六大核心能力 –Medical knowledge & Patient care

2016.09.10

Presenter: PGY曾家瑜
Supervisor: Vs 蘇正熙

Patient’s Profile

- Chart no./ Name: xxxxxxx/ OOO
- Age/ Gender: 65/ Female

Chief complaint

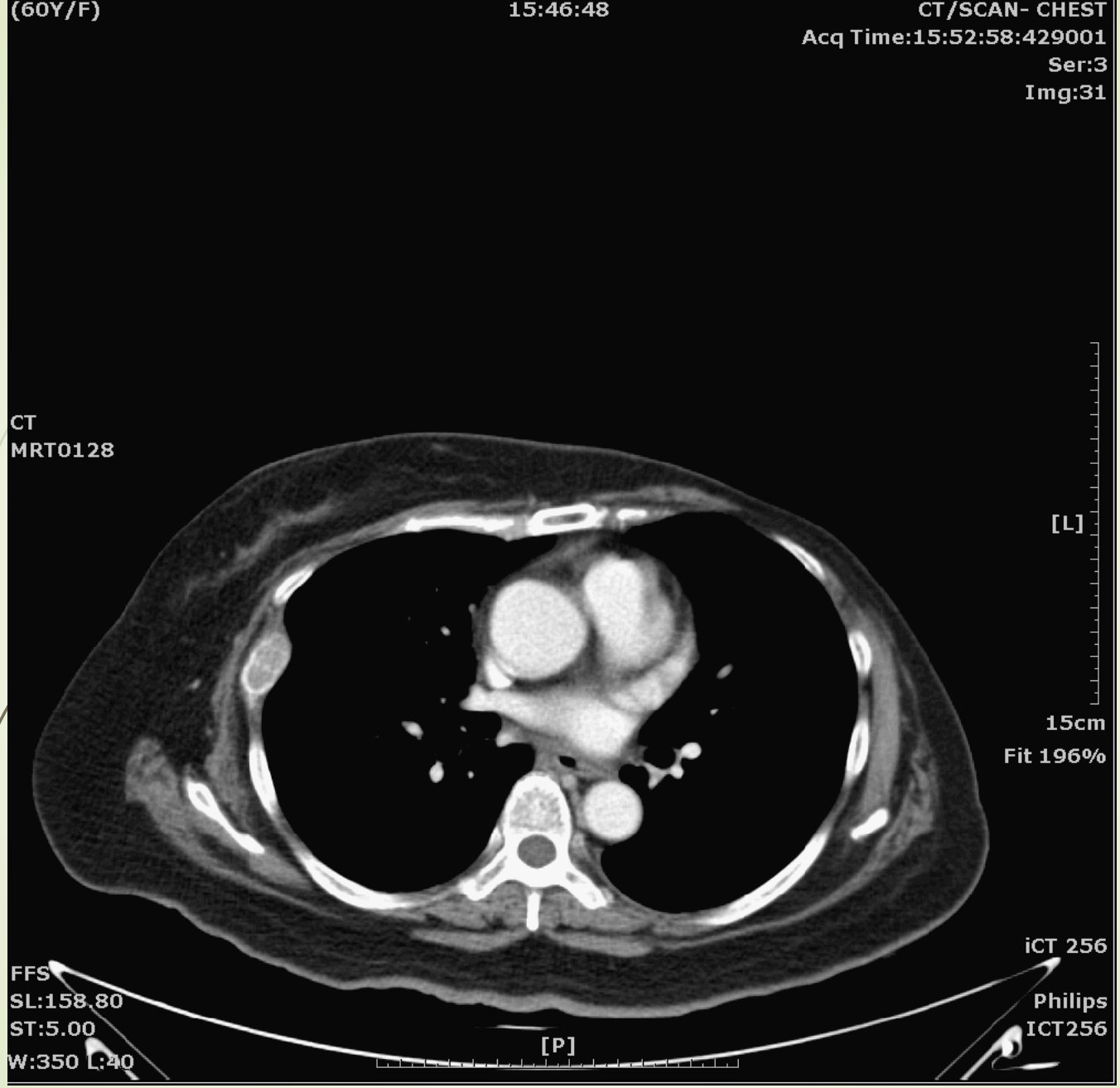
- Painful while coughing on right lower chest wall for 1 month.
- chronic cough for 6 months, voice hoarseness since 2016/4.

Past History

- 1998.7.28 : Infiltrating ductal carcinoma of left breast s/p MRM on, pT2N20 stage IIIA, ER:14.30, PR: (-), LN:6/19, FECx6, Tamoxifen x5Y
- 2000.2.3 : hysterectomy and BSO.
- 2004.7.16 : excision of thyroglossal duct cyst
- Hypertensive cardiovascular disease
- GERD

present illness

- She was under regular f/u at xxxx 醫院 anually, which 2015/9/23 breast sono showed negative findings.(routine f/u)
- This time she she complained about chronic cough for 6 months, hoarseness of voice since this April, and pain on right lower chest wall for 1 month. Nausea and vomiting were noticed in June 2016.
- PE showed right chest wall tenderness, no left chest wall reccurence, no mass over right breast, no axillary LNs.
- Lab data in normal range(including CEA and CA153),no leukocytosis, normal liver and renal function, normal electrolytes .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15cm
Fit 196%
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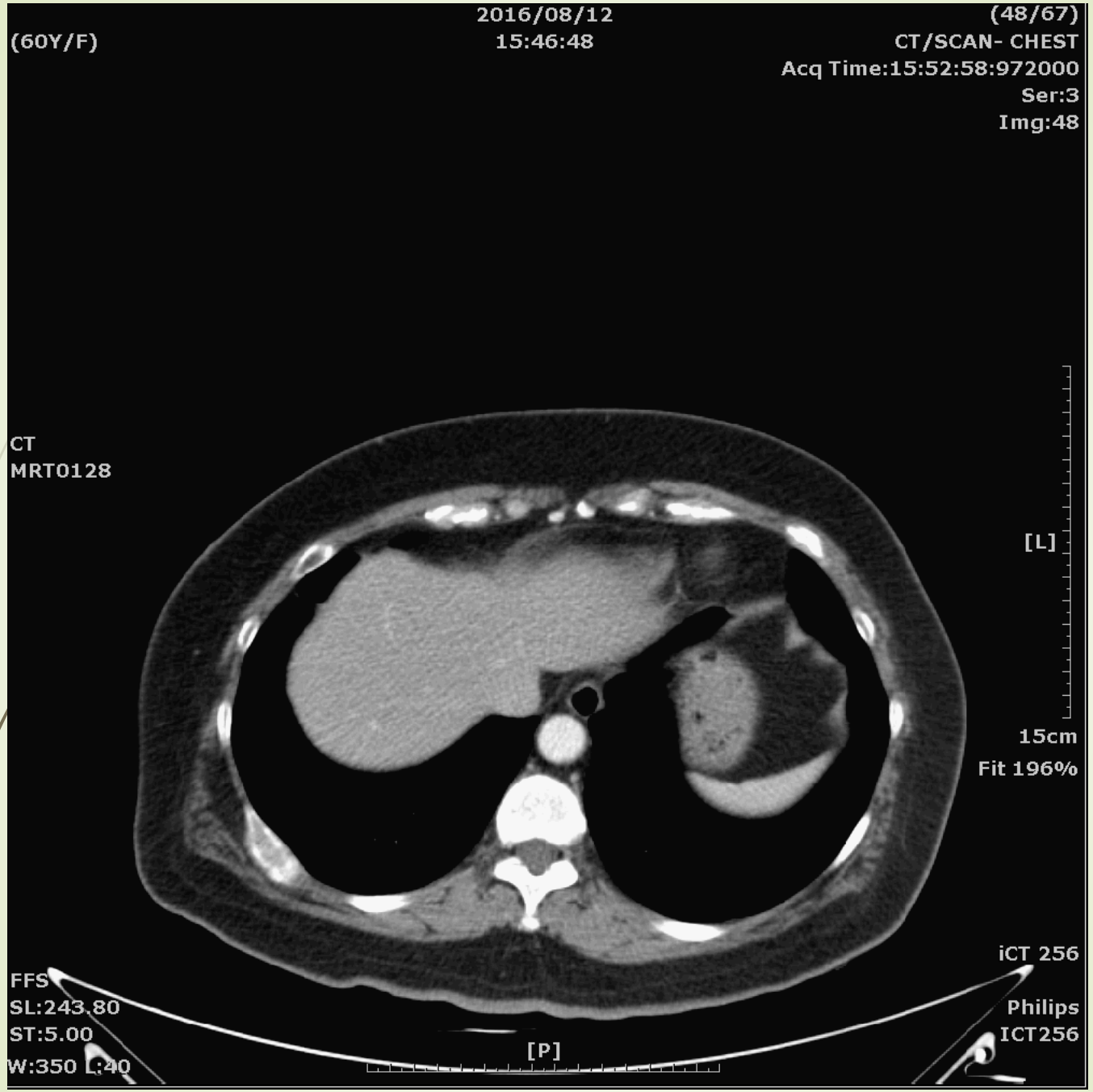
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15cm
Fit 196%
iCT 256
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SL:243.80
ST:5.00
W:350 L:40
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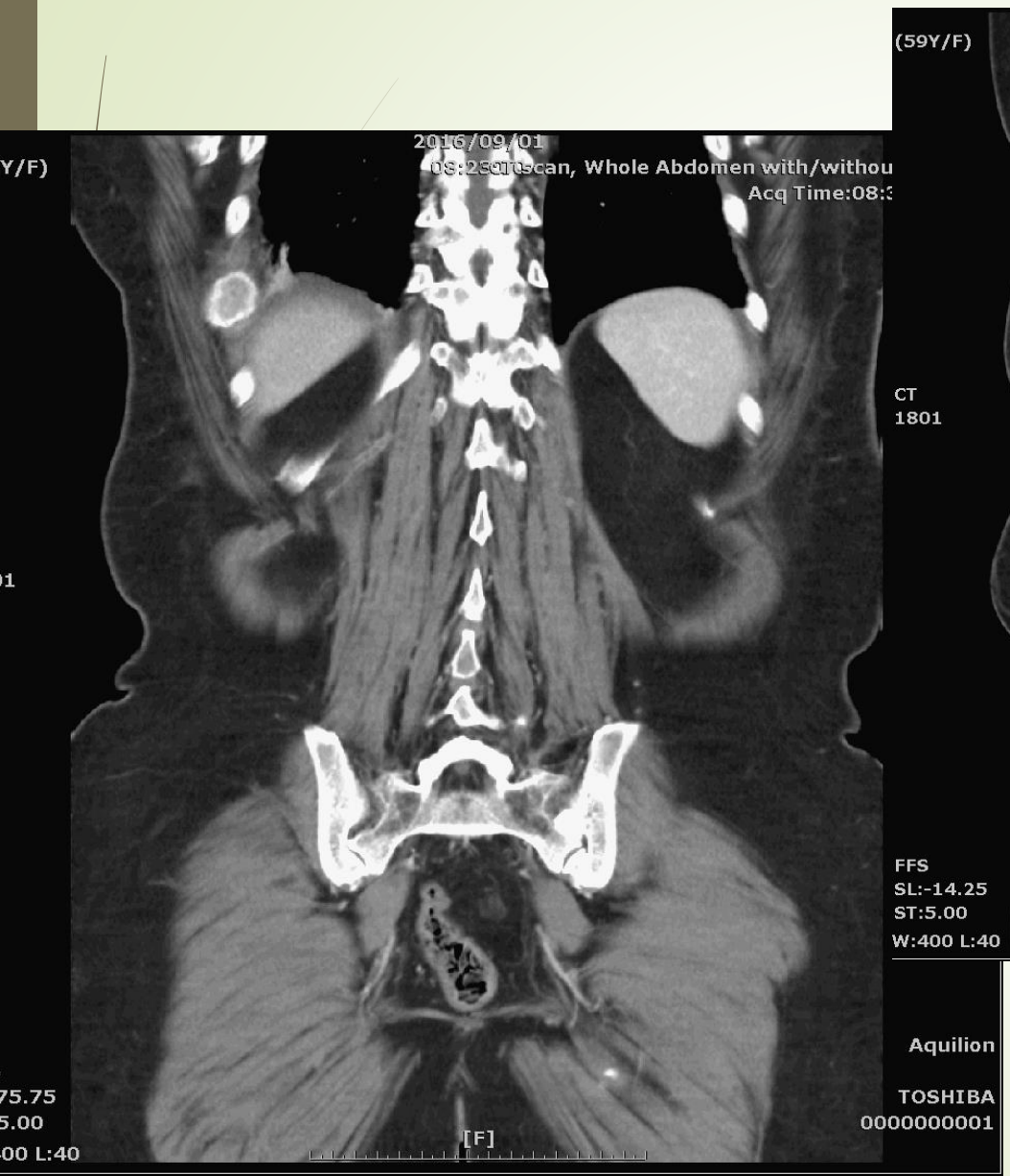
ICT256
[P]

2016/8/12 xxxx 醫院 Chest CT (2016.8.12) : **expansile soft tissue lesion noted at right 5th, 9thand 10th rib, and osteolytic nodules at C7and T10 vertebral body, bone metastases is compatible**, suggest bone scan correlation.

Subsegemntal atelectasis over right apical lung, paramediasitnum region, cause to be determined. Focal thickening and increased pleural infiltration over RLL of lung.

No enlarged lymph node within the mediastinum.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Aquilion
TOSHIBA
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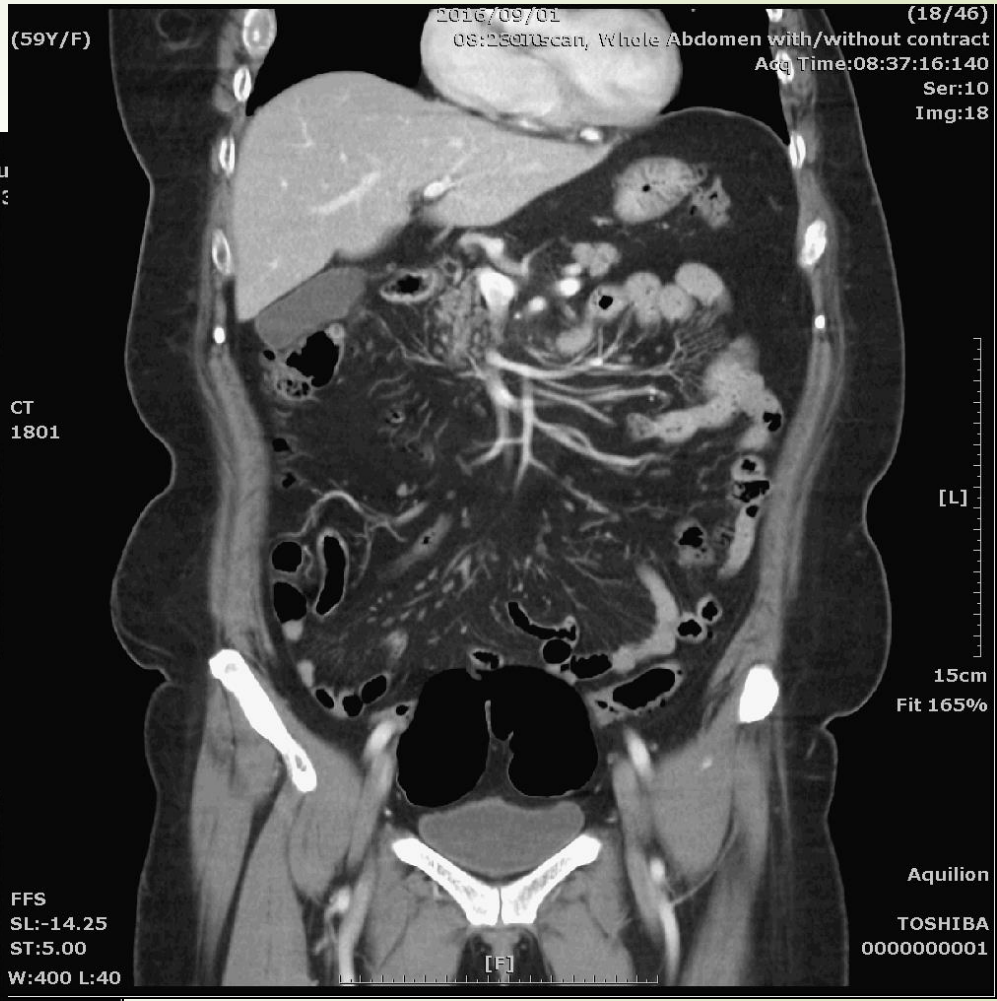
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(18/46)
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CT
1801
[L]
15cm
Fit 165%
FFS
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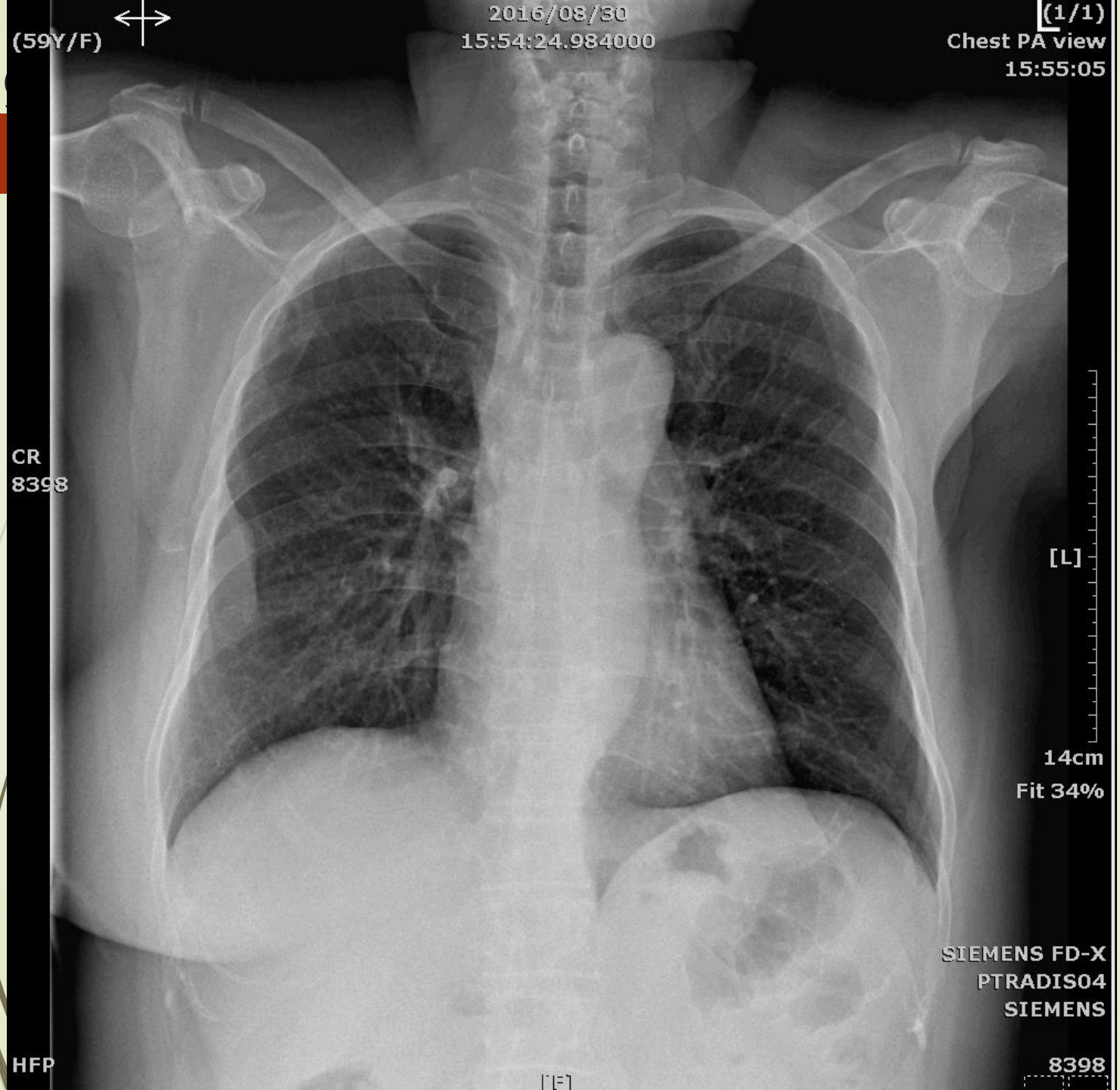
Ima


(59Y/F)
2016/08/30
15:54:24.984000
(1/1)
Chest PA view
15:55:05
CR
8398
[L]
14cm
Fit 34%
SIEMENS FD-X
PTRADIS04
SIEMENS
HFP
8398

8/31 Chest x ray:

Impression:

1.Atherosclerosis of thoracic aorta.

2.Normal heart size.

3.Clear lung fields,bil.

4.Hypertrophy of thoracic spine.

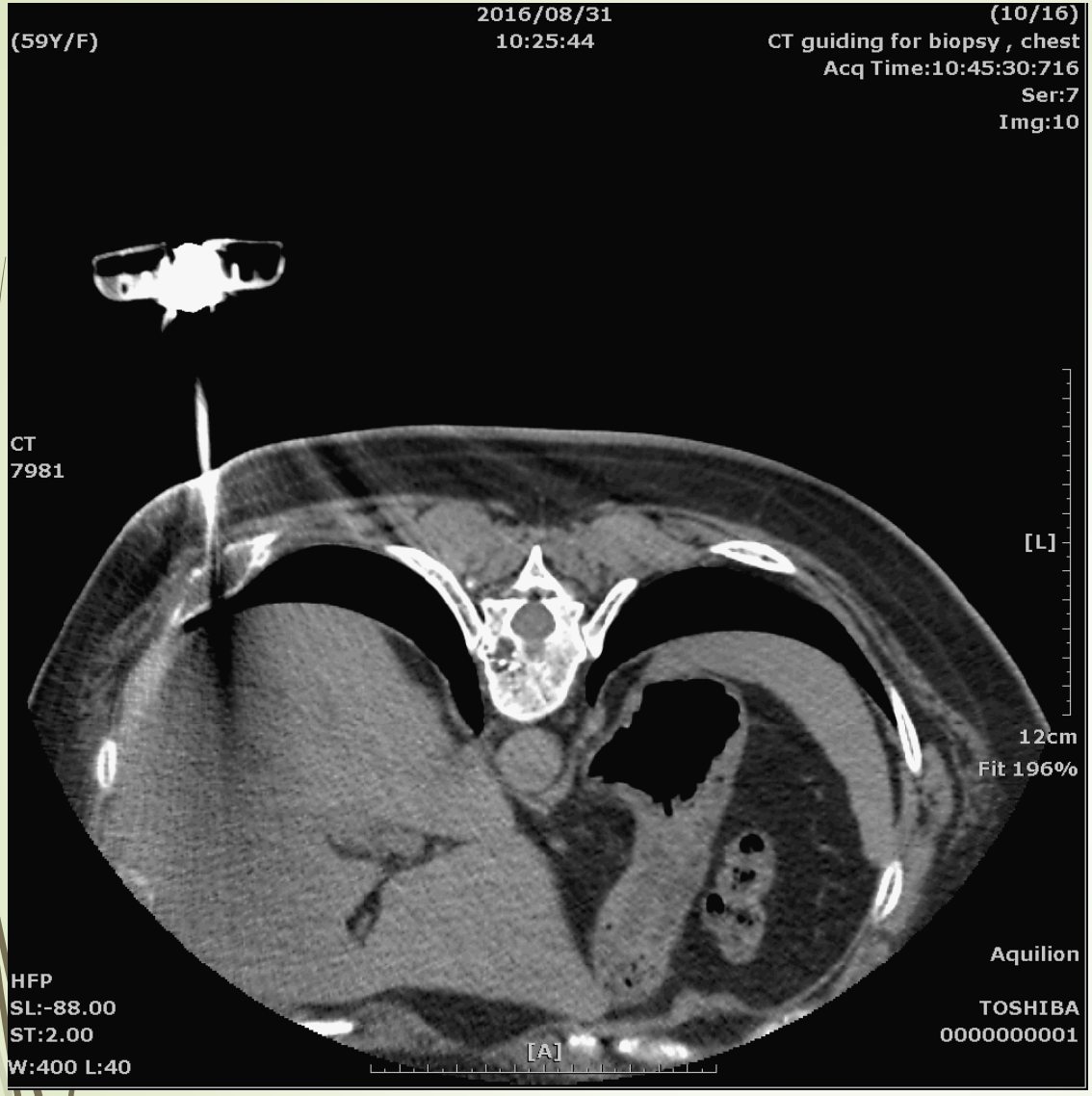
5.Scoliosis of thoracolumbar spine.

6.Expansive bony mass over 5th rib,right R/I metastasis.

7.S/P MRM,left.

Admission course

- 8/30 Admission
  CT-guide biopsy(check origin)
  port-A implantation
  zometa
  9/2 bone scan
  bronchoscopy: pleural wash for cytology(-)
  consult ENT for laryngoscopy
  consult RT for palliative radiotherapy
  neck sono
  9/5 radiotherapy



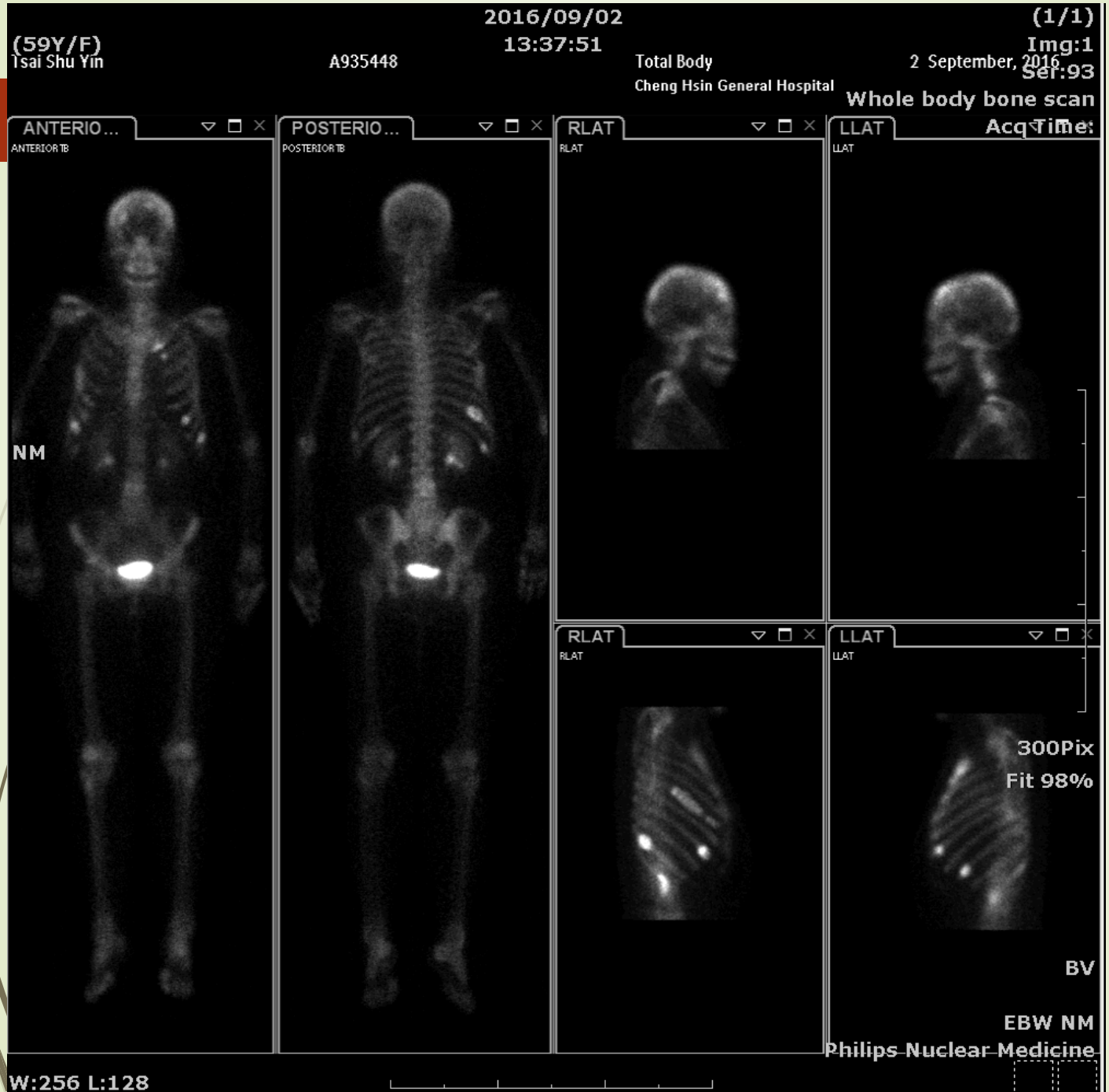
An expansile bone lesion (3.28x1.3cm) was noted in the posterior aspect of right 10th rib.

Pathology report

- PATHOLOGICAL DIAGNOSIS:
- Bone, rib, ?site, CT guided biopsy, **carcinoma, metastatic.**
- MICRO:
- Sections show a metasatic carcinoma with neoplastic cells arranged in single files and small clusters, consistent with metastasis from breast carcinoma.

- **IMMUNOHISTOLOGY: ER: + (60%)**
- **PR: - (0%)**
- **Her-2: 0+**
- **MIB-1: 15%**
- **GATA3: +**

1998: ER:14.30, PR: (-),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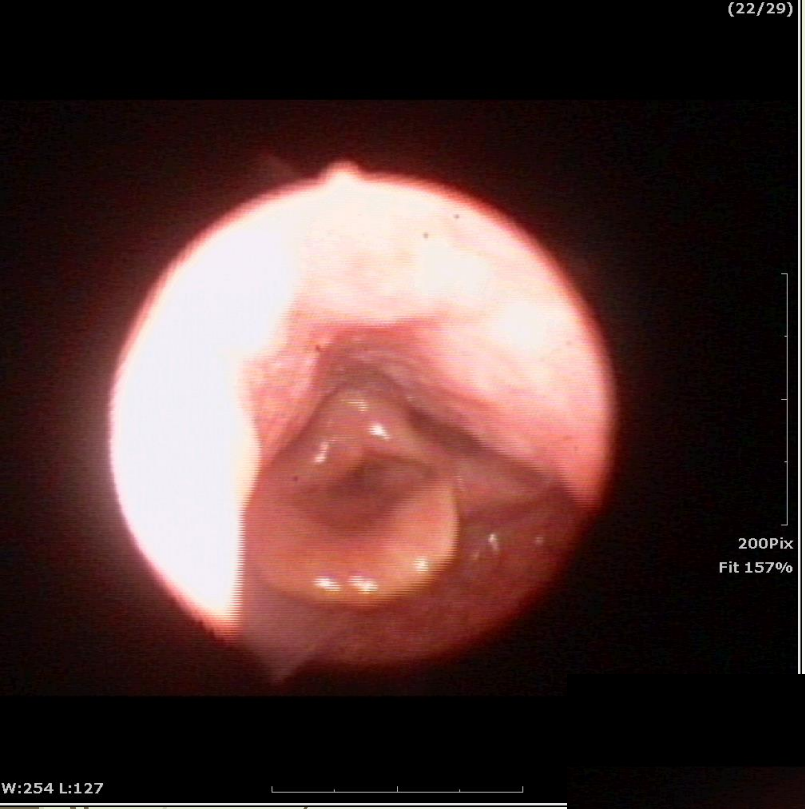
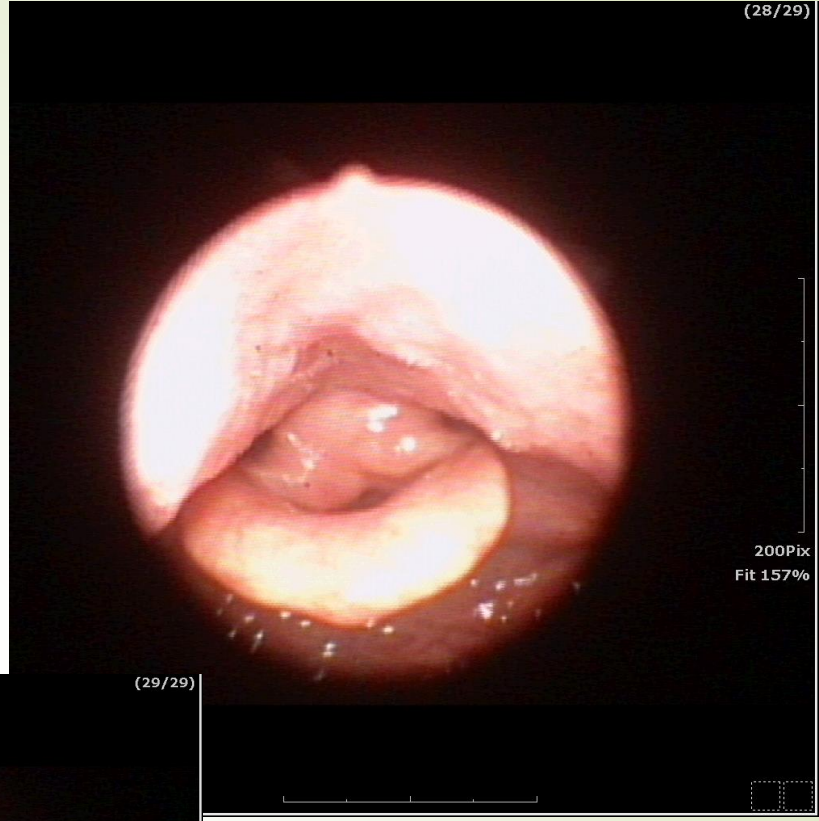
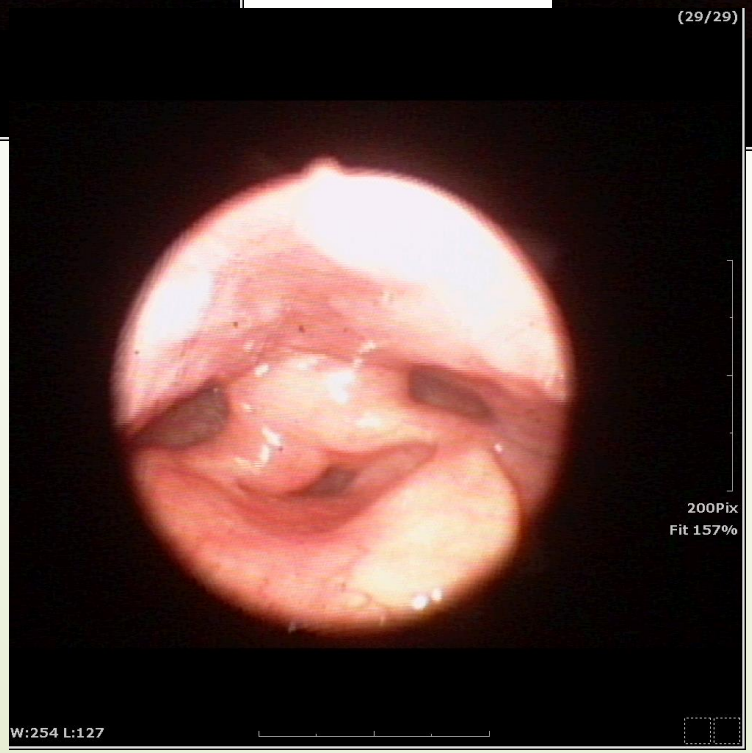
(1/1)
(59Y/F)
Tsai Shu Yin
A935448
Total Body
Cheng Hsin General Hospital
2 September, 2016
Img:1
Ser:93
Whole body bone scan
Acq Time:
ANTERIO...
ANTERIOR TB
POSTERIO...
POSTERIOR TB
RLAT
RLAT
LLAT
LLAT
NM
RLAT
RLAT
LLAT
LLAT
300Pix
Fit 98%
BV
EBW NM
Philips Nuclear Medicine
W:256 L:128







Left vocal cord palsy with big closure gap

9/5 Neck sono

- No identified enlarged LAPs.
- A few small L-N(<6mm)over left supraclavucular region,suggest f/u.

Current diagnosis

- metastatic breast carcinoma with multiple bony metastasis, ER: + (60%),PR(-),Her-2: 0+
  MIB-1: 15%
  GATA3: +

- Infiltrating ductal carcinoma of left breast s/p MRM, pT2N20 stage IIIA, ER:14.30, PR: (-), LN:6/19, FECx6, Tamoxifen x5Y

Treatment plans

- Major treatment: Hormone therapy
- For bone destruction: Zometa + radiotherapy
- Pain control

6 Core Competecnies

Patient Care
What You Do to the patient?

Medical Knowledge
What You Know?

Professionalism

How You Act?

Interpersonal and Communication Skill

How You Interact with Others?

System-Based Practice

How You Work Within the System?

Practice-Based Learning and Improvment

How You Get Better?

Hormone receptor(+) Metastatic breast cancer

2016 treatment guideline

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JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

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

The ASCO Expert Panel was convened to conduct a systematic review of evidence from 2008 through 2015 to create recommendations informed by that evidence. Outcomes of interest included sequencing of hormonal agents, hormonal agents compared with chemotherapy, targeted biologic therapy, and treatment of premenopausal women.

Key Guideline for HR(+)MBC patient

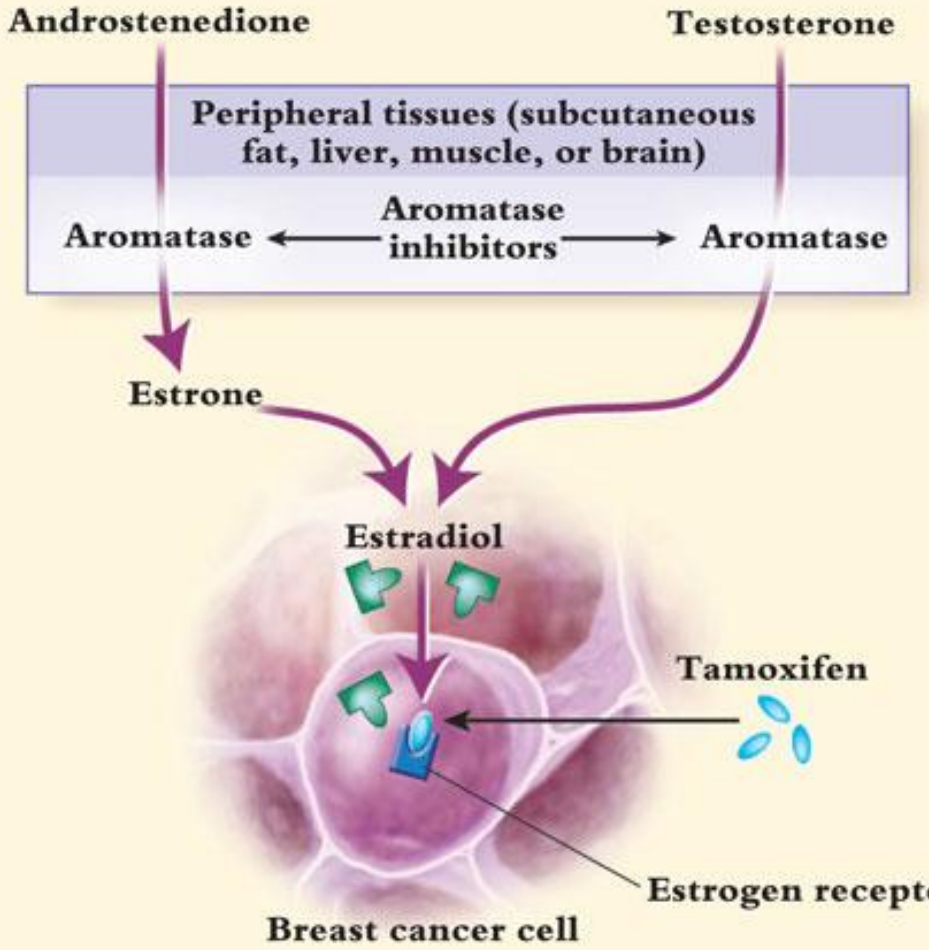
- Hormone therapy should be offered to patients whose tumors express **any level** of ER/PR receptors.

- Endocrine therapy should be recommended **as initial** treatment for patients with HR-positive MBC, **except for patients with immediately life-threatening disease or rapid visceral recurrence during adjuvant endocrine therapy.(and HER2 +)**

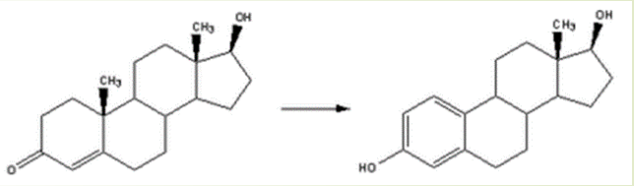
=>consider adding chemotherapy

- Treatment should be administered **until there is unequivocal evidence of disease progression** as documented by imaging, clinical examination, or disease-related symptoms.
- The use of combined endocrine therapy and chemotherapy is not recommended.

Figure 2. Mechanism of action of the aromatase inhibitors.

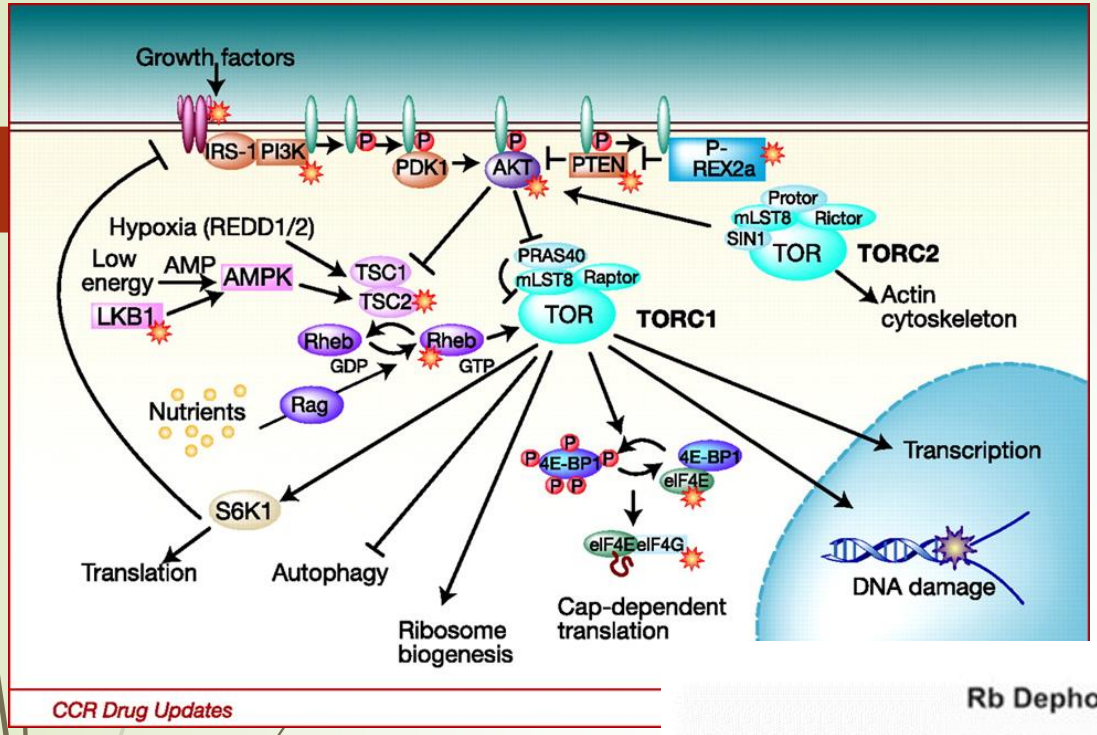


Source: Smith IE, Dowsett M. Aromatase inhibitors in breast cancer. N Engl J Med. *2003;348:2431-2442. Copyright © 2003 Massachusetts Medical Society. All rights reserved.*



regimen

- **AI(non steroidal):** such as **anastrozole (Arimidex) and letrozole (Femara),** inhibit the synthesis of estrogen via **reversible competition** for the aromatase enzyme.
- **Fulvestrant**(Faslodex): a **complete estrogen receptor antagonis**t with no agonist effects, which in addition, accelerates the proteasomal degradation of the estrogen receptor.[1] The drug has poor oral bioavailability, and is administered monthly via intramuscular injection.
- **Palbociclib**(Ibrance,125mg capsule**)**: a selective inhibitor of the cyclin-dependent kinases **CDK4 and CDK6**
- **Tamoxifen**(Nolvadex): selective estrogen-receptor modulator **(SERM)**
- **Everolimus**: **an inhibitor of** mammalian target of rapamycin (**mTOR**).


Growth factors
IRS-1
PI3K
PDK1
AKT
PTEN
P-REX2a
Protor
mLST8
Rictor
SIN1
TOR
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Actin cytoskeleton
Hypoxia (REDD1/2)
Low energy
AMP
AMPK
LKB1
TSC1
TSC2
PRAS40
mLST8
Raptor
TOR
TORC1
Rheb
GDP
Rheb
GTP
Nutrients
Rag
S6K1
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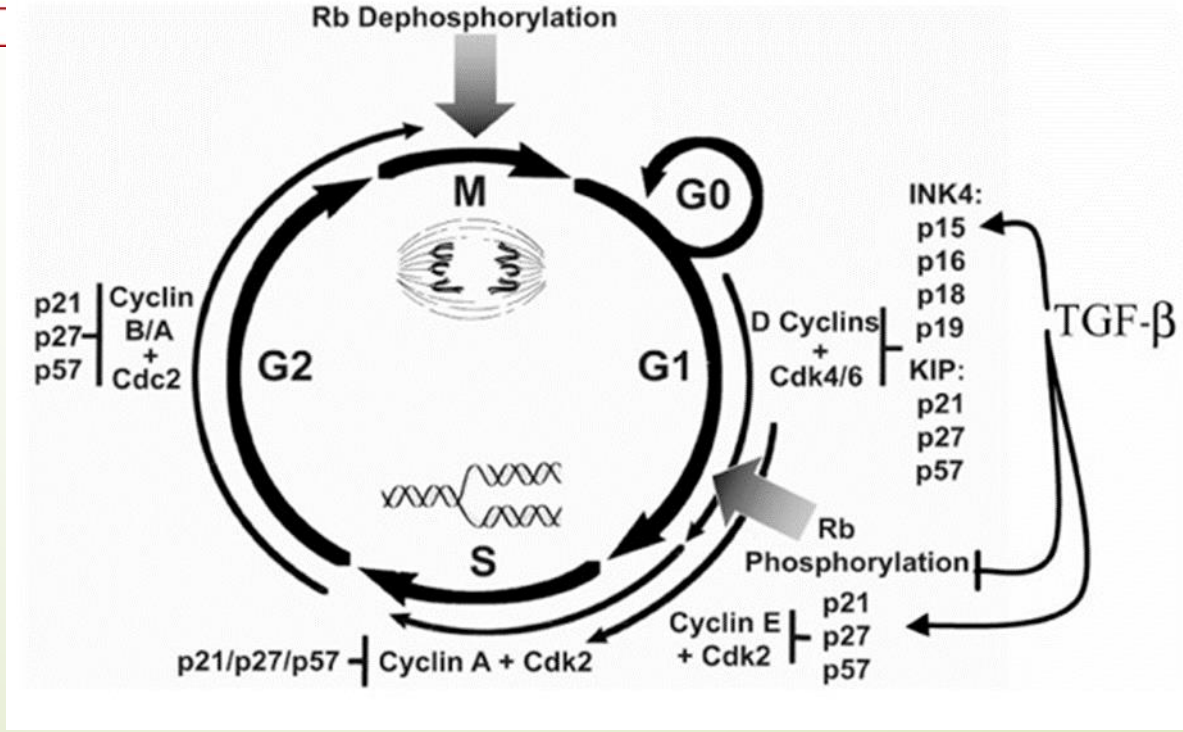
Transcription
DNA damage
Translation
Autophagy
Ribosome biogenesis
Cap-dependent translation
CCR Drug Updates


Rb Dephosphorylation
M
G0
G1
G2
S
p21
p27
p57
Cyclin B/A + Cdc2
D Cyclins + Cdk4/6
INK4:
p15
p16
p18
p19
KIP:
p21
p27
p57
TGF-β
Rb Phosphorylation
Cyclin E + Cdk2
p21
p27
p57
p21/p27/p57
Cyclin A + Cdk2

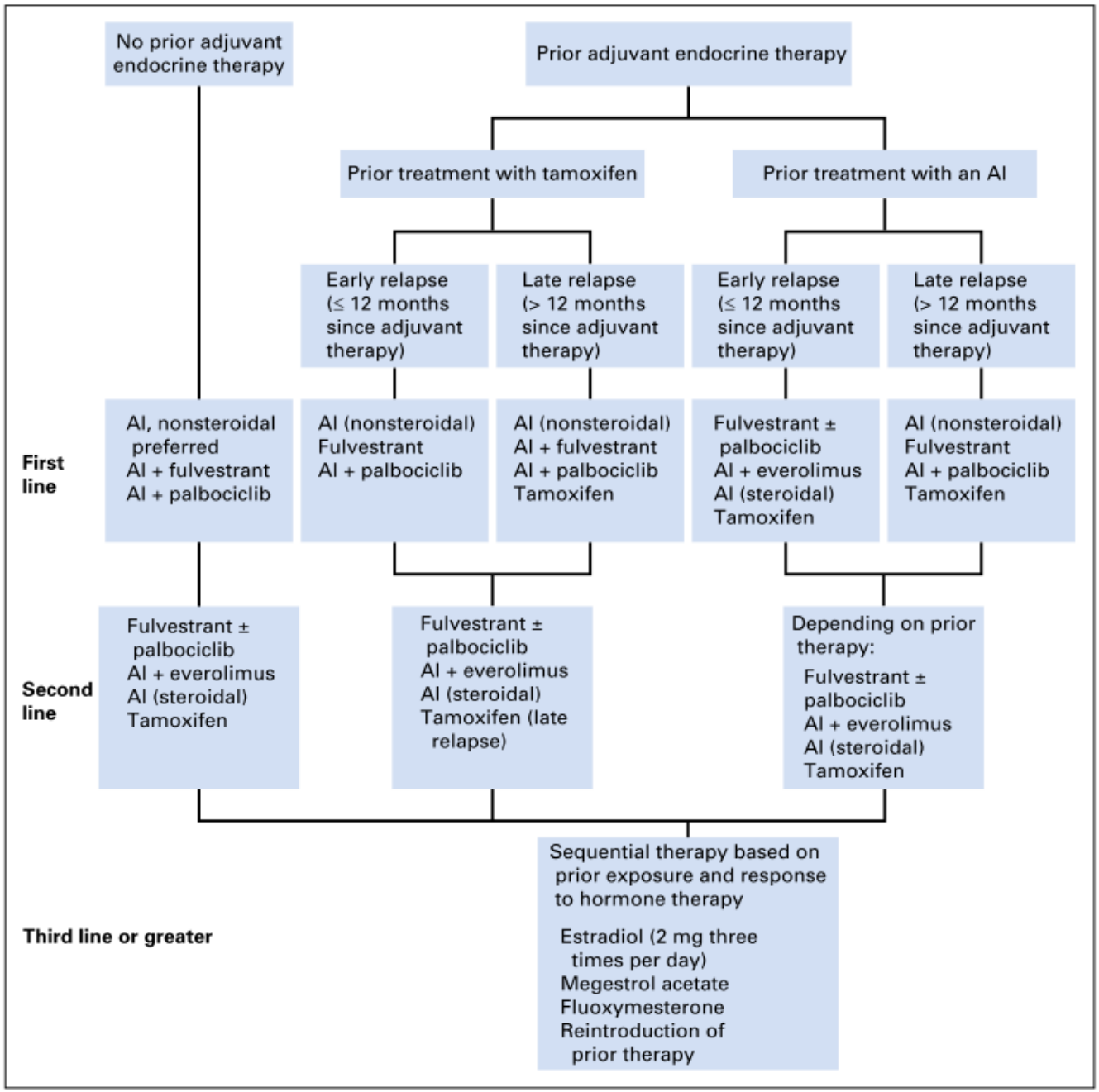


Fig 1. Hormone therapy for postmenopausal women with hormone receptor–positive metastatic breast cancer by line of therapy and adjuvant treatment. NOTE. Use of palbociclib should be reserved for patients without prior exposure to cyclin-dependent kinase 4/6 inhibitors. Fulvestrant should be administered at 500 mg every 2 weeks for three cycles, then once per month as an intramuscular injection. Withdrawal of tamoxifen or progestins was reported to result in short-term disease responses in older literature. Steroidal indicates exemestane; nonsteroidal indicates anastrozole or letrozole. AI, aromatase inhibitor.

Endocrine therapy
Single agent

- AI (anastrozole)
- Fulvestrant
- Tamoxifen

anastrozole(Arimidex) v.s. fulvestrant

Endocrine therapy combined agents

- **anastrozole(Arimidex) + Fulvestrant**

v.s. anastrozole(Arimidex) alone

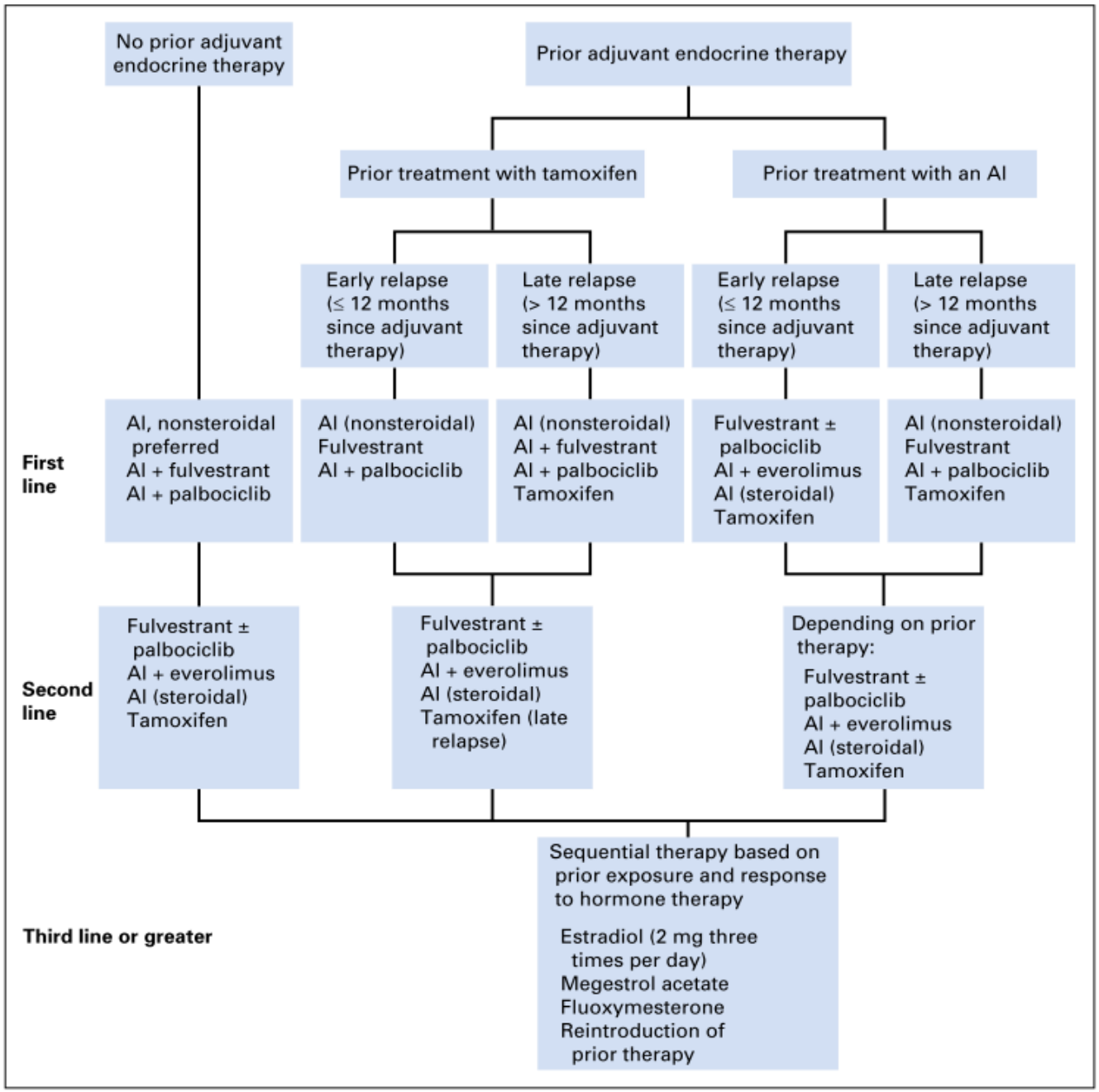
->1.FACT(most s/p hormone therapy) **+/-**

->2.SWOG0226 trial (never s/p hormone therapy) **combined 效果較好**

Letrozole(AI) + palociclib

v.s. letrozole alone

->PALOMA I trial **combined效果較好**



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First-Line Therapy for MBC patient

- **Postmenopausal** women with HR-positive MBC should be offered **aromatase inhibitors (AIs)** as part of first-line endocrine therapy.
- Combination hormone therapy with a **nonsteroidal AI and fulvestrant** may be offered for patients with MBC **without prior exposure to** adjuvant endocrine therapy.
- When fulvestrant is administered, it should be administered using the 500-mg dose and with a loading schedule (treatment start, day 15, day 28, then once per month).

- **Premenopausal** women with HR-positive MBC should be offered **ovarian suppression** or ablation and hormone therapy.

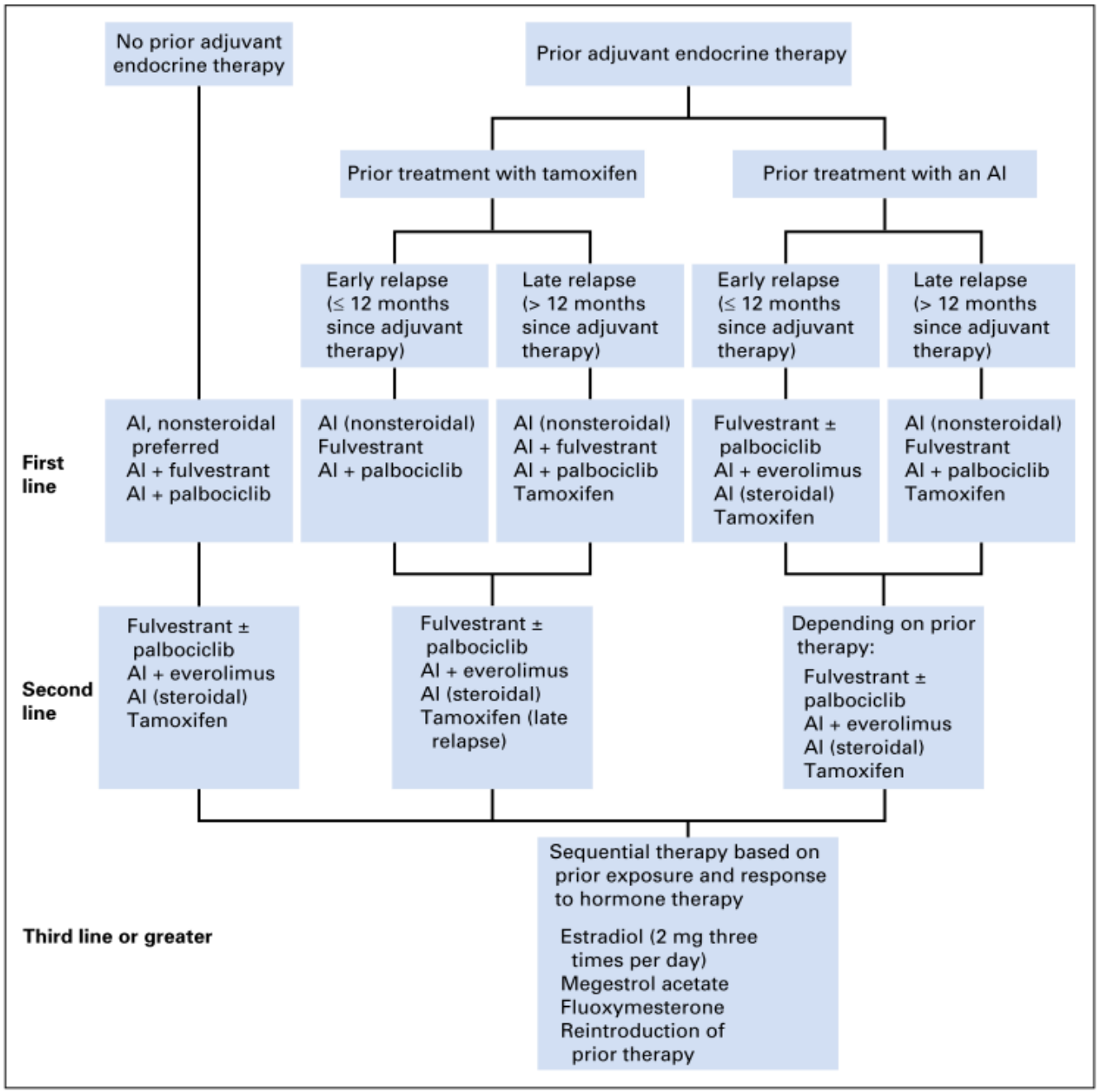
Second-Line Therapy

- Everolimus + steroidal AI (Exemestane)

↓

Prominent side effects (Oral ulcer, infection, fatigue,rash)

Fulvestrant+ palbociclib ->PALOMA III



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Treatment for bone destruction

Zometa(Zoledronic acid)

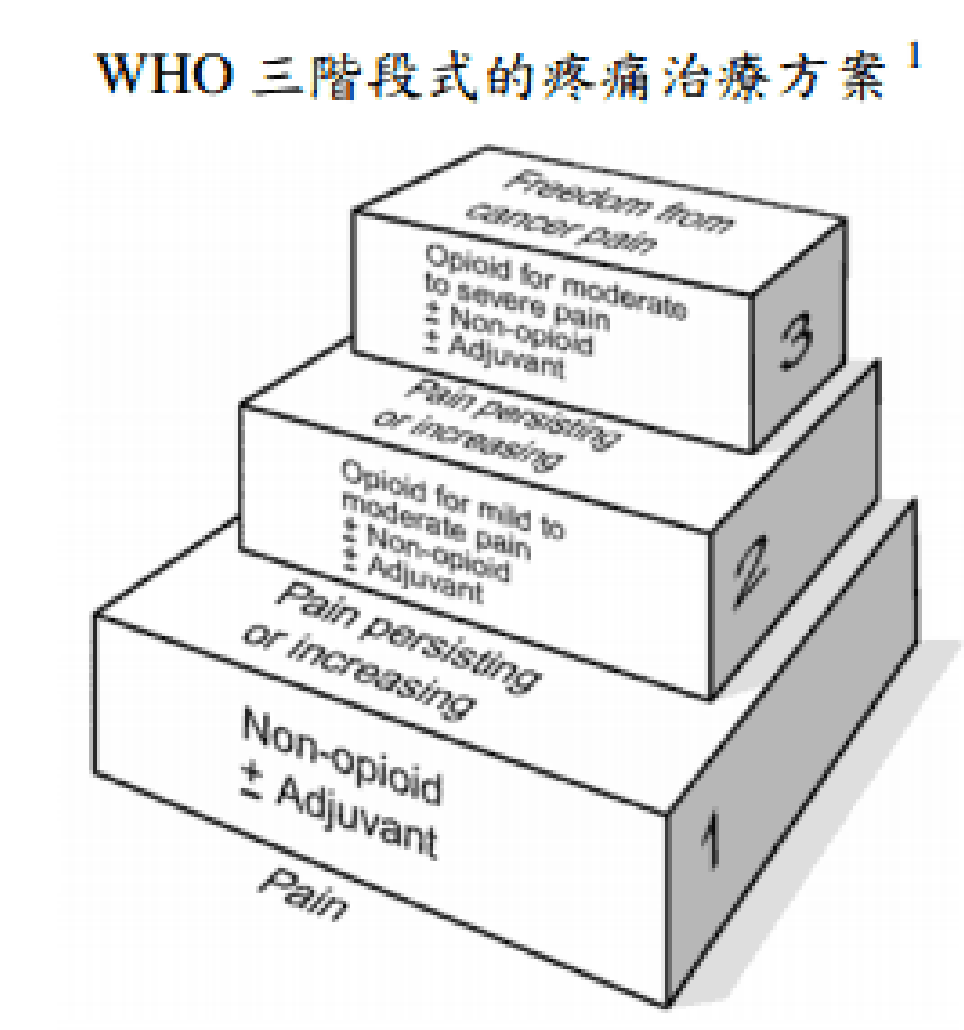
- 雙磷酸鹽 (Bisphosphonate) 化合物，作用在降低噬骨細胞的活力，活化造骨細胞的活動力；減少骨質流失，骨折、骨疼痛、高鈣血症。
- 適應症: 惡性腫瘤之蝕骨性骨頭轉移之病患，在使用嗎啡、可待因等止痛劑後仍不易控制者。惡性腫瘤之高血鈣症。
- 預防性: 更年期後接受AI治療之病患若骨密度檢查T Score小於-2.0、年齡大於65歲、BMI值小於20kg/m2、有家族股骨頭骨折史，個人在50歲後曾發生骨折或類固醇使用超過六個月以上時，考慮接受雙磷酸鹽治療
- Zometa的使用，對**乳癌病人復發率的降低**，具有統計上的差異，可是在死亡率及骨轉移率方面，使用Zometa與否在統計上並沒有意義的差異。
- 有腎臟功能受損的可能副作用。滴注時間 30 分鐘。建議在每一次投予Zometa 前監控血中之creatinine,
- 注意有無低血Ca,Mg情形

Palliative Radiotherapy

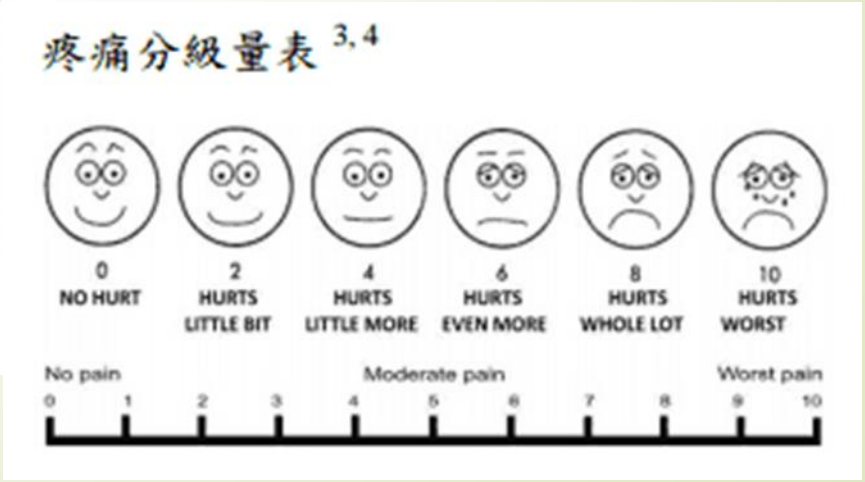
- 癌症病人骨轉移後發生病理性骨折的機率約為10%，至於在脊椎轉移後所引起脊椎不穩定的背痛約佔所有癌症病人的10%。因此，一旦癌症轉移到病人的骨骼後，將會引起病人背痛、高血鈣、病理性骨折及脊隨壓迫等症，而降低病人的生活品質和增加死亡率。

- **骨轉移之處理原則若骨轉移之部位涵蓋身體承重之肢體骨骼及軀幹骨骼（如脊椎及骨盆腔），或骨轉移疼痛無法控制時則應優先局部放射治療**以預防病理性骨折導致癱瘓及長期臥床

Pain control



- 免於疼痛是一種基本人權 (WHO 1990)。疼痛的治療，應該在最少的藥物副作用下，控制在疼痛量表的分數小於 3 的程度 。



- 第一階段: Acetaminophen 或者NSAIDs) 做為起始治療，同時考慮併用輔助藥物。
- 第二階段，使用弱效的鴉片類藥物，同時考慮併用輔助藥物。
- 第三階段，使用強效的鴉片類藥物，如 Morphine、Fentanyl、Oxycodone等，同時考慮併用非鴉片類的止痛藥以及輔助藥物。

- 輔助藥物例如抗憂鬱藥物、抗癲癇藥物、類固醇、局部麻醉劑、肌肉鬆弛劑等，可增加疼痛控制的效果，也可以減低止痛藥的副作用及耐受性的發生，尤其是用於神經性疼痛。

- 於2012年Cochrane Database發表「組合藥物用於治療成人神經性疼痛」的整合分析報告中 ，證實多種藥物併用可得到更好的止痛效果，多重機轉的疼痛控制策略已廣為被各學會所接受。

6 Core Competecnies

Patient Care
What You Do to the patient?

Medical Knowledge
What You Know?

Professionalism

How You Act?

Interpersonal and Communication Skill

How You Interact with Others?

System-Based Practice

How You Work Within the System?

Practice-Based Learning and Improvment

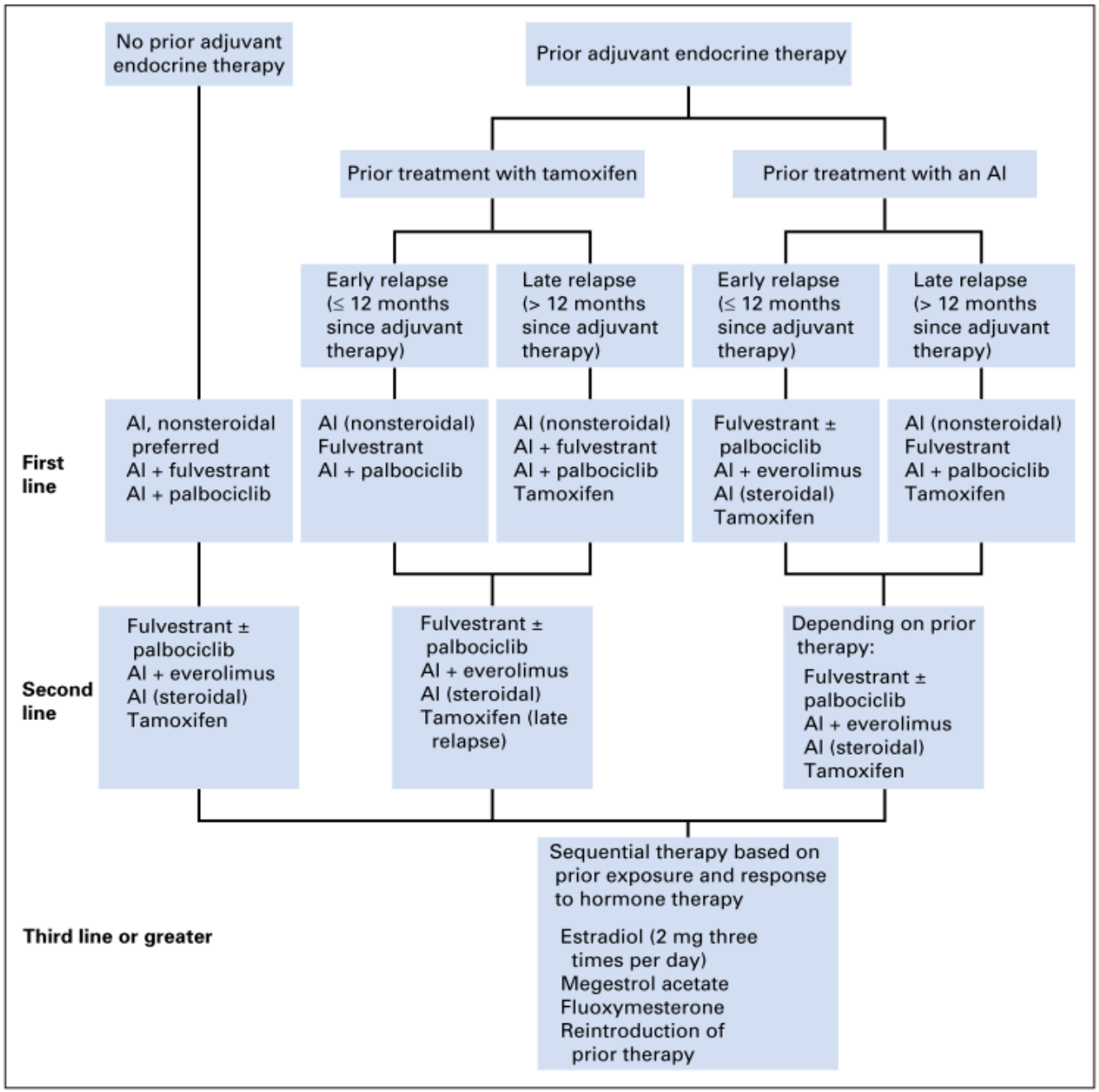
How You Get Better?

Take home messages

- **Endocrine therapy** should be recommended as initial treatment for patients with HR-positive MBC, except for patients with **immediately life-threatening disease or rapid visceral recurrence during adjuvant endocrine therapy.(and HER2 +)**
- =>consider adding chemotherapy

- **Postmenopausal** women with HR-positive MBC should be offered aromatase **inhibitors (AIs) as part of first-line endocrine therapy.**

- When fulvestrant is administered, it should be administered using the **500-mg dose and with a loading schedule (treatment start, day 15, day 28, then once per month**).



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REFERENCE

- 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 Fallow fi eld, 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

- 肺癌醫療暨衛教網頁
- 1. WHO cancer pain relief programme. Cancer Surv 1988; 7: 195-208.
- 2. Combination pharmacotherapy for the treatment of neuropathic pain in adults. Cochrane Database Sys Rev. 2012 Jul 11;7:CD008943
- 3. The Faces Pain Scale - Revised: Toward a common metric in pediatric pain measurement. Pain 2001; 93: 173-183.
- 4. New Clinical-Practice Guidelines for the Management of Pain in Patients with Cancer. N Engl J Med 1994; 330:651-655.


A Big
THANK
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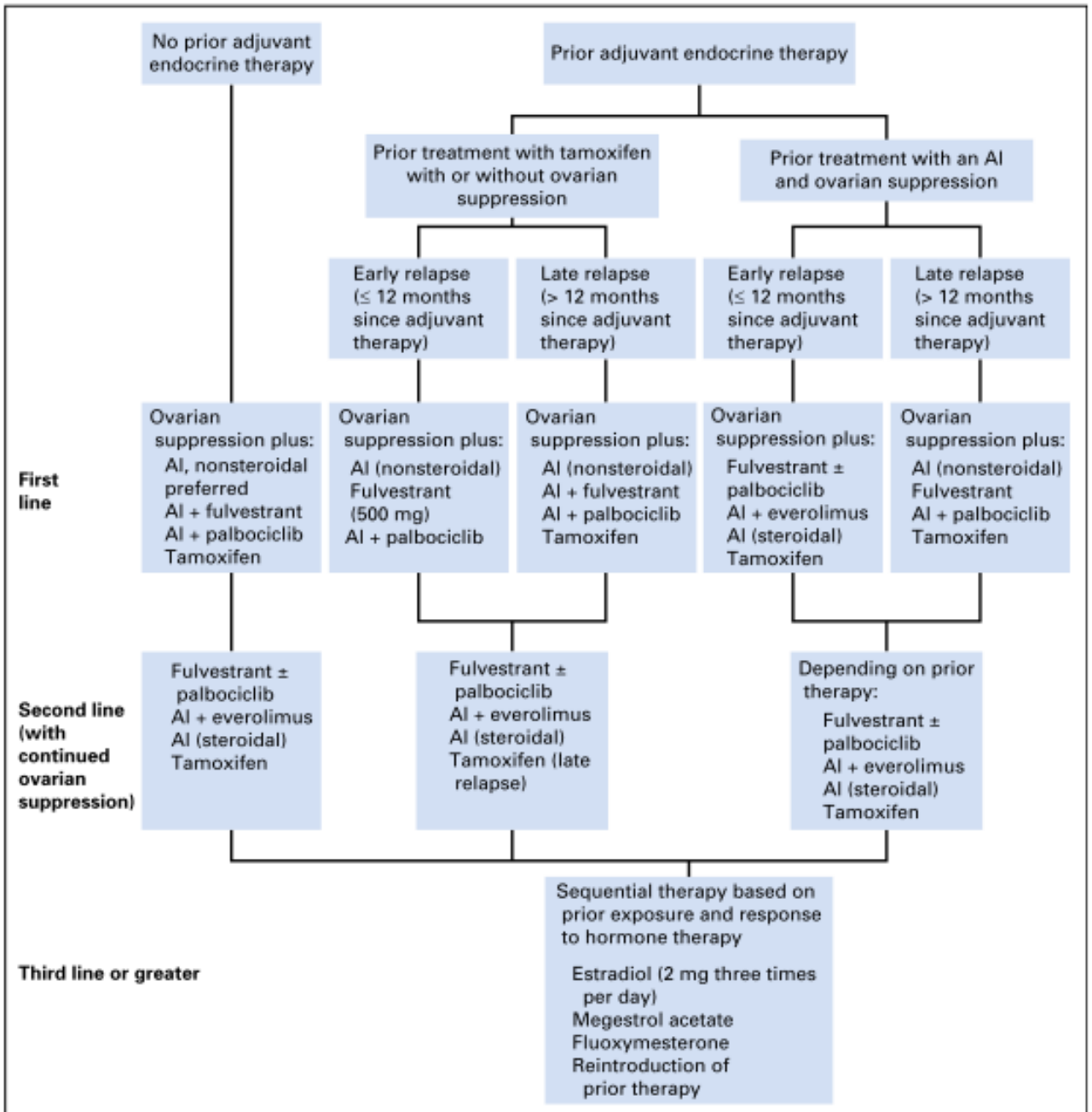

Fig 2. Hormone therapy for premenopausal women with hormone receptor–positive metastatic breast cancer by line of therapy and adjuvant treatment. NOTE. Use of palbociclib should be reserved for patients without prior exposure to cyclin-dependent kinase 4/6 inhibitors. Fulvestrant should be administered at 500 mg every 2 weeks for three cycles, then monthly as an intramuscular injection. Withdrawal of tamoxifen or progestins was reported to result in short-term disease responses in older literature. Steroidal indicates exemestane; nonsteroidal indicates anastrozole or letrozole. AI, aromatase inhibitor.