Optimizando el tratamiento de las pacientes con mutación en *PIK3CA*, con la primera terapia dirigida a la mutación: Piqray (Alpelisib)

Webinar

Javier Pascual

Pregunta 1

Además de los RH y del HER2, ¿que biomarcadores se pueden usar para la selección de terapias en pacientes con cáncer de mama metastásico HR+/HER2-?

- Mutaciones germinales en *BRCA1/BRCA2* en pacientes con criterios para estudio genético
- Mutaciones somáticas en *PIK3CA*
- Mutacione somáticas en *ESR1*
- **Todas las anteriores**

Pregunta 2

Tras progresión a una primera línea con CDK4/6i + IA en una paciente con cáncer de mama metastásico HR+/HER2-, mutación en *PIK3CA,* ECOG 1 y enfermedad visceral*,* ¿que estrategia terapéutica usarías preferentemente?

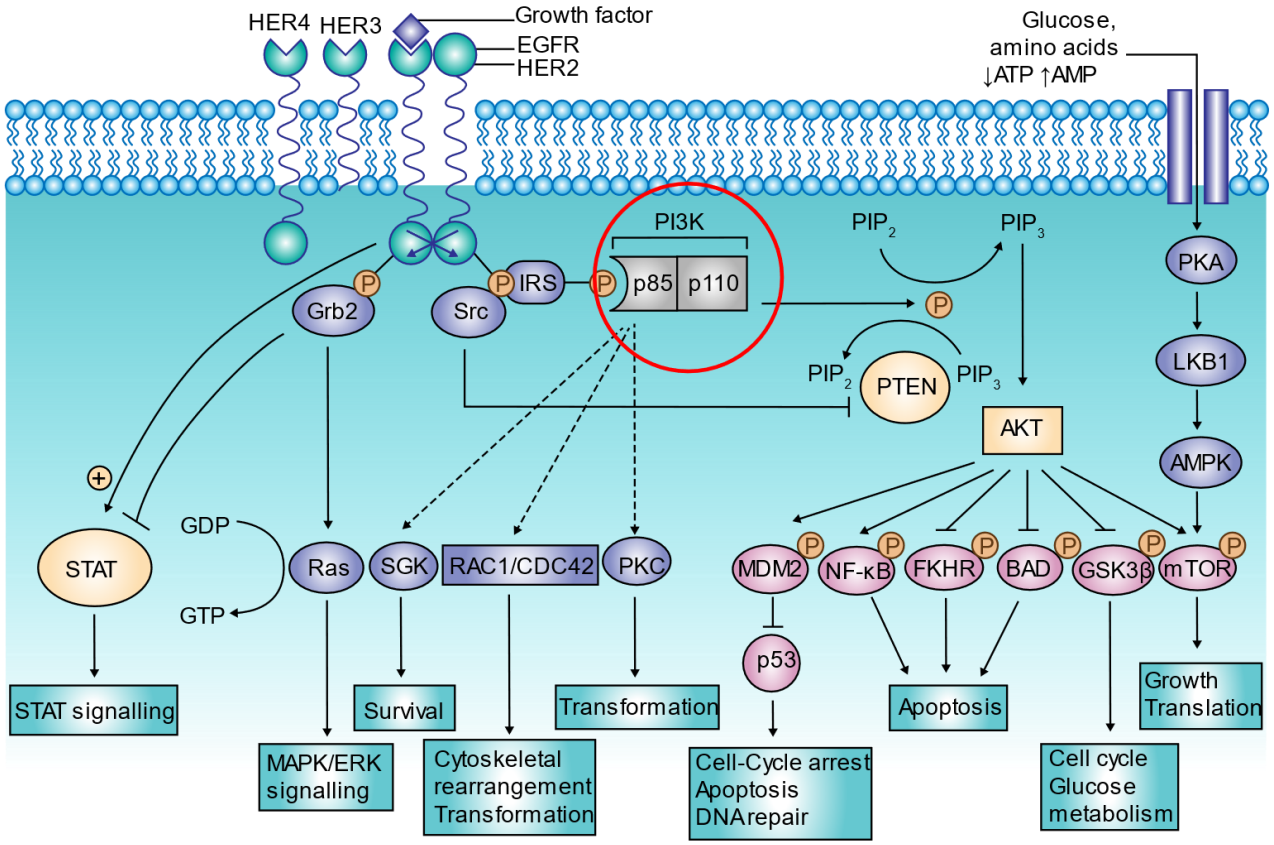
- Fulvestrant
- Quimioterapia
- **Alpelisib + Fulvestrant**
- Ninguna de las anteriores

- La vía de de la fosfoinositol 3-quinasas (**PI3K**) es una vía de señalización intracelular canónica, comúnmente desregulada en cáncer.

- Las PI3K clase I son las más comúnmente alteradas en cáncer y se componente de un heterodímero compuesto por una subunidad reguladora (**p85α and p85β**) y una subunidad catalítica (**p110α, β, γ and δ**).

- Las fosfoinositol 3-quinasas son una familia de enzimas que fosforilan la molécula del grupo 3´-hidroxilo de las fosfatidilinositol bifosfato (**PIP2**) en la membrana celular, resultando en fosfatidilinositol trifosfato (**PIP3)**.

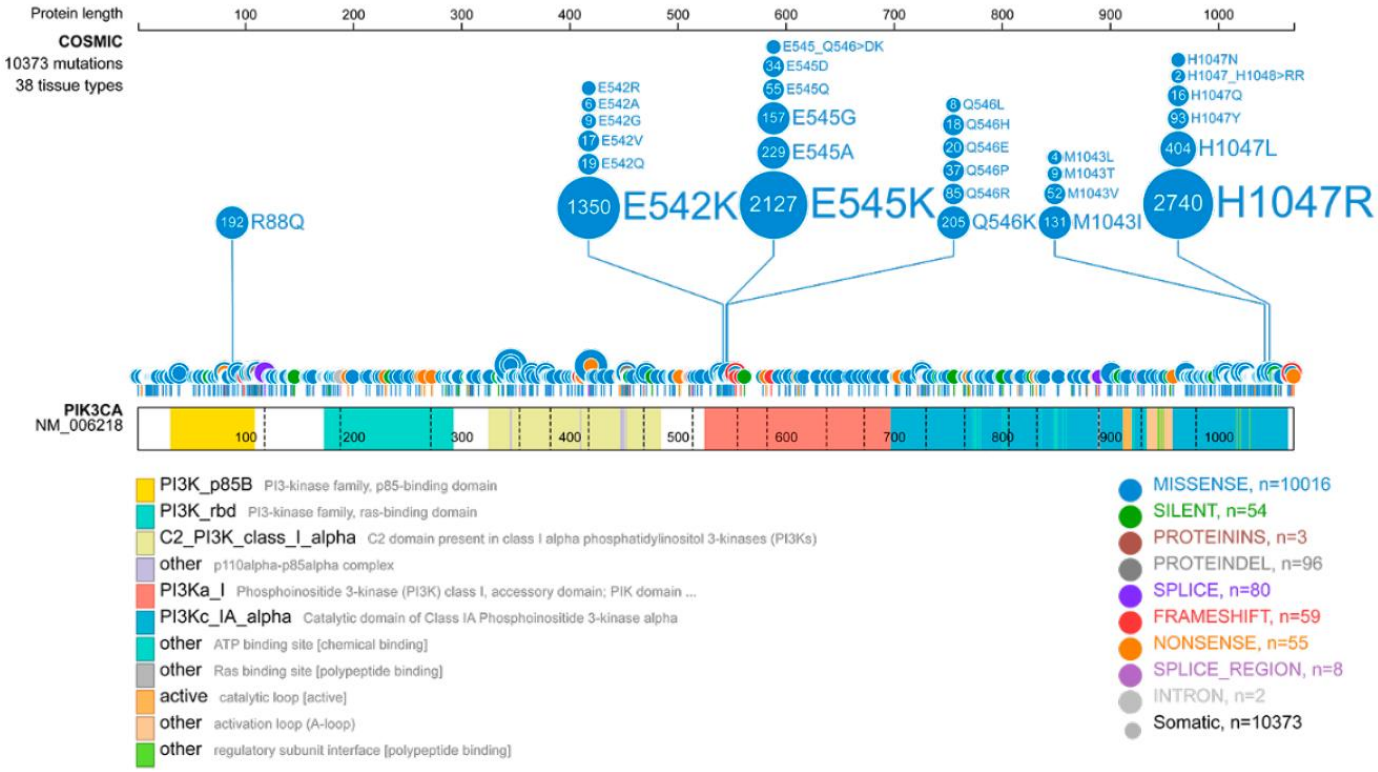
- **PIP3** desencadena la activación a través de la vía, fosforilando los nodos **AKT**, **mTOR**, resultando en un estímulo al crecimiento y proliferación cellular

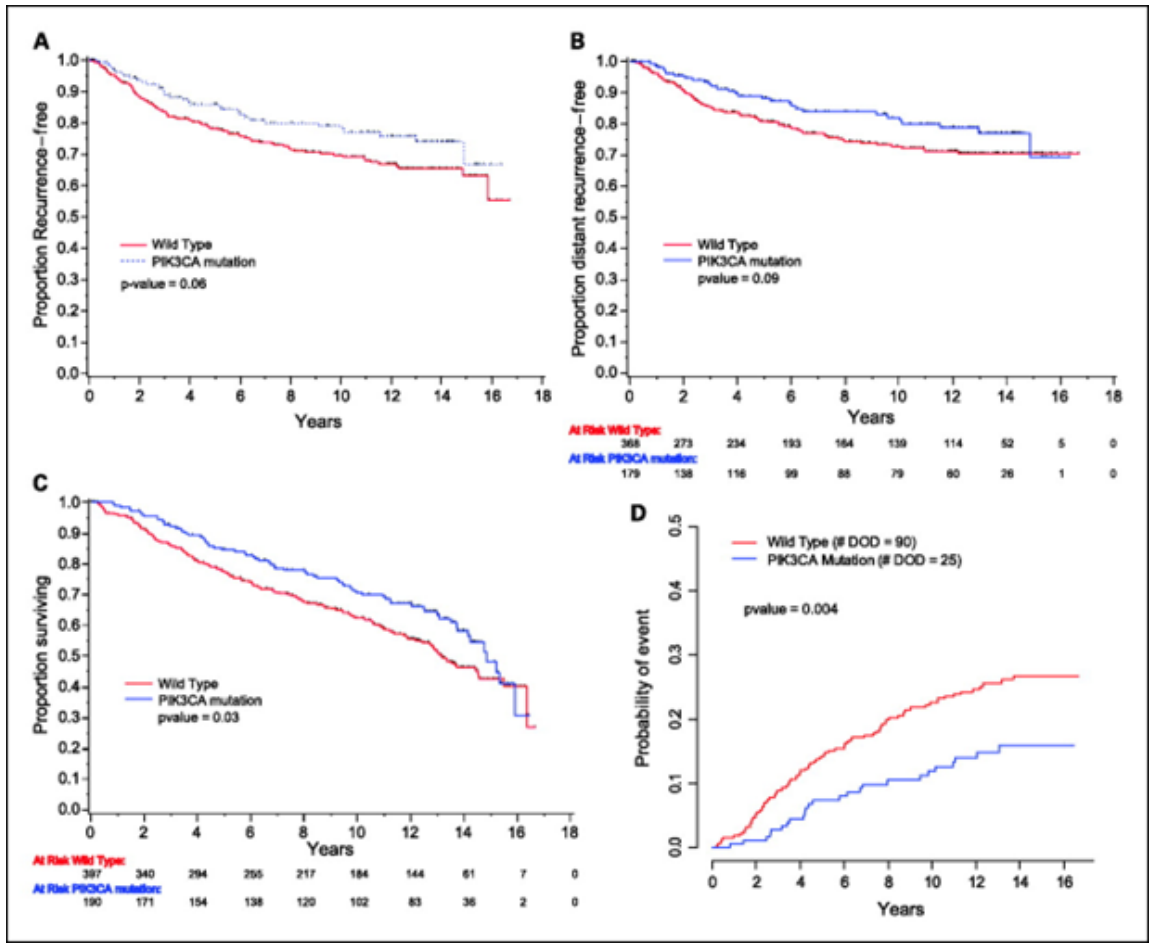


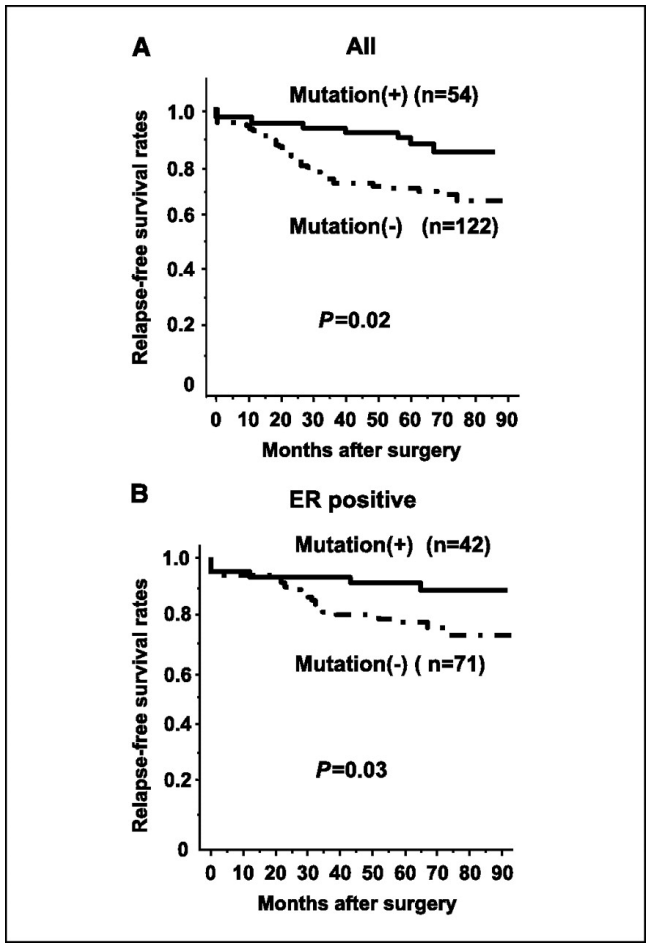
Hennessy BT et al. Nat Rev Drug Discov 2005

- La mayoría de las mutaciones activadoras que hiperactivan la vía ocurren en la subunidad 110α, codificada por el gen *PIK3CA*, aproximadamente en el **40% de las pacientes con CMM HR+/HER2-**

- *PIK3CA* se localiza en el cromosoma 3 y la mayoría de las mutaciones ocurren en regions *hotspot* localizadas en los dominios helicasa del **exon 9 (E542K and E545K)** y catalítico del **exon 20 (H1047L and H1047R)**







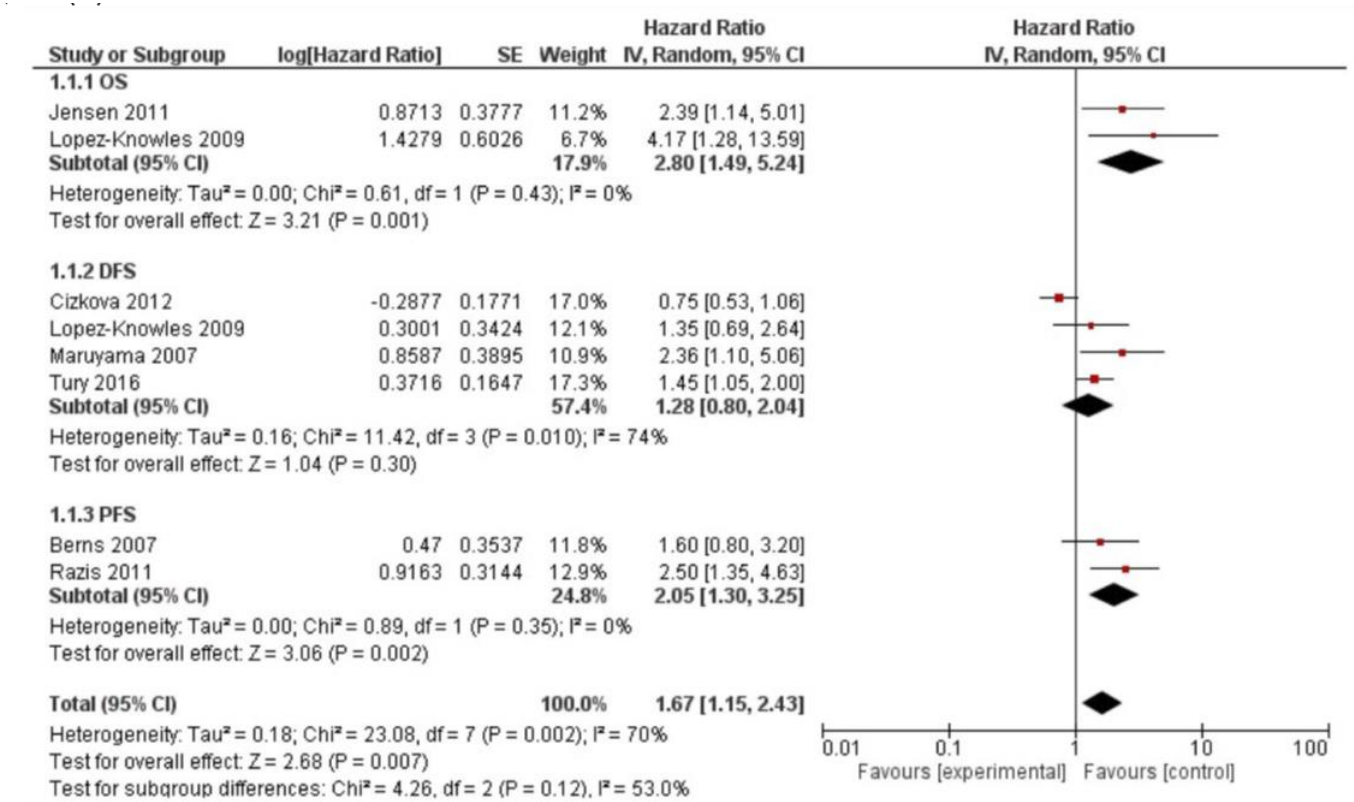
Kalinsky K et al. Clin Cancer Res 2009
Maruyama N et al. Clin Cancer Res 2007

Background

- Meta-analysis investigating the role of *PIK3CA* mutation status as a prognostic factor
- A total of 7 studies and 1,929 cases of breast cancer were included

Results

- The pooled analysis, including an analysis of OS, DFS, and PFS, revealed that the presence of a *PIK3CA* mutation is a negative prognostic factor

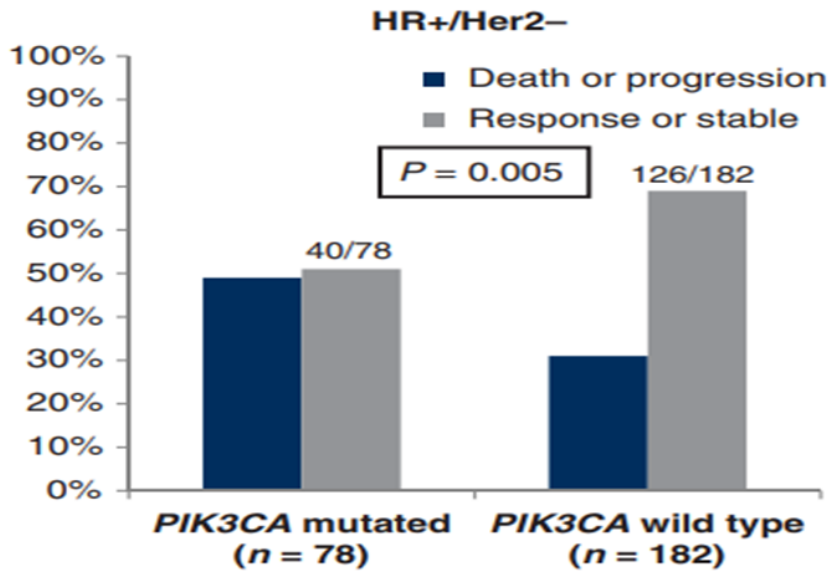


Summary

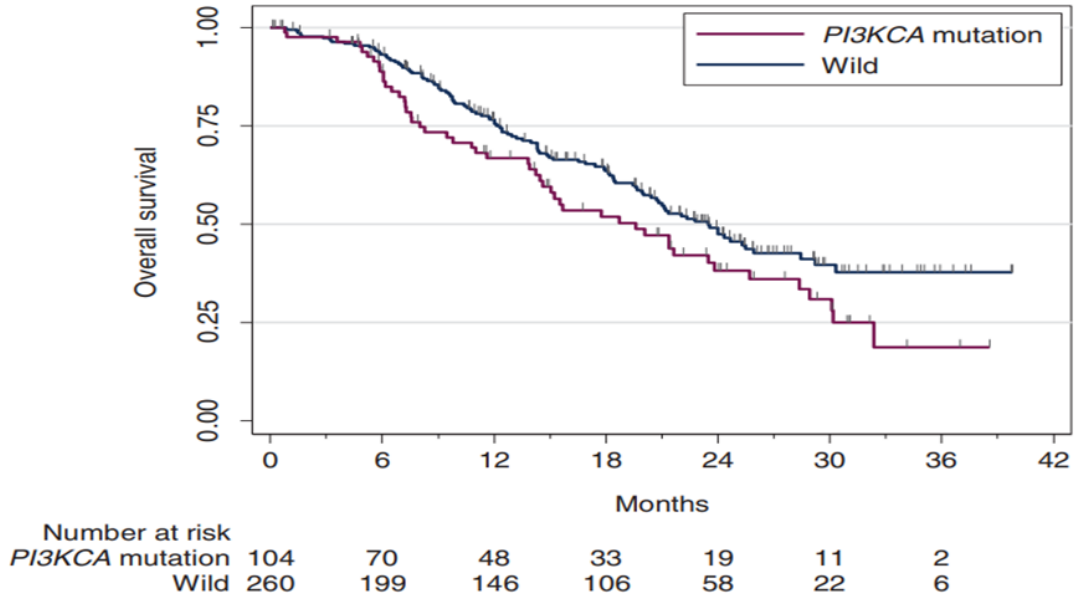
Pooled analysis demonstrated that a *PIK3CA* mutation is a negative prognostic factor for OS, DFS, and PFS

Sobhani N et al. J Cell Biochem 2018

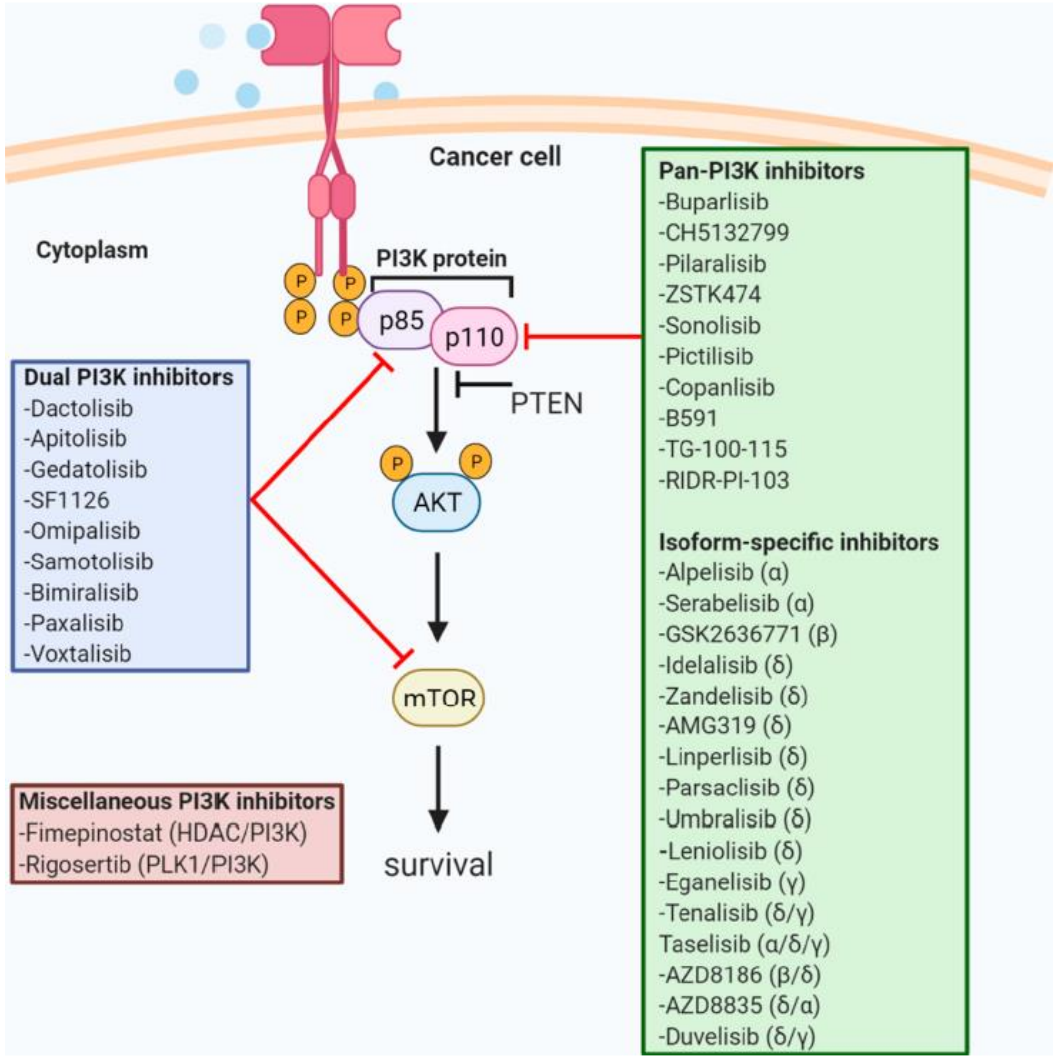
Response rate to chemotherapy



Overall survival

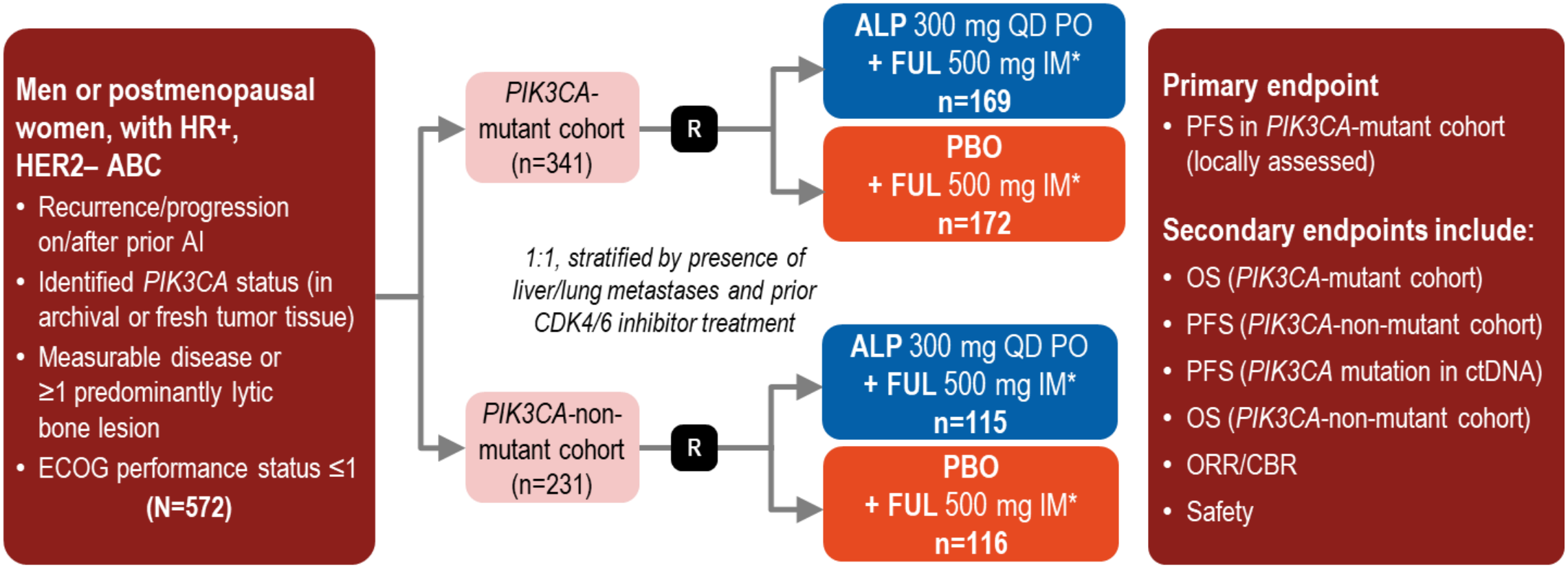


Mosele F et al. Annals of Oncology 2020



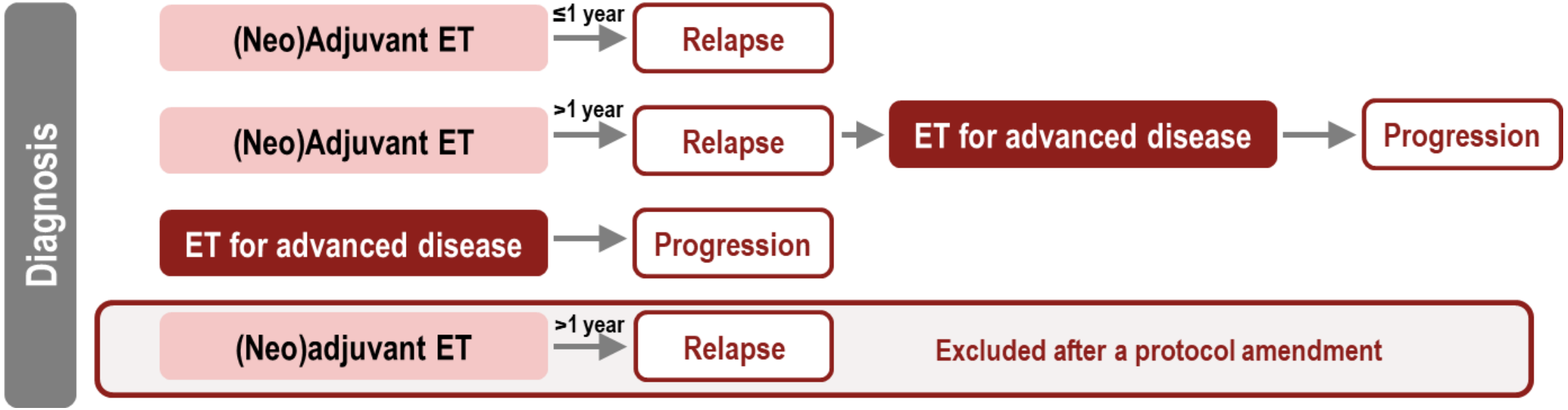
Mishra R et al. Int J Mol Sci 2021

SOLAR-1: A Phase III randomized, controlled trial (NCT02437318)



André F et al. ESMO 2018

Inclusion criteria: Prior exposure to AI



Se consideró tratamiento en “primera línea” en las pacientes que no habían recibido terapia endocrina para enfermedad avanzada

André F et al. ESMO 2018

Baseline characteristics

Characteristic*	*PIK3CA*-mutant		*PIK3CA*-non-mutant	
	Alpelisib + fulvestrant (N=169)†	Placebo + fulvestrant (N=172)‡	Alpelisib + fulvestrant (N=115)	Placebo + fulvestrant (N=116)
Median age, years (range)	63 (25–87)	64 (38–92)	62 (39–82)	63 (32–88)
Race				
Caucasian	117 (69.2)	109 (63.4)	82 (71.3)	69 (59.5)
Asian	34 (20.1)	40 (23.3)	25 (21.7)	26 (22.4)
Other/unknown	18 (10.7)	23 (13.4)	8 (7.0)	21 (18.1)
Metastatic sites				
Visceral disease	93 (55.0)	100 (58.1)	66 (57.4)	74 (63.8)
Lung/liver metastases	84 (49.7)	86 (50.0)	56 (48.7)	56 (48.3)
Bone-only disease	42 (24.9)	35 (20.3)	26 (22.6)	23 (19.8)
Line of advanced anti-cancer treatment				
First line	88 (52.1)	89 (51.7)	71 (61.7)	62 (53.4)
Second line	79 (46.7)	82 (47.7)	42 (36.5)	53 (45.7)
Endocrine resistance status§				
Primary resistance	23 (13.6)	22 (12.8)	31 (27.0)	26 (22.4)
Secondary resistance	120 (71.0)	127 (73.8)	66 (57.4)	65 (56.0)
Sensitive	20 (11.8)	19 (11.0)	16 (13.9)	20 (17.2)
Prior chemotherapy				
Neo-adjuvant	25 (14.8)	29 (16.9)	20 (17.4)	23 (19.8)
Adjuvant	78 (46.2)	86 (50.0)	64 (55.7)	58 (50.0)
Prior CDK4/6 inhibitor treatment	9 (5.3)	11 (6.4)	7 (6.1)	8 (6.9)

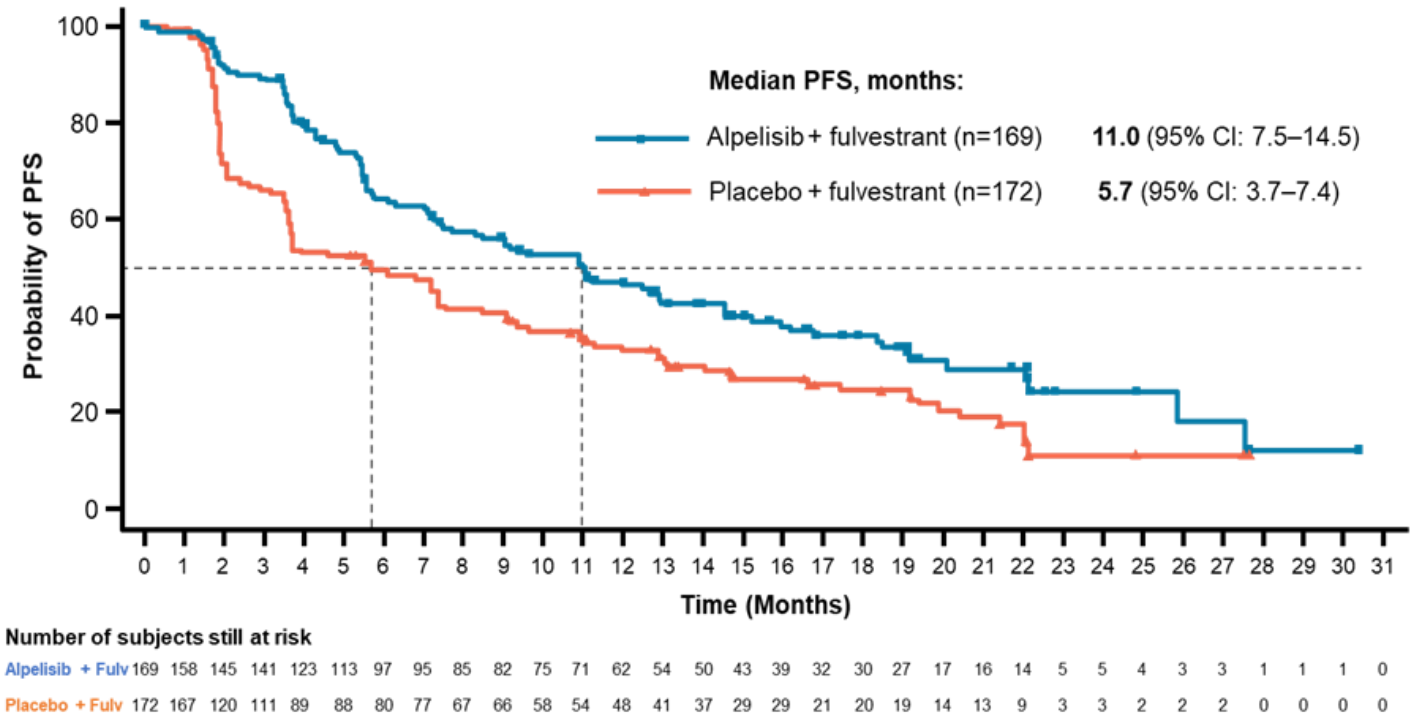
André F et al. ESMO 2018

Patient disposition

Disposition*	*PIK3CA*-mutant		*PIK3CA*-non-mutant	
	Alpelisib + fulvestrant (N=169)	Placebo + fulvestrant (N=172)†	Alpelisib + fulvestrant (N=115)	Placebo + fulvestrant (N=116)
On Treatment	42 (24.9)	32 (18.6)	13 (11.3)	14 (12.1)
Discontinued	127 (75.1)	139 (80.8)	102 (88.7)	102 (87.9)
Reasons for discontinuation (alpelisib/placebo and fulvestrant)				
Adverse Event	5 (3.0)	3 (1.7)	9 (7.8)	0
Death	3 (1.8)	4 (2.3)	1 (0.9)	0
Physician Decision	6 (3.6)	6 (3.5)	5 (4.3)	4 (3.4)
Progressive Disease	93 (55.0)	117 (68.0)	80 (69.6)	91 (78.4)
Protocol Deviation	4 (2.4)	3 (1.7)	1 (0.9)	3 (2.6)
Patient/Guardian Decision	16 (9.5)	6 (3.5)	6 (5.2)	4 (3.4)
Median follow-up (months)	20.2	19.9	7.3	7.4

André F et al. ESMO 2018

Primary endpoint:
Locally assessed PFS in the *PIK3CA*-mutant cohort

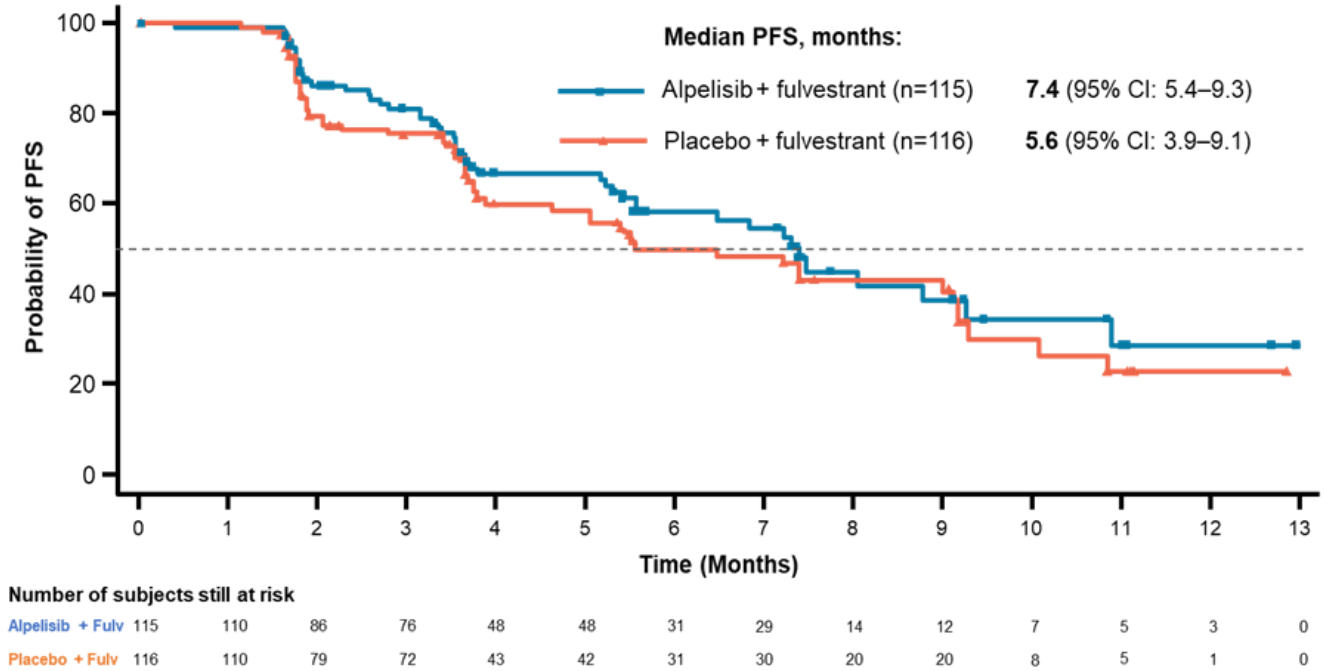


Data cut-off: Jun 12, 2018	Alpelisib + fulvestrant (N=169)	Placebo + fulvestrant (N=172)
Number of PFS events, n (%)	103 (60.9)	129 (75.0)
Progression	99 (58.6)	120 (69.8)
Death	4 (2.4)	9 (5.2)
Censored	66 (39.1)	43 (25.0)
Median PFS (95% CI)	11.0 (7.5–14.5)	5.7 (3.7–7.4)
HR (95% CI)	0.65 (0.50–0.85)	
p-value	0.00065	

André F et al. ESMO 2018

Proof of Concept: PFS in the *PIK3CA*-non-mutant cohort

Proof of concept criteria were not met in the PIK3CA-non-mutant cohort



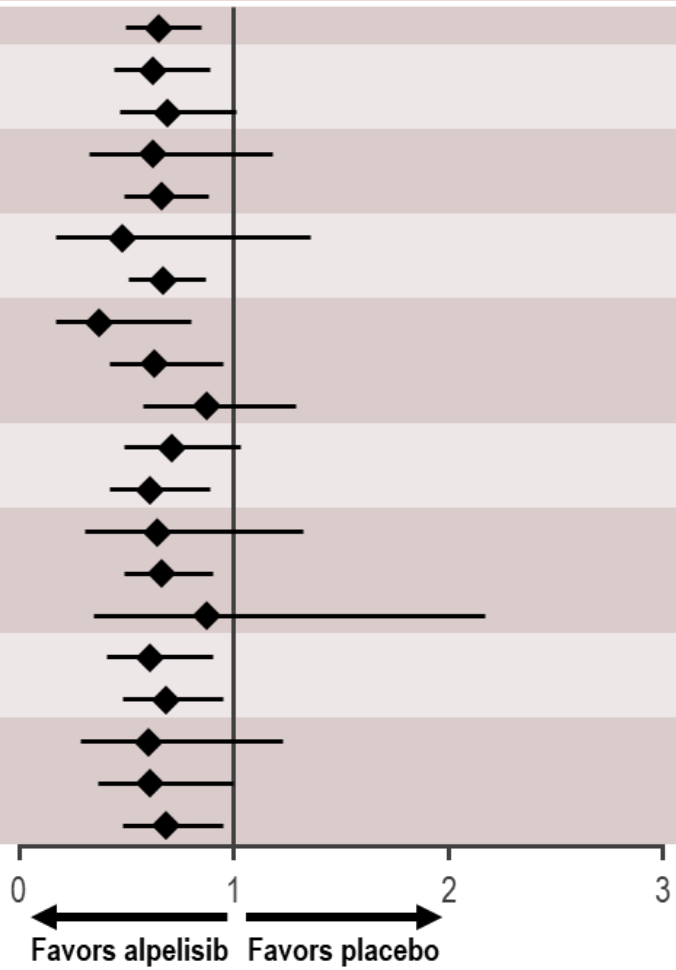
Data cut-off: Dec 23, 2016	Alpelisib + fulvestrant (N=115)	Placebo + fulvestrant (N=116)
Number of PFS events, n (%)	49 (42.6)	57 (49.1)
Progression	47 (40.9)	57 (49.1)
Death	2 (1.7)	0
Censored	66 (57.4)	59 (50.9)
Median PFS (95% CI)	7.4 (5.4–9.3)	5.6 (3.9–9.1)
HR (95% CI)	0.85 (0.58–1.25)	
Posterior probability HR<1, %	79.4	

- Proof of concept criteria: estimated hazard ratio ≤0.60 and posterior probability ≥90% that the hazard ratio was <1
- Patients with *PIK3CA*-non-mutant disease were followed up for safety alongside the *PIK3CA*-mutant cohort

André F et al. ESMO 2018

PFS by subgroup (*PIK3CA*-mutant cohort)

Subgroup		No. of patients	Hazard Ratio (95% CI)
All subjects		341	0.65 (0.50–0.85)
Lung/liver metastases	Yes	170	0.62 (0.44–0.89)
	No	171	0.69 (0.47–1.01)
Bone-only disease	Yes	77	0.62 (0.33–1.18)
	No	264	0.66 (0.49–0.88)
Prior CDK4/6 inhibitor treatment	Yes	20	0.48 (0.17–1.36)
	No	321	0.67 (0.51–0.87)
Prior chemotherapy	Neoadjuvant	46	0.37 (0.17–0.80)
	Adjuvant	161	0.63 (0.42–0.95)
	None	133	0.87 (0.58–1.29)
Line of advanced anti-cancer treatment	First line	177	0.71 (0.49–1.03)
	Second line	161	0.61 (0.42–0.89)
Endocrine status	Primary resistance	45	0.64 (0.31–1.32)
	Secondary resistance	247	0.66 (0.49–0.90)
	Sensitive	39	0.87 (0.35–2.17)
PIK3CA mutation exon	Exon 9	165	0.61 (0.41–0.90)
	Exon 20	193	0.68 (0.48–0.95)
PIK3CA mutation subtype*	*E542K*	60	0.60 (0.29–1.23)
	E545X†	105	0.61 (0.37–1.00)
	H1047X†	193	0.68 (0.48–0.95)



*Mutations detected in tissue. Patients may have had more than one *PIK3CA* mutation; †Includes multiple subtypes of *E545* and *H1047*.

André F et al. ESMO 2018

SOLAR-1: Alpelisib Demonstrated Long-term Disease Control[1]

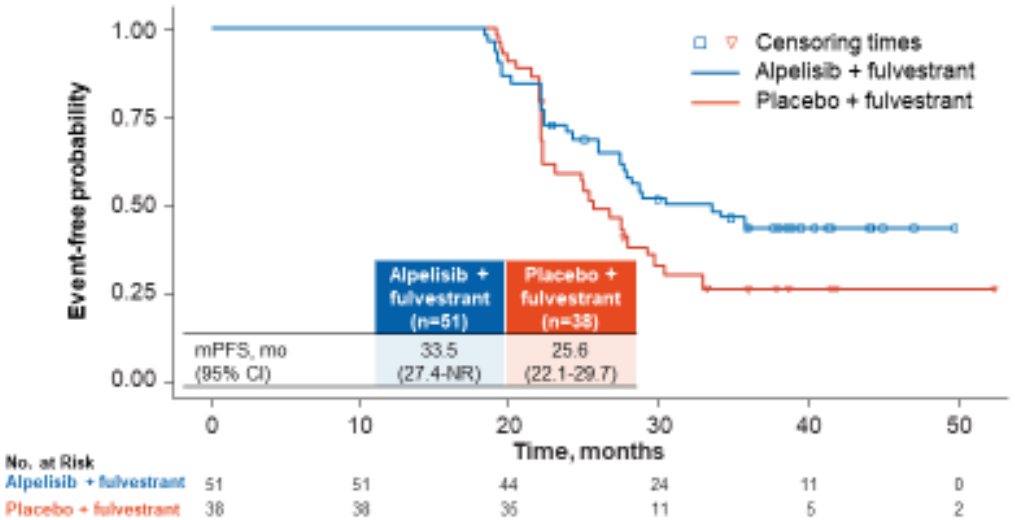
- **30.2%** of patients receiving alpelisib + fulvestrant (n=51/169) had LTDC, defined **as PFS ≥18 mo**[1,a]
  - **The majority (72.5%) of LTDC patients had PFS ≥24 mo**

Top 5 baseline predictors of LTDC based on the validated SVM model

1. Longer time from initial diagnosis to first recurrence
2. Absence of liver metastases
3. Low number of metastatic sites
4. Low ECOG PS
5. Absence of liver and/or lung metastases

- Further investigations of predictive biomarkers are necessary to better characterize this subgroup of patients achieving LTDC

PFS in Patients With Long-term Disease Control (Weighted Analysis)[1,b]



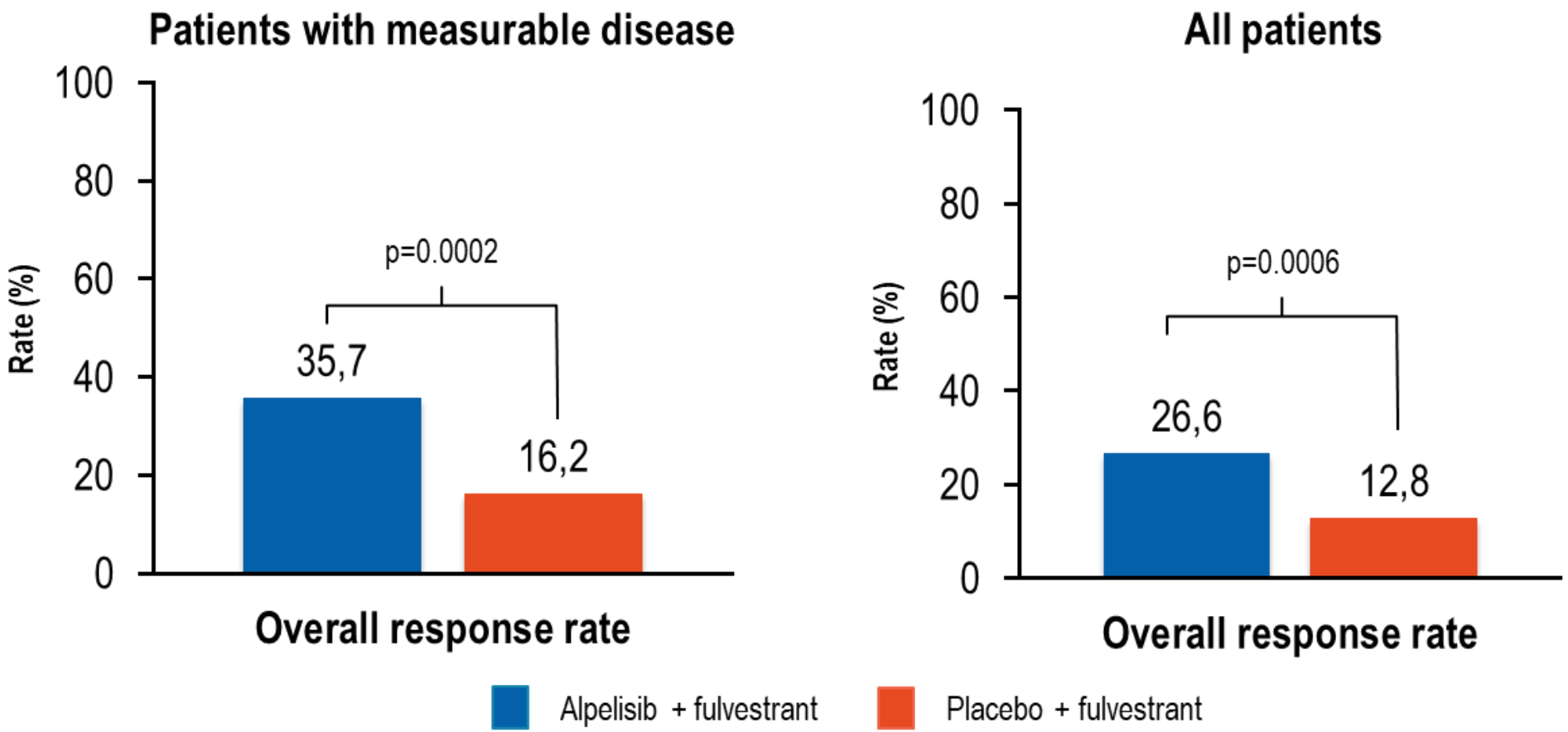
Poor prognosis, diabetes/prediabetes at baseline, and heavy pretreatment did not preclude long-term disease control

[a]mPFS from clinical trials in HR+, HER2–, endocrine-resistant ABC, regardless of presence of *PIK3CA* mutation, ranges from 4.6 to 9.3 months and 9.5 to 16.4 months with fulvestrant alone and with cyclin-dependent kinase 4/6 inhibitors (CDK4/6is), respectively[2-5]; thus, a PFS ≥18 months is clinically meaningful for this patient population with *PIK3CA*-mutated disease; [b]Post hoc exploratory analysis of patients who achieved LTDC (PFS ≥18 mo) in the alpelisib arm.

1. Juric D, et al. ASCO 2021. Abstract 1054 (poster); 2. André F, et al. *N Engl J Med*. 2019;380(20):1929-1940; 3. Cristofanilli M, et al. *Lancet Oncol*. 2016;17(4):425-439; 4. Slamon DJ, et al. ASCO 2018. Abstract 1000 (oral); 5. Sledge GW, et al. *J Clin Oncol*. 2017;35(25):2875-2884.

André F et al. ESMO 2018

Overall response rate in the *PIK3CA*-mutant cohort



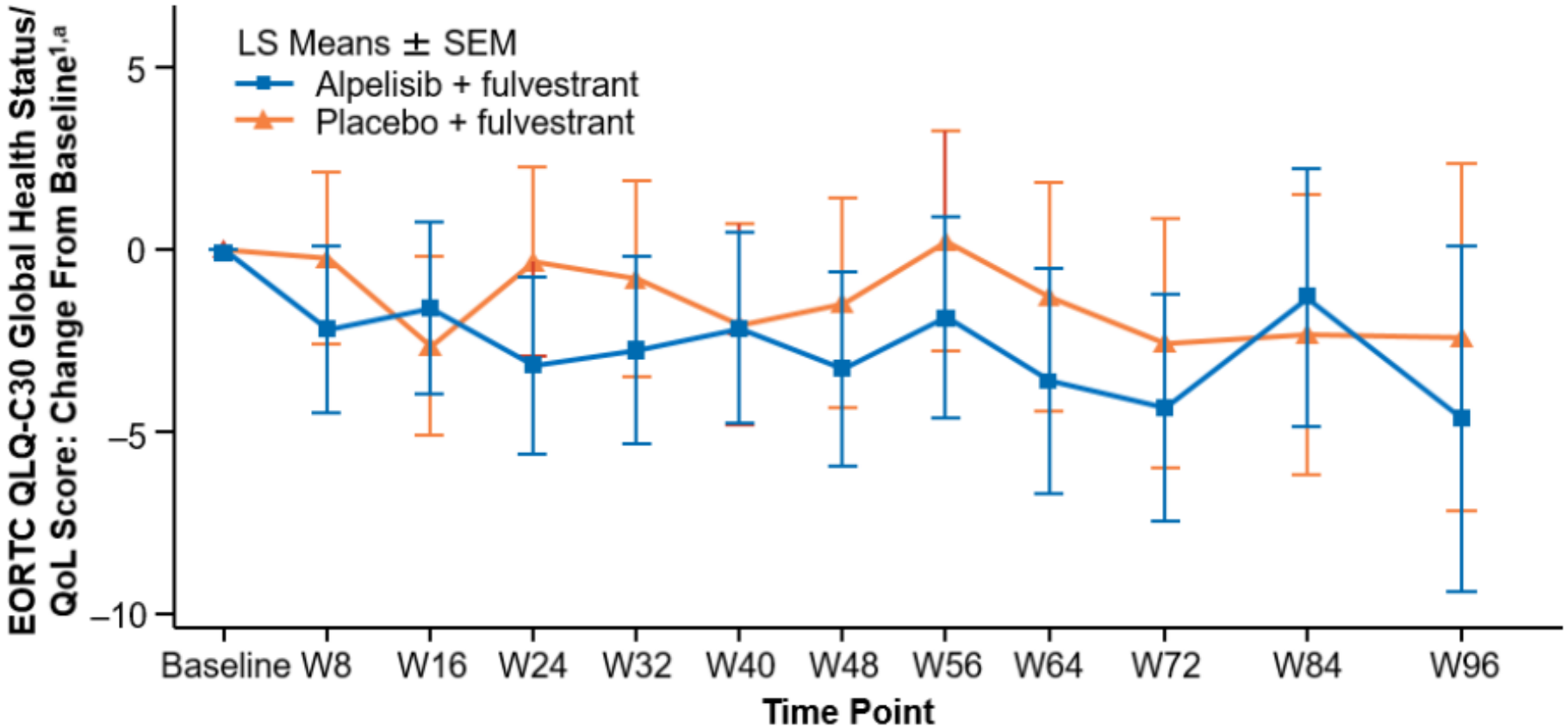
André F et al. ESMO 2018

Adverse events in the total population

AEs ≥20% in either arm, %	Alpelisib + fulvestrant N=284			Placebo + fulvestrant N=287		
	All	Grade 3	Grade 4	All	Grade 3	Grade 4
Any adverse event	282 (99.3)	183 (64.4)	33 (11.6)	264 (92.0)	87 (30.3)	15 (5.2)
Hyperglycemia	181 (63.7)	93 (32.7)	11 (3.9)	28 (9.8)	1 (0.3)	1 (0.3)
Diarrhea	164 (57.7)	19 (6.7)	0	45 (15.7)	1 (0.3)	0
Nausea	127 (44.7)	7 (2.5)	0	64 (22.3)	1 (0.3)	0
Decreased appetite	101 (35.6)	2 (0.7)	0	30 (10.5)	1 (0.3)	0
Rash*	101 (35.6)	28 (9.9)	0	17 (5.9)	1 (0.3)	0
Vomiting	77 (27.1)	2 (0.7)	0	28 (9.8)	1 (0.3)	0
Decreased weight	76 (26.8)	11 (3.9)	0	6 (2.1)	0	0
Stomatitis	70 (24.6)	7 (2.5)	0	18 (6.3)	0	0
Fatigue	69 (24.3)	10 (3.5)	0	49 (17.1)	3 (1.0)	0
Asthenia	58 (20.4)	5 (1.8)	0	37 (12.9)	0	0

- Eighteen patients (6.3%) discontinued alpelisib due to hyperglycemia and 9 patients (3.2%) due to rash; no patients discontinued placebo due to either hyperglycemia or rash
- Maculopapular rash was observed in 14.1% of patients (all-grade) and 8.8% (grade 3) in the alpelisib arm, vs 1.7% and 0.3%, respectively, in the placebo arm
- The safety profile of the alpelisib group and the placebo group was similar in *PIK3CA*-mutant and *PIK3CA*-non-mutant cohorts

André F et al. ESMO 2018

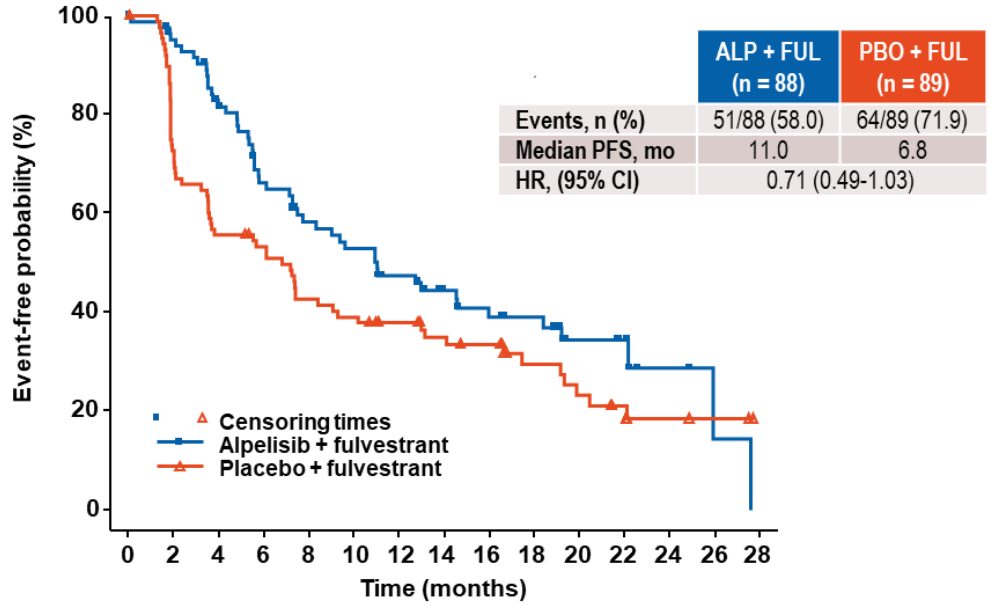


Mayer et al. ASCO 2019

PFS by Line of Therapy in the *PIK3CA*-mutant Cohort[a]

First-line (n = 177)

Defined as patients whose disease progressed ≤ 1 year after (neo)adjuvant ET (endocrine resistant) **or** whose disease progressed > 1 year after (neo)adjuvant ET (endocrine sensitive) (later excluded after protocol amendment)

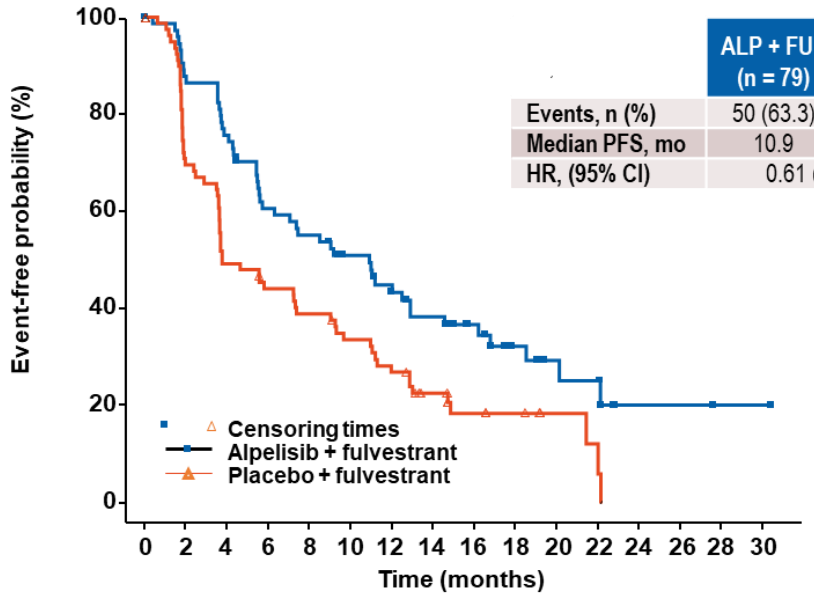


	ALP + FUL (n = 88)	PBO + FUL (n = 89)
Events, n (%)	51/88 (58.0)	64/89 (71.9)
Median PFS, mo	11.0	6.8
HR, (95% CI)	0.71 (0.49-1.03)	

	Endocrine sensitive patients		Endocrine resistant patients	
	ALP + FUL (n = 20)	PBO + FUL (n = 19)	ALP + FUL (n = 68)	PBO + FUL (n = 70)
Events, n (%)	11 (55.0)	9 (47.4)	40 (58.8)	55 (78.6)
Median PFS, mo	22.1	19.1	9.0	4.7
HR, (95% CI)	0.87 (0.35-2.17)		0.69 (0.46-1.05)	

Second-line (n = 161)

Defined as patients whose disease progressed > 1 year after (neo)adjuvant ET and while on or after 1 line of ET for ABC **or** patients with newly diagnosed ABC whose disease progressed while on or after 1 line of ET

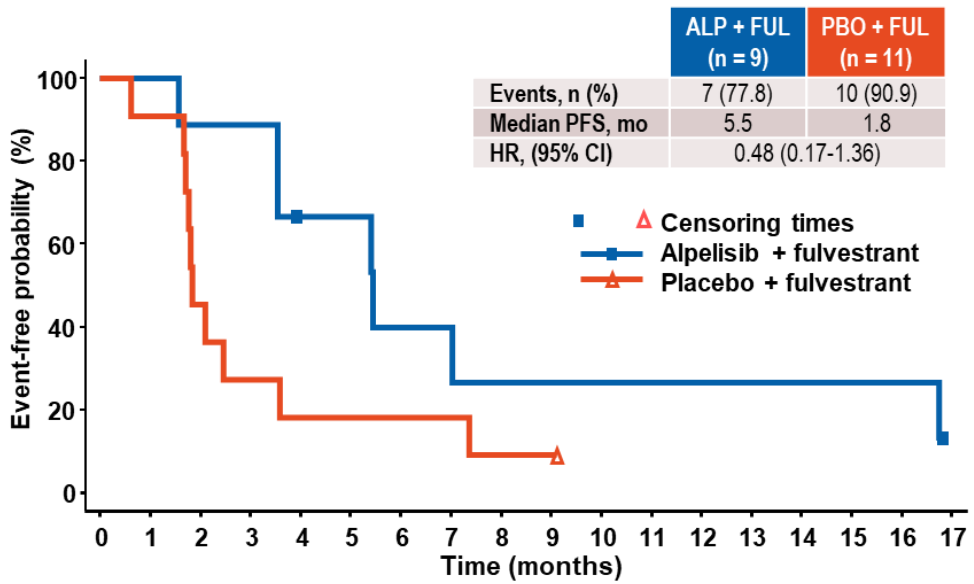


	ALP + FUL (n = 79)	PBO + FUL (n = 82)
Events, n (%)	50 (63.3)	65 (79.3)
Median PFS, mo	10.9	3.7
HR, (95% CI)	0.61 (0.42-0.89)	

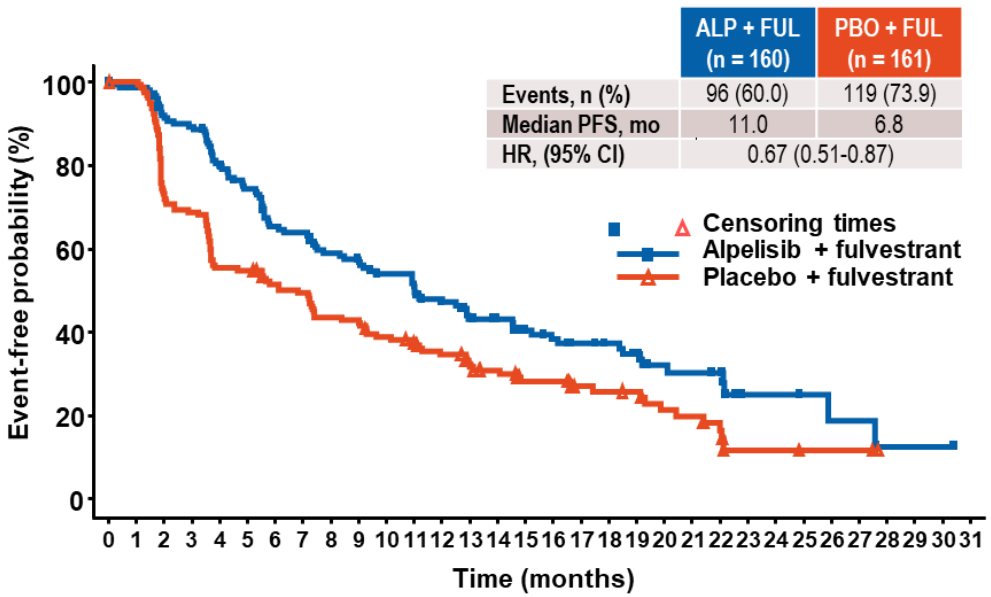
Juric D et al. SABCS 2018

PFS by Prior CDK4/6 Inhibitor Treatment in the *PIK3CA*-mutant Cohort[a]

With Prior CDK4/6 inhibitor therapy



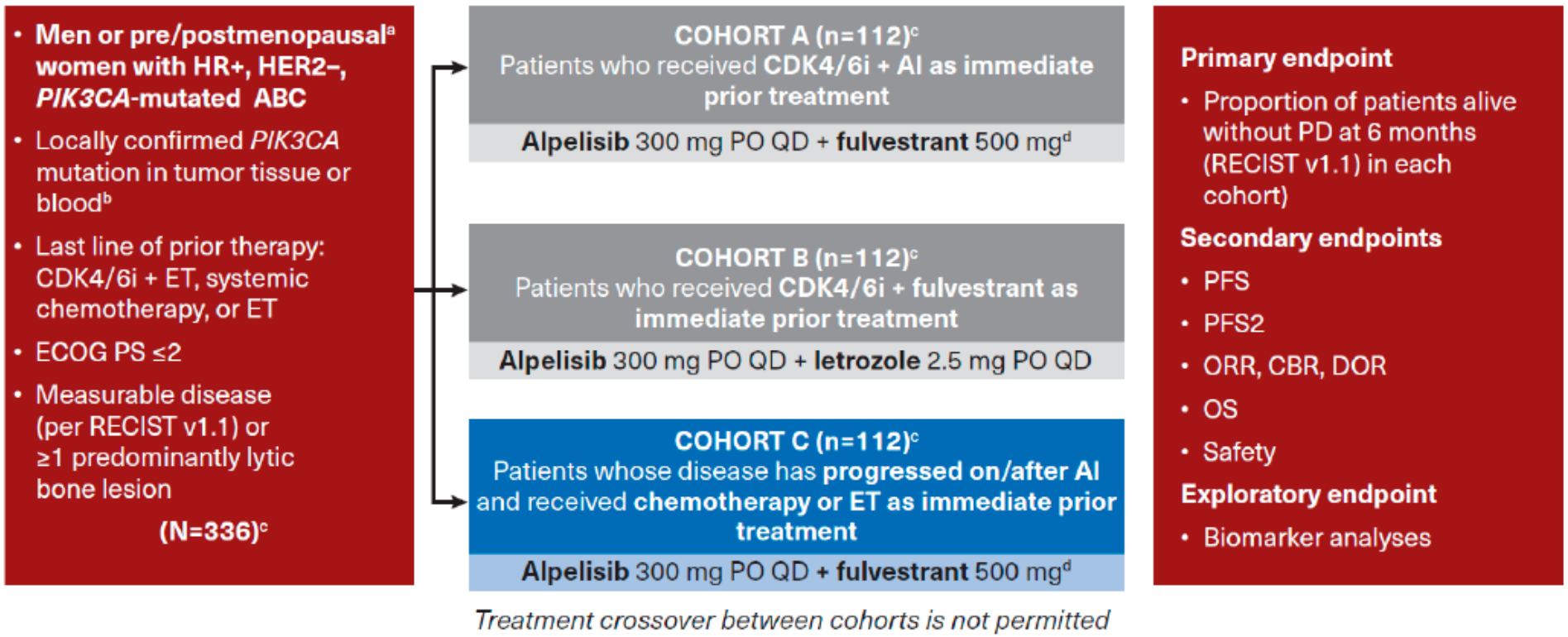
Without Prior CDK4/6 inhibitor therapy



- Previous treatment with any CDK4/6 inhibitor was a stratification factor, however the number of patients enrolled who had received prior CDK4/6 inhibitor therapy was small
- Treatment benefit with alpelisib was observed regardless of prior use with a CDK4/6 inhibitor

Juric D et al. SABCS 2018

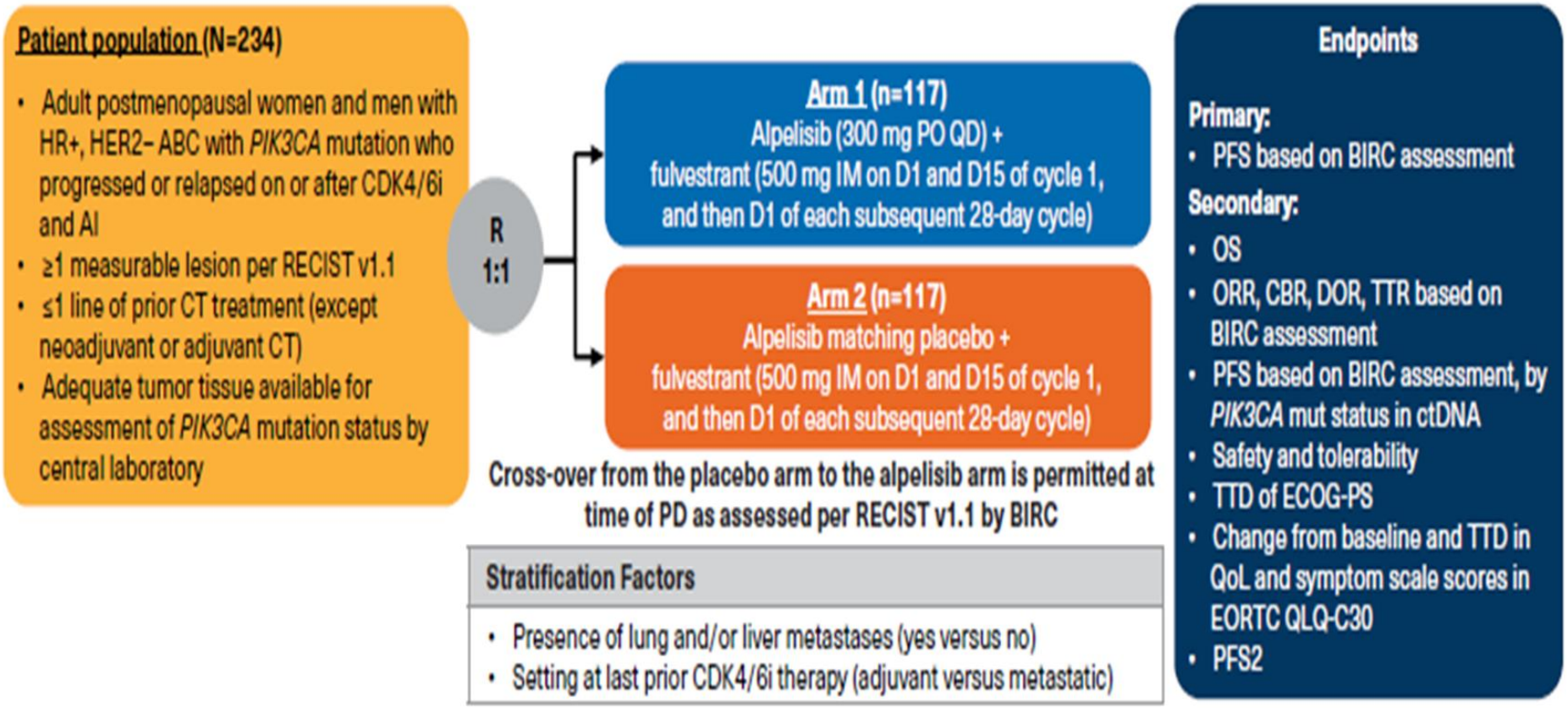
BYLieve (NCT03056755) Study Design



Treatment crossover between cohorts is not permitted

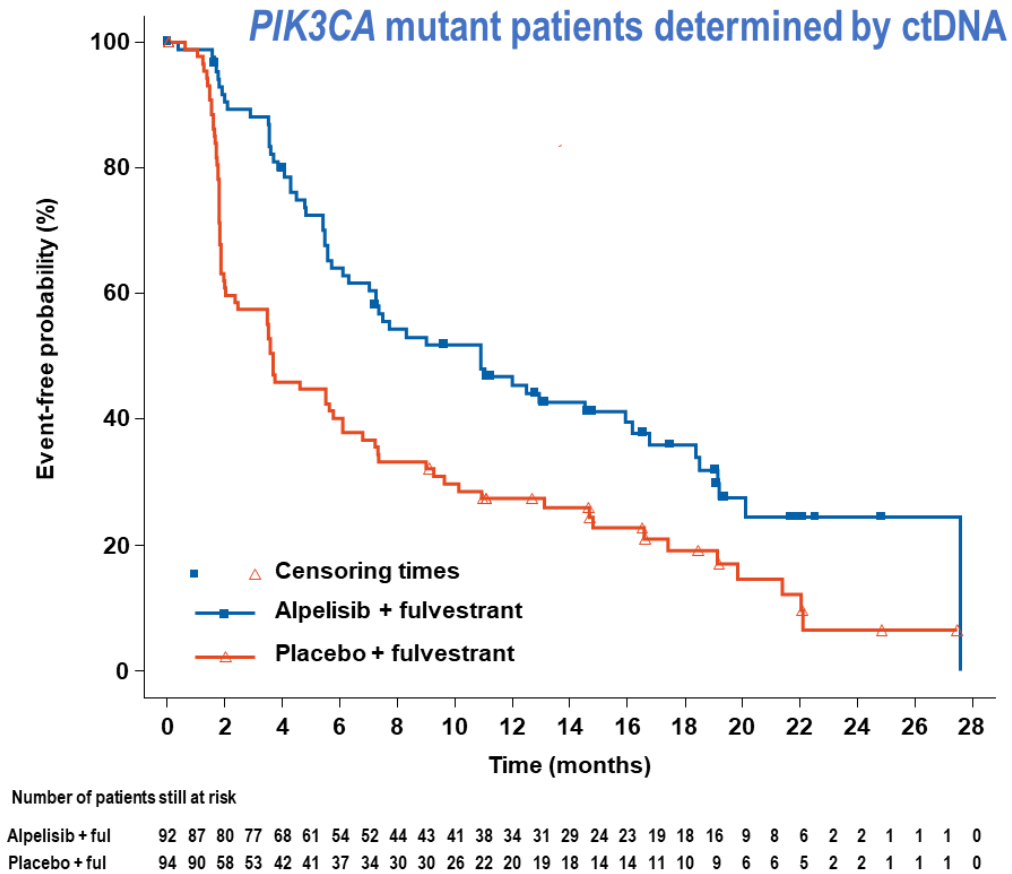
Rugo H et al. Lancet Oncol 2021

EPIK B5 Study Design



De Laurentiis et al. ASCO 2022

Locally Assessed PFS by Tissue or Plasma ctDNA-determined Mutation Status



	ALP + FUL		PBO + FUL		
	Event n/N (%)	Median PFS	Event n/N (%)	Median PFS	HR
Patients with *PIK3CA* mutation: tissue	103/169 (60.9)	11.0	129/172 (75.0)	5.7	0.65
Patients with *PIK3CA* mutation: plasma	57/92 (62.0)	10.9	75/94 (79.8)	3.7	0.55
Patients without *PIK3CA* mutation: tissue	49/115 (42.6)	7.4	57/116 (49.1)	5.6	0.85
Patients without *PIK3CA* mutation: plasma	92/181 (50.8)	8.8	103/182 (56.6)	7.3	0.80

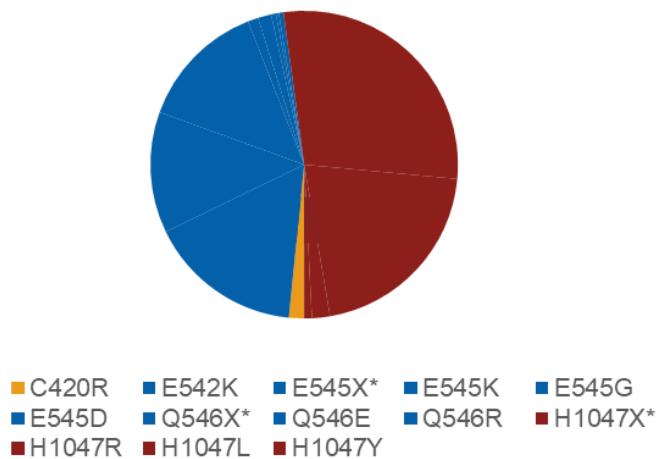
Juric D et al. SABCS 2018

Most frequent mutations found in the helical domain (exon 9) and kinase domain (exon 20) by PCR in SOLAR-1

Exon	Mutation	Base Change	SOLAR-1 tissue mutant cohort‡ N=370 (%)
7	C420R	1258 T>C	6 (1.6)
9	**E542K**	**1624 G>A**	**60 (16.2)**
	E545X* (A/D/G/K)		**47 (12.7)**
	E545K	**1634 A>C**	**50 (13.5)**
	E545G	1634 G>A	4 (1.1)
	E545D	1634 A>G	5 (1.4)
	Q546X* (E/K/R)		2 (0.5)
	Q546E	1637 A>G	1 (0.3)
	Q546R	1636 C>G	2 (0.5)
20	**H1047X*** (L/R/Y)		**106 (28.6)**
	H1047R	**3140 A>T**	**77 (20.8)**
	H1047L	3140 A>G	7 (1.9)
	H1047Y	3139 C>T	3 (0.8)

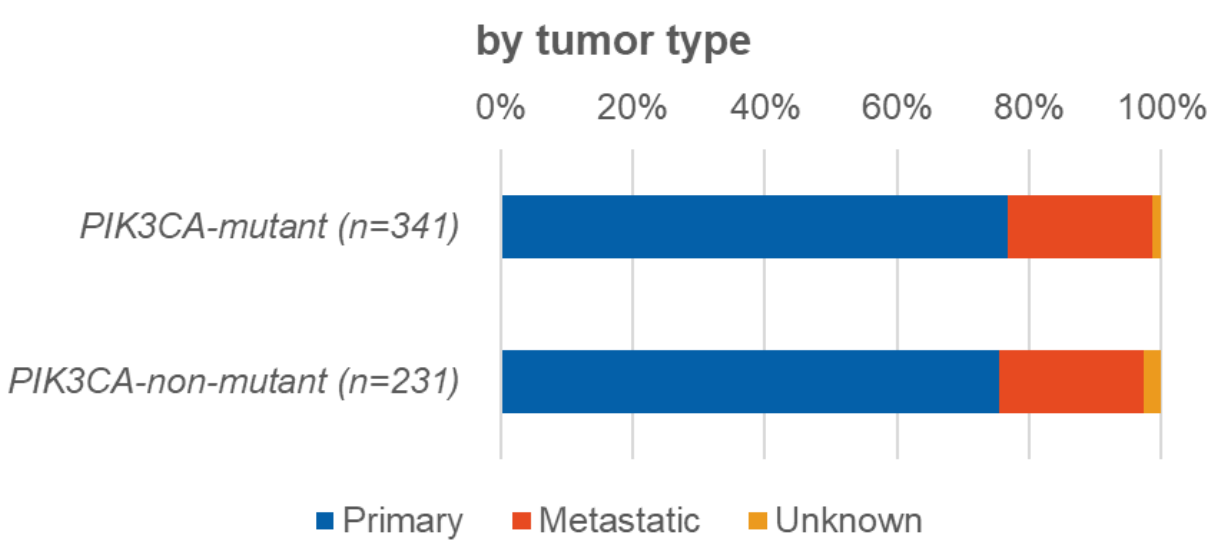
- Of the 341 patients whose tumors were *PIK3CA*-mutant per PCR at screening, 28 (8%) had multiple mutations.
  - 370 mutations detected in the 341 patients

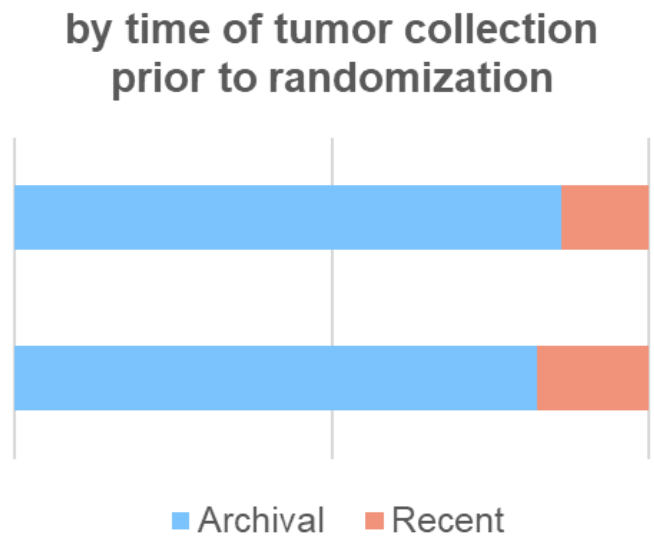
Variant frequency in *PIK3CA* mutations in SOLAR-1 tissue mutant cohort (n=370)*



Rugo H et al. AACR 2019

Majority of tissue samples used for *PIK3CA* screening at enrollment in SOLAR-1 were from primary tumors (vs. metastatic sites)



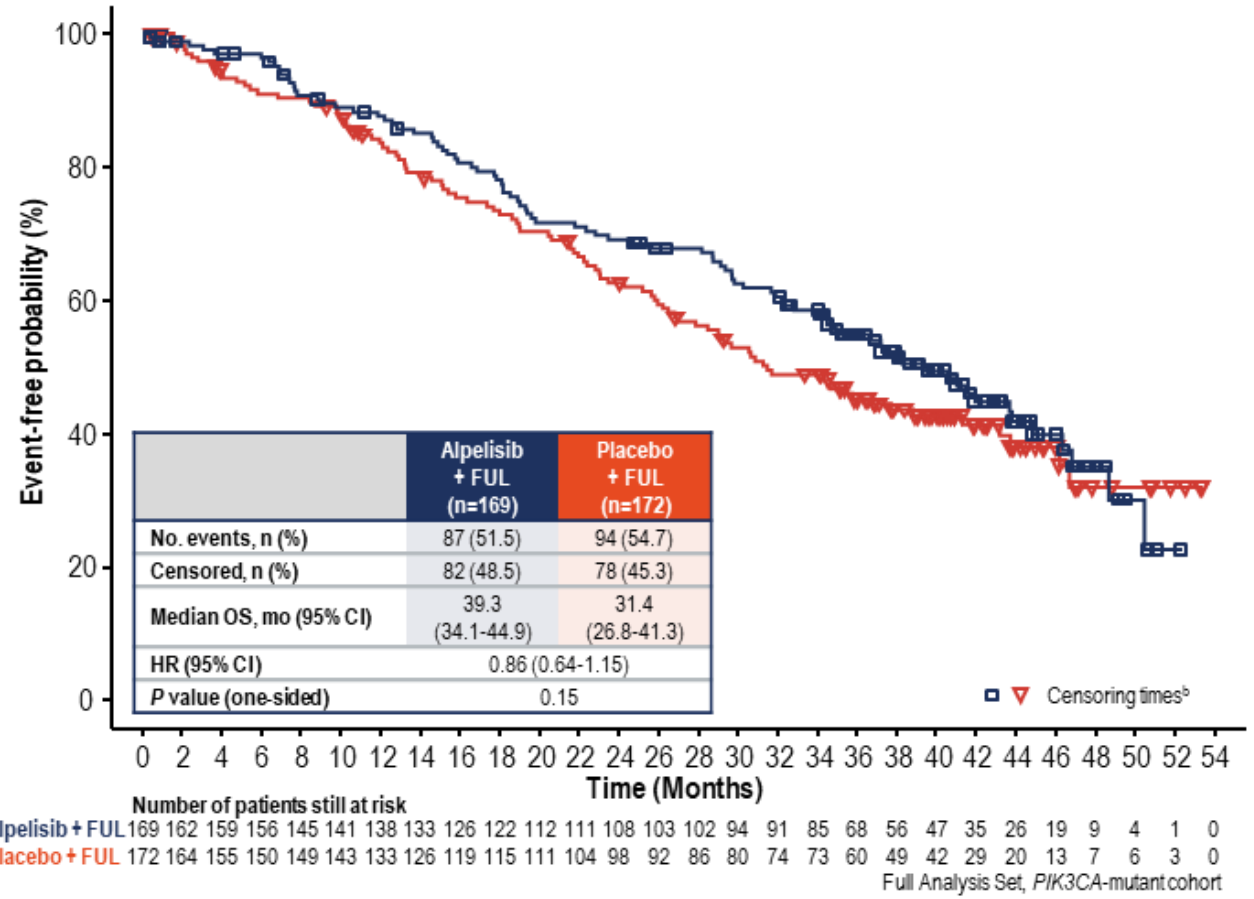


Freshly collected (≤3 months prior to randomization) vs archival (>3 months prior to randomization)

Rugo H et al. AACR 2019

SOLAR-1: OS in Patients in *PIK3CA*-mutant Cohort[a]

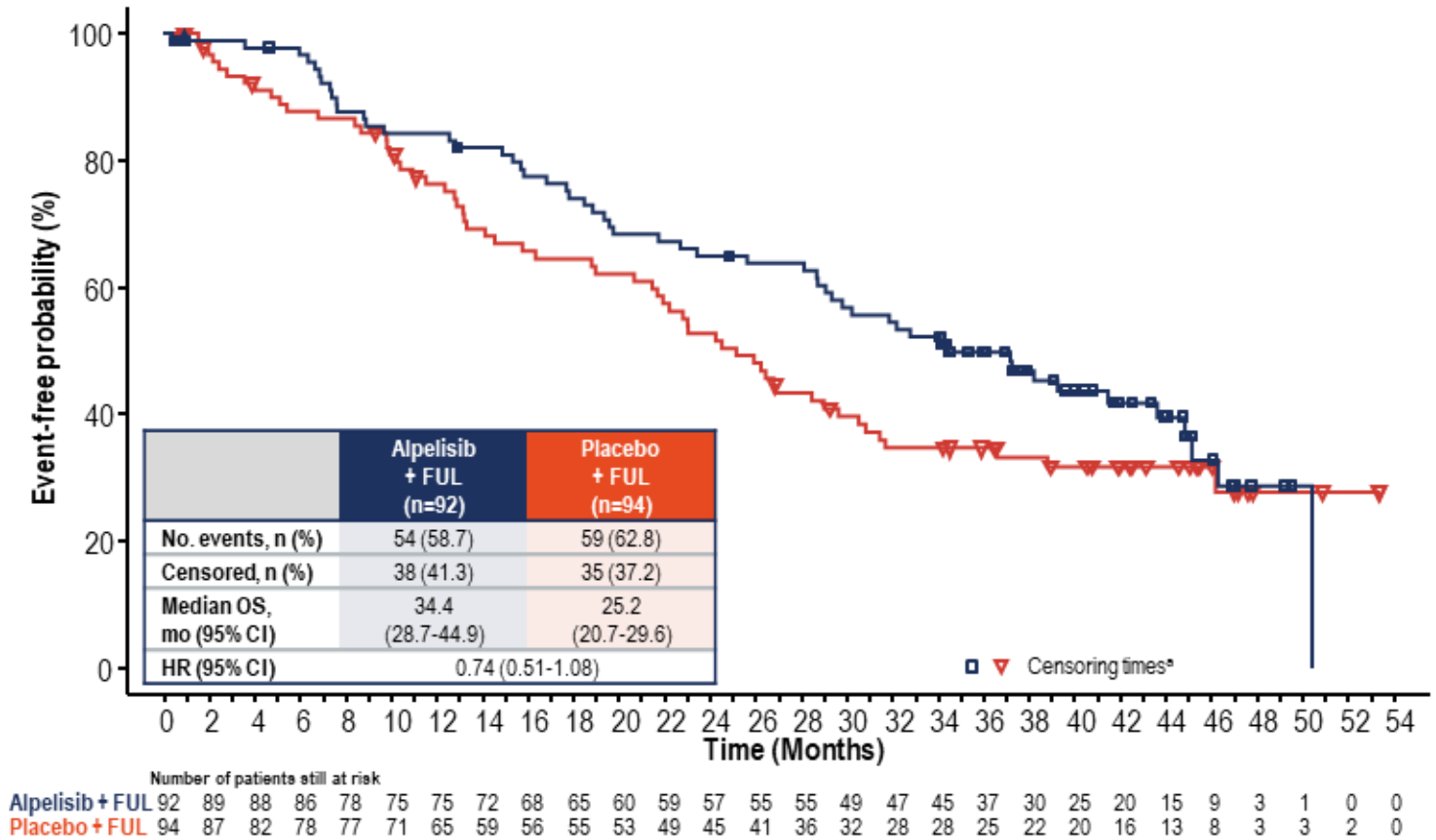
- mOS was prolonged by 7.9 mo for patients in the alpelisib + fulvestrant arm
- Final OS analysis in the *PIK3CA*-mutant cohort did not cross the prespecified O'Brien-Fleming efficacy boundary (1-sided $P \leq 0.0161$)



	Alpelisib + FUL (n=169)	Placebo + FUL (n=172)
No. events, n (%)	87 (51.5)	94 (54.7)
Censored, n (%)	82 (48.5)	78 (45.3)
Median OS, mo (95% CI)	39.3 (34.1-44.9)	31.4 (26.8-41.3)
HR (95% CI)	0.86 (0.64-1.15)	
P value (one-sided)	0.15	

André F et al. ASCO 2020

SOLAR-1: OS in Patients With *PIK3CA* Mutation in Plasma ctDNA



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SOLAR-1: First New Antineoplastic Medication After Discontinuation of Study Treatment

	Alpelisib + FUL (n=169)	Placebo + FUL (n=172)
Patients who discontinued study treatment, n	148	164
Any medication type, n (%)[a]	116 (78.4)	134 (81.7)
Chemotherapy	38 (25.7)	49 (29.9)
Chemotherapy + other[b]	20 (13.5)	26 (15.9)
Hormonal therapy alone	20 (13.5)	21 (12.8)
Hormonal therapy + targeted therapy/other[c]	37 (25.0)	35 (21.3)
Targeted therapy alone	1 (0.7)	2 (1.2)
Other	0	1 (0.6)

Full Analysis Set, *PIK3CA*-mutant cohort

- A CDK4/6 inhibitor was first new antineoplastic medication after discontinuation of study treatment in 17 (11.5%) patients in the alpelisib + fulvestrant arm and 22 (13.4%) patients in the placebo + fulvestrant arm

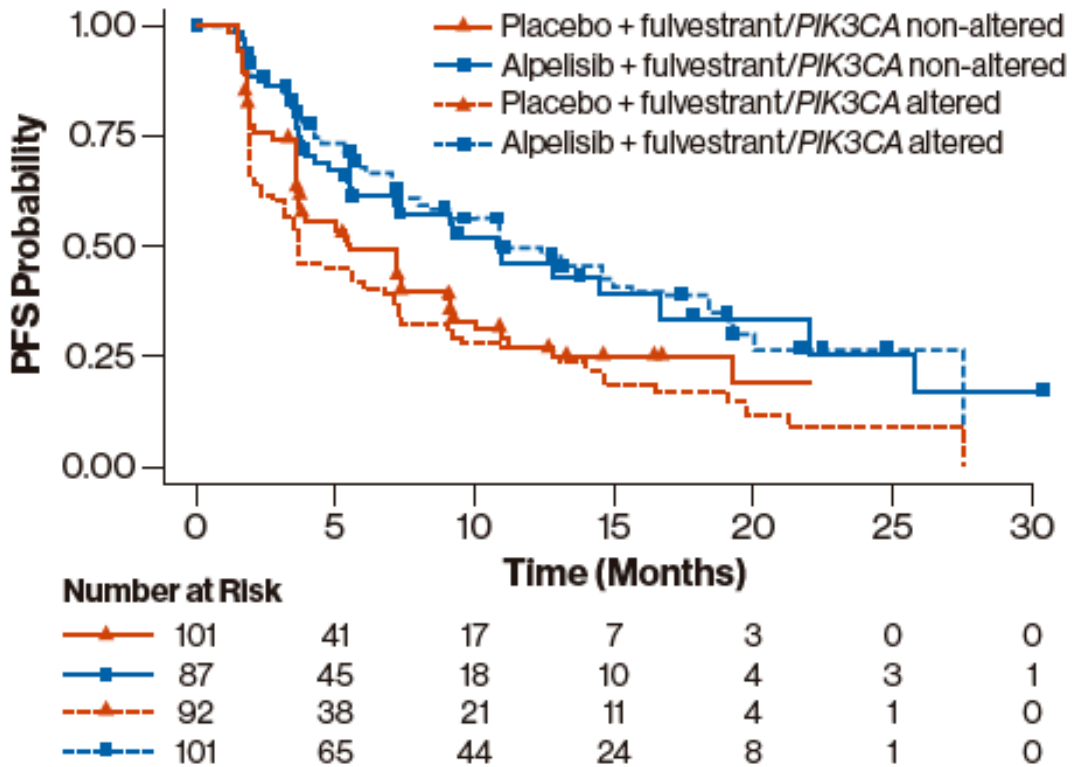
André F et al. ASCO 2020

	Patients With a *PIK3CA* Alteration per NGS (n=193)
Number of alterations, n (%)	
Single alteration	147 (76)
Multiple alterations	46 (24)
Detectable by PCR, n (%)	
Yes	168 (87)
No	25 (13)
Exon 7 alteration, n (%)[a]	11 (6)
Exon 9 alteration, n (%)	70 (36)
Exon 20 alteration, n (%)	102 (53)

[a]No further analysis was performed on patients with alterations in exon 7 due to the low number.
ctDNA, circulating tumor DNA; NGS, next-generation sequencing; PCR, polymerase chain reaction; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha.

Ciruelos E et al. SABCS 2020

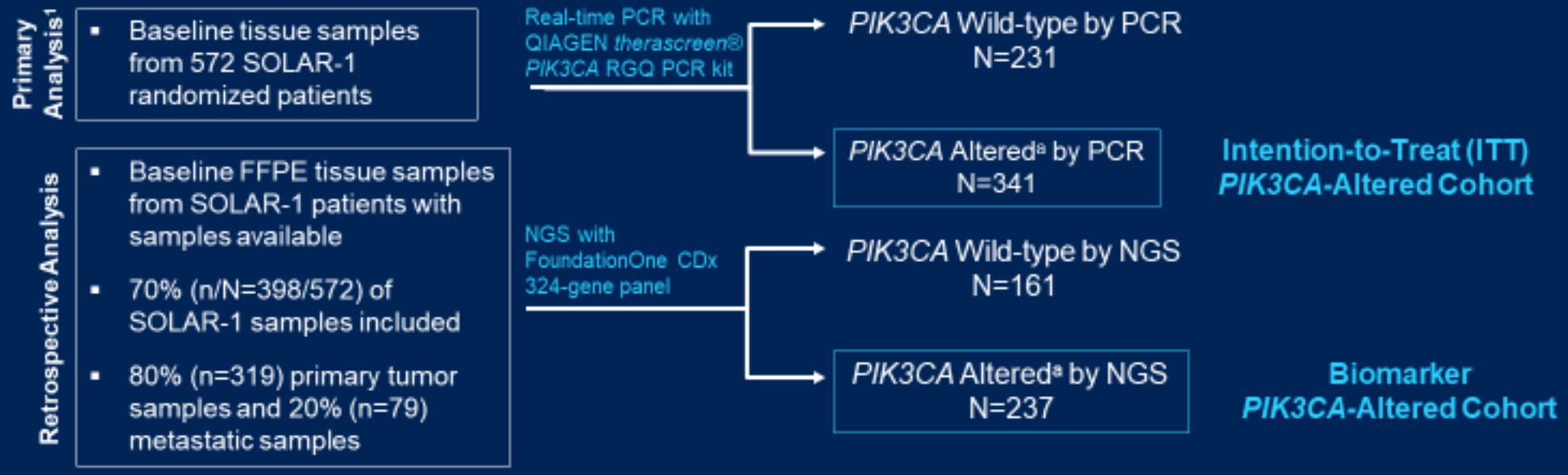
Figure 2. Kaplan–Meier mPFS in Patients by *PIK3CA* Alteration Status[a] in Plasma ctDNA as Detected by NGS



Group[a]	Events	N	mPFS (95% CI)	HR (95% CI)
Placebo + fulvestrant/ *PIK3CA* non-altered	60	101	5.5 (3.8-9.0)	0.60 (0.40-0.91)
Alpelisib + fulvestrant/ *PIK3CA* non-altered	40	87	10.9 (5.6-16.8)	
Placebo + fulvestrant/ *PIK3CA* altered	73	92	3.7 (2.9-6.8)	0.47 (0.33-0.67)
Alpelisib + fulvestrant/ *PIK3CA* altered	58	101	11.0 (7.7-16.2)	

Ciruelos E et al. SABCS 2020

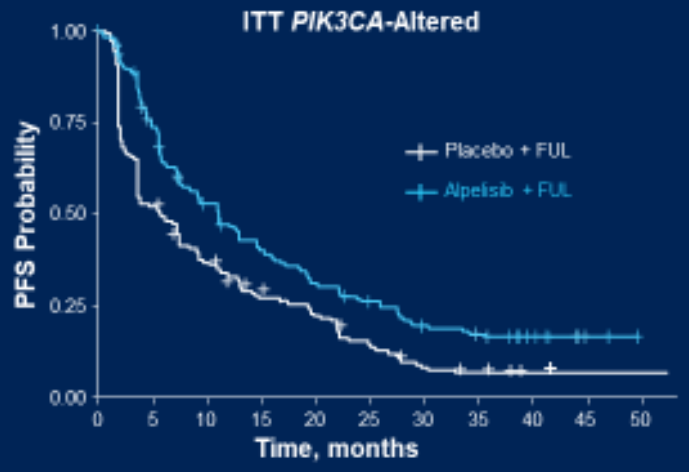
Planned Exploratory Biomarker Analysis With SOLAR-1 Baseline Tumor Samples

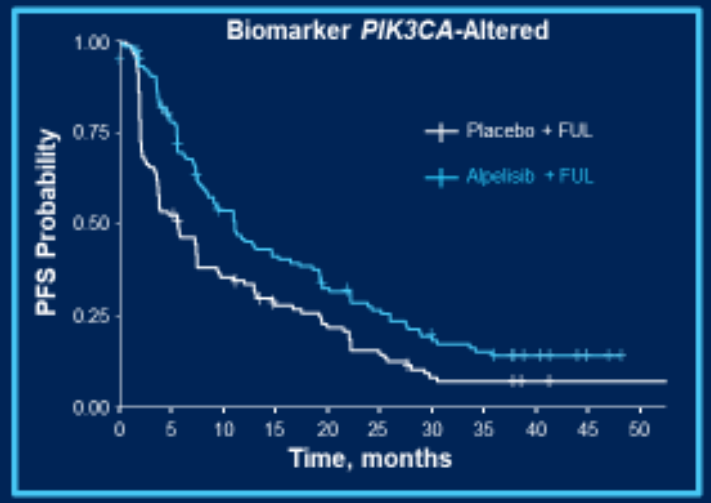


- Clinical benefit was assessed using progression-free survival (PFS) and hazard ratio (HR)
- HR (95% CI) was estimated using a multivariate Cox PH model by adjusting multiple clinical covariates including age, ECOG PS, bone lesion, lung/liver metastases, and prior CDK4/6 inhibitor treatment
- No multiple testing adjustments were made in this subgroup analysis

Juric D et al. ASCO 2022

Efficacy of Alpelisib + FUL in Patients With Altered *PIK3CA* Is Consistent in SOLAR-1 ITT and Biomarker Cohorts





- Biomarker *PIK3CA*-altered cohort includes 70% of the ITT *PIK3CA*-cohort
- *PIK3CA* alterations were detected by PCR in the ITT cohort and NGS in the Biomarker cohort

	Placebo + FUL		Alpelisib + FUL		
Cohort	n/N	mPFS, mo (95% CI)	n/N	mPFS, mo (95% CI)	HR (95% CI)
ITT *PIK3CA*-Altered	149/172	**5.7** (3.7-7.4)	124/169	**11.0** (7.5-14.5)	0.59 (0.43-0.81)
Biomarker *PIK3CA*-Altered	101/117	**5.6** (3.6-7.4)	90/120	**11.0** (8.3-15.2)	0.56 (0.42-0.76)

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Clinical Benefit Across TMB Quartiles of Patients Treated With Alpelisib + FUL

Quartile	Placebo + FUL[a]		Alpelisib + FUL[a]		HR by Quartile	HR (95% CI)
	n/N	mPFS, mo (95% CI)	n/N	mPFS, mo (95% CI)		
Quartile 1 0-<2.52 mut/mb	26/30	3.2 (1.8-7.4)	24/32	18.5 (7.7-22.1)		0.38 (0.21-0.68)
Quartile 2 2.52-<3.78 mut/mb	14/17	12.8 (3.7-22.1)	13/18	12.0 (4.5-33.5)		0.81 (0.38-1.77)
Quartile 3 3.78-<5.04 mut/mb	14/15	3.6 (1.8-7.4)	14/16	10.9 (3.8-11.2)		0.68 (0.32-1.47)
Quartile 4 ≥5.04 mut/mb	31/37	5.1 (1.9-7.4)	27/35	7.4 (5.5-17.3)		0.68 (0.40-1.17)

- Clinical benefit was consistent in patients treated with alpelisib with high TMB (Quartile 4) and more pronounced in patients with a low TMB (Quartile 1) who were treated with alpelisib

[a]TMB data available for 200 of 237 patients with *PIK3CA*-altered tumors tested by FoundationOne® CDx. Data should be interpreted with caution because of the small sample size.
FUL, fulvestrant; HR, hazard ratio; mb, megabase; mPFS, median progression-free survival; mut, mutations; n, number of events; N, number of patients; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; TMB, tumor mutational burden.

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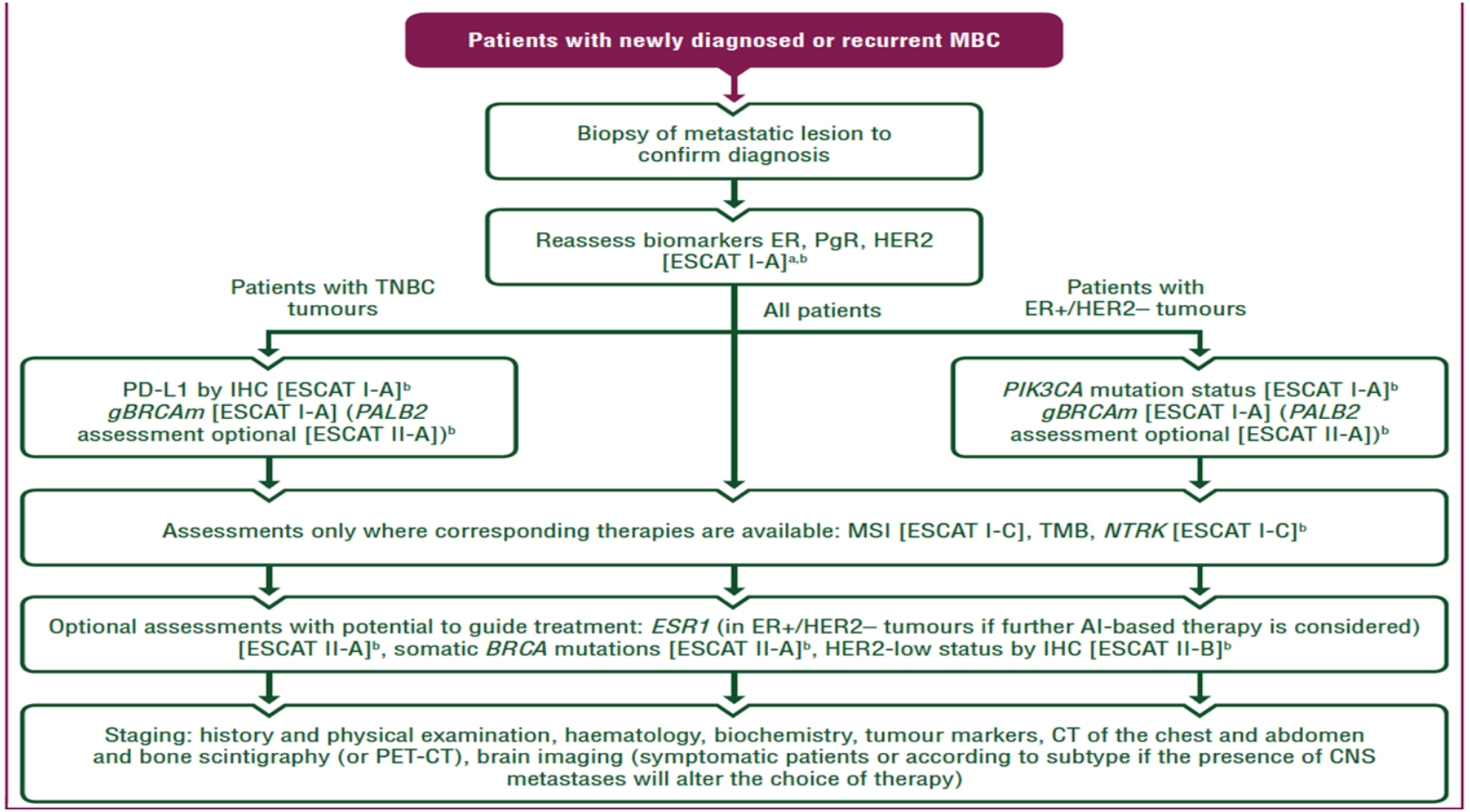

Mateo J et al. Annals of Oncology 2018

¿Donde hacer solicitudes de diagnóstico de mutaciones PIK3CA para pacientes con CMM HR+ HER2-?

Registrándose en la web:

www.diagnosticopi3k.es

Conclusiones

- En pacientes con CMM HR+/HER2- con mutación en *PIK3CA* la combinación de alpelisib + fulvestrant ha demostrado actividad clínica y estadísticamente significativa.
- El beneficio clínico parece consistente en el análisis de subgrupos.
  - En marcha fase III para testar formalmente la eficacia a la progresión al estándar en 1ª línea de CDK4/6i + ET.
- La hiperglicemia y el rash son los efectos secundarios de clase más destacables.
- La determinación de mutaciones en *PIK3CA* puede hacerse en tejido y sangre.

Muchas gracias