ADVANCES IN THE TREATMENT OF EARLY STAGE HORMONE RECEPTOR POSITIVE BREAST CANCER

Yael Zack, MD White Plains Hospital Center for Cancer Care



Disclosure of Conflicts of Interest

Yael Zack, MD, has no relevant financial relationships to disclose.





AC – 44yo Woman, BRCA2 Mutation +, left breast lump.

• <u>MAMMOGRAM/SONOGRAM:</u>

Suspicious palpable mass within the left 4:00 axis - Corresponding to the palpable nodule, is an irregular, hypoechoic, slightly vascular mass, measuring 1.1 x 1.2 x 1.1 cm

•<u>MRI:</u>

Biopsy-proven malignancy in the left breast at 4:00, measuring up to 1.6 cm. Small enhancing masses noted inferior to the index malignancy, highly suspicious for satellite lesions.

No adenopathy noted.

• <u>LEFT LUMPECTOMY + SLNB:</u>

INVASIVE DUCTAL CARCINOMA, POORLY DIFFERENTIATED 3.5CM ER and PR - 91-100%/Strong/Positive; Her2 - 0/Negative; Ki67 - 40%. 1/2 LN POSITIVE FOR MACROMET





Does everyone need chemo?

21 genes⁹



16 Cancer Genes and 5 Reference Genes



The Oncotype DX test reveals individual tumour biology based on measuring the expression of













A Invasive Disease-free Survival

TAILORX

No. at Risk Chemoendocrine therapy Endocrine therapy

B Freedom from Recurrence at a Distant Site

No. at Risk Chemoendocrine therapy Endocrine therapy

Sparano, et al. NEJM, 2018.







TAILORX – women under 50yo do benefit from chemo.

End Point and

Invasive disease

Score of ≤10

Score of 11-

Score of 11-

Score of 16-

Score of 16-

Score of 21-

Score of 21-

Score of ≥ 2

Sparano, et al. NEJM, 2018.

Table 3. Estimated Survival Rates According to Recurrence Score and Assigned Treatment among Women 50 Years of Age or Younger in the Intention-to-Treat Population.*

Treatment Group	Rate at 5 Yr	Rate at 9 Yr
	perc	cent
e-free survival†		
0, endocrine therapy	95.1±1.1	87.4±2.0
–15, endocrine therapy	95.1±1.1	85.7±2.2
–15, chemoendocrine therapy	94.3±1.3	89.2±1.9
-20, endocrine therapy	92.0±1.3	80.6±2.5
–20, chemoendocrine therapy	94.7±1.1	89.6±1.7
–25, endocrine therapy	86.3±2.3	79.2±3.3
–25, chemoendocrine therapy	92.1±1.8	85.5±3.0
6, chemoendocrine therapy	86.4±1.9	80.3±2.9





What about node-positive disease?

RxPONDER: Adjuvant ET ± Chemotherapy in HR+/HER2-EBC With 1-3 Positive Lymph Nodes and RS \leq 25

Randomized phase III trial

Stratified by RS score (0-13 vs 14-25), menopausal status (pre vs post), axillary surgery (ALND vs SLNB)

Adults with HR+/HER2- EBC and 1-3 positive LN without distant mets*; able to receive adjuvant taxane and/or anthracycline-based CT[†]; axillary staging by SLNB or ALND; RS 0-25[‡] (N = 5015)

*Protocol amended to exclude patients with pN1mic as only nodal disease after 2493 patients randomized. ⁺Approved CT regimens: TC, FAC (or FEC), AC/T (or EC/T), FAC/T (or FEC/T); AC alone or CMF not allowed. *Patients with RS > 25 recommended to be treated with CT followed ET off study.

Primary endpoint: iDFS

Key secondary endpoints: OS, distant DFS, local DFI, toxicity, QoL

Kalinsky. SABCS 2020. Abstr GS3-00.



(CO Slide credit: clinicaloptions.com







Kalinsky, et al. NEJM Dec 2021.



Women < 50yo BENEFIT from Chemo.

Kalinsky, et al. *NEJM* Dec 2021.

A Postmenopausal Women				
Subaroun	No. of	No. of	Hazard Ratio for Invasive Disease Re	currence,
Subgroup	Participants	Events	New Primary Cancer, or Death (9:	5% CI)
Age				
>65 yr	1180	138	⊢I	1.05 (0.75–1.47)
55–65 yr	1637	145		0.94 (0.68–1.30)
<55 yr	511	49		1.15 (0.66–2.03)
Grade				
Intermediate or high	2433	265	⊢	1.06 (0.83–1.35)
Low	850	62		0.91 (0.55–1.50)
Tumor size			- - -	
T2 or T3	1360	173		1.07 (0.80–1.45)
Τ1	1966	159		0.95 (0.70–1.30)
Nodes				
2 or 3 positive	1146	133		1.22 (0.87–1.71)
1 positive	2181	199		0.90 (0.68–1.19)
Sentinel node	1306	118		0.78 (0.54–1.12)
Full axillary lymph-node dissection	2022	214		1.19 (0.91–1.55)
Recurrence score				
14–25	1837	206	⊢	1.01 (0.77-1.33)
0-13	1492	126	⊦ł	1.01 (0.71-1.44)
Overall	3328	332	⊢ i	1.02 (0.82–1.26)
			0.50 0.75 1.00 1.50 2.00	
			Chemoendocrine Endocrine Therapy	
			Therapy Better Alone Better	
B Premenopausal Women				
B Premenopausal Women	No. of	No. of	Hazard Ratio for Invasive Disease Re	currence,
B Premenopausal Women Subgroup	No. of Participants	No. of Events	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (99	currence, 5% Cl)
B Premenopausal Women Subgroup Age	No. of Participants	No. of Events	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9	currence, 5% CI)
B Premenopausal Women Subgroup Age ≥50 yr	No. of Participants 509	No. of Events 44	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (99	ecurrence, 5% CI) 0.98 (0.54–1.78)
B Premenopausal Women Subgroup Age ≥50 yr 45-49 yr	No. of Participants 509 615	No. of Events 44 46	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (99)	ecurrence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86)
B Premenopausal Women Subgroup Age ≥50 yr 45-49 yr <45 yr	No. of Participants 509 615 531	No. of Events 44 46 59	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (99)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84)
B Premenopausal Women Subgroup Age ≤50 yr ≤50 yr ≤45 yr Grade	No. of Participants 509 615 531	No. of Events 44 46 59	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (99)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84)
B Premenopausal Women Age 50 yr 45-49 yr <45 yr Grade Intermediate or high	No. of Participants 509 615 531 1280	No. of Events 44 46 59 125	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (99)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84)
B Premenopausal Women Subgroup Age >50 yr 45-49 yr <45 yr	No. of Participants 509 615 531 1280 357	No. of Events 44 46 59 125 23	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55)
B Premenopausal Women Subgroup Age >50 yr 45-49 yr <45 yr	No. of Participants 509 615 531 1280 357	No. of Events 44 46 59 125 23	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55)
B Premenopausal Women Subgroup Age ≤50 yr 45-49 yr <45 yr Grade Intermediate or high Low Tumor size T2 or T3	No. of Participants 509 615 531 1280 357 728	No. of Events 44 46 59 125 23 23	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99)
B Premenopausal Women Subgroup Age ≥50 yr 45-49 yr <45 yr Grade Intermediate or high Low Tumor size T2 or T3 T1	No. of Participants 509 615 615 1280 357 728 925	No. of Events 44 46 59 125 23 23 80 69	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99) 0.53 (0.32–0.88)
B Premenopausal Women Subgroup Age 250 yr 45-49 yr 45-49 yr 45 yr Crade Intermediate or high Low Tumor size T2 or T3 T1 Nodes	No. of Participants 509 615 615 1280 357 728 925	No. of Events 44 46 59 125 23 80 69	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99) 0.53 (0.32–0.88)
B Premenopausal Women Subgroup Age ≥50 yr 45-49 yr <45 yr Grade Intermediate or high Low Tumor size T2 or T3 T1 Nodes 2 or 3 positive	No. of Participants 509 615 615 1280 1280 357 925 574	No. of Events 44 46 59 125 23 80 69 69	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99) 0.53 (0.32–0.88) 0.62 (0.36–1.06)
B Premenopausal Women Subgroup Age S0 yr 45-49 yr 45-49 yr 45 yr Grade Intermediate or high Low Tumor size T1 Nodes 2 or 3 positive 1 positive	No. of Participants 509 615 615 1280 1280 357 925 925 574 1081	No. of 244 44 46 59 125 23 80 69 555 94	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99) 0.53 (0.32–0.88) 0.62 (0.36–1.06) 0.57 (0.37–0.87)
B Premenopausal Women Subgroup Age ≥50 yr 45–49 yr <45 yr Grade Intermediate or high Low Tumor size T2 or T3 T1 Nodes 2 or 3 positive 1 positive Sentinel node	No. of Participants 509 615 615 1280 357 728 925 574 1081 556	No. of Events 44 46 59 125 23 (125 23 (125) 24 (125) 23 (125) 24 (125) 24 (125) 25 (Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	ECURTEENCE, 5% CI) 0.98 (0.54-1.78) 0.46 (0.25-0.86) 0.49 (0.28-0.84) 0.58 (0.41-0.84) 0.67 (0.29-1.55) 0.64 (0.41-0.99) 0.53 (0.32-0.88) 0.62 (0.36-1.06) 0.57 (0.37-0.87) 0.61 (0.36-1.02)
B Premenopausal Women Subgroup Age SO yr 45-49 yr <45 yr Grade Intermediate or high Low Tumor size T2 or T3 T1 Nodes 2 or 3 positive 1 positive Sentinel node Full axillary lymph-node dissection	No. of Participants 509 615 615 1280 357 925 574 1081 1081 1099	No. of Events 44 46 59 125 23 3 4 80 69 4 55 94 60 89	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (99)	ECURTEENCE, 5% CI) 0.98 (0.54-1.78) 0.46 (0.25-0.86) 0.49 (0.28-0.84) 0.58 (0.41-0.84) 0.67 (0.29-1.55) 0.64 (0.41-0.99) 0.53 (0.32-0.88) 0.62 (0.36-1.06) 0.57 (0.37-0.87) 0.61 (0.36-1.02) 0.60 (0.39-0.91)
B Premenopausal Women Subgroup Age So yr Age So yr A5-49 yr <srade 2="" 3="" axillary="" dissection="" full="" high="" i="" intermediate="" low="" lymph-node="" node="" nodes="" or="" positive="" recurrence="" score<="" sentinel="" size="" t1="" t2="" t3="" td="" tumor=""><td>No. of 509 615 615 531 1280 357 925 925 1081 1081 1099</td><td>No. of Events 44 46 59 125 23 80 69 69 55 94 60 89</td><td>Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)</td><td>Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99) 0.53 (0.32–0.88) 0.53 (0.32–0.88) 0.57 (0.37–0.87) 0.61 (0.36–1.02) 0.60 (0.39–0.91)</td></srade>	No. of 509 615 615 531 1280 357 925 925 1081 1081 1099	No. of Events 44 46 59 125 23 80 69 69 55 94 60 89	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99) 0.53 (0.32–0.88) 0.53 (0.32–0.88) 0.57 (0.37–0.87) 0.61 (0.36–1.02) 0.60 (0.39–0.91)
B Premenopausal Women Age Subgroup Age S0 yr 45-49 yr <45 yr Crade Intermediate or high Low Low Tumor size T2 or T3 T1 Nodes 2 or 3 positive 1 positive Sentinel node Full axillary lymph-node dissection Recurrence score 14-25	No. of Participants 509 615 615 1280 1280 357 925 1081 1081 1099 1015	No. of Events 44 46 59 125 23 80 69 60 69 55 94 60 89 60 89	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	ECUITERICE, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99) 0.53 (0.32–0.88) 0.62 (0.36–1.06) 0.57 (0.37–0.87) 0.61 (0.36–1.02) 0.60 (0.39–0.91) 0.63 (0.43–0.91)
B Premenopausal Women Subgroup Age S0 yr 45-49 yr 45-49 yr 45-49 yr 45 yr Grade Intermediate or high Low Tumor size T2 or T3 T1 Nodes 2 or 3 positive 1 positive Sentinel node Full axillary lymph-node dissection Recurrence score 14-25 0-13	No. of Participants 509 615 615 1280 1280 357 728 925 1081 556 1099 1015 640	No. of Events 44 46 59 125 23 80 69 55 94 60 89 4 60 89 113 36	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (99)	ECUITENCE, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99) 0.53 (0.32–0.88) 0.62 (0.36–1.06) 0.57 (0.37–0.87) 0.61 (0.36–1.02) 0.60 (0.39–0.91) 0.63 (0.43–0.91) 0.49 (0.24–0.99)
B Premenopausal Women	No. of Participants 509 615 615 1280 357 728 925 1081 556 1081 1015 640 1655	No. of Events 44 46 59 125 23 80 69 55 94 60 89 4 60 89 113 36 149	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	Currence, 5% CI) 0.98 (0.54–1.78) 0.46 (0.25–0.86) 0.49 (0.28–0.84) 0.58 (0.41–0.84) 0.67 (0.29–1.55) 0.64 (0.41–0.99) 0.53 (0.32–0.88) 0.62 (0.36–1.06) 0.57 (0.37–0.87) 0.61 (0.36–1.02) 0.60 (0.39–0.91) 0.60 (0.43–0.91) 0.49 (0.24–0.99) 0.60 (0.43–0.83)
B Premenopausal Women Subgroup Age ≥50 yr 45-49 yr <45 yr Grade Intermediate or high Low Tumor size T1 Nodes 2 or 3 positive 2 or 3 positive 1 positive Sentinel node Full axillary lymph-node dissection Recurrence score 14-25 0-13 Overall	No. of Participants 509 615 615 1280 357 728 925 1081 556 1009 1015 640 1655	No. of 44 44 46 59 125 23 80 69 55 94 60 89 113 36 149	Hazard Ratio for Invasive Disease Re New Primary Cancer, or Death (9)	ECURTENCE, 5% CI) 0.98 $(0.54-1.78)$ 0.46 $(0.25-0.86)$ 0.49 $(0.28-0.84)$ 0.58 $(0.41-0.84)$ 0.67 $(0.29-1.55)$ 0.64 $(0.41-0.99)$ 0.53 $(0.32-0.88)$ 0.62 $(0.36-1.06)$ 0.57 $(0.37-0.87)$ 0.61 $(0.36-1.02)$ 0.60 $(0.39-0.91)$ 0.63 $(0.43-0.91)$ 0.49 $(0.24-0.99)$ 0.60 $(0.43-0.83)$

Post menopausal

Pre menopausal



Chemoendocrine Therapy Better

Endocrine Therapy Alone Better





HEMATOLOGY & ONCOLOGY SOCIETY

Our Pt AC, 44yo woman, pT2N1, left breast cancer.

•Underwent chemo with dose dense AC-T

•Underwent bilateral mastectomies LEFT MASTECTOMY - RESIDUAL INVASIVE DUCTAL CARCINOMA, POORLY DIFFERENTIATED, WITH THERAPEUTIC CHANGES, MEASURING 3MM IN GREATEST DIMENSION.

•Underwent prophylactic BSO





Can we further improve her outcomes??

monarchE: Adjuvant Abemaciclib + ET in High-Risk, Node-Positive, HR+/HER2-EBC

International, randomized, open-label phase III trial .



- Primary endpoint: iDFS .

 - Current primary outcome efficacy analysis occurred after 395 iDFS events in ITT population
- •

Johnston, JCO. 2020;38:3987. Rastogi. SABCS 2020. Abstr GS1-01.

Planned for after ~ 390 iDFS events (~ 85% power, assumed iDFS HR of 0.73, cumulative 2-sided α = 0.05)

Key secondary endpoints: iDFS in Ki-67 high (≥ 20%) population, distant RFS, OS, safety, PRO, PK

Slide credit: clinicaloptions.com





Harbeck, Ann of Oncology, 2021.

Time (months)

MONARCH-E

DFS At 3 yrs: 86 vs 79% in Ki67 high

91.7 vs 87.2% in Ki67 low

45













































The NEW ENGLAND JOURNAL of MEDICINE

NAL ARTICLE neous-Breathing Trials essure-Support tion or a T-Piece



Gain remote access to your institution's NEJM.org site license subscription. \rightarrow

EDITORIAL John Jarcho, M.D., Beloved Colleague and Friend, 1957–2022

Adjuvant Olaparib for Patients with BRCA1- or BRCA2-Mutated Breast Cancer

Andrew N.J. Tutt, M.B., Ch.B., Ph.D., Judy E. Garber, M.D., M.P.H., Bella Kaufman, M.D., Giuseppe Viale, M.D., Debora Fumagalli, M.D., Ph.D., Priya Rastogi, M.D., Richard D. Gelber, Ph.D., Evandro de Azambuja, M.D., Ph.D., Anitra Fielding, M.B., Ch.B., Judith Balmaña, M.D., Ph.D., Susan M. Domchek, M.D., Karen A. Gelmon, M.D., <u>et al.</u>, for the OlympiA Clinical Trial Steering Committee and Investigators^{*}

≔	Artic	e Figures/Media	

-1832 patients with mutation in BRCA1 or BRCA2 with early HER2- breast cancer -If triple neg, tumor at least 2cm or LN+ or lack of pathCR after neoadjuvant chemo -If HR+, at least 4 involved LN or lack of pathCR after neoadjuvant chemo



ORIGINAL ARTICLE

 Metrics
 June 24, 2021

 N Engl J Med 2021; 384:2394-2405



Adjuvant Olaparib significantly improved DFS.

Figure 1. Kaplan-Meier Estimates of Survival.



Tutt, et al. *NEJM* Dec 2021.

81.5 77.1 Between-group difference in 3-yr invasive disease-free surviv 8.8 percentage points (95% Cl, 4.5-13.0) Stratified hazard ratio for invasive disease or death, 0.58 (99.5% Cl, 0.41-0.82) 74 30 74 36 477 361 276 452 353 256	89.2		85.9		
81.5 77.1 Placebo (178 events) Between-group difference in 3-yr invasive disease-free surviv 8.8 percentage points (95% CI, 4.5-13.0) Stratified hazard ratio for invasive disease or death, 0.58 (99.5% CI, 0.41-0.82) P<0.001 1 1 24 30 36 42 Randomization 477 477 361 276 477 361 276 452 353 256				_	Olaparib (106 events)
Between-group difference in 3-yr invasive disease-free surviv 8.8 percentage points (95% Cl, 4.5-13.0) Stratified hazard ratio for invasive disease or death, 0.58 (99.5% Cl, 0.41-0.82) P<0.001 ATT 361 276 183 452 353 256 173	81.5		77.1		Placebo (178 events)
24 30 36 42 Randomization 477 361 276 183 452 353 256 173					Between-group difference in 3-yr invasive disease-free surviv 8.8 percentage points (95% CI, 4.5-13.0) Stratified hazard ratio for invasive disease or death, 0.58 (99.5% CI, 0.41-0.82) P<0.001
Randomization 477 361 276 183 452 353 256 173	24	30	36	42	
477 361 276 183 452 353 256 173	Randomiza	ation			
452 353 256 173	477	361	276	183	
	452	353	256	173	



Adjuvant Olaparib Even Improved OS.



between-group difference did not cross the prespecified multiple-testing The procedure boundary for significance of P<0.01

Tutt, et al. *NEJM* Dec 2021.



Table 3. Summary of Adverse Events in the Safety Ana		
Adverse Event	0 (1	
Any adverse event	83	
Serious adverse event	7	
Adverse event of special interest†	3	
MDS or AML		
Pneumonitis <u></u>		
New primary cancer§	1	
Grade ≥3 adverse event	22	
Grade 4 adverse event¶	1	
Adverse event leading to permanent discon- tinuation of olaparib or placebo	9	
Adverse event leading to death**		

Tutt, et al. NEJM Dec 2021.

alysis Set.*		
)la N =	parib =911)	Placebo (N = 904)
I	no. of patie	nts (%)
5	(91.7)	753 (83.3)
79	(8.7)	76 (8.4)
0	(3.3)	46 (5.1)
2	(0.2)	3 (0.3)
9	(1.0)	11 (1.2)
9	(2.1)	32 (3.5)
21	(24.3)	102 (11.3)
.7	(1.9)	4 (0.4)
90	(9.9)	38 (4.2)
1	(0.1)	2 (0.2)





Our pt - AC



Radiation



Endocrine tx + Olaparib

Endocrine tx + Abemaciclib







2 MAJOR PRACTICE CHANGING TRIALS FOR METASTATIC HORMONE-RECEPTOR POSITIVE IN 2022:

- •DESTINY-04
- •TROPiCS-02





HR+/HER2- advanced breast cancer.



NCI, 2020.

TROPICS-02: A randomized phase 3 study of Sacituzumab govitecan (SG) versus treatment of physician's choice (TPC) in patients with

- **INCLUSION CRITERIA:**
- -543 patients randomized 1:1
- -unresectable locally advanced or metastatic
- -2 to 4 prior lines of chemotherapy, or 1 prior therapy if disease progressed </= 12 months after (neo)adjuvant therapy
- -must have received taxane, CDK4/6 inhibitor, and endocrine therapy

SG 10mg/kg day 1, 8, q21d

TPC: Capecitabine, eribulin, vinorelbine, or gemcitabine





TROPICS-02 RESULTS

Rugo, et al. ASCO 2022.

- p=0.0003
- •PFS at 6 months improved with SG: 46% vs 30% •PFS at 12 months improved with SG: 21% vs 7%
- (HR 0.84; p=0.143)
- •Improved ORR with SG: 21% vs 14%
- •Improved Clinical Benefit rate with SG: 34% vs 22%

•Improved median PFS with SG – 5.5 vs 4 months, HR 0.66; 95% Cl, 0.53-0.83;

•No statistically significant difference in OS with SG: 13.9 months vs 12.3 months







DESTINY-04: Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer

Modi, et al. *NEJM* July 2022.

Patients^a

 HER2-low (IHC 1+ vs IHC 2+/ISH-), unresectable, and/or mBC treated with 1-2 prior lines of chemotherapy in the metastatic setting



 HR+ disease considered endocrine refractory

Stratification factors

- Centrally assessed HER2 status^d (IHC 1+ vs IHC 2+/ISH-)
- 1 versus 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6 inhibitor) versus HR-

T-DXd 5.4 mg/kg Q3W (n = 373)

> HR+ ≈ 480 HR- ≈ 60

TPC

Capecitabine, eribulin, gemcitabine, paclitaxel, nab-paclitaxel^c (n = 184)

Primary endpoint

• PFS by BICR (HR+)

Key secondary endpoints^b

- PFS by BICR (all patients)
- OS (HR+ and all patients)







DESTINY-Breast04: PFS (BICR) and OS in HR+^{33,34}



TPC (n = 163): 163 146 105 85 84 69 57 48 43 32 30 27 24 20 14 12 8 4 3 2 1 1 1 1 1 1 0

Median duration of follow-up: 18.4 months



Thank you!





References

Harbeck, et al. Adjuvant abemaciclib combined with endocrine therapy for high-risk early breast cancer: updated efficacy and Ki-67 analysis from the monarchE study. Annals of Oncology. Volume 32. 2021.

Johnston, et al. Abemaciclib Combined with Endocrine Therapy for the Adjuvant Treatment of HR+, HER2-, Node-Positive, High Risk, Early Breast Cancer (monarchE). JCO. 38, no. 34 (December 01, 2020) 3987-3998.

Kalinsky, et al. 21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer. NEJM. 2021;385:2336-47.

Modi, et al. Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer. NEJM 2022;387:9-20.

Rugo, et al. Primary results from TROPiCS-02: A randomized phase 3 study of Sacituzumab govitecan (SG) versus treatment of physician's choice (TPC) in patients (Pts) with hormone rectpro-positive/HER2-negative (HR+/HER2-) advanced breast cancer. JCO 2022.

Sparano, et al. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. NEJM. 2018;379:111-21.

Sparano, et al. Clinical and Genomic Risk to Guide the Use of Adjuvant Therapy for Breast Cancer. NEJM. 2019;380:2395-405.

Tutt, et al. Adjuvant Olaparib for Patients with BRCA1- or BRCA2-Mutated Breast Cancer. NEJM 2021;384:2394-405.







