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BASES BIOLÓGICAS DEL CÁNCER
E INNOVACIÓN TERAPÉUTICA



MIÉRCOLES 17 DE MAYO 2023

Opciones de tratamiento tras progresión (*inmediata*) a iCDK4/6:

Lo que hay y lo que hay por llegar

Meritxell Bellet , MD PhD

Hospital de la Vall d'Hebron de Barcelona y Vall d'Hebron Institute of Oncology (VHIO)



Empecemos por una pregunta...

- ¿Qué cree menos importante en la valoración de tratamiento para un/una paciente cuya enfermedad progresa a iCDK4/6?
 - Determinación de mutaciones en PIK3CA
 - Determinación de mutaciones germinales en BRCA si hay sospecha razonable
 - Valoración de la PFS durante el tto con iCDK4/6, de la agresividad de la enfermedad actual y de las preferencias del/de la paciente
 - Valoración de todas las alteraciones en las alteraciones en la vía AKT (PIK3CA, PTEN y AKT)
 - Valoración del estado mutacional de *ESR1* en plasma en el momento de la progresión
 - No creo que haya una menos importante

Opciones de tratamiento tras progresión a iCDK4/6:
Lo que hay y lo que hay por llegar ...

mmm... difícil de diferenciar...



<https://twitter.com/PTarantinoMD/status/1628036984957464578?t=UWPtEn616miDTsvtyeulqQ&s=08>

NEW!

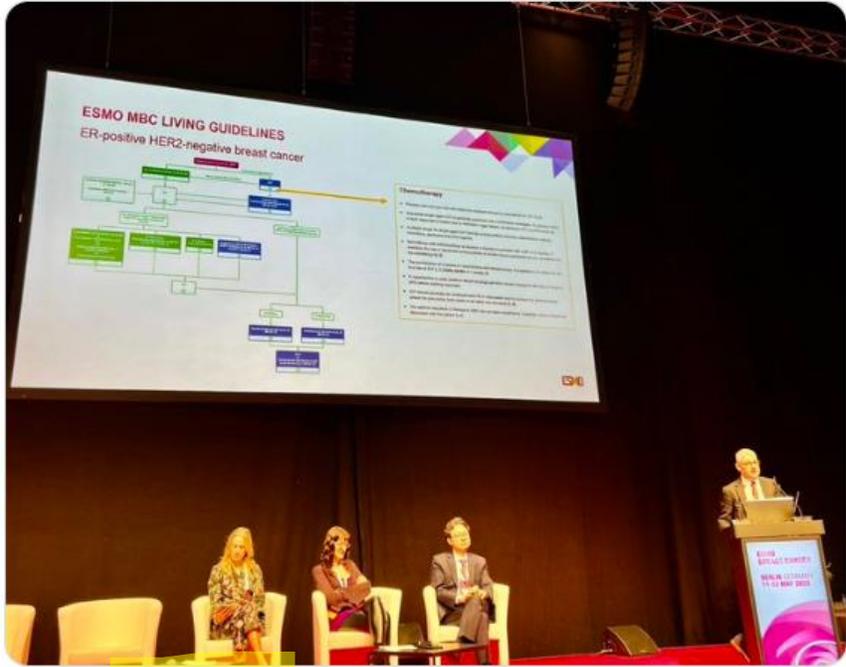
ESMO LIVING GUIDELINES
Metastatic Breast Cancer v1.1 MAY 2023

ESMO - Eur. Oncology retweeted

 **Paolo Tarantino**
@PTarantinoMD

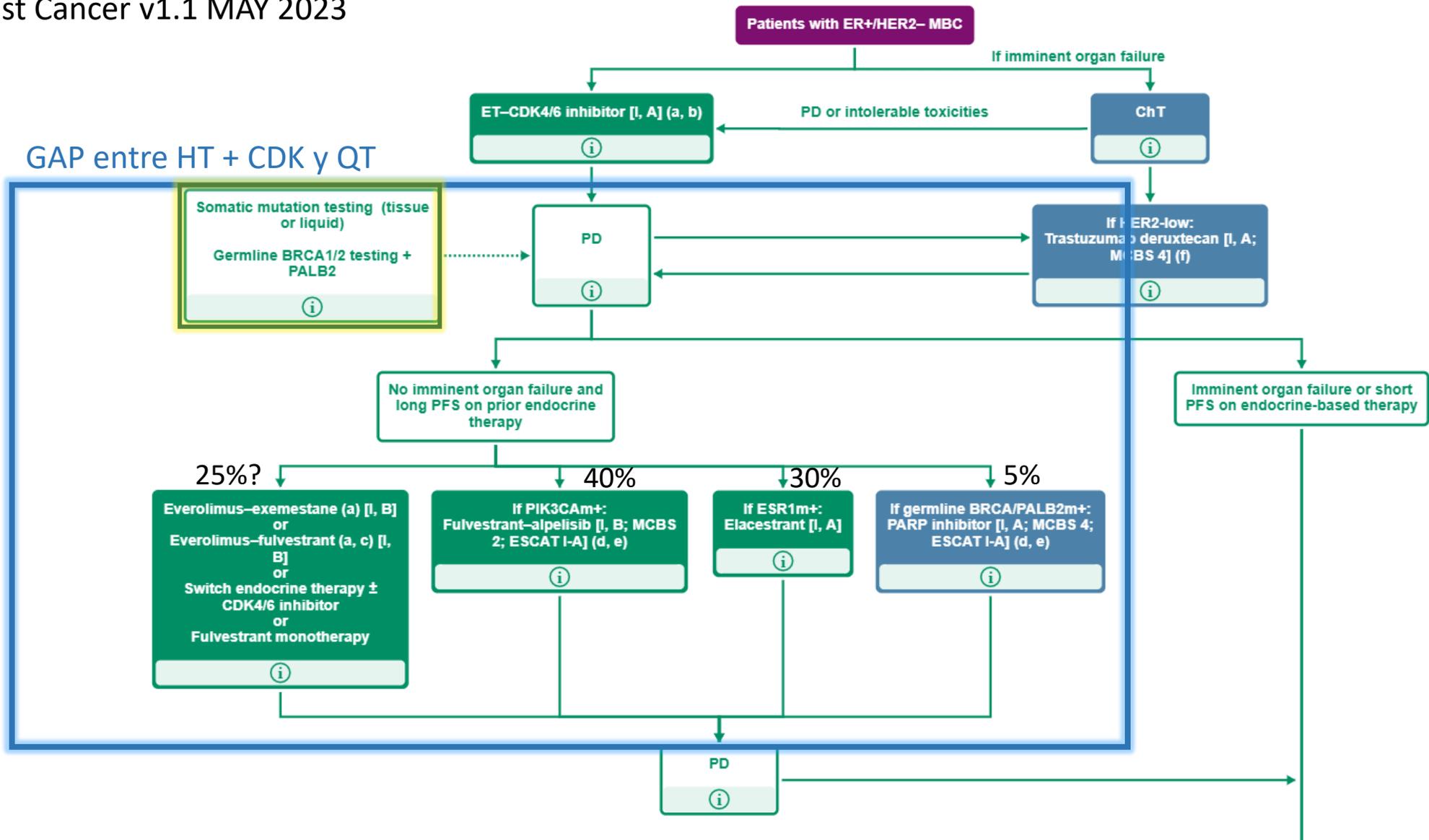
ESMO Guidelines Committee Chair [@curijoey](#) introduces the [@myESMO](#) Living Guidelines, a tremendous new resource for clinicians to have constantly updated guidance on the treatment of cancer. First live guidelines: metastatic breast cancer. [#bcsm](#) [#ESMOBreast23](#) [@IEOufficiale](#)

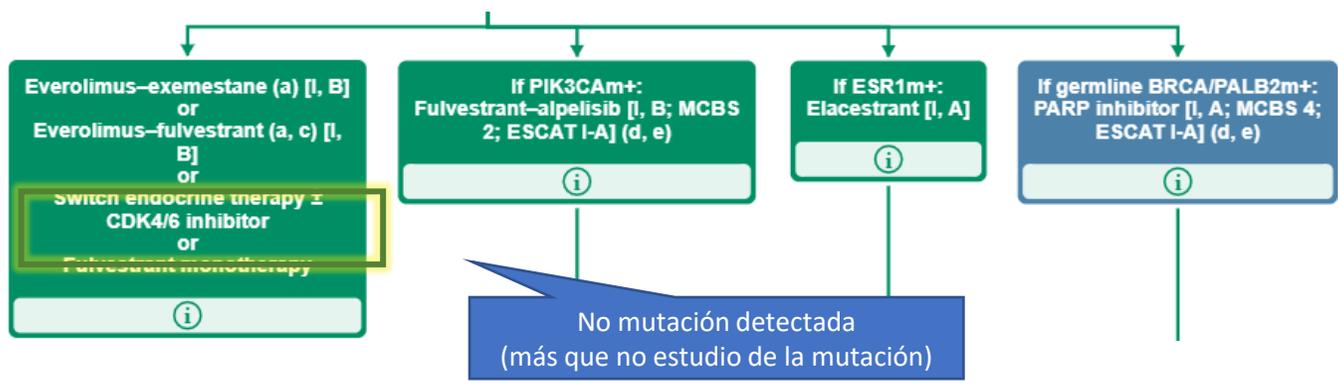
[Traducir Tweet](#)



1:21 p. m. · 11 may. 2023 · 5.468 Reproducciones

9 Retweets 2 Citas 47 Me gusta 3 Elementos guardados



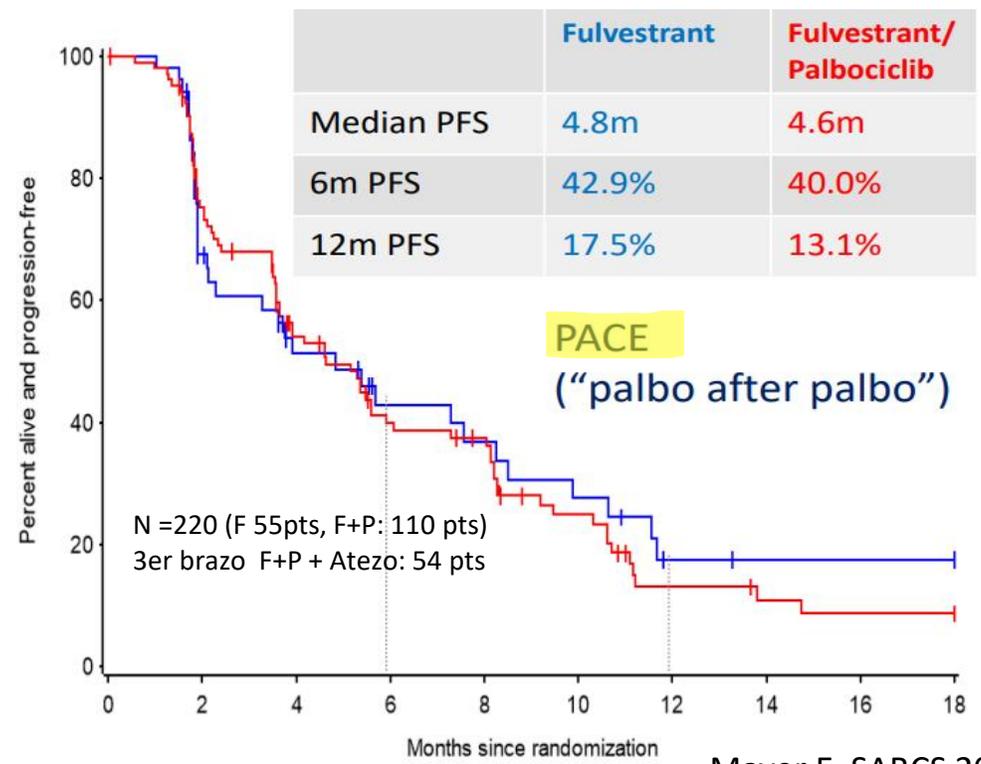


PACE

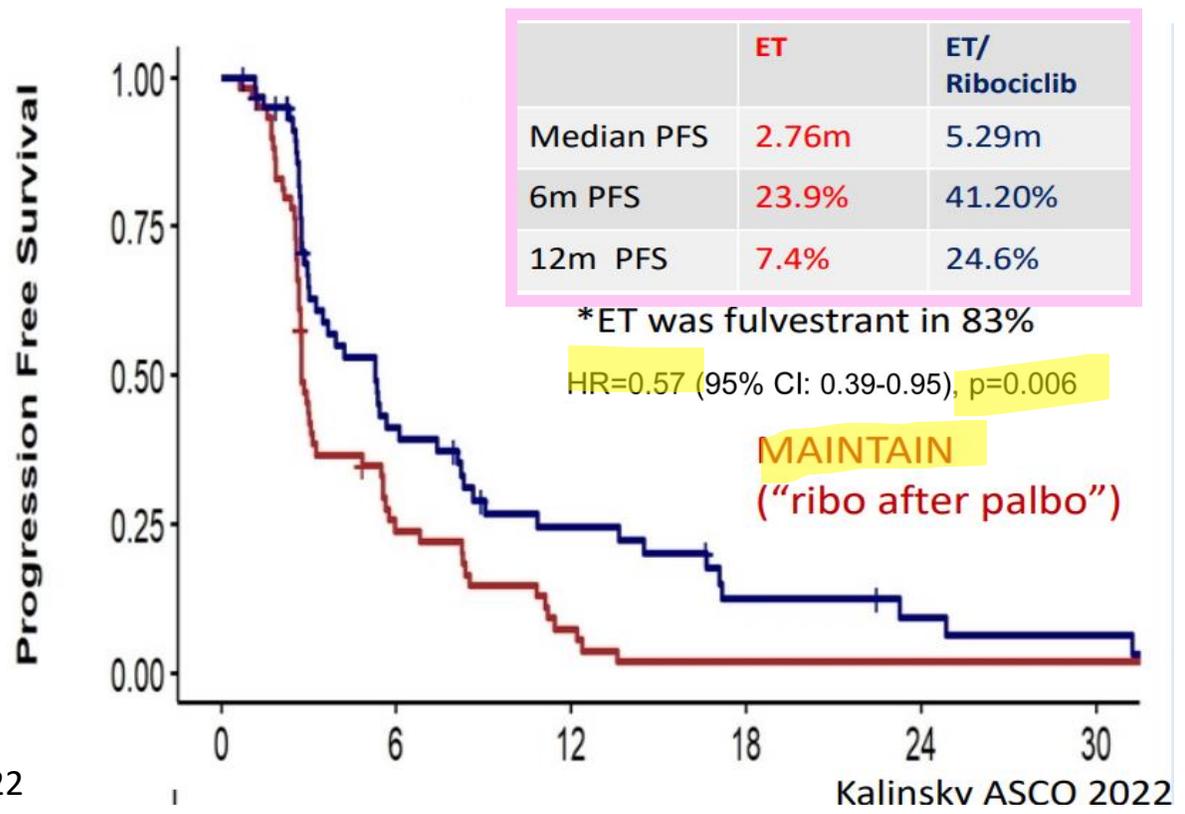
N = 165 (solo F vs F+P)
 Prior palbo: 90%
 Prior CDK4 for > 12 m 75%
 CT for MBC 16.4%
 Any systemic Rx bw CDK and PACE 12%

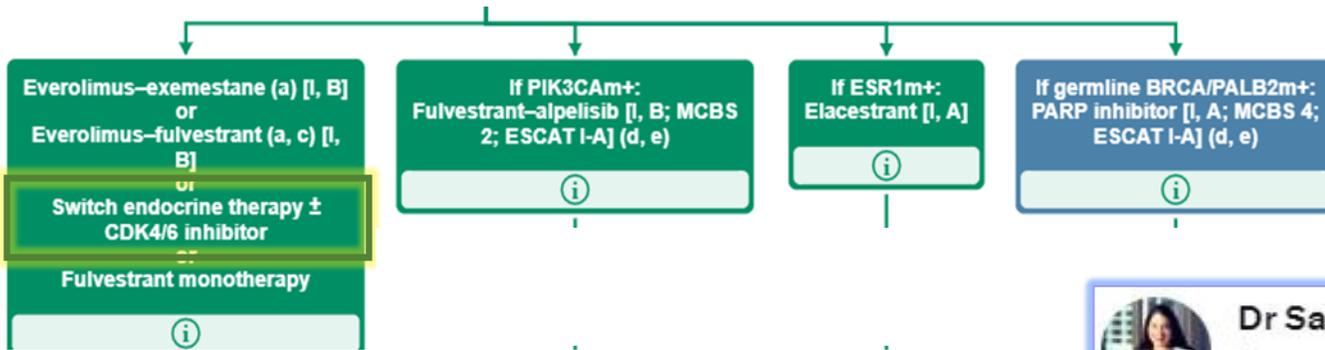
MAINTAIN

N=110
 89% prior palbo
 10% prior ribo
 Prior CDK>12m: 70%
 CT : 10%
 Intercurrent tx: 6.3%



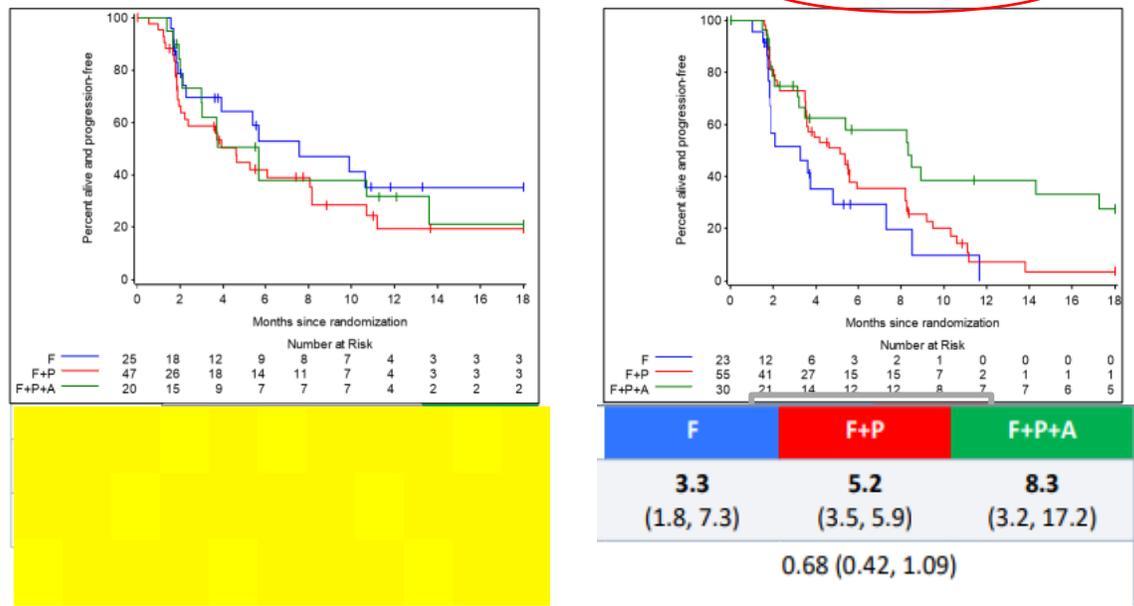
Mayer E, SABCS 2022





¿Y si existiera mutación en ESR1?

PACE: Exploratory Analysis of Baseline ESR1 Mutation and Outcome
 ESR1 WT ESR1 altered 54%



Dr Sarah Sammons @drsarahsam · 4 jun. 2022
 Interesting exploratory analysis for ESR1 mutations in MAINTAIN. Appears to be less benefit to ribo after palbo here, though small numbers.

Lasofoxifene/Abemaciclib in ESR1 mutants is in the poster session Monday!

#bcs #ASCO22

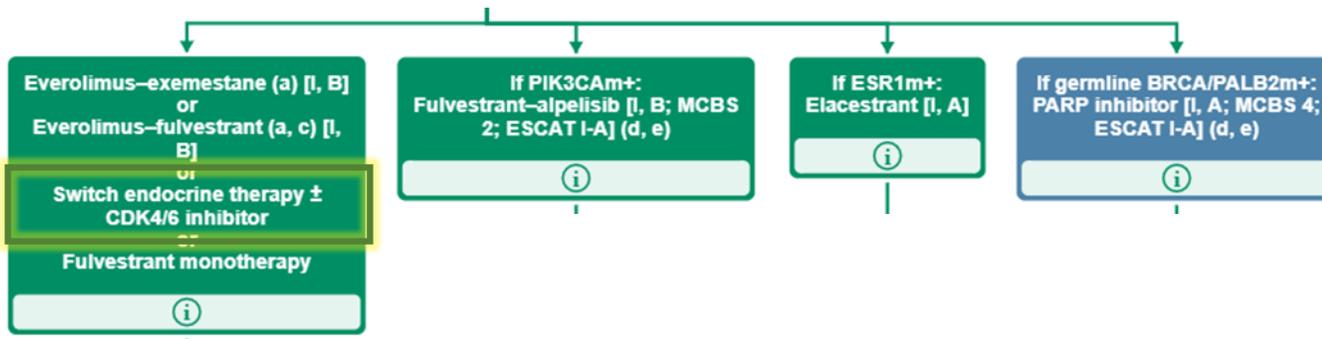
PFS: Fulvestrant and ESR1 Mutation Status

ESR1 WT (n=45)

	Placebo (n=21)	Ribociclib (n=24)
Median (95% CI) (mos)	2.76 (2.66-5.49)	8.32 (5.65-16.63)

ESR1 Mutant (n=33) 42%

	Placebo (n=15)	Ribociclib (n=18)
Median (95% CI) (mos)	3.02 (2.53-5.62)	2.96 (2.66-4.21)



¿Y si existiera mutación en PIK3CA?

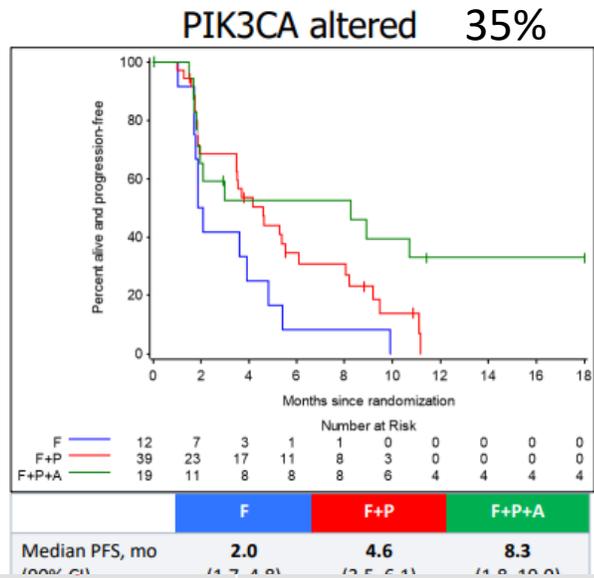
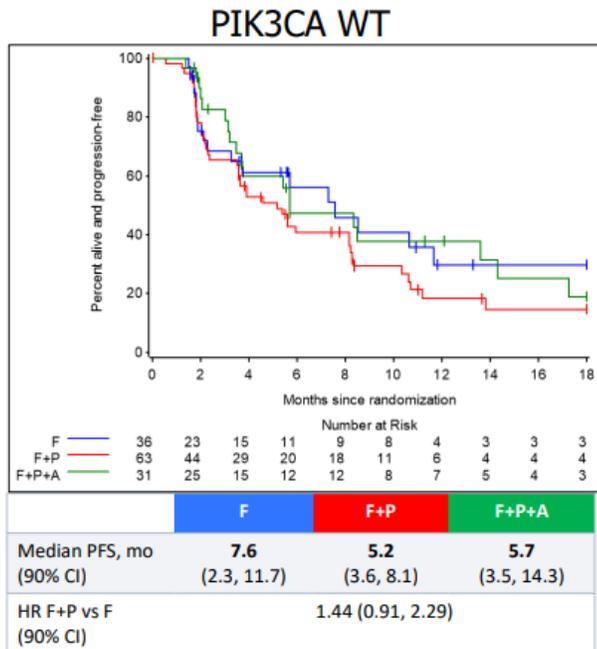
PACE: Exploratory Analysis of Baseline PIK3CA Mutation and Outcome

MAINTAIN

PIK3CA^{mut} 22/78 : 28%

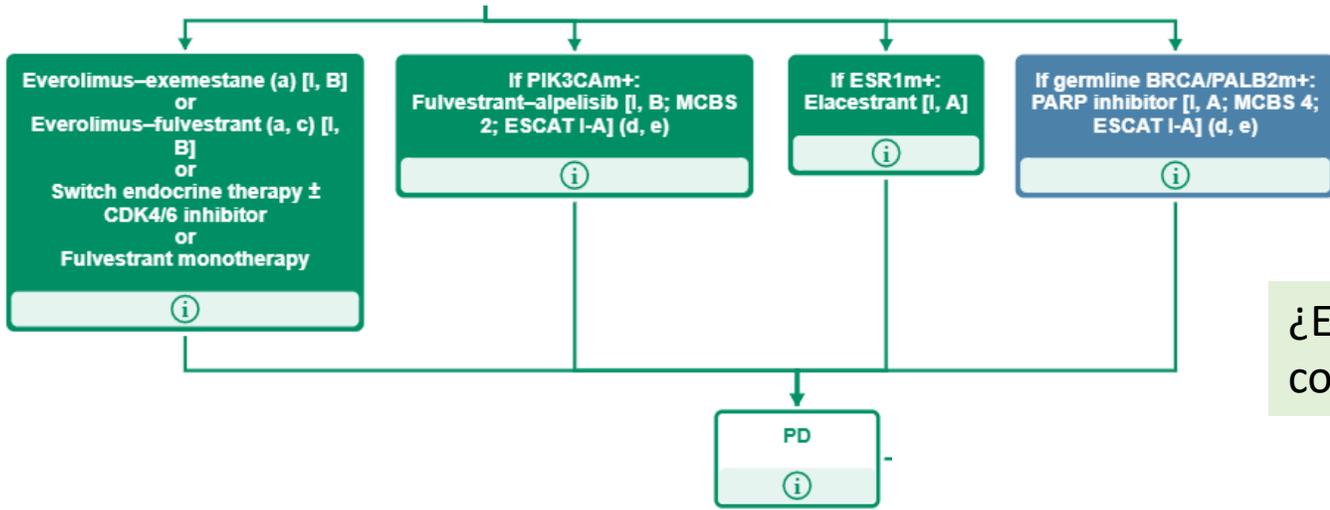


Pending results of studies with bigger sample sizes



PALMIRA	ET +/- Palbociclib (after palbociclib)	198
EMBER-3	ET vs Imlunestrant vs Imlunestrant/ Abemaciclib (after any CDK4/6i)	800
PostMONARCH	Fulvestrant +/- Abemaciclib (after any CDK4/6i)	350

ELAINE 2 lasofoxi+ abema : median PFS 13.9 mos (95% CI, 8.0–NE), ORR 33.3% (95% CI, 16.3–56.3) .CBR 62.1% (95% CI, 44.0–77.3) Damodaran S, ASCO 2022



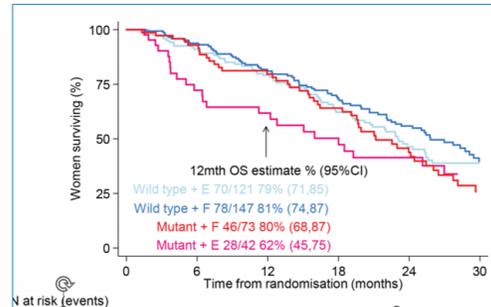
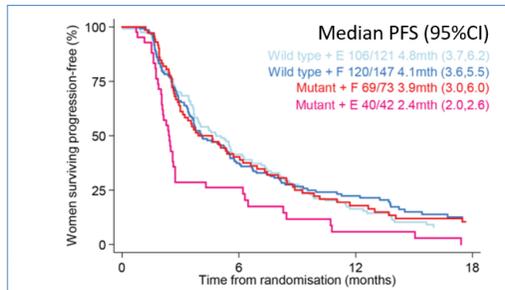
¿Exemestane es todavía válido en monoterapia o con iCDK4/6 tras CDK4/6?

Fulvestrant activity in ESR1^{mut} BC: Combined analyses of EFECT and SOFEA trials

Turner N, Clin Cancer Res Published OnlineFirst August 19, 2020

ESR1 mutation: independent prognostic factor (PFS)
 HR 1.96 (1.34, 2.86), p < 0.001
 Test interaction ESR1 status/treatment: 0.61 (0.38, 1.00), p=0.05

2 Trials with similar randomized design in mBC
 Anastrozol + Exemestane vs Anastrozol + fulvestrant after progression to NSAI
 N=383; Baseline ESR1 mut : 30% (ctDNA)

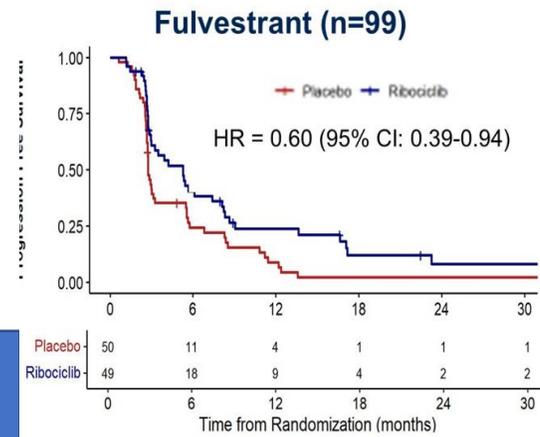


2 line
No prior
CDK

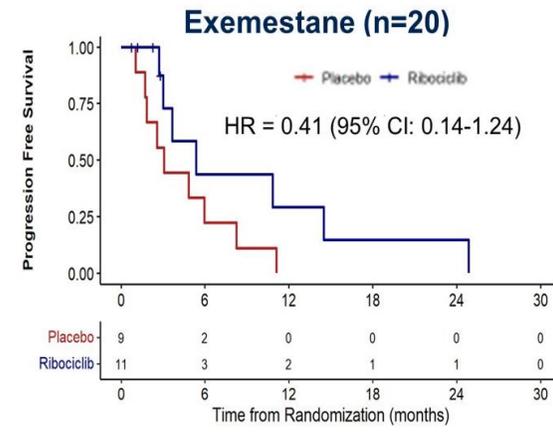
Detection of ESR1 mutations in baseline ctDNA is associated with inferior PFS and 12mOS in patients treated with exemestane versus fulvestrant

MAINTAIN

PFS in Fulvestrant or Exemestane Subgroups

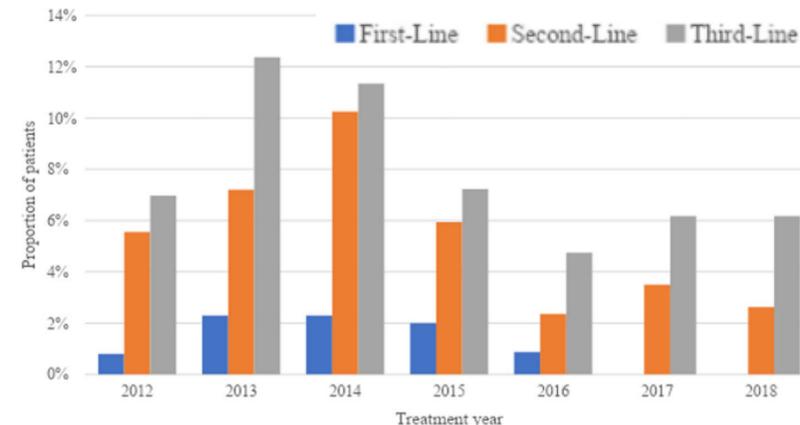
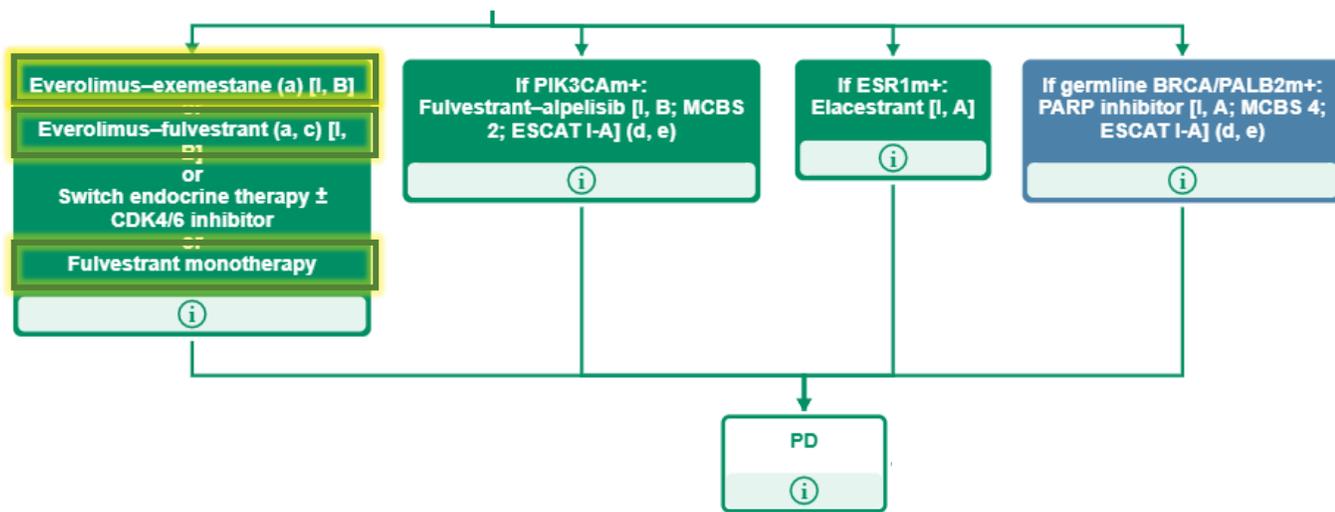


	Placebo (n=50)	Ribociclib (n=49)
Median (95% CI) (mos)	2.76 (2.66-3.25)	5.29 (2.96-8.12)



	Placebo (n=9)	Ribociclib (n=11)
Median (95% CI) (mos)	3.06 (1.84-5.95)	5.36 (3.02-14.50)

Uso de Exemestane-everolimus (RWD: Flatiron)



Rozenblit et al. Breast Cancer Research (2021)

Linea de tto	N, Tiempo a nuevo tto (TNT)		Valor <i>p</i>
	No iCDK previo	CDK previo	
2 L	6.2m (95% CI 5.2, 7.3)	4.3m (95% CI 3.2, 5.7)	0.03
3 L	5.6 m (95% CI 4.4, 6.9)	4.1m (95% CI 4.4, 6.9)	0.08 (NS)

Rozenblit et al. Breast Cancer Research (2021)

Exemestane-everolimus: Series retrospectivas

<i>n</i>	Prior Lines of Therapy	Prior CDK4/6i	PFS	Response Rate	Reference
41	<ul style="list-style-type: none"> Must have had CDK4/6i Median 4 prior lines of therapy 	100%	4.2 months	ORR 17.1% CBR 17.1%	1
20	<ul style="list-style-type: none"> Must have had CDK4/6i 	100%	5.8 months	NA	2
17	<ul style="list-style-type: none"> Must have had CDK4/6i 	100%	5.7 months	6-month PFS 18%	3
12	<ul style="list-style-type: none"> Prior therapy CDK4/6i 	100%	11.7 months	NA	4

1. Hakal, A.; Breast Cancer. 2020, 14, 1178223420944864.
2. Lupichuk, S.M.; Cancer Res. 2019, 79, 4. Abstract
- 3- Cook, M.M. Oncologist 2021, 26, 101–106.
- 4 Nakayama, T.; Future Oncol. 2020, 16, 1851–1862.

No se ha reportado en función de mutación de ESR1 en el contexto post CDK
 Valoración perfil tóxico:
 Inicialmente preocupados por la mucositis,
 hoy por la pneumonitis que pueda comprometer un tto ulterior con T-Dxd

If PIK3CAm+:
Fulvestrant–alpelisib [I, B; MCBS
2; ESCAT I-A] (d, e)



FabriceAndre @FAndreMD · 29 may. 2020

.@EMA_News approval of **alpelisib**: ONLY after ET SINGLE AGENT: almost no pts will get access to it. it comes the same day when everyone is favorably impressed by **Bylieve** trial at #ASCO20 . let s try to get the drug accessible !!! ABC5: alpe is recommended by 90% of panel... (COI)

EU Medicines Agency @EMA_News · 29 may. 2020

EMA's human medicines committee (#CHMP) recommends 8 #medicines for approval at its May 2020 meeting: ema.europa.eu/en/news/meetin...

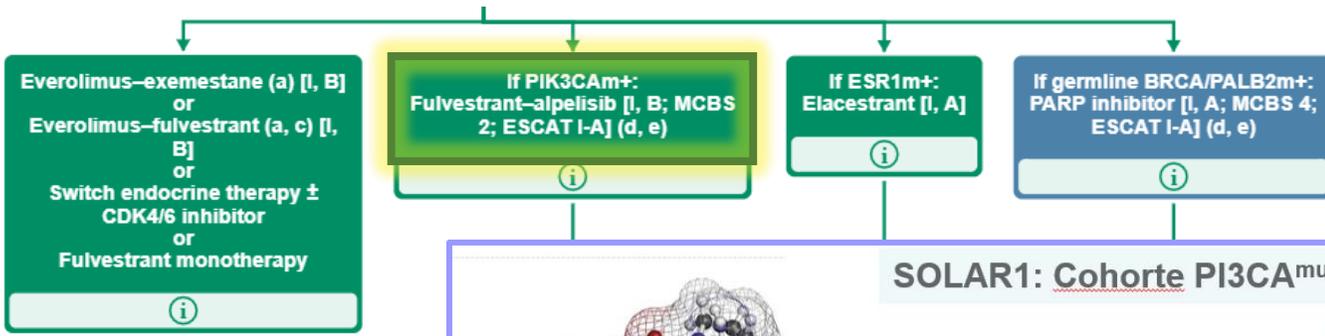
CHMP statistics: May 2020

Positive opinions on new medicines	8 Total	41 Total 2020
New [non-orphan] medicines	5	
Orphan medicines	1	
Biosimilars	1	
Generic / hybrids / informed consent	1	

Negative opinions on new medicines	0 Total	0 Total 2020
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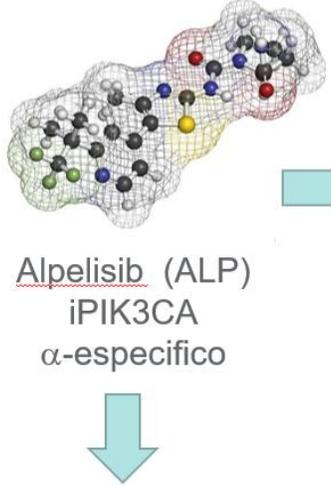
Positive opinions on extensions of therapeutic indications	5 Total	29 Total 2020
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Withdrawn applications for new medicines	2 Total	6 Total 2020
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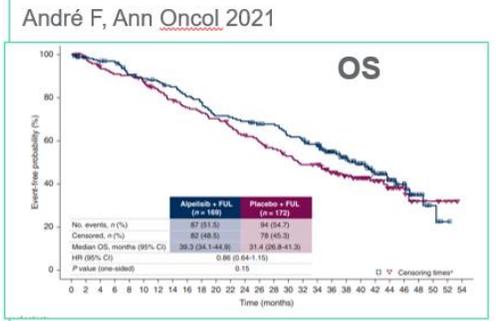
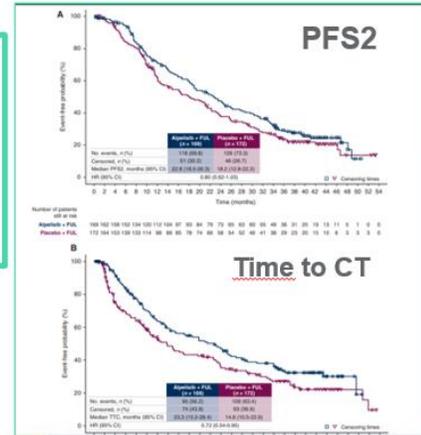
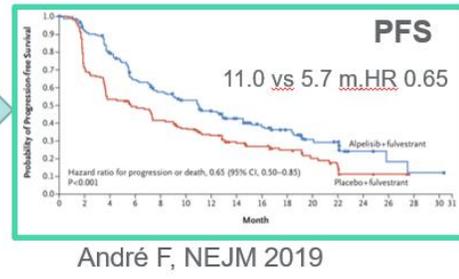


TOXICIDAD

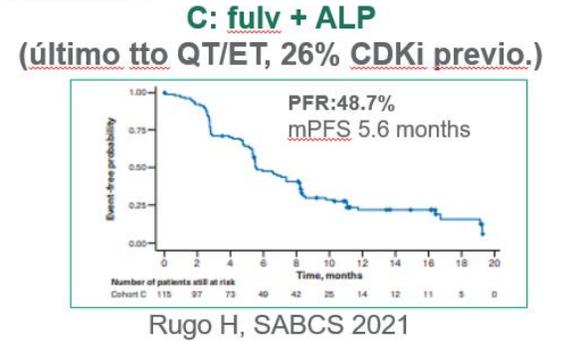
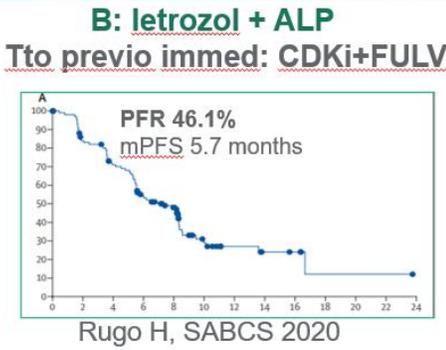
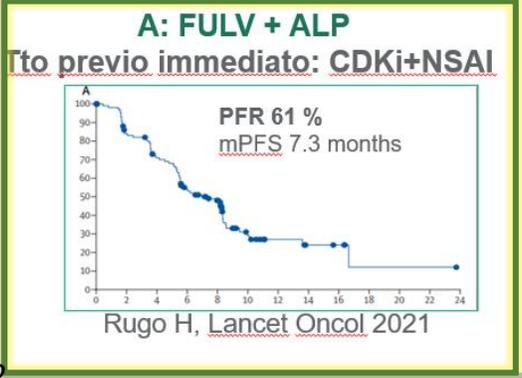
- Hiperglicemia
- Rash
- Diarrea



SOLAR1: Cohorte PI3CA^{mut} (CDK4/6 previo:6%); fulvestrant + ALP/placebo



BYLIEVE 3 cohortes, Obj 1^{ario}: alive and progression-free rate (PFR) at 6 m

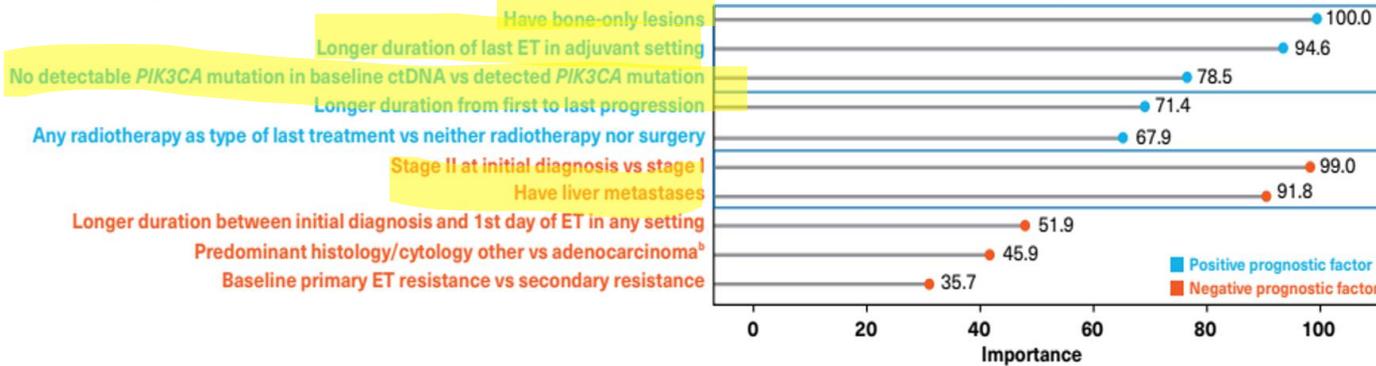


PFS actualizada: 8 meses
Existencia de un 25% de pts con enfermedad controlada > 12meses y 16% de pacientes con control enfermedad > 18 meses

Long term responders with alpelisib. Who are they?

Hope Rugo et al, PD 13-06, SABCS 2022

Top 10 Prognostic Factors Associated With LT Disease Control Identified by SVM Model^a



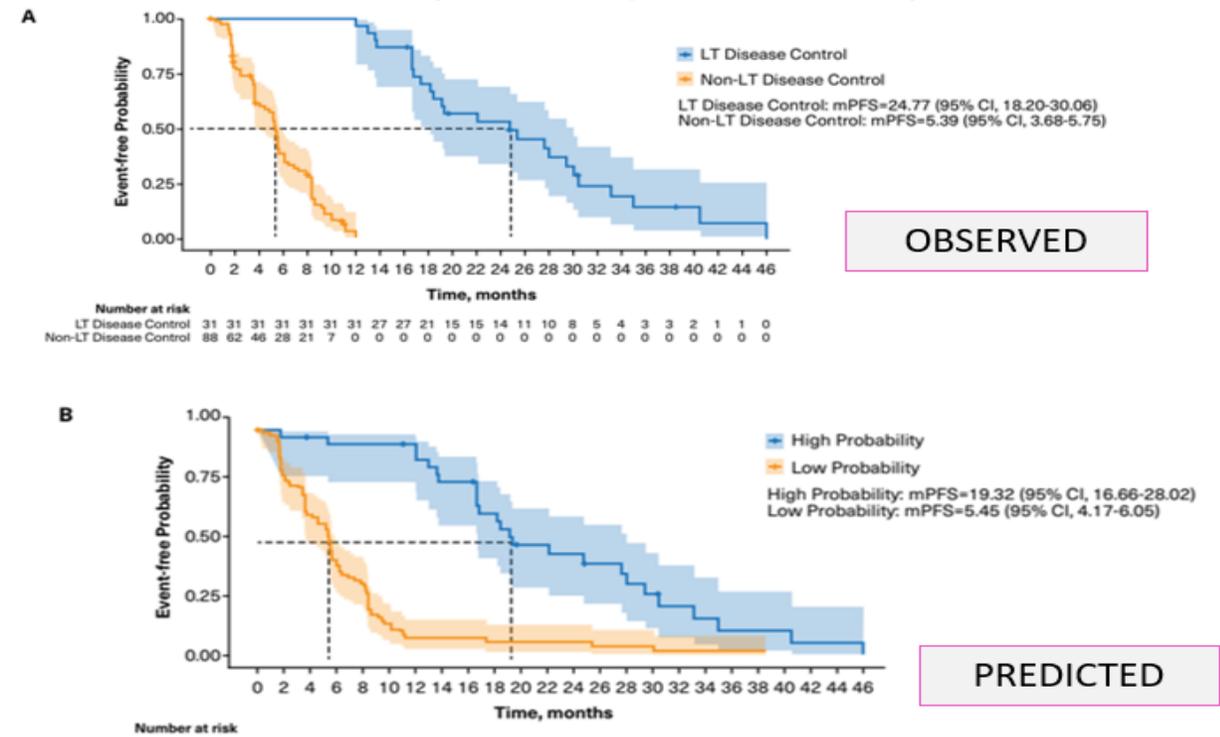
8 machine learning models were evaluated on a
-training set: 70% of the BYLieve Cohort
 A mFAS population (randomly selected)
-the remaining 30% of the population
comprised the test set

Patients were **classified as having high or low probability of LT disease control** according to the predicted probabilities (\geq or $<$ cutoff point)

Biomarker Analysis using baseline ctDNA samples In LT cohort

- Genes differentially altered
- Tumor complexity less predominant
- Low ctDNA fraction($<10\%$)

Figure 3. Kaplan-Meier Curves for (A) Observed PFS in Patients Who Experienced LT or Non-LT Disease Control or (B) PFS in Patients Predicted to Have High or Low Probability of LT Disease Control Using the SVM Model

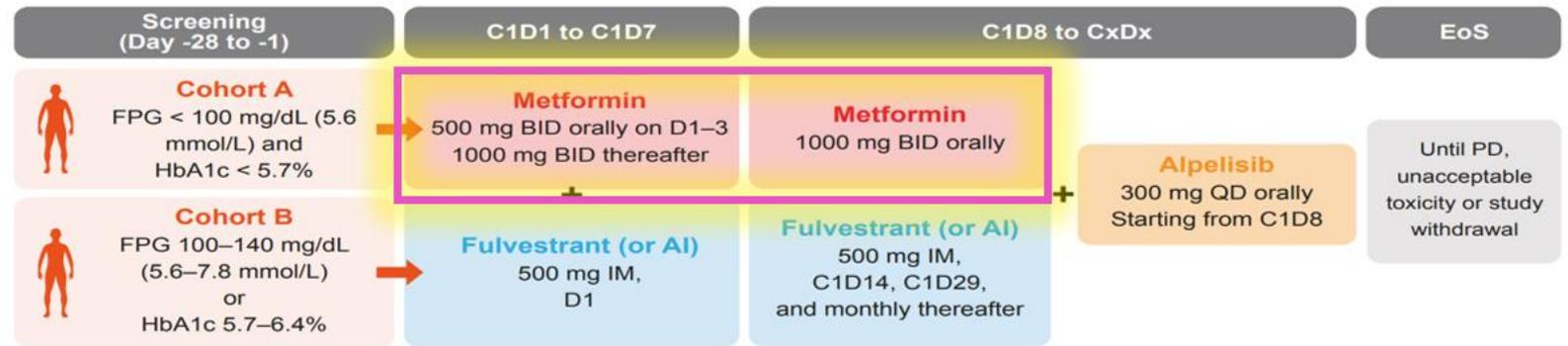


OBSERVED

PREDICTED

Metallica study

Metformine for the prevention of alpelisib-related hyperglycemia in PIK3CA mutated, HR+HER2-ABC



Primary Endpoint

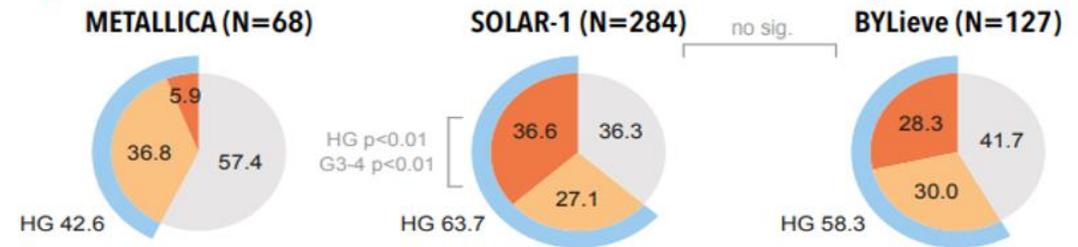
Incidence rate of G3–4 HG by CTCAE criteria 4.03 over the first two cycles of treatment with ALP (8 weeks).

- Cohort A (n=48):** H0: $\geq 25\%$ G3–4 HG pts / HA: $\leq 10\%$ G3–4 HG pts.
- Cohort B (n=20):** H0: $\geq 40\%$ G3–4 HG pts / HA: $\leq 15\%$ G3–4 HG pts.
- Positive finding in: **Cohort A:** ≤ 7 among 48 pts with G3–4 HG in the first 2 cycles;
Cohort B: ≤ 4 among 20 pts with G3–4 HG in the first 2 cycles.
- No study discontinuations were caused by hyperglycemia.

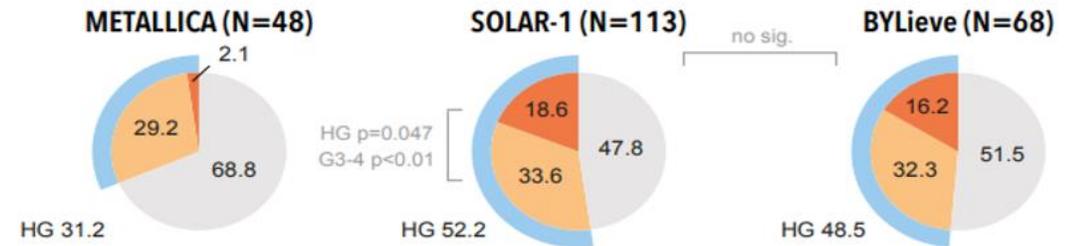


	Cohort A (N=48)	Cohort B (N=20)	Total (N=68)
PFS in months	7.5 (4.2-NA)	6.9 (5.8-NA)	7.3(5.8-NA)

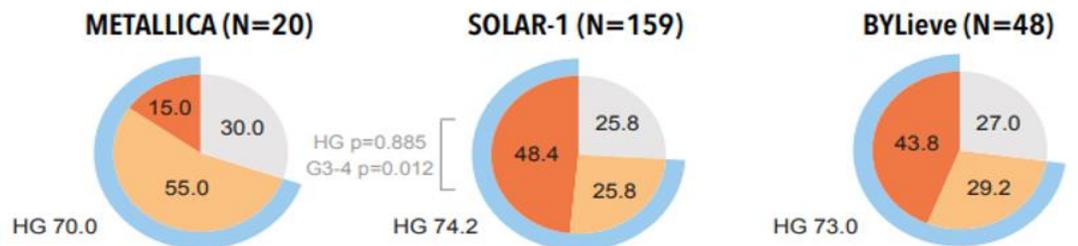
A) All patients



B) Cohort A: Patient with normal blood glucose at baseline



C) Cohort B: Prediabetics at baseline



Everolimus–exemestane (a) [I, B]
or
Everolimus–fulvestrant (a, c) [I, B]
or
Switch endocrine therapy ±
CDK4/6 inhibitor
or
Fulvestrant monotherapy

If PIK3CAm+:
Fulvestrant–alpelisib [I, B; MCBS
2; ESCAT I-A] (d, e)

If ESR1m+:
Elacestrant [I, A]

If germline BRCA/PALB1
PARP inhibitor [I, A; MCBS
2; ESCAT I-A] (d, e)

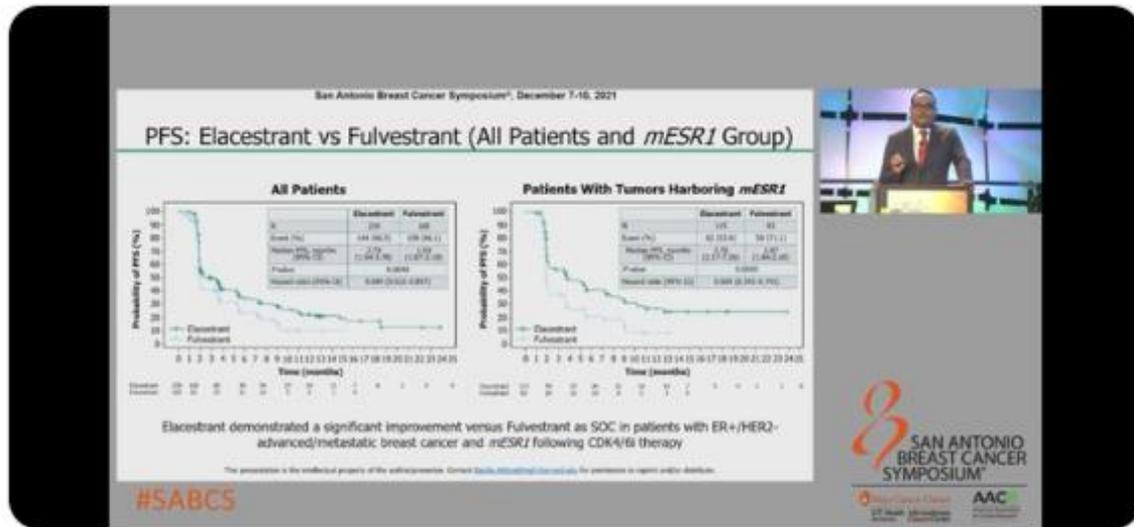
Hilo



Philippe Aftimos, MD
@aftimosp

Fulvestrant was one of the physician's choice endocrine therapy in EMERALD. The novel oral SERD Elacestrant was superior to Fulvestrant in this analysis of the phase 3 study both in all patients and in patients with ESR1-mutant tumors #SABCS21 #bcm @OncoAlert

Traducir Tweet



4:10 p. m. · 8 dic. 2021

Hilo



Paolo Tarantino
@PTarantinoMD

Primary results were published on @JCO ASCO: elacestrant significantly improved PFS vs SoC E1 & was well tolerated.

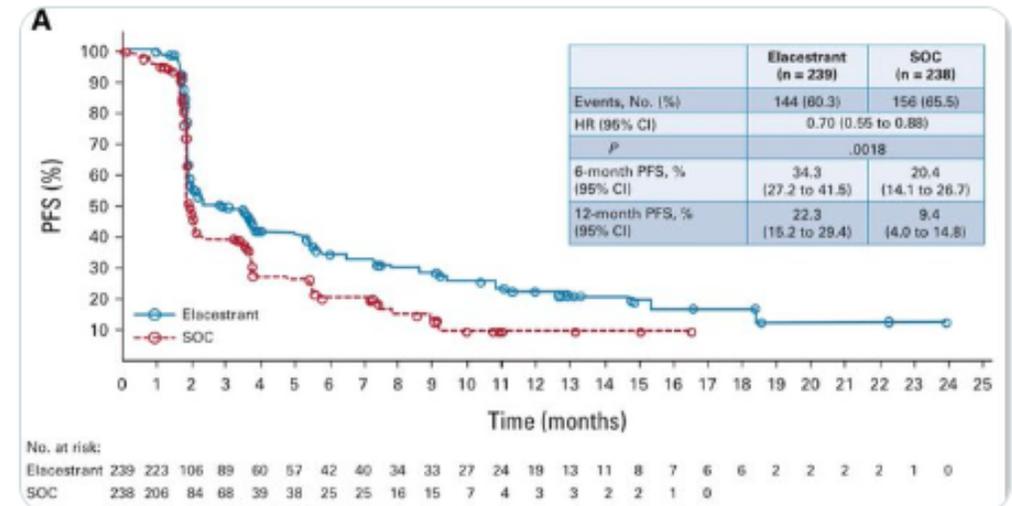
However, the absolute PFS benefit was small, and many pts progressed at the first scan in both arms

How to enrich for responders?

/5

ascopubs.org/doi/full/10.12...

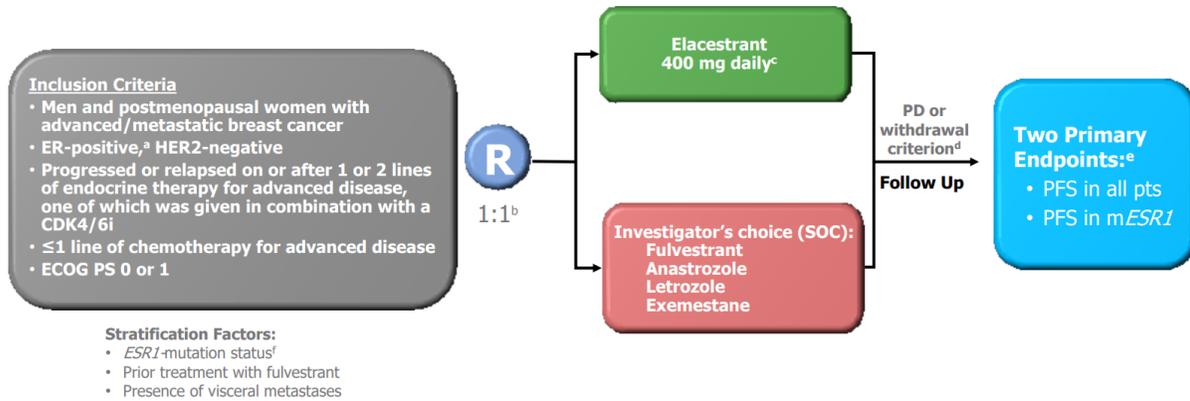
Traducir Tweet



3:20 p. m. · 21 feb. 2023 · 1.268 Reproducciones

3 Retweets 9 Me gusta

EMERALD (elacestrant vs ET)



	EMERALD ¹	SERENA-2 ⁷	EMBER-3 ²	AMEERA-3 ^{3,4,9}	acelERA ^{4-6, 10}
Treatment	Elacestrant	Camizestrant	Imlunestrant +/- abemaciclib	Amcenestrant	Giredestrant
Control Arm	fulvestrant / AIs	fulvestrant	fulvestrant / exemestane	fulvestrant / AIs / tamoxifen	fulvestrant / AIs
Phase (n)	Phase 3 (477)	Phase 2 (240)	Phase 3 (800)	Phase 2 (367)	Phase 2 (303)
Patients	Men or postmenopausal women	Postmenopausal women	Men or postmenopausal women	Men or women (any menopausal status)	Men or women (any menopausal status)
Prior CDK4/6i	Required (100%)	Permitted	Permitted	Permitted (79.7%)	Permitted (42%)
Allowed Prior Fulvestrant	YES	NO	NO	YES	YES
Allowed Prior Chemotherapy in MBC	YES	YES	NO	YES	YES

Duration on CDK4/6i in the metastatic setting

All patients	At least 6 mo		At least 12 mo		At least 18 mo	
	Elacestrant (n=202)	SOC (n=205)	Elacestrant (n=150)	SOC (n=160)	Elacestrant (n=98)	SOC (n=119)
Median PFS Months (95% CI)	2.79 (1.94 - 3.78)	1.91 (1.87 - 2.14)	3.78 (2.33 - 6.51)	1.91 (1.87 - 3.58)	5.45 (2.33 - 8.61)	3.29 (1.87 - 3.71)
PFS rate at 6 months (95% CI)	34.40 (26.70 - 42.10)	19.88 (12.99 - 26.76)	41.56 (32.30 - 50.81)	21.72 (13.65 - 29.79)	44.72 (33.24 - 56.20)	25.12 (15.13 - 35.10)
PFS rate at 12 months (95% CI)	21.00 (13.57 - 28.43)	6.42 (0.75 - 12.09)	25.64 (16.49 - 34.80)	7.38 (0.82 - 13.94)	26.70 (15.61 - 37.80)	8.23 (0.00 - 17.07)
PFS rate at 18 months (95% CI)	16.24 (8.75 - 23.74)	3.21 (0.00 - 8.48)	19.34 (9.98 - 28.70)	3.69 (0.00 - 9.77)	21.03 (9.82 - 32.23)	4.11 (0.00 - 11.33)
Hazard ratio (95% CI)	0.688 (0.535 - 0.884)		0.613 (0.453 - 0.828)		0.703 (0.482 - 1.019)	

Well Balanced b/w arms (all pts and *ESR1mut* cohort)

Prior CDK4/6 in MBC: 100%

Visceral disease: ≈70%

Prior Fulvestrant: ≈30%

2 prior ET lines: ≈43%

CT in MBC: ≈22%

SABCS 2021: Positive trial

PFS all pts (2.8 m v 1.9 m)

ESR1 mutation cohort:(3.8 m v 1.9m)

Bardia, JCO SEP 2022

Bardia A et al. GS3-01, SABCS 2022

EMERALD : Updated results by duration of prior CDK4/6i in metastatic setting

Duration on CDK4/6i in the metastatic setting

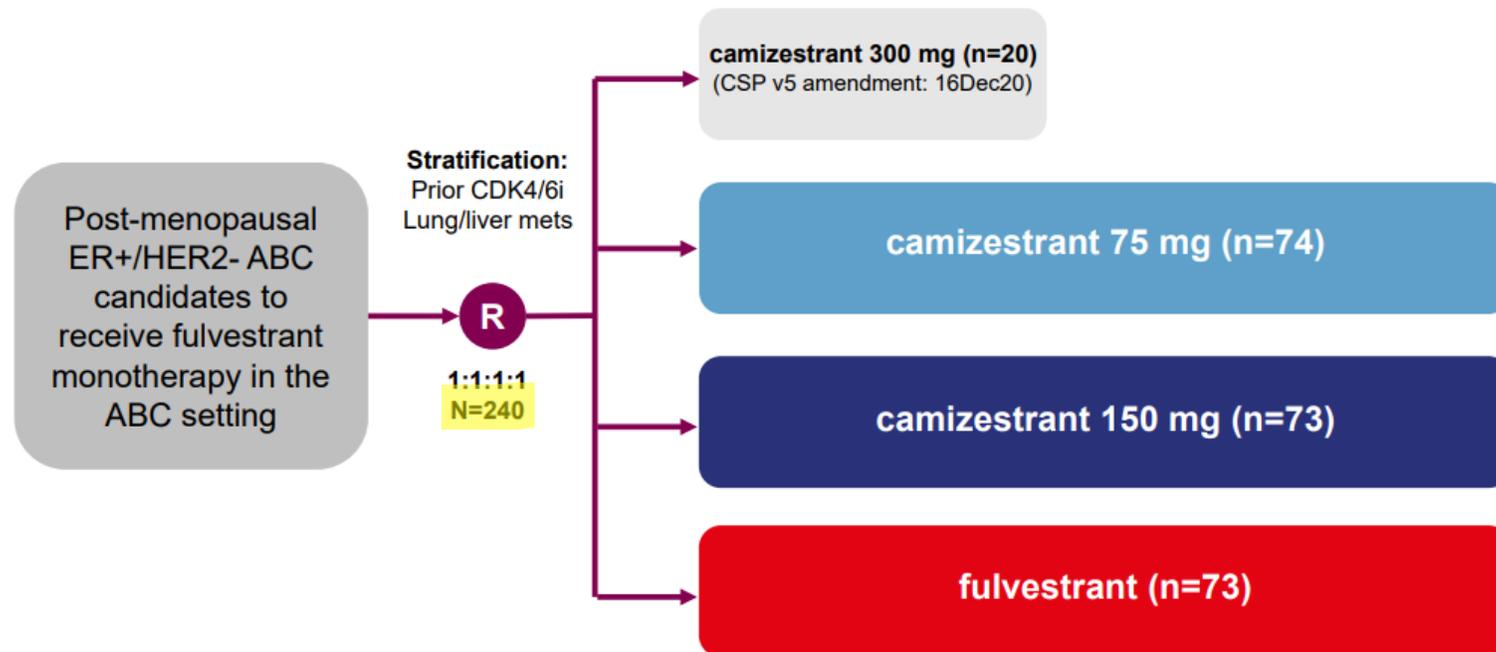
<i>ESR1</i> ^{mut} population	At least 6 mo		At least 12 mo		At least 18 mo	
	Elacestrant (n=103)	SOC (n=102)	Elacestrant (n=78)	SOC (n=81)	Elacestrant (n=55)	SOC (n=56)
Median PFS Months (95% CI)	4.14 (2.20 - 7.79)	1.87 (1.87 - 3.29)	8.61 (4.14 - 10.84)	1.91 (1.87 - 3.68)	8.61 (5.45 - 16.89)	2.10 (1.87 - 3.75)
PFS rate at 6 months (95% CI)	42.43 (31.15 - 53.71)	19.15 (9.95 - 28.35)	55.81 (42.69 - 68.94)	22.66 (11.63 - 33.69)	58.57 (43.02 - 74.12)	27.06 (13.05 - 41.07)
PFS rate at 12 months (95% CI)	26.02 (15.12 - 36.92)	6.45 (0.00 - 13.65)	35.81 (21.84 - 49.78)	8.39 (0.00 - 17.66)	35.79 (19.54 - 52.05)	7.73 (0.00 - 20.20)
PFS rate at 18 months (95% CI)	20.70 (9.77 - 31.63)	0.00 (. - .)	28.49 (14.08 - 42.89)	0.00 (. - .)	30.68 (13.94 - 47.42)	0.00 (. - .)
Hazard ratio (95% CI)	0.517 (0.361 - 0.738)		0.410 (0.262 - 0.634)		0.466 (0.270 - 0.791)	

SERENA-2

Key inclusion/exclusion criteria:

- Recurrence or progression on at least one line of ET
- No prior fulvestrant or oral SERD in ABC
- No more than one line of ET in ABC setting
- No more than one line CT in ABC setting
- Measurable and non-measurable disease

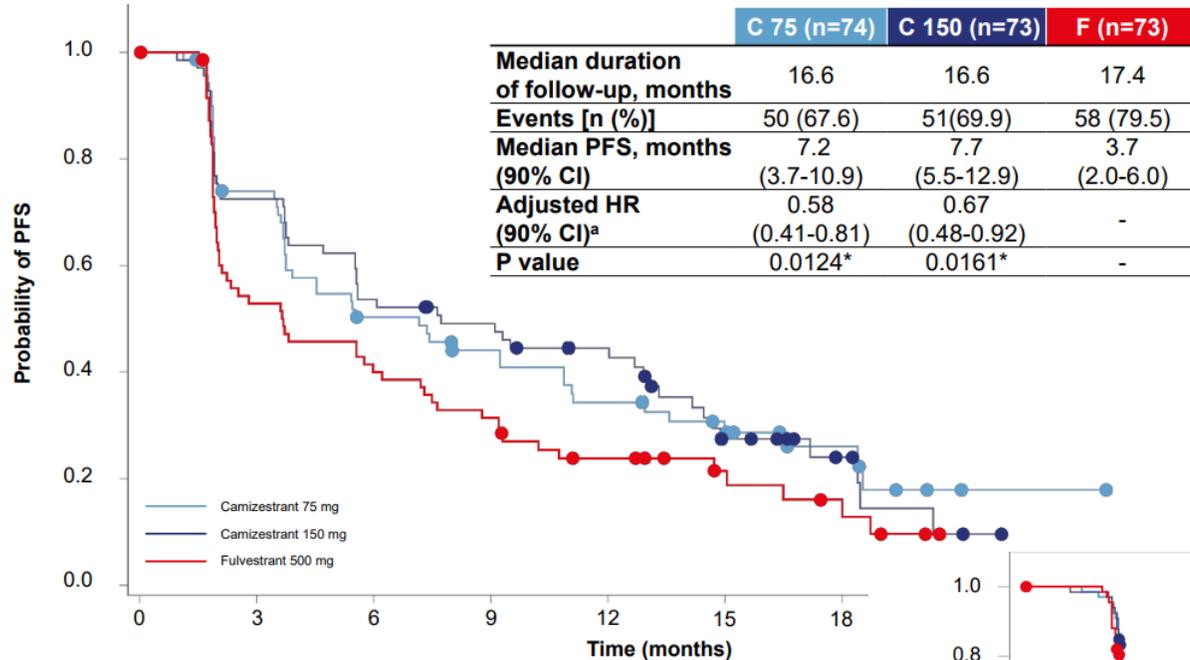
Treatment with CDK4/6i not required



- **Primary endpoint:** PFS (investigator assessment*)
- **Secondary endpoints:** CBR24, ORR, OS, safety
- **Translational endpoints:** serial ctDNA analysis including *ESR1m*, serial CTCs analysis

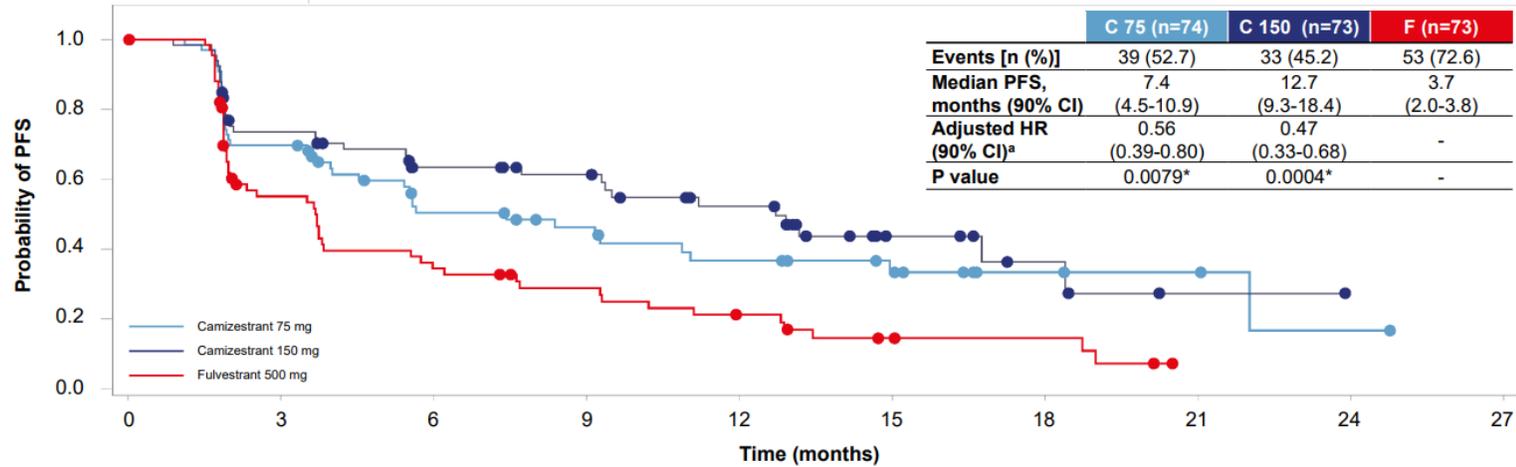
Study not powered to compare between camizestrant doses •
108 events for the pairwise comparison versus fulvestrant
provided **86% power** at the **2-sided 10% significance level** assuming the true hazard ratio was **0.59**
and the median PFS in the control arm was **5 months**

SERENA-2 trial: PFS by local assessment (Primary endpoint)



	C 75	C 150	F
74	50	33	27
73	50	37	32
73	37	28	22
			14
			8
			5

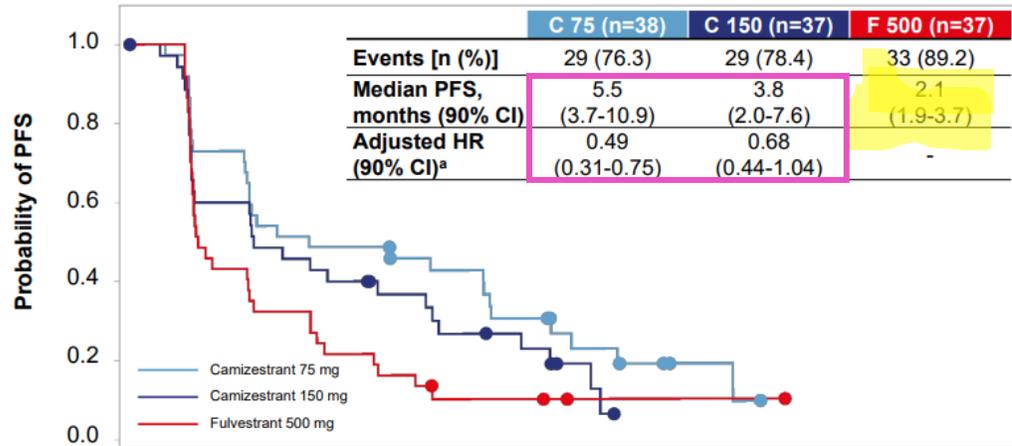
PFS by independent review



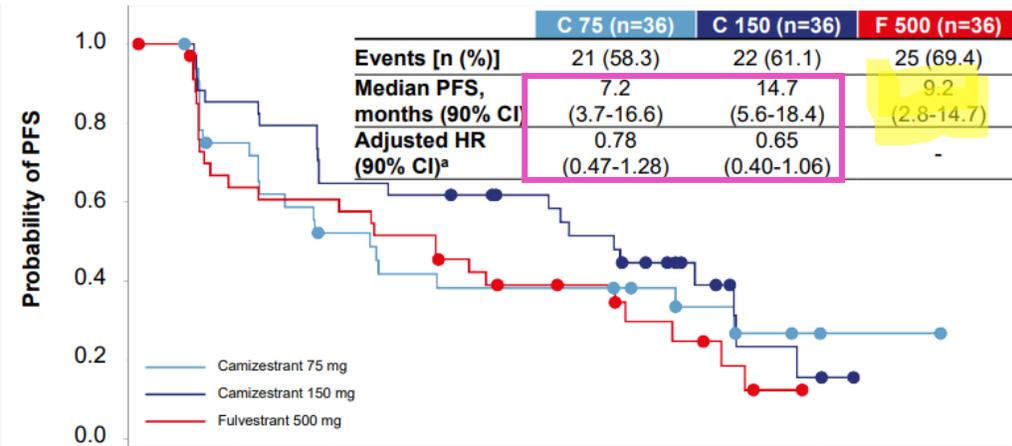
	C 75	C 150	F
74	46	27	21
73	45	33	29
73	32	20	15
			15
			10
			5
			4
			3
			1
			0
			1
			0
			0

SERENA-2 trial: PFS by subgroups (1)

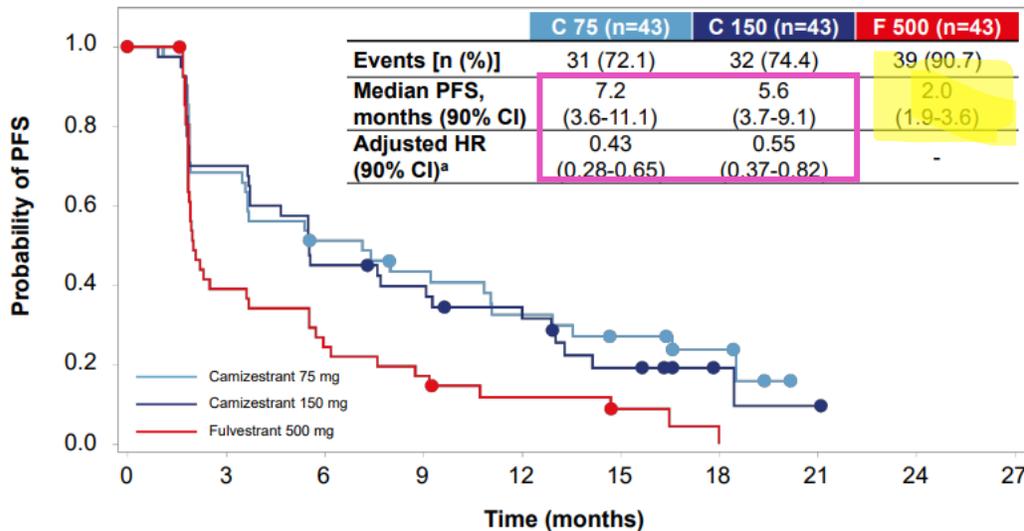
Prior CDK4/6i



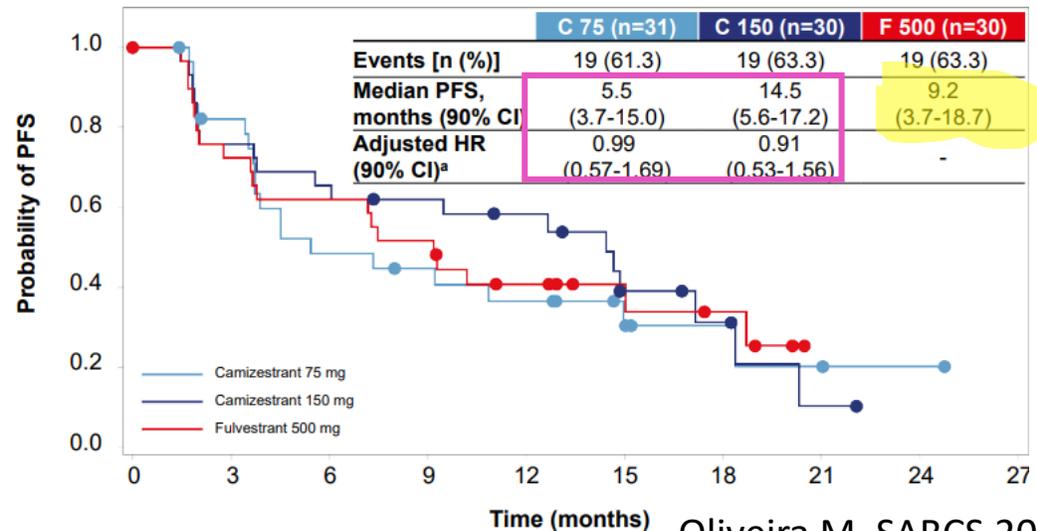
No prior CDK4/6i



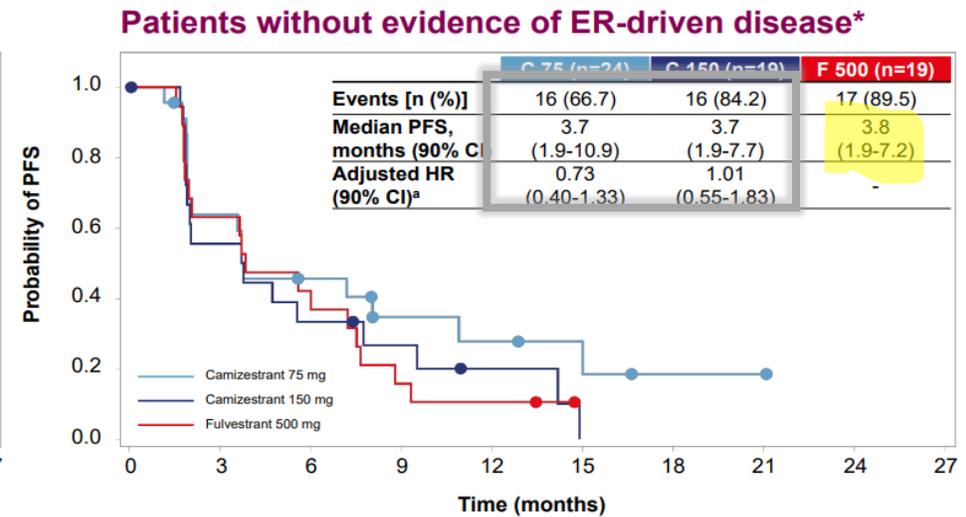
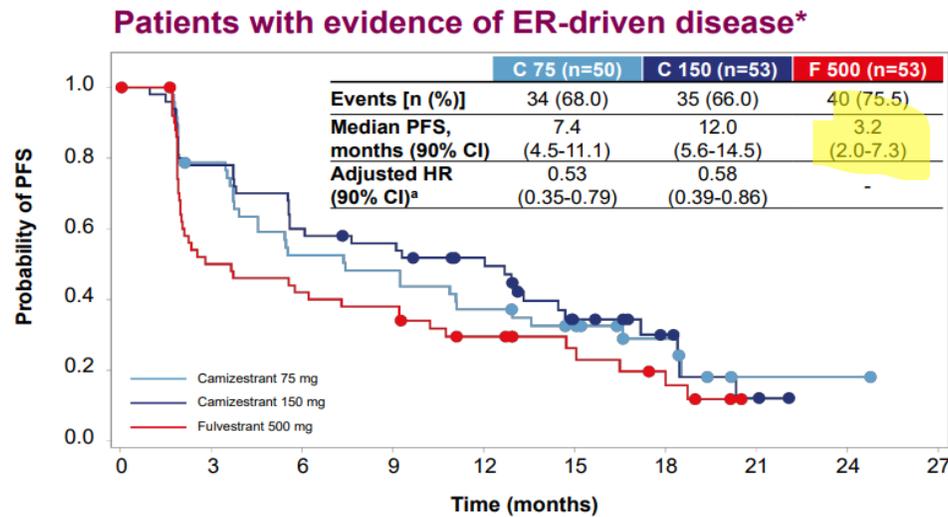
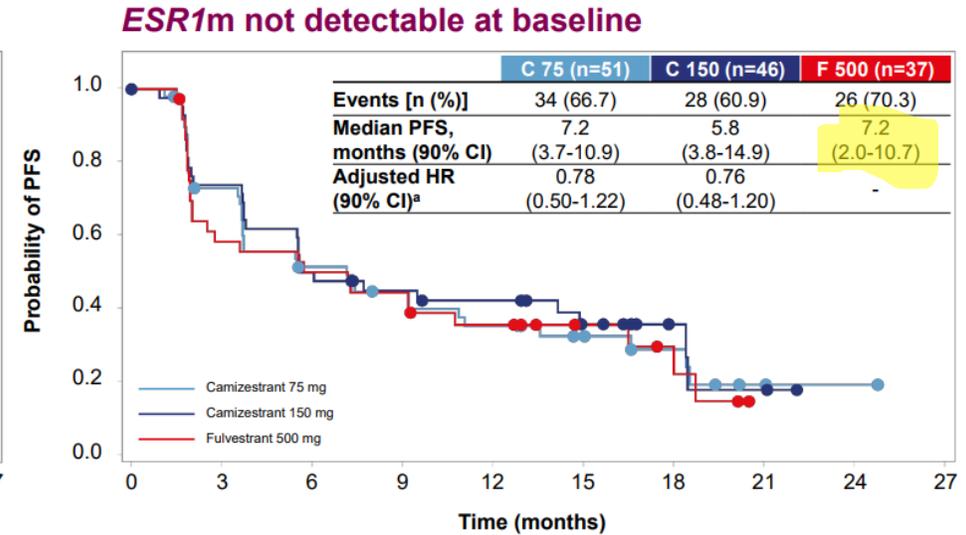
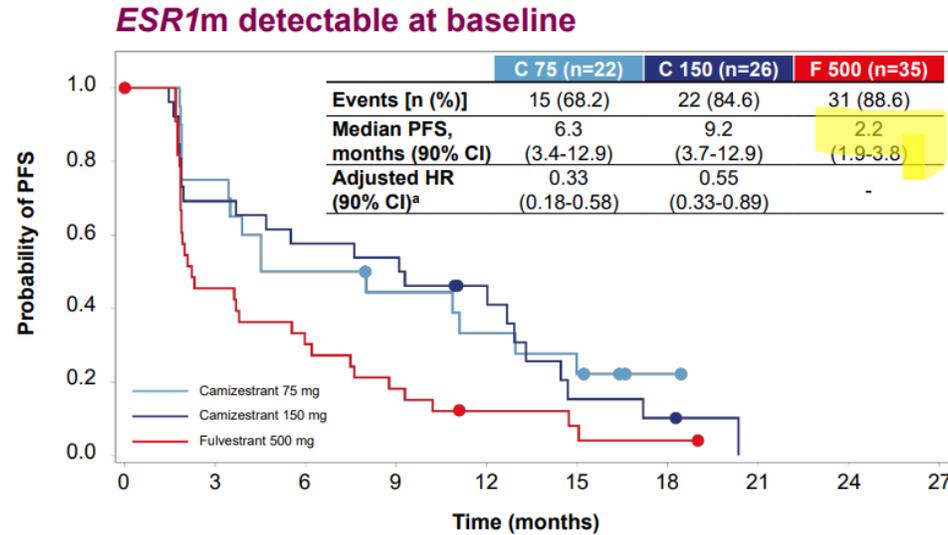
Presence of lung and/or liver metastases



No lung or liver metastases



SERENA-2 trial: PFS by subgroups (2)



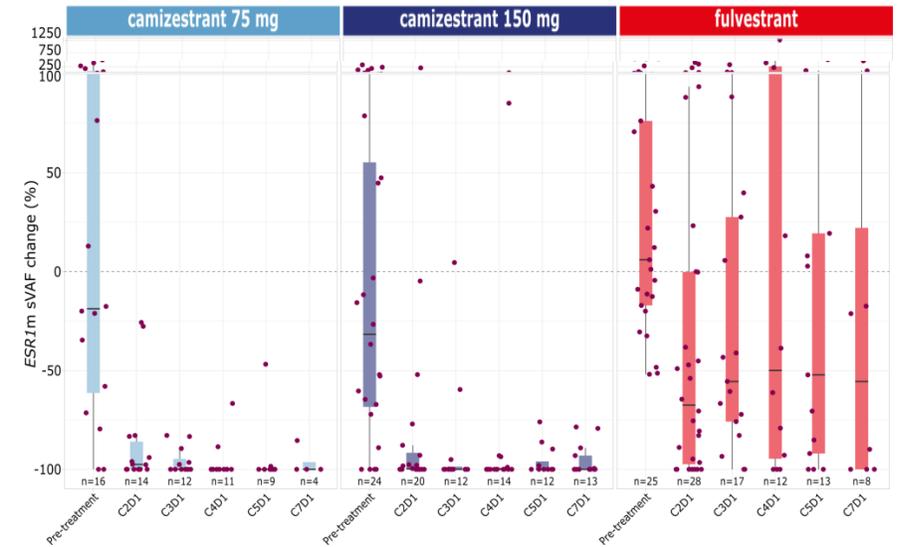
* Defined in accordance with 5th ESOESMO ABC guidelines where the cutpoint is increased to 12 months for patients receiving ET+CDK4/6i therapy in MBC

SERENA-2 trial: Other endpoints

ORR and CBR (all patients)

Group	n	Number (%) of patients with response	Adjusted response rate (%)	Comparison against fulvestrant		
				Odds ratio	90% CI	2-sided p-value
ORR						
Camizestrant 75 mg	70	11 (15.7)	15.7	1.43	0.63-3.33	0.4789
Camizestrant 150 mg	65	13 (20.0)	20.3	1.96	0.88-4.51	0.1675
Fulvestrant	68	8 (11.8)	11.5			
CBR24						
Camizestrant 75 mg	74	35 (47.3)	48.8	1.48	0.84-2.64	0.2554
Camizestrant 150 mg	73	36 (49.3)	51.0	1.62	0.91-2.89	0.1658
Fulvestrant	73	28 (38.4)	39.1			

Changes in *ESR1*^{mut} ctDNA variant allele frequency



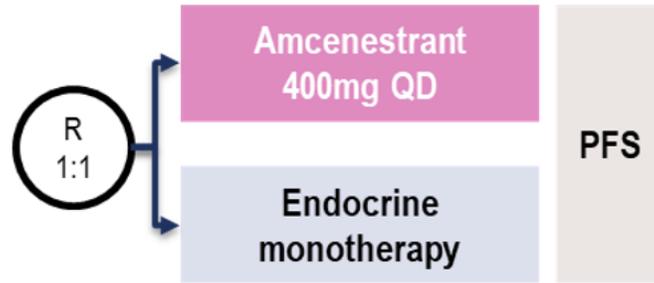
Other Trials of Oral SERD after CDK4/6i

AMEERA-3

NCT04059484

N = 282

- ER+/HER2- ABC
- 0-2 lines for ABC
- 0-1 CT for ABC
- 80% prior CDK4/6



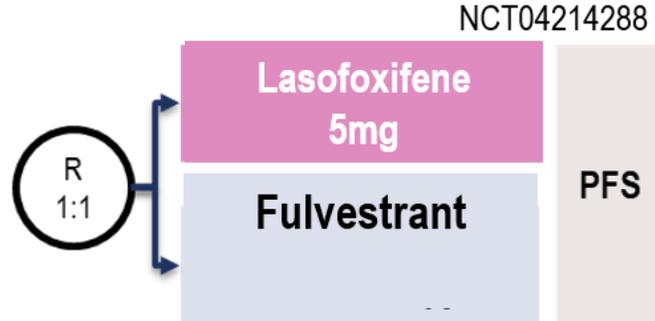
Negative trial. HR PFS 1.051; in ESR1mut pts 0.9
Amcenestrant development discontinued

ELAINE-1

NCT04214288

N=103

- ER+/HER2- ABC
- 100% prior AI+CDK4/6i (>12m)
- ≤1 CT
- All ESR1mut (ctDNA)



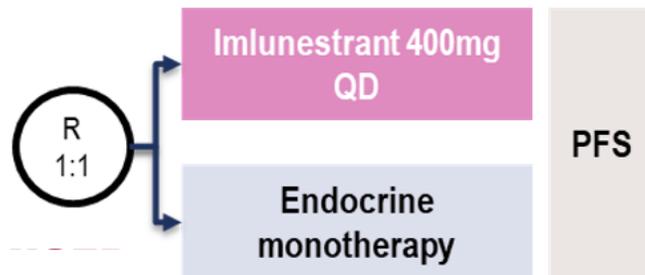
Negative trial. LAS numerically superior to Fulv for all 1ary (HR 0.69 (6.04 vs 4.04 mo, NS) and 2ary outcomes, no thrombosis..

EMBER-3

NCT04975308

N=500

- ER+/HER2- ABC
- Prior treatment with AI +/-CDK4/6i

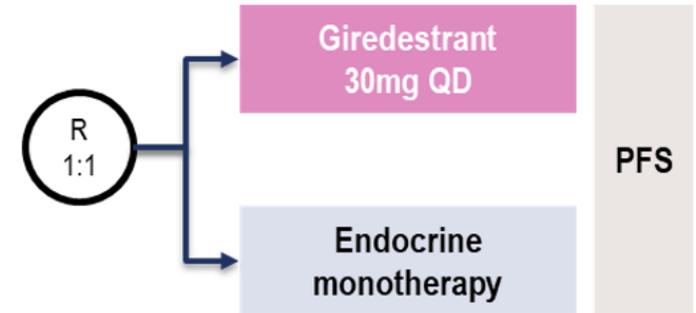


aceLERA

NCT04576455

N=300

- ER+/HER2- ABC
- After 1-2 lines of systemic therapy for ABC (prior CDK4/6:42%)



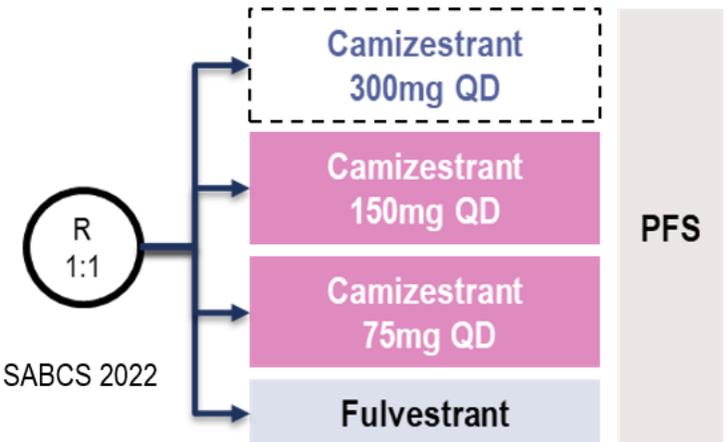
Negative trial; PFS; HR 0.81 (all pts), HR 0.60 (p0.06) in ESR1mut pts
Numerically superior in secondary outcomes

SERENA-2

NCT04214288

N=288

- ER+/HER2- ABC
- ≤2 ET / ≤1 CT
- 50% prior CDK4/6i

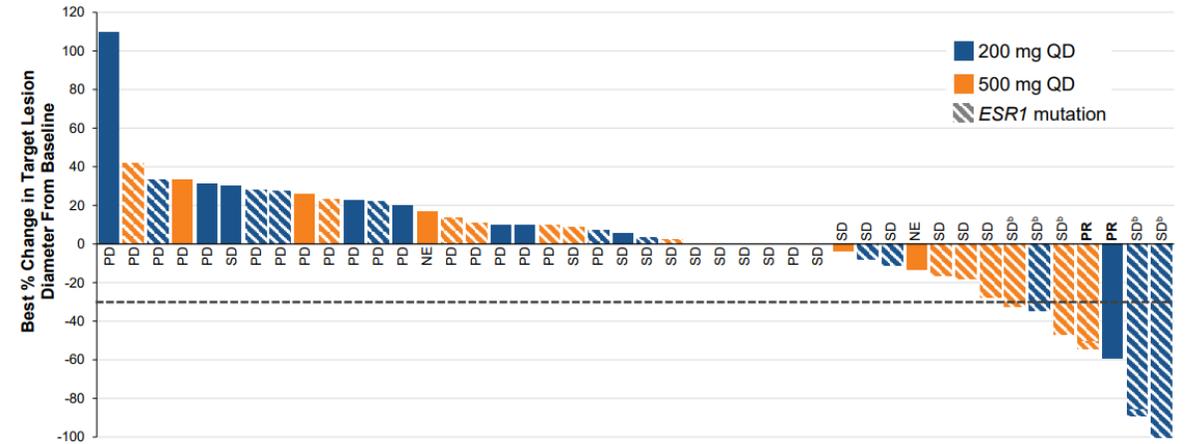


Positive trial (press release), SABCS 2022

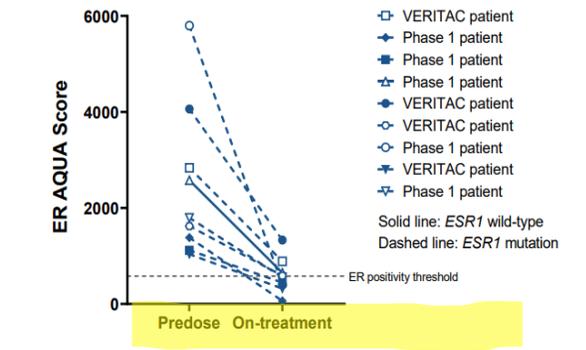
Tolaney S, Abstract 212MO, ESMO2022 (AMEERA-3)
Martin, M, Abstract 211 MO, ESMO 2022 (aceLERA)
Goetz, MP, Abstract 210 MO, ESMO 2022 (ELAINE-1)

VERITAC trial (PH2 in ET pretreated pts with ARV-471)

	200 mg QD (n=35)	500 mg QD (n=36)	Total (N=71)
CBR, % (95% CI)	37.1 (21.5–55.1)	38.9 (23.1–56.5)	38.0 (26.8–50.3)
Patients with mutant <i>ESR1</i>			
	(n=19)	(n=22)	(n=41)
CBR, % (95% CI)	47.4 (24.4–71.1)	54.5 (32.2–75.6)	51.2 (35.1–67.1)



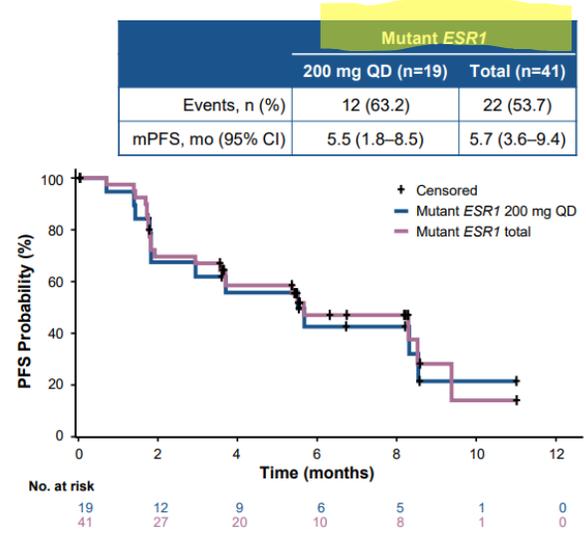
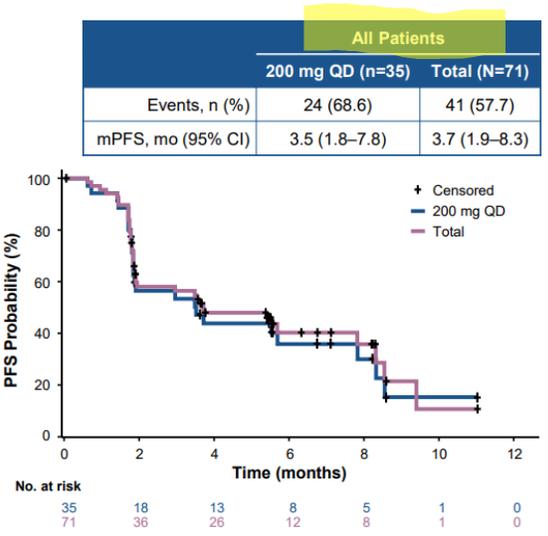
ARV-471 200 mg QD was selected as the phase 3 monotherapy dose based on comparable efficacy, favorable tolerability, and robust ER degradation



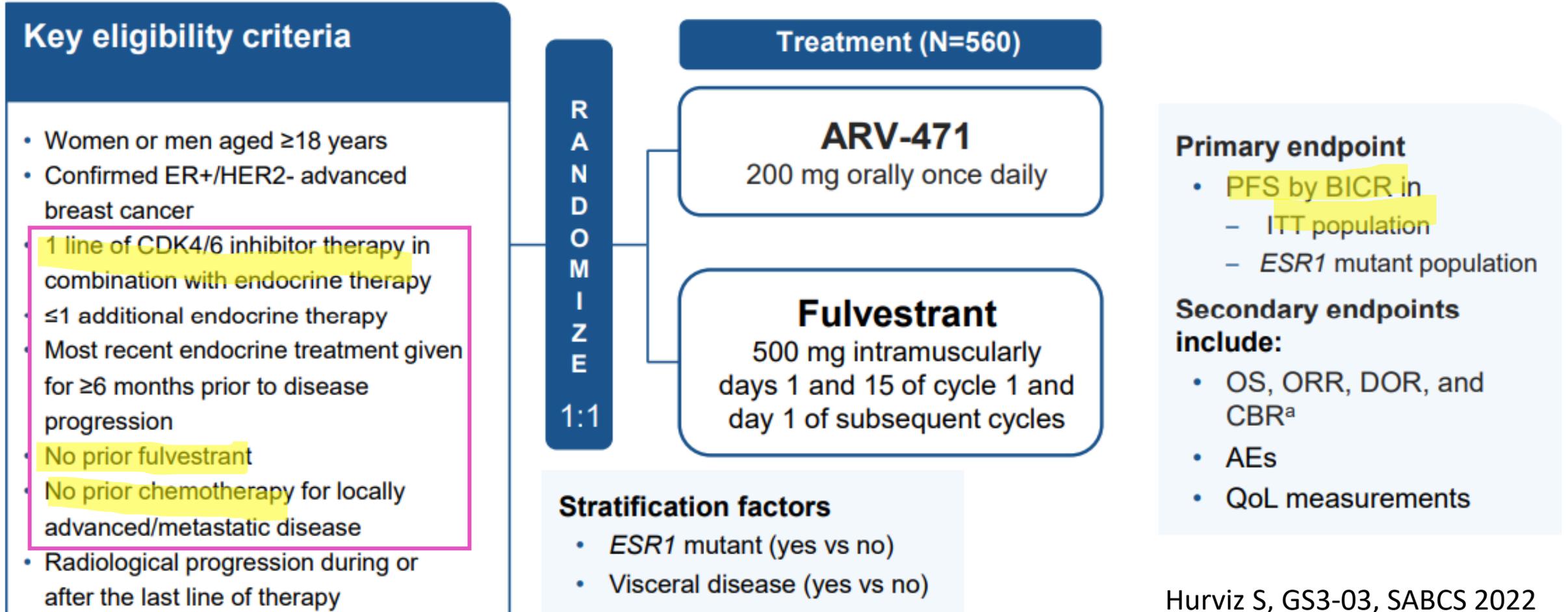
Median ER degradation was 69% (range: 28%–95%)

Is the dose well selected?
How to explain such interpatient heterogeneity?

Discussant: Fabrice André



Phase 3 VERITAC -2 trial



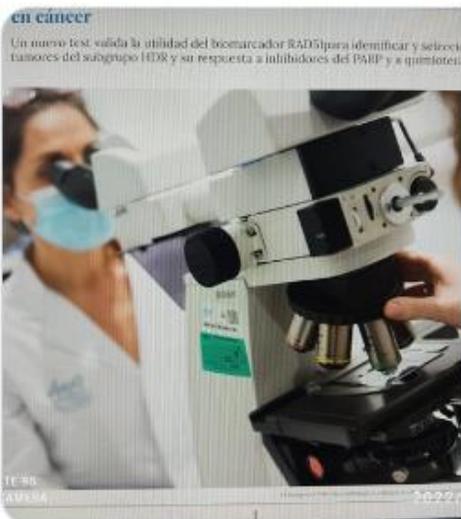
If germline BRCA/PALB2m+:
PARP inhibitor [I, A; MCBS 4;
ESCAT I-A] (d, e)

PARPi sin aprobación en contexto metastático

No hay datos sobre eficacia postCDK

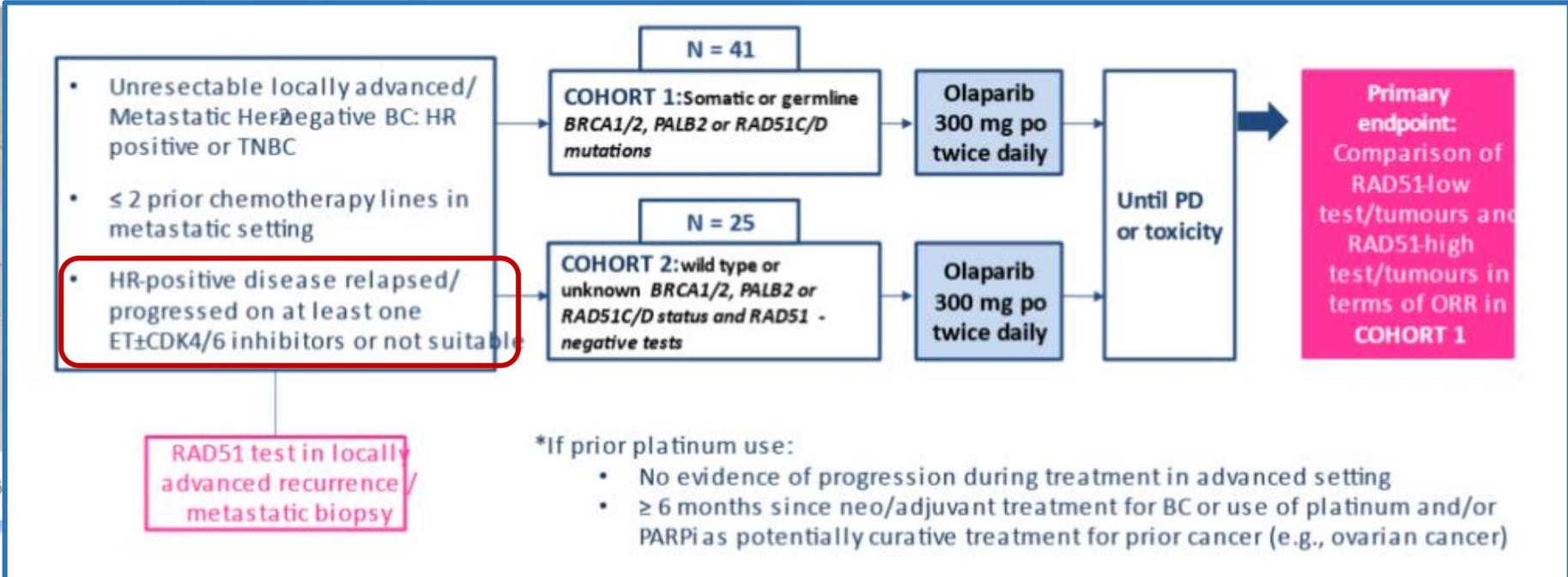


Meritxell Bellet @BelletMeritxell · 18 abr. 2022
 Cómo identificar a l@s pacientes "realmente HDR" que responderán a los inhibidores de PARP?
 Descubre RAD51 y el nuevo estudio de @_SOLTI, RADIOLA. Veeery cool!
 diariomedico.com/medicina/oncol...
 @vserra_elizalde; @judithbalmana; Dra Cristina Cruz; @prat_aleix @VHIO



10 26

En marcha estudio
RADIOLA



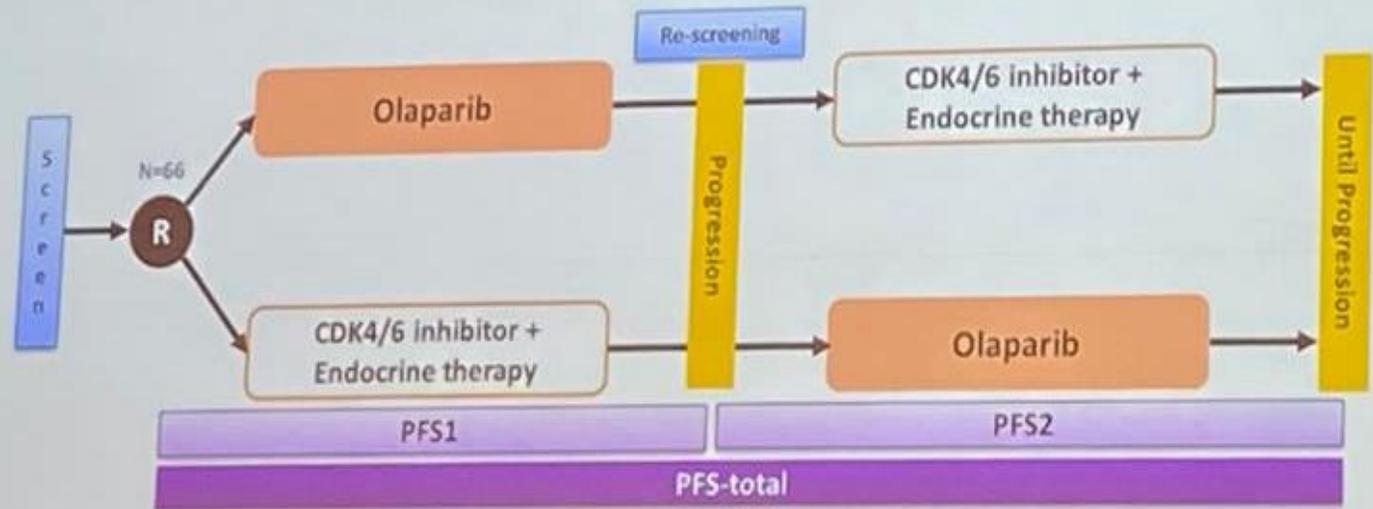
If germline BRCA/PALB2m+:
PARP inhibitor [I, A; MCBS 4;
ESCAT I-A] (d, e)



Propuestas: introducción de PARPi en primera línea.

OPERA trial: KCSG BR21-08

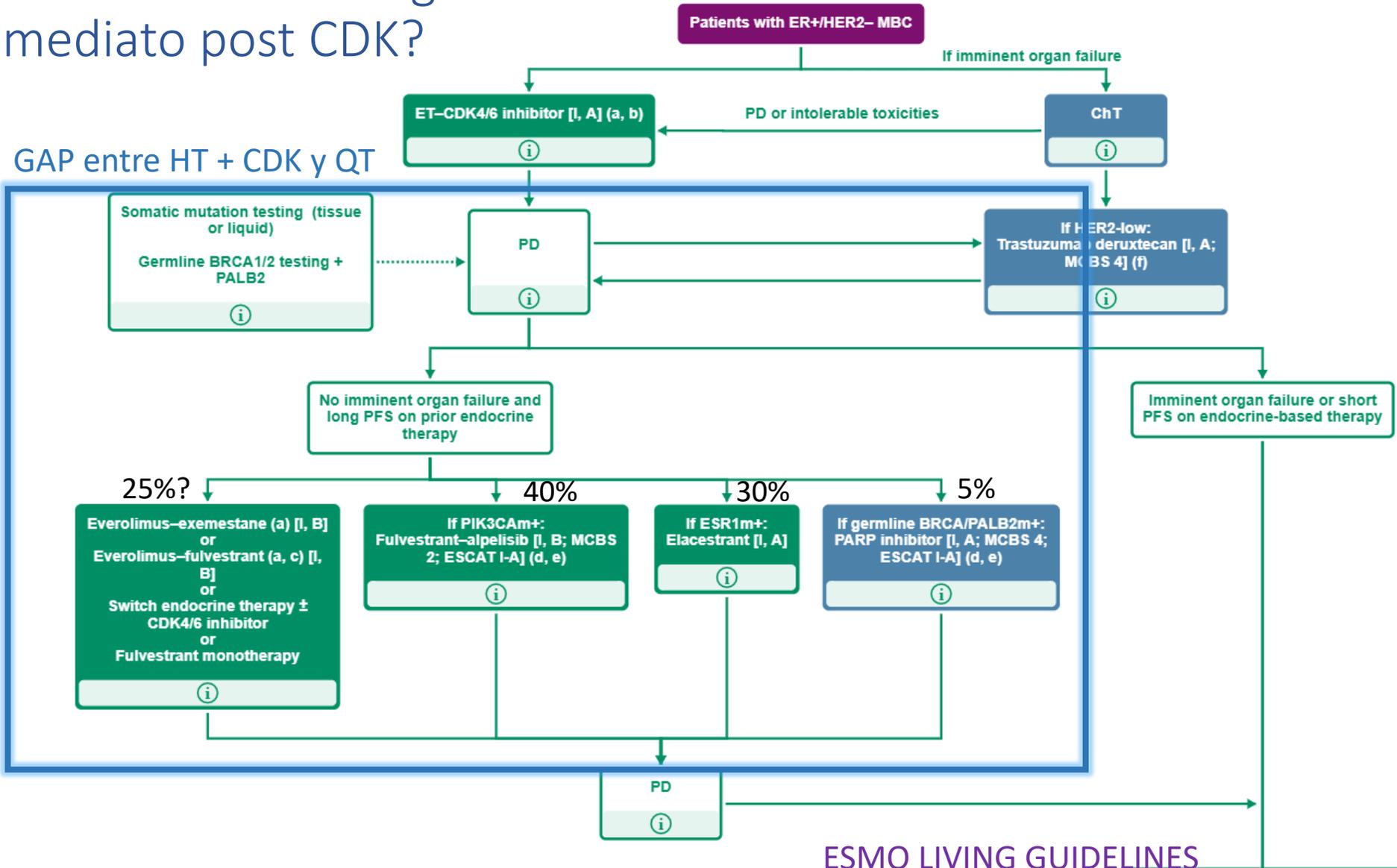
Randomized open-label multicenter phase II trial comparing first-line Olaparib versus CDK4/6i plus endocrine therapy in patients with gBRCAmut-associated HR(+)/HER2(-) recurrent unresectable and/or metastatic breast cancer



PI. Kyong Hwa Park

ESMO BREAST

¿Qué no recogen las ESMO LIVING guidelines en el contexto inmediato post CDK?

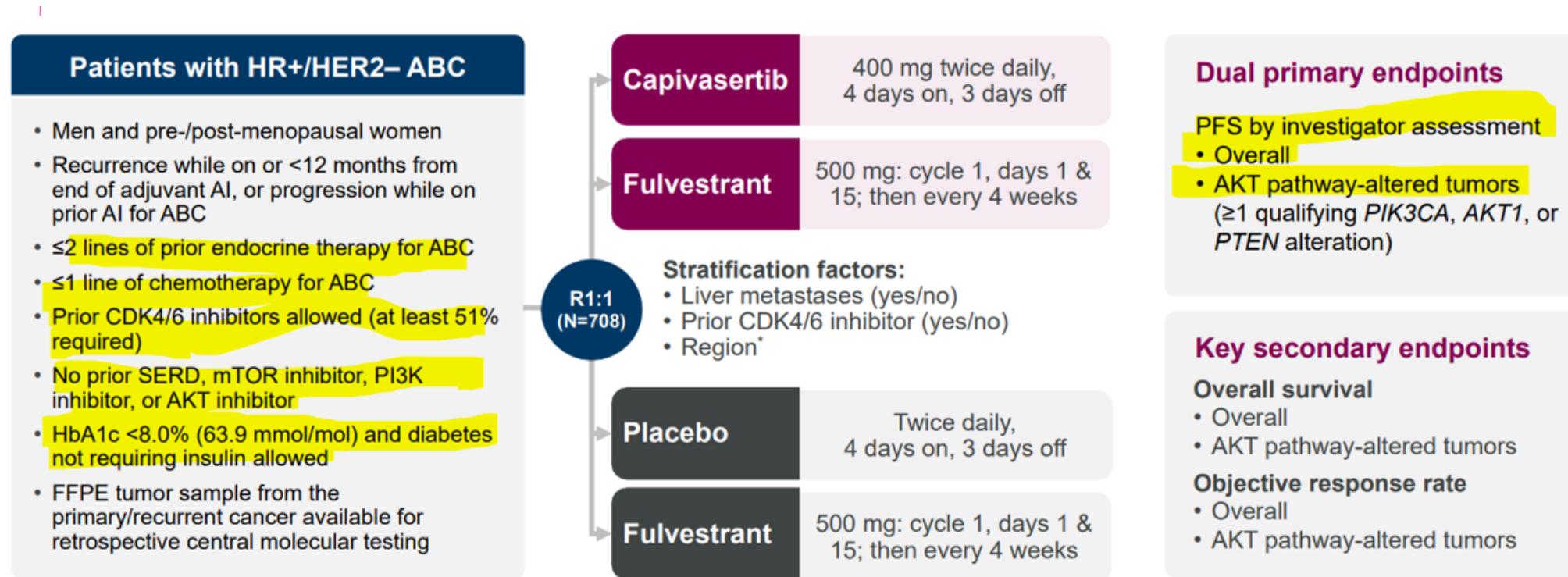


CAPIVASERTIB
(inh de AKT)

¿Qué no recogen las ESMO LIVING guidelines en el contexto inmediato post CDK?

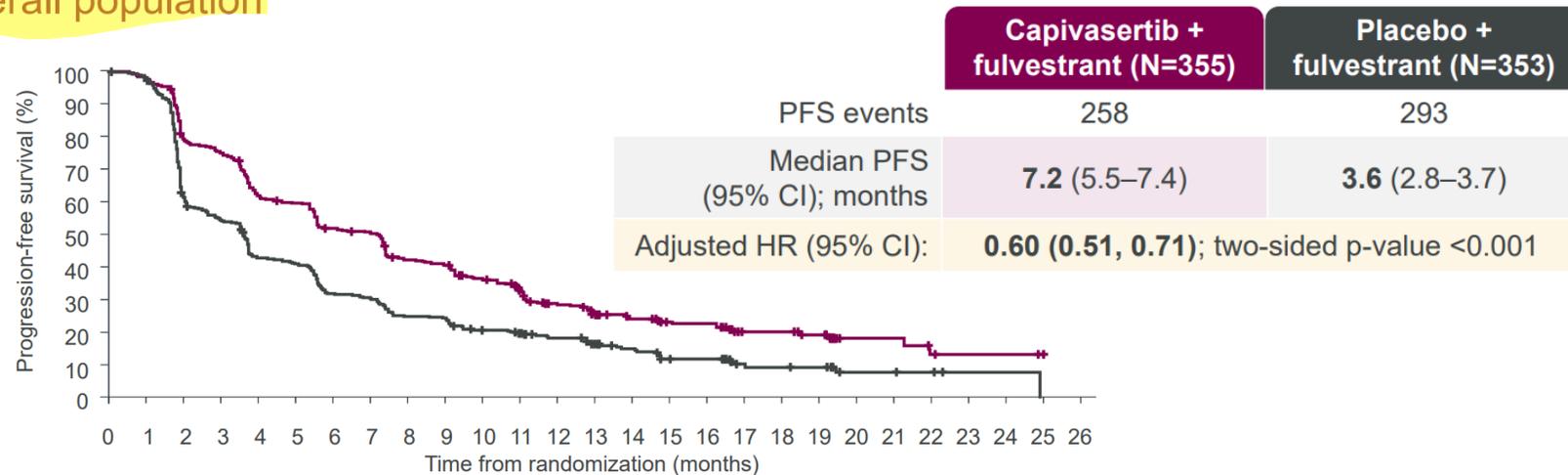
Estudio CAPItello-291

Probablemente porque sólo el 49% de la población había recibido iCDK 4/6 previo

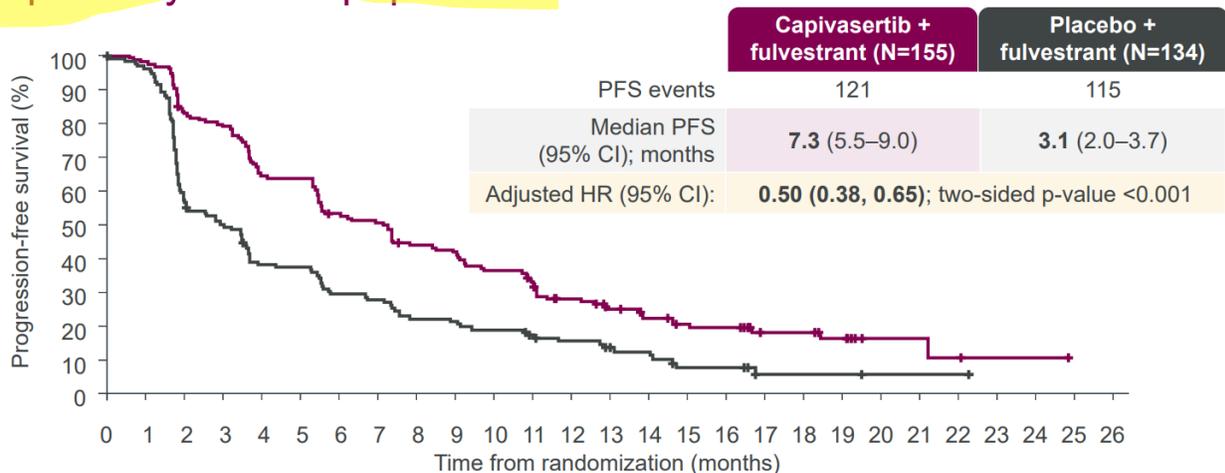


CAPitello-291: PFS

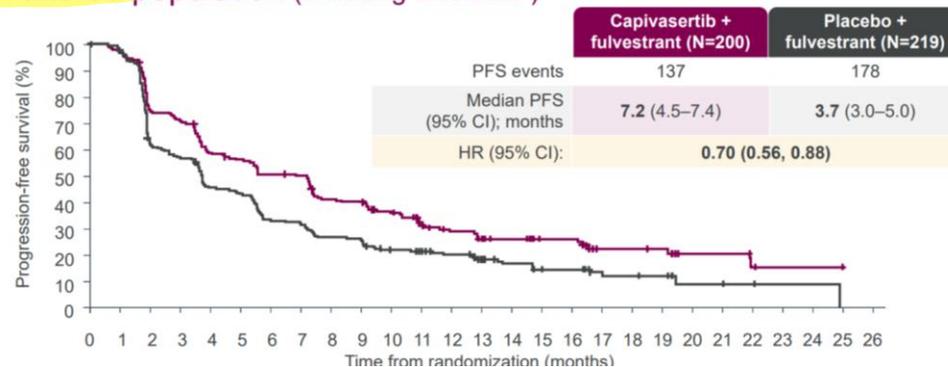
Dual-primary endpoint: Investigator-assessed PFS in the overall population



Dual-primary endpoint: Investigator-assessed PFS in the AKT pathway-altered population

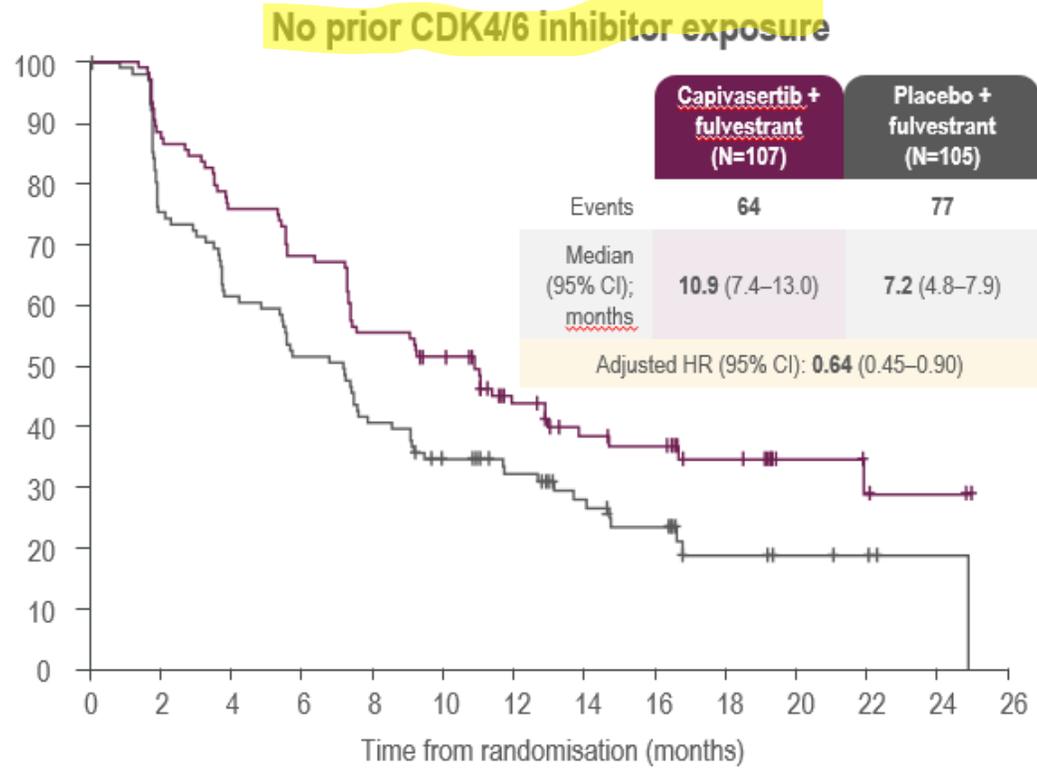
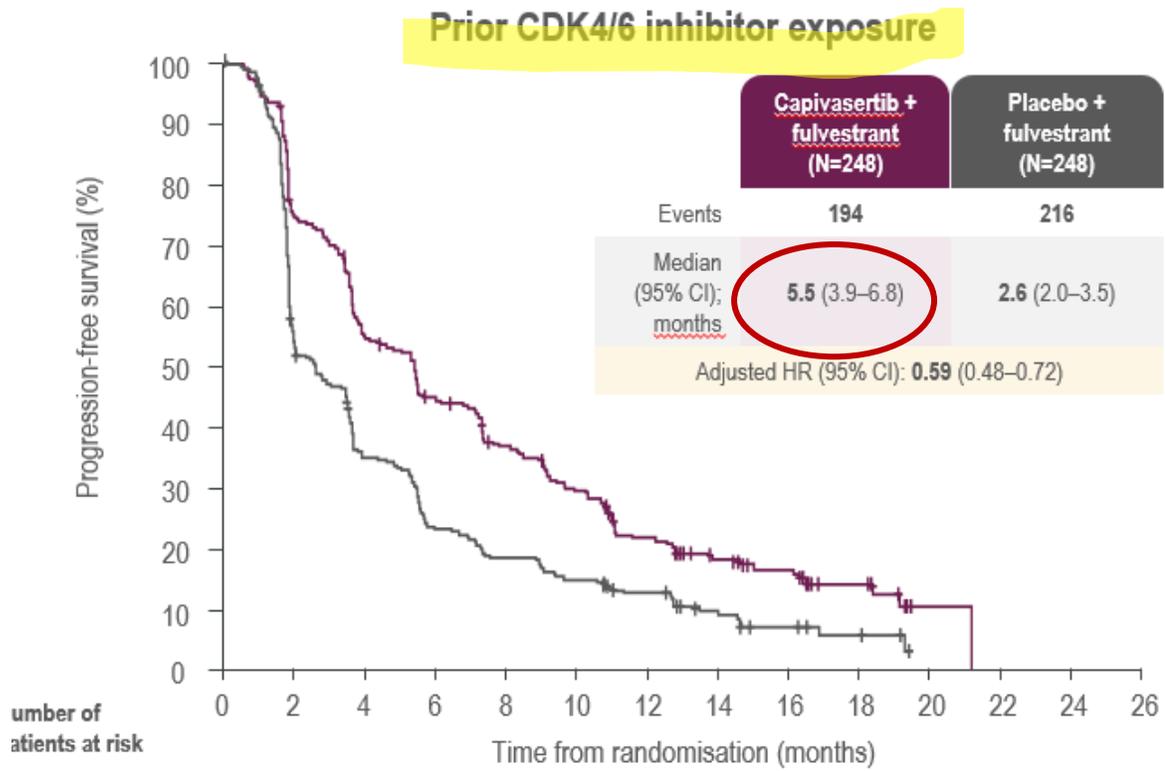


Exploratory analysis: Investigator-assessed PFS in the non-altered population (including unknown†)



PFS by prior CDK4/6 inhibitor (overall population)

In the overall population, consistent clinically meaningful benefit with capivasertib + fulvestrant was observed in patients with and without prior CDK4/6 inhibitor exposure



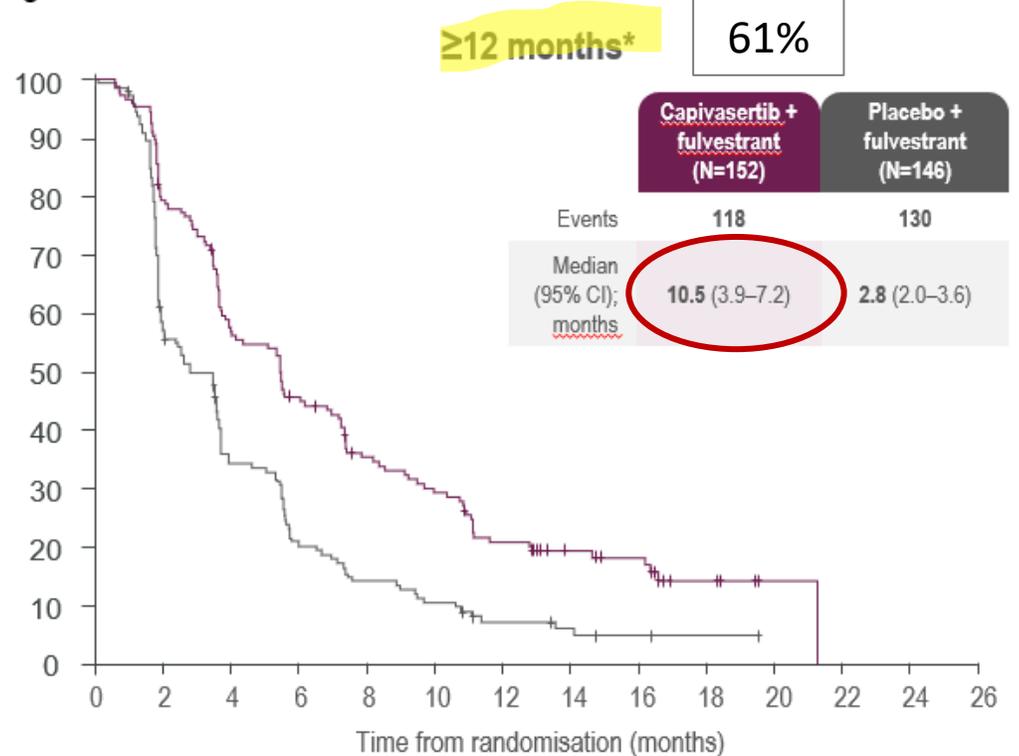
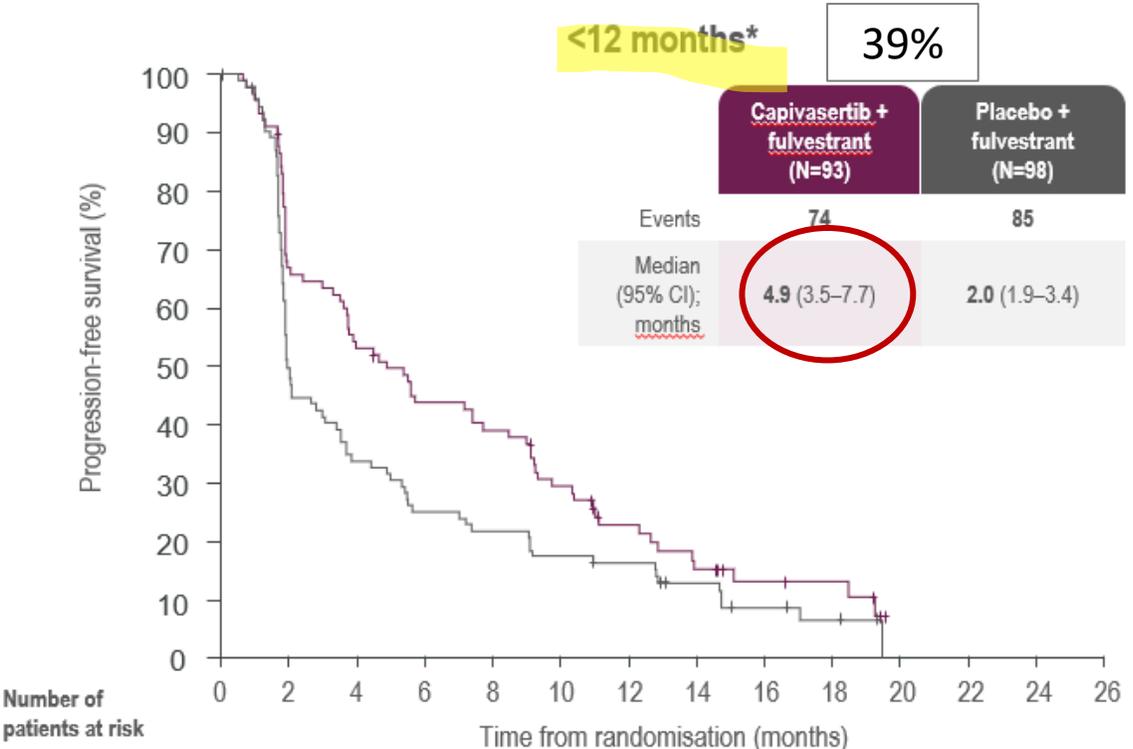
	0	2	4	6	8	10	12	14	16	18	20	22	24	26
Capivasertib + fulvestrant	248	175	129	102	81	64	43	29	21	10	1	0	0	0
Placebo + fulvestrant	248	131	80	54	42	34	25	14	8	4	0	0	0	0

	0	2	4	6	8	10	12	14	16	18	20	22	24	26
Capivasertib + fulvestrant	107	91	78	70	57	51	35	26	22	15	7	5	2	0
Placebo + fulvestrant	105	76	62	52	41	32	26	19	15	7	4	3	1	0

+ indicates a censored observation. HR was estimated using the Cox proportional hazard model stratified by the presence of liver metastases and geographic region. n=22 patients received >1 prior CDK4/6 inhibitor.

PFS by duration of prior CDK4/6 inhibitor (overall population; post-hoc exploratory analyses)

In the overall population, clinically meaningful benefit with capivasertib + fulvestrant was observed in patients regardless of duration of prior CDK4/6 inhibitor therapy in the advanced setting



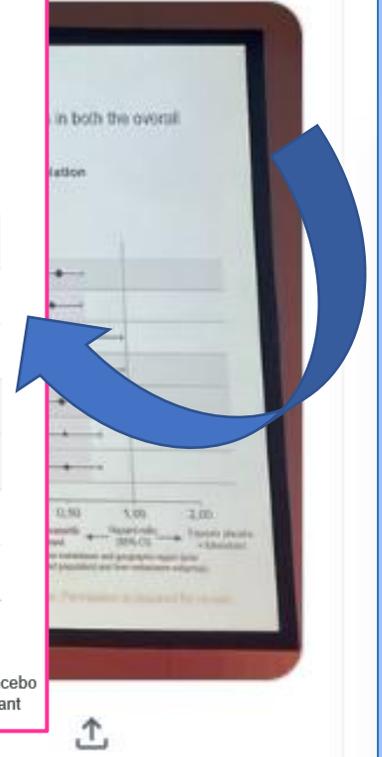
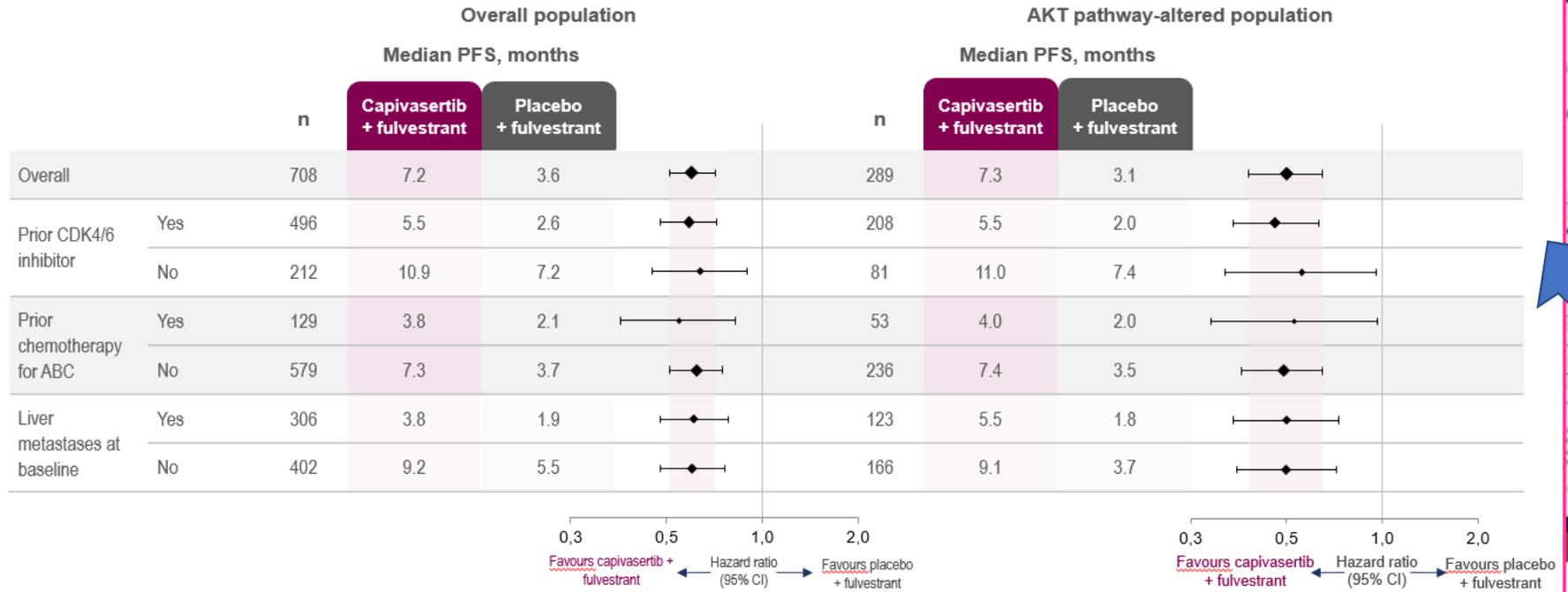


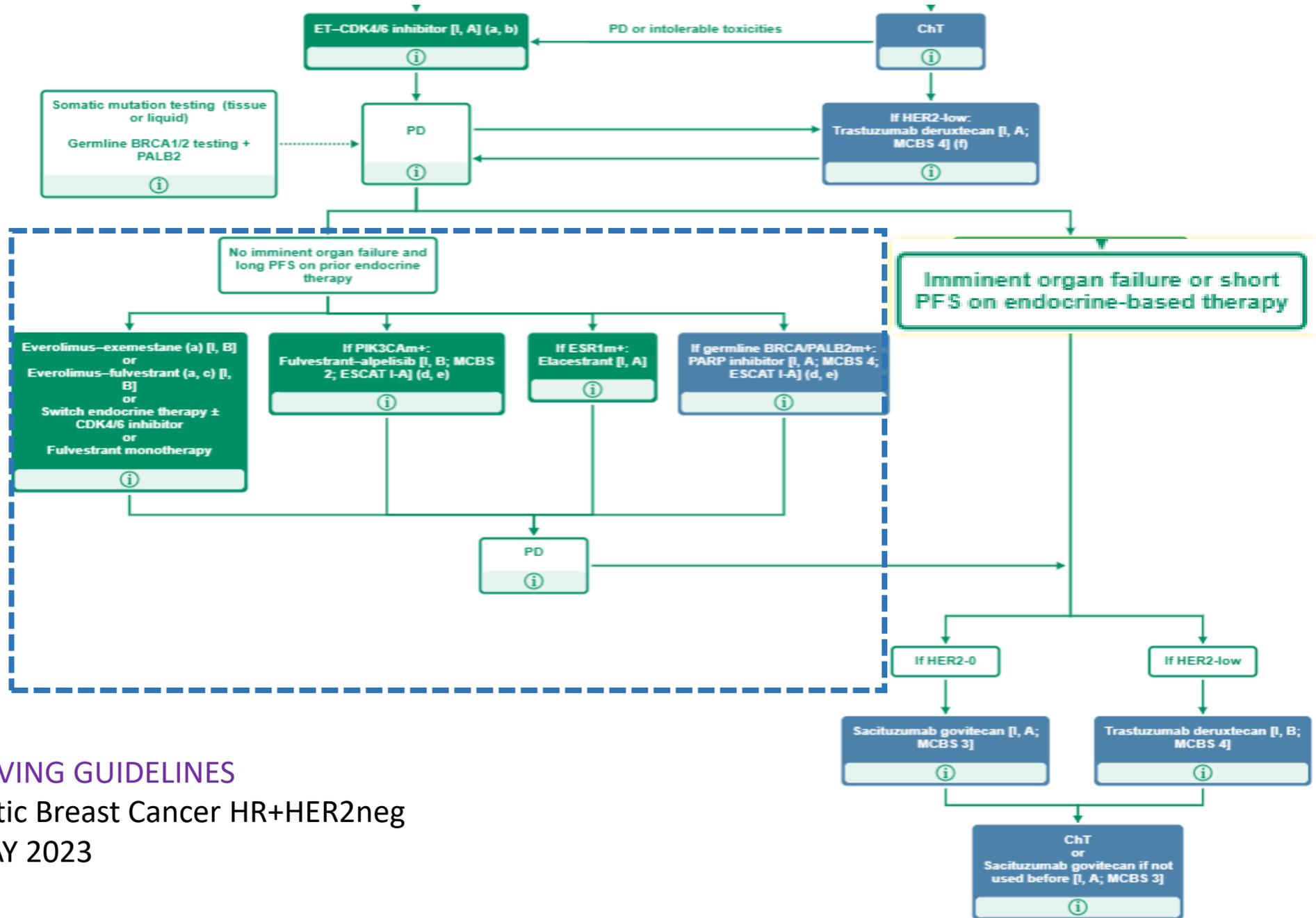
Stephanie Graff, MD, FACP @DrSGraff · 11 May

CAPitello291: **Capivasertib + fulvestrant** improves PFS compared to fulvestrant alone in patients:
 • prev tx w/CDK4/6 inhibitor

Summary of PFS by subgroups

Consistent clinically meaningful benefit with capivasertib + fulvestrant was observed across clinically relevant subgroups in both the overall population and AKT pathway-altered population





ESMO LIVING GUIDELINES

Metastatic Breast Cancer HR+HER2neg

v1.1 MAY 2023

...Y acabamos con la misma pregunta...

- ¿Qué cree menos importante en la valoración de tratamiento para un/una paciente cuya enfermedad progresa a iCDK4/6?
 - Determinación de mutaciones en PIK3CA
 - Determinación de mutaciones germinales en BRCA si hay sospecha razonable
 - Valoración de la PFS durante el tto con iCDK4/6, de la agresividad de la enfermedad actual y de las preferencias del/de la paciente
 - Valoración de todas las alteraciones en las alteraciones en la vía AKT (PIK3CA, PTEN y AKT)
 - Valoración del estado mutacional de *ESR1* en plasma en el momento de la progresión
 - No creo que haya una menos importante

Gracias por vuestra atención,
(presencial o virtual)

<https://twitter.com/PTarantinoMD/status/1640698971147448320?t=qaN1h9XkjHtZ0oqT7-JOvg&s=08>

And thank you,
Paolo!!

← Tweet

 Paolo Tarantino
@PTarantinoMD

Elacestrant, alpelisib, capivasertib, everolimus, ribo maintenance. A rapidly expanding arsenal to fill the critical gap between CDK4/6-inh and chemo. Check our latest open access review, led by @abhenilmittal, for a deep dive into this evolving landscape!
mdpi.com/2072-6694/15/7...
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 **cancers**
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Filling the Gap after CDK4/6 Inhibitors: Novel Endocrine and Biologic Treatment Options for Metastatic Hormone Receptor Positive Breast Cancer

Abhenil Mittal; Consolacion Molto Valiente; Faris Tamimi; Ilana Schlam; Sarah Sammons; Sara M. Tolaney; Paolo Tarantino

Cancers 2023, Volume 15, Issue 7, 2015

 Abhenil Mittal y 4 más

2:54 p. m. · 28 mar. 2023 · **21,3 mil** Reproducciones

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