



**UNIVERSITY
OF UDINE**
hic sunt futura



The **Liquid biopsy**
Research Team

Liquid biopsy and breast cancer

A role that is being defined?

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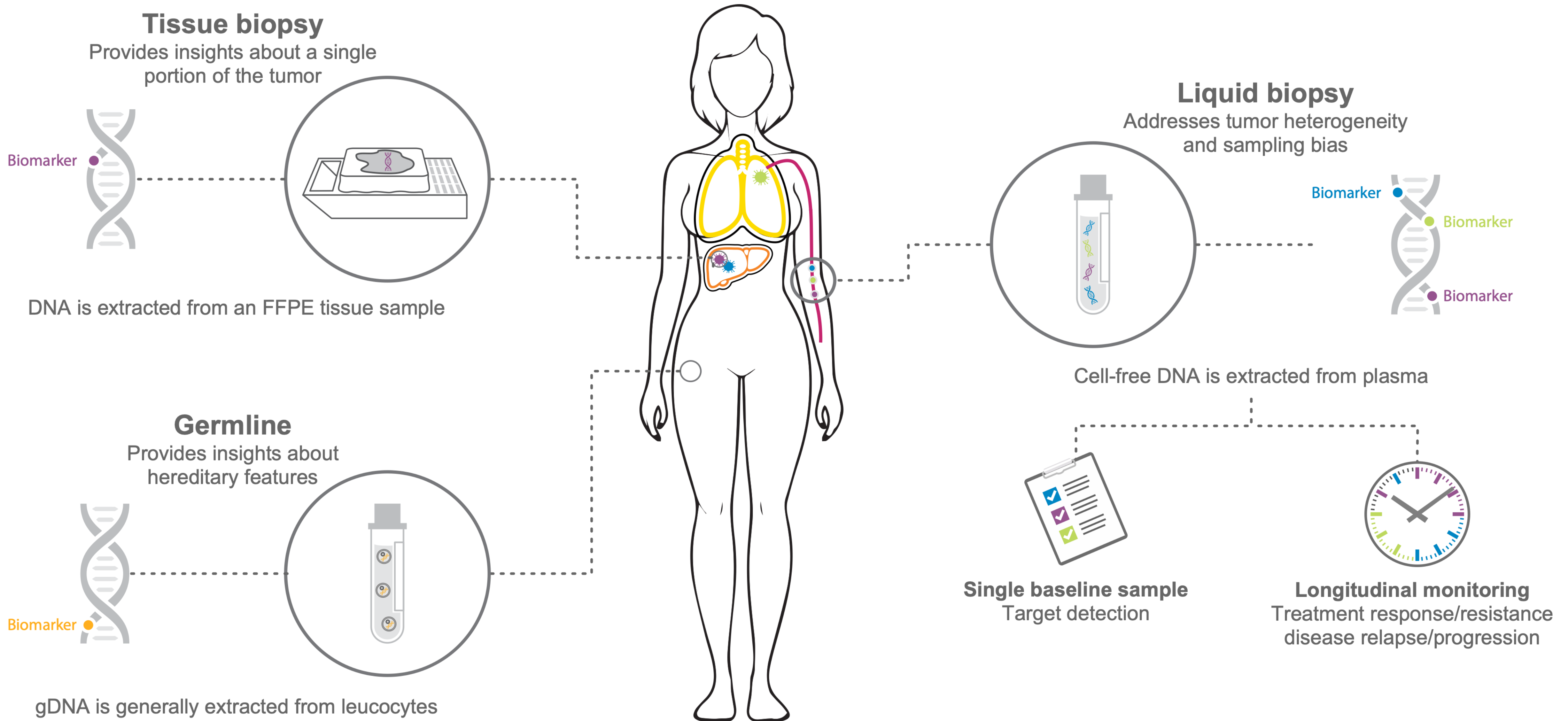
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The right tool for the right question

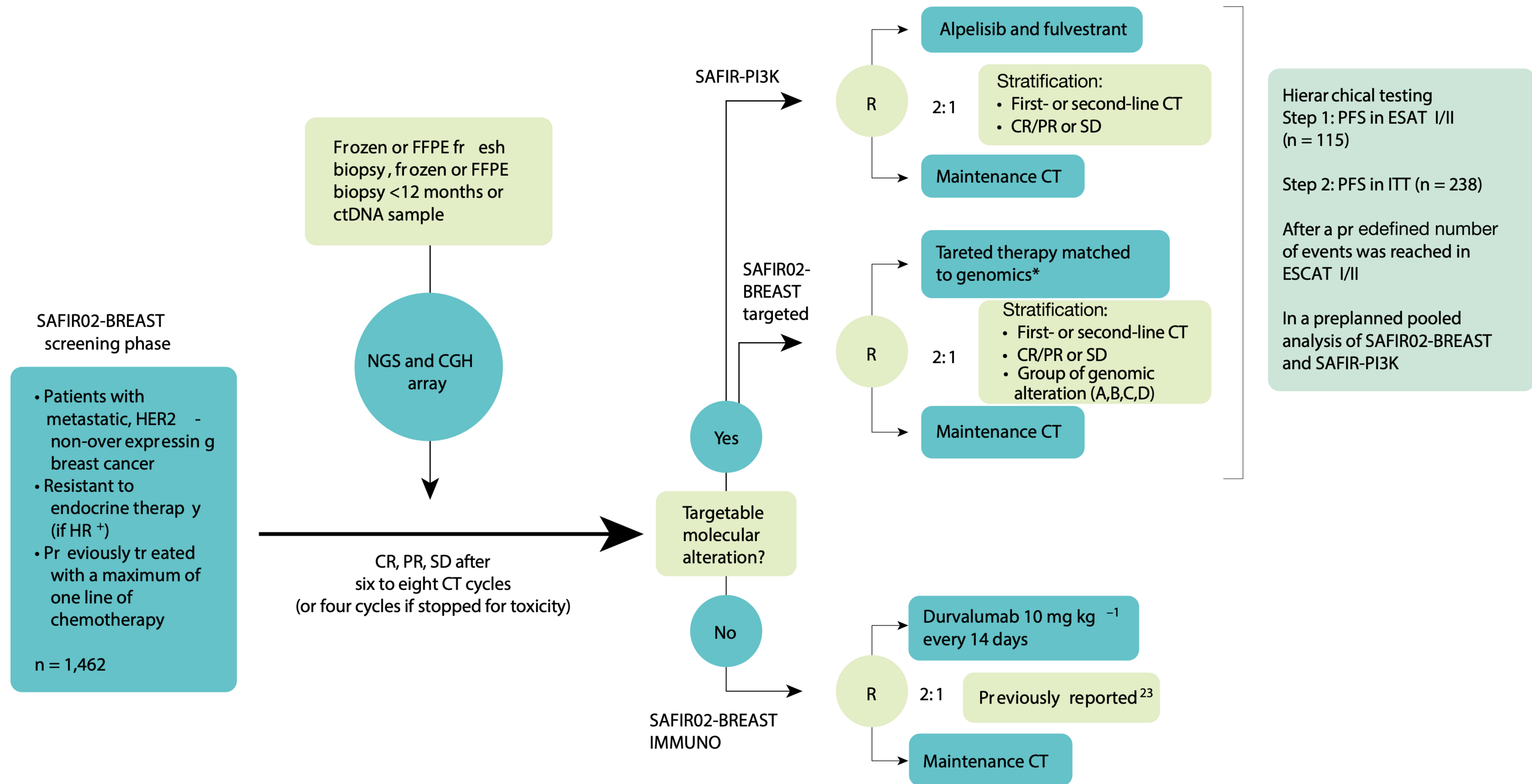
Tissue vs liquid vs germline



What's the role for ctDNA in MBC? **SAFIR02**

What's the role for ctDNA in BC?

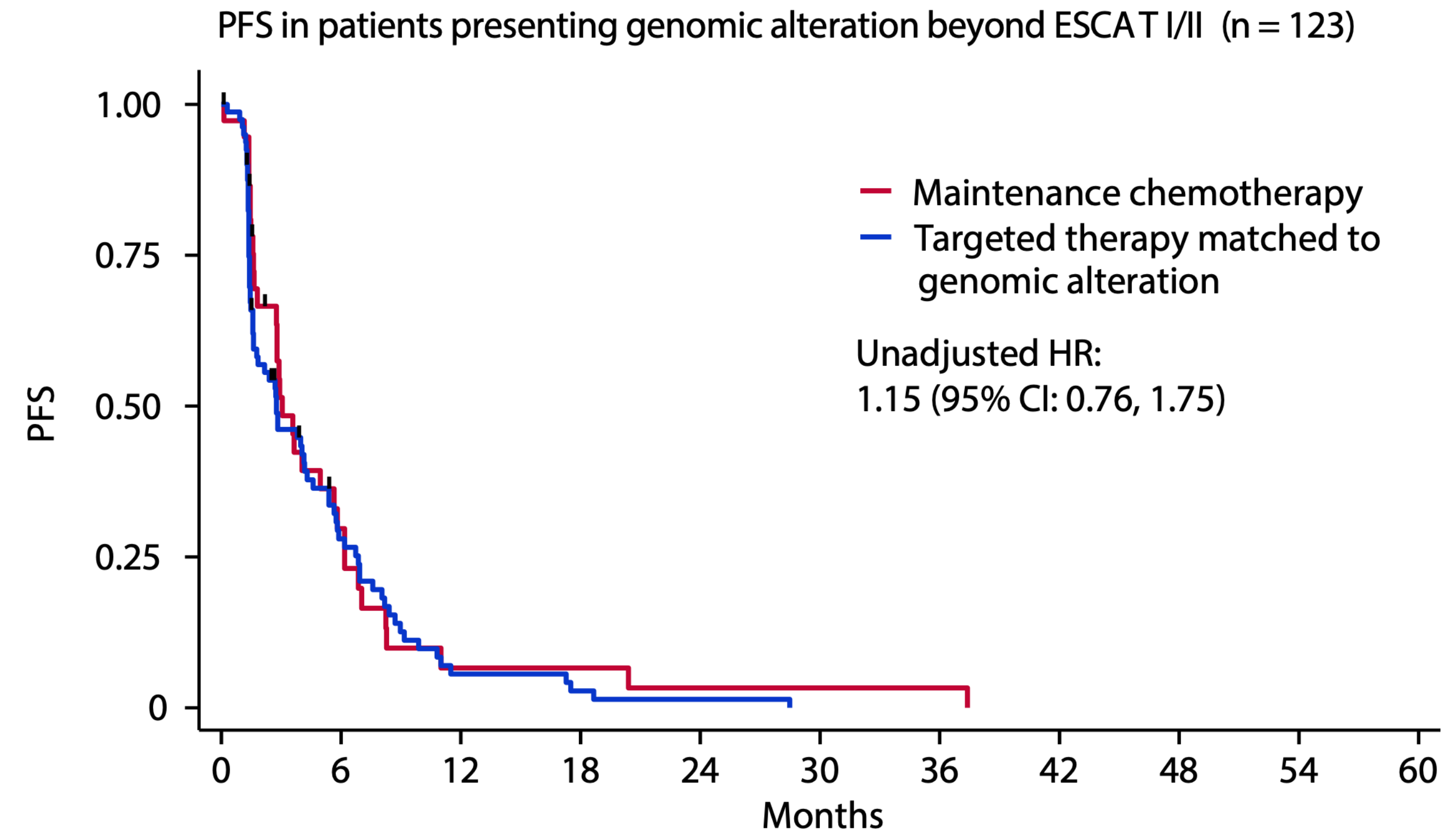
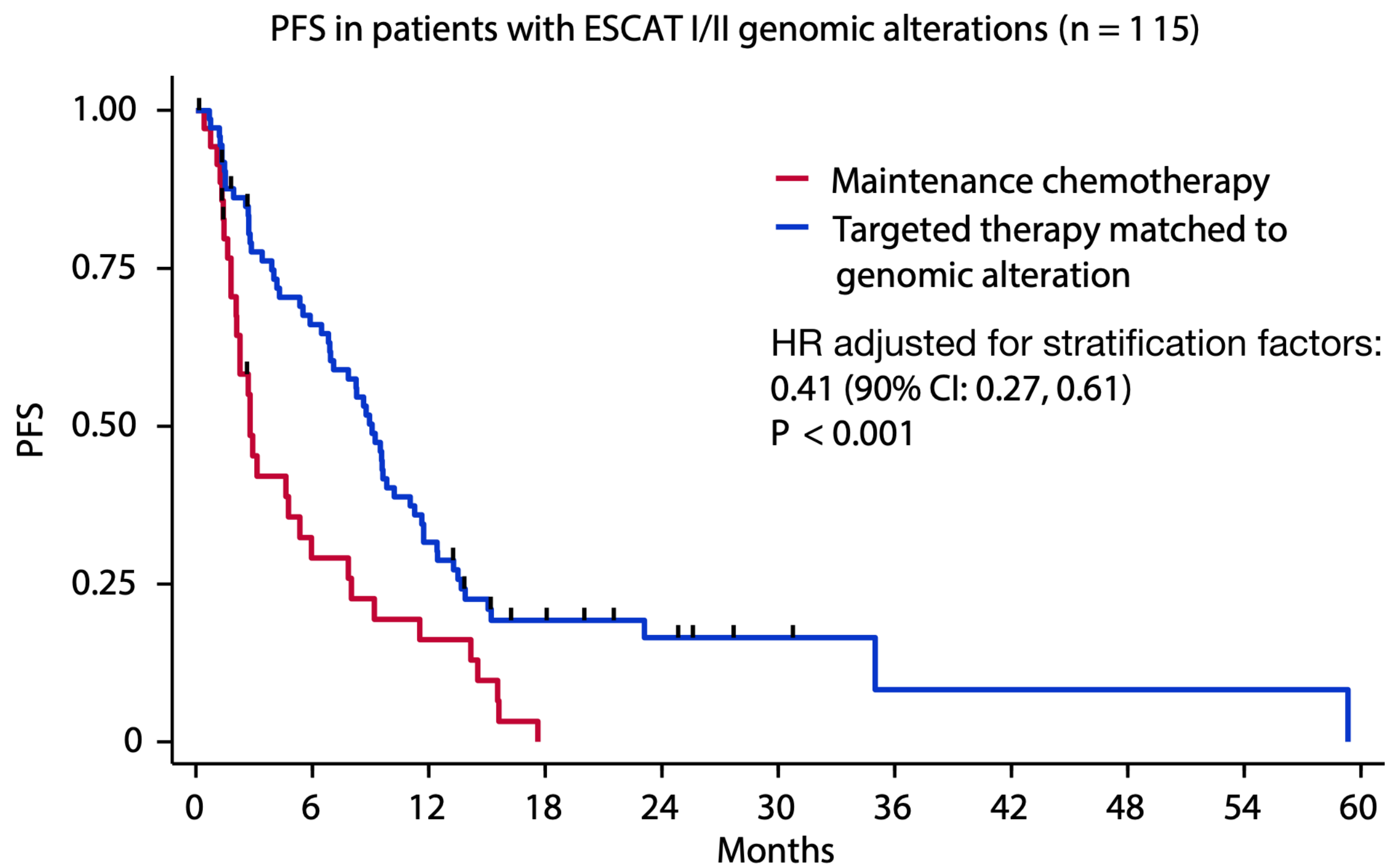
Genomics to select treatment for patients with metastatic breast cancer



*olaparib, capivasertib, vistusertib, AZD8931, vandetanib, bicalutamide, AZD4547, selumetinib

Genomics to select treatment for patients with MBC

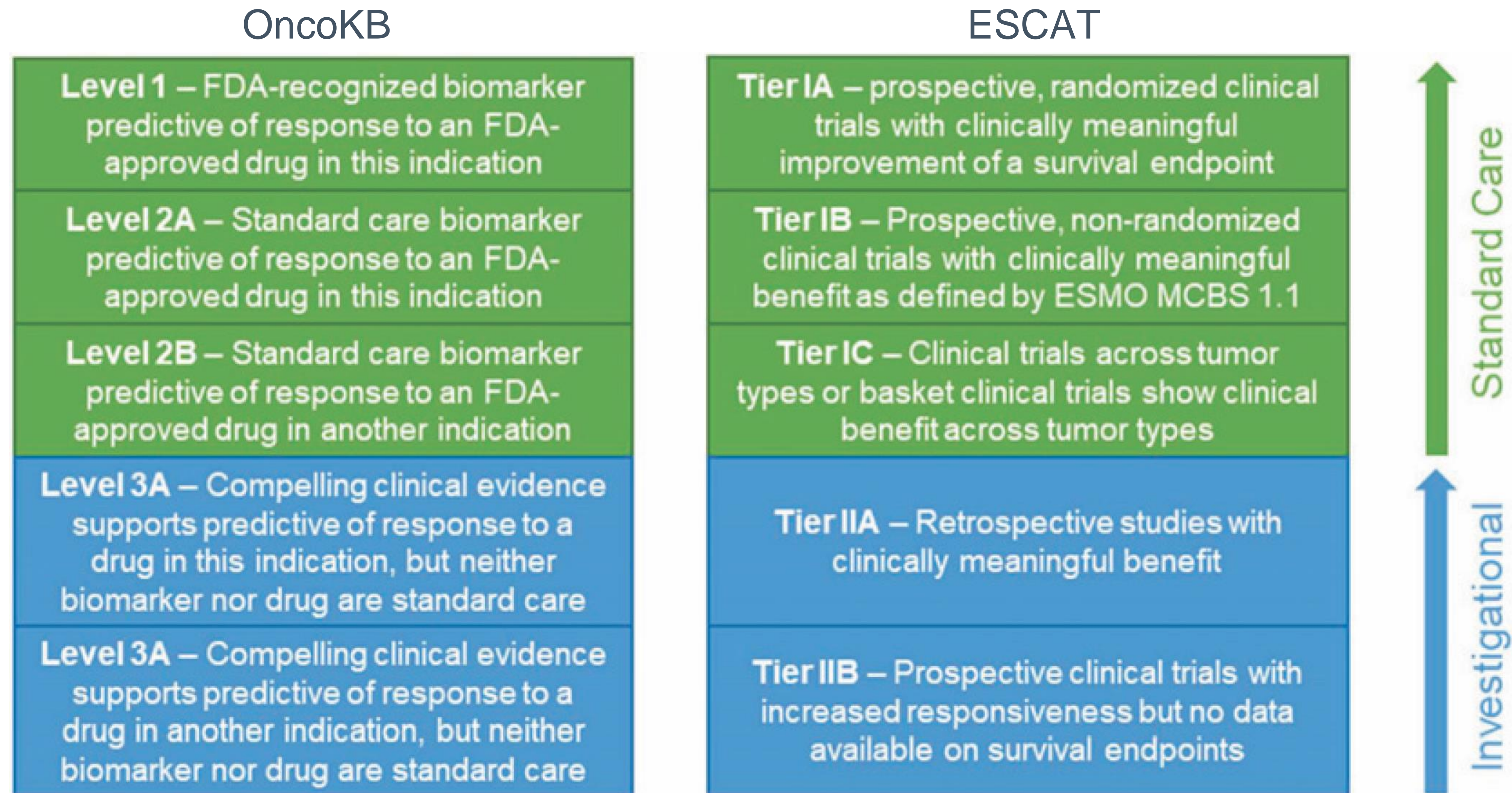
 PFS according to ESCAT classification



Is this really **unexpected**?

How to translate all of this to the clinic?

 The ESCAT classification



How to translate all of this to the clinic?

 The ESCAT classification

OncoKB

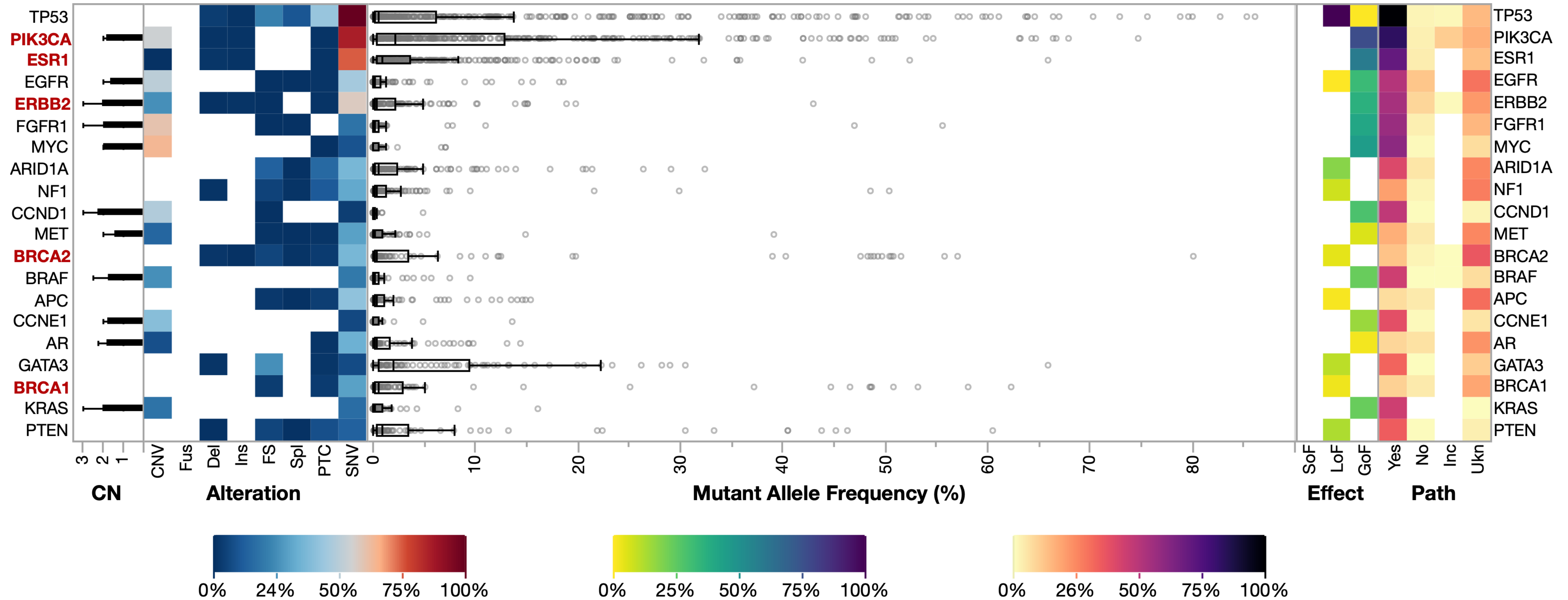
ESCAT



Do we have any ESCAT tier I/II in **breast cancer**?

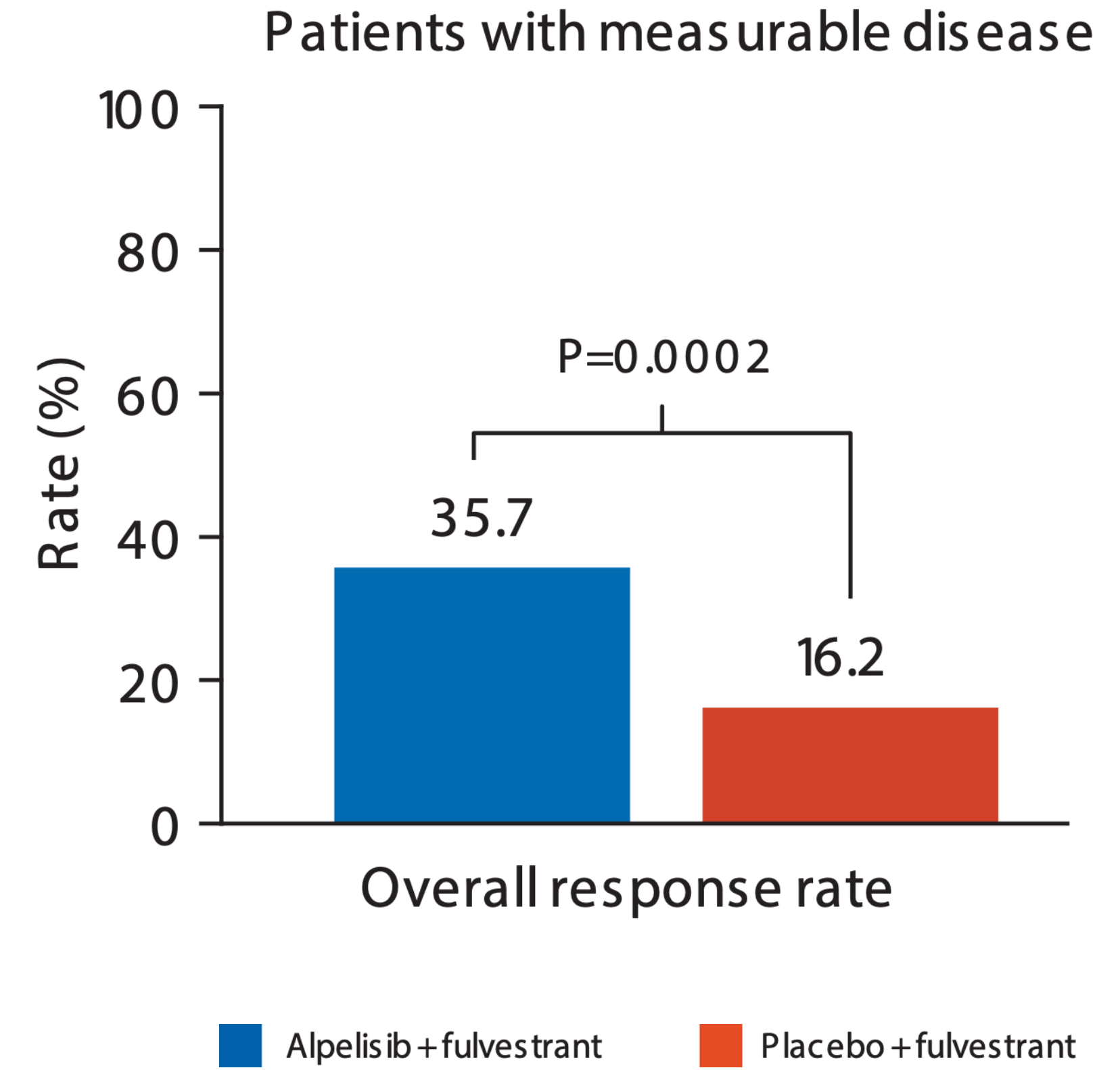
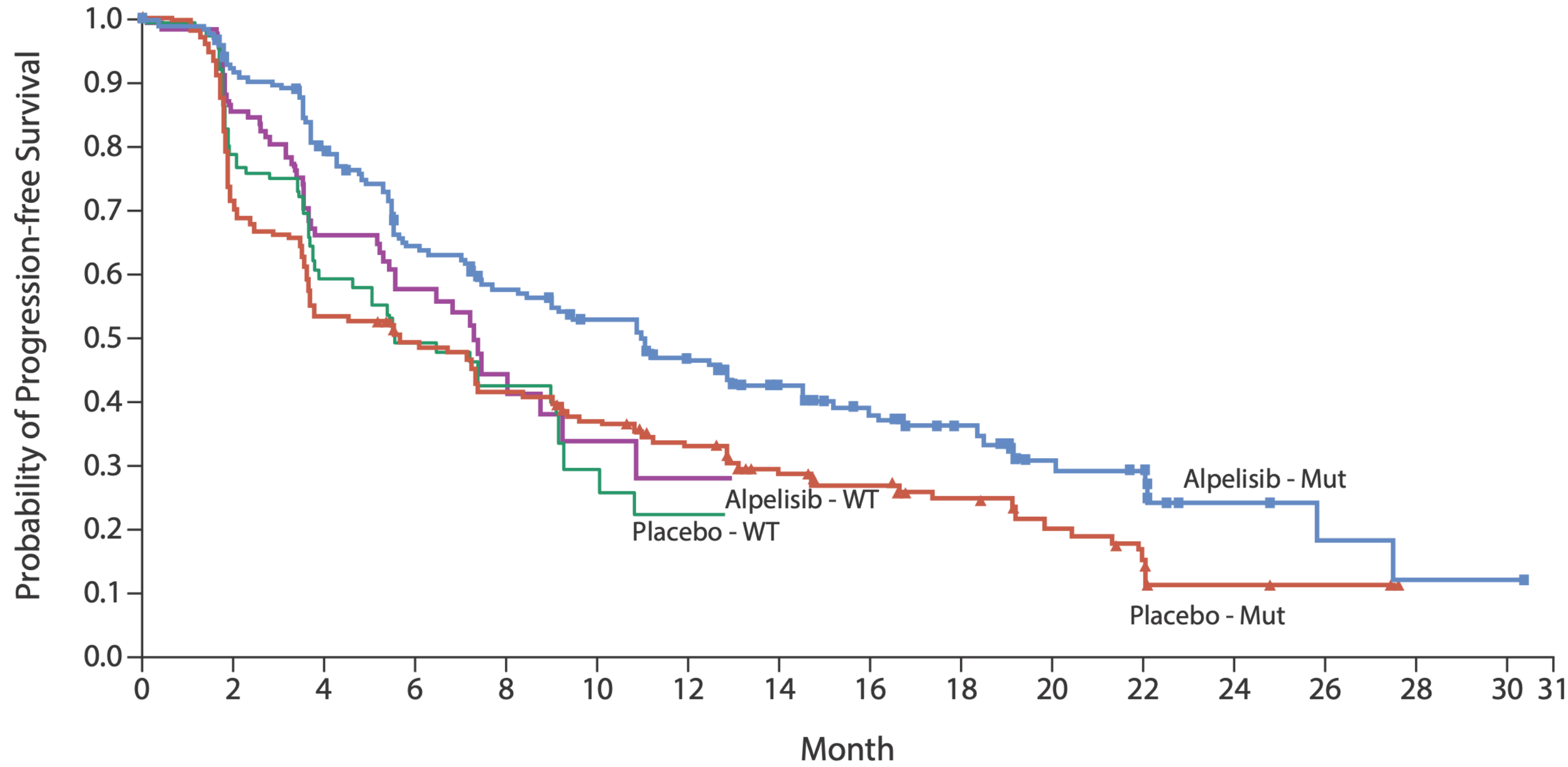
Do we have any ESCAT tier I/II in breast cancer?

Apparently all over the place



The SOLAR-1 trial

Treatment response and PIK3CA mutation

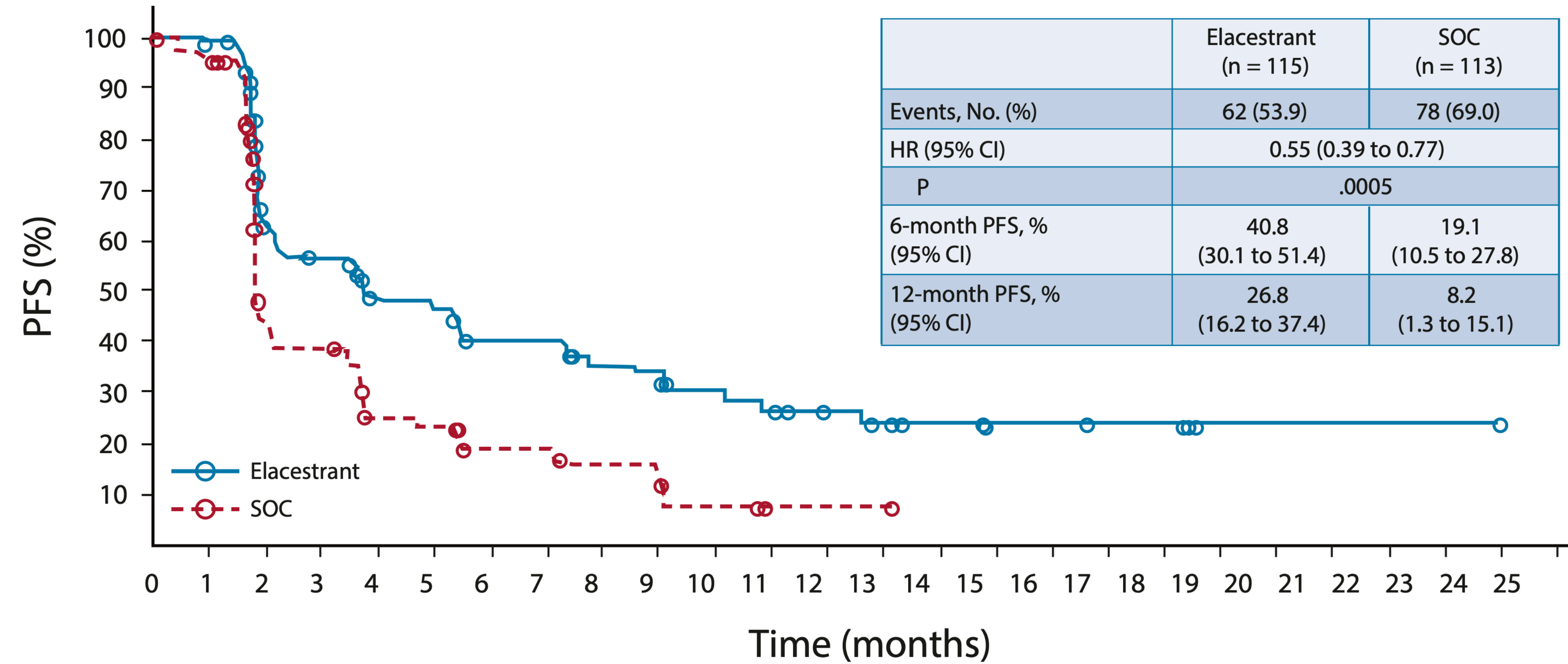


No. at Risk	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	31
Alpelisib - Mut	169	145	123	97	85	75	62	50	39	30	17	14	5	3	1	1	0
Placebo - Mut	172	120	89	80	67	58	48	37	29	20	14	9	3	2	0	0	0
Alpelisib - WT	115	86	48	31	14	7	3	0									
Placebo - WT	116	79	43	31	20	8	1	0									

From resistance to selection: **a new life** for *ESR1*

The Phase III trial EMERALD

Progression Free Survival in the ESR1 mutated subgroup

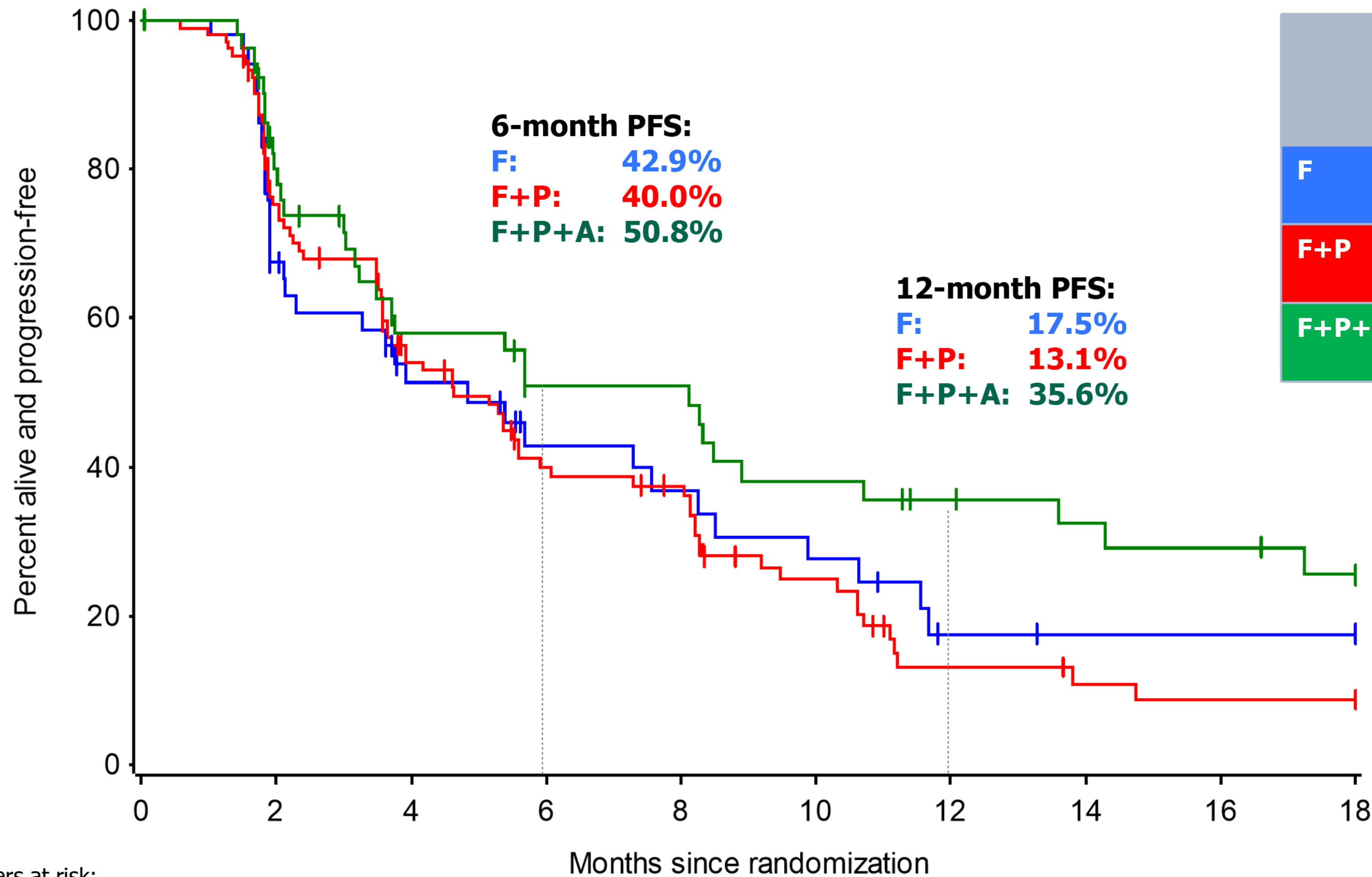


No. at risk:

Elacestrant	115	105	54	46	35	33	26	26	21	20	16	14	11	9	7	5	5	4	4	1	1	1	1	1	0
SOC	113	99	39	34	19	18	12	12	9	9	4	1	1	1	0										

Another unexpected role?

The PACE study: all comers, PFS



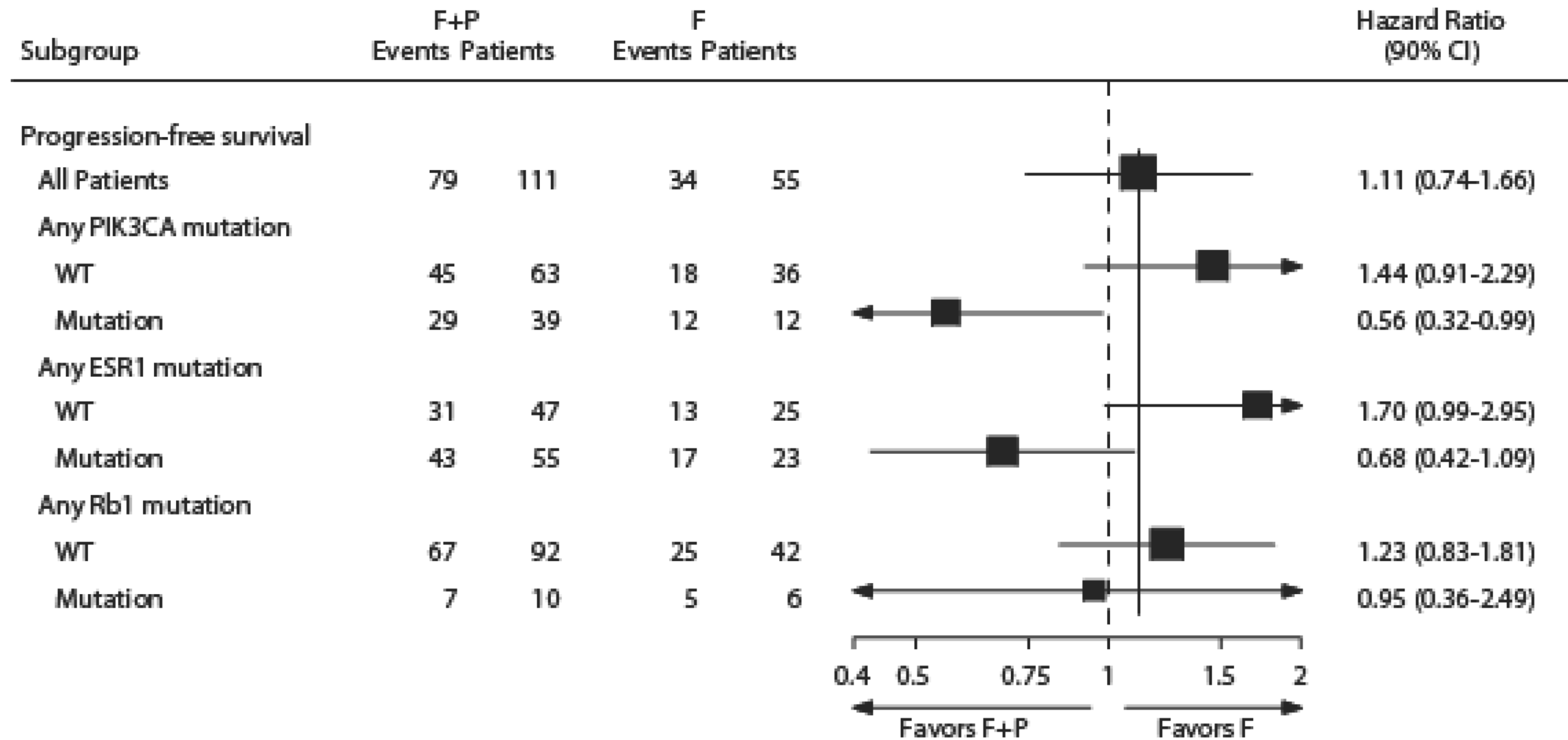
	Pts	PFS Events	Median PFS, mo (90% CI)	HR vs F (90% CI)	P-value
F	55	34	4.8 (2.1, 8.2)	--	--
F+P	111	79	4.6 (3.6, 5.9)	1.11 (0.74-1.66)	P=0.62
F+P+A	54	35	8.1 (3.2, 10.7)	0.75 (0.47-1.20)	P=0.23

Numbers at risk:

	0	2	4	6	8	10	12	14	16	18
F	55	31	20	14	12	9	4	3	3	3
F+P	111	73	48	32	28	16	7	5	4	4
F+P+A	54	38	25	20	20	15	12	10	9	7

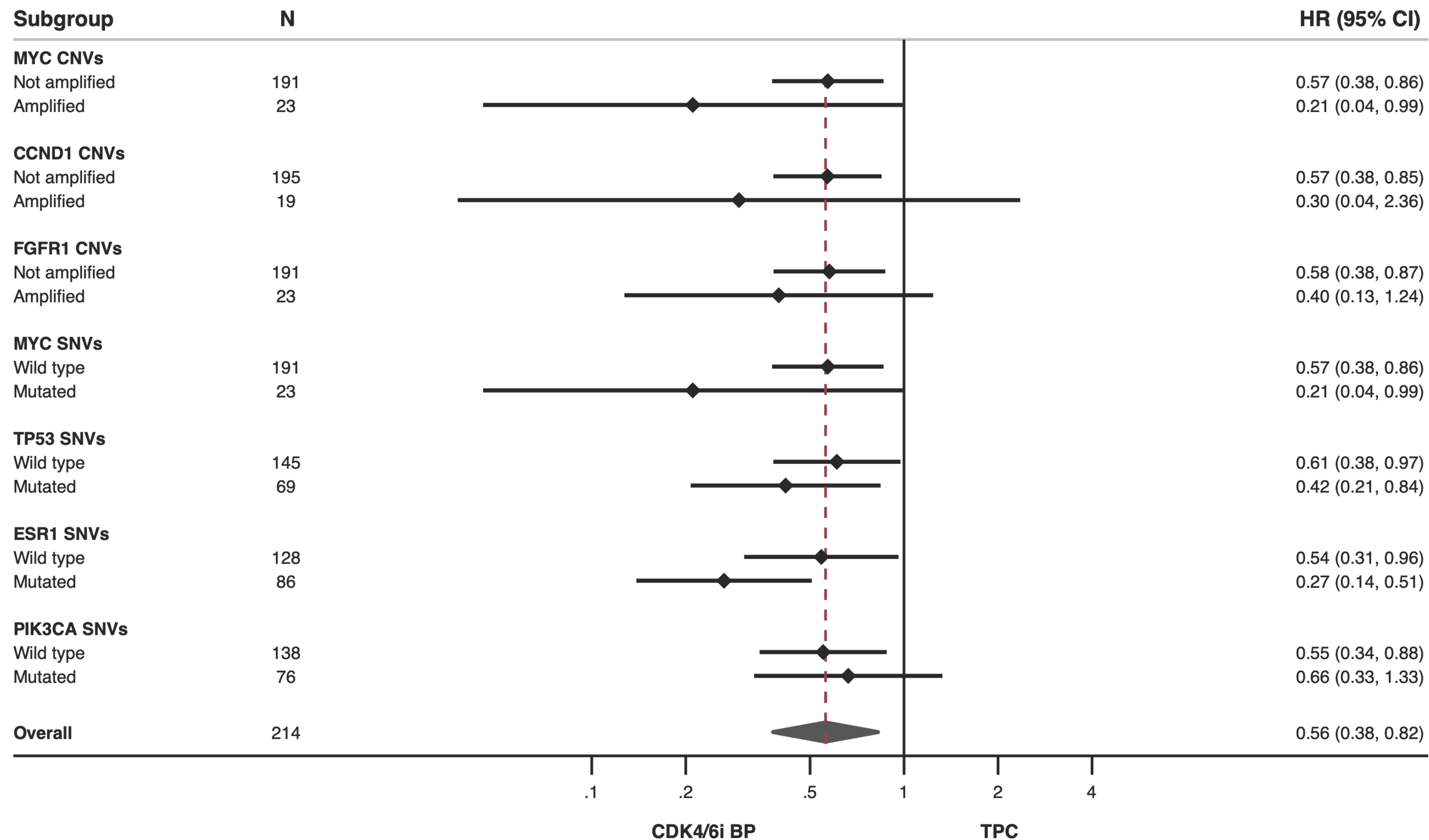
The PACE study

Subgroup analysis according to PIK3CA, ESR1 and RB1 status



What about real world practice?

CDK4/6i beyond progression: subgroup analysis, PFS

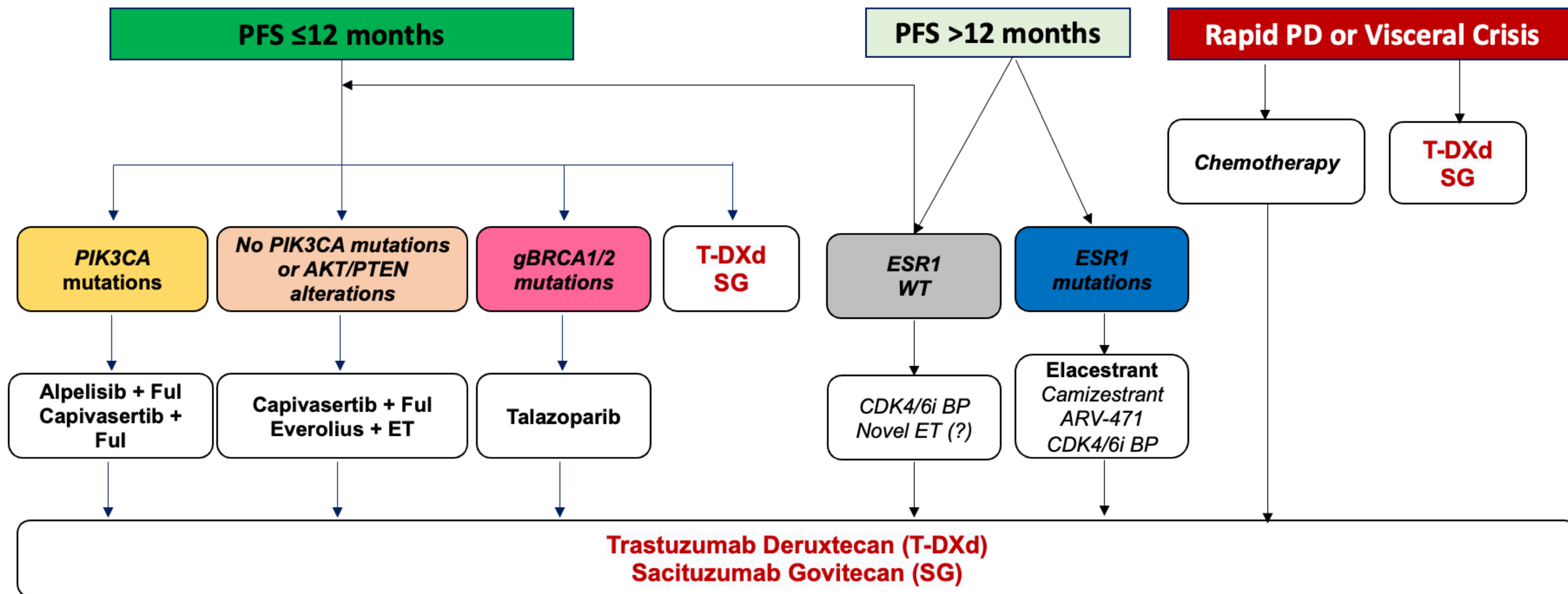


Can we leverage these data tomorrow?

Putting together all available evidence

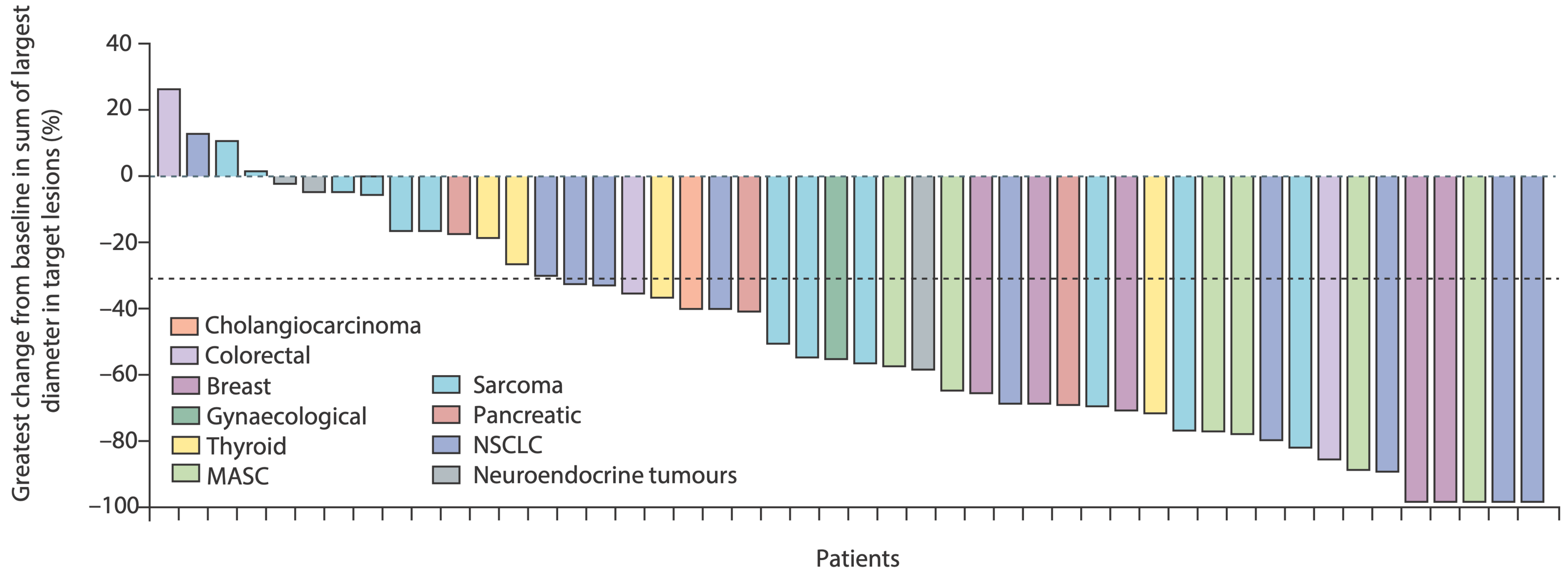
Progression on first-line endocrine therapy + CDK4/6 inhibitor

Status evaluation of *PIK3CA* (\pm PI3K pathway components), *gBRCA1/2*, *ESR1*



Is the future histotype agnostic?

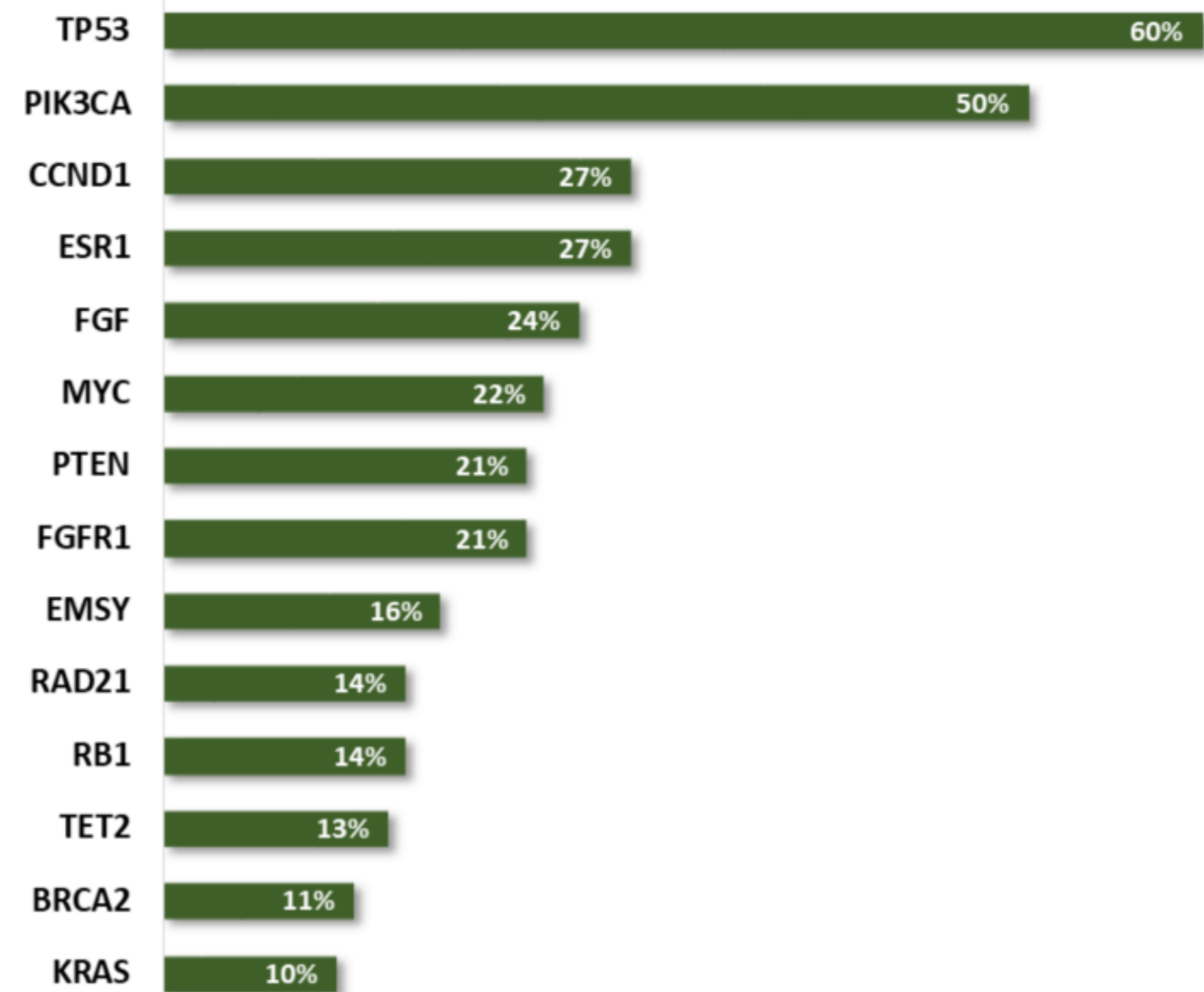
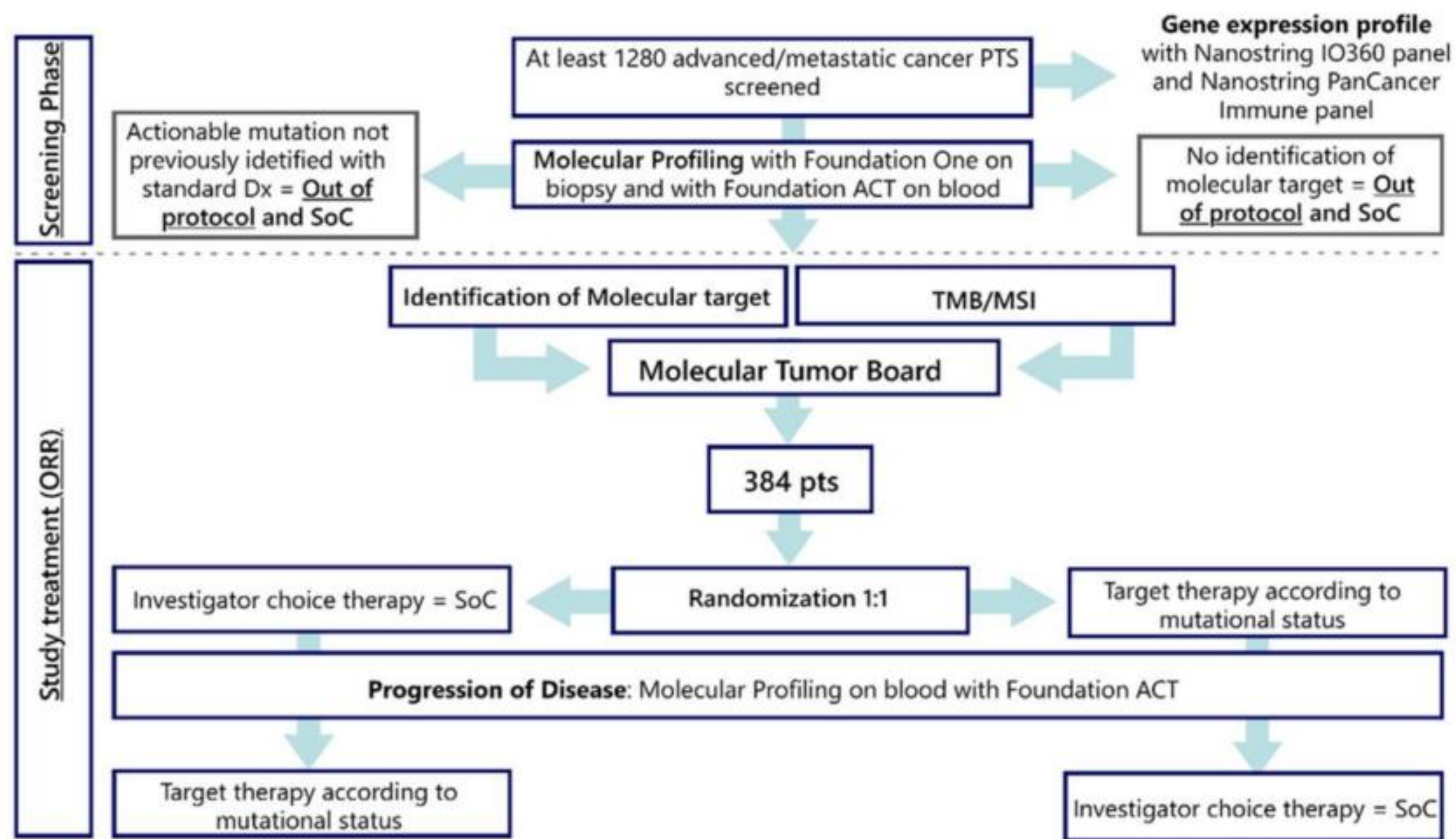
 The NTRK story: Entrectinib



Looking at the big picture: **extended profiling**

An Italian Twist

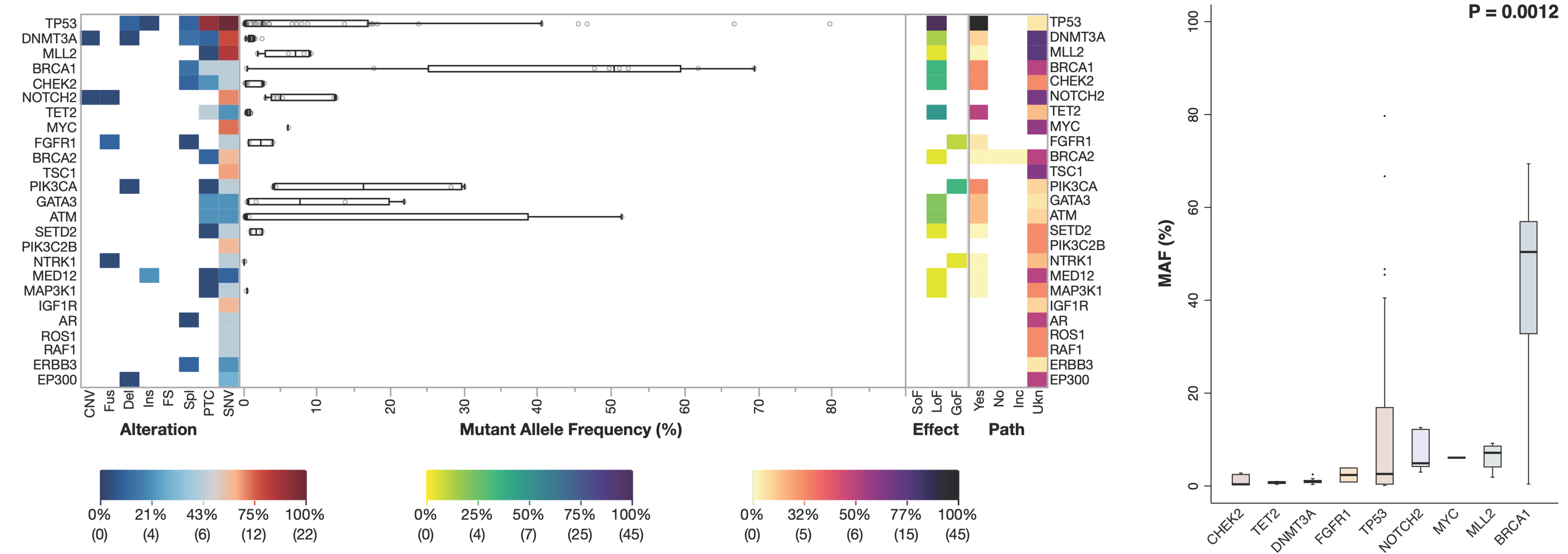
The Rome Trial



The Rome Trial is a randomized phase II trial (NCT04591431). The aim is to evaluate efficacy and safety of a tailored treatment compared to standard of care (SoC in patients with solid tumors)

The complex and nuanced landscape of GIM25-CAPT

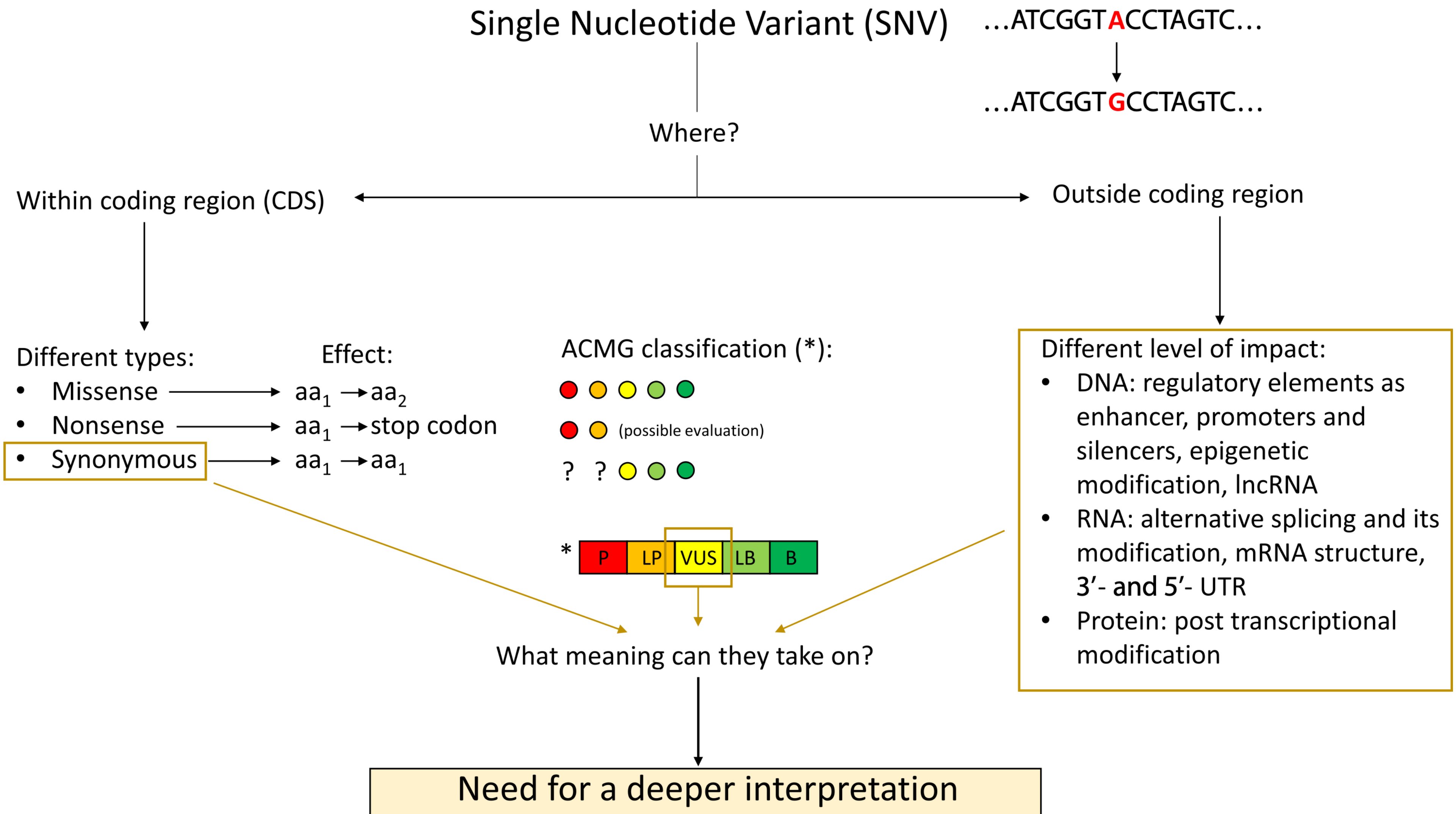
What people call serendipity sometimes is just having your eyes open



Of the overall gene variants, 62% were classified as class 1, 10% as class 2. Class 3A mutations were 5%, with an **impact on potential investigational studies.**

Are all gene variants made equal?

The noise of silence: synonymous mutations and variants of unknown significance



From snapshots to the **full video**

Targeting what you cannot see

 Minimal residual disease and treatment intensity



Wrapping up

 Brace yourself, Winter Has Come

1

Don't miss the technology for the methodology

Expect a higher benefit with solid biomarkers

Breast Cancer has ESCAT I/II mutations that soon will be part of our algorithms

2

Extended and targeted characterizations are different

Targeted panels will be recommended as new, mutation driven, drugs will be introduced in the clinic

Extended panels should be used in clinical trials only to select future ESCAT I/II mutations or MTBs

3

The world as we know it will end up soon

Adjuvant treatments will likely benefit from MRD approaches, but appropriate trial design is crucial

Alternative resistance mechanisms are emerging as new agents are being introduced to the clinic



Scan to **Link**

Thank you

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The **Liquid biopsy**
Research Team

