Scoops de l'année 2025 en sénologie

Jeudi 29 janvier 2026

Palais de la Bourse - Bordeaux

Dr Laura POETSCH
Oncologue médicale
Polyclinique Bordeaux Nord Aquitaine

- **Les scoops 2025 en oncologie médicale en Nouvelle-Aquitaine**

Cancer du sein RH+ stade précoce

lidERA

MonarchE

NATALEE

Improving Overall Survival in HR+ Early Breast Cancer

A. Tamoxifen vs No Treatment[1]

30% reduction in risk of death

Breast cancer mortality Δ at 15 years: 9.2%

B. Aromatase inhibitor (AI) vs Tamoxifen[2]

15% reduction in risk of death

Breast cancer mortality Δ at 10 years: 2.1%

C. 5 years ET vs extended AI[3]

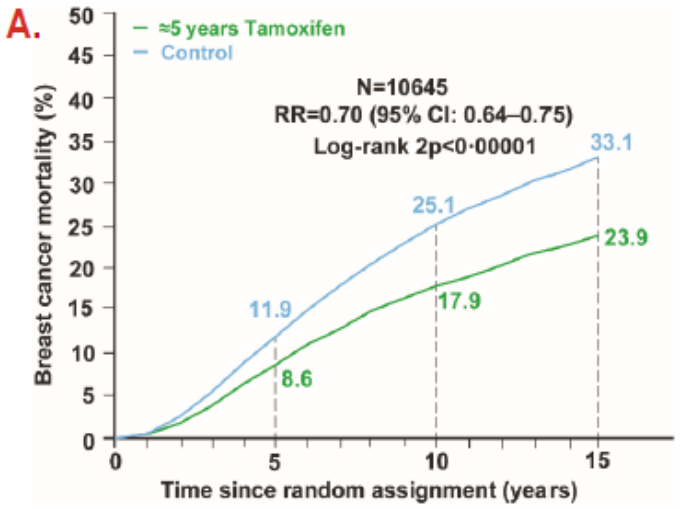
10% reduction is risk of death

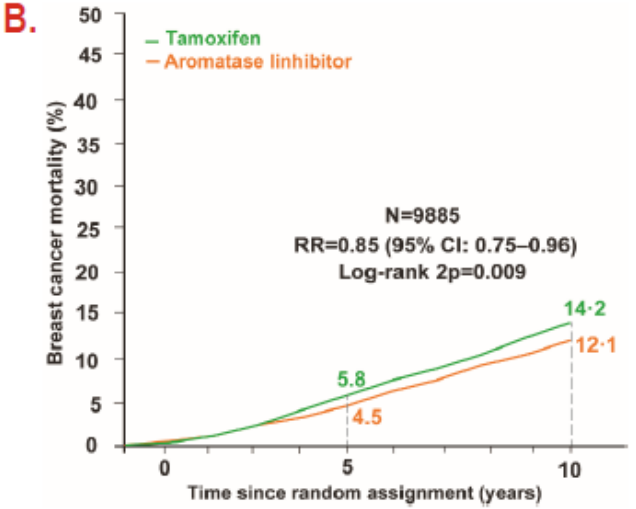
Breast cancer mortality Δ at 15 years: 0.6%

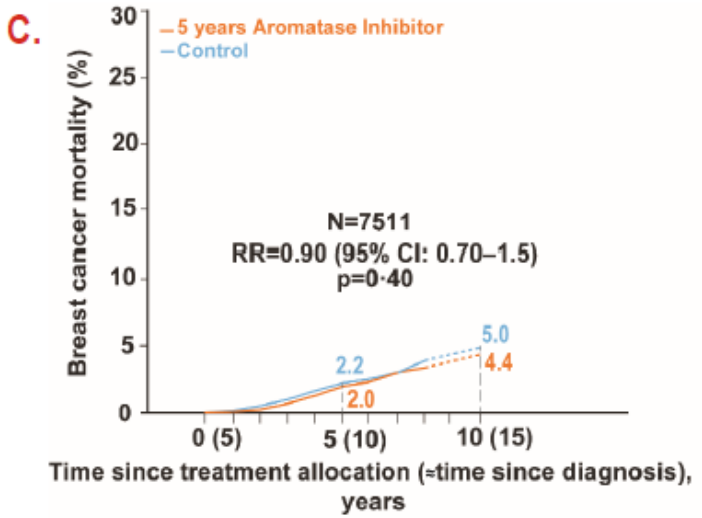
D. Exemestane + Ovarian Function Suppression (OFS) vs Tamoxifen[4]

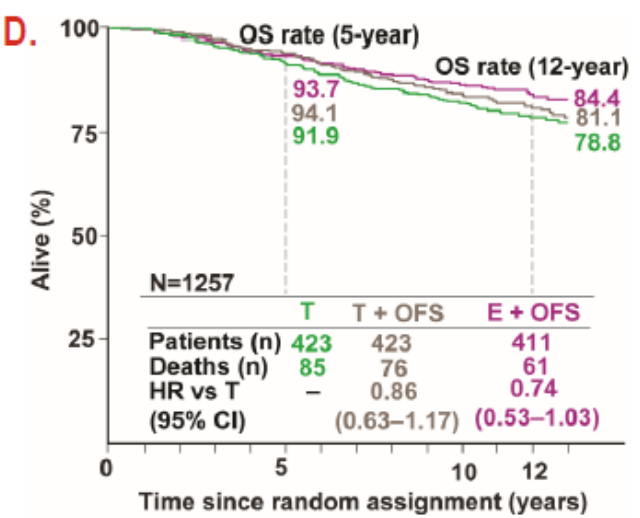
26% reduction in risk of death

Breast cancer mortality Δ at 12 years: 5.6%









E, exemestane; OFS, ovarian function suppression; RR, rate ratio; T, tamoxifen

Data form:

1. Early Breast Cancer Trialists' Collaborative Group. *Lancet*. 2011;378(9793):771–784.
2. Early Breast Cancer Trialists' Collaborative Group. *Lancet*. 2015;386(10001):1341–1352.
3. Early Breast Cancer Trialists' Collaborative Group. *Lancet*. 2025;406(10503):603–614.
4. Francis PA. *J Clin Oncol*. 2023;41(7):1370–1375.

Stephen Johnston, MD, PhD

BERLIN 2025 ESMO congress

monarchE: Primary overall survival results of adjuvant abemaciclib plus endocrine therapy for HR+, HER2-, high-risk early breast cancer

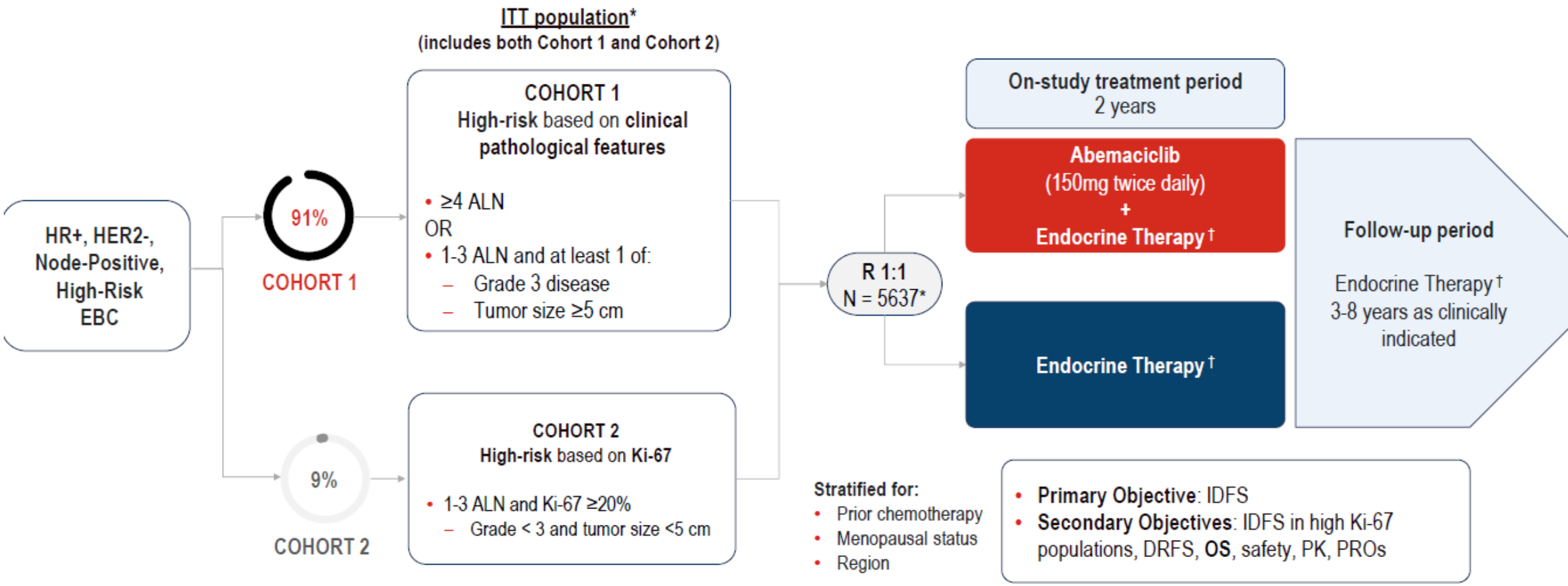
Stephen Johnston, Miguel Martin, Joyce O'Shaughnessy, Roberto Hegg, Sara M. Tolaney, Valentina Guarneri, Lucia Del Mastro, Mario Campone, Joohyuk Sohn, Frances Boyle, Javier Cortes, Hope S. Rugo, Matthew P. Goetz, Erika P. Hamilton, Chiun-Sheng Huang, Elzbieta Senkus, Irfan Cicin, Laura Testa, Patrick Neven, Jens Huober, Zhimin Shao, Ran Wei, Maria Munoz, Belen San Antonio, Ashwin Shahir, Priya Rastogi, Nadia Harbeck

Stephen Johnston, MD, PhD

Breast Unit, The Royal Marsden, NHS Foundation Trust, London, UK

ESMO EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY

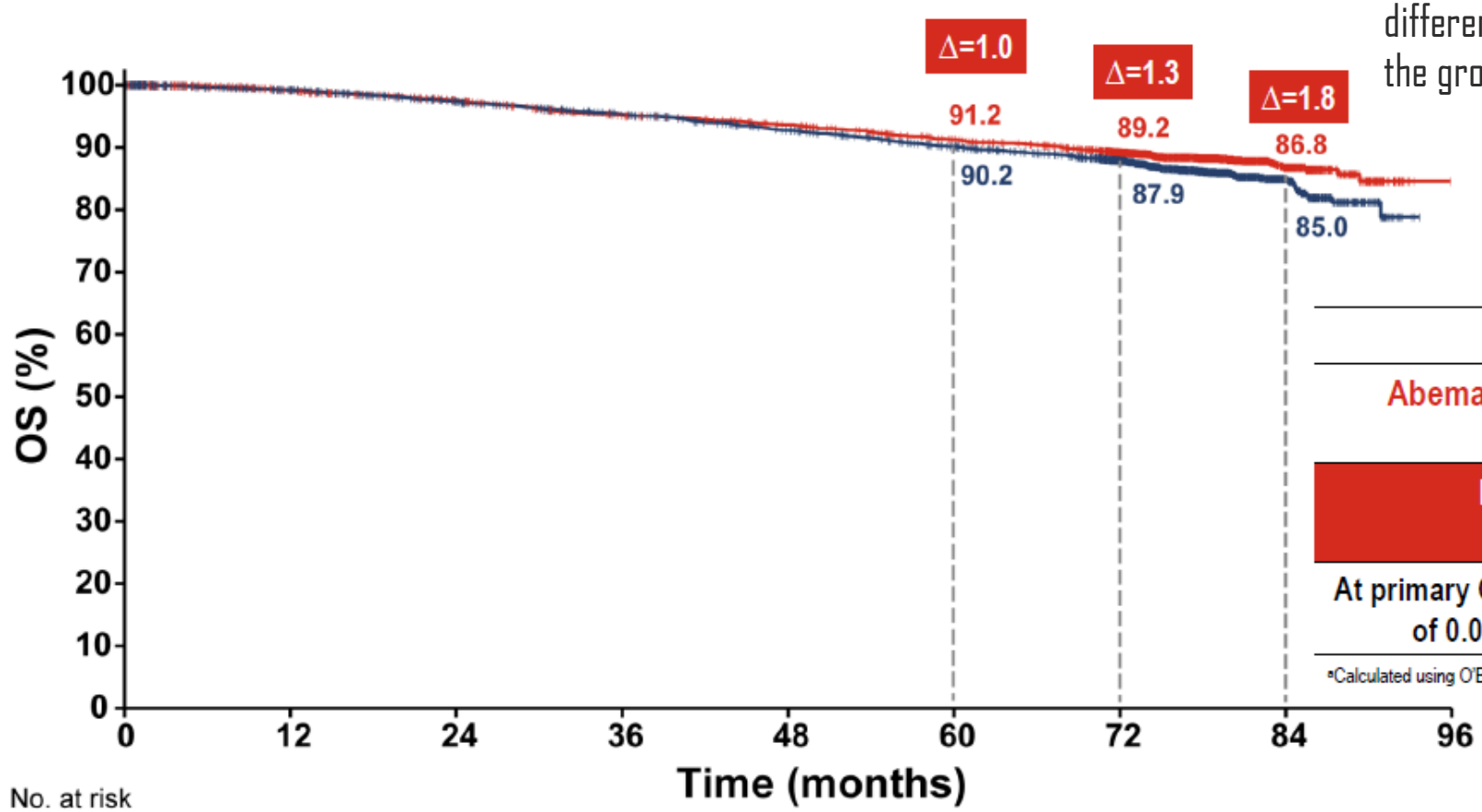
monarchE Trial Design (NCT03155997)



*Recruitment from July 2017 to August 2019. †Endocrine therapy of physician's choice (e.g. AI, Tamoxifen, GnRH). Data for the monarchE Cohort 1 population that forms the basis of multiple global approvals is in the supplement.
AI: aromatase inhibitor; ALN: axillary lymph nodes; DRFS: distant relapse-free survival; EBC: Early Breast Cancer; GnRH: gonadotropin-releasing hormone; HER2-: human epidermal growth factor receptor 2 negative; HR+: hormone receptor positive; IDFS: invasive disease-free survival; ITT: Intent-to-treat population; OS: overall survival; PK: pharmacokinetics; PRO: patient-reported outcome; R: randomized.

Key Secondary Endpoint: Overall Survival in ITT

IDFS benefit : HR 0·664 (95% CI 0·578–0·762, nominal p<0·0001). At 4 years, the absolute difference in invasive disease-free survival betweer the groups was 6·4%



No. at risk

Abemaciclib + ET	2808	2614	2518	2407	2342	2236	1967	425	0
ET	2829	2664	2546	2443	2338	2215	1908	433	0

Number of OS events	
Abemaciclib + ET	ET
301	360

HR (95% CI): 0.842 (0.722, 0.981)
***P*=0.0273**

At primary OS testing, OS in ITT met the critical boundary of 0.0434 (2-sided)[a] for statistical significance

[a]Calculated using O'Brien-Fleming type stopping boundary based on the observed number of events

At a median follow-up of 6.3 years, abemaciclib + ET reduced the risk of death by 15.8% compared to ET alone

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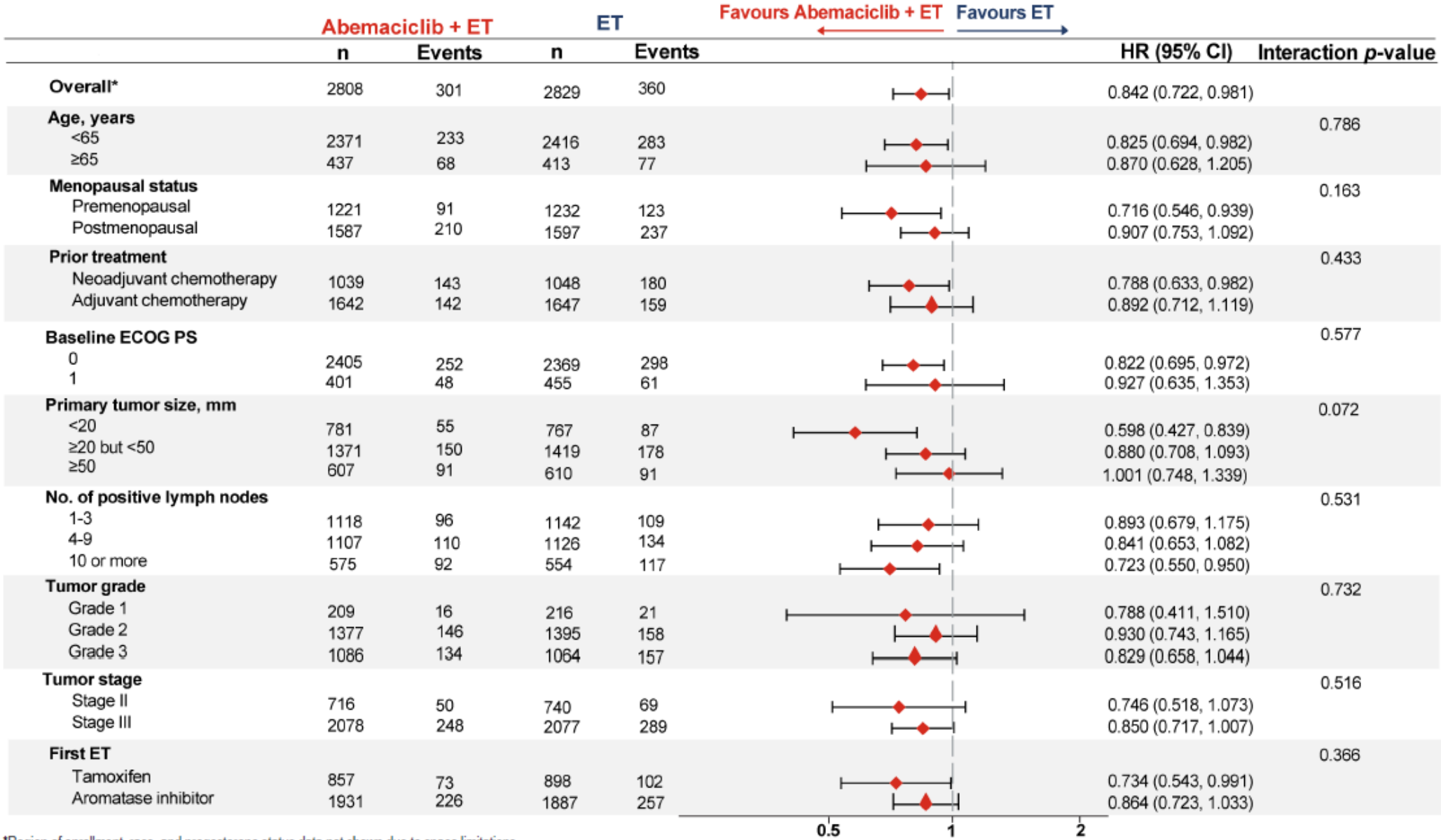
Consistent OS Benefit Across Prespecified Subgroups



*Region of enrollment, race, and progesterone status data not shown due to space limitations

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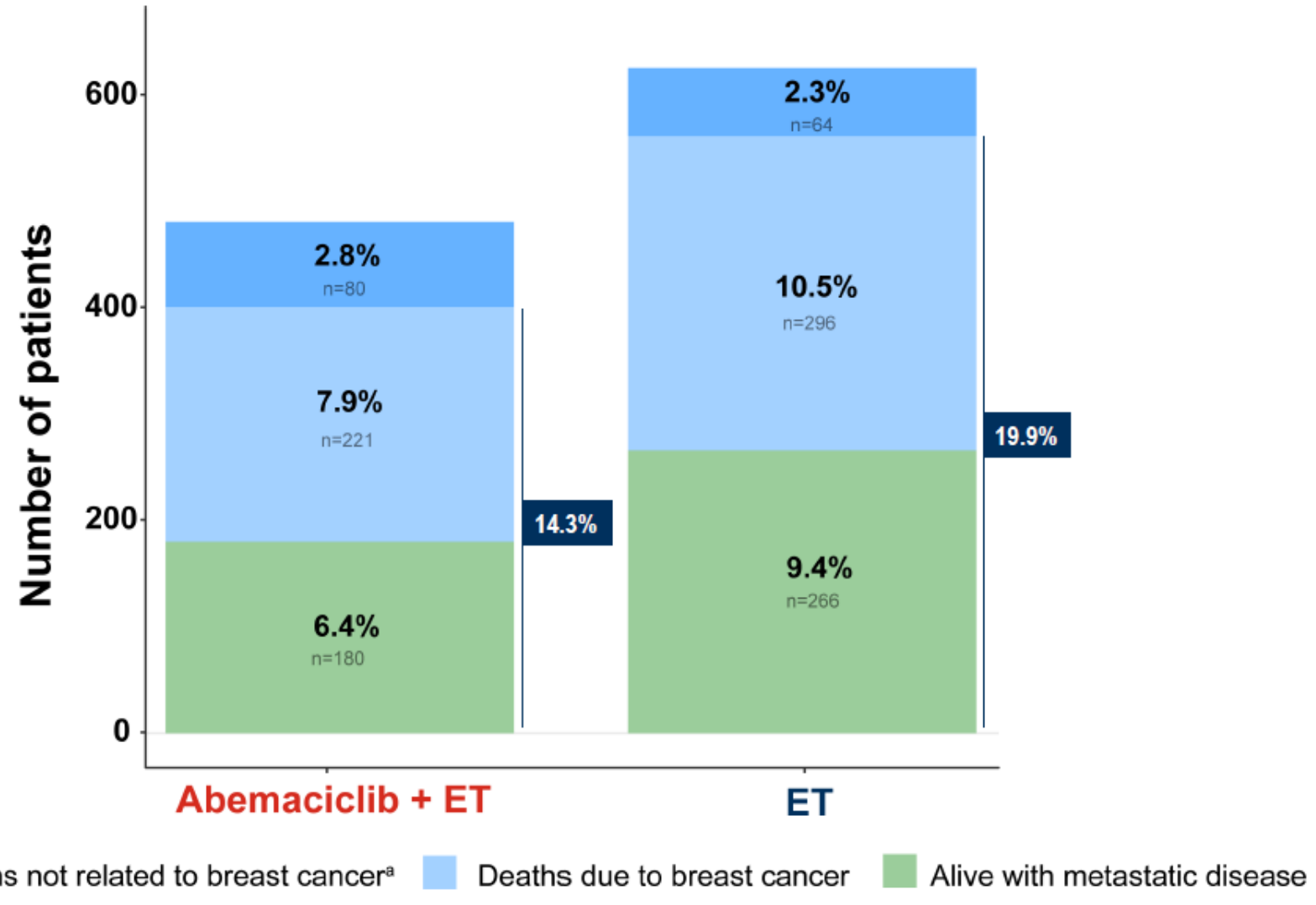
~30% Fewer Patients in Abemaciclib Arm Living with Metastatic Disease



Percentages based on ITT populations (abemaciclib + ET, N=2808; ET, N=2829). [a]Deaths due to AEs and due to unknown cause.

Stephen Johnston, MD, PhD

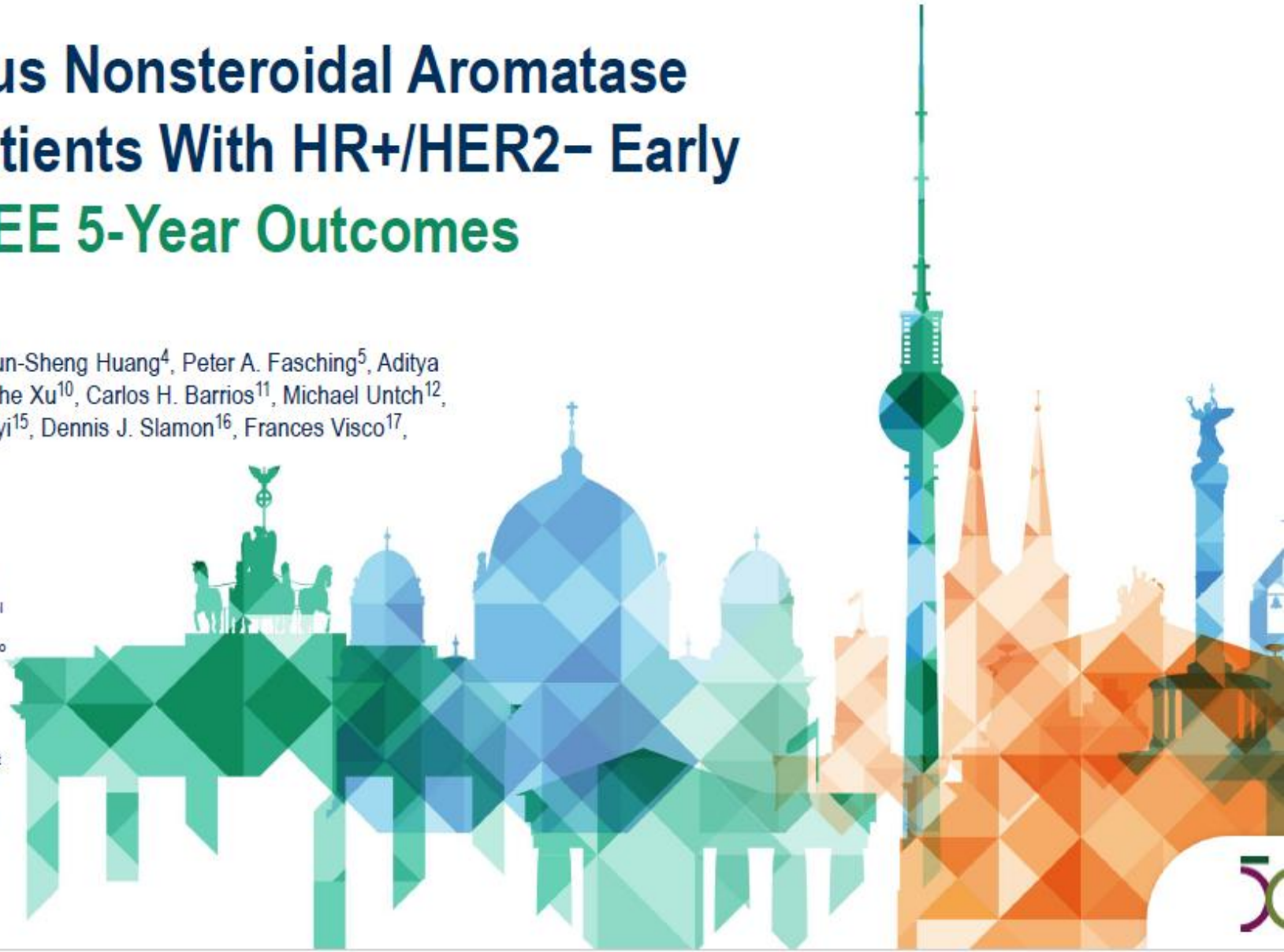
BERLIN 2025 ESMO congress

Adjuvant Ribociclib Plus Nonsteroidal Aromatase Inhibitor Therapy in Patients With HR+/HER2– Early Breast Cancer: NATALEE 5-Year Outcomes

John Crown[1], Daniil Stroyakovskii[2], Denise A. Yardley[3], Chiun-Sheng Huang[4], Peter A. Fasching[5], Aditya Bardia[6], Stephen Chia[7], Seock-Ah Im[8], Miguel Martin[9], Binghe Xu[10], Carlos H. Barrios[11], Michael Untch[12], Rebecca Moroose[13], Sara A. Hurvitz[14], Gabriel N. Hortobagyi[15], Dennis J. Slamon[16], Frances Visco[17], Gonzalo Spera[18], Zheng Li[19], Sherene Loi[20]

[1]St. Vincent's University Hospital, Dublin, Ireland; [2]Moscow City Oncology Hospital #62 of Moscow Healthcare Department, Moscow, Russia; [3]Sarah Cannon Research Institute, Nashville, TN, USA; [4]National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan; [5]University Hospital Erlangen Comprehensive Cancer Center Erlangen-EMN, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany; [6]David Geffen School of Medicine at UCLA and the UCLA Health Jonsson Comprehensive Cancer Center; Los Angeles, CA, USA; [7]BC Cancer, Vancouver, BC, Canada; [8]Cancer Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul National University, Seoul, Republic of Korea; [9]Instituto de Investigación Sanitaria Gregorio Marañon, Centro de Investigación Biomédica en Red de Cáncer, Grupo Español de Investigación en Cáncer de Mama, Universidad Complutense, Madrid, Spain; [10]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [11]Latin American Cooperative Oncology Group (LACOG), Porto Alegre, Brazil; [12]Interdisciplinary Breast Cancer Center, Helios Klinikum Berlin-Buch, Berlin, Germany; [13]Orlando Health Cancer Institute, Orlando, FL, USA; [14]University of Washington, Fred Hutchinson Cancer Center, Seattle, WA, USA; [15]Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; [16]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [17]National Breast Cancer Coalition (NBCC), Washington, DC, USA; [18]Translational Research in Oncology (TRIO), Montevideo, Uruguay; [19]Novartis Pharmaceuticals, East Hanover, NJ, USA; [20]Peter MacCallum Cancer Centre, Melbourne, Australia

Speaker: John Crown, M.D.



Study Design: NATALEE

An open-label, multicenter, randomized, phase 3 trial[1,2]

Adult patients with stage II and III HR+/HER2− EBC

- Prior ET allowed up to 12 months
- **Anatomical stage IIA**[a]
  - N0 with:
    - Grade 2 and evidence of high risk:
      - Ki-67 ≥ 20%
      - Oncotype DX Breast Recurrence Score ≥ 26 *or*
      - High risk via genomic risk profiling
    - Grade 3
  - N1
- **Anatomical stage IIB**[a]
  - N0 or N1
- **Anatomical stage III**
  - N0, N1, N2, or N3

R 1:1

RIB
400 mg/day
3 weeks on/1 week off for **3 y**
+
NSAI
Letrozole or anastrozole[b] for **≥5 y**
+ goserelin in men and premenopausal women

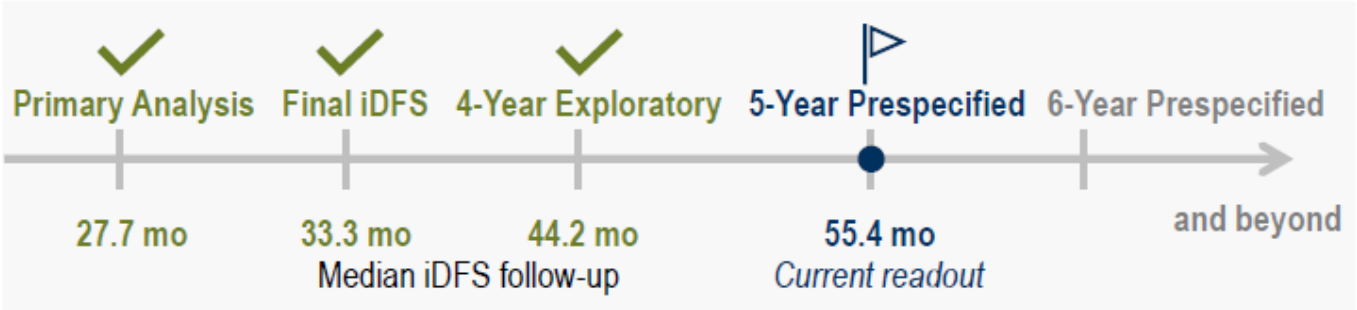
NSAI
Letrozole or anastrozole[b] for **≥5 y**
+ goserelin in men and premenopausal women

Primary End Point
iDFS using STEEP criteria

Secondary End Points
- RFS, DDFS, OS
- PROs
- Safety and tolerability
- PK

Exploratory End Points
- DRFS
- Gene expression and alterations in tumor ctDNA/ctRNA samples

Efficacy outcomes for the 5-year analysis were estimated by the Kaplan-Meier method, and results are descriptive. The Cox proportional hazards model was used to estimate the HRs and 95% CIs.



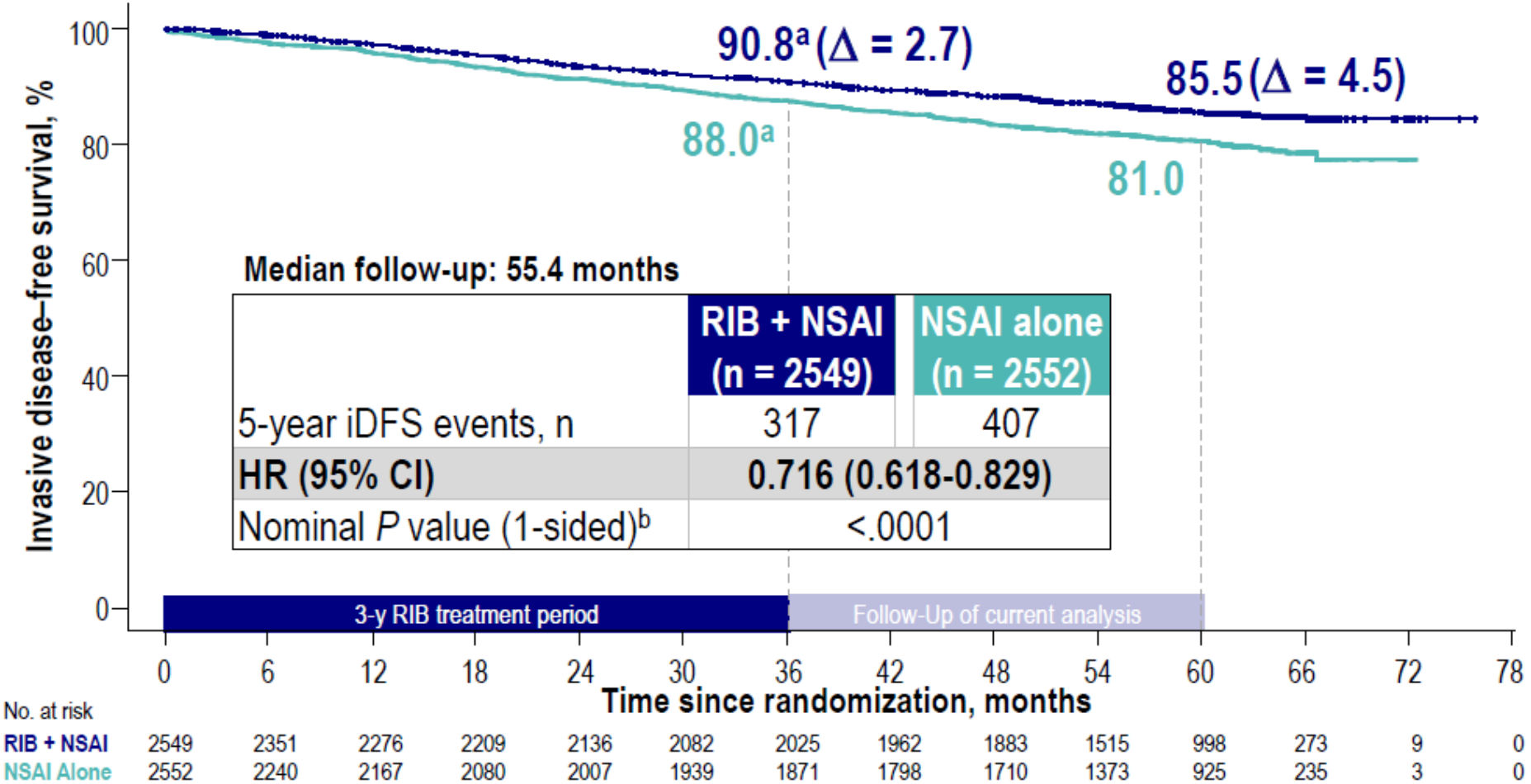
[a] Enrollment of patients with stage II disease was capped at 40%. [b] Per investigator choice.
ctDNA/RNA, circulating tumor DNA/RNA; DDFS, distant disease–free survival; DRFS, distant recurrence–free survival; EBC, early breast cancer; ET, endocrine therapy; HR, hazard ratio; iDFS, invasive disease–free survival; ITT, intention to treat; N, node; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; PK, pharmacokinetics; PRO, patient-reported outcomes; RIB, ribociclib; RFS, recurrence-free survival; STEEP, Standardized Definitions for Efficacy End Points.

1. ClinicalTrials.gov. Accessed November 8, 2023. https://clinicaltrials.gov/study/NCT03701334.
2. Slamon D et al. *Ther Adv Med Oncol*. 2023;15:1-16.

John Crown, M.D.

iDFS in the ITT Population

With 55.4 months of follow-up, RIB continues to demonstrate a durable iDFS benefit



[a] The difference between percentages does not equal 2.7 due to rounding. [b] Comparison of survival between treatment arms was generated by stratified log-rank test (1-sided *P* value, informational and not preplanned).
HR, hazard ratio; IDFS, invasive disease–free survival; ITT, intention to treat; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.

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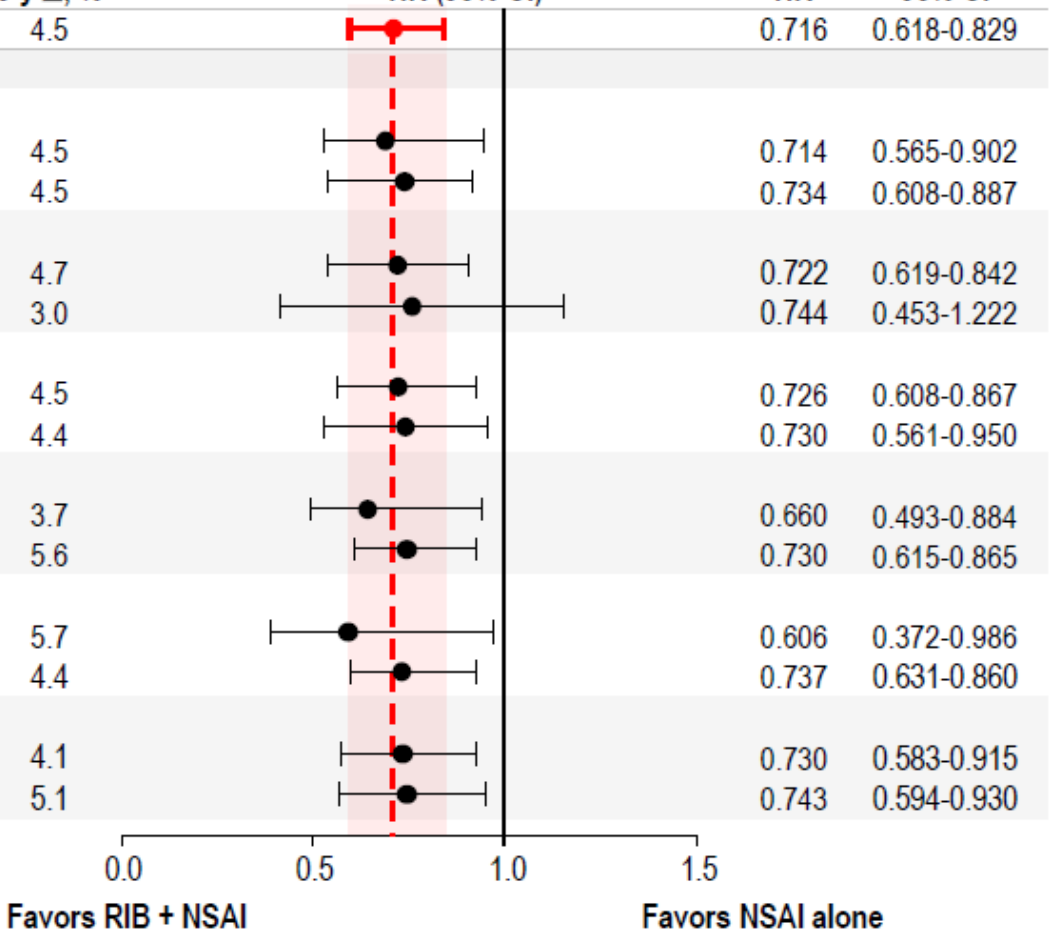
Consistent iDFS Outcomes Across Key Prespecified Subgroups

	RIB + NSAI		NSAI alone					
	Events/n	5-y iDFS rate, %	Events/n	5-y iDFS rate, %	5-y Δ, %	HR (95% CI)	HR	95% CI
ITT	317/2549	85.5	407/2552	81.0	4.5		0.716	0.618-0.829
SUBGROUPS								
Menopausal status								
Premenopausal women and men	124/1126	87.1	162/1132	82.6	4.5		0.714	0.565-0.902
Postmenopausal women	193/1423	84.3	245/1420	79.7	4.5		0.734	0.608-0.887
Prior CT[a]								
Yes	290/2249	84.9	370/2245	80.2	4.7		0.722	0.619-0.842
No	27/300	89.6	37/307	86.6	3.0		0.744	0.453-1.222
Prior ET								
Yes	220/1832	85.8	278/1807	81.3	4.5		0.726	0.608-0.867
No	97/717	84.6	129/745	80.3	4.4		0.730	0.561-0.950
AJCC stage								
Stage II	75/1012	91.7	113/1034	87.9	3.7		0.660	0.493-0.884
Stage III	241/1527	81.2	294/1512	75.6	5.6		0.730	0.615-0.865
Nodal status[b]								
N0	25/285	90.3	46/329	84.6	5.7		0.606	0.372-0.986
N1-N3	292/2261	84.9	360/2218	80.5	4.4		0.737	0.631-0.860
Ki-67 status[c]								
Ki-67 ≤20%	132/1200	87.0	177/1241	83.0	4.1		0.730	0.583-0.915
Ki-67 >20%	138/919	83.2	172/932	78.1	5.1		0.743	0.594-0.930



[a] Includes neoadjuvant and adjuvant chemotherapy. [b] Nodal status classification according to AJCC staging. Nodal status is from the most advanced stage derived per surgical specimen or at diagnosis. [c] From archival tumor tissue.
AJCC, American Joint Committee on Cancer; CT, chemotherapy; ET, endocrine therapy; iDFS, invasive disease–free survival; HR, hazard ratio; ITT, intent to treat; N, node; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.

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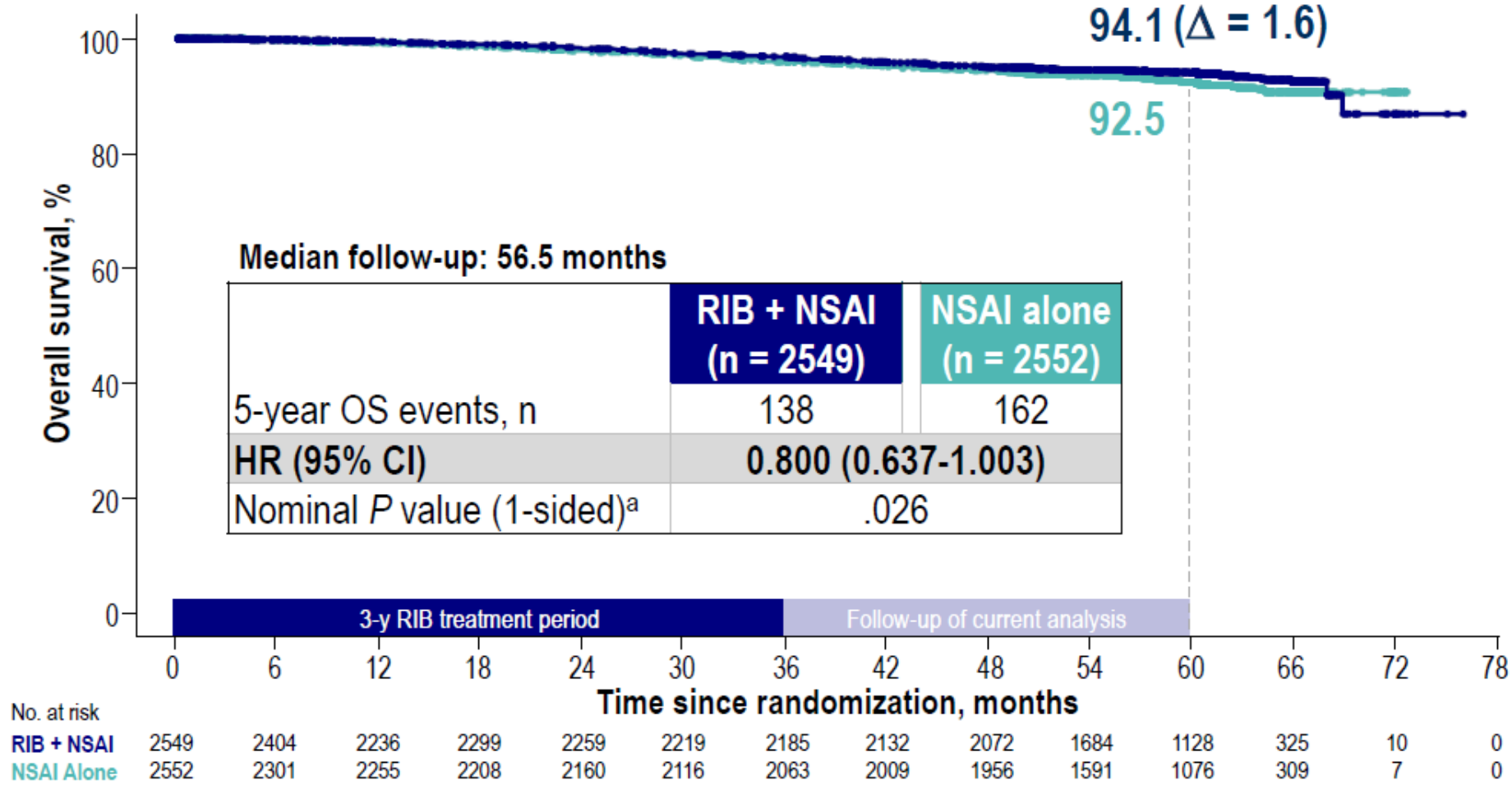
OS in the ITT Population

As OS data matures, a positive trend favoring RIB + NSAI treatment continues to emerge



[a] Comparison of survival between treatment arms was generated by stratified log-rank test (1-sided *P* value, informational and not preplanned).
HR, hazard ratio; ITT, intention to treat; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; RIB, ribociclib.

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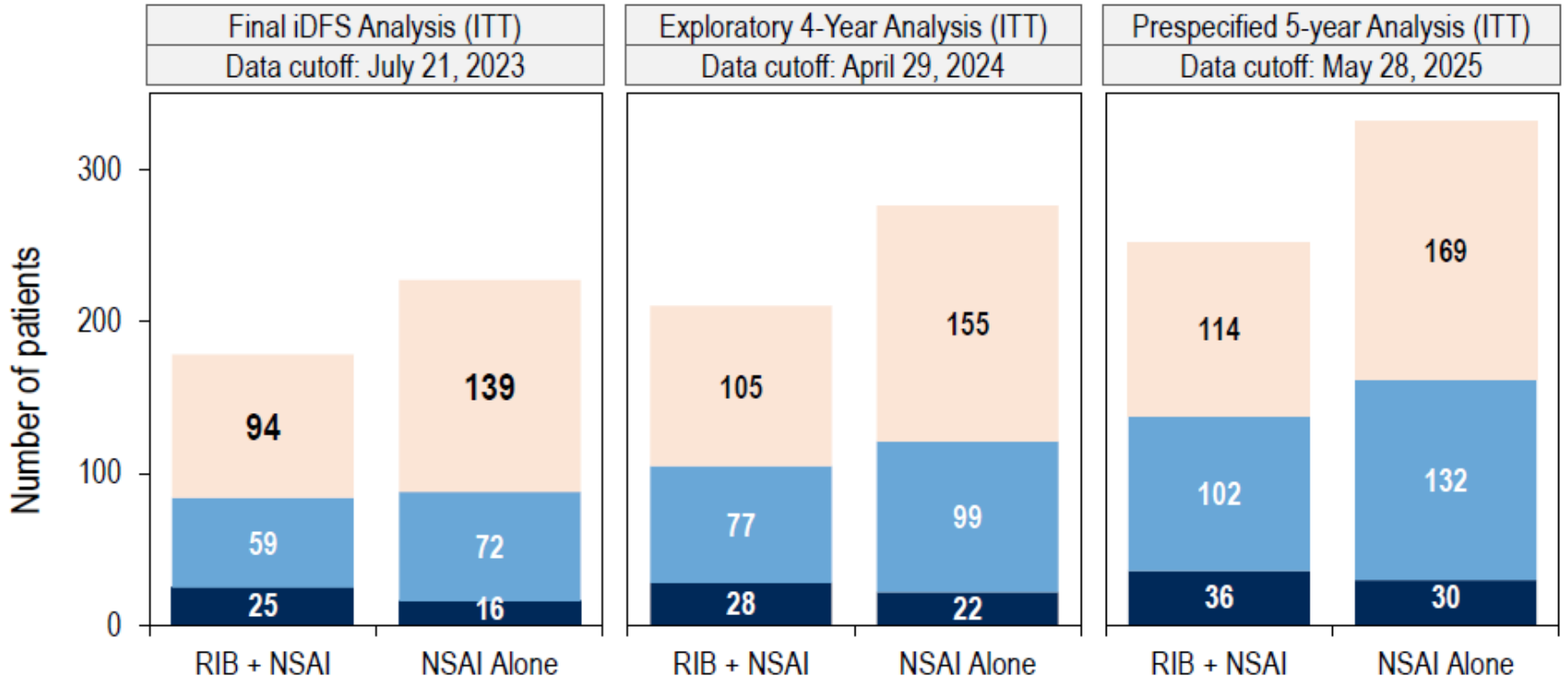
Survival Status Over Time: Fewer BC-Related Deaths in RIB Arm

A positive OS signal in favor of RIB + NSAI treatment has been observed at earlier timepoints



Approximate median follow-up (months)	36	44	57
OS HR (95% CI)	0.89 (0.66-1.20)	0.83 (0.64-1.07)	0.800 (0.637-1.003)

BC, breast cancer; HR, hazard ratio; iDFS, invasive disease–free survival; ITT, intention to treat; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib; OS, overall survival.

John Crown, M.D.

SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center
AACR American Association for Cancer Research
DECEMBER 9–12, 2025
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

Giredestrant vs standard-of-care endocrine therapy as adjuvant treatment for patients with estrogen receptor-positive, HER2-negative early breast cancer: Results from the global Phase III lidERA Breast Cancer trial

Presenting author: Aditya L. Bardia, MD
University of California, Los Angeles, Los Angeles, CA, USA

Aditya L. Bardia,* Peter Schmid,* Miguel Martín, Sara A. Hurvitz, Kyung Hae Jung, Mothaffar F. Rimawi, Shigehira Saji, Gustavo Werutsky, Nadia Harbeck, Sherene Loi, Akiko Ogiya, Manuel Ruiz-Borrego, Ahmet Alacacıoğlu, Jiong Wu, Chenglin Ye, Mario Liste-Hermoso, Nimali P. Withana, Tanja Badovinac Crnjevic, Mona D. Shah, Pablo Pérez-Moreno, Charles E. Geyer, Jr.*

* Equal contributions

lidERA Breast Cancer study design

A global, randomized, open-label, multicenter Phase III trial

SAN ANTONIO BREAST CANCER SYMPOSIUM®

UT Health San Antonio Mays Cancer Center | AACR American Association for Cancer Research

Key eligibility criteria

- Participants with ER+, HER2-negative early breast cancer
- Stage I–III disease (anatomical)
  - pN0 and pT > 1 cm with Grade 3, or Ki67 ≥ 20%, or high score on genomic assay,* or pT4N0
  - Node-positive
- Pre- or post-menopausal†
- Breast cancer surgery within 12 months
- (Neo)adjuvant chemotherapy if indicated

Stratification factors

- Risk: Medium-‡ vs high-risk§ Stage I–III breast cancer
- Region: USA/Canada/Western Europe vs Asia–Pacific vs RoW
- Previous chemotherapy: No vs yes
- Menopausal status: Pre-menopausal vs post-menopausal

Primary endpoint

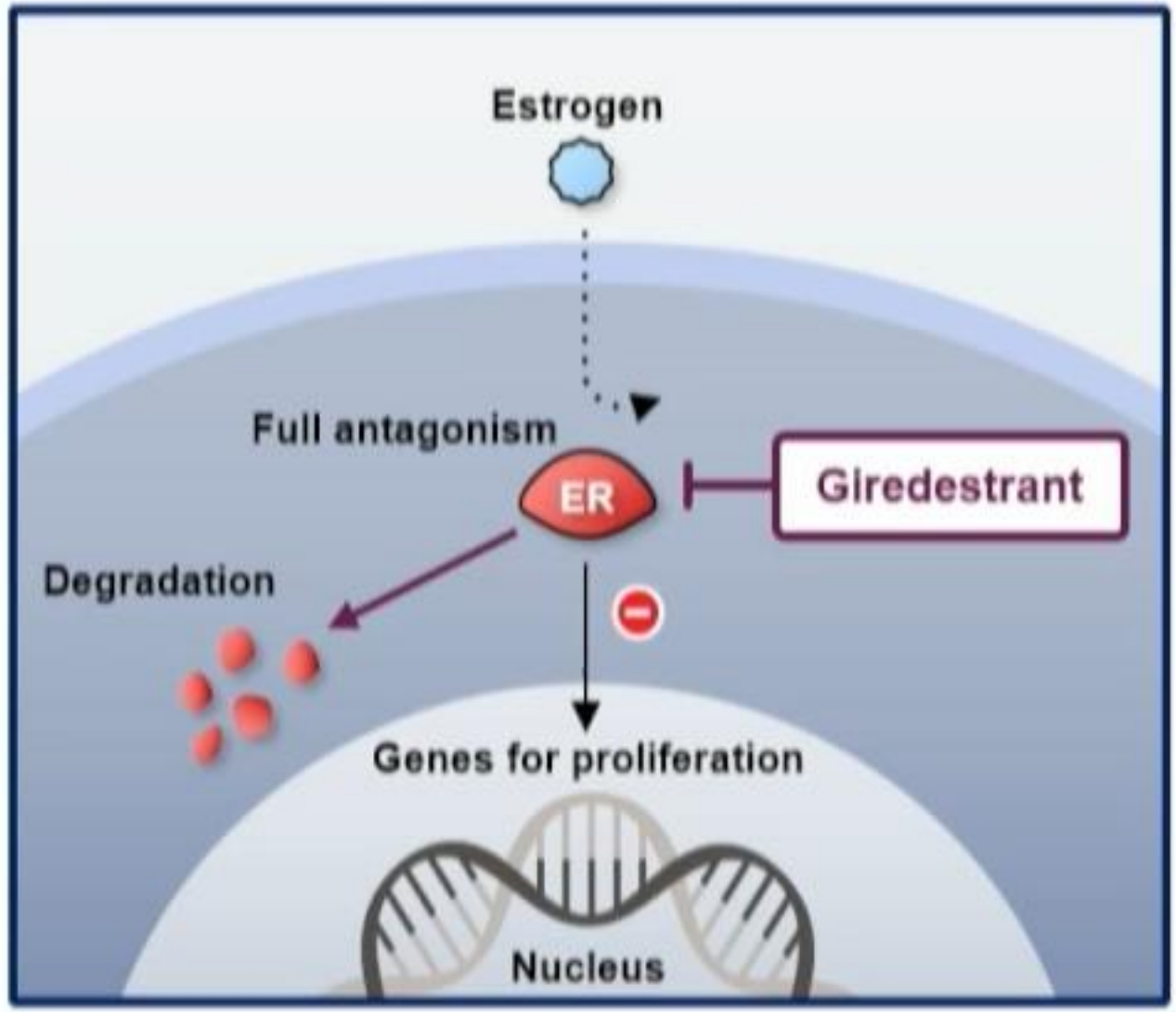
- IDFS (excluding second primary non-breast cancer)

Key secondary endpoints

- DFS, DRFI, IDFS (including second primary non-breast invasive cancer with exception of non-melanoma skin cancers and *in situ* carcinomas of any site), LRRFI, OS, safety

Giredestrant is currently also being investigated in combination with abemaciclib in the adjuvant setting (lidERA Breast Cancer substudy 1)

Enrollment: August 2021 to September 2023. Up to 12 weeks of ET ± CDK4/6i were allowed. ER+ was defined as ≥ 1% positive cells by immunohistochemistry. * OncotypeDx ≥ 26 or high-risk Mammaprint.
† Pre-menopausal patients on aromatase inhibitors or giredestrant had to receive ovarian function suppression with an approved luteinizing hormone-releasing hormone agonist. ‡ Medium risk: pN0 and primary tumor > 1 cm with high-risk biologic features (Grade 3, or Ki67 ≥ 20%, or high score on genomic assay [if available]) and pN1 with low-risk biologic features (Grade 1/2 and Ki67 < 20% and tumor ≤ 5 cm and low score on genomic assay [if available]). § High risk: pT4, or pN2, or pN3 and pN1 with high-risk biologic features (Grade 3, or Ki67 ≥ 20%, or tumor > 5 cm, or high score on genomic assay [if available]).
CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DFS, disease-free survival; DRFI, distant recurrence-free interval; ER+, estrogen receptor-positive; ET, endocrine therapy; IDFS, invasive disease-free survival; LRRFI, locoregional recurrence-free interval; OS, overall survival; PO, orally; QD, once daily; R, randomization; RoW, rest of the world; SOC, standard-of-care.
ClinicalTrials.gov number, NCT04961996. Adapted from Geyer CE, *et al.* ASCO 2023 (TPS616), with permission.



Giredestrant mechanism of action
(selective estrogen receptor antagonist and degrader)

Baseline demographics and characteristics

	Giredestrant n = 2084	SOC ET n = 2086
Median age, years (range)	54.0 (22–91)	54.0 (25–89)
Female sex, n (%)	2073 (99.5)	2075 (99.5)
Race, n (%)		
American Indian or Alaska Native	77 (3.7)	62 (3.0)
Asian	461 (22.1)	467 (22.4)
Black or African American	50 (2.4)	50 (2.4)
Other*	263 (12.6)	232 (11.1)
White	1233 (59.2)	1275 (61.1)
Region, n (%)		
Asia–Pacific	544 (26.1)	544 (26.1)
USA/Canada/Western Europe	860 (41.3)	905 (43.4)
Latin America/Africa/Eastern Europe	680 (32.6)	637 (30.5)
Menopausal status, n (%)†		
Pre-menopausal	849 (41.0)	838 (40.4)
Post-menopausal	1220 (59.0)	1236 (59.6)

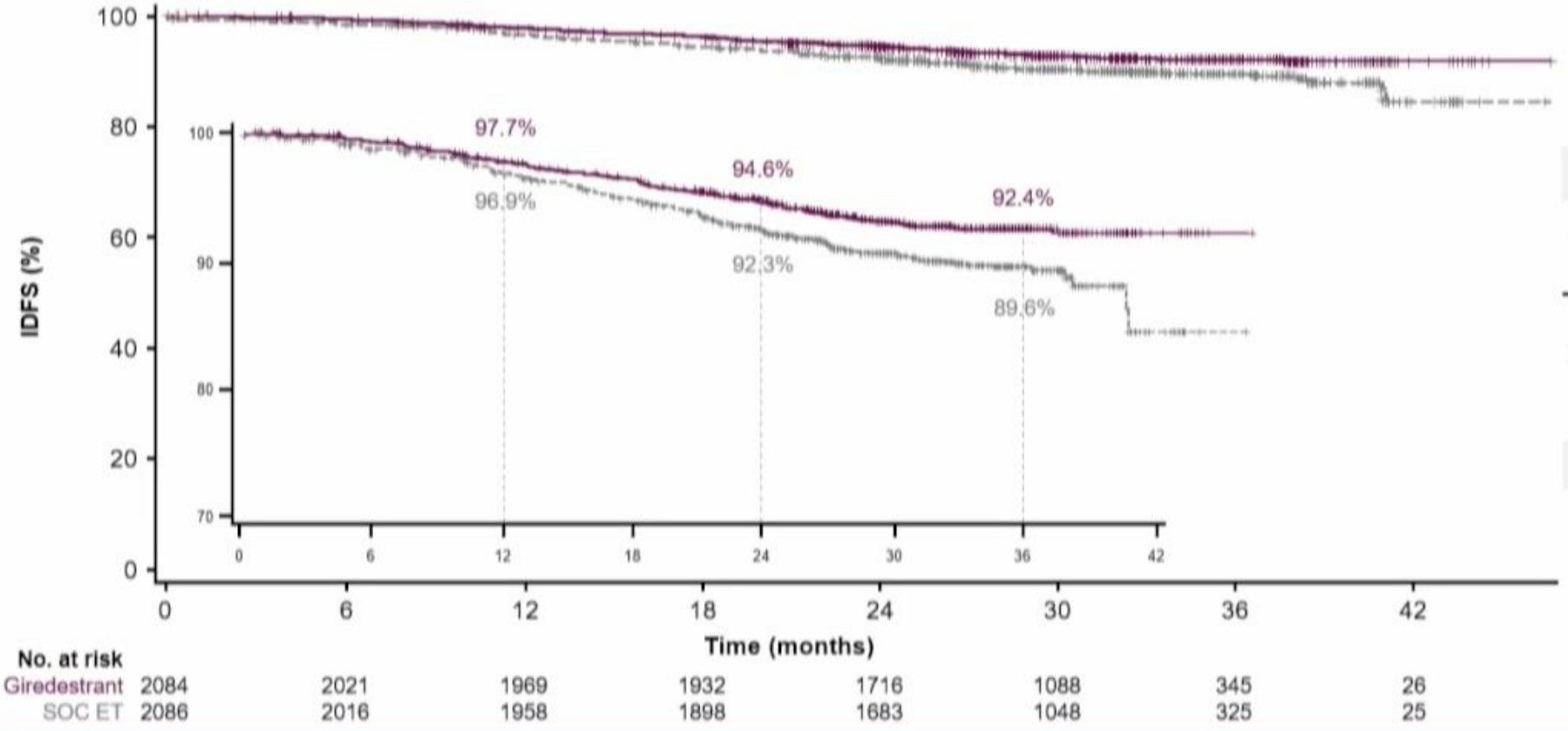
	Giredestrant n = 2084	SOC ET n = 2086
ER status, n (%)‡		
Low-positive (1–10% of cells positive)	45 (2.2)	52 (2.5)
Positive (> 10% of cells positive)	2030 (97.8)	2031 (97.5)
AJCC stage at surgery, n (%)§		
I	254 (12.3)	283 (13.6)
II	1013 (49.0)	950 (45.7)
III	799 (38.7)	844 (40.6)
Nodal status, n (%) on surgical specimen‖		
pN0	449 (21.6)	441 (21.2)
pN1	968 (46.6)	953 (45.7)
pN2–3	662 (31.8)	691 (33.1)
Risk, n (%)		
High	1448 (69.5)	1447 (69.4)
Medium	636 (30.5)	639 (30.6)
Previous chemotherapy, n (%)		
No	396 (19.0)	450 (21.6)
Yes	1688 (81.0)	1636 (78.4)

Baseline demographics and characteristics were balanced

Data cutoff: August 8, 2025. * "Other" refers to "multiple", "Native Hawaiian or Other Pacific Islander", "not reported", or "unknown". † Twenty-seven patients had unknown menopausal status (15 in the giredestrant arm and 12 in the SOC ET arm). ‡ Twelve patients had unknown ER status (nine in the giredestrant arm and three in the SOC ET arm). § One patient had Stage 0 disease (SOC ET arm); 26 had unknown Stage (18 in the giredestrant arm and eight in the SOC ET arm). ‖ Six patients had unknown nodal status (five in the giredestrant arm and one in the SOC ET arm). AJCC, American Joint Committee on Cancer; ER, estrogen receptor; ET, endocrine therapy; SOC, standard-of-care.

Presented by: Aditya L. Bardia, MD.

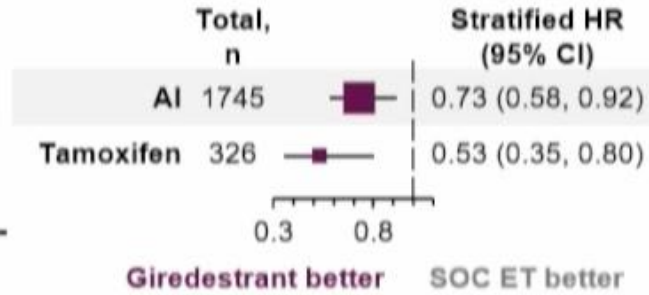
Primary endpoint: IDFS



No. at risk								
Giredestrant	2084	2021	1969	1932	1716	1088	345	26
SOC ET	2086	2016	1958	1898	1683	1048	325	25

	Giredestrant n = 2084	SOC ET n = 2086
Events, n (%)	140 (6.7)	196 (9.4)
Stratified HR (95% CI)	**0.70** (0.57, 0.87); **p = 0.0014***	

Exploratory analysis: IDFS by SOC ET



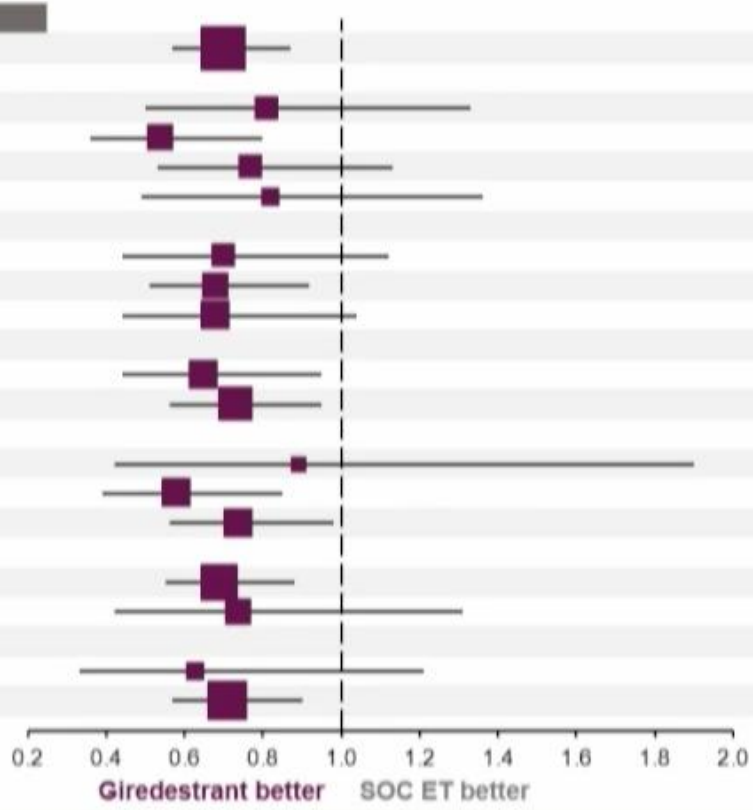
Median follow-up: 32.3 months

Statistically significant and clinically meaningful improvement in IDFS:
Giredestrant reduced the risk of invasive disease recurrence or death by 30% compared with SOC ET

Data cutoff: August 8, 2025. Median follow-up, 32.4 months in the giredestrant arm and 32.3 months in the SOC ET arm; maximum follow-up, 46.6 months and 46.3 months, respectively. * Log-rank (2-sided). p-value boundary for IDFS interim analysis was 0.0217 (2-sided). AI, aromatase inhibitor; CI, confidence interval; ET, endocrine therapy; HR, hazard ratio; IDFS, invasive disease-free survival; SOC, standard-of-care.

IDFS in key subgroups

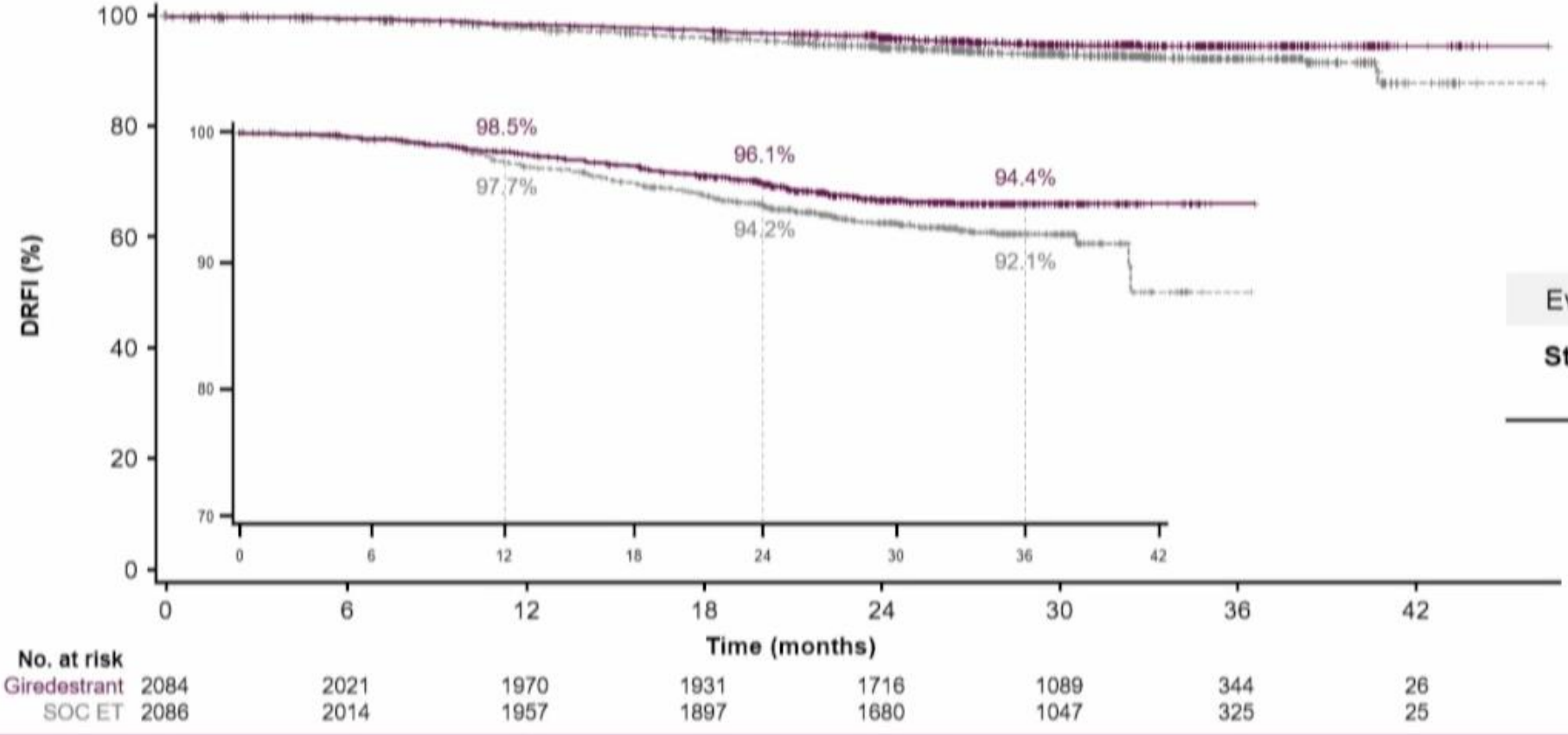
	Total, n	Patients, n: Giredestrant	Patients, n: SOC ET	HR (95% CI)
All patients	4170	2084	2086	0.70 (0.57, 0.87)
Age group, years				
≤ 45	906	472	434	0.81 (0.50, 1.33)
> 45 to ≤ 55	1355	660	695	0.54 (0.36, 0.80)
> 55 to ≤ 65	1118	567	551	0.77 (0.53, 1.13)
> 65	791	385	406	0.82 (0.49, 1.36)
Region				
Asia–Pacific	1088	544	544	0.70 (0.44, 1.12)
Latin America/Africa/Eastern Europe	1317	680	637	0.68 (0.51, 0.92)
USA/Canada/Western Europe	1765	860	905	0.68 (0.44, 1.04)
Menopausal status				
Pre-menopausal	1680	841	839	0.65 (0.44, 0.95)
Post-menopausal	2490	1243	1247	0.73 (0.56, 0.95)
AJCC stage at surgery*				
I	537	254	283	0.89 (0.42, 1.90)
II	1963	1013	950	0.58 (0.39, 0.85)
III	1643	799	844	0.74 (0.56, 0.98)
Risk				
High	2895	1448	1447	0.69 (0.55, 0.88)
Medium	1275	636	639	0.74 (0.42, 1.31)
Previous chemotherapy				
No	787	392	395	0.63 (0.33, 1.21)
Yes	3383	1692	1691	0.71 (0.57, 0.90)



IDFS benefit was consistent across key prespecified subgroups

Data cutoff: August 8, 2025. HR estimates are unstratified. Median follow-up of 32.4 months in the giredestrant arm and 32.3 months in the SOC ET arm; maximum follow-up, 46.6 months and 46.3 months, respectively.
* One patient had Stage 0 disease (SOC ET arm); 26 had unknown Stage (18 in the giredestrant arm and eight in the SOC ET arm).
AJCC, American Joint Committee on Cancer; CI, confidence interval; ET, endocrine therapy; HR, hazard ratio; IDFS, invasive disease-free survival; SOC, standard-of-care.

Distant recurrence-free interval



	Giredestrant n = 2084	SOC ET n = 2086
Events, n (%)	102 (4.9)	145 (7.0)
Stratified HR (95% CI)	**0.69** (0.54, 0.89)	

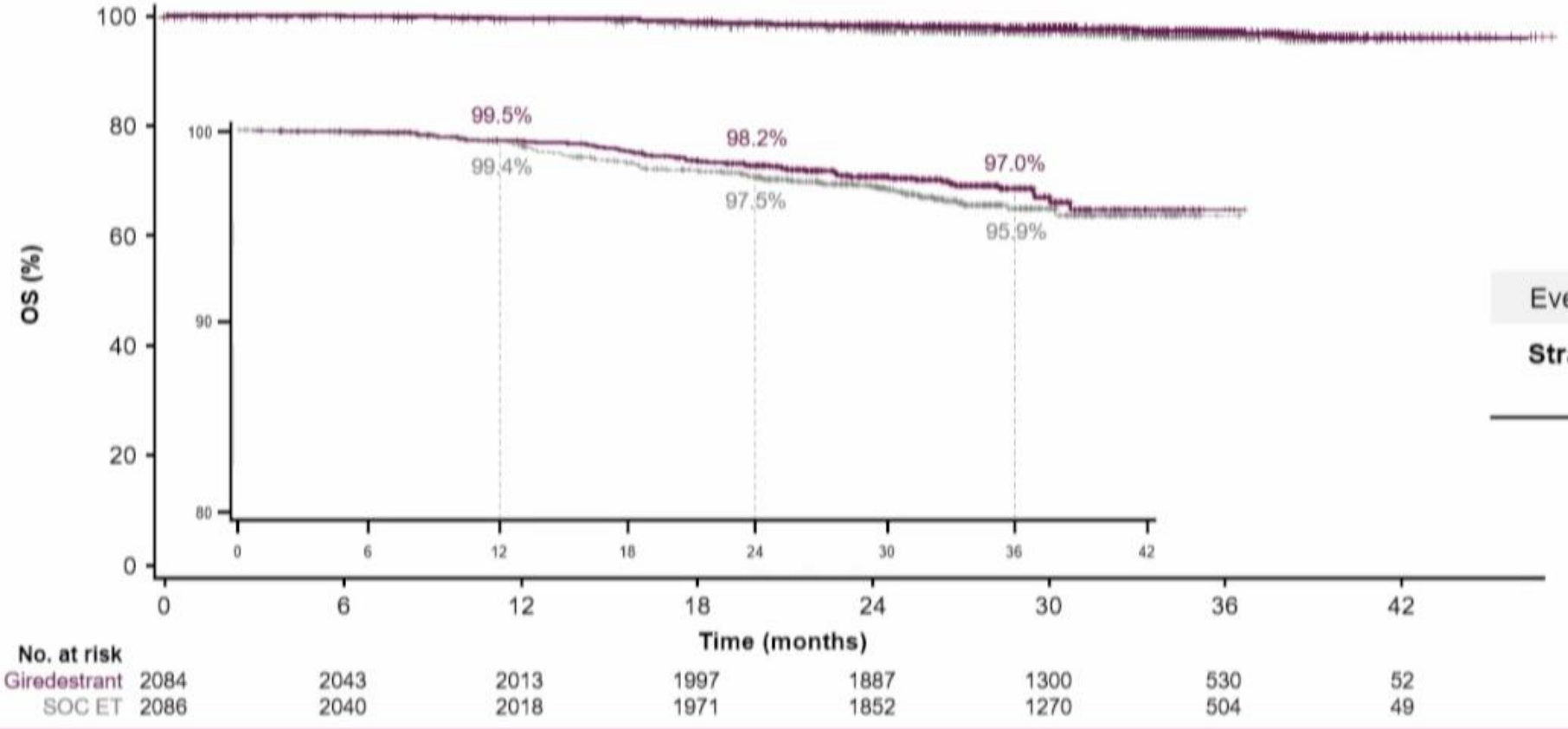
Median follow-up: 32.3 months

DRFI was improved vs SOC ET, with a 31% reduction in risk of developing metastatic disease

Data cutoff: August 8, 2025. Median follow-up, 32.4 months in the giredestrant arm and 32.3 months in the SOC ET arm; maximum follow-up, 46.6 months and 46.3 months, respectively.
CI, confidence interval; DRFI, distant recurrence-free interval; ET, endocrine therapy; HR, hazard ratio; SOC, standard-of-care.

Presented by: Aditya L. Bardia, MD.

Interim overall survival



	Giredestrant n = 2084	SOC ET n = 2086
Events, n (%)	57 (2.7)	71 (3.4)
Stratified HR (95% CI)	**0.79** (0.56, 1.12); p = 0.1863*	

Median follow-up: 32.3 months

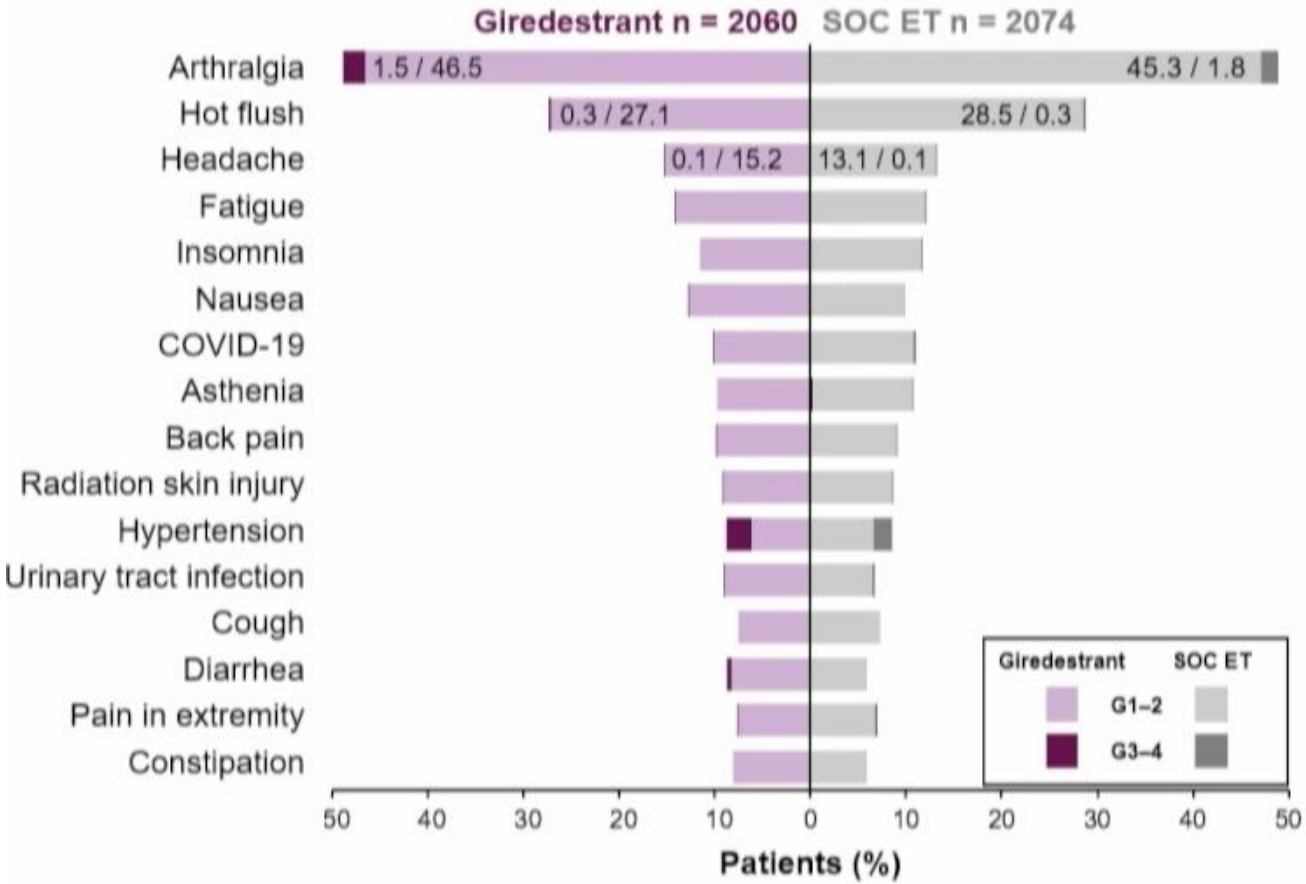
While OS data were immature, a clear positive trend was observed. OS testing will continue at future analyses

Data cutoff: August 8, 2025. Median follow-up, 32.4 months in the giredestrant arm and 32.3 months in the SOC ET arm; maximum follow-up, 46.6 months and 46.3 months, respectively. At the data cutoff, the 1st OS IA was conducted (maturity 31.2% with respect to the final OS analysis). * Log-rank (2-sided). p-value boundary for the 1st OS IA was 0.0001 (2-sided). Includes one death from a patient who was randomized but never dosed. Excludes one death from a patient with missing date of death. CI, confidence interval; ET, endocrine therapy; HR, hazard ratio; IA, interim analysis; OS, overall survival; SOC, standard-of-care.

Presented by: Aditya L. Bardia, MD.

AE overview *(safety-evaluable population)*

Common TEAEs (≥ 7.5% of patients in either arm at any grade)



Selected AEs

	Giredestrant n = 2060	SOC ET n = 2074
Patients, n (%) with treatment discontinuations due to AEs		
Musculoskeletal disorders	38 (1.8)	92 (4.4)
• Arthralgias (PT)	32 (1.6)	76 (3.7)
Vasomotor disorders	2 (< 0.1)	18 (0.9)
• Hot flush (PT)	1 (< 0.1)	16 (0.8)

	Giredestrant n = 2060			SOC ET n = 2074		
Patients, n (%) with selected AEs by medical concept*						
	G1	**G2**	**G3–4**	**G1**	**G2**	**G3–4**
Bradycardia†	217 (10.5)	15 (0.7)	0	64 (3.1)	2 (< 0.1)	0
Venous thromboembolic events	4 (0.2)	12 (0.6)	2 (< 0.1)‡	3 (0.1)	7 (0.3)	7 (0.3)

Data cutoff: August 8, 2025. * Assessed as medical concepts using grouped terms; all other AEs by medical concept were comparable between arms, including four patients per arm (0.2%) who experienced photopsia. † G2 events occurred in 17 patients; 13 resolved, four patients discontinued treatment and the events resolved. ‡ G3 only. AE, adverse event; ET, endocrine therapy; G, grade; PT, preferred term; SOC, standard-of-care; TEAE, treatment-emergent adverse event.

Presented by: Aditya L. Bardia, MD.

Conclusion

- Confirmation de la place de l'abemaciclib en adjuvant dans notre pratique courante
- Quid du ribociclib : aurons nous un remboursement ?
- Quid du Giredestrant ? Quelle place dans nos schéma adjuvant ? Pour quelles patientes ? Remboursement ?

Cancer du sein RH + avancé/métastatique

- evERA

Giredestrant (GIRE), an oral selective oestrogen receptor (ER) antagonist and degrader, + everolimus (E) in patients (pts) with ER-positive, HER2-negative advanced breast cancer (ER+, HER2– aBC) previously treated with a CDK4/6 inhibitor (i): Primary results of the Phase III evERA BC trial

Erica L. Mayer, Sara M. Tolaney, Miguel Martin, Gregory A. Vidal, Luca Moscetti, Komal L. Jhaveri, Adam Brufsky, William J. Gradishar, Andreas Schneeweiss, Naoki Niikura, Anne Favret, Margarita Alfie, Keun Seok Lee, Sarah Khan, Merilin B. Feldman, Bann-mo Day, Lisa Lam, Walter C. Darbonne, Pablo Perez-Moreno, Hope S. Rugo

Presenting author: Erica L. Mayer, MD, MPH
Dana-Farber Cancer Institute, Boston, MA, USA

Study design

A global, randomised, open-label, Phase III trial

Key eligibility criteria*

- ER+, HER2– aBC (1–3L of therapy)
- ≤ 2 prior lines of ET in the aBC setting
- PD or relapse during/post-CDK4/6i + ET
- No prior chemotherapy in the aBC setting
- Measurable disease per RECIST v1.1 or evaluable bone metastases

Enrolment period: August 2022 to October 2024

N = 373*

R 1:1

Giredestrant (30 mg) + everolimus (10 mg)†

SOC ET‡ + everolimus (10 mg)†
‡Exemestane/fulvestrant/tamoxifen

Until PD or unacceptable toxicity

† Dexamethasone mouthwash prophylaxis and treatment was strongly recommended per SWISH trial protocol[1]

* Trial was enriched to 55% of patients with *ESR1*m at baseline (centrally tested via circulating tumour DNA)

Stratification factors

- Prior treatment with fulvestrant (yes vs no)
- *ESR1*m (yes vs no/indeterminate)
- Site of disease (visceral [lung and/or liver involvement] vs non-visceral)

Co-primary endpoints (RECIST v1.1)

- INV-PFS in patients whose tumours had *ESR1*m
- INV-PFS in the ITT population

Key secondary endpoints

- OS
- INV-assessed ORR, DoR

ClinicalTrials.gov number, NCT05306340. Adapted from Mayer EL, *et al*. SABCS 2022 (poster OT2-01-07) with permission.
1–3L, first to third line; aBC, advanced breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DoR, duration of response; ER+, oestrogen receptor-positive; *ESR1*m, *ESR1* mutation; ET, endocrine therapy; HER2–, HER2-negative; INV, investigator-assessed; ITT, intention to treat; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; SOC ET, standard of care endocrine therapy.

1. Rugo HS, *et al*. *Lancet Oncology* 2017; 18:654–662.

Presented by: Erica L. Mayer, MD, MPH.

Baseline demographics and characteristics (ITT population)

	Giredestrant + everolimus n = 183	SOC ET + everolimus n = 190
Median age, years (range)	62.0 (27–83)	60.0 (28–84)
Female sex, n (%)	182 (99.5)	187 (98.4)
Race, n (%)		
White	103 (56.3)	119 (62.6)
Asian	66 (36.1)	57 (30.0)
Black	9 (4.9)	9 (4.7)
Other	5 (2.7)	5 (2.6)
Region, n (%)		
Asia–Pacific	58 (31.7)	49 (25.8)
North America	69 (37.7)	75 (39.5)
Western Europe	36 (19.7)	43 (22.6)
Other	20 (10.9)	23 (12.1)
Visceral disease (CRF), n (%)*	126 (68.9)	131 (68.9)
Disease involvement in liver	89 (48.6)	100 (52.6)
Bone-only involvement at screening, n (%)	24 (13.1)	22 (11.6)

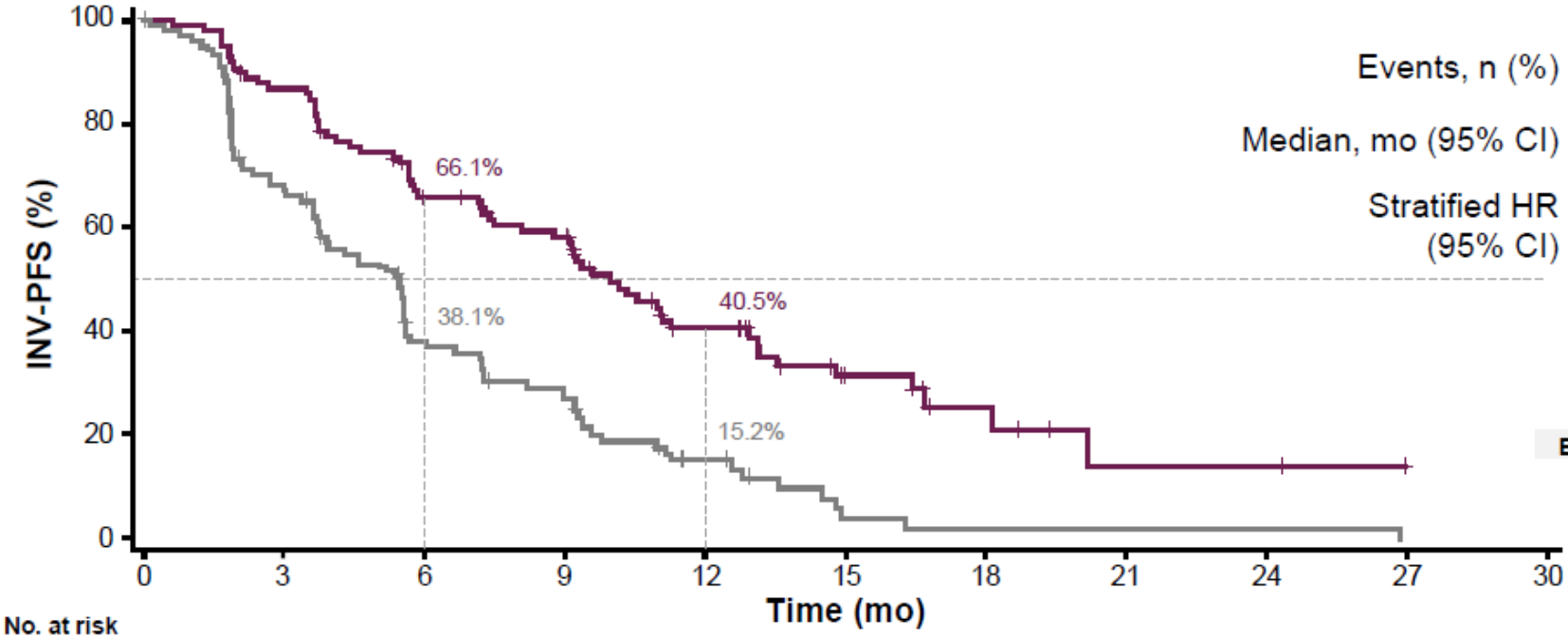
	Giredestrant + everolimus n = 183	SOC ET + everolimus n = 190
Post-menopausal at screening (eCRF), n (%)	156 (85.2)	159 (83.7)
***ESR1*m detected at baseline (central assessment), n (%)**	102 (55.7)	105 (55.3)
***PIK3CA*m detected at baseline (central assessment), n (%)**	64 (35.0)	51 (26.8)
Prior lines of therapy in aBC, n (%)†		
0	3 (1.6)	5 (2.6)
1	140 (76.5)	132 (69.5)
2	40 (21.9)	52 (27.4)
Prior fulvestrant treatment (CRF), n (%)	86 (47.0)	89 (46.8)
Prior CDK4/6i, n (%)	183 (100)	190 (100)
Abemaciclib	53 (29.0)	49 (25.8)
Palbociclib	104 (56.8)	119 (62.6)
Ribociclib	52 (28.4)	54 (28.4)
Prior PI3Ki, n (%)	6 (3.3)	7 (3.7)

Baseline characteristics were balanced in the ITT as well as in the *ESR1*m population

Data cutoff: 16 July 2025; First patient in: 3 August 2022; last patient in: 15 October 2024. * Visceral disease is defined as any lung and/or liver involvement. † None of the patients in the giredestrant + everolimus arm and one patient in SOC ET + everolimus arm had three prior lines of therapy in the aBC setting. aBC, advanced breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CRF, case report form; eCRF, electronic case report form; *ESR1*m, *ESR1* mutation; ET, endocrine therapy; ITT, intention to treat; PI3Ki, phosphatidylinositol 3-kinase inhibitor; *PIK3CA*m, *PIK3CA* mutation; SOC ET, standard of care endocrine therapy.

Presented by: Erica L. Mayer, MD, MPH.

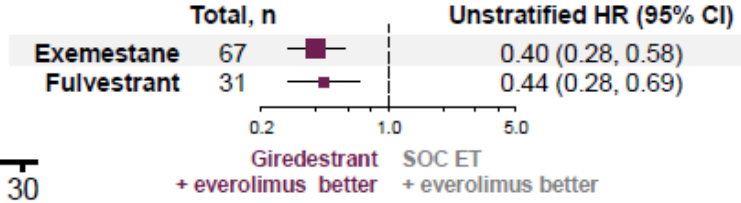
Co-primary endpoint – INV-PFS in the *ESR1*m population



No. at risk									
Giredestrant + everolimus	102	85	61	52	28	13	6	2	2
SOC ET + everolimus	105	67	35	25	10	2	1	1	1

	Giredestrant + everolimus n = 102	SOC ET + everolimus n = 105
Events, n (%)	63 (61.8)	89 (84.8)
Median, mo (95% CI)	**9.99** (8.08, 12.94)	**5.45** (3.75, 5.62)
Stratified HR (95% CI)	**0.38** (0.27, 0.54); p < 0.0001	

Exploratory analysis: INV-PFS by SOC ET

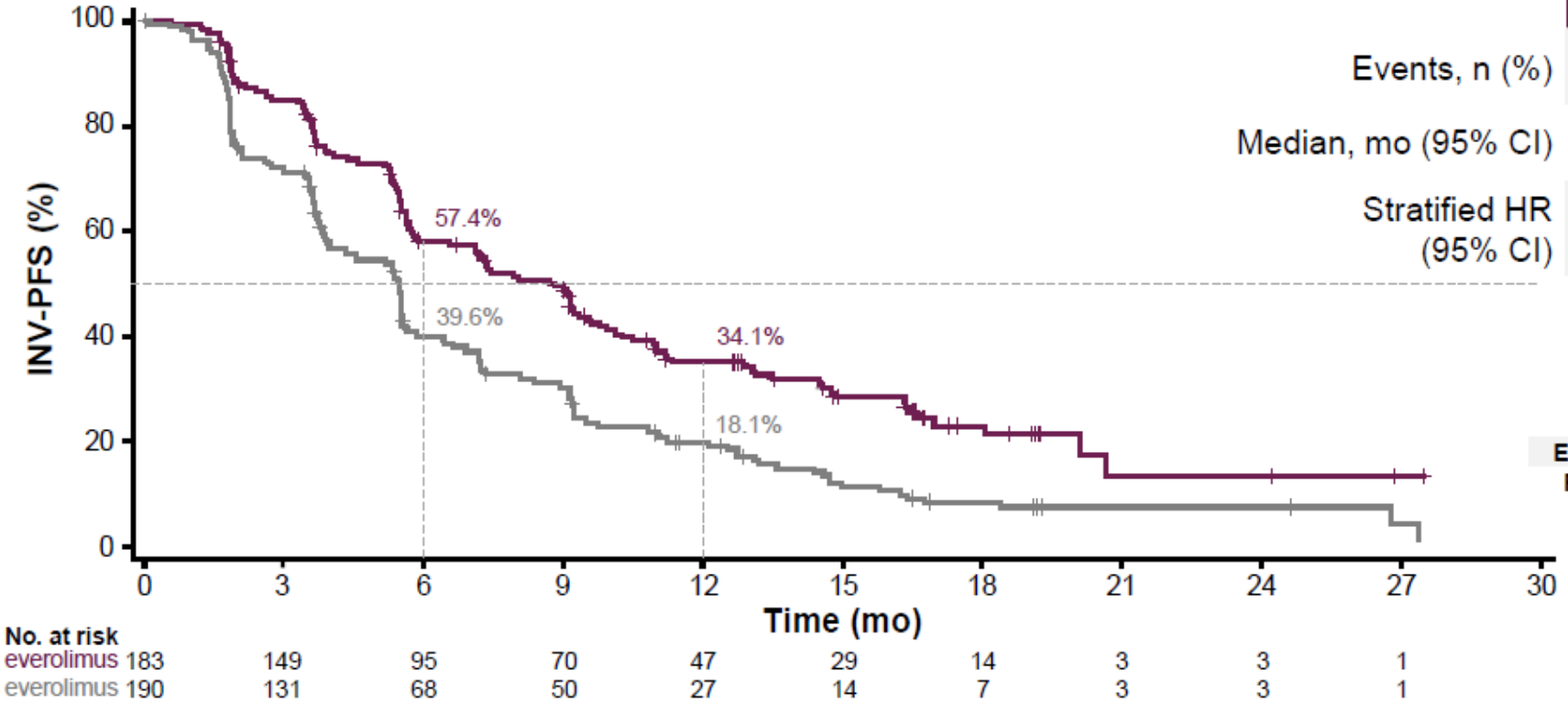


Combination therapy with giredestrant + everolimus led to a clinically meaningful 62% reduction in the risk of progression or death in patients with *ESR1*m

Data cutoff: 16 July 2025. PFS by blinded independent radiologist was similar to INV-PFS: Median PFS was 11.14 mo (giredestrant + everolimus) and 5.68 mo (SOC ET + everolimus); stratified HR, 0.49; 95% CI: 0.34, 0.71.
CI, confidence interval; *ESR1*m, *ESR1* mutation; HR, hazard ratio; INV, investigator-assessed; mo, months; PFS, progression-free survival; SOC ET, standard of care endocrine therapy.

Presented by: Erica L. Mayer, MD, MPH.

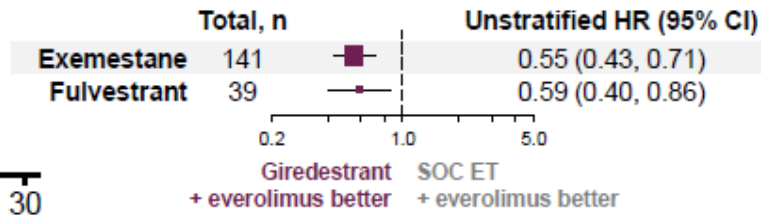
Co-primary endpoint – INV-PFS in the ITT population



No. at risk										
Giredestrant + everolimus	183	149	95	70	47	29	14	3	3	1
SOC ET + everolimus	190	131	68	50	27	14	7	3	3	1

	Giredestrant + everolimus n = 183	SOC ET + everolimus n = 190
Events, n (%)	126 (68.9)	163 (85.8)
Median, mo (95% CI)	8.77 (6.60, 9.59)	5.49 (4.01, 5.59)
Stratified HR (95% CI)	**0.56** (0.44, 0.71); p < 0.0001	

Exploratory analysis: INV-PFS by SOC ET



Combination therapy with giredestrant + everolimus led to a clinically meaningful 44% reduction in the risk of progression or death in patients in the ITT population

Data cutoff: 16 July 2025. PFS by blinded independent radiologist was similar to INV-PFS: Median PFS was 10.32 mo (giredestrant + everolimus) and 7.26 mo (SOC ET + everolimus); stratified HR, 0.66; 95% CI: 0.50, 0.87.
CI, confidence interval; HR, hazard ratio; INV, investigator-assessed; ITT, intention to treat; mo, months; PFS, progression-free survival; SOC ET, standard of care endocrine therapy.

Presented by: Erica L. Mayer, MD, MPH.

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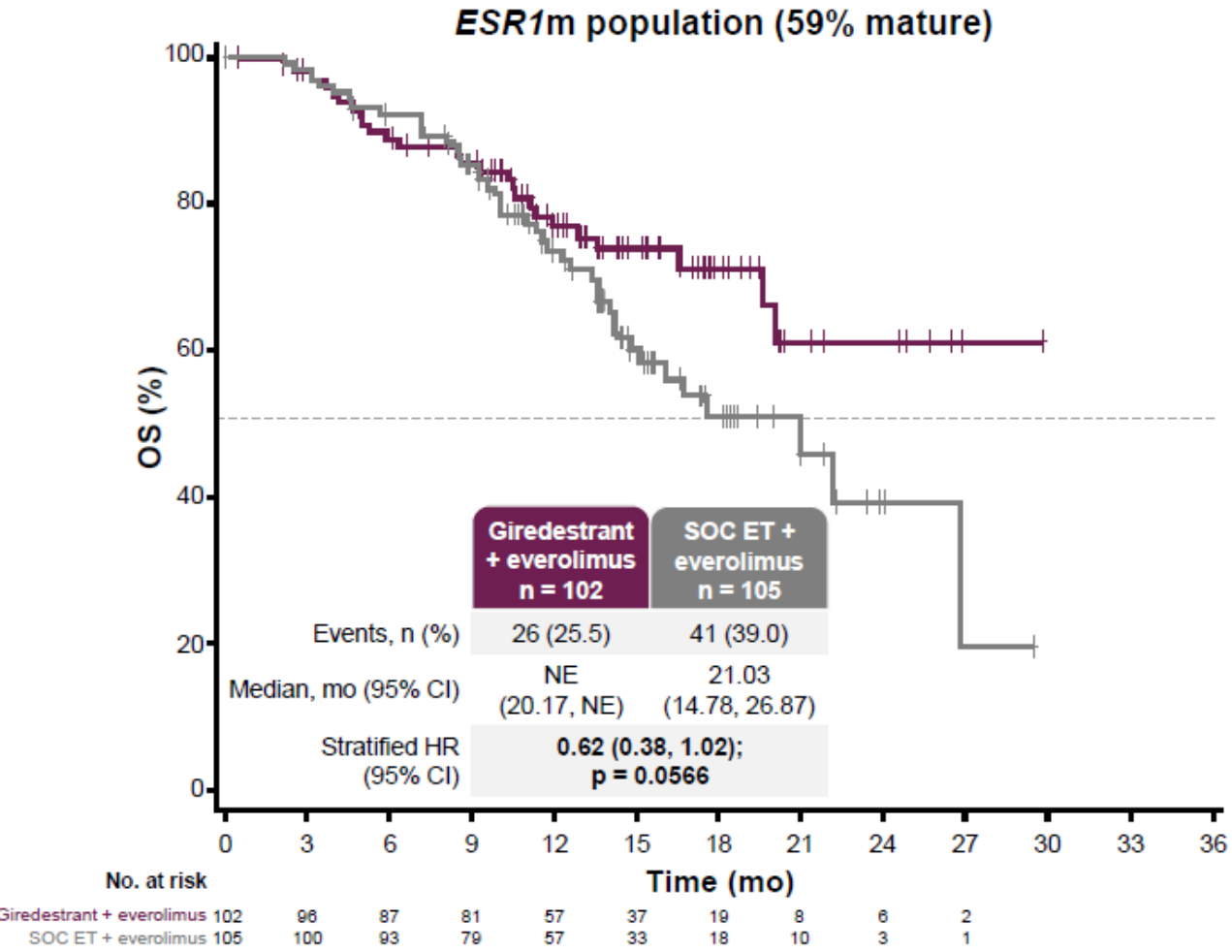
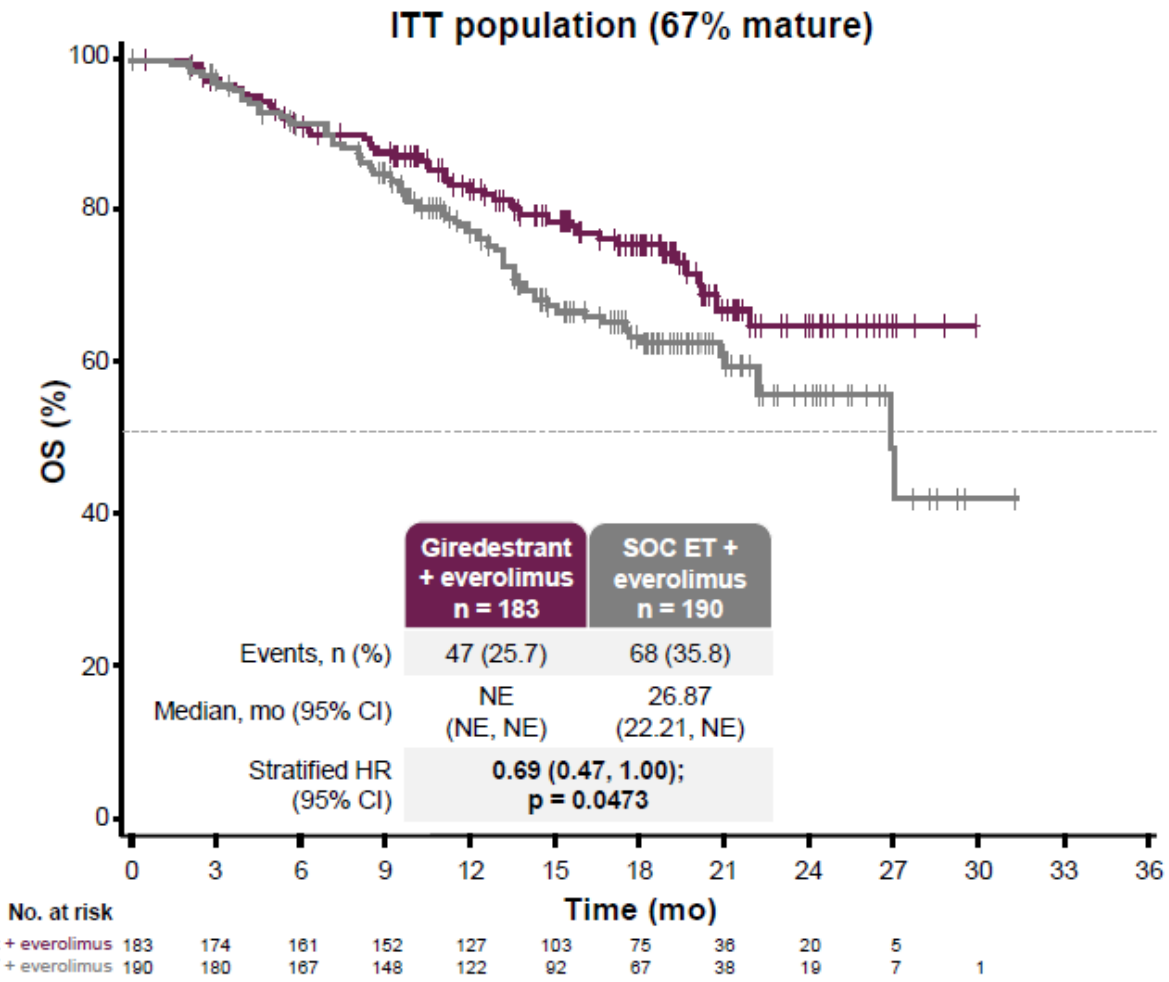
Interim OS in the *ESR1*m and ITT populations

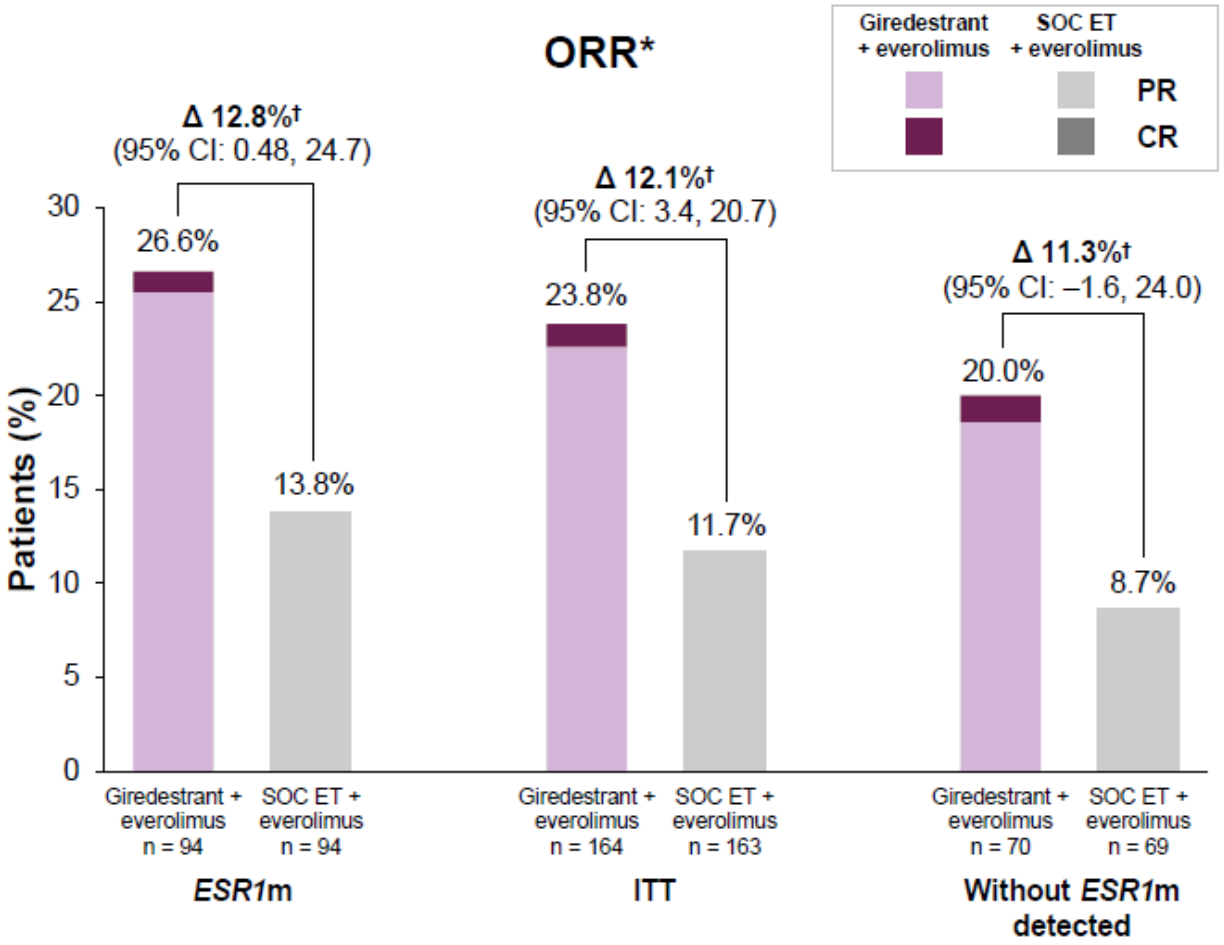


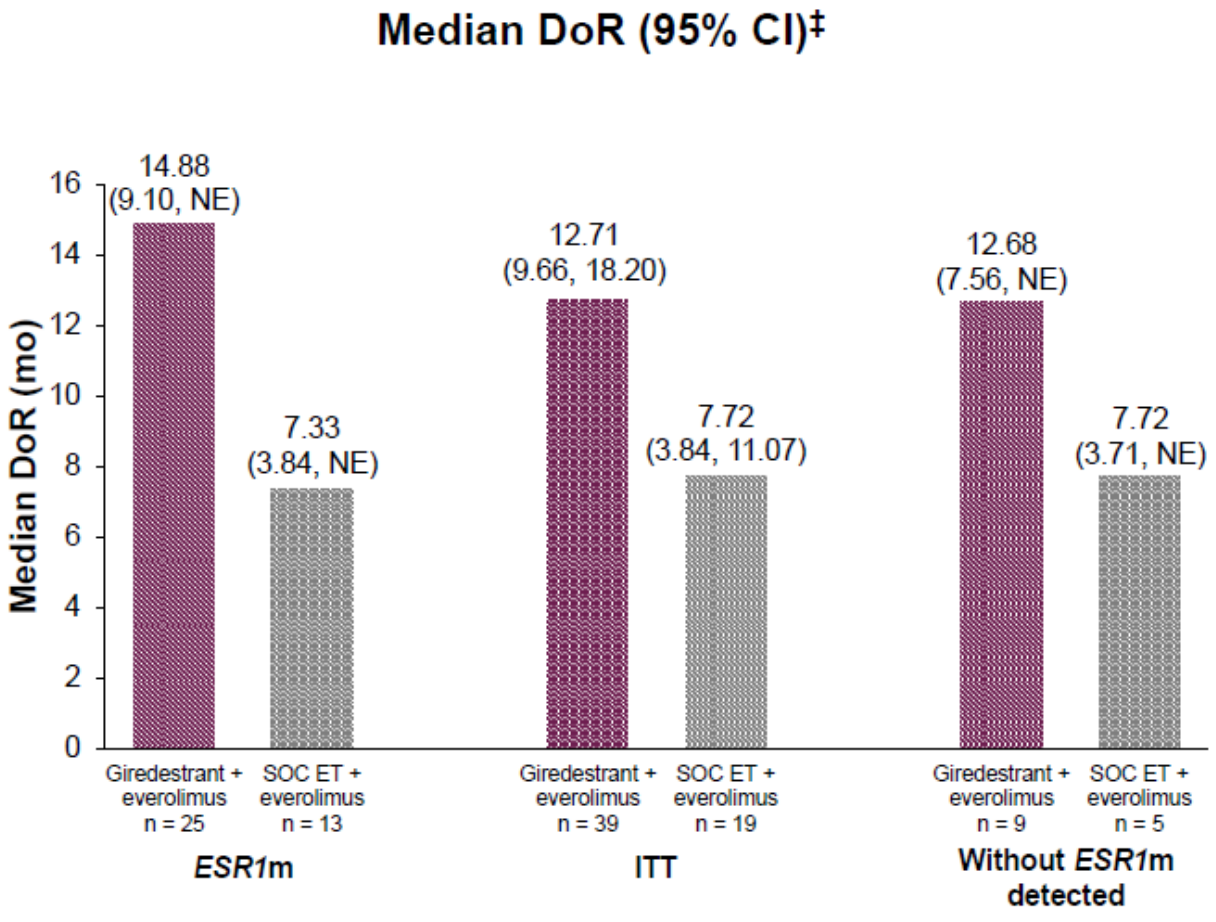


Data cutoff: 16 July 2025. CI, confidence interval; *ESR1*m, *ESR1* mutation; HR, hazard ratio; ITT, intention to treat; mo, months; NE, not evaluable; OS, overall survival; SOC ET, standard of care endocrine therapy.

Presented by: Erica L. Mayer, MD, MPH.

ORR and DoR in the *ESR1*m and ITT populations, and in patients without *ESR1*m detected



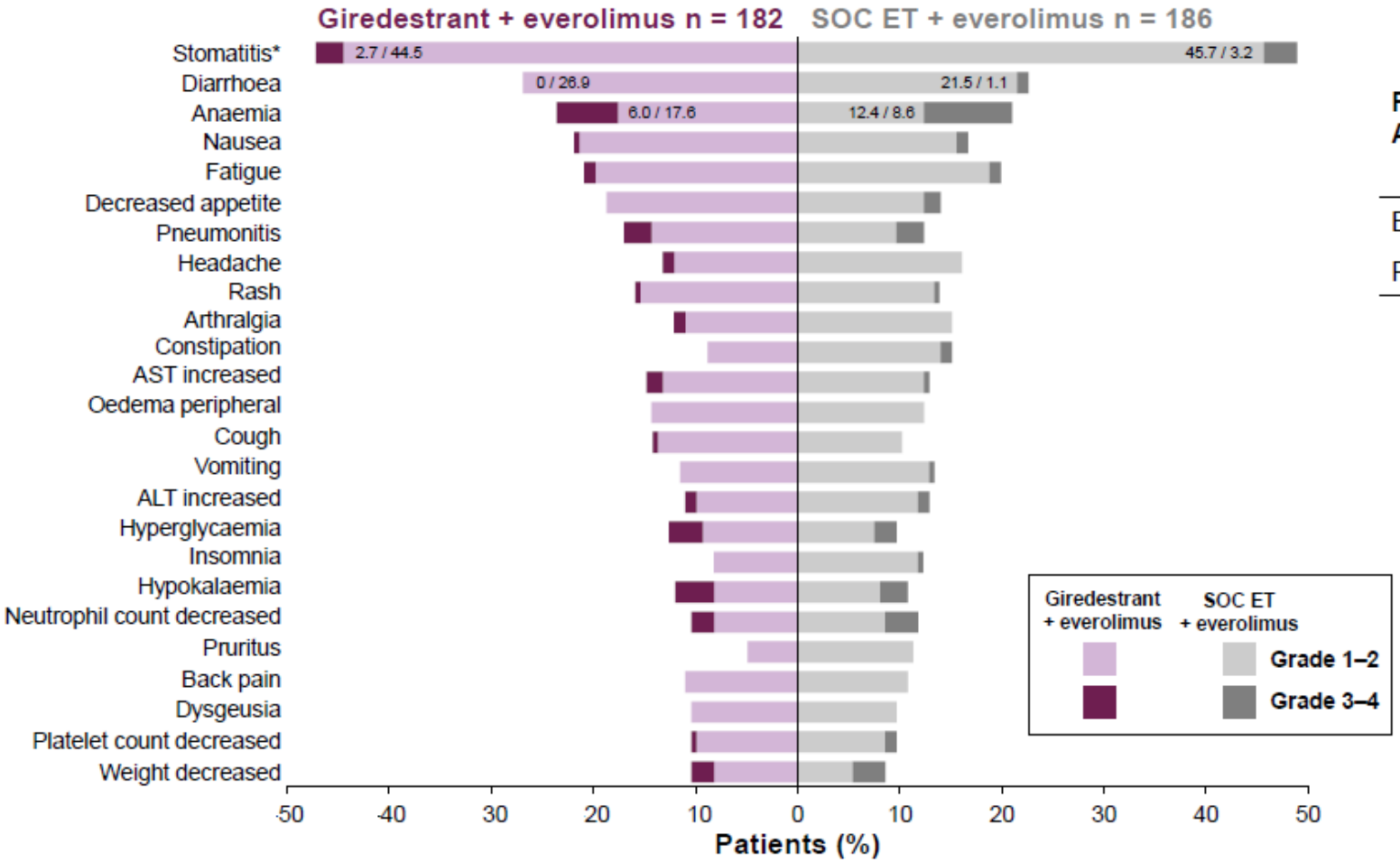


Data cutoff: 16 July 2025. * Patients who had measurable disease at baseline; all responses were confirmed on two consecutive occasions ≥ 4 weeks apart. † Stratified analysis. ‡ Patients who had measurable disease at baseline and an objective response.
CI, confidence interval; CR, complete response; DoR, duration of response; *ESR1*m, *ESR1* mutation; ITT, intention to treat; mo, months; NE, not evaluable; ORR, objective response rate; PR, partial response; SOC ET, standard of care endocrine therapy.

Presented by: Erica L. Mayer, MD, MPH.

AEs overview

Common TEAEs (≥ 10% of patients in either arm)



Selected AEs

Patients with AE, n	Giredestrant + everolimus n = 182		SOC ET + everolimus n = 186	
	Grade 1–2	Grade 3–4	Grade 1–2	Grade 3–4
Bradycardia†	7 (3.8)	0	1 (0.5)	0
Photopsia	0	0	0	0

Data cutoff: 16 July 2025. * Dexamethasone mouthwash prophylaxis and treatment was strongly recommended per SWISH trial protocol (Rugo HS, *et al. Lancet Oncology* 2017; **18**:654–662).
† Assessed as a medical concept using grouped terms; all events were Grade 1, non-serious and no treatment interruptions/interventions were needed. All events had resolved by data cutoff.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; SOC ET, standard of care endocrine therapy; TEAE, treatment-emergent adverse event.

Presented by: Erica L. Mayer, MD, MPH.

Cancer du sein HER2 positif stades précoces

- DB 05
- DB 011

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DESTINY Breast05

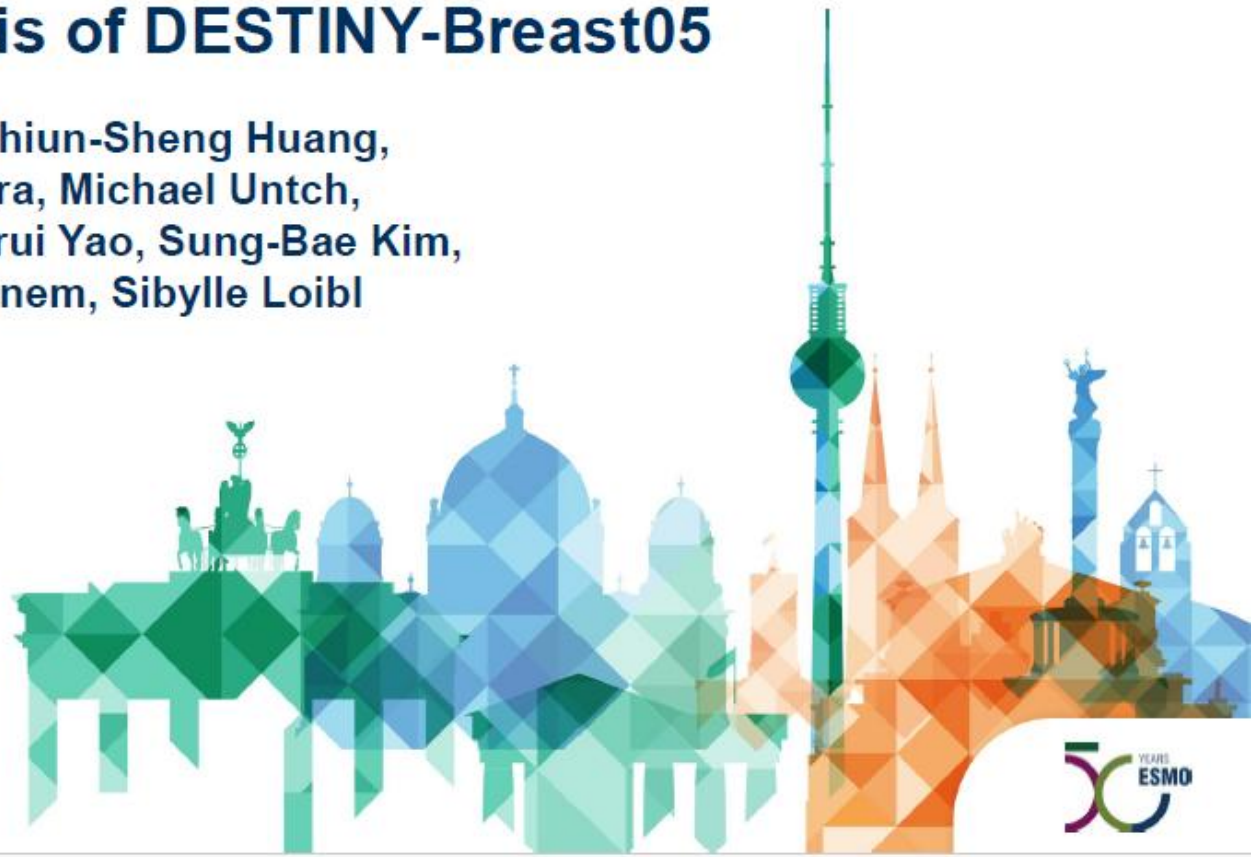
Trastuzumab deruxtecan (T-DXd) vs trastuzumab emtansine (T-DM1) in patients with high-risk human epidermal growth factor receptor 2–positive (HER2+) primary breast cancer with residual invasive disease after neoadjuvant therapy: Interim analysis of DESTINY-Breast05

Charles E Geyer Jr,[a,b] Yeon Hee Park, Zhiming Shao, Chiun-Sheng Huang, Carlos Barrios, Jame Abraham, Aleix Prat, Naoki Niikura, Michael Untch, Seock-Ah Im, Wei Li, Huiping Li, Yongsheng Wang, Herui Yao, Sung-Bae Kim, Elton Mathias, Yuta Sato, Wenjing Lu, Hanan Abdel-Monem, Sibylle Loibl

On behalf of the DESTINY-Breast05 investigators

[a]NSABP Foundation, Pittsburgh, PA, USA
[b]University of Pittsburgh Hillman Cancer Center, Pittsburgh, PA, USA

Saturday, October 18, 2025
Presentation LBA1



NSABP National Surgical Adjuvant Breast and Bowel Project · GBG German Breast Group · AGO-B Breast Study Group · SOLTI

50 YEARS ESMO

DESTINY-Breast05 study design

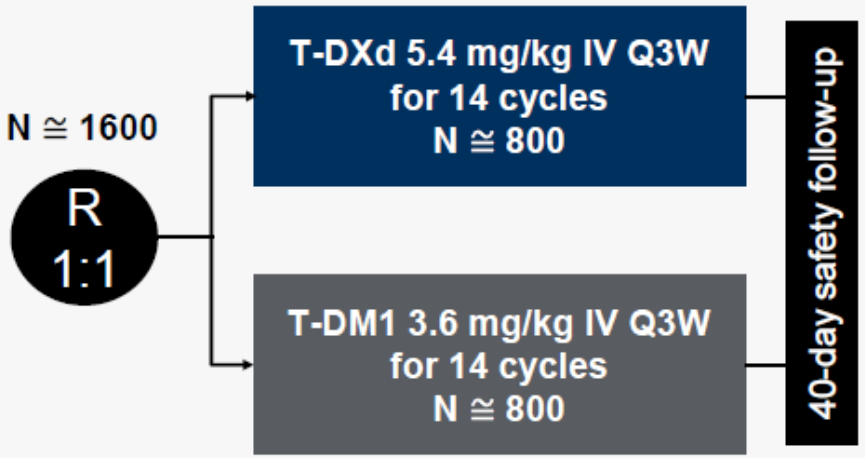
A global, multicenter, randomized, open-label, phase 3 trial (NCT04622319)

Key Eligibility Criteria

- **Residual invasive disease in the breast and/or axillary lymph nodes** after neoadjuvant chemotherapy with HER2-directed therapy (NAT)[a]
- **High-risk defined as presentation prior to NAT with:**
  - **Inoperable eBC (cT4,N0-3,M0 or cT1-3,N2-3,M0) OR**
  - **Operable eBC (cT1-3,N0-1,M0) with axillary node–positive disease (ypN1-3) after NAT**
- **Centrally confirmed HER2+** (IHC 3+ or ISH+) eBC
- ECOG PS 0 or 1

Stratification factors

- Extent of disease at presentation (inoperable, operable)
- HER2-targeted NAT (single, dual)
- Hormone receptor status (positive, negative)
- Post-NAT pathologic nodal status (positive, negative)



Primary endpoint

- IDFS

Key secondary endpoint

- DFS

Other secondary endpoints

- OS
- DRFI
- BMFI
- Safety

- **Concomitant adjuvant ET was allowed per local practices**
- **If administered, RT could be initiated concurrent with study therapy or completed prior to initiation of study therapy (sequential) per investigator**
- **ILD monitoring program for patients treated with RT**
  - All patients had baseline non-contrast, low dose (LD) chest CT during screening
  - All RT patients (concurrent and sequential) had LD chest CT 6 weeks after start of study therapy, then every 12 weeks while on therapy, and at 40-day follow-up
  - Sequential RT patients had additional LD chest CT after completion of RT prior to start of study therapy

BMFI, brain metastasis–free interval; CT, computed tomography; eBC, early breast cancer; DCO, data cutoff; DFS, disease-free survival; DRFI, distant recurrence–free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; IDFS, invasive disease–free survival; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; IV, intravenous; NAT, neoadjuvant therapy; OS, overall survival; Q3W, every 3 weeks; R, randomization; RT, radiotherapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]NAT is defined as ≥16 weeks' NAT with ≥9 weeks trastuzumab ± pertuzumab and ≥9 weeks taxane-based chemotherapy.

Dr Charles E Geyer Jr

Baseline demographics and clinical characteristics

	T-DXd n = 818	T-DM1 n = 817
Age, median (range), years	50.3 (24-78)	50.6 (21-83)
<65	735 (89.9)	736 (90.1)
≥65	83 (10.1)	81 (9.9)
Female sex, n (%)	814 (99.5)	814 (99.6)
Race		
White	301 (36.8)	333 (40.8)
Black or African American	22 (2.7)	13 (1.6)
Asian	**399 (48.8)**	**386 (47.2)**
Other	96 (11.7)	85 (10.4)
Region, n (%)		
Asia	**392 (47.9)**	**380 (46.5)**
Europe	222 (27.1)	223 (27.3)
North America + Australia	57 (7.0)	72 (8.8)
Rest of world[a]	147 (18.0)	142 (17.4)
ECOG PS score, n (%)		
0	656 (80.2)	652 (79.8)
1	162 (19.8)	165 (20.2)
HER2 expression,[b] n (%)		
IHC 3+	**676 (82.6)**	**670 (82.0)**
IHC 2+ and ISH+	129 (15.8)	133 (16.3)
IHC 2+ and ISH−	2 (0.2)	0
IHC 1+ and ISH+	11 (1.3)	14 (1.7)
Hormone receptor status,[c] n (%)		
Positive	**581 (71.0)**	**583 (71.4)**
Negative	237 (29.0)	234 (28.6)

	T-DXd n = 818	T-DM1 n = 817
Operative status at disease presentation,[c] n (%)		
Operable (cT1-3, N0-1, M0)	387 (47.3)	393 (48.1)
Inoperable (cT4, N0-3, M0 or cT1-3, N2-3, M0)	**431 (52.7)**	**424 (51.9)**
Post-NAT pathologic nodal status,[c] n (%)		
Positive	**660 (80.7)**	**658 (80.5)**
Negative	158 (19.3)	159 (19.5)
Neoadjuvant HER2-targeted therapy, n (%)		
Trastuzumab alone	176 (21.5)	171 (20.9)
Trastuzumab + pertuzumab	**637 (77.9)**	**641 (78.5)**
Trastuzumab + other HER2-targeted therapy	3 (0.4)	3 (0.4)
Trastuzumab + pertuzumab + other HER2-targeted therapy	2 (0.2)	2 (0.2)
Neoadjuvant chemotherapy, n (%)		
Taxanes	818 (100)	817 (100)
Platinum compounds	386 (47.2)	392 (48.0)
Anthracycline	**423 (51.7)**	**399 (48.8)**
Radiotherapy treatment, n (%)		
Adjuvant radiotherapy	**764 (93.4)**	**759 (92.9)**
Concurrent	438 (53.5)	480 (58.8)
Sequential	326 (39.9)	279 (34.1)
No radiotherapy	54 (6.6)	58 (7.1)

ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; NAT, neoadjuvant therapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]Included regions: Argentina, Brazil, Chile, Czech Republic, Israel, Mexico, Peru, Poland, Romania, Russian Federation. [b]Centrally confirmed. [c]As reported in electronic data capture.

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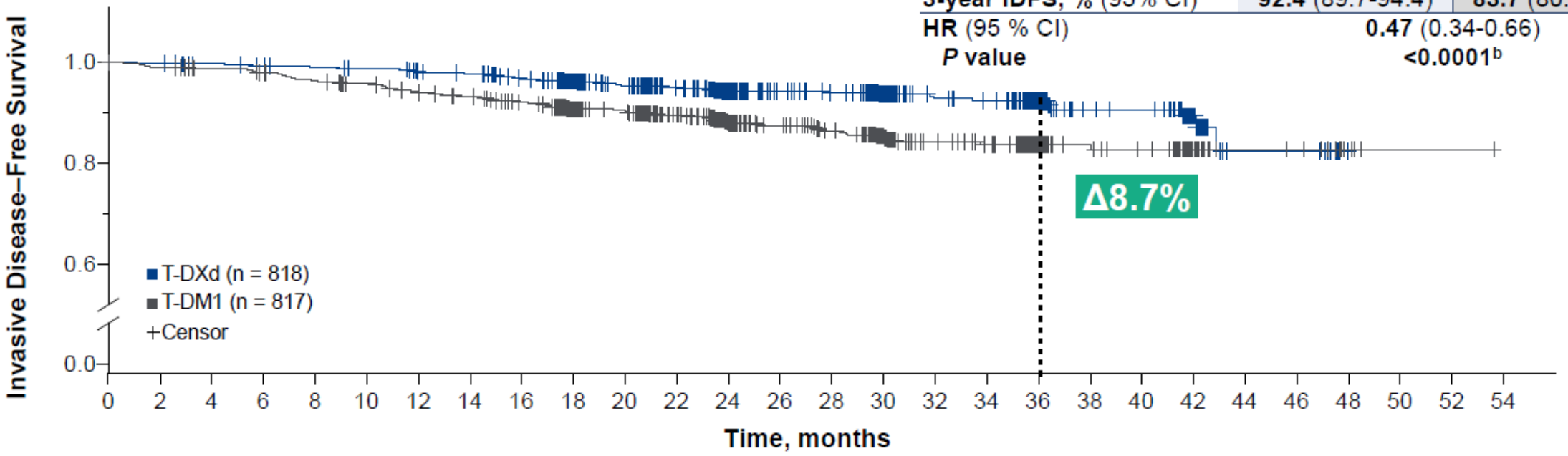
Primary endpoint: IDFS[a]

	T-DXd n = 818	T-DM1 n = 817
Patients with events, n (%)	**51** (6.2)	**102** (12.5)
3-year IDFS, % (95% CI)	**92.4** (89.7-94.4)	**83.7** (80.2-86.7)
HR (95 % CI)	**0.47** (0.34-0.66)	
***P* value**	**<0.0001[b]**	



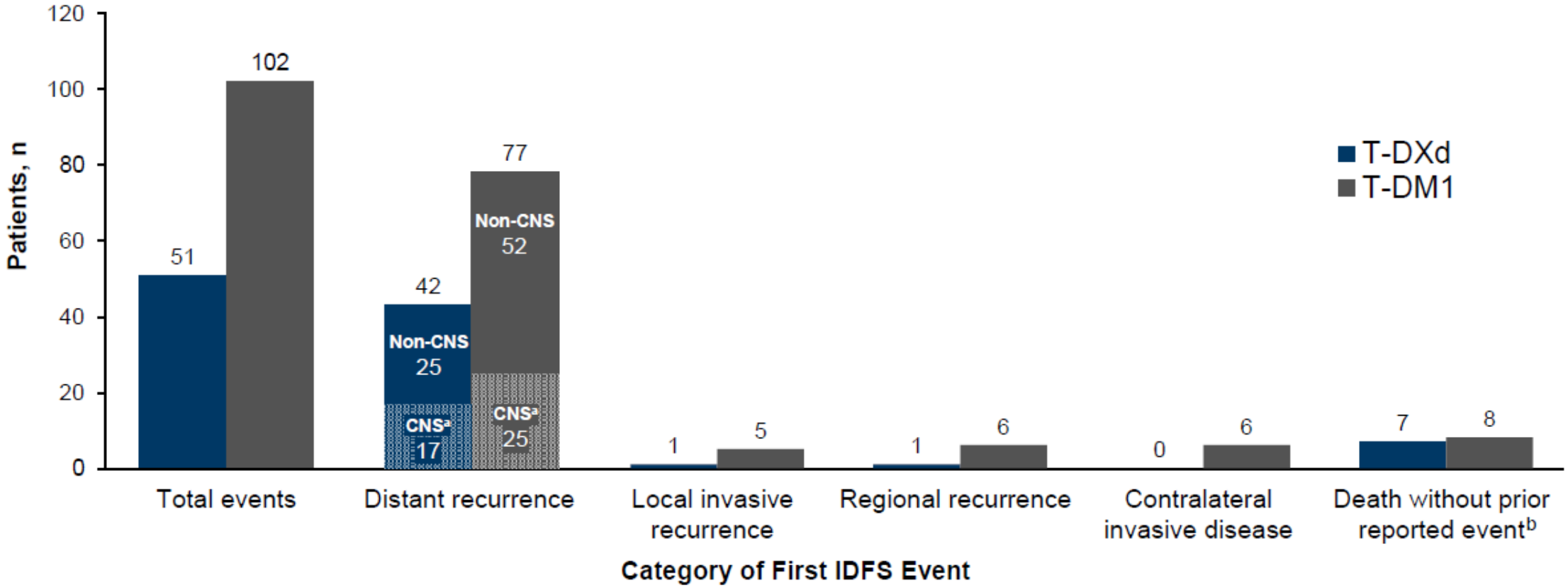
Number at Risk:

T-DXd	818	788	781	776	771	768	758	753	731	684	634	544	440	380	370	275	218	212	129	92	90	46	14	14	0	0	0	0
T-DM1	817	781	769	760	745	734	719	708	687	632	599	527	417	355	337	233	186	177	120	84	79	38	14	13	4	1	1	0

53% reduction in the risk of invasive disease recurrence or death for T-DXd compared with T-DM1

HR, hazard ratio; IDFS, invasive disease–free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Efficacy stopping boundary, *P* = 0.0183.
[a]IDFS is defined as the time from randomization until the date of first occurrence of one of the following events: recurrence of ipsilateral invasive breast tumor, recurrence of ipsilateral locoregional invasive breast cancer, contralateral invasive breast cancer, a distant disease recurrence, or death from any cause. [b]Two-sided *P* value from stratified log-rank test. Hazard ratio and 95% CI from stratified Cox proportional hazards model with stratification factor of operative status at disease presentation.

Categories of first IDFS events



Lower distant and locoregional recurrences were observed with T-DXd vs T-DM1, including CNS recurrences

IDFS, invasive disease–free survival; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
Participants who experienced multiple types of IDFS events within 61 days of their first event are reported in the category according to the following hierarchy: distant recurrence CNS, distant recurrence non-CNS, local invasive recurrence, regional recurrence, contralateral breast cancer, and death without a previous event.
[a]CNS as sole site for distant recurrence or one of multiple distance recurrent sites [b]Causes of death in the T-DXd arm were 2 drug-related ILD, unrelated respiratory tract infection, acute respiratory failure (outside AE reporting period), acute respiratory distress syndrome (outside AE reporting period), and 2 disease progression, and in the T-DM1 arm were drug-related sepsis, unrelated ovarian cancer, unrelated aneurysm, unrelated pneumothorax, unrelated leiomyosarcoma, self-inflicted gun wound, and 2 disease progression.

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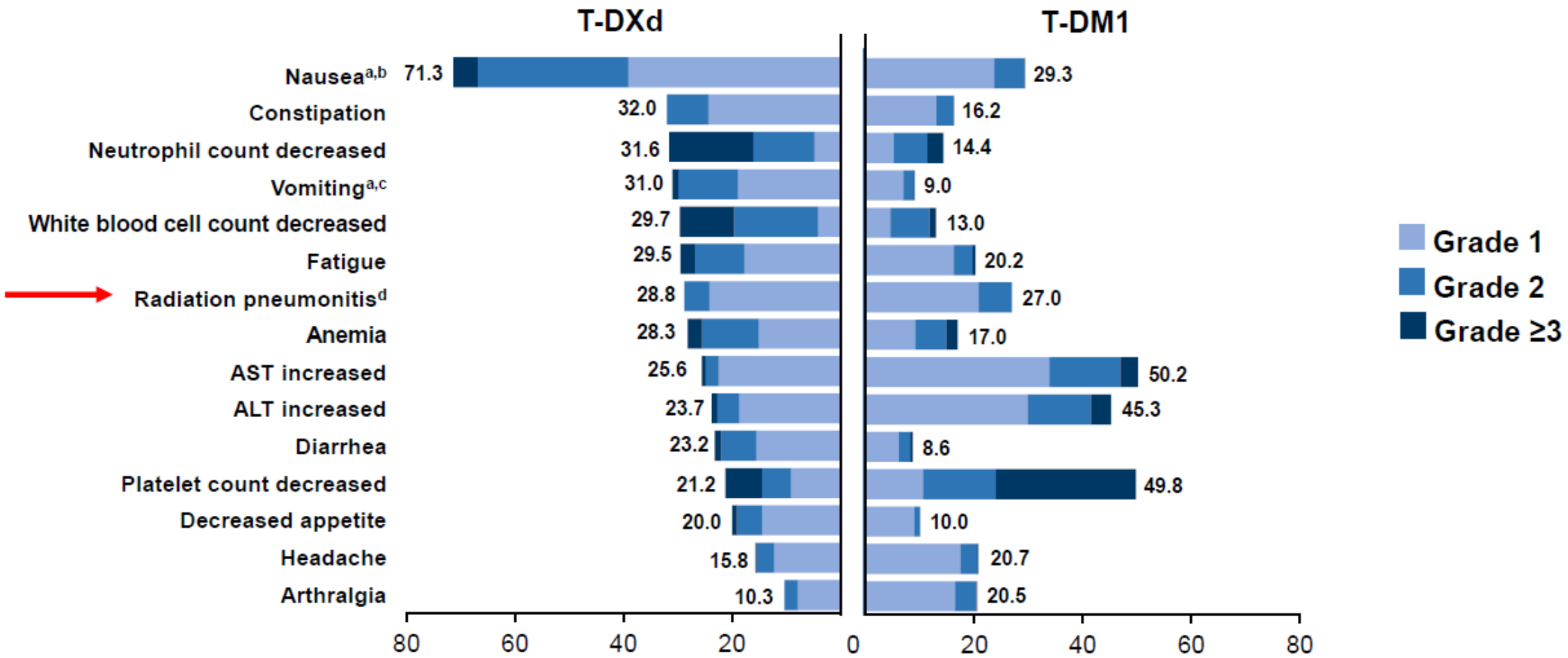
TEAEs in ≥20% of patients (either arm)



ALT, alanine aminotransferase; AST, aspartate aminotransferase; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event.
[a]Prophylactic antiemetics were recommended but not mandatory. [b]In the T-DXd and T-DM1 arms: 39.1% and 23.7% grade 1, 27.8% and 5.5% grade 2, and 4.5% and 0.1% grade 3 events, respectively. [c]In the T-DXd and T-DM1 arms: 19.0% and 6.9% grade 1, 10.9% and 2.0% grade 2, and 1.1% and 0.1% grade 3 events. [d]In the T-DXd and T-DM1 arms: 24.2% and 20.8% grade 1, 4.6% and 6.1% grade 2 events.

Adverse events of special interest: ILD/pneumonitis and LV dysfunction

n (%)	Adjudicated Drug-related ILD					
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
T-DXd (n = 806)[a]	77 (9.6)	16 (2.0)	52 (6.5)	7 (0.9)	0	2 (0.2)
T-DM1 (n = 801)[a]	13 (1.6)	8 (1.0)	5 (0.6)	0	0	0

Adjuvant radiotherapy timing (sequential or concurrent) showed no differences in adjudicated drug-related ILD

Similar distributions of any grade adjudicated drug-related ILD events were observed with sequential and concurrent radiotherapy in both treatment arms (T-DXd: 10.7% and 9.6.% vs T-DM1: 2.6% and 1.0%, respectively)

n (%)	LV dysfunction					
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
T-DXd (n = 806)[a]	23 (2.9)	1 (0.1)	20 (2.5)	2 (0.2)	0	0
T-DM1 (n = 801)[a]	14 (1.7)	0	11 (1.4)	3 (0.4)	0	0

CT, computed tomography; ILD, interstitial lung disease; LV, left ventricular; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.
[a]All patients who received at least 1 dose of study treatment.

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BERLIN 2025 ESMO congress

DESTINY Breast11

DESTINY-Breast11: neoadjuvant trastuzumab deruxtecan alone or followed by paclitaxel + trastuzumab + pertuzumab vs ddAC-THP for high-risk HER2+ early breast cancer

Nadia Harbeck

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Co-authors: Shanu Modi, Lajos Pusztai, Shinji Ohno, Jiong Wu, Sung-Bae Kim, Alessandra Fabi, Xuchen Cao, Rona Joseph, Rubi Li, Bogdan Żurawski, Santiago Escrivá-de-Romaní, Shin-Cheh Chen, Catherine Kelly, Giuseppe Curigliano, William Fraser Symmans, Shoubhik Mondal, Shahana Safdar, Pia Herbolsheimer, Jean-François Boileau
On behalf of the DESTINY-Breast11 investigators

Saturday October 18, 2025

Presentation 291O

50 YEARS ESMO

DESTINY-Breast11 study design

A randomized, global, multicenter, open-label, Phase 3 study (NCT05113251)

Patient population

- Previously untreated HER2+ eBC
- HR-positive or HR-negative
- High-risk defined as:
  - ≥cT3 and N0–3 or cT0–4 and N1–3
  - Inflammatory BC

Randomized 1:1:1

- n=321 → T-DXd* → THP† (4 + 4 cycles)
- n=320 → ddAC‡ → THP§ (4 + 4 cycles)
- n=286 → T-DXd* (8 cycles)

→ Surgery¶

Recommended post-neoadjuvant treatment per study protocol‖

pCR: radiotherapy and concomitant trastuzumab ± pertuzumab for up to 1 year

No pCR: radiotherapy and T-DM1 for up to 14 cycles

HR-positive: endocrine therapy

Stratification factors

- HR status: ER and/or PR-positive or negative
- HER2 status: (IHC 3+ or ISH+ in the absence of IHC 3+ status)

The T-DXd alone arm closed on March 13 2024, following Independent Data Monitoring Committee recommendation

The reasons were multifactorial, including a lower pCR rate, low likelihood that T-DXd alone would be superior to ddAC-THP, and the timing of surgery

Data cutoff: March 12, 2025

Primary endpoint

- pCR (ypT0/is ypN0) by blinded central review

Secondary endpoints

- pCR (ypT0 ypN0) by blinded central review
- EFS
- Safety
- Pharmacokinetics and immunogenicity
- Invasive disease-free survival
- Overall survival
- Health-related quality of life

Additional outcome measures

- Residual cancer burden (RCB)

High-resolution computed tomography chest scans were performed every 6 weeks during treatment; if ILD/pneumonitis was suspected while receiving T-DXd, treatment was interrupted and a full investigation completed. Echocardiograms or multigated acquisition scans were performed during screening (<28 days prior to randomization), during treatment (<3 days before Cycle 5), and at end of treatment to assess left ventricular ejection fraction. *5.4 mg/kg Q3W; †paclitaxel (80 mg/m² QW) + trastuzumab (6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W); ‡doxorubicin (60 mg/m² Q2W) + cyclophosphamide (600 mg/m² Q2W); §paclitaxel (80 mg/m² QW) + trastuzumab (8 mg/kg loading dose followed by 6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W); ¶the recommended window for surgery was 3–6 weeks following administration of the last dose of neoadjuvant study treatment; ‖administered as part of the patient's SOC at the investigator's discretion. cT, clinical tumor stage; ER, estrogen receptor; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH+, in situ hybridization–positive; N, nodal stage; PR, progesterone receptor; QXW, every X weeks; T-DM1, trastuzumab emtansine; ypT0/is ypN0, absence of invasive cancer in the breast and axillary nodes; ypT0 ypN0, absence of invasive and in-situ cancer in the breast and axillary nodes

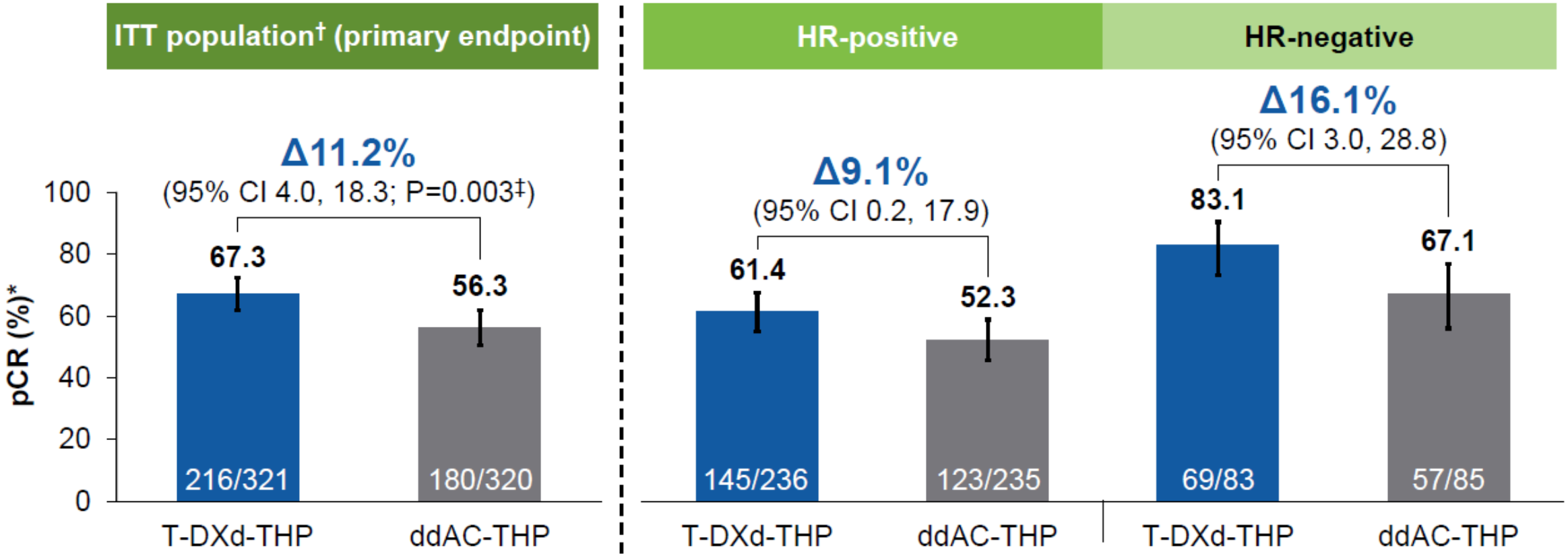
Nadia Harbeck, MD

Patient demographics and key baseline characteristics

		T-DXd-THP (n=321)	ddAC-THP (n=320)	T-DXd (n=286)
Median (range) age, years		50 (25–82)	50 (23–79)	50 (23–79)
Female, n (%)		321 (100)	320 (100)	286 (100)
Geographical region, n (%)	Asia	152 (47.4)	152 (47.5)	124 (43.4)
	Western Europe	69 (21.5)	77 (24.1)	66 (23.1)
	North America	43 (13.4)	41 (12.8)	52 (18.2)
	Rest of world*	57 (17.8)	50 (15.6)	44 (15.4)
Race, n (%)†	Asian	160 (49.8)	157 (49.1)	127 (44.4)
	White	140 (43.6)	137 (42.8)	139 (48.6)
	Black or African American	5 (1.6)	7 (2.2)	7 (2.4)
	Other	12 (3.7)	10 (3.1)	8 (2.8)
Eastern Cooperative Oncology Group performance status score, n (%)	0	278 (86.6)	280 (87.5)	252 (88.1)
	1	43 (13.4)	40 (12.5)	34 (11.9)
HER2 status, n (%)‡	IHC 3+	280 (87.2)	283 (88.4)	254 (88.8)
	Other	40 (12.5)	36 (11.3)	32 (11.2)
HR status, n (%)§	Positive¶	236 (73.5)	235 (73.4)	205 (71.7)
Clinical tumor stage, n (%)	cT0–2	176 (54.8)	188 (58.8)	157 (54.9)
	cT3–4	145 (45.2)	132 (41.3)	129 (45.1)
Nodal status, n (%)‖	N0	26 (8.1)	35 (10.9)	20 (7.0)
	N+	287 (89.4)	281 (87.8)	254 (88.8)

*Brazil, Bulgaria, Peru, Poland, Russia, and Saudi Arabia; †not reported for four patients (1.2%), nine patients (2.8%) and five patients (1.7%) in the T-DXd-THP, ddAC-THP, and T-DXd alone arms, respectively; ‡centrally confirmed. Not categorized for one patient (0.3%) in the T-DXd-THP arm and missing for one patient (0.3%) in the ddAC-THP arm; §the proportion of patients with HR-negative disease was capped at 30% to reflect natural prevalence. Missing for two patients (0.6%) and one patient (0.3%) in the T-DXd-THP and T-DXd alone arms, respectively; ¶ER and/or PR-positive per electronic case report form data; ‖unknown in eight patients (2.5%), four patients (1.3%), and 12 patients (4.2%) in the T-DXd-THP, ddAC-THP, and T-DXd alone arms, respectively

pCR (ypT0/is ypN0): primary endpoint



Neoadjuvant T-DXd-THP demonstrated a statistically significant and clinically meaningful improvement in pCR vs ddAC-THP

Improvement was observed in both the HR-positive and HR-negative subgroups

For the ITT population, treatment effects were estimated by the difference in pCR with 95% CIs and P-values based on the stratified Miettinen and Nurminen's method, with strata weighting by sample size (ie Mantel–Haenszel weights)

Patients with no valid records regarding pCR status for any reason were considered to be non-responders (including but not limited to withdrawal from the study, progression of disease or death before surgery, lack of surgical specimen, or defined as not evaluable by the central pathologist). Subgroup analyses were unstratified. *By blinded central review; †pCR responders were defined as patients who only received randomized study treatment (at least one dose) and had pCR; ‡two-sided P-value crossed the 0.03 prespecified boundary. ITT, intent-to-treat

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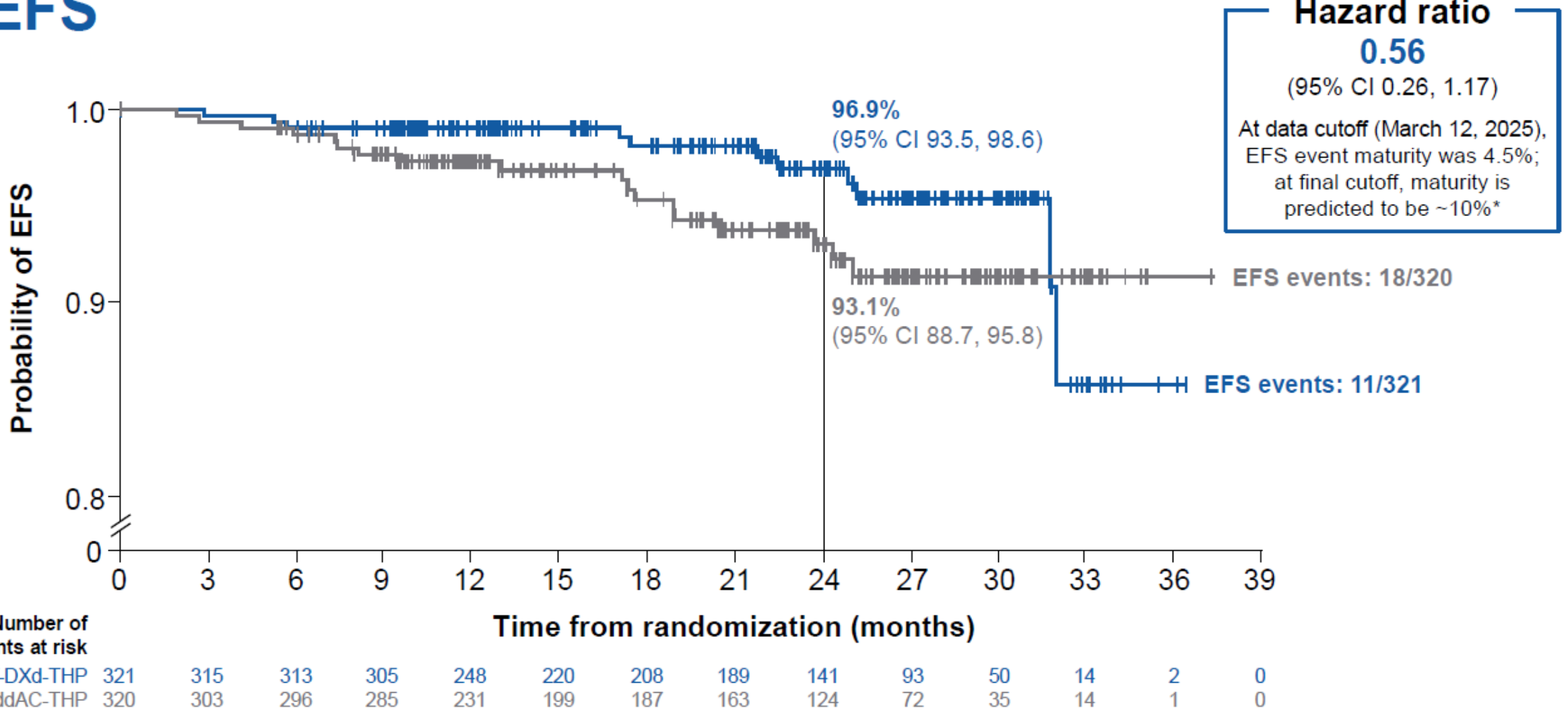
EFS

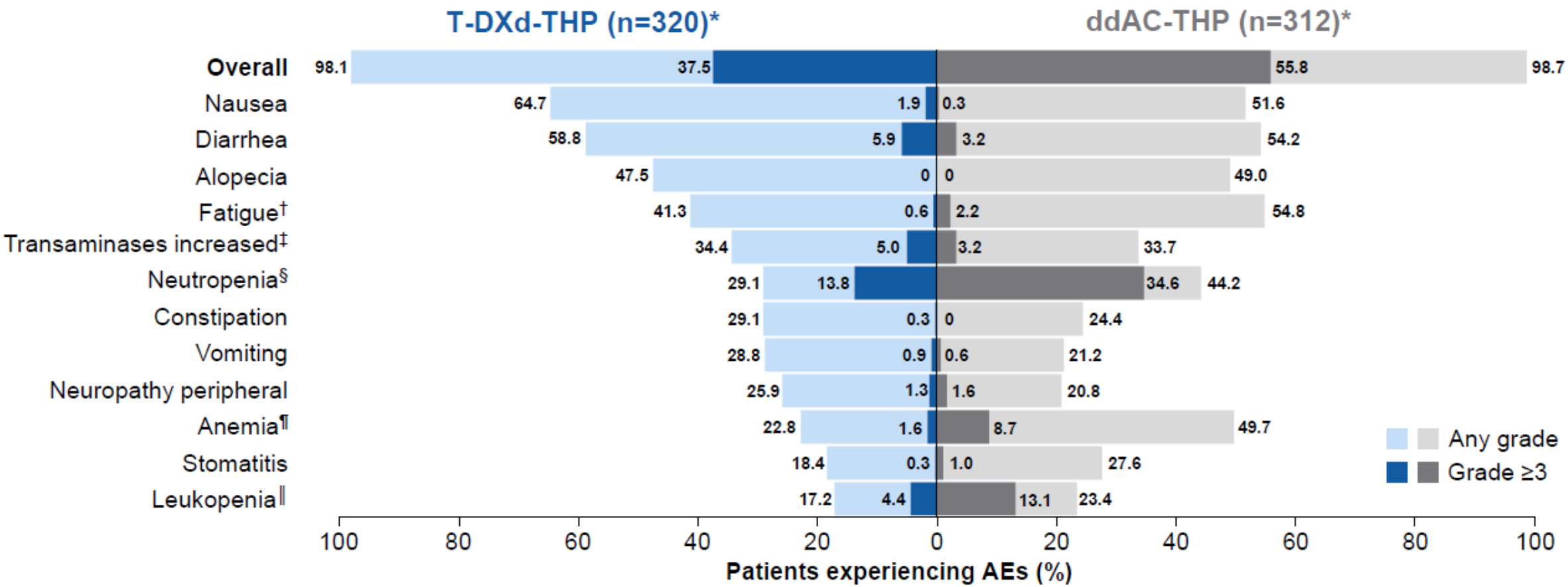


Number of patients at risk														
T-DXd-THP	321	315	313	305	248	220	208	189	141	93	50	14	2	0
ddAC-THP	320	303	296	285	231	199	187	163	124	72	35	14	1	0

An early positive trend in EFS was observed, favoring T-DXd-THP vs ddAC-THP

The median duration of follow up was 24.3 months with T-DXd-THP and 23.6 months with ddAC-THP. *Predicted maturity assumes that the observed EFS hazard ratio continues after data cutoff (March 12, 2025)

TEAEs in at least 20% of patients in either arm



T-DXd-THP had fewer any-grade and Grade ≥3 hematological and fatigue events than ddAC-THP
Aside from nausea, gastrointestinal toxicity was comparable between arms

*Safety analyses included all patients who received at least one dose of any study treatment; †grouped term: fatigue, asthenia, malaise, and lethargy; ‡grouped term: transaminases increased, aspartate transaminase increased, alanine transaminase increased, gamma-glutamyl transferase increased, liver function test abnormal, hypertransaminasemia, hepatic function abnormal, and liver function test increased; §grouped term: neutrophil count decreased and neutropenia; ¶grouped term: hemoglobin decreased, red blood cell count decreased, and anemia and hematocrit decreased; ‖grouped term: white blood cell count decreased and leukopenia. TEAE, treatment-emergent adverse event

Nadia Harbeck, MD

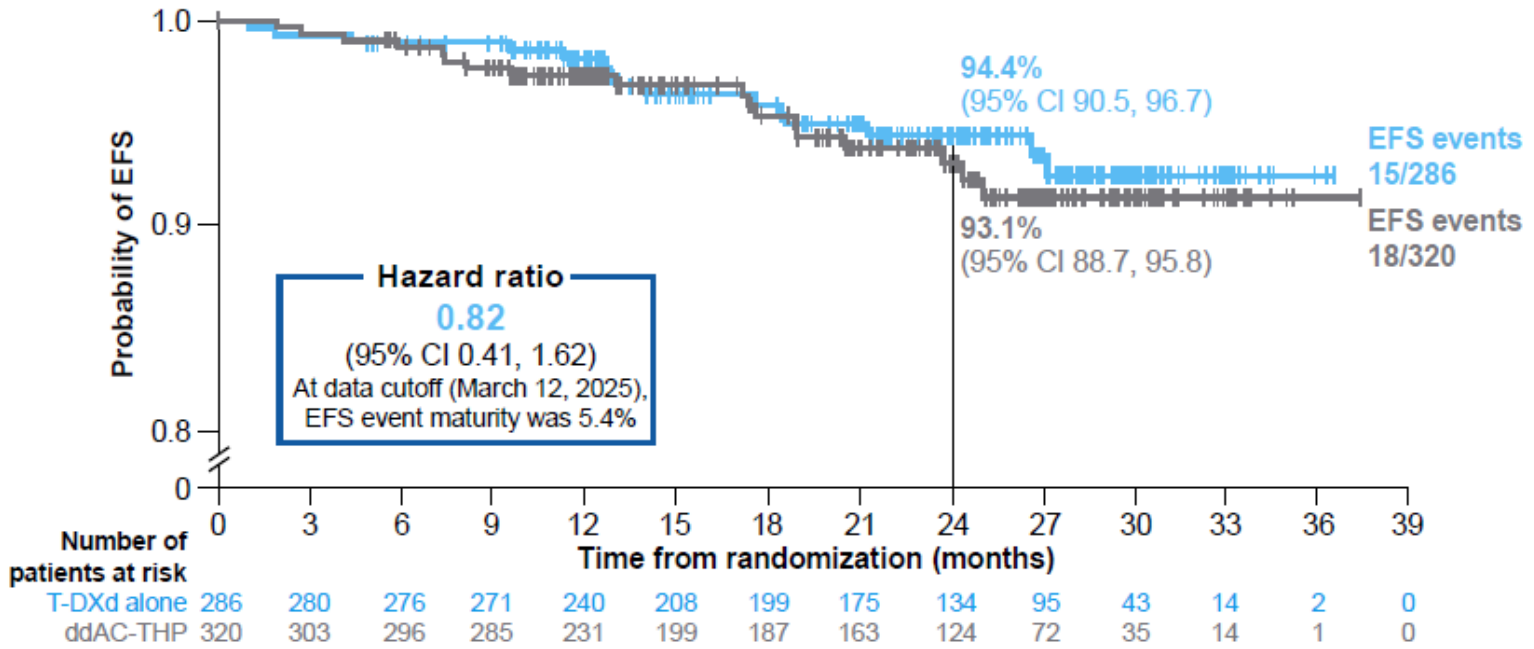
T-DXd alone arm: efficacy summary

On March 13, 2024, the T-DXd alone arm closed following Independent Data Monitoring Committee recommendation.* Patients who were still receiving T-DXd alone could remain on therapy or immediately switch to local SOC

pCR rate

%	T-DXd (n=286)	ddAC-THP (n=320)
Primary analysis Switch to local SOC classified as non-pCR		
pCR†	43.0	56.3
Δ (95% CI)	−13.2 (−20.8, −5.4)	
Prespecified supplementary analysis Switch to local SOC not automatically classified as non-pCR		
pCR†	51.4	57.2
Δ (95% CI)	−5.8 (−13.4, 1.9)	

EFS



T-DXd alone showed inferior but robust pCR compared with the five-agent ddAC-THP
EFS data were similar for T-DXd alone and ddAC-THP

Treatment effects were estimated by the difference in pCR with 95% CIs based on the stratified Miettinen and Nurminen's method, with strata weighting by sample size (ie Mantel–Haenszel weights). Median duration of follow up was 24.9 months (T-DXd) and 23.6 months (ddAC-THP). Analyses are reported in the ITT population. *The reasons were multifactorial, including a lower pCR rate, low likelihood that T-DXd alone would be superior to ddAC-THP, and the timing of surgery; †by blinded central review

Conclusion

- TDXD adjuvant ou néoadjuvant ?
- Schéma néo adjuvant permettant de s'affranchir des anthracyclines
- Quid du Kadcyla en post néoadjuvant si TDXD utilisé en premier lieu ?
- Place du score HER2 DX dans cette stratégie ?
- Attente des données d'EFS avant utilisation en néoadjuvant

- Toxicités non négligeables du TDXD en adjuvant

Cancer du sein HER2 positif métastatique

- Etude DESTINY BREAST 09

DESTINY-Breast09 study design

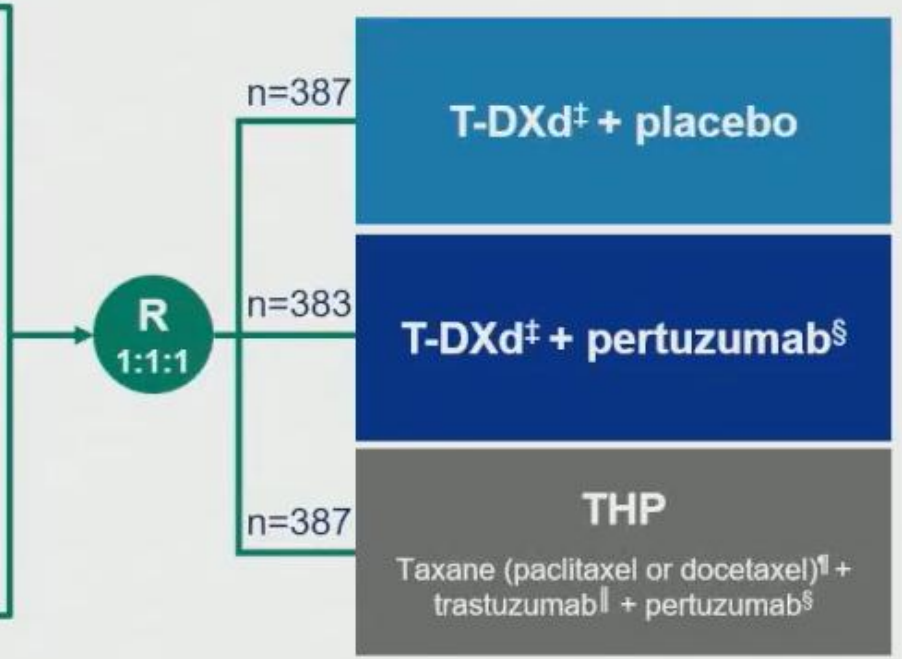
A randomized, multicenter, open-label,* Phase 3 study (NCT04784715)

Eligibility criteria

- HER2+ a/mBC
- Asymptomatic/inactive brain mets allowed
- DFI >6 mo from last chemotherapy or HER2-targeted therapy in neoadjuvant/adjuvant setting
- One prior line of ET for mBC permitted
- **No other prior systemic treatment for mBC†**

Stratification factors

- De-novo vs recurrent mBC
- HR+ or HR−
- *PIK3CA*m (detected vs non-detected)



Endpoints

Primary

- PFS (BICR)

Key secondary

- OS

Secondary

- PFS (INV)
- ORR (BICR/INV)
- DOR (BICR/INV)
- PFS2 (INV)
- Safety and tolerability

- If T-DXd was discontinued due to AEs (except Grade >2 ILD), patients could switch to trastuzumab**
- Concurrent use of ET (AI or tamoxifen) was allowed for those with HR+ disease after six cycles of T-DXd or discontinuation of taxane in THP arm

*Open label for THP arm. Double blinded for pertuzumab in experimental arms; †HER2-targeted therapy or chemotherapy; ‡5.4 mg/kg Q3W; §840 mg loading dose, then 420 mg Q3W; ¶paclitaxel 80 mg/m² QW or 175 mg/m² Q3W, or docetaxel 75 mg/m² Q3W for a minimum of six cycles or until intolerable toxicity; ‖8 mg/kg loading dose, then 6 mg/kg Q3W; **without loading dose

AE, adverse event; AI, aromatase inhibitor; a/mBC, advanced/metastatic breast cancer; BICR, blinded independent central review; DFI, disease-free interval; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HER2+, HER2-positive; HR+/−, hormone receptor–positive/–negative; ILD, interstitial lung disease; INV, investigator; mets, metastases; mo, months; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PFS2, second progression-free survival; *PIK3CA*m, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha mutation; Q3W, every 3 weeks; QW, once every week; R, randomization; T-DXd, trastuzumab deruxtecan

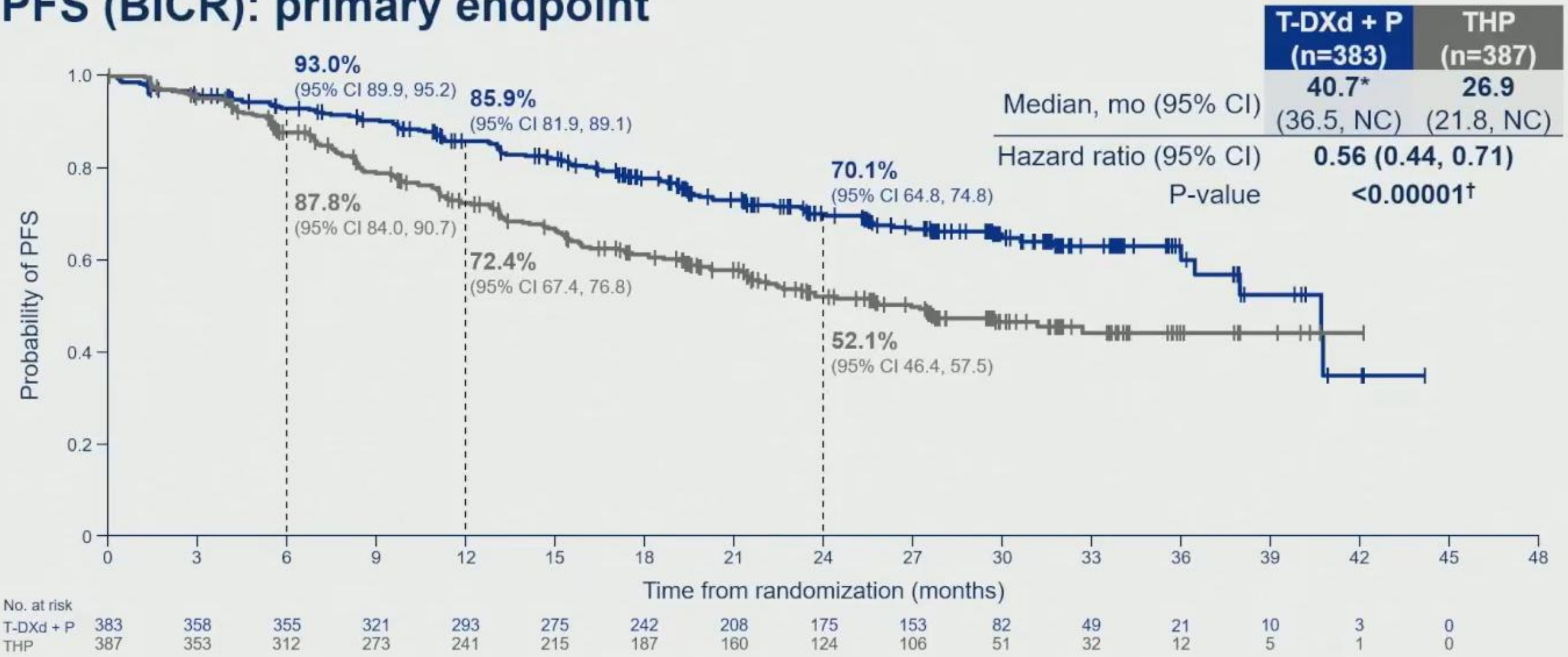
NCT04784715. Updated May 6, 2025. Available from: https://clinicaltrials.gov/study/NCT04784715 (Accessed May 29, 2025)

Patient demographics and key baseline characteristics

	T-DXd + P (n=383)	THP (n=387)
Age, median (range), years	54 (27–85)	54 (20–81)
Female, n (%)	383 (100)	387 (100)
Geographical region, n (%)		
Asia	188 (49.1)	191 (49.4)
Western Europe and North America	87 (22.7)	78 (20.2)
Rest of World	108 (28.2)	118 (30.5)
ECOG performance status, n (%)		
0 (normal activity)	256 (66.8)	246 (63.6)
1 (restricted activity)	127 (33.2)	141 (36.4)
HER2 score by central test, n (%)		
IHC 3+	318 (83.0)	315 (81.4)
IHC <3 / ISH+	62 (16.2)	71 (18.3)
IHC NR / ISH+	3 (0.8)	1 (0.3)
HR status, n (%)		
Positive*	207 (54.0)	209 (54.0)
Negative	176 (46.0)	178 (46.0)
De-novo disease at diagnosis, n (%)	200 (52.2)	200 (51.7)
***PIK3CA* mutations detected, n (%)**	116 (30.3)	121 (31.3)
Brain metastases, n (%)†	25 (6.5)	22 (5.7)
Visceral metastases, n (%)	281 (73.4)	268 (69.3)

*Defined as estrogen receptor–positive and/or progesterone receptor–positive (≥1%); †participants were eligible if they had brain metastases that were clinically inactive or treated/asymptomatic
ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; NR, not recorded; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

PFS (BICR): primary endpoint

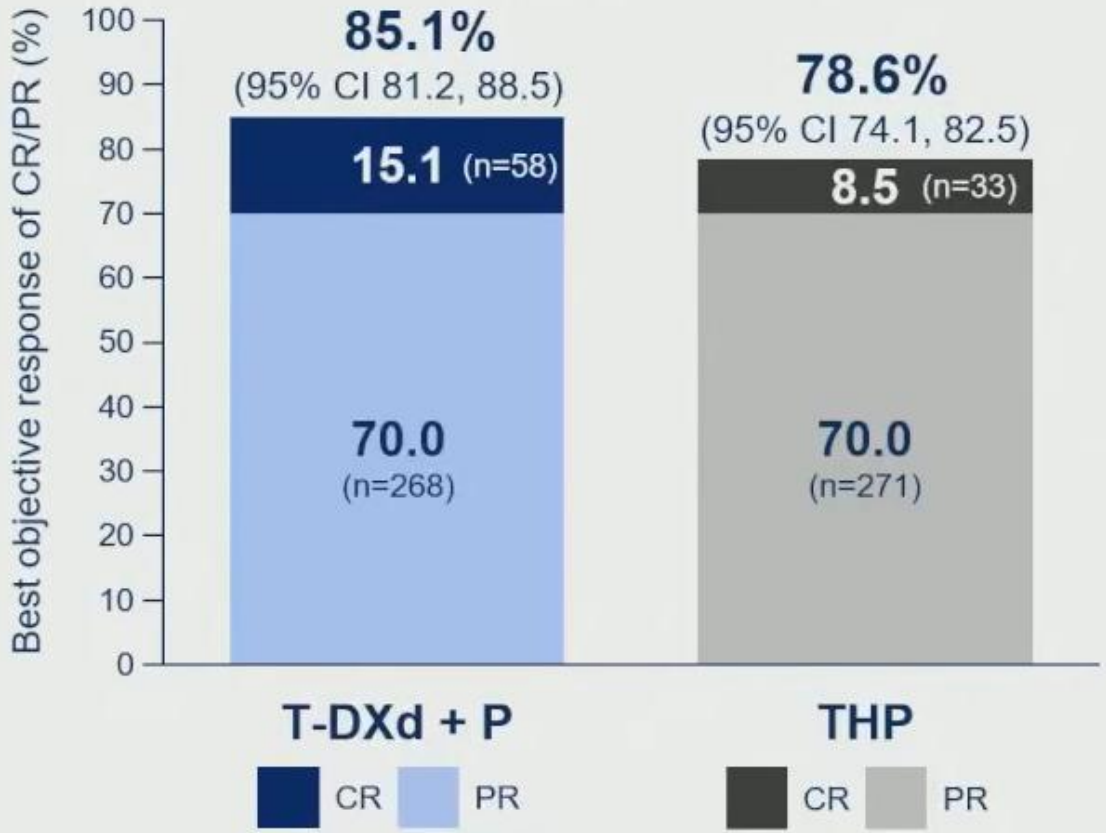


Statistically significant and clinically meaningful PFS benefit with T-DXd + P (median Δ 13.8 mo)

*Median PFS estimate for T-DXd + P is likely to change at updated analysis; †stratified log-rank test. A P-value of <0.00043 was required for interim analysis superiority
BICR, blinded independent central review; CI, confidence interval; mo, months; (m)PFS, (median) progression-free survival; NC, not calculable; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

ORR and DOR (BICR)

Confirmed ORR*



	T-DXd + P (n=383)	THP (n=387)
Median DOR, mo (95% CI)	39.2 (35.1, NC)	26.4 (22.3, NC)
Remaining in response at 24 mo (%)	73.3	54.9
Stable disease, n (%)	38 (9.9)	56 (14.5)

Response rates were greater with T-DXd + P vs THP and were durable

*Based on RECIST v1.1; response required confirmation after 4 weeks
BICR, blinded independent central review; CI, confidence interval; CR, complete response; DOR, duration of response; mo, months; NC, not calculable; ORR, objective response rate; P, pertuzumab; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

dverse events of special interest

Adjudicated drug-related ILD/pneumonitis*

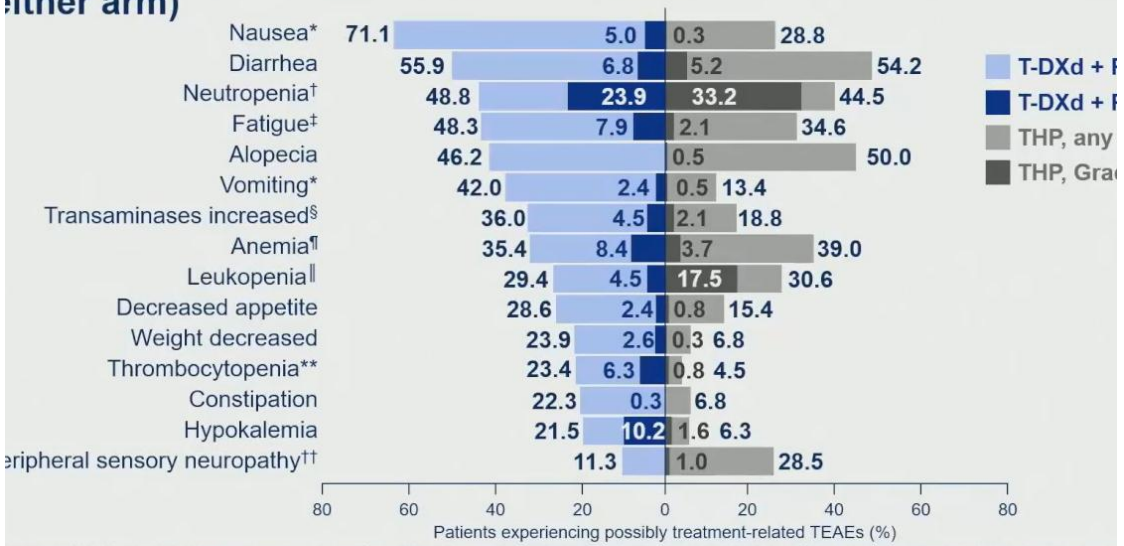
n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	An
T-DXd + P (n=381)	17 (4.5)	27 (7.1)	0	0	2 (0.5)	46
THP (n=382)	2 (0.5)	2 (0.5)	0	0	0	4

Left ventricular dysfunction†

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	An
T-DXd + P (n=381)	4 (1.0)	30 (7.9)	7 (1.8)	1 (0.3)	0	42
THP (n=382)	1 (0.3)	19 (5.0)	7 (1.8)	0	0	2

analysis set
icated drug-related ILD/pneumonitis (grouped term) includes: chronic obstructive pulmonary disease, interstitial lung disease, organizing pneumonia, pneumonia, and pneumonitis, †left ventricular dysfunction (g
, cardiac failure, cardiac failure chronic, ejection fraction decreased, left ventricular dysfunction, and right ventricular failure
terstitial lung disease; P, pertuzumab; T-DXd, trastuzumab deruxtecan; THP, taxane + trastuzumab + pertuzumab

ossibly treatment-related (investigator assessed) TEAEs in ≥20% ither arm)



emetic prophylaxis was recommended but not mandated by protocol; †neutropenia (grouped term) includes: neutropenia and neutrophil count decreased; ‡fatigue (grouped term) includes: fatigue, asthenia, malaise,
ased (grouped term) includes: transaminases increased, aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyltransferase increased, liver function test abnormal, hepatic functi
ncrease; ¶anemia (grouped term) includes: anemia, hemoglobin decreased, hematocrit decreased, and red blood cell count decreased; ‖leukopenia (grouped term) includes: leukopenia and white blood cell count de
ped term) includes: platelet count decreased and thrombocytopenia; ††peripheral sensory neuropathy (grouped term) includes: neuropathy peripheral, peripheral sensory neuropathy, and polyneuropathy
rtuzumab; T-DXd, trastuzumab deruxtecan; TEAE, treatment-emergent adverse event; THP, taxane + trastuzumab + pertuzumab

Evolution of T-DXd in HER2+ a/mBC

Observed mPFS*

*Comparisons are hypothesis-generating only as it is not possible to directly compare the studies due to differences in trial population and design; †capecitabine plus trastuzumab or lapatinib

1L, first line; 2L, second line; 3L, third line; a/mBC, advanced/metastatic breast cancer; CTx, chemotherapy; HER2+, human epidermal growth factor receptor 2–positive; mo, months; mPFS, median progression-free survival; P, pertuzumab; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice; THP, taxane + trastuzumab + pertuzumab

1. Baselga J, et al. *N Engl J Med*. 2012;366:109–119; 2. Cottu P, et al. *Breast Cancer Res Treat*. 2024;209:419–430; 3. Hurvitz SA, et al. *Lancet*. 2023;401:105–117; 4. André F, et al. *Lancet*. 2023;401:1773–1785; 5. Modi S, et al. *N Engl J Med*. 2020;382:610–621

Conclusion

- Attente des données d'OS
- Maintenance par pertuzumab seul? Car qualité de vie différente sous TdXD au long cours ..
- Pertinence du schéma Patina chez les patientes RH+ ?
- Pertinence du tucatinib en maintenance chez les RH- (HER- Climb 05) ?

Cancer du sein triple négatif métastatique

- Ascent 03
- Tropion Breast 02

BERLIN 2025 ESMO congress

Primary Results From ASCENT-03: A Randomized Phase 3 Study of Sacituzumab Govitecan vs Chemotherapy in Patients With Previously Untreated Metastatic Triple-Negative Breast Cancer Who Are Unable to Receive PD-(L)1 Inhibitors

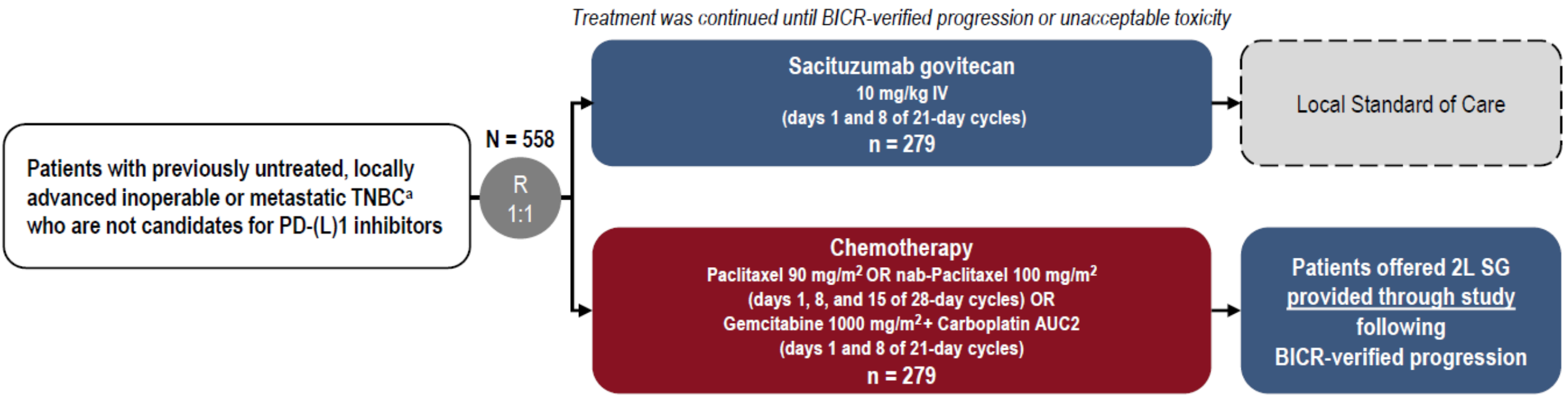
Javier Cortés[1-5], Aditya Bardia[6], Kevin Punie[7], Carlos Barrios[8], Sara Hurvitz[9], Andreas Schneeweiss[10], Joohyuk Sohn[11], Eriko Tokunaga[12], Adam Brufsky[13], Yeon Hee Park[14], Binghe Xu[15], Roberto Hegg[16], Mafalda Oliveira[17], Alessandra Fabi[18], Natalya Vaksman[19], Theresa Valdez[19], Xinrui Zhang[19], Catherine Lai[19], Sara M Tolaney[20]

[1]International Breast Cancer Center (IBCC), Pangaea Oncology, Quiron Group, Barcelona, Spain; [2]IOB Madrid, Institute of Oncology, Hospital Beata María Ana, Madrid, Spain; [3]Oncology Department, Hospital Universitario Torrejón, Ribera Group, Madrid, Spain; [4]Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain; [5]Medica Scientia Innovation Research (MEDSIR), Barcelona, Spain and Ridgewood, NJ, USA; [6]David Geffen School of Medicine, University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [7]Ziekenhuis Aan de Stroom, Antwerp, Belgium; [8]Latin American Cooperative Oncology Group (LACOG), Porto Alegre, Brazil; [9]Department of Medicine, UW Medicine, Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA USA; [10]Heidelberg University Hospital and German Cancer Research Center, Heidelberg, Germany; [11]Yonsei Cancer Center, Seoul, Republic of Korea; [12]National Hospital Organization Kyushu Cancer Center, Fukuoka, Japan; [13]Magee-Womens Hospital and the Hillman Cancer Center, University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [14]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [15]Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [16]University of São Paulo, São Paulo, Brazil; [17]Vall d'Hebron University Hospital, Breast Cancer Group, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [18]Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy; [19]Gilead Sciences Inc., Foster City, CA, USA; [20]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Sunday, October 19, 2025; 9:15-9:25 am
LBA 20

YEARS ESMO

ASCENT-03: Study Design



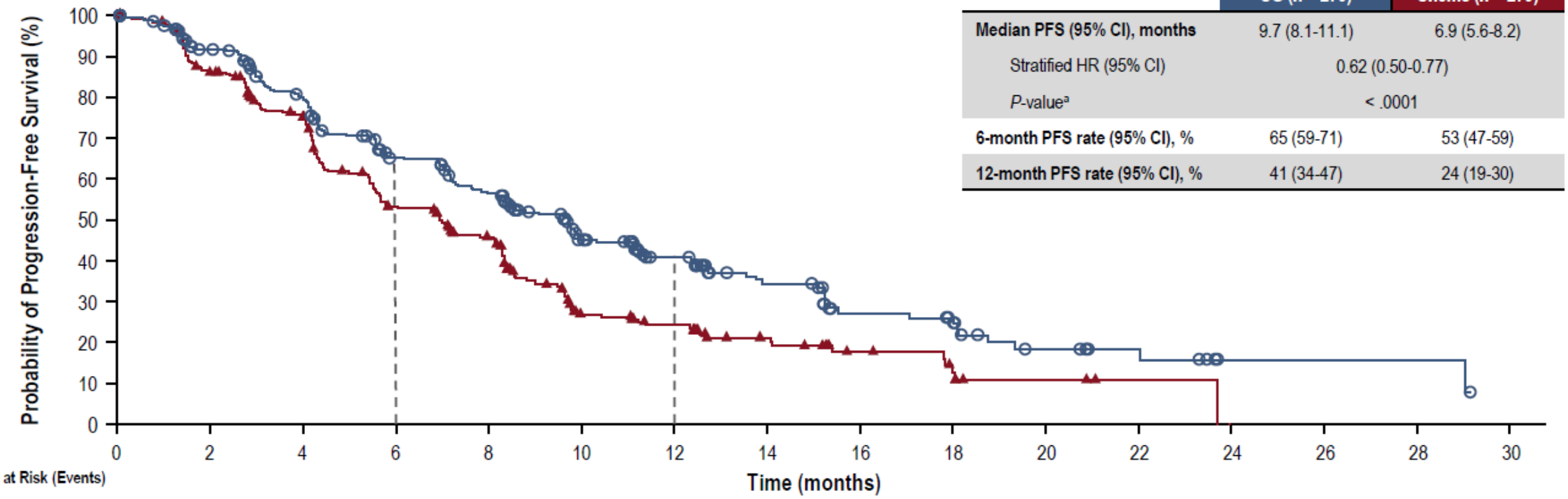
Stratification factors:

- United States/Canada/Western Europe vs rest of the world
- De novo mTNBC[b] vs recurrent within 6 to 12 months of treatment vs recurrent after > 12 months from treatment in curative setting

ClinicalTrials.gov identifier: NCT05382299. [a]TNBC status was centrally confirmed and determined according to standard American Society of Clinical Oncology-College of American Pathologists criteria. [b]Up to 35% de novo mTNBC.
2L, second-line; **BICR**, blinded independent central review; **IV**, intravenous; **mTNBC**, metastatic triple-negative breast cancer; **PD-1**, programmed cell death protein-1; **PD-L1**, programmed cell death ligand 1; **PD-(L)1**, PD-1 or PD-L1; **R**, randomization; **SG**, sacituzumab govitecan; **TNBC**, triple-negative breast cancer.

Javier Cortés, MD

Progression-Free Survival by BICR



	SG (n = 279)	Chemo (n = 279)
Median PFS (95% CI), months	9.7 (8.1-11.1)	6.9 (5.6-8.2)
Stratified HR (95% CI)	0.62 (0.50-0.77)	
P-value[a]	< .0001	
6-month PFS rate (95% CI), %	65 (59-71)	53 (47-59)
12-month PFS rate (95% CI), %	41 (34-47)	24 (19-30)

SG demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo by BICR analysis, with a 38% reduction in risk of disease progression or death

Data cutoff date: April 2, 2025. [a]Two-sided *P*-value from stratified log-rank test.
BICR, blinded independent central review; **chemo**, chemotherapy; **HR**, hazard ratio; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

Javier Cortés, MD

Subgroup Analysis of Progression-free Survival by BICR

	SG		Chemo		Unstratified HR (95% CI)	Unstratified HR (95% CI)
	n	Median PFS, mo (95% CI)	n	Median PFS, mo (95% CI)		
ITT population	279	9.7 (8.1-11.1)	279	6.9 (5.6-8.2)		0.66 (0.53-0.82)
Age group						
< 65 years	214	9.6 (7.6-10.3)	201	5.7 (4.4-7.0)		0.58 (0.45-0.74)
≥ 65 years	65	11.1 (7.3-13.9)	78	9.0 (8.3-10.0)		0.91 (0.58-1.44)
ECOG PS						
0	183	11.2 (9.7-13.5)	187	7.3 (6.0-8.3)		0.61 (0.47-0.80)
1	96	7.1 (5.4-8.5)	92	5.5 (4.2-7.2)		0.74 (0.52-1.05)
Geographic region						
United States/Canada/Western Europe	89	9.9 (7.8-13.9)	89	7.1 (5.4-8.3)		0.54 (0.36-0.79)
Rest of the world	190	9.6 (7.2-11.1)	190	6.9 (5.5-8.3)		0.72 (0.55-0.92)
Disease Status						
De novo	87	8.3 (5.6-12.4)	88	5.5 (4.2-7.3)		0.65 (0.45-0.94)
Recurrent 6-12 mo	58	8.3 (5.6-9.9)	57	5.6 (4.2-6.7)		0.46 (0.29-0.72)
Recurrent > 12 mo	134	11.1 (8.4-13.5)	134	8.4 (7.2-9.8)		0.72 (0.52-1.00)
PD-L1 status						
CPS < 1	102	8.5 (7.2-12.5)	98	8.3 (5.4-9.6)		0.74 (0.51-1.06)
1 ≤ CPS < 10	175	9.8 (7.6-11.3)	180	6.9 (5.5-8.1)		0.64 (0.49-0.83)
Chemo selected prior to randomization						
Taxane	154	11.1 (8.1-12.7)	155	5.7 (4.3-8.1)		0.51 (0.38-0.68)
Gemcitabine/carboplatin	125	8.5 (6.9-9.9)	124	8.1 (5.7-8.3)		0.89 (0.64-1.22)

PFS benefit of SG over chemo was observed across key prespecified subgroups

Data cutoff date: April 2, 2025. **BICR**, blinded independent central review; **chemo**, chemotherapy; **CPS**, combined positive score; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **HR**, hazard ratio; **ITT**, intent-to-treat; **PD-L1**, programmed cell death ligand 1; **PFS**, progression-free survival; **SG**, sacituzumab govitecan.

Javier Cortés, MD

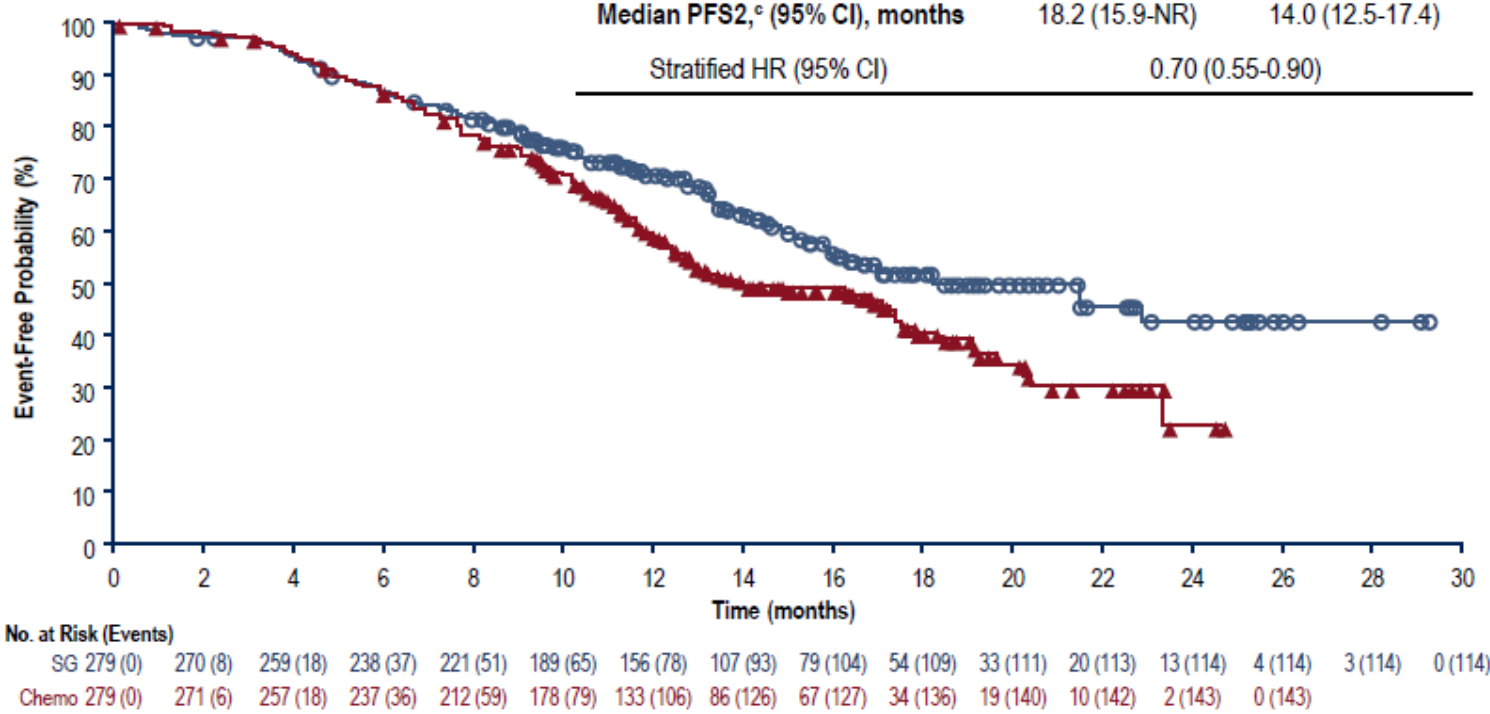
Descriptive Overall Survival and PFS2

- **Overall survival not yet mature[a]**
- Study continues to first formal OS analysis
- Of 179 patients who initiated subsequent treatment after chemo, 147 (82%) received SG

Overall survival	SG (n = 279)	Chemo (n = 279)
Number of events, %	103 (37)	103 (37)
Median (95% CI) , months	21.5 (17.7-NR)	20.2 (18.2-NR)
Stratified HR (95% CI)	0.98 (0.75-1.30)	
OS rate (95% CI), %		
12-month	75 (70-80)	73 (67-78)
24-month	46 (36-56)	42 (29-54)

Progression-Free Survival 2[b]

	SG (n = 279)	Chemo (n = 279)
Median PFS2,[c] (95% CI), months	18.2 (15.9-NR)	14.0 (12.5-17.4)
Stratified HR (95% CI)	0.70 (0.55-0.90)	

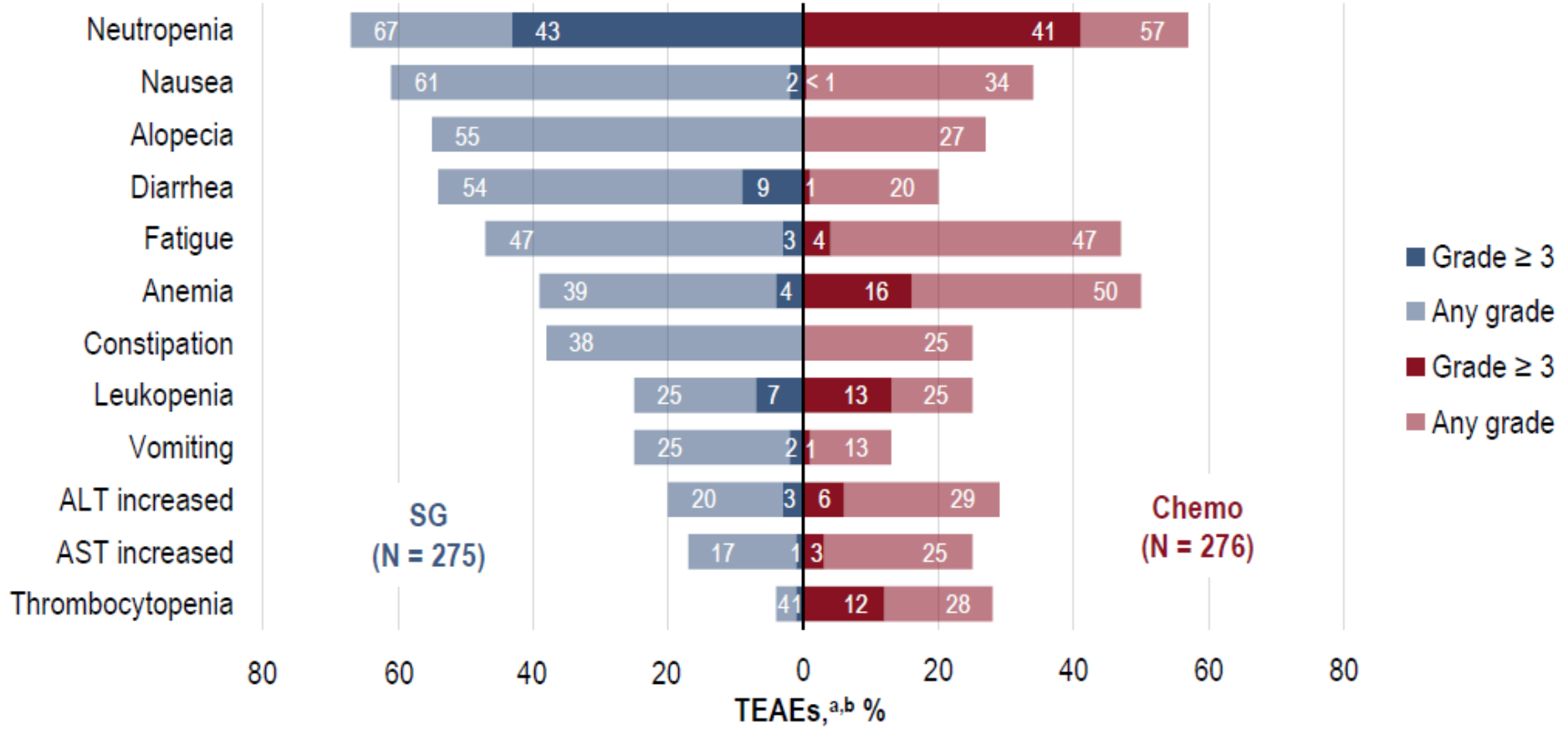


At the time of primary analysis, overall survival was immature and PFS2 was longer with SG vs chemo by investigator assessment

Data cutoff date: April 2, 2025. [a]At the time of this analysis, OS data maturity was 37%. [b]PFS2 is defined as the time from date of randomization to the first documented progression on next-line therapy based on investigator assessment of progressive disease or death due to any cause, whichever occurs first. [c]By investigator assessment.
2L, second line; **chemo**, chemotherapy; **HR**, hazard ratio; **NR**, not reached; **OS**, overall survival; **PFS2**, progression-free survival 2; **SG**, sacituzumab govitecan.

Javier Cortés, MD

Safety Summary: Most Common Adverse Events



The AEs observed are consistent with the known safety profile of SG

Data cutoff date: April 2, 2025. [a]TEAEs were included if they occurred in ≥ 20% of patients in either group. [b]Combined preferred terms of Neutropenia includes neutrophil count decreased, Fatigue includes asthenia, Anemia includes hemoglobin decreased and red blood cell count decreased, Leukopenia includes white blood cell count decreased, and Thrombocytopenia includes platelet count decreased.
AE, adverse event; **ALT**, alanine aminotransferase; **AST**, aspartate aminotransferase; **chemo**, chemotherapy; **SG**, sacituzumab govitecan; **TEAE**, treatment-emergent adverse event.

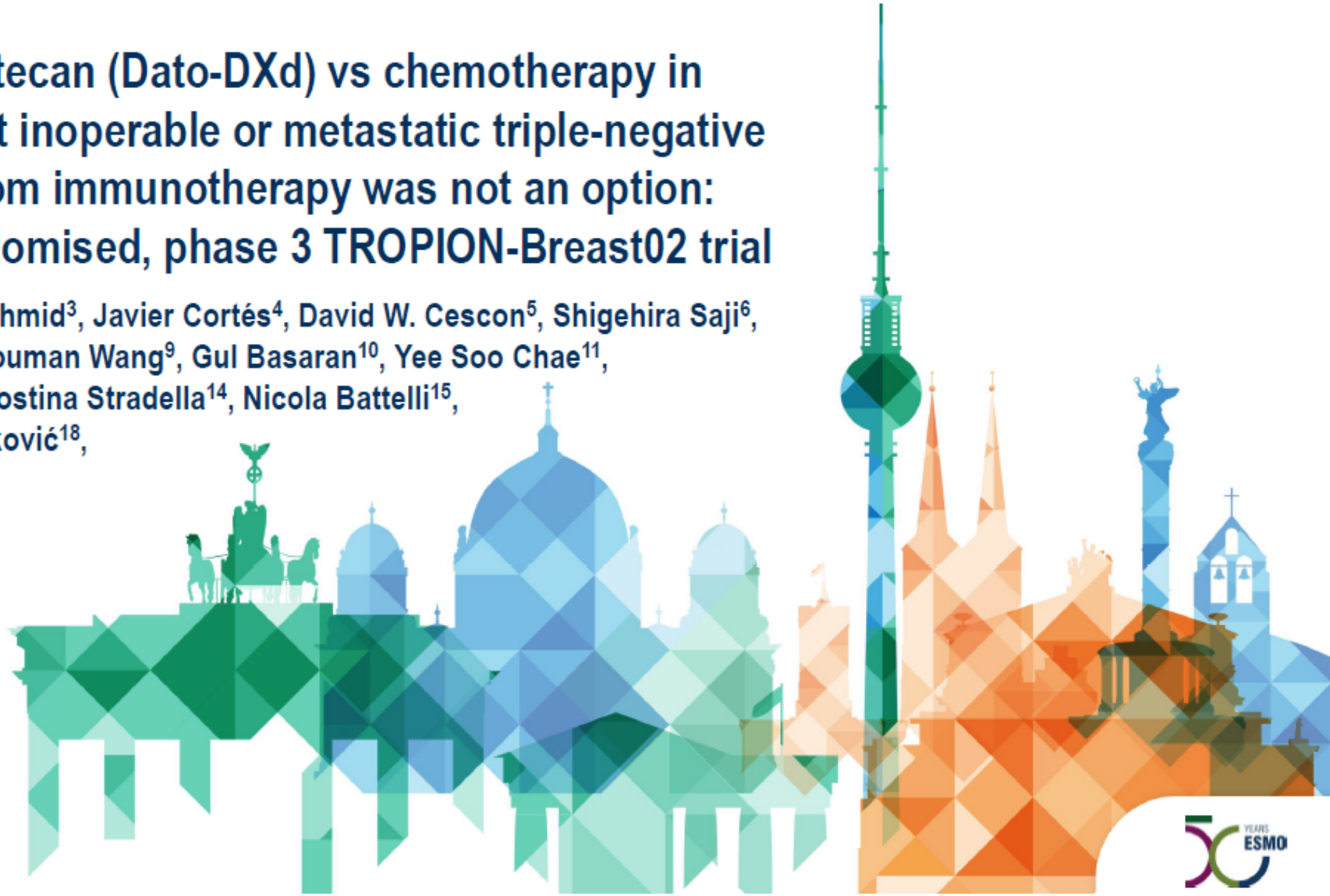
Javier Cortés, MD

BERLIN 2025 ESMO congress

First-line datopotamab deruxtecan (Dato-DXd) vs chemotherapy in patients with locally recurrent inoperable or metastatic triple-negative breast cancer (TNBC) for whom immunotherapy was not an option: Primary results from the randomised, phase 3 TROPION-Breast02 trial

Rebecca A. Dent[1], Zhimin Shao[2], Peter Schmid[3], Javier Cortés[4], David W. Cescon[5], Shigehira Saji[6], Kyung Hae Jung[7], Thomas Bachelot[8], Shouman Wang[9], Gul Basaran[10], Yee Soo Chae[11], Rofhiwa Mathiba[12], Shin-Cheh Chen[13], Agostina Stradella[14], Nicola Battelli[15], Naoki Niikura[16], Kechen Zhao[17], Petra Vuković[18], Micah J. Maxwell[19], Tiffany A. Traina[20]

[1]National Cancer Center Singapore, Singapore; [2]Fudan University Shanghai Cancer Center, Fudan, China; [3]Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, London, UK; [4]International Breast Cancer Center (IBCC), Pangaea Oncology, Barcelona, Spain; [5]Princess Margaret Cancer Centre, Toronto, ON, Canada; [6]Fukushima Medical University, Fukushima, Japan; [7]Asan Medical Center – University of Ulsan College of Medicine, Seoul, Republic of Korea; [8]Centre Léon Bérard, Lyon, France; [9]Xiangya Hospital of Central South University, Changsha, China; [10]MAA Acibadem University, School of Medicine, Medical Oncology Department, Istanbul, Türkiye; [11]Kyungpook National University Chilgok Hospital, Kyungpook National University School of Medicine, Kyungpook, Republic of Korea; [12]Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa; [13]Chang Gung Medical Foundation – Taipei Chang Gung Memorial Hospital, Taipei City, Taiwan; [14]Institut Catala d'Oncologia - Hospital Duran i Reynals (ICO L'Hospitalet), Barcelona, Spain; [15]Ospedale Generale Provinciale Macerata, Macerata, Italy; [16]Tokai University School of Medicine, Kanagawa, Japan; [17]Biometrics, Late-Stage Development, Oncology R&D, AstraZeneca, Wilmington, DE, USA; [18]Clinical Development, Late-Stage Development, Oncology R&D, AstraZeneca, Cambridge, UK; [19]Clinical Development, Late-Stage Development, Oncology R&D, AstraZeneca, Gaithersburg, MD, USA; [20]Memorial Sloan Kettering Cancer Center (MSKCC), New York, NY, USA



50 YEARS ESMO

TROPION-Breast02: Study Design

Randomised, phase 3, open-label, global study (NCT05374512)

Key inclusion criteria:

- Patients with histologically or cytologically documented locally recurrent inoperable or metastatic TNBC*
- No prior chemotherapy or targeted systemic therapy in the locally recurrent inoperable or metastatic setting
- Immunotherapy not an option†
- ECOG PS 0 or 1
- No minimum DFI‡

1:1

Dato-DXd
6 mg/kg IV Day 1 Q3W
(n=323)

Investigator's choice of chemotherapy (ICC)#
Paclitaxel, nab-paclitaxel, capecitabine, eribulin mesylate/eribulin, carboplatin
(n=321)

Endpoints

Dual primary:

- OS
- PFS by BICR per RECIST v1.1

Secondary included:

- PFS (investigator-assessed)
- ORR, DoR
- Safety

Randomisation stratified by:

- Geographic region (US/Canada/Europe vs other geographic regions)
- PD-L1 status (high [CPS ≥10] vs low [CPS <10])§
- DFI history (*de novo* vs prior DFI 0–12 months vs prior DFI >12 months)¶

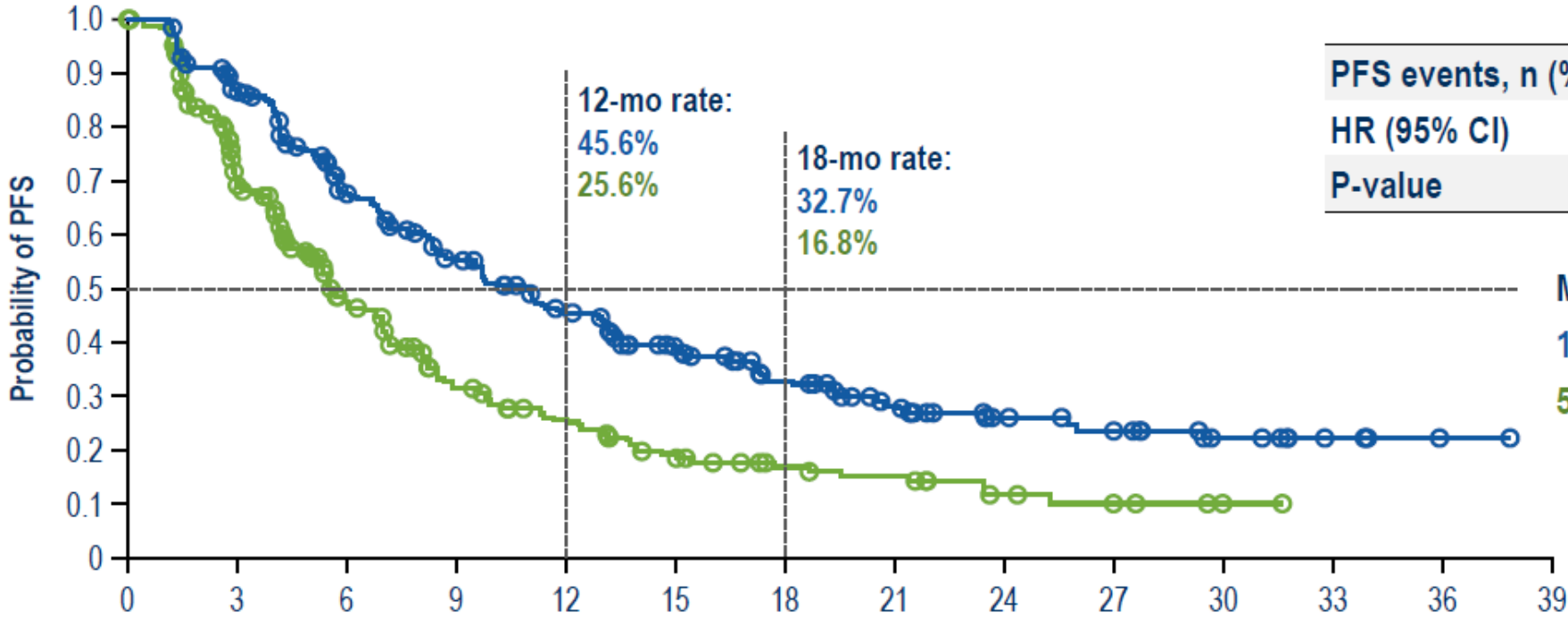
- Treatment continued until investigator-assessed RECIST v1.1 progressive disease, unacceptable toxicity, or another discontinuation criterion was met
- Following progression or discontinuation of study treatment, patients could receive subsequent therapies, including approved ADCs or chemotherapy, at the investigator's discretion‖

*According to ASCO/CAP criteria. †Including patients with PD-L1-low tumours, or patients with PD-L1-high tumours with (a) disease relapse after prior PD-(L)1 inhibitor therapy for early-stage breast cancer, (b) comorbidities precluding PD-(L)1 inhibitor therapy, or (c) no regulatory access to PD-(L)1 inhibitor therapy. ‡DFI defined as time between date of completion of treatment with curative intent and date of first documented local or distant disease recurrence. §Recruitment of patients with PD-L1-high tumours who would otherwise be eligible for pembrolizumab if regulatory access was available was capped at ~10% of randomised patients. ¶Recruitment of patients with DFI 0–12 months was capped at ~20% of randomised patients. #If no prior taxane, or prior taxane in the (neo)adjuvant setting and DFI >12 months: paclitaxel 80 mg/m² IV, D1, 8, 15, Q3W, or nab-paclitaxel 100 mg/m² IV, D1, 8, 15, Q4W; if prior taxane and DFI 0–12 months: capecitabine 1000 or 1250 mg/m² orally twice daily, D1–14, Q3W (dose determined by standard institutional practice), or eribulin mesylate 1.4 mg/m² / eribulin 1.23 mg/m² IV, Day 1, 8, Q3W, or carboplatin AUC6 IV, D1, Q3W. ‖In the Dato-DXd vs ICC arm, 65% vs 72% of patients received any subsequent therapy in any treatment line; 14% vs 30% received a subsequent ADC (sacituzumab govitecan, sacituzumab tirumotecan, trastuzumab deruxtecan).

ADC, antibody-drug conjugate; BICR, blinded independent central review; CPS, combined positive score; D, day; DFI, disease-free interval; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenously; ORR, objective response rate; PD-(L)1, programmed cell death (ligand) 1; PFS, progression-free survival; QXW, every X weeks.

Rebecca A. Dent

Progression-Free Survival by BICR



	Dato-DXd	ICC
PFS events, n (%)	199 (62)	209 (65)
HR (95% CI)	0.57 (0.47–0.69)	
P-value	<0.0001	

Median PFS (95% CI)

10.8 mo (8.6–13.0)

5.6 mo (5.0–7.0)

Δ 5.3 mo*

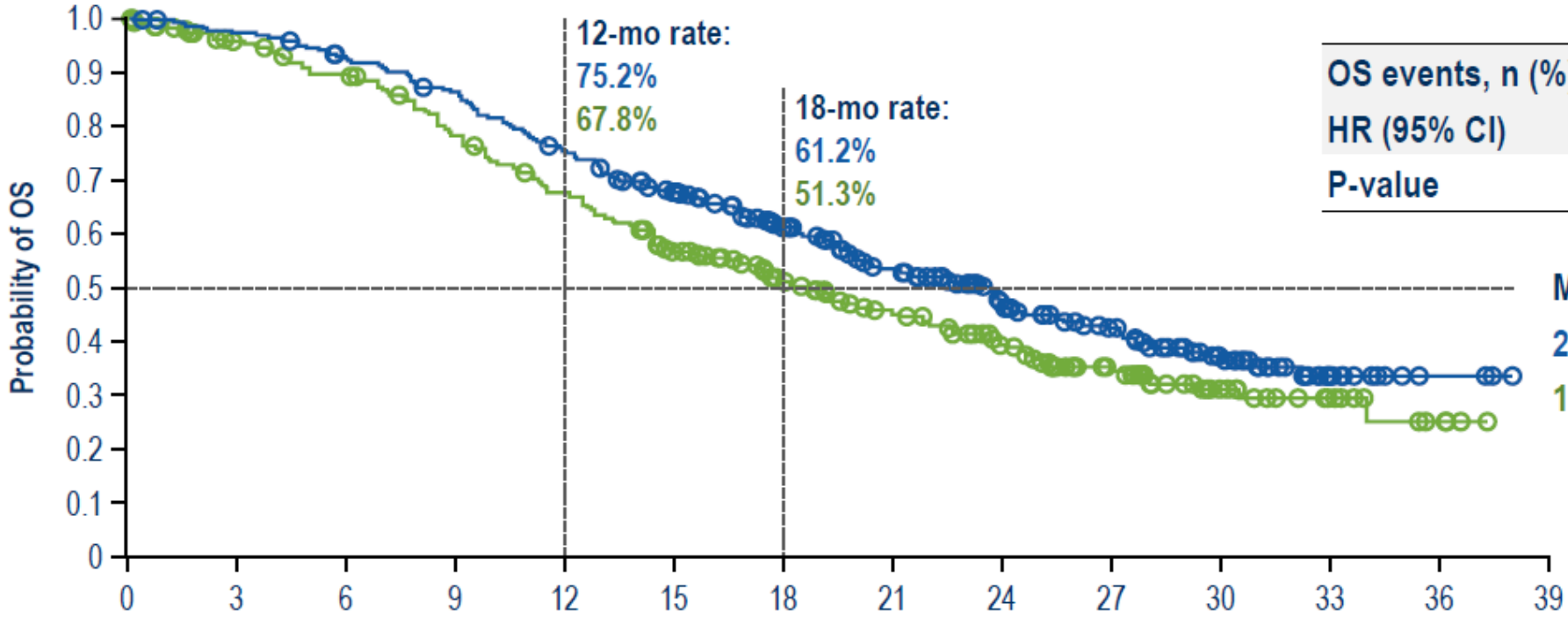
Number at risk														
Data-DXd	323	265	191	150	116	84	56	41	24	20	10	5	1	0
ICC	321	191	107	64	46	29	19	16	8	6	1	0	0	0

Dato-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with ICC, reducing the risk of progression or death by 43%

Rebecca A. Dent

*Numbers are rounded. To two decimal points: median PFS 10.84 (95% CI 8.57–12.98) with Dato-DXd, 5.55 (95% CI 4.96–6.97) with ICC; Δ 5.29 months.
CI, confidence interval; HR, hazard ratio; mo, months.

Overall Survival



	Dato-DXd	ICC
OS events, n (%)	168 (52)	181 (56)
HR (95% CI)	0.79 (0.64–0.98)	
P-value	0.0291	

Median OS (95% CI)

23.7 mo (19.8–25.6)

18.7 mo (16.0–21.8)

Δ 5.0 mo

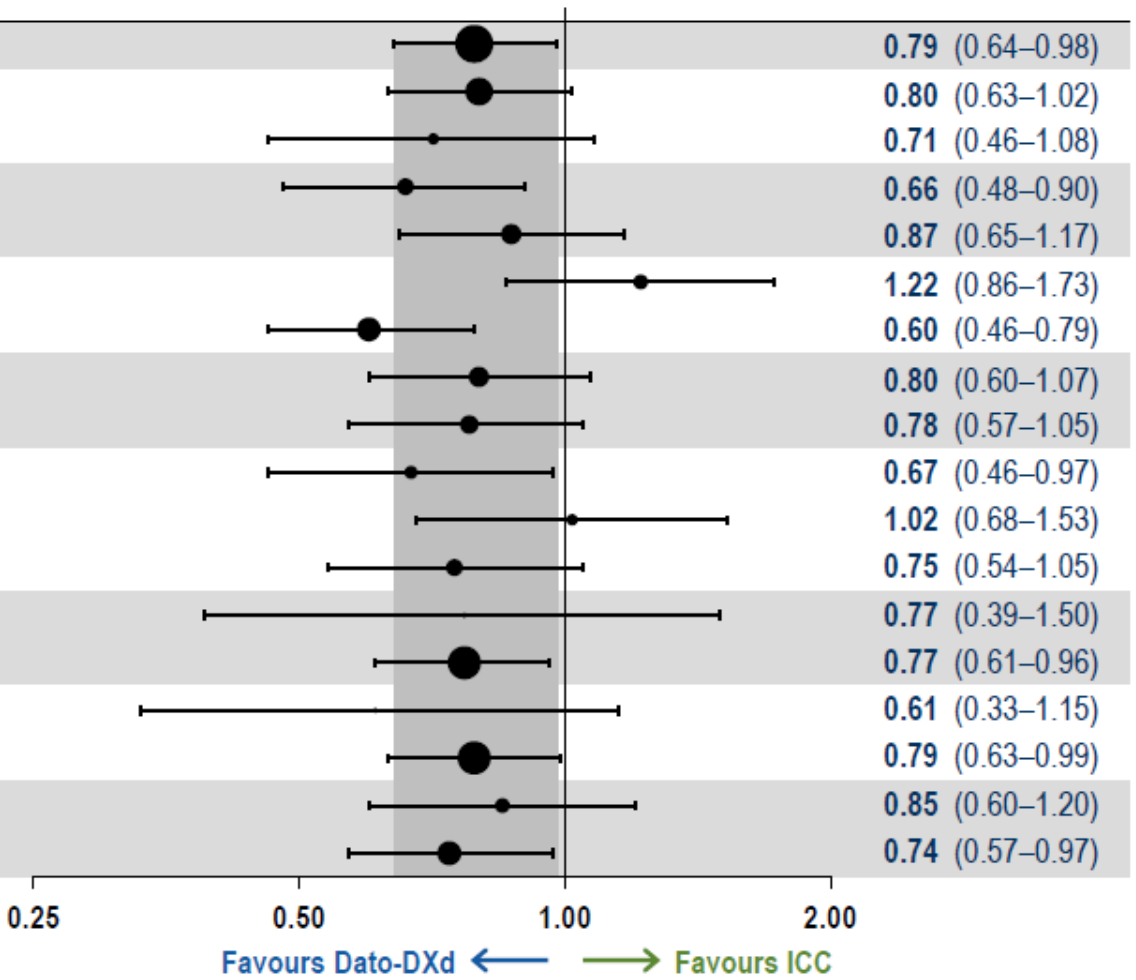
Number at risk

Data-DXd	323	311	291	272	235	201	157	122	86	64	37	14	3	0
ICC	321	290	268	231	199	158	122	93	70	48	27	12	4	0

Dato-DXd demonstrated a statistically significant and clinically meaningful improvement in OS compared with ICC, reducing the risk of death by 21%

OS Subgroup Analysis

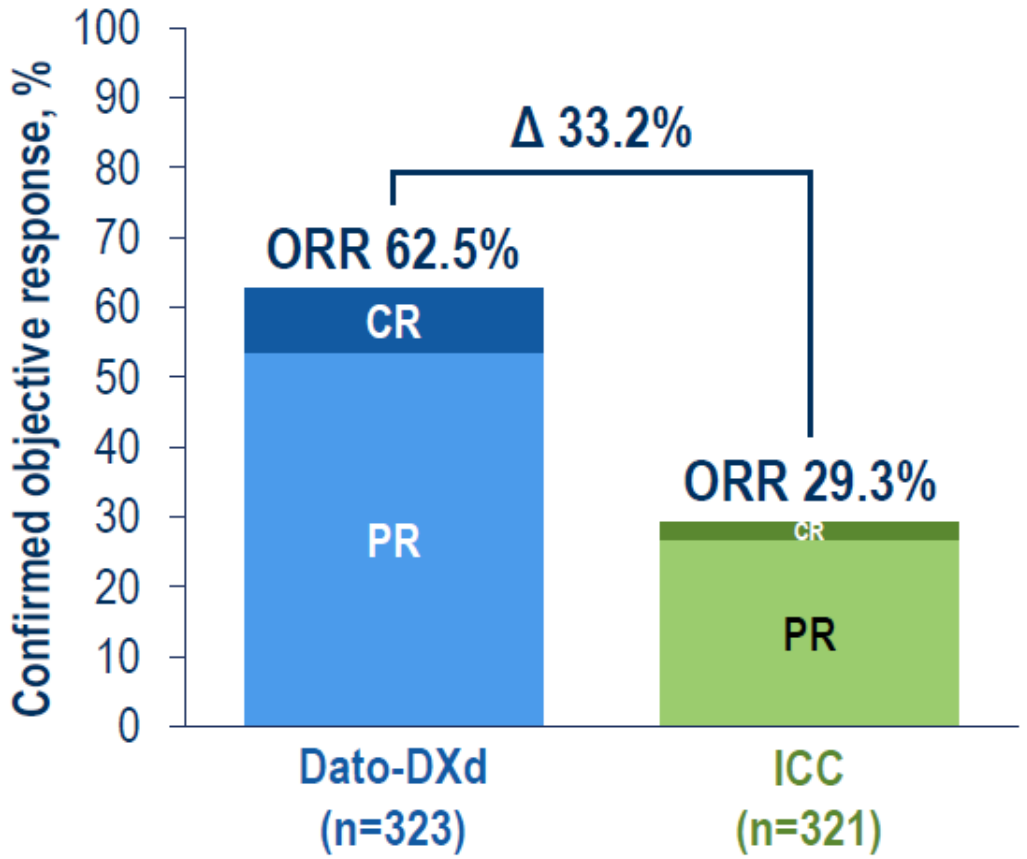
		Events/patients, n		Hazard ratio (95% CI)
		Dato-DXd	ICC	
All patients		168/323	181/321	**0.79** (0.64–0.98)
Age at randomisation	<65 years	128/245	132/239	**0.80** (0.63–1.02)
	≥65 years	40/78	49/82	**0.71** (0.46–1.08)
Race	Asian	76/151	78/131	**0.66** (0.48–0.90)
	Non-Asian	82/151	98/173	**0.87** (0.65–1.17)
Geographic region	US, Canada, Europe†	72/120	59/120	**1.22** (0.86–1.73)
	Other geographic regions	96/203	122/201	**0.60** (0.46–0.79)
ECOG PS	0	93/195	92/182	**0.80** (0.60–1.07)
	1	75/128	89/139	**0.78** (0.57–1.05)
DFI history	*De novo*	51/109	63/110	**0.67** (0.46–0.97)
	Prior DFI 0–12 months	51/67	45/66	**1.02** (0.68–1.53)
	Prior DFI >12 months	66/147	73/145	**0.75** (0.54–1.05)
PD-L1 status	High (CPS ≥10)	17/34	18/29	**0.77** (0.39–1.50)
	Low (CPS <10)	149/287	163/291	**0.77** (0.61–0.96)
Brain metastases*	Yes	21/36	19/28	**0.61** (0.33–1.15)
	No	147/287	162/293	**0.79** (0.63–0.99)
Liver metastases	Yes	64/93	66/98	**0.85** (0.60–1.20)
	No	104/230	115/223	**0.74** (0.57–0.97)



*Patients with asymptomatic, stable brain metastases were permitted in the study.
†Ad hoc analysis of the US cohort showed comparable OS HR to the ITT population.

Rebecca A. Dent

Response by BICR



	Dato-DXd (n=323)	ICC (n=321)
Confirmed objective response, n (%)	202 (62.5)	94 (29.3)
Odds ratio (95% CI)	4.24 (3.03–5.95)	
Best confirmed objective response, n (%)		
Complete response	29 (9.0)	8 (2.5)
Partial response	173 (53.6)	86 (26.8)
Stable disease	87 (26.9)	151 (47.0)
Progressive disease	27 (8.4)	52 (16.2)
Not evaluable	7 (2.2)	24 (7.5)

With Dato-DXd, confirmed ORR was more than double that with ICC, and confirmed complete response rate was more than three times that with ICC

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Treatment-Related AESIs for Dato-DXd

AESI category, n (%) Preferred term*	Dato-DXd (n=319)			ICC (n=309)		
	Grade 1	Grade 2	Grade ≥3	Grade 1	Grade 2	Grade ≥3
Oral mucositis/stomatitis†	78 (24)	87 (27)	27 (8)	22 (7)	8 (3)	0
Stomatitis	72 (23)	83 (26)	27 (8)	19 (6)	8 (3)	0
Ocular surface events‡§	76 (24)	50 (16)	23 (7)	9 (3)	5 (2)	1 (<1)
Dry eye	51 (16)	21 (7)	4 (1)	6 (2)	3 (1)	0
Keratitis	21 (7)	14 (4)	7 (2)	1 (<1)	0	0
Conjunctivitis	7 (2)	13 (4)	1 (<1)	0	0	0
Adjudicated drug-related ILD/pneumonitis¶	1 (<1)	7 (2)	1 (<1)#	1 (<1)	1 (<1)	0

Treatment-related oral mucositis/stomatitis:

- In the Dato-DXd arm, events led to dose interruption, reduction, and discontinuation in 11 (3%), 36 (11%), and 0 patients, respectively
- Grade ≥2 events resolved to grade ≤1 in 103/114 patients (90%) at data cutoff

Treatment-related ocular surface events:

- In the Dato-DXd arm, events led to dose interruption, reduction, and discontinuation in 18 (6%), 14 (4%), and 3 (<1%) patients, respectively
- Grade ≥2 events resolved to grade ≤1 in 49/73 patients (67%) at data cutoff

*Details for preferred terms included if reported in ≥20 patients in either arm. †Comprising the preferred terms of aphthous ulcer, mouth ulceration, oral pain, oropharyngeal pain, pharyngeal inflammation, and stomatitis. ‡Comprising the preferred terms of acquired corneal dystrophy, blepharitis, conjunctivitis, corneal disorder, corneal epithelium defect, corneal erosion, corneal exfoliation, corneal lesion, corneal toxicity, dellen, dry eye, keratitis, keratopathy, lacrimation increased, limbal stem cell deficiency, meibomian gland dysfunction, photophobia, punctate keratitis, ulcerative keratitis, vision blurred, visual acuity reduced, visual impairment, and xerophthalmia. §In the Dato-DXd arm only, ophthalmologic assessments were required every 3 cycles while on therapy; this was not required in the ICC arm. For all patients in both arms, ophthalmologic assessments were required at baseline, as clinically indicated, and at end of therapy. ¶Comprising the preferred terms of interstitial lung disease and pneumonitis. #Grade 5 – this event was characterised by the investigator as grade 3 pneumonitis, with death assessed as related to breast cancer.

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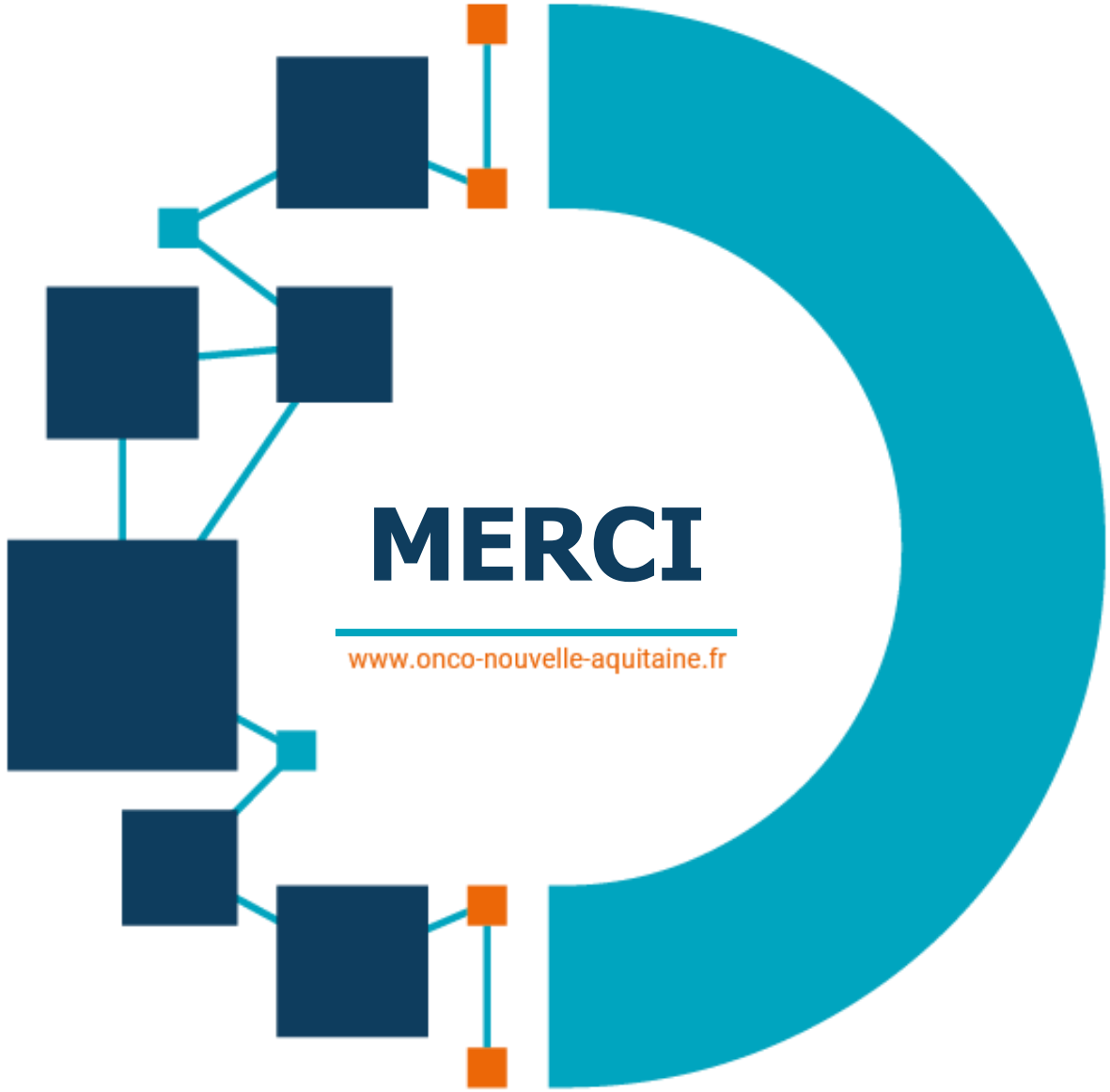
AESI, adverse event of special interest; ILD, interstitial lung disease.

Conclusion

- Intérêt indiscutable de ces anticorps conjugués en L1
- OS significative seulement pour le Datopotamab Deruxtecan
- Attention cross over dans l'étude ASCENT 03
- Données positives également de l'étude ASCENT 04 (SG + Pembrolizumab chez les patientes éligibles à l'immunothérapie) mais obtention ? Patientes déjà +++ traitée en néo adjuvant par de l'immunothérapie aujourd'hui)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