Breast Cancer
Best of ASCO
GASCO Annual meeting
Atlanta, GA, September 9th 2017

Ruth M. O'Regan, MD
Professor and Division Chief Hematology
and Medical Oncology,
Department of Medicine,
University of Wisconsin

Carbone Cancer Center
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

NCCN National Comprehensive Cancer Network®

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Topics to cover

- Early stage:
  - Omitting anthracyclines in HER2-negative breast cancer (Abstract 504)
  - Adjuvant HER2-positive breast cancer (Abstracts LBA 500, 511)
  - Neoadjuvant pembrolizumab (Abstract 506)
- Metastatic disease:
  - Single agent pembrolizumab (Abstract 1008)
  - Olaparib in BRCA-mutated cancers (Abstract LBA 4)
  - CDK inhibitors in ER-positive MBC (Abstracts 1000, 1001
- Local therapy:
  - Impact of change in margin definition on surgical approaches (Abstract 508)

Prospective WSG Phase III PlanB trial: Final analysis on adjuvant 4xEC→4xDoc vs. 6xDocetaxel/Cyclophosphamide in high clinical and intermediate/high genomic risk HER2-negative early breast cancer

Nadia Harbeck, Oleg Gluz, Michael Clemens, Wolfram Malter, Toralf Reimer, Benno Nuding, Bahriye Aktas, Andrea Stefek, Anke Pollmanns, Fatemeh Lorenz-Salehi, Christoph Uleer, Petra Krabisch, Sherko Kuemmel, Cornelia Liedtke, Steven Shak, Rachel Wuerstlein, Matthias Christgen, Ronald E. Kates, Hans H. Kreipe, and Ulrike Nitz,
on behalf of the WSG PlanB investigators

PlanB: Design

HER2-negative early breast cancer

WSG
WOMEN'S HEALTHCARE STUDY GROUP

- Age≤75 years
- cM0
- free margins
- pN+
- pN0 high risk

- pT≥2
- G2-3
- uPA/PAI-1↑
- HR-
- age ≤35 years

HR-

HR+

RECURRENCE SCORE

0-3 LN and RS>11 or >/= 4 LN

0-3 LN and RS≤11

Recurrence Score: after early amendment

RANDOMIZATION

$Doc_{75}C_{600}$ x 6*

$E_{90}C_{600}$x4 →Doc_{100} x4*

Endocrine therapy*

* Endocrine Therapy and RT according to national guidelines
E: Epirubcin; Doc: Docetaxel;
C: Cyclophosphamide

Presented by: Nadia Harbeck, MD

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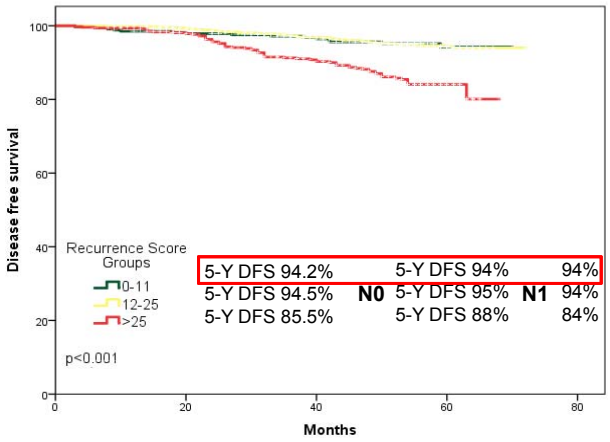
PlanB: Translational subprotocol

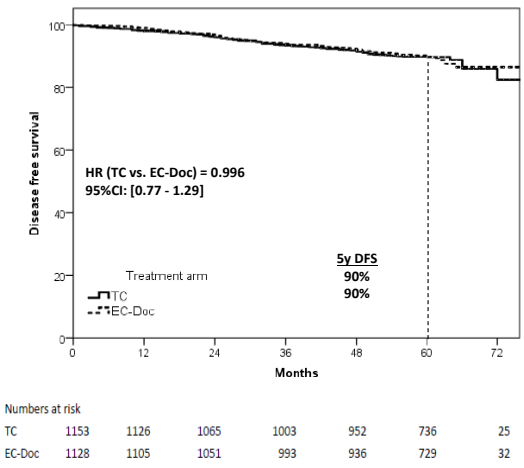
5-year DFS in per-protocol population
(no chemotherapy in pN0-1 and Recurrence Score 0-11)



Gluz et al, EBCC 2016, plenary lecture

5

PlanB: Disease-free survival (DFS) by chemotherapy arm (ITT population)



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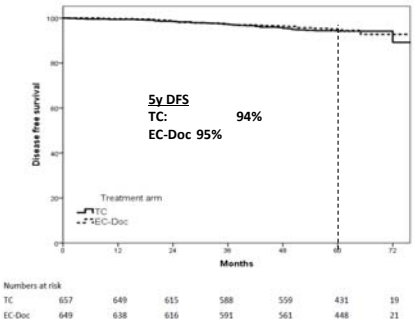
PlanB: Disease-free survival (DFS) according to Recurrence Score (HR+)*

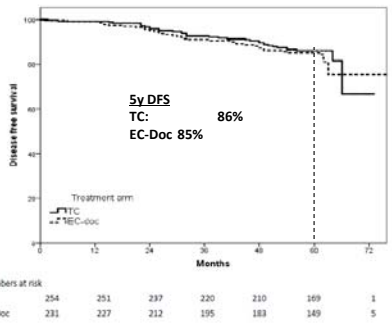
RS≤25



Numbers at risk

TC	657	649	615	588	559	431	19
EC-Doc	649	638	616	591	561	448	21

RS>25

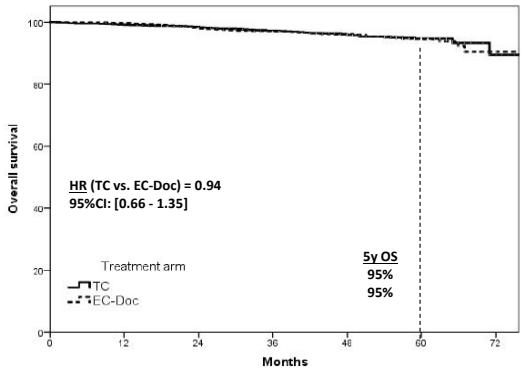


Numbers at risk

TC	254	251	237	220	210	169	1
EC-Doc	231	227	212	195	183	149	5

*ITT patients with RS measured; after early amendment

PlanB: Overall survival (OS) by chemotherapy arm (ITT population)



Numbers at risk

TC	1153	1137	1087	1032	979	751	16
EC-Doc	1128	1112	1063	1016	963	751	25

WSG PlanB trial: Summary

WSG
WOMEN'S HEALTHCARE STUDY GROUP

- First trial to evaluate the A-free TC regimen vs. a conventional A-T sequence in clinically high-risk or genomically intermediate/high-risk HER2-negative early BC.
- TC and EC-Doc both result in 90% 5-year DFS:
  - HR (TC vs. EC-Doc) = 0.996, 95%CI: [0.77 - 1.29].
  - DFS difference within non-inferiority margin of original trial design.
- Subgroup analyses do not reveal any subgroup with a particular benefit from the A-containing regimen.
  - Recurrence Score risk group not predictive for A-benefit.
- EC-Doc associated with more grade 3-4 toxicity.

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The APHINITY Study

Adjuvant Pertuzumab and Herceptin in Initial Therapy

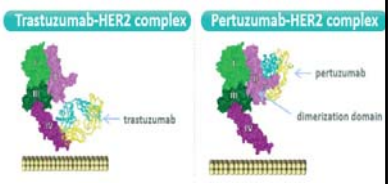
BIG 4-11 / BO25126 / TOC4939g

A randomized comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with HER2-positive early breast cancer

G. von Minckwitz, M. Procter, E. de Azambuja, D. Zardavas, M. Benyunes, G. Viale, T. Suter, A. Arahmani, N. Rouchet, E. Clark, A. Knott, I. Lang, C. Levy, D. Yardley, J. Bines, R. Gelber, M. Piccart, J. Baselga
for the APHINITY Steering Committee and Investigators

APHINITY: Rationale

- Pertuzumab has complementary mechanisms o action with trastuzumab.[1-3]
  - Trastuzumab binds close to the transmembrane domain, inhibiting HER2 dimerization
  - Pertuzumab binds to the dimerization domain, inhibiting HER2 hetero-dimerization with other H family receptors [4-7]
- In patients with HER2-positive metastatic breast cancer
  pertuzumab added to trastuzumab and docetaxel significantly improved both progression-free and overall survival.[8,9]
- In the neoadjuvant setting, the addition of pertuzumab to trastuzumab plus docetaxel significantly improved pathological complete response rate.[10,11]



[1]Baselga J, Nat Rev Cancer 2009; [2]Scheuer W, Cancer Res 2009; [3]Hubbard SR Cancer Cell 2005; [4]Molina MA et al. Cancer Res 2001; [5]Junttila TT et al. Cancer Cell 2009; [6]Franklin MC et al. Cancer Cell 2004; [7]Agus DB et al. Cancer Cell 2002 [8]Baselga J, NEJM 2012; [9]Swain SM, NEJM 2015; [10]Swain SM, Oncologist 2013; [11]Gianni L, Lancet Oncol 2012; [12]Cameron D, Lancet 2017

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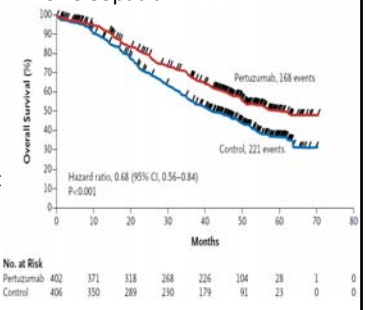
- Recurrences of HER2-positive early breast cancer still occur for
  a significant proportion of patients in the long-term.[12]

Final Overall Survival Analysis of Cleopatra



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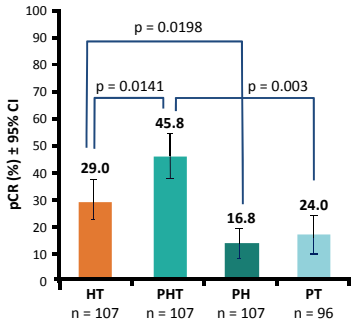
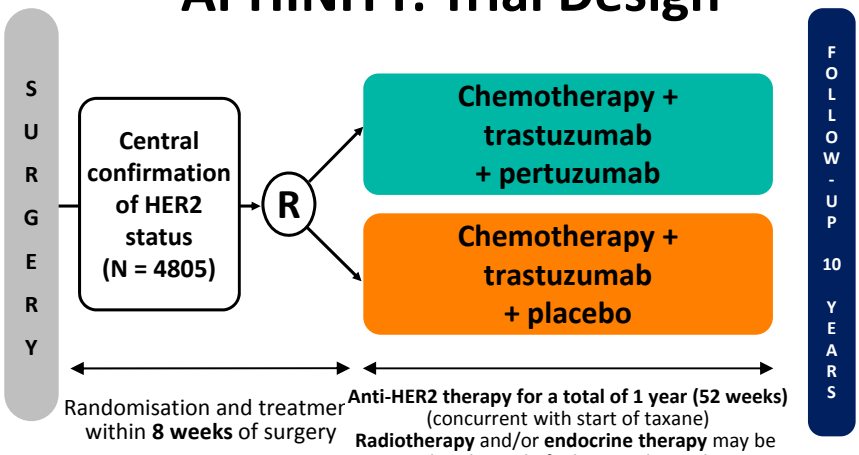
NeoSphere PCR rates: ITT population summ



[1]Baselga J, Nat Rev Cancer 2009; [2]Scheuer W, Cancer Res 2009; [3]Hubbard SR Cancer Cell 2005; [4]Molina MA et al. Cancer Res 2001; [5]Junttila TT et al. Cancer Cell 2009; [6]Franklin MC et al. Cancer Cell 2004; [7]Agus DB et al. Cancer Cell 2002 [8]Baselga J, NEJM 2012; [9]Swain SM, NEJM 2015; [10]Swain SM, Oncologist 2013; [11]Gianni L, Lancet Oncol 2012; [12]Cameron D, Lancet 2017

APHINITY: Trial Design



- HER2 status confirmed centrally
- Node-positive (unless T0)
- Node-negative if:
  - T ≥ 1cm
  - or 0.5 to 1cm with grade 3, ER/PR-negative or age < 35

APHINITY: Primary Endpoint: Invasive Disease-Free Survival (IDFS)

Time from randomisation until the date of the first occurrence of one of the following events:

- Ipsilateral invasive breast tumour recurrence
- Ipsilateral local-regional invasive breast cancer recurrence
- Distant recurrence
- Contralateral invasive breast cancer
- Death attributable to any cause including breast cancer, non-breast cancer, or unknown cause

- Secondary endpoints

This IDFS definition

- was the FDA's recommended definition for a trial intended to support a regulatory filing
- differs from the STEEP definition[1] of IDFS since it excludes second primary non-breast cancers as event

[1] Hudis CA, J Clin Oncol 2007

APHINITY: Statistical Assumptions

	EXPECTED 3-year IDFS rate Placebo vs. Pertuzumab
HR=0.75	**89.2% vs. 91.8% (Δ=2.6%)**

- Placebo arm IDFS rate was based on BCIRG 006 data[1], assuming a 35% / 65% node-negative / node-positive split
- 379 events and 4800 patients required for 80% power and alpha of 5%

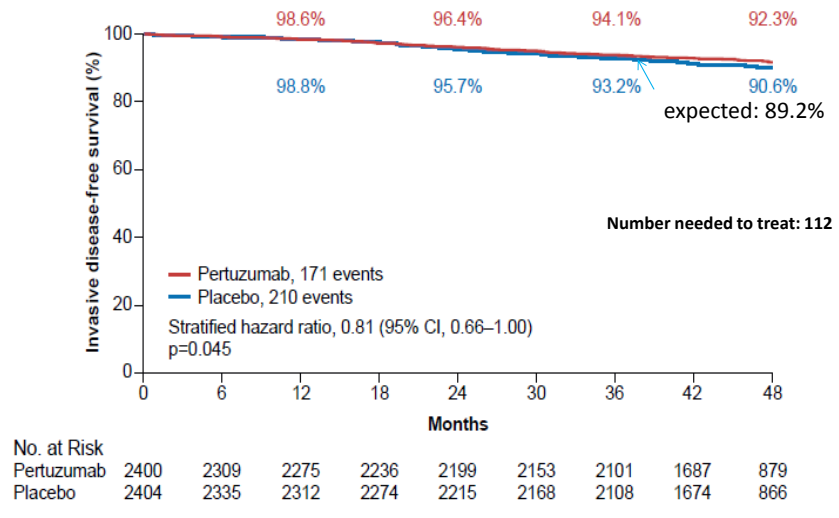
[1] Slamon D, NEJM 2011

APHINITY: Randomization Stratification Factors by Treatment

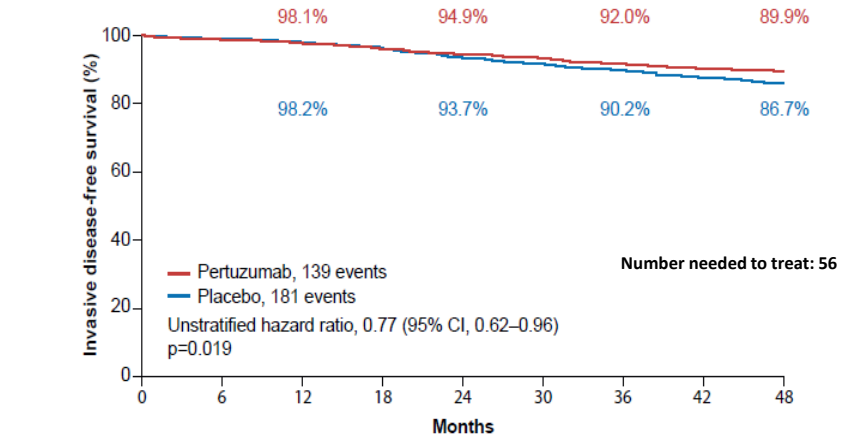
	Pertuzumab n=2400	Placebo n=2404*
Nodal status, n (%)		
0 positive nodes and T ≤1 cm*	90 (3.8)	84 (3.5)
0 positive nodes and T >1 cm*	807 (33.6)	818 (34.0)
1–3 positive nodes	907 (37.8)	900 (37.4)
≥ 4 positive nodes	596 (24.8)	602 (25.0)
Adjuvant chemotherapy regimen (randomised), n (%)		
Anthracycline-containing regimen	1865 (77.7)	1877 (78.1)
Non-anthracycline-containing regimen	535 (22.3)	527 (21.9)
Hormone receptor status (central), n (%)		
Negative (ER- and PgR-negative)	864 (36.0)	858 (35.7)
Positive (ER- and/or PgR-positive)	1536 (64.0)	1546 (64.3)
Geographical region, n (%)		
USA	296 (12.3)	294 (12.2)
Canada/Western Europe/Australia – New Zealand/South Africa	1294 (53.9)	1289 (53.6)
Eastern Europe	200 (8.3)	200 (8.3)
Asia Pacific	550 (22.9)	557 (23.2)
Latin America	60 (2.5)	64 (2.7)
Protocol Version, n (%)		
Protocol A	1828 (76.2)	1827 (76.0)
Protocol Amendment B	572 (23.8)	577 (24.0)

*One patient was excluded from the ITT population due to her falsification of personal information

APHINITY: ITT Primary Endpoint Analysis Invasive Disease-free Survival



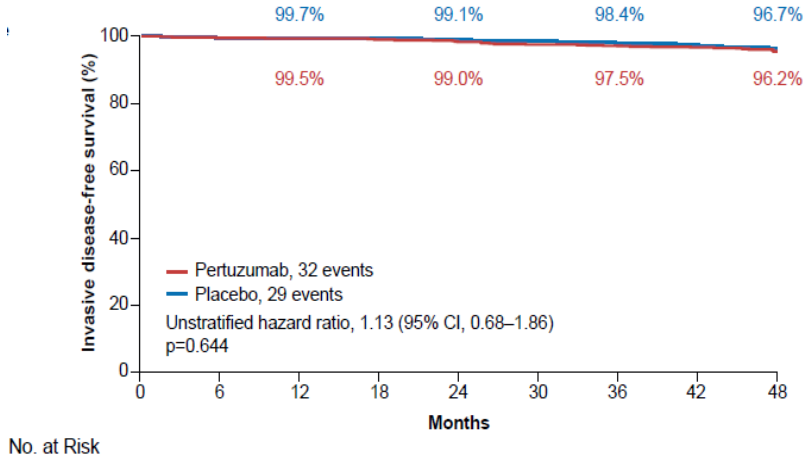
APHINITY: Node-positive Subgroup



No. at Risk

Pertuzumab	1503	1444	1419	1387	1358	1327	1283	912	423
Placebo	1502	1453	1439	1408	1359	1319	1264	882	405

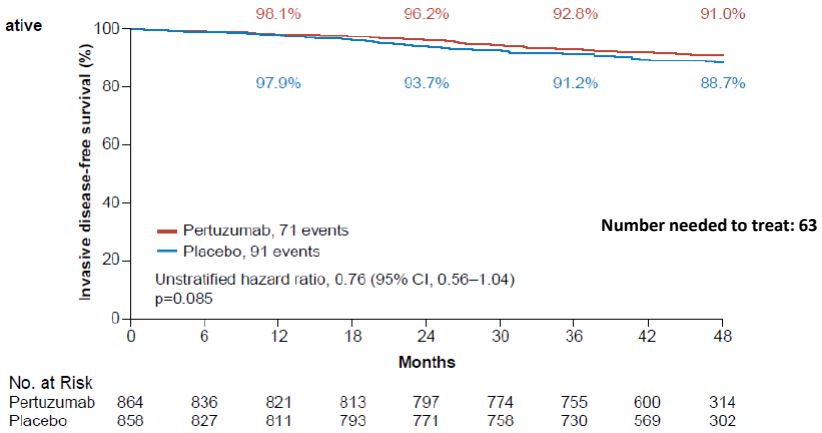
APHINITY: Node-negative Subgroup



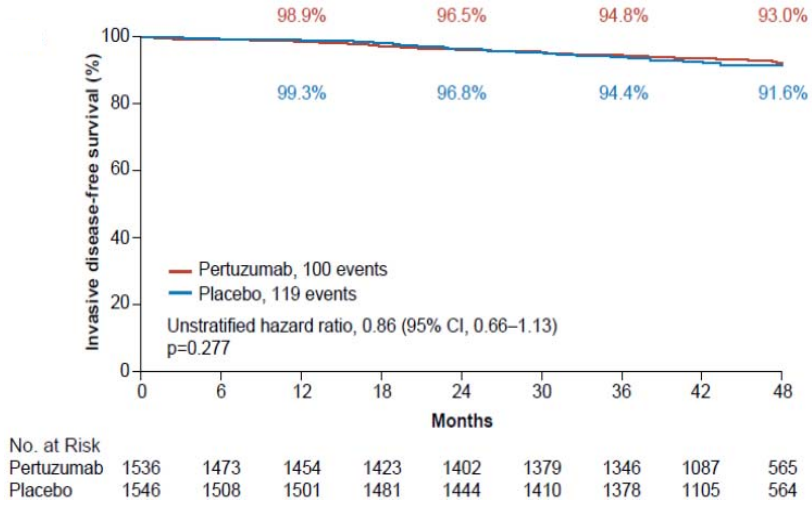
No. at Risk

Pertuzumab	897	865	856	849	841	826	818	775	456
Placebo	902	882	873	866	856	849	844	792	461

APHINITY: Hormone Receptor-negative Subgroup



APHINITY: Hormone Receptor-positive Subgroup



APHINITY: Secondary Efficacy Endpoints

3-year	Pertuzumab n=2400	Placebo n=2404	Hazard ratio (95% CI)	p value
IDFS (primary endpoint), %	94.1	93.2	**0.81 (0.66, 1.00)**	**0.045**
Secondary efficacy endpoints, %				
IDFS incl. second primary non-BC events (STEEP definition)	93.5	92.5	**0.82 (0.68, 0.99)**	**0.043**
Disease-free interval	93.4	92.3	**0.81 (0.67, 0.98)**	**0.033**
Recurrence-free interval	95.2	94.3	**0.79 (0.63, 0.99)**	**0.043**
Distant recurrence-free interval	95.7	95.1	**0.82 (0.64, 1.04)**	**0.101**
Overall survival (first interim analysis)*	97.7	97.7	**0.89 (0.66, 1.21)**	**0.467**

*** 1st interim analysis at 26% of the target events for the final overall survival analysis**

APHINITY: Cardiac Endpoints

N (%)	Pertuzumab n=2364	% Treatment difference (95% CI)	Placebo n=2405
Primary cardiac endpoint	17 (0.7)	0.4 (0.0, 0.8)	8 (0.3)
• Heart failure NYHA III/IV + LVEF drop* • Cardiac death**	15 (0.6) 2 (0.08)		6 (0.2) 2 (0.08)
• Recovered according to LVEF	7		4
Secondary cardiac endpoint Asymptomatic or mildly symptomatic LVEF drop*	64 (2.7)	-0.1 (-1.0, 0.9)	67 (2.8)

***LVEF drop = ejection fraction drop ≥10% from baseline AND to below 50%;**
****Identified by the Cardiac Advisory Board for the trial according to a prospective definition**

APHINITY: Common Grade ≥ 3 Adverse Events

	Pertuzumab n=2364	Placebo n=2405
Neutropenia	385 (16.3%)	377 (15.7%)
Febrile Neutropenia	287 (12.1%)	266 (11.1%)
Anaemia	163 (6.9%)	113 (4.7%)
Diarrhoea	232 (9.8%)	90 (3.7%)
- with chemotherapy and targeted therapy	232 (9.8%)	90 (3.7%)
- with targeted therapy (post-chemotherapy)	12 (0.5%)	4 (0.2%)
- with AC->T (N=1834; 1894)	137 (7.5%)	59 (3.1%)
- with TCH (N= 528; 510)	95 (18.0%)	31 (6.1%)

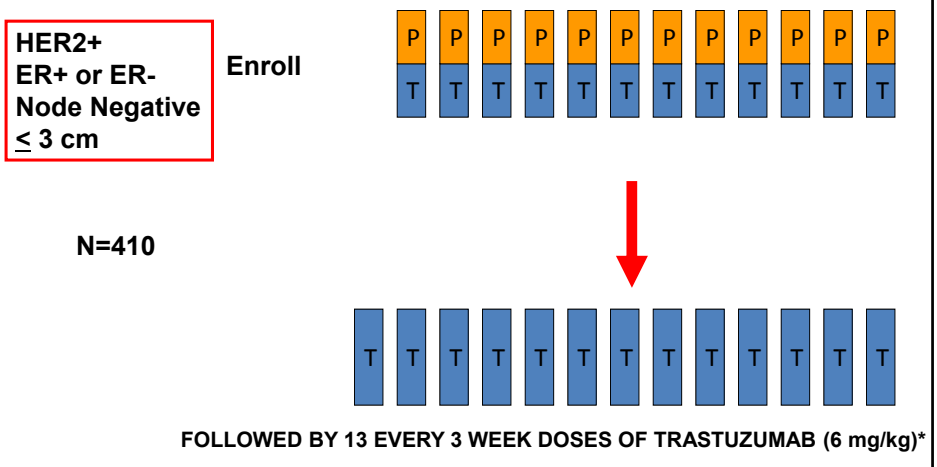
APHINITY: Conclusions

- The APHINITY study met its primary objective
  - Pertuzumab reduced the risk of an IDFS event by 19% compared with placebo (HR 0.81; 95% CI 0.66, 1.00; p=0.045) at a median follow up of 45.4 months (3 years IDFS of 94.1% with pertuzumab and 93.2% with placebo)
- Treatment effect was homogenous throughout all subgroups, however the N+ and HR-negative cohorts appeared to derive most benefit at the current point of time
  - with a relative risk reduction of 23% and 24%, respectively and
  - a 3-year IDFS absolute increase of 1.8% and 1.6% respectively
- Cardiac toxicity was low and not different between the two arms.
- The incidence of diarrhea was increased in the pertuzumab arm and occurred predominantly during chemotherapy and with TCH.

Seven-year follow-up of adjuvant paclitaxel and trastuzumab (APT Trial) for node-negative, HER2+ Breast Cancer

Sara M. Tolaney, William T. Barry, Hao Guo, Deborah A. Dillon, Chau T. Dang, Denise A. Yardley, Beverly Moy, P. Kelly Marcom, Kathy S. Albain, Hope S. Rugo, Matthew Ellis, Iuliana Shapira, Antonio C. Wolff, Lisa A. Carey, Beth A. Overmoyer, Ann H. Partridge, Clifford A. Hudis, Ian E. Krop, Harold J. Burstein, Eric P. Winer

APT: Study Design

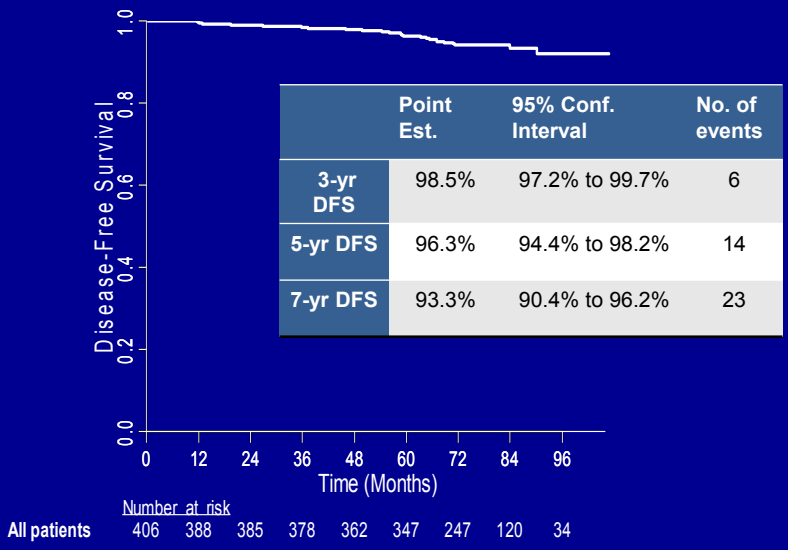


Presented by: Sara M. Tolaney

Patient Characteristics

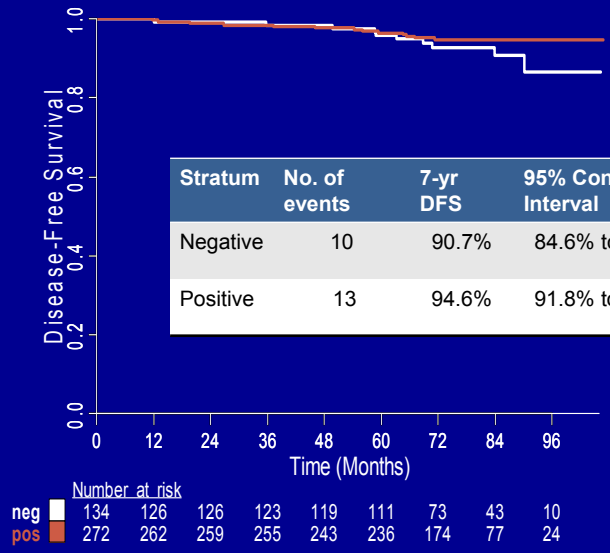
	N	%
Age		
<50	132	33
50-70	233	57
≥70	41	10
Size of Primary Tumor		
T1a ≤0.5 cm	77	19
T1b >0.5-≤1.0	124	31
T1c >1.0-≤2.0	169	42
T2 >2.0-≤3.0	36	9
Histologic Grade		
I Well differentiated	44	11
II Moderately differentiated	131	32
III Poorly differentiated	228	56
HR Status (ER and/or PR)		
Positive	272	67
Negative	134	33

Disease-Free Survival



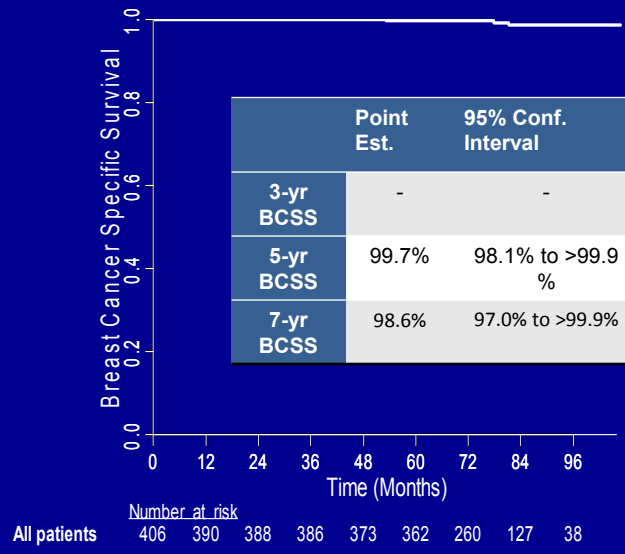
	Point Est.	95% Conf. Interval	No. of events
3-yr DFS	98.5%	97.2% to 99.7%	6
5-yr DFS	96.3%	94.4% to 98.2%	14
7-yr DFS	93.3%	90.4% to 96.2%	23

Disease-Free Survival by HR status



Stratum	No. of events	7-yr DFS	95% Conf. Interval
Negative	10	90.7%	84.6% to 97.2%
Positive	13	94.6%	91.8% to 97.5%

Breast Cancer Specific Survival



	Point Est.	95% Conf. Interval	No. of events
3-yr BCSS	-	-	0
5-yr BCSS	99.7%	98.1% to >99.9 %	1
7-yr BCSS	98.6%	97.0% to >99.9%	3

Presented by:

Conclusions

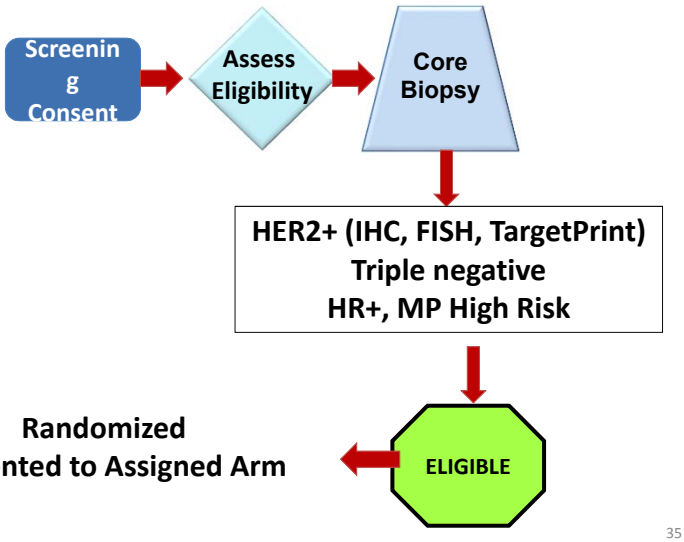
- With a median follow-up of 6.5 years, the 7-yr DFS was 93.3%, with just 4 distant recurrences
- The 7-yr RFI (including invasive local/regional + distant recurrences + deaths due to breast cancer) was 97.5%
- With longer term follow-up, adjuvant paclitaxel and trastuzumab is associated with excellent outcomes, suggesting that it remains a standard regimen for the majority of patients with stage I HER2+ breast cancer

Presented by:

Pembrolizumab plus standard neoadjuvant therapy for high-risk breast cancer: Results from the I-SPY 2 Trial

Rita Nanda, Minetta C. Liu, Douglas Yee, Angela M. DeMichele, Christina Yau, Smita M. Asare, Nola M. Hylton, Laura J. van't Veer, Jane Perlmutter, Anne M. Wallace, A. Jo Chien, Andres Forero-Torres, Erin D. Ellis, Heather S. Han, Amy S. Clark, Kathy S. Albain, Judy C. Boughey, Anthony D. Elias, **Claudine Isaacs, Kathleen Kemmer, Hope S. Rugo**, **Michelle Melisko**, **Fraser Symmans**, Donald A. Berry, Laura J. Esserman, I-SPY 2 TRIAL Investigators.

I-SPY 2 TRIAL Eligibility



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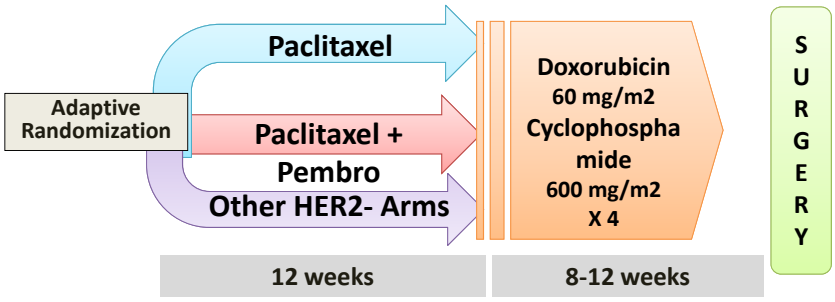
I-SPY 2 TRIAL Schema: HER2- Signatures



Control
Paclitaxel 80 mg/m2 every wk x 12

Experimental
Paclitaxel 80 mg/m2 every wk x 12
Pembro 200 mg every 3 wks x 4

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Pembrolizumab graduated in all HER2- signatures: Both HR+/HER2- and TN

Signature	Estimated pCR rate (95% probabilty interval)		Probability pembro is superior to control	Predictive probability of success in phase 3
	Pembro	Control		
All HER2-	**0.46** (0.34 – 0.58)	**0.16** (0.06 – 0.27)	**> 99%**	**99%**
TNBC	**0.60** (0.43 – 0.78)	**0.20** (0.06 – 0.33)	**>99%**	**>99%**
HR+/HER2-	**0.34** (0.19 – 0.48)	**0.13** (0.03 – 0.24)	**>99%**	**88%**

The Bayesian model estimated pCR rates appropriately adjust to characteristics of the I-SPY 2 population.
The raw pCR rates (not shown) are higher than the model estimate of 0.604 in TNBC.

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Adverse Events of Special Interest (including immune-related toxicities)

	Pembrolizumab (n=69) % (n)		Control (n=180) % (n)	
	All grades	Grade 3-5	All grades	Grade 3-5
Hypothyroidism	8.7 (6)	1.4 (1)	0.6 (1)	0 (0)
Hyperthyroidism	4.3 (3)	0 (0)	0 (0)	0 (0)
Adrenal Insufficiency^	8.7 (6)	7.2 (5)	0 (0)	0 (0)
Hepatitis	2.9 (2)	2.9 (2)	0 (0)	0 (0)
Pneumonitis	2.9 (2)	0 (0)	1.1 (2)	0.6 (1)
Colitis	1.4 (1)	1.4 (1)	0.6 (1)	0.6 (1)
Pruritis	24.6 (17)	0 (0)	11.1 (20)	0.6 (1)

*includes both hyperthyroidism and hypothyroidism
^includes primary and secondary causes of AI

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Conclusions

- Pembrolizumab x 4 cycles plus paclitaxel has graduated for all HER2- signatures studied
  - Tripling of the estimated pCR rate in TNBC (60% vs 20%)
  - Near tripling of the estimated pCR rate in HR+/HER2- (34% vs 13%)
  - First agent to graduate in HR+/HER2- signature
- Adrenal insufficiency was observed at a higher rate than previously reported in advanced cancer; pts are doing well on replacement therapy; follow-up of patient outcomes is ongoing

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Early stage disease: my take

- Omission of anthracyclines feasible in high risk HER2-negative breast cancer
- Addition of pertuzumab to adjuvant HER2-directed regimens results in modest benefit, especially in node-negative disease
- Paclitaxel plus trastuzumab remains reasonable choice for lower risk HER2+ cancers
- Addition of pembrolizumab to paclitaxel:
  - Triples PCR rate in TNBC (but control only 20%)
  - Improves PCR for high risk ER+

Phase 2 Study of Pembrolizumab Monotherapy for Previously Treated Metastatic Triple-Negative Breast Cancer: KEYNOTE-086 Cohort A

Sylvia Adams,[1] Peter Schmid,[2] Hope S. Rugo,[3] Eric P. Winer,[4] Delphine Loirat,[5] Ahmad Awada,[6] David W. Cescon,[7] Hiroji Iwata,[8] Mario Campone,[9] Rita Nanda,[10] Rina Hui,[11] Giuseppe Curigliano,[12] Deborah Toppmeyer,[13] Joyce O'Shaughnessy,[14] Sherene Loi,[15] Shani Paluch-Shimon,[16] Deborah Card,[17] Jing Zhao,[17] Vassiliki Karantza,[17] Javier Cortés[18]

[1]Perlmutter Cancer Center, New York University School of Medicine, New York, NY, USA; [2]Barts Health NHS Trust, London, UK;[3]University of California San Francisco Comprehensive Cancer Center, San Francisco, CA, USA; [4]Dana-Farber Cancer Institute, Boston, MA, USA; [5]Institut Curie, Paris, France; [6]Institut Jules Bordet, Universite Libre de Bruxelles, Brussels, Belgium; [7]Princess Margaret Cancer Center, Toronto, ON, Canada; [8]Aichi Cancer Center Hospital, Nagoya, Japan; [9]Institut de Cancerologie de l'Ouest, Nantes, France; [10]University of Chicago, Chicago, IL, USA; [11]Westmead Hospital, The University of Sydney, Australia; [12]Istituto Europeo di Oncologia, Milan, Italy; [13]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA; [14] Baylor University Medical Center, Texas Oncology, US Oncology, Dallas, TX, USA; [15]Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia; [16]Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel; [17]Merck & Co., Inc., Kenilworth, NJ, USA; [18]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [18]Ramon y Cajal University Hospital, Madrid, Spain

Study Design – KEYNOTE-086 Cohort A

Patients

- Age ≥18 y
- Centrally confirmed TNBC[a]
- ≥1 prior systemic treatment for mTNBC with documented progression
- ECOG PS 0-1
- LDH <2.5 x ULN
- Tumor biopsy sample for PD-L1 evaluation
- No radiographic evidence of CNS metastases
- Measurable disease per RECIST v1.1 by central review

Pembrolizumab 200 mg IV Q3W

for 2 years or until PD, intolerable toxicity, patient withdrawal, or investigator decision

Protocol-specified follow-up

- Primary end points: ORR[b] and safety
- Secondary end points[b]: DOR, DCR,[c] PFS, OS

[a]<1% tumor cells positive for ER and PR by IHC, irrespective of intensity, and HER2 IHC 0 or 1+ or FISH negative. [b]Assessed in the total population and in the PD-L1–positive population. [c]DCR = disease control rate = SD ≥24 wk + CR + PR.

Enrollment and Disposition

Median Follow-Up: 10.9 mo (range, 7.7-15.5)

386 patients screened

170 patients enrolled and treated
- 105 (61.8%) PD-L1 positive
- 64 (37.6%) PD-L1 negative
- 1 (0.6%) PD-L1 unknown

- 9 (5.3%) remain on treatment
- 161 (94.7%) discontinued
  - 108 (63.5%) radiologic PD
  - 42 (24.7%) clinical PD
  - 7 (4.1%) AE
  - 4 (2.4%) patient withdrawal

- PD-L1: assessed at a central laboratory
  - Samples: newly obtained core needle or excisional biopsy samples from non-irradiated metastatic lesions or archival samples from the primary tumor
  - Assay: PD-L1 IHC 22C3 pharmDx (Agilent Technologies [formerly Dako])
  - Measure of expression: combined positive score (CPS)
    - Number of PD-L1-positive cells (tumor cells, lymphocytes, and macrophages) out of the total number of tumor cells × 100
    - PD-L1 positive: CPS ≥1%

Follow-up defined as time from first dose to database cutoff date.
Data cutoff date: Nov 10, 2016.

KEYNOTE 086: Baseline Demographics

Characteristic, n (%)	Total Population[a] n = 170	PD-L1 Positive n = 105	PD-L1 Negative n = 64
Female	170 (100)	105 (100)	64 (100)
Age, y, median (range)	53.5 (28-85)	53.0 (30-85)	55.0 (28-80)
Postmenopausal	140 (82.4)	85 (81.0)	54 (84.4)
ECOG PS 1	80 (47.1)	54 (51.4)	26 (40.6)
LDH >1×ULN	87 (51.2)	51 (48.6)	36 (56.2)
Visceral ± nonvisceral disease	126 (74.1)	74 (70.4)	51 (79.7)
Prior taxanes and anthracycline	163 (95.9)	102 (97.1)	60 (93.8)
Prior (neo)adjuvant therapy	142 (83.5)	86 (81.9)	55 (85.9)
Prior lines of therapy for metastatic disease			
1	53 (31.2)	36 (34.3)	17 (26.6)
2	43 (25.3)	27 (25.7)	15 (23.4)
≥3	74 (43.5)	42 (40.0)	32 (50.0)

[a]Includes 1 patient with unknown PD-L1 status.
Data cutoff date: Nov 10, 2016.

KEYNOTE 086: Best Overall Response
(RECIST v1.1, Central Review)

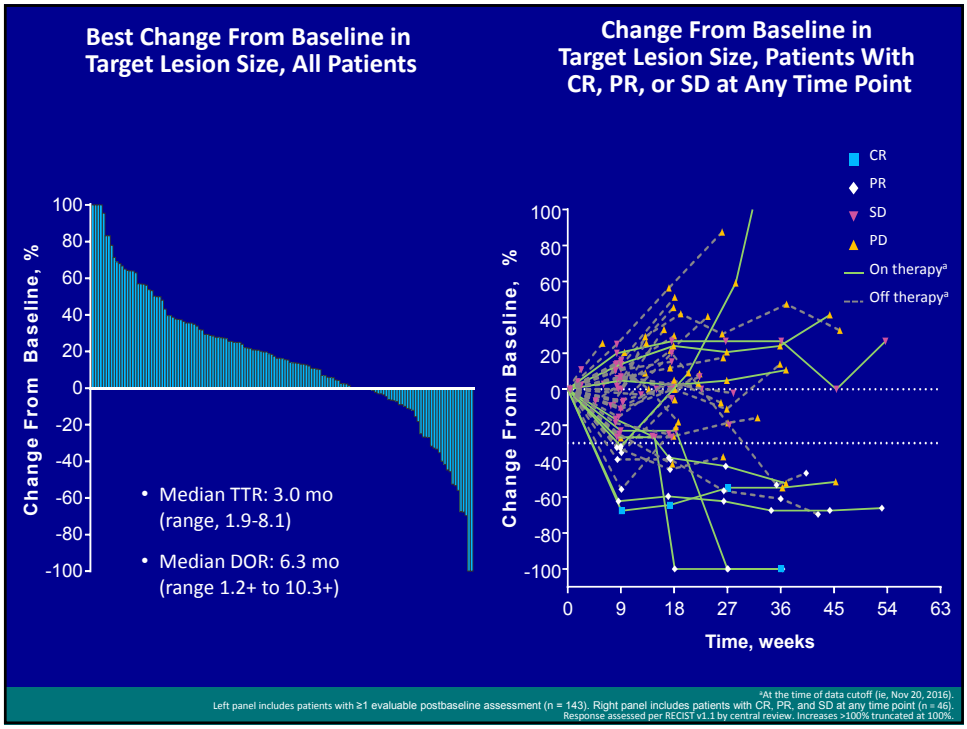
	Total Population[a] N = 170
ORR, n (%) [95% CI]	8 (4.7) [2.3-9.2]
DCR,[b] n (%) [95% CI]	13 (7.6) [4.4-12.7]
Best Overall Response, n (%)	
Complete response	1 (0.6)
Partial response	7 (4.1)
Stable disease	35 (20.6)
Progressive disease	103 (60.6)
Not evaluable[c]	5 (2.9)
Not able to be assessed[d]	19 (11.2)

[a]Includes the patient with unknown PD-L1 status. [b]DCR = disease control rate = SD ≥24 wk + CR + PR. [c]Patients who had ≥1 postbaseline tumor assessment, none of which were evaluable. [d]Patients who had no postbaseline tumor assessment because of death, withdrawal of consent, loss to follow-up, or start of new anticancer therapy. Data cutoff date: Nov 10, 2016.

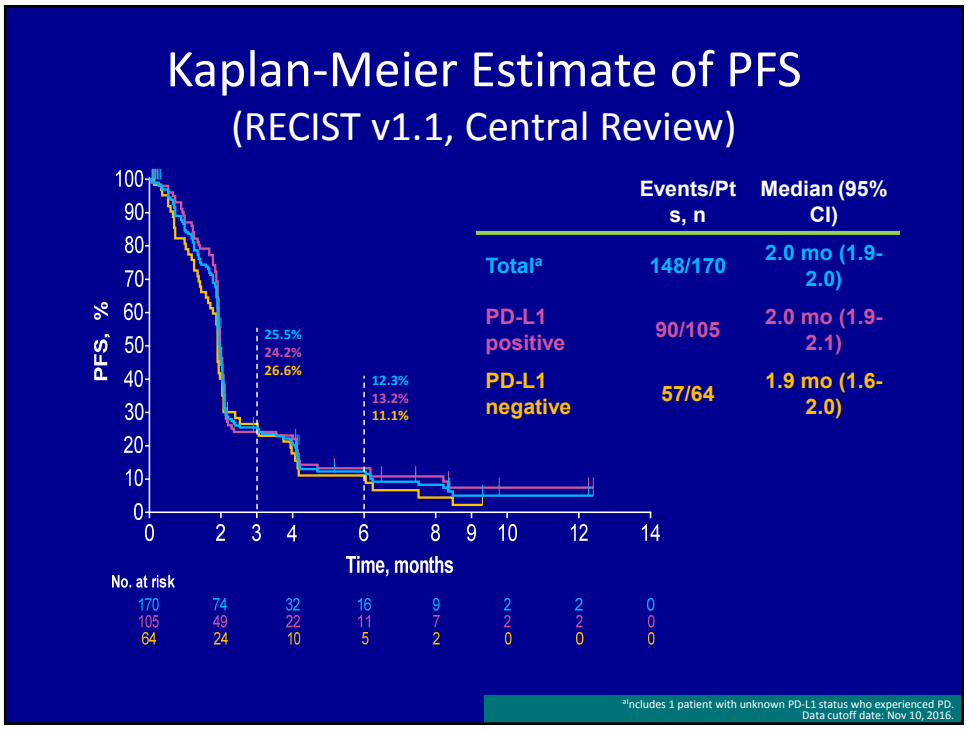
KEYNOTE 086: Best Overall Response
(RECIST v1.1, Central Review)

	Total Population[a] N = 170	PD-L1 Positive n = 105	PD-L1 Negative n = 64
ORR, n (%) [95% CI]	8 (4.7) [2.3-9.2]	5 (4.8) [1.8-10.9]	3 (4.7) [1.1-13.4]
DCR,[b] n (%) [95% CI]	13 (7.6) [4.4-12.7]	10 (9.5) [5.1-16.8]	3 (4.7) [1.1-13.4]
Best Overall Response, n (%)			
Complete response	1 (0.6)	1 (1.0)	0
Partial response	7 (4.1)	4 (3.8)	3 (4.7)
Stable disease	35 (20.6)	22 (21.0)	12 (18.8)
Progressive disease	103 (60.6)	66 (62.9)	37 (57.8)
Not evaluable[c]	5 (2.9)	2 (1.9)	3 (4.7)
Not able to be assessed[d]	19 (11.2)	10 (9.5)	9 (14.1)

[a]Includes the patient with unknown PD-L1 status. [b]DCR = disease control rate = SD ≥24 wk + CR + PR. [c]Patients who had ≥1 postbaseline tumor assessment, none of which were evaluable. [d]Patients who had no postbaseline tumor assessment because of death, withdrawal of consent, loss to follow-up, or start of new anticancer therapy. Data cutoff date: Nov 10, 2016.

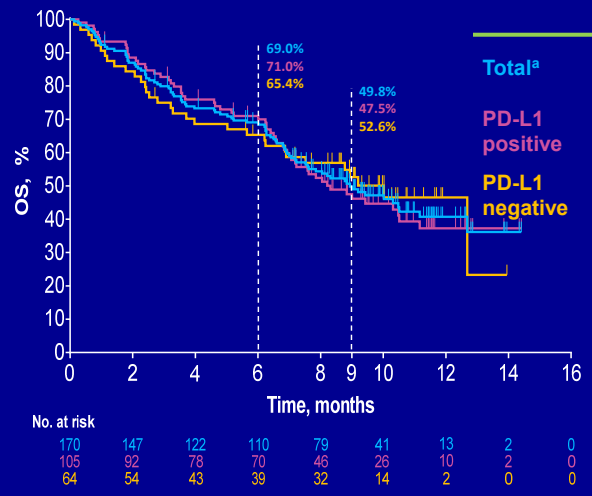


[a]At the time of data cutoff (ie, Nov 20, 2016).
Left panel includes patients with ≥1 evaluable postbaseline assessment (n = 143). Right panel includes patients with CR, PR, and SD at any time point (n = 46).
Response assessed per RECIST v1.1 by central review. Increases >100% truncated at 100%.



[a]Includes 1 patient with unknown PD-L1 status who experienced PD.
Data cutoff date: Nov 10, 2016.

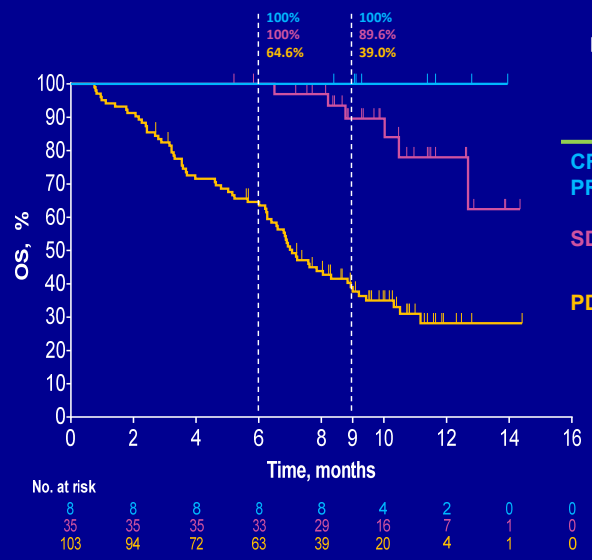
Kaplan-Meier Estimate of OS



	Events/Pts, n	Median (95% CI)
Total[a]	90/170	8.9 mo (7.2-11.2)
PD-L1 positive	58/105	8.3 mo (6.9-10.5)
PD-L1 negative	32/64	10.0 mo (6.2-NR)

NR, not reportable.
[a]Includes 1 patient with unknown PD-L1 status who was alive at data cutoff.
Data cutoff date: Nov 10, 2016.

Overall Survival by Best Overall Response



Exploratory Analysis

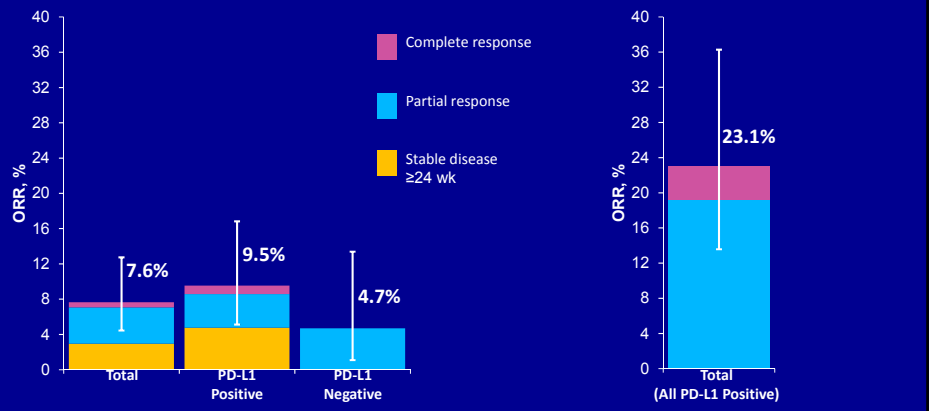
	Events/Pts, n	Median (95% CI)
CR or PR	0/8	Not reached (NR-NR)
SD	6/35	Not reached (12.7-NR)
PD	66/103	7.1 mo (6.3-8.8)

NR, not reportable.
Patients with response that was nonevaluable (n = 5) or not assessed (n = 19) per RECIST v1.1 by central review are not included. Data cutoff date: Nov 10, 2016.

Pembrolizumab Antitumor Activity in Previously Treated and Previously Untreated mTNBC

Cohort A (N = 170): Previously Treated, Regardless of PD-L1 Expression

Cohort B (N = 52)[1]: Previously Untreated, PD-L1 Positive

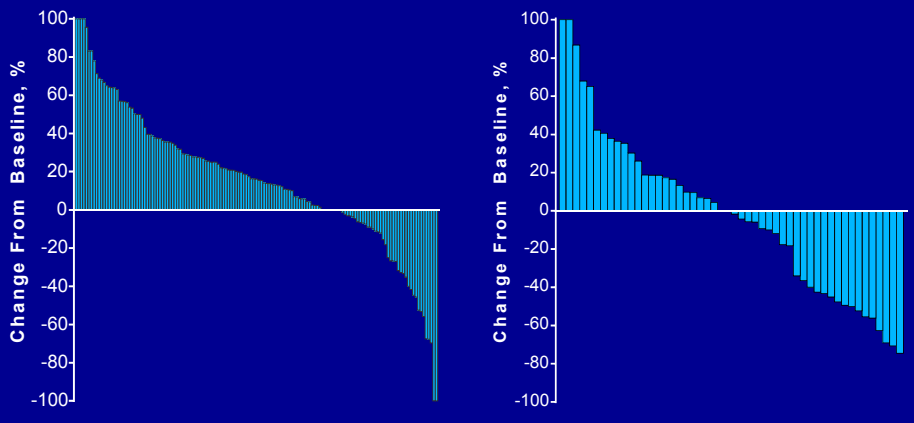


1. Adams S et al. ASCO Annual Meeting; Jun 2-6, 2017; Chicago, IL; abstr 1088; presented Sunday, Jun 4, from 8:00-11:30 am on poster board #80.

Pembrolizumab Antitumor Activity in Previously Treated and Previously Untreated mTNBC

Cohort A (N = 170): Previously Treated, Regardless of PD-L1 Expression

Cohort B (N = 52)[1]: Previously Untreated, PD-L1 Positive



Plots include patients with ≥1 evaluable postbaseline assessment (n = 143 for cohort A, n = 50 for cohort B).
1. Adams S, et al. ASCO Annual Meeting; Jun 2-6, 2017; Chicago, IL; abstr 1088; presented Sunday, Jun 4, from 8:00-11:30 am on poster board #80.

Summary and Conclusions

- Pembrolizumab monotherapy showed durable antitumor activity in a subset of patients with heavily pretreated mTNBC
  - Activity appeared independent of tumor PD-L1 expression
  - ORR was numerically lower in patients with poor prognostic factors
  - Survival is promising, particularly in patients with CR, PR, or SD
- Activity may be greater in patients with less heavily pretreated disease
- Analyses of non–PD-L1 biomarkers, including TILs, are ongoing
- Treatment was well tolerated
- Randomized studies of pembrolizumab monotherapy and pembrolizumab-based combination therapy are ongoing for TNBC

OlympiAD: Phase III trial of olaparib monotherapy versus chemotherapy for patients with HER2-negative metastatic breast cancer and a germline *BRCA* mutation

Mark Robson,[1] Seock-Ah Im,[2] Elżbieta Senkus,[3] Binghe Xu,[4] Susan M Domchek,[5] Norikazu Masuda,[6] Suzette Delaloge,[7] Wei Li,[8] Nadine Tung,[9] Anne Armstrong,[10] Wenting Wu,[11] Carsten Goessl,[11] Sarah Runswick,[12] Pierfranco Conte[13]

ClinicalTrials.gov identifier: NCT02000622. This study was sponsored by AstraZeneca

OlympiAD study design

- HER2-negative metastatic BC
  - ER+ and/or PR+ or TNBC
- Deleterious or suspected deleterious g*BRCA*m
- Prior anthracycline and taxane
- ≤2 prior chemotherapy lines in metastatic setting
- HR+ disease progressed on ≥1 endocrine therapy, or not suitable
- If prior platinum use
  - No evidence of progression during treatment in the advanced setting
  - ≥12 months since (neo)adjuvant treatment

Olaparib 300 mg tablets bd

Chemotherapy treatment of physician's choice (TPC)
- Capecitabine
- Eribulin
- Vinorelbine

Treat until progression

Primary endpoint:
- Progression-free survival (RECIST 1.1, BICR)

Secondary endpoints:
- Time to second progression or death
- Overall survival
- Objective response rate
- Safety and tolerability
- Global HRQoL (EORTC-QLQ-C30)

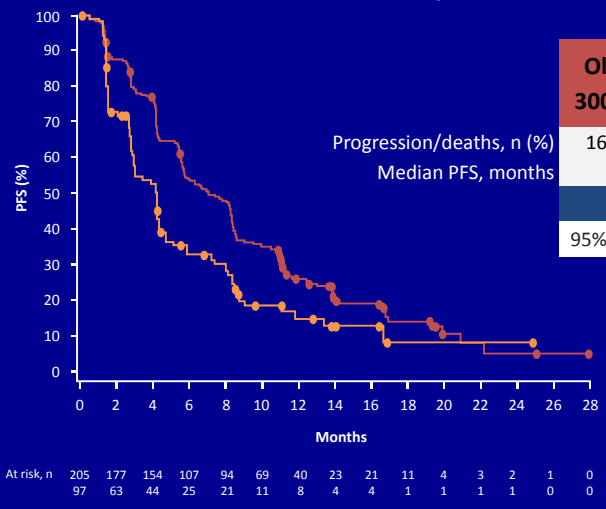
OlympiAD: Patient characteristics

	Olaparib 300 mg bd (N=205)	Chemotherapy TPC (N=97)
Age, years (median, range)	44 (22–76)	45 (24–68)
Male, n (%)	5 (2)	2 (2)
White race, n (%)	134 (65)	63 (65)
***BRCA* mutation status, n (%)**		
BRCA1	117 (57)	51 (53)
BRCA2	84 (41)	46 (47)
Both	4 (2)	0
Hormonal receptor status, n (%)		
ER+ and/or PR+	103 (50)	49 (51)
TNBC	102 (50)	48 (49)
Prior chemotherapy for metastasis, n (%)	146 (71)	69 (71)
Prior platinum treatment, n (%)	60 (29)	26 (27)

OlympiAD: Patient characteristics

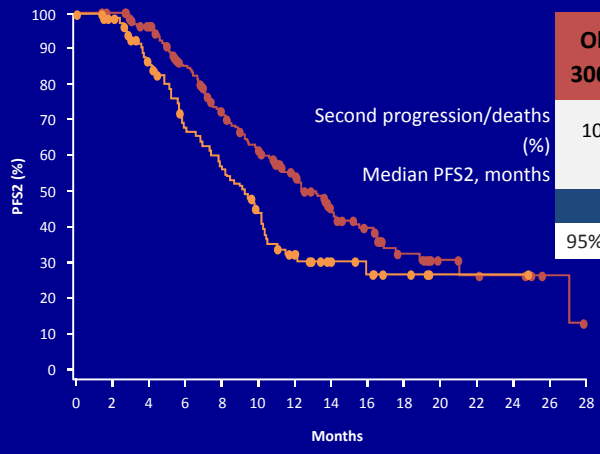
n (%)	Olaparib 300 mg bd (N=205)	Chemotherapy TPC (N=97)
***De novo* metastatic breast cancer**	26 (13)	12 (12)
Measurable disease	167 (82)	66 (68)
≥2 sites	159 (78)	72 (74)
Bone metastases only	16 (8)	6 (6)
Prior lines of chemotherapy for metastases		
0	68 (33)	31 (32)
1	80 (39)	42 (43)
2	57 (28)	24 (25)
Chemotherapy TPC*		
Capecitabine	NA	41 (45)
Eribulin		34 (37)
Vinorelbine		16 (18)

Primary endpoint: progression-free survival by BICR



	Olaparib 300 mg bd	Chemotherapy TPC
Progression/deaths, n (%)	163 (79.5)	71 (73.2)
Median PFS, months	7.0	4.2
HR 0.58		
95% CI 0.43 to 0.80; *P*=0.0009		

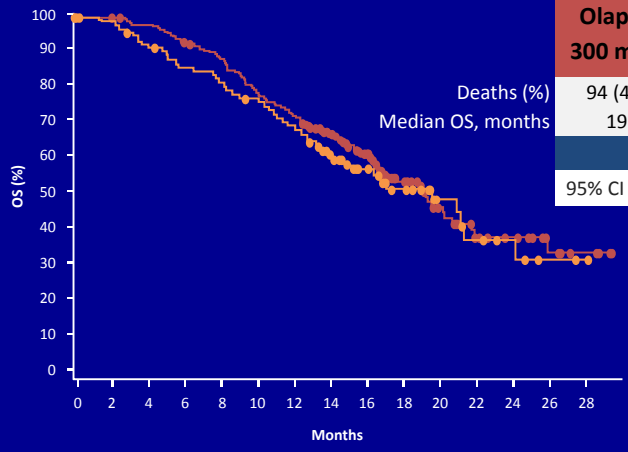
Time to second progression or death (PFS2) by investigator assessment



	Olaparib 300 mg bd	Chemotherapy TPC
Second progression/deaths (%)	104 (50.7)	53 (54.6)
Median PFS2, months	13.2	9.3
HR 0.57		
95% CI 0.40 to 0.83; *P*=0.0033		

At risk, n															
Olaparib 300 mg bd	205	199	185	152	123	102	75	44	34	18	8	6	5	2	0
Chemotherapy TPC	97	85	69	51	42	31	19	10	7	4	1	1	1	0	0

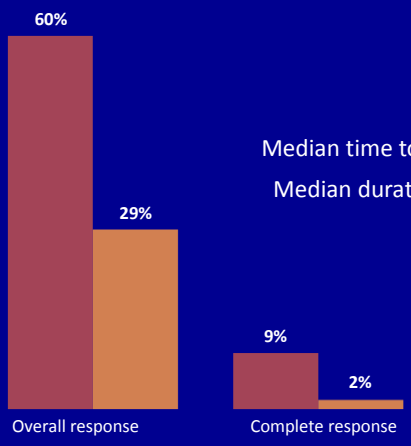
Overall survival (interim analysis; 46% data maturity)



	Olaparib 300 mg bd	Chemotherapy TPC
Deaths (%)	94 (45.9)	46 (47.4)
Median OS, months	19.3	19.6
HR 0.90		
95% CI 0.63 to 1.29; *P*=0.5665		

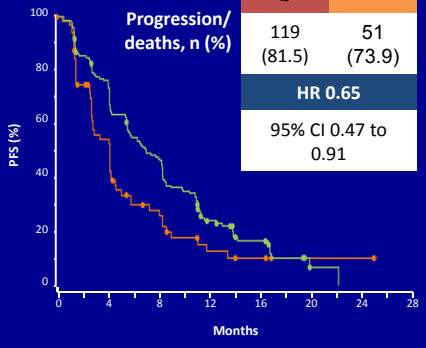
At risk, n															
Olaparib 300 mg bd	205	205	199	189	178	159	146	109	78	46	30	18	14	8	4	0
Chemotherapy TPC	97	92	85	78	74	69	62	50	34	24	13	9	7	4	2	0

Objective response by BICR



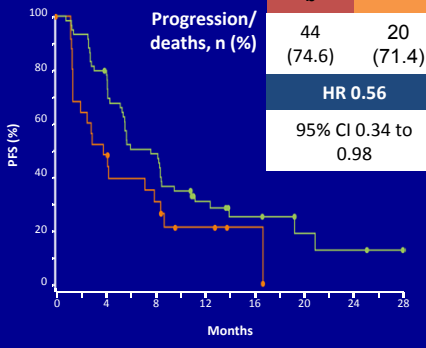
	Olaparib 300 mg bd	Chemotherapy TPC
n	167	66
Median time to response, days	47	45
Median duration of response, months	6.2 (4.6–7.2)	7.1 (2.8–12.2)

Subgroup analyses: PFS by BICR



	Olaparib	TPC
Progression/ deaths, n (%)	119 (81.5)	51 (73.9)
HR 0.65		
95% CI 0.47 to 0.91		

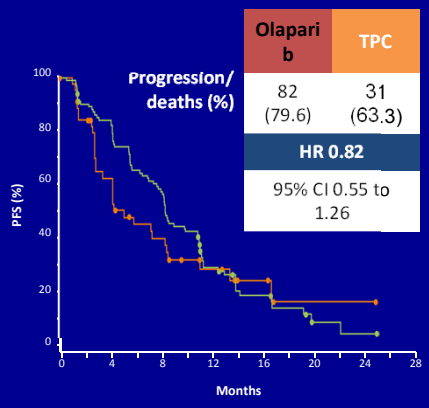
Prior chemotherapy



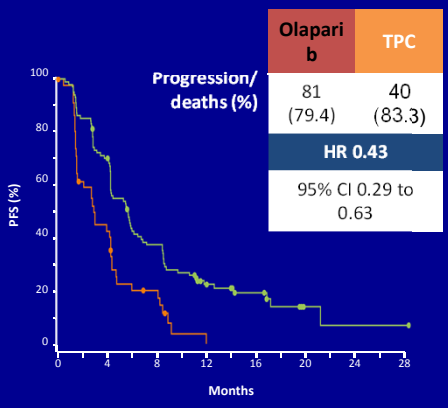
	Olaparib	TPC
Progression/ deaths, n (%)	44 (74.6)	20 (71.4)
HR 0.56		
95% CI 0.34 to 0.98		

No prior chemotherapy

Subgroup analyses: PFS by BICR

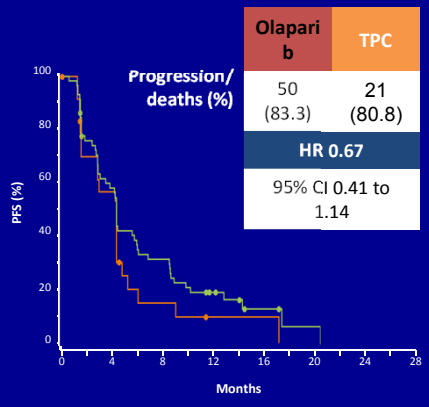


ER+ and/or PR+

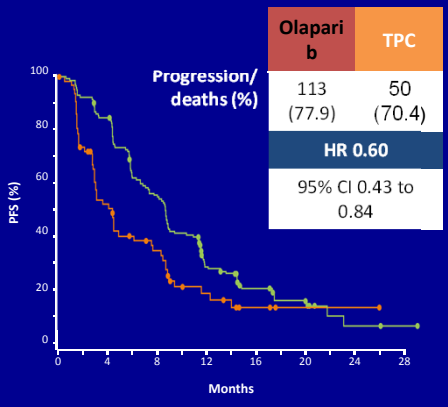


TNBC

Subgroup analyses: PFS by BICR



Prior platinum



No prior platinum

Conclusions

- Olaparib tablet monotherapy provided a statistically significant and clinically meaningful PFS benefit versus standard-of-care chemotherapy for patients with HER2-negative metastatic breast cancer and a g*BRCA*m
- Olaparib was generally well tolerated with <5% discontinuing treatment for toxicity and a lower rate of Grade ≥3 AEs compared with chemotherapy
- OlympiAD is the first Phase III study in metastatic breast cancer patients demonstrating benefit for a PARP inhibitor over an active comparator

MONARCH 2: Abemaciclib in Combination with Fulvestrant in Patients with HR+/HER2- Advanced Breast Cancer Who Progressed On Endocrine Therapy

George W. Sledge, Jr[1], Masakazu Toi[2], Patrick Neven[3], Joohyuk Sohn[4], Kenichi Inoue[5], Xavier B. Pivot[6], Olga Nikolaevna Burdaeva[7], Meena Okera[8], Norikazu Masuda[9], Peter A. Kaufman[10], Han A. Koh[11], Eva-Maria Grischke[12], Martin Frenzel[13], Yong Lin[13], Susana Barriga[14], Ian C. Smith[13], Nawel Bourayou[15], and Antonio Llombart[16]

[1]Stanford University, Stanford, CA; [2]Kyoto University, Kyoto, Japan; [3]Universitaire Ziekenhuizen Leuven - Campus Gasthuisberg, Leuven, Belgium; [4]Yonsei Cancer Center, Seoul, Korea; [5]Saitama Cancer Center, Saitama, Japan; [6]CHU de Besancon Hopital Jean Minjoz, Besancon Cedex, France; [7]Arkhangelsk Regional Clinical Oncology Dispensary, Arkhangelsk, Russian Federation; [8]Adelaide Cancer Centre, Adelaide, Australia; [9]National Hospital Organization Osaka National Hospital, Osaka, Japan; [10]Norris Cotton Cancer Center at Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA; [11]Kaiser Permanente Medical Group, Bellflower, CA, USA; [12]Universitätsklinikum Tübingen Frauenklinik, Tübingen, Germany; [13]Eli Lilly and Company, Indianapolis, IN, USA; [14]Eli Lilly and Company, Madrid, Spain; [15]Eli Lilly and Company, Paris, France; [16]Hospital Arnau Vilanova, Valencia, Spain

MONARCH 2: Study Design

N=669

- HR+/HER2- ABC
- Pre/peri-[a] or postmenopausal
- ET resistant:
  - Relapsed on neoadjuvant or on/within 1 yr of adjuvant ET
  - Progressed on first-line ET
- No chemo for MBC
- No more than 1 ET for MBC
- ECOG PS ≤ 1

2:1 Randomization

abemaciclib: 150 mg[b] BID (continuous schedule)
fulvestrant: 500 mg[c]

placebo: BID (continuous schedule)
fulvestrant: 500 mg[c]

Primary endpoint:
Investigator-assessed PFS

Secondary endpoint:
OS, Response, Clinical Benefit Rate, Safety

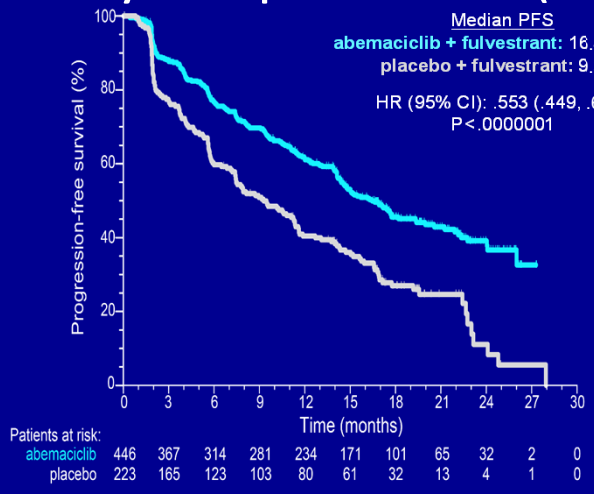
Stratification factors:
- Metastatic site
- ET resistance (primary vs secondary)[4,5]

[b]Dose reduced by protocol amendment in all new and ongoing patients from 200 mg to 150 mg BID after 178 patients enrolled

Patient and Disease Characteristics

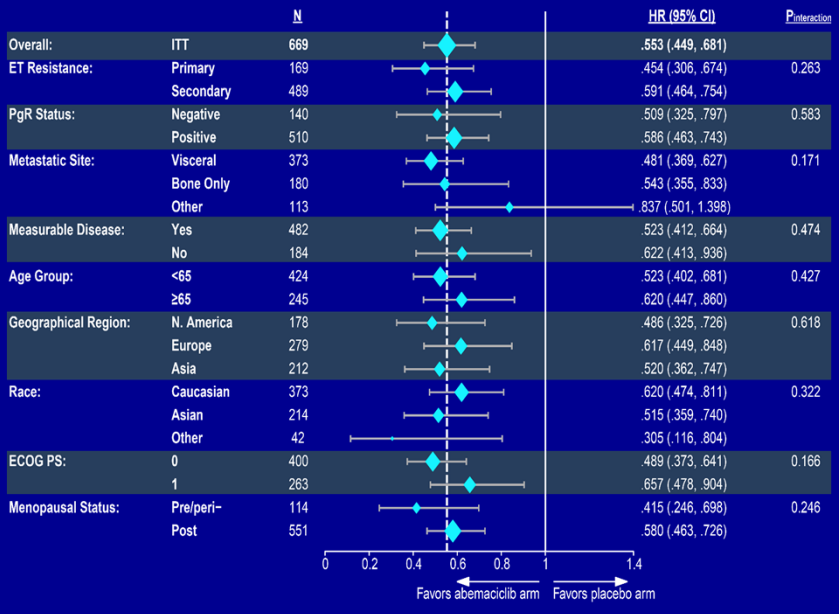
		abemaciclib + fulvestrant N = 446	placebo + fulvestrant N = 223
Median age (range)		59 (32-91)	62 (32-87)
ET resistance[a]	Primary	111 (24.9)	58 (26.0)
	Secondary	326 (73.1)	163 (73.1)
Most recent ET[a,b]	Neoadjuvant or adjuvant	263 (59.0)	133 (59.6)
	Metastatic	171 (38.3)	85 (38.1)
Prior AI	Yes	316 (70.9)	149 (66.8)
	No	130 (29.1)	74 (33.2)
PgR status[a]	Positive	339 (76.0)	171 (76.7)
	Negative	96 (21.5)	44 (19.7)
Metastatic site[a]	Visceral	245 (54.9)	128 (57.4)
	Bone only	123 (27.6)	57 (25.6)
	Other (non-visceral soft tissue)	75 (16.8)	38 (17.0)
Measurable disease	Yes	318 (71.3)	164 (73.5)
	No	128 (28.7)	59 (26.5)
Menopausal status[a]	Pre/peri-	72 (16.1)	42 (18.8)
	Post-	371 (83.2)	180 (80.7)

Primary Endpoint: PFS (ITT)



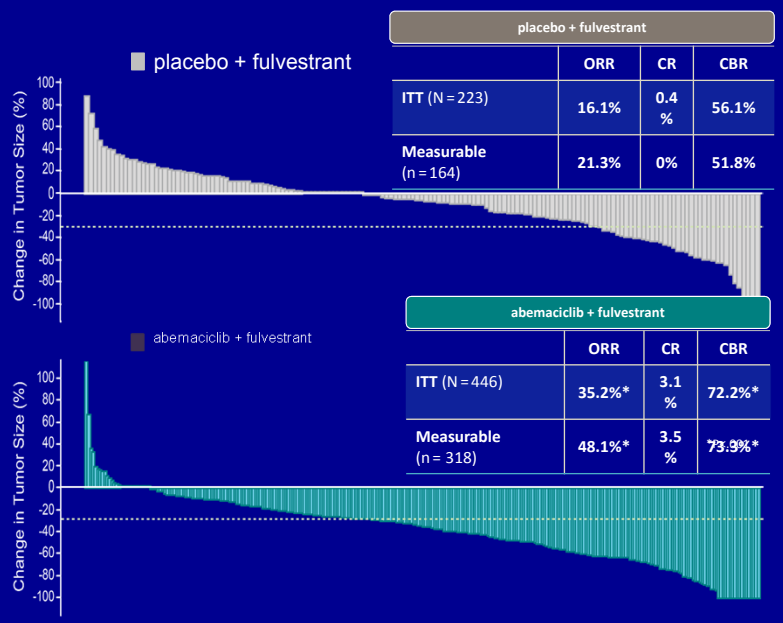
PFS benefit confirmed by blinded independent central review (HR: .460; 95% CI: .363, .584; P<.000001)

PFS: Patient Subgroup Analysis (ITT)



		N	HR (95% CI)	$P_{interaction}$
Overall:	ITT	669	.553 (.449, .681)	
ET Resistance:	Primary	169	.454 (.306, .674)	0.263
	Secondary	489	.591 (.464, .754)	
PgR Status:	Negative	140	.509 (.325, .797)	0.583
	Positive	510	.586 (.463, .743)	
Metastatic Site:	Visceral	373	.481 (.369, .627)	0.171
	Bone Only	180	.543 (.355, .833)	
	Other	113	.837 (.501, 1.398)	
Measurable Disease:	Yes	482	.523 (.412, .664)	0.474
	No	184	.622 (.413, .936)	
Age Group:	<65	424	.523 (.402, .681)	0.427
	≥65	245	.620 (.447, .860)	
Geographical Region:	N. America	178	.486 (.325, .726)	0.618
	Europe	279	.617 (.449, .848)	
	Asia	212	.520 (.362, .747)	
Race:	Caucasian	373	.620 (.474, .811)	0.322
	Asian	214	.515 (.359, .740)	
	Other	42	.305 (.116, .804)	
ECOG PS:	0	400	.489 (.373, .641)	0.166
	1	263	.657 (.478, .904)	
Menopausal Status:	Pre/peri-	114	.415 (.246, .698)	0.246
	Post	551	.580 (.463, .726)	

Change in Tumor Size



placebo + fulvestrant	ORR	CR	CBR
ITT (N = 223)	16.1%	0.4 %	56.1%
Measurable (n = 164)	21.3%	0%	51.8%

abemaciclib + fulvestrant	ORR	CR	CBR
ITT (N = 446)	35.2%*	3.1 %	72.2%*
Measurable (n = 318)	48.1%*	3.5 %	73.3%*

TEAE (Safety Population)

	abemaciclib + fulvestrant n = 441			placebo + fulvestrant n = 223		
≥ 20 % in either arm, n (%)	All	G3	G4	All	G3	G4
Any	435 (98.6)	241 (54.6)	26 (5.9)	199 (89.2)	46 (20.6)	5 (2.2)
Diarrhea[a]	381 (86.4)	59 (13.4)	0	55 (24.7)	1 (0.4)	0
Neutropenia[b]	203 (46.0)	104 (23.6)	13 (2.9)	9 (4.0)	3 (1.3)	1 (0.4)
Nausea	199 (45.1)	12 (2.7)	-	51 (22.9)	2 (0.9)	-
Fatigue	176 (39.9)	12 (2.7)	-	60 (26.9)	1 (0.4)	-
Abdominal pain	156 (35.4)	11 (2.5)	-	35 (15.7)	2 (0.9)	-
Anemia	128 (29.0)	31 (7.0)	1 (0.2)	8 (3.6)	2 (0.9)	0
Leukopenia	125 (28.3)	38 (8.6)	1 (0.2)	4 (1.8)	0	0
Decreased appetite	117 (26.5)	5 (1.1)	0	27 (12.1)	1 (0.4)	0
Vomiting	114 (25.9)	4 (0.9)	0	23 (10.3)	4 (1.8)	0
Headache	89 (20.2)	3 (0.7)	-	34 (15.2)	1 (0.4)	-

[a] Grade 2 diarrhea: abemaciclib + fulvestrant n = 140 (31.7%); placebo + fulvestrant n = 11 (4.9%).
[b] Febrile neutropenia was uncommon [6 patients in the abemaciclib arm (1 incorrectly coded; 1 post-chemotherapy)] and was not associated with severe infection

Conclusions

- Abemaciclib at 150 mg BID plus fulvestrant was an effective treatmwomen with HR+/HER2- ABC whose disease progressed on prior ent for endocrine therapy
- Abemaciclib plus fulvestrant significantly improved PFS (16.4 vs 9.3 months; HR: .553) and ORR (48.1% vs 21.3% in patients with measurable disease)
- Abemaciclib dosed on a continuous schedule was generally well-tolerated
  - Grade 3 & 4 neutropenia was 26.5%
  - Diarrhea typically occurred early and was managed with dose adjustment and antidiarrheal medication

Based on these results, abemaciclib in combination with endocrine therapy as adjuvant treatment of HR+/HER2- high-risk breast cancer will begin recruitment 3Q2017 (monarchE)

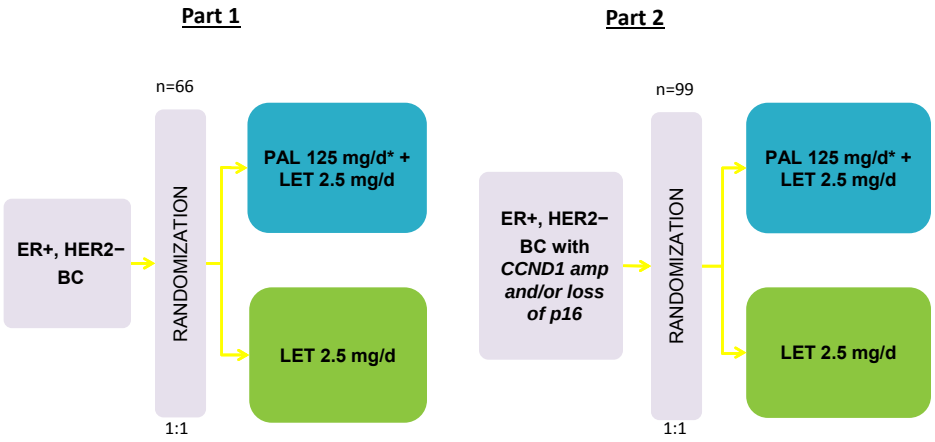
Overall Survival Results From the Randomized Phase 2 Study of Palbociclib in Combination With Letrozole vs Letrozole Alone for First-Line Treatment of ER+/HER2– Advanced Breast Cancer (PALOMA-1; TRIO-18)

Richard S. Finn,[1] John Crown,[2] Istvan Lang,[3] Katalin Boer,[4] Igor Bondarenko,[5] Sergey O. Kulyk,[6] Johannes Ettl,[7] Ravindranath Patel,[8] Tamas Pinter,[9] Marcus Schmidt,[10] Yaroslav V. Shparyk,[11] Anu Thummala,[12] Nataliya L. Voytko,[13] Camilla Fowst,[14]
Xin Huang,[15] Sindy Kim,[15] Dennis J. Slamon[1]

[1]David Geffen School of Medicine, Los Angeles, CA, USA; [2]Irish Cooperative Oncology Research Group, Dublin, Ireland; [3]National Institute of Oncology, Budapest, Hungary; [4]Szent Margit Korhaz, Onkologia, Budapest, Hungary; [5]Dnepropetrovsk State Medical Center, Dnipropetrovsk, Ukraine; [6]Municipal Treatment-and-Prophylactic Institution, Donetsk, Ukraine; [7]Technical University of Munich, Munich, Germany; [8]Comprehensive Blood and Cancer Center, Bakersfield, CA, USA; [9]Petz Aladar Megyei Oktato Korhaz, Gyor, Hungary; [10]Johannes Gutenberg University, Mainz, Germany; [11]Lviv State Oncologic Regional Treatment and Diagnostic Center, Lviv, Ukraine; [12]Comprehensive Cancer Centers of Nevada, Las Vegas, NV, USA; [13]Kyiv City Clinical Oncology Center, Kyiv, Ukraine; [14]Pfizer Inc, Milan, Italy; [15]Pfizer Inc, La Jolla, CA, USA

Presented at the 2017 ASCO Annual Meeting

PALOMA-1: Phase 2 Study Design

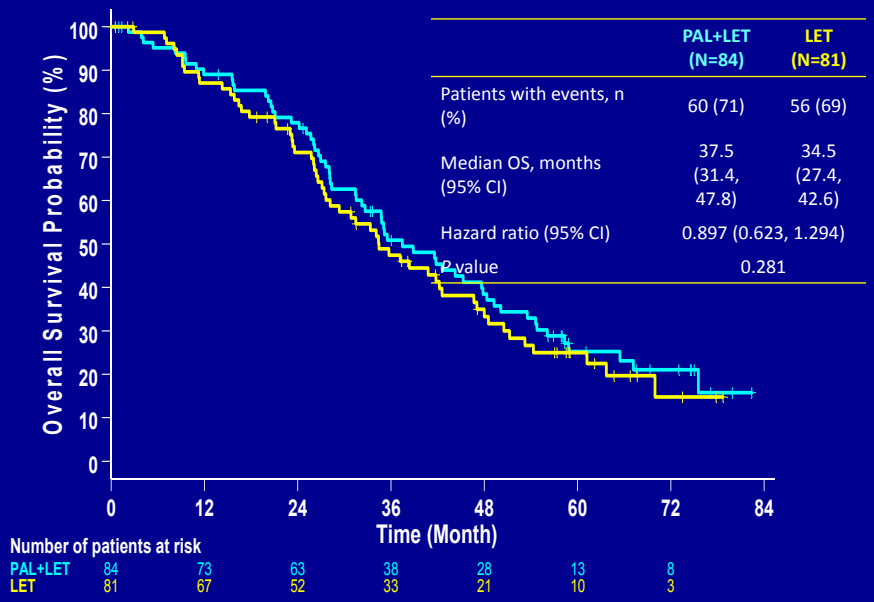


Stratification factors:
- Disease site (visceral vs bone only vs other)
- Disease-free interval (>12 vs ≤12 months from end of adjuvant therapy to recurrence or de novo advanced disease)

*Palbociclib schedule: 3 weeks on/1 week off (28-day cycle)
Amp=amplification; BC=breast cancer; ER=estrogen receptor; HER2=human epidermal growth factor receptor 2; LET=letrozole; PAL=palbociclib.

1.clinicaltrials.gov

OS: Phase 2 (ITT)



	PAL+LET (N=84)	LET (N=81)
Patients with events, n (%)	60 (71)	56 (69)
Median OS, months (95% CI)	37.5 (31.4, 47.8)	34.5 (27.4, 42.6)
Hazard ratio (95% CI)	0.897 (0.623, 1.294)	
P value	0.281	

Metastatic disease: my take

- Single agent pembrolizumab disappointing in pretreated TNBC
  - Await further results from first line cohort
- Olaparib significantly better than chemotherapy in BRCA-related cancers
- Abemaciclib effective in second-line setting
- No survival advantage for first-line palbociclib
  - Await PALOMA 2 survival results

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CANCER SURVEILLANCE AND OUTCOMES RESEARCH TEAM

ASCO 2017
Chicago, IL

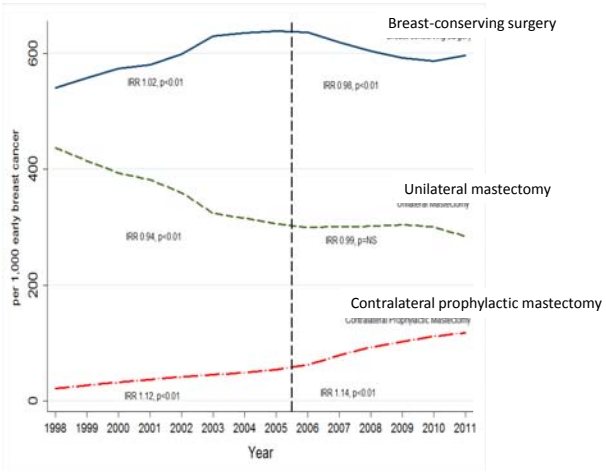
5 June 2017

Mastectomy Rates in Relation to Adoption of a Margin Guideline

Monica Morrow, Steven J. Katz, Reshma Jagsi
Memorial Sloan Kettering Cancer Center / University of Michigan

Overtreatment in Breast Cancer

n = 1,856,702



Albornoz C, Plast Reconstr Surg 2015;135:1518

SSO-ASTRO Consensus Guidelines on Margins for BCS+WBRT in Stage I and II Breast Cancer

Endorsed no ink on tumor

Presented Fall 2013

Epub Feb 2014

Print March, May 2014

Moran M, Ann Surg Oncol 2014;21:704
Moran M, J Clin Oncol 2014;32:1057

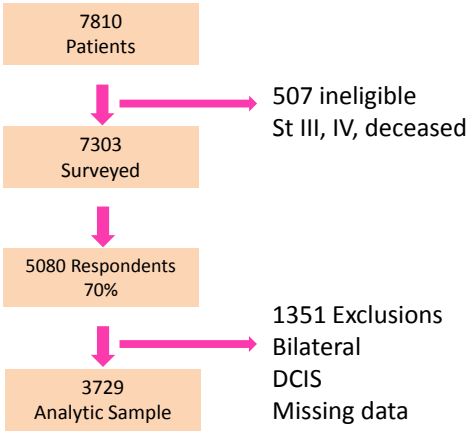
Moran M, Int J Radiat Oncol Biol Phys 2014;88:503

Objectives

- Examine time trends in the use of additional surgery after lumpectomy before and after guideline dissemination
- To determine the impact of these trends on rates of BCS

Patient Sample

- Age: 20-79 years
- Stage I+II breast cancer
- Dx 4/2013-4/2015
- LA + Georgia SEER



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Final Surgical Treatment

	April 2013	April 2015
BCS	52%	65%
Unilat Mastectomy	27%	18%
Bilat Mastectomy	21%	16%

p = .002

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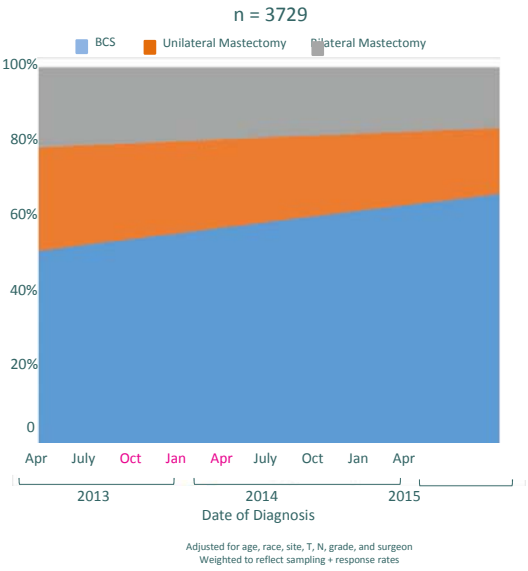
Trends in Final Surgical Treatment
Multinomial Logistic Regression



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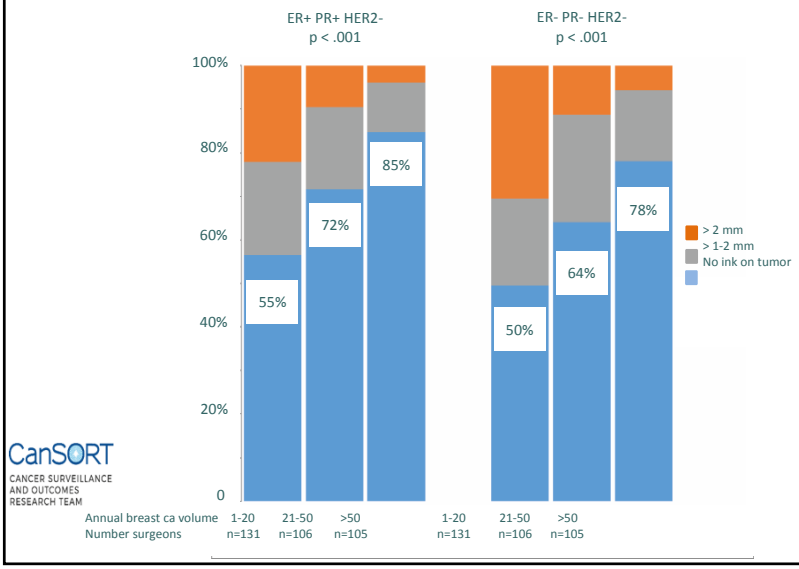
Relationship of Surgeon Volume to Preferred Margin Status



Summary

During the 2 year time period immediately before and after the SSO-ASTRO margin guideline, we observed:

- 16% decrease in additional surgery after initial lumpectomy
- 13% increase in final BCS
  - Decrease in both unilateral and bilateral mastectomy

Practice changing?

- Probably:
  - Olaparib in BRCA-mutated cancers
  - Abemaciclib as 3rd CDKi on the block
  - Pembrolizumab with chemotherapy pre-operatively
- Possibly not:
  - Adjuvant pertuzumab
- Confirmatory:
  - Adjuvant paclitaxel and trastuzumab
  - Margin definition
  - Omission of anthracyclines
- May need a change of heart
  - All patients receiving a CDKi in first-line setting
- Disappointing:
  - Single agent pertuzumab in TNBC