HR-Positive Metastatic Breast Cancer: 2025 Update

共識會議

主編-----台灣乳房醫學會

Preface

承先啟後，共譜 HR+ 轉移性乳癌治療的 HAPPY 新篇章

乳癌治療的進展一日千里，每一次的共識凝聚，都是為了讓臨床決策更清晰，讓病患的生命更有品質。繼 2023 年學會發布具指標性的 HR+ 轉移性乳癌共識後，面對後 CDK4/6 抑制劑時代的挑戰，我們再次集結專家智慧，期望透過這份嶄新的共識手冊，為台灣的乳癌治療帶來 HAPPY 的新願景：

- H - Hope（新藥帶來的希望）： 隨著抗體藥物複合體（ADC）、口服 SERD 及 AKT 路徑抑制劑等新型藥物的問世，我們看見了更多突破抗藥性的曙光。這些「新武器」的加入，為過往治療選項有限的病患，重新燃起了控制疾病的希望（Hope）。
- A - Advance（治療策略的躍進）： 醫學的腳步從未停歇，從單一藥物到合併療法，從傳統化療到標靶精準打擊。這份共識見證了我們在治療序列上的躍進（Advance），確保每一位醫師都能掌握最前沿的證據，做出最有利於病人的判斷。
- P - Precision（檢測導向的精準）： 精準醫療已非口號，而是現在進行式。我們特別強調抗藥性機制的檢測時機（如ESR1、PIK3CA 等生物標記），唯有透過精準（Precision）的診斷，才能在對的時間，給予對的病人，最準確的藥物。
- P - Partnership（醫病攜手的夥伴）： 共識的制定不僅是專家的對話，更是為了深化醫病關係。我們期許這份指引能成為醫病溝通的橋樑，透過醫病共享決策（SDM），建立堅實的夥伴關係（Partnership），陪伴病患走過漫長的抗癌路。
- Y - Years of Quality Life（優質長存的歲月）： 治療的終極目標，不僅是數字上的存活期，更是有品質的生活。我們致力於為病患爭取更多美好的歲月（Years），讓她們在延長生命的同時，依然能保有身心靈的圓滿。

這本共識手冊的誕生，凝聚了工作小組無數個夜晚的心血。感謝所有參與的專家學者與理監事團隊，因為有各位的努力，我們才能將這份 HAPPY 的祝福，轉化為具體的臨床指引，造福每一位台灣的乳癌病友。

台灣乳房醫學會 理事長 陳芳銘 謹識 2026.01.21

特別感謝以下專家提供寶貴建議（依姓氏筆畫排列、職稱省略概以醫師稱謂）

于承平、李忠良、周旭桓、
林季宏、林金瑤、洪志強、
洪進昇、高理鈞、張献崑、
張耀仁、沈士哲、游啟昌、
黃其晟、黃俊升、廖國秀、
劉峻宇、賴峻毅、鍾為邦、
饒坤銘　等諸位醫師。

本治療共識僅做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不作為醫療訴訟用。

(2025 UPDATE)

Preface

乳癌至今仍居高台灣女性癌症發生率第一名，隨著醫學知識和技術的不斷演進，我們期望能夠提供更有效的方法和更全面的照護。然而，由於臨床醫事人員能夠使用的工具日益增多，且病人需求與背景多元化，治療方式的選擇變得更加複雜。

為了整合更多關於荷爾蒙受體陽性的轉移性乳癌治療的參考資訊，因此在 2023 年 5 月學會邀請多位專家成立共識會議工作小組，進行共識會議籌備，擬定 HR+ MBC 治療的重要議題，包含 HR+ risk evaluation and biomarker testing、Selection of first-linetreatment、Selection of second-line treatment、Treatment options other than endocrine-based approaches 等議題，本人衷心感謝工作小組的辛勞付出。

本會於 2023 年 11 月 19 日舉辦「2023 HR+ MBC Consensus」，與眾多專家學者們共同討論，會後彙整專家建議，經台灣乳房醫學會第九屆理監事審議通過，期望本次共識會議手冊能夠成為臨床醫師治療時的參考依據。

透過這份共識的制定和實施，我們期望在臨床實踐中引領方向，促進更高水平的乳癌治療，並進一步改善患者的生存率和生活品質。同時，我們也能夠加強醫療專業人員之間的溝通和協調，提升整體醫療水平，為台灣的乳房疾病治療作出更大的貢獻。

最後，我代表台灣乳房醫學會衷心感謝各位醫療專業人士的參與和支持，期待這份共識的實施能夠為病人和乳房疾病治療帶來更多的福祉和價值。

台灣乳房醫學會 前理事長陳守棟 于 2024 年 1 月

特別感謝以下專家提供寶貴建議（依姓氏筆畫排列、職稱省略概以醫師稱謂）

于承平、王明暘、朱崧肇、吳建廷、
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張耀仁、郭文宏、郭玟伶、陳守棟、
陳怡君、陳芳銘、陳訓徹、陳偉武、
陳達人、曾令民、曾彥敦、黃其晟、
黃俊升、葉顯堂、廖國秀、趙大中、
趙祖怡、劉良智、劉峻宇、蔡青樺、
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鍾奇峰、鍾為邦、饒坤銘　等諸位
醫師。

本治療共識僅做為參考，因每人狀況不同，而由各醫師選擇最適當之處置方式，不作為醫療訴訟用。

Contents

Strength of the Recommendation and Quality of Evidence

Strength	Recommendation
A	Strong recommendation for use
B	Moderaterecommendation for use
C	Marginal recommendation for use
D	Recommendation against use

Quality	Evidence
I	Evidence from at least 1 properly designed randomized, controlled trial
II	Evidence from at least 1 well-designed clinical trial, without randomization; from cohortor case-controlled analytic studies (preferably from > 1 center); from multiple time series; or from dramatic results of uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive case studies

1.AGREE Next Steps Consortium. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ 2012; 182: E839–E842
2.Grading quality of evidence and strength of recommendations in clinical practice guidelines part 3 of 3. The GRADE approach to developing recommendations. Allergy 2011; 66:8
3.Annals of Hematology (2018) 97:1271–1282

The Principle of Voting for Strength of Recommendation

Strength	Recommendation
A	Strong recommendation for use
B	Moderaterecommendation for use
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D	Recommendation against use

For the “Strength of Recommendation A and B”, a majority panel vote of at least 85% is required. For the “Strength of Recommendation C”, a panel vote of at least 50% (but less than 85%) is required.
For recommendations where there is strong panel disagreement regardless of the quality of the evidence, “Strength of Recommendation D” requires a panel vote of at least 25%.

1. NCCN giudelines. Development and Update of Guidelines.

HR+ Risk Evaluation and Biomarker Testing (I)

—— 長庚醫院 / 郭玟伶 醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
Single hormone receptor-positive (ER-/PR+ and ER+/PR-) metastatic breast cancer is associated with worse OS than double hormone receptor-positive metastatic breast cancer.	II	A	1, 4, 5
Histological type (lobular vs. ductal) is inconsistently associated with worse OS and PFS.	II	B	1
High Ki67 in primary tumor or metastatic site is associated with worse OS and PFS.	II	B	1, 7
Disease-free intervala < 2 years is associated with worse OS and PFS.	II	A	1, 6, 11
De novo metastasis is associated with better OS compared with relapsed disease.b	II	A	1, 6, 8
Oligometastasis is associated with better OS and PFS.	II	A	1, 6,12

a.Disease-free interval or recurrence-free interval is often defined as the date of surgery for early breast cancer to the date of first recurrence.
b.Late recurrence with disease free interval > 5 years has similar survival outcome with de novo metastasis6.

HR+ Risk Evaluation and Biomarker Testing (I)

—— 長庚醫院 / 郭玟伶 醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
Bone metastasis is associated with better outcome.c	II	A	1, 6
Endocrine resistanced is associated with poor PFS and OS. **Primary endocrine resistance** is defined as a relapse within 2 years of adjuvant endocrine treatment or disease progression during the first 6 months of first-line endocrine therapy for advanced or metastatic breast cancer (MBC). **Secondary endocrine resistance** is defined in early breast cancer as a relapse that occurs after at least 2 years of endocrine therapy and during or within the first year of completing adjuvant endocrine therapy. In advanced breast cancer or MBC, secondary resistance is defined as disease progression after more than 6 months of endocrine therapy.	III	A	12, 13

c. Liver metastasis in HR+ HER2- breast cancer has poor outcome13.
d. With more modern or advanced endocrine-based treatment approaches, endocrine resistance might be better defined more by the nature of the resistance and the availability of precision medicine tools to address it, but less by the relapse or progression-free interval15.

Reference

1. Prognostic Factors in Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative (HR+/HER2-) Advanced Breast Cancer: A Systematic Literature Review. Gebra Cuyún Carter , Maitreyee Mohanty , Keri Stenger , Claudia Morato Guimaraes , Shivaprasad Singuru , Pradeep Basa , Sheena Singh , Vanita Tongbram, Sherko Kuemmel , Valentina Guarneri , Sara M TolaneyCancer Management and Research 2021:13 6537–6566.

2. Endocrine-Based Treatments in Clinically-Relevant Subgroups of Hormone Receptor-Positive/HER2-Negative Metastatic Breast Cancer: Systematic Review and Meta-Analysis. Francesco Schettini , Mario Giuliano, Fabiola Giudici , Benedetta Conte , Pietro De Placido , Sergio Venturini , Carla Rognoni , Angelo Di Leo , Mariavittoria Locci , Guy Jerusalem , Lucia Del Mastro , Fabio Puglisi , PierFranco Conte , Michelino De Laurentiis , Lajos Pusztai , Mothaffar F Rimawi , Rachel Schiff , Grazia Arpino , Sabino De Placido , Aleix Prat, Daniele GeneraliCancers (Basel) . 2021 Mar 22;13(6):1458. DOI: 10.3390/cancers13061458.

3. Is progression-free survival a more relevant endpoint than overall survival in first-line HR+/HER2 − metastatic breast cancer? Anna Forsythe , David Chandiwana , Janina Barth , Marroon Thabane , Johan Baeck , Anastasiya Shor , Gabriel Tremblay Cancer Management and Research 2018:10 1015–1025. DOI: 10.2147/CMAR.S162714.

4. Prognostic factors for stage IV hormone receptor-positive primary metastatic breast cancer. Akiko Kawano1 , Chikako Shimizu, Kenji Hashimoto, Takayuki Kinoshita, Hitoshi Tsuda, Hirofumi Fujii, Yasuhiro Fujiwara Breast Cancer . 2013 Apr;20(2):145-51. DOI: 10.1007/s12282-011-0320-3. Epub 2011 Dec 3.

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15. Abstract Book of The Advanced Breast Cancer Seventh International Consensus Conference (ABC7).Lisa A. Carey. The Breast 2023 Oct. Vol 71, Supplement 1. page S22.

Risk Evaluation & Biomarker Testing

—by 賴峻毅醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
1. For *PIK3CA* gene, both somatic tissue and liquid biopsy testing can be used for determining mutation status.	I	A	
2. Mutations in somatic *PIK3CA/AKT1/PTEN, ESR1*, and germline pathogenic *BRCA1/2* mutations are associated with improved treatment outcome to relevant targeted therapies. (QoE:I;SoR:A)	I	A	
3. In HR(+) mBC with *HER2*-low (IHC 1+ or IHC 2+/ISH-) or *HER2*-ultralow (IHC 0 with membrane staining) status is predictive of trastuzumab deruxtecan treatment efficacy.	I	A	
4. *ESR1* mutation, determined by circulating tumor DNA has both predictive and prognostic indicator values.	I	A	

(2025 UPDATE)

Risk Evaluation & Biomarker Testing

—by 賴峻毅醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
5. Determination of TROP2 expression status is not required for decision of TROP2 antibody drug conjugates use (such as sacituzumab govitecan, datopotamab deruxtecan)	II	B	8
6. There is data to support replacing AI with a SERD (e.g. camizestrant) in combination to first line CDK4/6 inhibitor use upon emergence of mutant ESR1 ctDNA before clinical progression #	I	A	9
7. Biopsy of metastatic sites may be considered for guiding treatment options if no risk of major complications.	II	A	10

testing for ESR1 ctDNA started at least 6 months after initiation of CDK4/6 inhibitors plus aromatase inhibitors

(2025 UPDATE)

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1. André F, et al. Alpelisib for PIK3CA-Mutated, Hormone Receptor-Positive Advanced Breast Cancer. N Engl J Med. 2019.

2. Oliveira M, et al. Capivasertib and fulvestrant for patients with hormone receptor-positive, HER2-negative advanced breast cancer (CAPItello-291). Lancet Oncol. 2024.

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(2025 UPDATE)

Selection of First-line Treatment (I)

—by 洪志強醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
CDK4/6 inhibitors combined with endocrine treatment(ET) are advised for first line treatment of HR–positive, HER2–negative MBC, including those with clinically aggressive diseasea, regardless of primary or secondary resistance of ET.[b] In the case of premenopausal patients, ovarian function suppression is recommended.	I	A	1-6
For patients who did not relapse on an aromatase inhibitor (AI), or did not recurrence within 12 months of stopping adjuvant AI, a CDK4/6 inhibitor in combination with an AI is advised. Otherwise, SERDc combined with a CDK4/6 inhibitor is considered.	I	A	7-9
For patients who relapse on adjuvant ET or within 12 months after completing adjuvant treatment, in the presence of a PIK3CA mutation, a combination of inavolisib+palbociclib+fulvestrant is recommended.	I	A	10-11

a. Definition of aggressive ABC: symptomatic visceral metastases, rapid disease progression or impending visceral compromise, marked non–visceral disease but with total bilirubin <1.5 ULN.
b. Ribociclib and Abemaciclib have shown OS benefit in phase 3 randomized controlled trial.
c. Imlunestrant (FDA-approved as monotherapy for ESR1 mutation) or Fulvestrant

(2025 UPDATE)

Selection of First-line Treatment (I)

—by 洪志強醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
For patients on first-line CDK4/6 inhibitor plus AI therapy, substitution of the AI with camizestrant upon ESR1 mutation detection by liquid biopsy may be appropriate before disease progression.[d]	I	B	12
Delayed combination of CDK4/6 inhibitor to second line treatment is acceptable.e	I	B	13-14
If recurrence develops at least one year after the completion of adjuvant CDK4/6 inhibitor treatment, the re-introduction of a CDK4/6 inhibitor could be considered.	III	B	15

d. At least 6 months of treatment with AI+CDK 4/6 inhibitor and no evidence of disease progression
e. ET alone is acceptable for patients with comorbidities or a poor performance status. Palbociclib may be safer for older patients.

(2025 UPDATE)

Reference

1. Finn RS, Martin M, Rugo HS, et al. Palbociclib and letrozole in advanced breast cancer. N Engl J Med. 2016;375(20):1925-1936.

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(2025 UPDATE)

Selection of First-Line Treatment (II)

——臺大醫院 / 陳怡君 醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
ET with CDK 4/6 inhibitor is standard of care in 1st line therapy for themajority of ER+/ HER2-advancedbreast cancer patients, including those with clinically aggressive disease. #Definition of aggressive ABC:symptomatic visceral metastases, rapid disease progression or impending visceral compromise, marked non- visceral-diseasebut withtotal bilirubin <1.5ULN.	I	A	1
ET with CDK 4/6 inhibitor maybe consideredafter surgical resection or radiotherapy for clinically stable CNS metastasis.	II	B	2
ET with CDK4/6 inhibitor is effective both in luminal A and luminal B subgroups.* *The subgroups refer to PAM50 defined intrinsic subtypes, rather than clinicopathologic subtypes.	II	B	3

Reference

1. Yen-Shen Lu, et al. Primary results from the randomized Phase II RIGHT Choice trial of premenopausal patients with aggressive HR+/HER2 − advanced breast cancer treated with ribociclib + endocrine therapy vs physician's choice combination chemotherapy [abstract]. In: Proceedings of the 2022 San Antonio Breast Cancer Symposium; 2022 Dec 6-10; San Antonio, TX. Philadelphia (PA): AACR; Cancer Res 2023;83(5 Suppl):Abstract nr GS1-10.

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Selection of Second-line Treatment (I)

— by 林金瑤醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
Fulvestrant in combination with a CDK 4/6 inhibitor may be offered to patients who experienced disease progression during prior treatment with endocrine therapy.	I	A	1-5
Alpelisib plus fulvestrant or AI is a treatment option for patients with PIK3CA-mutanted breast cancer who have progressed on endocrine therapy with or without a CDK4/6 inhibitor.	I	B	6-8
Everolimus plus any other endocrine therapy is an option for patients who have progressed on prior endocrine therapy.	I-II	B	9-13
CDK4/6 inhibitor combined with switching endocrine therapy is a treatment option for HR+, HER2- advanced breast cancer after CDK4/6 progression with endocrine therapy.	II	B	14-15
Capivasertib plus fulvestrant is a treatment choice for one or more *PIK3CA/AKT1/PTEN* alterations metastatic breast cancer after at least one line of endocrine therapy in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.	I	A	16

(2025 UPDATE)

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(2025 UPDATE)

Selection of Second-Line Treatment (II)

— by 李忠良醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
Elacestrant is a treatment option for patients with ESR1-mutated ER-positive, HER2-negative advanced or metastatic breast cancer progressing after at least one line of endocrine therapy.	I	A	1
Tucidinostat plus exemestane might be consider for alternative treatment for ER-positive HER2-negative advanced or metastatic breast cancer. * Only in Asia, not gobal trial	II*	A	2
Imlunestrant with or without abemaciclib is a treatment option for ESR1-mutated ER-positive, HER2-negative advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy. * * FDA proven monotherapy imlunestrant	I	A	3
Giredestrant combined with everolimus is a treatment option for ER-positive, HER2-negative advanced or metastatic breast cancer after prior CDK4/6 inhibitor progression with endocrine therapy	I	A	4
Vepdegestrant, a proteolysis-targeting chimera (PROTAC) estrogen receptor degrader, is a treatment option for with ESR1-mutated ER-positive, HER2-negative advanced or metastatic breast cancer breast cancer progressing after at least one line of endocrine therapy.	I	B	5

(2025 UPDATE)

Reference

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(2025
UPDATE)

Non-Endocrine Based Approaches

—by 鍾為邦醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
1.PARP inhibitors could be used for patients bearing deleterious germline BRCA1/2 mutations who fail or are not suitable for endocrine therapy (ET) and have received at least one line of chemotherapy either in early or metastatic setting.	I	A	1, 2
2.Trastuzumab deruxtecan could be used for patients with HR+/HER2-low (HER2IHC 1+ or HER2IHC 2+ with negative FISH) or HER2-ultralow (HER2IHC 0 with membrane staining) metastatic breast cancer who fail ≥ 2 lines of ET or 1 line of ET but with indicated conditions.a	I	A	3, 4, 5
3.Datopotamab deruxtecan could be used for patients with HR+/HER2-negative metastatic breast cancer who fail ET and ≥ 1 line of chemotherapy.b	I	A	6

a. If patients only experience 1 line of ET, the condition can be as follows: progression ≤ 6 months of starting first-line ET + CDK4/6i, recurrence ≤ 24 months of starting adjuvant ET, or failure of ≥ 1 line of chemotherapy.
b. TROPION-Breast01 trial did not enroll patients who received more than two lines of chemotherapy.

(2025 UPDATE)

Non-Endocrine Based Approaches

—by 鍾為邦醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
4.Sacituzumab govitecan could be used for patients with HR+/HER2- metastatic breast cancer who fail ET and ≥2 lines of chemotherapy.c	I	A	7, 8 ,9
5.Abemaciclib as monotherapy could be considered for patients with HR+/HER2- metastatic breast cancer with disease progression following ET and prior chemotherapy in the metastatic setting.d	II	B	10

c. TROPiCS-02 trial did not enroll patients who received more than four lines of chemotherapy.
d. The dosage of Abemaciclib used in MONARCH 1 trial was 200mg twice a day, which caused notable diarrhea.

(2025 UPDATE)

Reference

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(2025 UPDATE)

Treatment Options Other Than Endocrine-Based Approaches (II)

—— 臺大醫院 / 陳偉武 醫師

Consensus Statement	Quality of Evidence	Strength of Recommendation	Key Reference
Chemotherapy is an option for patients with clinically aggressive metastatic breast cancer or evidence of endocrine resistance.a	I	A	1
The optimal sequence of chemotherapeutic agents has not been established.b	II	A	2,3
Metronomic chemotherapy is an option for patients with advanced hormone-receptor positive disease.c, d	I	B	4,5

a.Please refer to previous points about the definition endocrine resistance
b.Anthracyclines (including liposomal doxorubicin) and taxanes (paclitaxel, docetaxel, nab-paclitaxel), vinorelbine, capecitabine, cisplatin/ carboplatin, gemcitabine, eribulin, and ixabepilone could be considered as options for MBCpatients when chemotherapy is considered.
c.Metronomic chemotherapy treatment refers to the chronic administration of low doses of chemotherapeutic agent(s). The availability of NHI coverage makes metronomic chemotherapy a reasonable alternative.
d.Metronomic chemotherapy regimens that have been validated in prospective clinical trials includes single agent oral vinorelbine andcapecitabine or combinations such as oral methotrexate plus oral cyclophosphamide, oral vinorelbine plus capecitabine, oral cyclophosphamide plus capecitabine, and triple combination of oral vinorelbine, oral cyclophosphamide, and capecitabine.

Reference

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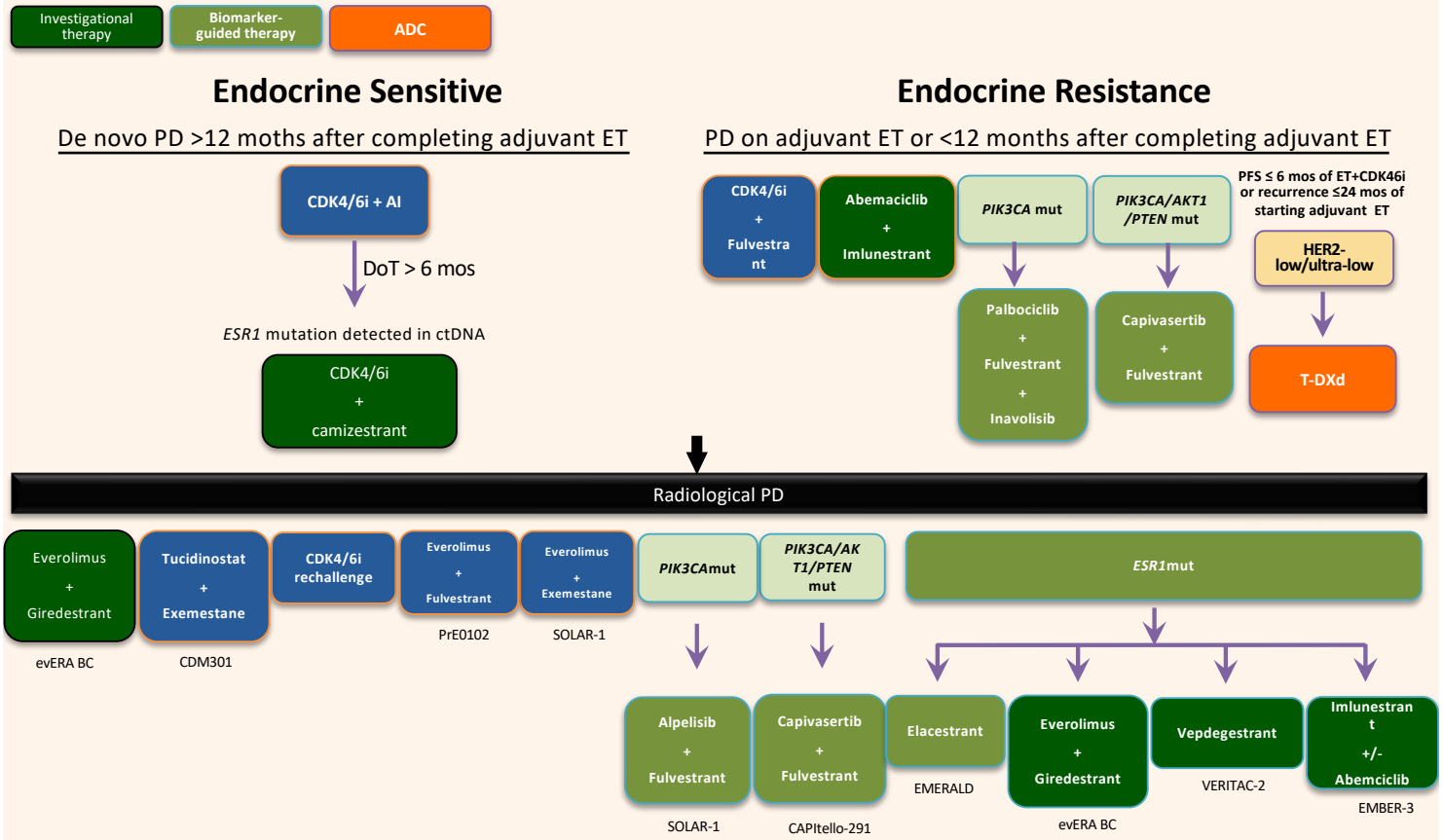
Online Consensus

Treatment Algorithm


Investigational therapy
Biomarker-guided therapy
ADC
Endocrine Sensitive
De novo PD >12 moths after completing adjuvant ET
CDK4/6i + AI
DoT > 6 mos
ESR1 mutation detected in ctDNA
CDK4/6i + camizestrant
Endocrine Resistance
PD on adjuvant ET or <12 months after completing adjuvant ET
CDK4/6i + Fulvestrant
Abemaciclib + Imlunestrant
PIK3CA mut
PIK3CA/AKT1 /PTEN mut
PFS ≤ 6 mos of ET+CDK46i or recurrence ≤24 mos of starting adjuvant ET
HER2-low/ultra-low
Palbociclib + Fulvestrant + Inavolisib
Capivasertib + Fulvestrant
T-DXd
Radiological PD
Everolimus + Giredestrant
evERA BC
Tucidinostat + Exemestane
CDM301
CDK4/6i rechallenge
Everolimus + Fulvestrant
PrE0102
Everolimus + Exemestane
SOLAR-1
PIK3CAmut
PIK3CA/AKT1/PTEN mut
ESR1mut
Alpelisib + Fulvestrant
SOLAR-1
Capivasertib + Fulvestrant
CAPItello-291
Elacestrant
EMERALD
Everolimus + Giredestrant
evERA BC
Vepdegestrant
VERITAC-2
Imlunestrant +/- Abemaciclib
EMBER-3

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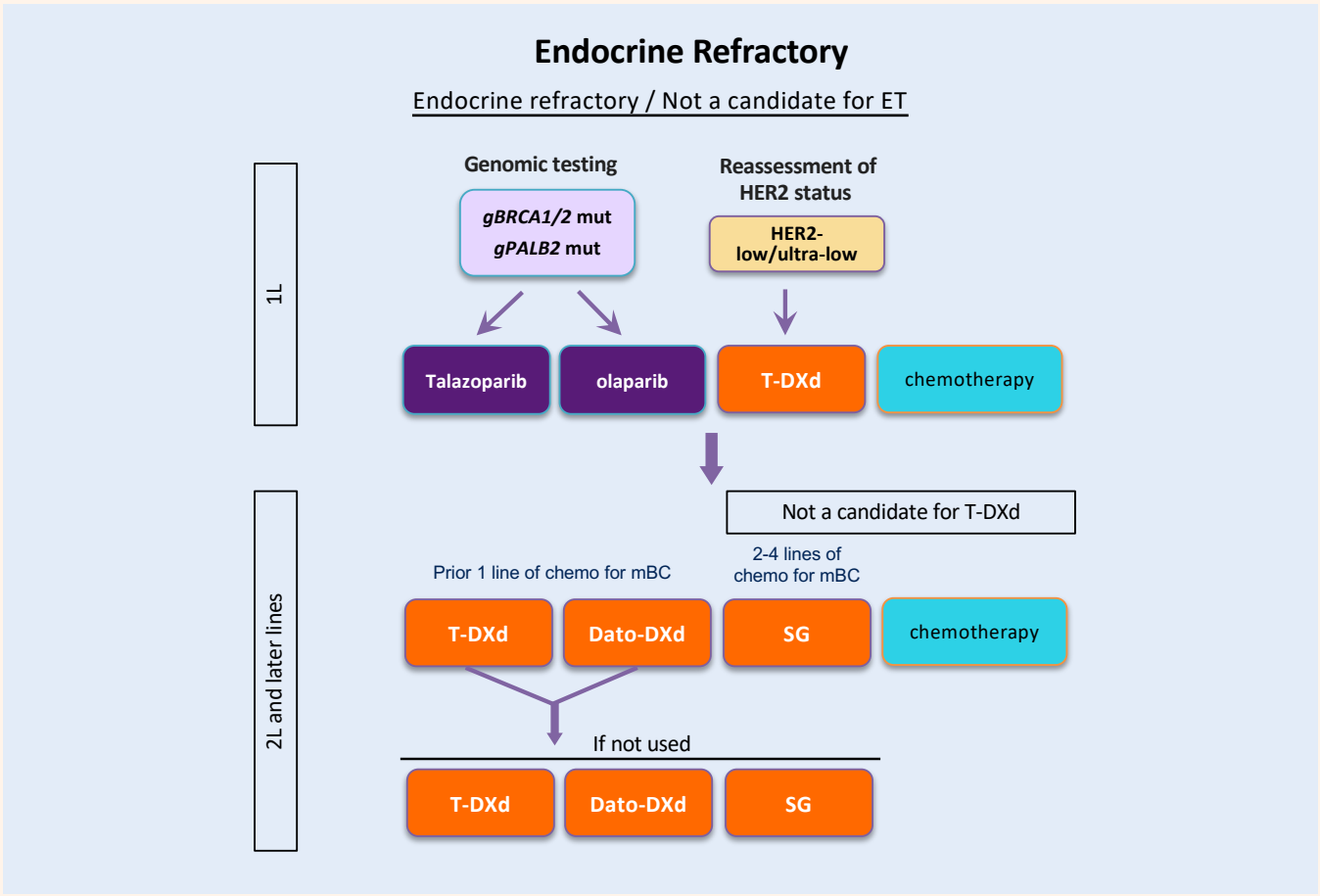
Investigational therapy | Biomarker-guided therapy | ADC | PARPi



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THANK YOU

主編-----台灣乳房醫學會