THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

New Directions in Adjuvant Endocrine Therapy:

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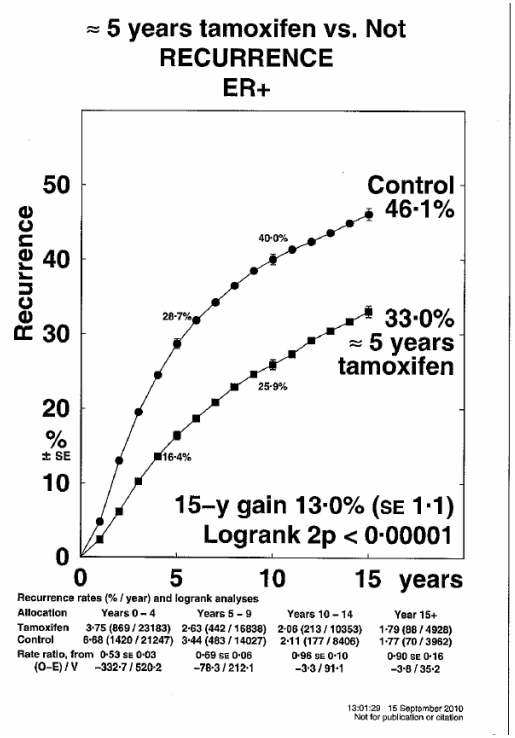
15th Annual New Orleans Summer Cancer Meeting

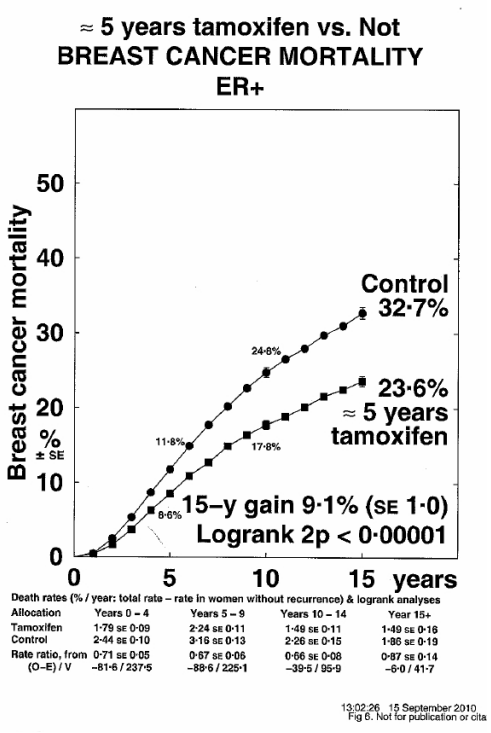
Disclosures

- Research support: Novartis
- Advisory Board/Consultant: Roche, Pfizer, AZ, Abbott; Genomic Health

Adjuvant endocrine therapy

- Cornerstone of the treatment of patients with HR+ breast cancer





Long term risk of recurrence

Lee Cheng et al. Cancer Epidemiol Biomarkers Prev 2012;21:800-809

AACR American Association for Cancer Research
Cancer Epidemiology, Biomarkers & Prevention

THE LONGER, THE BETTER?

Trial	Treatments											De Facto Comparisons (years)	HR for DFS	Exposed to AI Years 0-5, %
Year after diagnosis	1	2	3	4	5	6	7	8	9	10	15			
Studies of tamoxifen after 5 years of tamoxifen														
ATLAS					*							5 *v* 10	0.75-0.99†	0
ATTOM					*							5 *v* 10	0.75-0.99†	0
Studies of AI after 5 years of tamoxifen														
MA.17					*							5 *v* 10	0.57	0
NSAPB B-33					*							5 *v* 10	0.68	0
ABCSG 6a‡					*							5 *v* 8	0.62	0
Studies of extended AI after 5 years therapy that included AI														
DATA			*									6 *v* 9	0.79	100
NSABP B-42					*							5 *v* 10	0.85	100
MA.17R										§		10 *v* 15	0.66	100
Studies of optimal duration or dosing in years 5 to 10														
BOOG 2006-05 IDEAL					*							7.5 *v* 10	0.92	88
ABCSG 16					*							7 *v* 10	1.007	49
SOLE					*							Continuous *v* intermittent	1.08	81

Tamoxifen
Tam/AI
AI

Burnstein, J Clin Oncol 2018

Extended Endocrine Trials-Tamoxifen

Extended Endocrine Trials	Meno-pausal Status	Treatment	Trial Size	Median follow-up	Risk of Recurrence (Extended vs Not Extended)
ATLAS	Pre- and Post	Tamoxifen (5y) vs no treatment	6,846	10+ y	**21.4% vs 25.1%** **Δ 3.7%**
aTTom	Pre- and Post	Tamoxifen (5y) vs no treatment	6,953	8.6 y	**28.0% vs 32.9%** **Δ 4.9%**

Davies C et al., Lancet. 2013 ;381(9869):805-16.
Gray et al., J Clin Oncol 31, 2013 (suppl; abstr 5).

MA.17R Trial Design

Oct 2004 - May 2009

N=1928

Any duration of prior Tamoxifen

4.5-6 yrs of Aromatase Inhibitor

Letrozole 2.5 mg qd

RANDOMIZE

Letrozole 2.5 mg qd

Placebo

5 yrs

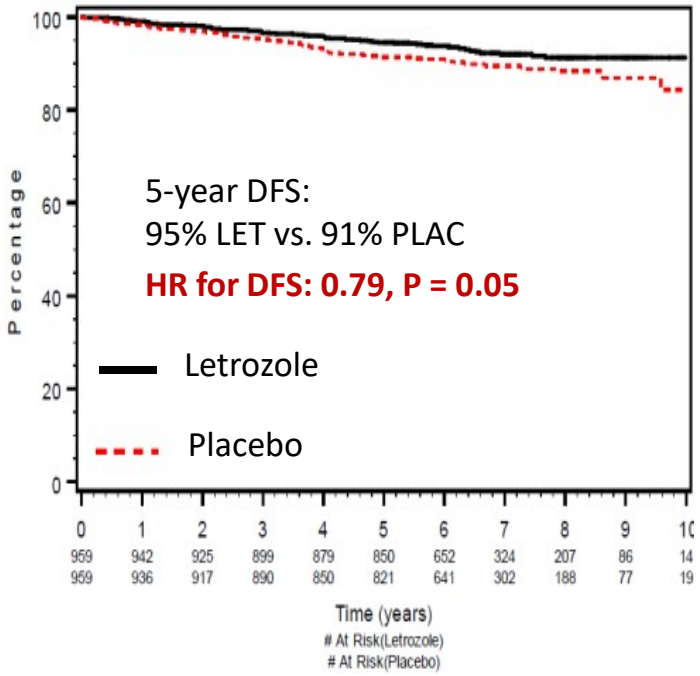
ER+ and/or PR+ breast cancer
Postmenopausal and disease-free
Completed 4.5-6 years of adjuvant AI
Any time of prior TAM
Minimum life expectancy ≥5 years (no exclusion for age alone)

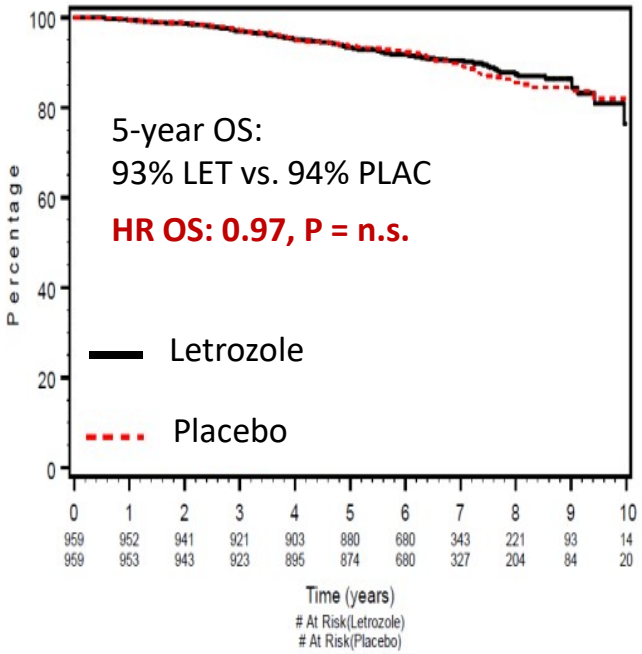
STRATIFICATION FACTORS
- Lymph node status at diagnosis
- Prior adjuvant chemotherapy
- Interval between the last dose of AI and randomization
- Duration of prior tamoxifen (0; >0 to <2; 2 to 4.5; >4.5)

54% N+
58% Adjuvant chemotherapy

ASCO 2016, Presented by: P.E. Goss

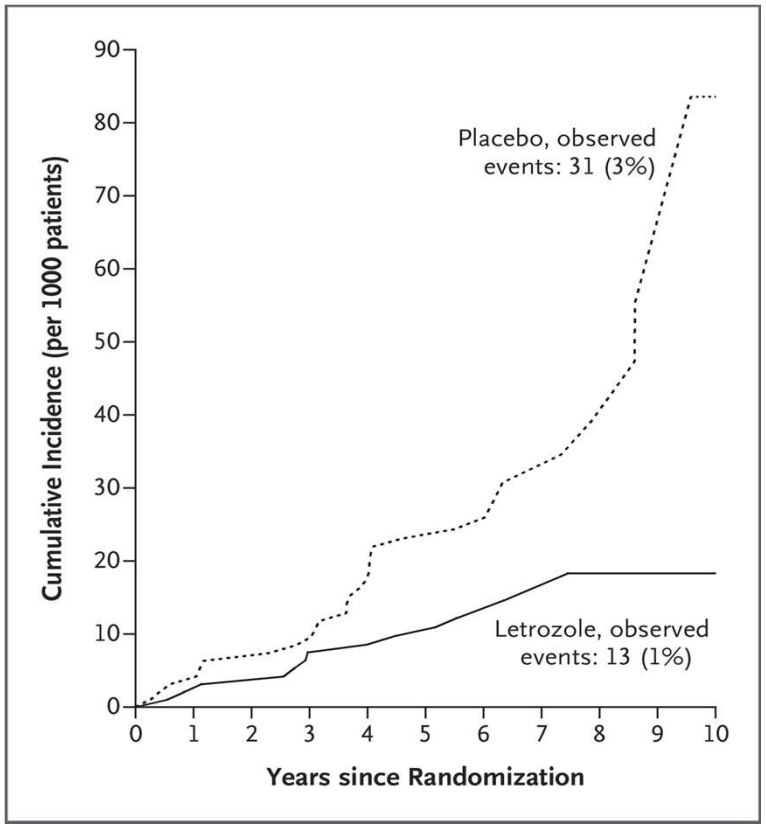
MA.17R –DFS (med F/U of 6.3 yrs)





Goss et al, NEJM, 2016

MA.17R - Contralateral Breast Cancer



HR CBC: 0.42

P = 0.007

58% Reduction in CBC

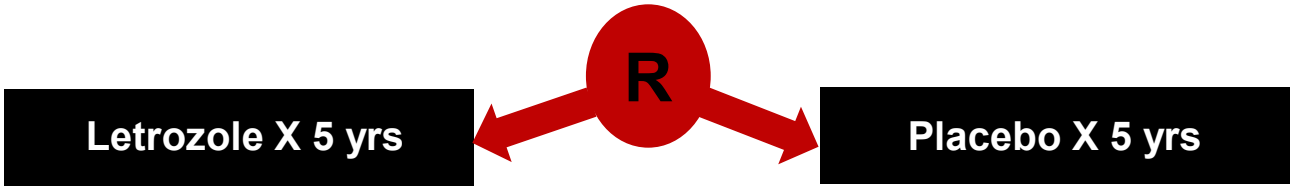
ASCO 2016, Presented by: P.E. Goss

NSABP B-42: Schema

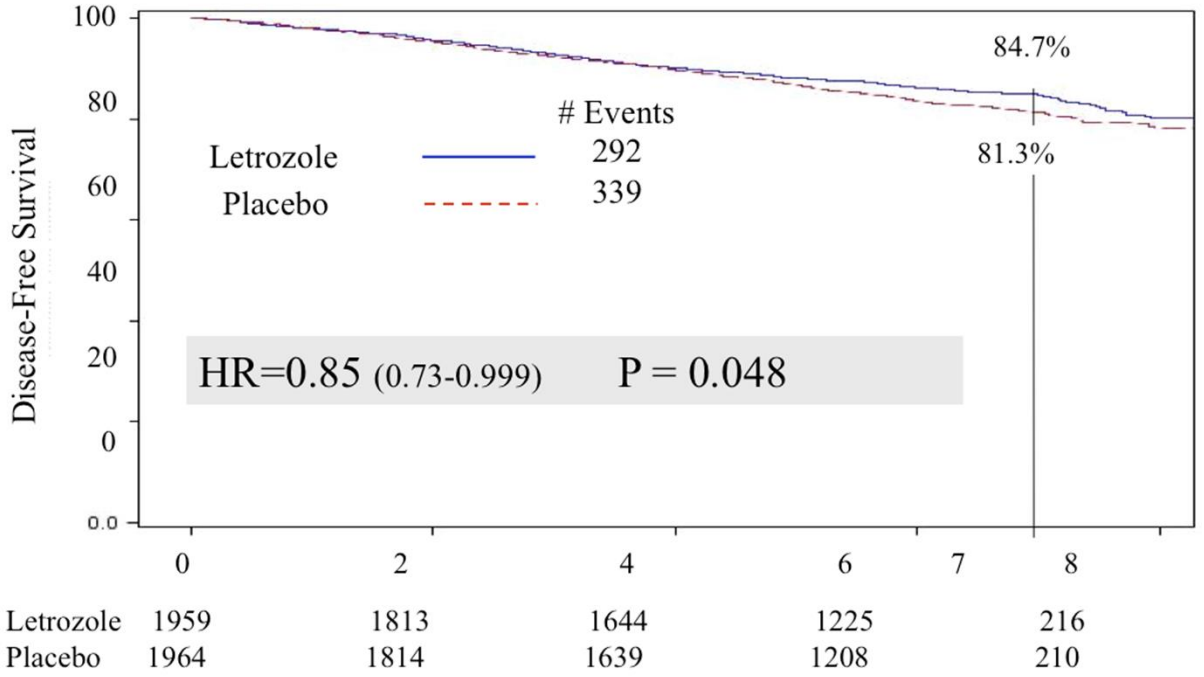
- Postmenopausal Pts with ER+ or PR+ Breast Cancer
- Stage I, II, or IIIa invasive BC at diagnosis
- Disease-free After 5 Years of Endocrine Therapy

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)

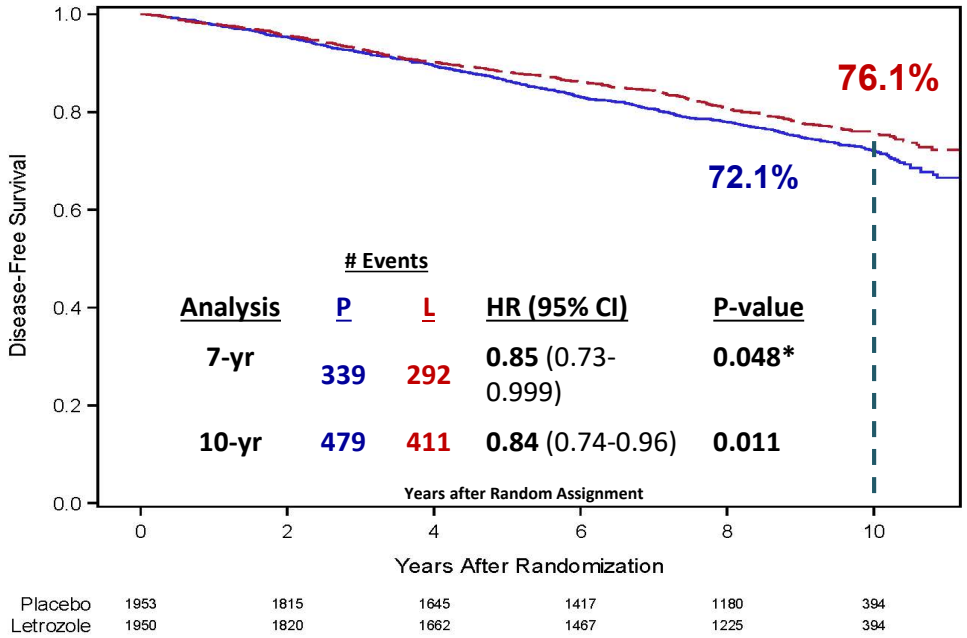


NSABP B-42: Disease-Free Survival



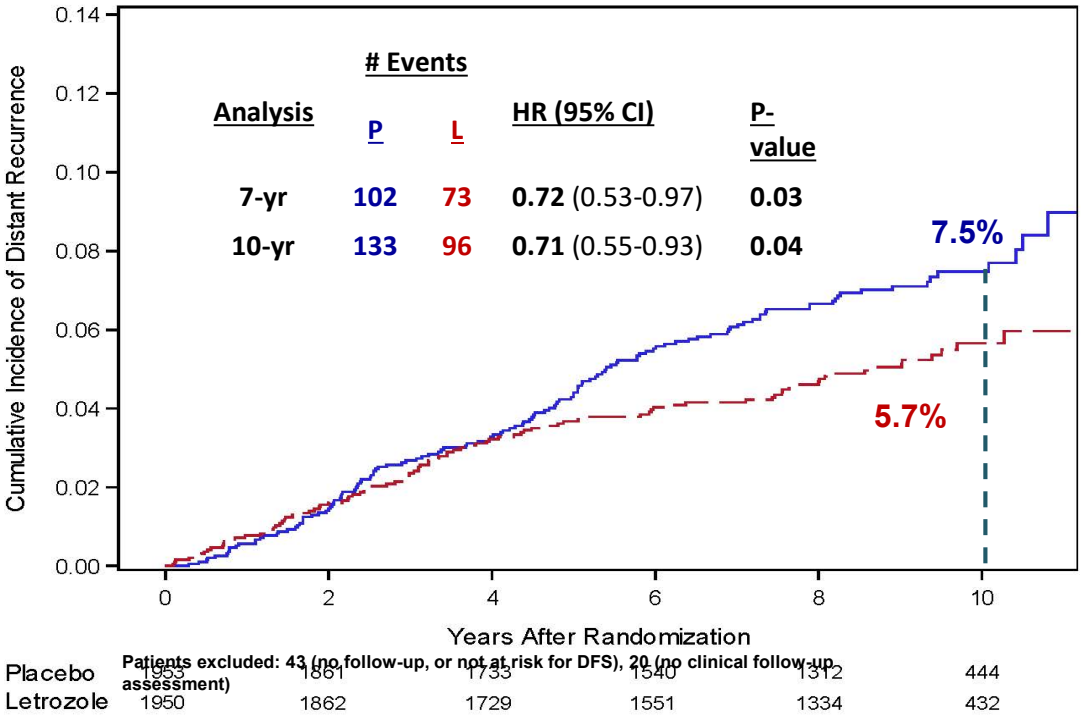
*P-value did not reach statistical significance level of 0.0418

10-year Disease-Free Survival



Patients excluded: 43 (no follow-up, or not at risk for DFS), 20 (no clinical follow-up assessment)

10-year Distant Recurrence



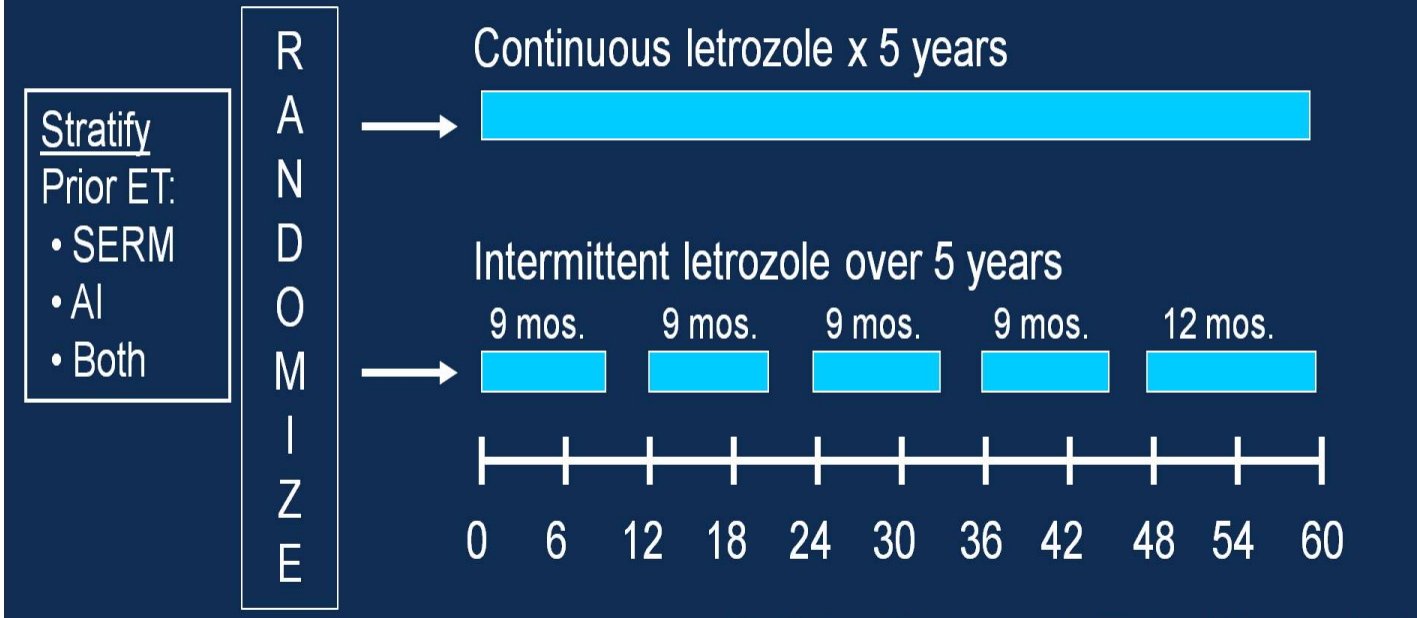
Patients excluded: 43 (no follow-up, or not at risk for DFS), 20 (no clinical follow-up assessment)

DFS First Events by Treatment

First Event	Placebo (n=1953) #	Placebo (n=1953) %	Letrozole (n=1950) #	Letrozole (n=1950) %
Distant Recurrence	**111**	**5.7**	**81**	**4.2**
Local Recurrence	**43**	**2.2**	**45**	**2.3**
Second Primary Cancer	**230**	**11.8**	**183**	**9.4**
Breast	81	4.1	52	2.7
Non-Breast	149	7.6	131	6.7
Death	**95**	**4.9**	**102**	**5.2**
Total First Event	**479**	**24.5**	**411**	**21.1**

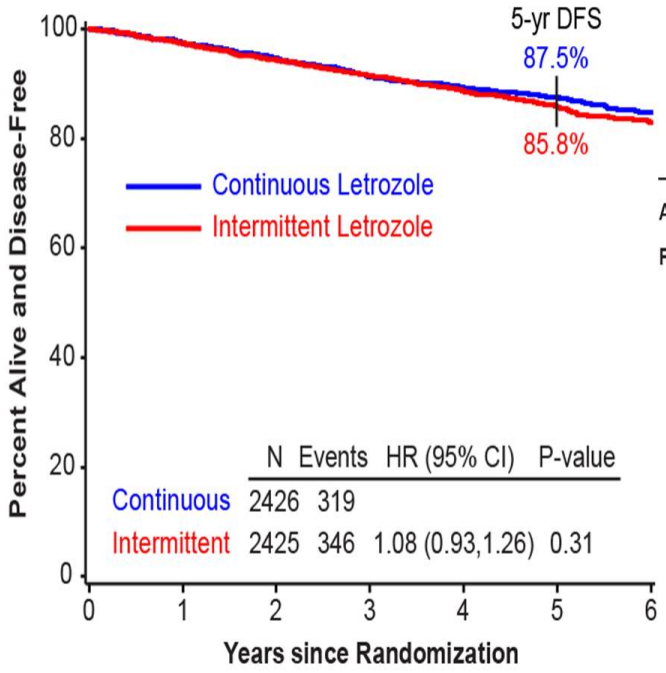
SOLE: Study of Letrozole Extension

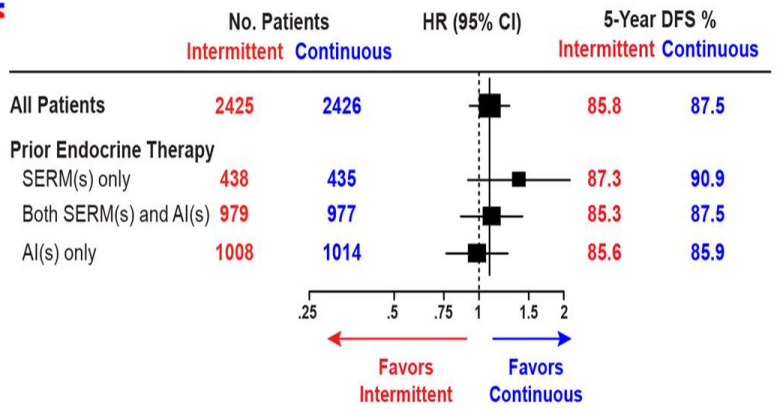
After 4 to 6 years of Prior Adjuvant Endocrine Therapy
Postmenopausal, HR-positive, Node-positive



4884 Patients Randomized in ITT, Nov 2007 - July 2012

Primary Endpoint: Disease-Free Survival



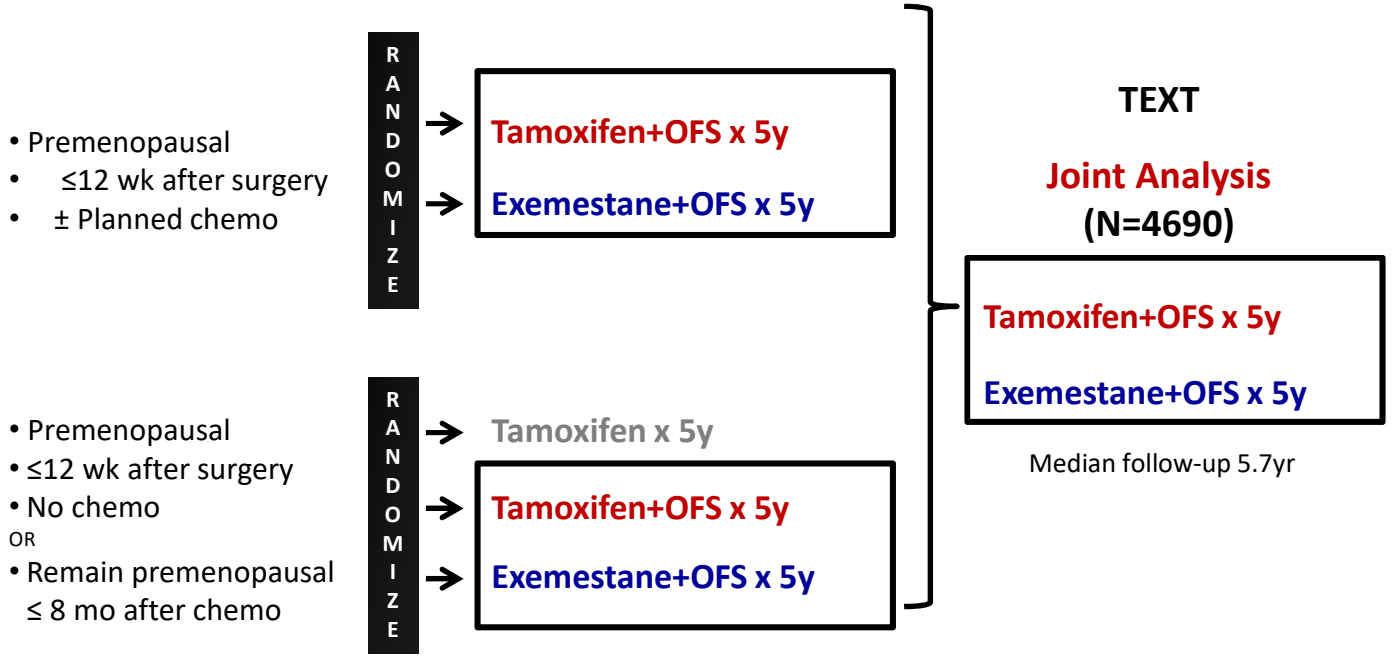


Median age: 60 60 mos. median follow-up

THE MORE, THE BETTER?

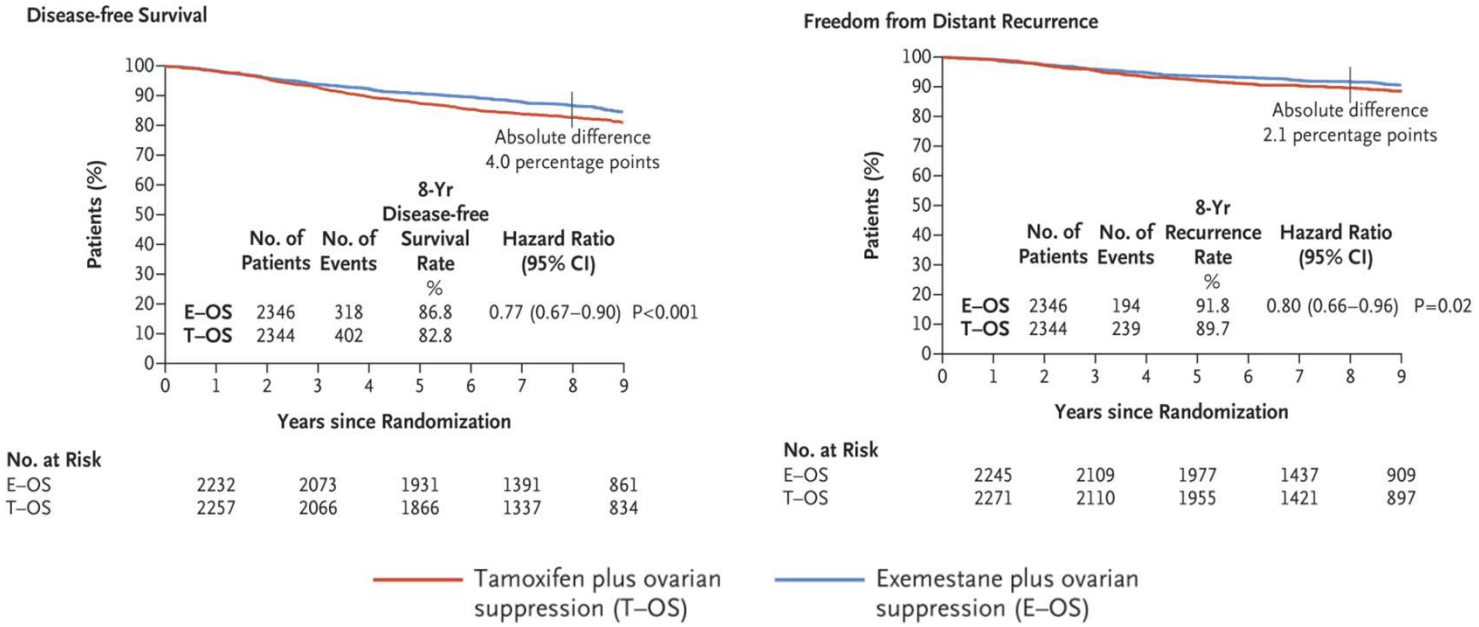
TAMOXIFEN AND EXEMESTANE TRIAL

(N=2672)



SUPPRESSION OF OVARIAN FUNCTION TRIAL (N=3066)

Combined analysis: Exemestane+OFS Improved DFS

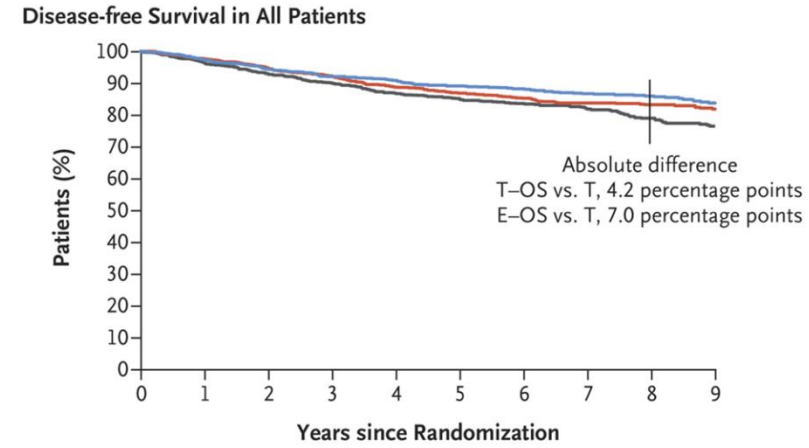


8 years median follow-up: 4% improvement in iDFS

Fracis el at NEJM 2018

SOFT updated results

Difference at 8 years= 7.0% iDFS



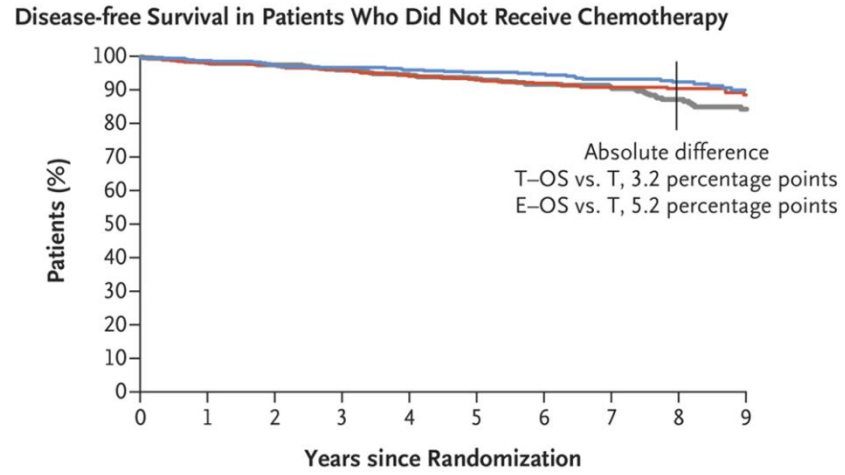
No. at Risk					
T	957	858	771	522	221
T–OS	968	888	795	558	252
E–OS	956	875	805	562	246

	No. of Patients	No. of Events	8-Yr Disease-free Survival Rate %	Hazard Ratio (95% CI) vs. T
T	1018	208	78.9	
T–OS	1015	167	83.2	0.76 (0.62–0.93)
E–OS	1014	143	85.9	0.65 (0.53–0.81)

Tamoxifen alone (T)
Tamoxifen plus ovarian suppression (T–OS)
Exemestane plus ovarian suppression (E–OS)

Fracis el at NEJM 2018

Results- SOFT: No chemotherapy



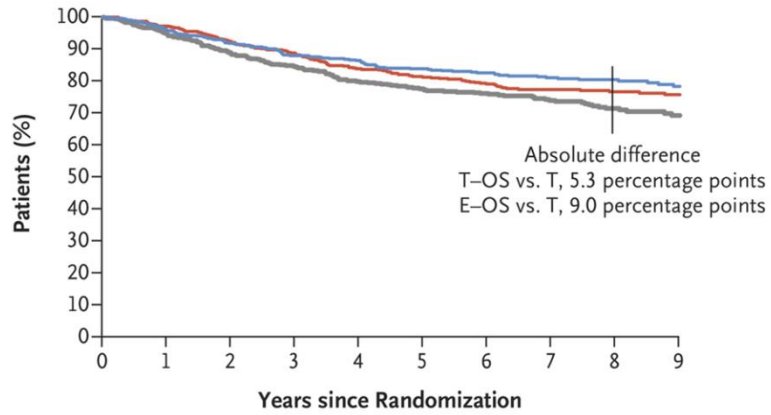
No. at Risk					
T	460	431	398	272	118
T–OS	453	433	399	276	124
E–OS	443	419	390	270	132

	No. of Patients	No. of Events	8-Yr Disease-free Survival Rate %	Hazard Ratio (95% CI) vs. T
T	476	60	87.4	
T–OS	473	47	90.6	0.76 (0.52–1.12)
E–OS	470	35	92.5	0.58 (0.38–0.88)

Tamoxifen Tamoxifen–OS Exemestane–OS

Francis el at NEJM 2018

Results- SOFT: Chemotherapy



No. at Risk					
T	496	427	373	249	102
T–OS	515	456	396	282	129
E–OS	513	456	414	291	115

	No. of Patients	No. of Events	8-Yr Disease-free Survival Rate %	Hazard Ratio (95% CI) vs. T
T	542	148	71.4	
T–OS	542	120	76.7	0.76 (0.60–0.97)
E–OS	544	108	80.4	0.68 (0.53–0.88)

Tamoxifen — Tamoxifen–OS — Exemestane–OS

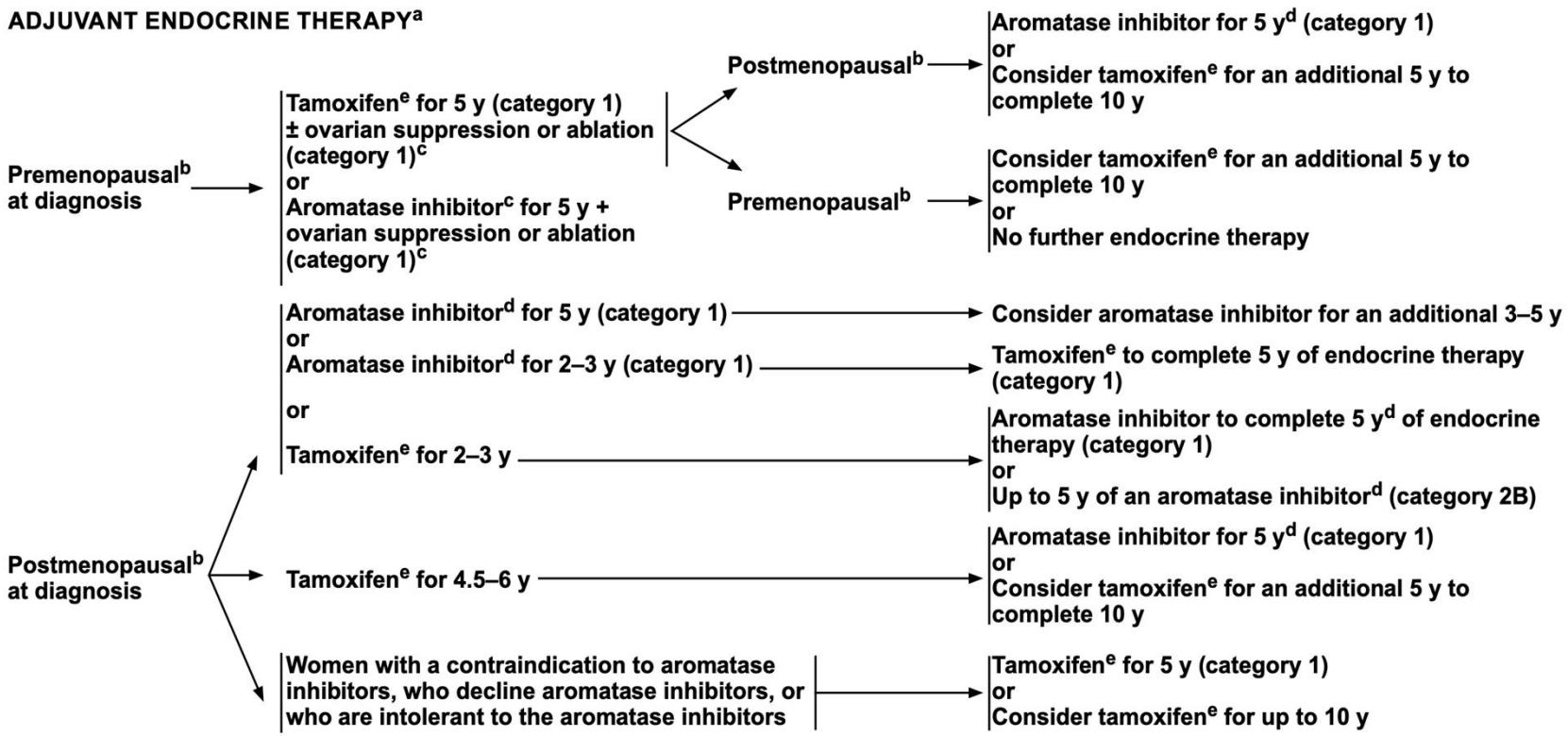
The bottom line, among high-risk patients: 4.3 % improvement with Tam+OS and **9.0 % absolute improvement with OS+Exemestane**

Francis el at NEJM 2018

Selected Adverse Events SOFT/TEXT

Adverse Event	Tamoxifen (N=1005)		Tamoxifen plus Ovarian Suppression (N=2326)		Exemestane plus Ovarian Suppression (N=2317)	
	Any Event	Grade 3 or 4 Event	Any Event	Grade 3 or 4 Event	Any Event	Grade 3 or 4 Event
	number of patients (percent)					
Any targeted adverse event	962 (95.7)	247 (24.6)	2295 (98.7)	721 (31.0)	2288 (98.7)	748 (32.3)
Allergic reaction or hypersensitivity	35 (3.5)	2 (0.2)	110 (4.7)	9 (0.4)	122 (5.3)	12 (0.5)
Injection-site reaction	4 (0.4)	0	189 (8.1)	1 (<0.1)	174 (7.5)	1 (<0.1)
Hot flushes	808 (80.4)	78 (7.8)	2175 (93.5)	284 (12.2)	2141 (92.4)	234 (10.1)
Depression	476 (47.4)	41 (4.1)	1195 (51.4)	108 (4.6)	1197 (51.7)	95 (4.1)
Sweating	492 (49.0)	NA	1391 (59.8)	NA	1286 (55.5)	NA
Insomnia	470 (46.8)	30 (3.0)	1383 (59.5)	105 (4.5)	1375 (59.3)	89 (3.8)
Fatigue	612 (60.9)	34 (3.4)	1496 (64.3)	70 (3.0)	1450 (62.6)	75 (3.2)
Hypertension	181 (18.0)	57 (5.7)	550 (23.6)	188 (8.1)	564 (24.3)	168 (7.3)
Cardiac ischemia or infarction†	5 (0.5)	4 (0.4)	10 (0.4)	6 (0.3)	17 (0.7)	7 (0.3)
Thrombosis or embolism	22 (2.2)	17 (1.7)	53 (2.3)	47 (2.0)	27 (1.2)	20 (0.9)
Nausea	241 (24.0)	0	692 (29.8)	14 (0.6)	747 (32.2)	17 (0.7)
Musculoskeletal symptom	703 (70.0)	67 (6.7)	1809 (77.8)	132 (5.7)	2082 (89.9)	263 (11.4)
Osteoporosis	138 (13.7)	1 (0.1)	648 (27.9)	7 (0.3)	977 (42.2)	10 (0.4)
Fracture	53 (5.3)	8 (0.8)	140 (6.0)	23 (1.0)	179 (7.7)	37 (1.6)
Vaginal dryness	426 (42.4)	NA	1144 (49.2)	NA	1245 (53.7)	NA
Decreased libido	434 (43.2)	NA	981 (42.2)	NA	1056 (45.6)	NA
Dyspareunia	242 (24.1)	16 (1.6)	636 (27.3)	35 (1.5)	733 (31.6)	56 (2.4)

Francis et al NEJM 2018

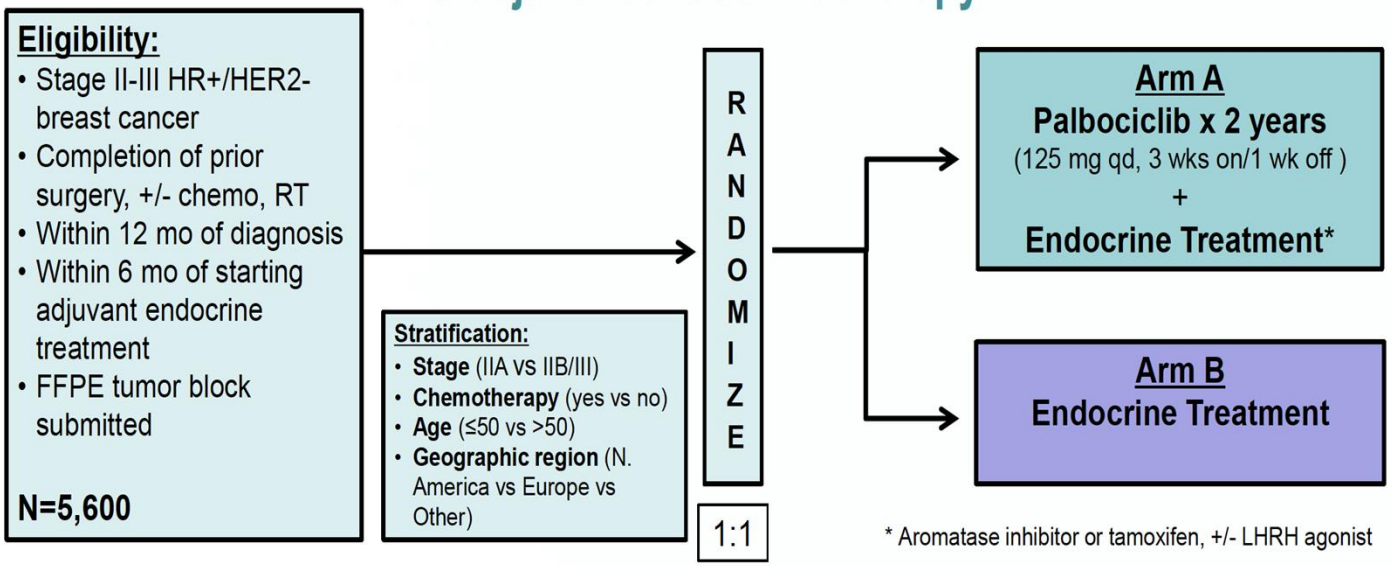


National Comprehensive Cancer Network®

ADDING NEW MOLECULES?

VIRTUAL 2020 ESMO congress

PALLAS: Phase III open-label study of palbociclib and adjuvant endocrine therapy



Primary Endpoint: invasive Disease-Free Survival (iDFS)

VIRTUAL ESMO congress 2020

PALLAS: Patient Characteristics

- Between 9/2015 and 11/2018, 5,760 patients were randomized and included in the ITT set.
- The majority had higher stage disease and had received prior chemotherapy.
- 58·7% had high clinical risk disease, described as:
  - ≥4 nodes involved (≥N2), or
  - 1-3 nodes with either T3/T4 and/or G3 disease

Variable	Palbociclib + ET (N=2,883)	ET (N=2,877)
Age (y) – median (range)	52 (25 – 90)	52 (22 – 85)
Stage		
IIA	504 (17·5%)	509 (17·7%)
IIB	968 (33·6%)	951 (33·1%)
III	1402 (48·6%)	1408 (48·9%)
T-Stage		
T0/T1/Tis/TX	557 (19·3%)	500 (17·4%)
T2	1603 (55·6%)	1636 (56·9%)
T3/T4	722 (25·0%)	741 (25·8%)
N-Stage		
N0	367 (12·7%)	383 (13·3%)
N1	1427 (49·5%)	1415 (49·2%)
N2	703 (24·4%)	709 (24·6%)
N3	385 (13·4%)	370 (12·9%)
Histologic Grade		
G1	300 (10·4%)	313 (10·9%)
G2	1622 (56·3%)	1658 (57·6%)
G3	836 (29·0%)	767 (26·7%)
Prior Chemotherapy	2384 (82·7%)	2370 (82·4%)
Initial Adjuvant Endocrine Therapy		
Aromatase inhibitor	1954 (67·8%)	1918 (66·7%)
Tamoxifen	923 (32·0%)	949 (33·0%)
Concurrent Adjuvant LHRH Agonist	532 (18·5%)	604 (21.1%)

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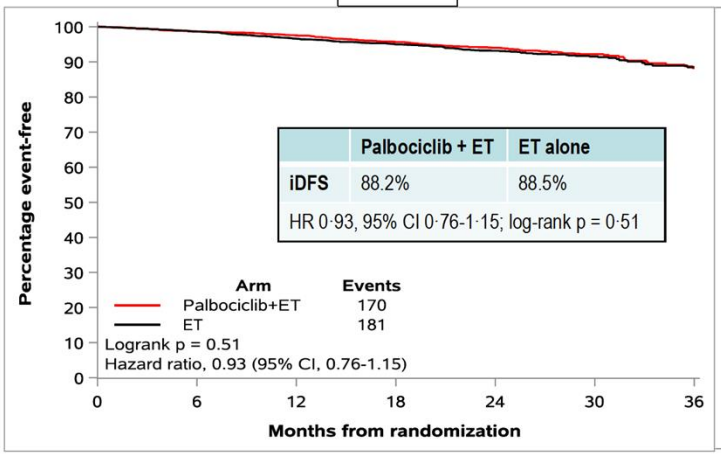
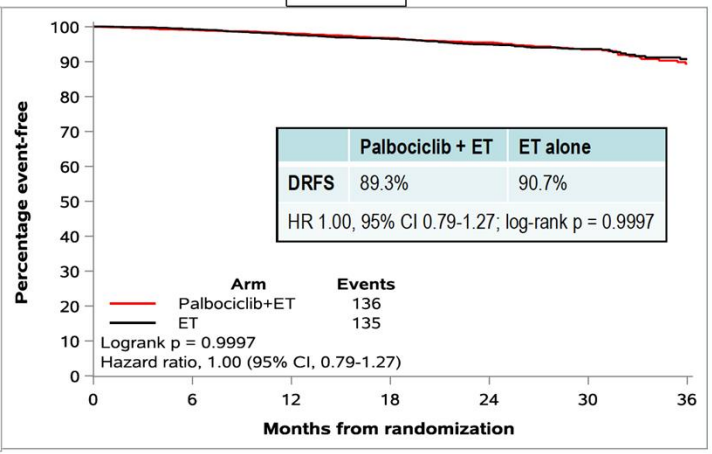
PALLAS: Primary Endpoint iDFS

iDFS



DRFS



At a median follow-up of 23.7 months, no significant difference in either 3-year iDFS or DRFS was observed

PALLAS
ABCSG 42 / AFT-05 / BIG 14-03

Sponsored by AFT and ABCSG, in cooperation with PrECOG, BIG, GBG, NSABP, and supported by Pfizer.

Efficacy population: Intent-to-treat (ITT) principle, with patients withdrawing consent for all analysis excluded

ABCSG · ALLIANCE FOUNDATION TRIALS, LLC · BIG · Pfizer Oncology

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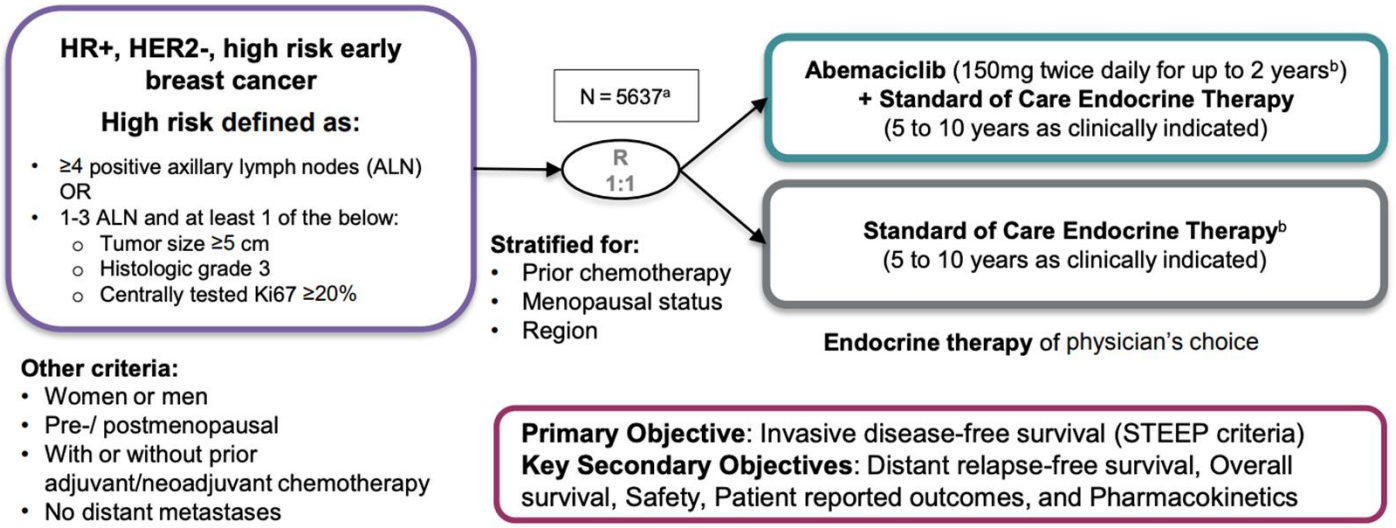
PALLAS: Subgroup Analysis

Subgroup	Palbociclib+ET *Events / N*	ET *Events / N*	Hazard Ratio (95% CI)	P Value for Interaction
All patients	170 / 2883	181 / 2877	0.93 (0.75 - 1.14)	
Stage				0.99
IIA	21 / 504	25 / 509	0.91 (0.51 - 1.63)	
IIB/III	149 / 2370	156 / 2359	0.92 (0.73 - 1.15)	
T-Stage				0.60
T0/T1/Tis/TX	26 / 557	22 / 500	1.10 (0.62 - 1.94)	
T2	84 / 1603	101 / 1636	0.84 (0.63 - 1.12)	
T3/T4	60 / 722	58 / 741	1.01 (0.70 - 1.44)	
N-Stage				0.50
N0	14 / 367	23 / 383	0.65 (0.33 - 1.26)	
N1	53 / 1427	53 / 1415	1.02 (0.70 - 1.50)	
N2/N3	103 / 1088	105 / 1079	0.89 (0.68 - 1.17)	
Histologic grade				0.56
G1/G2	86 / 1922	100 / 1971	0.88 (0.66 - 1.18)	
G3	73 / 836	72 / 767	0.89 (0.65 - 1.24)	
GX	11 / 122	9 / 139	1.43 (0.59 - 3.44)	
Neo/adjuvant chemotherapy				0.36
No	18 / 498	27 / 507	0.71 (0.39 - 1.28)	
Yes	152 / 2384	154 / 2370	0.96 (0.77 - 1.20)	
Age group				0.29
≤50	79 / 1309	73 / 1304	1.06 (0.77 - 1.45)	
>50	91 / 1573	108 / 1573	0.84 (0.64 - 1.11)	
Clinical Risk				0.87
High risk	131 / 1710	136 / 1672	0.89 (0.70 - 1.13)	
Low risk	39 / 1172	45 / 1205	0.93 (0.61 - 1.43)	

PALLAS
ABCSG 42 / AFT-05 / BIG 14-03

BIG Pfizer Oncology

monarchE Study Design



[a] Recruitment from July 2017 to August 2019; [b] Treatment period = first 2 years on study treatment after randomization

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Patient Demographics

monarchE EARLY BREAST CANCER

		Abemaciclib + ET N = 2808, n (%)	ET Alone N = 2829, n (%)
Age	Median (range)	51 (23-89)	51 (22-86)
Age categories	<65 years	2371 (84.4)	2416 (85.4)
	≥65 years	437 (15.6)	413 (14.6)
Gender	Female	2787 (99.3)	2814 (99.5)
	Male	21 (0.7)	15 (0.5)
Region [a]	North America/Europe	1470 (52.4)	1479 (52.3)
	Asia	574 (20.4)	582 (20.6)
	Other	764 (27.2)	768 (27.1)
Menopausal status [a]	Premenopausal	1221 (43.5)	1232 (43.5)
	Postmenopausal	1587 (56.5)	1597 (56.5)
Prior treatment [a]	Neoadjuvant chemotherapy	1039 (37.0)	1048 (37.0)
	Adjuvant chemotherapy	1642 (58.5)	1647 (58.2)
	No chemotherapy	127 (4.5)	134 (4.7)
Baseline ECOG PS	0	2405 (85.7)	2369 (83.8)
	1	401 (14.3)	455 (16.1)

Note: where values do not add up to 100%, remaining data are missing, unavailable or could not be assessed; [a] per Interactive Web Response System (IWRS)

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High Risk Disease Characteristics

monarchE EARLY BREAST CANCER

		Abemaciclib + ET N = 2808, n (%)	ET Alone N = 2829, n (%)
Number of positive lymph nodes	0	7 (0.2)	7 (0.2)
	1-3	1119 (39.9)	1143 (40.4)
	≥4 or more	1680 (59.8)	1679 (59.3)
Histological grade	Grade 1	209 (7.4)	215 (7.6)
	Grade 2	1373 (48.9)	1395 (49.3)
	Grade 3	1090 (38.8)	1066 (37.7)
Primary tumor size by pathology following definitive surgery	<2 cm	780 (27.8)	765 (27.0)
	2-5 cm	1369 (48.8)	1419 (50.2)
	≥5 cm	610 (21.7)	612 (21.6)
Central Ki-67	<20%	953 (33.9)	973 (34.4)
	≥20%	1262 (44.9)	1233 (43.6)
	Unavailable	593 (21.1)	623 (22.0)
Progesterone receptor status	Positive	2421 (86.2)	2453 (86.7)
	Negative	298 (10.6)	294 (10.4)

Note: where values do not add up to 100%, remaining data are missing, unavailable or could not be assessed

Additional high risk eligibility criteria for patients with 1-3 nodes	Abemaciclib + ET N = 2808, n (%)	ET Alone N = 2829, n (%)
Tumor size ≥5 cm (pathology) [a]	249 (8.9)	236 (8.3)
Tumor size ≥5 cm (imaging) [a, b]	152 (5.4)	158 (5.6)
Histologic grade 3 [a]	629 (22.4)	618 (21.8)
Central Ki-67 ≥20% only [c]	216 (7.7)	237 (8.4)

[a] Patients could be counted in more than one of the sub-categories under 1-3 positive lymph nodes; [b] Patients who received neoadjuvant chemotherapy may have been eligible based on imaging tumor size prior to receiving systemic therapy; [c] Patients not double counted; patients did not have tumor size ≥5 cm (either by pathology or imaging) or histologic grade 3

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Invasive Disease-Free Survival

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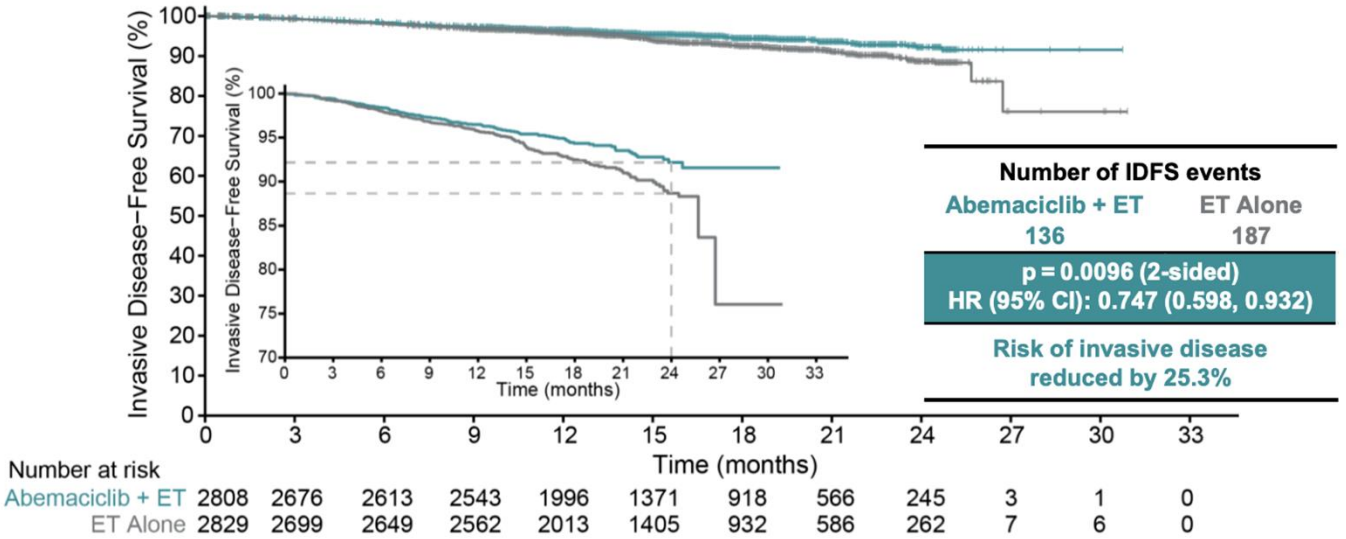

Number of IDFS events

Abemaciclib + ET	ET Alone
136	187

p = 0.0096 (2-sided)
HR (95% CI): 0.747 (0.598, 0.932)

Risk of invasive disease reduced by 25.3%

Number at risk

Abemaciclib + ET	2808	2676	2613	2543	1996	1371	918	566	245	3	1	0
ET Alone	2829	2699	2649	2562	2013	1405	932	586	262	7	6	0

Two-year IDFS rates were 92.2% (abemaciclib + ET arm) and 88.7% (ET arm) – 3.5% absolute difference

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IDFS in Prespecified Subgroups

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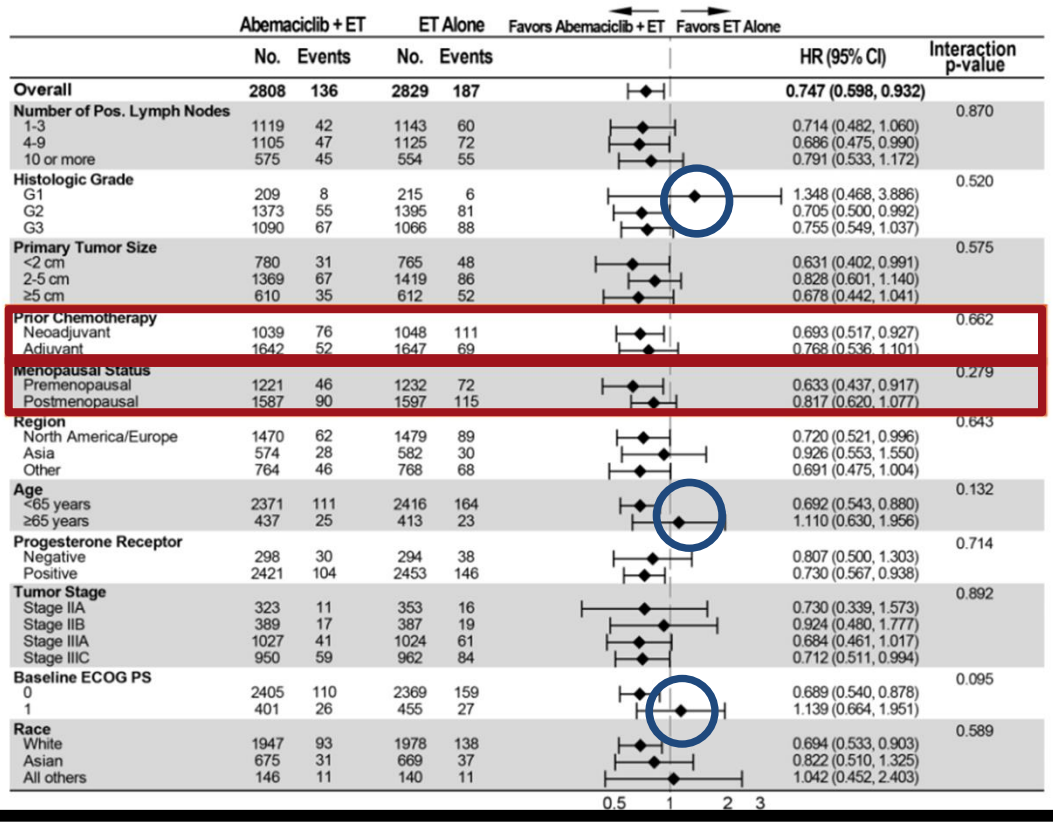
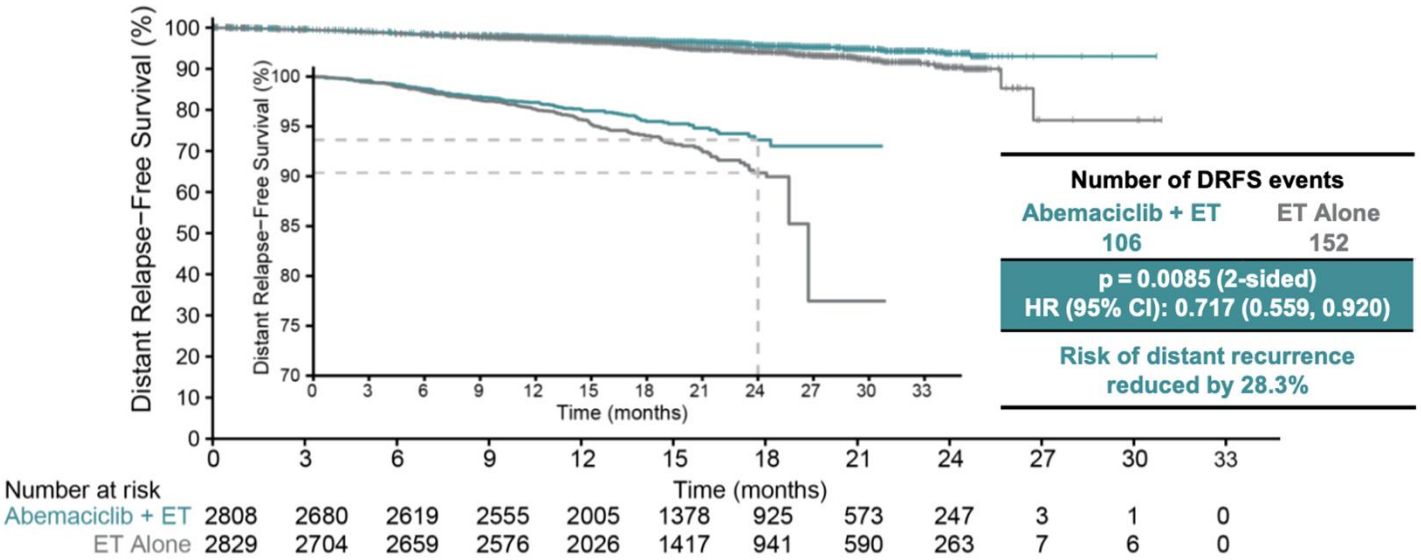


	Abemaciclib + ET		ET Alone		HR (95% CI)	Interaction p-value
	No.	Events	No.	Events		
Overall	**2808**	**136**	**2829**	**187**	**0.747 (0.598, 0.932)**	
Number of Pos. Lymph Nodes						0.870
1-3	1119	42	1143	60	0.714 (0.482, 1.060)	
4-9	1105	47	1125	72	0.686 (0.475, 0.990)	
10 or more	575	45	554	55	0.791 (0.533, 1.172)	
Histologic Grade						0.520
G1	209	8	215	6	1.348 (0.468, 3.886)	
G2	1373	55	1395	81	0.705 (0.500, 0.992)	
G3	1090	67	1066	88	0.755 (0.549, 1.037)	
Primary Tumor Size						0.575
<2 cm	780	31	765	48	0.631 (0.402, 0.991)	
2-5 cm	1369	67	1419	86	0.828 (0.601, 1.140)	
≥5 cm	610	35	612	52	0.678 (0.442, 1.041)	
Prior Chemotherapy						0.662
Neoadjuvant	1039	76	1048	111	0.693 (0.517, 0.927)	
Adjuvant	1642	52	1647	69	0.768 (0.536, 1.101)	
Menopausal Status						0.279
Premenopausal	1221	46	1232	72	0.633 (0.437, 0.917)	
Postmenopausal	1587	90	1597	115	0.817 (0.620, 1.077)	
Region						0.643
North America/Europe	1470	62	1479	89	0.720 (0.521, 0.996)	
Asia	574	28	582	30	0.926 (0.553, 1.550)	
Other	764	46	768	68	0.691 (0.475, 1.004)	
Age						0.132
<65 years	2371	111	2416	164	0.692 (0.543, 0.880)	
≥65 years	437	25	413	23	1.110 (0.630, 1.956)	
Progesterone Receptor						0.714
Negative	298	30	294	38	0.807 (0.500, 1.303)	
Positive	2421	104	2453	146	0.730 (0.567, 0.938)	
Tumor Stage						0.892
Stage IIA	323	11	353	16	0.730 (0.339, 1.573)	
Stage IIB	389	17	387	19	0.924 (0.480, 1.777)	
Stage IIIA	1027	41	1024	61	0.684 (0.461, 1.017)	
Stage IIIC	950	59	962	84	0.712 (0.511, 0.994)	
Baseline ECOG PS						0.095
0	2405	110	2369	159	0.689 (0.540, 0.878)	
1	401	26	455	27	1.139 (0.664, 1.951)	
Race						0.589
White	1947	93	1978	138	0.694 (0.533, 0.903)	
Asian	675	31	669	37	0.822 (0.510, 1.325)	
All others	146	11	140	11	1.042 (0.452, 2.403)	

Distant Relapse-Free Survival



Number at risk												
Abemaciclib + ET	2808	2680	2619	2555	2005	1378	925	573	247	3	1	0
ET Alone	2829	2704	2659	2576	2026	1417	941	590	263	7	6	0

Two-year DRFS rates were 93.6% (abemaciclib + ET arm) and 90.3% (ET arm) – 3.3% absolute difference
DRFS benefit consistent across all prespecified subgroups

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Treatment-Emergent Adverse Events

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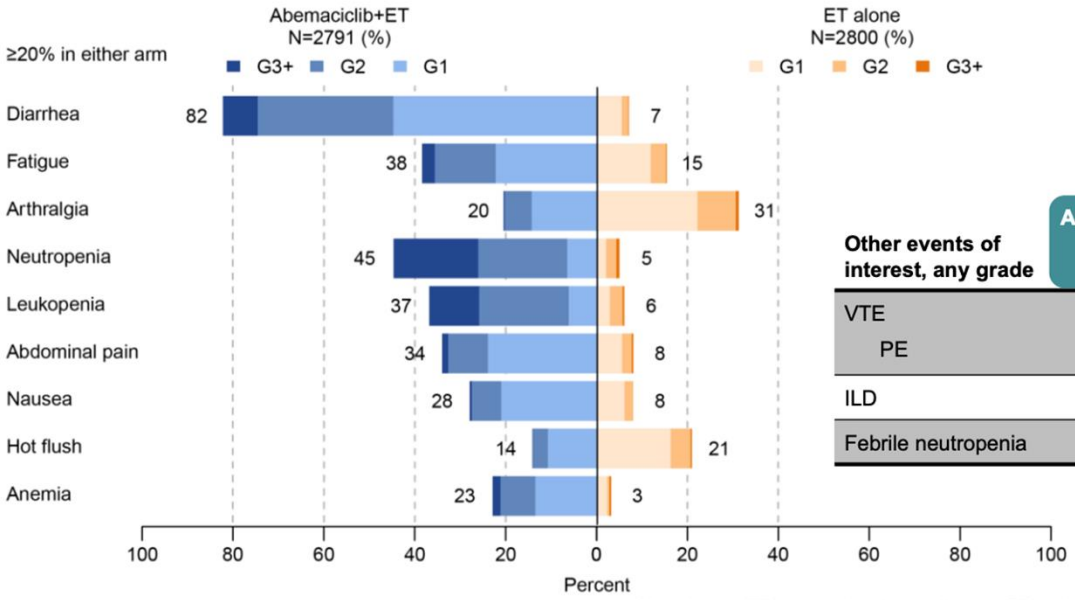


Other events of interest, any grade	Abemaciclib + ET N = 2791, n (%)	ET Alone N = 2800, n (%)
VTE	63 (2.3%)	14 (0.5%)
PE	25 (0.9%)	3 (0.1%)
ILD	75 (2.7%)	33 (1.2%)
Febrile neutropenia	7 (0.3%)	1 (<0.1%)

Abbreviations: VTE = venous thromboembolic event; PE = pulmonary embolism; ILD = Interstitial lung disease

Conclusions

Abemaciclib combined with ET showed a statistically significant improvement in IDFS in patients with high risk HR+, HER2- EBC

- HR = 0.747; (95% CI, 0.598 to 0.932; p = 0.0096)
- A 3.5% absolute improvement in 2-year IDFS rates was observed: 92.2% vs 88.7%
- There was a consistent treatment benefit across all prespecified subgroups

Results indicate the prevention of early recurrence and a reduction in the risk of distant recurrence (metastatic disease) by a clinically meaningful 28.3%

- The greatest reduction in distant metastases was to the liver and bone

Safety was consistent with the known profile of abemaciclib

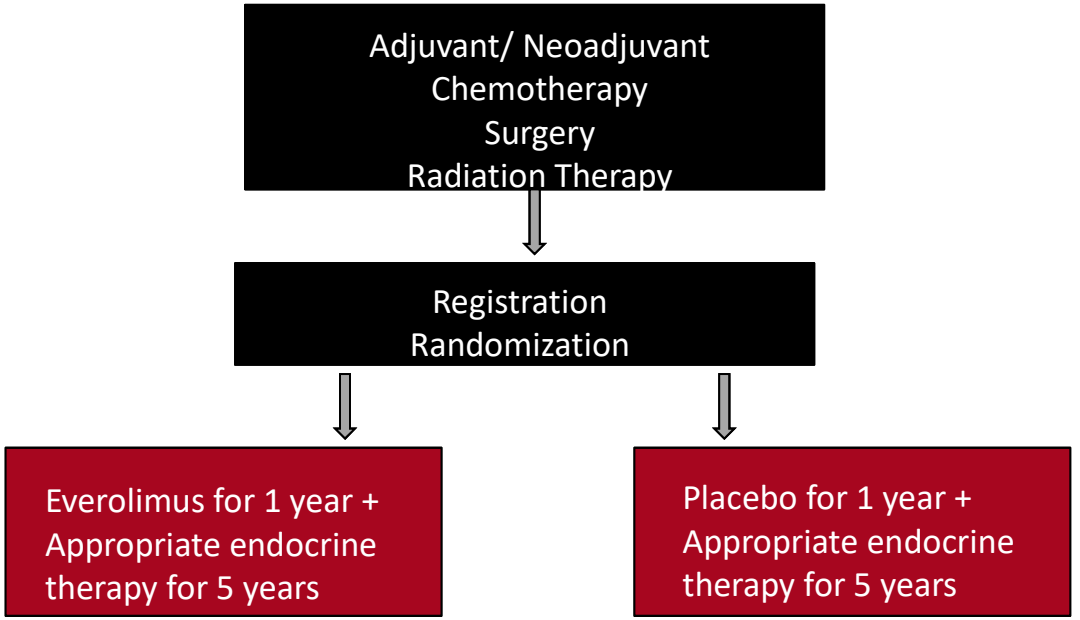
- Diarrhea was manageable with anti-diarrheal medication and dose adjustments
- There were significant reductions in arthralgia and hot flush when abemaciclib was added to ET

Abemaciclib is the first CDK4 & 6 inhibitor to show a significant improvement in IDFS when combined with ET compared with ET alone in patients with HR+, HER2-, high risk EBC

MonarchE vs PALLAS

	MonarchE	PALLAS
Treatment	Abemaciclib	Palbociclib
Duration of Treatment	2 years	2 years
Total # Patients	5591	5760
Discontinuation rate	18.8%	42.2%
N0 patients	14	750
Stage IIA	676	1013

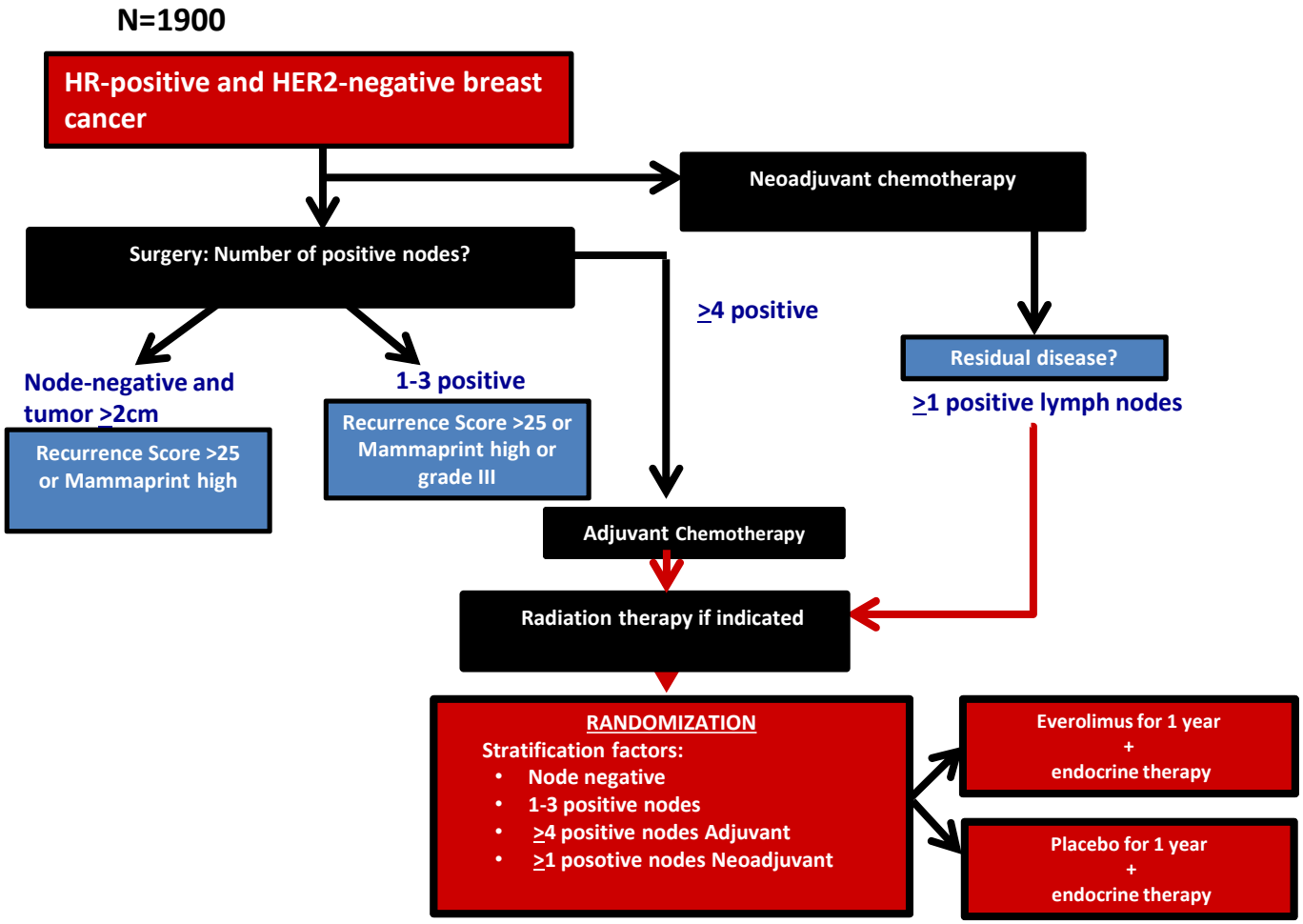
S1207: Phase III randomized, placebo-controlled trial adding 1 year of everolimus to adjuvant endocrine therapy for patients with high-risk, HR+, HER2- BC



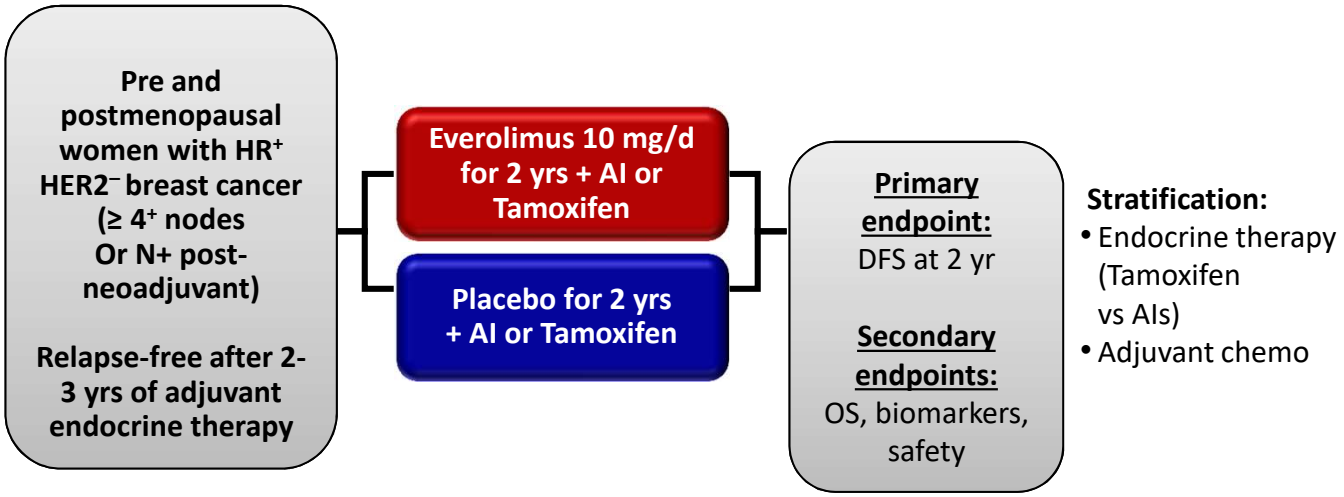
PI: Mariana Chavez-MacGregor, MD

SWOG
Leading cancer research. Together.

NSABP
National Surgical Adjuvant Breast and Bowel Project


N=1900
HR-positive and HER2-negative breast cancer
Neoadjuvant chemotherapy
Surgery: Number of positive nodes?
≥4 positive
Residual disease?
≥1 positive lymph nodes
Node-negative and tumor ≥2cm
Recurrence Score >25 or Mammaprint high
1-3 positive
Recurrence Score >25 or Mammaprint high or grade III
Adjuvant Chemotherapy
Radiation therapy if indicated
RANDOMIZATION
Stratification factors:
• Node negative
• 1-3 positive nodes
• ≥4 positive nodes Adjuvant
• ≥1 posotive nodes Neoadjuvant
Everolimus for 1 year + endocrine therapy
Placebo for 1 year + endocrine therapy

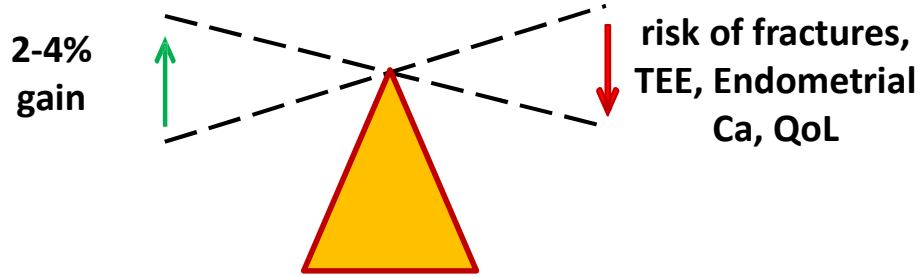
UNIRAD trial



Phase 3 study; N = 2010
Sponsor: UNICANCER
Funding: French NCI
PI: Fabrice Andre

Balancing act: Risks and Benefits

Predicted benefit versus side effects



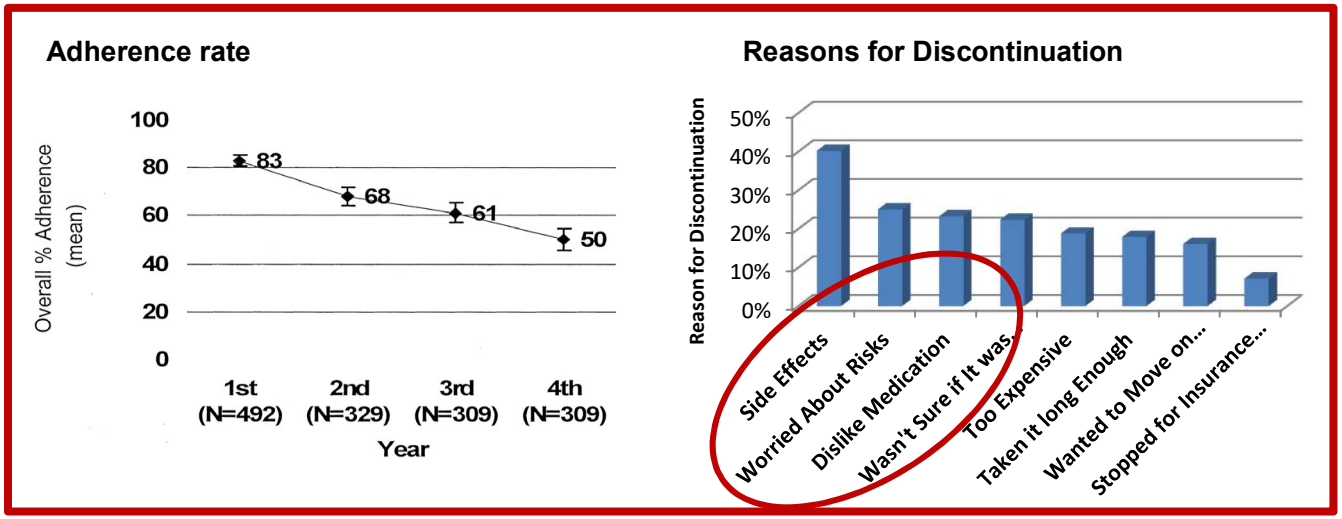
Decrease in risk of recurrence counterbalanced by treatment-associated risks?

No OS benefit

Adherence and Persistence with Endocrine Therapy is a Significant Challenge

- Endocrine therapy adherence and persistence are poor
- Discontinuation ranges from 31-73% during the first 5 years

Side effects are the primary reason for treatment discontinuation



Partridge, A. H. et al. J Clin Oncol; 21:602-606 2003
Murphy CC, et al Breast Can Res Treat. 2012;134:459-4
Sheppard VB, et al J Clin Oncol. 2014

Fontein DBY. EJSO. 2012;38:110-117
Friese CR et al. Breast Can Res Treat 2013; 138(3):931-39
Hershman et al. Breast Cancer Res Treat. 2011; 126(2): 529-537

Adherence rates in extended AI clinical trials

Trial	Adherence Rate (%)
MA.17R	62.5
NSABP-42	62.5
DATA	NR
IDEAL	57.5
ABCSG-16	59.4

Highly motivated patients that actually had already tolerated AIs

Take home points

- Endocrine therapy improves BC outcomes
- Significant risk of recurrence
  - High risk groups
  - Late recurrence

- Optimization/improvement
  - Improve adherence/ Management of side effects

- **Premenopausal patients**
  - Tamoxifen 10 years
  - Ovarian ablation + AI in selected groups of patients

- **Postmenopausal patients**
  - Extended endocrine therapy in high-risk patients

- Molecular assays may be helpful/ Predictive biomarkers
- Incorporate new drugs/Algorithms will change

- In the absence of a survival advantage this decision should be selective rather than for all.
  - Shared-decision making process

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