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T.C.
Yıldırım Beyazıt Üniversitesi
Tıp Fakültesi
Sağlık Uygulama ve Araştırma Merkezi

Meme Kanseri
‘Kongrelerden Esintiler’

Doç.Dr. Mehmet Ali Nahit ŞENDUR

İç Hastalıkları, Tıbbi Onkoloji

29.12.2016


June 3-7, 2016
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COPENHAGEN 2016
ESMO congress
7-11 OCTOBER 2016
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2016
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SAN ANTONIO
BREAST CANCER SYMPOSIUM
Henry B. Gonzalez Convention Center, San Antonio, Texas, USA

ERKEN EVRE MEME KANSERİ
GÜNCEL GELİŞMELER

- **ER+ Meme Kanseri**
  - **Kombinasyon Stratejileri**
    - **CDK 4/6 inhibisyonu**
  - **Monoterapi yaklaşımları**

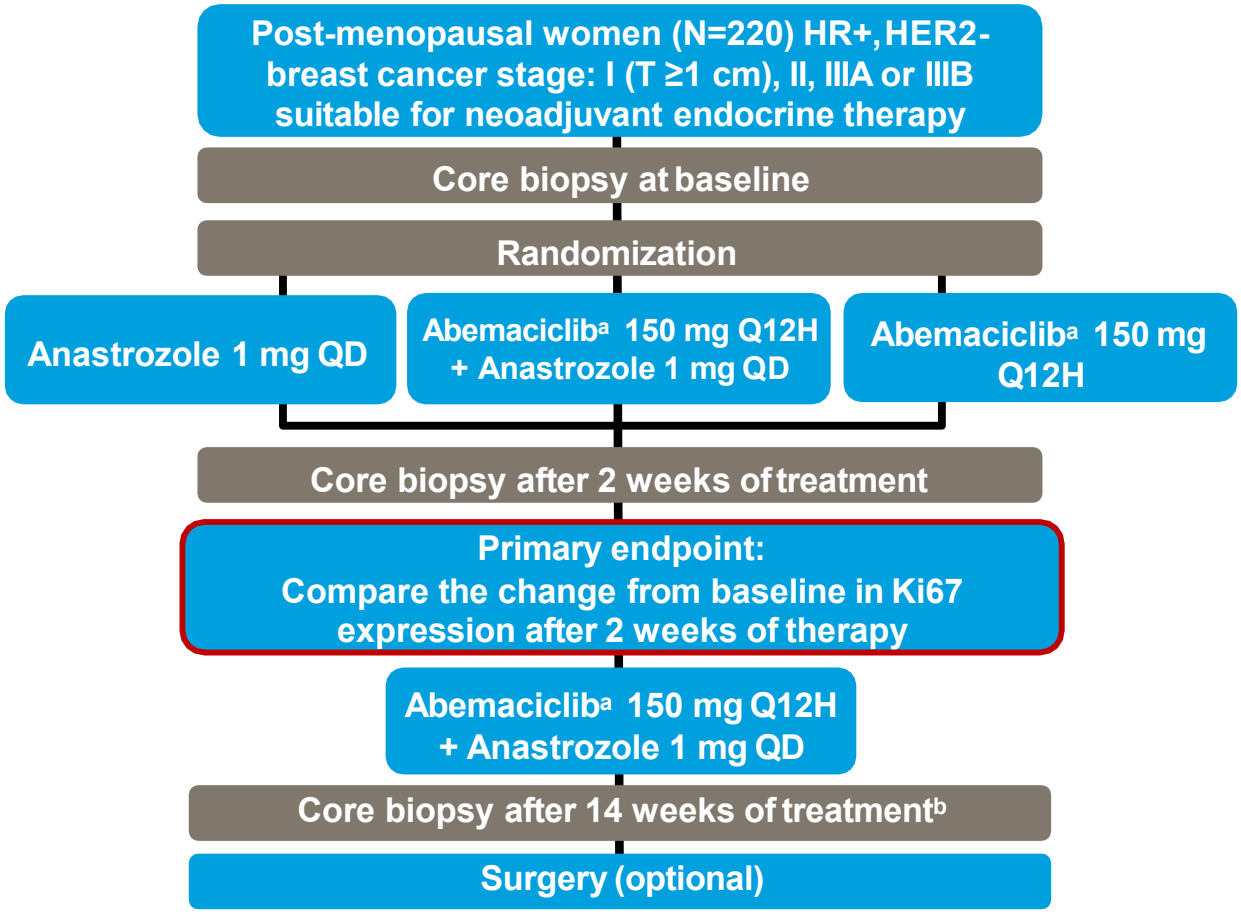
INTERIM RESULTS FROM neoMONARCH:A NEOADJUVANT PHASE II STUDY OF ABEMACICLIB IN POSTMENOPAUSAL WOMEN WITH HR+/HER2- BREAST CANCER

S. Hurvitz, et al.

Abstract: LBA1602

neoMONARCH: Faz 2 Çalışma Dizaynı

- Abemaciclib 150 mg BID is tolerable when dosed on a continuous schedule with endocrine therapy[1]
- The most common adverse event has been diarrhea
  - Typically occurred within the first 7 days of treatment
  - Manageable with use of loperamide or dose reduction
- Loperamide was administered prophylactically for the first 28 days then at discretion of investigator

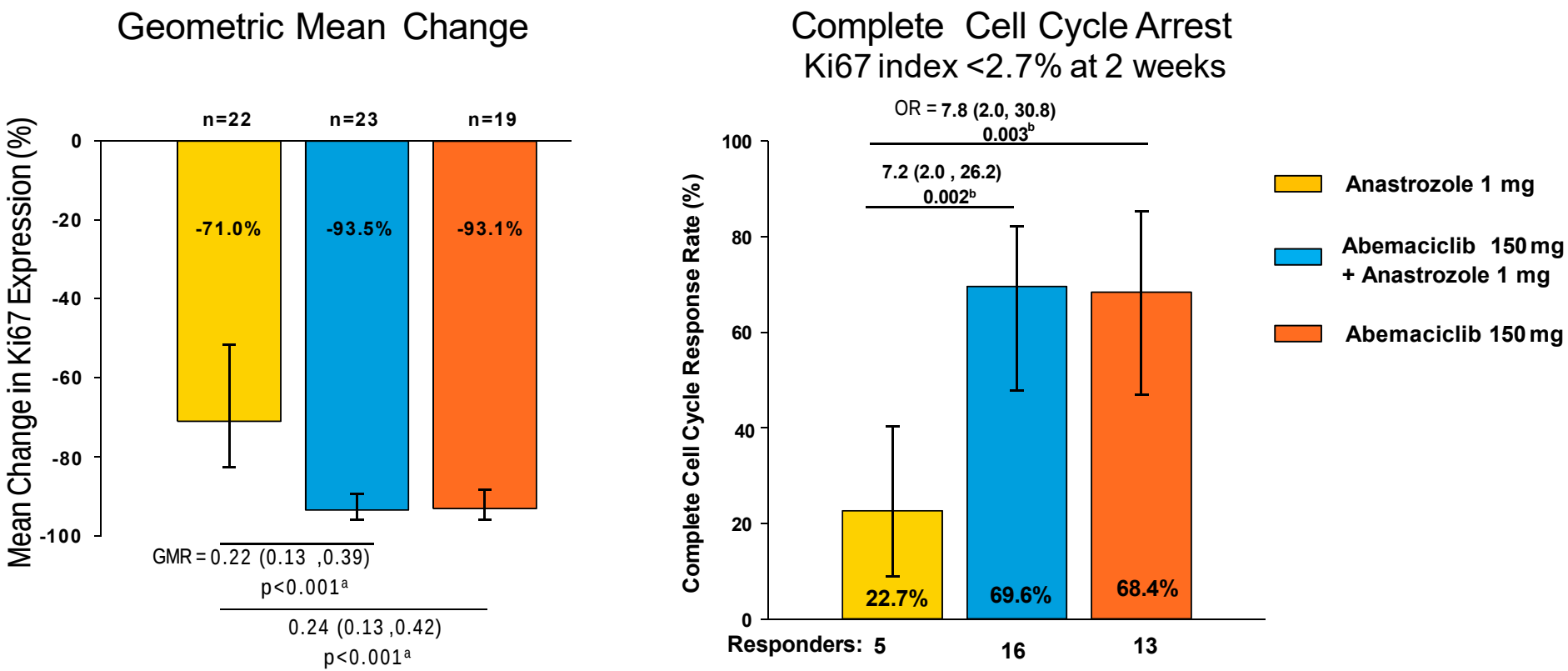


[1]Patnaik A et al. *Cancer Discovery* 2016;6:740-5

Abbreviations: HER2 = human epidermal growth factorreceptor 2; HR = hormone receptor; Q12H = every 12 hours; QD = once daily
[a]Participants receive loperamide with each dose of abemaciclib
[b]Participants who experience benefit following 14 weeks may remain on neoadjuvant therapy for up to 8 additional weeks

neoMONARCH: Ki67 Ekspresyonunda Değişim ve Yanıt

- Study met the boundary for statistical significance at the interim analysis (boundary p <0.03)



Abbreviations: GMR = geometric mean ratio, OR = odds ratio

[a]Geometric Mean Ratio (GMR), 2-sided 90% confidence interval (CI), p-value. p-values are based on a one-sided hypothesis test from a linear model with treatment, PR status (positive versus negative/unknown) and tumor size (<2 cm versus ≥2 cm and <5 cm versus ≥5 cm) as fixed effects.

[b]A responder is identified as a patient with a ln(Ki67) value of less than 1. Odds ratio (OR), 2-sided 90% CI, p value. p-value is calculated by Fisher's Exact test of a one-sided hypothesis.

neoMONARCH: Yan Etkiler

Investigator Assessed TEAEs >10% (N=173)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	All Grades n (%)
Diarrhea	59 (34.1)	15 (8.7)	5 (2.9)	0	79 (45.7)
Constipation	43 (24.9)	15 (8.7)	2 (1.2)	0	62 (35.8)
Nausea	39 (22.5)	17 (9.8)	2 (1.2)	0	58 (33.5)
Fatigue	31 (17.9)	16 (9.2)	1 (0.6)	0	49 (28.3)
Abdominal pain	22 (12.7)	6 (3.5)	5 (2.9)	0	33 (19.1)
Decreased appetite	19 (11.0)	5 (2.9)	4 (2.3)	0	28 (16.2)
Hot flush	17 (9.8)	3 (1.7)	0	0	20 (11.6)
Vomiting	12 (6.9)	5 (2.9)	2 (1.2)	0	19 (11.0)
Neutropenia	2 (1.2)	5 (2.9)	10 (5.8)	0	17 (9.8)
Laboratory Abnormalities[a]					
Creatinine increased[b]	106 (65.4)	44 (27.2)	1 (0.6)	0	151 (93.2)
Neutrophil count decreased	49 (30.2)	44 (27.2)	10 (6.2)	2 (1.2)	105 (64.8)
WBC decreased	50 (30.9)	45 (27.8)	3 (1.9)	1 (0.6)	99 (61.1)
ALT increased	52 (32.1)	7 (4.3)	3 (1.9)	0	63 (38.9)
AST increased	34 (21.0)	2 (1.2)	1 (0.6)	0	37 (22.8)
Anemia	0	27 (17.8)	0	0	27 (17.8)
Platelet count decreased	22 (13.6)	1 (0.6)	0	0	23 (14.2)

Abbreviations: ALT= alanine aminotransferase, AST= aspartate aminotransferase, TEAE=treatment-emergent adverse event, WBC = white blood cell; [a]N=162 for lab abnormalities listed, except anemia (N=152), [b]Abemaciclib is a competitive inhibitor of OCT2, MATE1, and MATE2-K, efflux transporters of creatinine

S1-03: First results from the multicenter phase III DATA study comparing 3 versus 6 years of anastrozole after 2-3 years of tamoxifen in postmenopausal women with hormone receptor-positive early breast cancer

Vivianne Tjan-Heijnen,[1] Irene van Hellemond,[1] Petronella Peer,[2] Astrid Swinkels,[3] Carolien Smorenburg,[4] Maurice van der Sangen,[5] Judith Kroep,[6] Hiltje De Graaf,[7] Aafke Honkoop,[8] Frans Erdkamp,[9] Franchette van den Berkmortel,[10] Jos Kitzen,[11] Maaike de Boer,[1] Wilfred de Roos,[12] Sabine Linn,[13] Alexander Imholz,[14] Caroline Seynaeve,[15] on behalf of the Dutch Breast Cancer Research Group (BOOG) for the DATA Investigators

[1]Maastricht University Medical Center, Maastricht; [2]Radboud University Medical Center, Nijmegen; [3]Netherlands Comprehensive Cancer Organization IKNL, Utrecht; [4]Medical Center Alkmaar, Alkmaar; [5]Catharina Hospital, Eindhoven; [6]Leiden University Medical Center, Leiden; [7]Medical Center Leeuwarden, Leeuwarden; [8]Isala Clinics, Zwolle; [9]Zuyderland Medical Center, Sittard; [10]Zuyderland Medical Center, Heerlen; [11]Albert Schweitzer Hospital, Dordrecht; [12]Gelderse Vallei Hospital, Ede; [13]Netherlands Cancer Institute, Amsterdam; [14]Deventer Hospital, Deventer; [15]Erasmus MC Cancer Institute, Rotterdam; all in The Netherlands

Design DATA study

San Antonio Breast Cancer Symposium, December 6-10, 2016

DATA Study Design

- ✓ Postmenopausal at randomization
- ✓ ER+ and/or PR+
- ✓ No sign of disease recurrence
- ✓ M0 breast cancer
- ✓ After 2-3 years adjuvant tamoxifen

Stratification
- Nodal status
- ER/PR status
- HER2 status
- Tamoxifen duration

→ 6 years anastrozole, 1 mg daily

→ 3 years anastrozole, 1 mg daily

- 80% power to detect an increase in 3-year adapted Disease-Free Survival (aDFS) from 90% to 94%, i.e., a hazard ratio (HR) of 0.60 and a significance level of 0.05
- Accounting for 10% drop-out: 950 patients per group to be included (n=1912 patients actually included)
- Minimum follow-up: ≥6 years after randomization, i.e., ≥ 3 years of adapted follow-up (last patient included in August 2009)

Maastricht UMC+ DATA
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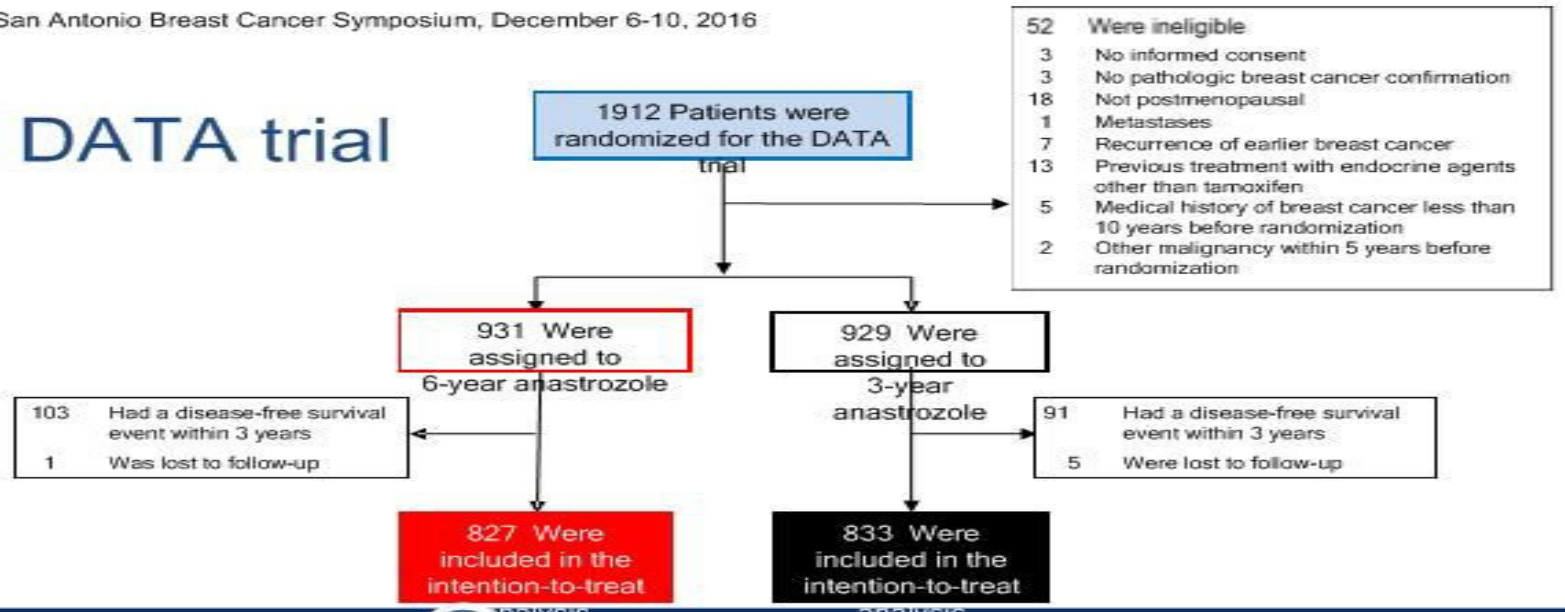
DATA trial



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Patient and tumor characteristics well balanced

Characteristic		6-year Anastrozole (N=827)	3-year Anastrozole (N=833)
Age at randomization – no. (%)			
	< 49 years	141 (17.0)	160 (19.2)
	50-59 years	342 (41.4)	328 (39.4)
	≥ 60 years	344 (41.6)	345 (41.4)
Tumor status – no. (%)			
	pT1	376 (45.5)	383 (46.0)
	pT2	392 (47.4)	382 (45.9)
	pT3/4	58 (7.0)	67 (8.0)
Nodal status – no. (%)			
	pN0 / pN0(i+)	266 (32.2)	282 (33.8)
	pN1	434 (52.5)	457 (54.9)
	pN2 / pN3	127 (15.3)	94 (11.3)
Histological grade – no. (%)			
	Grade I	139 (16.8)	158 (19.0)
	Grade II	430 (52.0)	415 (49.8)
	Grade III	229 (27.7)	238 (28.6)
Hormone-receptor status – no. (%)			
	ER *and* PR positive	627 (75.8)	633 (76.0)
	ER *or* PR positive	200 (24.2)	200 (24.0)
HER2 status – no. (%)			
	Positive	18 (2.2)	22 (2.6)
	Negative	745 (90.1)	748 (89.8)
	Unknown	64 (7.7)	63 (7.6)

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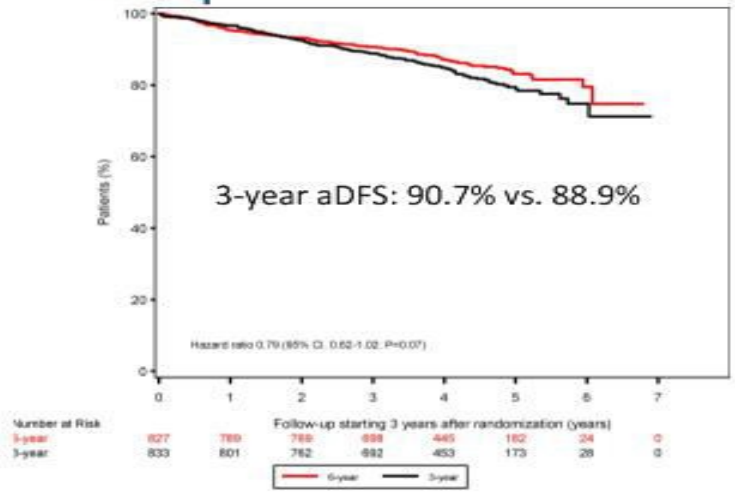
adapted Disease-Free Survival (aDFS)



N=1660	6-year Anastrozole (N=827)	3-year Anastrozole (N=833)
5-year aDFS (%)	83.1	79.4
HR (95% CI)	0.79 (0.62 – 1.02)	
P-value	0.07	

Maastricht UMC+

DATA

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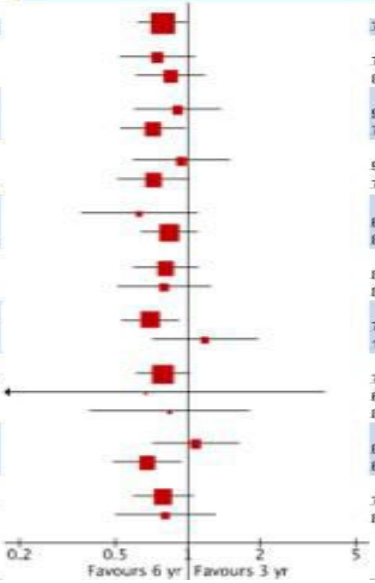
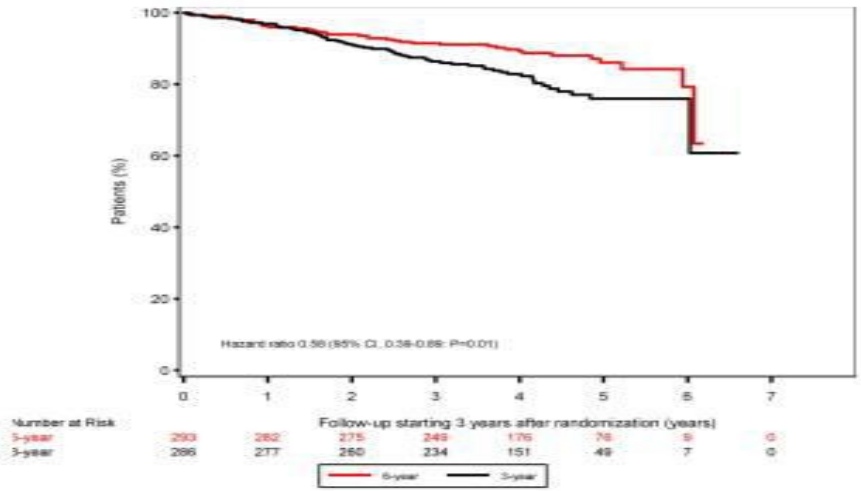
Subgroup analyses

Adapted Disease-free Survival	No. of patients		No. of Events		Hazard ratio (95% CI)	5 -yr adapted Disease-free Survival (%)	
	6-year	3-year	6-year	3-year		6-year	3-year
All	827	833	116	145	79 (0.62 - 1.02)	83.1	79.4
Age at randomization							
< 60 years	483	488	49	64	75 (0.52 - 1.10)	88.2	85.1
≥ 60 years	344	345	67	81	85 (0.61 - 1.19)	75.3	70.9
Tumor status							
pT1	376	383	45	50	91 (0.60 - 1.38)	85.0	84.4
pT2 and pT3/4	450	459	71	94	72 (0.51 - 0.98)	81.5	75.3
Nodal status							
pN negative	286	282	32	39	94 (0.59 - 1.50)	85.4	83.4
pN positive	561	551	84	106	72 (0.52 - 1.00)	82.2	77.4
Histology							
Lobular	154	140	24	32	63 (0.36 - 1.12)	83.0	72.4
Other	673	693	92	113	84 (0.64 - 1.11)	83.2	80.8
Histological grade							
Grade I and II	589	573	76	93	81 (0.59 - 1.10)	84.6	80.9
Grade III	229	238	36	49	80 (0.51 - 1.26)	80.3	75.4
Hormone receptor status							
ER and PR positive	627	633	83	117	70 (0.53 - 0.92)	84.8	78.8
ER or PR positive	200	200	33	28	18 (0.71 - 1.96)	77.4	81.3
HER2 status							
Negative	745	748	102	126	79 (0.61 - 1.03)	83.2	79.7
Positive	18	22	2	4	67 (0.12 - 3.80)	88.9	85.0
Unknown	64	63	12	15	84 (0.39 - 1.81)	79.8	75.8
Chemotherapy (neo)adjuvant							
No	262	263	48	49	88 (0.71 - 1.64)	77.1	78.0
Yes	565	570	68	96	68 (0.49 - 0.92)	85.8	80.1
Duration prior tamoxifen							
≤ 2.5 years	606	598	85	104	79 (0.59 - 1.05)	82.5	78.9
> 2.5 years	221	235	31	41	81 (0.50 - 1.29)	85.2	80.7



DATA

aDFS if ER+ *and* PR+, HER2-, pN+, Chemo+



N=597	6-year Anastrozole (N=293)	3-year Anastrozole (N=286)
5-year aDFS (%)	86.0	75.9
HR (95% CI)	0.58 (0.39 – 0.89)	
P-value	0.01	

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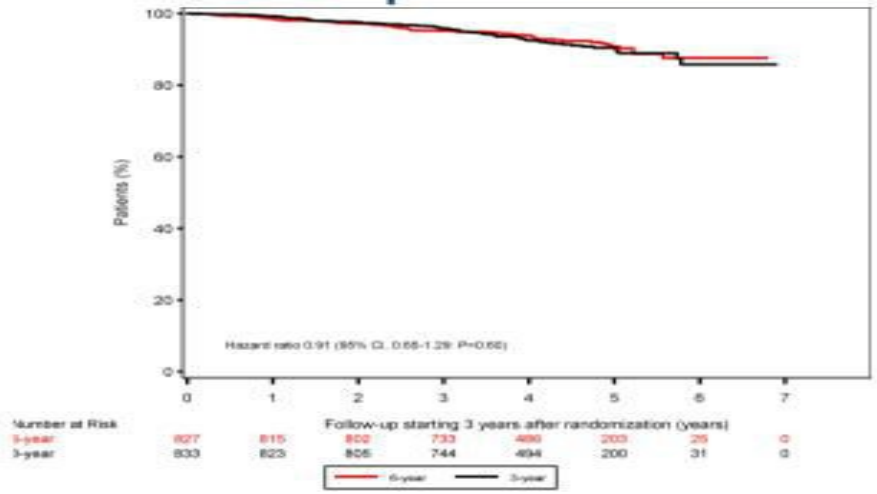
adapted Overall Survival (aOS)



N=1660	6-year Anastrozole (N=827)	3-year Anastrozole (N=833)
5-year aOS (%)	90.8	90.4
HR (95% CI)	0.91 (0.65 – 1.29)	
P-value	0.60	

Median adapted follow-up of 4.1 years (P_5=2.9, P_{95}=5.8 years)

DATA ÇALIŞMASI: SONUÇLAR

- The findings of the DATA study do not support extended adjuvant AI use after 5 years of sequential endocrine therapy for all postmenopausal hormone receptor-positive breast cancer patients.
- It suggests benefit for a selected group of patients, i.e., those with both ER *and* PR positive disease, HER2-negative disease, large tumor load, and prior chemotherapy.
- Extended AI use is associated with an increased number of bone and muscle adverse events.
- We will perform a follow-up analysis when all patients have reached a minimum adapted follow-up of 9 years.

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A Randomized, Double-blinded, Placebo-controlled Clinical Trial of Extended Adjuvant Endocrine Therapy with Letrozole in Postmenopausal Women with Hormone-receptor (+) Breast Cancer who have Completed Previous Adjuvant Tx with an Aromatase Inhibitor: Results from NRG Oncology/NSABP B-42

Eleftherios P. Mamounas, MD,[1,2] Hanna Bandos, PhD[1,3] Barry C. Lembersky, MD,[1,4] Charles E. Geyer, Jr., MD,[1,5] Louis Fehrenbacher, MD,[1,6] Mark L. Graham, MD,[1,7] Stephen L. Chia, MD, FRCPC[1,8] Adam M. Brufsky, MD, PhD,[1,4] Bryan T. Hennessy, MD,[1,9] Gamini S. Soori, MD,[1,10] Shaker R. Dakhil, MD,[1,11] Thomas E. Seay, MD,[1,12] James L. Wade, III, MD,[1,13] Edward C. McCarron, MD,[1,14] Soonmyung Paik, MD,[1,15] Sandra M. Swain, MD,[1,16] D. Lawrence Wickerham, MD,[1,17] Norman Wolmark, MD[1,17]

[1]NRG Oncology/NSABP (NSABP Legacy trials are now part of the NRG Oncology portfolio), Pittsburgh, PA; [2]UF Cancer Center at Orlando Health, Orlando, FL; [3]University of Pittsburgh, Pittsburgh, PA; [4]University of Pittsburgh Cancer Institute, Pittsburgh, PA; [5]Massey Cancer Center, Virginia Commonwealth University, Richmond, VA; [6]Kaiser Permanente Oncology Clinical Trials Norther California, Vallejo, CA; [7]Southeast Cancer Control Consortium, Goldsboro, NC; [8]British Columbia Cancer Agency (BCCA),Vancouver, British Columbia, Canada; [9]Cancer Trials Ireland (Formerly known as Irish Clinical Oncology Research Group - ICORG), Dublin, Ireland; [10]Missouri Valley Cancer Consortium, Omaha, NE; [11]CCOP, Wichita Cancer Center of Kansas, Wichita, KS; [12]Georgia NCI Community Oncology Research Program, Atlanta, GA; [13]CCOP, Central Illinois, Decatur, IL; [14]MedStar Franklin Square Medical Center/Weinberg Cancer Institute, Baltimore, MD; [15]Severance Biomedical Science Institute and Department of Medical Oncology, Yonsei University College of Medicine, Seoul, Korea; [16]Washington Cancer Institute, MedStar Washington Hospital Center, Washington, DC; [17]Allegheny Health Network Cancer Institute, Pittsburgh, PA

NSABP B-42: Schema

- Postmenopausal Pts with ER+ or PR+ Breast Cancer
- Stage I, II, or IIIa invasive BC at diagnosis
- Disease-free After 5 Years of Endocrine Therapy

AI X 5 yrs **or** TAM X ≤ 3 yrs → AI to Complete 5 yrs

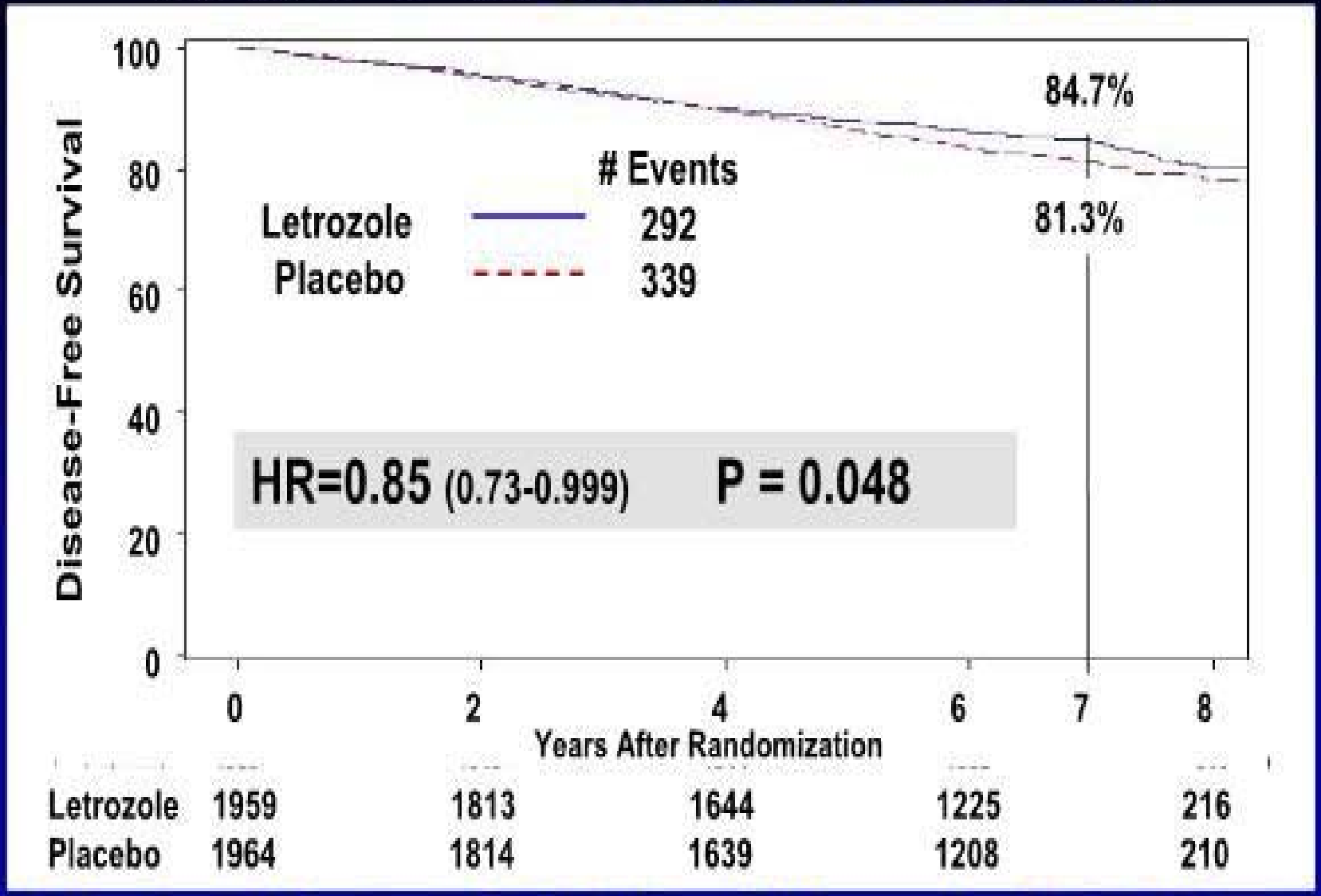
Stratification:

Pathological nodal status (Negative, Positive)

Prior adjuvant TAM (Yes, No)

Lowest BMD T score: spine, hip, femur (>-2.0, ≤ -2.0 SD)

NSABP B-42: Disease-Free Survival



***P-value did not reach statistical significance level of 0.0418**

NSABP B-42: Multivariate Analysis for DFS

Characteristic		No. of pts (N=3,923)	% DFS events	HR (95%CI)	P
Treatment	Placebo Letrozole	1964 1959	17.3 14.9	0.86 (0.73,1.00)	0.05
Age	<60 ≥60	1350 2573	12.1 18.2	1.55 (1.29,1.86)	<0.01
Path Nodal Status	Negative Positive	2251 1672	14.3 18.5	1.33 (1.13,1.56)	<0.01
Prior Tamoxifen	No Yes	2388 1535	17.6 13.7	0.78 (0.66,0.92)	<0.01
Surgery Type	Lumpectomy Mastectomy	2386 1537	14.6 18.4	1.24 (1.05,1.45)	<0.01

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NSABP B-42: Letrozole Effect on DFS in Subgroups

		HR	P	P Interaction
All Patients		0.85	0.048	
Nodes	Negative	0.86	0.17	0.99
	Positive	0.85	0.16	
Prior TAM	No	0.91	0.34	0.27
	Yes	0.75	0.04	
T-score	≤ -2.0	0.70	0.03	0.16
	> -2.0	0.92	0.34	
Age	<60	0.86	0.32	0.87
	≥60	0.84	0.06	

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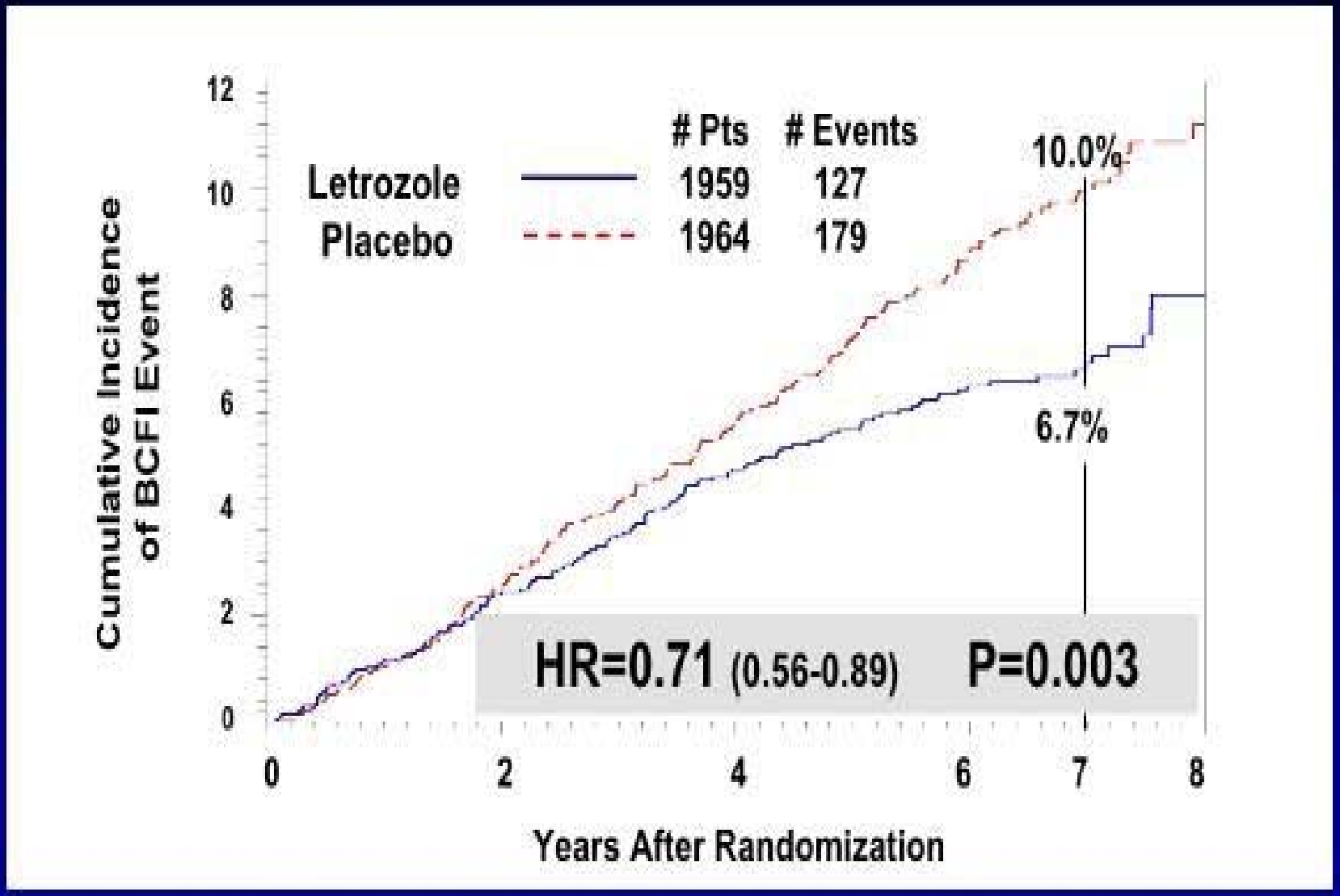
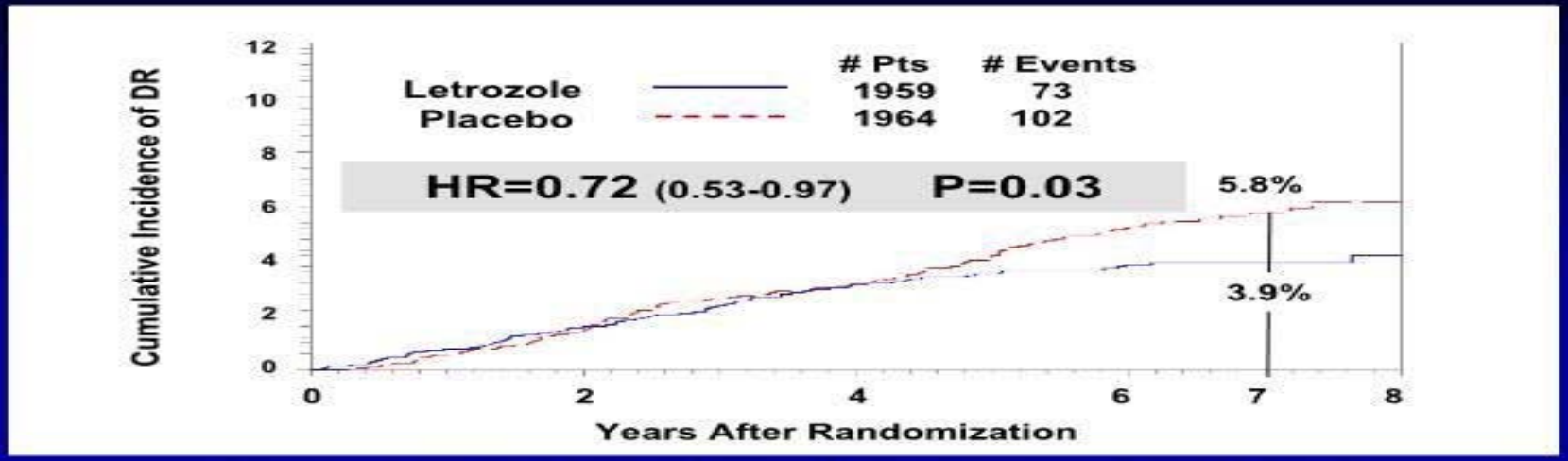
NSABP B-42:
Cumulative Incidence of BCFI Event



NSABP B-42: Cumulative Incidence of Distant Recurrence



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NSABP B-42: Overall Survival

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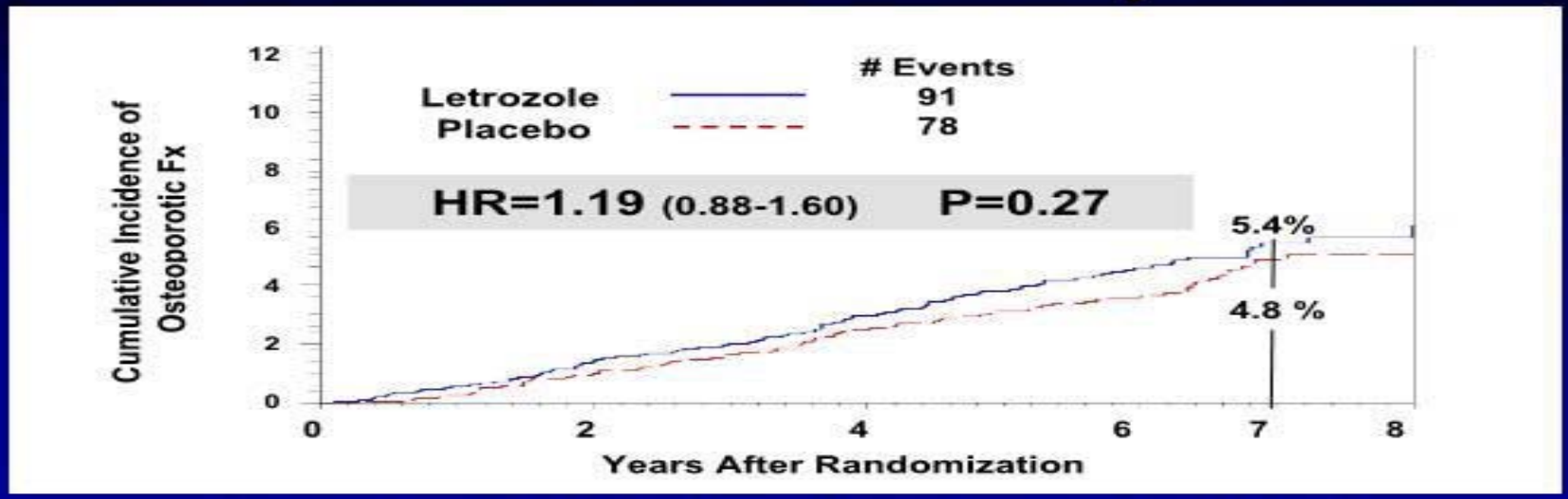
NSABP B-42:
Cumulative Incidence of Osteoporotic Fx



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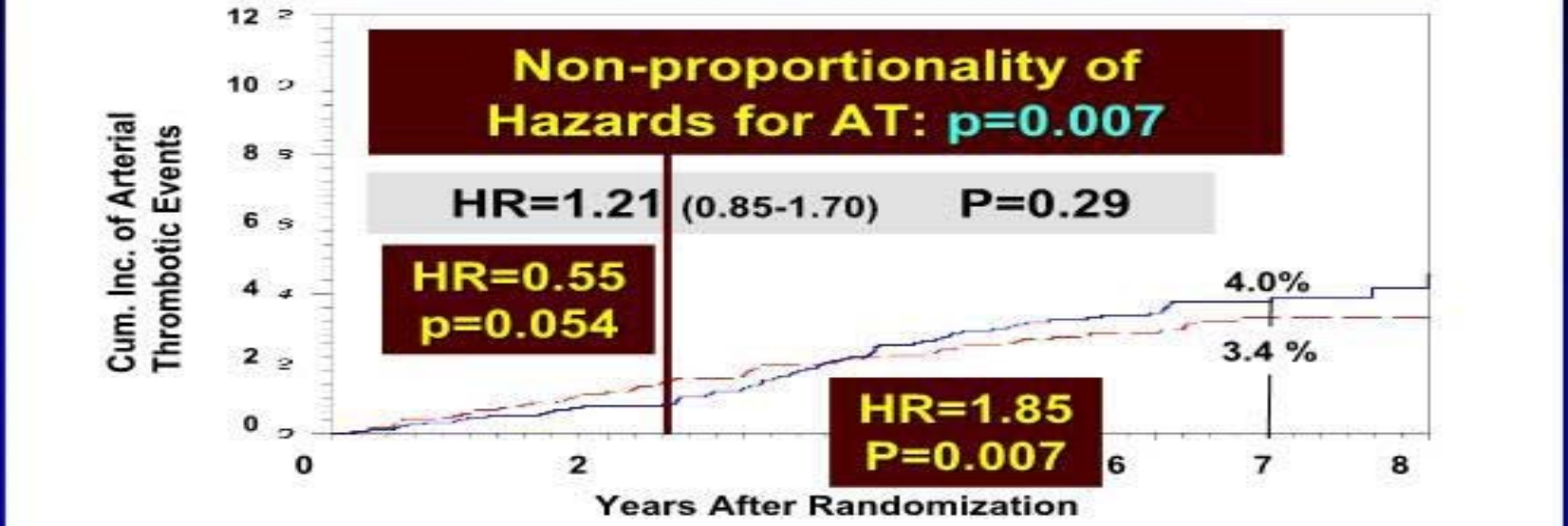
NSABP B-42:
Cum. Inc. of Arterial Thrombotic Events



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NSABP B-42: Summary

- The beneficial effect of extended L therapy on DFS did not reach statistical significance (15% reduction)
- No significant difference in overall survival with L vs. P
- Extended L provided:
  - Statistically significant improvement in BCFI (29% reduction in BCFI event)
  - Statistically significant reduction in the rate of DR (28% reduction in DR)
- L did not significantly increase risk of osteoporotic fractures
- Risk of arterial thrombotic events was elevated for L after 2.5 years

NSABP B-42 and NCIC MA.17R
Comparison of HRs for Various Endpoints

Trial	Effect	Endpoint			
		DFS	BCFI	DR	OS
B-42 (n=3,923 631 events)	HR	0.85*	0.71	0.72	1.15
	P-value	0.048	0.003	0.03	0.22
MA.17R[1] (n=1,918 165 events)	HR	0.80***	0.66**	NR	0.97
	P-value	0.06	0.01	NR	0.83

* DFS (Recurrence + CBC + Non-breast CA + Deaths as first Events)

** Selected as DFS in MA.17R (Recurrence + CBC)

*** DFS (Recurrence + CBC + Deaths from any cause)

[1]Goss P. et al: NEJM 2016

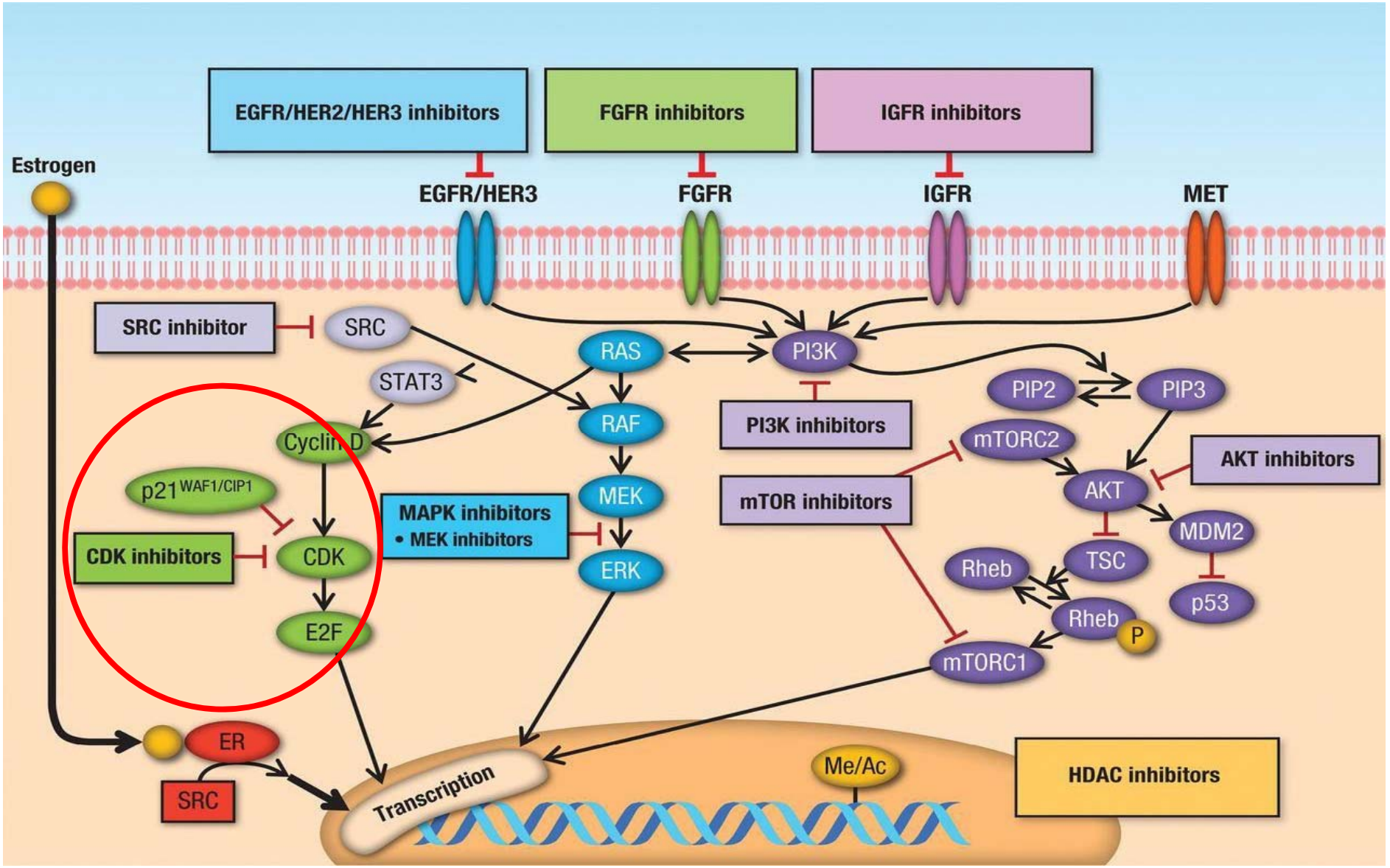
METASTATİK MEME KANSERİ
GÜNCEL GELİŞMELER

- **ER+ Metastatik Meme Kanseri**
  - **Kombinasyon Stratejileri**
    - **CDK 4/6 inhibisyonu**
    - **MTOR inhibisyonu**
  - **Monoterapi yaklaşımları**
- **Her-2 + Metastatik Meme Kanseri**
  - **Trastuzumab**
- **Umut vadeden Çalışmalar**
  - **Umut vadeden Sonuçlar**
  - **Yeni Potansiyel Hedefler**

METASTATİK MEME KANSERİ
GÜNCEL GELİŞMELER

- **ER+ Metastatik Meme Kanseri**
  - **Kombinasyon Stratejileri**
    - **CDK 4/6 inhibisyonu**
    - **MTOR inhibisyonu**

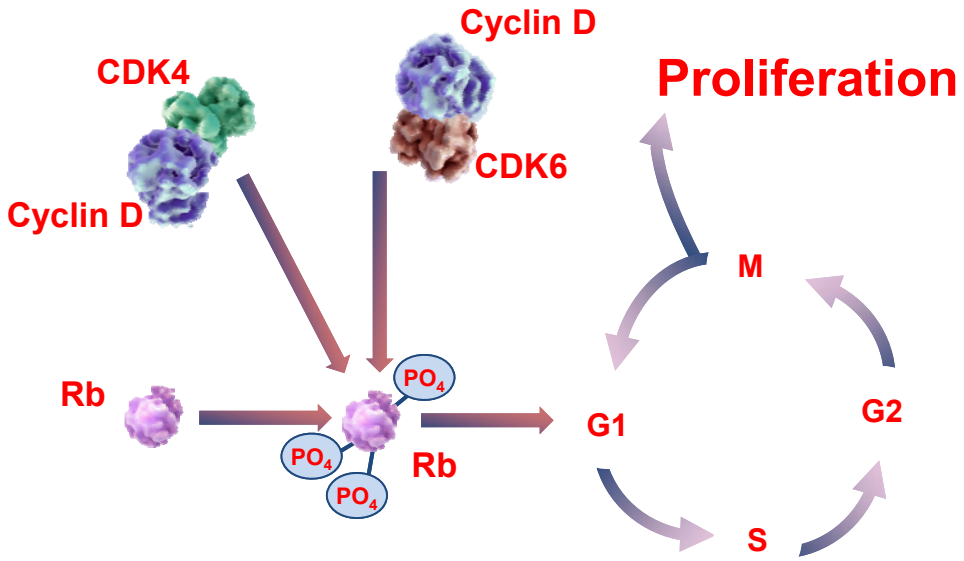
ER+ Metastatik Meme Kanserinde Hedefler



Johnston SRD. J Natl Cancer Inst 2015; Aug 6;107(10). 107:djv212

Meme kanserinde CDK4 & 6'nın Rolü

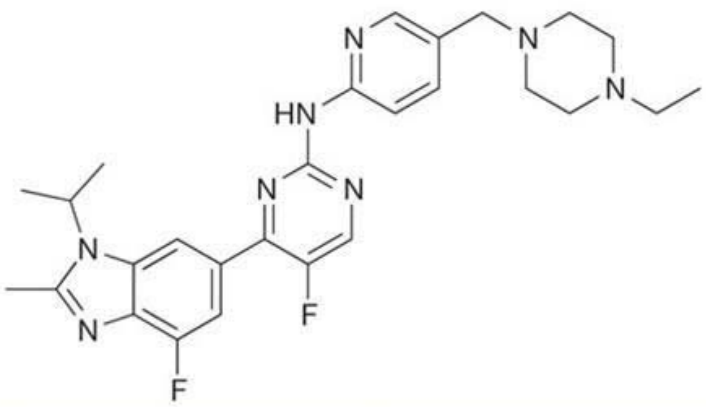
- D type cyclins activate CDK4 & 6 which phosphorylate Rb resulting in G1 to S progression
- Estrogen stimulates cyclin D1 in HR+ breast cancer[1]
- Short term inhibition of CDK4 & 6 leads to G1 arrest that rebounds upon withdrawal[2]
- Continuous inhibition leads to prolonged cell cycle arrest with initiation of apoptosis or senescence[3]
- This led to the hypothesis that continuous target inhibition may be an effective strategy



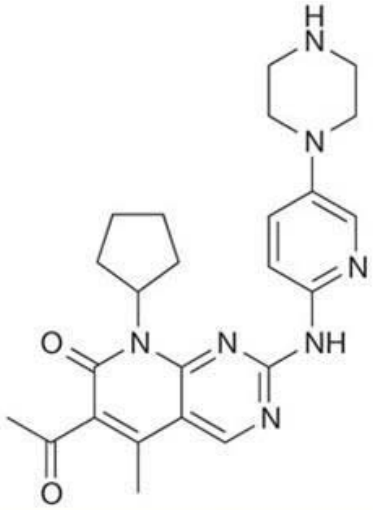
[1]Altucci L et al. 1996 *Oncogene* 12:2315-24
[2]Gelbert et al. 2014 *Invest New Drugs* 32: 825-37
[3]Beckman et al. *AACR Annual Meeting* 2016

Selektif CDK 4/6 İnhibitörleri

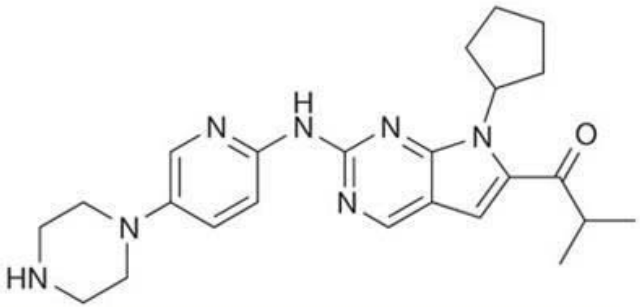
Abemaciclib



Palbociclib



Ribociclib



	Abemaciclib (LY-2835219)	Palbociclib (PD-0332991)	Ribociclib (LEE011)
IC_{50}	CDK1: >1 μM	CDK1: >10 μM	CDK1: >100 μM
	CDK2: >500 nM	CDK2: >10 μM	CDK2: >50 μM
	CDK4: 2 nM	CDK4: 9–11 nM	CDK4: 10 nM
	CDK5: ND	CDK5: >10 μM	CDK5: ND
	CDK6: 5 nM	CDK6: 15 nM	CDK6: 39 nM
	CDK7: 300 nM	CDK7: ND	CDK7: ND
	CDK9: 57 nM	CDK9: ND	CDK9: ND

Nature Reviews | Clinical Oncology

O'Leary B, et al. Nat Rev Clin Oncol. 2016;13(7):417–430.

Abstract 512

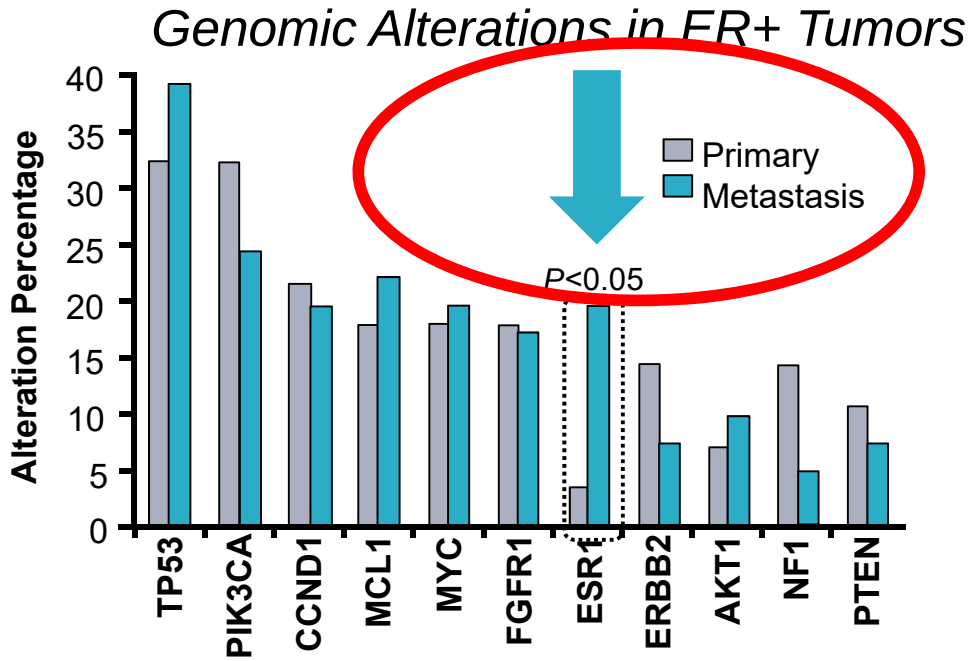
Efficacy of Palbociclib Plus Fulvestrant in Patients With Metastatic Breast Cancer and *ESR1* Mutations in Circulating Tumor DNA

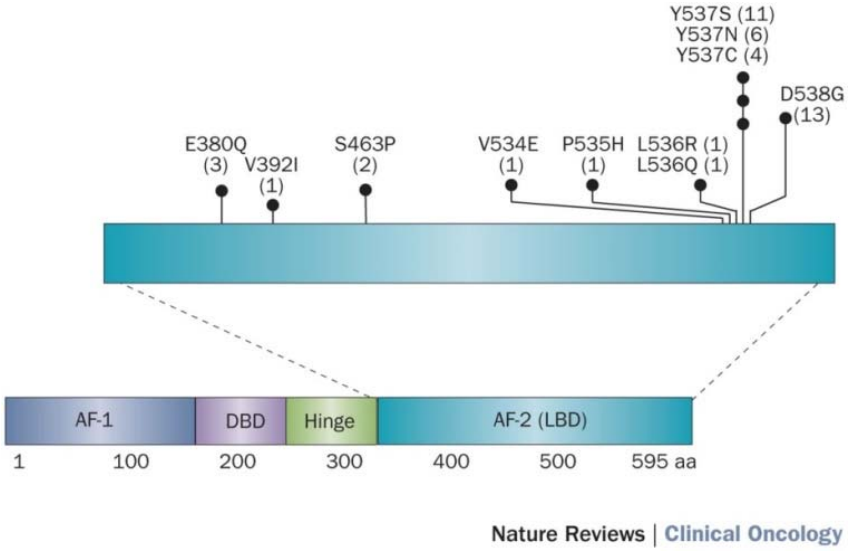
Nicholas C. Turner,[1] Yuqiu Jiang,[2] Ben O'Leary,[1] Sarah Hrebien,[1] Massimo Cristofanilli,[3] Fabrice André,[4] Sibylle Loibl,[5] Patricia A. English,[2] Ke Zhang,[2] Sophia Randolph,[2] Cynthia Huang Bartlett,[6] Maria Koehler,[6] Sherene Loi[7]

[1]Royal Marsden Hospital and Institute of Cancer Research, London, UK; [2]Pfizer Inc, La Jolla, CA, USA; [3]Robert H Lurie Comprehensive Cancer Center, Feinberg School of Medicine, Chicago, IL, USA; [4]Institut Gustave Roussy, Villejuif, France; [5]German Breast Group Forschungs GmbH, Neu-Isenburg, Germany; [6]Pfizer Inc, New York, NY, USA; [7]Peter MacCallum Cancer Centre, East Melbourne, Victoria, Australia

Presented at ASCO 2016; June 3, 2016; Chicago, IL, USA

ESR1 Mutasyonları



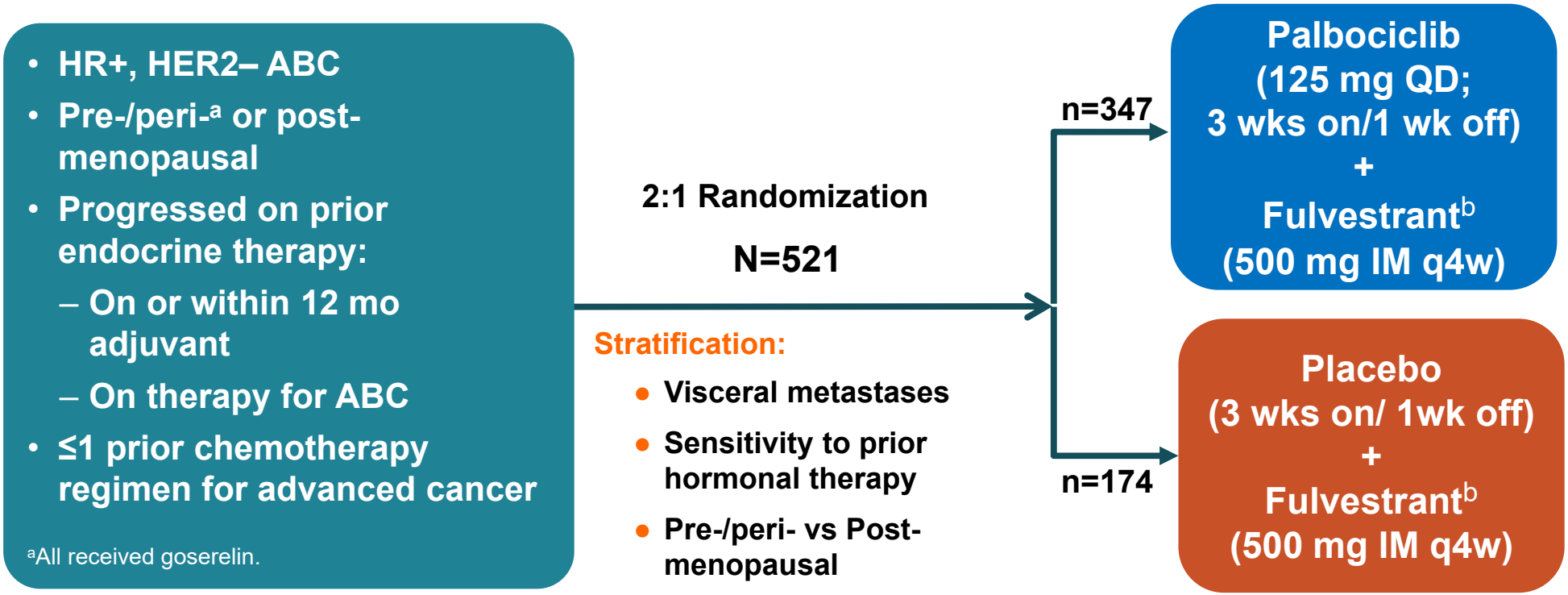


ESR1 mutations occur in ~20% of AI-resistant, ER+ breast cancer

AI=aromatase inhibitor; ER=estrogen receptor.

Toy et al. *Nat Genet*, 2013.
Robinson et al. *Nat Genet*, 2013.
Merenbakh-Lamin et al. *Cancer Res*, 2013.
Jeselsohn et al. *Clin Cancer Res*, 2014.
Jeselsohn et al. *Nat Rev Clin Oncol*, 2015.

PALOMA-3 Çalışma Dizaynı

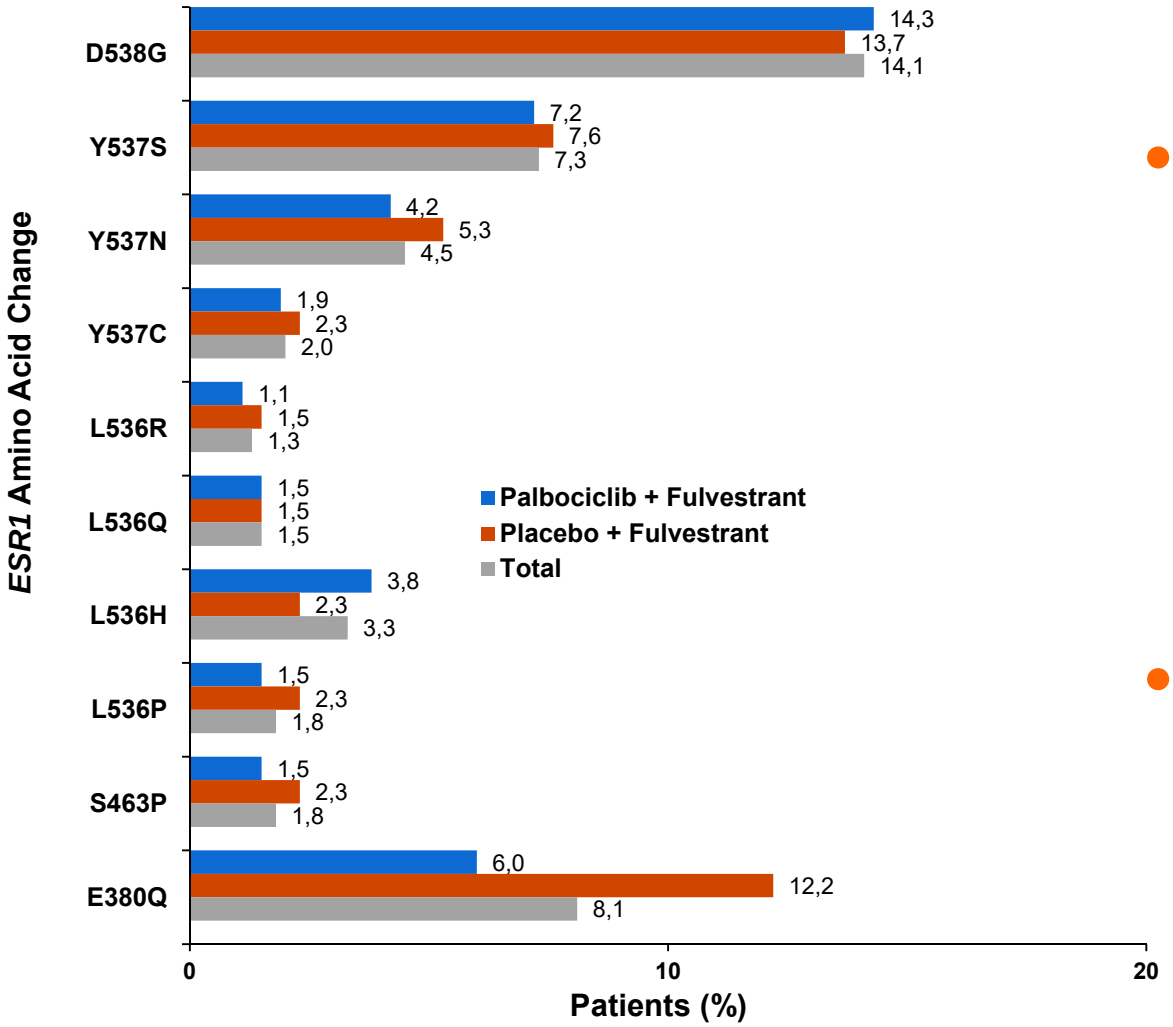


- **Baseline plasma samples collected for circulating tumor DNA analysis were processed within 1 hour of venipuncture.**

[b]Administered on Days 1 and 15 of Cycle 1.

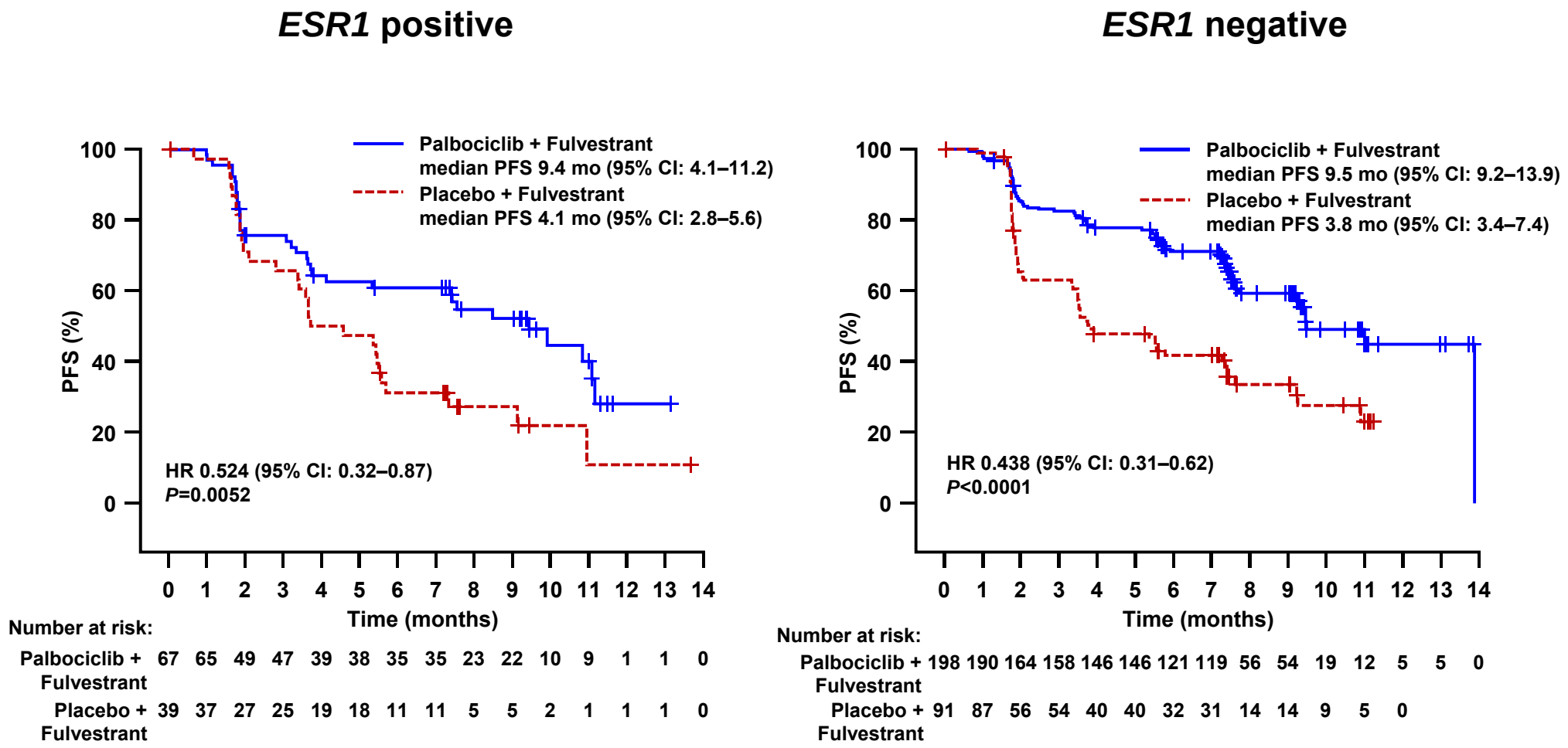
Clinicaltrials.gov NCT01942135. Turner et al *NEJM*. 2015.

PALOMA-3'de ESR1 Mutasyonları



- *ESR1* mutations were detected in 27% (106/396) of patients with plasma samples
  - Amino acid changes P535H and V534E were not detected
- *ESR1* mutations were polyclonal in 38% (40/106) of mutation-positive patients

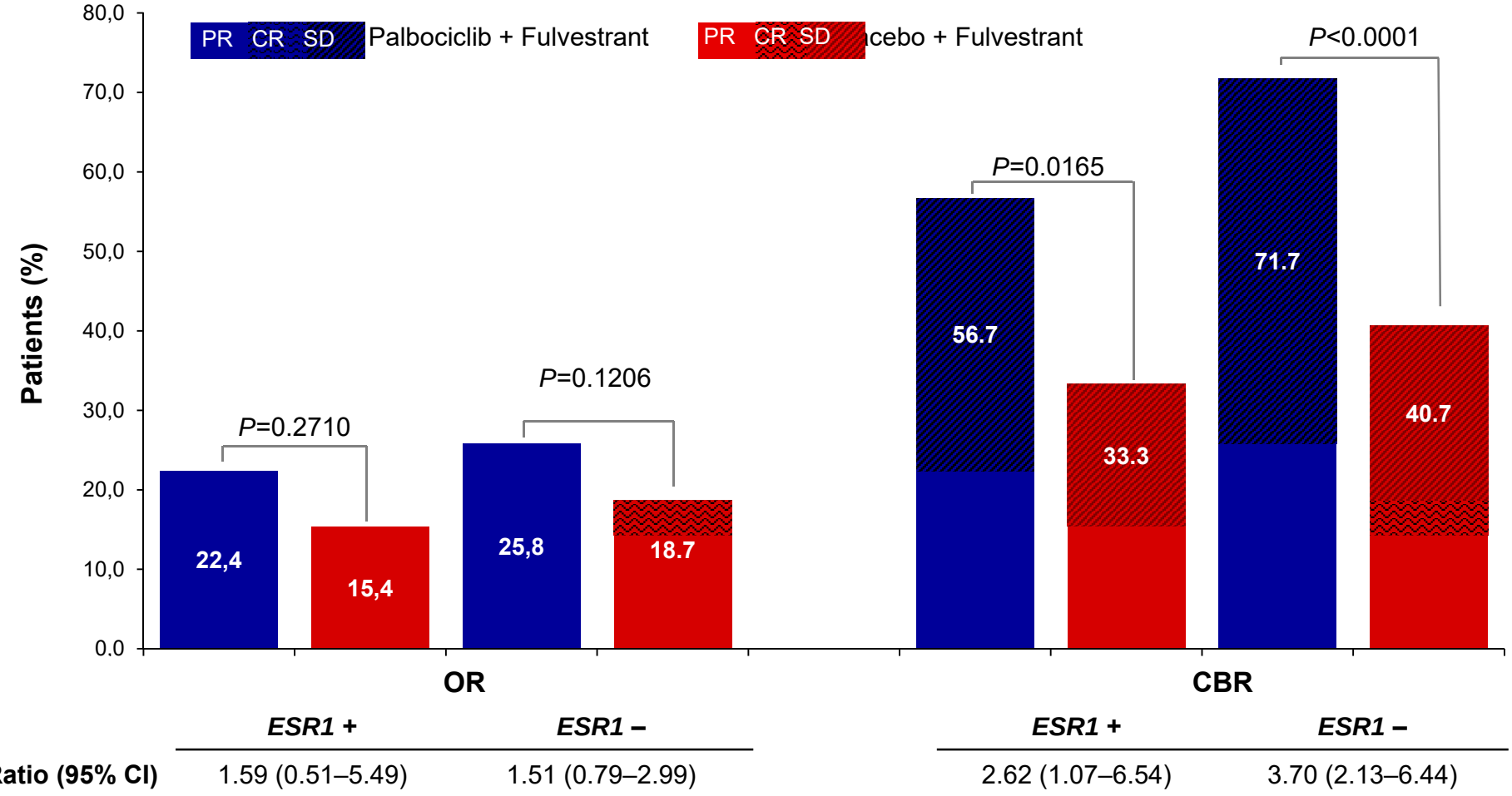
ESR1 Mutasyon Durumuna Göre PFS



PFS=progression-free survival.

March 2015 final PFS data cut, Cristofanilli et al. *Lancet Oncol,* 2016.

ESR1 Mutasyon Durumuna Göre Yanıt Oranları



CBR=clinical benefit response; CR=complete response; OR=objective response; PR=partial response; SD=stable disease ≥24 months.

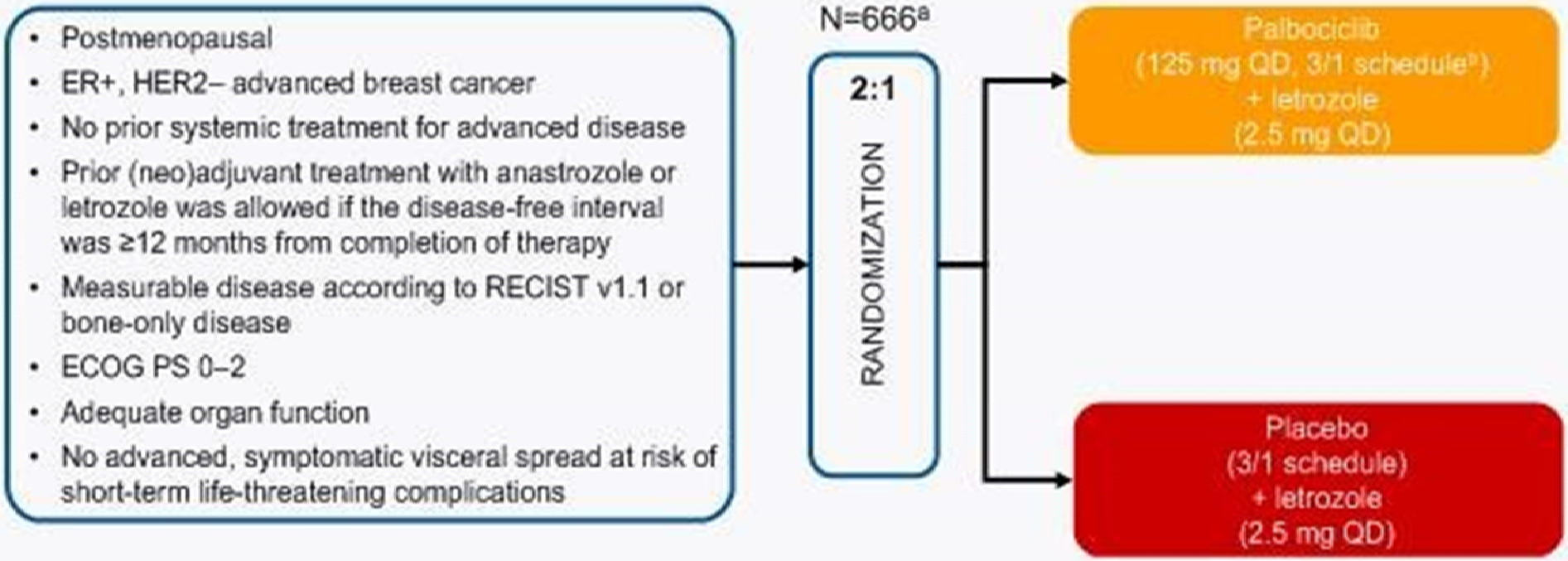
PALOMA-2: Primary Results From a Phase 3 Trial of Palbociclib Plus Letrozole Compared With Placebo Plus Letrozole in Postmenopausal Women With ER+/HER2– Advanced Breast Cancer

Richard S. Finn,[1] Miguel Martin,[2] Hope S. Rugo,[3] Stephen Jones,[4] Seock-Ah Im,[5] Karen Gelmon,[6] Nadia Harbeck,[7] Oleg N. Lipatov,[8] Janice M. Walshe,[9] Stacy Moulder,[10] Eric Gauthier,[11] Dongrui R. Lu,[11] Sophia Randolph,[11] Veronique Dieras,[12] Dennis J. Slamon[1]

[1]David Geffen School of Medicine, Los Angeles, CA, USA; [2]Hospital Gregorio Maranon, Universidad Complutense, Madrid, Spain; [3]University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA, USA; [4]US Oncology Research, The Woodlands, TX, USA; [5]Seoul National University Hospital, Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea; [6]British Columbia Cancer Agency, Vancouver, BC, Canada; [7]Brustzentrum der Universitaet Muenchen (LMU), Munich, Germany; [8]SBMI Republican Clinical Oncologic Dispensary, Ufa, Russian Federation; [9]All-Ireland Cooperative Oncology Research Group (ICORG), Ireland; [10]University of Texas, MD Anderson Cancer Center, Houston, TX, USA; [11]Pfizer Inc, La Jolla, CA, USA; [12]Institut Curie, Paris, France

PALOMA-2: Phase III Study Design in Postmenopausal Patients with ER+, HER2– Advanced Breast Cancer

- Phase III, randomized, double-blind trial at 186 centers in 17 countries
- Treatment continued until objective disease progression, unacceptable toxicity, or withdrawal of consent. Crossover was not allowed
- Palbociclib/placebo dose reductions were allowed per protocol. Letrozole dose reductions were not permitted



Finn RS, et al. *N Engl J Med* 2016 Nov 17;375(20): 1925–1936