Abemaciclib plus endocrine therapy for HR+, HER2-, node-positive, high-risk early breast cancer: results from a pre-planned monarchE overall survival interim analysis, including 4-year efficacy outcomes

Stephen R.D. Johnston[1], Masakazu Toi, Joyce O'Shaughnessy, Priya Rastogi, Mario Campone, Patrick Neven, Chiun-Sheng Huang, Jens Huober, Georgina Garnica Jaliffe, Irfan Cicin, Sara M. Tolaney, Matthew P. Goetz, Hope S. Rugo, Elzbieta Senkus, Laura Testa, Lucia Del Mastro, Chikako Shimizu, Ran Wei, Ashwin Shahir, Maria Munoz, Belen San Antonio, Valérie André, Nadia Harbeck, Miguel Martin

[1]Royal Marsden NHS Foundation Trust, London, United Kingdom

Disclosures

Stephen Johnston

Consulting or Advisory Role:
Eli Lilly and Company, Puma Biotechnology, Pfizer, Novartis, Sanofi Genzyme

Speaker Honoraria:
Pfizer, Novartis, Eisai, Eli Lilly and Company, AstraZeneca, Roche/Genentech, Sanofi Genzyme

Research Funding:
Laboratory Studies: Pfizer, Puma Biotechnology
Clinical Trials: Eli Lilly and Company, Pfizer, AstraZeneca, Novartis, Roche/Genentech

monarchE: Adjuvant Abemaciclib in Early Breast Cancer

- Adjuvant abemaciclib combined with ET previously demonstrated significant improvement in IDFS and DRFS in high-risk, HR+/HER2-, node-positive EBC[1, 2]
  - When statistical significance was first met, follow-up was limited (median 15.5 months)[1]
  - A subsequent analysis confirmed abemaciclib treatment benefit persisted beyond the 2-year treatment period[2]
- Data presented today are from a pre-planned OS interim analysis defined to occur 2 years following the primary outcome analysis
  - All patients are now off abemaciclib
  - Median follow-up is 42 months
  - Includes a 4-year landmark analyses

[1]Johnston SRD, et al. J Clin Oncol. 2020;38(34):3987-3998
[2]Harbeck* N, Rastogi* P, et al. Ann Oncol. 2021;32(12):1571-1581
***co-first authors**

Overview of monarchE Data Cuts

Current Analysis

Analysis Time points	Interim Analysis[1]	Primary Outcome	Additional Follow-up 1[2] (AFU1)	Overall Survival Interim Analysis (OS IA2)
Date	16 March 2020	08 July 2020	01 April 2021	**01 July 2022**
Median Follow-up (months)	15.5	19.1	27.1	**42.0**
IDFS Events	323	395	565	**835**
Off Study Treatment*	26.4%	41.0%	89.6%	**99.2%**

*0.8% of patients were randomized but never entered treatment period and are not included in these percentages

- OS IA2 was planned to occur 2 years after the primary outcome analysis
- Follow up will continue to final OS analysis

[1]Johnston SRD, et al. J Clin Oncol. 2020;38(34):3987-3998
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monarchE Study Design (NCT03155997)

HR+, HER2-, node positive high-risk EBC

- Women or men
- Pre-/postmenopausal
- With or without prior neo- and/or adjuvant chemotherapy
- No metastatic disease
- Maximum of 16 months from surgery to randomization and 12 weeks of ET following the last non-ET

Cohort 1: High risk based on **clinical pathological features**

- ≥4 ALN OR
- 1-3 ALN and at least 1 of the below:
  - Grade 3 disease
  - Tumor size ≥5 cm

Cohort 2: High risk based on **Ki-67**

- 1-3 ALN and
- Ki-67 ≥20% and
- Grade 1-2 and tumor size <5 cm

Stratified for:

- Prior chemotherapy
- Menopausal status
- Region

R 1:1
N = 5637

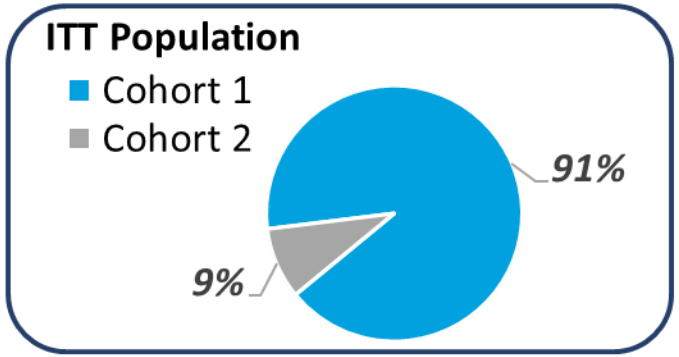
On-study treatment period
2 years

Abemaciclib
(150mg twice daily)
+
Endocrine Therapy: AI or tamoxifen

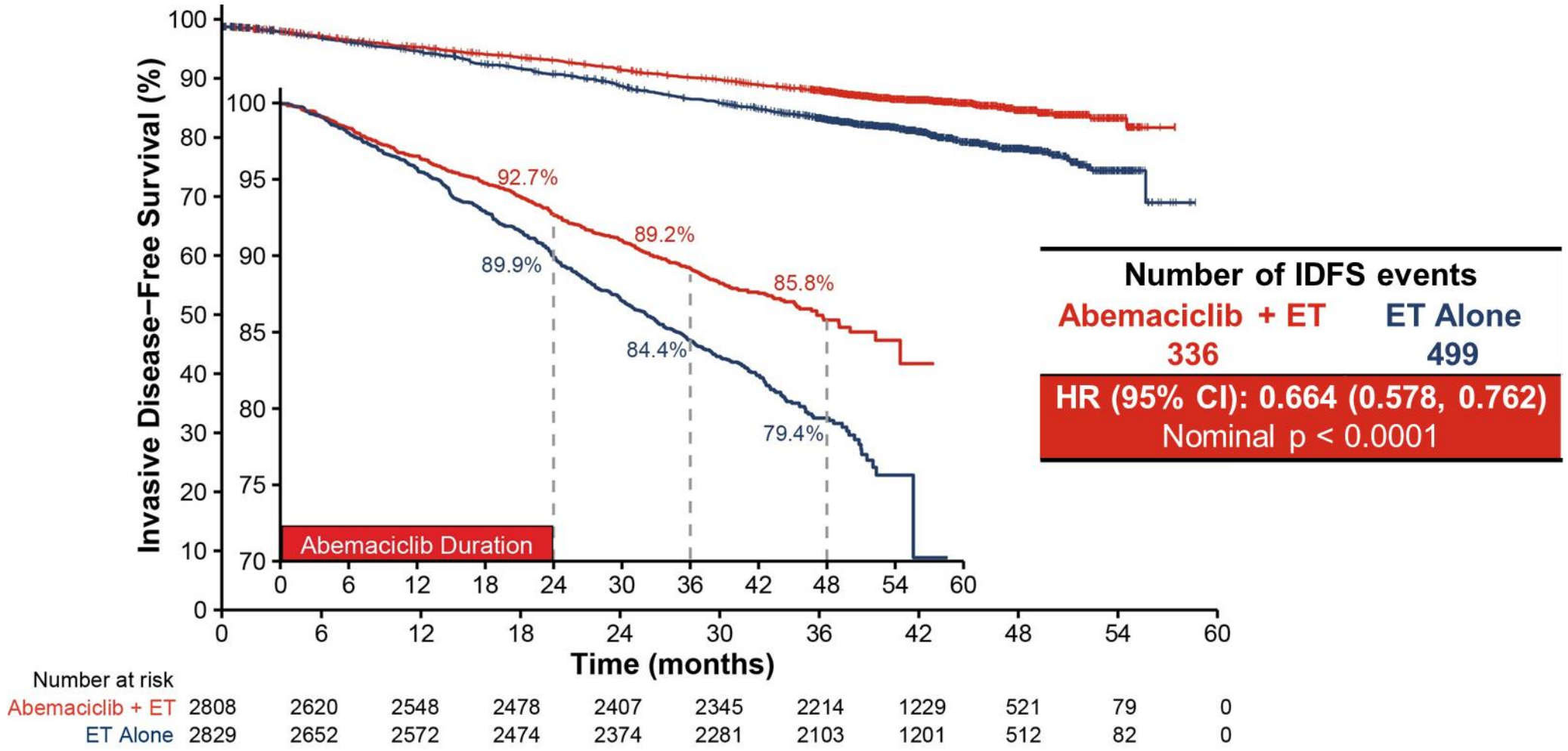
Endocrine Therapy: AI or tamoxifen

Follow-up period
Endocrine Therapy
3-8 years as clinically indicated

Primary Objective: IDFS
Secondary Objectives: IDFS in high Ki-67 populations, DRFS, OS, Safety, PK, PRO



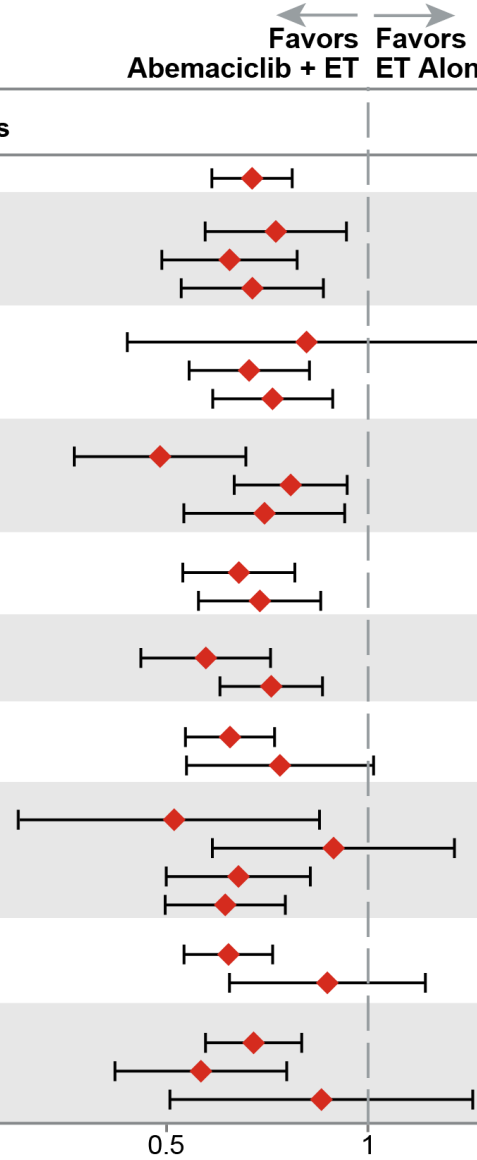
IDFS Benefit in ITT Persists Beyond Completion of Abemaciclib



33.6% reduction in the risk of developing an IDFS event with an increase in absolute benefit in IDFS 4-year rates (6.4%) compared to 2-and 3-year IDFS rates (2.8% and 4.8% respectively)

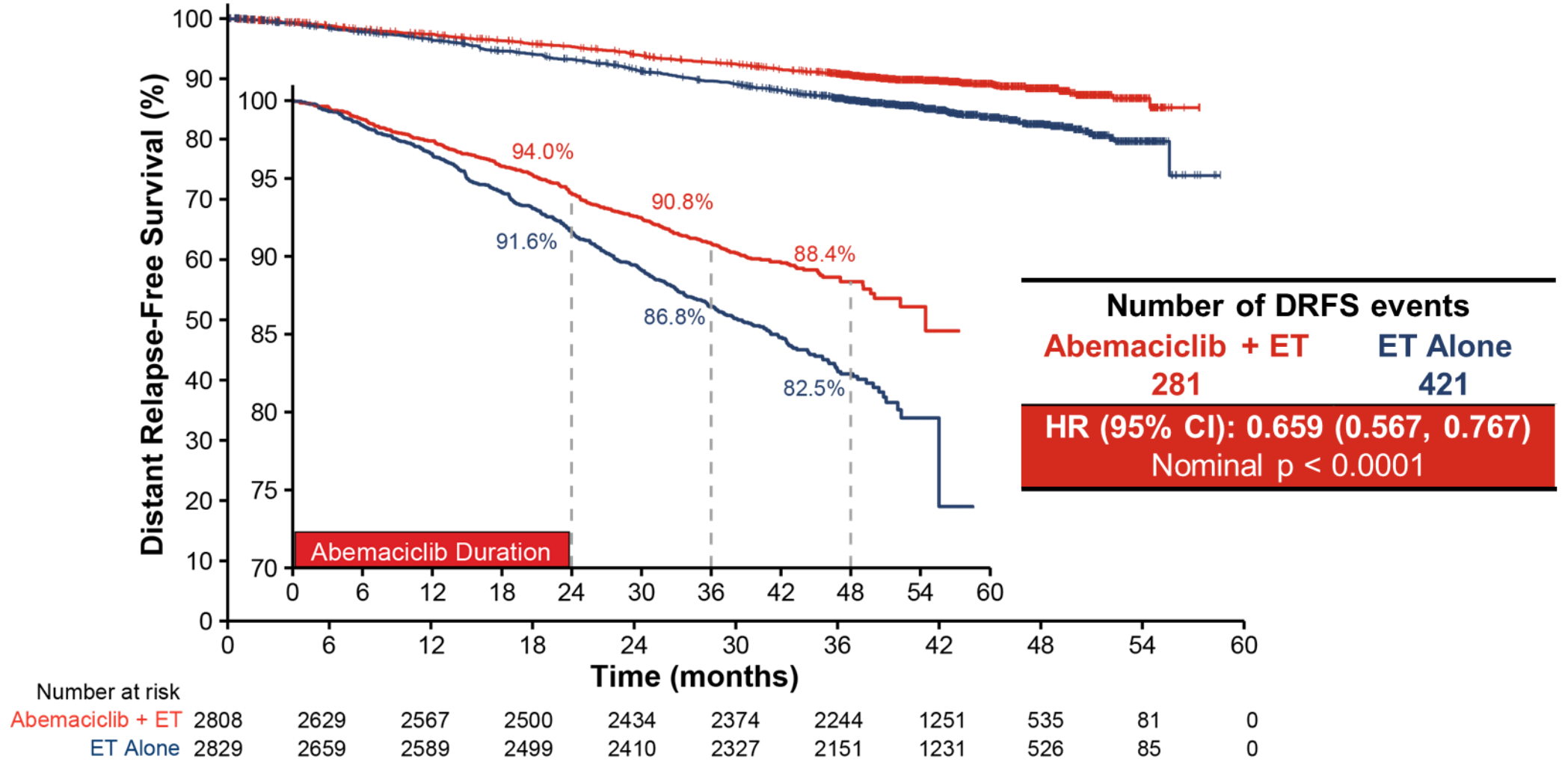
Consistent IDFS Benefit Observed in all Prespecified Subgroups*

	Abemaciclib + ET		ET Alone		HR (95% CI)	Interaction p-value
	No.	Events	No.	Events		
Overall	2808	336	2829	499	0.664 (0.578, 0.762)	
Number of Pos. lymph nodes						0.657
1-3	1118	111	1142	158	0.709 (0.556, 0.904)	
4-9	1107	113	1126	188	0.605 (0.479, 0.763)	
10 or more	575	110	554	153	0.654 (0.512, 0.835)	
Histologic Grade						0.754
Grade 1	209	18	216	23	0.797 (0.430, 1.478)	
Grade 2	1377	148	1395	226	0.654 (0.532, 0.805)	
Grade 3	1086	157	1064	213	0.709 (0.577, 0.872)	
Primary Tumor Size						0.044
<2 cm	781	66	767	131	0.481 (0.358, 0.646)	
2-5 cm	1371	177	1419	242	0.754 (0.621, 0.916)	
≥5 cm	607	86	610	121	0.689 (0.522, 0.908)	
Prior Chemotherapy						0.612
Neoadjuvant	1039	170	1048	261	0.631 (0.520, 0.765)	
Adjuvant	1642	147	1647	215	0.678 (0.549, 0.836)	
Menopausal Status						0.124
Premenopausal	1221	125	1232	205	0.583 (0.466, 0.728)	
Postmenopausal	1587	211	1597	294	0.730 (0.612, 0.871)	
Age						0.351
<65 years	2371	270	2416	414	0.646 (0.554, 0.753)	
≥65 years	437	66	413	85	0.767 (0.556, 1.059)	
Tumor Stage						0.351
Stage IIA	324	23	353	46	0.525 (0.318, 0.866)	
Stage IIB	392	42	387	47	0.909 (0.599, 1.378)	
Stage IIIA	1029	104	1026	157	0.655 (0.511, 0.839)	
Stage IIIC	950	148	963	227	0.626 (0.509, 0.770)	
Baseline ECOG PS						0.088
0	2405	277	2369	418	0.635 (0.545, 0.739)	
1	401	59	455	80	0.892 (0.637, 1.250)	
Race						
White	1947	236	1978	344	0.688 (0.583, 0.812)	0.337
Asian	675	71	669	116	0.574 (0.427, 0.771)	
All others	146	26	140	31	0.869 (0.516, 1.463)	



*Region of enrollment and Progesterone status data not shown

DRFS Benefit in ITT Persists Beyond Completion of Abemaciclib



34.1% reduction in the risk of developing a DRFS event with an increase in absolute benefit in DRFS 4-year rates (5.9%), compared to 2-and 3-year rates (2.5% and 4.1%, respectively)

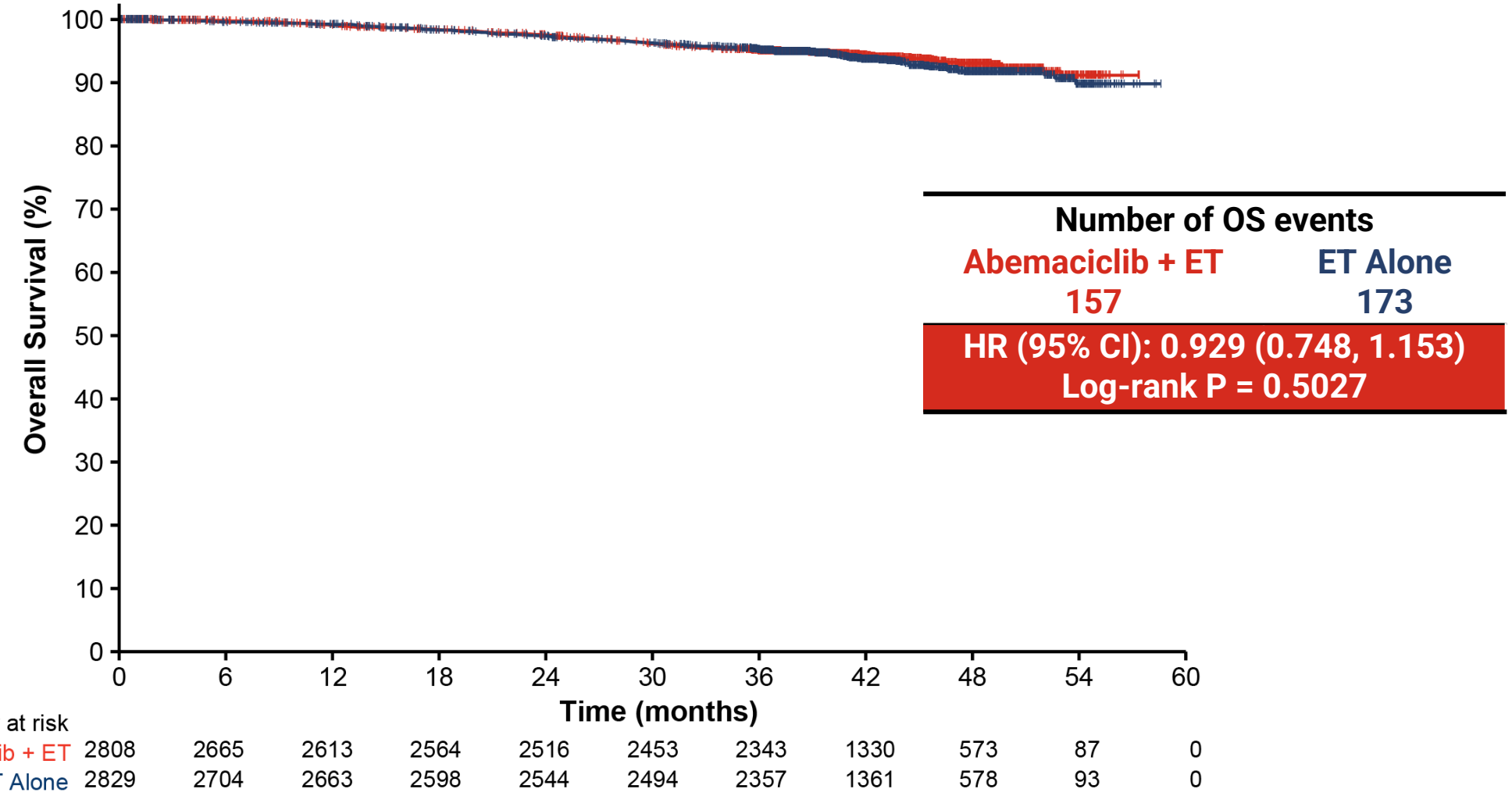
Abemaciclib Treatment Benefit Deepened Over Time

Analysis landmark	IDFS	DRFS
	Piecewise HR[a] (95% CI[b])	Piecewise HR[a] (95% CI[b])
Year 0-1	0.782 (0.583, 1.018)	0.725 (0.519, 0.983)
Year 1-2	0.674 (0.521, 0.858)	0.691 (0.521, 0.887)
Year 2-3	0.618 (0.477, 0.788)	0.651 (0.497, 0.851)
Year 3+	0.602 (0.428, 0.803)	0.581 (0.391, 0.818)

Study Treatment Period

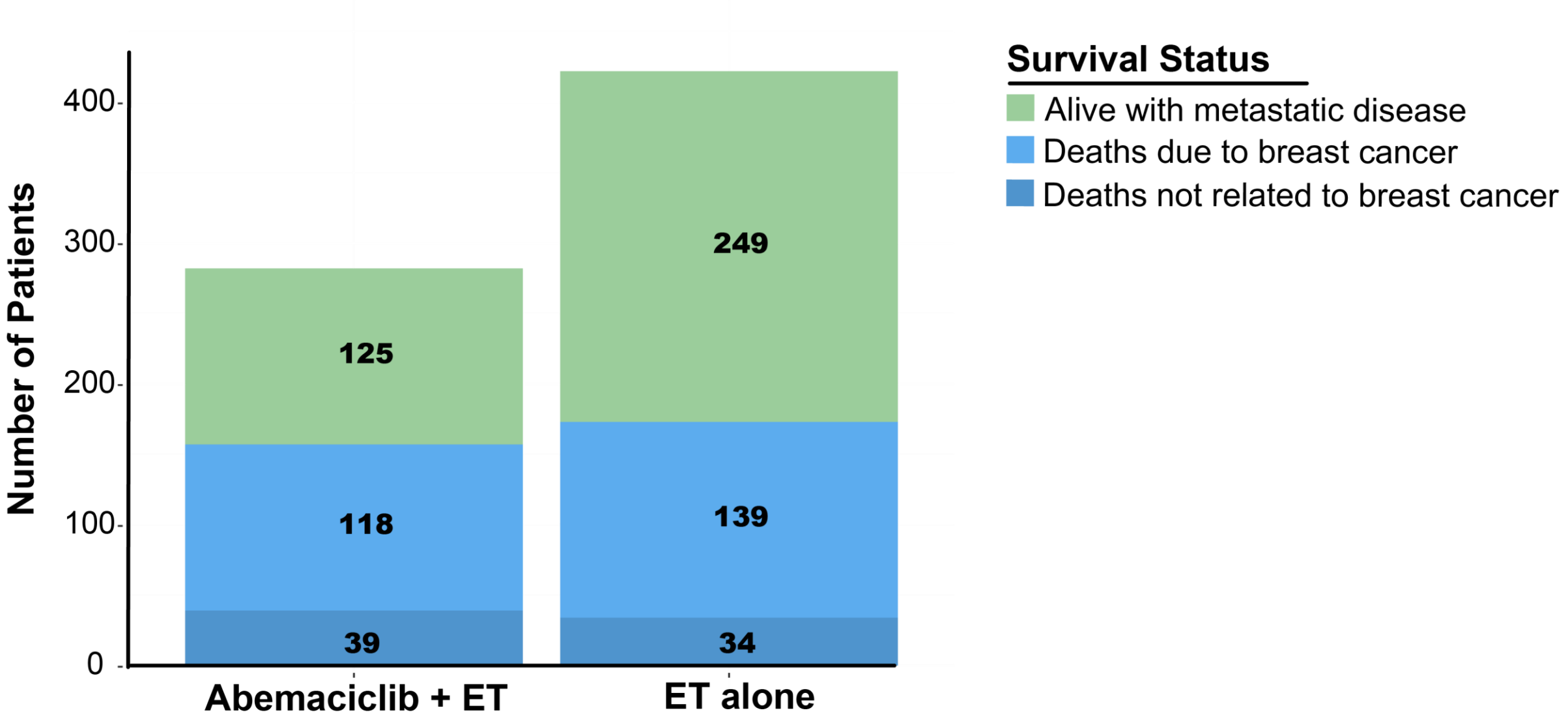
[a]Piecewise hazard ratio as a post-hoc analysis was estimated using piecewise exponential model to assess the yearly treatment effect size;
[b]95% credible intervals were calculated by equal tails in the posterior samples of Bayesian exponential models

OS Data Remain Immature in ITT



Fewer deaths (157 vs 173) were observed in the abemaciclib plus ET group versus the ET group

Fewer Patients with Metastatic Disease in the Abemaciclib arm



Efficacy in Subpopulations

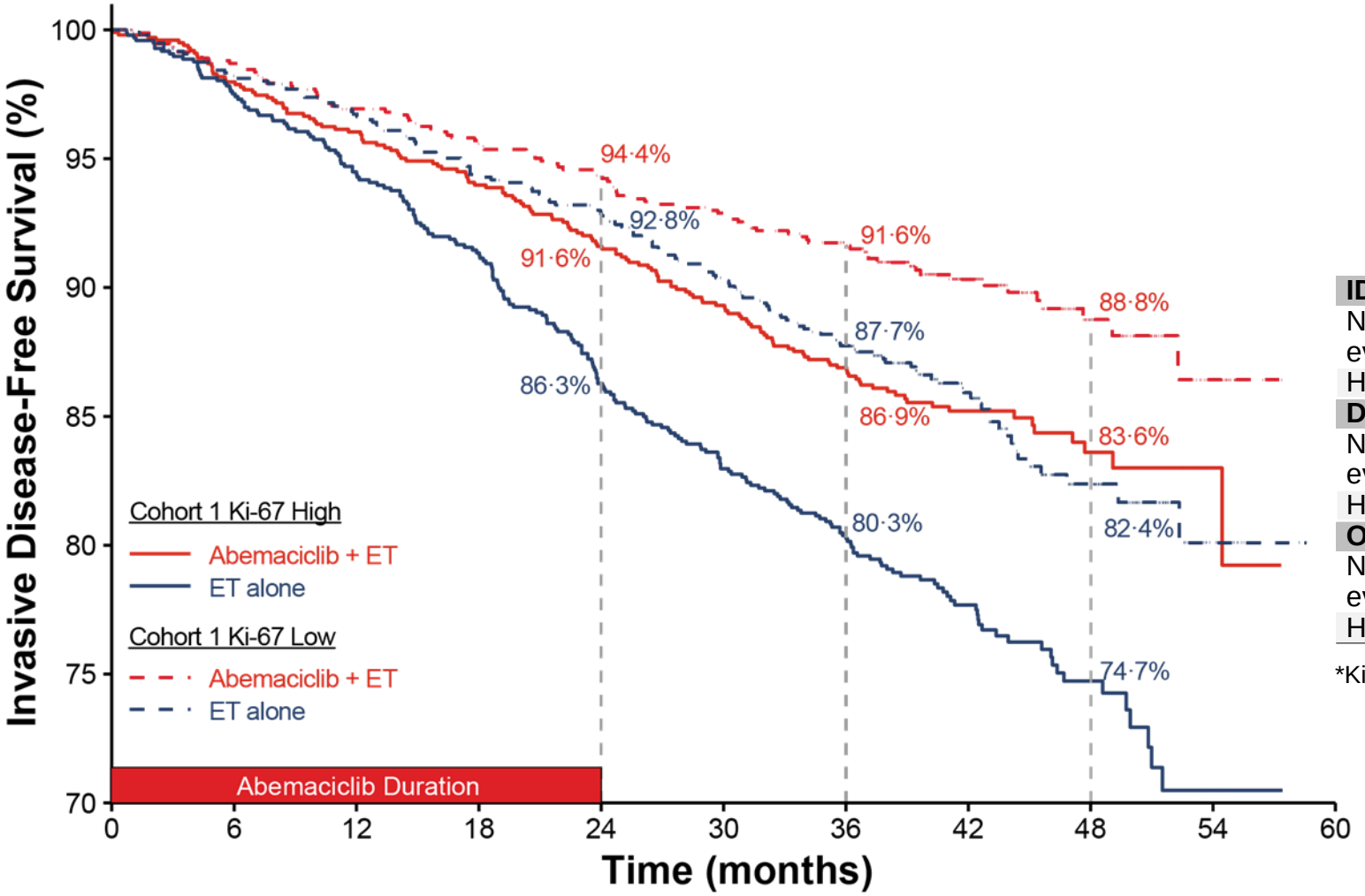
Efficacy Outcomes by Cohort

	Cohort 1		Cohort 2	
	Abemaciclib + ET N=2555	ET alone N=2565	Abemaciclib + ET N=253	ET alone N=264
IDFS				
Number of events, n	317	474	19	25
HR (95% CI)	**0.653 (0.567, 0.753)**		**0.773 (0.420, 1.420)**	
Nominal p-value	p<0.0001		p = 0.4048	
4-yr IDFS rate, (95% CI)	85.5 (83.8, 87.0)	78.6 (76.7, 80.4)	NR	NR
DRFS				
Number of events, n	267	402	14	19
HR (95% CI)	**0.652 (0.558, 0.761)**		**0.764 (0.383, 1.526)**	
Nominal p-value	p<0.0001		p = 0.4448	
4-yr DRFS rate, (95% CI)	87.9 (86.4, 89.3)	81.8 (79.9, 83.4)	NR	NR
OS (Immature)				
Number of events, n	147	168	10	5
HR (95% CI)	**0.890 (0.714, 1.111)**		NR	

NR: Not reported. Low event number does not allow reliable statistical analysis.

Cohort 2 enrolled patients with intermediate risk by clinicopathological features. Data remain immature

Ki-67 is Prognostic, but Not Predictive of Abemaciclib Benefit

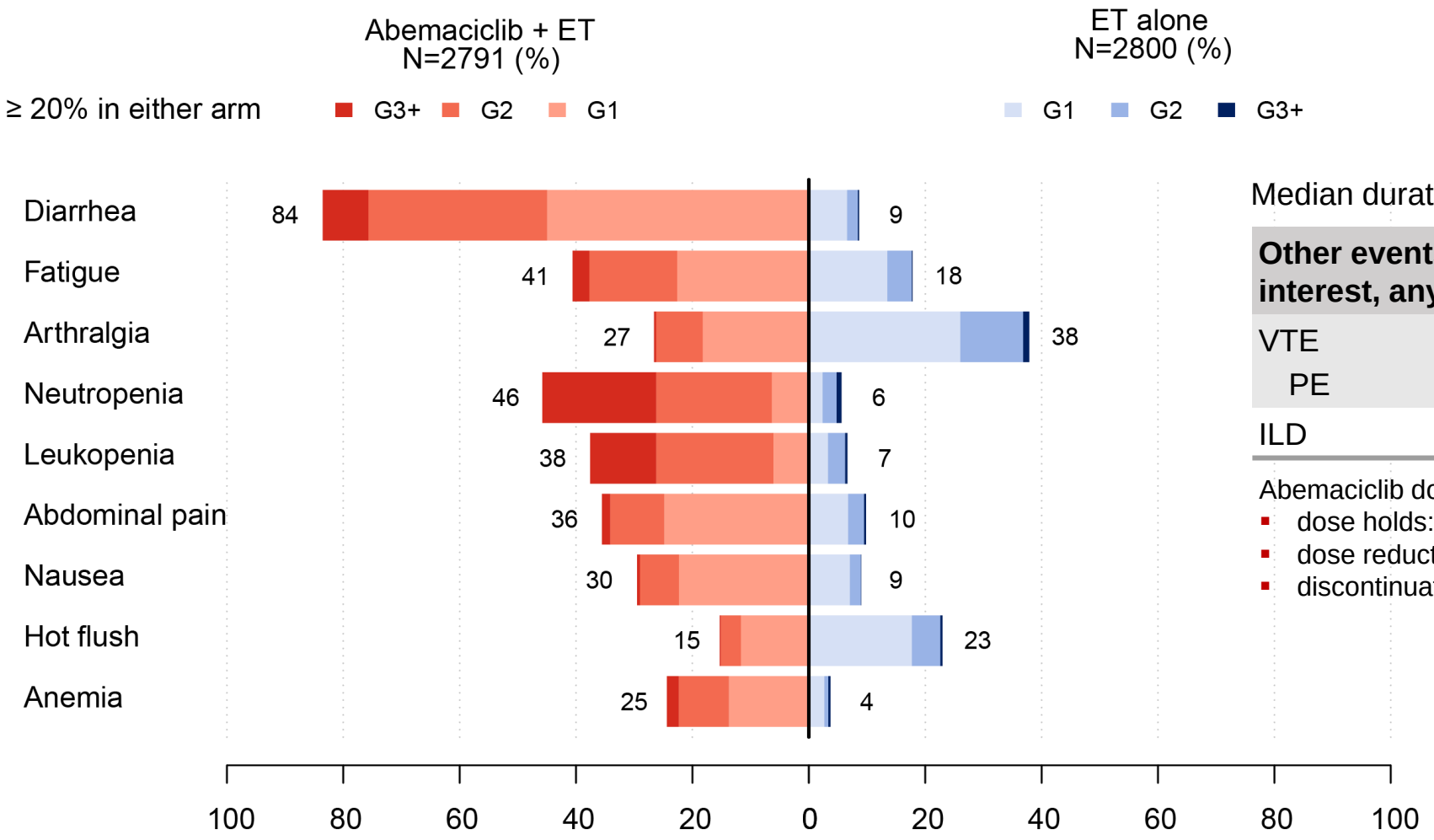


	Cohort 1*			
	C1 Ki-67 High		C1 Ki-67 Low	
	Abemaciclib + ET N=1017	ET alone N=986	Abemaciclib + ET N=946	ET alone N=968
IDFS				
Number of events, n	147	224	91	141
HR (95% CI)	**0.618** (0.501, 0.762)		**0.624** (0.478, 0.814)	
DRFS				
Number of events, n	126	193	74	119
HR (95% CI)	**0.612** (0.488, 0.767)		**0.613** (0.458, 0.821)	
OS (Immature)				
Number of events, n	68	88	39	50
HR (95% CI)	**0.733** (0.533, 1.007)		**0.772** (0.506, 1.175)	

*Ki-67 value was missing in 1203 (23.5%) patients

Within Cohort 1, similar abemaciclib treatment effects were observed regardless of Ki-67 index

Safety Findings Consistent with Previous Analyses



Median duration of abemaciclib: 23.7 months.

Other events of interest, any grade	Abemaciclib + ET N = 2791, %	ET Alone N = 2800, %
VTE	2.5	0.7
PE	1.0	0.1
ILD	3.3	1.3

Abemaciclib dose adjustments due to AEs
- dose holds: 61.7%
- dose reductions: 43.6%
- discontinuations 18.5% [8.9% after dose reduction]

All patients who received at least one dose of study treatment were included in the safety population

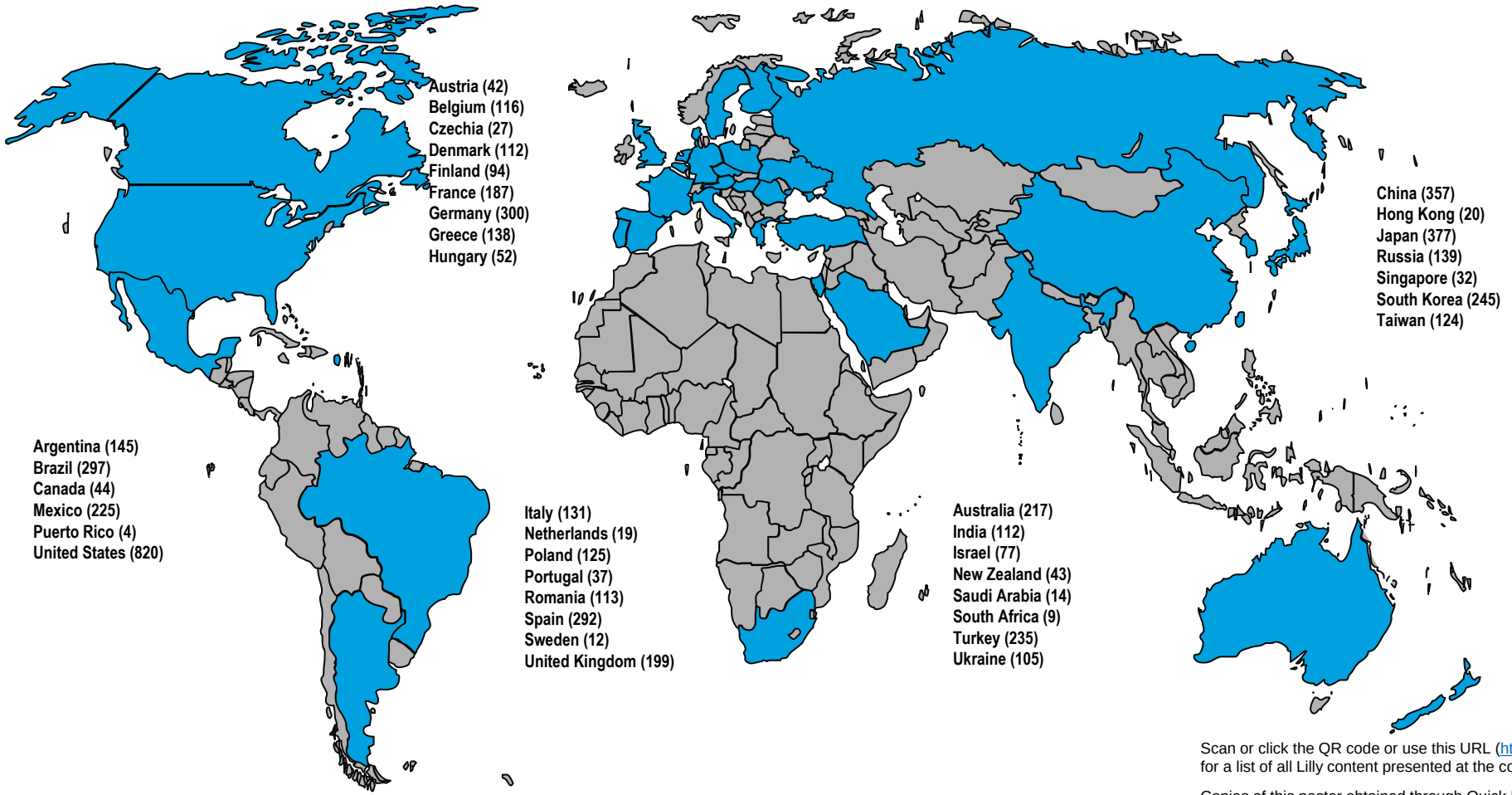
The safety profile of abemaciclib is considered manageable and acceptable for this high-risk population

Conclusions

- With additional follow-up, the benefit of adjuvant abemaciclib deepened in magnitude with an increase in absolute IDFS and DRFS benefit at 4 years as compared to 2- and 3-year rates
  - Benefit demonstrated across all prespecified subgroups for IDFS and DRFS
  - Ki-67 remains prognostic but abemaciclib benefit is similar regardless of Ki-67 index
- While OS data remain immature at this time, fewer deaths were observed with abemaciclib plus ET group compared to ET alone
  - Continued follow-up is ongoing until final assessment of OS
- These data further support the addition of adjuvant abemaciclib to ET for patients with HR+, HER2-, node-positive, high-risk EBC

Acknowledgements

We thank the 5,637 patients and their families/caregivers from 603 sites in the following 38 countries for participating in this trial:



- We would like to generously thank the investigators and their support staff who participated in this work
- We are very grateful for the time and efforts of the monarchE Executive and Steering Committees
- This study was sponsored by Eli Lilly and Company

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Published online December 6, 2022
https://doi.org/10.1016/S1470-2045(22)00694-5