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breast
Journal
club

L'IMPORTANZA DELLA RICERCA IN ONCOLOGIA

**THE
OXFORD DEBATE
EDITION**

**20 - 21 APRILE
2023
ROMA**

**THE HIVE HOTEL
Via Torino, 6**

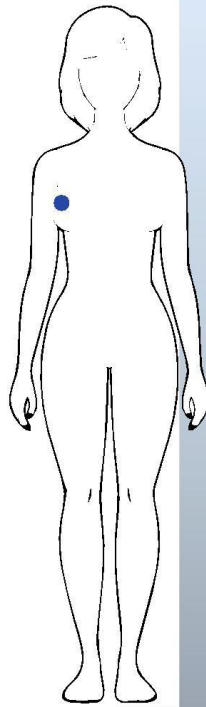


**UNIVERSITÀ
DEGLI STUDI
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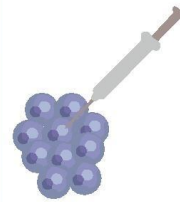

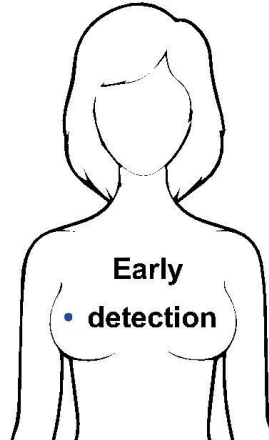
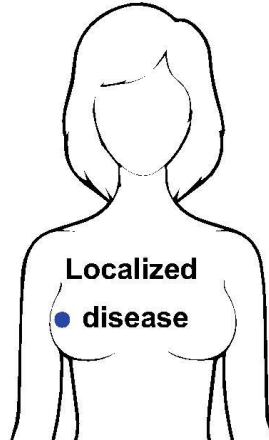
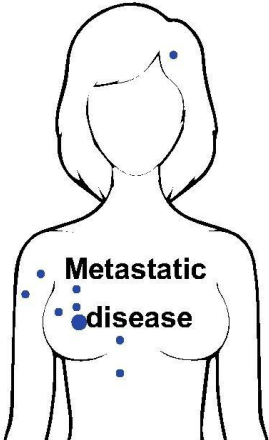
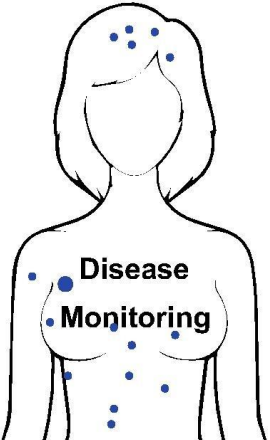
**Biopsia liquida:
siamo pronti per un
uso clinico**

Linda Cucciniello

Tissue versus Liquid Biopsy



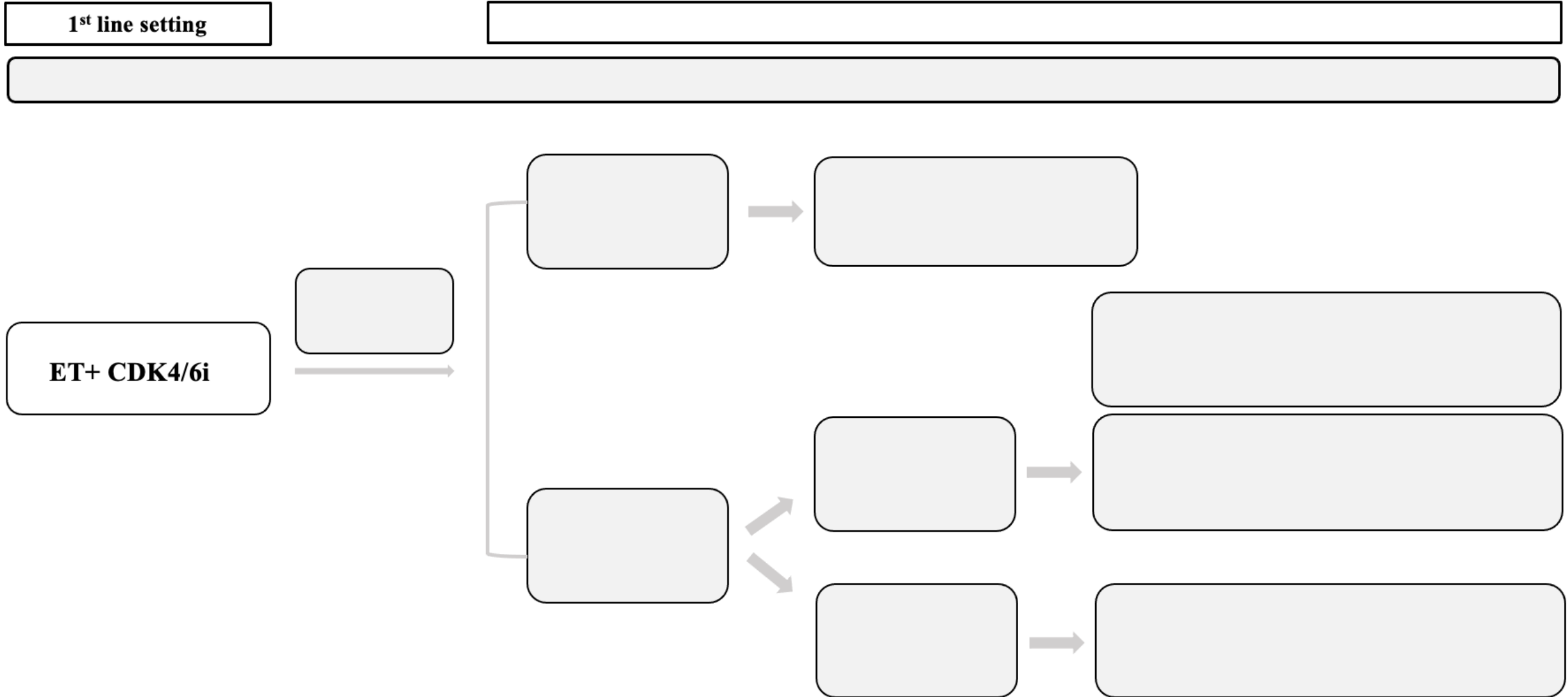
Evolving diagnostics

		Tissue biopsy			
 <ul style="list-style-type: none"> - Often difficult, invasive and multiple sampling are not always feasible - Not always representative of tumor heterogeneity - Single snapshot over time and space 	Does not allow early detection	Allows histological diagnosis and staging	Allows metastasis characterization	Does not allow monitoring disease	
	 <ul style="list-style-type: none"> - Non-invasive procedure, easily repeatable and highly reproducible - Representative of tumor heterogeneity - Real-time monitoring of disease 	 <p>Early detection</p>	 <p>Localized disease</p>	 <p>Metastatic disease</p>	 <p>Disease Monitoring</p>
	Diagnose cancer earlier through screening	Determine the risk of recurrence	Determine treatment selection through biomarkers	Determine mechanisms of resistance	
		Liquid biopsy			

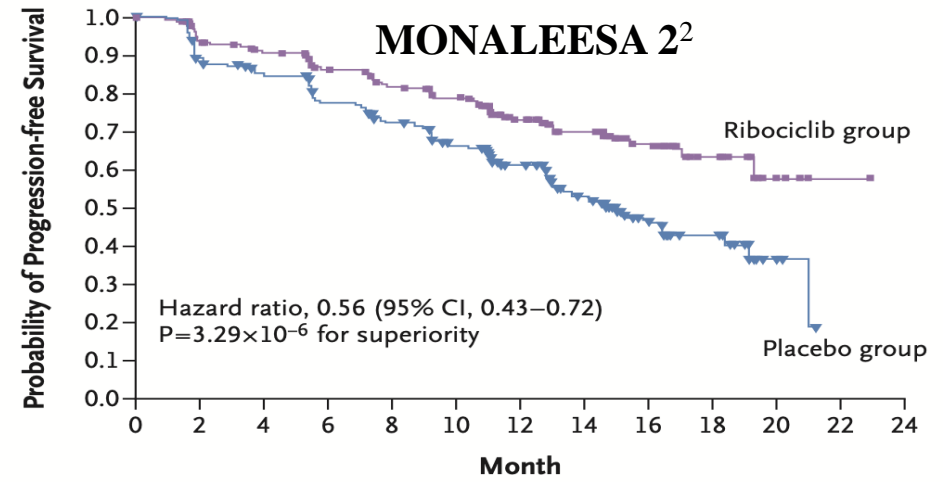
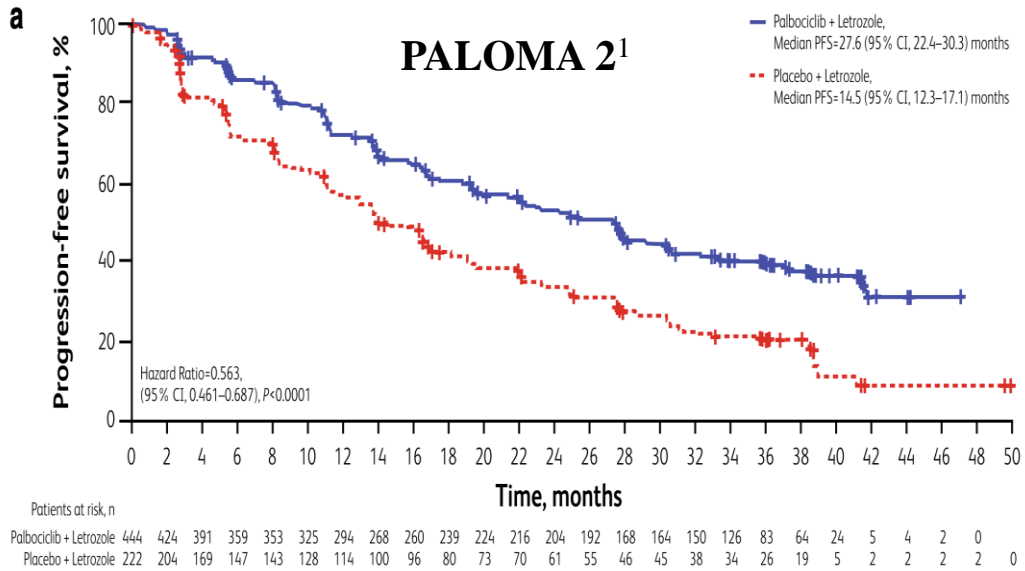
An **essential** tool for the management of **luminal-like MBC**

Drawing together a **Liquid Biopsy-based therapeutic algorithm**

Luminal-like MBC

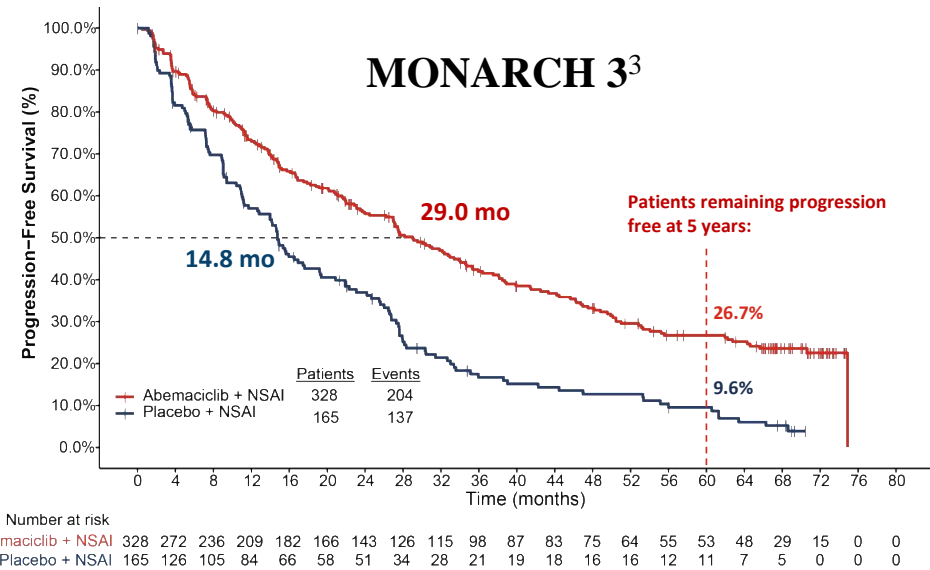


PFS for the currently approved CDK4/6 inhibitors + AI



No. at Risk

Ribociclib	334	294	277	257	240	226	164	119	68	20	6	1	0
Placebo	334	279	264	237	217	192	143	88	44	23	5	0	0



¹ Rugo HS et al. *Breast Cancer Res Treat* 2019;174:719–29

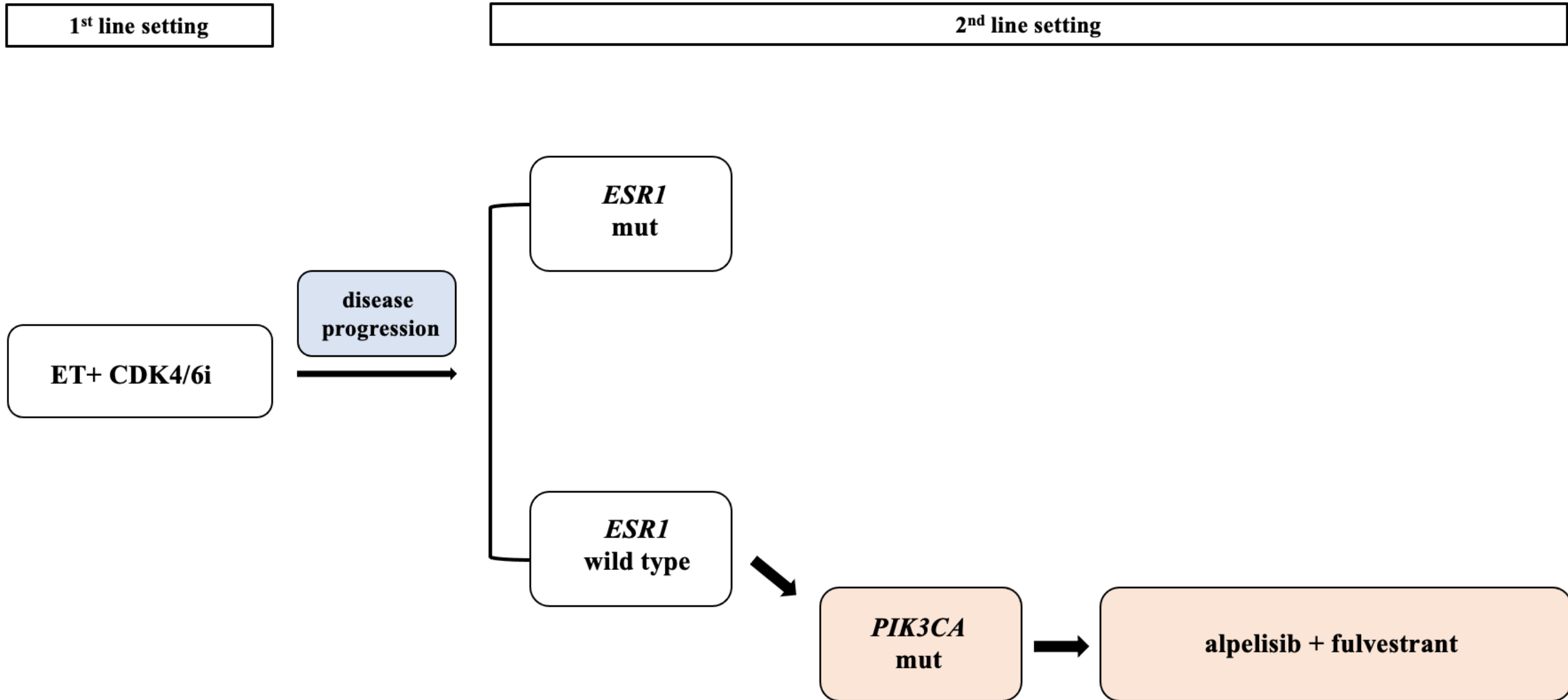
² Hortobagyi GN et al. *N Engl J Med* 2016;375:1738–48

³ Goetz MP et al. *Ann Oncol* 2022;33:S1384

identifying mechanisms of resistance

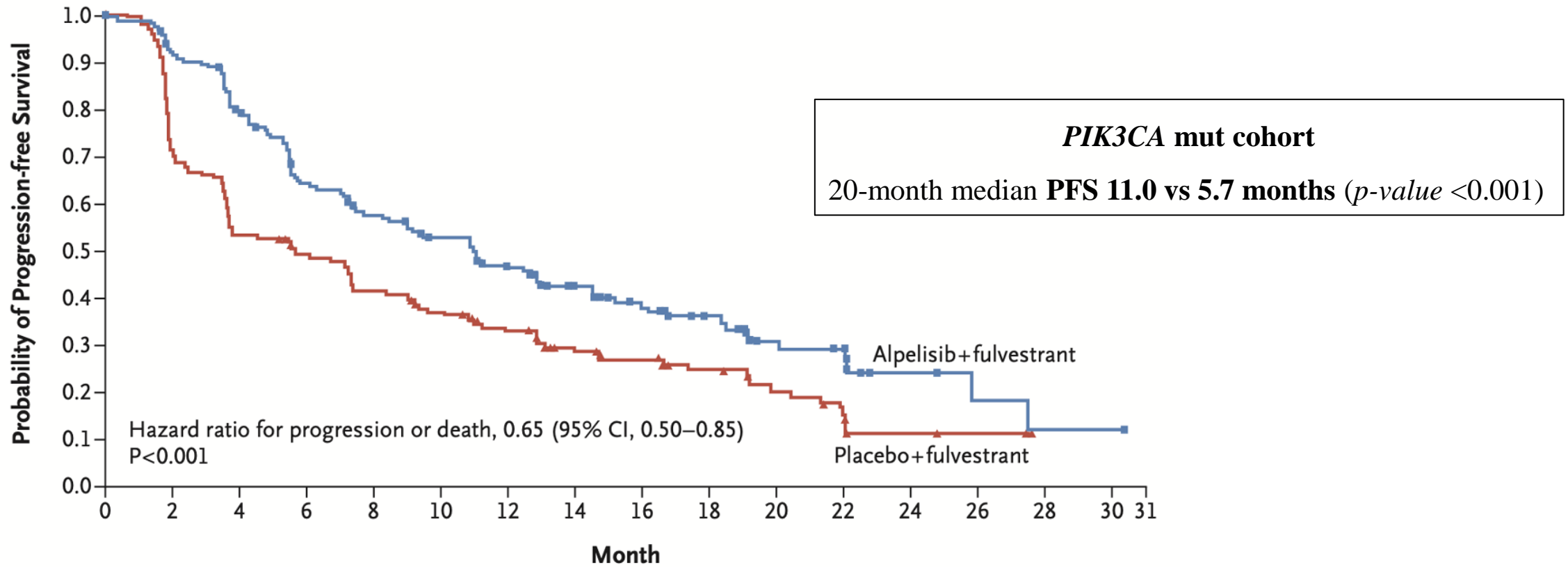
Drawing together a **Liquid Biopsy-based therapeutic algorithm**

Luminal-like MBC



SOLAR-1

Cohort with *PIK3CA*-Mutated Cancer



No. at Risk

Alpelisib+fulvestrant	169	145	123	97	85	75	62	50	39	30	17	14	5	3	1	1	0
Placebo+fulvestrant	172	120	89	80	67	58	48	37	29	20	14	9	3	2	0	0	0

SOLAR-1

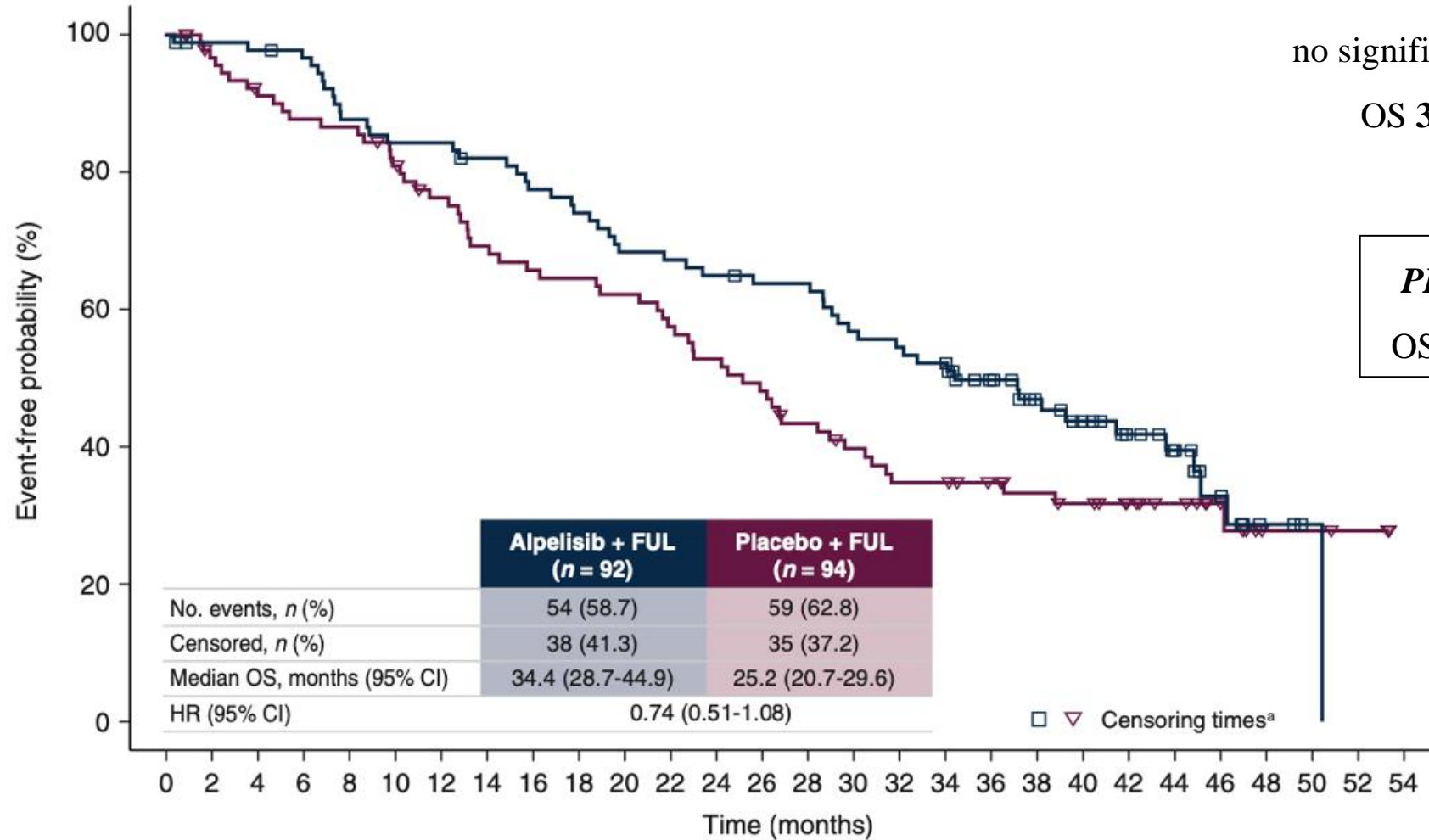
no significant OS benefit in *PIK3CA* mut cohort

OS 39.3 vs 31.4 months (*p*-value 0.15)

but

PIK3CA mut detected in ctDNA

OS 34.4 vs 25.2 months (HR 0.74)



Number of patients
still at risk

Alpelisib + FUL
Placebo + FUL

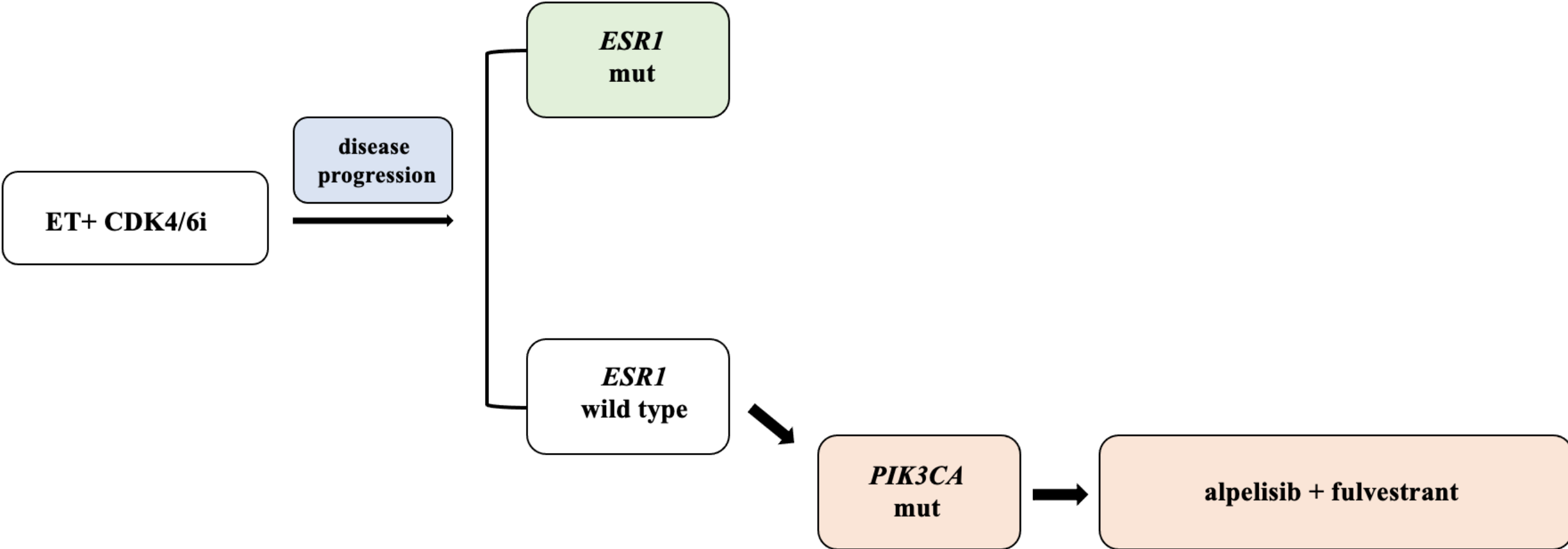
92	89	88	86	78	75	75	72	68	65	60	59	57	55	55	49	47	45	37	30	25	20	15	9	3	1	0	0
94	87	82	78	77	71	65	59	56	55	53	49	45	41	36	32	28	28	25	22	20	16	13	8	3	3	2	0

Drawing together a **Liquid Biopsy-based therapeutic algorithm**

Luminal-like MBC

1st line setting

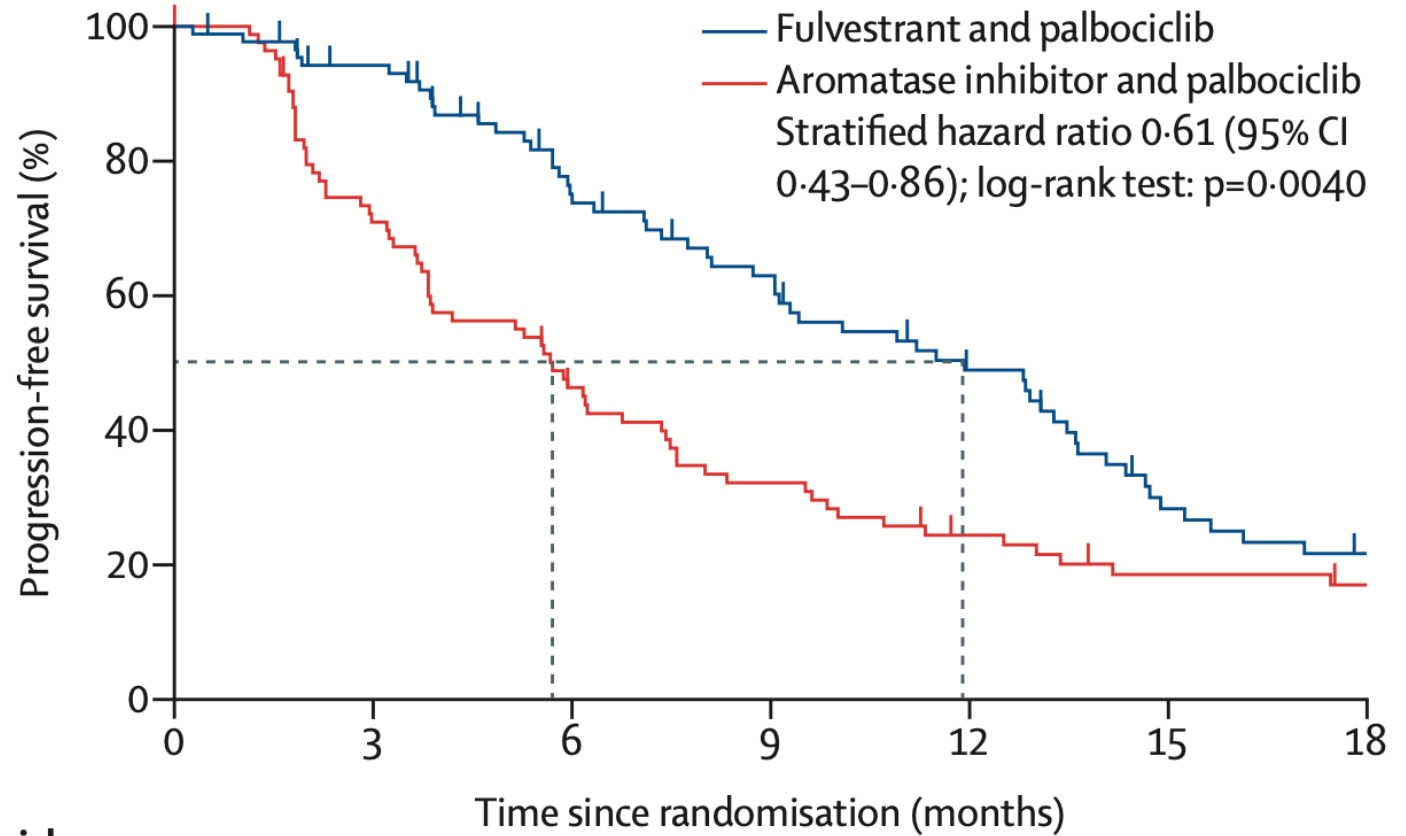
2nd line setting



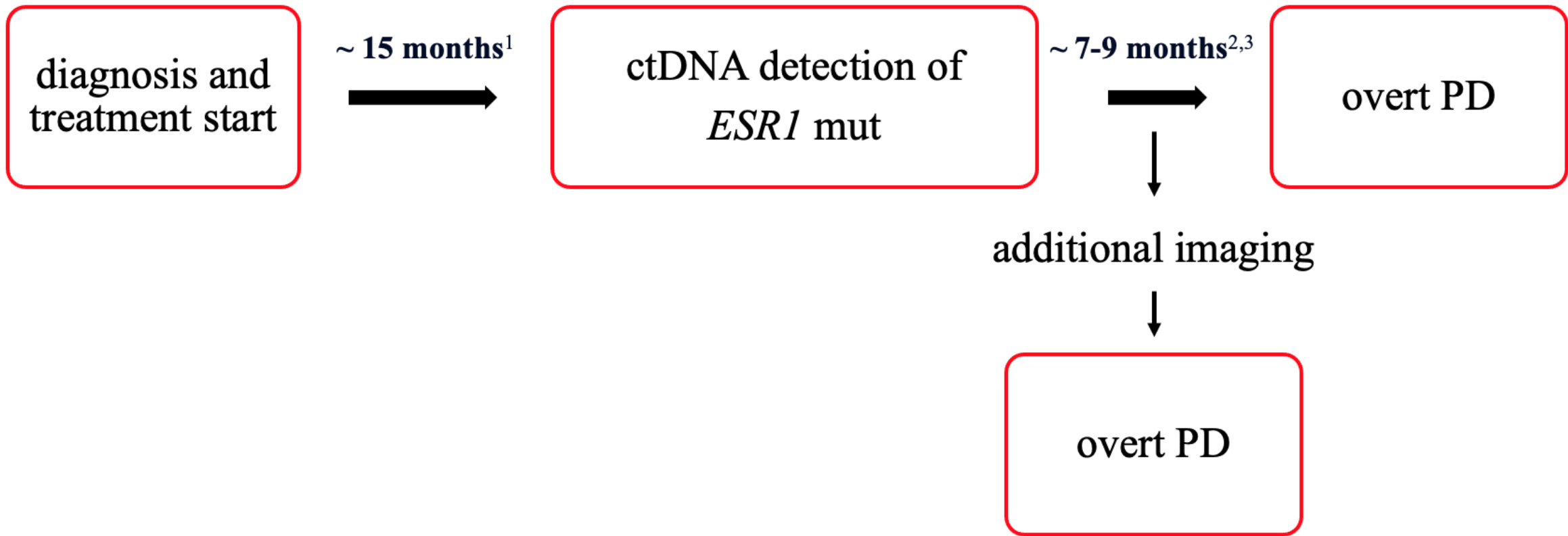
PADA-1

ESR1 mut

35-month PFS **11.9** vs **5.7** months (*p*-value 0.004)

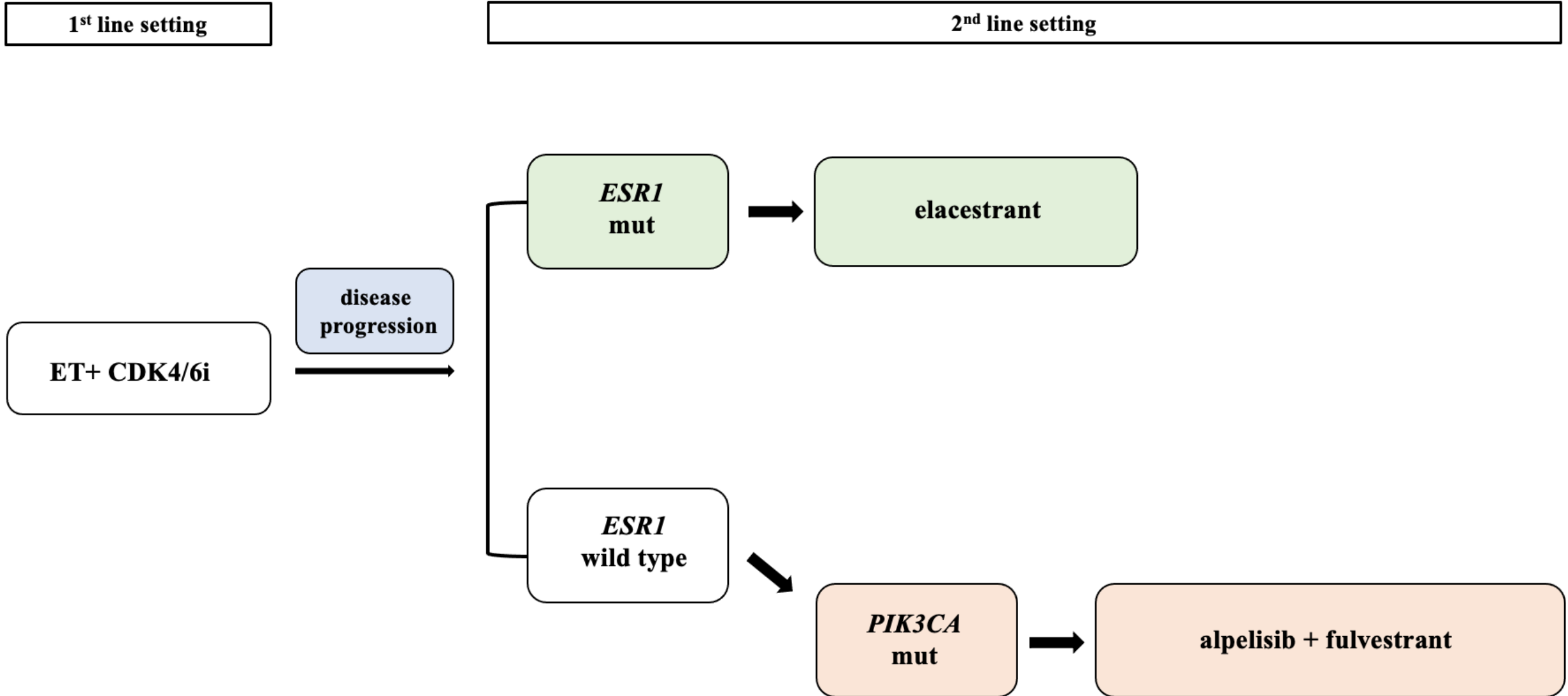


	Number at risk (number censored)						
	0	3	6	9	12	15	18
Fulvestrant and palbociclib	88 (0)	78 (5)	57 (11)	46 (13)	32 (17)	17 (19)	12 (20)
Aromatase inhibitor and palbociclib	84 (1)	58 (2)	36 (4)	25 (4)	17 (6)	12 (7)	10 (8)

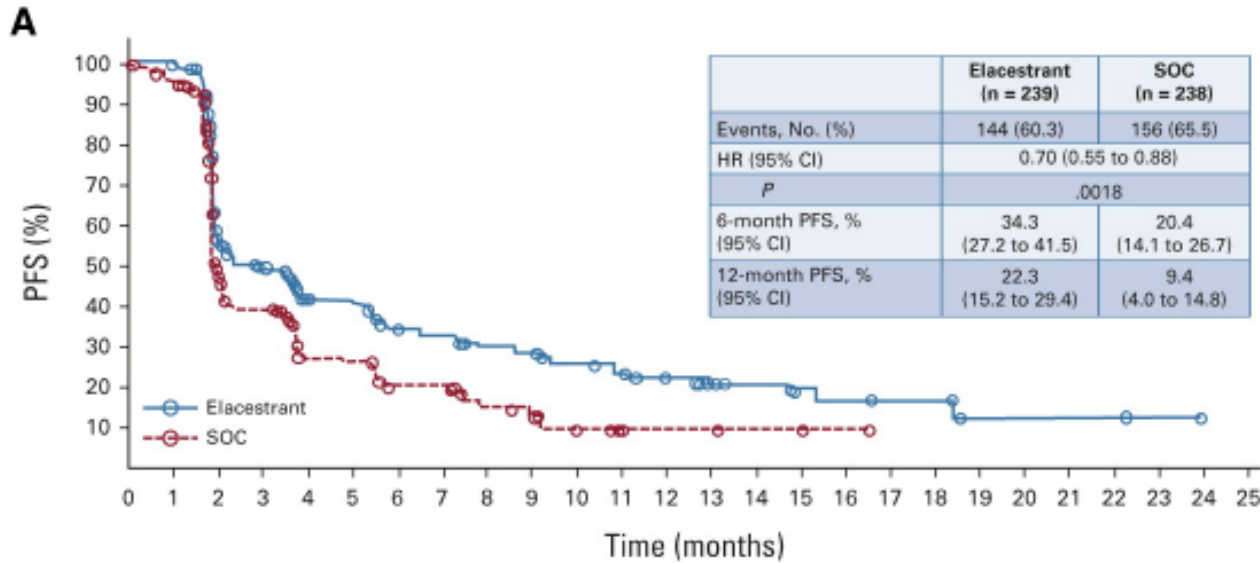


Drawing together a **Liquid Biopsy-based therapeutic algorithm**

Luminal-like MBC



EMERALD

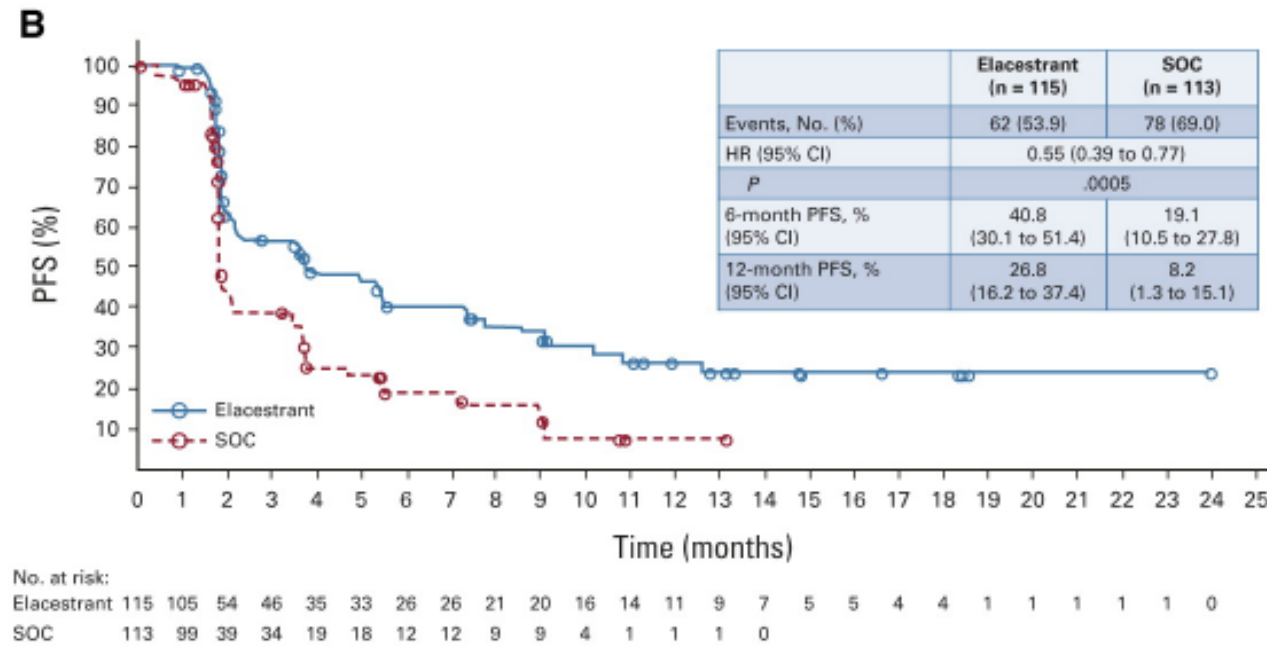


← PFS for all patients

No. at risk:

	239	223	106	89	60	57	42	40	34	33	27	24	19	13	11	8	7	6	6	2	2	2	2	1	0	
Elacestrant	239	223	106	89	60	57	42	40	34	33	27	24	19	13	11	8	7	6	6	2	2	2	2	1	0	
SOC	238	206	84	68	39	38	25	25	16	15	7	4	3	3	2	2	1	0								

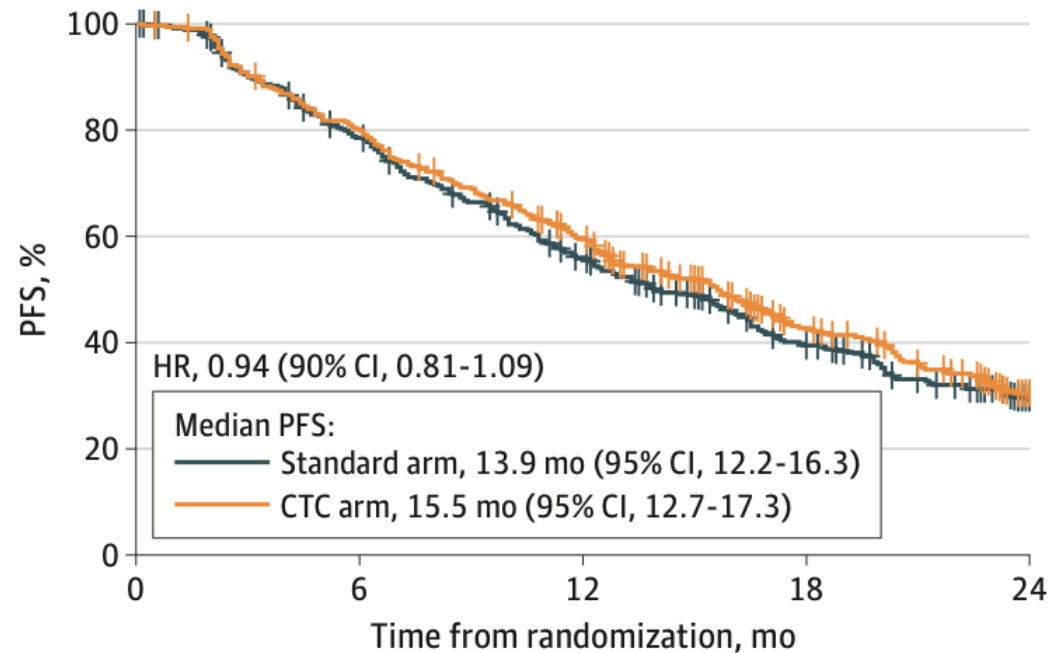
→ PFS for subgroup with *ESR1* mutations



How do we define endocrine resistance? STIC CTC

STIC CTC

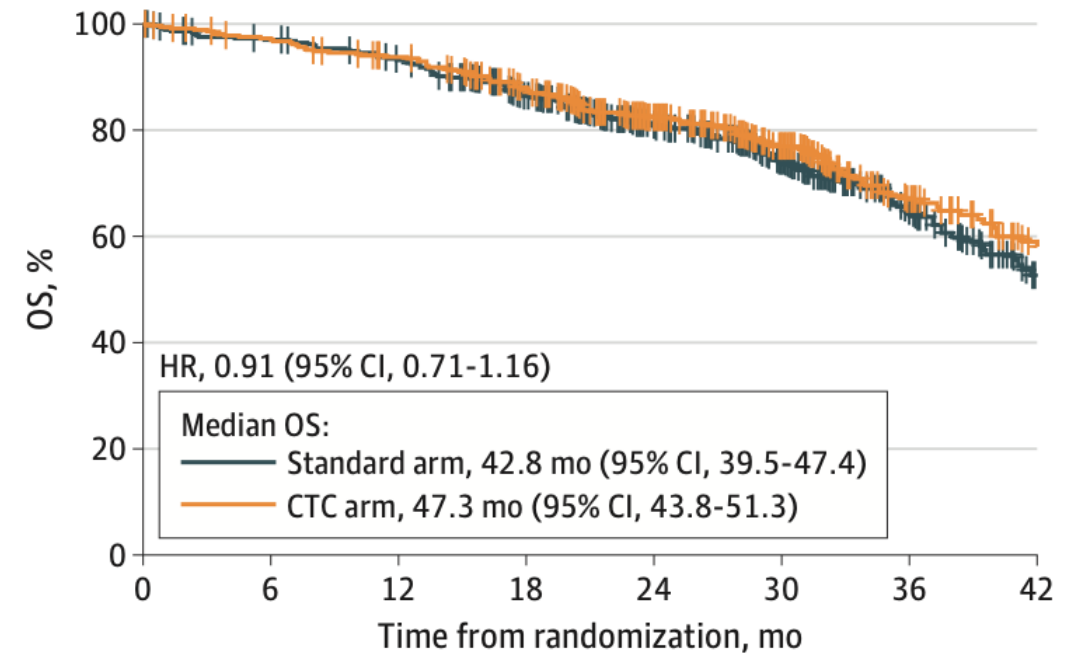
A PFS in the per-protocol population after 498 events



No. at risk (patients censored)

Standard arm	378(0)	287(12)	195(22)	120(46)	56(83)
CTC arm	377(0)	300(3)	216(11)	127(44)	63(80)

B OS in the per-protocol population when considering all events

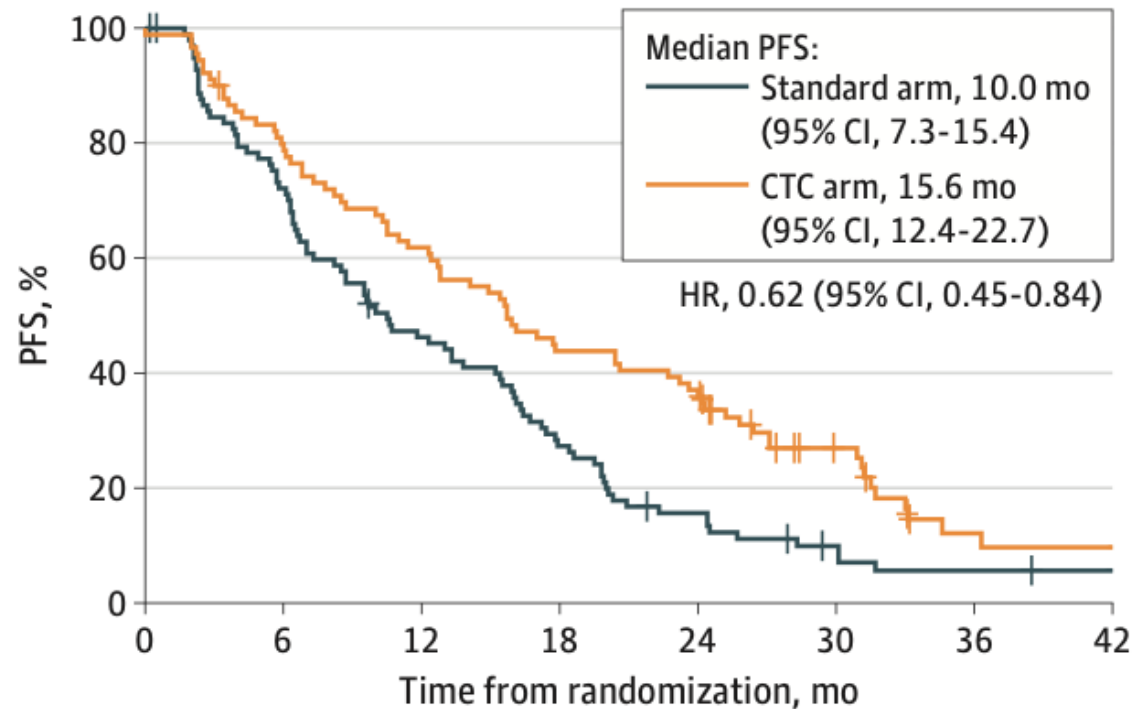


No. at risk (patients censored)

Standard arm	378(0)	359(8)	340(13)	290(39)	231(84)	169(127)	97(186)	50(214)
CTC arm	377(0)	361(6)	342(12)	300(32)	233(84)	166(138)	98(187)	63(212)

No significant differences in PFS or OS amongst CTC arm and standard arm

STIC CTC



No. at risk (patients censored)

Standard arm	99(0)	70(2)	44(3)	26(3)	14(4)	7(6)	4(6)	3(7)
CTC arm	90(0)	71(1)	55(1)	39(1)	33(1)	16(10)	5(13)	4(13)

Higher PFS benefit for clinical low/CTC high group with chemotherapy versus ET

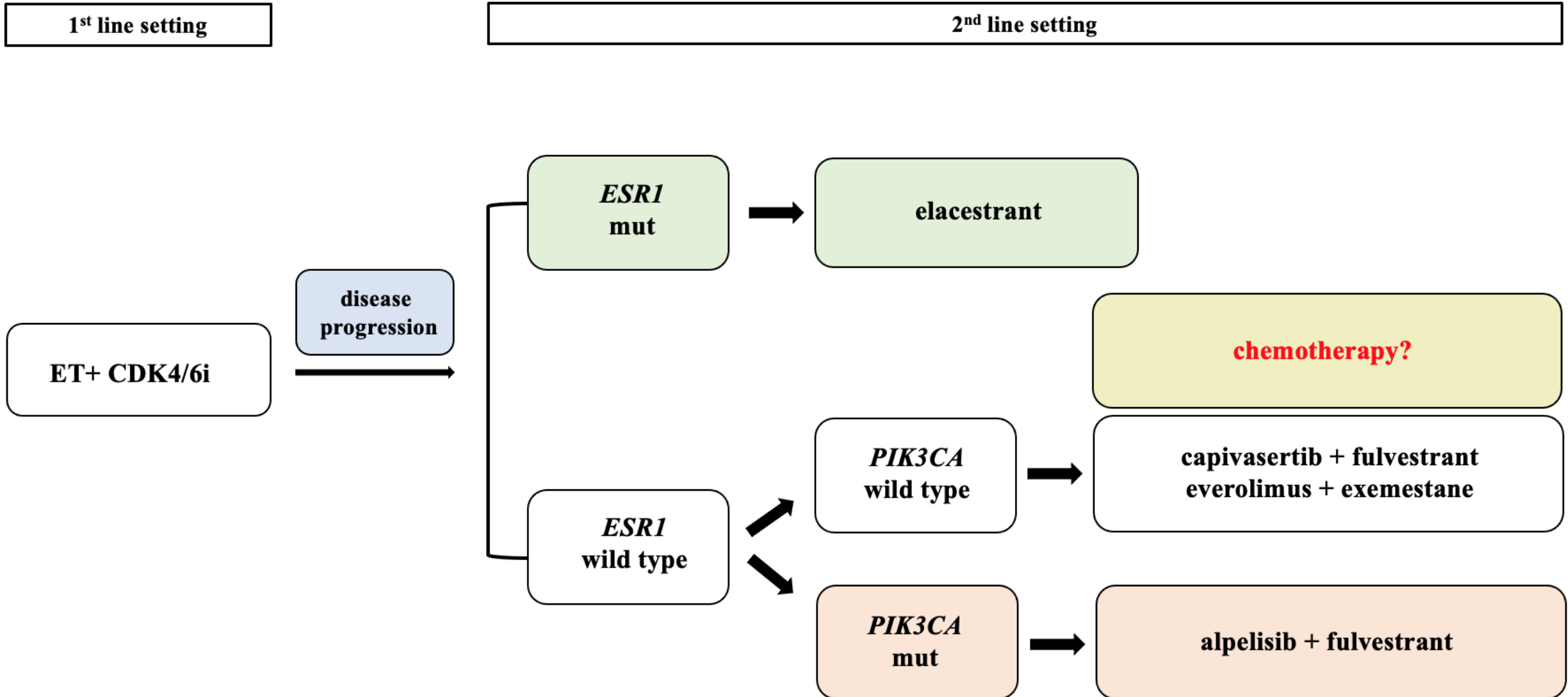


Updated results at SABCS22 showing **higher OS benefit for clinical low/CTC high with chemotherapy versus ET** (51.8 vs 35.4 months, *p-value* 0.001)

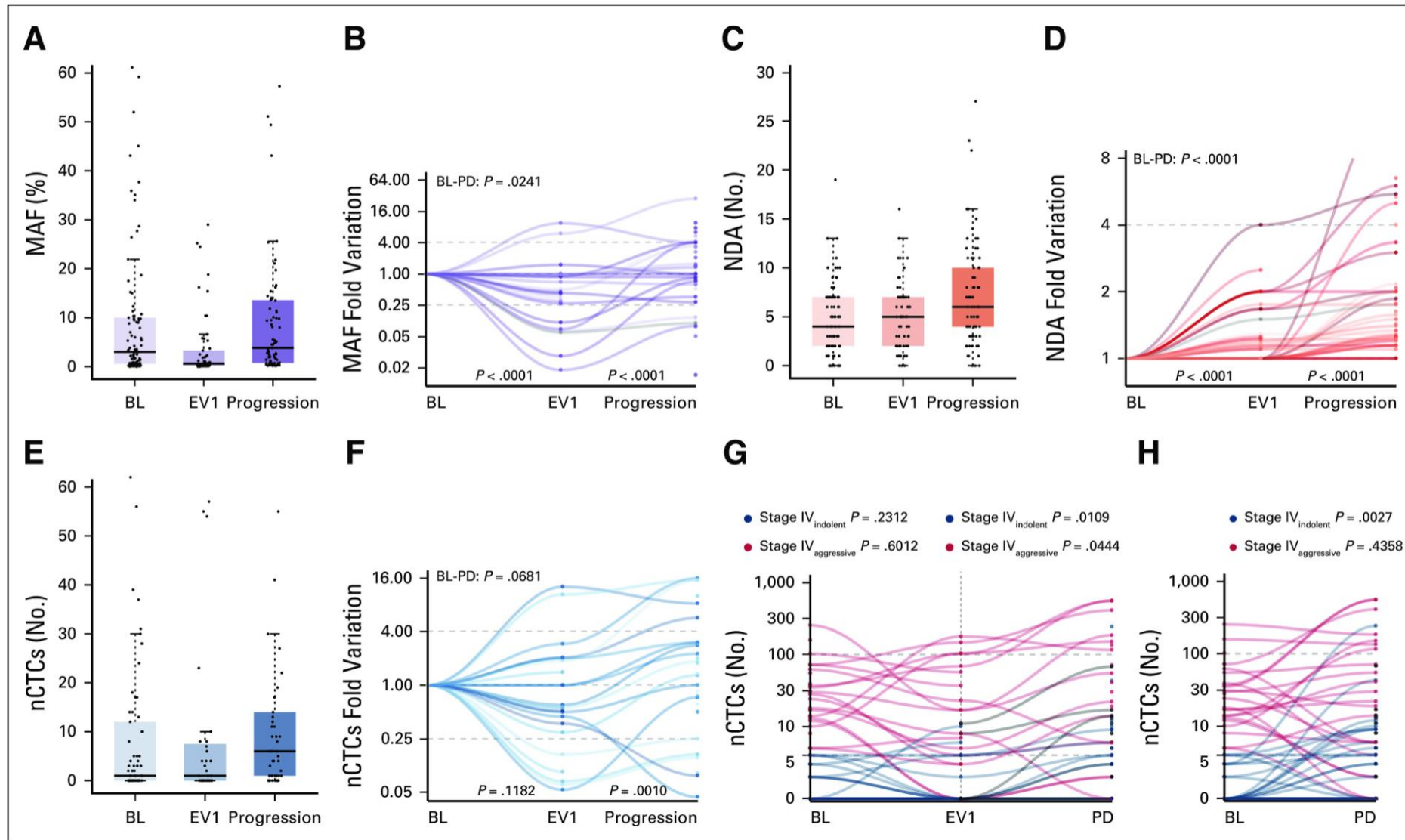
- CTC count is a reliable biomarker and should be considered in the decision-making process
- Patients with ≥ 5 CTCs/7.5 mL of blood should receive chemotherapy

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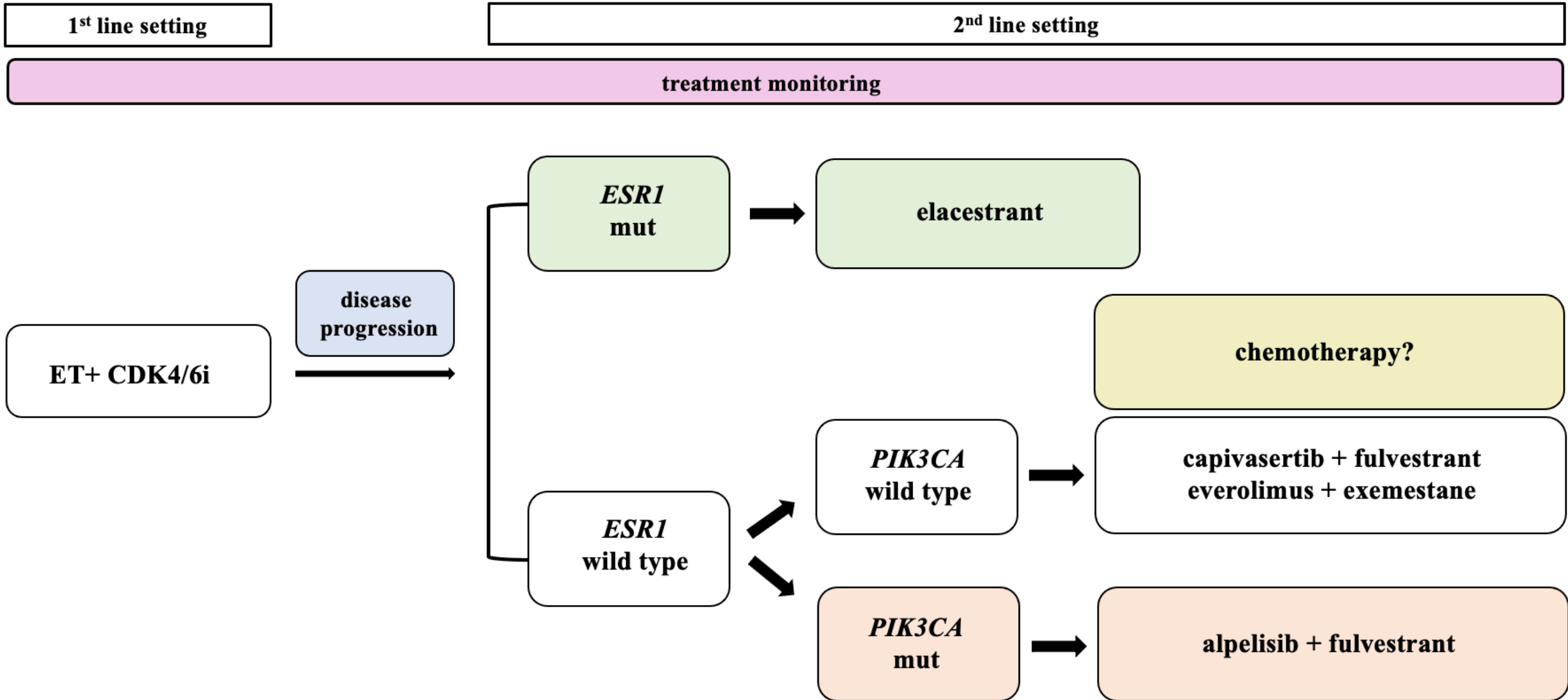


CTCs and ctDNA longitudinal monitoring to predict treatment response



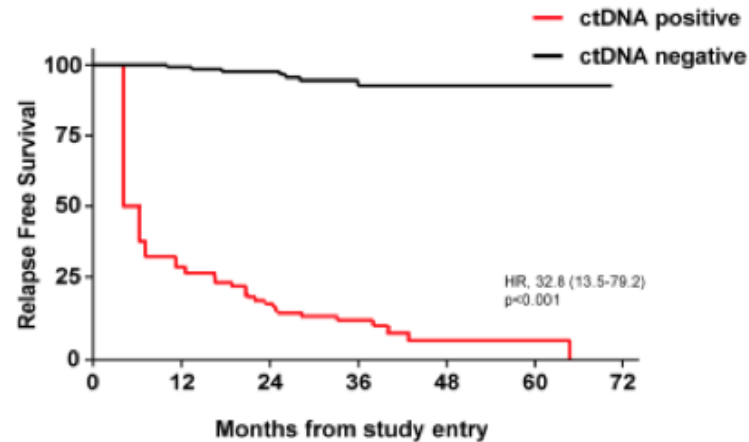
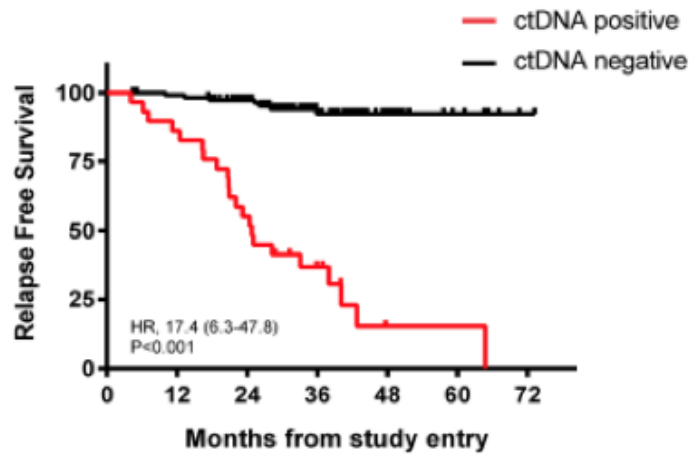
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Luminal-like MBC



Clinical utility *beyond* MBC

ctDNA identification as a predictor of distant relapse with a lead time of 10.7 months in early BC

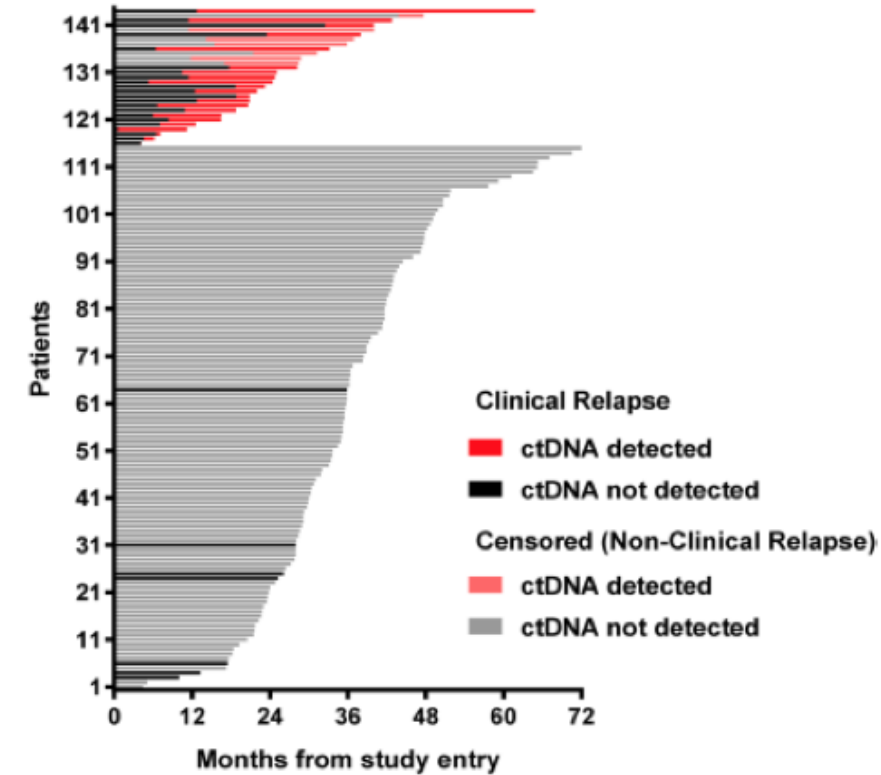


Number at risk

ctDNA negative	115	112	93	51	18	7	1
ctDNA positive	29	25	16	7	1	1	0

Number at risk

ctDNA negative	144	125	95	52	18	7	1
ctDNA positive	0	12	14	6	1	1	0



Does liquid biopsy have a clinical utility? **YES!**

PROs

CONs

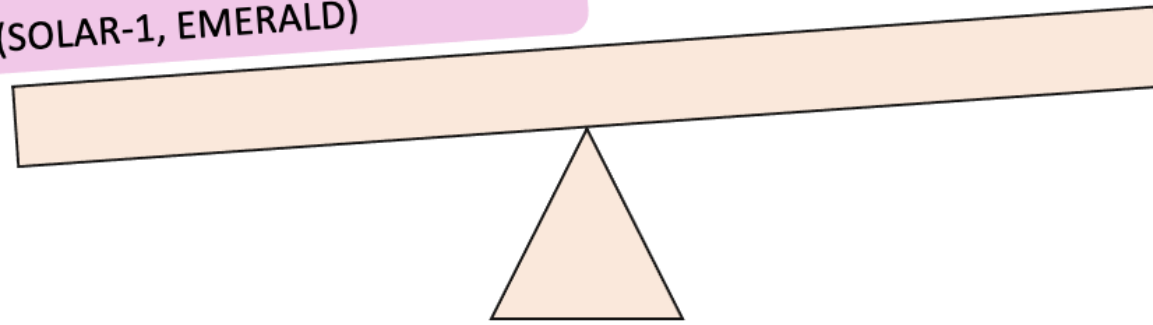
early identification of distant relapse
(Garcia-Murillas et al.)

treatment monitoring
(Gerratana et al.)

identification of resistance mechanisms
(PADA-1)

early identification of disease progression
(PADA-1)

target therapy
(SOLAR-1, EMERALD)



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hic sunt futura

**Thank you for your
attention!**

Linda Cucciniello