



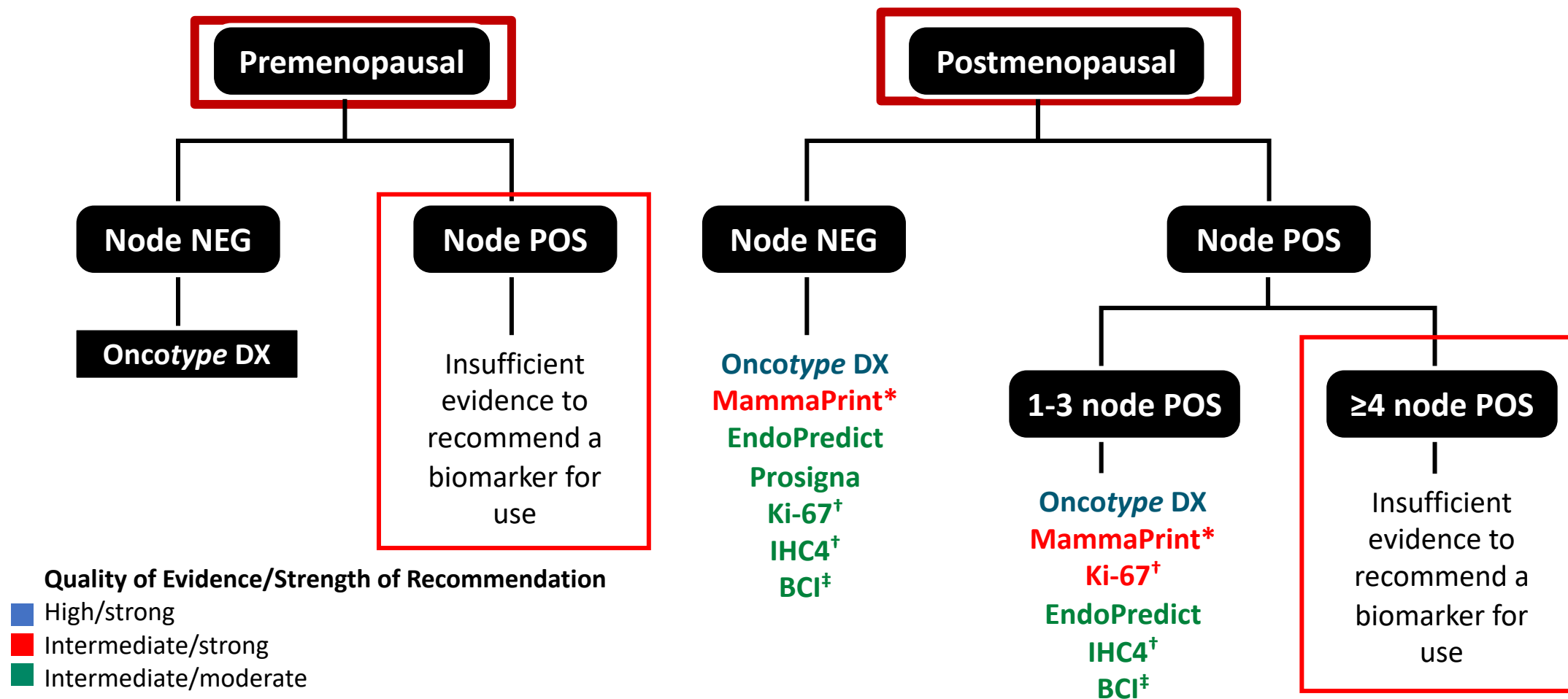
How I treat hormone receptor-positive, HER2-negative breast cancer

Ruth O'Regan, MD, MSc, FASCO,
Executive Vice Dean & Chief Academic Officer,
Charles A. Dewey Professor of Medicine,
University of Rochester

Early-stage HR-positive breast cancer

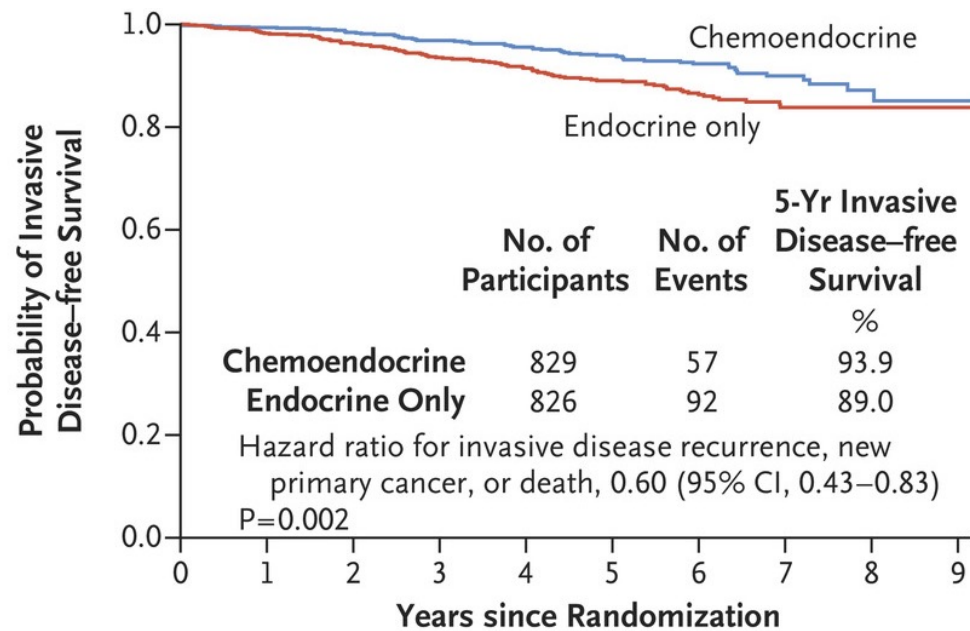
- Chemotherapy use based on genomic assays for node-negative and N1 disease (and now N2) and menopausal status
- Aromatase inhibitors standard for postmenopausal patients
 - Adjuvant giredestrant awaited
- Tamoxifen for premenopausal with low-risk cancers and OFS + AI for higher-risk cancers
- CDK 4/6 inhibitors added for node-positive and high-risk node-negative cancers
- PARP inhibitor if BRCA mutation and high risk
- Effective pre-operative systemic therapy is a critical need

ASCO-CAP Guidelines



RxPONDER: Chemo Benefit Different by Menopausal Status if RS 0-25

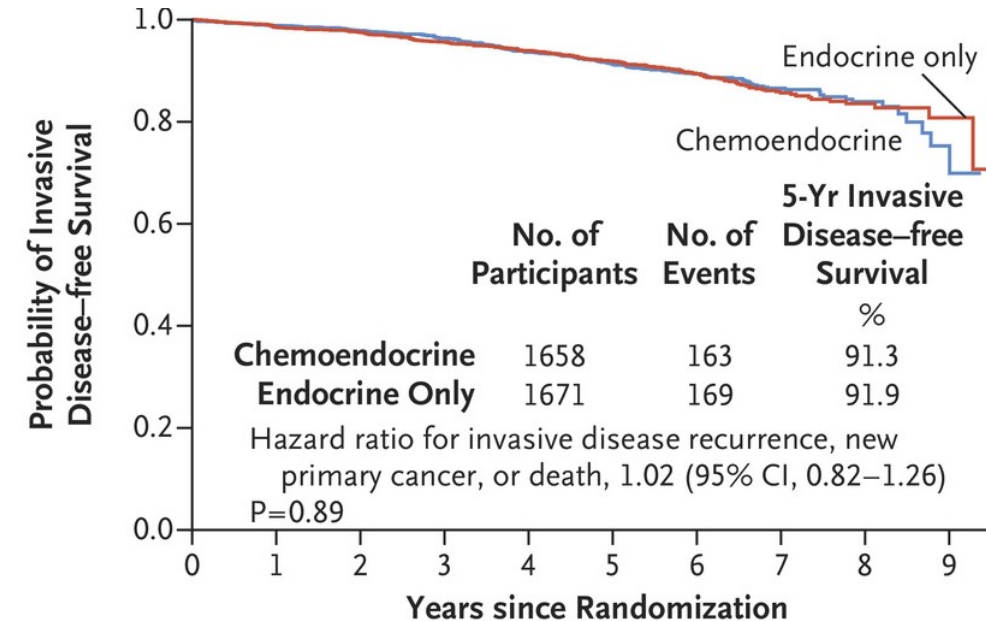
Premenopausal (1/3rd Trial)



Why the Chemo Benefit?

OFS rate low (~ 16% in ET only)

Postmenopausal (2/3rd Trial)

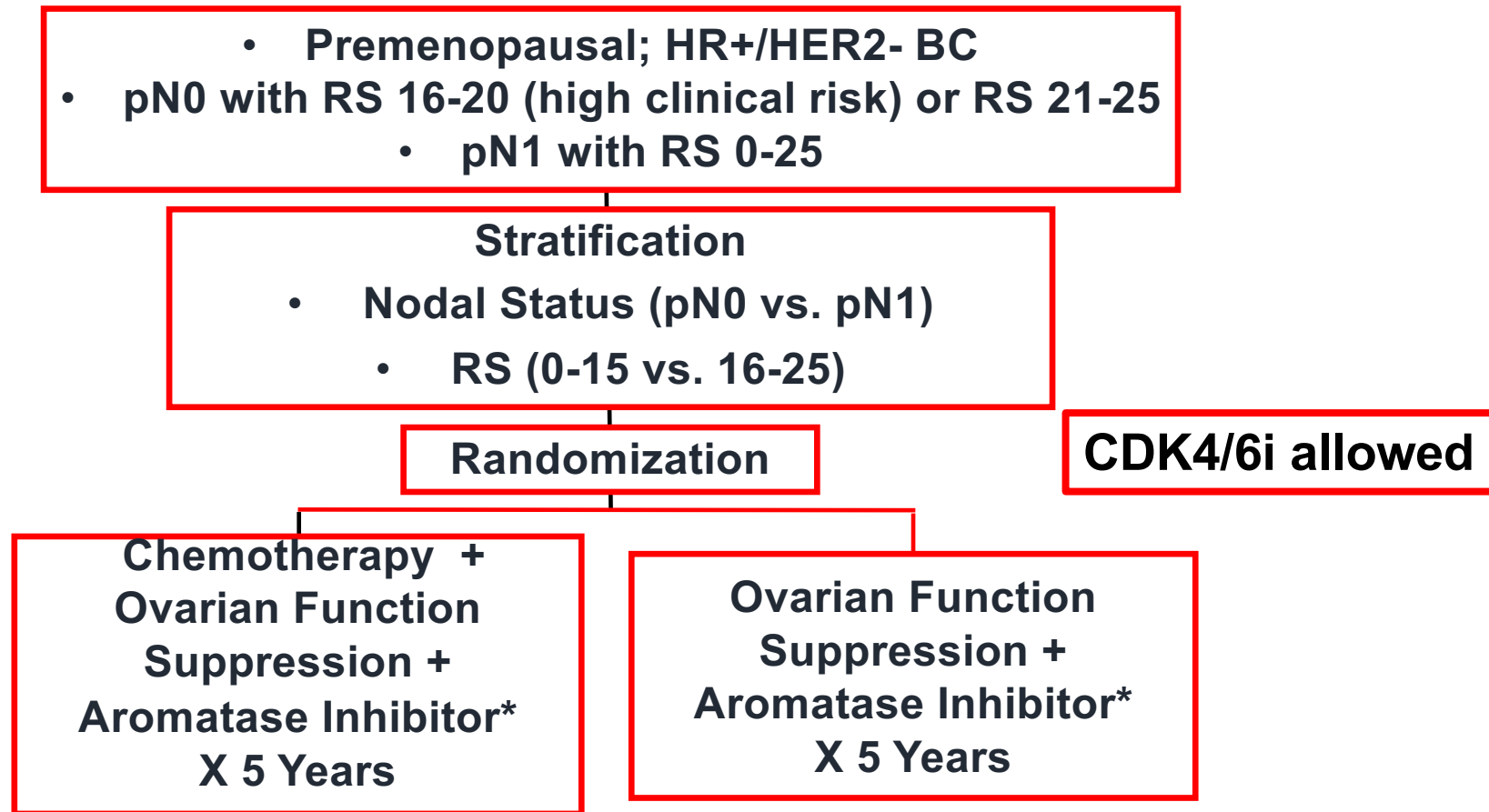


What about if > 3 Lymph Nodes?

What about RS > 25?

postmenopausal: LMP > 12 mo or BSO; premenopausal: LMP < 6 mo; if neither: age 50 as cutoff

BR009: The OFSET Study Schema (N=3960)

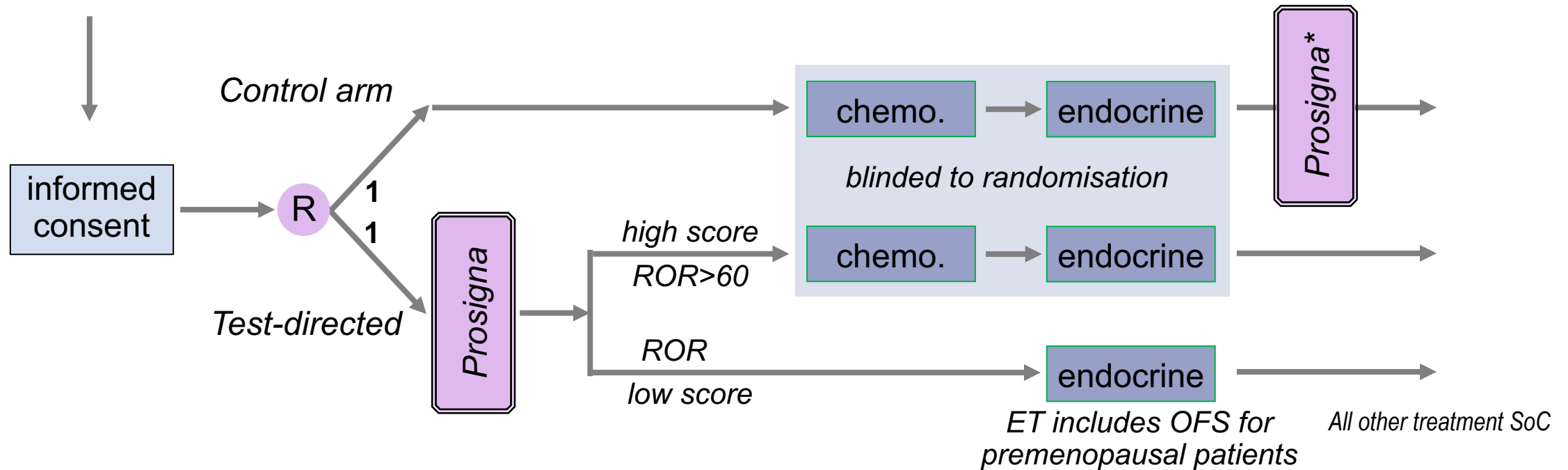


* Tamoxifen can be used if AI is not tolerated

OPTIMA Trial Design

Main eligibility criteria

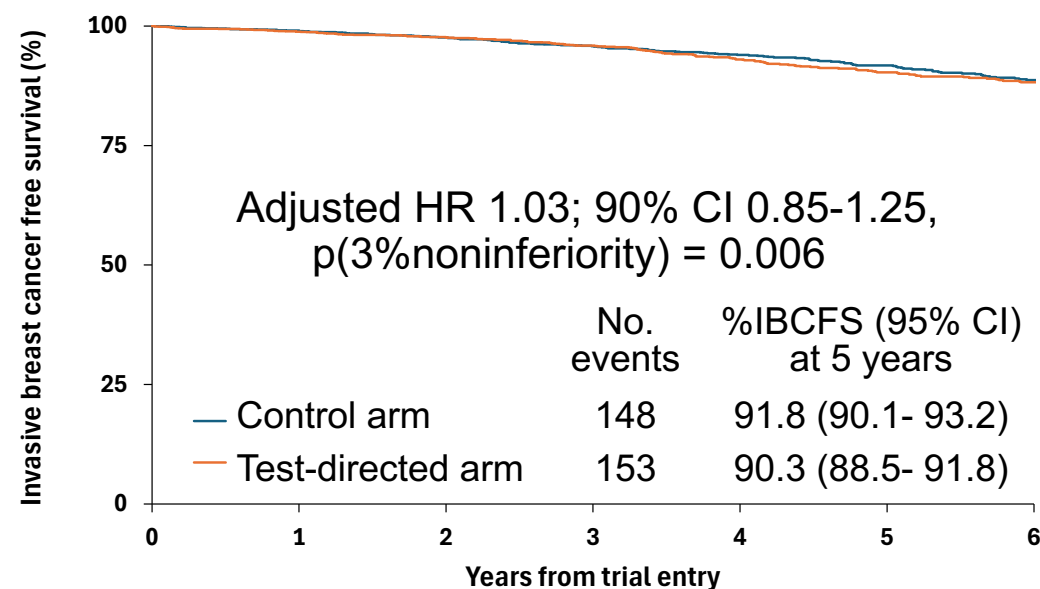
- Women & men age ≥ 40 with excised breast cancer
- ER-pos (IHC $> 10\%$) & HER2-neg
- Nodes: $\geq 0-9N+$,
 - ▶ minimum T-size requirement if N0/ N1mi
- Neoadjuvant chemotherapy prohibited



*Control arm Prosigna testing used for analysis only. U.K. control arm testing performed following recruitment completion

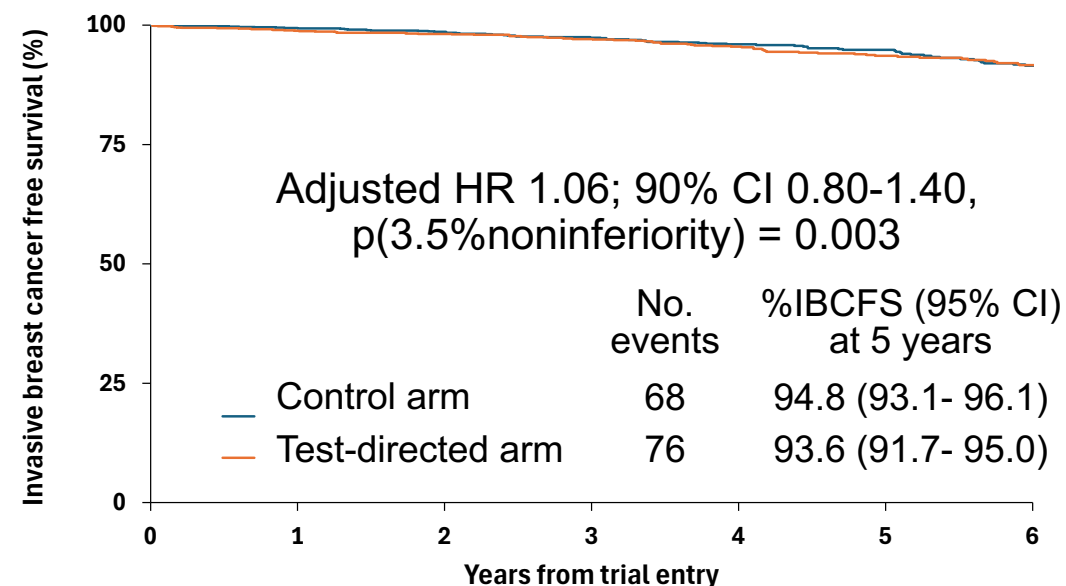
Invasive Breast Cancer Free Survival (IBCFS)

Complete Per Protocol



Number at risk:							
Control	2059	1818	1563	1283	999	741	485
Test-directed	2094	1857	1591	1303	989	724	481

ROR ≤ 60 (2/3rd)

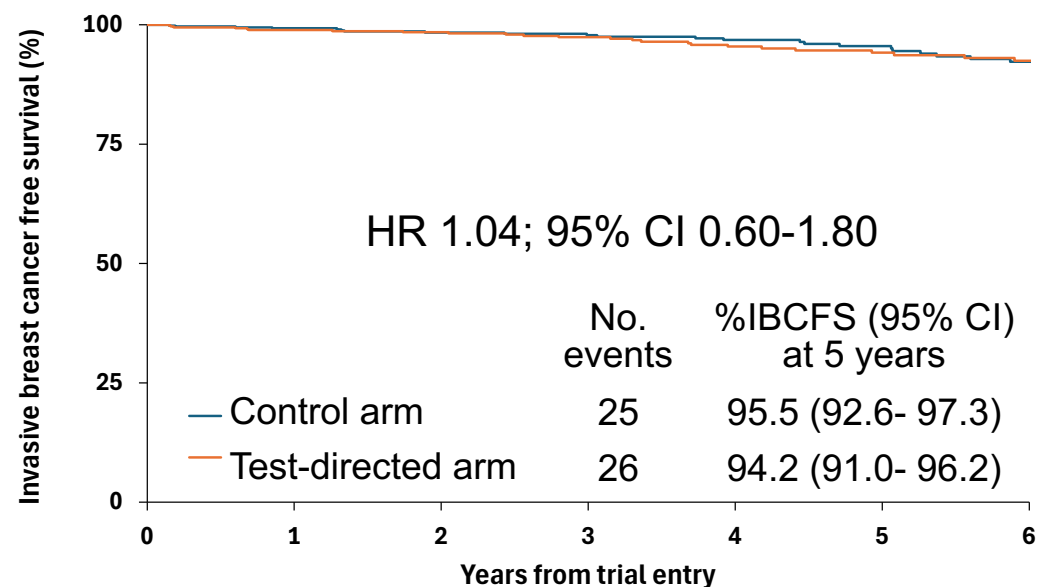


Number at risk:							
Control	1358	1207	1043	862	672	504	337
Test-directed	1421	1257	1086	905	694	503	342

Median follow-up 4.0 years: IQR 2.0-6.0 years

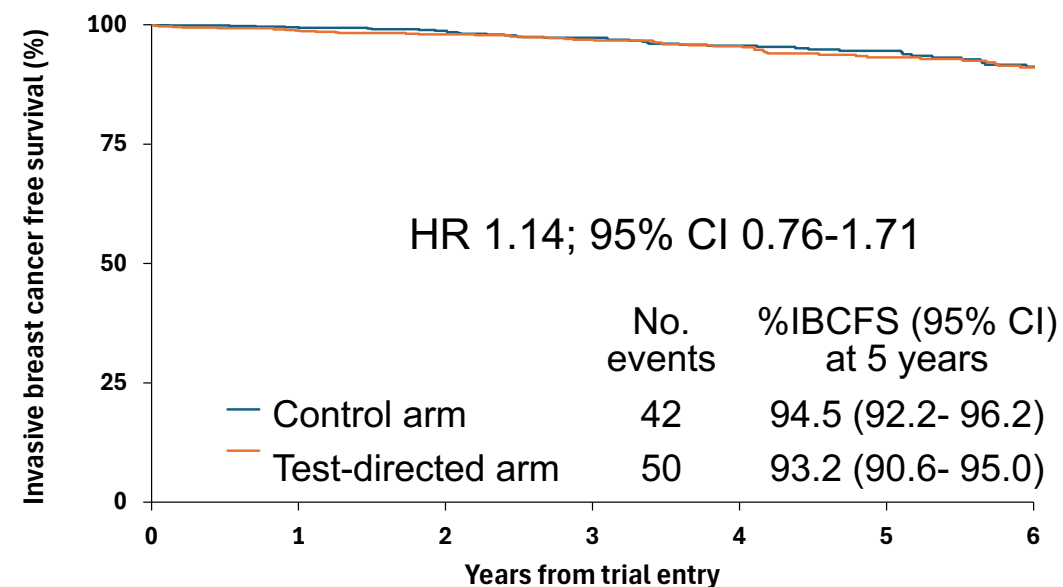
IBCFS vs menopausal status: low ROR score

Premenopausal (40%)



Number at risk:							
Control	561	481	409	338	258	200	140
Test-directed	559	487	410	347	256	195	135

Postmenopausal (60%)

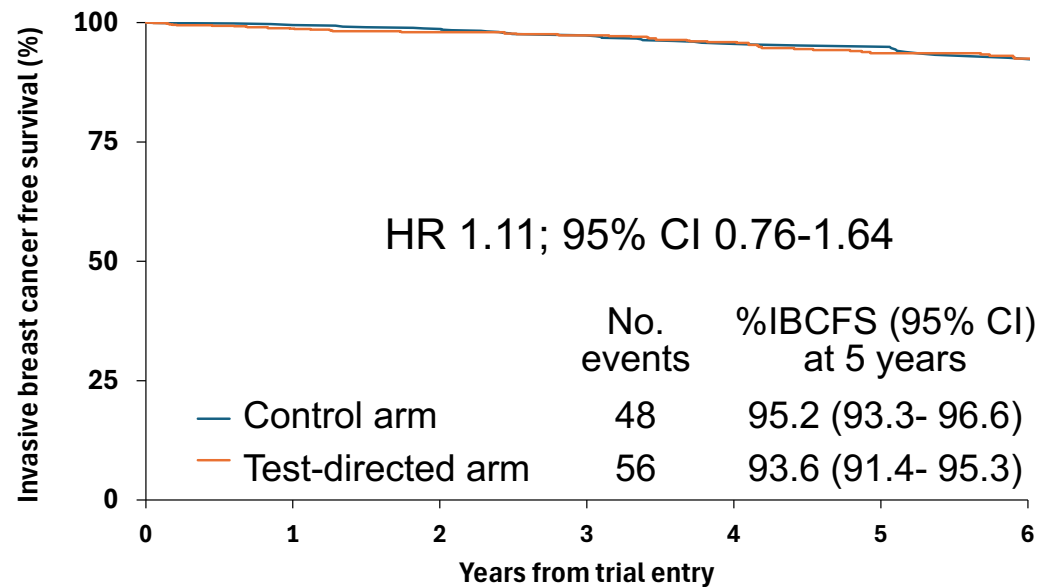


Number at risk:							
Control	791	721	631	522	414	304	197
Test-directed	858	766	673	556	437	307	207

Postmenopausal: age > 45 and LMP > 12 months; BSO; or estradiol and FSH in postmenopausal range

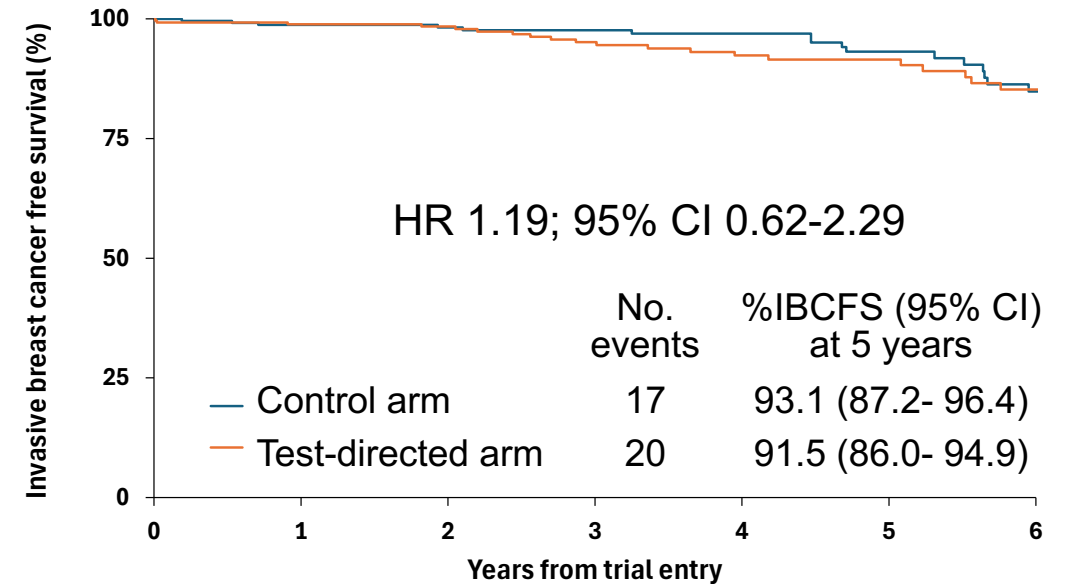
IBCFS vs menopausal status: low ROR score

N1 (1-3 LN+) (80%)



Number at risk:							
Control	1015	914	798	651	499	382	264
Test-directed	1063	953	829	700	539	389	270

N2 (4-9 LN+) (20%)



Number at risk:							
Control	243	214	181	155	125	84	48
Test-directed	269	232	197	158	118	86	49

lidERA: Study design

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

N = 4170

R
1:1

At least 5-year treatment duration

Giredestrant (30 mg PO QD)

SOC ET

Tamoxifen/anastrozole/letrozole/exemestane

5-year follow-up

Long-term
follow-up

Primary endpoint

- IDFS (excluding second primary non-breast cancer)

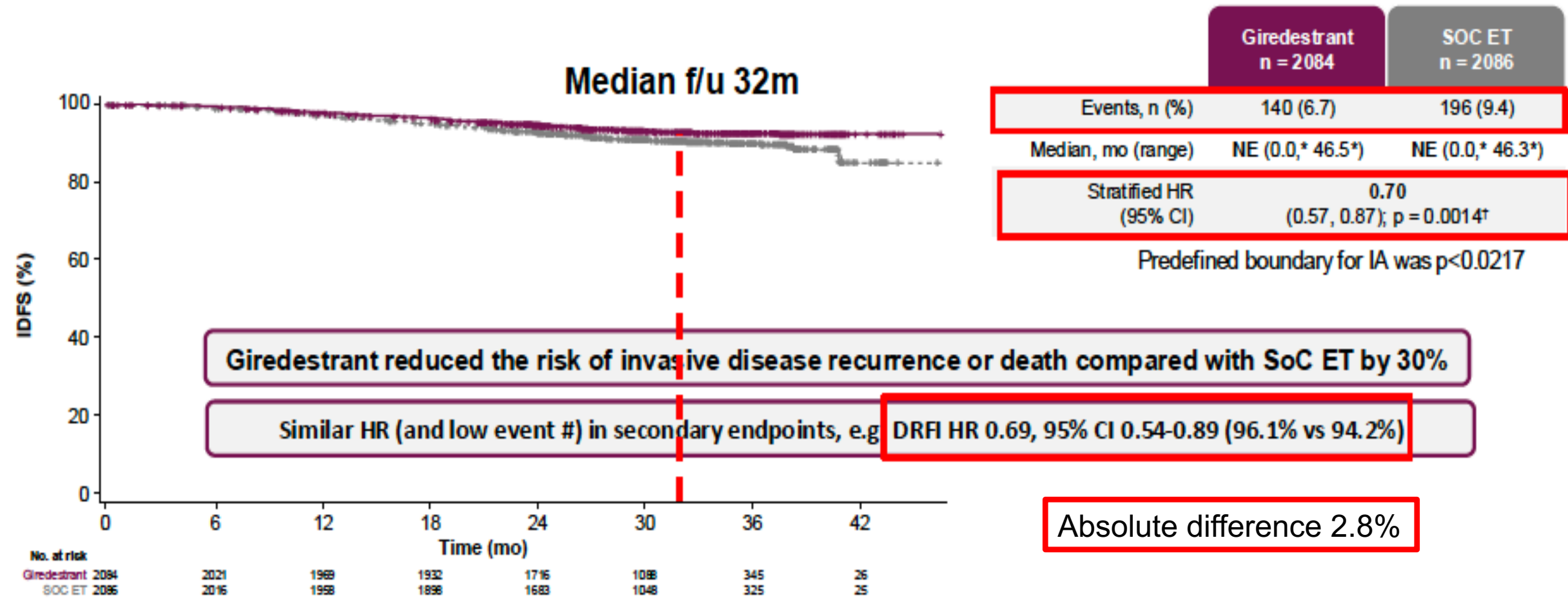
Key secondary endpoints

- 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

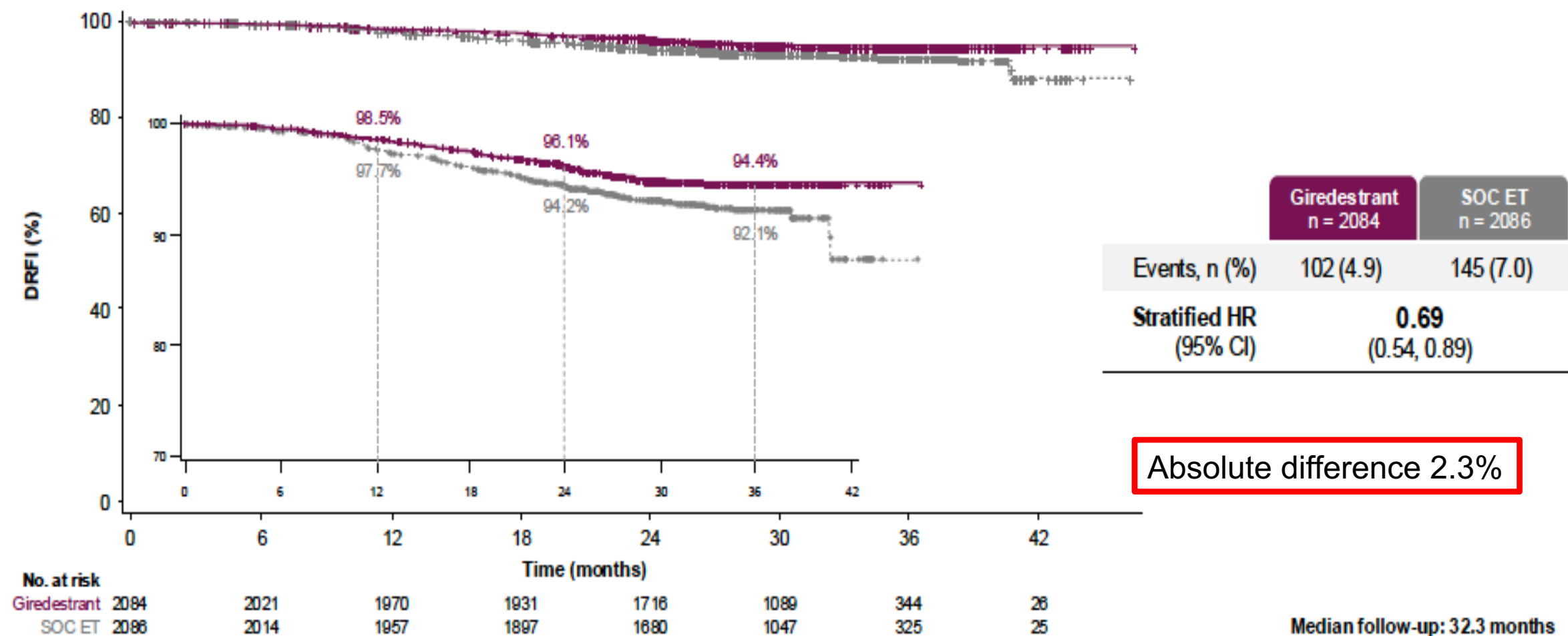
No CDK 4/6i

† Premenopausal patients received LHRH agonist with giredestrant or AI

lidERA: IDFS

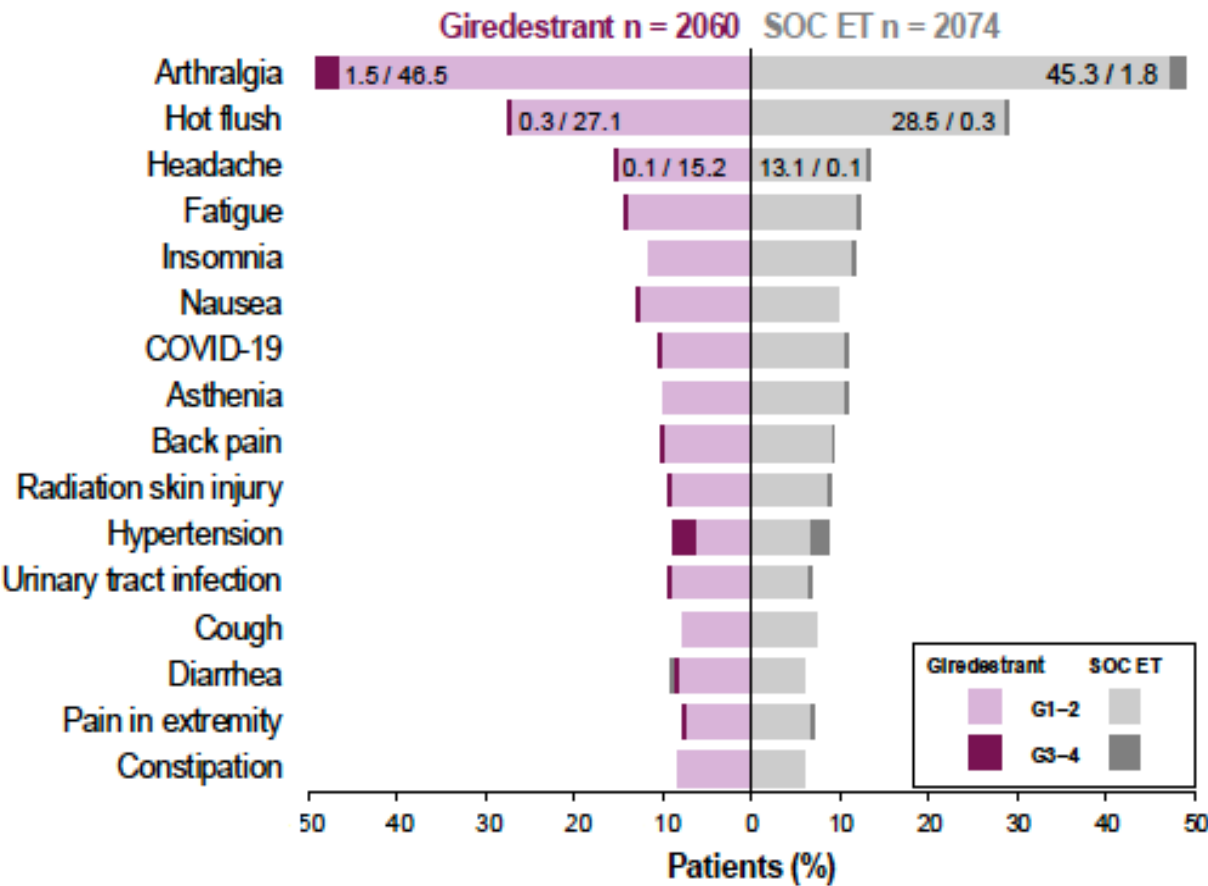


lidERA: DRFS



lidERA: Adverse events

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

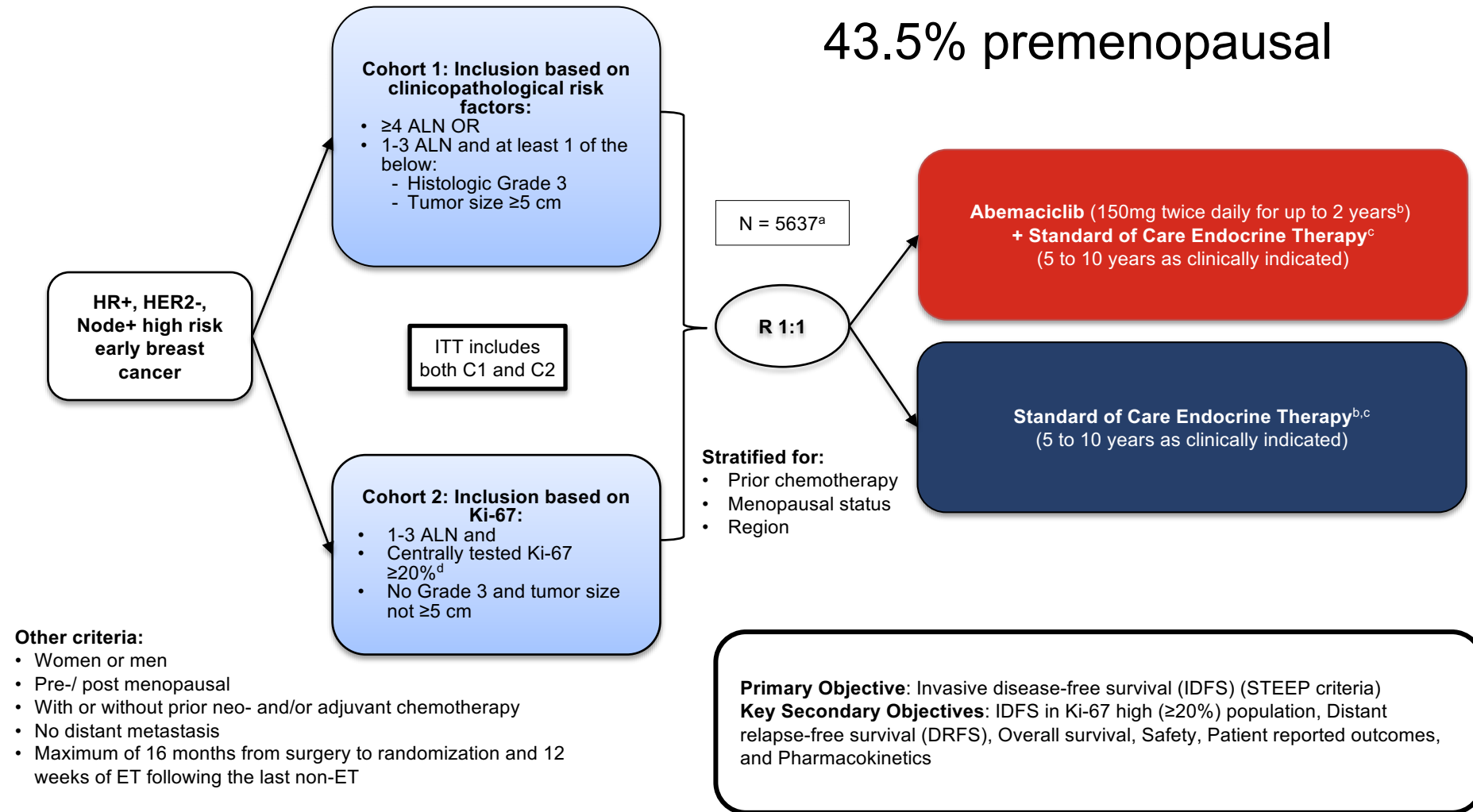


Selected AEs

	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)

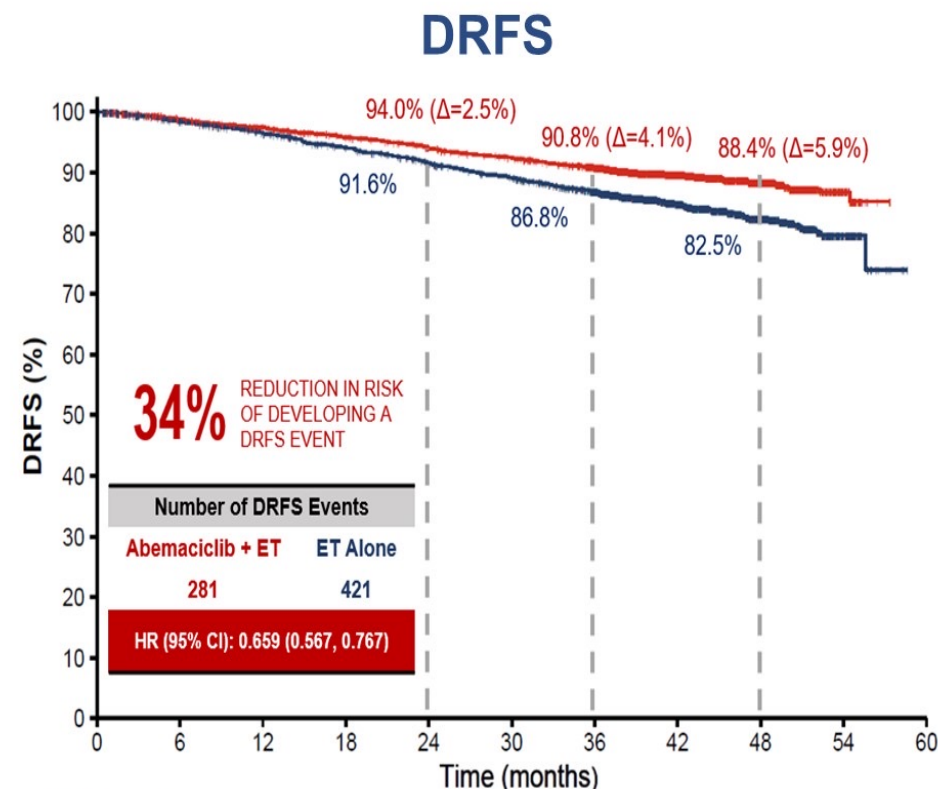
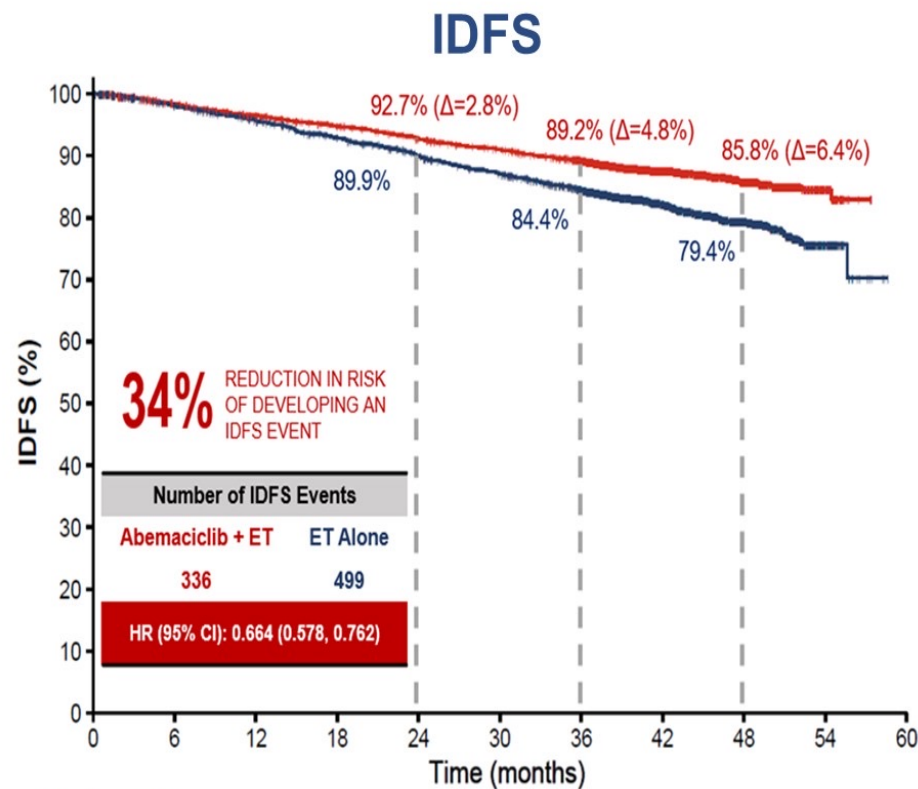
	Giredestrant n = 2060			SOC ET n = 2074		
Patients, n (%) with selected AEs by medical concept*						
	G1	G2	G3–4	G1	G2	G3–4
Bradycardia†	217 (10.5)	15 (0.7)	0	64 (3.1)	2 (< 0.1)	0
Venous thromboembolic events	4 (0.2)	12 (0.6)	2 (< 0.1)‡	3 (0.1)	7 (0.3)	7 (0.3)

Monarch E: Study Design



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

IDFS and DRFS Benefit Persist and Deepen Beyond Completion of 2-Year Abemaciclib Treatment Period^{*3}



Number at risk

2808	2620	2548	2478	2407	2345	2214	1229	521	79	0
2829	2652	2572	2474	2374	2281	2103	1201	512	82	0

Number at risk

2808	2629	2567	2500	2434	2374	2244	1251	535	81	0
2829	2659	2589	2499	2410	2327	2151	1231	526	85	0

*From ITT analysis

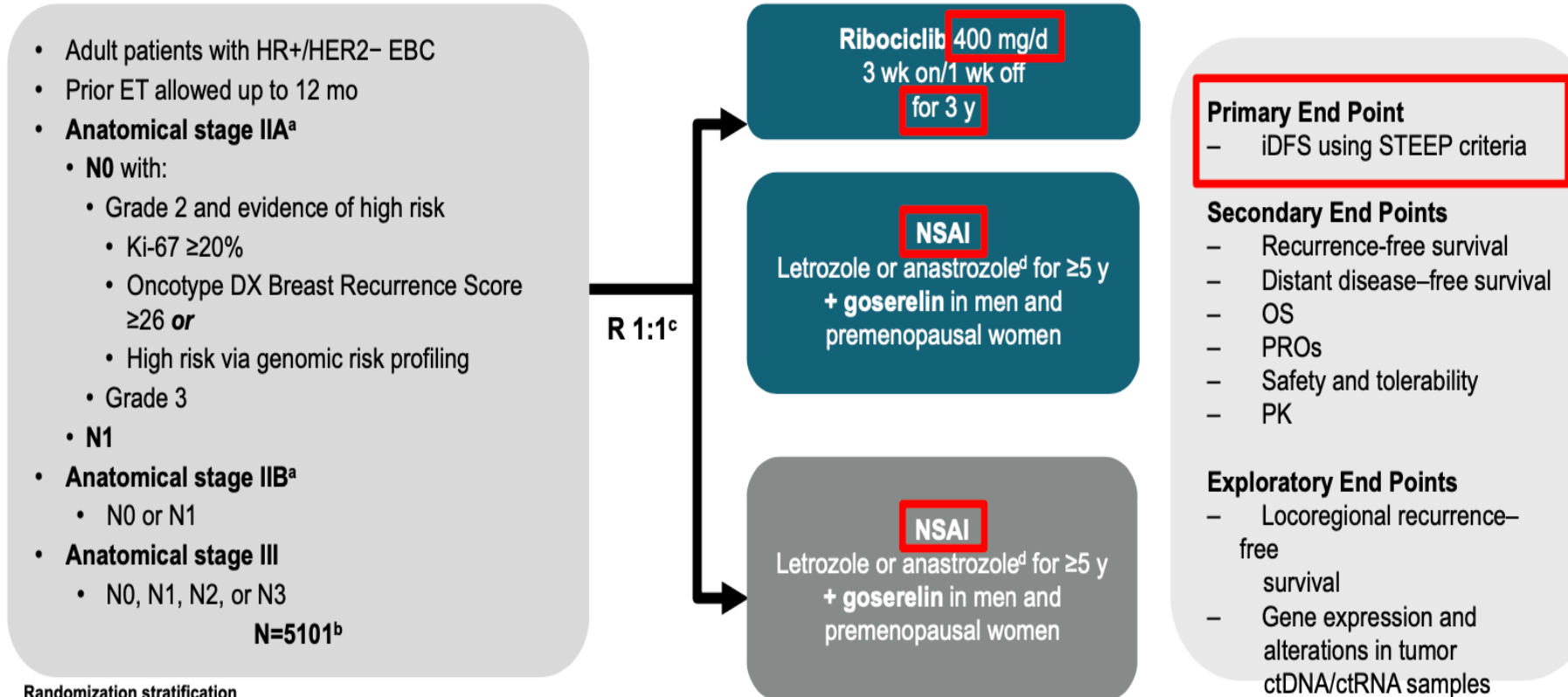
Hamilton et al. ASCO 2023

³Johnston SRD et al. 2023 The Lancet Oncol;24(01):77-90

Copyright ©2023 Eli Lilly and Company. All rights reserved.

NATALEE: Schema

44% of patients were premenopausal or male



Randomization stratification

Anatomical stage: II vs III

Menopausal status: men and premenopausal women vs postmenopausal women

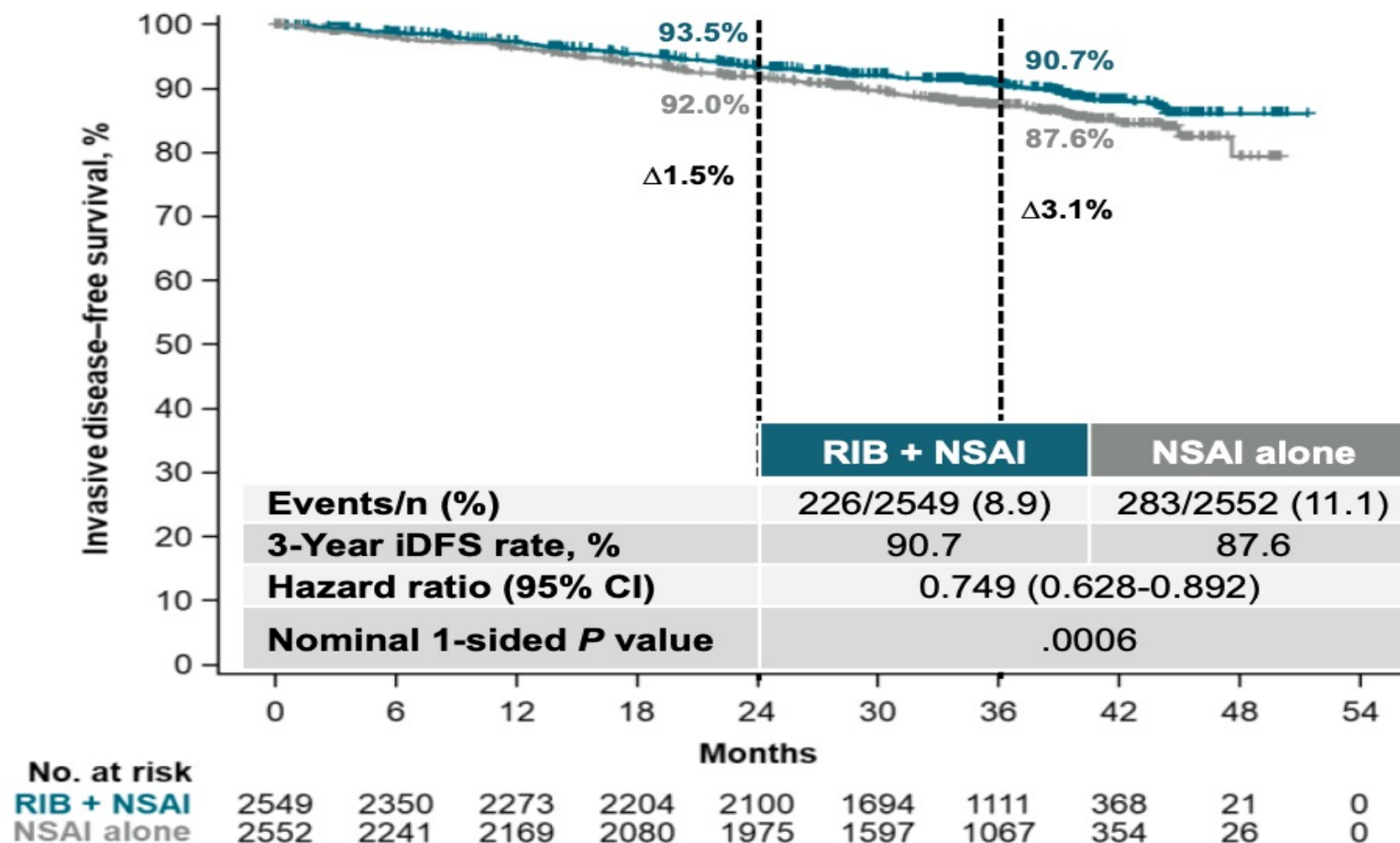
Receipt of prior (neo)adjuvant chemotherapy: yes vs no

Geographic location: North America/Western Europe/Oceania vs rest of world

ct, circulating tumor; EBC, early breast cancer; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; iDFS, invasive disease-free survival; N, node; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; PK, pharmacokinetics; PRO, patient-reported outcome; R, randomized; STEEP, Standardized Definitions for Efficacy End Points in Adjuvant Breast Cancer Trials.

^a Enrollment of patients with stage II disease was capped at 40%. ^b 5101 patients were randomized from Jan 10, 2019 to April 20, 2021. ^c Open-label design. ^d Per investigator choice.

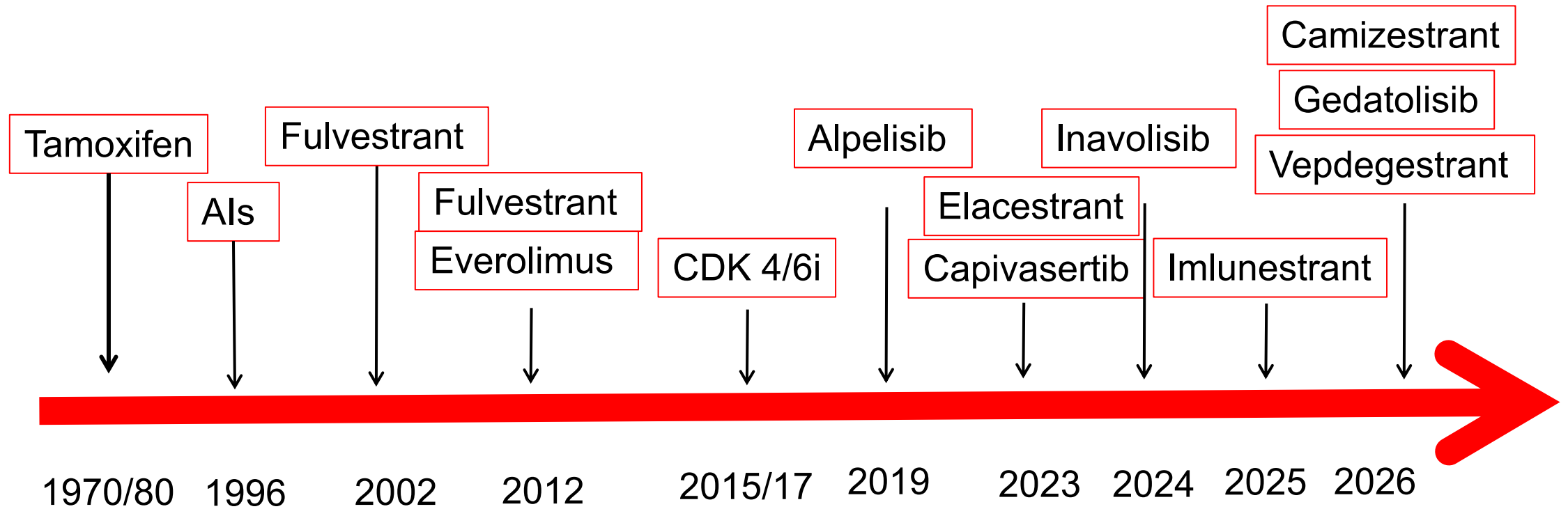
NATALEE: Invasive disease-free survival



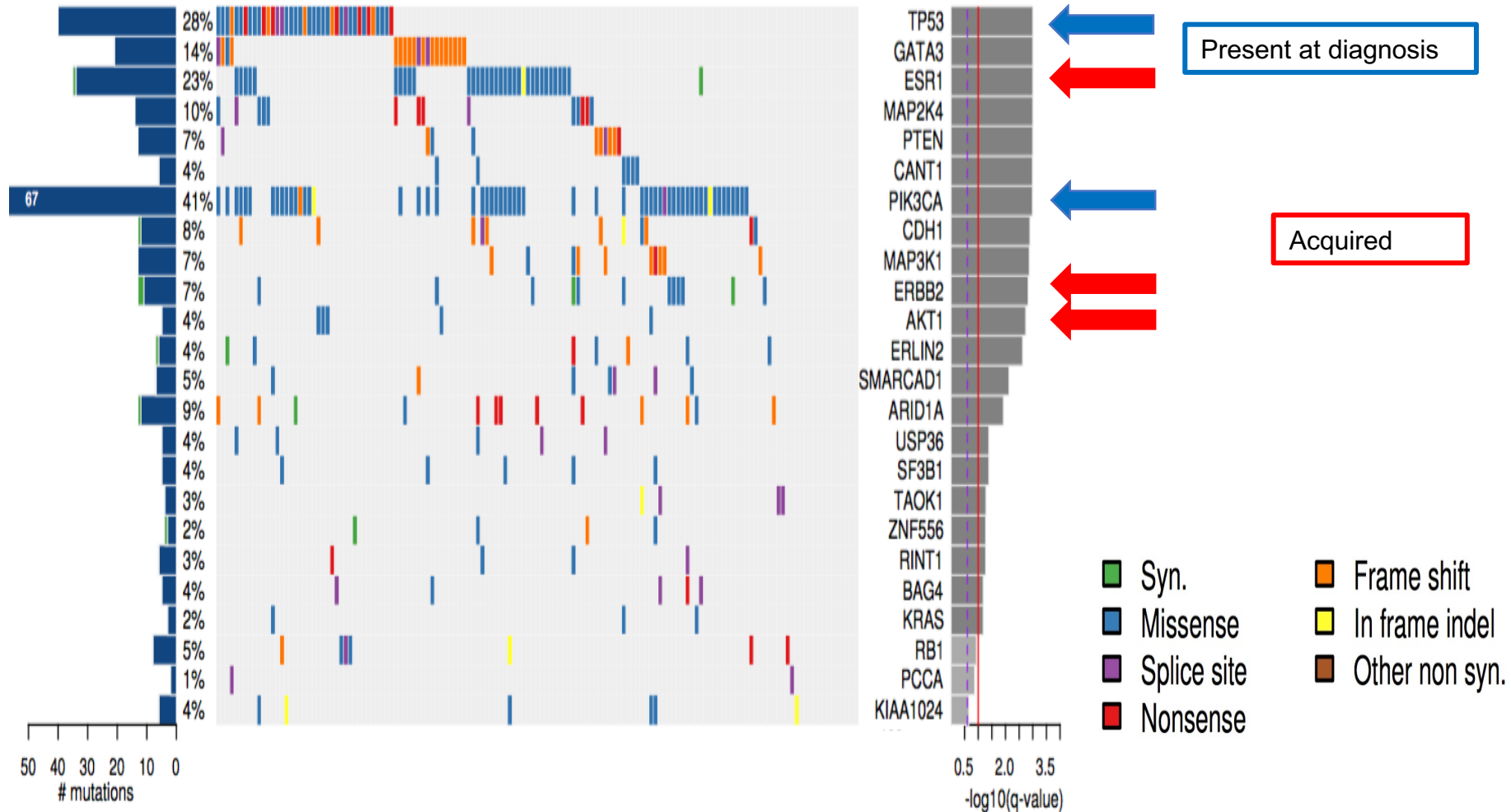
Metastatic HR-positive breast cancer

- First line treatment is endocrine therapy with a CDK 4/6 inhibitor (+/- inavolisib in endocrine-resistant and PIK3ca mutant)
 - Ribociclib and abemaciclib preferred as positive impact on overall survival
- Second line therapy decisions are based on genomics
- Antibody-drug-conjugates replacing standard chemotherapy
- Median survival around 5-years
 - Can we extend this further with new agents?

Ongoing changing landscape of targeted agents in ER-positive metastatic breast cancer



Genomic landscape of metastatic HR-positive breast cancer

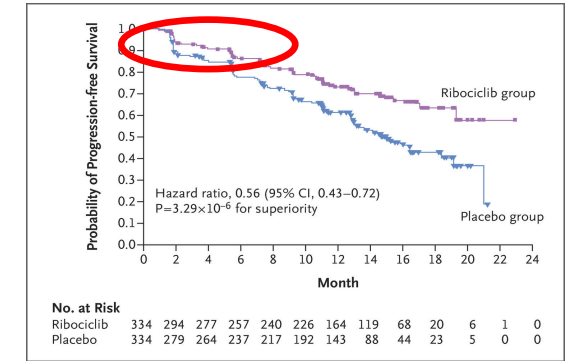
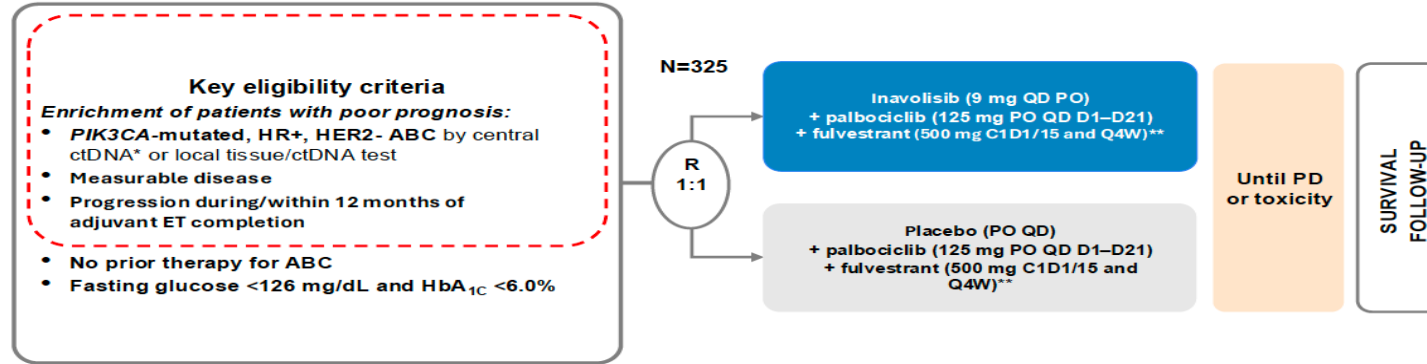


When and how should we check tumor genomics?

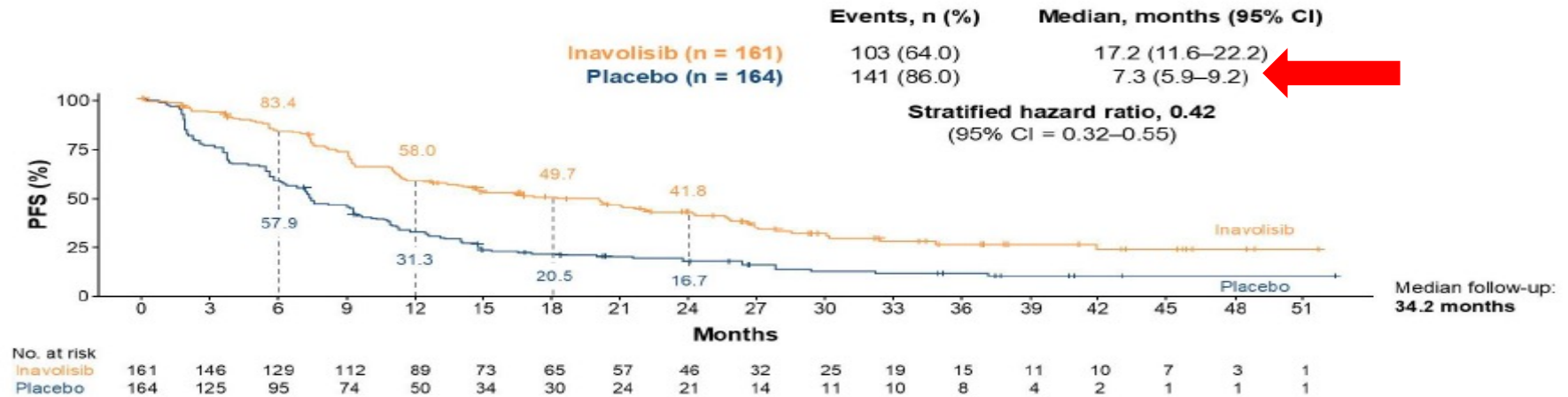
- Check genomics on metastatic tissue and/or via ctDNA
 - Tumor genomics on biopsy from diagnosis of metastatic disease
 - Recheck genomics in ctDNA at disease progression
 - Looking for acquired alterations: ESR1, ERB2, AKT1
 - If needed can test genomics on primary tissue for non-acquired alterations
 - PI3-kinase
 - Determine combinational partner with endocrine therapy based on presence or absence of genomic alterations

INAVO 120 Trial: Fulvestrant and palbociclib ± inavolisib

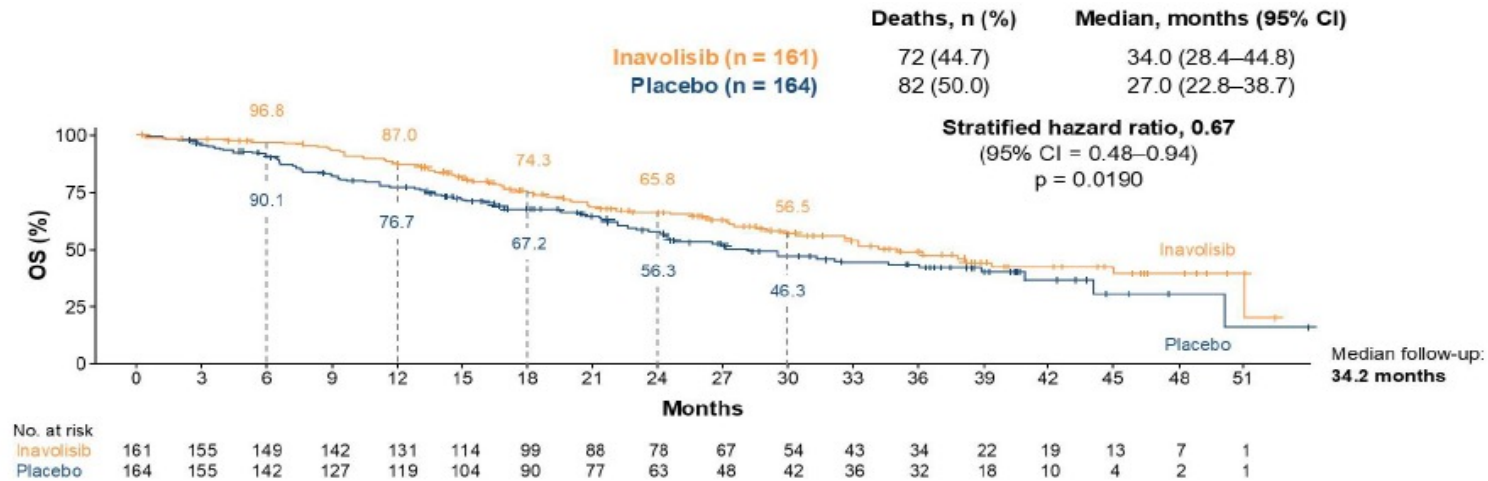
Monaleesa 2



Despite patients being off ET for at least 12- months

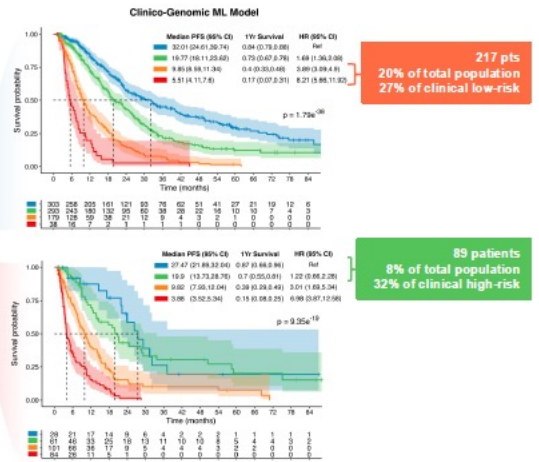
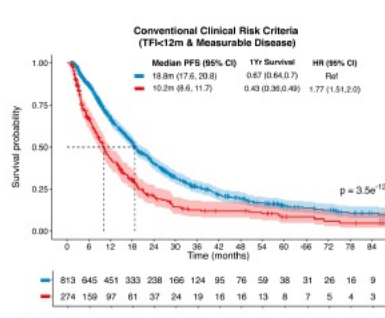
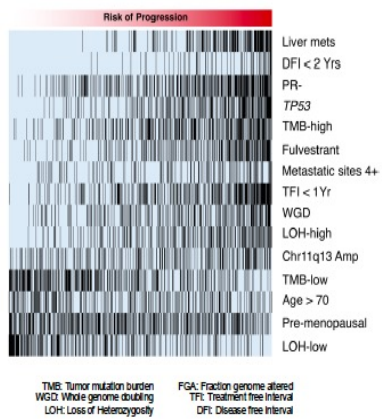
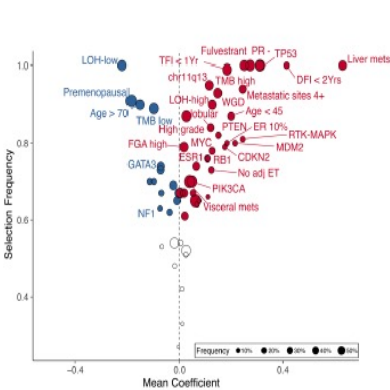
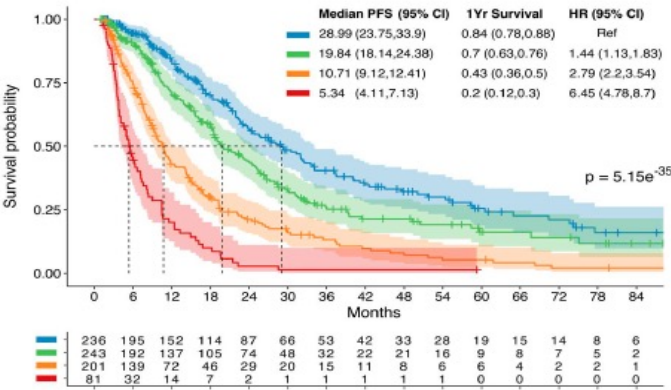
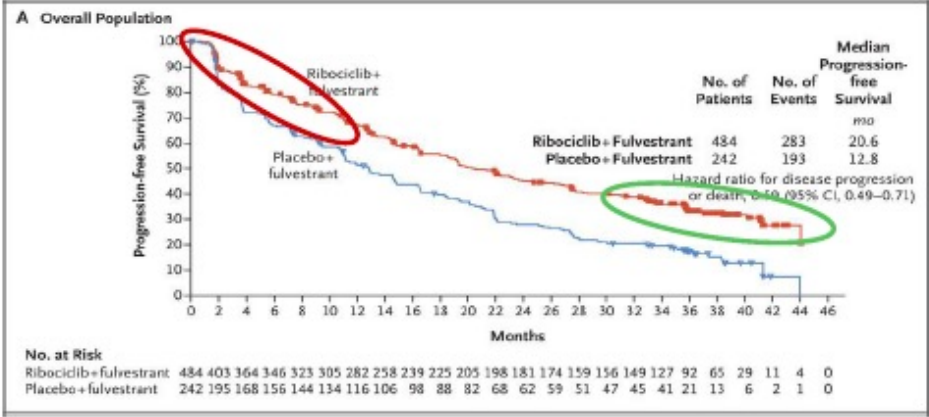


INAVO 120: Final overall survival



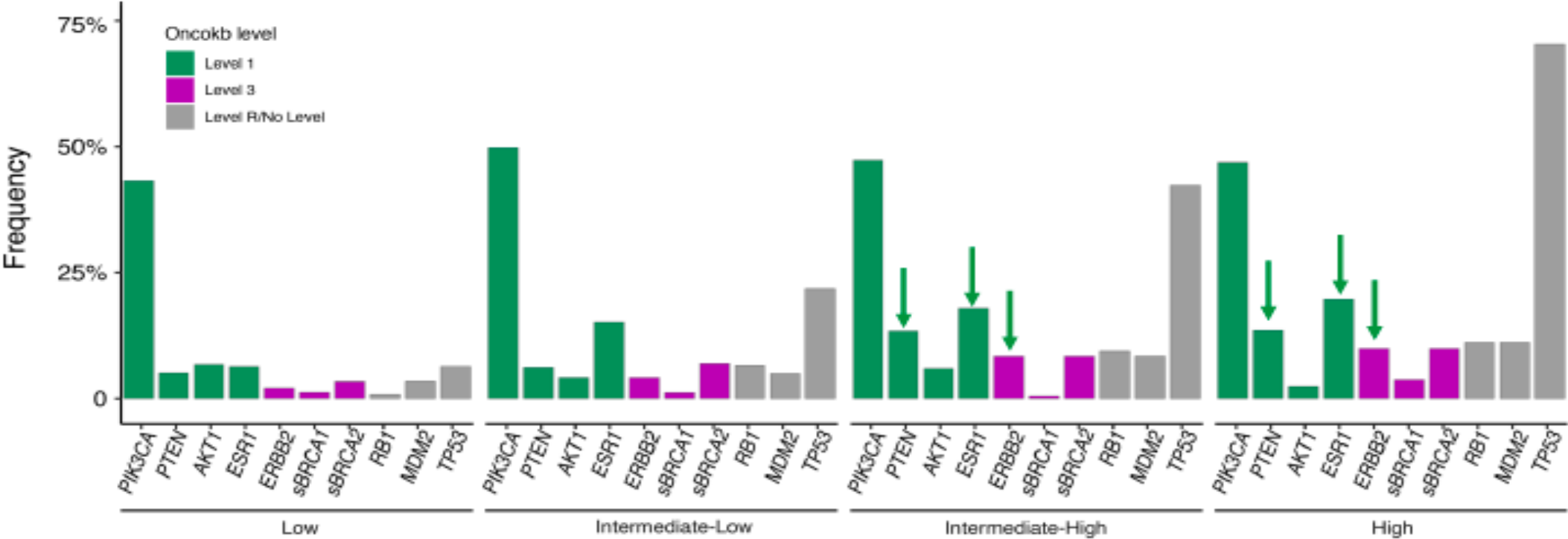
	Inavolisib		Placebo	
Patients, n (%)	Second line	Third line or greater	Second line	Third line or greater
Discontinued treatment	111/161 (68.9)		144/164 (87.8)	
No subsequent therapy – death	17/161 (10.6)		22/164 (13.4)	
Received subsequent therapy*	83/111 (74.8)	48/111 (43.2)	109/144 (75.7) [†]	56/144 (38.9)
Chemotherapy (any)	46/83 (55.4)	41/48 (85.4)	79/109 (72.5)	49/56 (87.5)
Capecitabine	26/83 (31.3)	14/48 (29.2)	37/109 (33.9)	24/56 (42.9)
Paclitaxel	12/83 (14.5)	17/48 (35.4)	20/109 (18.3)	16/56 (28.6)
Eribulin	1/83 (1.2)	11/48 (22.9)	6/109 (5.5)	17/56 (30.4)
Antibody–drug conjugate (any)	1/83 (1.2)	8/48 (16.7)	1/109 (0.9)	20/56 (35.7)
Trastuzumab deruxtecan	0	6/48 (12.5)	1/109 (0.9)	16/56 (28.6)
Sacituzumab govitecan	0	2/48 (4.2)	0	8/56 (14.3)
PI3K inhibitor (any)	5/83 (6.0)	2/48 (4.2)	11/109 (10.1)	3/56 (5.4)
Alpelisib	5/83 (6.0)	2/48 (4.2)	9/109 (8.3)	2/56 (3.6)
mTOR kinase inhibitor (everolimus)	8/83 (9.6)	4/48 (8.3)	10/109 (9.2)	9/56 (16.1)
CDK4/6 inhibitor (any)	8/83 (9.6)	3/48 (6.2)	5/109 (4.6)	3/56 (5.4)
Ribociclib	1/83 (1.2)	1/48 (2.1)	5/109 (4.6)	0
Abemaciclib	2/83 (2.4)	2/48 (4.2)	0	2/56 (3.6)
Other (any)	6/83 (7.2)	0	3/109 (2.8)	5/56 (8.9)

Machine-learning model of clinical and genomic data to predict outcome from CDK 4/6i

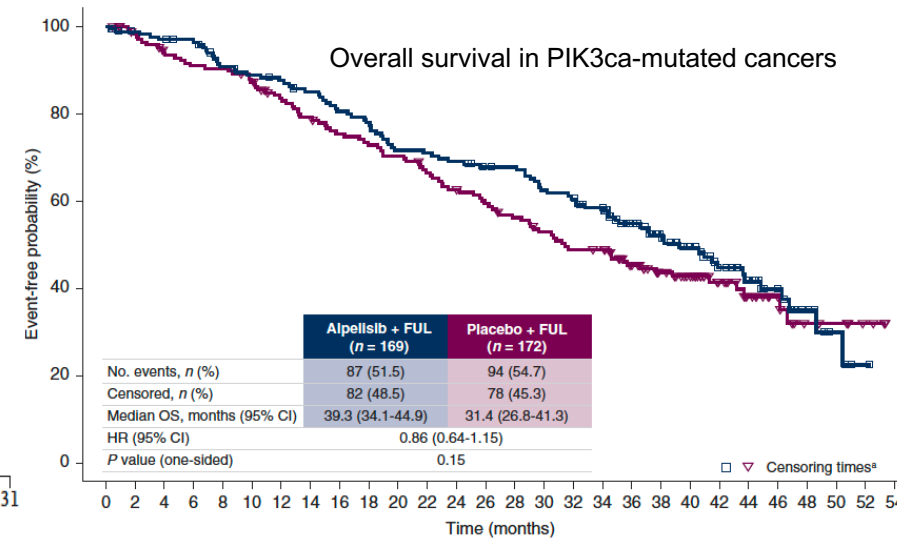
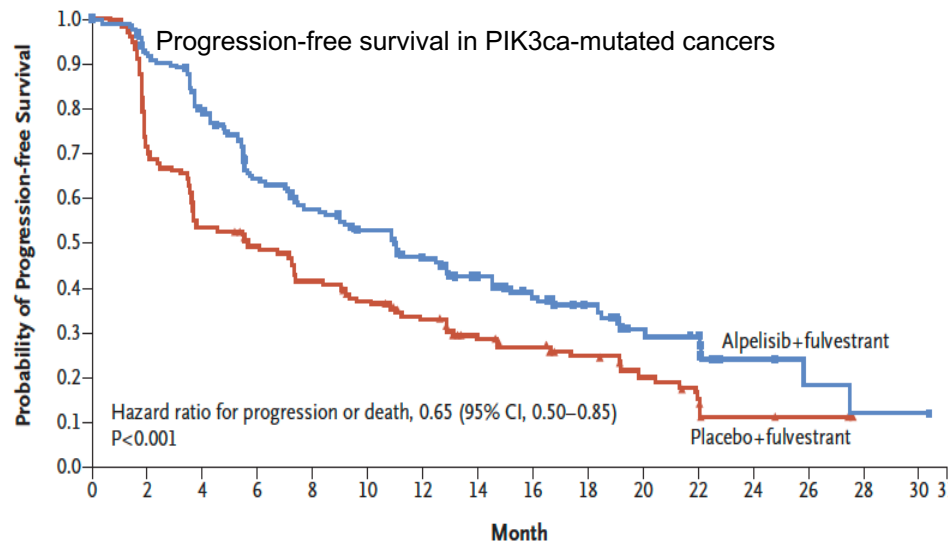
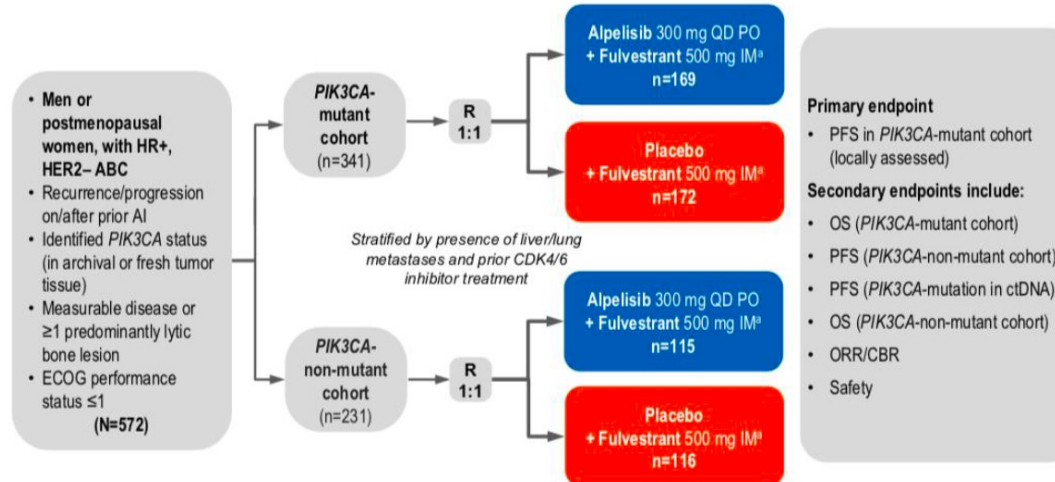


1087 patients split 70/30 between training and test sets

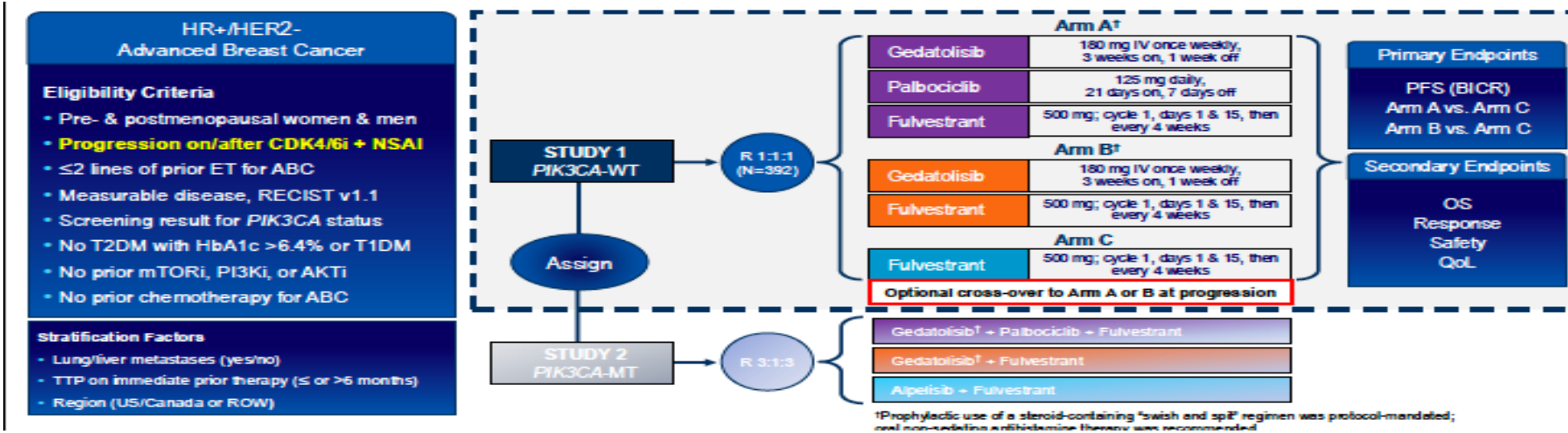
Increase in actionable mutations in higher risk disease



SOLAR 1: Addition of alpelisib to fulvestrant in PIK3ca-mutated cancers



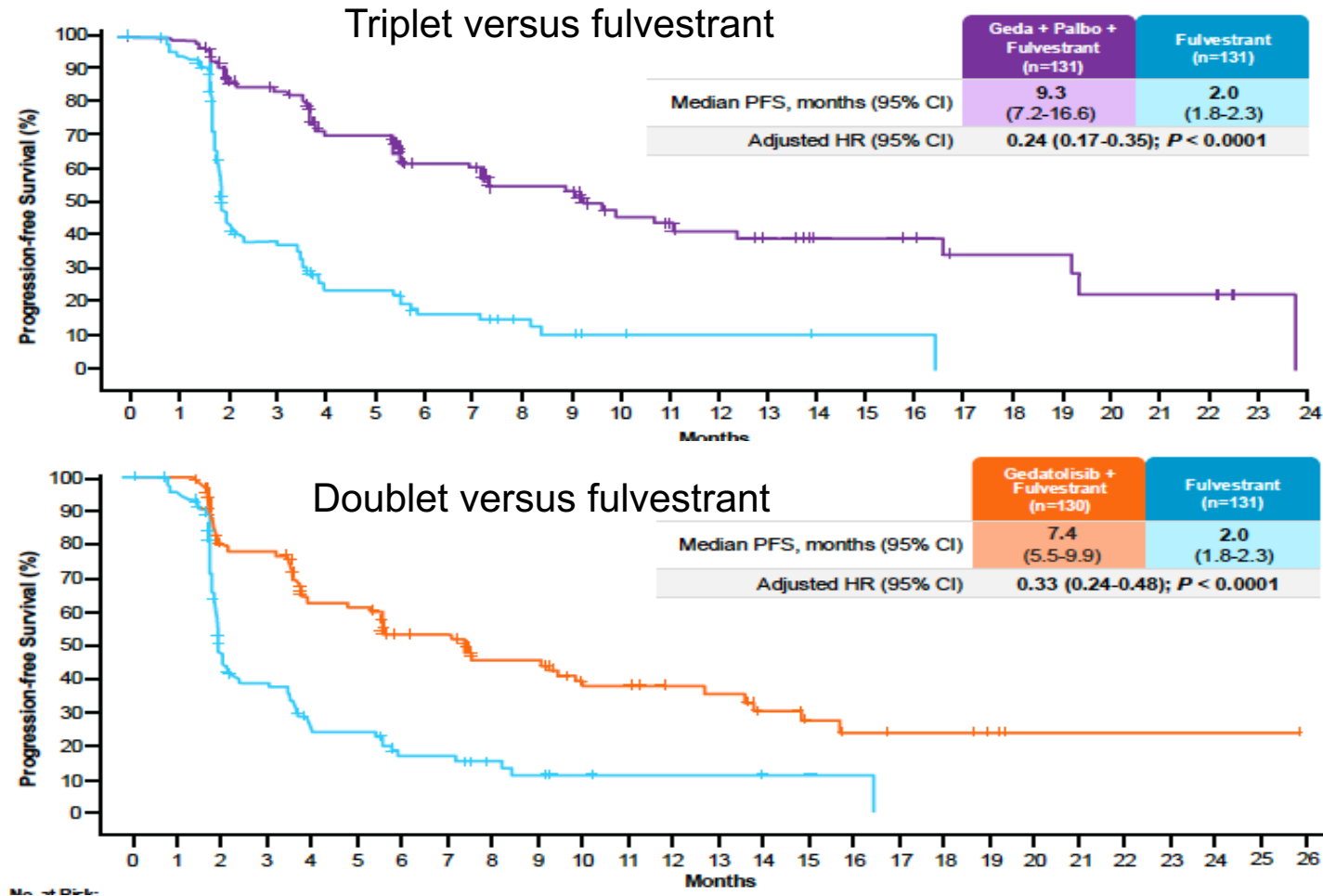
VIKTORIA1: Gedatolisib + fulvestrant ± palbociclib



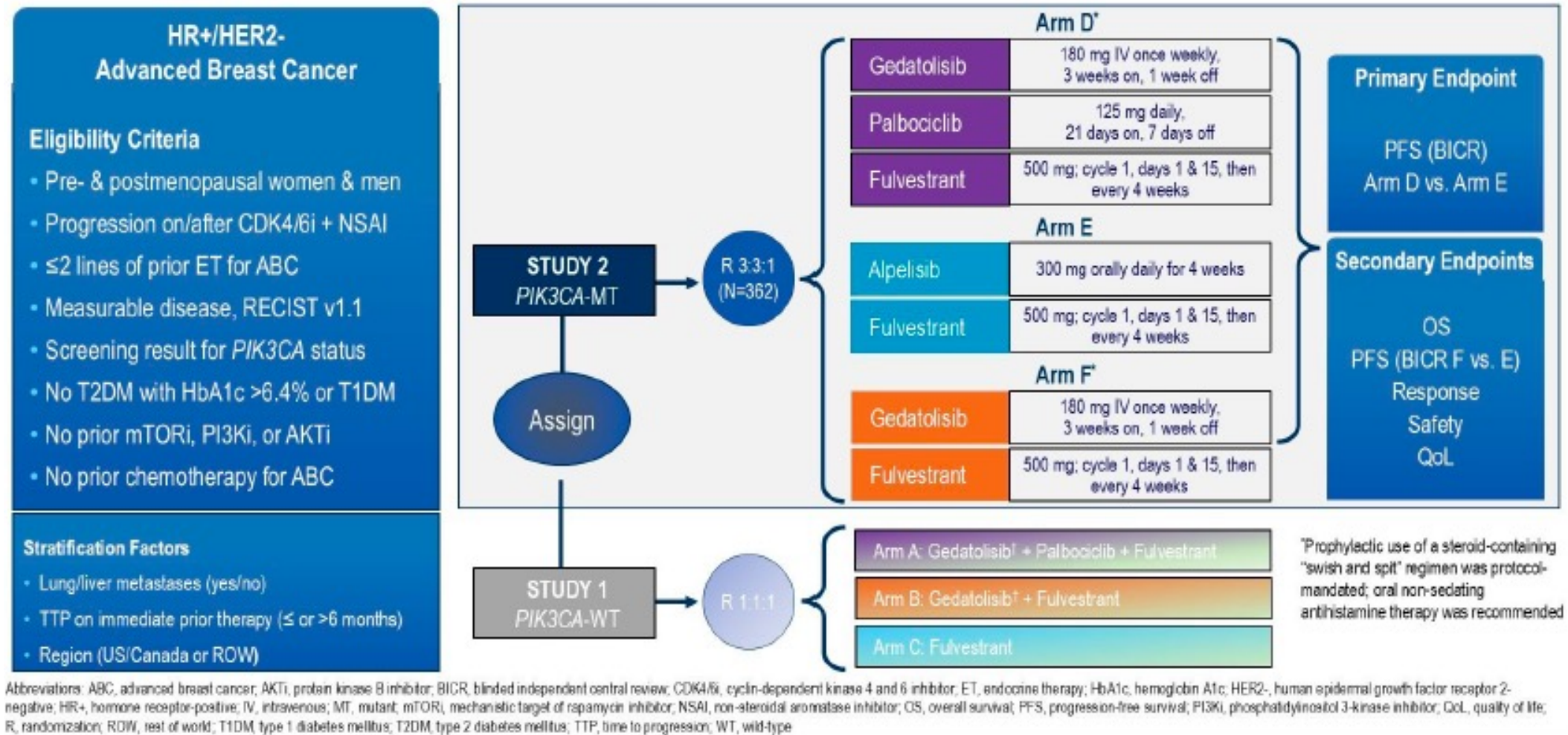
Characteristic	Gedatolisib + Palbo + Fulvestrant (n=131)	Gedatolisib + Fulvestrant (n=130)	Fulvestrant (n=131)
Age, yr, median (range)	57 (33-83)	57 (32-81)	54 (28-83)
Female sex, n (%)	129 (98.5)	130 (100)	128 (97.7)
Postmenopausal, n (%)	101 (77.1)	93 (71.5)	92 (70.2)
Race/ethnic group, n (%)			
White	85 (64.9)	95 (73.1)	95 (72.5)
Asian	18 (13.7)	19 (14.6)	25 (19.1)
Black/African American	5 (3.8)	3 (2.3)	1 (0.8)
Other/Unknown	23 (17.6)	13 (10.0)	10 (7.6)
Geographic region, n (%)			
United States/Canada	21 (16.0)	21 (16.2)	22 (16.8)
Asia Pacific	18 (13.7)	18 (13.8)	26 (19.8)
Latin America	35 (26.7)	36 (27.7)	35 (26.7)
Europe	57 (43.5)	55 (42.3)	48 (36.6)
ABC at diagnosis, n (%)	63 (48.1)	51 (39.2)	45 (34.4)
ECOG PS score, n (%)			
0	70 (53.4)	85 (65.4)	77 (58.8)
1	61 (46.6)	45 (34.6)	54 (41.2)

Characteristic	Gedatolisib + Palbo + Fulvestrant (n=131)	Gedatolisib + Fulvestrant (n=130)	Fulvestrant (n=131)
Liver or lung mets, n (%)	102 (77.9)	104 (80.0)	109 (83.2)
Prior (neo)adjuvant tx, n (%)			
Chemotherapy	33 (25.2)	39 (30.0)	38 (29.0)
Endocrine therapy	46 (35.1)	57 (43.8)	64 (48.9)
Prior lines, ET for ABC, n (%)			
0	3 (2.3)	2 (1.5)	4 (3.1)
1	113 (86.3)	113 (86.9)	115 (87.8)
2	15 (11.5)	15 (11.5)	12 (9.2)
TTP on immediate prior tx, n (%)			
≤6 months	21 (16.0)	19 (14.6)	20 (15.3)
>6 months	109 (83.2)	111 (85.4)	111 (84.7)
Prior adjuvant CDK4/6i, n (%)	3 (2.3)	6 (4.6)	4 (3.1)
Prior CDK4/6i for ABC, n (%)			
Palbociclib	56 (42.7)	47 (36.2)	52 (39.7)
Ribociclib	59 (45.0)	62 (47.7)	70 (53.4)
Abemaciclib	23 (17.6)	26 (20.0)	16 (12.2)
Prior CDK4/6i for ABC, mo., median duration (IQR)	21.7 (13.7-35.0)	18.1 (10.8-30.0)	20.0 (12.0-34.2)

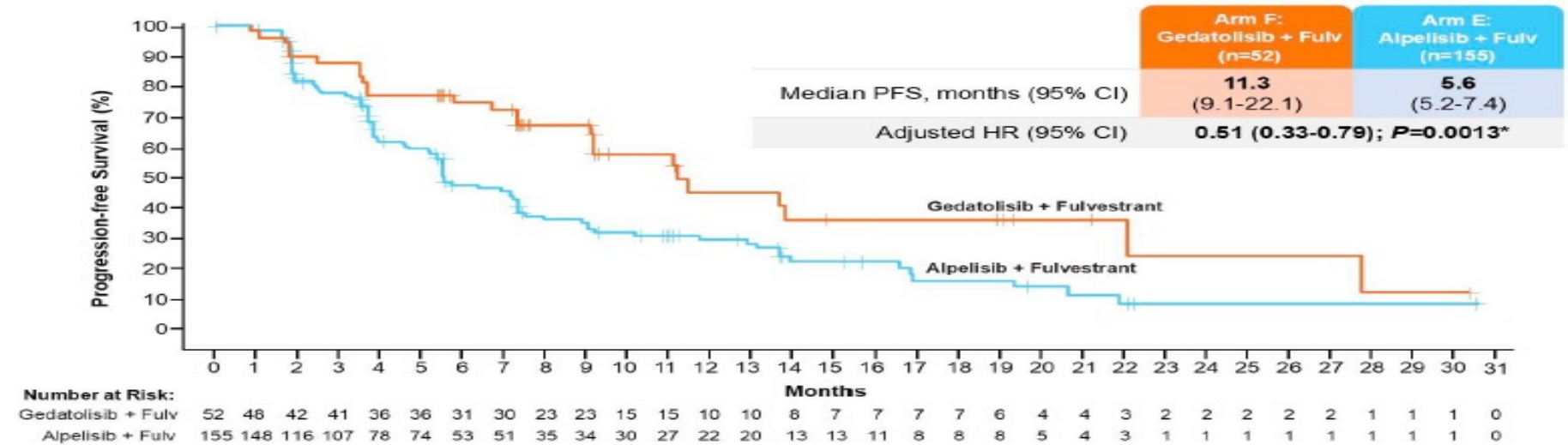
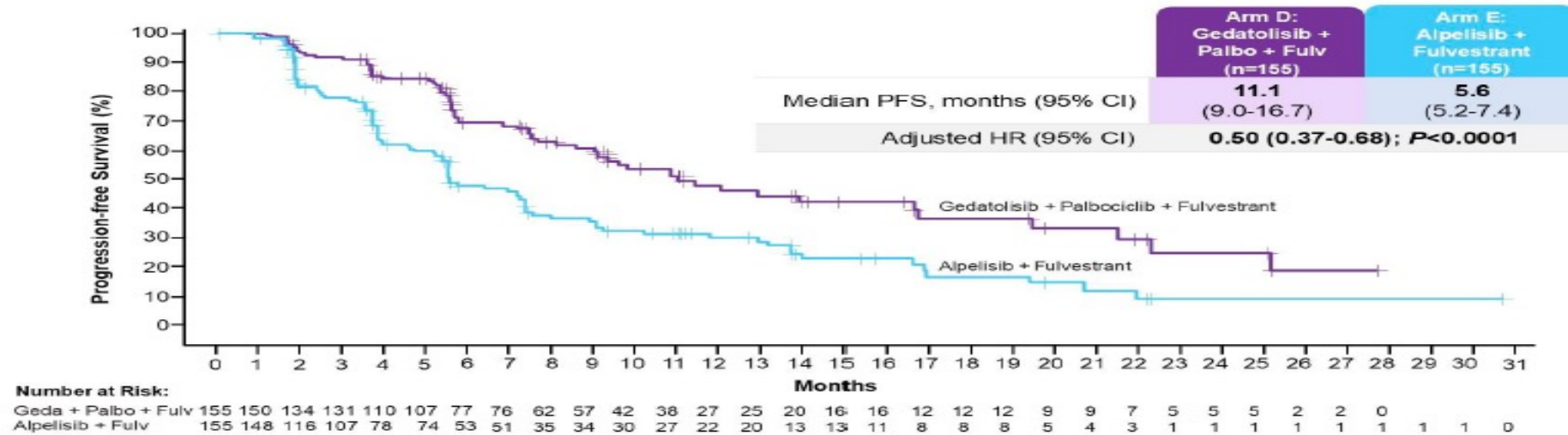
VIKTORIA1: PFS by BICR PIK3ca-wt



VIKTORIA-1: PIK3ca-mutant cohort schema



VIKTORIA-1: Primary endpoint PFS triplet versus alpelisib + fulvestrant PIK3ca-mutant



VIKTORIA-1: Safety and tolerability

Exposure	Arm D: Gedatolisib + Palbociclib + Fulvestrant (n=153)			Arm F: Gedatolisib + Fulvestrant (n=52)			Arm E: Alpelisib + Fulvestrant (n=152)		
Median RDI, Geda (IQR)	93.3 (80.6-100)			100 (97.8-100)			--		
Median RDI, Alpe (IQR)	--			--			81.7 (64.8-96.2)		
TRAE and TR-SAE, n (%)									
Pts with ≥1 TRAE	150 (98.0)			50 (96.2)			147 (96.7)		
Study tx D/C for TRAE	4 (2.6)			2 (3.8)			11 (7.1)		
Pts with ≥1 TR-SAE	16 (10.5)			2 (3.8)			20 (13.2)		
Deaths due to TR-SAE*	1 (0.7)			0			2 (1.3)		
TRAE, n (%)†	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
Neutropenia‡	97 (63.4)	73 (47.7)	17 (11.1)	1 (1.9)	0	0	2 (1.3)	0	1 (0.7)
Stomatitis‡	94 (61.4)	25 (16.3)	0	32 (61.5)	3 (5.8)	0	52 (34.2)	8 (5.3)	0
Nausea	70 (45.8)	5 (3.3)	0	21 (40.4)	1 (1.9)	0	50 (32.9)	2 (1.3)	0
Rash‡	40 (26.1)	10 (6.5)	0	17 (32.7)	3 (5.8)	0	56 (36.8)	23 (15.1)	0
Vomiting	39 (25.5)	0	0	10 (19.2)	0	0	23 (15.1)	1 (0.7)	0
Fatigue	33 (21.6)	5 (3.3)	0	11 (21.2)	1 (1.9)	0	32 (21.1)	4 (2.6)	0
Diarrhea§	23 (15.0)	2 (1.3)	0	5 (9.6)	0	0	61 (40.1)	9 (5.9)	1 (0.7)
Hyperglycemia‡,§	23 (15.0)	4 (2.6)	0	6 (11.5)	0	0	88 (57.9)	21 (13.8)	1 (0.7)

*Grade 5 events include fatal cerebral hemorrhage (gedatolisib triplet), urosepsis (alpelisib + fulvestrant group), and general physical health decline (alpelisib + fulvestrant group)

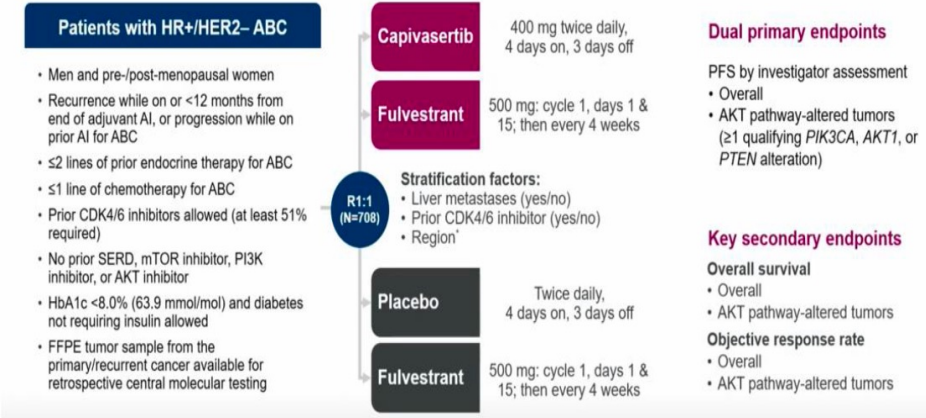
†Shown are treatment-related adverse events of any grade that occurred in at least 20% of the patients in any trial group unless otherwise noted

‡For stomatitis, neutropenia, rash, and hyperglycemia, combined preferred terms are used in the table; if a patient experienced multiple terms, it was counted once for the highest grade.

§Additional events of clinical importance

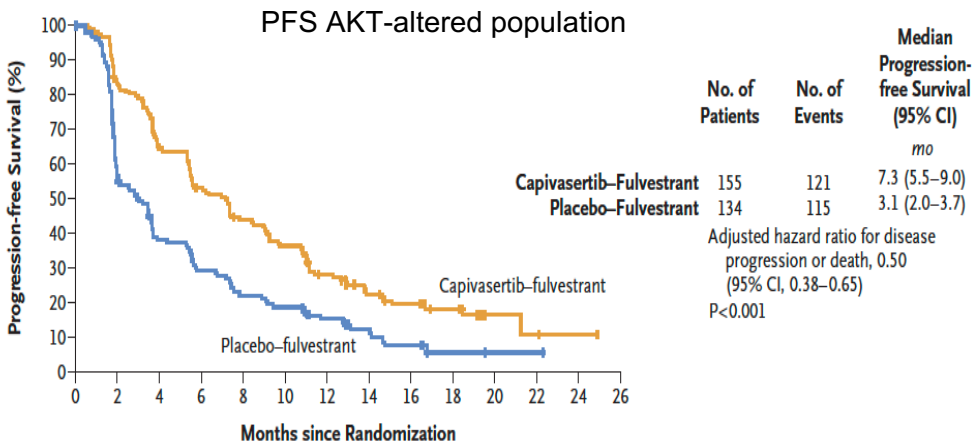
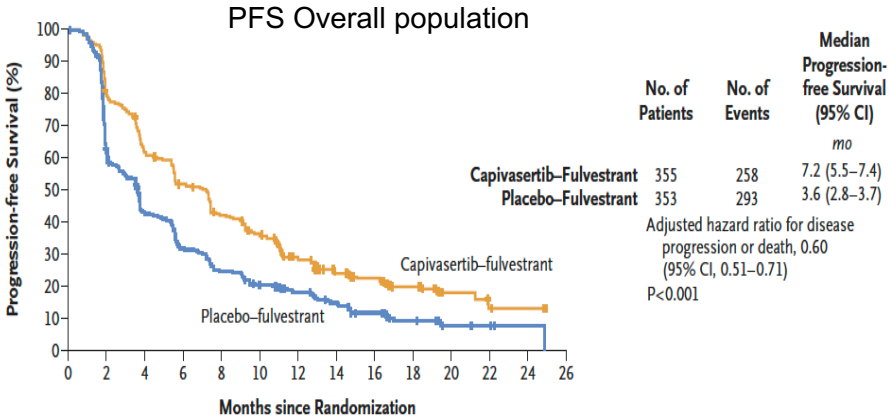
Abbreviations: Alpe, alpelisib; D/C, discontinued; Geda, gedatolisib; IQR, interquartile range; Pts, patients; RDI, relative dose intensity; TRAE, treatment-related adverse event; TR-SAE, treatment-related serious adverse events; tx, treatment

CAPItello-291: Phase III trial of capiivasertib in HR+ metastatic breast cancer

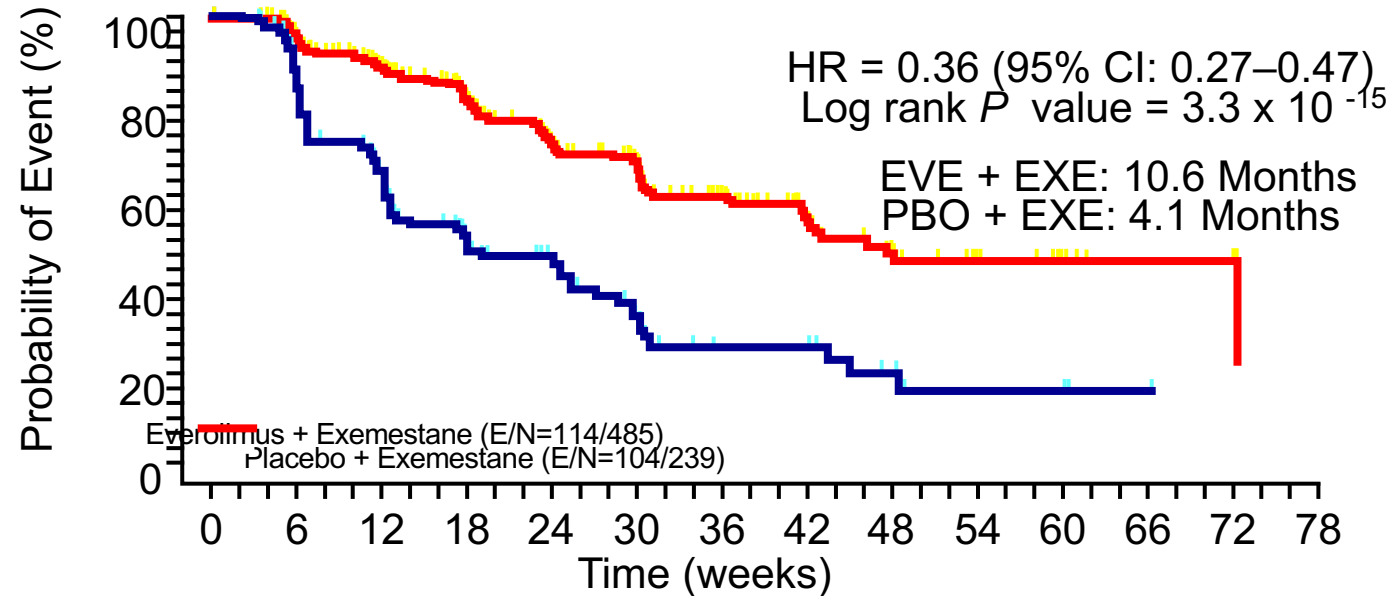
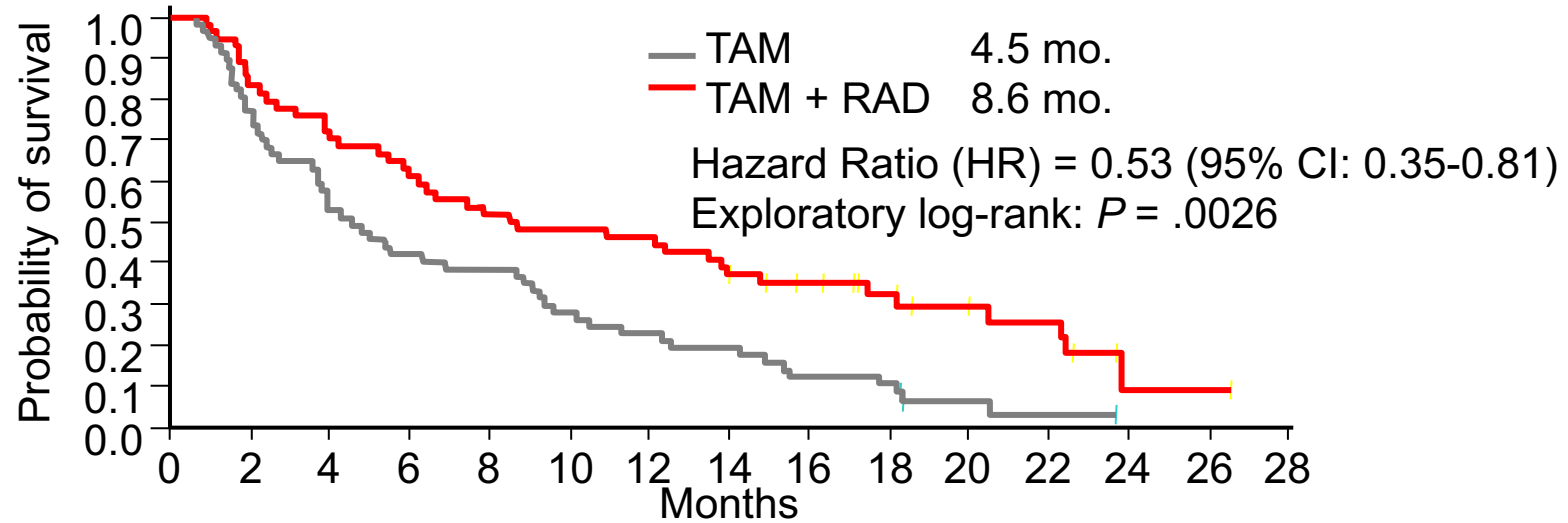


AKT pathway alterations

Alteration; n (%)	Capiivasertib + fulvestrant (N=355)	Placebo + fulvestrant (N=353)
Any AKT pathway alteration	155 (43.7)	134 (38.0)
PIK3CA		
Any	116 (32.7)	103 (29.2)
PIK3CA only	110 (31.0)	92 (26.1)
PIK3CA and AKT1	2 (0.6)	2 (0.6)
PIK3CA and PTEN	4 (1.1)	9 (2.5)
AKT1 only	18 (5.1)	15 (4.2)
PTEN only	21 (5.9)	16 (4.5)
Non-altered	200 (56.3)	219 (62.0)
AKT pathway alteration not detected	142 (40.0)	171 (48.4)
Unknown	58 (16.3)	48 (13.6)
No sample available	10 (2.8)	4 (1.1)
Preanalytical failure	39 (11.0)	34 (9.6)
Post analytical failure	9 (2.5)	10 (2.8)



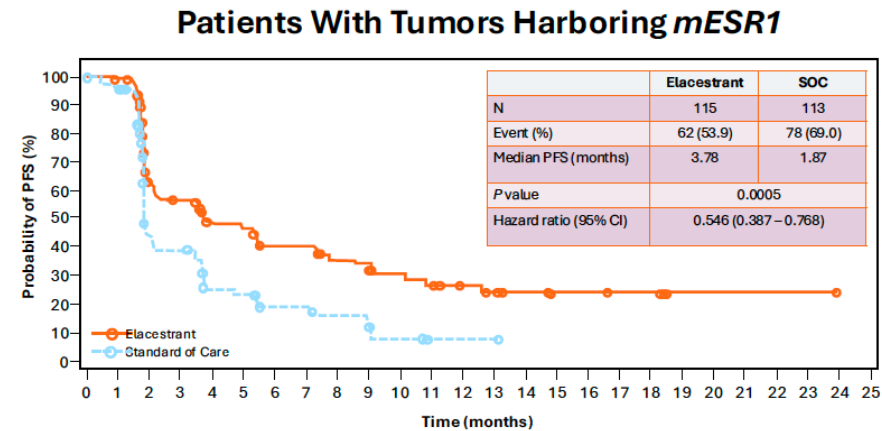
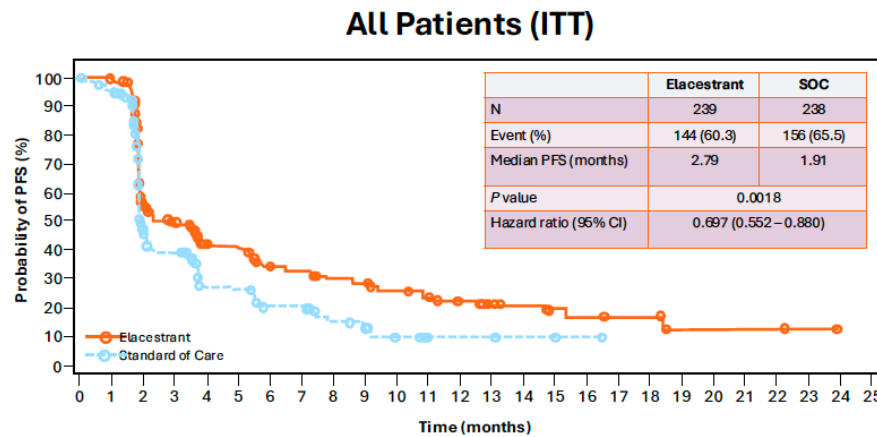
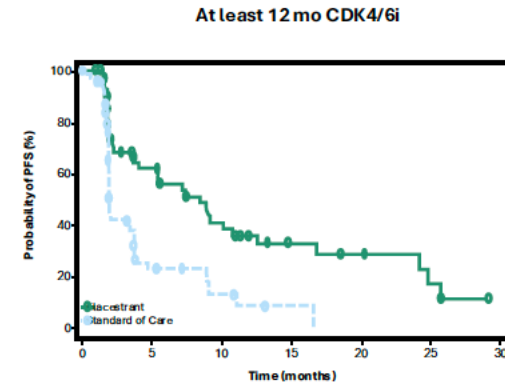
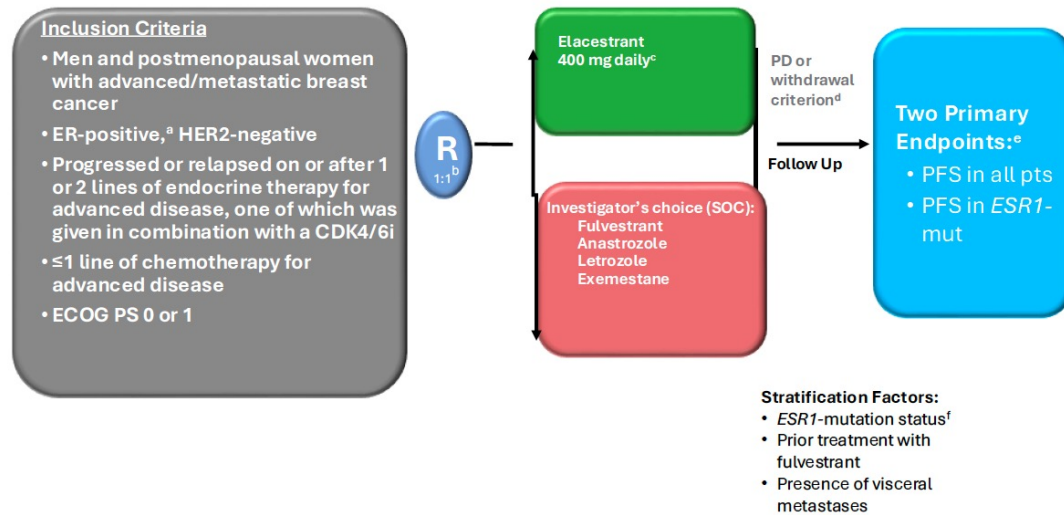
Everolimus in hormone-refractory MBC



Post progression CDKi trials

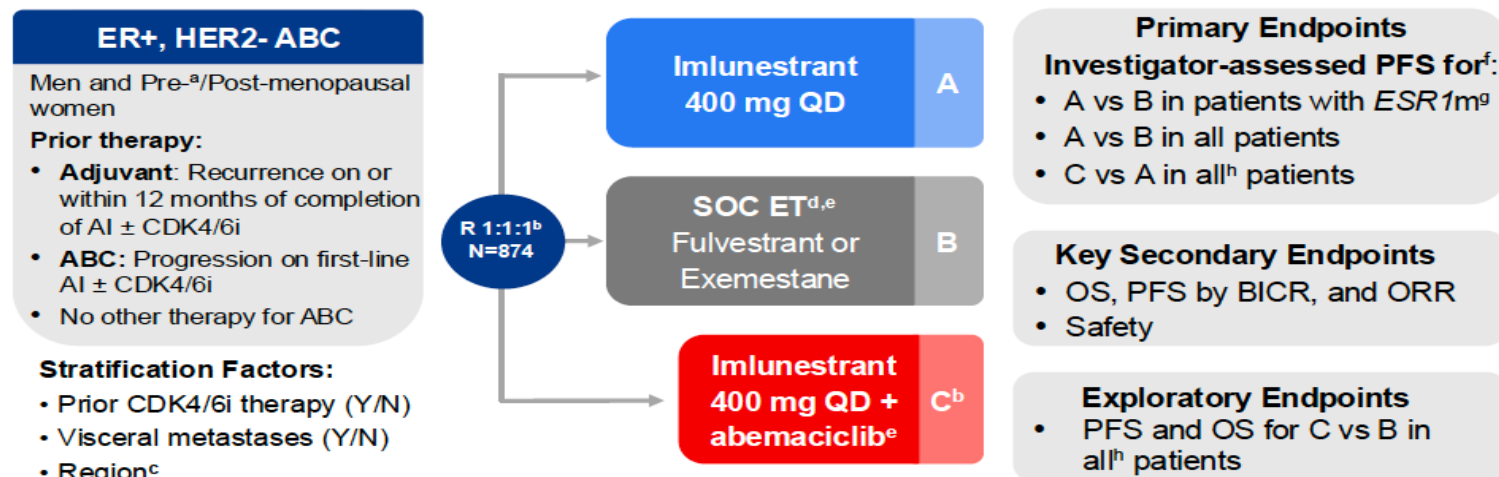
	postMONARCH		MAINTAIN		PALMIRA		PACE	
ARM	ABEMA	PLAC	RIBO	PLAC	PALBO	CONT	PALBO	CONT
PFS	6.0 mos.	5.3 mos.	5.3 mos.	2.8 mos.	4.9 mos.	3.6 mos.	4.6 mos	4.8 mos.
▲	0.7 mos.		2.5 mos.		1.3 mos		-0.2 mos	
HR	0.73		0.57		0.84		1.11	
P value	0.02		0.006		0.149		0.06	

EMERALD trial: Elacestrant vs endocrine therapy in HR+ metastatic breast cancer



Bidard et al J Clin Oncol 2022;40:3246, Bardia et al Clin Cancer Res 2024;30:4299

EMBER3: Schema

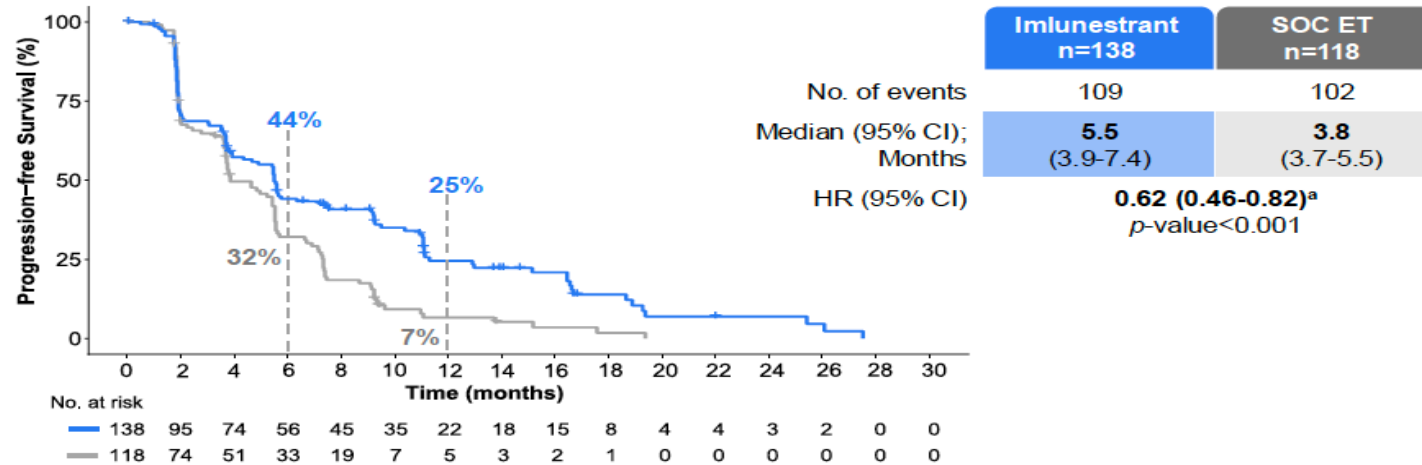


Characteristic	Imlunestrant n=331	SOC ET n=330	Imlunestrant + abemaciclib n=213
Median age, years (range)	61 (28-87)	62 (27-89)	62 (36-87)
Female, %	99	99	99
Post-menopausal, %	84	86	86
Race, %			
White	56	58	52
Asian	28	29	34
Black or African American	3	2	4
Region, %			
East Asia	25	26	31
North America/ Western Europe	38	39	45
Other	37	36	24
PR-positive, %	78	79	74
<i>ESR1</i> mutation, % ^a	42	36	32
PI3K pathway mutations, % ^b	39	39	41

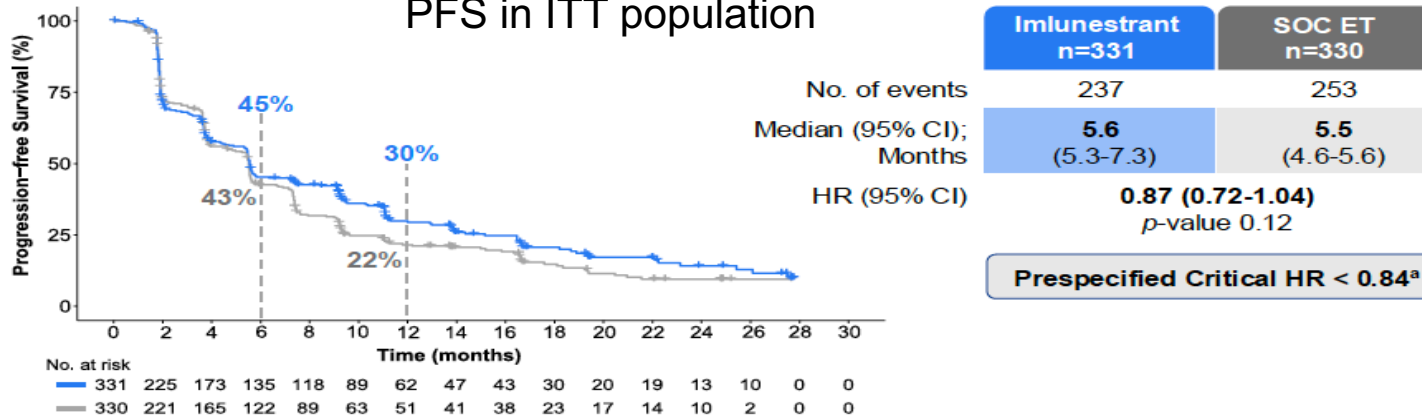
Characteristic	Imlunestrant n=331	SOC ET n=330	Imlunestrant + abemaciclib n=213
Site of metastases, %			
Visceral	57	54	56
Liver	32	30	27
Bone-only	22	26	24
Endocrine resistance, % ^c			
Primary	8	11	8
Secondary	92	89	93
Most recent ET, % ^d			
Adjuvant	32	34	30
ABC	63	63	68
Previous CDK4/6i, %			
Overall	59	57	65
Adjuvant	4	5	3
ABC	55	53	62
Previous CDK4/6i therapy, % ^e			
Palbociclib	61	69	65
Ribociclib	29	27	27
Abemaciclib	10	4	7

EMBER3: Imlunestrant versus SOC

PFS in ESR1-mutated population

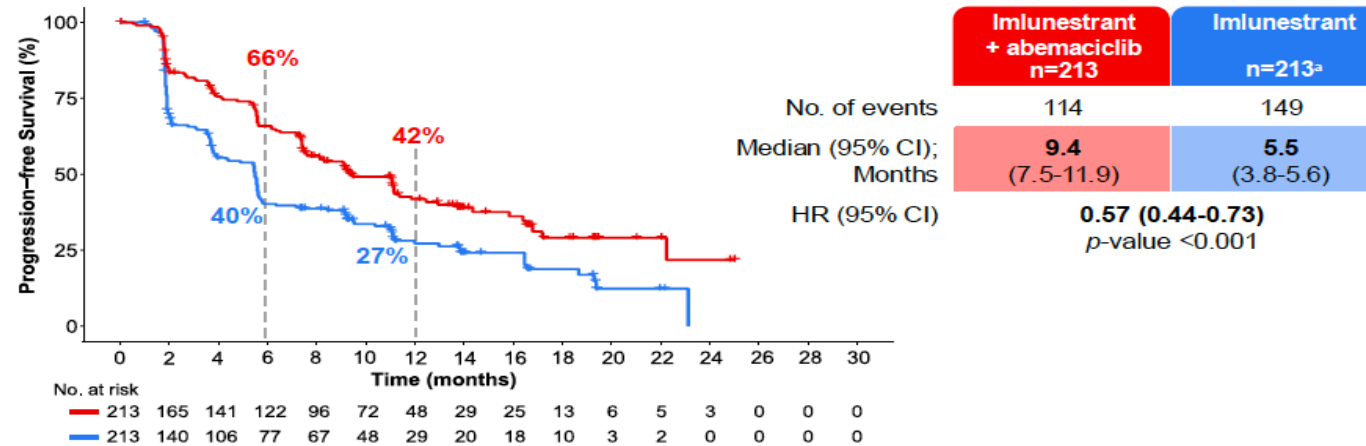


PFS in ITT population

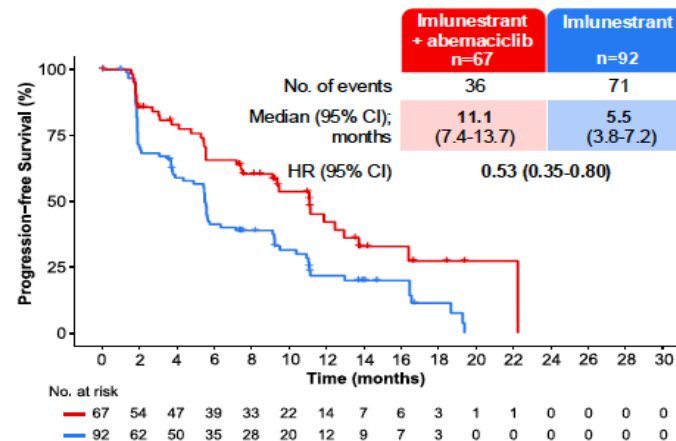


EMBER3: Imlunestrant + abemaciclib versus imlunestrant

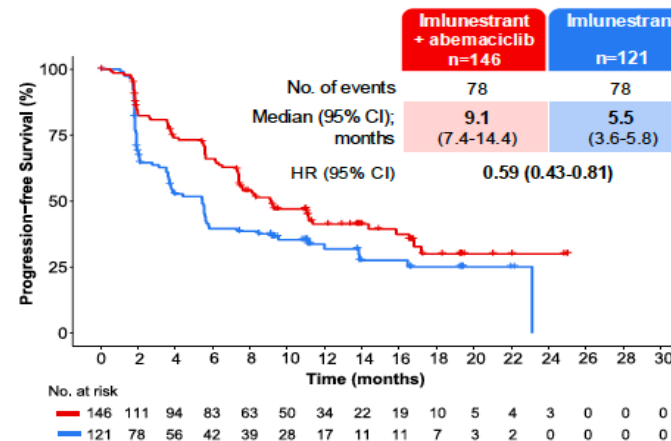
PFS in ITT population



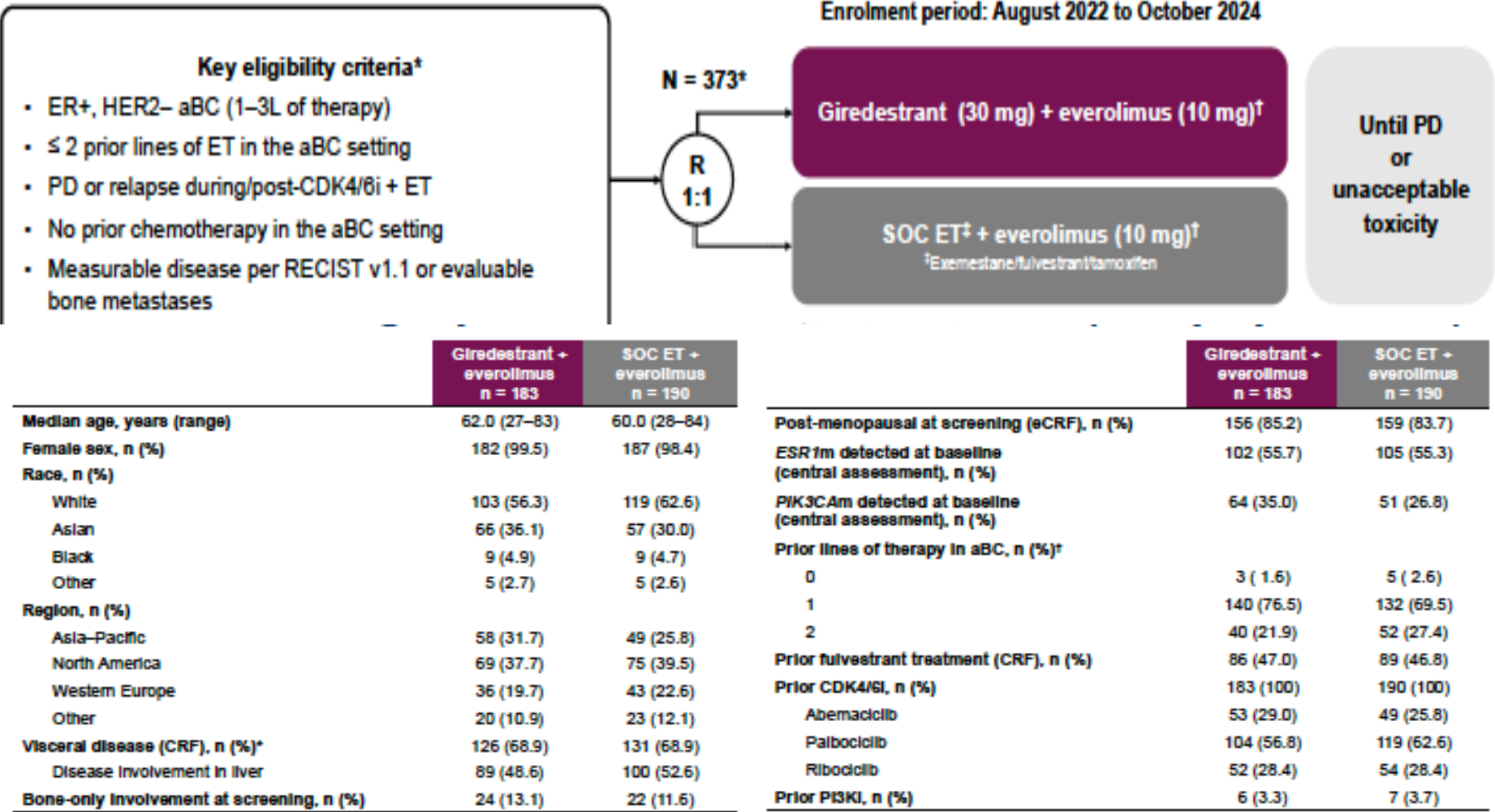
Patients with ESR1m



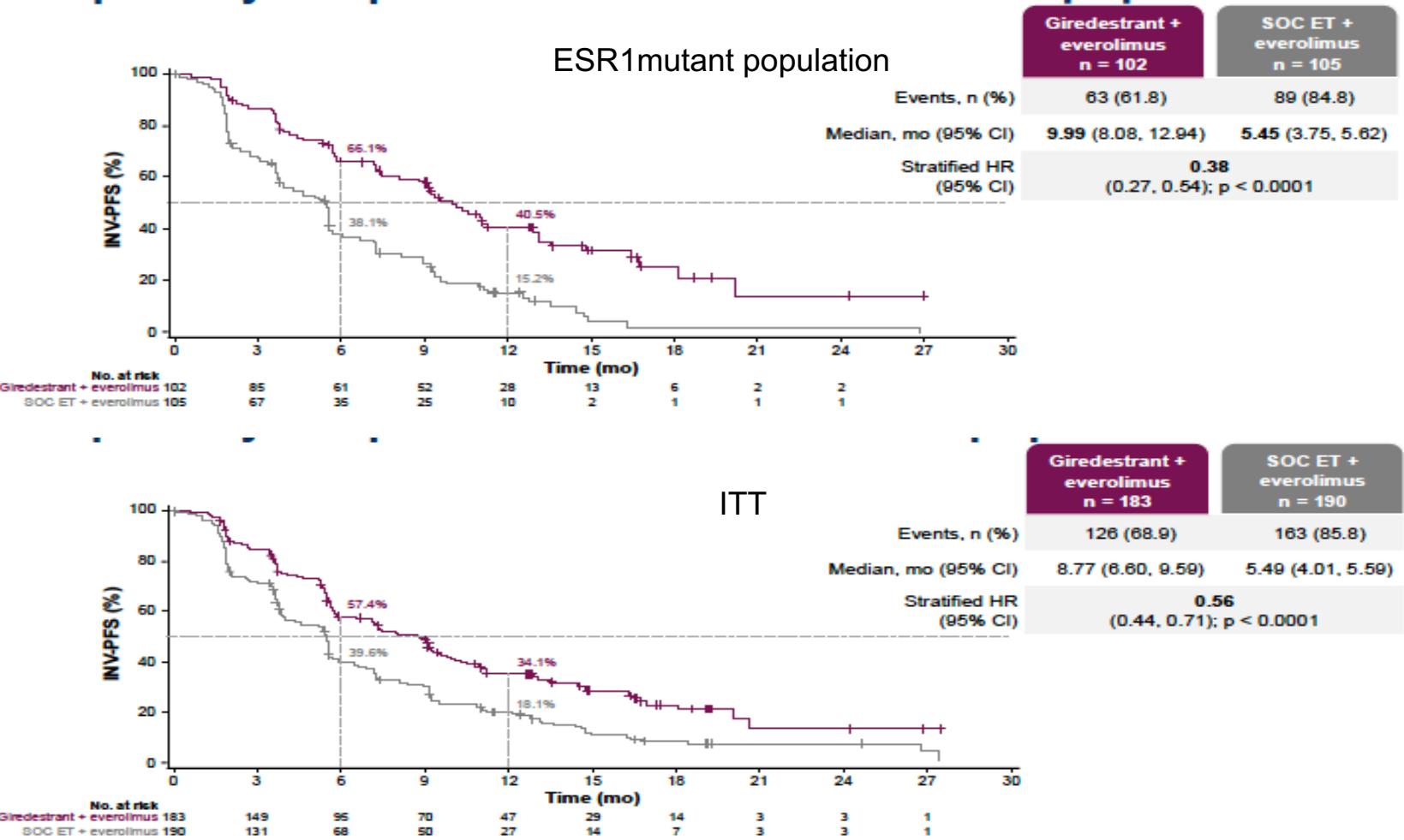
Patients without ESR1m



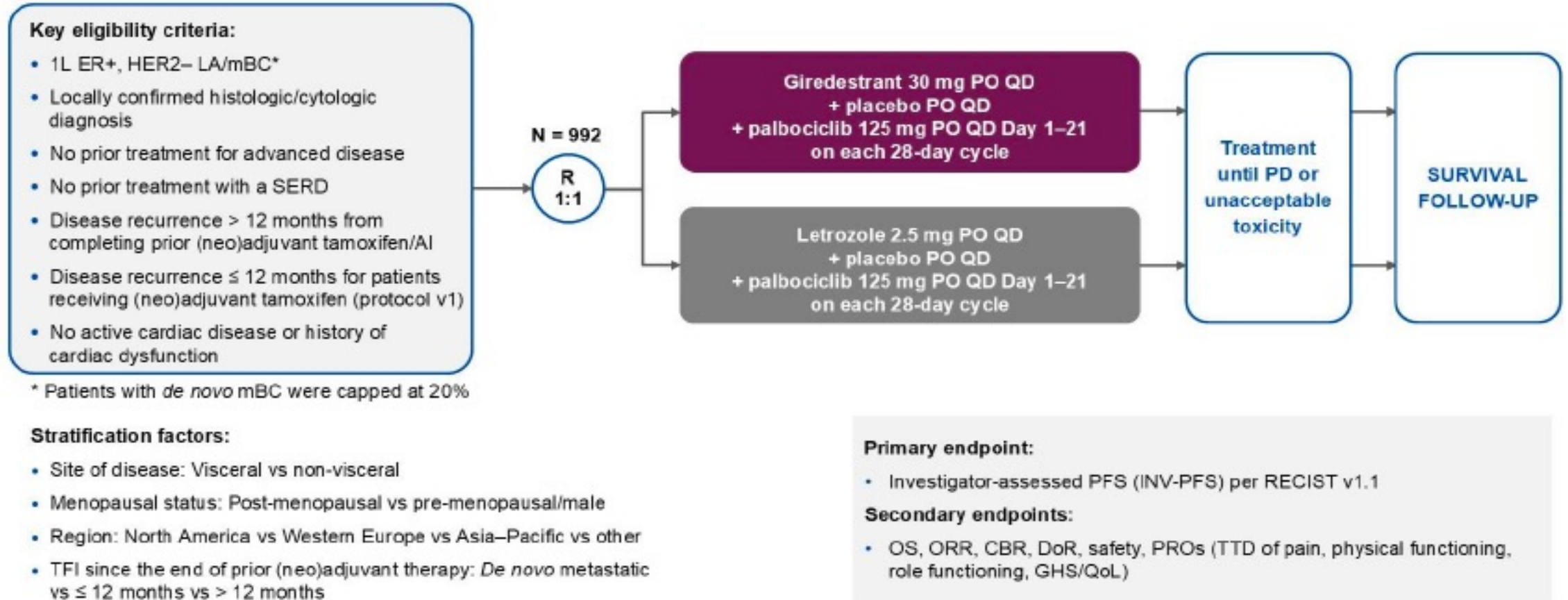
Giredestrant + everolimus versus SOC endocrine therapy + everolimus in pretreated HR+ MBC



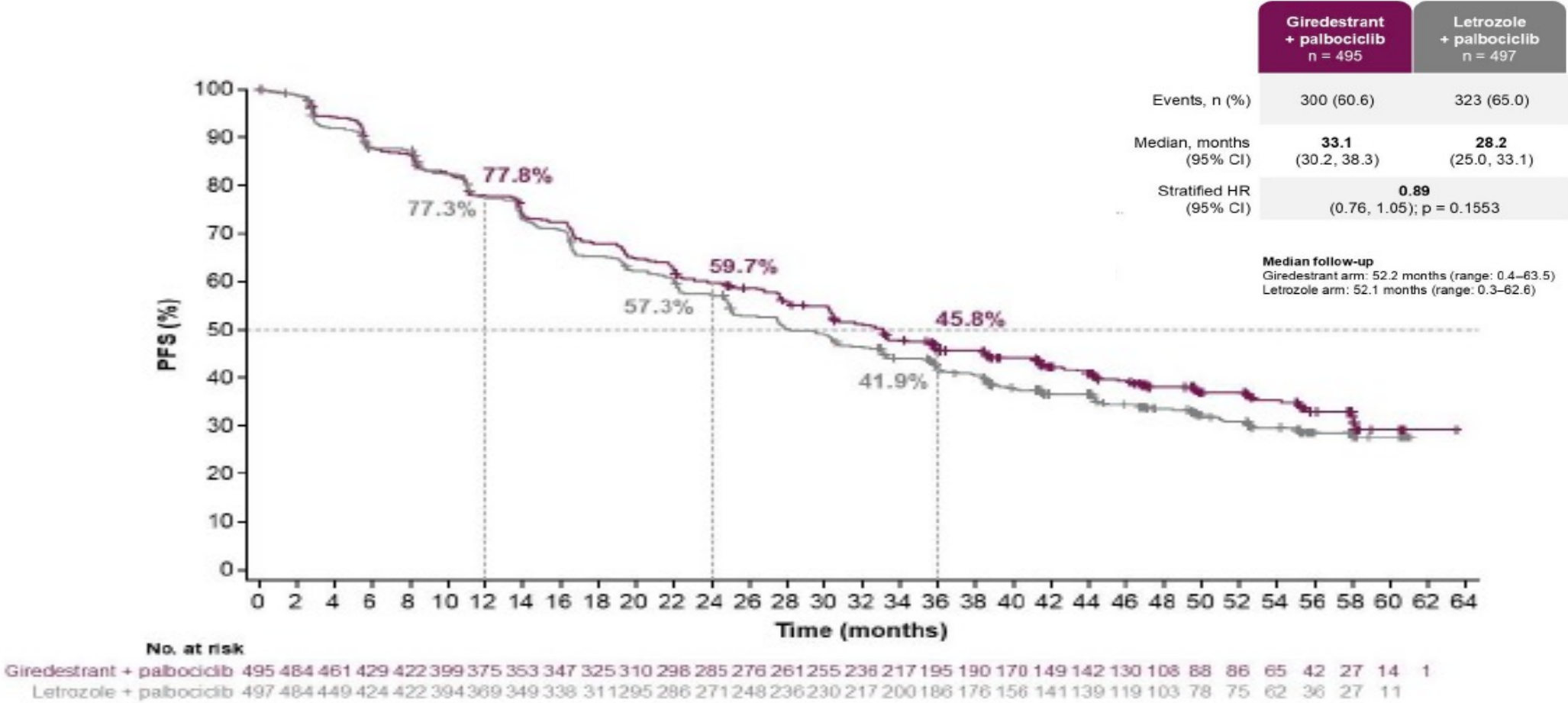
Giredestrant + everolimus versus SOC endocrine therapy + everolimus in pretreated HR+ MBC: PFS



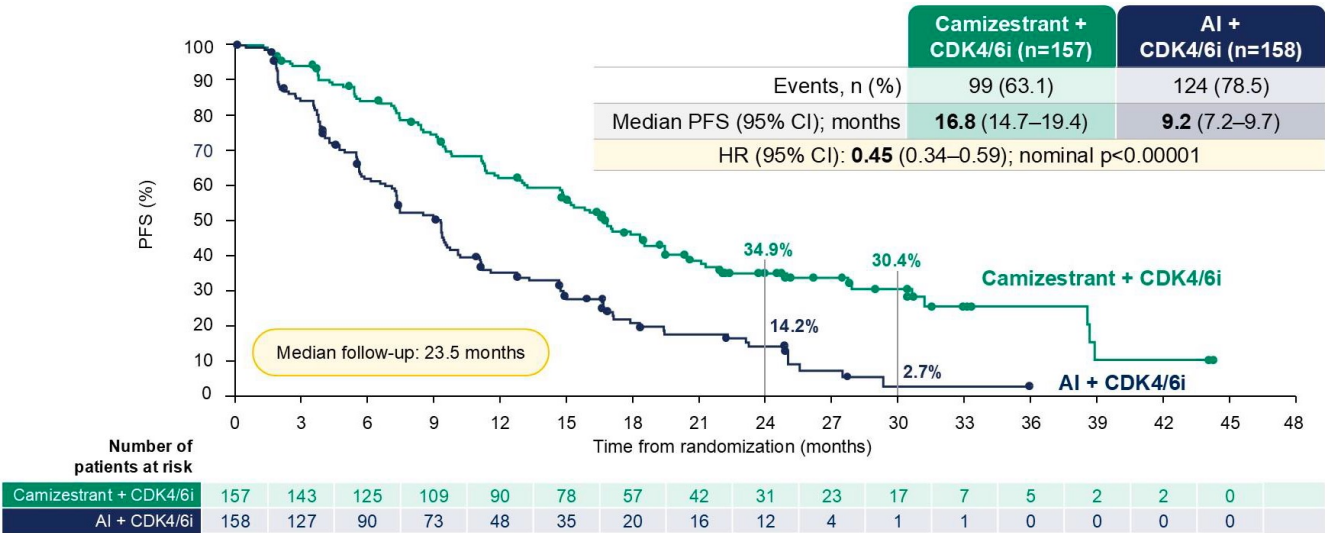
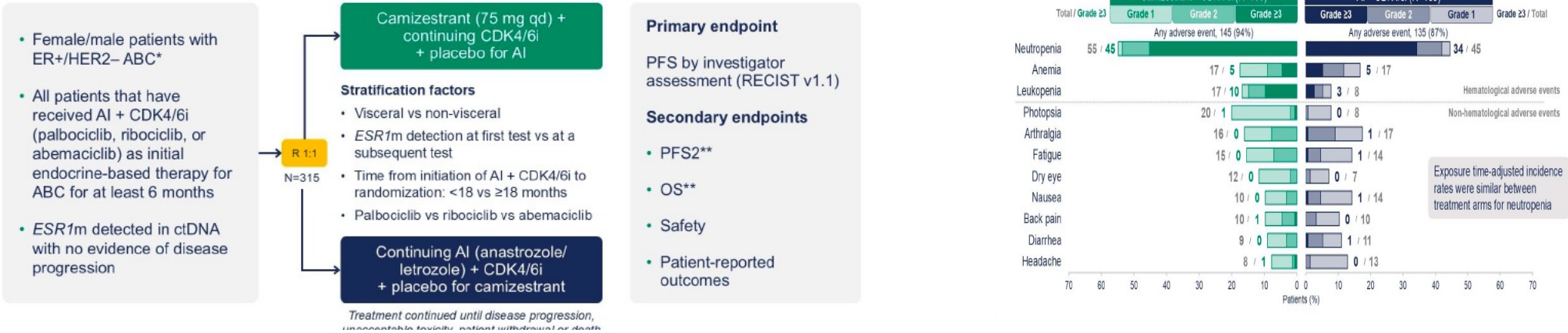
persevERA BC: Schema



persevERA BC: PFS

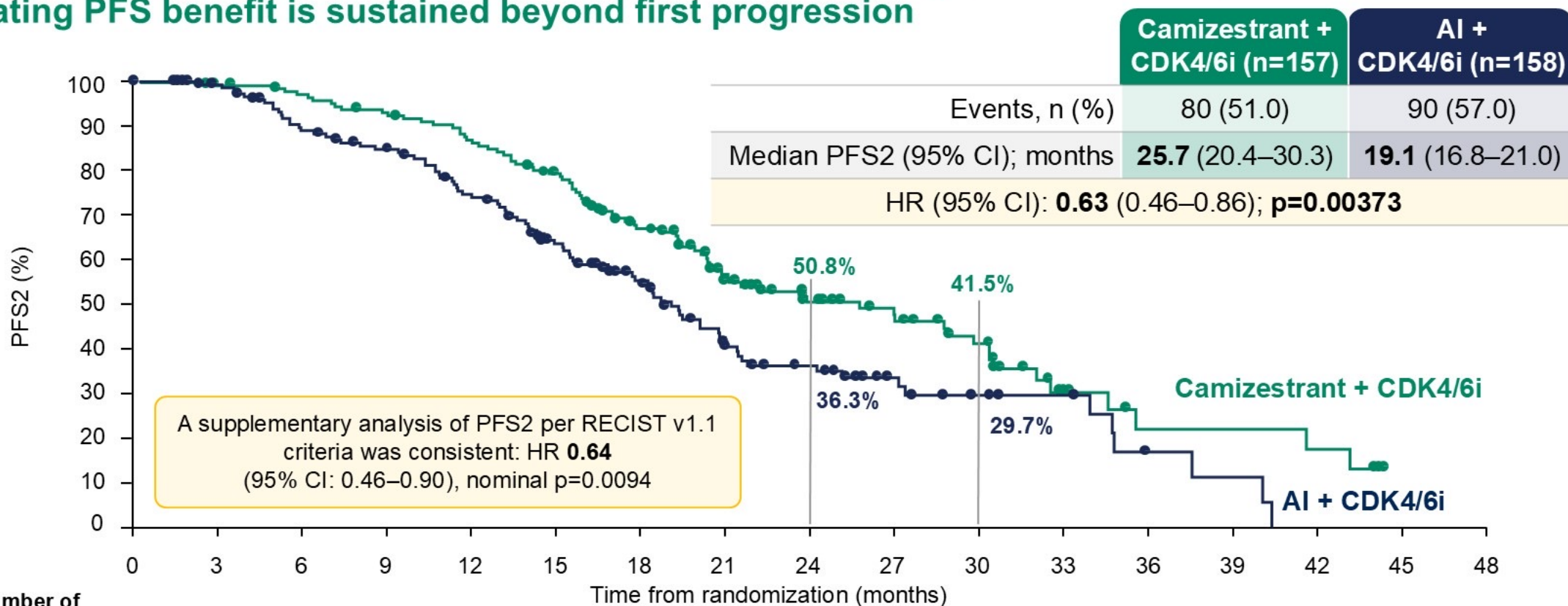


SERENA 6: Camizestrant versus AI upon detection of ESR1 mutation



Final second progression-free survival (PFS2)

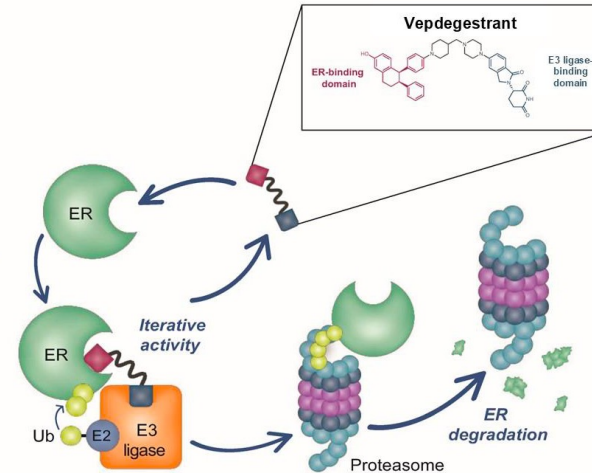
Camizestrant + CDK4/6i significantly extended time to second progression or death, demonstrating PFS benefit is sustained beyond first progression



DCO3 (Jan 02, 2026). PFS2, defined in a standard manner (assessed by the investigator according to local standard clinical practice) as the time from randomisation to the earliest of disease progression after first subsequent therapy or death in the primary analysis. The p value is based on the stratified log-rank test, stratified by disease site (visceral vs non-visceral), timing of *ESR1m* detected (first vs subsequent test), and time from initiation of AI+CDK4/6i to randomization (<18 months vs ≥18 months).

VERITAC-2: Vepdegestrant versus fulvestrant

- Vepdegestrant is a selective, oral PROTAC ER degrader that targets WT and mutant ER^{5,6}
- In a first-in-human, phase 1/2 study (NCT04072952), vepdegestrant was well tolerated and demonstrated encouraging clinical activity in heavily pretreated patients with ER+/HER2- advanced breast cancer⁷



Key Eligibility Criteria

- Age ≥18 years old
- ER+/HER2- advanced or metastatic breast cancer
- Prior therapy:
 - 1 line of CDK4/6i + ET
 - ≤1 additional ET
 - Most recent ET for ≥6 months
 - No prior SERD (eg, fulvestrant, elacestrant)
 - No prior chemotherapy for advanced or metastatic disease
- Radiological progression during or after the last line of therapy

Randomization (1:1)

28-day Treatment Cycles

Vepdegestrant (n=313)
200 mg orally (once daily)

Fulvestrant (n=311)
500 mg IM
(days 1 and 15 of cycle 1; day 1 of subsequent cycles)

Stratification Factors:

- ESR1 mutation^a (yes vs no)
- Visceral disease (yes vs no)

Primary Endpoint:

- PFS by BICR in
 - ESR1m population
 - All patients

Secondary Endpoints:

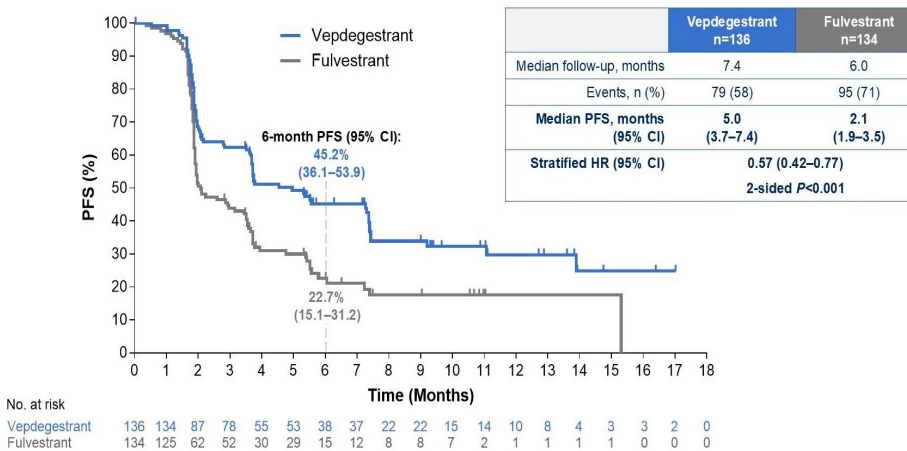
- OS (key secondary)
- CBR and ORR by BICR
- AEs

VERITAC-2: Vepdegestrant versus fulvestrant

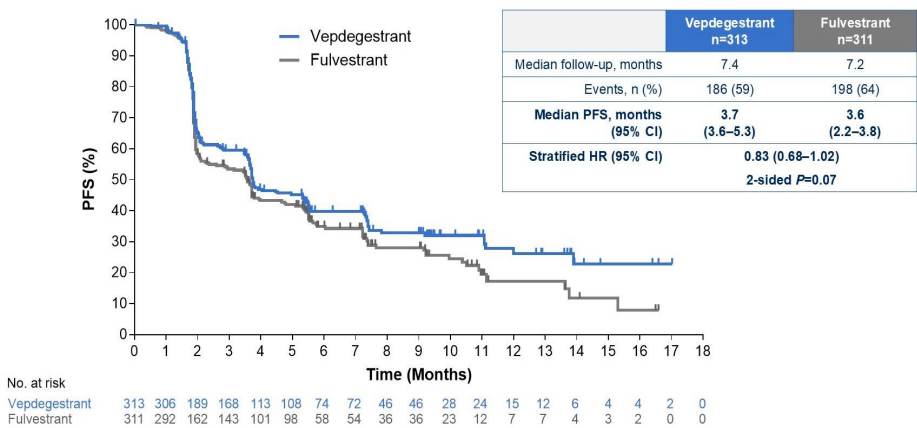
Characteristic	Patients With ESR1m		All Patients	
	Vepdegestrant (n=136)	Fulvestrant (n=134)	Vepdegestrant (n=313)	Fulvestrant (n=311)
Median age (range), y	60 (26–87)	60 (34–85)	60 (26–89)	60 (28–85)
Female, %	99	100	99	100
Postmenopausal, %	79	79	78	78
Race, %				
White	43	51	47	46
Black or African American	3	4	2	2
Asian	45	37	39	41
Unknown/NR	9	7	12	9
ECOG PS, %				
0	57	57	61	64
1	43	43	39	36
ESR1m, % ^a	100	100	43	43
Sites of disease, %				
Visceral disease	68	68	63	63
Liver metastasis	46	44	40	36
Bone-only disease	18	18	18	20

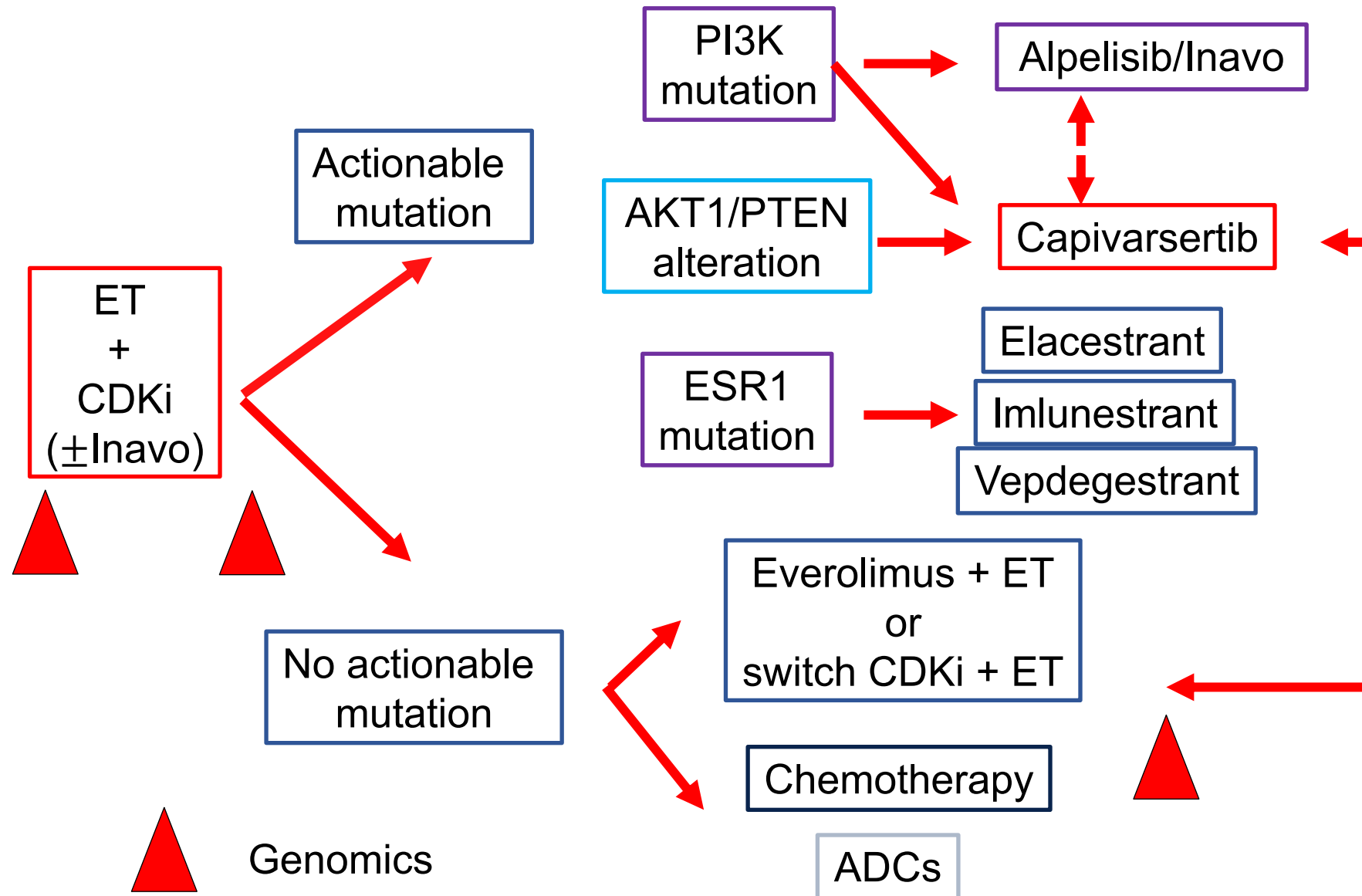
Characteristic, %	Patients With ESR1m		All Patients	
	Vepdegestrant (n=136)	Fulvestrant (n=134)	Vepdegestrant (n=313)	Fulvestrant (n=311)
Measurable disease ^b	71	75	71	71
Prior lines of therapy in advanced/metastatic setting ^c				
1	82	80	82	76
2	18	20	18 ^d	23 ^d
Prior endocrine therapy	100	100	100	100 ^e
Aromatase inhibitor	99	100	99	99
SERM	15	16	16	20
Prior CDK4/6 inhibitor	100	100	100	100
Palbociclib	50	54	46	52
Ribociclib	38	28	36	31
Abemaciclib	16	25	20	21
Other ^f	1	5	4	4

ESR1-mutated



ESR1-wt







UR
MEDICINE

WILMOT
CANCER INSTITUTE



A Cancer Center Designated by the
National Cancer Institute