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hic sunt futura



The **Liquid biopsy**
Research Group

Looking for a target in breast cancer

Tissue or liquid biopsy?

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Precision Medicine Academic Consortium (PMAC)

Conflict of Interest Disclosure Statement

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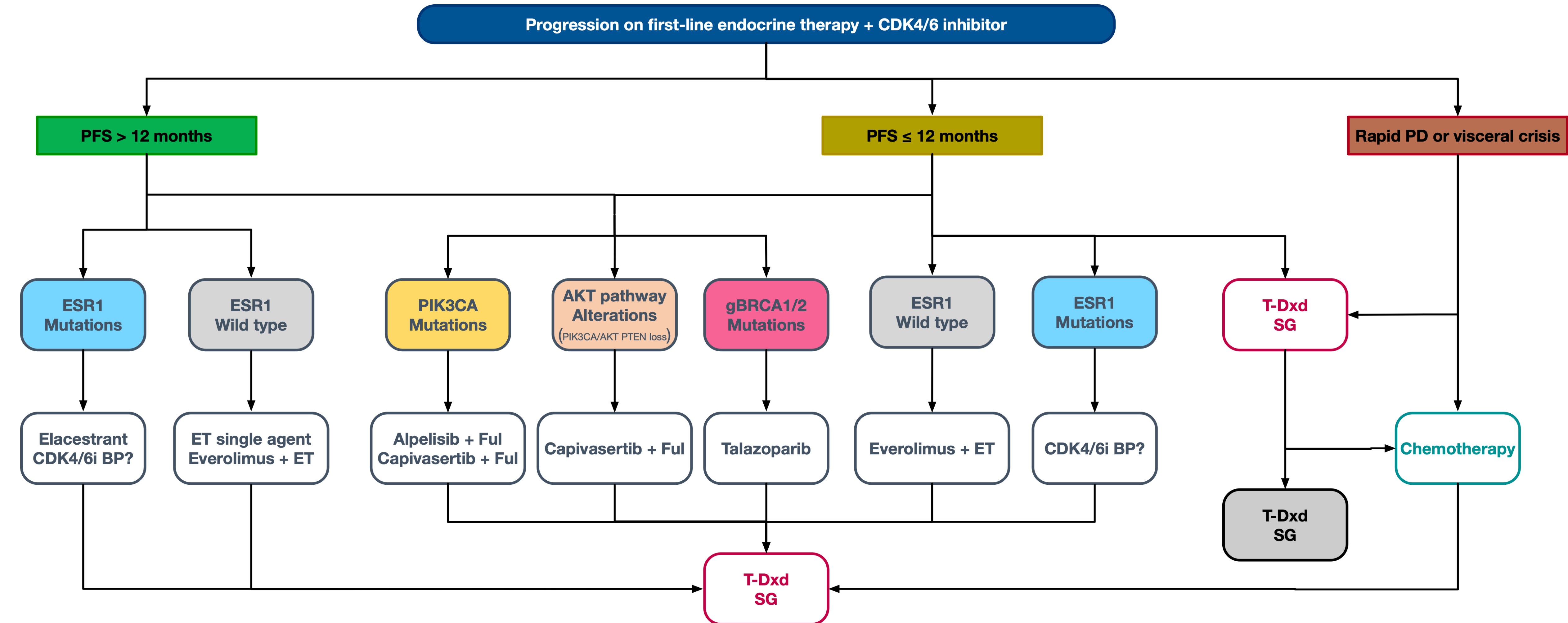
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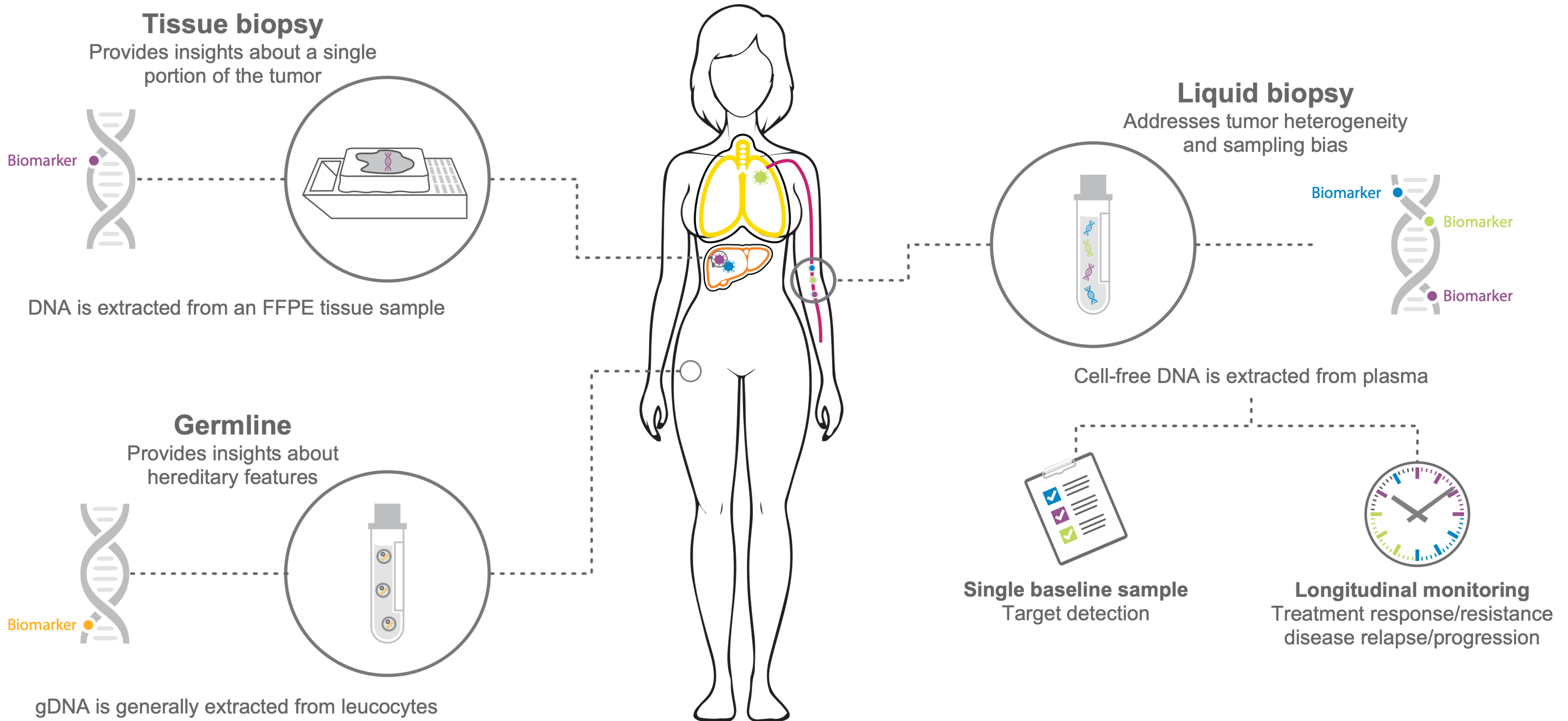
Let's connect the dots

Which targets are you looking for?



The right tool for the right question

Tissue vs liquid vs germline



Concordance Analysis in Single Gene Alteration

 The BioltaLEE Study

Gene	LB, % (n)	TS, % (n)	Kappa (95% C.I.)
<i>PIK3CA</i>	20.1 (29)	40.3 (58)	0.48 (0.34; 0.62)
<i>TP53</i>	16.0 (23)	24.3 (35)	0.44 (0.27- 0.62)
<i>PTEN</i>	4.2 (6)	7.6 (11)	0.56 (0.28; 0.85)
<i>KMT2C</i>	4.2 (6)	4.2 (6)	
<i>MAP2K4</i>	3.5 (5)	4.2 (6)	
<i>ATM</i>	2.1 (4)	0.7 (1)	0.49 (-0.11-1.00)
<i>AKT1</i>	2.8 (4)	5.6 (8)	0.48 (0.13; 0.83)
<i>MAP3K1</i>	1.4 (2)	4.9 (7)	0.43 (0.03; 0.83)
<i>ESR1</i>	1.4 (2)	2.8 (4)	-0.02 (-0.04; 0.00)
<i>GATA3</i>	0.7 (1)	5.6 (8)	0.21 (-0.14; 0.56)
<i>ERBB2</i>	0.7 (1)	2.1 (3)	0.49 (-0.11; 1.00)

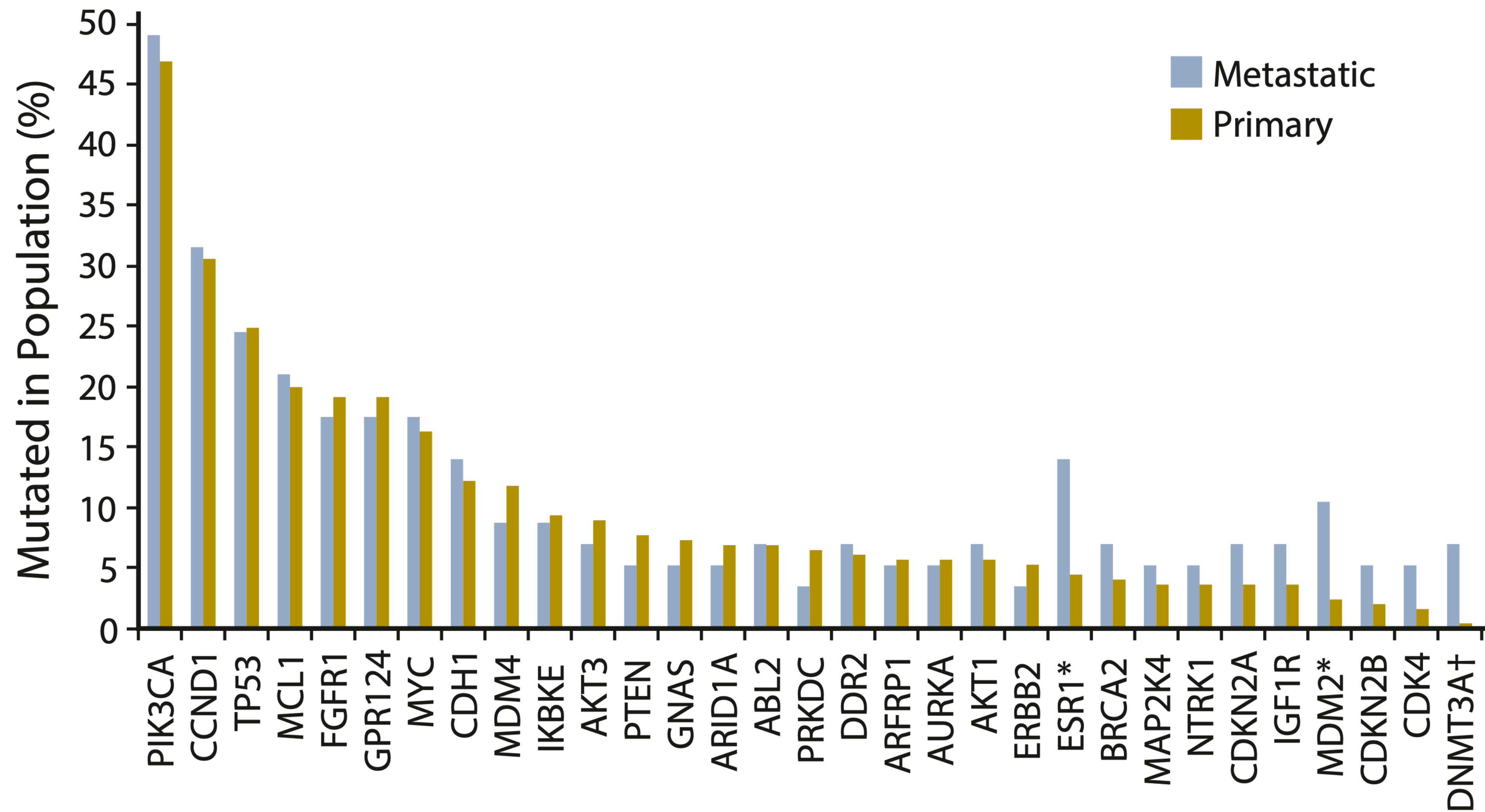
What about the real world?

Liquid vs Tissue NGS concordance

	Observed Agreement	Kappa	95% C.I.		P
<i>TP53</i>	79.05%	0.5809	0.4061	0.7147	< 0.0001
<i>PIK3CA</i>	80.95%	0.5513	0.36	0.6988	< 0.0001
<i>ERBB2</i>	79.05%	0.3675	0.1572	0.5596	0.0001
<i>ESR1</i>	84.76%	0.4167	0.1808	0.6167	< 0.0001
<i>MYC</i>	80.00%	0.386	0.1736	0.577	< 0.0001
<i>EGFR1</i>	80.00%	0.0541	-0.1053	0.2352	0.1421
<i>FGFR1</i>	90.48%	0.6313	0.3984	0.7929	< 0.0001
<i>CCNE1</i>	83.81%	0.3014	0.0622	0.5153	0.0001
<i>NF1</i>	83.81%	0.1748	-0.0131	0.4325	0.0325
<i>ARID1A</i>	89.52%	0.2979	0.0611	0.5753	0.0009

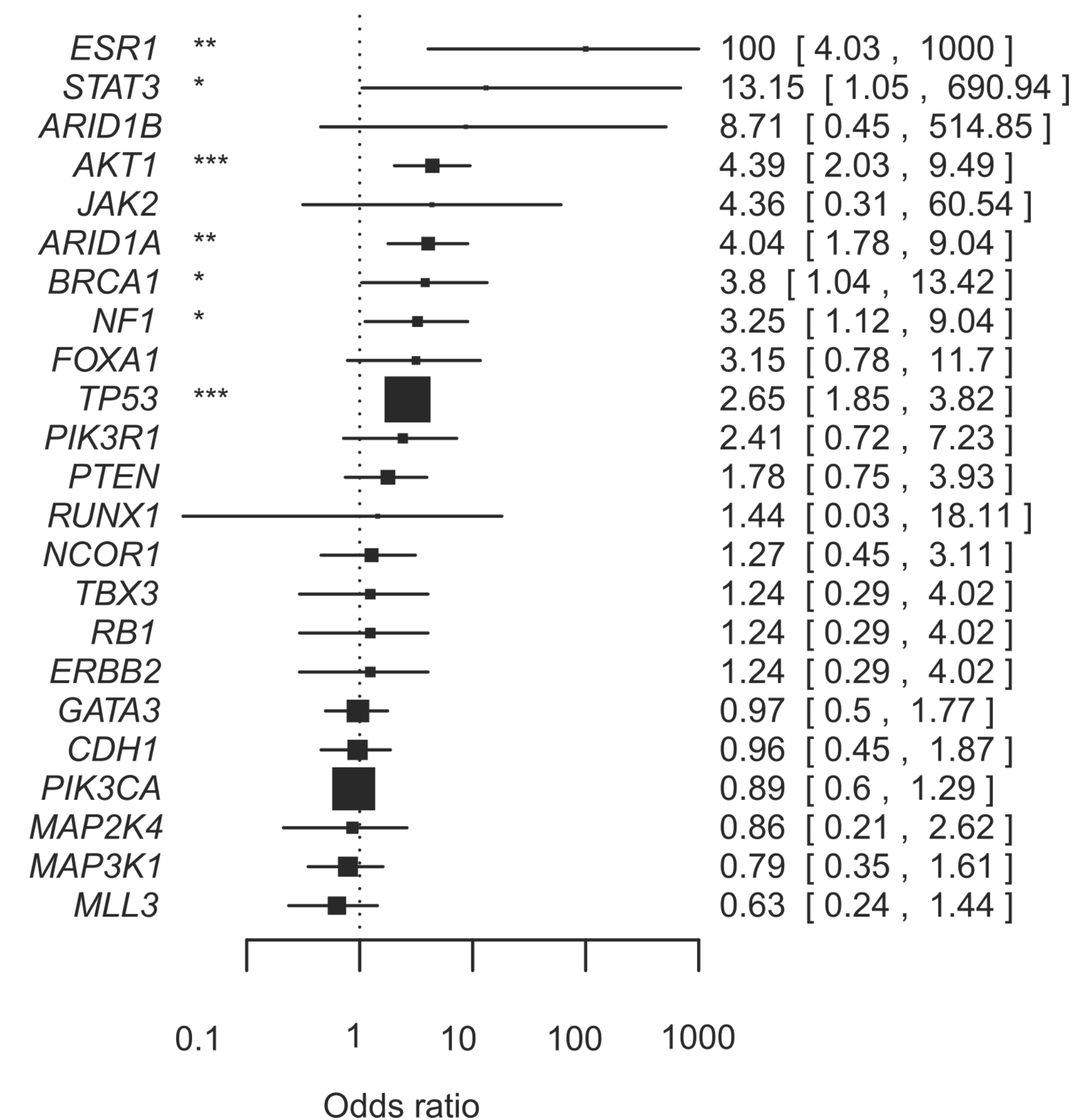
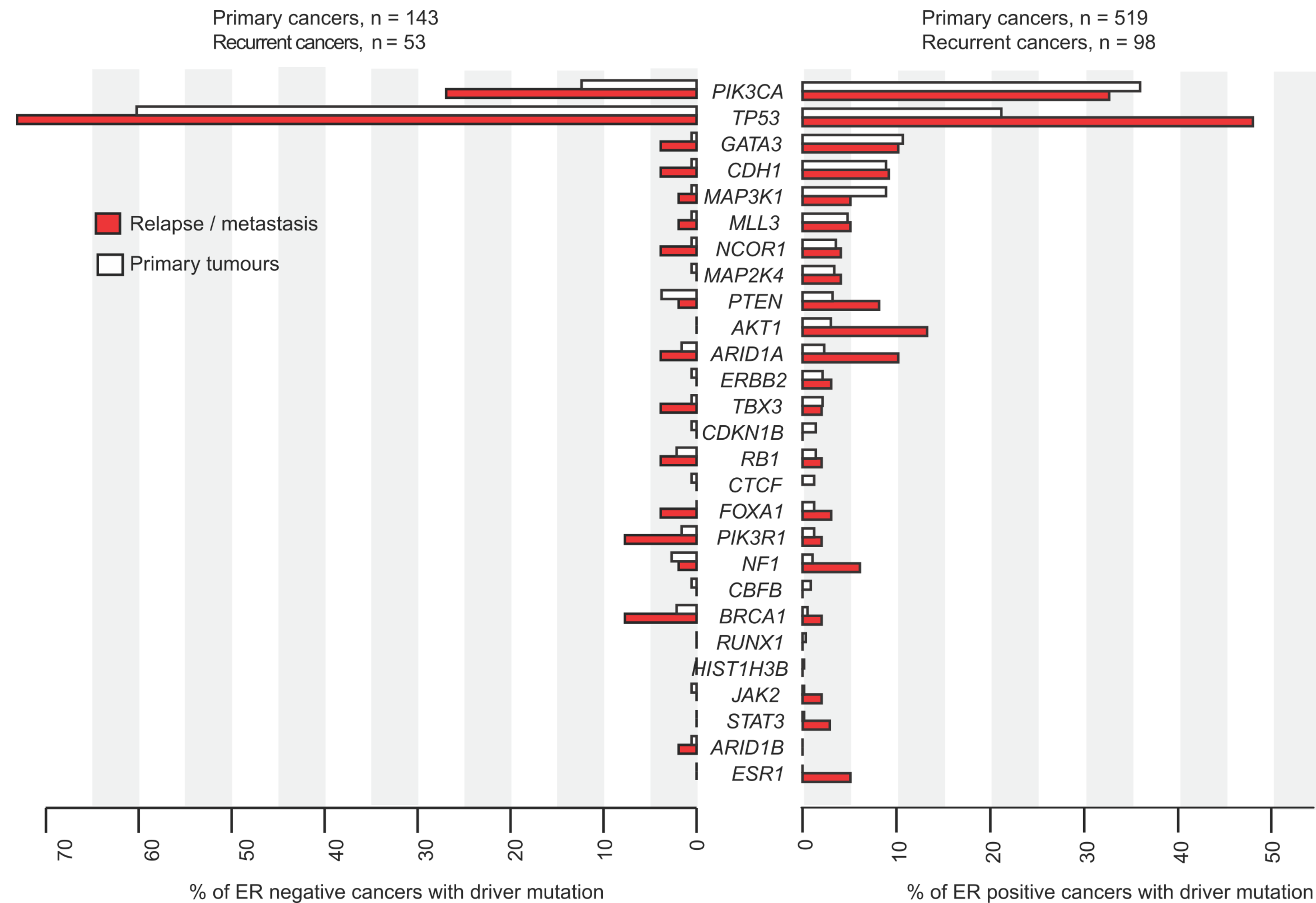
Another bolero turn

 The translational side of the BOLERO trial



What about the real world?

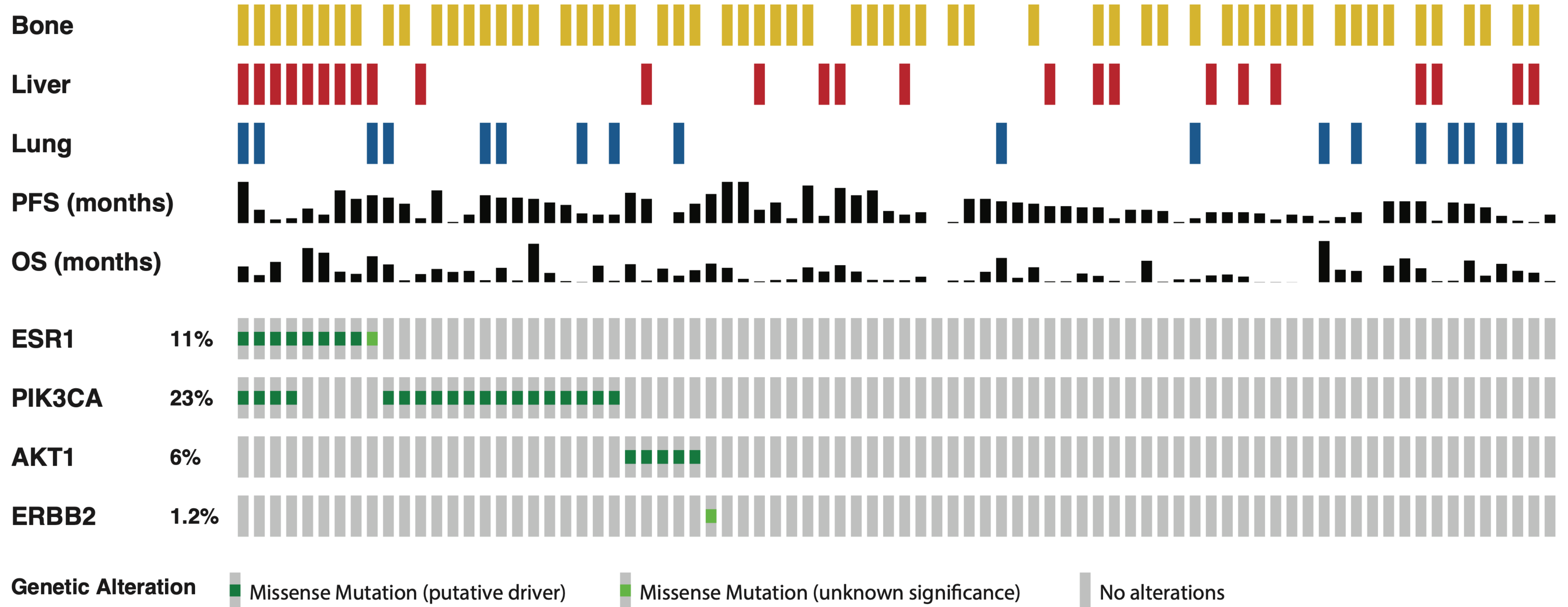
Driver Landscapes of 163 Recurrent and 705 Primary Breast Cancers



Not just **primary** vs **recurrence**

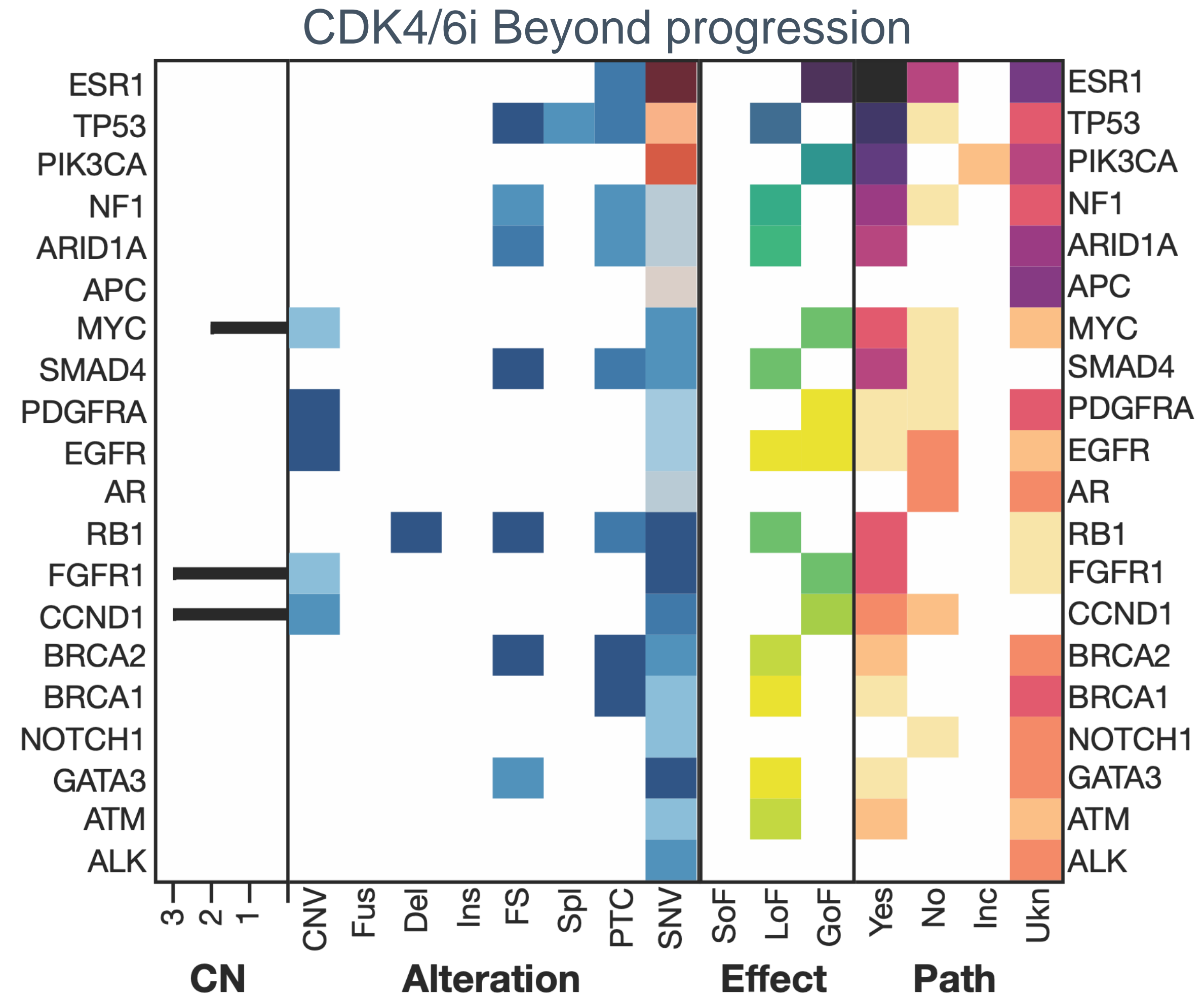
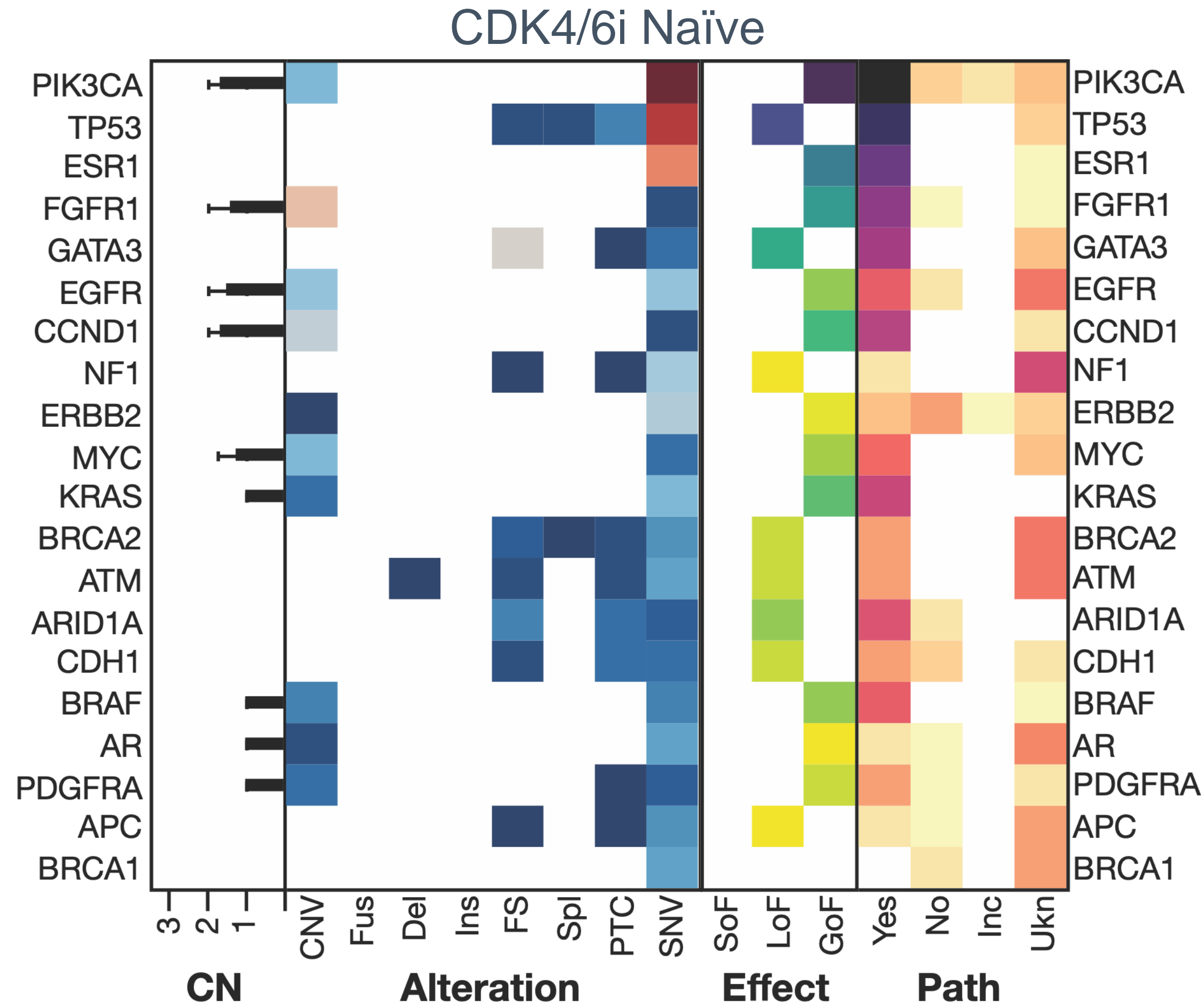
An ever-changing disease

 Actionable targets at baseline



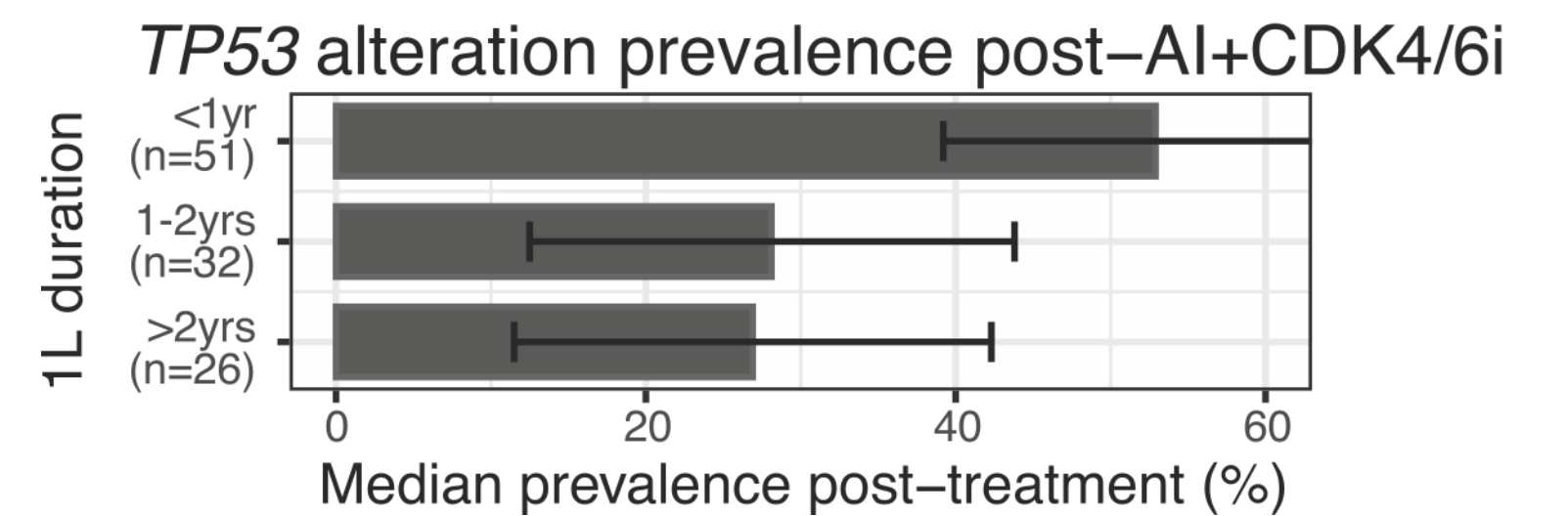
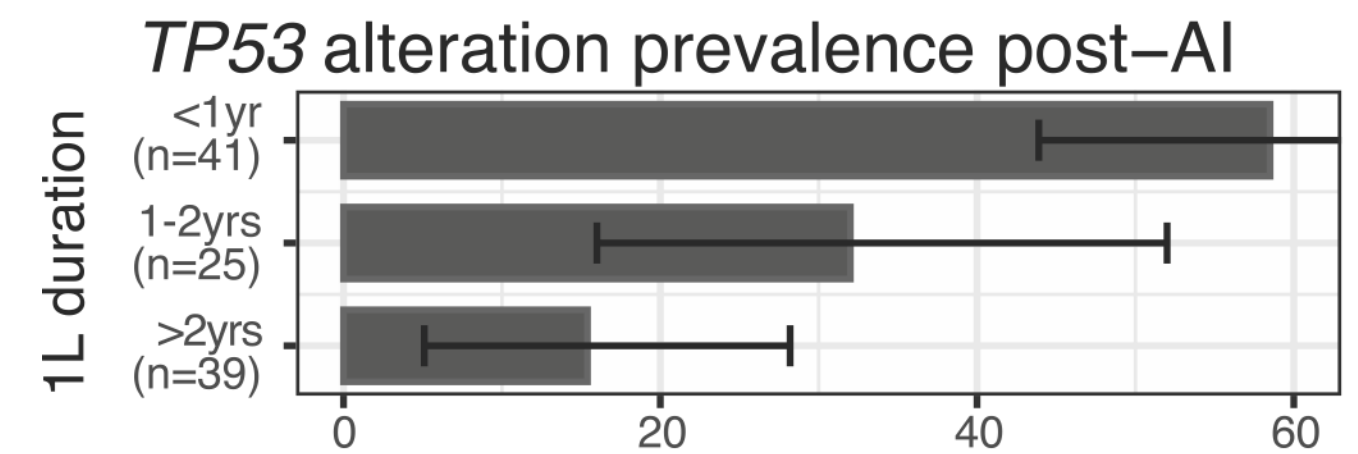
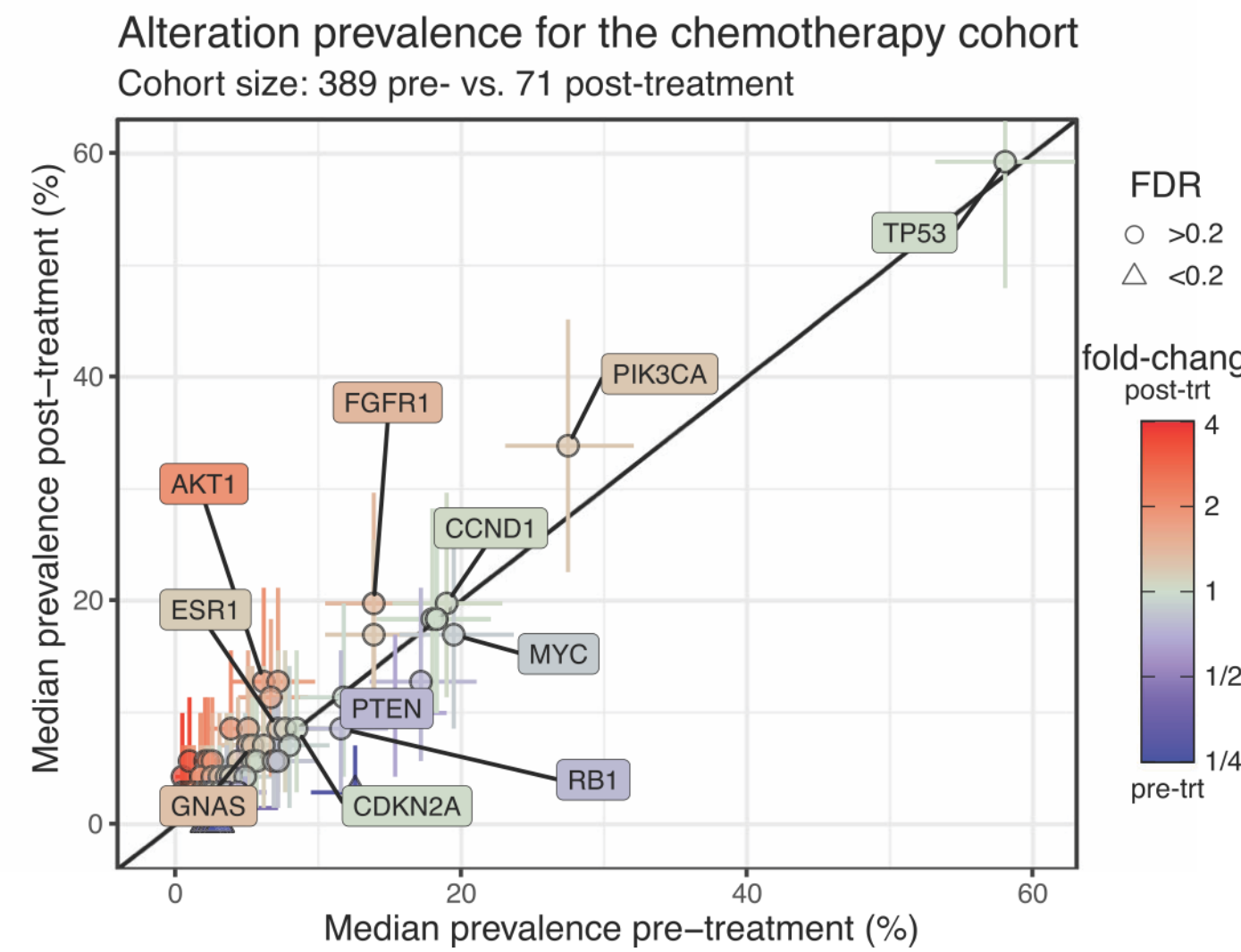
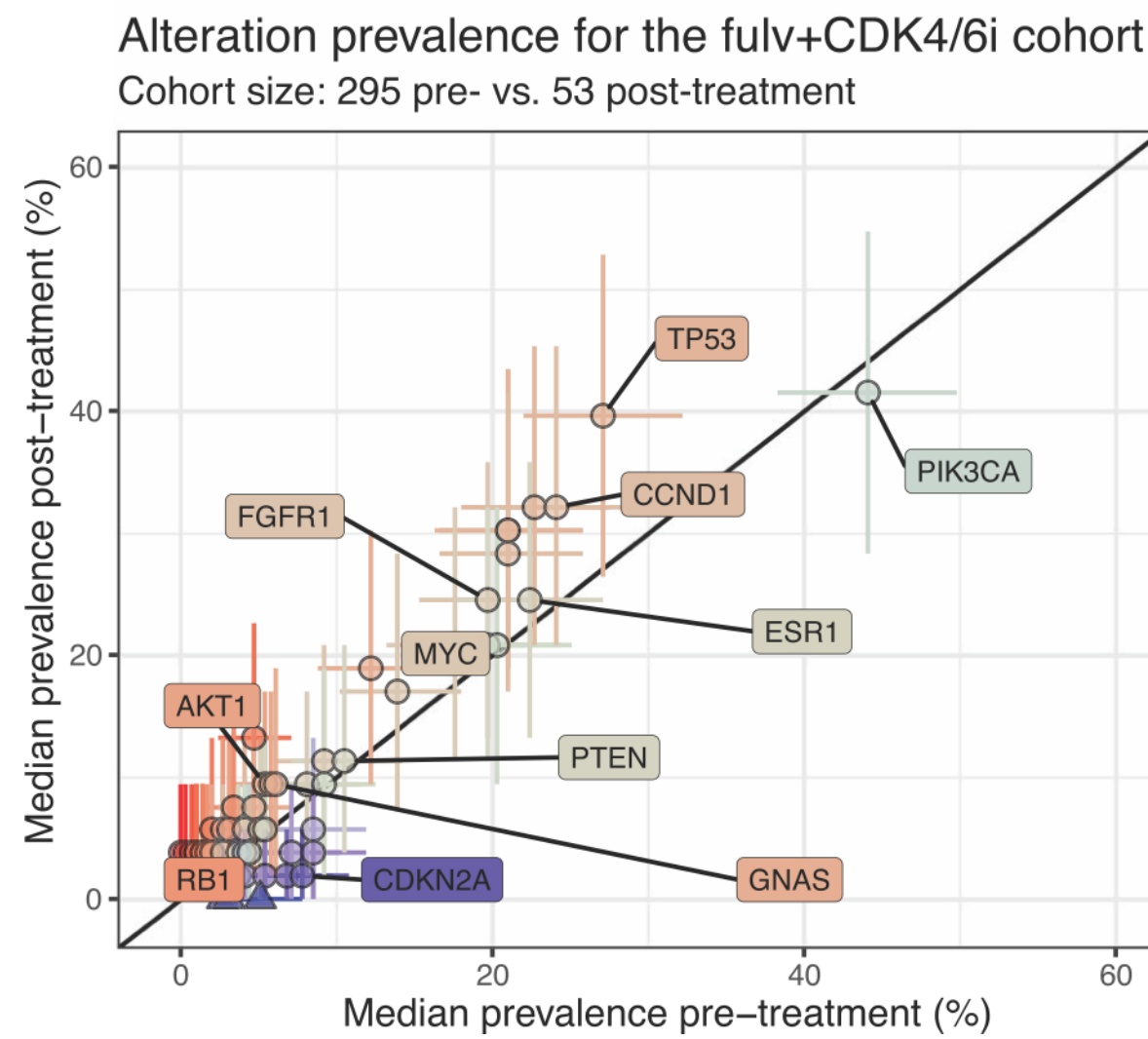
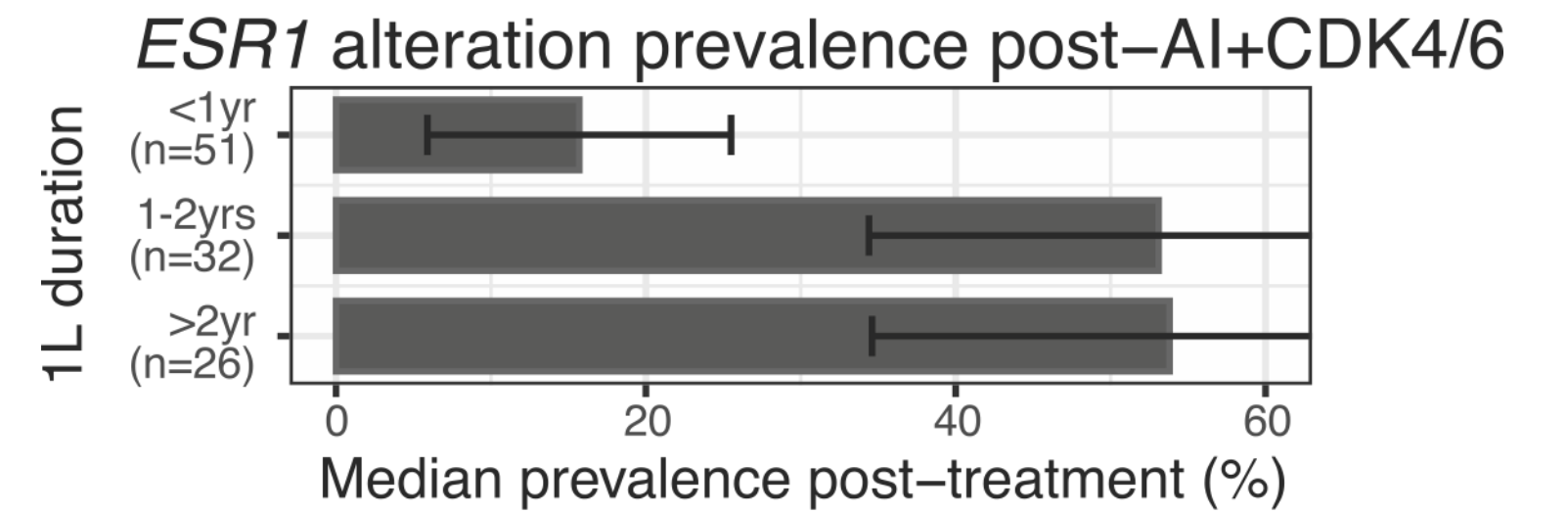
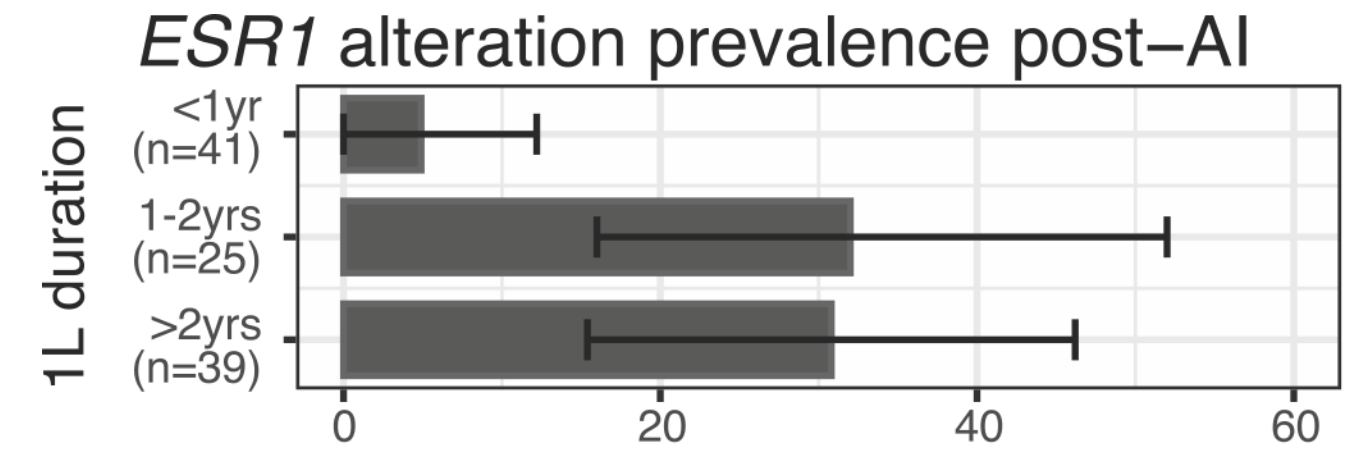
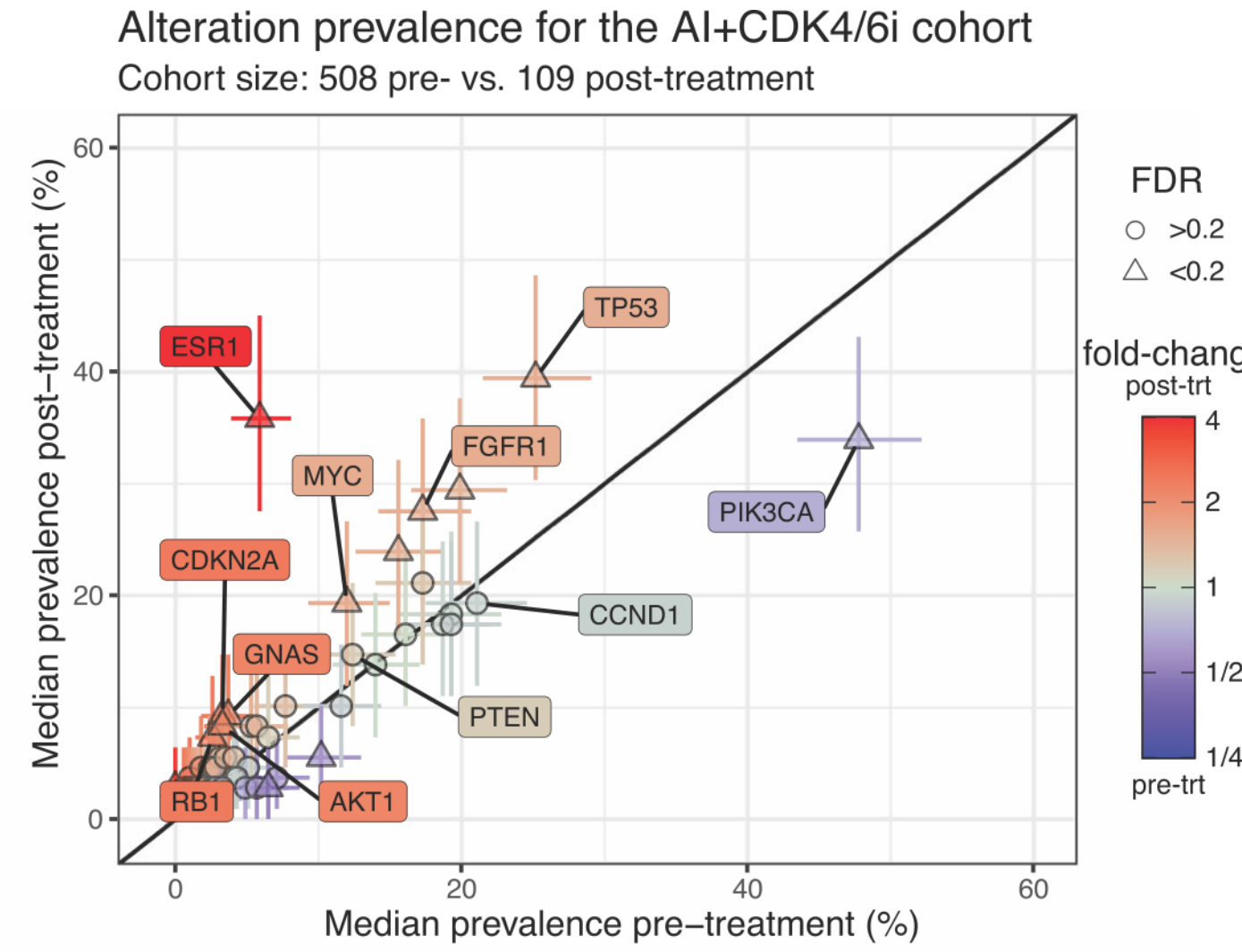
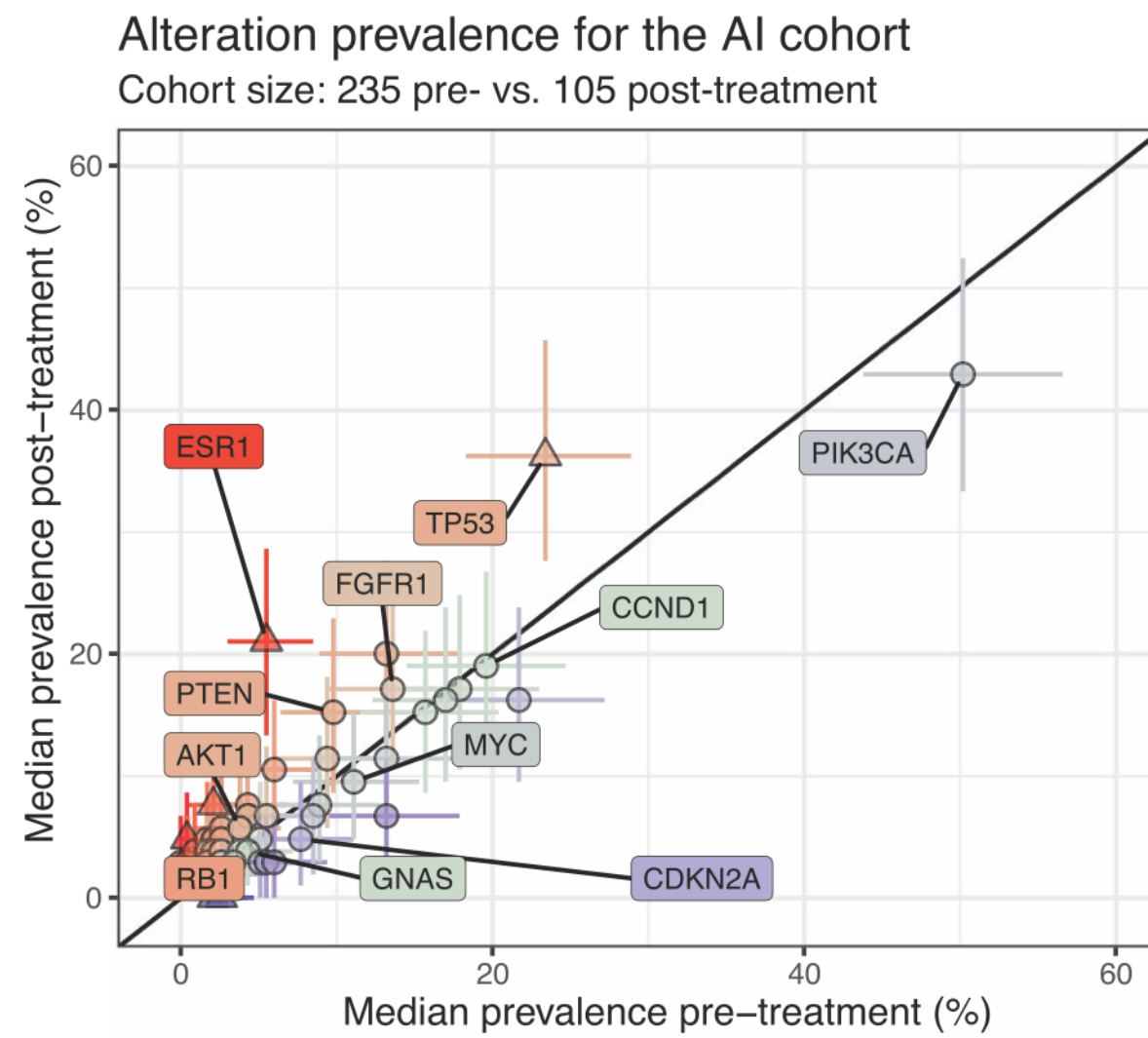
An ever-changing disease

Mutational landscape of the CDK4/6i Naïve and Beyond Progression subgroups



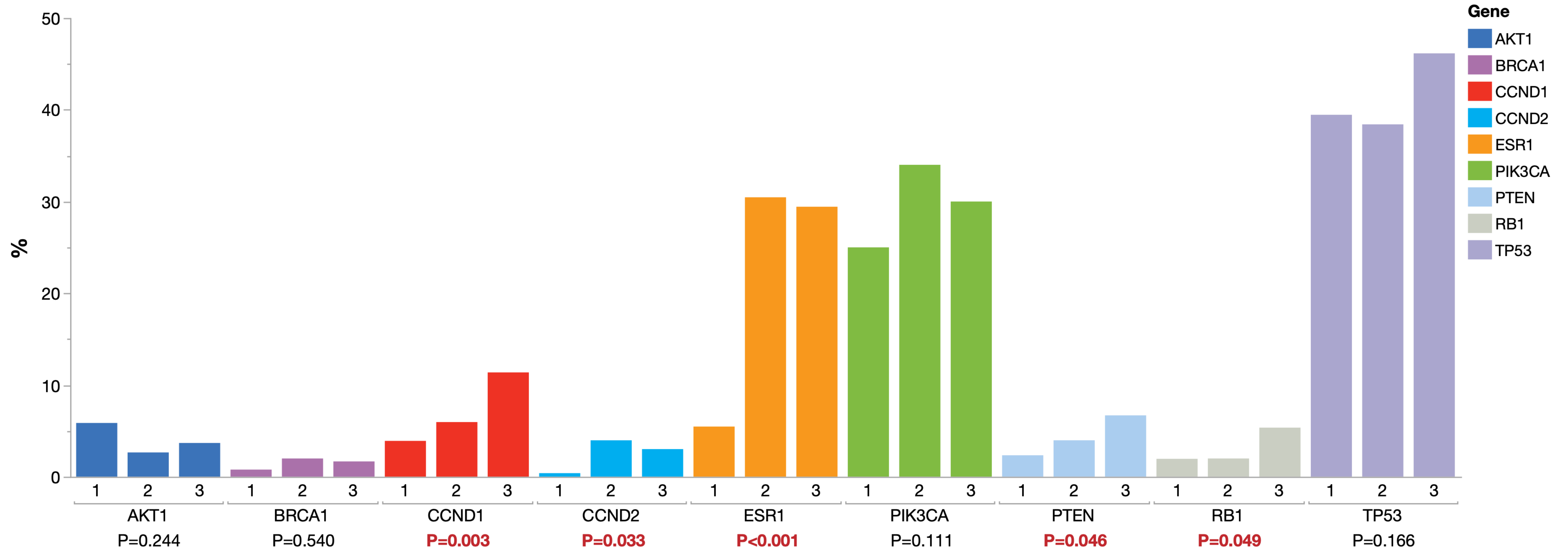
An ever-changing disease

Should we follow the *PIK3CA* north star?



An ever-changing disease

How do gene alterations change across lines?



Wrapping up

 To infinity... and beyond

1

The right tool for the right question

DNA-based targets can be either somatic or germinal, the former can be tested at any time point
Tissue biopsy can guarantee a higher DNA yield, but can't address spatial and temporal heterogeneity

2

Archival samples are not always reliable

Truncal mutations, such as PIK3CA, are conserved across time points
Resistance-driven biomarkers, such as ESR1, are usually present in metastatic samples

3

Biomarkers can change across treatment lines

Several gene alterations can be selected during treatments (e.g. ESR1, PTEN)
Liquid biopsy can be better suited when differential resistance levels could result in spatial heterogeneity



Thank you

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