Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress

CDK4/6 Inhibitors in the Management of HR-Positive Breast Cancer

Saturday, May 16, 2026

6:00 AM – 7:30 AM

Faculty

Kelly Fischer, MSN, FNP-BC
Marissa Marti-Smith, DNP, APRN, AGNP-C, AOCNP
Ruth M O'Regan, MD

Moderator

Rita Nanda, MD

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Ms Fischer — Disclosures

No relevant financial relationships to disclose.

Ms Marti-Smith — Disclosures

Consulting Agreements	Amplity
Speakers Bureaus	AstraZeneca Pharmaceuticals LP, Biotheranostics Inc, A Hologic Company, Daiichi Sankyo Inc, Stemline Therapeutics Inc
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Dr O’Regan — Disclosures

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Consulting Agreements	Biotheranostics Inc, A Hologic Company, Gilead Sciences Inc, Lilly, Puma Biotechnology Inc, Regor Pharmaceuticals
Contracted Research	Novartis, Puma Biotechnology Inc
Data and Safety Monitoring Boards/Committees	Gilead Sciences Inc

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Dr Nanda — Disclosures

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Contracted Research	Arvinas, AstraZeneca Pharmaceuticals LP, Corcept Therapeutics Inc, Genentech, a member of the Roche Group, Gilead Sciences Inc, Jazz Pharmaceuticals Inc, Mabwell Therapeutics Inc, Merck, Pfizer Inc, Relay Therapeutics

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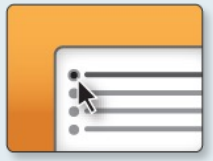
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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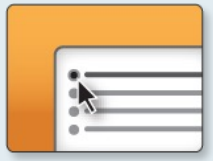
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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RTP RESEARCH TO PRACTICE ONCOLOGY NURSING UPDATE WITH NEIL LOVE, MD

NONMELANOMA SKIN CANCERS
Check out our recent program with Dr Nikhil I Khushalni from Moffitt Cancer Center in Tampa, Florida. Published May 7, 2026.

Overview of nonmelanoma skin cancers (12 min)

Systemic therapy for nonmelanoma skin cancers (8 min)

Immune checkpoint inhibitors for special patient populations (12 min)

Hedgehog inhibitors for basal cell carcinoma (6 min)

New developments in therapy for nonmelanoma skin cancers (5 min)

CASE: A man in his early 70s with cutaneous squamous cell carcinoma receives cemiplimab (8 min)

CASE: A man in his mid 70s with a history of basal cell carcinoma presents with disease of the ocular surface and receives immunotherapy (6 min)

CASE: A man in his early 70s with recurrent metastatic basal cell carcinoma receives vismodegib followed by cemiplimab on disease progression (6 min)

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Feedback (Please!)

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“Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse”
Eighteenth Annual RTP-ONS NCPD Symposium Series

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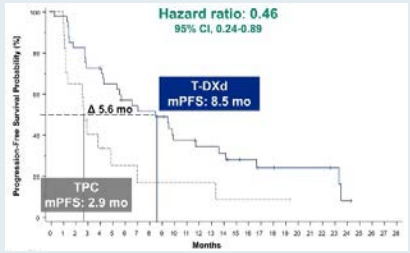
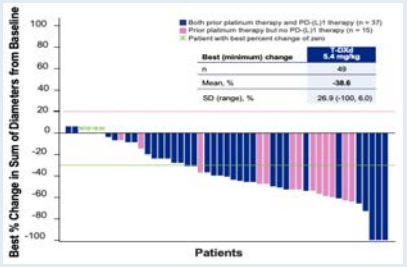
Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

New Agents, Therapies and Regimens

- When should it be used, for whom and why?
- How to prevent and manage side effects: dose holds and reductions
  - Kaplan Meier curves — HR and absolute benefit



  - Waterfall plots



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Agenda

Introduction: Advent of CDK4/6 Inhibitors in HR-Positive Breast Cancer (BC)

Module 1: Risk Assessment for Patients with HR-Positive, HER2-Negative Localized BC

Module 2: Adjuvant CDK4/6 Inhibitor Therapy

Module 3: Practical Considerations with CDK4/6 Inhibitors

Module 4: Monitoring and Management of Cytopenias

Module 5: CDK4/6 Inhibitors in HR-Positive Metastatic BC

Module 6: Management of Gastrointestinal Adverse Events

Module 7: CDK4/6 Inhibitors in Unique Populations

Module 8: Rarer CDK4/6 Inhibitor-Associated Toxicities

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The Advent of CDK 4/6 Inhibitors

- **Before 2015, aromatase inhibitors, fulvestrant, tamoxifen, and everolimus were the only endocrine options we had for treating HR+ breast cancer**
- **After that, patients had to move on to capecitabine and then to IV chemotherapies, making prognosis and quality of life quite limited**
- **In 2015, palbociclib, the first CDK 4/6 inhibitor, was approved**
- **In 2018, ribociclib and abemaciclib followed**
- **These drugs very quickly changed the landscape for patients with metastatic HR+ breast cancer**

Courtesy of Jane Lowe Meisel, MD

J Clin Oncol 42, 994-1000(2024). npj Breast Cancer volume 8, Article number: 114 (2022)

CDK 4/6 Inhibitors in High-Risk Early-Stage Disease

- **A decade ago, CDK 4/6 inhibitors revolutionized the care of women with stage IV HR+ breast cancer and became a mainstay of first-line treatment**
- **As history has shown, the next step for many drugs that do well in the metastatic setting (especially if well tolerated) is to study them upfront**
- **Can we cure more high-risk patients with early-stage disease if we use these newer agents in the adjuvant setting?**

Courtesy of Jane Lowe Meisel, MD

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AT THE FOREFRONT
UChicago Medicine

Risk Assessment for Patients with HR+/HER2- Early Breast Cancer (BC): Rationale for CDK4/6 Inhibitors in Those at High Risk for Recurrence

Rita Nanda, M.D.

RTP Satellite Symposium at ONS

May 16, 2026

Clinicopathologic Factors Impacting Risk of Recurrence in HR+/HER2- Early-Stage Breast Cancer

- Size, node status, grade/Ki-67, ER/PR expression level, LVI
- Genomic assay results
  - Oncotype Dx, MammaPrint, Breast Cancer Index
- Response to NAT
- Age, menopausal status
- Type of treatment
  - +/-chemo, AI vs tam, +/- OS, 5yrs vs extended, +/-CDK4/6i
- Duration of ET
  - 5 yrs vs extended
- Adherence to ET
  - Up to 40% non-adherent; higher rates in young women and Black women

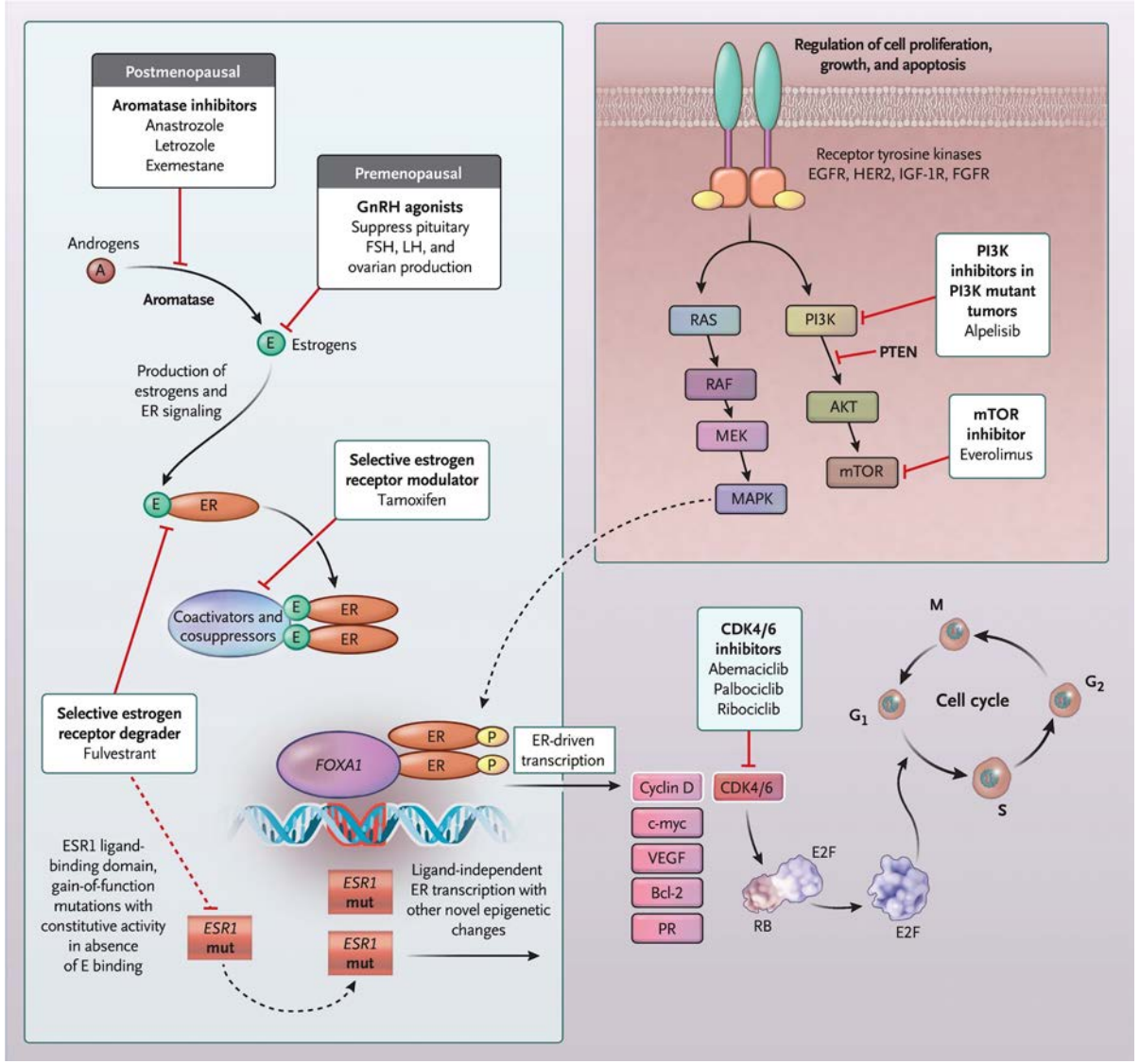
Summary of Longterm Outcomes by Treatment

Population	Treatment	Key Outcome	References
T1N0 (EBCTCG)	5 yr ET	20-yr distant recurrence: ~13%	Pan et al, NEJM 2017
T2N4–9 (EBCTCG)	5 yr ET	20-yr distant recurrence: ~41%	
Node-negative, RS 0–10	ET alone	12-yr distant recurrence-free: **93.2%**	Sparano et al, NEJM 2024
Node-negative, RS 11–25	ET alone vs. Chemo+ET	1% difference at 12 yr (all endpoints)	
Node-negative, RS 26–100	Chemo+ET	5-yr freedom from distant recurrence: **93%**	Sparano et al, JAMA Onc 2020
Premenopausal (SOFT)	Exemestane + OFS	15-yr DFS: 73.5%	Francis et al, JCO 2025
	Tamoxifen alone	15-yr DFS: 67.0%	

Mechanism of Action of CDK4/6 Inhibitors and Rationale for Adding CDK4/6i to ET

- Estrogen → turns the ignition key (cyclin D1) → starts the engine (CDK4/6) → releases the brake (Rb) → cell divides
- Cancer cells can develop resistance to ET by making more cyclin D1

- ET turns off the fuel supply (estrogen/ER → cyclin D1)
- CDK4/6 inhibitors shut down the engine (CDK4/6 → Rb)



Burstein et al, NEJM 2020

Adjuvant CDK4/6 Inhibitors

Trial	monarchE	NATALEE
Drug	**Abemaciclib**	**Ribociclib**
Schedule	150 mg PO BID continuously	400 mg PO QD, 3 on /1 off
Duration of CDK4/6i	**2 years**	**3 years**
Endocrine Partner	Tamoxifen or AI	NSAI + OS (in premen/men)
N (randomized)	5,637	5,101
Eligible Population	≥4+ LN 1-3+LN and gr 3 or T ≥5 cm 1-3+ LN and Ki-67 ≥20%	stage IIA (**high-risk N0** or N1) IIB III
Chemotherapy	~58% received (neo)adjuvant chemo	~58% received (neo)adjuvant chemo
Median Follow-Up	76.2 months (~6.4 years)	55.4 months (~4.6 years)
Primary Endpoint	iDFS	iDFS
iDFS HR (latest)	0.734 (95% CI 0.657–0.820)	0.716 (95% CI 0.618–0.829)
Absolute iDFS Benefit	**6.5% at 7 years** (77.4% vs 70.9%)	**4.5% at 5 years** (86.1% vs 81.6%)
DRFS / DDFS HR	DRFS: 0.746 (95% CI 0.662–0.840)	DDFS: 0.72 (95% CI 0.60–0.85) at 4 yr
Overall Survival HR	**0.842** (95% CI 0.722–0.981; P = 0.027) **significant**	**0.800** (95% CI 0.637–1.003; P = 0.026) **not yet significant**
OS Absolute Benefit	1.8% at 7 years (86.8% vs 85.0%)	Trend favoring ribociclib; data immature

Johnston et al, Annals of Oncology 2026; Crown et al, ESMO Open 2025.

Case Presentation

Case Presentation: EBC

- 35 yo premenopausal woman presents with palpable right breast mass
- Imaging reveals a 2.5 cm breast mass with 2 suspicious LNs
- Bx of mass and LN reveal grade 3, IDC, which is ER/PR+, HER2-, Ki-67 of 25%
- MammaPrint testing is performed and she is found to have MP-high risk disease; germline genetic testing is negative for gBRCA
- She receives NACT with T-AC
- Has lumpectomy and TAD, pathology reveals residual disease in breast and axilla; RCB II
- She undergoes adjuvant radiation therapy

Case Presentation: EBC

After completion of NACT, surgery, and radiation, she presents for discussion of adjuvant ET. What would you recommend:

1. Tamoxifen
2. Tamoxifen + Ovarian Suppression
3. Aromatase Inhibitor + Ovarian Suppression
4. Aromatase Inhibitor + Ovarian Suppression + CDK4/6 Inhibitor

Discussion Questions

Are you offering an adjuvant CDK4/6 inhibitor to all of your patients with high-risk, HR-positive, HER2-negative early BC who would have met the enrollment criteria for monarchE or NATALEE? When do you not do so?

Would you consider an adjuvant CDK4/6 inhibitor for any patients who would NOT have been eligible for the pivotal studies?

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Role of Adjuvant CDK4/6 Inhibitor Therapy in High-Risk, HR-Positive, HER2-Negative Early BC

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Chair, Department of Medicine
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Physician-in-Chief
Strong Memorial Hospital
Associate Director of Education and Mentoring
Wilmot Cancer Institute
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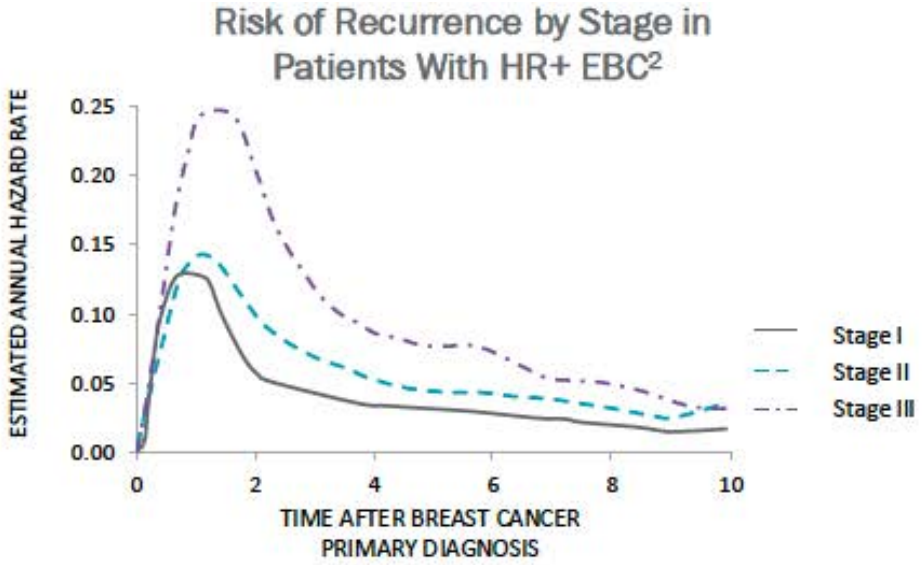
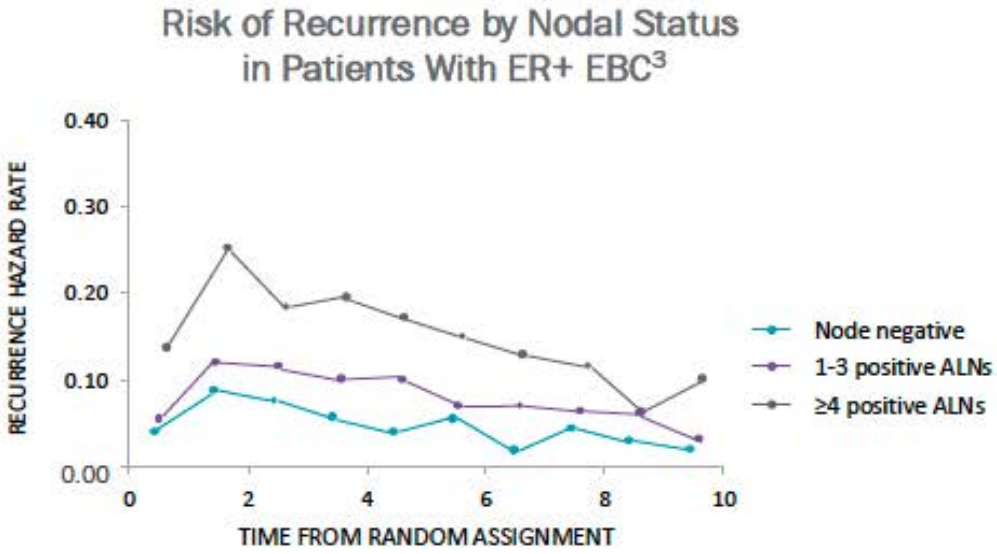
Case history

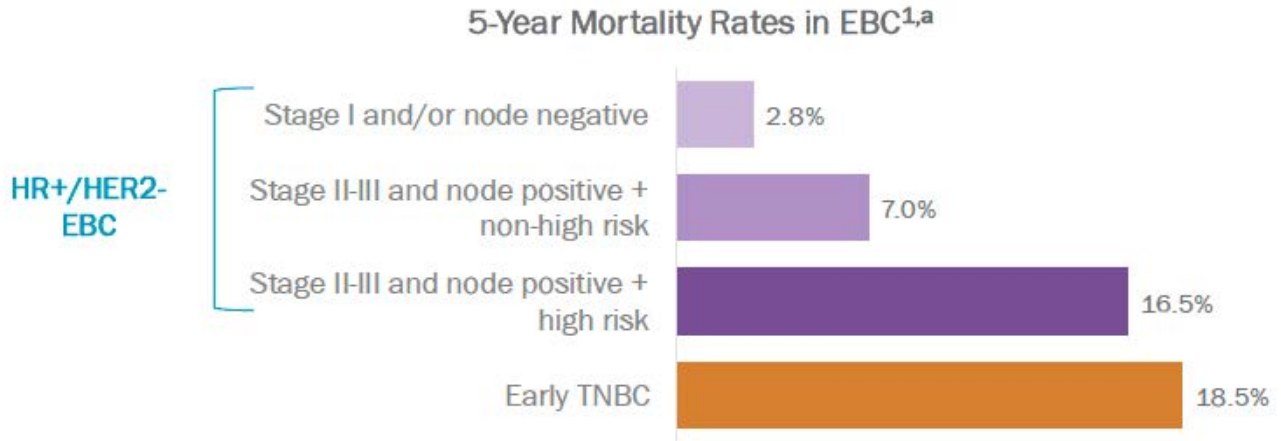
- 58-year-old postmenopausal female presents with a right breast mass
- Biopsy: Invasive ductal cancer, grade 3, ER 80%, PR 50%, HER2 IHC 0, Ki67 25% with involved axillary node
- Clinical stage cT2, cN1
- Received neo-adjuvant chemotherapy
- Undergoes mastectomy with residual disease ypT2 (3mm), ypN1 (2-positive nodes)
- Completes radiation and aromatase inhibitor planned

Recurrence rates for early hormone receptor (HR)-positive breast cancer





Almost 30% of patients with, node-positive, HR-positive breast cancer will experience disease recurrence or death within 5-years of diagnosis



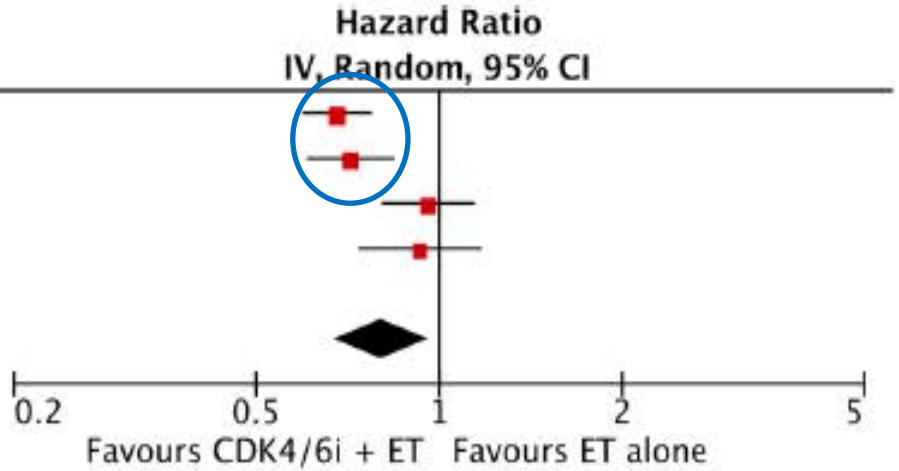
Cheng et al Cancer Epidemiol Biomarkers 2012, Colleoni et al J Clin Oncol 2016, Nelson et al Plos One 2022

Meta-analysis of CDKi adjuvant trials

CDKis improve invasive disease-free survival

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
monarchE	-0.38566248	0.06472524	28.0%	0.68 [0.60, 0.77]
NATALEE	-0.33547274	0.08203664	25.8%	0.72 [0.61, 0.84]
PALLAS	-0.04082199	0.08718094	25.1%	0.96 [0.81, 1.14]
PENELOPE-B	-0.07257069	0.1168645	21.1%	0.93 [0.74, 1.17]
Total (95% CI)			**100.0%**	**0.80 [0.67, 0.96]**

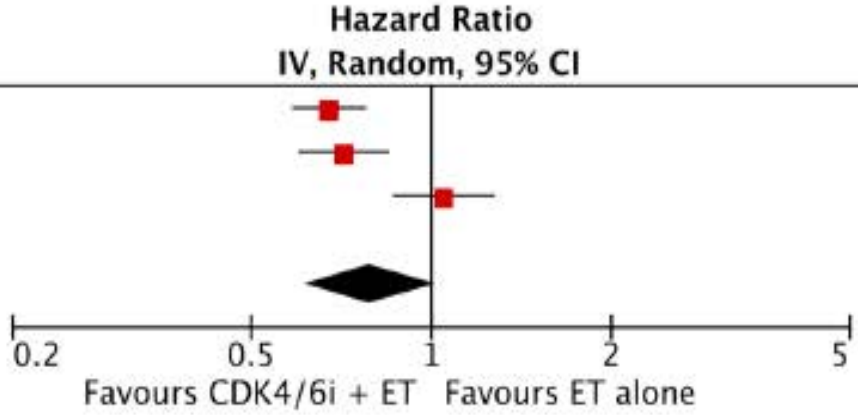
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 13.51$, df = 3 (P = 0.004); $I^2 = 78\%$
Test for overall effect: Z = 2.43 (P = 0.01)



CDKis improve distant disease-free survival

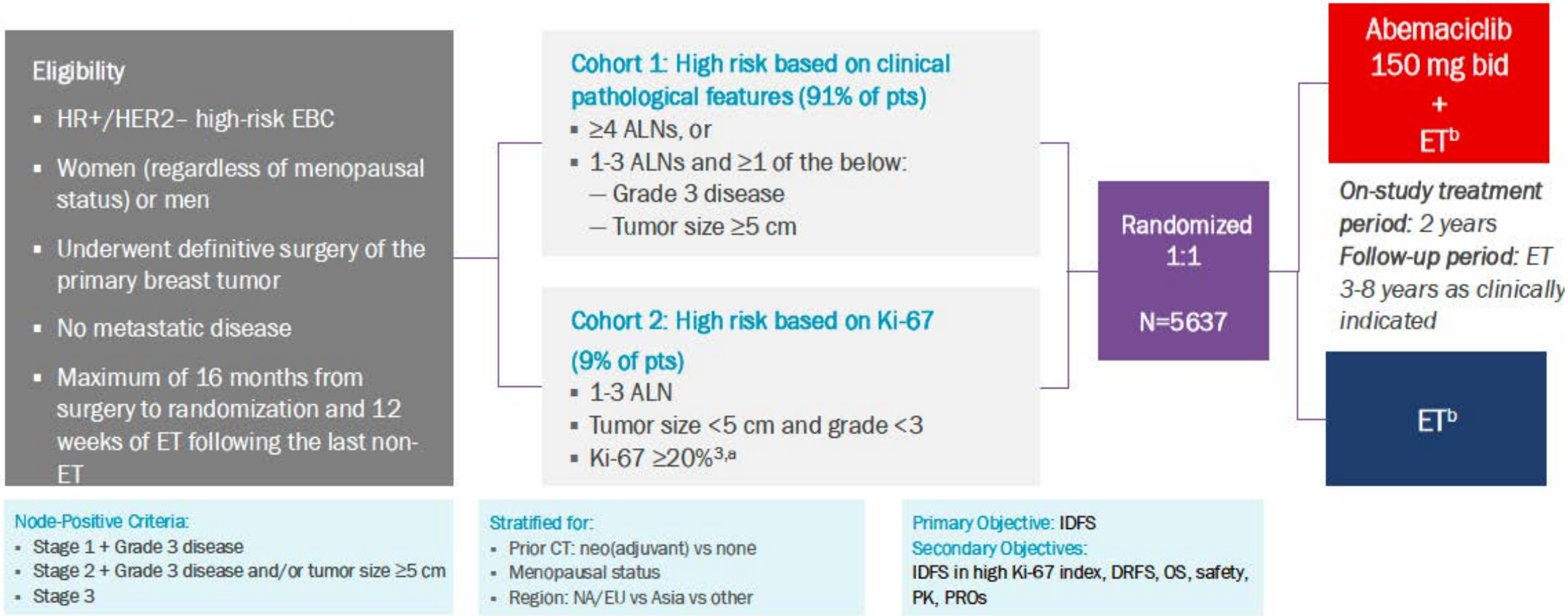
Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
monarchE	-0.39304259	0.0701135	35.0%	0.68 [0.59, 0.77]
NATALEE	-0.33547274	0.08625676	33.2%	0.72 [0.60, 0.85]
PALLAS	0.04879016	0.09850055	31.8%	1.05 [0.87, 1.27]
Total (95% CI)			**100.0%**	**0.79 [0.61, 1.02]**

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 14.13$, df = 2 (P = 0.0009); $I^2 = 86\%$
Test for overall effect: Z = 1.80 (P = 0.07)



Alexiou et al Cancers 2025

MonarchE: Study design

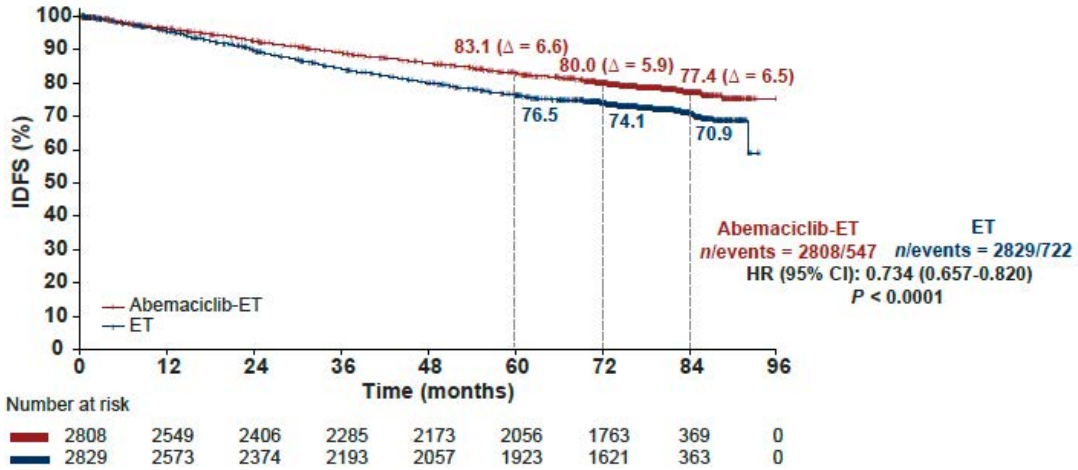


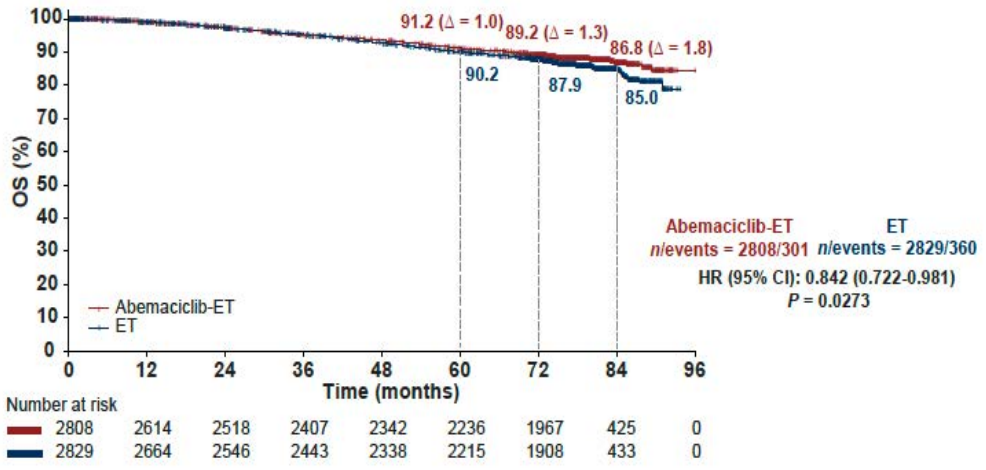
All patients had node-positive, HR-positive breast cancer
Abemaciclib given continuously twice daily for 2-years

https://clinicaltrials.gov/study/NCT03155997

MonarchE: Outcomes at 7 years

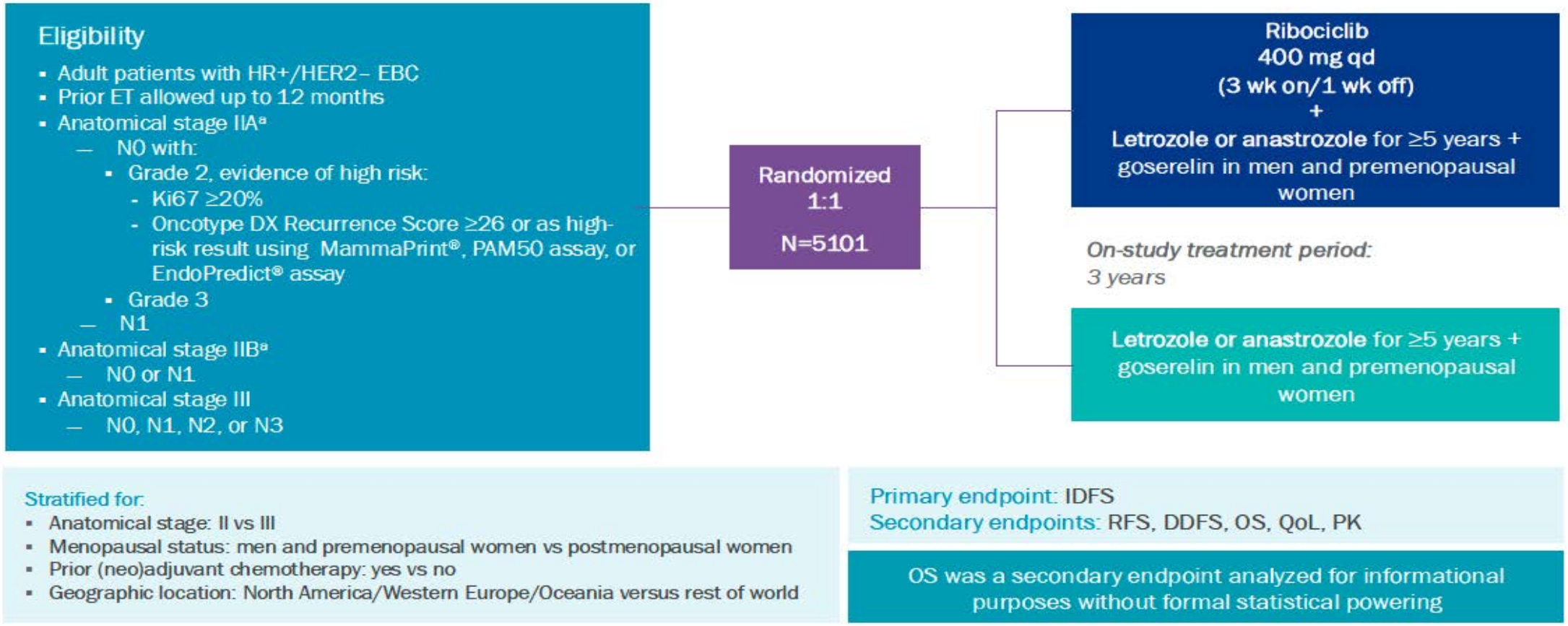
	ABEMA + ET	ET	Difference	P value
Invasive DFS	77%	71%	6%	P<.0001
Distant RFS	80%	75%	5%	P<.0001
Overall survival	87%	85%	2%	P=.027
Living with MBC	6%	9%	3%	





Johnston et al Ann Oncol 2025

NATALEE: Study design



Patients had node-positive or high risk node-negative, HR-positive breast cancer

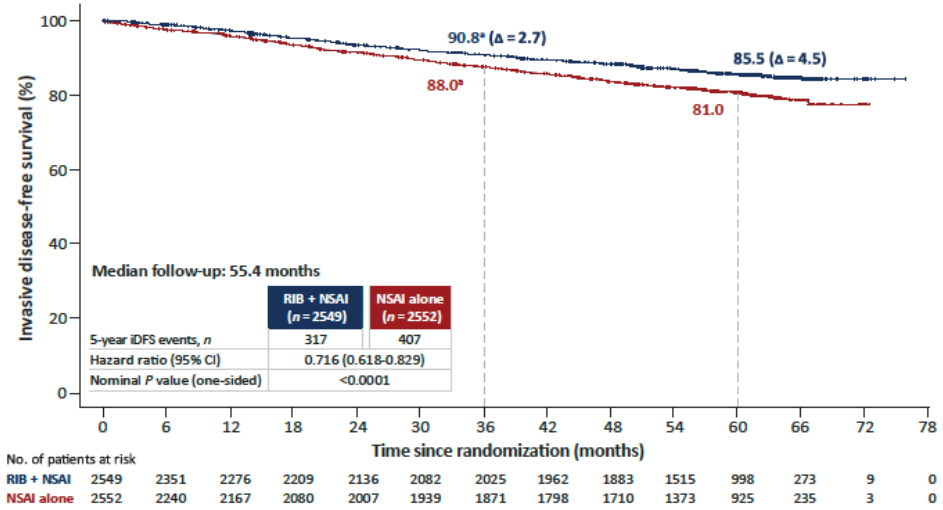
If node-negative had to have T2 with high-risk biology, T3 or T4 disease

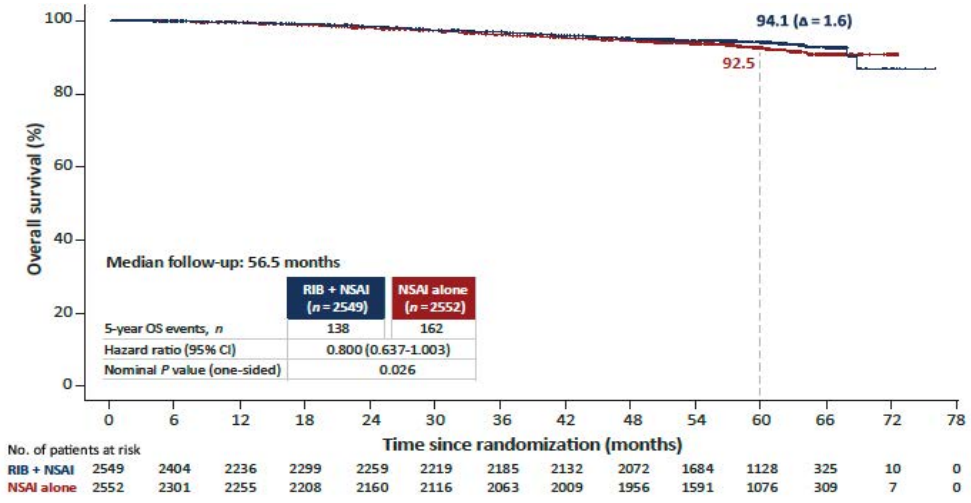
Ribociclib 400mg once daily for 3 out of 4-weeks for 3-years

https://clinicaltrials.gov/study/NCT03701334

NATALEE: Outcomes at 5 years

	RIBO + ET	ET	Difference	P value
Invasive DFS	86%	81%	5%	P<.0001
Distant RFS	88%	84%	4%	P<.0001
Overall survival	94%	93%	1.5%	P=.026





Crown et al Ann Oncol 2025

MonarchE and Natalee: Adverse events

AEs in Either Arm (≥20%), %	Abemaciclib + ET (n=2791)	
	Any Grade	Grade 3/4
Diarrhea[a]	83.6	7.8
Neutropenia	45.9	19.6
Fatigue[b]	40.8	2.9
Leukopenia	37.7	11.4
Abdominal pain[b]	35.7	1.4
Nausea	29.6	0.5
Arthralgia[b]	26.5	0.3
Anemia	24.5	2.1
Hot flush[b]	15.4	0.1

AEs of Special Interest and Clinical Relevance in Either Arm, %	Ribociclib + NSAI (n=2526)	
	Any Grade	Grade ≥3
Neutropenia[a]	62.8	44.4
Febrile neutropenia	0.3	0.3
Arthralgia	38.8	1.0
Liver-related AEs[b]	26.7	8.6
Nausea	23.5	0.2
Headache	22.9	0.4
Fatigue	22.8	0.8
Diarrhea	14.6	0.6
Prolonged QT interval[c]	5.4	1.0
Prolonged ECG QT	4.4	0.2
ILD pneumonitis[d]	1.6	0.0
VTE[e]	1.1	0.6

CDK4/6i	Trial(s)	Dose Reduction Rate Due to AE	Discontinuation Rate Due to AE	Common AEs Associated With Dose Reduction
Abemaciclib	monarchE[1,2]	44%	19%[a]	Diarrhea Neutropenia Fatigue
Ribociclib	NATALEE[3,4]	23%	20%	Neutropenia Neutrophil count decreased

Dose reductions did not impact efficacy

Johnston et al Lancet Onc 2023, Barrios et al ESMO Breast 2024, Goetz et al NPJ Breast Cancer 2024, Hamilton et al SABCS 2024

FDA-approved indications and identification of appropriate candidates

Abemaciclib

- In combination with fulvestrant for women with HR+, HER2- advanced or mBC with disease progression on ET
- As monotherapy for women with HR+, HER2- advanced or mBC with disease progression on ET and prior CT in the metastatic setting

Ribociclib

- In combination with AI as adjuvant therapy in women with HR+, HER2- stage II/III early BC and high risk of recurrence
- For women with HR+, HER2- advanced or mBC with AI as initial ET or fulvestrant as initial ET or ET following disease progression

Abemaciclib PI; Ribociclib PI

Case History

- 58-year-old with stage IIB, node-positive, hormone receptor-positive breast cancer
- Completed neo-adjuvant therapy, surgery and radiation
- Aromatase inhibitor planned
- Meets criteria for both MonarchE and Natalee
- Abemaciclib used for only 2-years but more diarrhea though dose escalation decreases this risk
- Ribociclib given for 3-years with different side-effect profile

Discussion Questions

How are you selecting between abemaciclib and ribociclib in the adjuvant setting? How do their tolerability/toxicity profiles affect your selection between them for individual patients?

Agenda

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Module 7: CDK4/6 Inhibitors in Unique Populations

Module 8: Rarer CDK4/6 Inhibitor-Associated Toxicities

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Practical Considerations with CDK4/6 Inhibitors

Kelly Fischer, MSN, FNP-BC
Family Nurse Practitioner
Dana-Farber Cancer Institute
Boston, Massachusetts

Optimal dosing and dose-adjustment strategies for CDK4/6 inhibitors in patients with localized and metastatic BC

Localized (adjuvant)

- Abemaciclib → 150 mg BID
- Ribociclib → 400 mg once daily x 21 days on, 7 days off

Metastatic

- Abemaciclib → 150 mg BID
- Ribociclib → 600 mg daily x 21 days on, 7 days off
- Palbociclib → 125 mg daily x 21 days on, 7 days off

Fasching PA et al. JAMA Oncol. 2025;11(11):1364–1372.
Johnston SRD et al. J Clin Oncol. 2020 Dec 1;38(34):3987-3998.

Recommended duration of CDK4/6 inhibitor therapy in the adjuvant setting: Abemaciclib and Ribociclib

Monarch-E

- Adjuvant **abemaciclib** for a total of **two years**
- HR-positive, HER2-negative, node positive, high risk early stage disease
- Abemaciclib + endocrine therapy demonstrated superior invasive disease-free survival vs endocrine therapy alone (IDFS rates of 92.2% vs 88.7%)

NATALEE

- Adjuvant **ribociclib** for a total of **three years**
- HR-positive, HER2-negative, stage II or III early breast cancer
- Ribociclib + endocrine therapy demonstrated 3-year iDFS rates of 90.8% vs 88.1%, and 4-year rates of 88.5% vs 83.6%

Fasching PA et al. JAMA Oncol. 2025;11(11):1364–1372.
Johnston SRD et al. J Clin Oncol. 2020 Dec 1;38(34):3987-3998.

Approaches for encouraging and assessing adherence in patients receiving CDK4/6 inhibitor therapy

- Recommend more frequent visits initially to assess side effect profile, tolerability, and lab monitoring
  - Check labs every 2 weeks for the first 2 months on CDK4/6 inhibitor therapy, then space out to monthly thereafter
- Ensure patients are aware of dosing and schedule
  - Palbociclib is taken once daily for 3 weeks on, 1 week off
  - Abemaciclib is taken twice a day
  - Ribociclib is taken once daily for 3 weeks on, 1 week off
- Ensure patients are set up for success at home
  - Loperamide at home to take as needed for diarrhea
  - Antiemetic RX's to take as needed for nausea
- If issues with tolerability, dose reduce/change/discontinue therapy if appropriate

Drug-drug interactions to consider with CDK4/6 inhibitor therapy

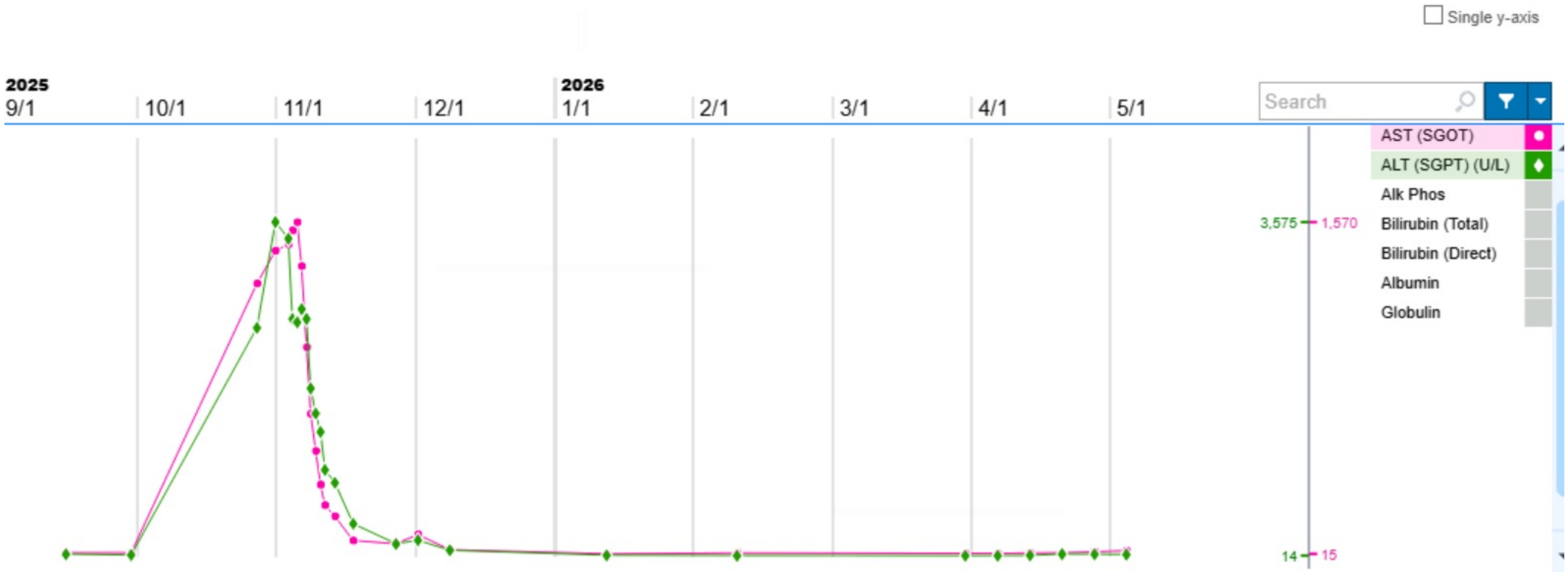
- CDK4/6 inhibitors interact with drugs that are metabolized by the CYP3A4 enzyme pathway
  - Increased toxicity with CYP3A4 inhibitors
  - Reduced efficacy with CYP3A4 inducers
- Strong CYP3A4 inhibitors: clarithromycin (azithromycin may be used in place of clarithromycin), ketoconazole, ritonavir
- Strong CYP3A4 inducers: rifampin, enzalutamide, phenytoin, St. John's wort
- QT-prolonging agents (caution with ribociclib): tricyclic antidepressants, some antipsychotics, amiodarone, moxifloxacin
- Gastric pH-elevating agents (caution with palbociclib): PPIs may reduce palbociclib absorption
- Grapefruit = strong inhibitor of CYP3A4

https://www.uspharmacist.com/article/drug-interactions-associated-with-cdk-4-6-inhibitors

Case Presentation

A 53 y/o female with HR-positive, HER2-negative breast cancer: Adjuvant CDK4/6 inhibitor therapy

- March 2025: Abnormal mammogram leads to biopsy
  - Right breast biopsy → invasive lobular carcinoma, grade 3, ER+, PR+, HER2 neg (0)
- May 2025: Bilateral mastectomy → right breast ILC multifocal, spanning 7.5 cm, + skin invasion into dermis. 1 of 4 SLN with microinvasion of 1.5 mm; 2 with ITCs. Oncotype = 13
- July/August: Radiation therapy
- September 2025: Starts adjuvant letrozole/leuprolide/**ribociclib**
  - Baseline LFTs normal
- October-November 2025: Ribociclib discontinued after LFTs **greater than 2000**. Hospitalized for persistent transaminitis and hyperbilirubinemia. Responded to high dose steroids
- March 2026: Initiates **abemaciclib** at 50 mg daily dose
  - Slowly increased abemaciclib to 100 mg BID over a 2-month period with weekly lab monitoring, LFTs remained normal


Single y-axis
2025
9/1
10/1
11/1
12/1
2026
1/1
2/1
3/1
4/1
5/1
Search
AST (SGOT)
ALT (SGPT) (U/L)
Alk Phos
Bilirubin (Total)
Bilirubin (Direct)
Albumin
Globulin
3,575
1,570
14
15

All Rows

Search

LIVER FUNCTION TES...

	2025 11/7/25 09:14	11/6/25 07:18	11/5/25 08:46	11/4/25 07:45	11/3/25 10:44	10/31/25 15:27	10/27/25 12:41	9/29/25 12:32	9/15/25 10:28
AST (SGOT)	983 ▲	1,364 ▲	1,570 ▲	1,531 ▲	1,466 ▲	1,436 ▲	1,282 ▲	20	20
ALT (SGPT) (U/L)	2,543 ▲	2,647 ▲	2,506 ▲	2,540 ▲	3,399 ▲	3,575 ▲	2,446 ▲	21	31
Alk Phos	384 ▲	316 ▲	322 ▲	306 ▲	352 ▲	331 ▲	224 ▲	88	101
Bilirubin (Total)	7.6 ▲	5.4 ▲	4.8 ▲	4.0 ▲	3.0 ▲	1.3 ▲	0.5	0.2	0.4
Bilirubin (Direct)	5.4 ▲	4.1 ▲	3.6 ▲	2.9 ▲					
Albumin	3.8	3.3 ▼	3.5	3.5	3.9	4.6	4.4	4.4	4.5
Globulin	3.2	2.6	2.8	2.7	3.2	3.1	3.2	3.0	3.1

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TEXAS ONCOLOGY

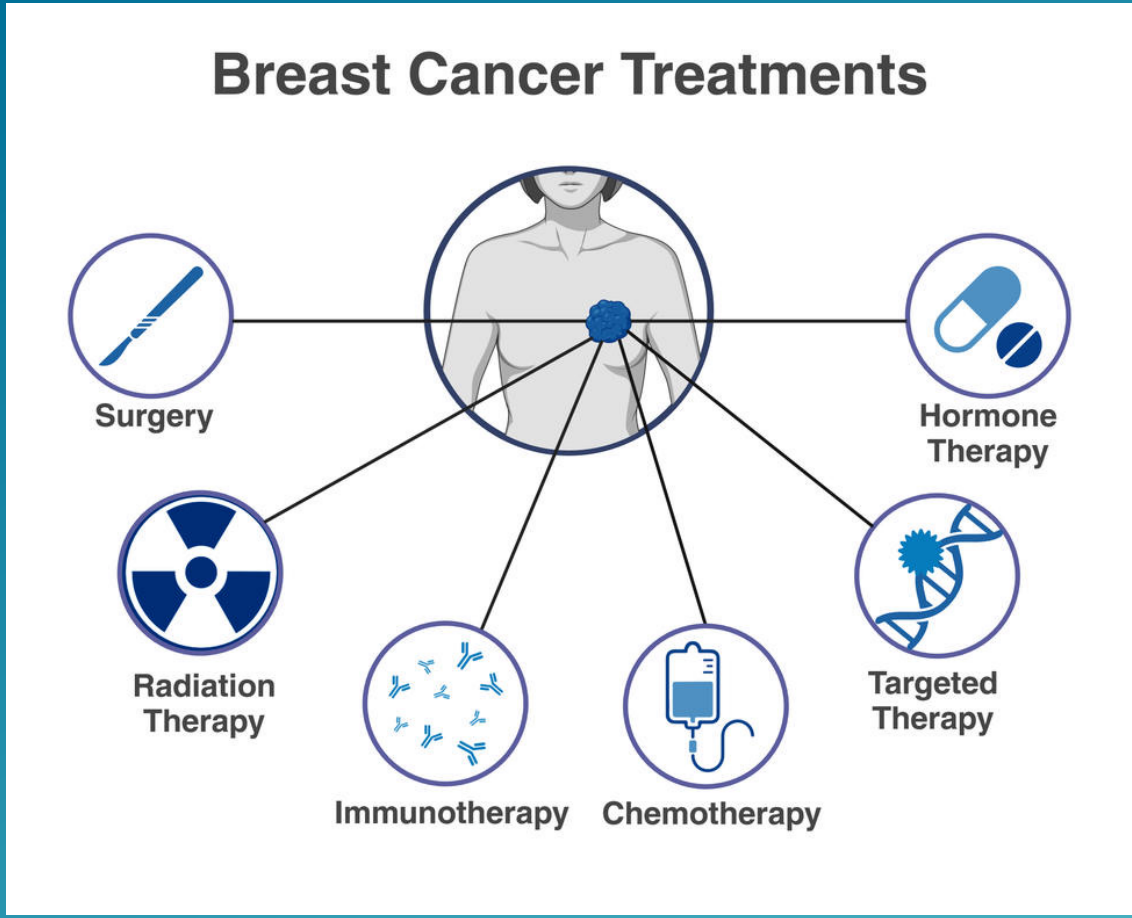
Cytopenias Associated with CDK4/6 Inhibitors

Marissa Marti-Smith
DNP, APRN, AGNP-C, AOCNP

Clinical Overview & Toxicities

- CDK4/6 inhibitors (Palbociclib, Ribociclib, Abemaciclib) have revolutionized the treatment landscape for HR+/HER2– breast cancer.

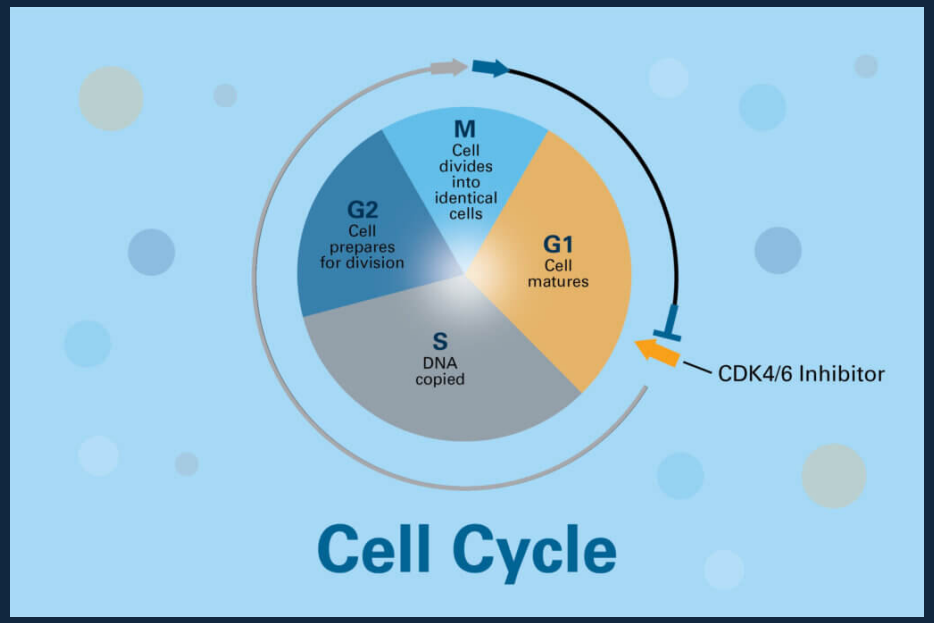
- FOCUS:
  - Frequency & severity of hematologic toxicities
  - Routine lab monitoring
  - Nursing management
  - Dose modification strategies



CDK 4/6 Inhibitor Mechanism

Palbociclib, Ribociclib, & Abemaciclib

in combo w/ endocrine therapy



Cell cycle arrest

Bone marrow suppression

Photo https://blog.dana-farber.org/insight/2018/02/cdk46-inhibitors-stop-breast-cancer-growth/

Incidence of Grade 3-4 Neutropenia

- **Palbociclib & Ribociclib:**
- 75% to 80% of patients
- **Grade 3/4 >50% of patients**

- **Abemaciclib :**
- 46% of patients
- **Grade 3/4 – 19.6%** in MonarchE trial

- Anemia (grade 1-2) and Thrombocytopenia – less frequent with all agents

- Freq grade 3/4 neutropenia
  - decreases with extended therapy, cumulative toxicity is unlikely and that dose adjustments adequately treat neutropenia

(Anders et al., 2020) (

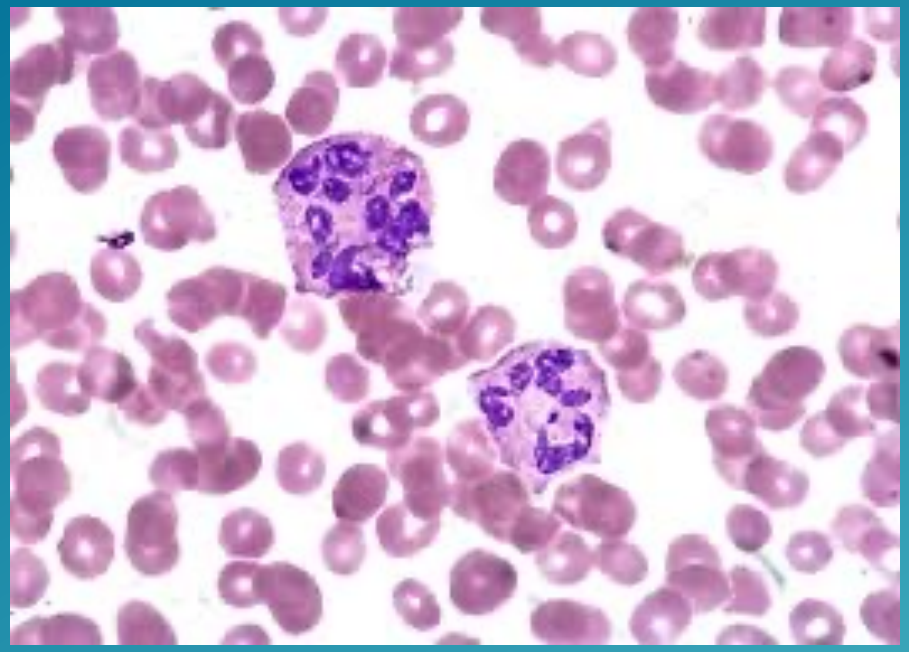
Predictability & Reversibility

Key Clinical Insights for Nursing Assessment:

- *Predictable:*
Typically occurs during the first 1-2 cycles of treatment.

- *Reversible:*
Neutrophil counts recover rapidly (median 7 days) upon treatment interruption.

- *Safety:*
Febrile neutropenia is exceptionally rare (incidence <2.5%).



Spring et al. (2020)

Monitoring Protocols

CBC prior to initiating therapy

1st 2 cycles

CBC q2 weeks

Future
Monitor monthly (C3+)

Adjust frequency if Grade 3 or 4 toxicity observed

ASCO (2023). Breast Cancer Management Guidelines: Practical Management of Targeted Therapy.

Change in Common Terminology Criteria for Adverse Events

Comparison of CTCAE v5 and CTCAE v6 neutrophil count grading criteria.

	CTCAE v5 (2017)	CTCAE v6 (2025)
Grade 1	LLN–1500/μL	<1500–1000/μL
Grade 2	<1500–1000/μL	<1000–500/μL
Grade 3	<1000–500/μL	<500–100/μL
Grade 4	<500/μL	<100/μL

(Merz, 2025)

Interruption vs. Discontinuation

1,000

ANC Threshold for resumption

Resumption criteria:

- Interrupt therapy for persistent Grade 3 or any Grade 4 cytopenia
- Resume only after recovery to Grade 2 (ANC>= 1000)
- Permanent dose reduction is preferred over growth factor support for chronic issues.

Supportive Care Considerations

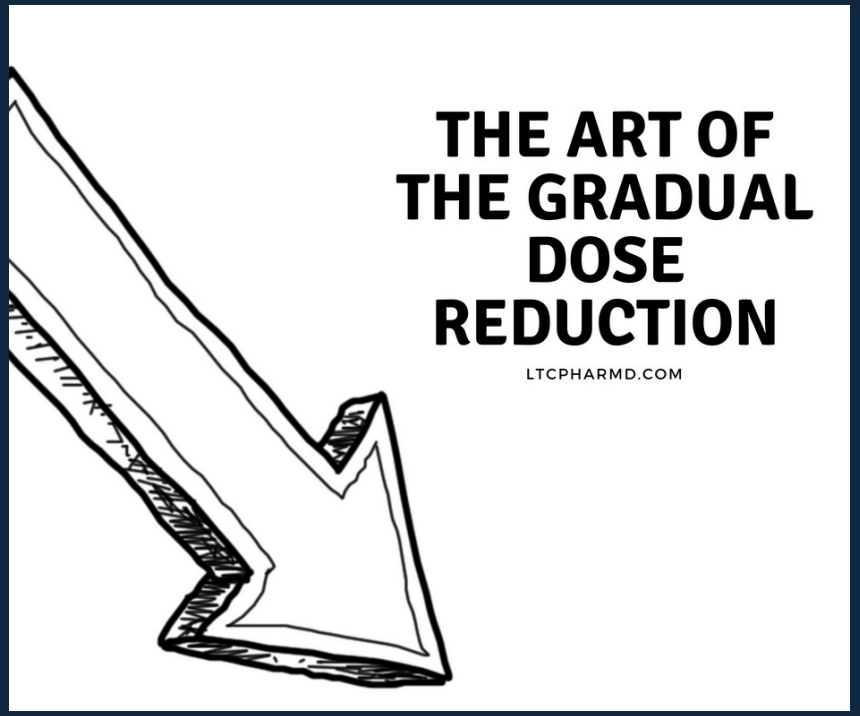
G-CSF: Rarely indicated

Infrequently associated with febrile neutropenia and responds rapidly to drug withdrawal

Anemia management: if symptomatic may require iron / blood transfusion

Gold standard ›››››››

Dose interruption & modification if needed



Case Presentation

Case Study

- 51 yo female
- T2 pN1a , left lumpectomy
- Adjuvant AC, weekly paclitaxel, followed by XRT
- Tamoxifen initially, leuprolide + AI, zoledronic acid IV 2x year
- Ins denied Ribociclib, given Abemaciclib 150mg PO BID

- Hx depression, controlled.
- Moved prior to initiating this CDK4/6 therapy

Management & Takeaway

- Q2 week lab checks x 2 months
- Diarrhea f/u

- At 2 week check, leukopenia WBC 3.8, but **ANC 0.4**
- Oral antibx while neutropenic
- Neutropenic precautions

- HELD x1 week till ANC >1
- Dose reduced to 100mg PO BID

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AT THE FOREFRONT
UChicago Medicine

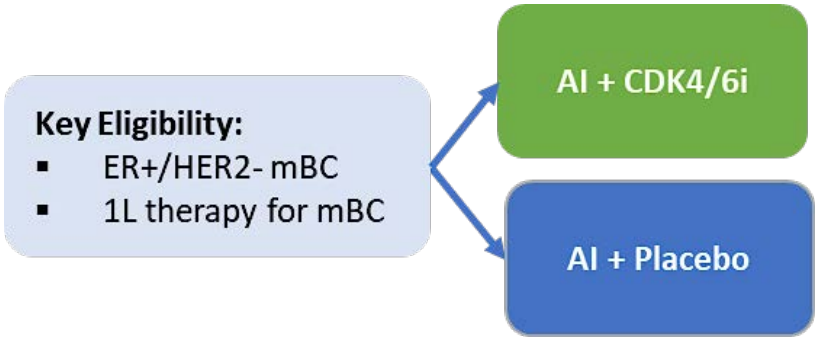
CDK4/6 Inhibitors in HR+/HER2 Metastatic BC (MBC)

Rita Nanda, M.D.

May 16, 2026

RTP Satellite Symposium at ONS
San Antonio, TX

HR+ MBC: Frontline Therapy with AI +/- CDK4/6i

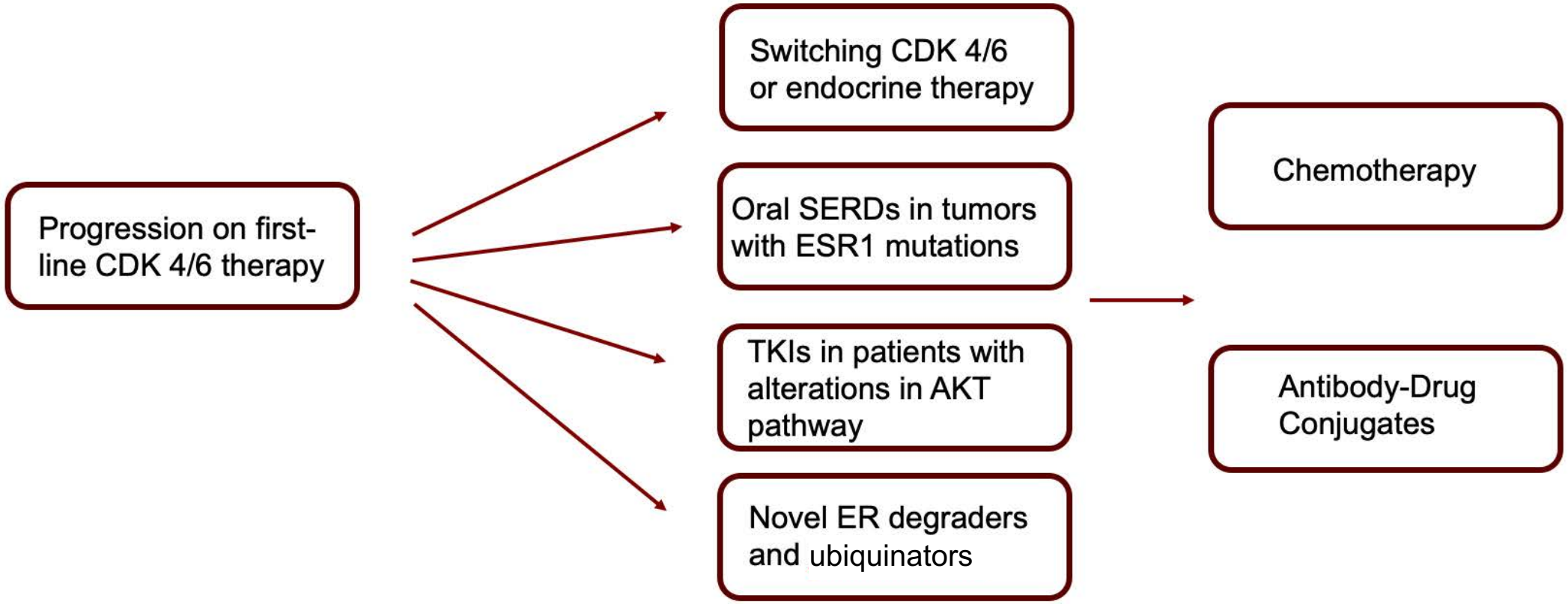


	PALOMA-2 N=666	MONALEESA-2 N=668	MONARCH-3 N=493
Endocrine Therapy	Letrozole	Letrozole	Letrozole or anastrozole
CDK4/i	Palbociclib	Ribociclib	Abemaciclib
Patients (n)	666	668	493
PFS Hazard Ratio	0.58**	0.56**	0.54**
PFS (months)	24.8 vs 14.5	25.3 vs 16	29 vs 14.8
OS Hazard Ratio	0.96	0.76**	0.80
OS (months)	53.9 vs 51.2	63.9 vs 51.4	66.8 vs 53.7

** statistically signficant

Finn NEJM 2016; Hortobagyi NEJM 2016; Goetz J Clin Oncol 2017; Finn, ASCO 2022; Hortobagyi NEJM 2022; Goetz SABCS 2023; GS01-12

Treatment in Second Line Setting After Progression on CDK4/6 Inhibition



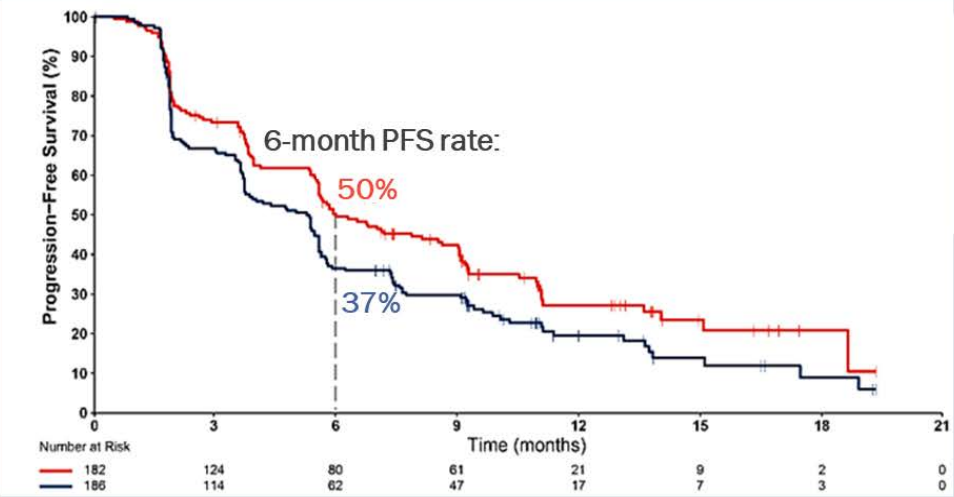
CDK4/6i post Progression on CDK4/6i: The postMONARCH Randomized Phase 3 Trial

Key Eligibility:
- ER+/HER2- aBC
- ABC: PD on 1L AI+CDK4/6i
- Adj: PD on/post ET+CDK4/6i
- No other Tx for ABC

→ Abema + Fulv

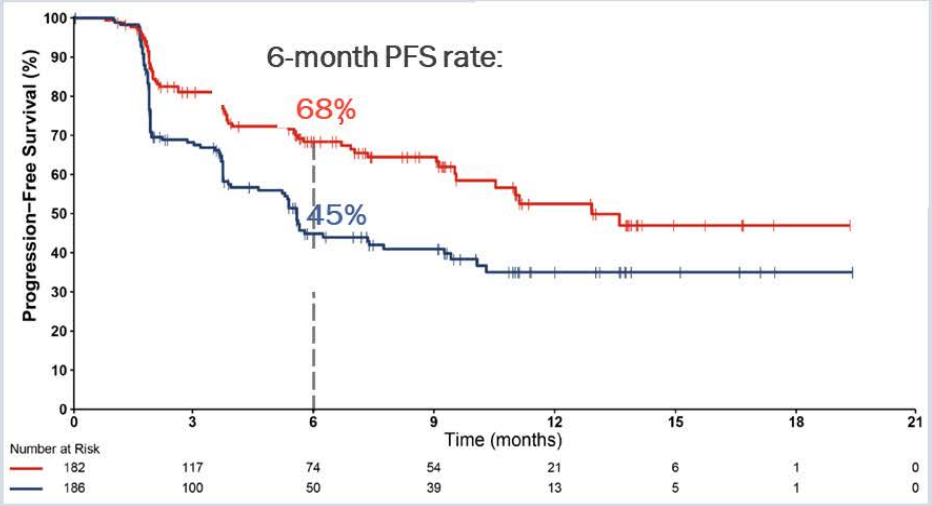
→ Placebo + Fulv

Primary Analysis: PFS by INV



PFS by INV	Abemaciclib + Fulv (n=182)	Placebo + Fulv (n=186)
No. events	117	141
Median PFS (95% CI), months	6.0 (5.6-8.6)	5.3 (3.7-5.6)
HR (95% CI)	0.73 (0.57-0.95)	
P value	0.017	

Key Secondary Endpoint: PFS by BICR



PFS by BICR	Abemaciclib + Fulv (n=182)	Placebo + Fulv (n=186)
Events	60	92
Median PFS (95% CI), mo	12.9 (9.5-NR)	5.6 (3.9-7.7)
HR (95% CI)	0.55 (0.39-0.77)	
P value	< .001	

Kalinsky et al, JCO 2025

CDK4/6i After Progression on First-Line CDK4/6i

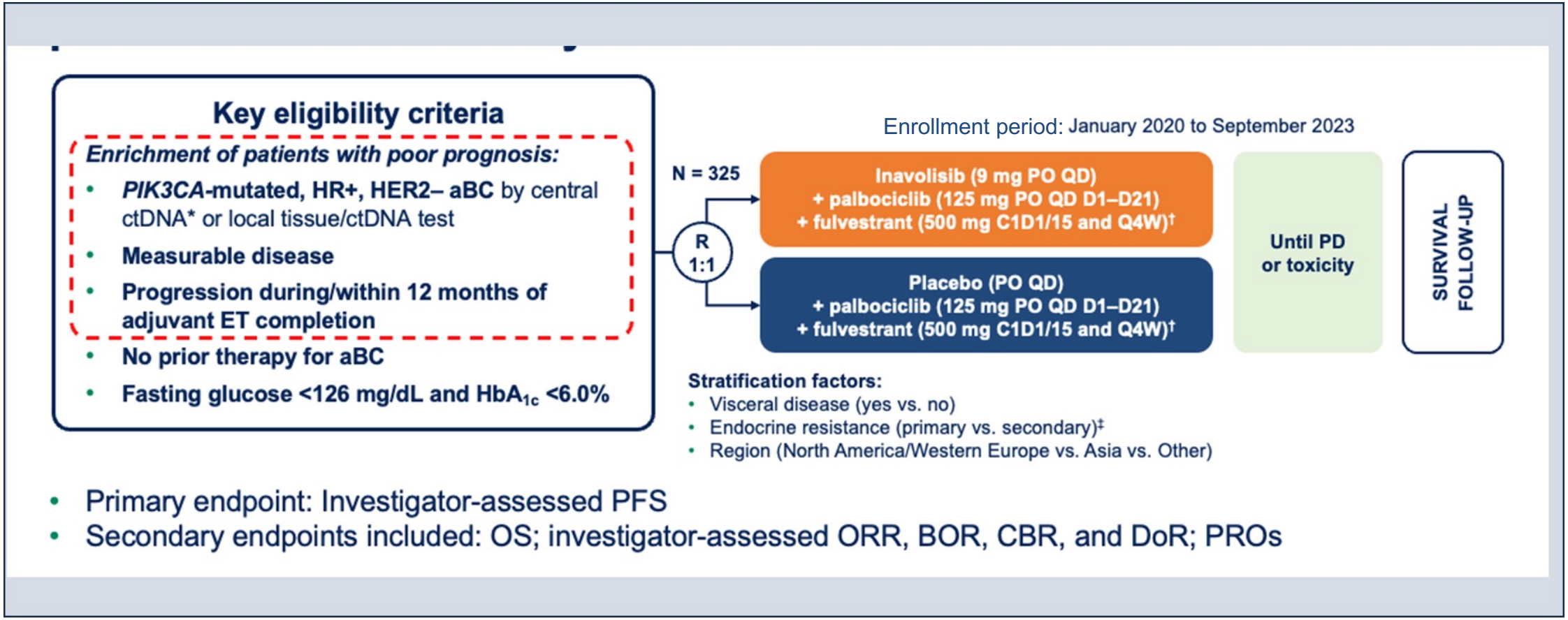
	POSTMONARCH[1]	MAINTAIN[2]	PACE[3]	PALMIRA[4]
Patients, n	368	120	166	198
1L CDK4/6i	Palbociclib (59%) Ribociclib (34%)	Palbociclib (84%)	Palbociclib (90%)	Palbociclib (100%)
1L CDK4/6i >12 mo	~71%	67%	75%	86%
Endocrine therapy	Fulv (100%)	Fulv (83%) or Exem	Fulv (100%)	Fulv (90%) or Let
"Continuation" CDK4/6i	Abemaciclib	Ribociclib	Palbociclib	Palbociclib
PFS ET only, mo	5.3 (5.6 BICR*)	2.8	4.8	3.6
PFS fulvestrant + CDK4/6i, mo	6.0 INV (12.9 BICR*)	5.3	4.6	4.9

Caveats regarding cross-trial comparisons: different studies, designs, populations, prior therapy, and subgroup definitions

* secondary endpoint

1.Kalinsky K, et al. ASCO 2024. LBA1001. 2. Kalinsky K et al. J Clin Oncol. 2023;41:4004-4013. 3. Mayer EL et al. SABCS 2022. Abstract GS3-06.
4. Llombart-Cussac A et al. ASCO 2023. Abstract 1001.

INAVO120: Palbo + Fulvestrant +/- Inavolisib in Patients with PIK3CAm progressing ≤ 12 mos of completing adjuvant ET



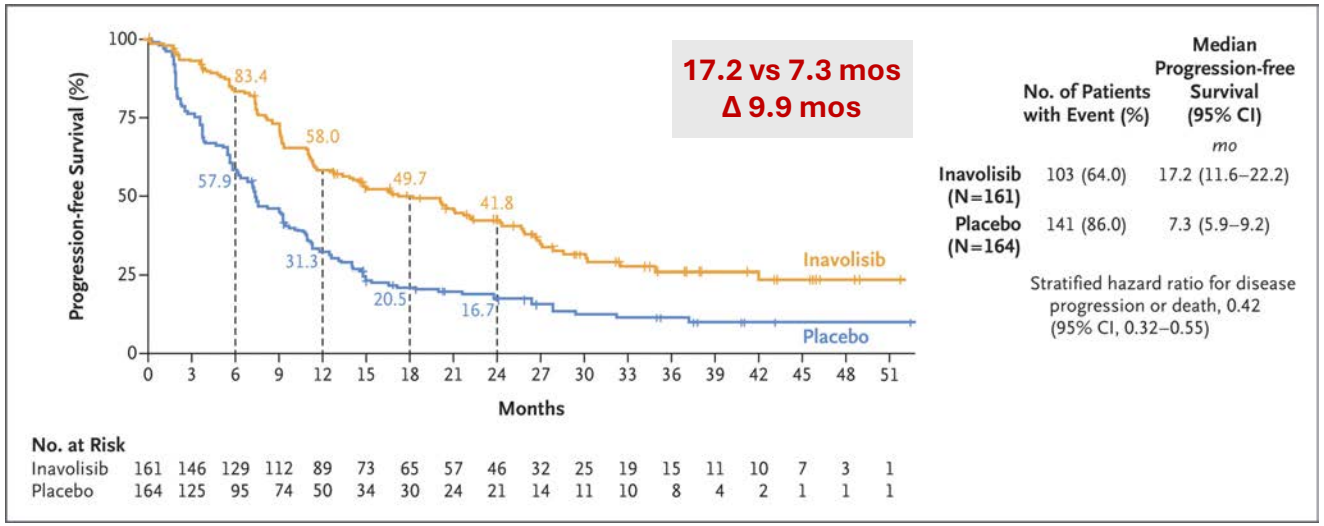
Select participant characteristics

- Asian 38%; White 58%; Black 1%
- Liver mets: 50%
- Prior (neo)adj therapy: chemo 82%; ET 99%; CDK4/6i 1%

Turner et al. NEJM 2024; Jhaveri et al. NEJM 2025

INAVO120: Palbo + Fulvestrant +/- Inavolisib

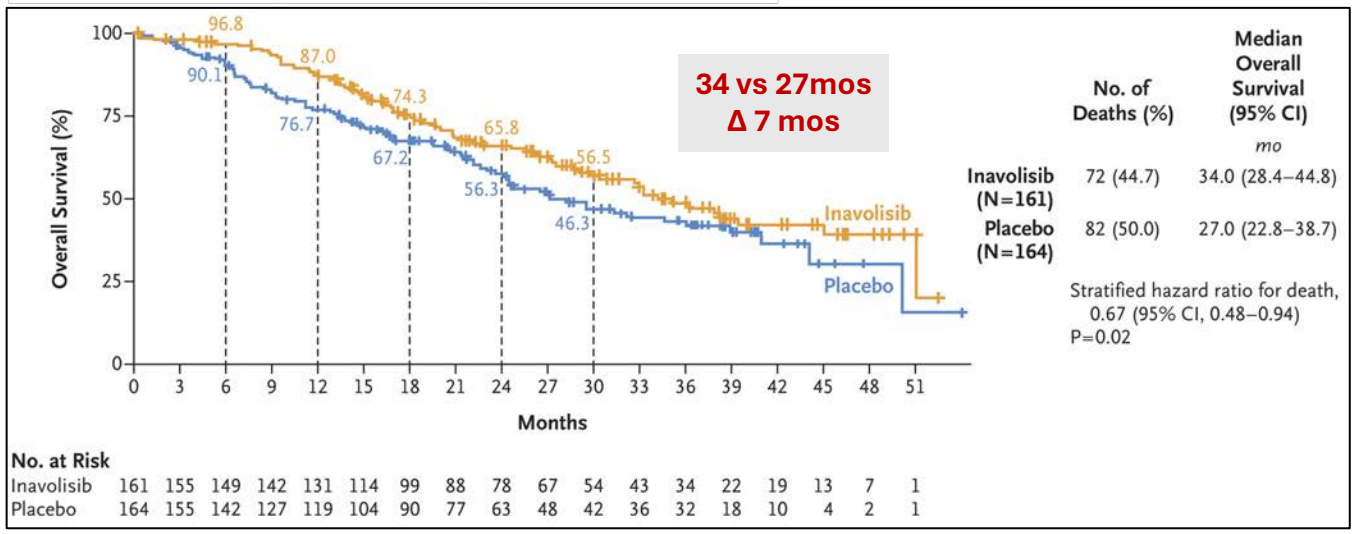
INAVO120 updated PFS



	No. of Patients with Event (%)	Median Progression-free Survival (95% CI) mo
Inavolisib (N=161)	103 (64.0)	17.2 (11.6–22.2)
Placebo (N=164)	141 (86.0)	7.3 (5.9–9.2)

Stratified hazard ratio for disease progression or death, 0.42 (95% CI, 0.32–0.55)

INAVO120 key secondary endpoint: OS



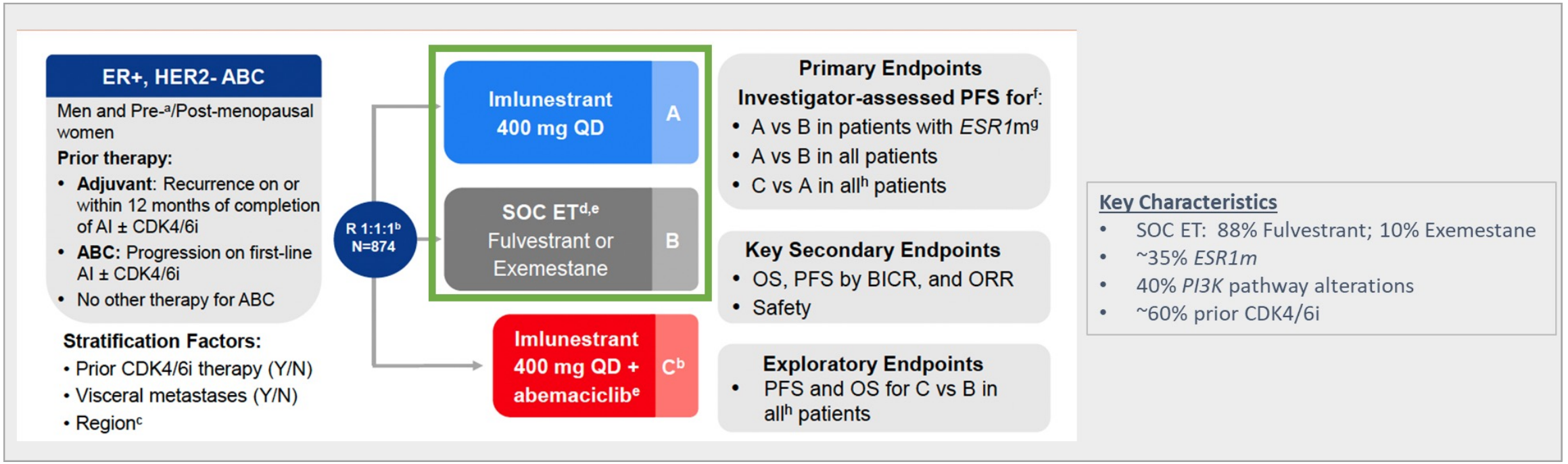
	No. of Deaths (%)	Median Overall Survival (95% CI) mo
Inavolisib (N=161)	72 (44.7)	34.0 (28.4–44.8)
Placebo (N=164)	82 (50.0)	27.0 (22.8–38.7)

Stratified hazard ratio for death, 0.67 (95% CI, 0.48–0.94)
P=0.02

- Time to 1st chemo: 35.6 vs 12.6 mo (HR 0.43, CI 0.3-0.6)
- Subsequent therapies (including 3L+)
  - Pbo arm: 15% PI3Ki 2L+
  - Pbo arm: more ADC (T-DXd 29% vs 12% inavo)

Turner et al. NEJM 2024
Jhaveri et al. NEJM 2025

Ember 3 Trial: Imlunestrant (oral SERD) vs SOC ET



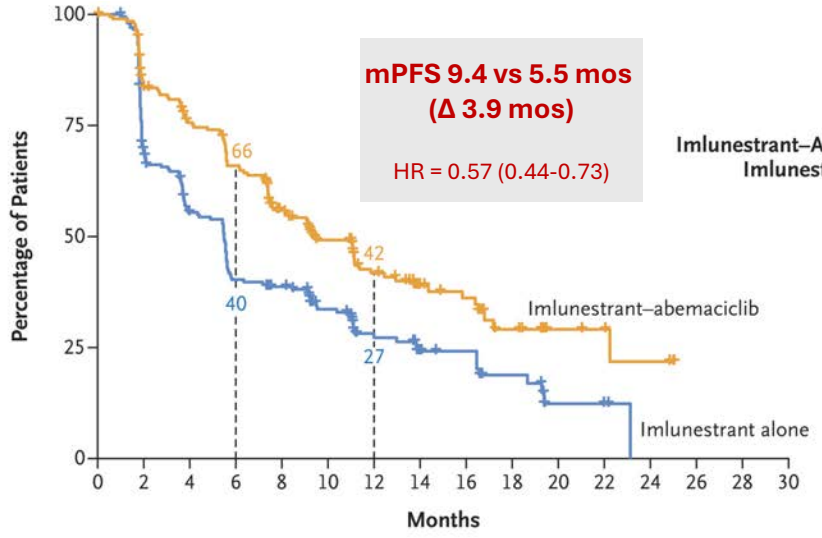
	Imlunestrant n=138	SOC ET n=118
No. of events	109	102
Median (95% CI); Months	**5.5** (3.9-7.4)	**3.8** (3.7-5.5)
HR (95% CI)	**0.62 (0.46-0.82)[a]** *p*-value<0.001	

FDA Approval 9/25/25

Jhaveri K, et al. NEJM 2025;392:12.

EMBER-3: Imlunestrant +/- Abemaciclib

A PFS Imlu + Abema vs Imlu Alone: Overall Population



mPFS 9.4 vs 5.5 mos (Δ 3.9 mos)

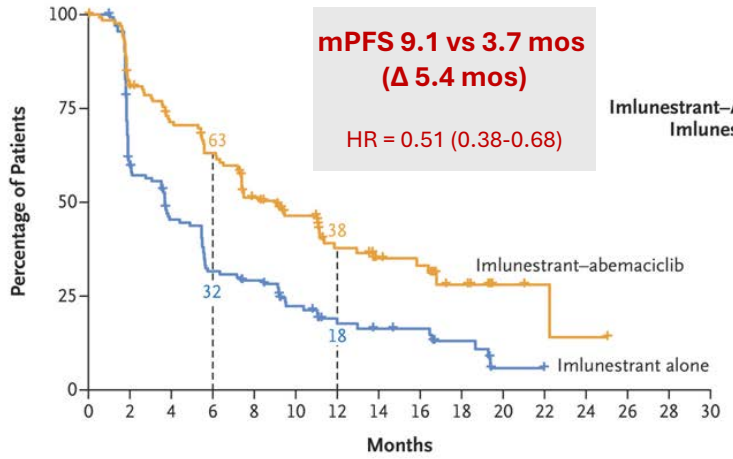
HR = 0.57 (0.44-0.73)

	No. of Patients	No. of Events	Median Progression-free Survival (95% CI)
			mo
Imlunestrant–Abemaciclib	213	114	9.4 (7.5–11.9)
Imlunestrant Alone	213	149	5.5 (3.8–5.6)

Hazard ratio for disease progression or death, 0.57 (95% CI, 0.44–0.73)
P<0.001

No. at Risk																
Imlunestrant–abemaciclib	213	165	141	122	96	72	48	29	25	13	6	5	3	0	0	0
Imlunestrant alone	213	140	106	77	67	48	29	20	18	10	3	2	0	0	0	0

B PFS Imlu + Abema vs Imlu Alone: Prior CDK4/6i



mPFS 9.1 vs 3.7 mos (Δ 5.4 mos)

HR = 0.51 (0.38-0.68)

	No. of Patients	No. of Events	Median Progression-free Survival (95% CI)
			mo
Imlunestrant–Abemaciclib	139	79	9.1 (7.2–11.2)
Imlunestrant Alone	140	109	3.7 (2.1–5.5)

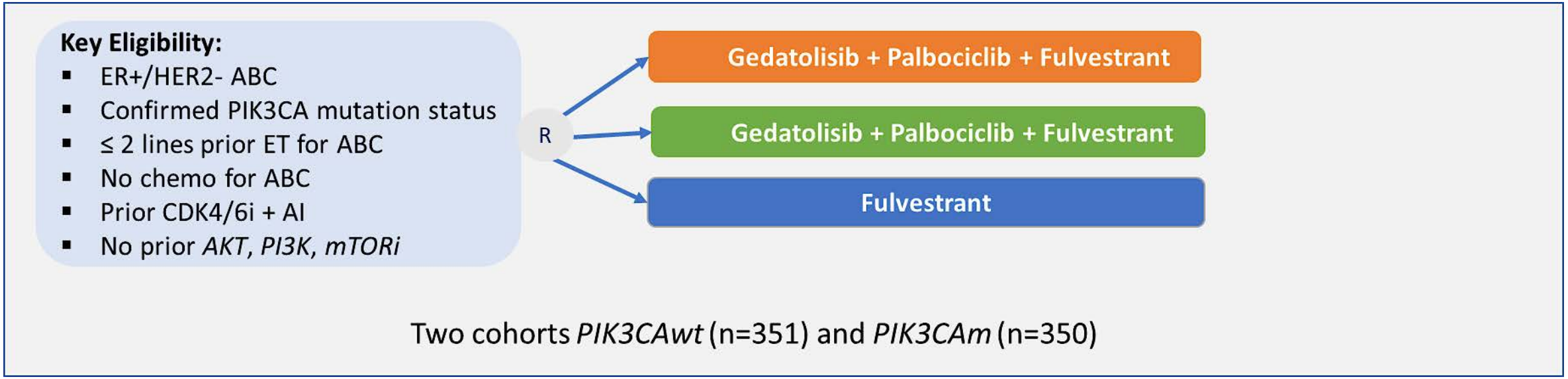
Hazard ratio for disease progression or death, 0.51 (95% CI, 0.38–0.68)

No. at Risk																
Imlunestrant–abemaciclib	139	105	87	76	58	43	29	19	17	8	3	2	1	0	0	0
Imlunestrant alone	140	79	56	39	32	21	13	11	10	6	1	0	0	0	0	0

Consistent benefit of Imlu + Abema regardless of ESR1m status, PI3Km, and prior CDK4/6i use

Jhaveri K, et al. NEJM 2025;392:12.

VIKTORIA-1: Randomized Phase 3 Trial of ET + CDK4/6i +/- Gedatolisib (pan PI3K and mTORC1/2 Inhibitor)



- Gedatolisib triplet:
  - mPFS (BICR) 9.3 mo triplet vs 2.0 mo fulv alone (HR, 0.24; 95% CI, 0.17–0.35; *P* <.0001).
- Gedatolisib doublet:
  - mPFS (BICR) 7.4 mo doublet vs 2.0 mo fulv alone (HR, 0.33; 95% CI, 0.24–0.48; *P* <.0001).

Hurvitz et al, JCO 2026

Case Presentation

Case: HR+/HER2- MBC

- 55 yo woman is diagnosed with *de novo* metastatic HR+/HER2- breast cancer to the bones after presenting with lower back pain
- NGS and germline genetic testing are performed at baseline and are unremarkable
- She begins treatment with letrozole plus palbociclib and zoledronic acid
- She does well until 9 years later, when she develops progressive bone metastases in multiple bones on bone scan (remains asymptomatic)
- A liquid biopsy is performed and is negative for actionable alterations (specifically NO ESR1 or AKT pathway alterations are present)

Case: HR+/HER2- MBC Continued

She is now 65 yo and presents for next steps. What treatment would you recommend next:

1. Continue letrozole plus palbociclib as she has done so well for so long
2. Continue the letrozole but switch to abemaciclib
3. Switch to fulvestrant plus abemaciclib
4. Discontinue endocrine therapy-based therapy and proceed with chemotherapy

Discussion Questions

Do you generally include a CDK4/6 inhibitor as part of first-line therapy for all of your patients with HR-positive, HER2-negative mBC? In which situations, if any, do you not?

How do you select among the three available CDK4/6 inhibitors in the metastatic setting, and what factors influence this decision?

In what situations, if any, do you rechallenge with a CDK4/6 inhibitor after disease progression on first-line CDK4/6 inhibitor/endocrine therapy?

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Module 7: CDK4/6 Inhibitors in Unique Populations

Module 8: Rarer CDK4/6 Inhibitor-Associated Toxicities

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GI Adverse Events Documented with CDK4/6 Inhibitors

Kelly Fischer, MSN, FNP-BC
Family Nurse Practitioner
Dana-Farber Cancer Institute
Boston, Massachusetts

Rates of various GI issues in patients taking CDK4/6 inhibitor therapy

Adverse Reaction	Abemaciclib	Ribociclib	Palbociclib
Diarrhea	82.2%	15.0%	19.1%
Nausea	27.9%	23.0%	35.0%
Vomiting	16.3%	8.0%	18.0%
Constipation	10.3%	13.2%	17.0%
Abdominal pain	34.0%	11.0%	10.0%

Dean B et al. J Adv Pract Oncol. 2024 Jul 22:1-8. Slamon D et al. N Engl J Med. 2024 Mar 21;390(12):1080-1091. Metzger O et al. N Engl J Med. 2026 Jan 29;394(5):451-462.

Strategies to mitigate and manage treatment-related GI AEs with CDK4/6 inhibitors

- Start over-the-counter loperamide at first sign of diarrhea and take as needed
- Stay hydrated and drink 8-10 glasses of water/clear liquids daily
- Modify diet if needed – limit alcohol and caffeine intake, avoid spicy foods, refrain from lactose-containing food or drink
- Start antiemetic like ondansetron or prochlorperazine at the first sign of nausea. Increase fluid intake
- Dose escalation approach with abemaciclib may help with diarrhea

The TRADE study: A phase 2 trial to assess the tolerability of abemaciclib dose escalation in early-stage HR+/HER2- breast cancer

- A prospective, single-arm study assessing whether dose escalation of abemaciclib improves tolerability
- All patients started abemaciclib at 50 mg BID x 2 weeks, then increased to 100 mg BID x 2 weeks, then increased to 150 mg BID thereafter
  - In order to increase to next dose level, patients could not be experiencing grade 3 or 4 or persistent grade 2 toxicity
- Use of dose escalation abemaciclib allowed 70.8% of patients enrolled on the study to reach and continue the 150 mg BID dose at 12-week
- There was a reduced incidence and severity of toxicity, such as diarrhea, with this dose escalation strategy

Mayer EL et al. ASCO 2025;Abstract 517

Role of nutritional counseling and diet modifications during CDK4/6 inhibitor treatment

- Avoid grapefruit and pomegranate
- Since abemaciclib can cause diarrhea, counsel patients to avoid foods that may worsen diarrhea, such as spicy, fatty, greasy, high-fiber foods
  - Bland/"BRAT" diet is best with diarrhea (bananas, rice, applesauce, toast)
- Small, frequent meals are recommended
- Avoid/limit alcohol intake
- Increase fluid intake, particularly if having diarrhea
  - Don't forget electrolytes (broth, popsicles, OTC rehydration drink)

Case Presentation

A 51 y/o female with pT1cN2a ER+, PR+, HER2- invasive lobular carcinoma

- 11/29/23: Left breast lumpectomy/SLN: **1.6 cm** invasive carcinoma with ductal and lobular features (predominantly lobular features) **grade 2**. **3**/4 positive SLN (largest metastatic focus is 1.2 cm, 1 macromet, 2 micromet), ENE present in association with macrometastases. **Oncotype RS 12.**
- 12/29/23 Left axillary ALND and re-excision: metastatic ductal carcinoma in **2** of 10 LN (1 macromet and 1 micromet, largest micromet focus 0.3 cm). Re-excision of left inferior and medial margin (DCIS is present on the inked margins). In total, 5/14 nodes positive. **pT1cN2a.**
- 1/16/24 - 04/23/24 **ddAC-T x 8 cycles.**
- 3/12/24 Started **leuprolide.**
- 6/1/2024: Started adjuvant **letrozole**.
- 8/2024: Completed adjuvant radiation.
- 8/27/2024: Started adjuvant **abemaciclib** (on **TRADE trial**).
- 9/2024: Start **adjuvant zoledronic acid**.

A 51 y/o female with pT1cN2a ER+, PR+, HER2- invasive lobular carcinoma

- Married, has two kids (13 y/o and 16 y/o), works remotely from home 3 days a week
- Premenopausal at the time of diagnosis
- Adjuvant therapy includes:
  - Ovarian suppression with monthly leuprolide injections
  - Letrozole
  - Abemaciclib
- Started to experience hot flashes and difficulty sleeping during chemotherapy, and has continued with similar side effect profile on OFS + AI
- Has been tolerating abemaciclib at 150 mg BID dose very well
  - Intermittent diarrhea (infrequent, ~2 episodes per month, well-controlled with PRN loperamide)

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Role of CDK4/6 Inhibitors in Unique Populations of Patients with HR-Positive mBC

Ruth M O'Regan, MD
Charles A Dewey Professor of Medicine and Oncology
Chair, Department of Medicine
University of Rochester Medical Center
Physician-in-Chief
Strong Memorial Hospital
Associate Director of Education and Mentoring
Wilmot Cancer Institute
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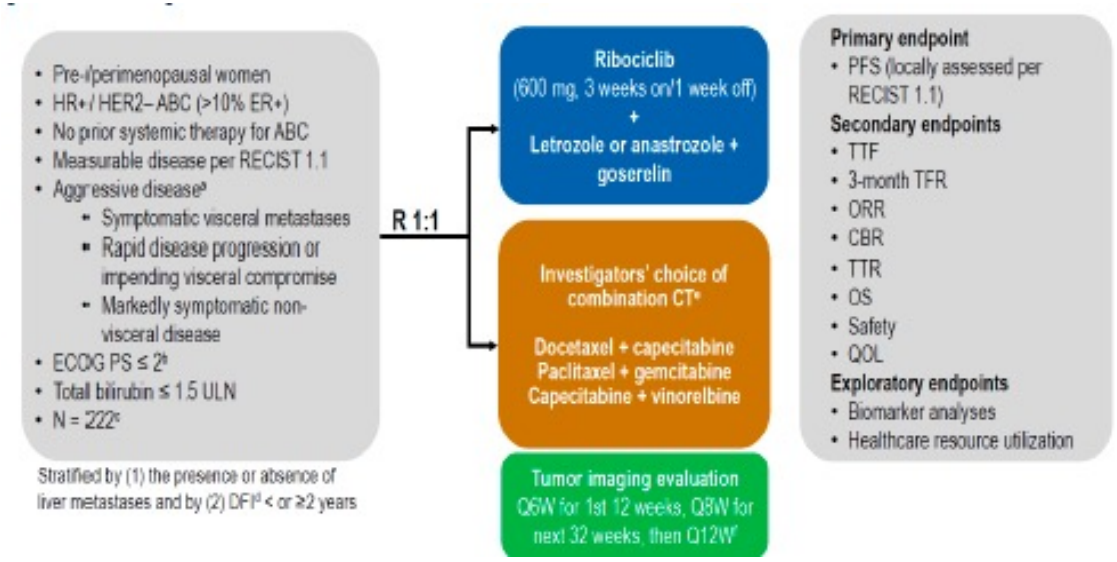
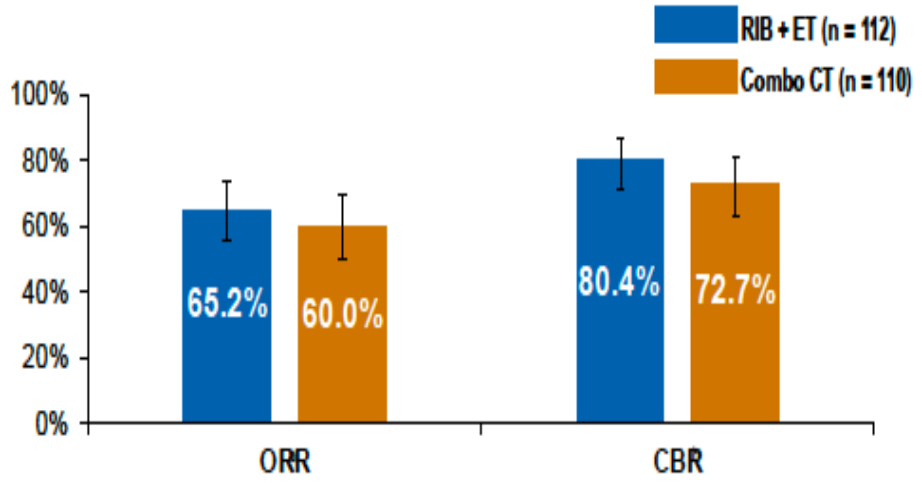
Case history

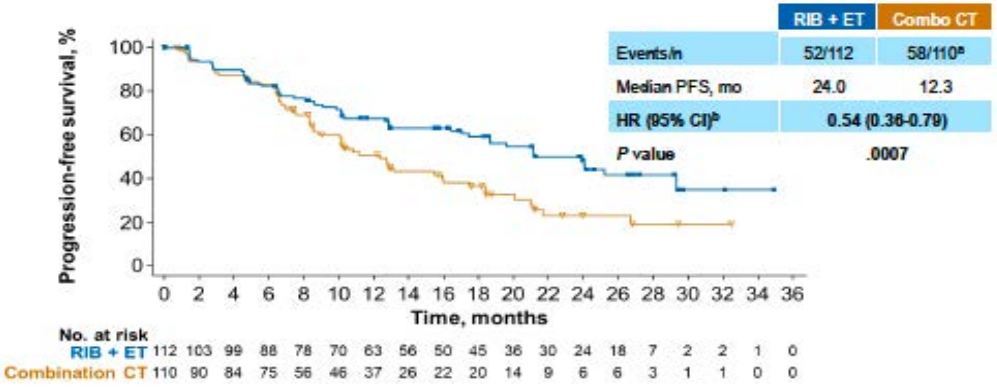
- 65-year-old female presents with 6-week history of abdominal pain with nausea
- Admits to 6-months history of back pain.
- Examination reveals a right breast mass with palpable axillary nodes and hepatomegaly
- Systemic imaging reveals extensive metastatic disease in her liver and bones and confirms the right breast mass and axillary nodes
- Liver biopsy: metastatic carcinoma consistent with a breast primary, ER-positive, PR-negative, HER2-negative
- LFTs with mild elevation in transaminases and normal bilirubin

RIGHT Choice (Phase 2): Ribociclib + endocrine therapy vs chemotherapy for patients with HR+/HER2– advanced breast cancer

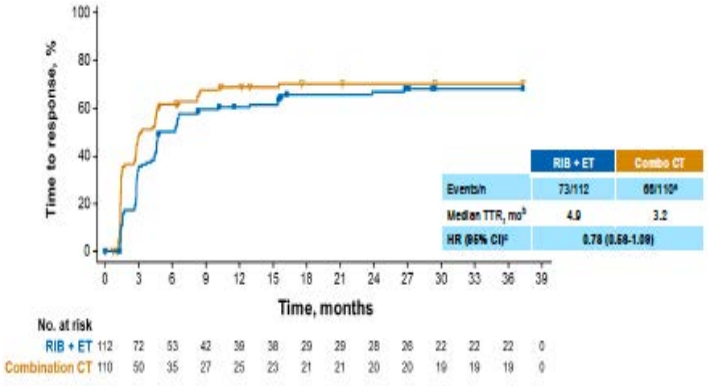




Progression-free survival



Time to response



Treatment discontinued due to adverse events 6.3% with ribo/ET versus 27% with chemo

No difference in PFS for patients with visceral crisis (n=88)

Gao M et al. Miami Breast Cancer Conference 2023; Lu et al J Clin Oncol 2024:42:2812

PADMA: Palbociclib plus endocrine therapy versus single agent chemotherapy

Patient Population
N=150
- HR-positive/HER2-negative
- Female or male
- Indication for mono-chemotherapy
- No prior treatment for metastatic/relapsed disease
- No asymptomatic bone-only, oligo-metastatic disease
- No uncontrolled/untreated CNS metastases
- Live-expectancy >6 months

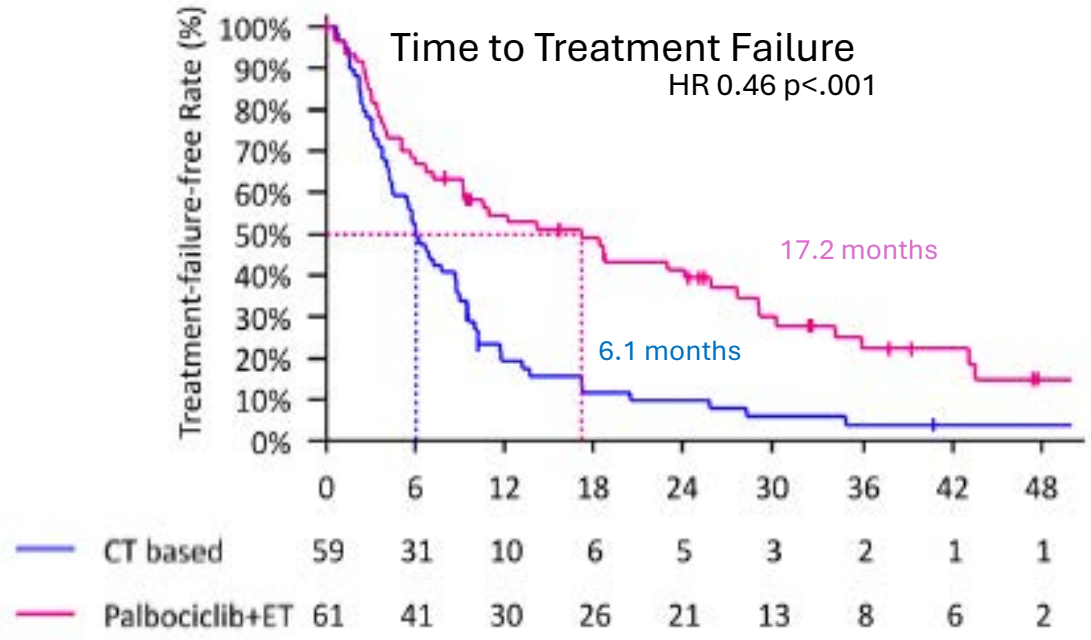
R → 1:1

Arm A: Endocrine therapy (ET) + palbociclib

Arm B: Chemotherapy (CT) of physician's choice ± ET maintenance therapy

Stratification:
- Endocrine resistant vs endocrine sensitive
- Symptomatic vs asymptomatic metastatic disease

ET with palbociclib: AI or fulvestrant ± GnRHa
ET maintenance: tamoxifen, AI or fulvestrant ± GnRHa
CT: paclitaxel, capecitabine, epirubicin, or vinorelbine

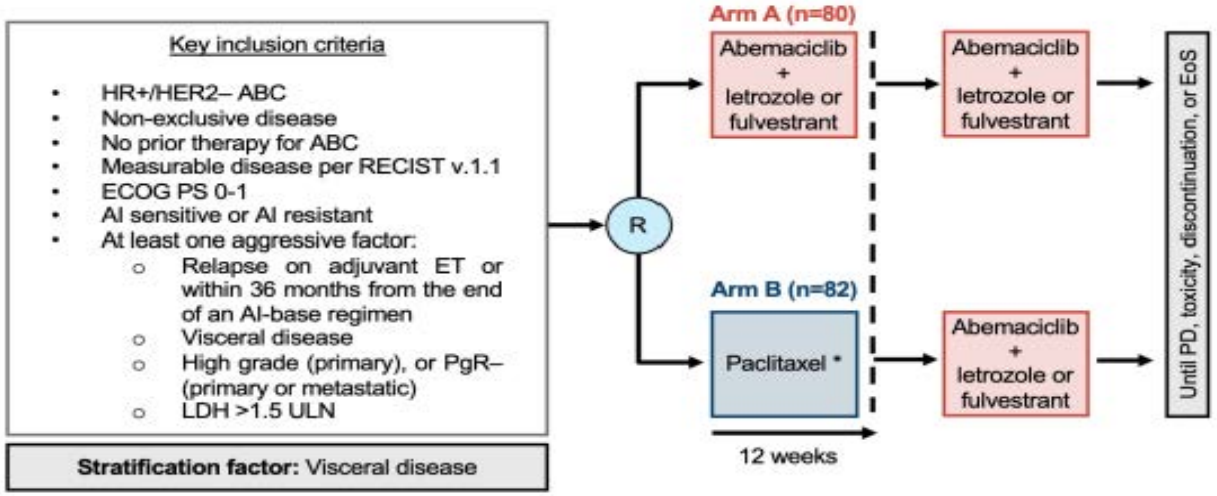


Indication for chemotherapy:
Symptomatic visceral metastases
Aggressive disease with rapid progression
Prior endocrine-resistance
High disease burden

	PALBO/ET	CHEMO	P VALUE
PFS	18.7 mos	7.8 mos.	P<.001
ORR	59%	40%	
OS	46 mos.	37 mos.	

Loibl et al SABCS 2024

ABIGAIL Trial: Abemaciclib ± induction paclitaxel in HR+ metastatic breast cancer plus real-world data



	Abemaciclib + ET N = 80	Paclitaxel N = 82	Odd ratio (95% CI)	p value
12-week ORR in ITT population				
Complete response, partial response	47 (58.8%)	33 (40.2%)	2.11 (1.13-3.96)	0.0193
Stable disease, progressive disease , or discontinuation	33 (41.2%)	49 (59.8%)		
Response at 12 weeks since randomization				
Complete response	0 (0%)	0 (0%)		
Partial response	47 (58.8%)	33 (40.2%)		
Stable disease	24 (30.0%)	37 (45.2%)		
Progressive disease	1 (1.2%)	7 (8.5%)		
Not evaluable	8 (10.0%)	5 (6.1%)		
Death*	2 (2.5%)	2 (2.4%)		
Withdrawal of consent	2 (2.5%)	1 (1.3%)		
Toxicity	2 (2.5%)	0 (0%)		
Non-radiological progression	1 (1.25%)	0 (0%)		
Incorrect randomization	1 (1.25%)	2 (2.4%)		

*Deaths were due to causes different from treatment-related toxicity.

De La Haba-Rodriquez et al ESMO 2024

UK real-world retrospective study compared CDKi versus Paclitaxel in patients (n=482) with impending or documented visceral crisis:
TTF 17 vs 4-months, OS 25 vs 4.5-months
Real-world analysis of 336 patients with visceral crisis:
Overall survival 11-months with CDKi versus 6-months with paclitaxel (p=.01)

Behrouzi et al BCRT 2023, Dawood JCO 2021

CDK4/6i versus chemotherapy in HR-positive aggressive disease

Outcome	Best treatment	Trials' results
Progression free-suvival	CDK4/6i + ET	RIGHT Choice: 21.8 vs 12.8 months (HR: 0.61, p=0.003) PADMA: 18.7 vs 7.8 months (HR: 0.45, p<0.001)
Overall Response Rate	CDK4/6i + ET	RIGHT Choice: 66.1% vs 61.8%; PADMA: 58.8% vs 40.2%; ABIGAIL: 58.8% vs 40.2% (p=0.0193)
Time to Treatment Failure	CDK4/6i + ET	PADMA: 17.2 vs 6.1 months (HR: 0.50, p<0.001)
Time to Response	= Comparable	RIGHT Choice: 4.9 vs 3.2 months (HR: 0.76, NS)
Safety Profile	CDK4/6i + ET	RIGHT Choice: lower discontinuation rate for AEs (6.3% vs 27.0%, p<0.001)
CDK4/6i + ET demonstrates superiority across all efficacy endpoints with comparable time to response and lower discontinuation rate for AEs.		

Orlandi Discover Oncology 2025

Phase II trial of abemaciclib in patients with HR-positive brain metastases

- Patients with HR-positive, HER2-negative breast cancer with brain metastases (cohort A, n=55)
  - Median number of brain mets was 2 and prior radiation in 82% (Whole brain 47%, SRS 35%)
  - Intracranial objective response 5%, intracranial disease control at 6-months 24%, intracranial PFS 5-months
- Patients with HR-positive leptomeningeal disease (cohort C, n=7)
  - Intracranial disease control at 6-months 14%
- CSF analysis showed high levels of abemaciclib compared to plasma
  - Confirms preclinical studies showing abemaciclib crosses the blood-brain-barrier

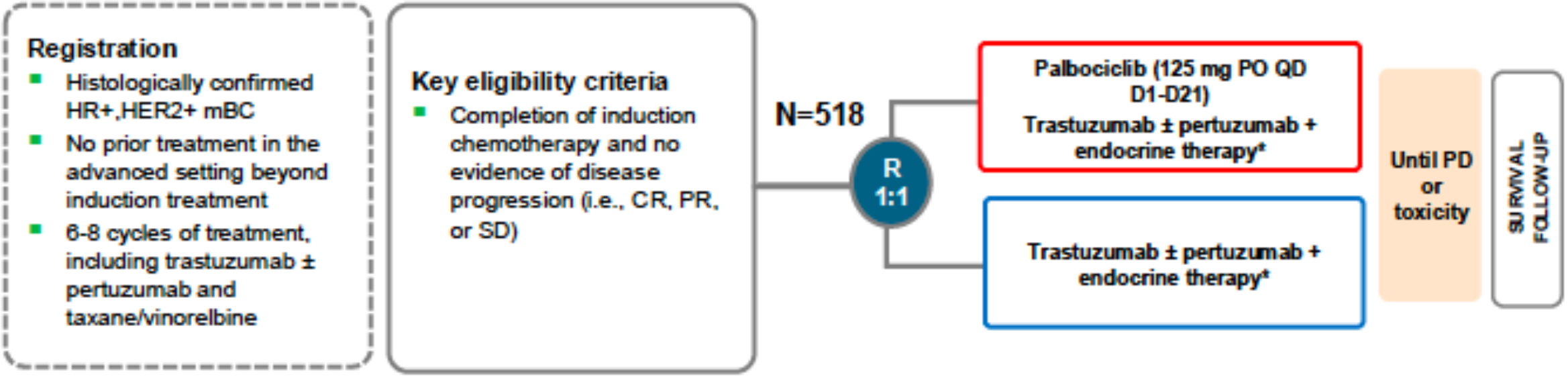
Tolaney et al Clin Cancer Res 2020

Radiotherapy with CDKi in patients with HR-positive brain metastases

- Patients (n=24) received radiotherapy to the brain before (n=11), during (n=6), and after (n=7)
- PFS at 6-months 77% and at 12-months 50%
- Local control at 6-months 80% and at 12-months 69%
- Radiotherapy with CDKi appears feasible (though patient numbers are small)

Kubeczko et al Clin Med 2023

PATINA: Addition of palbociclib to maintenance HER2 and ER-directed therapy in HR-positive, HER2-positive MBC

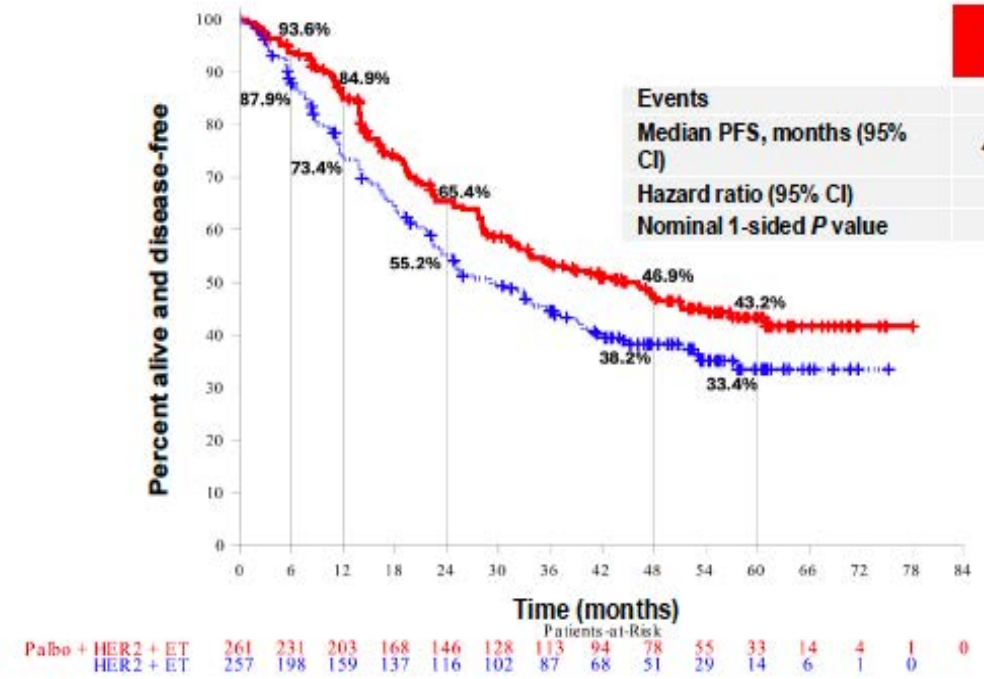


Stratification factors

- Pertuzumab use (yes vs no)
  - The non-pertuzumab option is limited to up to 20% of the population
- Prior anti-HER2 therapy in the (neo)adjuvant setting (yes vs no, including de novo)†
- Response to induction therapy (CR or PR vs SD) by investigator assessment†
- Type of endocrine therapy (fulvestrant vs aromatase inhibitor)

Metzger et al SABCS 2024; Metzger et al N Eng J Med 2026

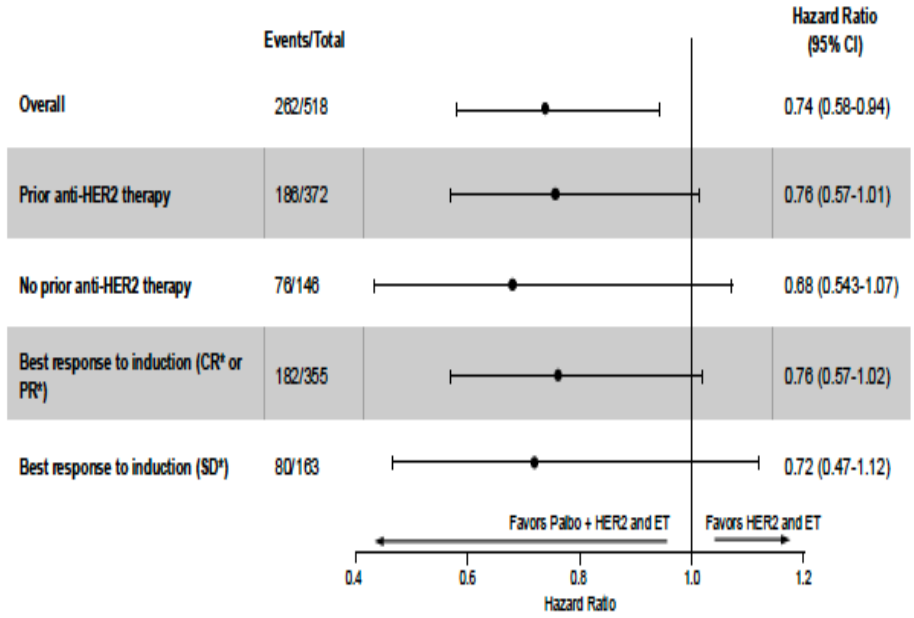
PATINA: Addition of palbociclib to maintenance HER2 and ER-directed therapy in HR-positive, HER2-positive MBC



	Palbo + anti-HER2 and ET	Anti-HER2 and ET
Events	126/261	136/257
Median PFS, months (95% CI)	44.3 (32.4-60.9)	29.1 (23.3-38.6)
Hazard ratio (95% CI)	0.74 (0.58-0.94)	
Nominal 1-sided *P* value	0.0074	

Median follow-up on patients who are alive and disease-free, 52.6 months

CI=confidence interval; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; palbo=palbociclib.



*Factors used in stratified analyses.
CR=Complete Response; Palbo=palbociclib; PR=Partial Response; SD=Stable Disease

Median lines of induction therapy = 6
CR/PR to induction therapy = 69%
SD following induction = 31%

Metzger et al SABCS 2024; Metzger et al N Eng J Med 2026

Discussion Questions

How do you think through the selection of initial therapy for patients with HR-positive, HER2-negative mBC with symptomatic visceral disease? How do you decide between a CDK4/6 inhibitor/endocrine therapy and chemotherapy?

How do CDK4/6 inhibitors fit into treatment for patients with brain metastases?

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Rarer but Potentially Serious Toxicities Associated with One or More CDK 4/6 Inhibitors

Marissa Marti-Smith
DNP, APRN, AGNP-C, AOCNP

The Rare 5 Safety Concerns

Lung Health

ILD monitoring

Liver Safety

Liver enzyme monitoring

Blood Clots

VTE, especially with abemaciclib.

Cardiac

Monitoring the rhythm (QTc) during ribociclib therapy.

Skin toxicity

Rare, severe skin reactions like SJS or DRESS.

(Spring et al., 2020)

Managing ILD

- **Incidence:** At the end of 2019, the FDA reviewed all clinical trials for the three approved CDK4/6 inhibitors and found that pneumonitis was identified in 1% to 3% of cases and less than 1% had a fatal outcome
- **Early Signs:** New cough or shortness of breath.
- **Action:** Hold treatment for any suspected symptoms. Scan.

TABLE 3. Grading for Pneumonitis* per the National Cancer Institute Common Terminology Criteria for Adverse Events

Grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Presentation	Asymptomatic	Symptomatic, limiting instrumental activities of daily living	Severe symptoms, limiting self-care activities of daily living	Life-threatening respiratory insufficiency	Death
Intervention	No intervention indicated	Medical intervention indicated	Medical intervention indicated (hospital admission, oxygen supplementation)	Urgent medical intervention indicated (ventilatory support)	
	Observation only	Cessation or dose adjustment	Discontinue therapy	Discontinue therapy	
		Consider corticosteroid use	Corticosteroid use	Corticosteroid use or other immunosuppressive treatment	

*Pneumonitis is a disorder characterized by inflammation focally or diffusely affecting lung parenchyma. Grading is based on the National Cancer Institute Common Terminology Criteria for Adverse Events (version 5.0).[41]

(Anders et al., 2020)

ILD Management Algorithm

- Stop drug OR dose reduction
- Steroids if needed
- Supportive measures
- Rechallenge can be considered

(Anders et al., 2020)

Liver Safety: Monitoring

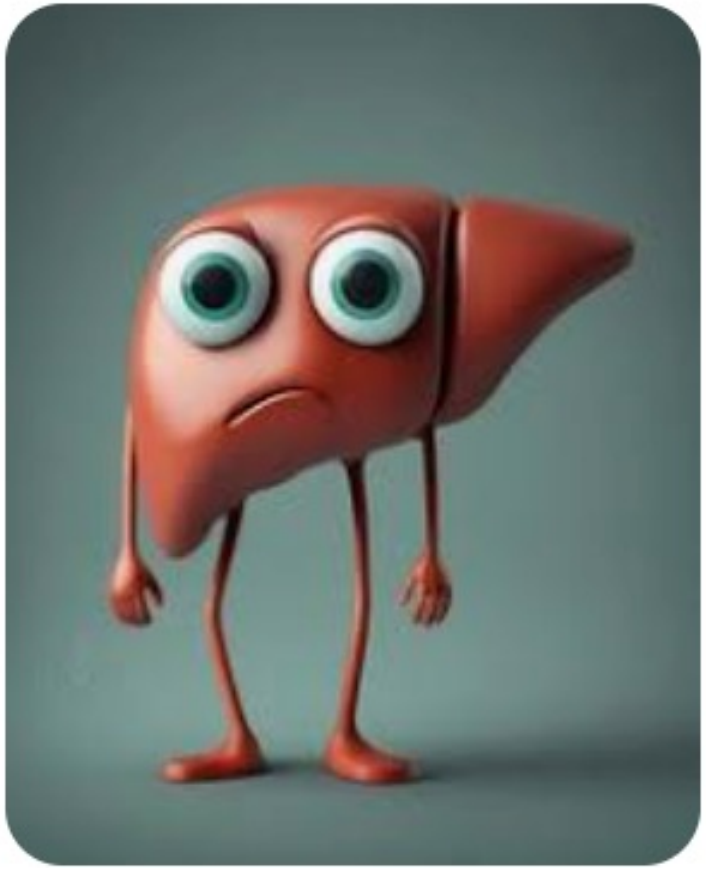
Phase	Monitoring Frequency	Nursing Focus
Baseline	Prior to Day 1	Establish "normal" filter health.
Cycles 1 & 2	Every 2 Weeks	Identify early spikes in enzymes.
Cycles 3 to 6	Every 4 Weeks (Start of Cycle)	Monitor for stable maintenance.
Cycle 7+	As Clinically Indicated	Check if patient reports fatigue or yellowing.

Monitoring applies to Ribociclib and Abemaciclib; adjust based on ALT/AST levels.

(Lipsyc-Sharf et al., 2025)

Handling Liver Enzyme Stress

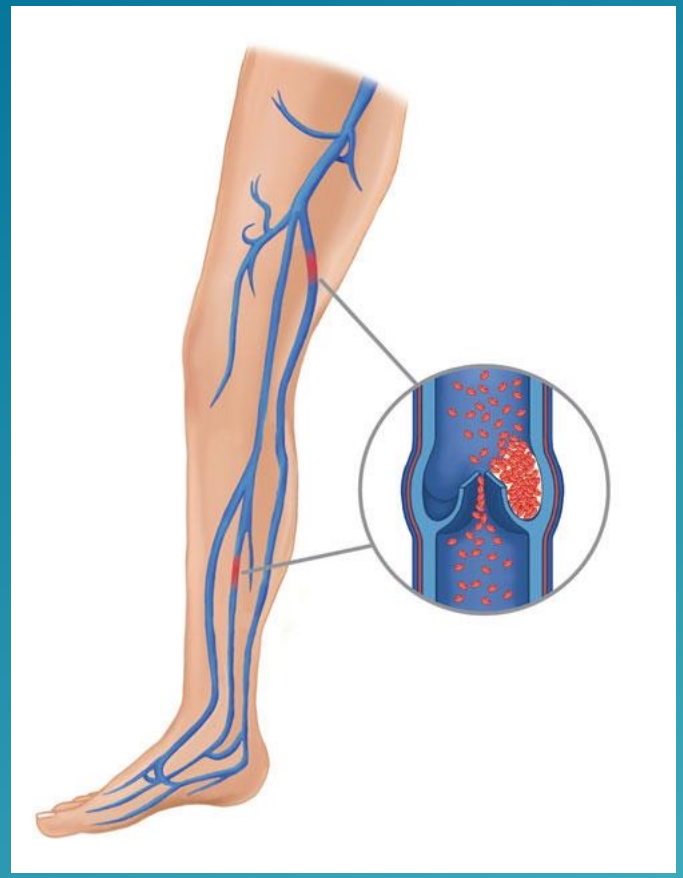
- Silent laboratory spike (AST/ALT)
- Pre-existing liver insufficiency, **Fatty liver disease**
  - Hepatitis
  - Hepatotoxic medications and alcohol abuse.
- Grade 1 (>3x ULN) & Grade 2 (>3-5x ULN) no dose mod req
- Persistent/Recurrent Grade 2 or **Grade 3 (>5-20x ULN):** Hold until Grade 1, then resume at lower dose.
- **Liver Injury:** If bilirubin also rises (>2x ULN), discontinue therapy permanently.



(Wekking et al., 2023), (U.S. Food and Drug Administration, 2023) Prescribing Information

VTE & Blood Clots

- **Circulation Blockage:**
  - Blood clots can form in the legs (DVT) or lungs (PE). This risk is notably higher with abemaciclib.
- Leg swelling, pain, redness, warmth, or sudden chest tightness.
- Rate: ~2.3% in monarchE trial participants.
- Screen for pre-existing risk factors at every cycle.



(Johnston et al., 2020)

Heart Rhythm: QTc monitoring

Ribociclib

- Ensuring safe electrical activity w/ heart
- **QTcF <450 ms**
- **Baseline ECG**
- ECG + check electrolytes (K, Mg, Phos, Ca)
- **Cycle 1 on D14 , Cycle 2 & as needed**
- Avoid QT prolonging drugs and/or strong CYP3A inhibitors

U.S. Food and Drug Administration. (2023). Ribociclib full prescribing information.

Skin Toxicities

- Less frequent with CDK's

- ***Red Flag Signs***
- **Painful rashes, mouth blisters, or peeling skin accompanied by a high fever.**
- Severe reactions (SJS/Toxic epidermal necrolysis TEN)
- Drug-induced hypersensitivity syndrome (diHS)
- Drug reaction with eosinophilia and systemic symptoms (DRESS)

(Anders et al., 2020),
U.S. Food and Drug Administration. (2023). ribociclib full prescribing information.

Case Presentation

Case Study

- 53 yo female
- Metastatic Breast CA pt, extensive bone and pleural mets, nodal mets
- Hx Fatty liver, Hypercholesterolemia, HTN
- Fulvestrant + abemaciclib 150mg PO BID , 1st line
- 6 week check
- AST 197, ALT 323, Alk Phos 250, Bili normal
- No alcohol / Tylenol
- Oxycodone for pain

Management & Takeaway

- Held x3 weeks, LFTs did not improve off meds, hospitalized
- U/S showed fatty liver, biopsy confirmed moderate to severe macrovesicular steatosis
- IV steroids, d/c'ed on oral steroids
- 1 mo later AST 345/ ALT 929, Alk Phos 163, Bili 1.1
- 4 months off therapy, began palbociclib

Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress

Relapsed/Refractory Multiple Myeloma

Saturday, May 16, 2026

12:15 PM – 1:45 PM

Faculty

Beth Faiman, PhD, MSN, APN-BC, AOCN, BMTCN, FAAN, FAPO
Hans Lee, MD
Mary Steinbach, PhD-c, DNP, FNP-C, APRN

Moderator

Natalie S Callander, MD

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Thank you for joining us! Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

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