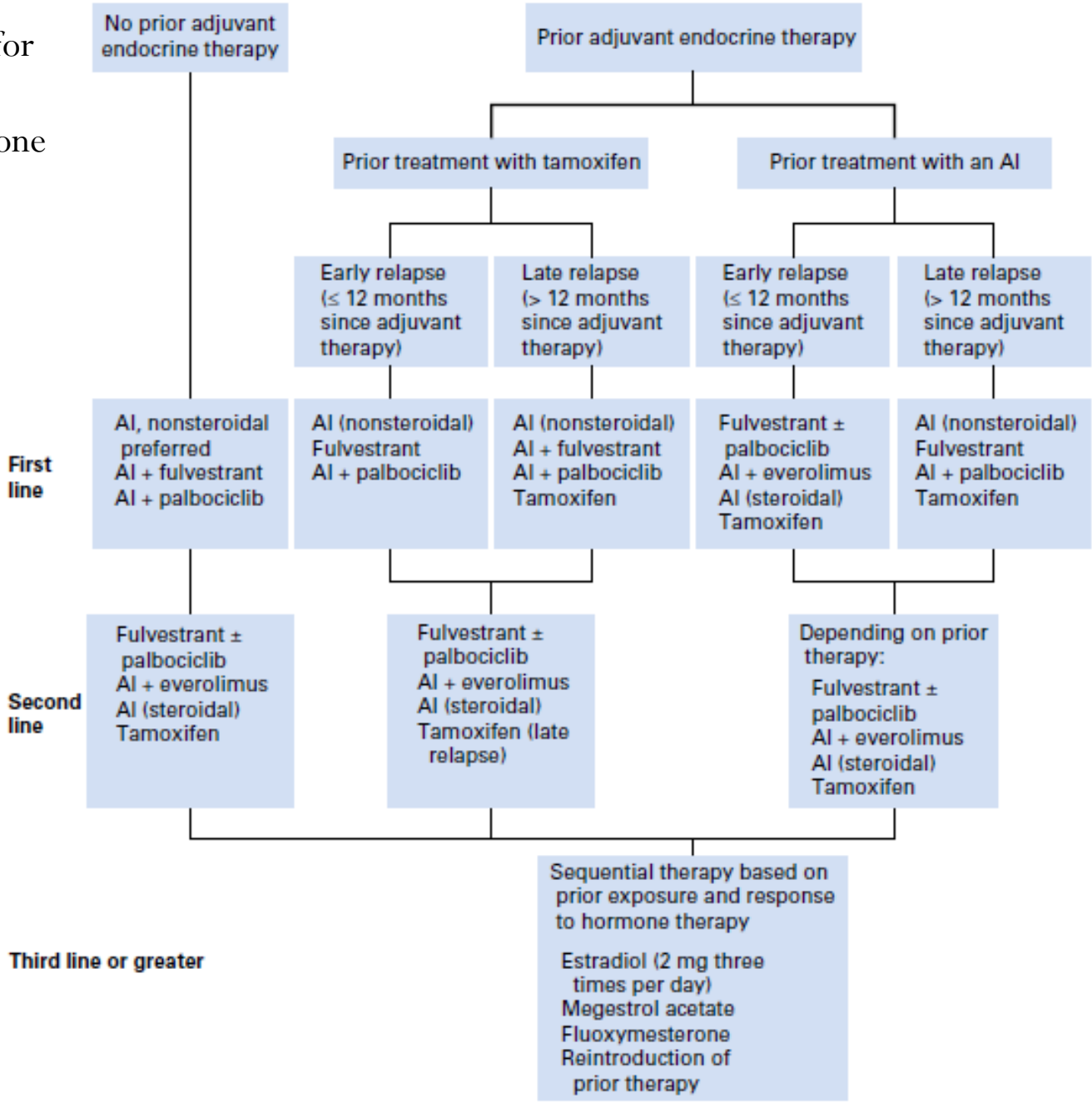


Steroidal indicates exemestane; nonsteroidal indicates anastrozole or letrozole

Postmenopausal women with HR-positive MBC

- Should be offered AIs as first-line endocrine therapy

Hormone therapy for postmenopausal women with hormone receptor–positive metastatic breast cancer

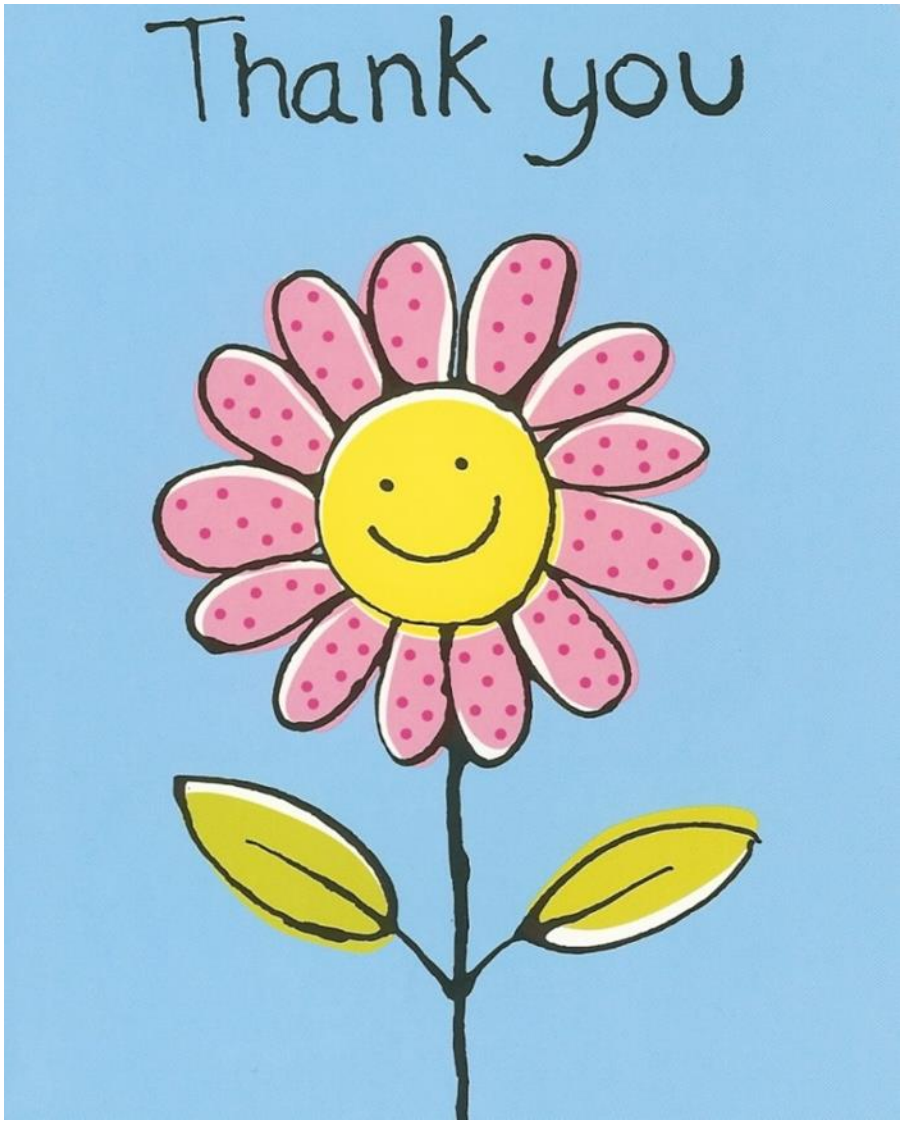


Hormone therapy vs chemotherapy

- Endocrine therapy should be recommended as initial treatment for patients with HR-positive MBC, except for patients with immediately life-threatening disease or for those who experience rapid visceral recurrence during adjuvant endocrine therapy
- The use of combined endocrine therapy and chemotherapy is not recommended

What is the optimal duration of treatment with hormone therapy?

- Treatment should be administered until there is unequivocal evidence of disease progression as documented by imaging, clinical examination, or disease-related symptoms.
- Tumor markers or circulating tumor cells should not be used as the sole criteria for determining progression.


Thank you