

乳癌的藥物治療

台大雲林分院

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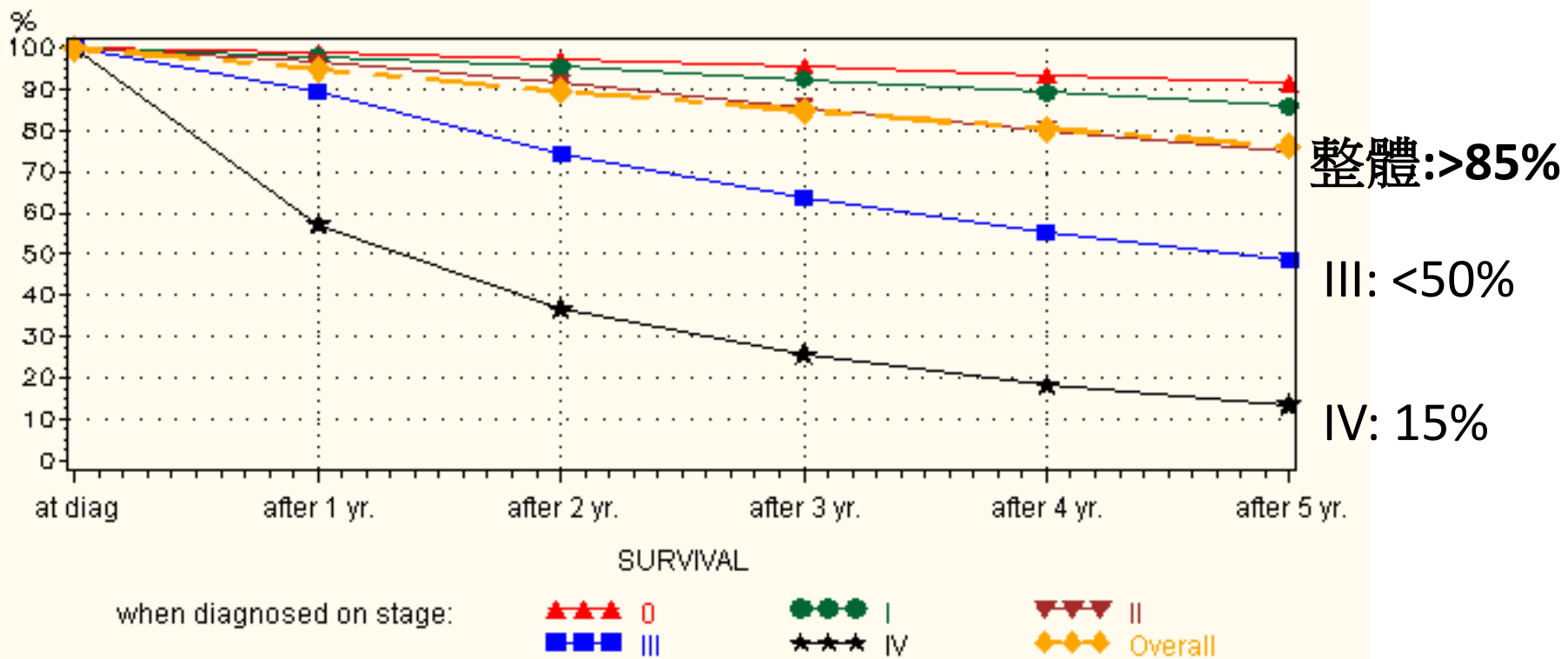
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乳癌五年存活率

Five Year Surv. Rates for Breast Cancer Cases Diagnosed in 1995 and 1996

All States / Data Reported from 608 Hospitals

Hospitals of Type: Community Cancer Center



Source: NCDB, Commission on Cancer, ACoS.

Survival Reports, v2.0 – January 31, 2005

病理報告：最重要的治療決定指標

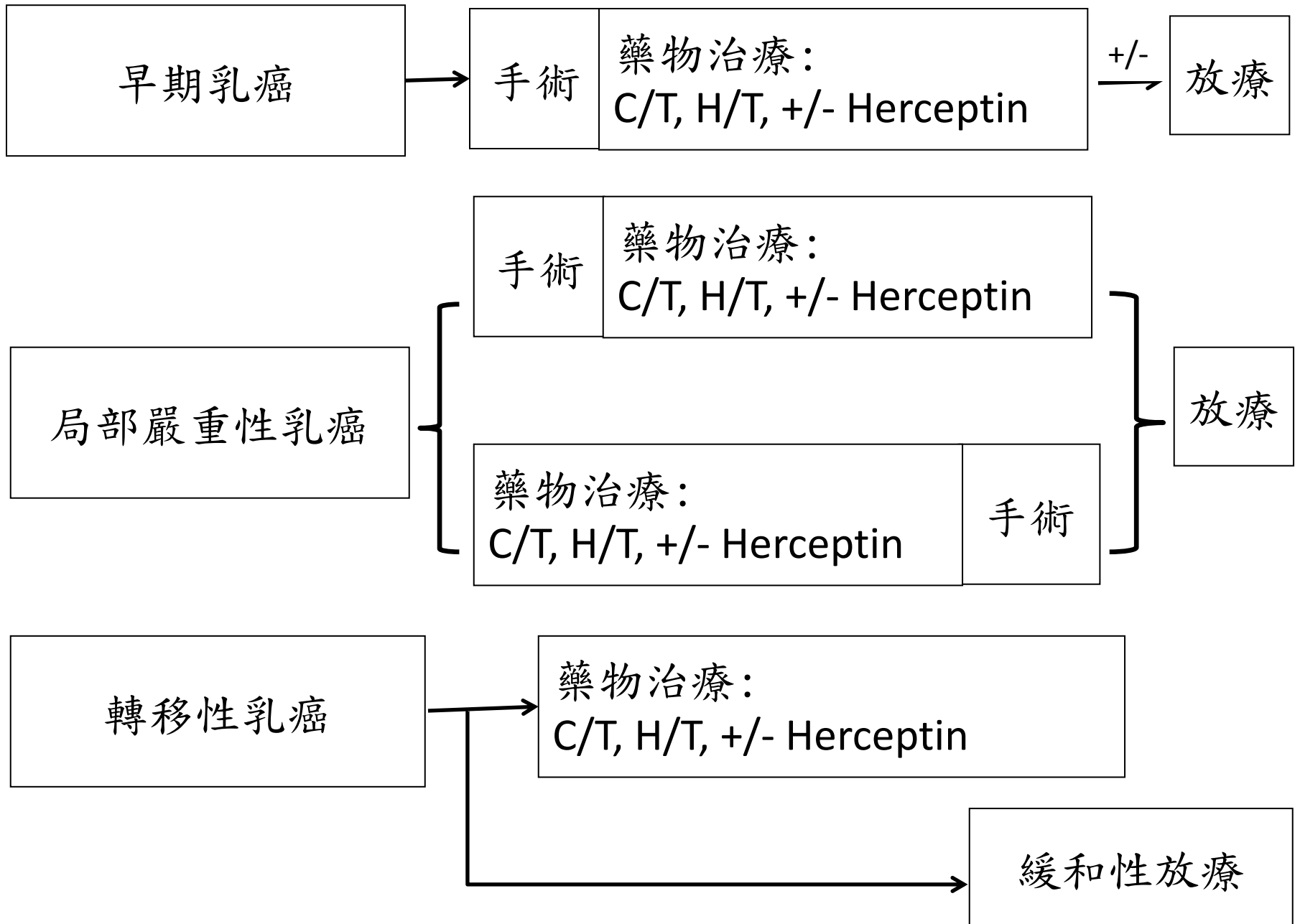
- 腫瘤本身
 - 腫瘤大小(最大徑)
 - 腫瘤分級(grade)
 - 低(Low), 中(intermediate), 高(high)
 - 以 mitosis, tubular formation, atypia 來決定
 - 免疫染色 (IHC)
 - ER (estrogen receptor)
 - PR (progesterone receptor)
 - Her-2/neu staining, 0~3+

病理報告：最重要的治療決定指標

- 腫瘤與旁邊組織的關係
 - 淋巴血管侵犯(Lymphovascular invasion)?
 - 神經叢侵犯(Perineural invasion)?
 - 手術邊緣是否切的乾淨(Margin)?
- 淋巴結取樣
 - 轉移顆數 / 取樣總顆數, 如: 3(+)/16
 - 前哨淋巴結取樣

Her-2/neu 表現

- 定義：
 - 病理免疫染色(IHC stain): 3+/3+，或
 - 染色體螢光檢驗(FISH): positive (fluorescence in situ hybridization)
- Her-2/neu (+):
 - 約占乳癌病人的20%



藥物治療

- 化學治療：輔助性或緩和性
- 荷爾蒙治療
- 標靶治療：anti-HER-2 therapy

常用的化療藥物

- Anthracyclines(小紅莓)
 - Doxorubicin
 - Epirubicin
 - Mitoxantrone
- Taxanes(紫杉醇類)
 - Paclitaxel
 - Docetaxel
- Others
 - Vinorelbine
 - Cyclophosphamide
 - 5-FU
 - Capecitabine
 - Methotrexate

Stage III 考量

- If Her-2/neu (+)
 - Herceptin (trastuzumab)
 - 治療期間：
 - 至少 9 周 (FinHer study)
 - 輔助性治療: 1 年 (HERA study)
- Her-2(+), ER(-): taxanes 很重要
- 小紅莓為常用主要處方
- 通常使用”併用處方”

Stage IV 考量

- 非根治性的治療
- 單獨使用一種藥：效果並沒有比較差
- 與藥物使用的順序無關
- 常用處方：與輔助性化療相似
 - CMF, CEF, CAF
 - EC, AC
 - Gemcitabine + paclitaxel
 - Docetaxel + capecitabine
 - EP, TP
 - N-HDFL

藥物治療

- 化學治療
- 荷爾蒙治療
 - Tamoxifen, aromatase inhibitors(AI)
- 標靶治療: anti-HER-2 therapy

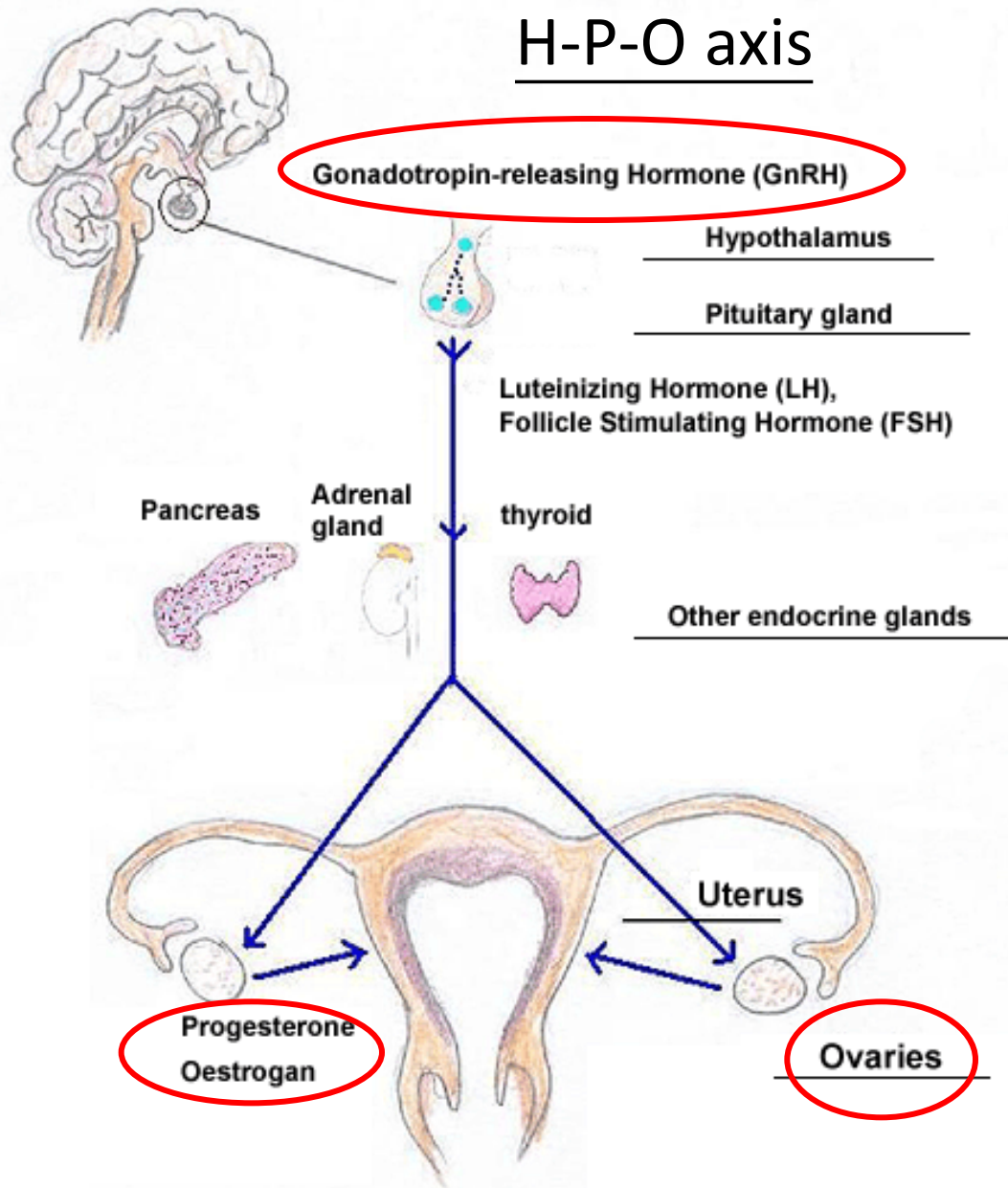
荷爾蒙治療

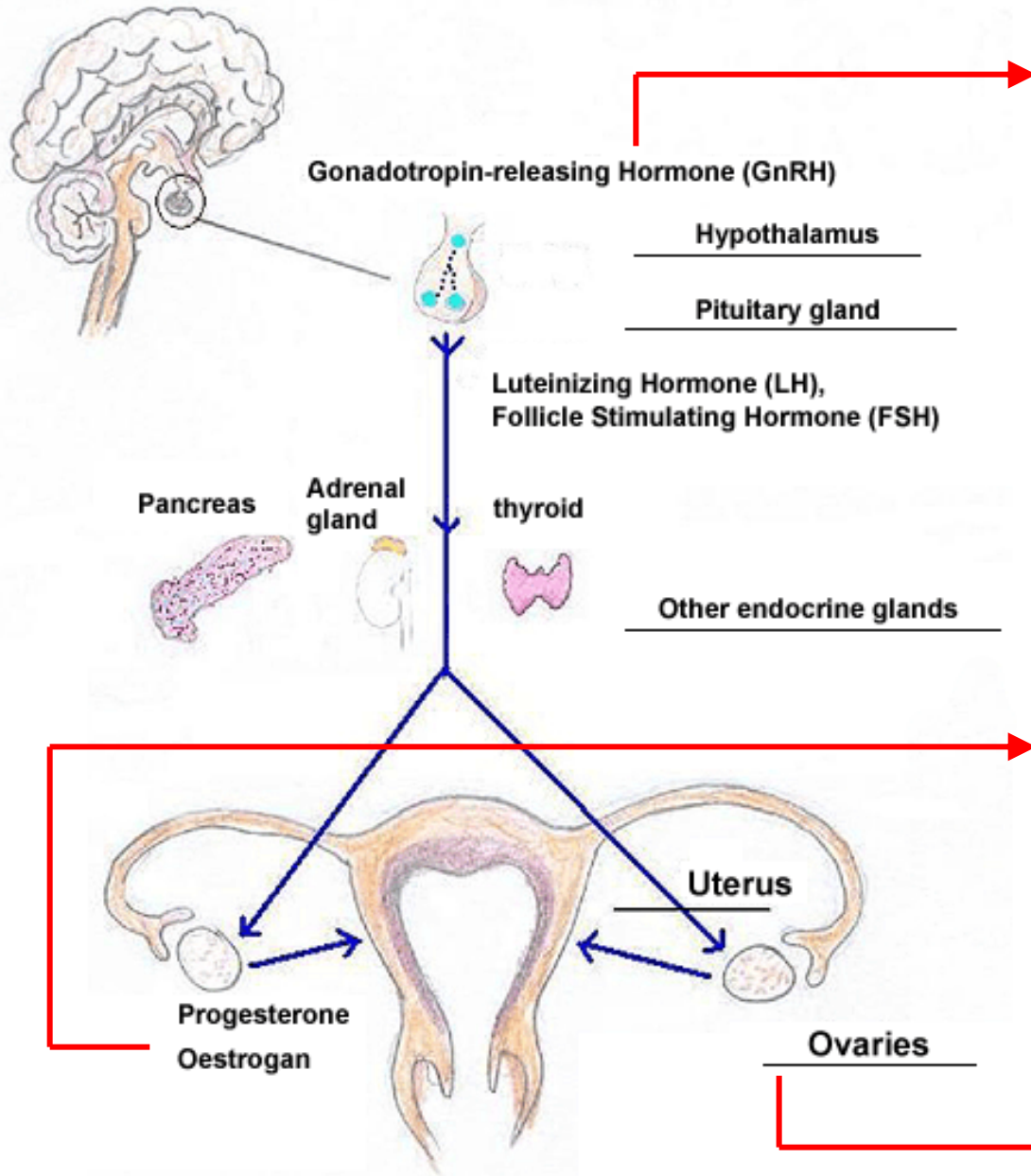
- 約 60% 乳癌是 ER(+)
- 腫瘤生長依靠荷爾蒙
- 荷爾蒙治療目標：
 - 拮抗estrogen的效果
 - 降低estrogen

Estrogen 來源

- 停經前：
 - 卵巢
- 停經後：
 - 周邊的androgen由aromatase代謝成estrogen
 - 卵巢
 - 腎上腺
 - 脂肪組織

H-P-O axis





GnRH agonist:
Leuprolide or Goserelin

SERM: Tamoxifen

PR: Megace, Farlutal

Aromatase inhibitors:
Anastrozole, letrozole, exemestane

ER antagonist: fulvestrant

Bilateral oophorectomy

作用機轉

- 降低estrogen
 - 切除卵巢 (Bilateral oophorectomy, BSO)
 - GnRH agonist
 - Aromatase inhibitor
- ER modulator or antagonist
 - Tamoxifen
 - Megace, Fulvestrant
 - Fulvestrant

輔助性荷爾蒙治療：停經前

- Standard:
 - Tamoxifen x 5 years
 - Also standard for postmenopausal women
- Bilateral oophorectomy
- GnRH + Tamoxifen > GnRH alone
- GnRH + Tamoxifen vs. Tamoxifen???

輔助性荷爾蒙治療：停經後

- Aromatase Inhibitors (AI)
 - Anastrozole (Arimidex[®])
 - Letrozole (Femara[®])
 - Exemestane (Aromasin[®])
- Tamoxifen x 5 yrs, or
- AI x 5 yrs, or
- Tamoxifen x 5 yrs + AI x 5 yrs, or
- Tamoxifen x 2-3 yrs + AI x 2-3 yrs

轉移性乳癌

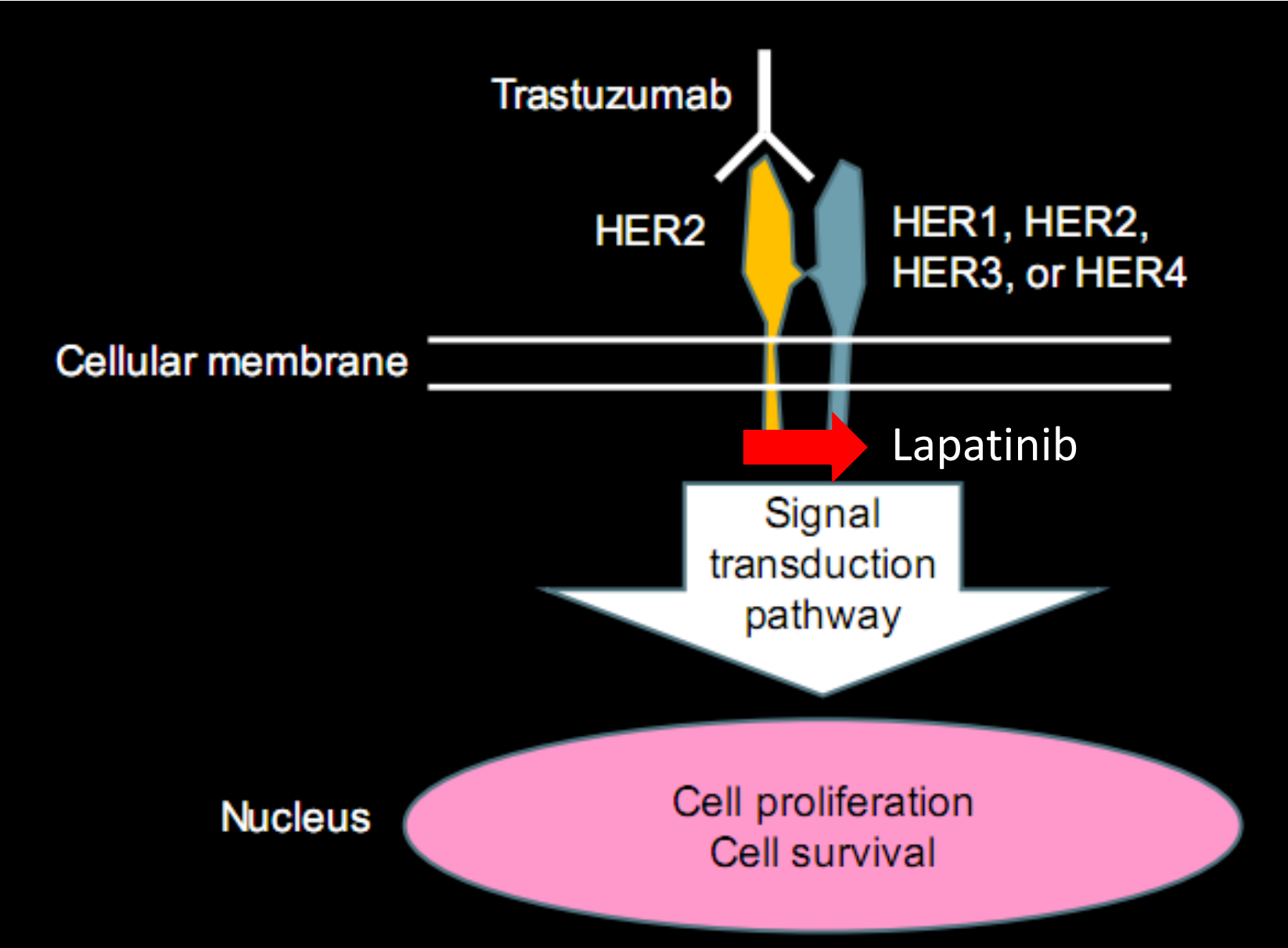
- 荷爾蒙治療仍可做為第一線治療考慮
 - 尤其是老年且 ER(+), PR(+) patients
 - 沒有重要器官轉移的病人
 - 病程進展較慢的病人
- Tamoxifen or AI
- 若失敗, 可再試其他荷爾蒙治療或是改用化療

荷爾蒙治療副作用

- Tamoxifen
 - Antagonist to breast
 - Agonist to bone, uterus
 - **↑** 子宮內膜癌、子宮肉癌
 - 血栓疾病機率增加
- AIs
 - 較多骨質疏鬆
 - 較多關節或肌肉疼痛
 - 也有血栓問題

藥物治療

- 化學治療
- 荷爾蒙治療
- 標靶治療: anti-HER-2 therapy
 - Trastuzumab (Herceptin): 賀癌平
 - Lapatinib(Tykerb): 泰嘉錠



Trastuzumab (Herceptin[®]): 賀癌平

- Anti-HER2 單株抗體
- 劑量:
 - 4 mg/kg ivd in week 1, 2 mg/kg IV Q1W from Week 2
 - 8mg/kg ivd in week 1, then 6mg/kg ivd q3w
- 適應症:
 - 乳癌 (與paclitaxel併用或單獨使用)
 - IHC (immunohistochemistry) **3+**
 - IHC **2+** → FISH (fluorescent in situ hybridization) +
- Side effects:
 - Infusion-related reaction
 - Cardiomyopathy

Lapatinib (Tykerb[®]): 泰嘉錠

- EGFR and HER2 tyrosine kinase inhibitor
- 劑量:
 - 1250 mg PO QD
- 適應症:
 - With Capecitabine
 - With Trastuzumab
- 副作用:
 - 皮膚疹
 - 腹瀉
 - Cardiomyopathy



因此，當我們準備治療病人，我們需要知道…

- 正確診斷：組織型態, IHC 染色 (ER/ PR/ HER-2)
- 分期與治療：
 - 怎麼手術呢? MRM/ BCT, ALND vs SLND
 - 化療: HER-2 status?
 - 荷爾蒙治療: ER/ PR? 停經了嗎? 藥物使用長度?
 - 放射線治療

Adjuvant! Online

Decision making tools for health care professionals

Adjuvant! for Breast Cancer (Version 8.0)

Patient Information

Age:

Comorbidity: ▼

ER Status: ▼

Tumor Grade: ▼

Tumor Size: ▼

Positive Nodes: ▼

Calculate For: ▼

10 Year Risk:

Adjuvant Therapy Effectiveness

Horm: ▼

Chemo: ▼

Hormonal Therapy:


Chemotherapy:

Combined Therapy:

No additional therapy:



 73.1 alive and without cancer in 10 years.

 24.7 relapse.

 2.2 die of other causes.

With hormonal therapy: Benefit = 9.0 without relapse.



With chemotherapy: Benefit = 8.2 without relapse.



With combined therapy: Benefit = 14.4 without relapse.



