Year in Review: ER-positive breast cancer, PARP inhibitors and sacituzumab govitecan

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HARVARD
MEDICAL SCHOOL

Dana-Farber
Cancer Institute

ER-Positive, HER2-Negative Breast Cancer

CDK4/6 Inhibitors in Advanced Breast Cancer

Courtesy of Harold J Burstein, MD, PhD

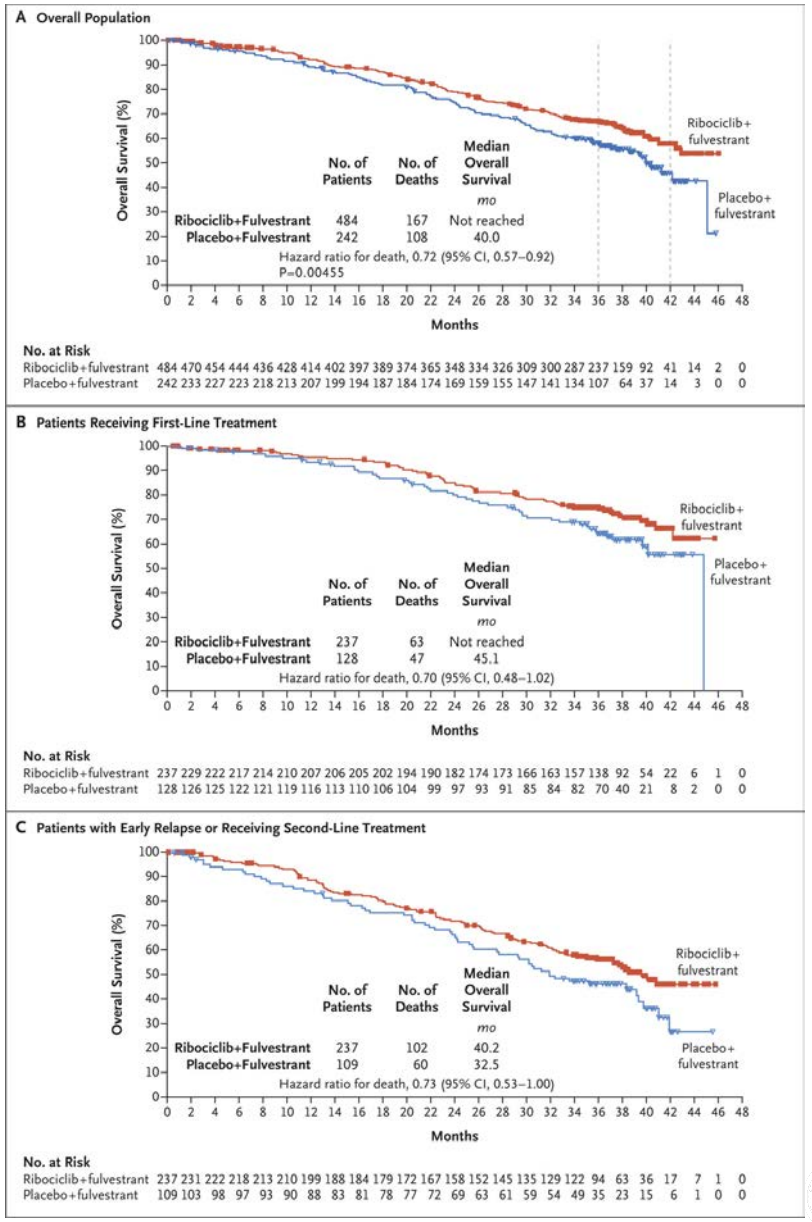
Phase 3 studies of Endocrine Therapy +/- CDK4/6 inhibitors In ER+ HER2- Advanced Breast Cancer

	1st Line Trials				2nd Line Trials		
Study/Arms	**[2]Paloma 2**	**[3]Monaleesa 2**	**[4]Monarch 3**	**[5]Monaleesa 7**	**[6]Paloma 3**	**[7]Monarch 2**	**[8]Monaleesa 3**
CDK4/6i ET partner	**Palbo AI**	**Ribo AI**	**Abema AI**	**Ribo AI/Tam + OS**	**Palbo Fulvestrant**	**Abema Fulvestrant**	**Ribo Fulvestrant**
N	**666**	**668**	**493**	**642**	**521**	**669**	**726**
Median PFS (months) Placebo	**14.5**	**16**	**14.7**	**13.0**	**4.6**	**9.3**	**12.8**
Median PFS (months) CDK 4/6i	**27.6**	**25.3**	**28.1**	**23.8**	**11.2**	**16.4**	**20.5**
HR 95% CI	**0.56 0.46-0.69**	**0.54 0.41-0.69**	**0.55 0.44-0.69**	**0.55 0.44-0.69**	**0.50 0.40-0.62**	**0.55 0.45-0.68**	**0.59 0.480-0.732**
P value	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**

[2]Rugo H, et al, et al. SABCS. 2017; [3]Hortobagyi GN, et al. ASCO; [4]Goetz MP, et al. J Clin Oncol. 2017 Nov 10;35(32):3638-3646; [5]Tripathy D, et al. Lancet Oncol. 2018 Jul;19(7):904-915. [6]Turner NC, et al. N Engl J Med. 2015;373:209-219; [7]Sledge GW, et al. JCO. 2017;35:2875-2884; [8]Slamon DJ, et al. J Clin Oncol. 2018 Aug 20;36(24):2465-2472.

Courtesy of Harold J Burstein, MD, PhD

Overall Survival in the Overall Population and According to Line of Treatment for Advanced Disease: MONALEESA-3.

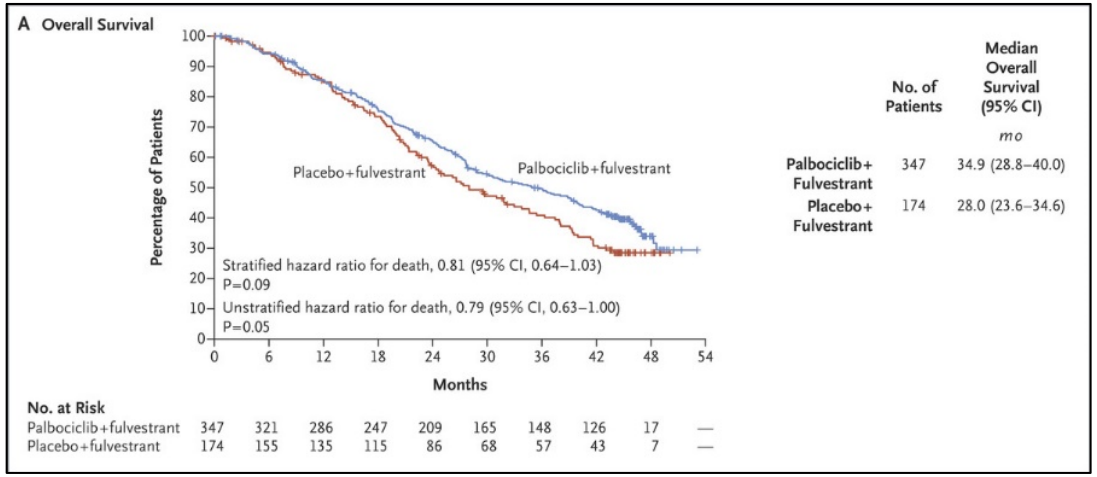


DJ Slamon et al. N Engl J Med 2020;382:514-524.

Courtesy of Harold J Burstein, MD, PhD

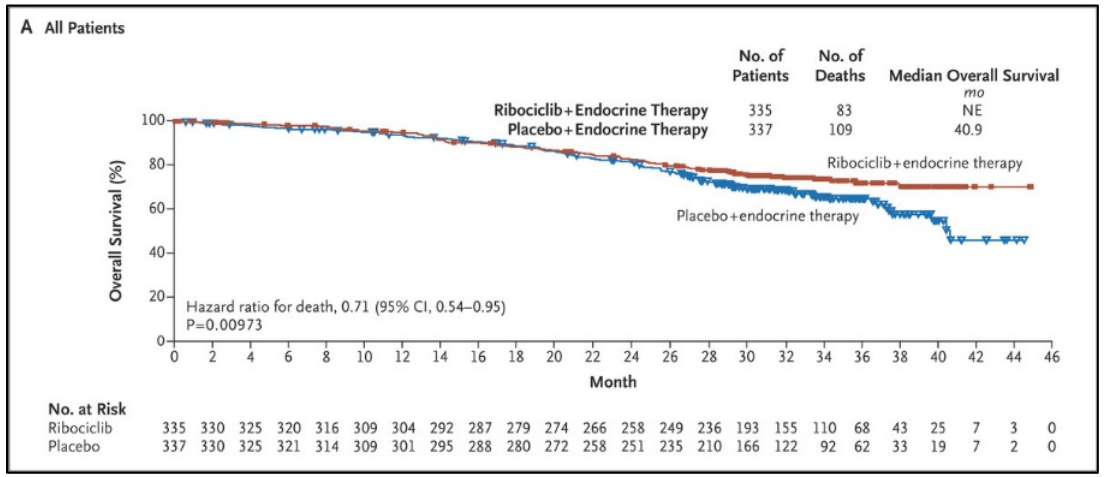
Overall Survival with CDK4/6i

Palbociclib



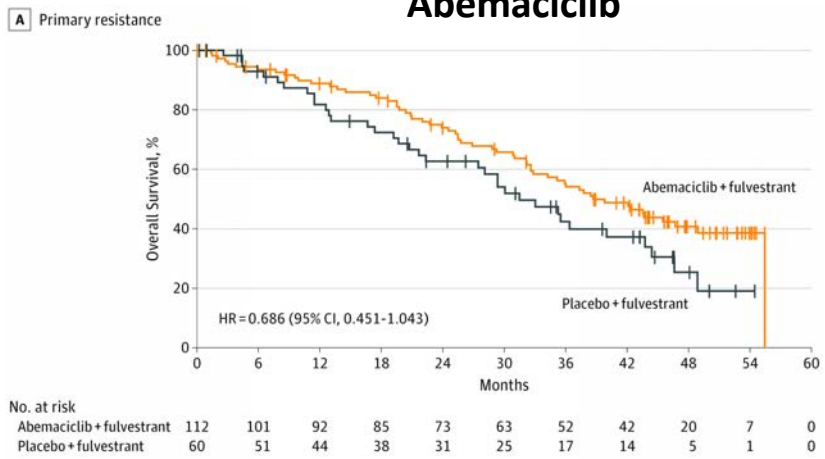
NC Turner et al. N Engl J Med 2018;379:1926-1936.

Ribociclib



S Im et al. N Engl J Med 2019;381:307-316.

Abemaciclib



Sledge GW et al. JAMA Oncol 2020;6:116-124.

Courtesy of Harold J Burstein, MD, PhD

nextMONARCH: Study Design

Same population as MONARCH 1 without prior taxane requirement

- HR+, HER2- mBC
- Prior treatment with ≥2 chemotherapy regimens
  - 1-2 of the prior chemotherapies must have been in metastatic setting
- Measurable disease
- ECOG PS ≤ 1

N=234

1:1:1 Randomization

- A: A+T → **abemaciclib: 150 mg Q12H plus tamoxifen: 20 mg QD (n=78)**
- B: A-150 → **abemaciclib: 150 mg Q12H (n=79)**
- C: A-200 → **abemaciclib: 200 mg Q12H plus prophylactic loperamide [a] (n=77)**

Primary endpoint:
Investigator-assessed PFS

Secondary endpoints:
Response rates, Safety, OS

Exploratory endpoints:
- Association between biomarker and clinical outcomes
- Evaluate relationship between abemaciclib and tamoxifen exposure and response

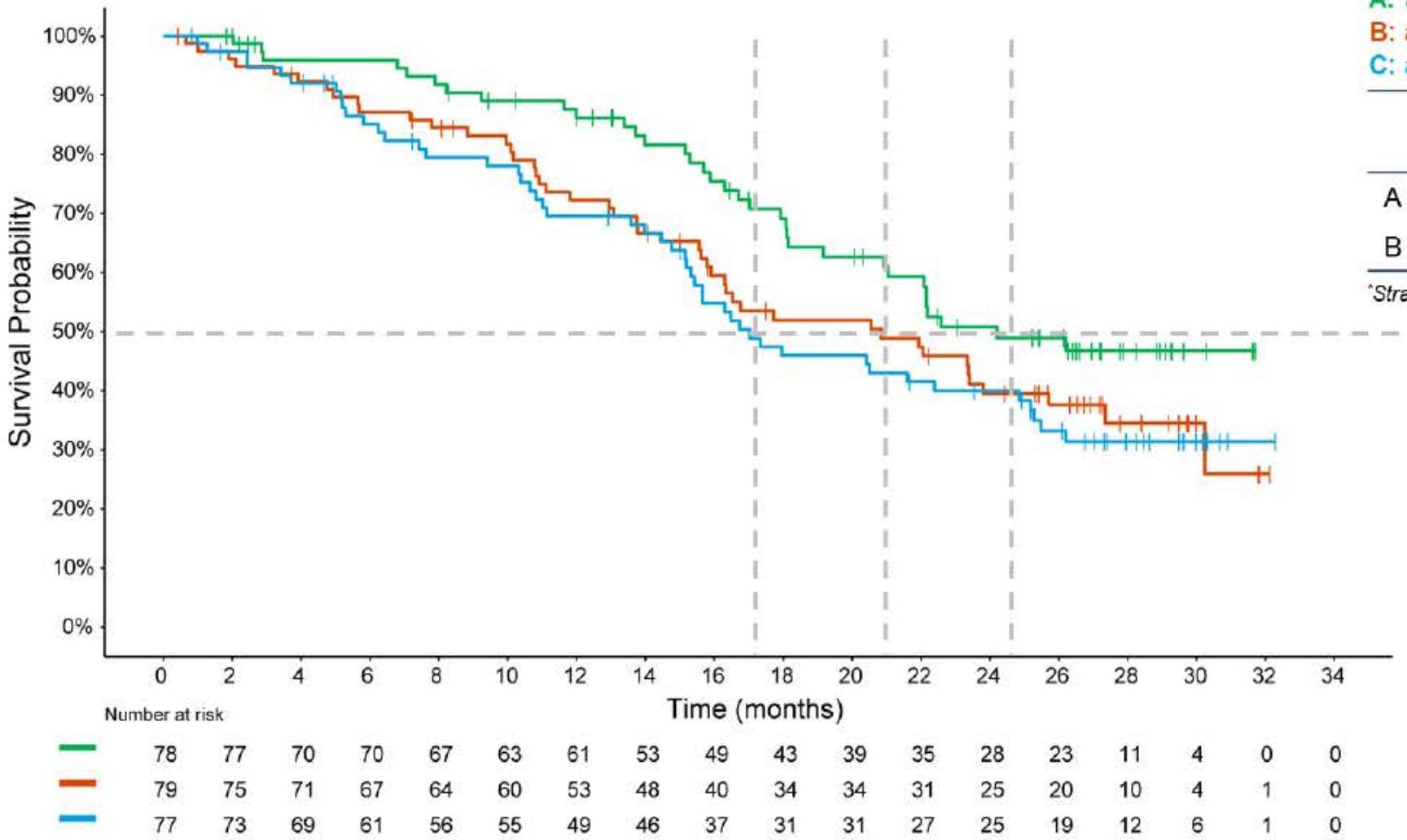
Stratification factors:
- Liver metastases (yes or no)
- Prior tamoxifen in advanced/metastatic setting (yes or no)

Data cutoff: 28 June 2019
Final OS planned 24 months after last patient entered treatment
Median Follow-up: 27.2 months
- 6 patients (A: A+T), 3 (B: A-150), and 3 patients (C: A-200) remained on treatment

Hamilton E et al. ESMO 2020;Abstract 273O.

Courtesy of Harold J Burstein, MD, PhD

nextMONARCH: Overall Survival



Median Overall Survival

A: abemaciclib-150 + Tamoxifen: 24.2 months
B: abemaciclib-150: 20.8 months
C: abemaciclib-200: 17.0 months

	HR*	95% CI	Log-rank p-value*
A vs C	0.62	0.40, 0.97	.0341
B vs C	0.96	0.64, 1.44	.8321

Stratified HR, 2-sided p-value

Hamilton E et al. ESMO 2020;Abstract 273O.

Courtesy of Harold J Burstein, MD, PhD

FLIPPER: Study design

Randomized, double-blind, parallel-group, multicenter, international phase II study

1. Postmenopausal
2. HR-positive & HER2-negative metastatic breast cancer
3. Endocrine sensitive disease
   a) relapse after adjuvant endocrine therapy ≥ 5 years and disease-free interval > 12 months
   or
   b) "de novo" metastatic disease
4. ECOG PS 0-2
5. No prior therapy for MBC

N=189

Stratification:
- Visceral vs non visceral metastases
- Disease presentation at study entry: metastatic "de novo" versus recurrent

RANDOMIZATION

1:1

Experimental Arm:
Fulvestrant + Palbociclib
n = 94

Control Arm:
Fulvestrant + Placebo
n = 95

Fulvestrant: 500mg days 1 & 15 of cycle 1 and then once every 28 days
Palbociclib/Placebo: 125mg, 3 weeks on/1week off, q 28-days
Treatment until objective disease progression, symptomatic deterioration, unacceptable toxicity, death or withdrawal of consent

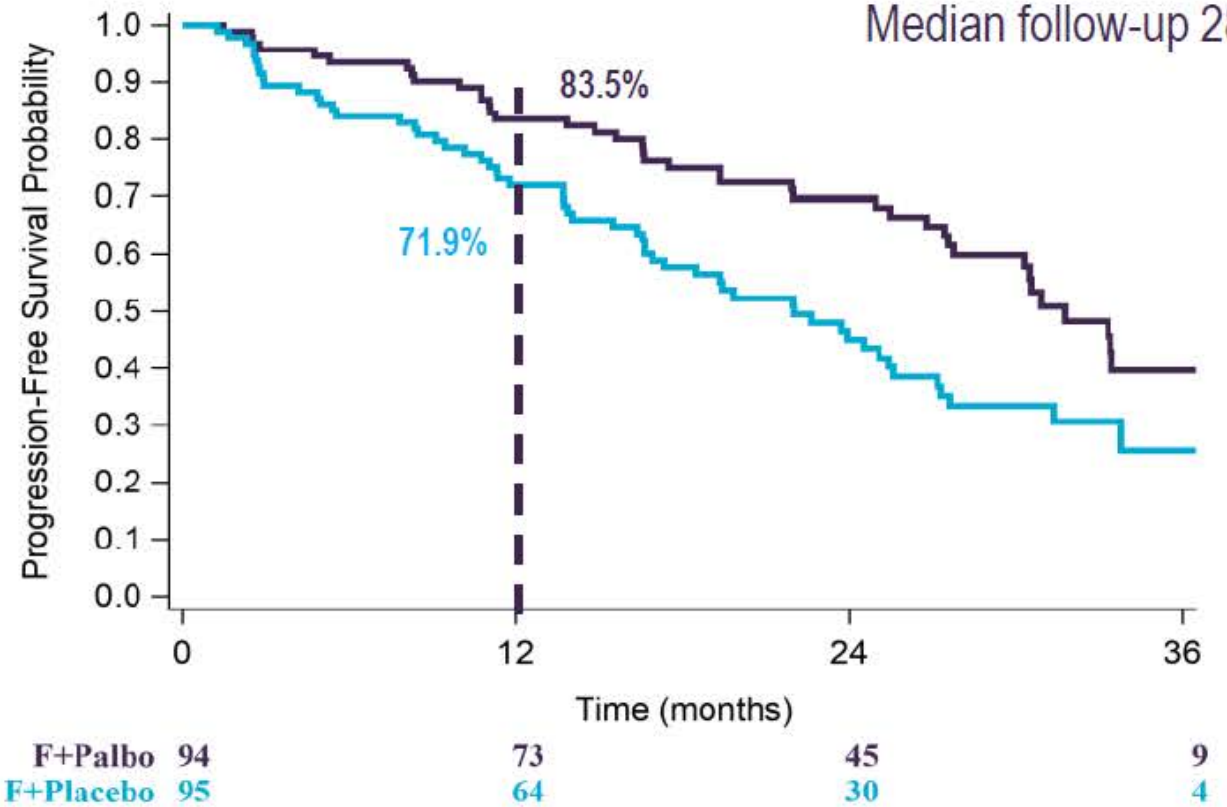
Abbreviations: HR=hormone receptor; HER2=human epidermal growth factor receptor 2; BC=breast cancer; ET=endocrine therapy. PD=progressive disease.

Courtesy of Harold J Burstein, MD, PhD

Albanell J et al. ESMO 2020;Abstract LBA19.

FLIPPER Primary end-point

Median follow-up 28.6 months (1.5-44.8)



	Fulvestrant + Palbociclib n=94	Fulvestrant + Placebo n=95
PFS rate at 1 year in ITT population (primary objective)		
No. of events (%)	15 (16.0)	26 (27.4)
No. of censored patients (%)	79 (84.0)	69 (72.6)
K-M **estimates** (80% CI)	**83.5% (78.5-88.5)**	**71.9% (65.8 - 77.9)**

HR (80% CI): 0.55 (0.36-0.83) **p=0.064**

Statistical design; Hazard Ratio (HR): 0.6; Power: 80%; Two-sided alpha: 0.2

Courtesy of Harold J Burstein, MD, PhD

Albanell J et al. ESMO 2020;Abstract LBA19.

Conclusions

- CDK4/6 inhibitors are appropriate in first- or second-line therapy of ER+ MBC in combination with endocrine treatments
- Three commercially available agents with similar activity/outcomes
- Don’t forget to re-consider late endocrine therapy!

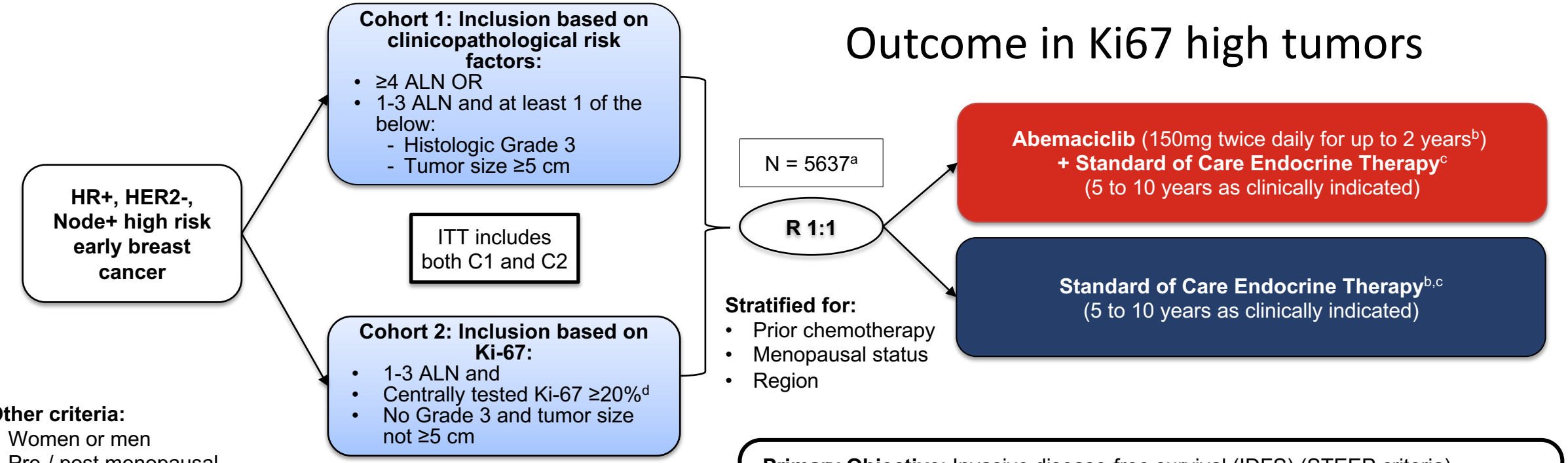
Courtesy of Harold J Burstein, MD, PhD

ER-Positive, HER2-Negative Breast Cancer

CDK4/6 Inhibitors in Early-Stage Breast Cancer

monarchE Study Design

New★
Additional 3.6-month F/up
67 additional IDFS events
Outcome in Ki67 high tumors



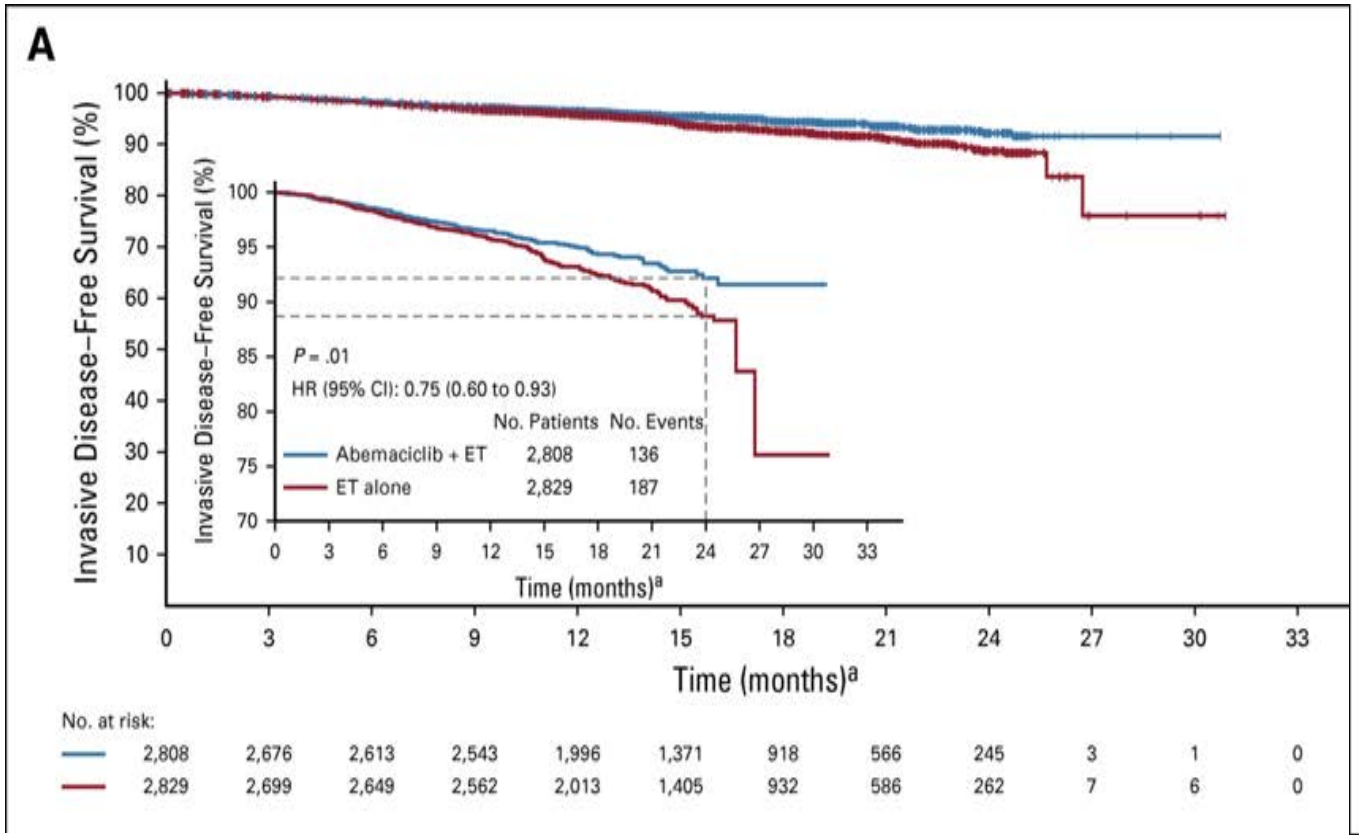
Other criteria:
- Women or men
- Pre-/ post menopausal
- With or without prior neo- and/or adjuvant chemotherapy
- No distant metastasis
- Maximum of 16 months from surgery to randomization and 12 weeks of ET following the last non-ET

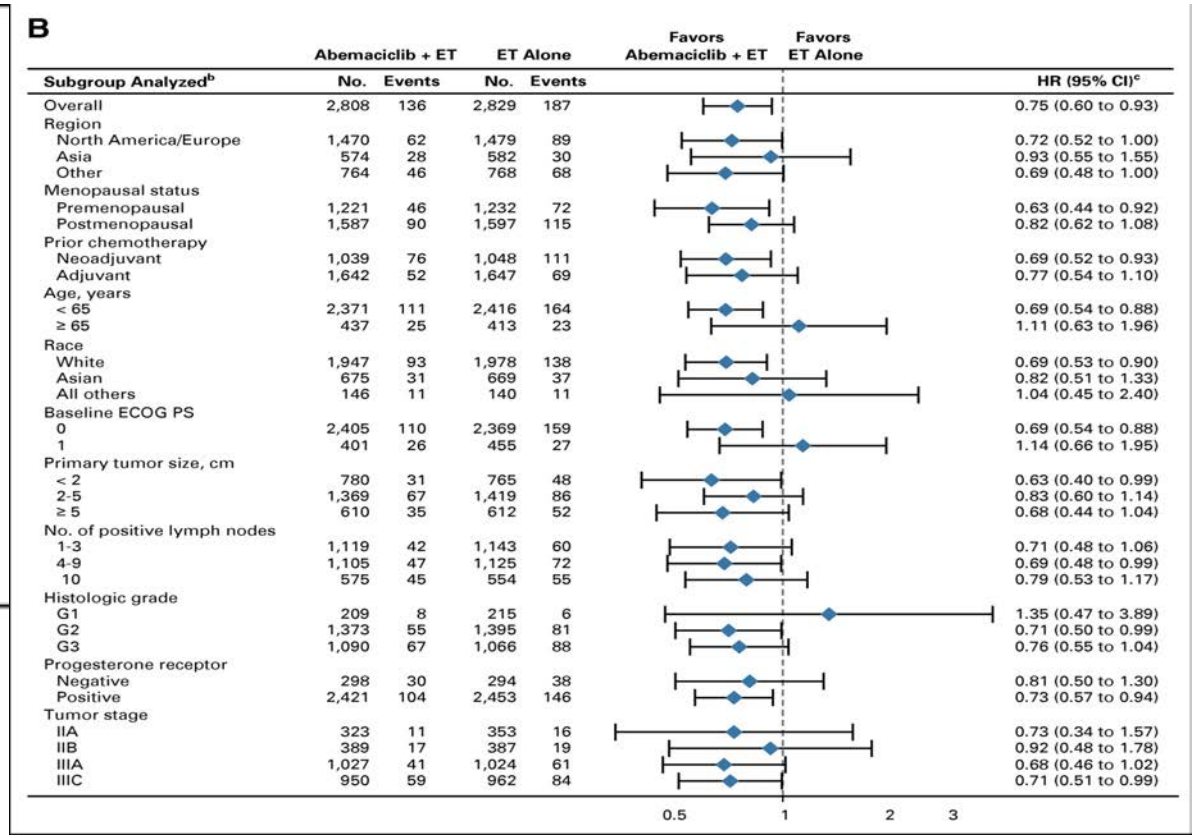
Primary Objective: Invasive disease-free survival (IDFS) (STEEP criteria)
Key Secondary Objectives: IDFS in Ki-67 high (≥20%) population, Distant relapse-free survival (DRFS), Overall survival, Safety, Patient reported outcomes, and Pharmacokinetics

[a]Recruitment from July 2017 to August 2019; [b]Treatment period = first 2 years on study treatment after randomization; [c]Endocrine therapy of physician's choice [e.g. aromatase inhibitors, tamoxifen, LHRH agonist]; [d]Ki-67 expression assessed in all patients from both cohorts with suitable untreated breast tissue using Ki-67 immunohistochemistry Assay by Dako/Agilent
Abbreviations: ALN, positive axillary lymph nodes; R, randomized

Courtesy of Harold J Burstein, MD, PhD

monarchE





Published in: Stephen R. D. Johnston; Nadia Harbeck; Roberto Hegg; Masakazu Toi; Miguel Martin; Zhi Min Shao; Qing Yuan Zhang; Jorge Luis Martinez Rodriguez; Mario Campone; Erika Hamilton; Joohyuk Sohn; Valentina Guarneri; Morihito Okada; Frances Boyle; Patrick Neven; Javier Cortés; Jens Huober; Andrew Wardley; Sara M. Tolaney; Irfan Cicin; Ian C. Smith; Martin Frenzel; Desirée Headley; Ran Wei; Belen San Antonio; Maarten Hulstijn; Joanne Cox; Joyce O'Shaughnessy; Priya Rastogi; *Journal of Clinical Oncology* 2020 383987-3998.
DOI: 10.1200/JCO.20.02514

Johnston SRD et al. *J Clin Oncol* 2020;38(34):3987-98.

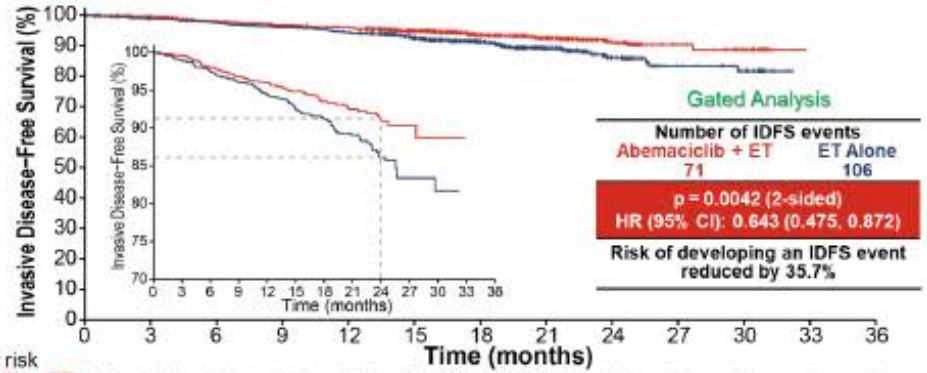
Courtesy of Harold J Burstein, MD, PhD

KEY RESULTS: Consistent Abemaciclib Treatment Benefit Was Observed Independent of Ki-67 Level (high or low)

- Previously presented data of ITT Ki-67 high: Statistically significant and clinically meaningful improvement in IDFS in patients with high Ki-67 tumors
  - 197 events, p-value = 0.0111; HR=0.691 (95% CI = 0.519, 0.920) - see monarchE Primary Outcome Presentation for additional details
  - Two-year IDFS rates were 91.6% in the abemaciclib + ET arm and 87.1% in the ET arm – 4.5% difference

Additional evaluations in patients from cohort 1 with either Ki-67 high (≥20%) or low (<20%)

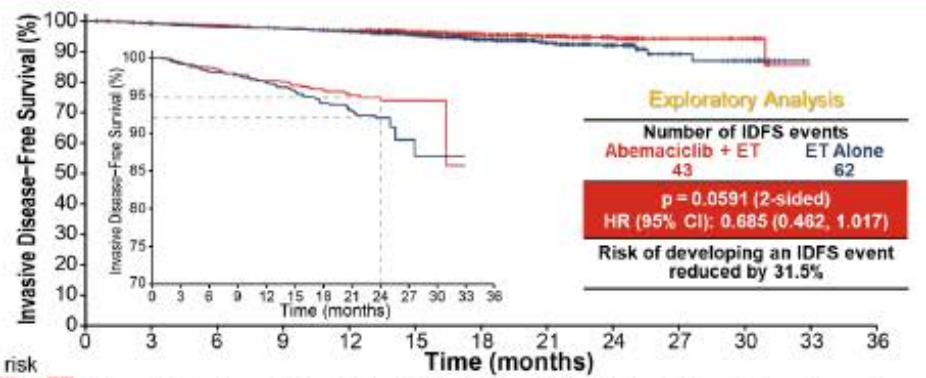
Statistically significant and clinically meaningful improvement in IDFS in patients with high Ki-67 tumors in Cohort 1



Number at risk													
Abemaciclib + ET	1017	989	961	943	929	774	565	394	253	55	36	0	0
ET Alone	986	955	939	923	906	756	556	384	236	57	43	0	0

Two-year IDFS rates were 91.3% in the abemaciclib + ET arm and 86.1% in the ET arm – 5.2% difference

While the magnitude of treatment benefit was numerically lower for patients with low Ki-67, all patients within Cohort 1 benefited from the addition of abemaciclib

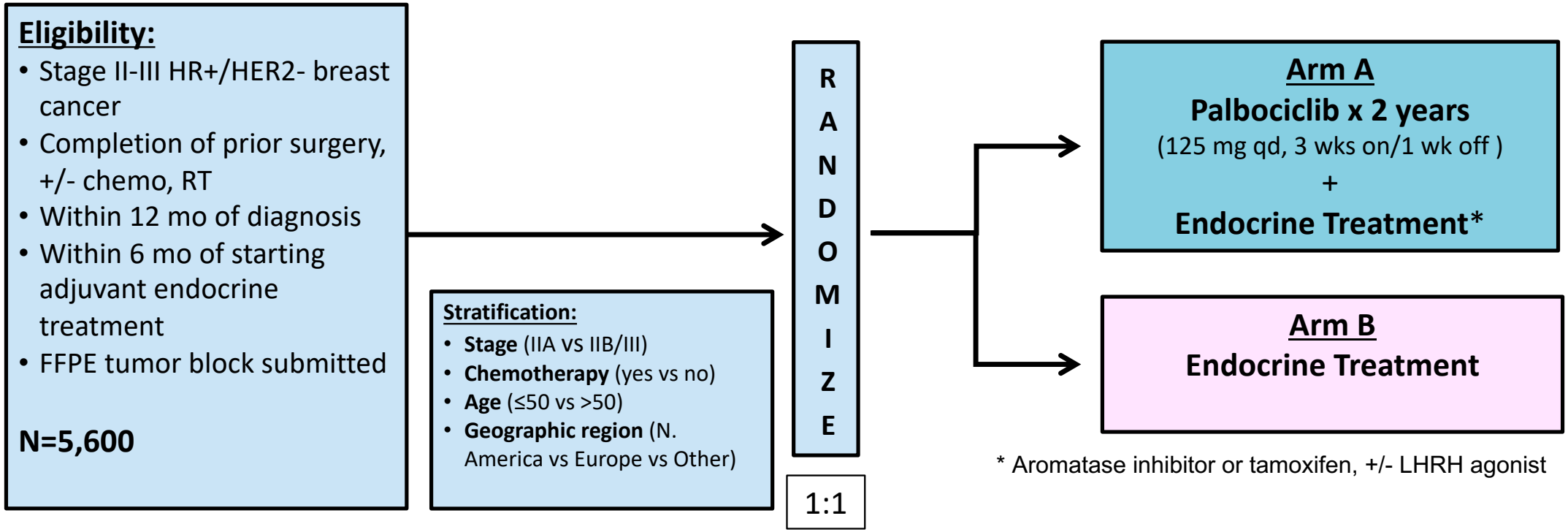


Number at risk													
Abemaciclib + ET	946	911	898	884	867	712	521	381	235	46	32	0	0
ET Alone	968	946	932	925	912	751	534	381	245	44	34	0	0

Two-year IDFS rates were 94.7% in the abemaciclib + ET arm and 92.0% in the ET arm – 2.7% difference

Courtesy of Harold J Burstein, MD, PhD

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



Primary Endpoint: invasive Disease-Free Survival (iDFS)

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

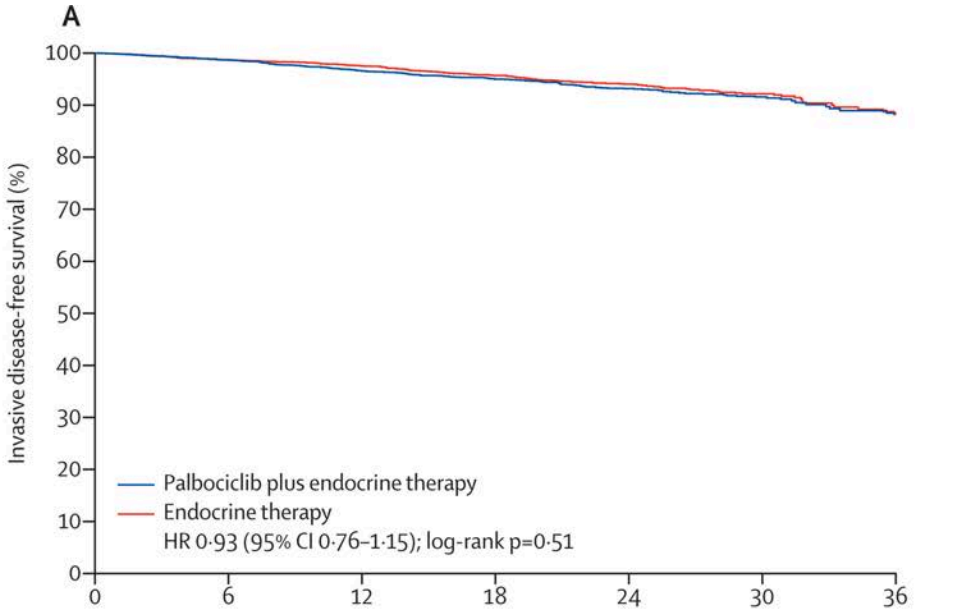
Sponsored by AFT and ABCSG, in cooperation with PrECOG, BIG, GBG, NSABP, and supported by Pfizer.

ABCSG ALLIANCE FOUNDATION TRIALS, LLC BIG Pfizer Oncology

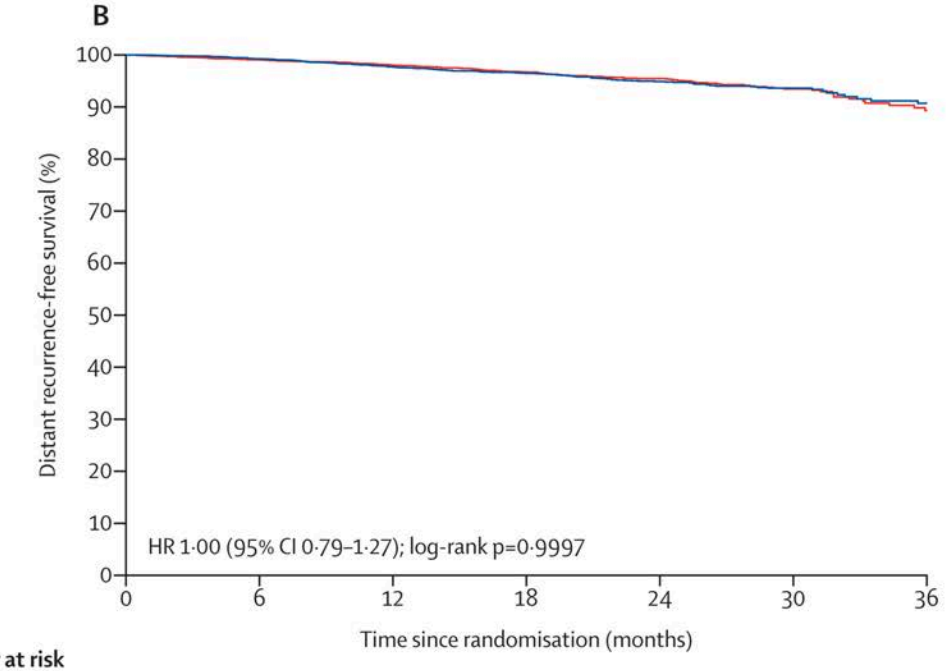
Courtesy of Harold J Burstein, MD, PhD

Mayer et al. ESMO 2020;Abstract LBA12.

PALLAS



Number at risk (number censored)							
Palbociclib plus endocrine therapy	2883 (0)	2684 (163)	2563 (253)	1946 (827)	1257 (1488)	583 (2145)	163 (2554)
Endocrine therapy	2877 (0)	1649 (192)	2535 (250)	1953 (796)	1275 (1444)	574 (2131)	172 (2524)



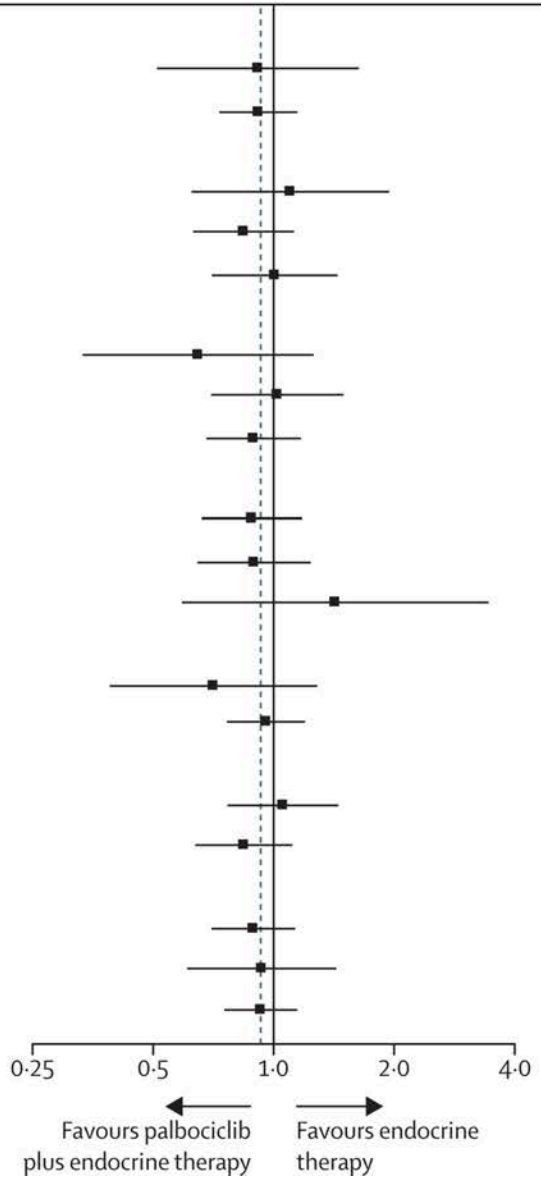
Number at risk (number censored)							
Palbociclib plus endocrine therapy	2883 (0)	2692 (165)	2573 (256)	1956 (843)	1270 (1508)	588 (2172)	163 (2586)
Endocrine therapy	2877 (0)	1662 (195)	2554 (261)	1976 (811)	1288 (1473)	579 (2171)	175 (2567)

Mayer EL et al. Lancet Oncol 2021

Courtesy of Harold J Burstein, MD, PhD

PALLAS Trial

	Palbociclib plus endocrine therapy group		Endocrine therapy alone group		Hazard ratio (95% CI)	$p_{interaction}$
	Events n/N	3-year invasive disease-free survival (95% CI)	Events n/N	3-year invasive disease-free survival (95% CI)		
Stage						0·99
IIA	21/504	94·7 (91·4–96·7)	25/509	92·9 (88·9–95·5)	0·91 (0·51–1·63)	
IIB or III	149/2370	85·6 (81·4–89·0)	156/2359	86·6 (82·7–89·6)	0·92 (0·73–1·15)	
T stage						0·60
T0, T1, Tis, or TX	26/557	92·8 (88·9–95·4)	22/500	93·3 (89·3–95·8)	1·10 (0·62–1·94)	
T2	84/1603	90·0 (86·4–92·7)	101/1636	89·0 (85·5–91·7)	0·84 (0·63–1·12)	
T3 or T4	60/722	79·8 (69·8–86·8)	58/741	82·4 (73·6–88·5)	1·01 (0·70–1·44)	
N Stage						0·50
N0	14/367	95·5 (92·3–97·4)	23/383	89·4 (83·0–93·5)	0·65 (0·33–1·26)	
N1	53/1427	93·7 (91·4–95·5)	53/1415	93·4 (90·2–95·6)	1·02 (0·70–1·50)	
N2 or N3	103/1088	75·0 (65·9–82·0)	105/1079	79·3 (71·7–85·1)	0·89 (0·68–1·17)	
Histological grade						0·56
G1 or G2	86/1922	91·0 (87·9–93·3)	100/1971	90·6 (87·5–93·0)	0·88 (0·66–1·18)	
G3	73/836	83·2 (76·2–88·4)	71/767	82·8 (76·7–87·5)	0·89 (0·65–1·24)	
GX	11/122	76·5 (42·5–92·0)	9/139	89·6 (78·6–95·1)	1·43 (0·59–3·44)	
Adjuvant or neoadjuvant chemotherapy						0·36
No	18/498	94·9 (91·4–97·0)	27/507	91·7 (86·7–94·8)	0·71 (0·39–1·28)	
Yes	152/2384	85·9 (81·7–89·1)	154/2370	87·4 (84·0–90·1)	0·96 (0·77–1·20)	
Age group, years						0·29
≤50	79/1309	85·9 (79·8–90·2)	73/1304	88·6 (86·7–94·8)	1·06 (0·77–1·45)	
>50	91/1573	89·7 (86·5–92·2)	154/1370	87·4 (84·0–90·1)	0·84 (0·64–1·11)	
Clinical risk						0·87
High	131/1710	81·9 (76·1–86·4)	136/1672	83·6 (78·7–87·7)	0·89 (0·70–1·13)	
Low	29/1172	95·0 (92·8–96·5)	45/1205	93·1 (89·8–95·3)	0·93 (0·61–1·43)	
All patients	**170/2883**	**88·2 (85·2–90·6)**	**181/2877**	**88·5 (85·8–90·7)**	**0·93 (0·75–1·14)**	



Mayer EL et al. Lancet Oncol 2021

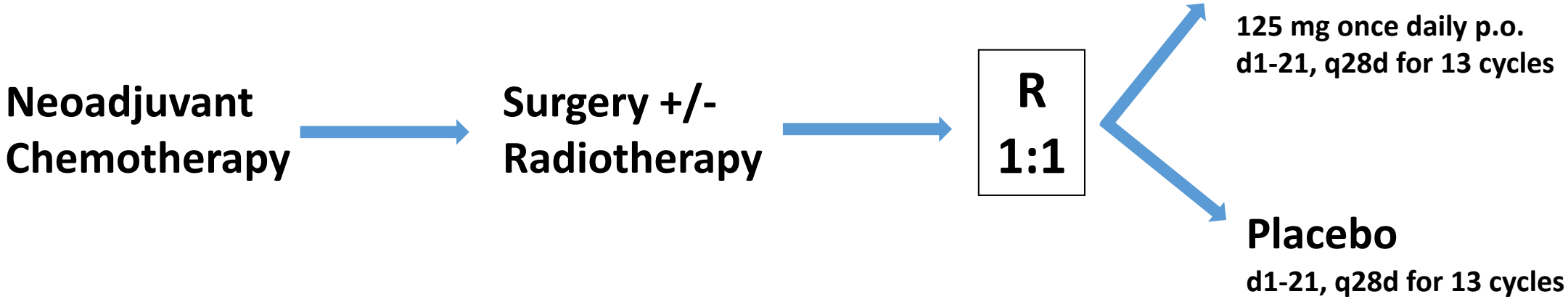
Courtesy of Harold J Burstein, MD, PhD

PENELOPE-B: Study Design

N=1250
- HR+/HER2- breast cancer
- no pCR after NACT
- CPS-EG score ≥3 or ≥2 with ypN+

Primary Endpoint: iDFS

Stratification factors
- Nodal status: ypN 0-1 vs ypN2-3
- Age: ≤50 vs >50 yrs
- Ki-67: >15% vs ≤ 15%
- Region: Asian vs non Asian
- CPS-EG Score: ≥3 vs 2 and ypN+



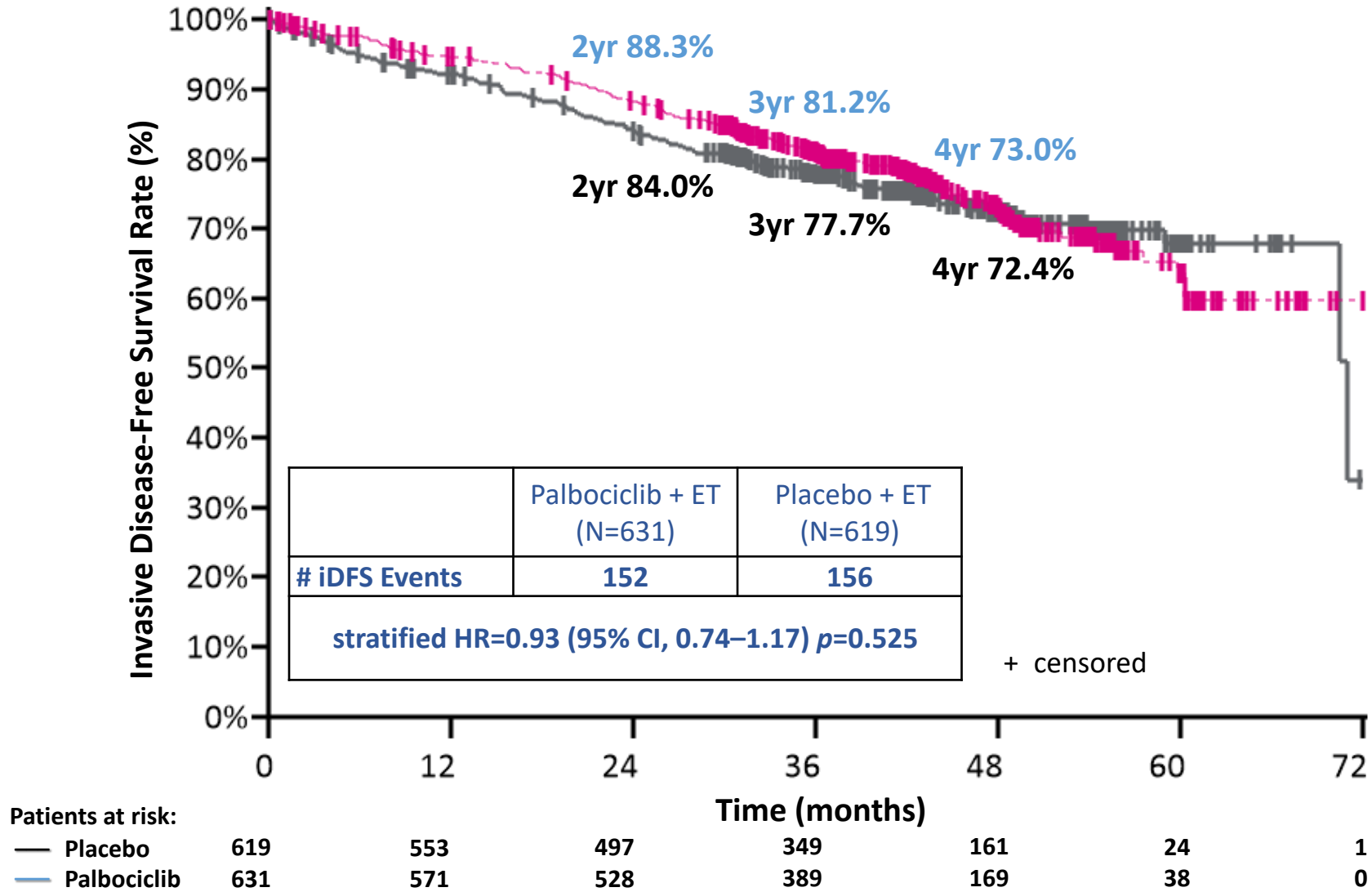
All patients will receive concomitantly endocrine therapy according to local standards

Penelope-B: ClinicalTrials.gov NCT01864746

Loibl S et al. SABCS 2020;Abstract GS1-02.

Courtesy of Harold J Burstein, MD, PhD

PENELOPE-B: Primary Endpoint iDFS



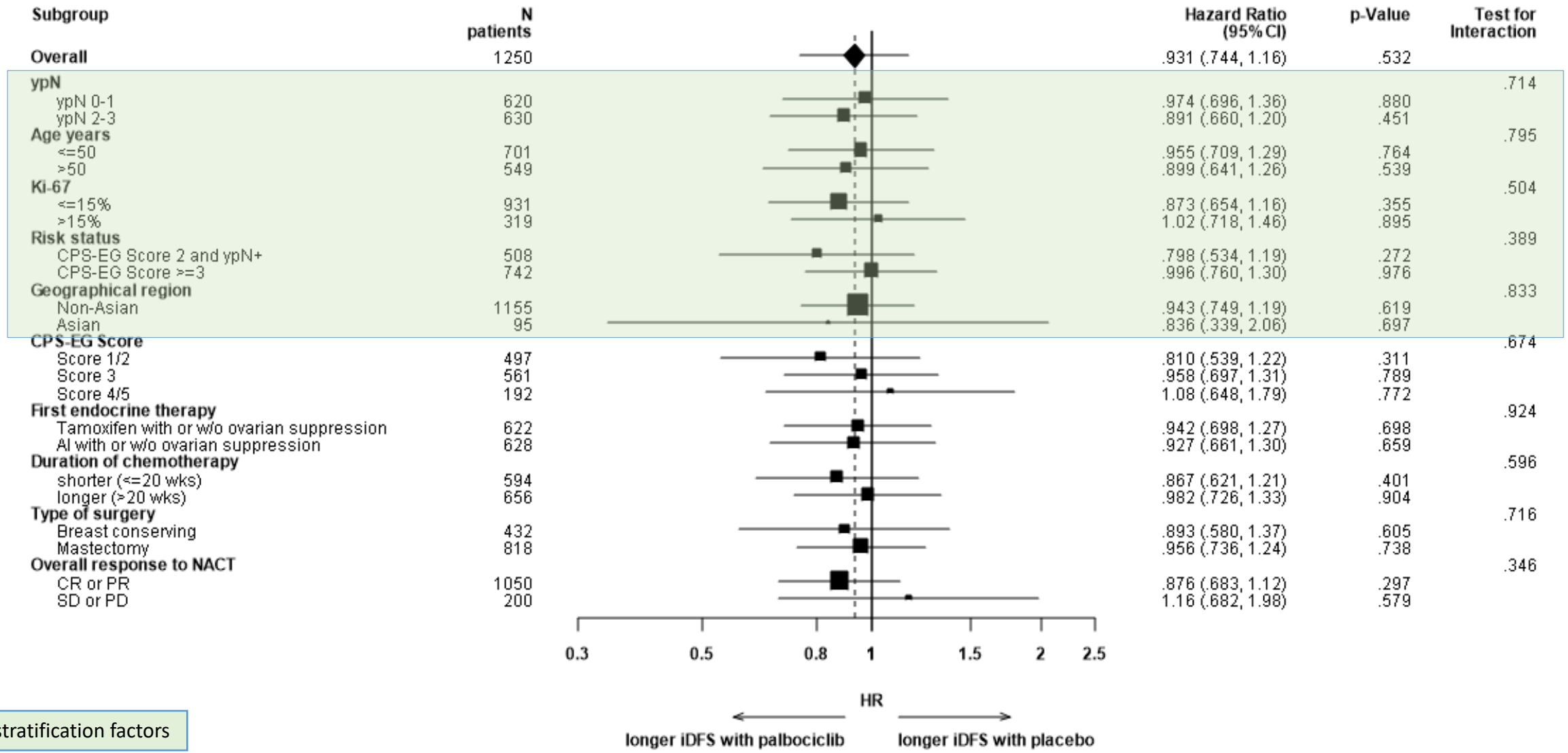
	Palbociclib + ET (N=631)	Placebo + ET (N=619)
# iDFS Events	152	156
stratified HR=0.93 (95% CI, 0.74–1.17) *p*=0.525		

Median Follow-Up
42.8 Months

* Weighted log-rank test based on the CHW method, taking into account the adaptive sample size re-estimation and group-sequential nature of the design

Courtesy of Harold J Burstein, MD, PhD

PENELOPE-B: Subgroups iDFS



stratification factors

Courtesy of Harold J Burstein, MD, PhD

Absolute events in adjuvant CDK4/6i trials

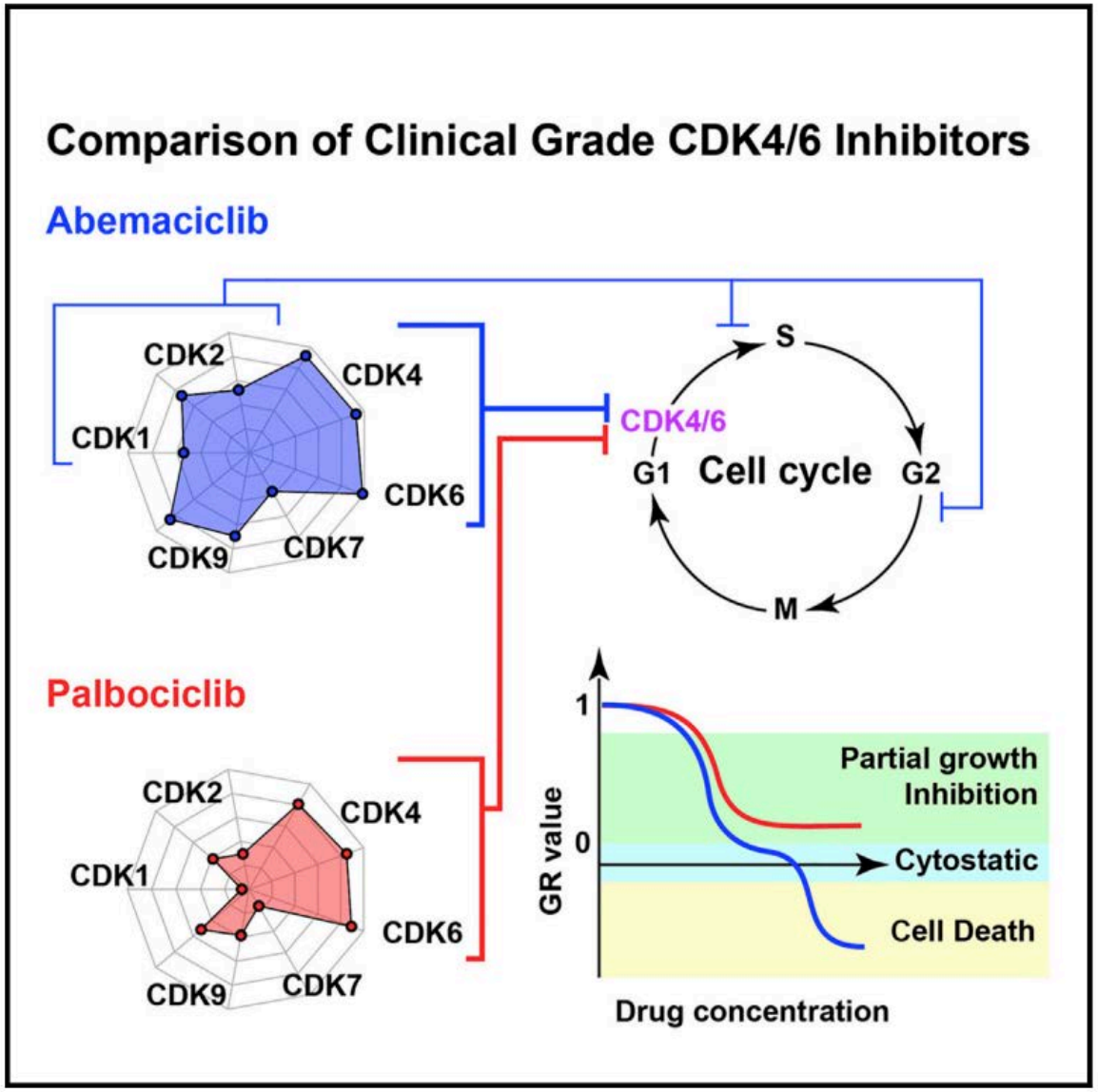
	Distant Metastasis		Local-Regional Recurrence	
	ET	ET + CDK4/6i	ET	ET + CDK4/6i
monarchE	138	87	26	17
PALLAS	116	114	13	11
PENELOPE-B	111	116	27	21

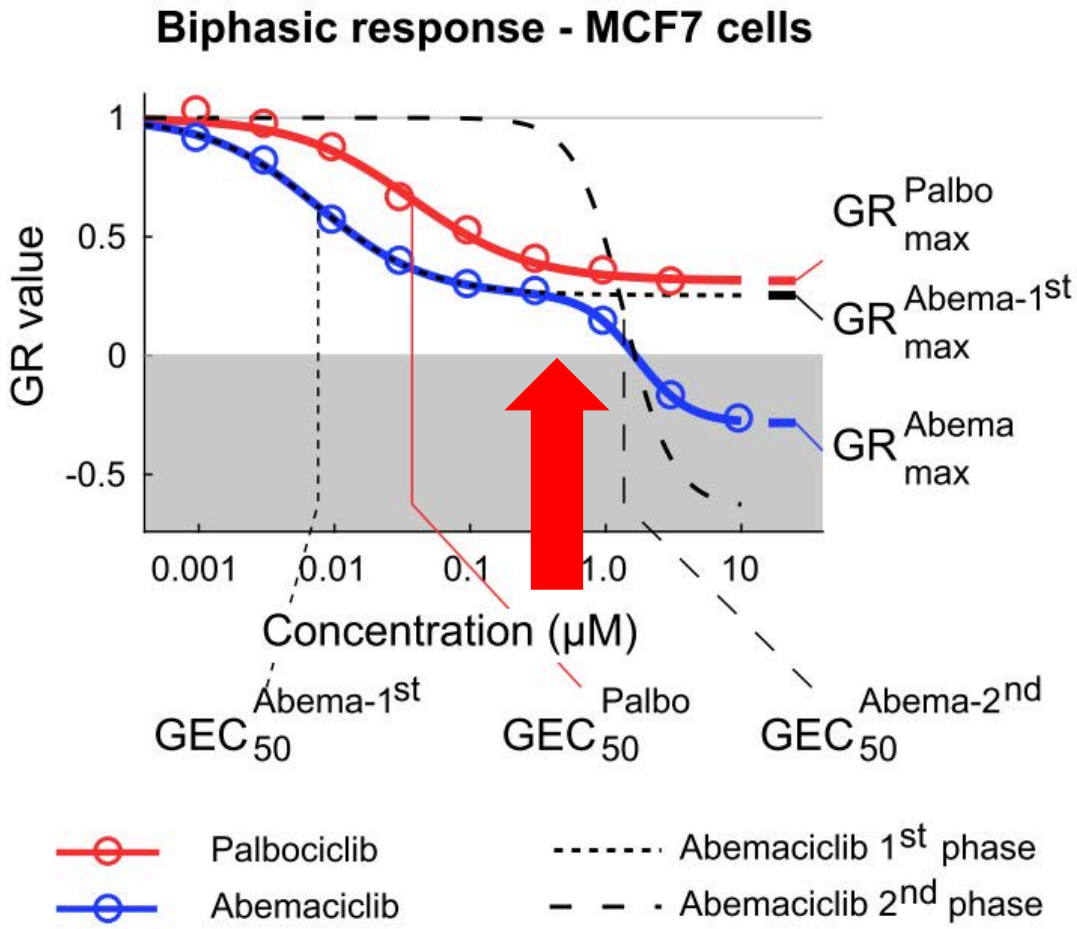
Courtesy of Harold J Burstein, MD, PhD

PALLAS, PENELOPE-B, monarchE: What accounts for differences?

- Chance? Maybe.
- High-risk cases? No.
- Ki-67 selection? No.
- Compliance? Not likely.
- Agent? Maybe but …
- Follow-up? Maybe.

Courtesy of Harold J Burstein, MD, PhD



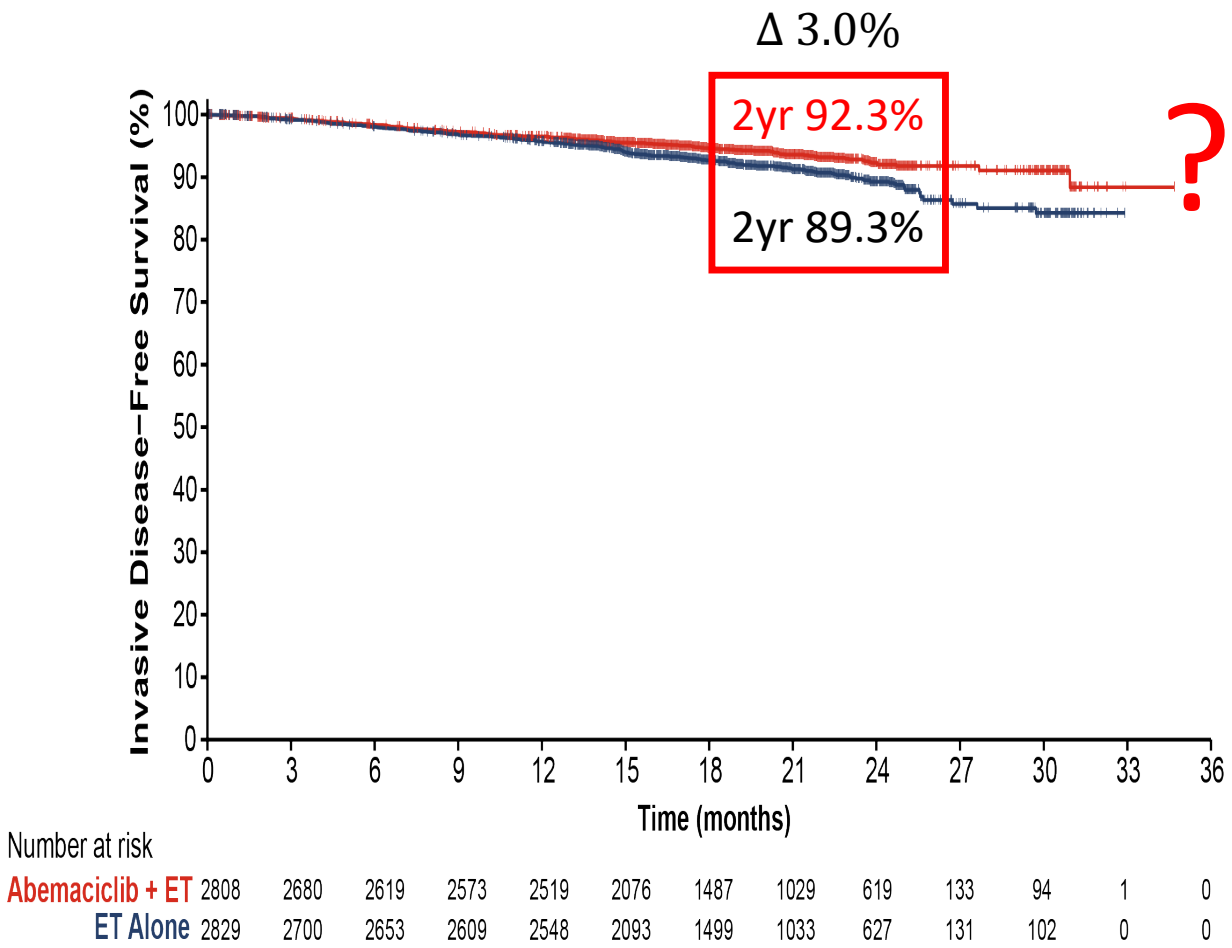


Hafner et al. Cell Chemical Biology 2019;26:1067.

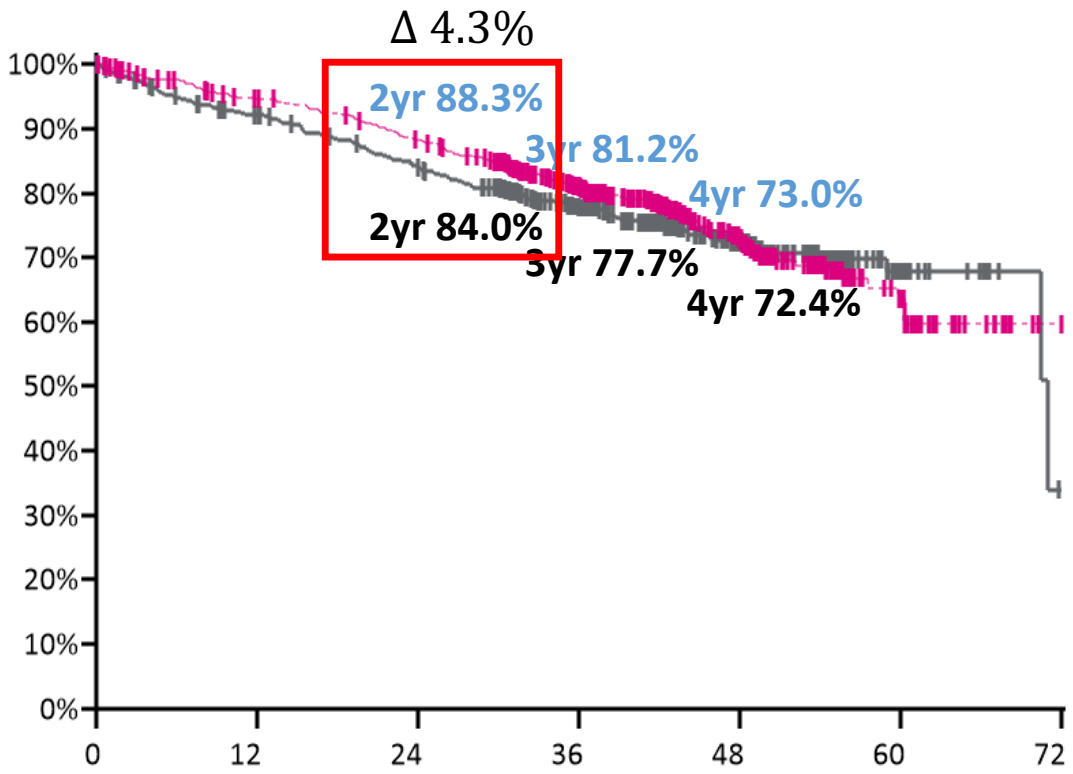
Courtesy of Harold J Burstein, MD, PhD

Do we have adequate followup? (slide courtesy of R. O'Regan)

monarchE



PENELOPE-B



Courtesy of Harold J Burstein, MD, PhD

Conclusions

- Despite three large, well-designed, well-conducted adjuvant trials, the clinical impact of CDK4/6 inhibitors on the longer-term natural history of ER-positive breast cancer remains undefined.

- In general, I am not recommending such therapy

- On a case-by-case basis in highly selected individuals, I consider such treatment

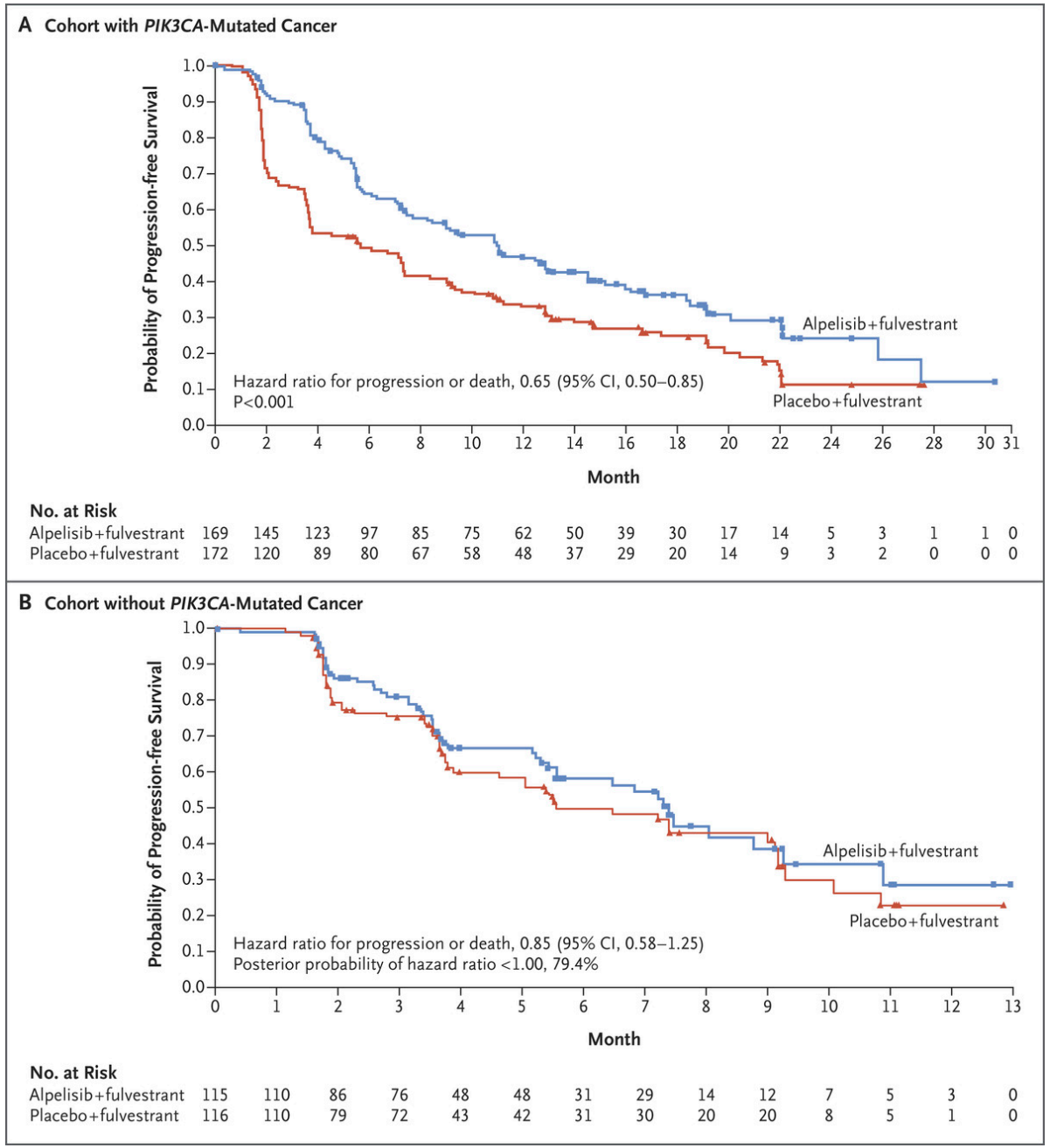
Courtesy of Harold J Burstein, MD, PhD

ER-Positive, HER2-Negative Breast Cancer

PI3K Inhibitors in Advanced Breast Cancer

Courtesy of Harold J Burstein, MD, PhD

SOLAR-1

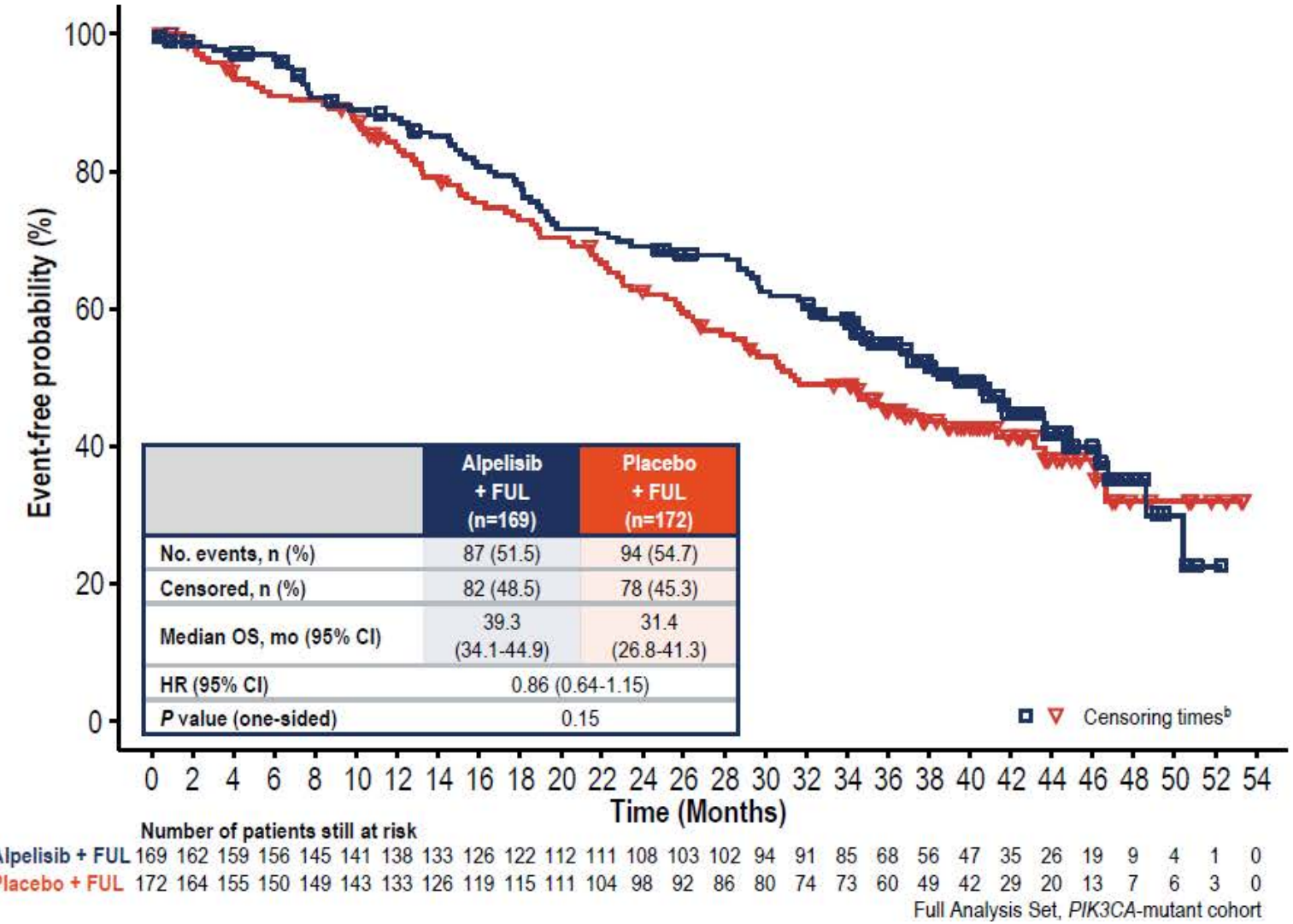


F André et al. N Engl J Med 2019;380:1929-1940.

Courtesy of Harold J Burstein, MD, PhD

SOLAR-1: OS in Patients in PIK3CA-mutant Cohort[a]

- mOS was prolonged by 7.9 mo for patients in the alpelisib + fulvestrant arm
- Final OS analysis in the *PIK3CA*-mutant cohort did not cross the prespecified O'Brien-Fleming efficacy boundary (1-sided $P \leq 0.0161$)



	Alpelisib + FUL (n=169)	Placebo + FUL (n=172)
No. events, n (%)	87 (51.5)	94 (54.7)
Censored, n (%)	82 (48.5)	78 (45.3)
Median OS, mo (95% CI)	39.3 (34.1-44.9)	31.4 (26.8-41.3)
HR (95% CI)	0.86 (0.64-1.15)	
P value (one-sided)	0.15	

[a] Between randomisation to OS event or censoring, median time was 30.8 mo.
[b] Date of censoring is defined as the last contact date for OS.

Andre F et al. ESMO 2020;Abstract LBA18.

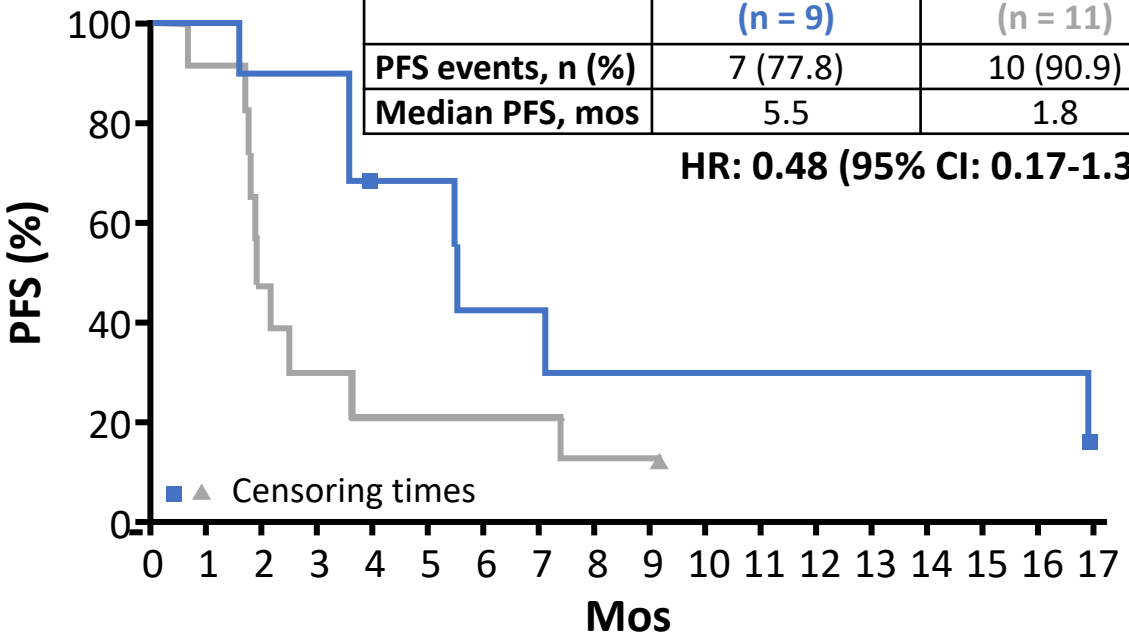
Courtesy of Harold J Burstein, MD, PhD

SOLAR-1: PFS by Prior CDK4/6 Exposure in PIK3CA-Mutant Cohort

With Prior CDK4/6 Inhibitor Therapy

	Alpelisib + FULV (n = 9)	Placebo + FULV (n = 11)
PFS events, n (%)	7 (77.8)	10 (90.9)
Median PFS, mos	5.5	1.8

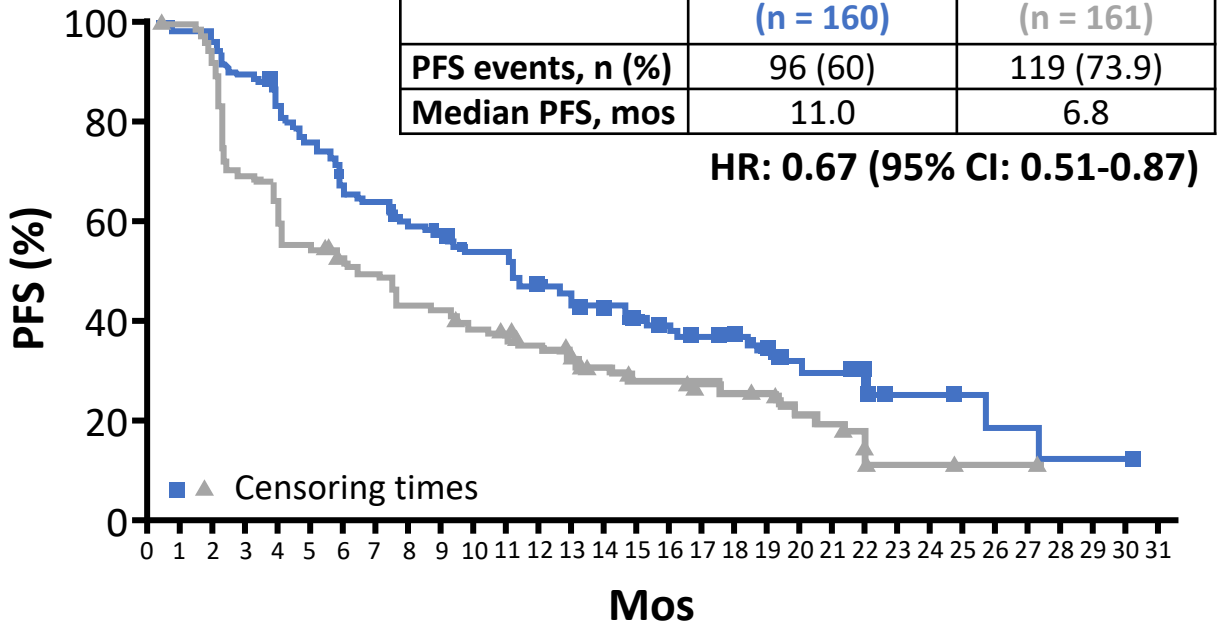
HR: 0.48 (95% CI: 0.17-1.36)



Without Prior CDK4/6 Inhibitor Therapy

	Alpelisib + FULV (n = 160)	Placebo + FULV (n = 161)
PFS events, n (%)	96 (60)	119 (73.9)
Median PFS, mos	11.0	6.8

HR: 0.67 (95% CI: 0.51-0.87)



- Randomization was stratified by prior treatment with any CDK4/6 inhibitor, but the number of patients enrolled who had received prior CDK4/6 inhibitor therapy was small
- Benefit with alpelisib observed regardless of prior CDK4/6 inhibitor therapy

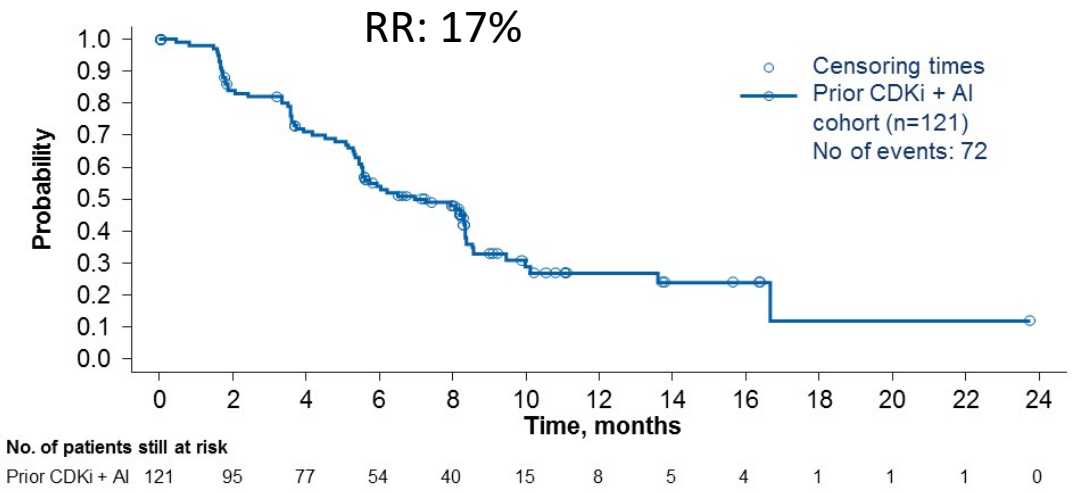
Juric. SABCS 2018. Abstr GS3-08.

Courtesy of Harold J Burstein, MD, PhD

BYLieve Trial Efficacy: Primary Endpoint and PFS Results

BYLieve
Alpelisib (BYL719) In patients with PIK3CA mutant, HR+, HER2- adVanced brEast cancer

Endpoint	Prior CDKi + AI (Cohort A) (n=121)
Primary endpoint: Patients who were alive without disease progression at 6 mo	**50.4%** (n=61; 95% CI, 41.2-59.6)
Secondary endpoint: Median PFS	**7.3 mo** [n=72 (59.5%) with event]; 95% CI, 5.6-8.3)



The primary endpoint for the prior CDKi + AI cohort was met (lower bound of 95% CI was > 30%), with 50.4% of patients alive without disease progression at 6 months

- In SOLAR-1, 44.4% of patients in the *PIK3CA*-mutant cohort with prior CDKi treated with alpelisib plus fulvestrant were alive without disease progression at 6 months

AI, aromatase inhibitor; CDKi, cyclin-dependent kinase inhibitor; CI, confidence interval; PFS, progression-free survival; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha.

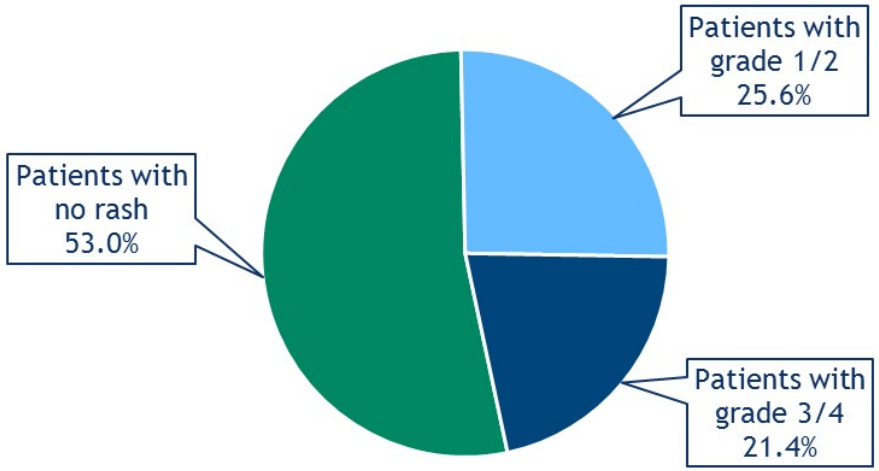
Presented By Hope Rugo at TBD

Courtesy of Harold J Burstein, MD, PhD

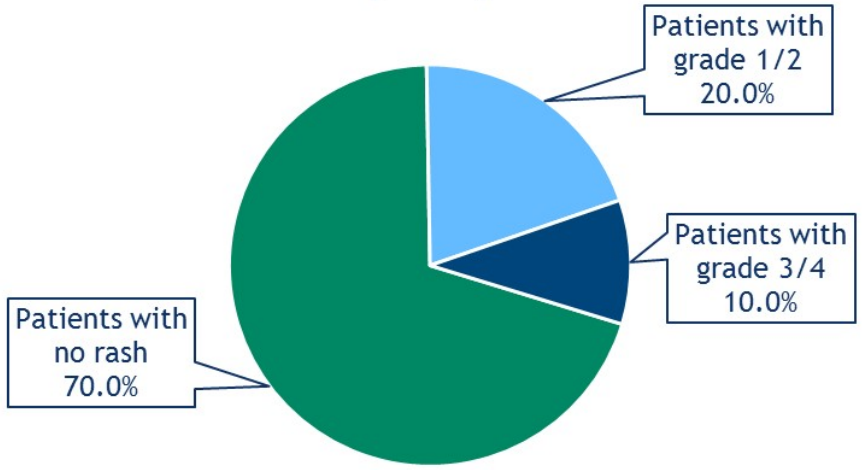
Incidence of Rash in Patients With/Without Prophylactic Antihistamines

BYLieve
Alpelisib (BYL719) In patients with PIK3CA mutant, HR+, HER2- adVanced brEast cancer

Patients who did not receive antihistamines or received antihistamines after rash (n=117)



Patients who received antihistamines before rash or had no event (n=10)



Presented By Hope Rugo at TBD

Courtesy of Harold J Burstein, MD, PhD

Conclusions

- PI3K inhibitor alpelisib has clinical activity in ER+, PIK3Ca mutant breast cancer
- Given survival benefit with CDK4/6i, we typically use CDK4/6i first, and alpelisib in subsequent lines of therapy
- This justifies testing ALL cases of ER+ MBC for PIK3Ca mutation
- Common side effects of hyperglycemia, rash are problematic and require additional management

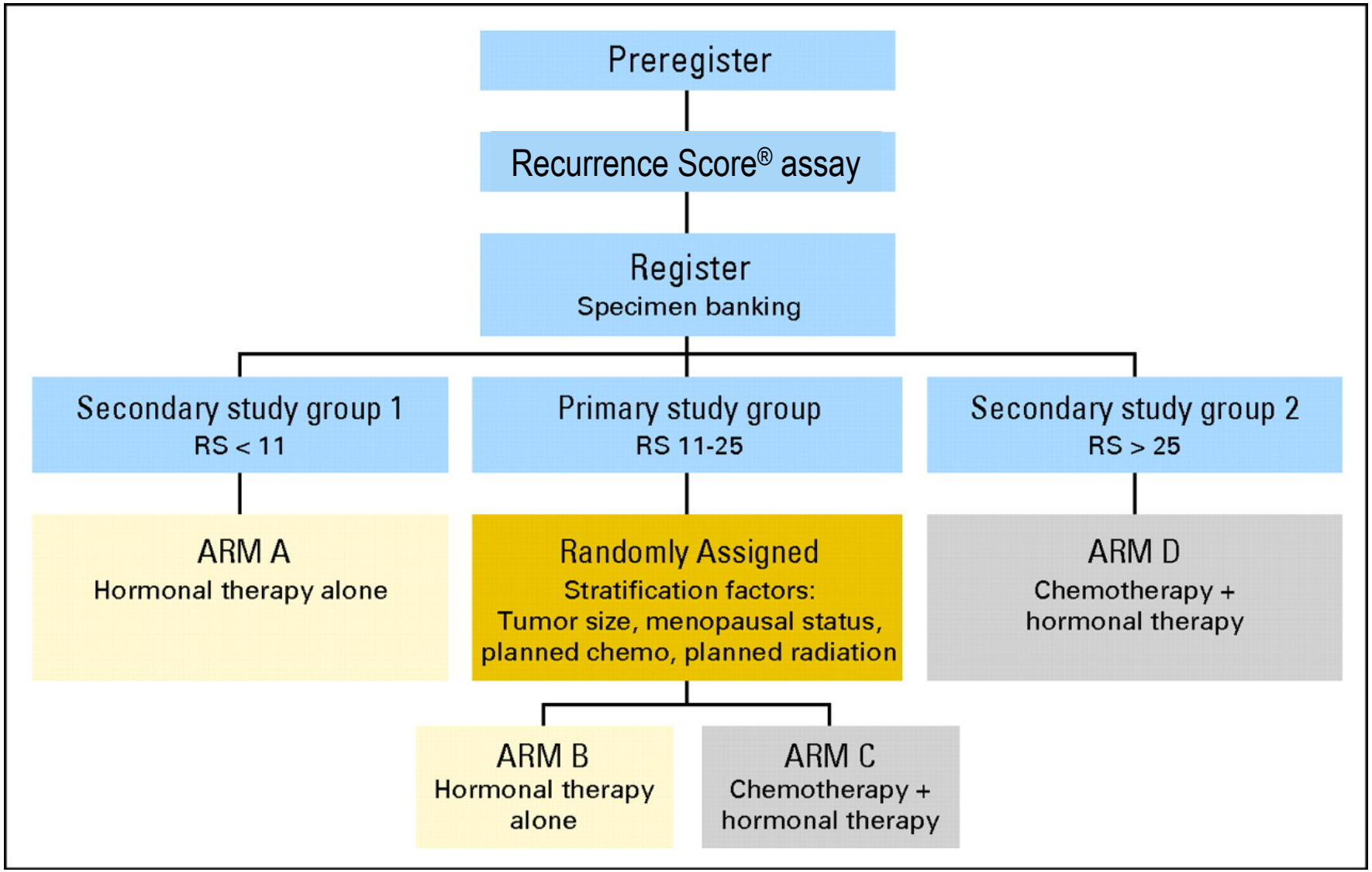
Courtesy of Harold J Burstein, MD, PhD

ER-Positive, HER2-Negative Breast Cancer

Genomic tests and chemotherapy for ER+ early-stage breast cancer

Courtesy of Harold J Burstein, MD, PhD

TAILORx



Sparano JA, et al. J Clin Oncol. 2008;26(5):721-728.

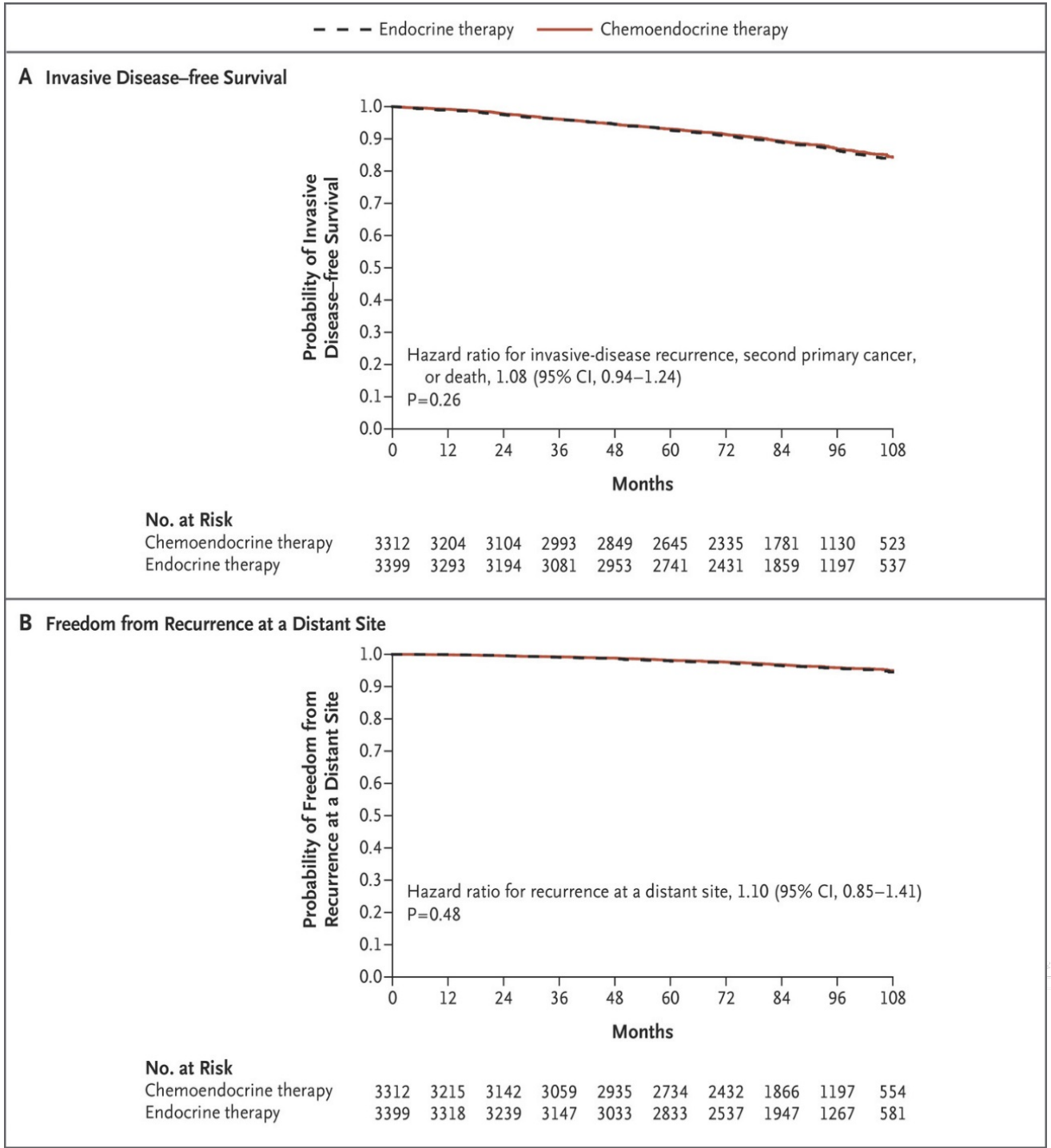
Courtesy of Harold J Burstein, MD, PhD

TAILORx –

RS 11-25

Overall

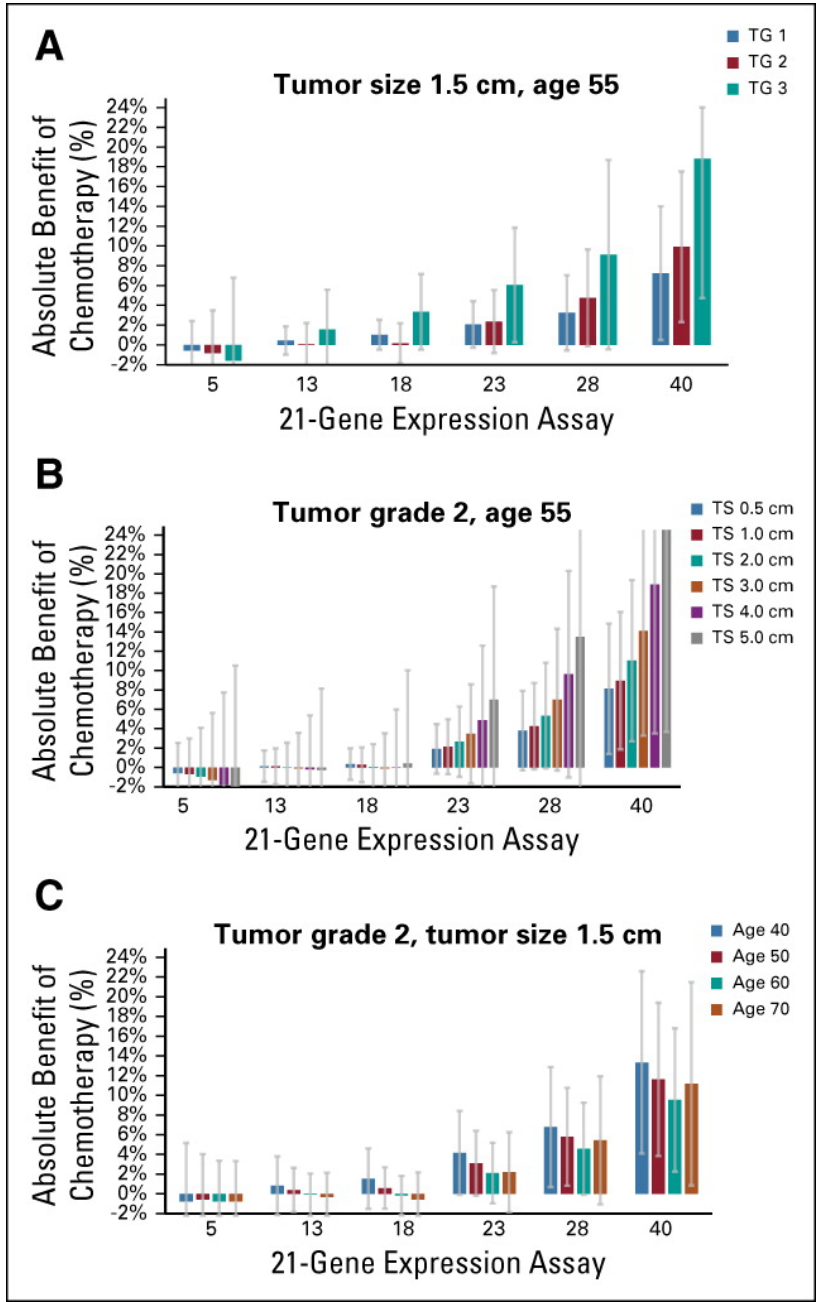
Result



JA Sparano et al.
N Engl J Med 2018.
DOI: 10.1056/NEJMoa1804710

Courtesy of Harold J Burstein, MD, PhD

The RSClin tool provides individualized estimates for chemotherapy benefit based on the entry of patient information for the RS result, age, tumor size, and tumor grade. Example estimates and 95% CIs provided by the RSClin tool for the absolute benefit of adjuvant chemotherapy for (A) tumor grade series, (B) tumor size series, and (C) patient age series. RS, recurrence score.



Sparano et al. JCO 2021

Sparano JA et al. *J Clin Oncol* 2020;[Online ahead of print].

Courtesy of Harold J Burstein, MD, PhD

RxPONDER Schema

Key Entry Criteria

- Women age ≥ 18 yrs
- ER and/or PR ≥ 1%, HER2- breast cancer with 1*-3 LN+ without distant metastasis
- Able to receive adjuvant taxane and/or anthracycline-based chemotherapy**
- Axillary staging by SLNB or ALND

REGISTRATION

Recurrence Score 0-25

Recurrence Score > 25

Off Study
Chemotherapy Followed by
Endocrine Therapy Recommended

RANDOMIZATION

N = 5,000 pts

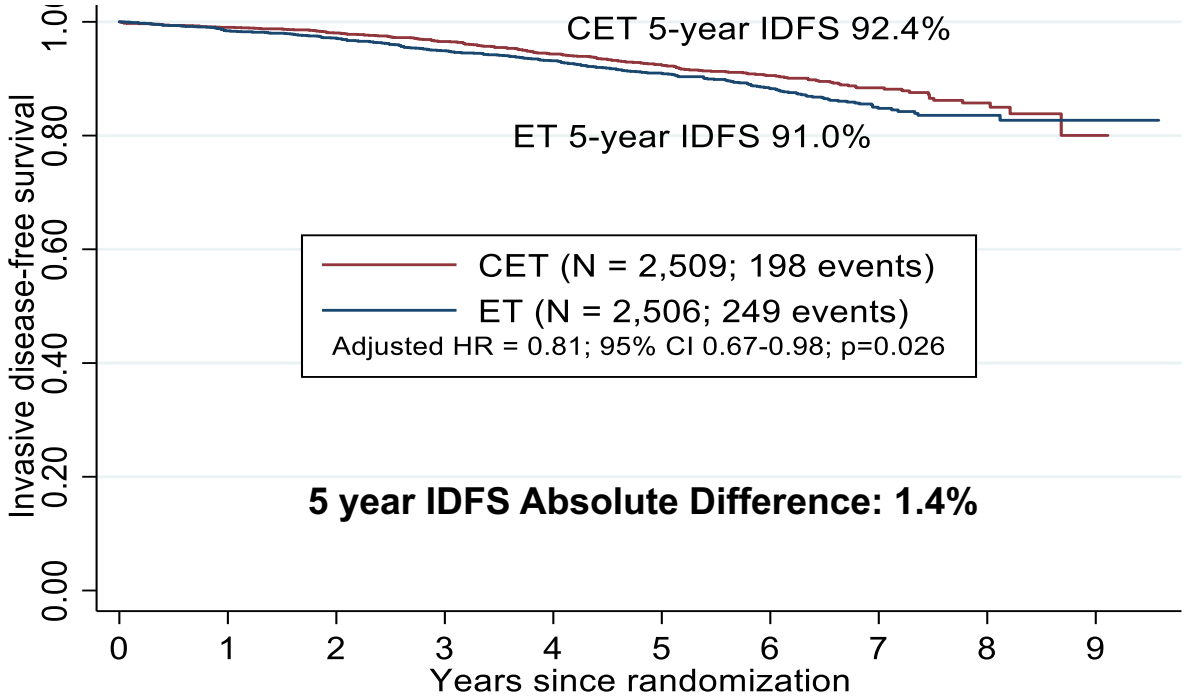
Arm 1:
Chemotherapy Followed by
Endocrine Therapy

Arm 2:
Endocrine Therapy Alone

Stratification Factors
Recurrence Score: 0-13 vs.14-25
Menopausal Status: pre vs. post
Axillary Surgery: ALND vs. SLNB

* After randomization of 2,493 pts, the protocol was amended to exclude enrollment of pts with pN1mic as only nodal disease.
** Approved chemotherapy regimens included TC, FAC (or FEC), AC/T (or EC/T), FAC/T (or FEC/T). AC alone or CMF not allowed.
ALND = Axillary Lymph Node Dissection, SLNB = Sentinel Lymph Node Biopsy

IDFS in Overall Population by Treatment Arm



Number at risk

CET	2509	2277	2104	1893	1648	1397	857	403	122	4
ET	2506	2327	2161	1910	1696	1404	846	397	135	11

CET = Chemotherapy + Endocrine Therapy; ET = Endocrine Therapy Alone

447 observed IDFS events (54% of expected at final analysis) at a median follow-up of 5.1 years

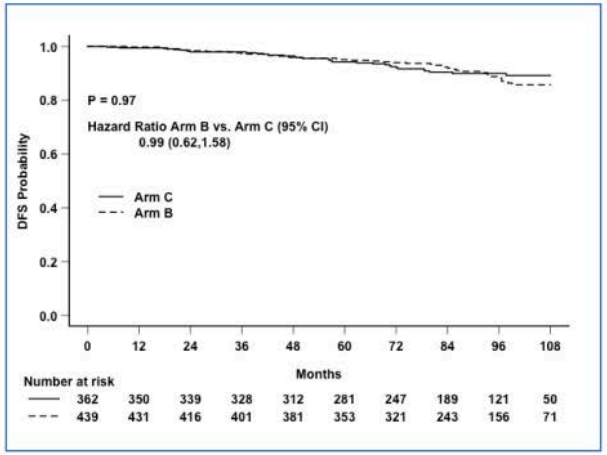
Kalinsky K et al. SABCS 2020;Abstract GS3-00.

Courtesy of Harold J Burstein, MD, PhD

What about *premenopausal* women?

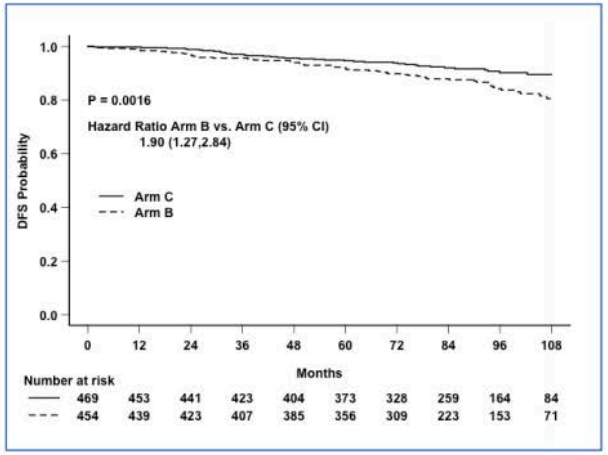
Courtesy of Harold J Burstein, MD, PhD

Outcomes for Women < 50 in TAILORx

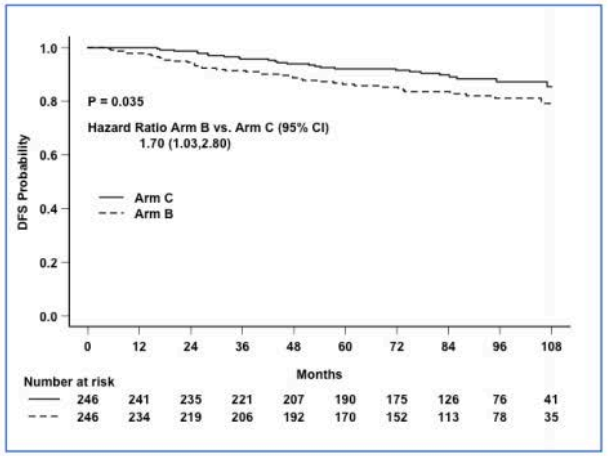


Recurrence Score

11-15



16-20



21-25

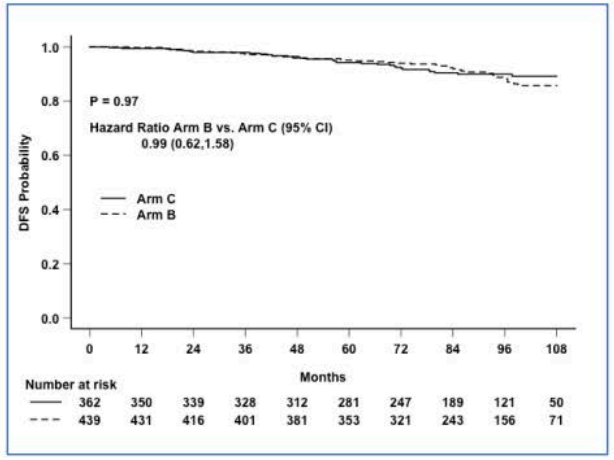
JA Sparano et al.
N Engl J Med 2018. DOI: 10.1056/NEJMoa1804710

Courtesy of Harold J Burstein, MD, PhD

Outcomes for Women < 50 in TAILORx

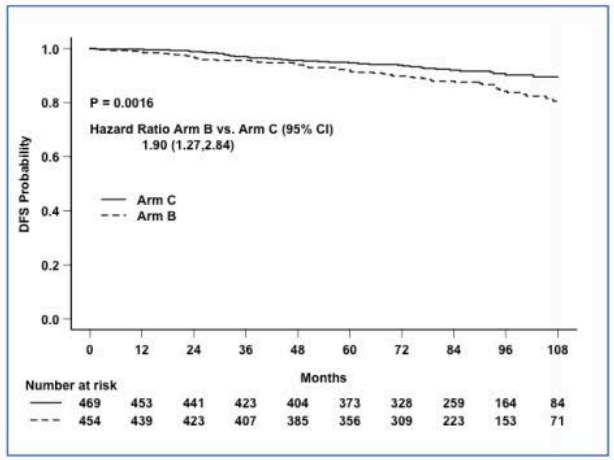
Q: How much is due to OFS effects of chemo?

A: A lot. All?

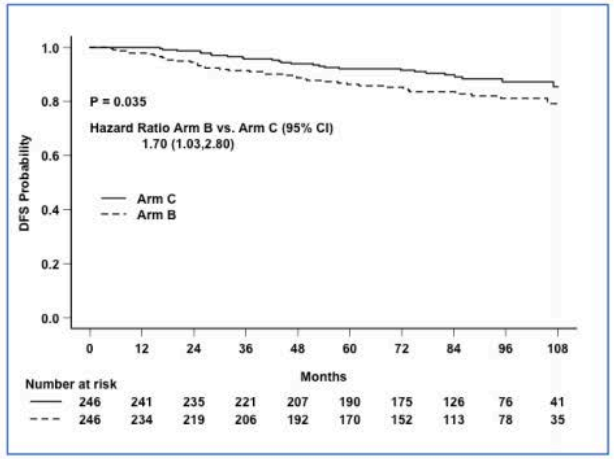


Recurrence Score

11-15



16-20



21-25

JA Sparano et al.
N Engl J Med 2018. DOI: 10.1056/NEJMoa1804710

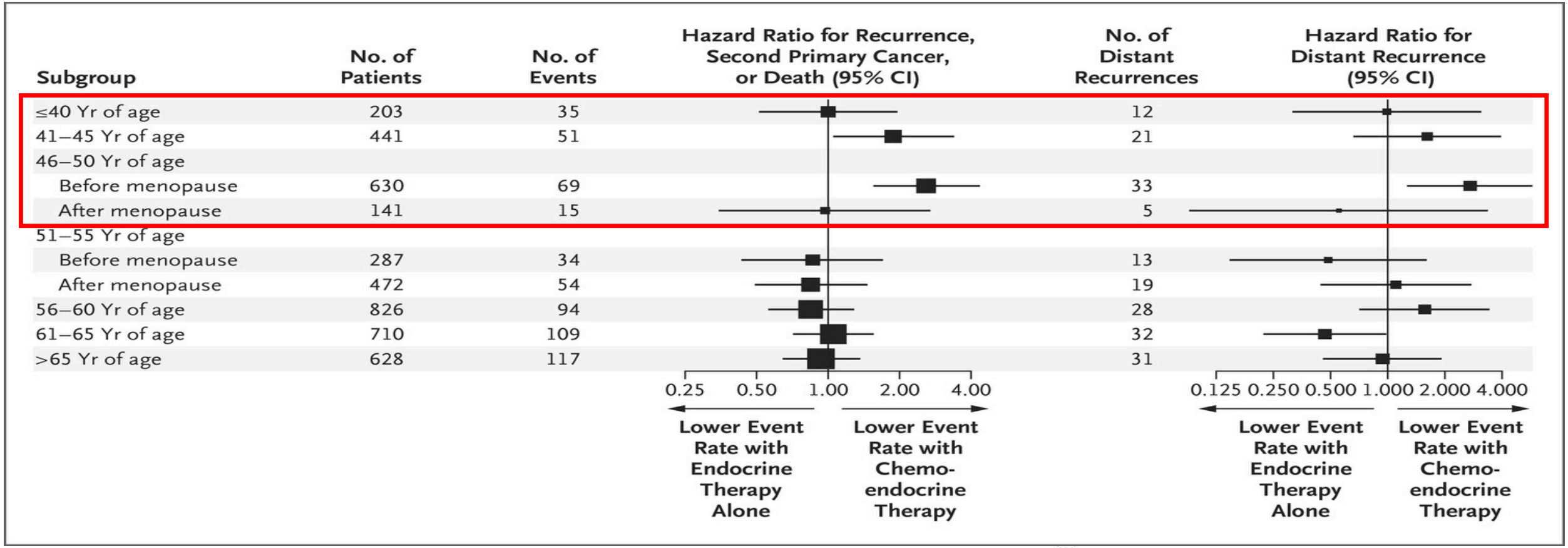
Courtesy of Harold J Burstein, MD, PhD

Hypothesis: benefits of chemotherapy in women ≤ age 50 with recurrence scores 16 to 25 ***are due to endocrine consequences of chemotherapy***

Population	Likelihood of chemotherapy – induced amenorrhea	Predicted benefit from chemotherapy if hypothesis is correct
Premenopausal ≤ Age 40	**Low**	**None**
Premenopausal Age 41 – 45	**Moderate**	**Yes; moderate**
Premenopausal Age 45 – 50	**High**	**Yes; high**
Postmenopausal Age < 50	**N/A**	**None**

Courtesy of Harold J Burstein, MD, PhD

Effect of Age and Menopausal Status on Chemotherapy Benefit.

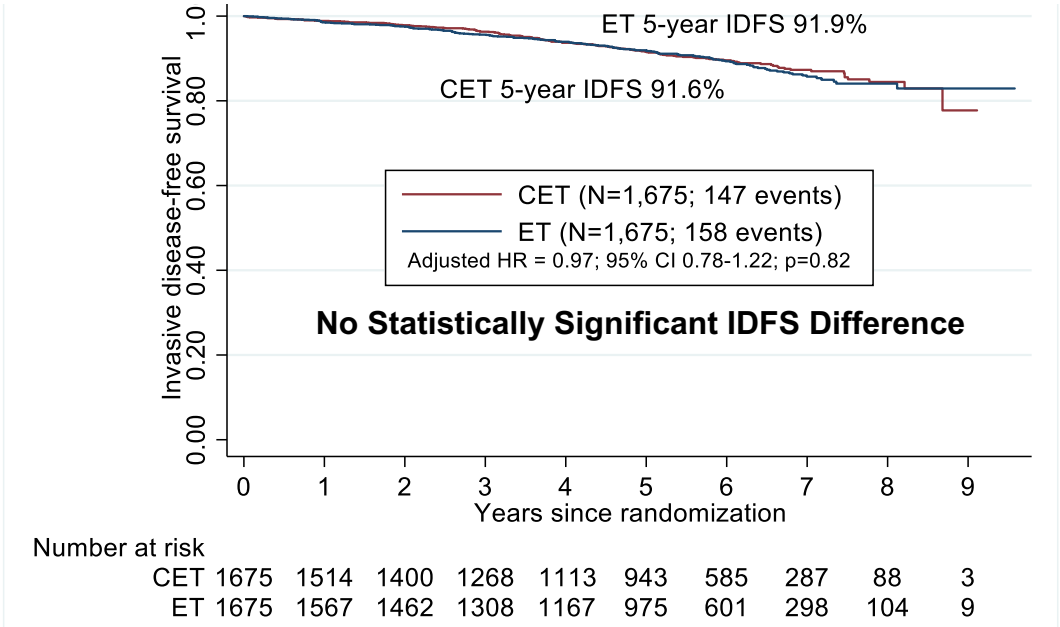


JA Sparano et al. N Engl J Med 2019. DOI: 10.1056/NEJMoa1904819

Courtesy of Harold J Burstein, MD, PhD

IDFS Stratified by Menopausal Status

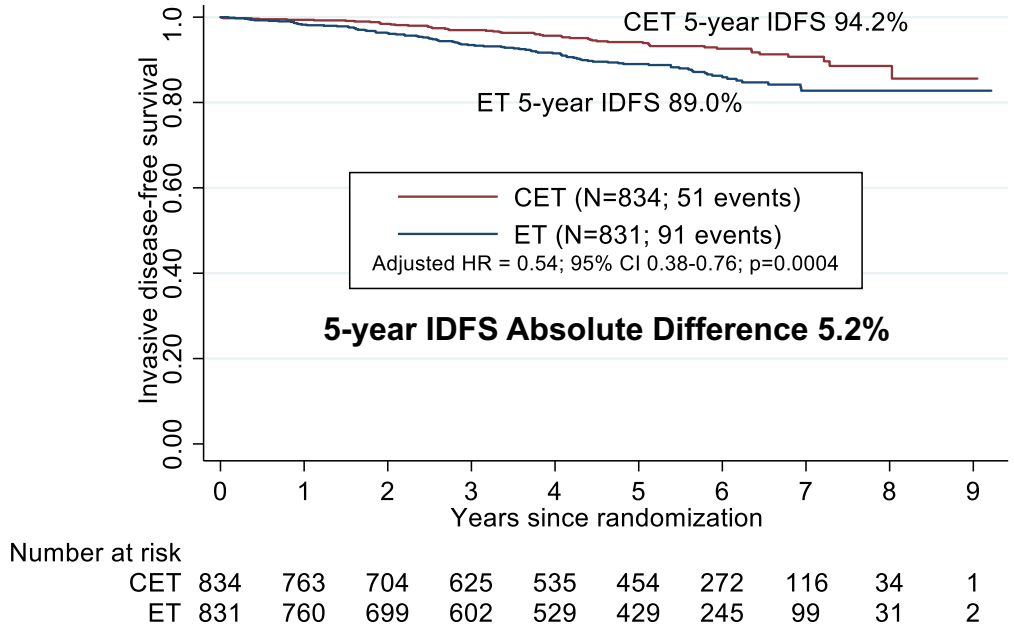
Postmenopausal



IDFS Event	CET	ET	Total (%)
Distant	39	44	83 (27%)
Local-Regional	10	14	24 (8%)
Contralateral	10	9	19 (6%)
Non-Breast Primary	44	47	91 (30%)
Recurrence Not Classified	9	7	16 (5%)
Death not due to Recurrence or Second Primary	35	37	72 (24%)

Absolute Difference in Distant Recurrence as 1st site: 0.3% (2.3% CET vs. 2.6% ET)

Premenopausal



IDFS Event	CET	ET	Total (%)
Distant	26	50	76 (54%)
Local-Regional	8	17	25 (18%)
Contralateral	4	8	12 (8%)
Non-Breast Primary	10	10	20 (14%)
Recurrence Not Classified	1	1	2 (1%)
Death not due to Recurrence or Second Primary	2	5	7 (5%)

Absolute Difference in Distant Recurrence as 1st site: 2.9% (3.1% CET vs. 6.0% ET)

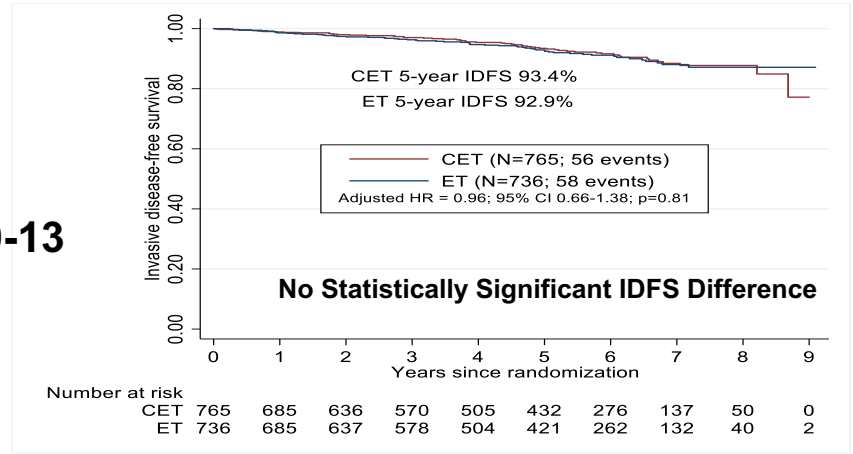
Courtesy of Harold J Burstein, MD, PhD

Kalinsky K et al. SABCS 2020.

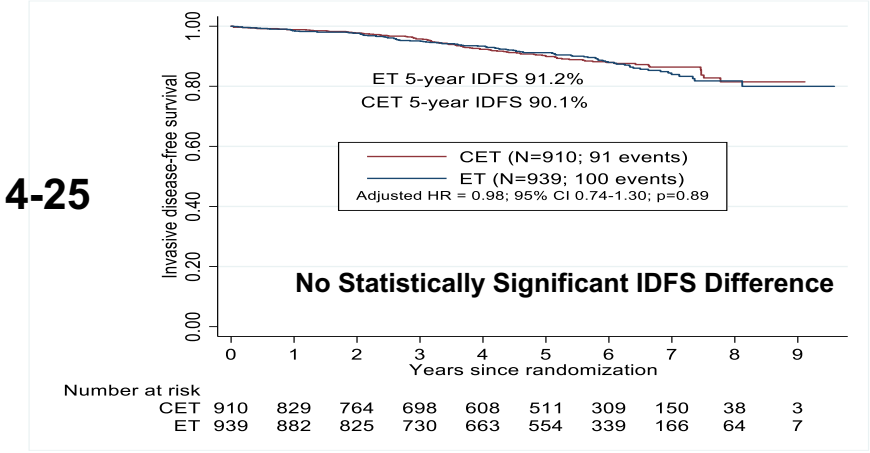
IDFS Stratified by Recurrence Score and Menopausal Status

Postmenopausal

RS 0-13

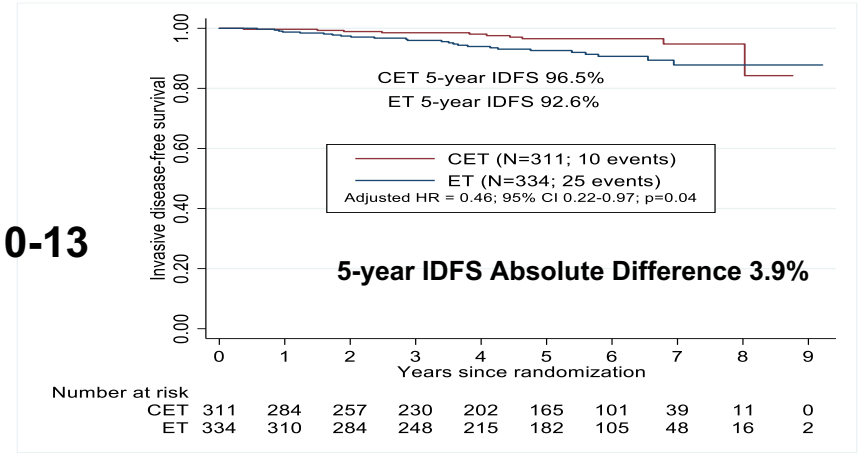


RS 14-25

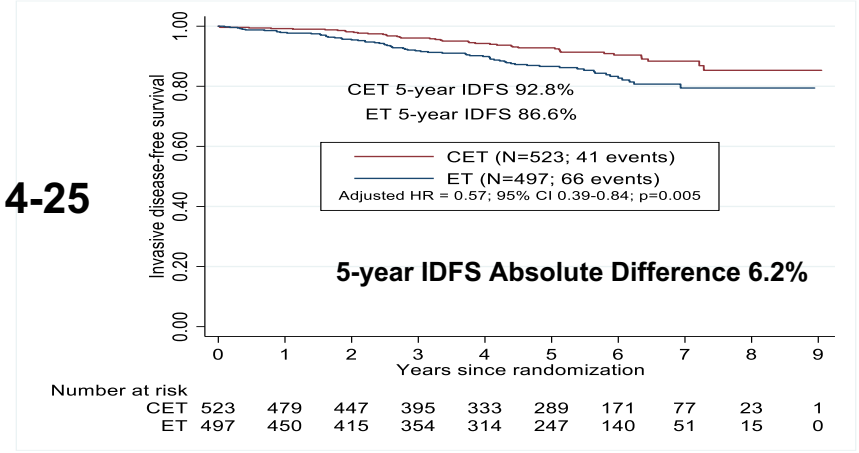


Premenopausal

RS 0-13



RS 14-25



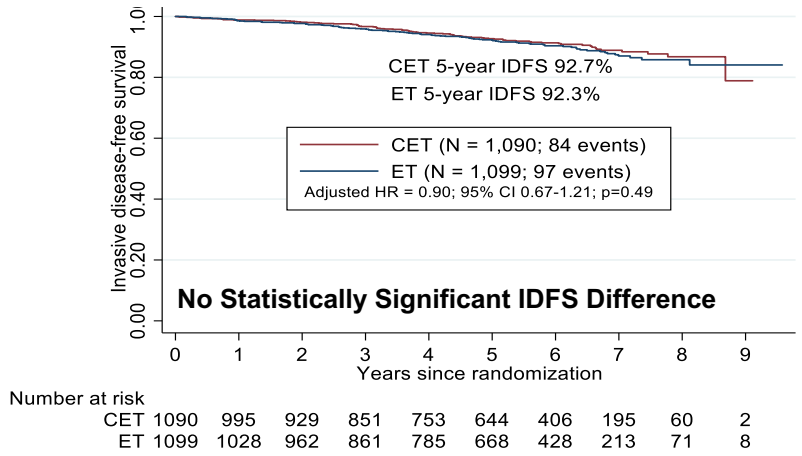
Courtesy of Harold J Burstein, MD, PhD

Kalinsky K et al. SABCS 2020.

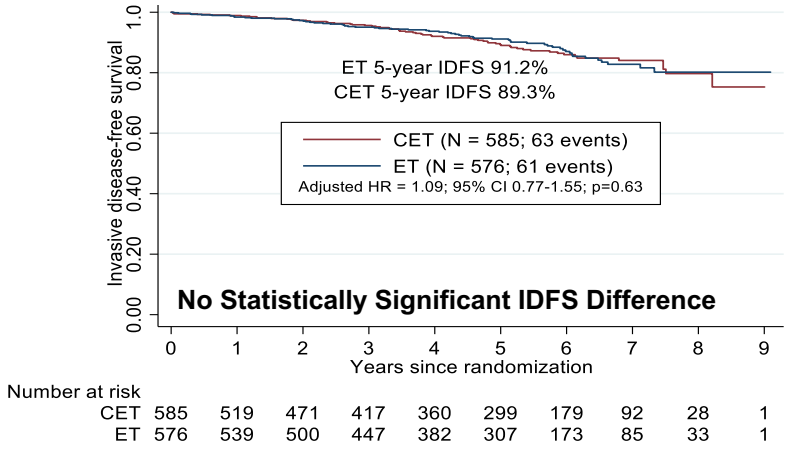
IDFS Stratified by Number of Nodes and Menopausal Status

Postmenopausal

1 Node

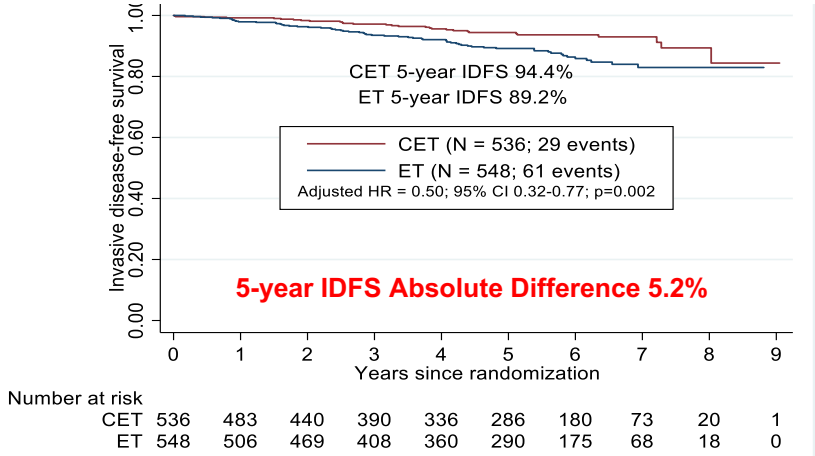


2-3 Nodes

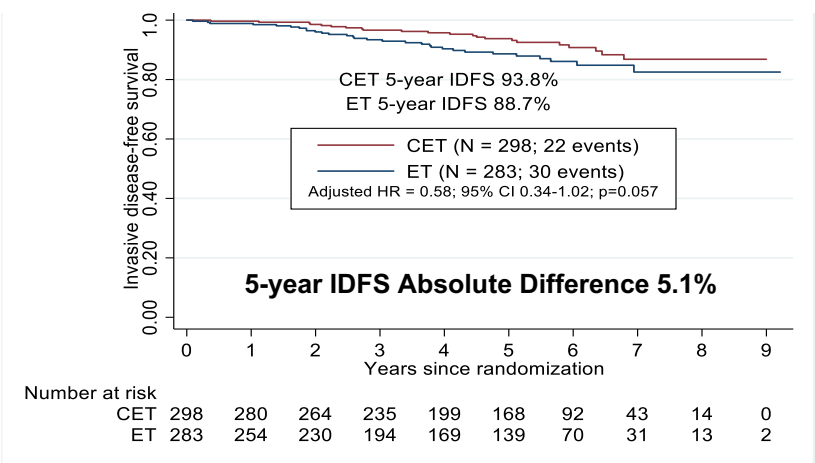


Premenopausal

1 Node



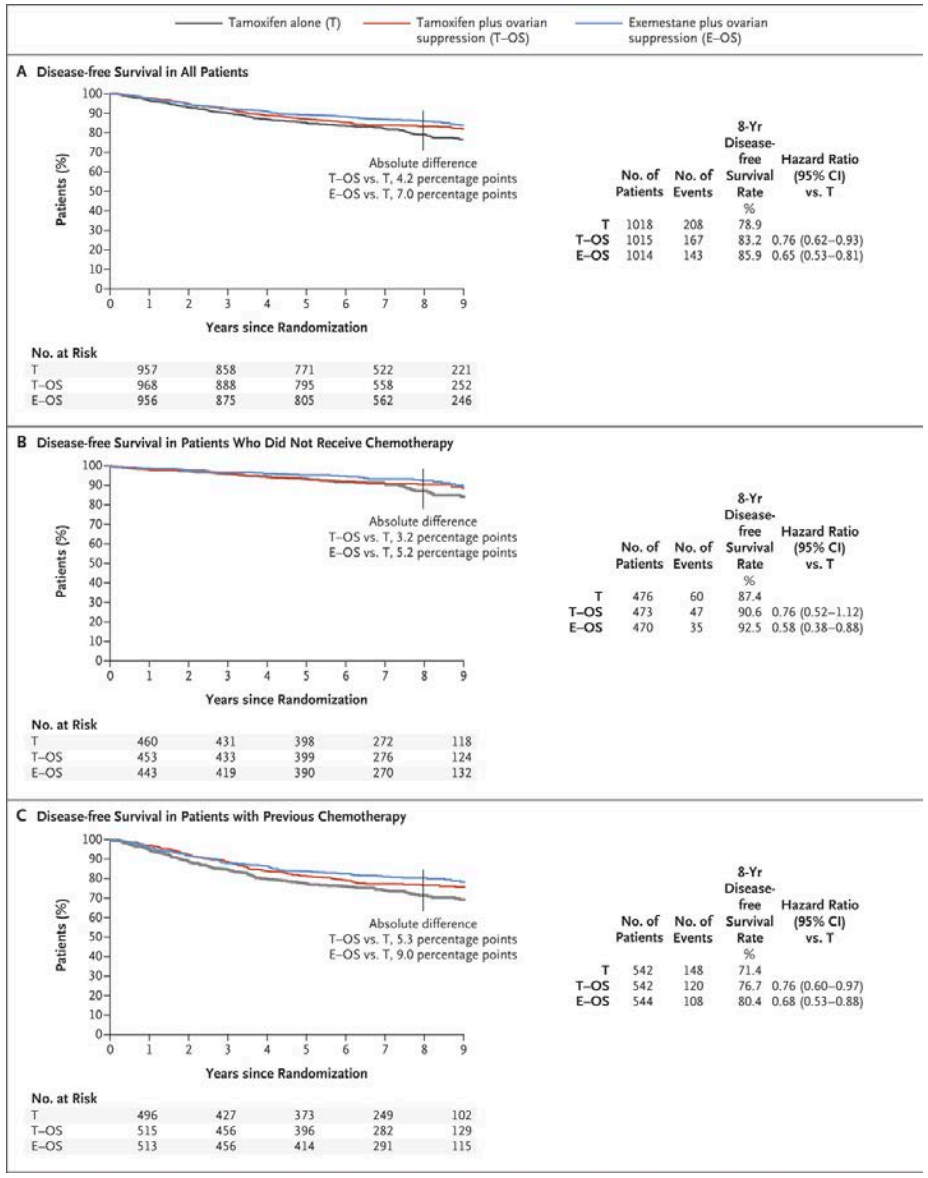
2-3 Nodes



Courtesy of Harold J Burstein, MD, PhD

Kalinsky K et al. SABCS 2020.

SOFT Trial: iDFS at 8 year median follow-up



Absolute Benefit of AI/OFS

Without chemo: 4.9%
With chemo: 9.0%

PA Francis et al. N Engl J Med 2018;379:122-137.

Courtesy of Harold J Burstein, MD, PhD

Conclusions

- Prospective data from randomized clinical trials show that women with ER+ breast cancers and a recurrence score ≤ 25 do not benefit from adjuvant chemotherapy.
  - Node-negative, TAILORx
  - One to three positive LN, RxPONDER

- There is a numerical benefit to chemotherapy among premenopausal women
  - The most plausible explanation for this finding is because of the ovarian suppression effects of chemotherapy, and not the 'cytotoxic' effects of chemotherapy
  - It is likely that OFS could achieve outcomes equivalent to chemotherapy in premenopausal women with low-int RS scores

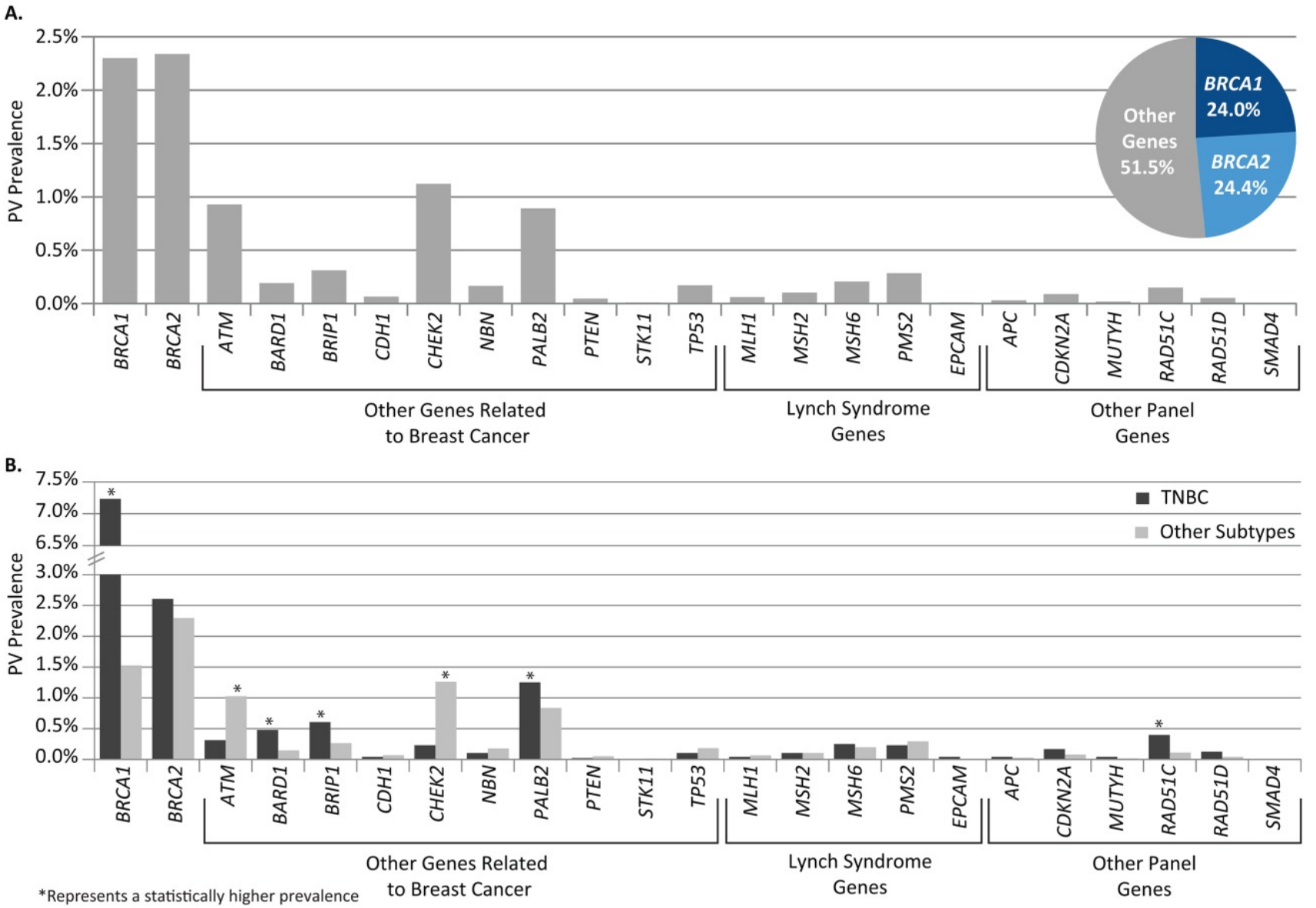
- We order RS in pre- and post-menopausal women and use it to guide treatment decisions

Courtesy of Harold J Burstein, MD, PhD

PARP inhibitors in advanced, hereditary breast cancer

Courtesy of Harold J Burstein, MD, PhD

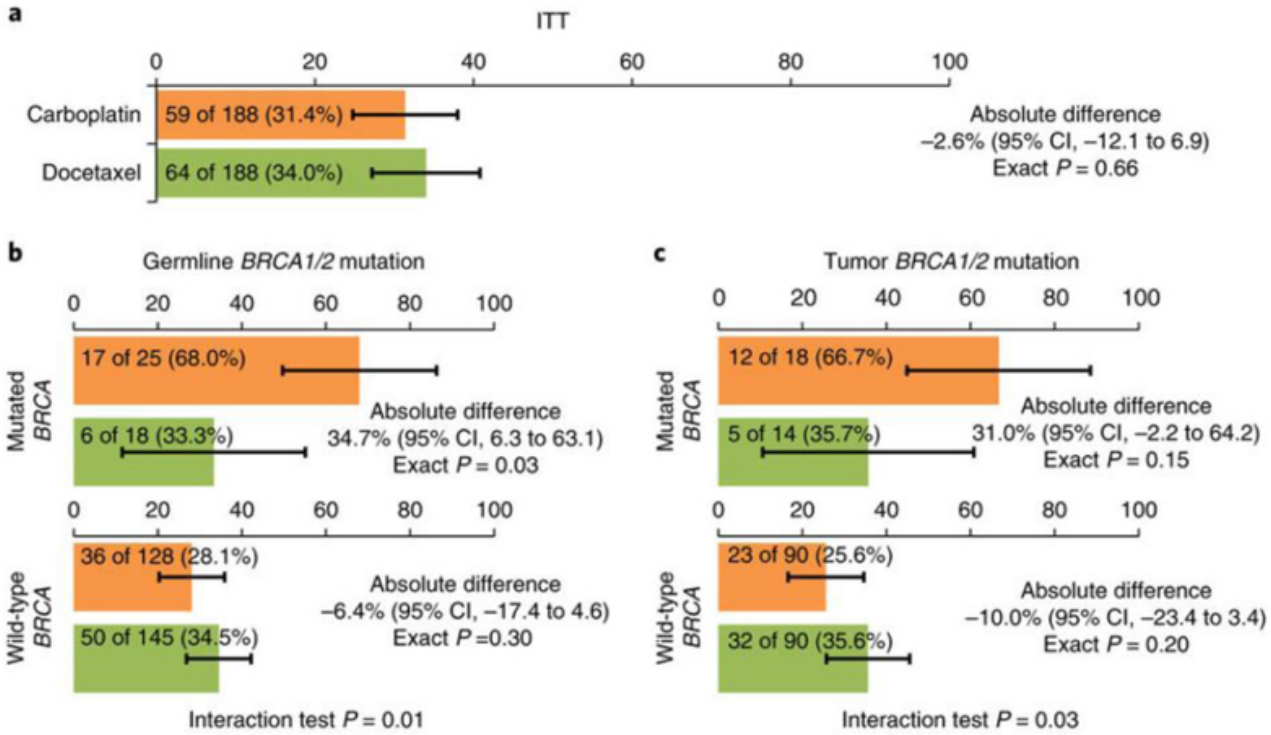
A study of over 35,000 women with breast cancer tested with a 25-gene panel of hereditary cancer genes

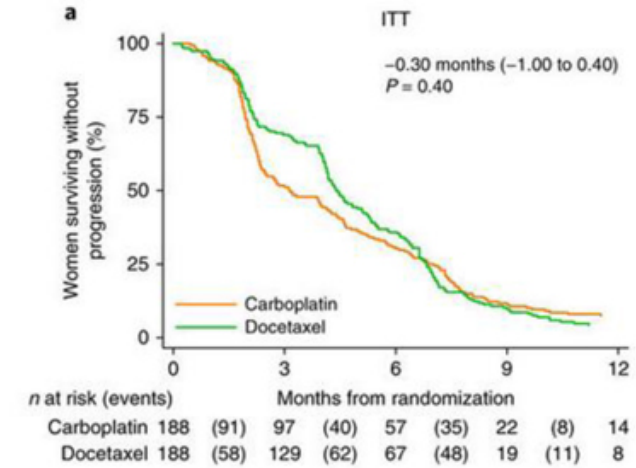


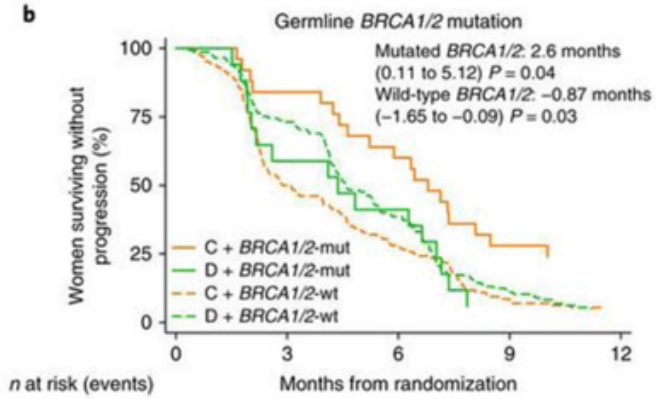
Buys, et al. Cancer, Volume: 123, Issue: 10, Pages: 1721-1730, First published: 13 January 2017, DOI: (10.1002/cncr.30498)

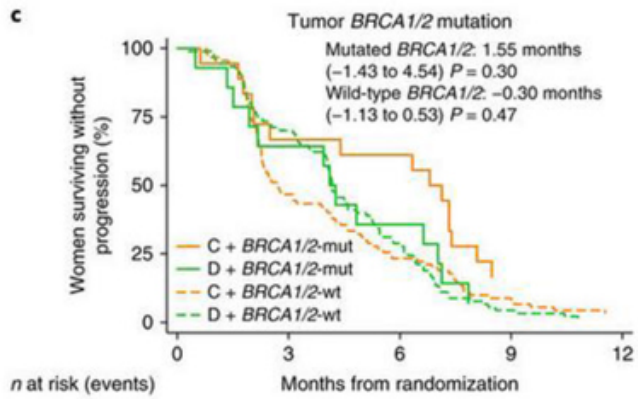
Courtesy of Harold J Burstein, MD, PhD

TNT Trial: carboplatin vs docetaxel in TNBC





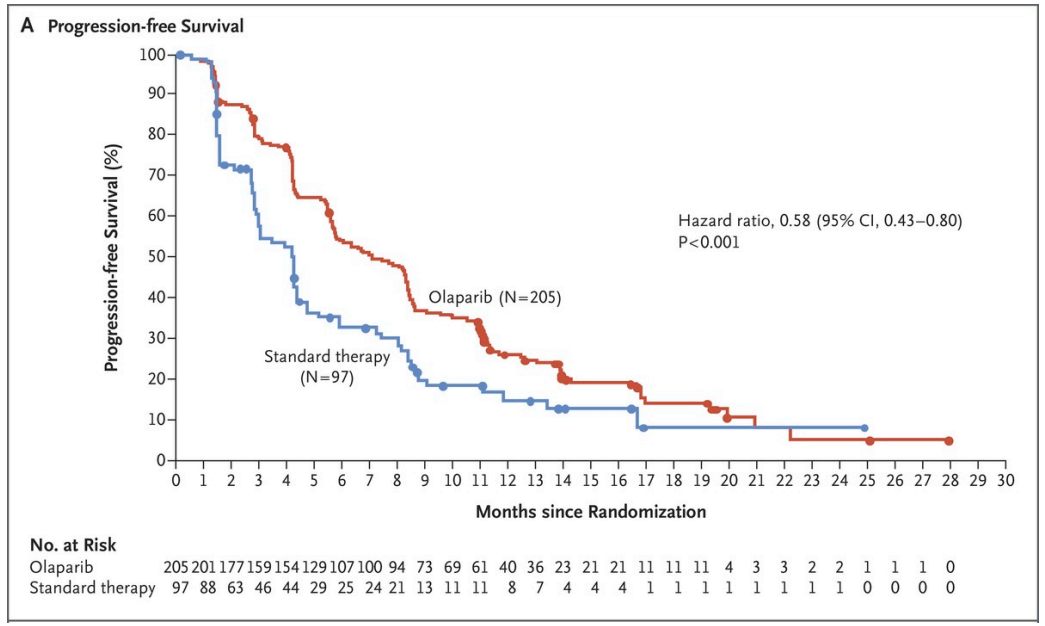




Tutt et al. Nature Med 2018;24:628

Courtesy of Harold J Burstein, MD, PhD

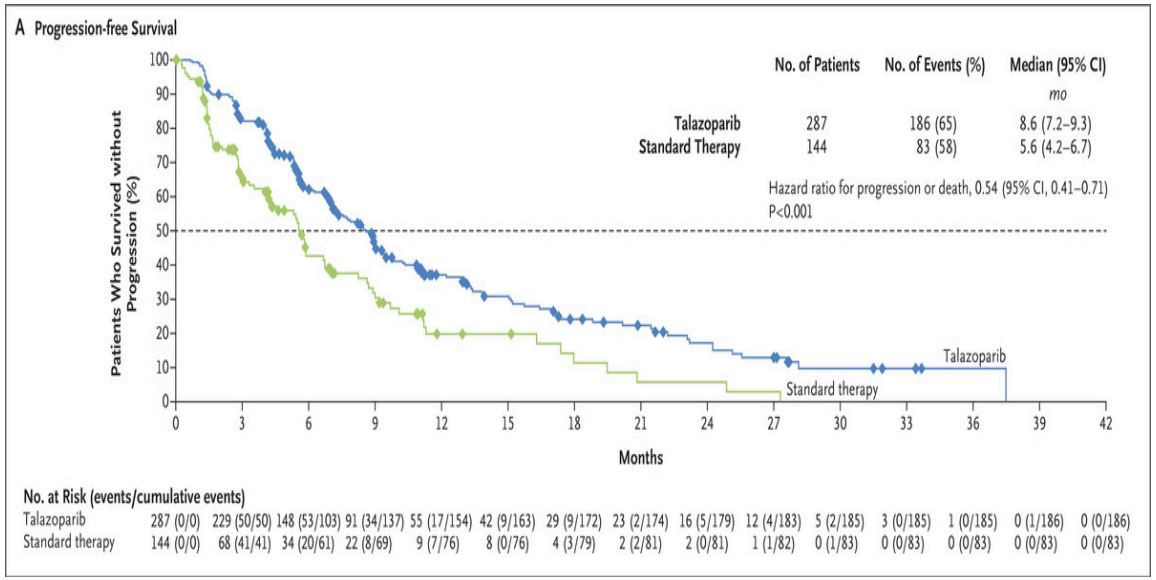
PARP Inhibitor vs Std Chemotherapy in BRCA-associated Advanced Breast Cancer



Robson M et al. N Engl J Med 2017;377:523-533.

Response rates

Olaparib 60% Std chemo 28%

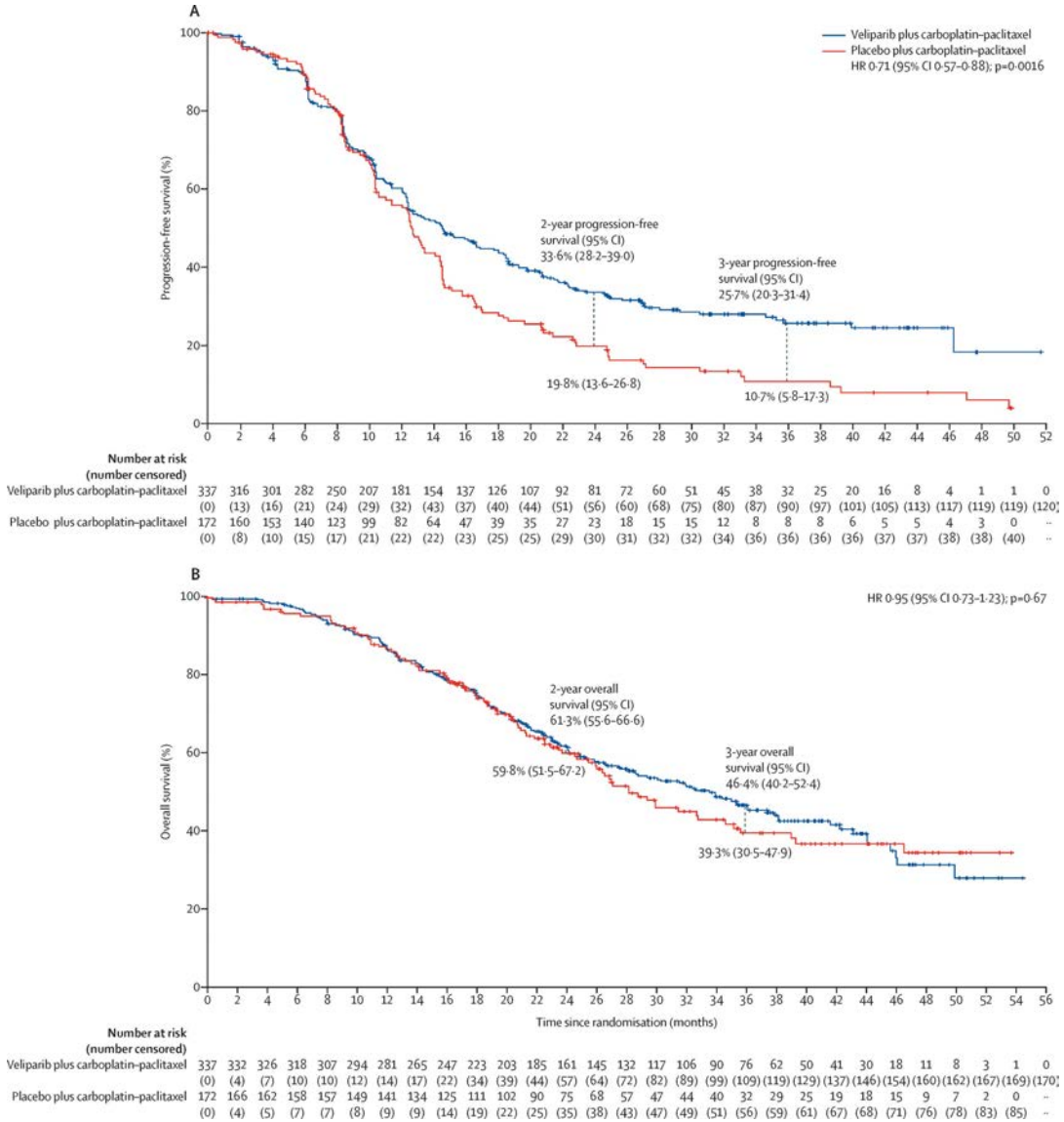


JK Litton et al. N Engl J Med 2018;379:753-763.

Talazoparib 62% Std chemo 27%

Courtesy of Harold J Burstein, MD, PhD

BROCADE3: carboplatin and paclitaxel w/w/o veliparib in BRCA associated breast cancer



<u>Response rates:</u>

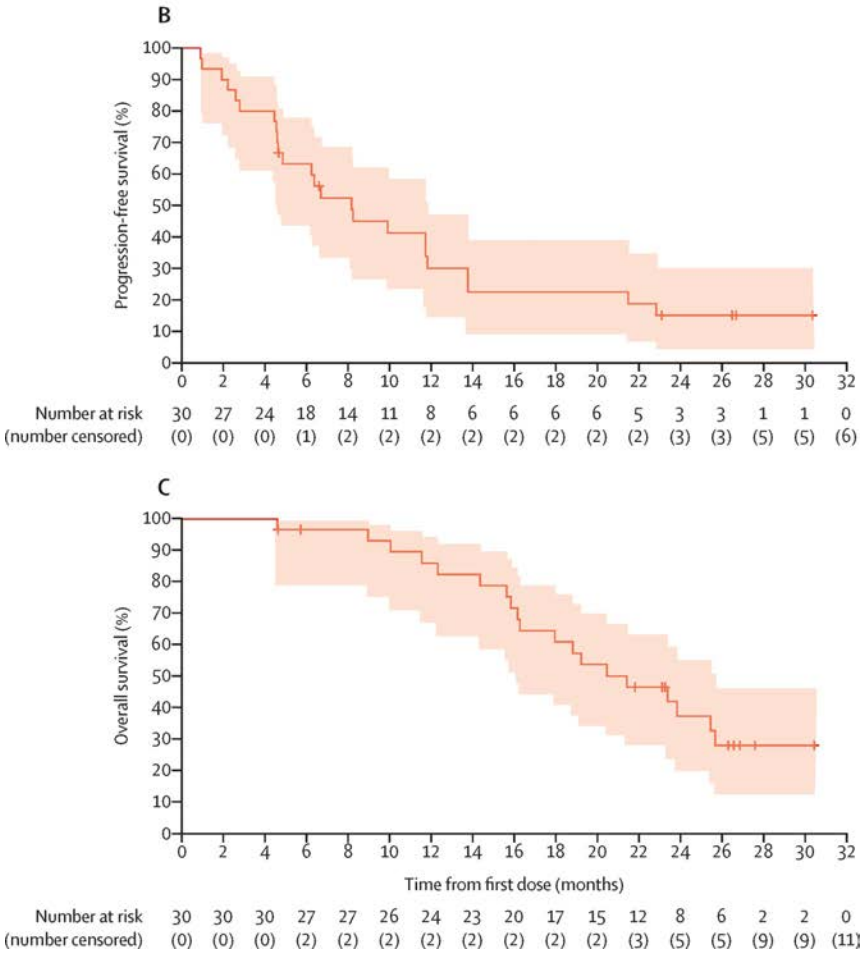
Carbo/Tax 74%

Carbo/Tax/Velip 76%

Dieras V et al. Lancet Oncol 2020;21(10):1269-82.

Courtesy of Harold J Burstein, MD, PhD

MEDIOLA: olaparib plus durvalumab (anti-PD-L1) in BRCA-associated advanced breast cancer



Response rate: 63%

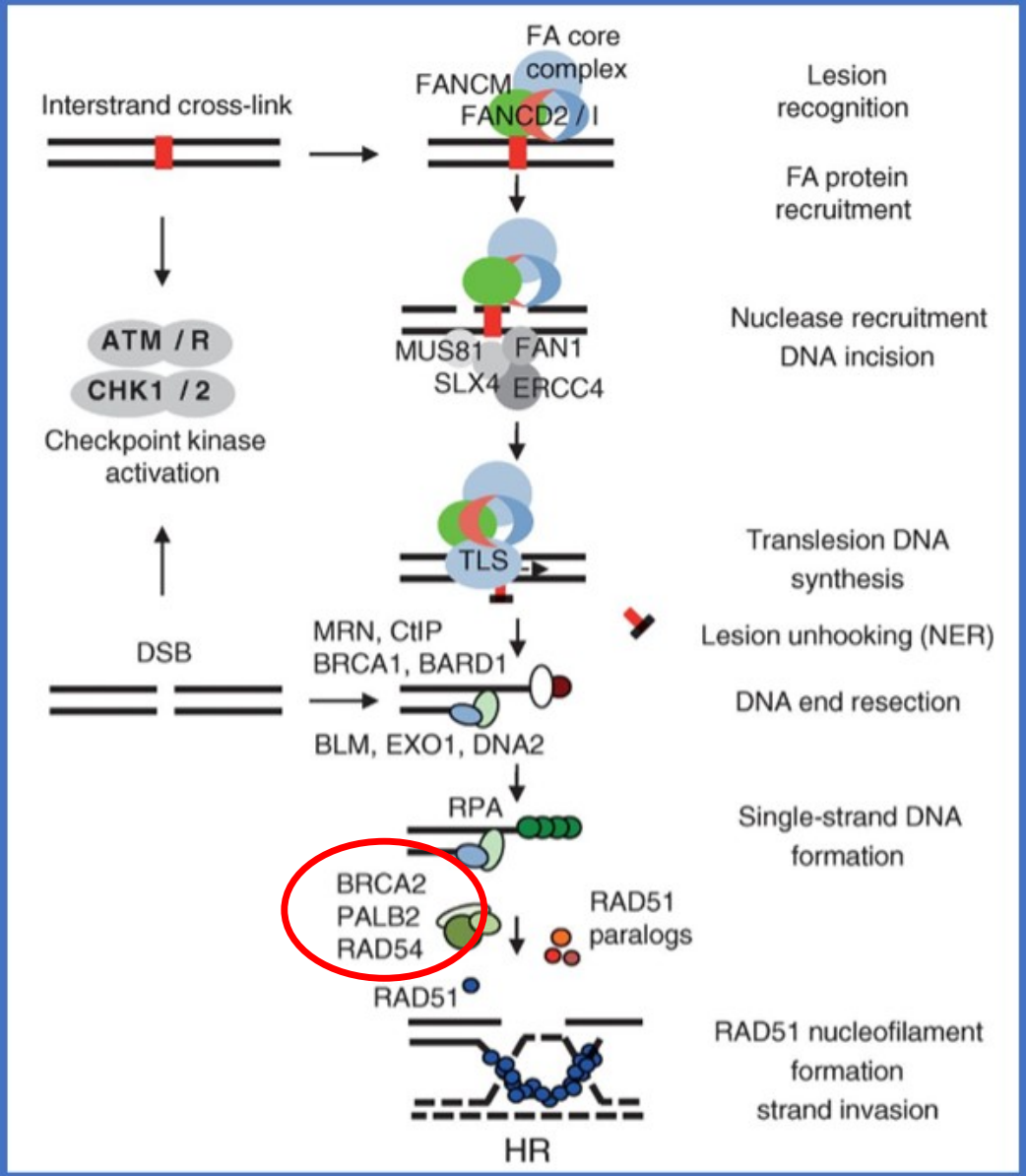
PFS:

TNBC	4.9m
ER+	9.9m

Domchek et al. Lancet Oncol 2020;21:1155

Courtesy of Harold J Burstein, MD, PhD

DNA double strand break repair pathway



Courtesy of Harold J Burstein, MD, PhD

Konstantinopoulos et al. Cancer Discov; 2015; 5; 1137–54

Beth Israel Deaconess Medical Center | HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Dana-Farber Cancer Institute

tbcrc Translational Breast Cancer Research Consortium

TBCRC 048: A phase II study of olaparib monotherapy in metastatic breast cancer patients with germline or somatic mutations in homologous recombination (HR) pathway genes (Olaparib Expanded)

Nadine Tung, Mark E. Robson, Steffen Ventz, Cesar Santa-Maria, Paul Kelly Marcom, Rita Nanda, Payal D. Shah, Tarah J. Ballinger, Eddy Yang, Michelle Melisko, Adam Brufsky, Shaveta Vinayak, Michelle DeMeo, Colby Jenkins, Susan Domchek, Gerburg Wulf, Ian E. Krop, Antonio C. Wolff, Eric P. Winer, Judy E. Garber

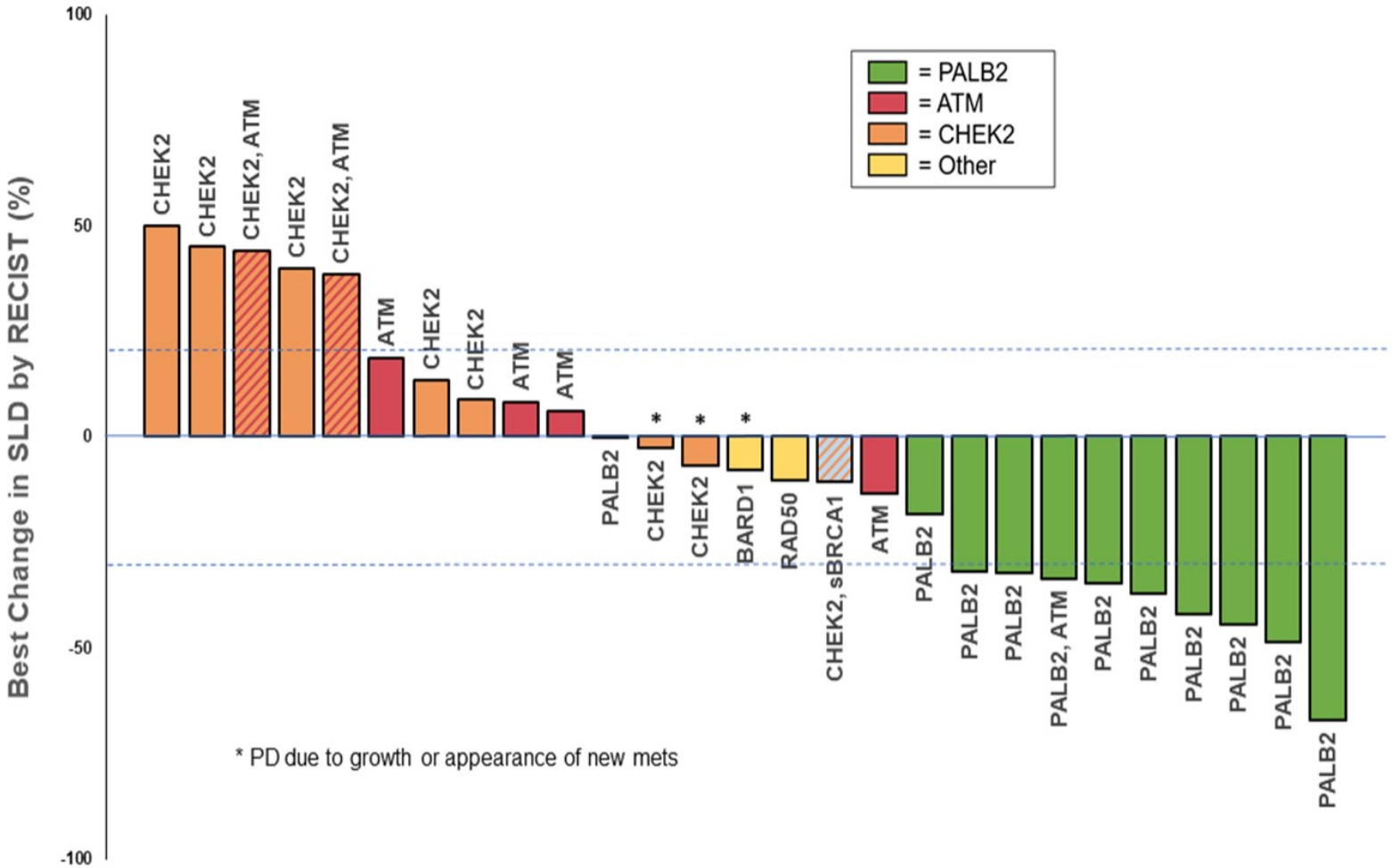
PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20

PRESENTED BY: Nadine Tung, MD

Presented By Nadine Tung at TBD

Courtesy of Harold J Burstein, MD, PhD

Best Overall Responses: Cohort 1 (Germline)



Datacut May 4, 2020

Presented By Nadine Tung at TBD

Courtesy of Harold J Burstein, MD, PhD

Results for g*PALB2*

g*PALB2* N=11	
Best Response	**Responses (rate, %)**
Complete Response (CR)	0 (0%)
Partial Response (PR)	9 (82%)
Stable Disease (SD)	2 (18%)
Progressive Disease (PD)	0 (0%)
ORR = 82% (9/11, 90%-CI: 48%-98%)	
CBR (18 wks) = 100% (10/10, 90%-CI: 74%-100%)	

Datacut May 4, 2020

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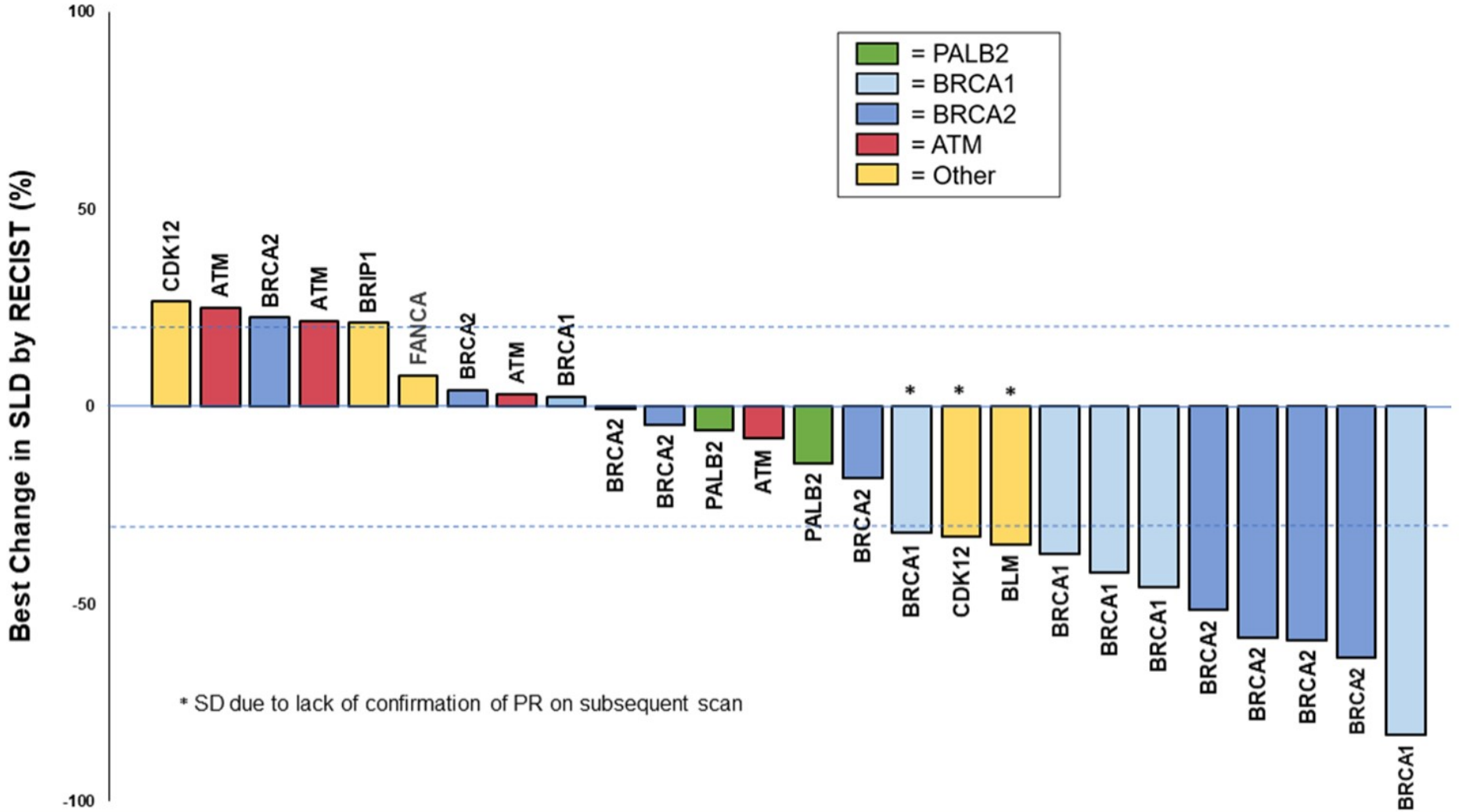
Best Overall Responses: Cohort 2 (Somatic)



Datacut May 4, 2020

Presented By Nadine Tung at TBD

Courtesy of Harold J Burstein, MD, PhD

Results for s*BRCA1/2*

sBRCA1/2 N=16*	
Best Response	**Responses, (rate, %)**
Complete Response (CR)	0 (0%)
Partial Response (PR)	8 (50%)
Stable Disease (SD)	6 (38%)
Progressive Disease (PD)	2 (12%)
ORR = 50% (8/16, 90%-CI: 25%-75%)	
CBR (18 wks) = 67% (10/15, 90%-CI: 47%-87%)	

* Includes patient from Cohort 1 with gCHEK2 and sBRCA1 mutations

Datacut May 4, 2020

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Courtesy of Harold J Burstein, MD, PhD

Responses for 5 most common genes (somatic and germline mutations)

PALB2 N=13	*sBRCA1/2* N=17^	*ATM & CHEK2*** N=17
Germline: 9/11 PR (82%) 10/11 had tumor regression; 1 SD > 1 yr **Somatic: 0/2 – both SD* (limited assessments)**	**8/16 PR (50%)**	**0/13 germline** **0/4 somatic**

15 patients remain on study

* 1 sPALB2- lost to follow-up after 1st tumor assessment with skin and tumor marker response
^ includes patient from Cohort 1 with sBRCA1 and gCHEK2
** Not included: patient with both gCHEK2 & sBRCA1; patient with gATM and gPALB2

Datacut May 4, 2020

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Courtesy of Harold J Burstein, MD, PhD

Conclusions

- PARP inhibitors are really active drugs in BRCA-associated breast cancer
- Justifies genetic testing in ALL women with advanced breast cancer for BRCA1, BRCA2, and PALB2 at a minimum
- Role in sBRCA is intriguing; more work needed

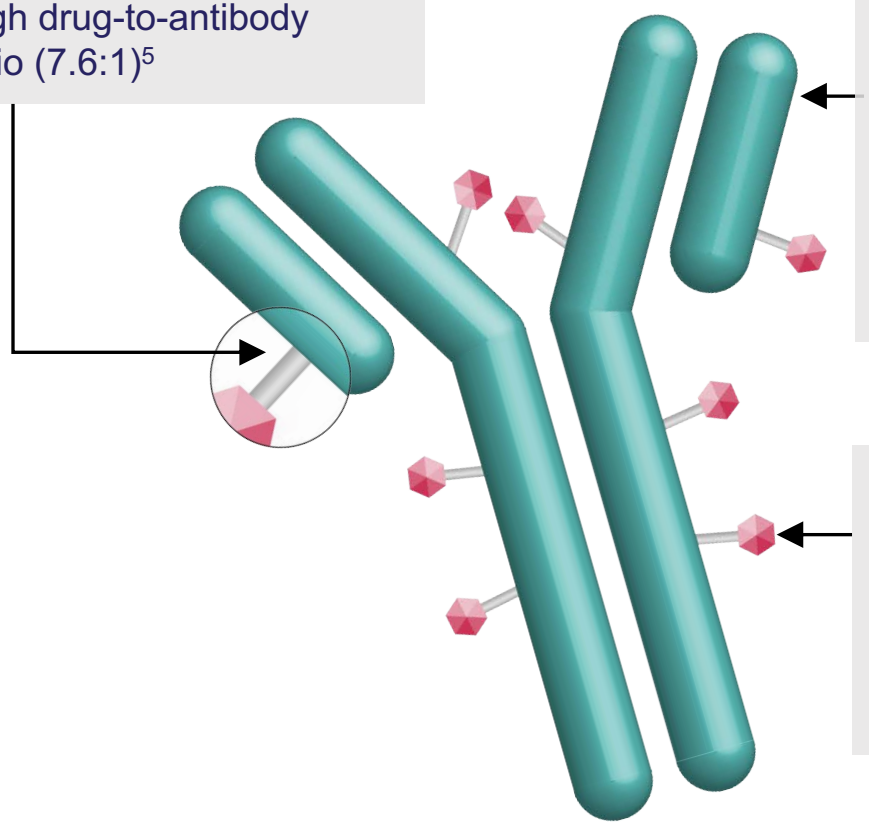
Courtesy of Harold J Burstein, MD, PhD

Sacituzumab govitecan in advanced TNBC

Courtesy of Harold J Burstein, MD, PhD

Sacituzumab Govitecan (SG) Is a First-In-Class Trop-2–Directed ADC

- Trop-2 is expressed in all subtypes of breast cancer and linked to poor prognosis[1,2]
- SG is distinct from other ADCs[3-5]
  - Antibody highly specific for Trop-2
  - High drug-to-antibody ratio (7.6:1)
  - Internalization and linker cleaver by tumor cell not required for the liberation of SN-38 from the antibody
  - Hydrolysis of the linker releases the SN-38 cytotoxic extracellularly in the tumor microenvironment, providing a bystander effect
- Granted accelerated approval by the FDA for metastatic TNBC and fast-track designation in metastatic urothelial cancer[6]

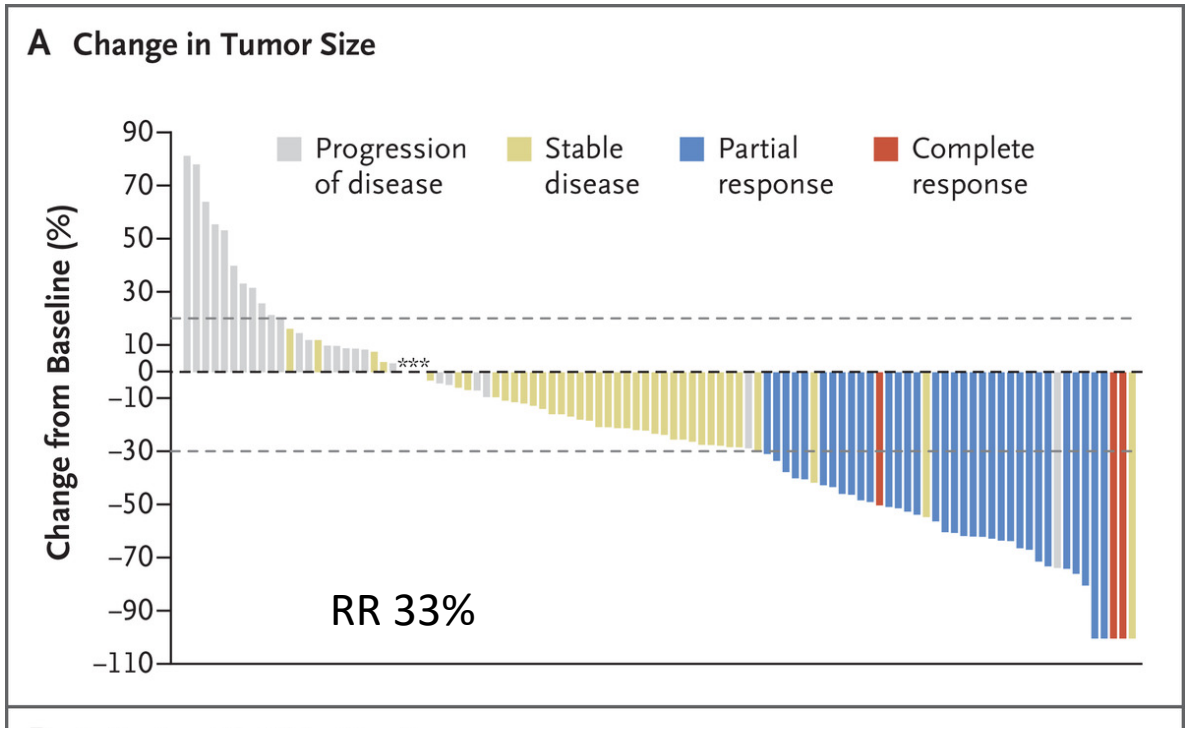


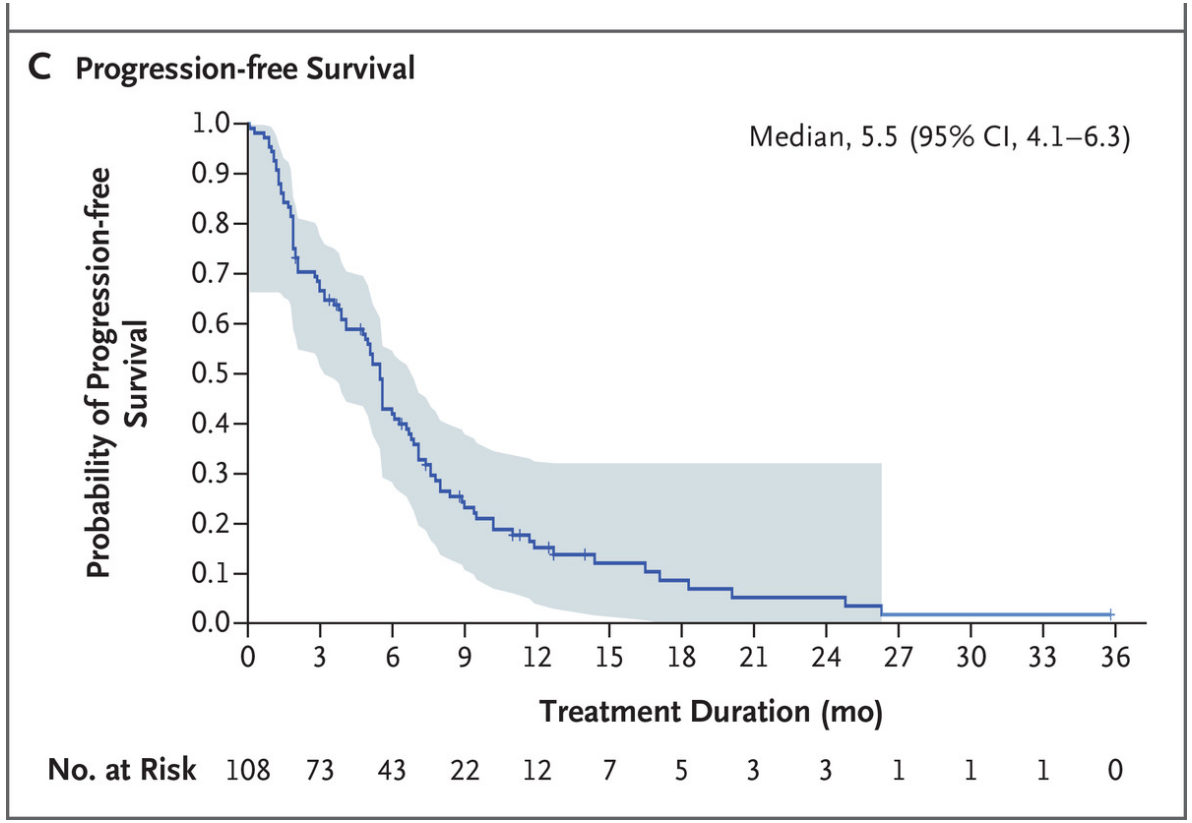
ADC, antibody−drug conjugate; TNBC, triple-negative breast cancer; Trop-2, trophoblast cell surface antigen 2.

1. Vidula et al. *J Clin Oncol.* 2017;35:15(suppl):Abstract 1075. 2. Ambrogi et al. *PLoS One.* 2014;9(5):e96993. 3. Goldenberg DM et al. *Expert Opin Biol Ther*. 2020 Aug;20(8):871-885. 4. Nagayama A, et al. *Ther Adv Med Oncol*. 2020;12:1758835920915980. 5. Cardillo TM, et al. *Bioconjugate Chem.* 2015;26:919-931. 6. Press Release. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-grants-accelerated-approval-sacituzumab-govitecan-hziy-metastatic-triple-negative-breast-cancer. Accessed August 26, 2020.

Courtesy of Harold J Burstein, MD, PhD

Sacituzumab govitecan: Response and Survival among 108 Patients with Metastatic Triple-Negative Breast Cancer.



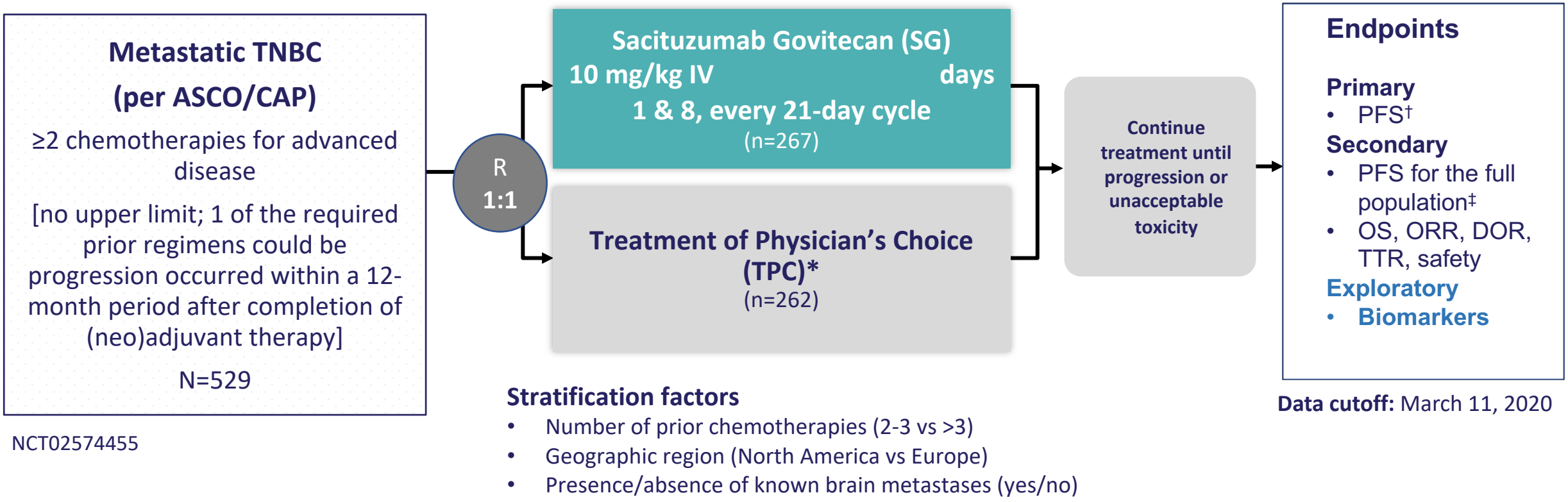


Common side effects: anemia, neutropenia, febrile neutropenia, diarrhea, vomiting/nausea, alopecia

A Bardia et al. N Engl J Med 2019;380:741-751.

Courtesy of Harold J Burstein, MD, PhD

ASCENT: A Phase 3 Confirmatory Study of Sacituzumab Govitecan in Refractory/Relapsed mTNBC



NCT02574455

Stratification factors
- Number of prior chemotherapies (2-3 vs >3)
- Geographic region (North America vs Europe)
- Presence/absence of known brain metastases (yes/no)

Data cutoff: March 11, 2020

We report the exploratory biomarker analysis in the brain metastases-negative (Brain Mets-Negative) population

*TPC: eribulin, vinorelbine, gemcitabine, or capecitabine. †PFS measured by an independent, centralized, and blinded group of radiology experts who assessed tumor response using RECIST 1.1 criteria in patients without brain metastasis. ‡The full population includes all randomized patients (with and without brain metastases). Baseline brain MRI only required for patients with known brain metastasis.
ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; DOR, duration of response; DSMC, Data Safety Monitoring Committee; IV, intravenous; mTNBC, metastatic triple-negative breast cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.
National Institutes of Health. https://clinicaltrials.gov/ct2/show/NCT02574455.

Bardia A et al. ESMO 2020;Abstract LBA17.

Courtesy of Harold J Burstein, MD, PhD

Demographics and Patient Characteristics

	SG (n=235)	TPC (n=233)
Female—no. (%)	233 (99)	233 (100)
Median age—yr (range)	54 (29-82)	53 (27-81)
Race or ethnic group—no. (%)		
White	188 (80)	181 (78)
Black	28 (12)	28 (12)
Asian	9 (4)	9 (4)
Other or not specified	10 (4)	15 (6)
ECOG PS—no. (%)		
0	108 (46)	98 (42)
1	127 (54)	135 (58)
***BRCA 1/2* mutational status—no. (%)**		
Positive	16 (7)	18 (8)
Negative	133 (57)	125 (54)
Unknown	86 (37)	90 (39)
TNBC at initial diagnosis*		
Yes	165 (70)	157 (67)
No	70 (30)	76 (33)

	SG (n=235)	TPC (n=233)
Previous Anticancer Regimens —median no. (range)†	4 (2-17)	4 (2-14)
Most common previous chemotherapy—no. (%)		
Taxane‡	235 (100)	233 (100)
Anthracycline§	181 (81)	193 (83)
Cyclophosphamide	192 (82)	192 (82)
Carboplatin	147 (63)	160 (69)
Capecitabine	147 (63)	159 (68)
Previous PARP inhibitor—no. (%)	17 (7)	18 (8)
Previous use of checkpoint inhibitors—no. (%)	67 (29)	60 (26)
Most common sites of disease‖—no. (%)		
Lung only	108 (46)	97 (42)
Liver	98 (42)	101 (43)
Bone	48 (20)	55 (24)

Brain metastases-negative population.
*Patients on study either had TNBC at initial diagnosis or had hormone receptor-positive disease that converted to hormone-negative at time of study entry. †Anticancer regimens refer to any treatment regimen that was used to treat breast cancer in any setting ‡ Includes: Paclitaxel, paclitaxel albumin, and docetaxel. §Includes: Doxorubicin, daunorubicin, epirubicin, and variations of those treatment names. ‖Based on independent central review of target and non-target lesions.
BRCA, breast cancer gene; ECOG PS, Eastern Cooperative Oncology Group performance score; PARP, poly-ADP ribose polymerase; TNBC, triple-negative breast cancer; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Bardia A et al. ESMO 2020;Abstract LBA17.

Courtesy of Harold J Burstein, MD, PhD

TRAEs (All Grade, >20%; Grade 3/4, >5% of Patients)

		SG (n=258)			TPC (n=224)		
	TRAE*	**All grade %**	**Grade 3, %**	**Grade 4, %**	**All grade, %**	**Grade 3, %**	**Grade 4, %**
Hematologic	**Neutropenia†**	**63**	**46**	**17**	**43**	**27**	**13**
	Anemia‡	**34**	**8**	**0**	**24**	**5**	**0**
	Leukopenia§	16	10	1	11	5	1
	Febrile neutropenia	6	5	1	2	2	<1
Gastrointestinal	**Diarrhea**	**59**	**10**	**0**	12	<1	0
	Nausea	**57**	**2**	**<1**	**26**	**<1**	**0**
	Vomiting	29	1	<1	10	<1	0
Other	**Fatigue**	**45**	**3**	**0**	**30**	**5**	**0**
	Alopecia	**46**	**0**	**0**	**16**	**0**	**0**

- Key grade ≥3 TRAEs (SG vs TPC): Neutropenia (51% vs 33%), diarrhea (10% vs <1%), leukopenia (10% vs 5%), anemia (8% vs 5%), and febrile neutropenia (6% vs 2%)
  - GCSF usage was 49% in the SG arm vs 23% in the TPC arm
- No severe cardiovascular toxicity, no grade >2 neuropathy or grade >3 interstitial lung disease
- No treatment-related deaths with SG; one treatment-related death (neutropenic sepsis) with TPC
- AE leading to treatment discontinuation were low for SG and TPC: 4.7% and 5.4%

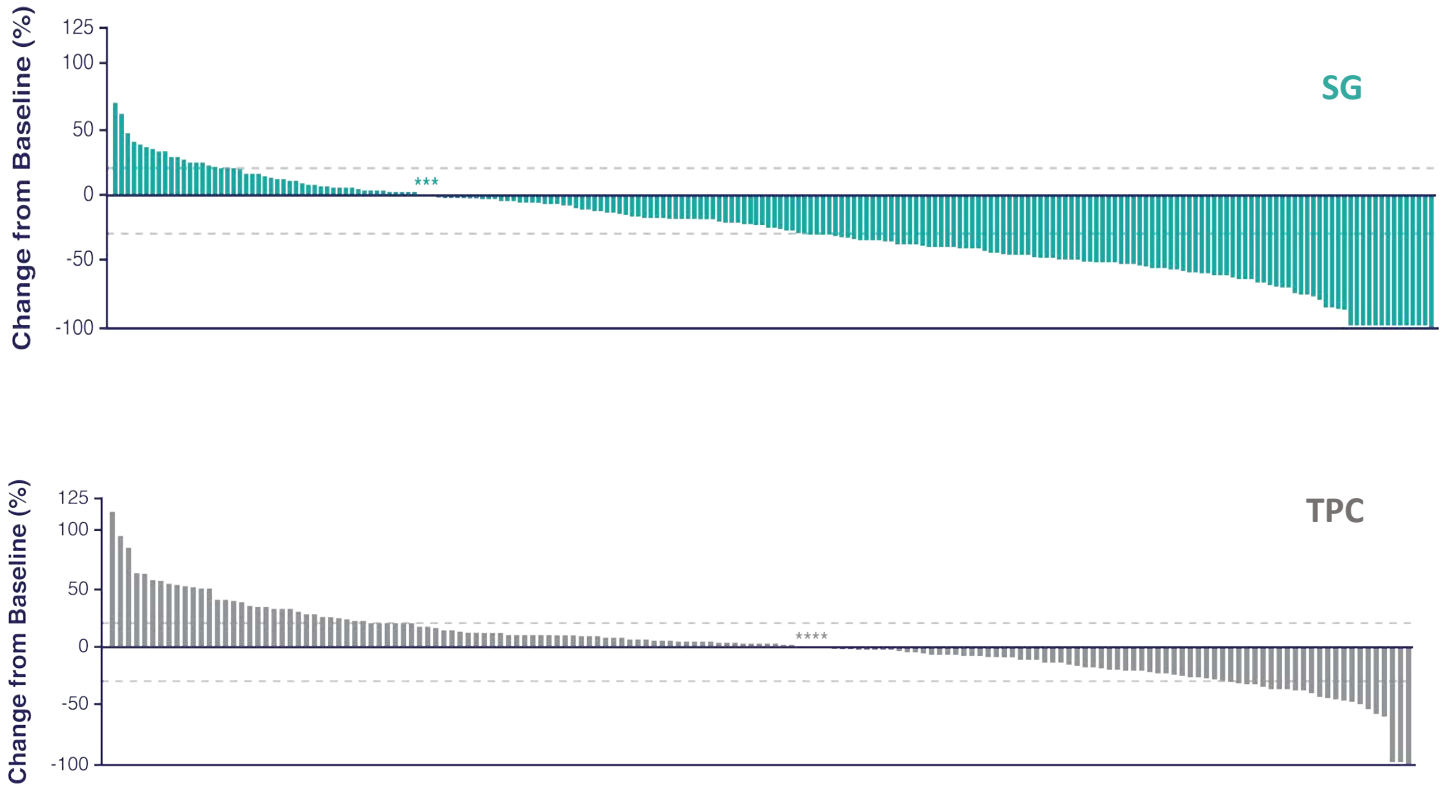
*Patients may report more than 1 event per preferred term. AEs were classified according to the MedDRA systems of preferred terms and system organ class and according to severity by NCI CTCAE v4.03. †Combined preferred terms of 'neutropenia' and 'decreased neutrophil count'. ‡Combined preferred terms of 'anemia' and 'decreased hemoglobin'. §Combined preferred terms of 'leukopenia' and 'decreased white blood cell count'.
BMNeg, brain metastasis-negative; MedDRA, Medical Dictionary for Regulatory Activities; NCI CTCAE, National Cancer Institute Common Terminology for AE; SG, sacituzumab govitecan; TPC, treatment of physician's choice; TRAE, treatment-related AE.

Bardia A et al. ESMO 2020;Abstract LBA17.

Courtesy of Harold J Burstein, MD, PhD

Overall Response and Best Percent Change From Baseline in Tumor Size (BICR)

BICR	SG (n=235)	TPC (n=233)	*P*-value
ORR—no. (%)	**82 (35)**	**11 (5)**	**<0.0001**
CR	10 (4)	2 (1)	
PR	72 (31)	9 (4)	
SD—no. (%)	81 (34)	62 (27)	
PD—no. (%)	54 (23)	89 (38)	
Not evaluable—no. (%)	18 (8)	71 (30)	
CBR—no. (%)	**105 (45)**	**20 (9)**	**<0.0001**
Median DOR—mo (95% CI)	**6.3 (5.5−9.0)**	**3.6 (2.8−NE)**	
Median TTR—mo (range)	1.5 (0.7-10.6)	1.5 (1.3-4.2)	

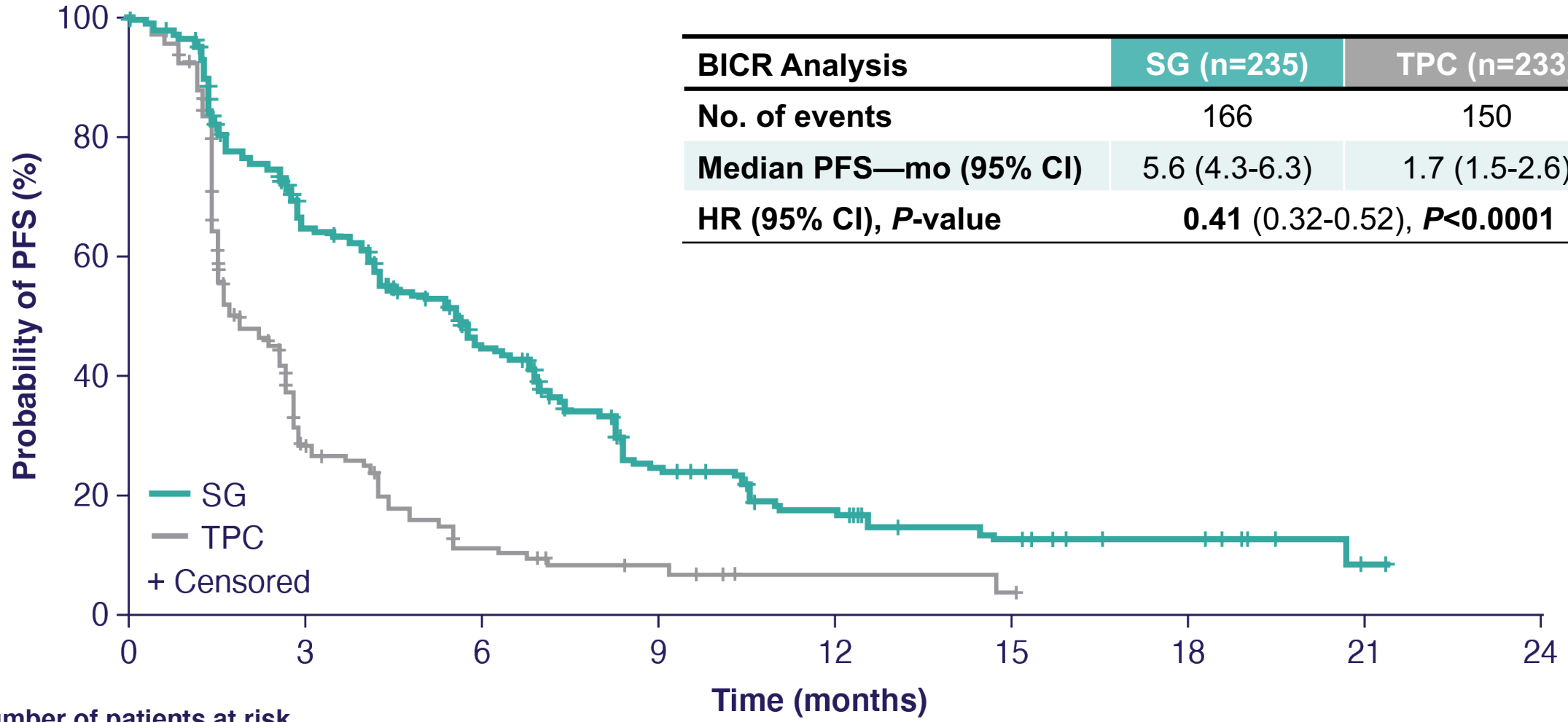


Assessed in the brain metastases-negative population. Assessed by independent central review in brain metastases negative population.
CBR, clinical benefit rate (CR + PR + SD ≥6 mo); CR, complete response; DOR, duration of response; NE, not evaluable, a patient can be designated not evaluable for a variety of reasons including lack of post-baseline images or unreadable images; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease; SG, sacituzumab govitecan; TPC, treatment of physician's choice; TTR, time to response.
*Denotes patients who had a 0% change from baseline in tumor size.
BICR, blind independent central review; SG, sacituzumab govitecan.

Bardia A et al. ESMO 2020;Abstract LBA17.

Courtesy of Harold J Burstein, MD, PhD

Progression-Free Survival (BICR Analysis)



BICR Analysis	SG (n=235)	TPC (n=233)
No. of events	166	150
Median PFS—mo (95% CI)	5.6 (4.3-6.3)	1.7 (1.5-2.6)
HR (95% CI), *P*-value	**0.41** (0.32-0.52), ***P*<0.0001**	

Number of patients at risk

SG	235	222	166	134	127	104	81	63	54	37	33	24	22	16	15	13	9	8	8	5	3	1	0
TPC	233	179	78	35	32	19	12	9	7	6	4	2	2	2	2	1	0	0	0	0	0	0	0

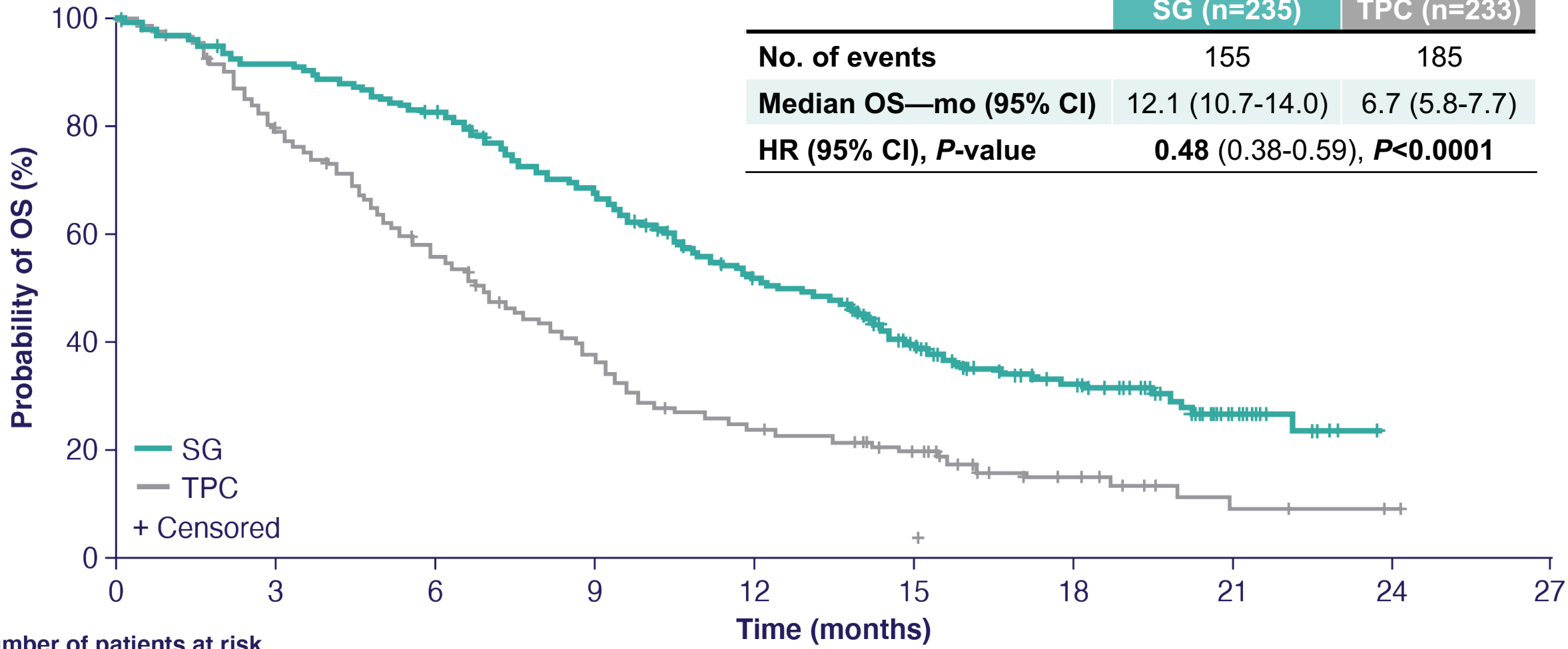
Assessed in the brain metastases-negative population.
BICR, blind independent central review; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician choice.

Bardia A et al. ESMO 2020;Abstract LBA17.

Courtesy of Harold J Burstein, MD, PhD

Overall Survival

	SG (n=235)	TPC (n=233)
No. of events	155	185
Median OS—mo (95% CI)	12.1 (10.7-14.0)	6.7 (5.8-7.7)
HR (95% CI), *P*-value	**0.48** (0.38-0.59), ***P*<0.0001**	



Number of patients at risk

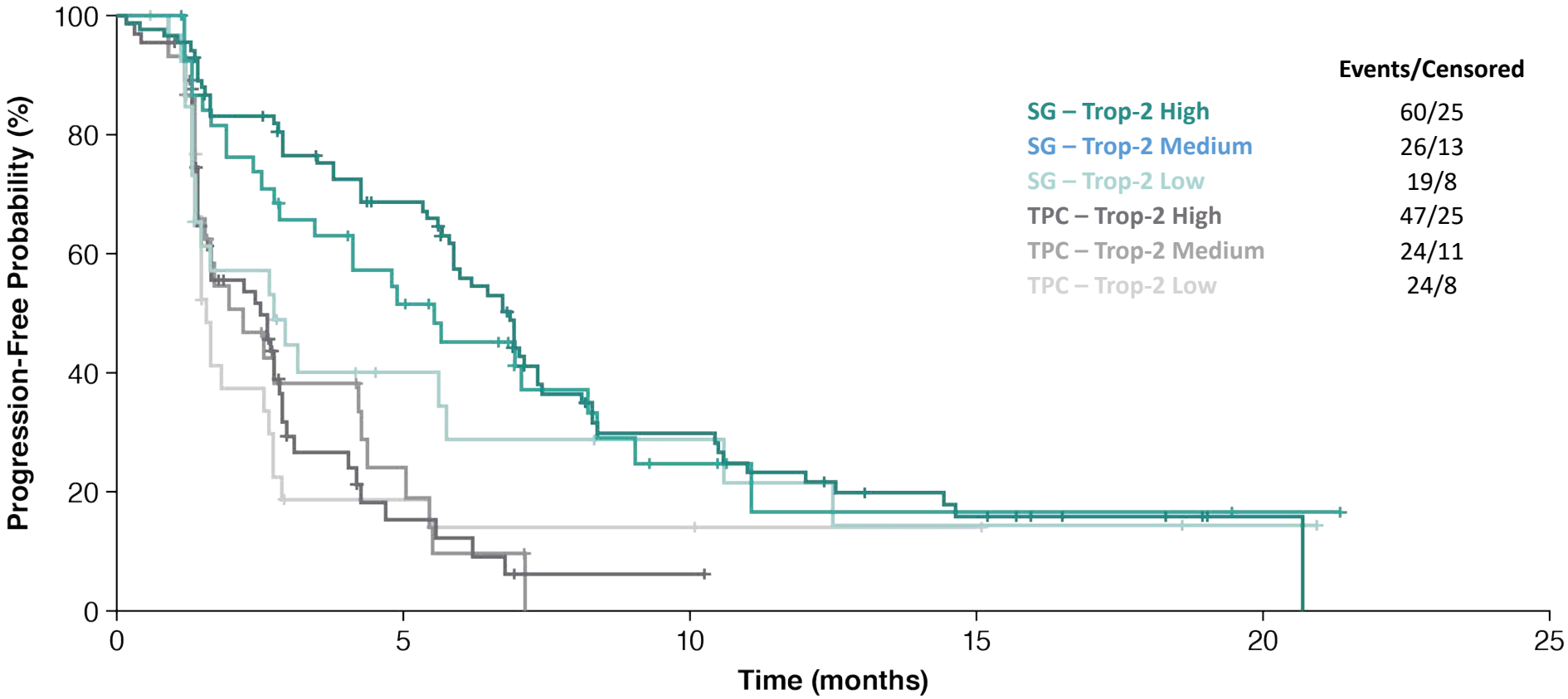
SG	235	228	220	214	206	197	190	174	161	153	135	118	107	101	90	70	52	43	37	30	21	13	8	1	0	0
TPC	233	214	200	173	156	134	117	99	87	74	56	50	45	41	37	30	20	14	11	7	4	3	3	2	1	0

Assessed by independent central review in the brain metastases-negative population.
OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician choice.

Bardia A et al. ESMO 2020;Abstract LBA17.

Courtesy of Harold J Burstein, MD, PhD

ASCENT: Progression-Free Survival by Trop-2 Expression



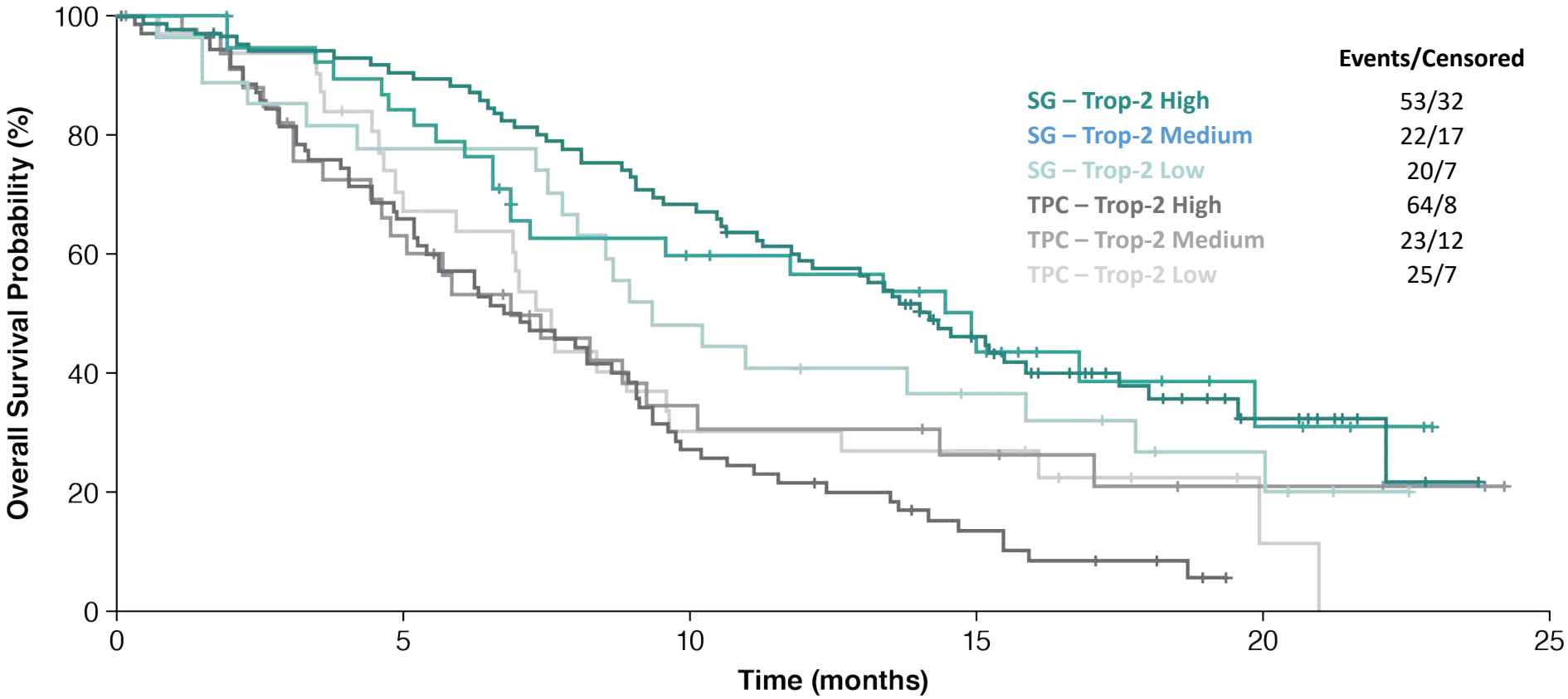
	Trop-2 High | H-score: 200-300		Trop-2 Medium | H-score: 100-200		Trop-2 Low | H-score: <100	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
Median PFS—mo (95% CI)	6.9 (5.8-7.4)	2.5 (1.5-2.9)	5.6 (2.9-8.2)	2.2 (1.4-4.3)	2.7 (1.4-5.8)	1.6 (1.4-2.7)

Assessed in brain metastases-negative population. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.
H-score, histochemical score; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice; Trop-2, trophoblast cell surface antigen-2.

Hurvitz SA et al. SABCS 2020;Abstract GS3-06.

Courtesy of Harold J Burstein, MD, PhD

Overall Survival by Trop-2 Expression



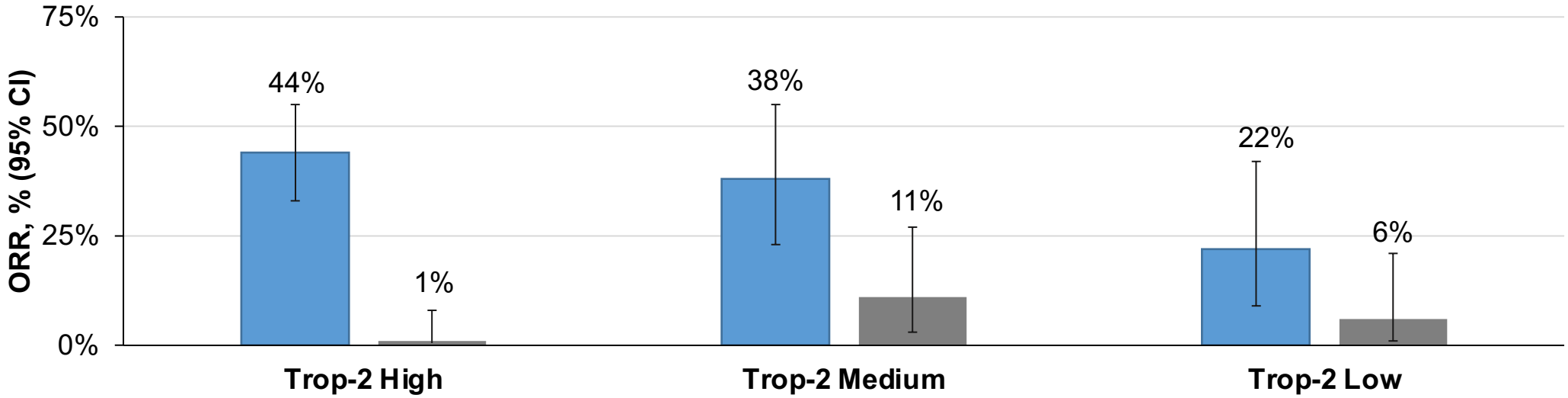
	Trop-2 High | H-score: 200-300		Trop-2 Medium | H-score: 100-200		Trop-2 Low | H-score: <100	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
Median OS—mo (95% CI)	14.2 (11.3-17.5)	6.9 (5.3-8.9)	14.9 (6.9-NE)	6.9 (4.6-10.1)	9.3 (7.5-17.8)	7.6 (5.0-9.6)

Assessed in brain metastases-negative population. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.
H-score, histochemical-score; OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice; Trop-2, trophoblast cell surface antigen-2.

Hurvitz SA et al. SABCS 2020;Abstract GS3-06.

Courtesy of Harold J Burstein, MD, PhD

ORR by Trop-2 Expression



	Trop-2 High H-score: 200-300 (n=157)		Trop-2 Medium H-score: 100-200 (n=74)		Trop-2 Low H-score: <100 (n=59)	
	SG (n=85)	TPC (n=72)	SG (n=39)	TPC (n=35)	SG (n=27)	TPC (n=32)
ORR—% (no.)	44% (37)	1% (1)	38% (15)	11% (4)	22% (6)	6% (2)
95% CI	33-55	0-8	23-55	3-27	9-42	1-21

Assessed in the brain metastases-negative population. ORR and PFS are assessed by BICR. Trop-2 expression determined in archival samples by validated immunohistochemistry assay and H-scoring.
BICR, blind independent central review; H-score, histochemical-score; ORR, objective response rate; SG, sacituzumab govitecan; TPC, treatment of physician's choice; Trop-2, trophoblast cell surface antigen-2.

Hurvitz SA et al. SABCS 2020;Abstract GS3-06.

Courtesy of Harold J Burstein, MD, PhD

Conclusions

- Sacituzumab govitecan is an active drug in TNBC
  - Side effects are more like ‘chemo’ than a targeted agent
  - Expression of the Trop-2 target does not seem to predict benefit

- Algorithm: PD-1/PD-L1 testing
  - Positive → 1st line chemo + CPI
  - Negative → 1st line chemo

  - 2nd line: sacituzumab

  - 3rd line and beyond: additional chemotherapy

Courtesy of Harold J Burstein, MD, PhD

Thank you.

Stay healthy.

Here’s to a better 2021.

Courtesy of Harold J Burstein, MD, PhD