

LIVING BEYOND
BREAST CANCER®

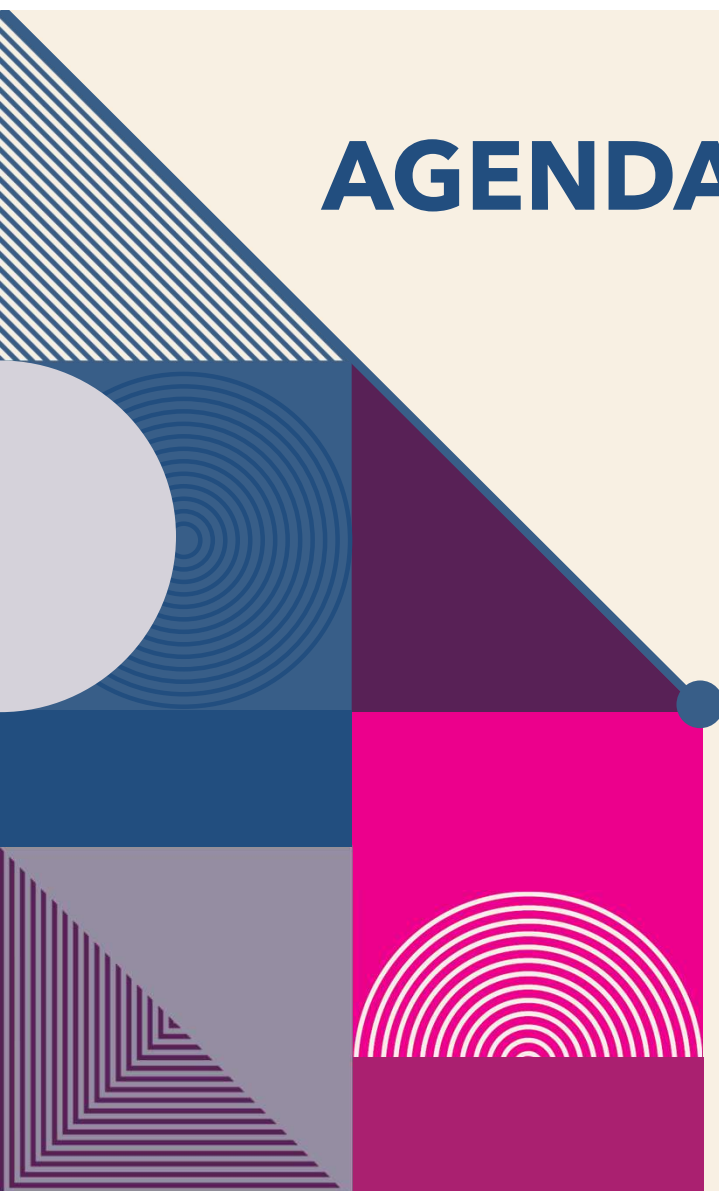
Session 2 | The right dose for you: Managing treatment & quality of life

Effective treatment & side effect support | Innovations in
breast cancer care



THE RIGHT DOSE FOR YOU: MANAGING TREATMENT AND SIDE EFFECTS

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AGENDA

- Why dose matters
- How dose is determined in MBC?
- What about dosing in early stage?
- Does dose reduction impact efficacy?

INTRODUCTION: WHY DOSE MATTERS

- Dose = how much medicine, how often (schedule), and for how long
- Goal: maximize cancer control while minimizing side effects
- The “right dose” is the one you can stay on safely and consistently

HOW DOSE IS DETERMINED IN MBC?

- Phase 1 dose-escalation: start low, increase in small cohorts until reach DLTs
- DLTs (dose-limiting toxicities): early serious side effects that define the Maximum Tolerated Dose (MTD)
- RP2D: recommended phase 2 dose based on MTD plus PK/PD, early activity, and overall tolerability.
- Targeted/oral drugs: optimal biologic dose may be below the MTD—**more isn't always better**.



Patient Centered Dosing Initiative

[THERIGHTDOSE.ORG](https://therightdose.org)

Shaping the Conversation Through Data

- 2020 MBC patient survey (1,200+ respondents)
- 82% reported meaningful relief after dose reductions
- Majority supported flexible dosing discussions
- ADC-focused patient survey presented at MASCC 2025
- Version 2 of the MBC patient survey to be presented at SABCS 2025



Patient Centered Dosing Initiative

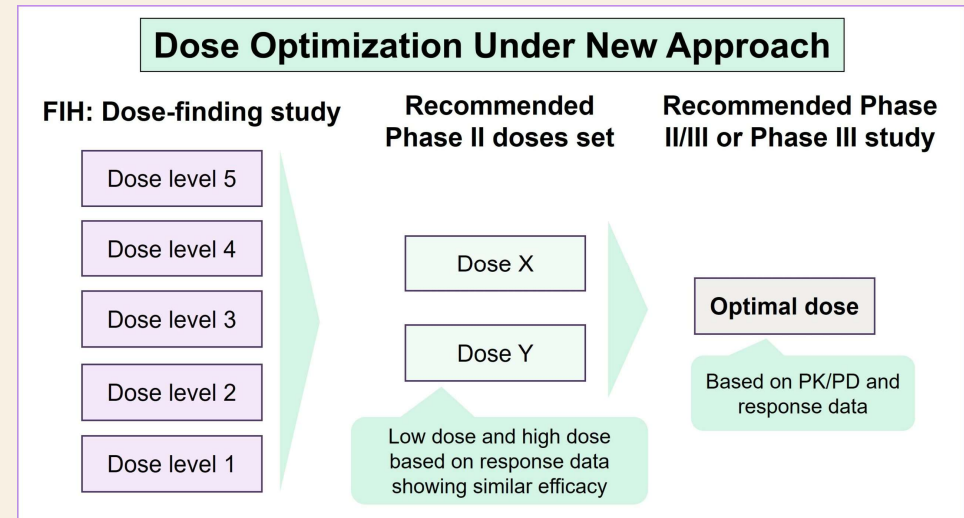
THE RIGHT DOSE.ORG

2025 ADC Survey: Key Findings (n = 170)

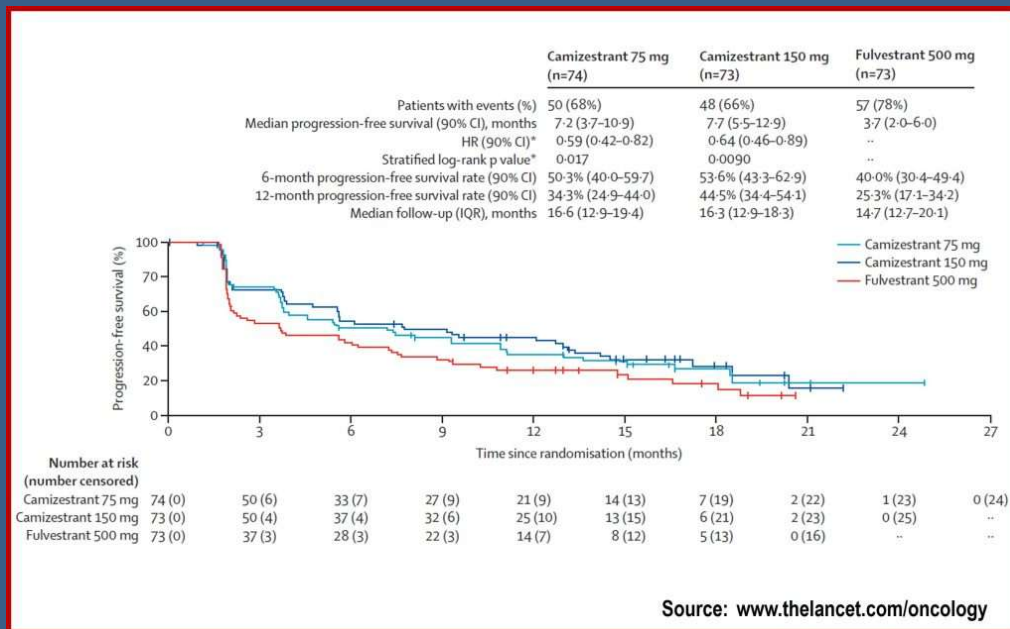
- 81.8% of patients experienced a bad side effect
- 17.1% started on a lower dose
- 94.1% started at the recommended dosing frequency
- 35.3% reduced dose after starting at the recommended dose
- Reasons for dose reduction (n=60):
 - 52% history of bad side effects
 - 35% concerns about side effects
 - 5% other health problems
 - 15% other reasons

PROJECT OPTIMUS

- Project Optimus (FDA): shift from “highest tolerable” to “optimal” dosing.
- Encourages randomized dose-finding, exposure-response analyses, and patient-reported outcomes.
- Focus on long-term tolerability, not just first-cycle safety; multiple doses may be studied/approved.
- What this means for you: clearer dose guidance, safer adjustments, and better quality of life without losing effectiveness.



EXAMPLES OF SUCCESS



1. Camizestrant 75 mg and 150 mg had similar efficacy
2. Camizestrant 75 mg had better side effect profile.
3. Phase III trials include 75 mg

- SERENA 2.



DOSE REDUCTIONS IN EARLY-STAGE BREAST CANCER

OVERVIEW

- Dose reductions are less common in early stage
 - Treatment duration is shorter than in MBC
 - Doctors may feel the need to “treat very aggressively”
- Regimens are based off of MBC dosing trials
- Not as much data to provide efficacy

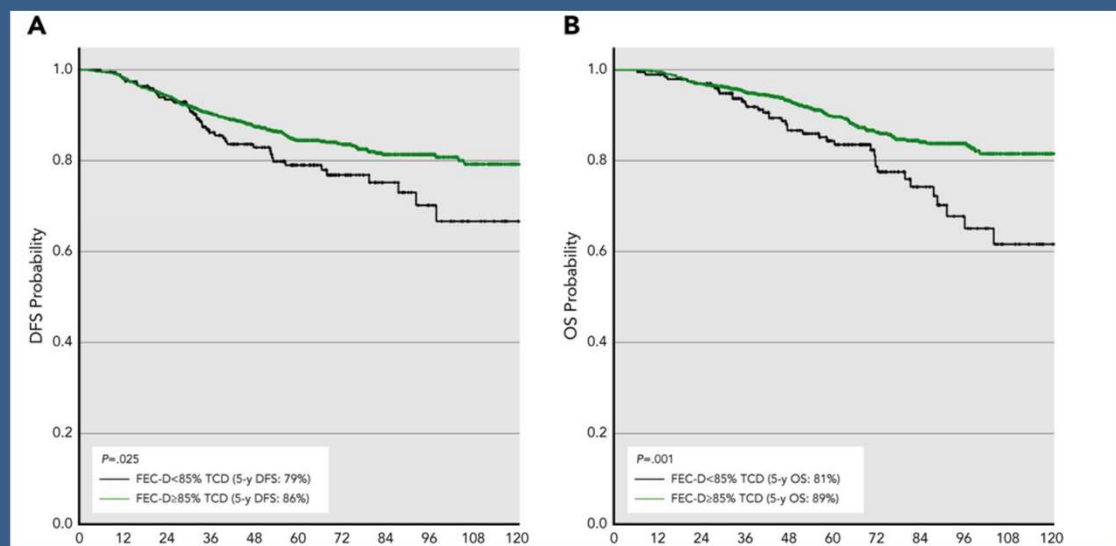
REASONS FOR DOSE REDUCTIONS

- Debilitating side effects
 - Potential life-long neuropathy (most common)
 - Constant nausea/diarrhea
- Interference with activities of daily living (ADLs)
- Dangerous medical situations
 - Low blood counts (platelets, RBCs, WBCs)
 - Heart toxicities
 - Interstitial lung disease



DOES DOSE REDUCTION IMPACT OUTCOMES IN EARLY STAGE?

EARLY CHEMOTHERAPY DOSE REDUCTION COULD LEAD TO WORSE OUTCOMES IN EBC

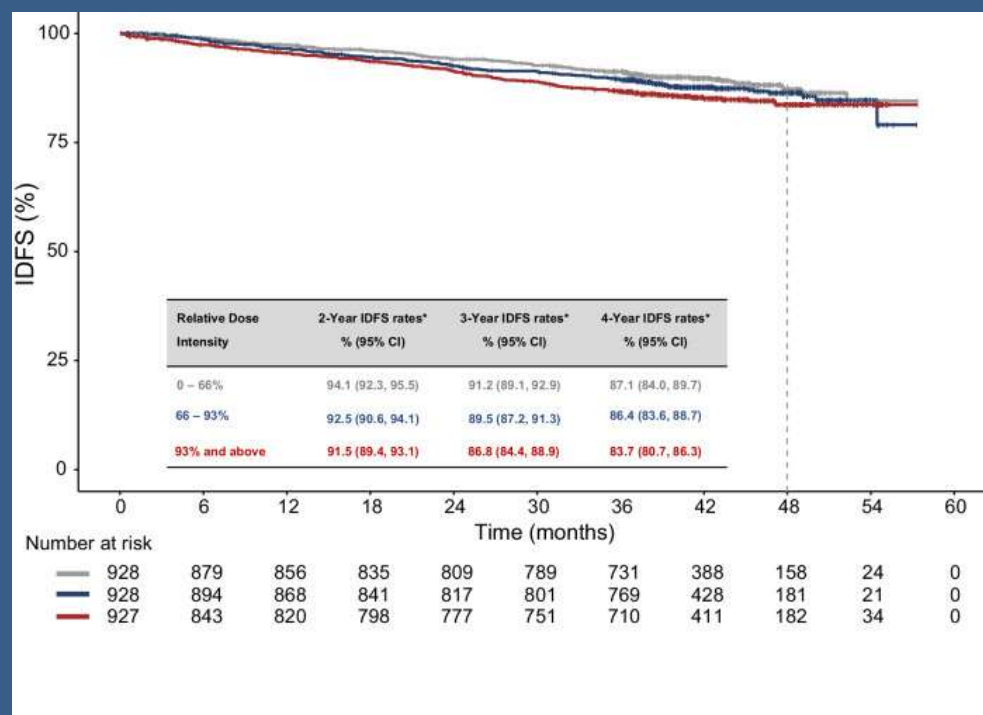


>1300 women with stage I-III, hormone receptor-positive/negative, HER2-negative breast cancer treated with adjuvant FEC-D chemotherapy from.

Total Dose for cycles 1 to 6 of <85% or ≥85% was calculated.

Vietch, J NCCN 2019

ABEMACICLIB DOSE REDUCTION DOES NOT IMPACT OUTCOMES IN EBC



Across the three patient subgroups as defined by relative dose intensity ($\leq 66\%$, $66-93\%$, $\geq 93\%$), the estimated 4-year IDFS rates were the same (87.1%, 86.4%, and 83.7%).

Goetz, NPJ Breast Cancer 2024.



TRADE STUDY

Focus: Investigated dose escalating (starting low and building) of abemaciclib in high risk, early Stage patients with breast cancer

Design: patients started at 50mg for 2 weeks, then increased to 100mg for 2 weeks, then went to the full dose of 150mg

Preliminary Results:

Dose reductions did not compromise effectiveness.

Less patients discontinued their medication

Patients reported less side effects

Significance: Promotes personalized dosing strategies for better patient management.

Mayer, ASCO 2025.

TALKING WITH YOUR PROVIDER

- Just because dose reductions are less common in early stage does not mean they can't or shouldn't happen
- Talk to your doctor about whether a change in dose or cadence may be right for you
 - Your care team will know the potential risks and benefits for your specific case
 - "Is a dose reduction right for me"
 - "Is it possible for me to safely take a break from this medication?"

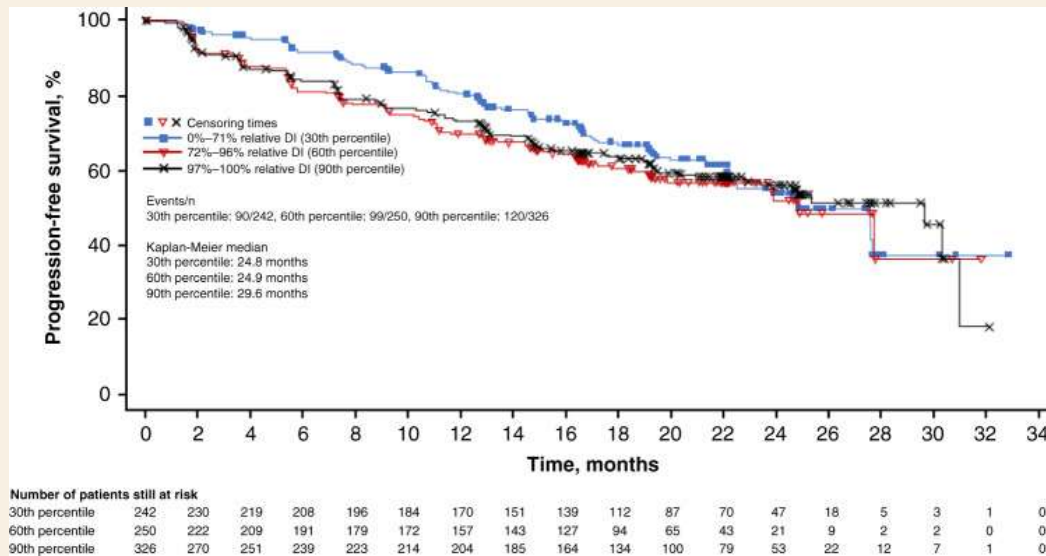


DOES DOSE REDUCTION IMPACT OUTCOMES IN MBC?

- Some trials report dose intensity impact on progression free and overall survival
- Some trials compare lower starting doses to higher doses

DOSE REDUCTION IN CDK4/6 INHIBITORS DOES NOT IMPACT OUTCOMES

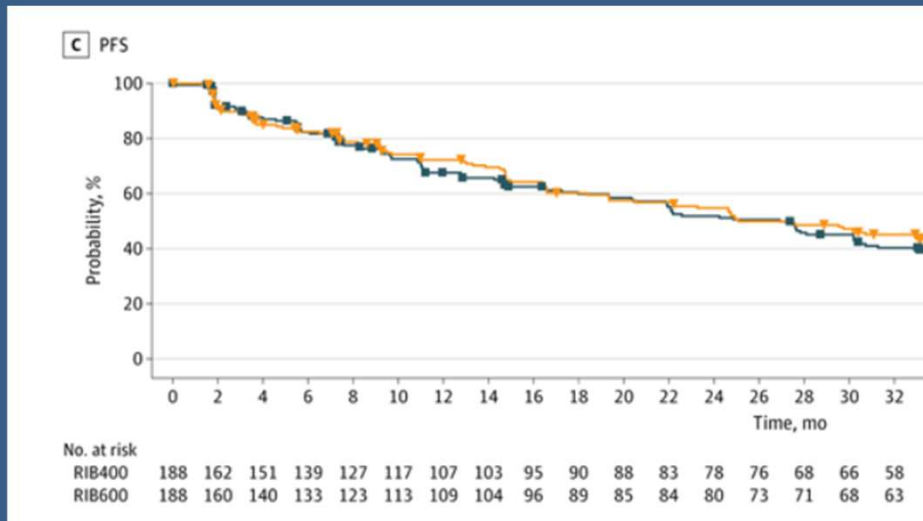
MONALEESA 2,3,7 RDI versus PFS



Relative Dose Intensity= ratio dose
Received versus dose intended

Burris, B J Cancer 2021

WHAT ABOUT STARTING AT A LOWER DOSE?



Cardosa, JAMA Oncol 2025.

AMELEE Study: 400mg versus 600 mg ribociclib

Same PFS, Slightly higher response with 600 mg, Less side effects with 400 mg

Table 2. Overall Response Rate (ORR), Best Overall Response (BOR), and Clinical Benefit Rate (CBR)

Characteristic	No. (%)						ORR ratio, RIB400/RIB600 (90% CI)
	All patients		Patients with liver/lung metastases at baseline		Patients without liver/lung metastases at baseline		
	RIB400 + NSAI	RIB600 + NSAI	RIB400 + NSAI	RIB600 + NSAI	RIB400 + NSAI	RIB600 + NSAI	
ORR, per-protocol set							
No.	182	180	110	112	72	68	NA
ORR, %	48.9	56.1	52.7	55.4	43.1	57.4	
ORR ratio in per-protocol set	NA	NA	NA	NA	NA	NA	0.87 (0.74-1.0f3)
ORR, BOR, and CBR: ITT population							
No.	188	188	114	115	74	73	NA
ORR, %	47.9	54.8	50.9	54.8	43.2	54.8	
ITT set	NA	NA	NA	NA	NA	NA	0.87 (0.74-1.03)
BOR							
Complete response	2 (1.1)	3 (1.6)	0	1 (0.9)	2 (2.7)	2 (2.7)	
Partial response	88 (46.8)	100 (53.2)	58 (50.9)	62 (53.9)	30 (40.5)	38 (52.1)	
Stable disease	77 (41.0)	53 (28.2)	43 (37.7)	30 (26.1)	34 (45.9)	23 (31.5)	
Noncomplete response/ nonprogressive disease	0	1 (0.5)	0	0	0	1 (1.4)	NA
Progressive disease	14 (7.4)	17 (9.0)	10 (8.8)	14 (12.2)	4 (5.4)	3 (4.1)	
Unknown	7 (3.7)	14 (7.4)	3 (2.6)	8 (7.0)	4 (5.4)	6 (8.2)	
CBR ^a	142 (75.5)	133 (70.7)	85 (74.6)	78 (67.8)	57 (77.0)	55 (75.3)	

Abbreviations: ITT, intent to treat; NA, not applicable; NSAI, nonsteroidal aromatase inhibitor; RIB400, ribociclib, 400 mg; RIB600, ribociclib, 600 mg.

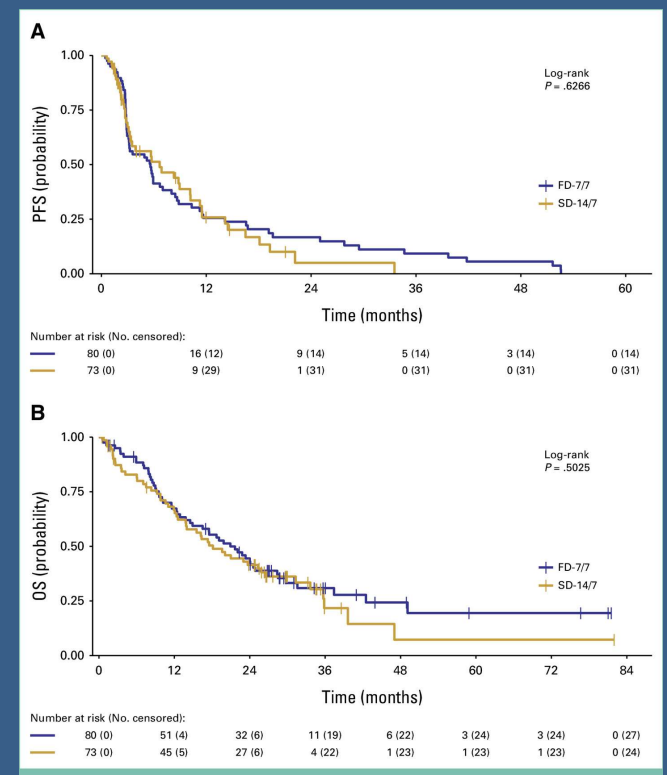
^a Includes complete and partial responses as well as stable disease lasting 24 weeks or longer.

CAPECITABINE DOSING STUDY

MBC and any previous lines of therapy were included.
Patients were randomly assigned 1:1 to either
FD-7/7 1500 mg BID or SD-14/7 or 1250 mg/m² BID

Key outcomes:
Response rate slightly lower with lower dose

PFS and OS same.



Khan, JCO Onc 2025.

LOWER DOSE CAPECITABINE HAS LESS SIDE EFFECTS

Event	FD-7/7 (n = 80), No. of Patients (%)	SD-14/7 (n = 73), No. of Patients (%)	P
Diarrhea			
Any grade	44 (55.0)	47 (64.4)	.2377
Grade 2 to 4	6 (7.5)	27 (37.0)	<.0001
Grade ≥3	2 (2.5)	18 (24.7)	<.0001
HFS			
Any grade	41 (51.3)	53 (72.6)	.0067
Grade 2 to 4	10 (12.5)	36 (49.3)	<.0001

CONCLUSIONS

- **Oncology drug development previously relied on MTD which was not patient friendly.**
- **Project Optimus has required companies to also study dose below MTD for efficacy**
- **Dose reductions do not impact PFS, OS for CDK 4/6 inhibitors or capecitabine**
- **Dose reductions increased compliance and decreased discontinuations of abemaciclib in early-stage breast cancer**
- **We must encourage industry to show data for all drugs**
- **QOL and side effects matter; one size fits all dosing is hard to justify**