

Supplementary Material to:

Westphalen CB, Fine AD, Andre F et al. 2021.

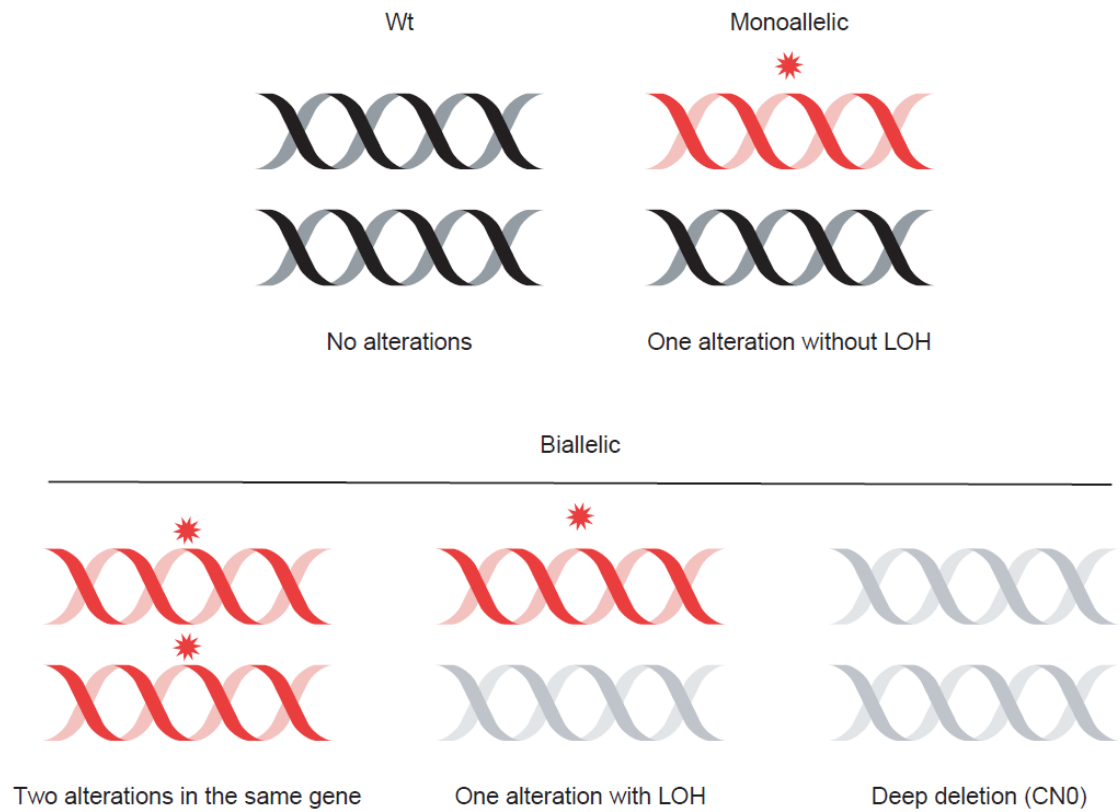
Pan-cancer Analysis of Homologous Recombination Repair-associated Gene
Alterations and Genome-wide Loss of Heterozygosity Score

- Supplementary Figures S1-S10
- Supplementary Tables S1-S8

Supplementary Figures

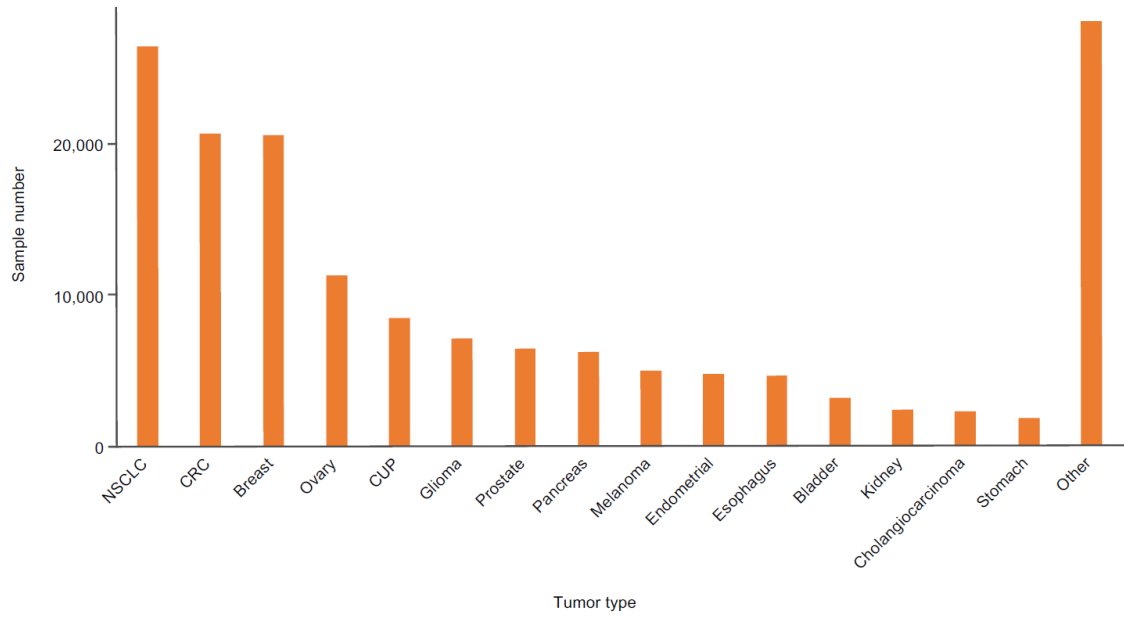
Supplementary Figure 1.

Graphic of biallelic and monoallelic alteration callings. LOH, loss of heterozygosity; wt, wildtype.



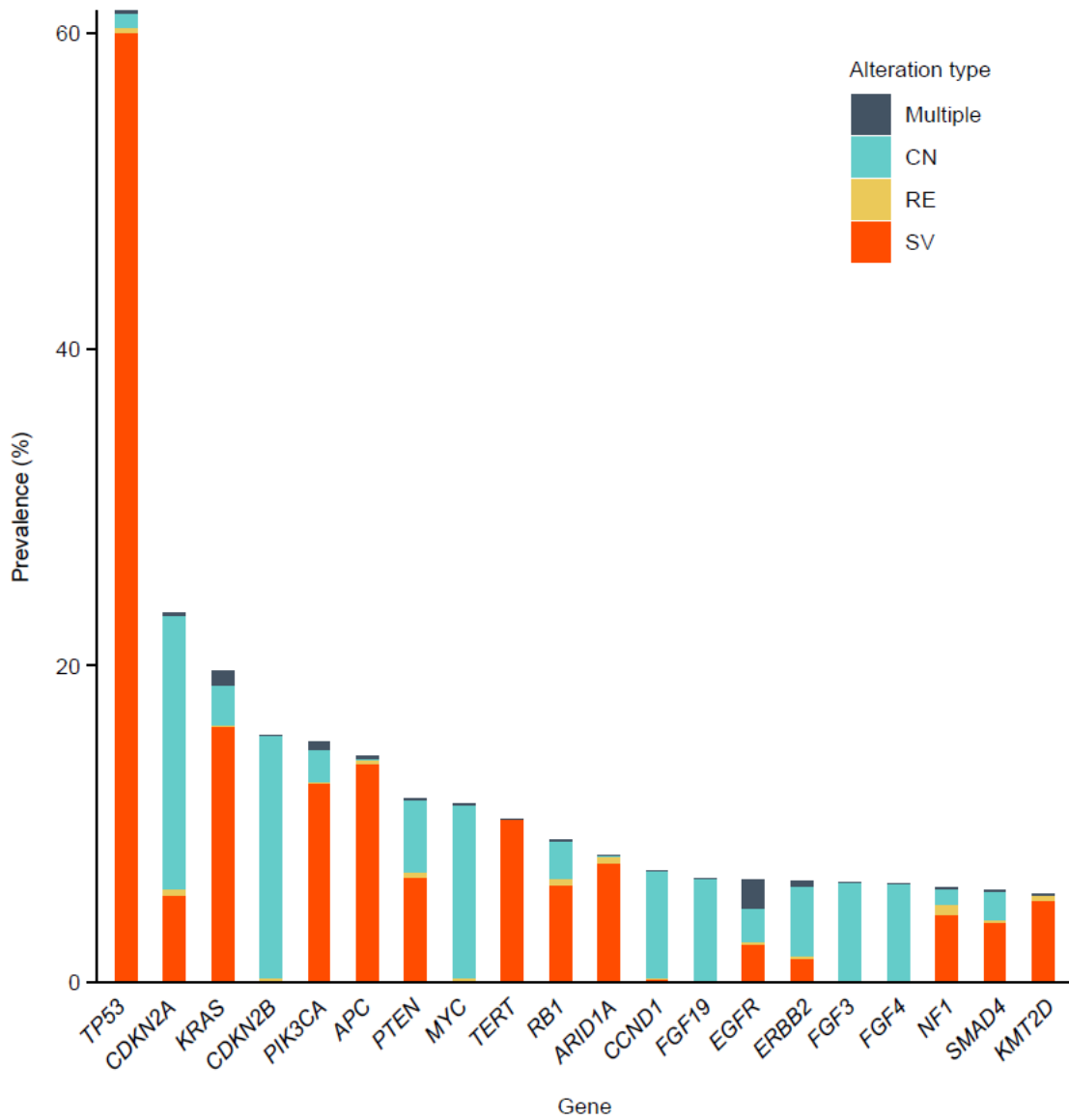
Supplementary Figure 2.

Cancer types represented in the study. CUP, carcinoma-of-unknown-primary-origin.



Supplementary Figure 3.

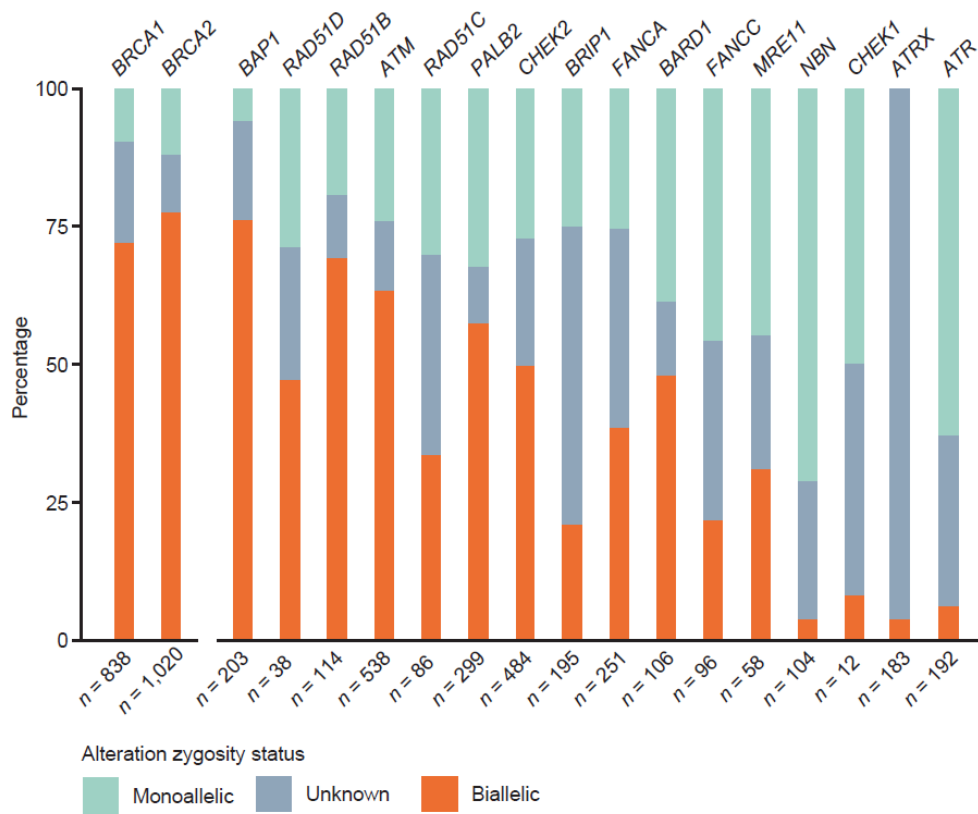
Mutational landscape of the overall cohort. CN, copy number; RE, rearrangement; SV, short variant; the top 20 most frequently altered genes are shown.

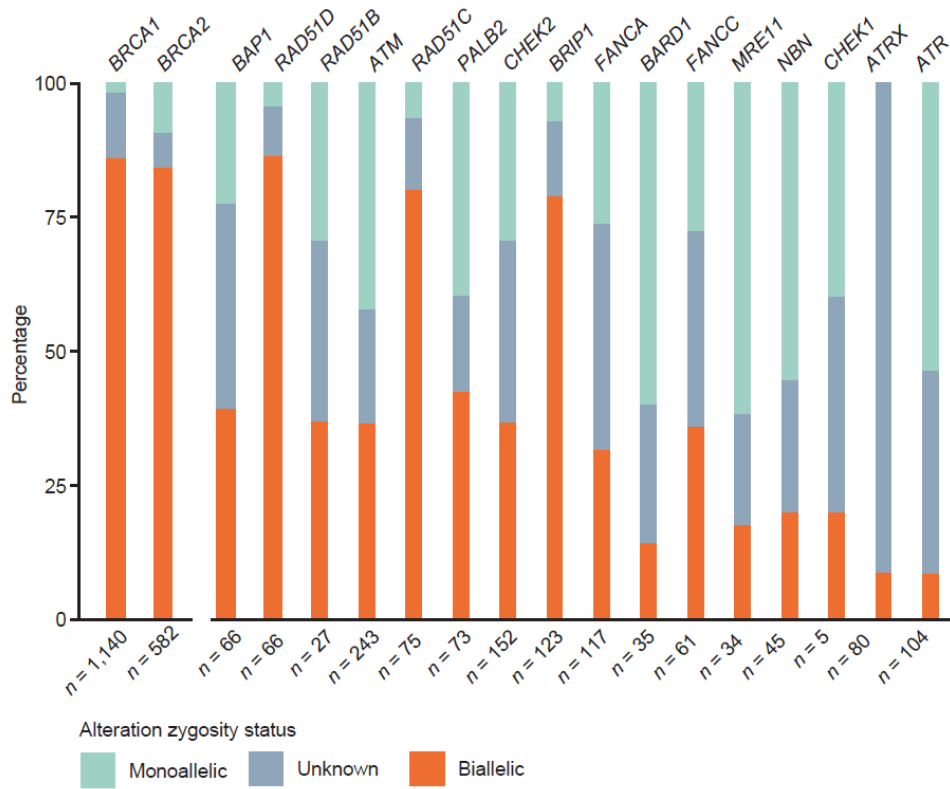
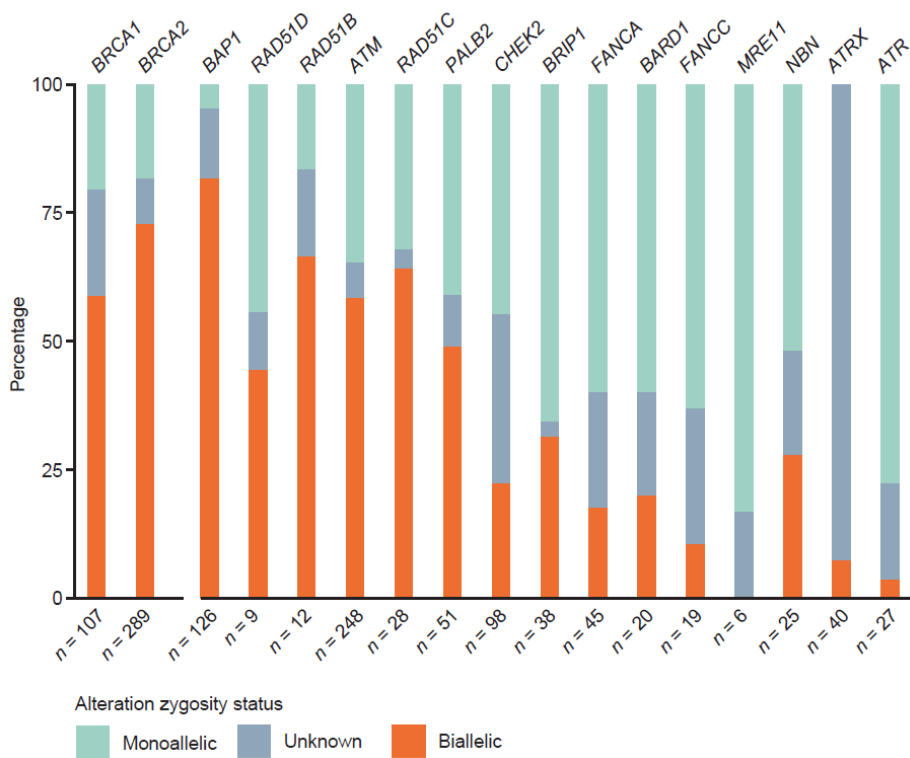


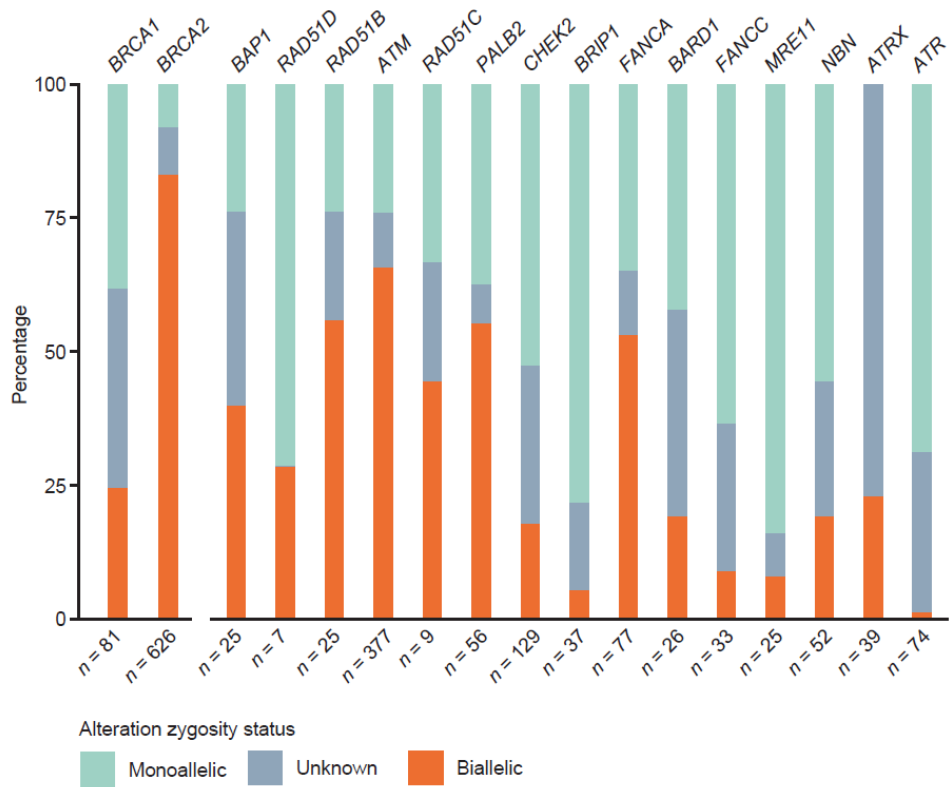
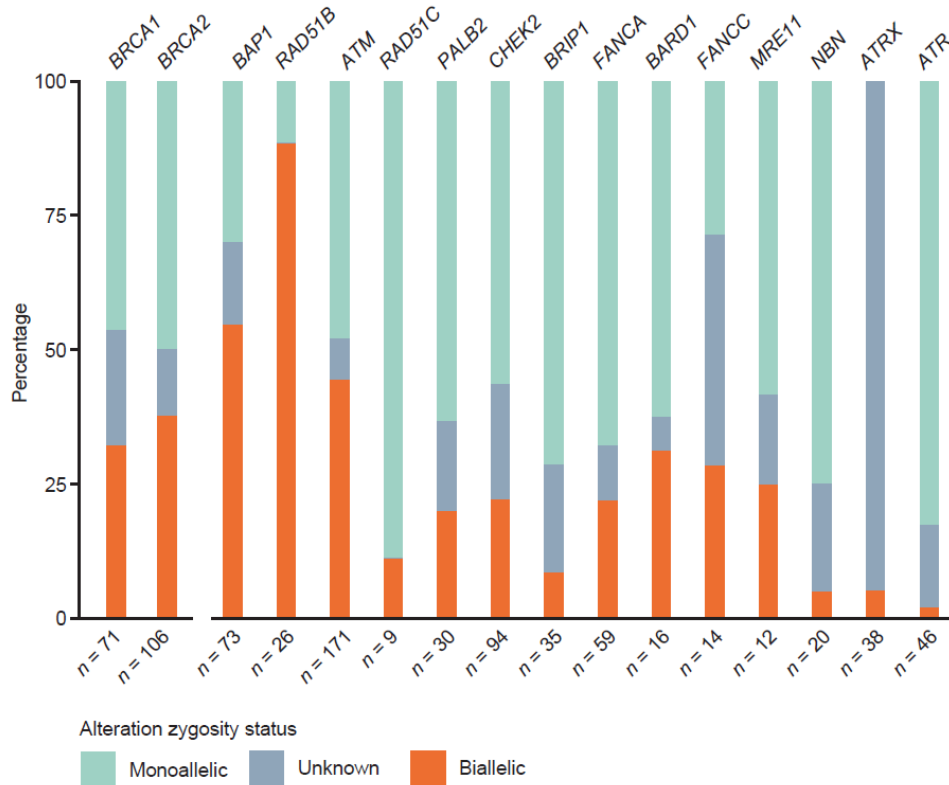
Supplementary Figure 4.

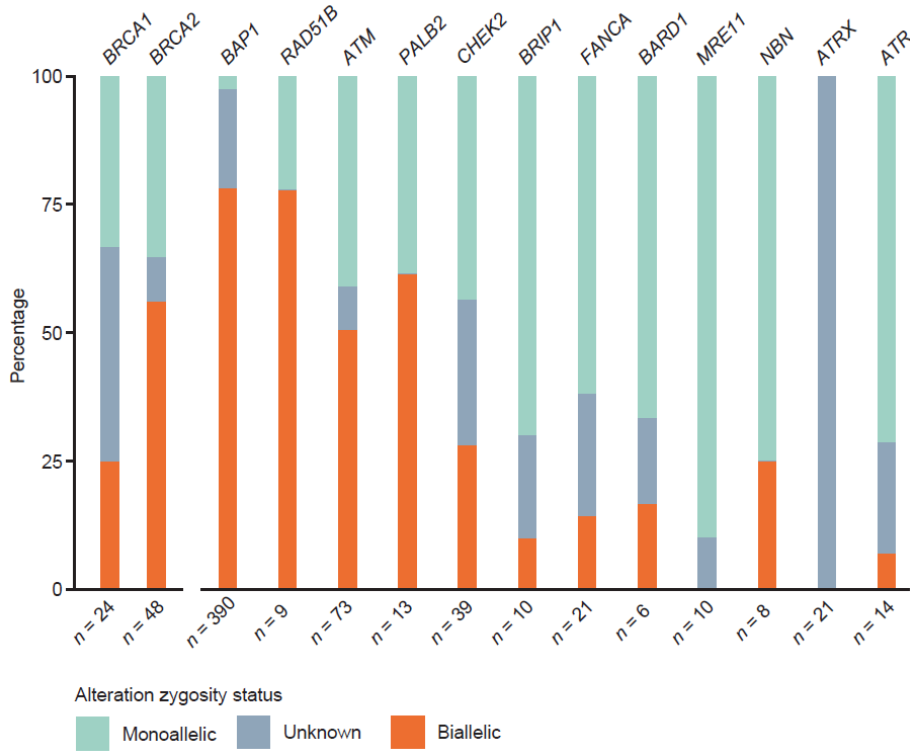
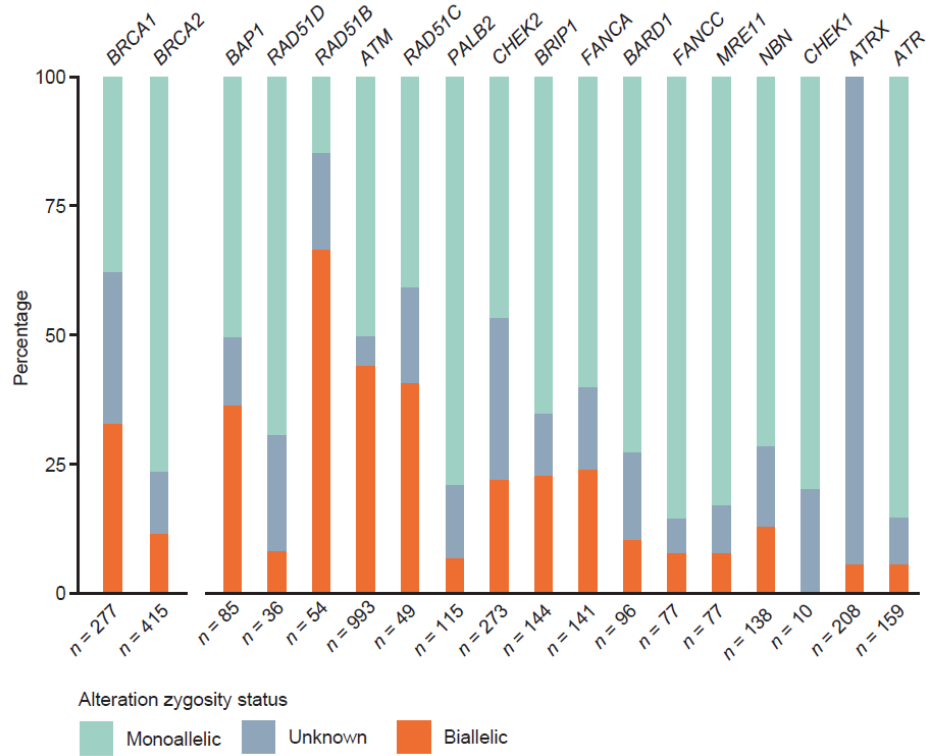
Association of HRR-associated gene alterations with biallelic loss in **A**, breast, **B**, ovarian, **C**, pancreatic, **D**, prostate, **E**, bladder, **F**, cholangiocarcinoma, **G**, CRC, **H**, CUP, **I**, endometrial, **J**, esophageal, **K**, glioma, **L**, kidney, **M**, melanoma, **N**, NSCLC, **O**, stomach, and **P**, other cancers. CUP, carcinoma-of-unknown-primary-origin.

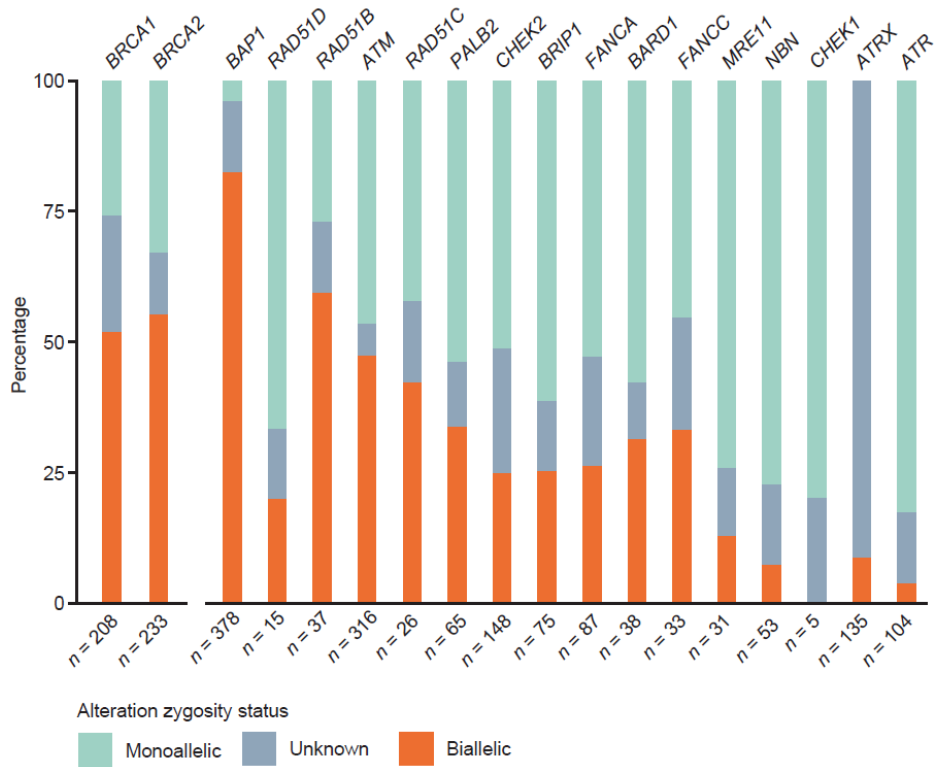
A

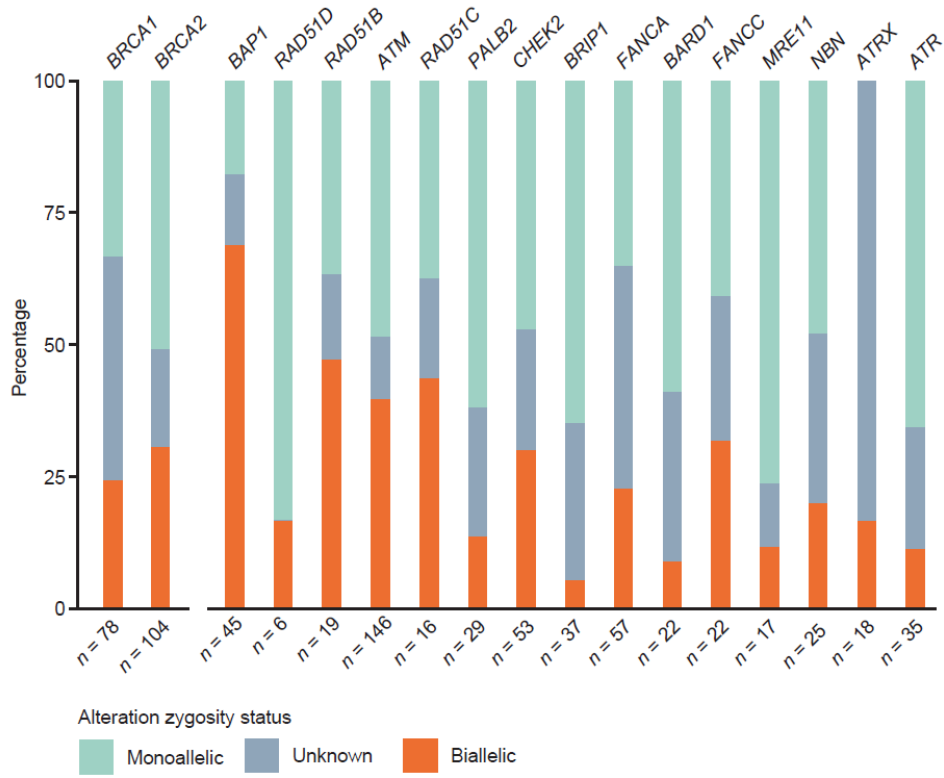
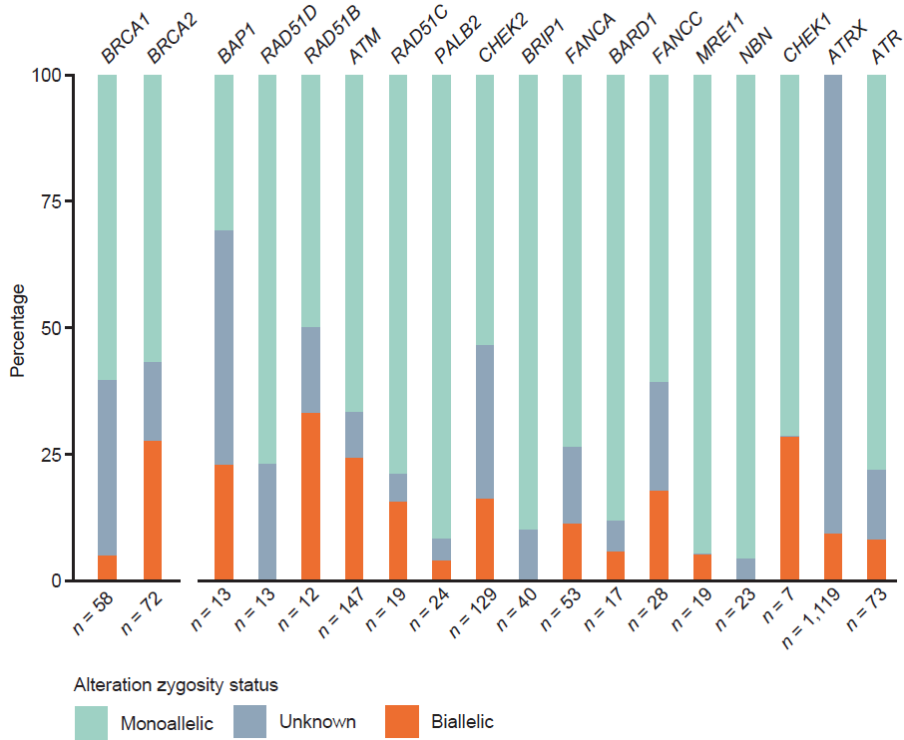


B**C**

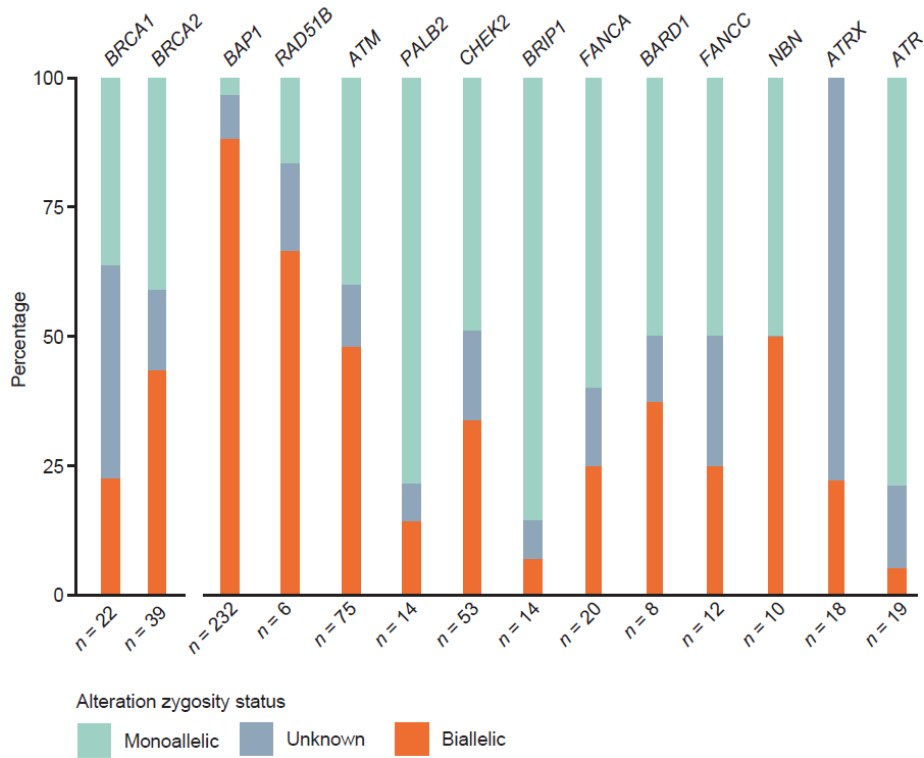
D**E**

F**G**

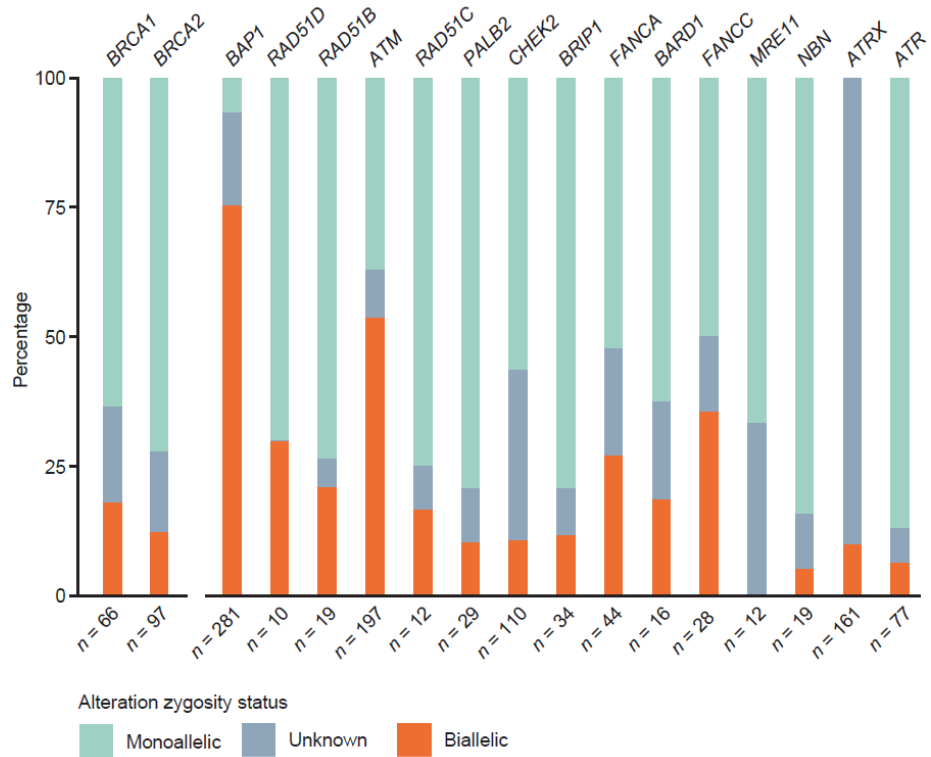
H**I**

J**K**

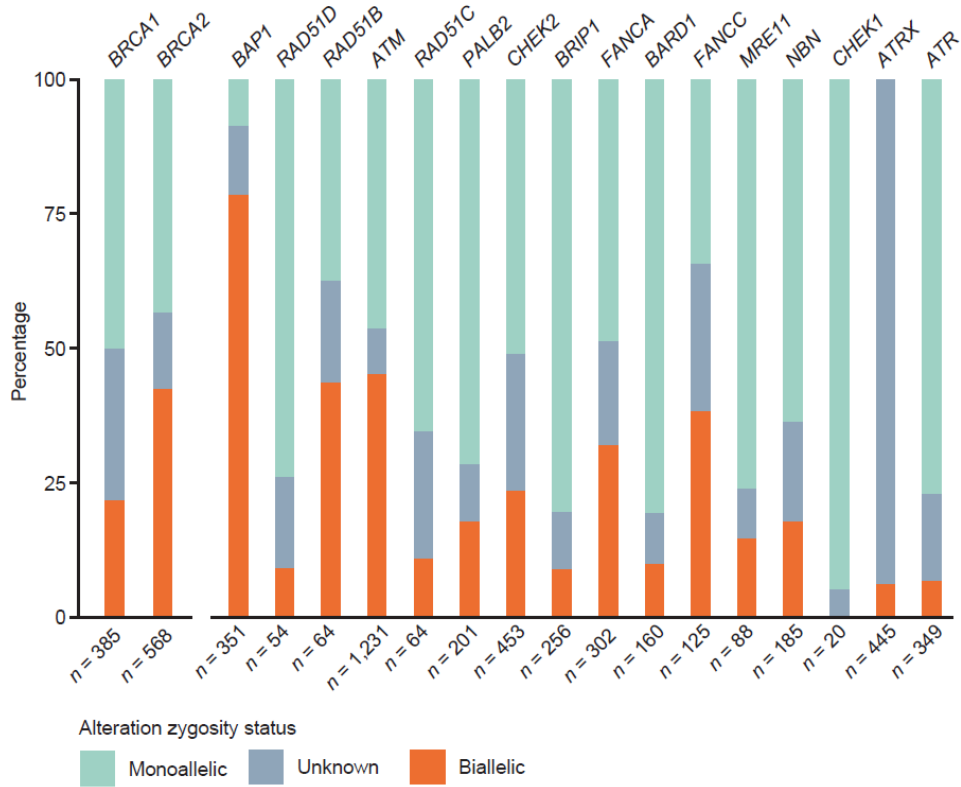
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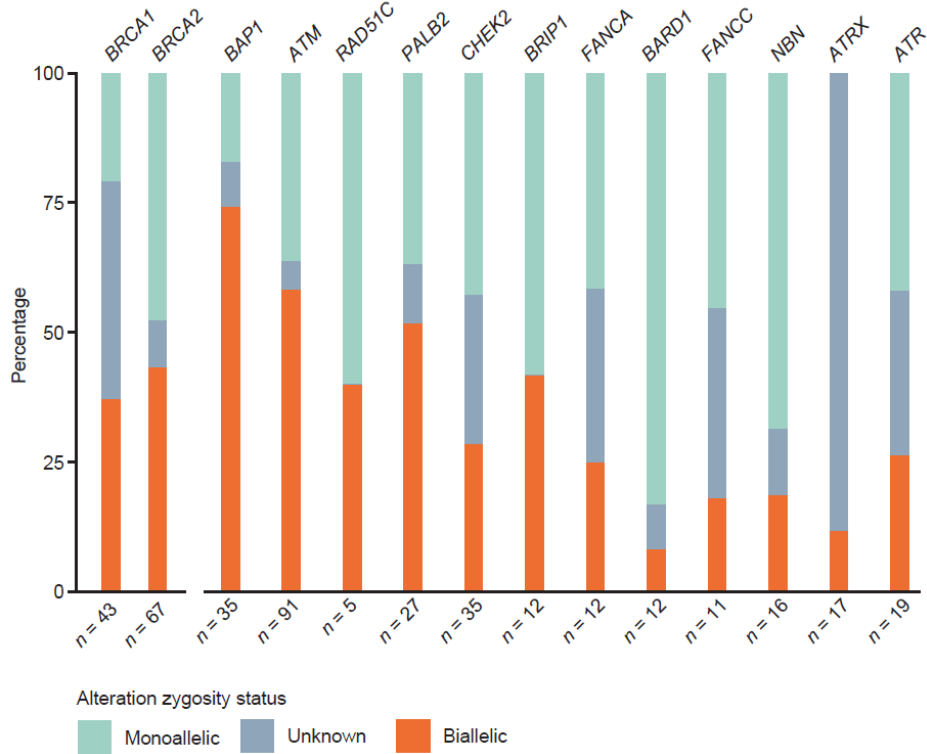
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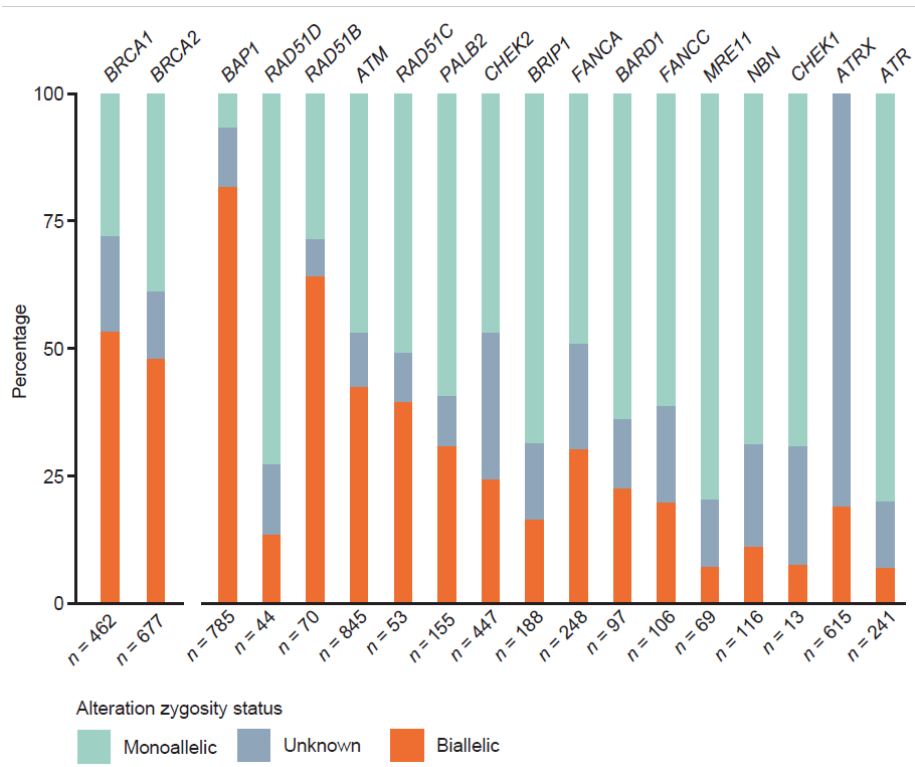
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O

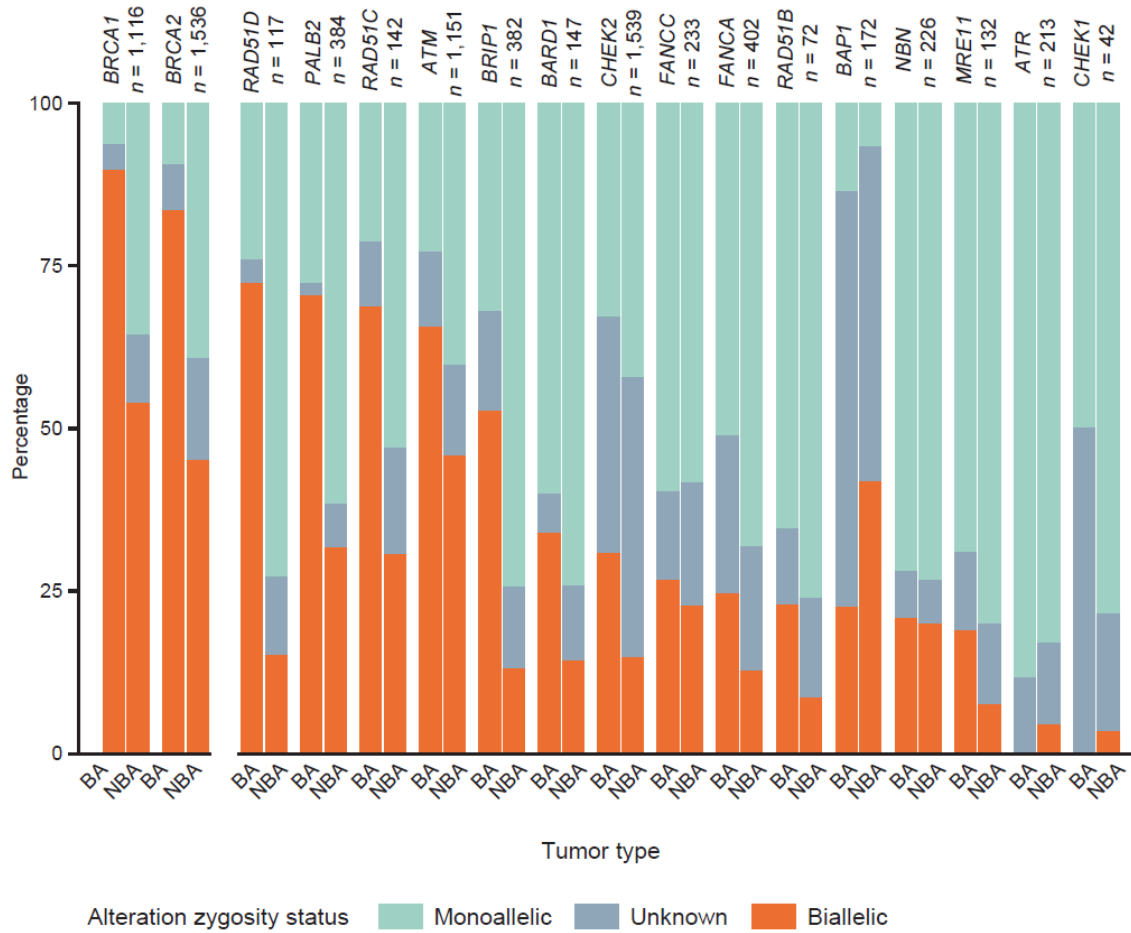


P



Supplementary Figure 5.

Association of HRR-associated gene alterations of predicted germline origin with biallelic loss.

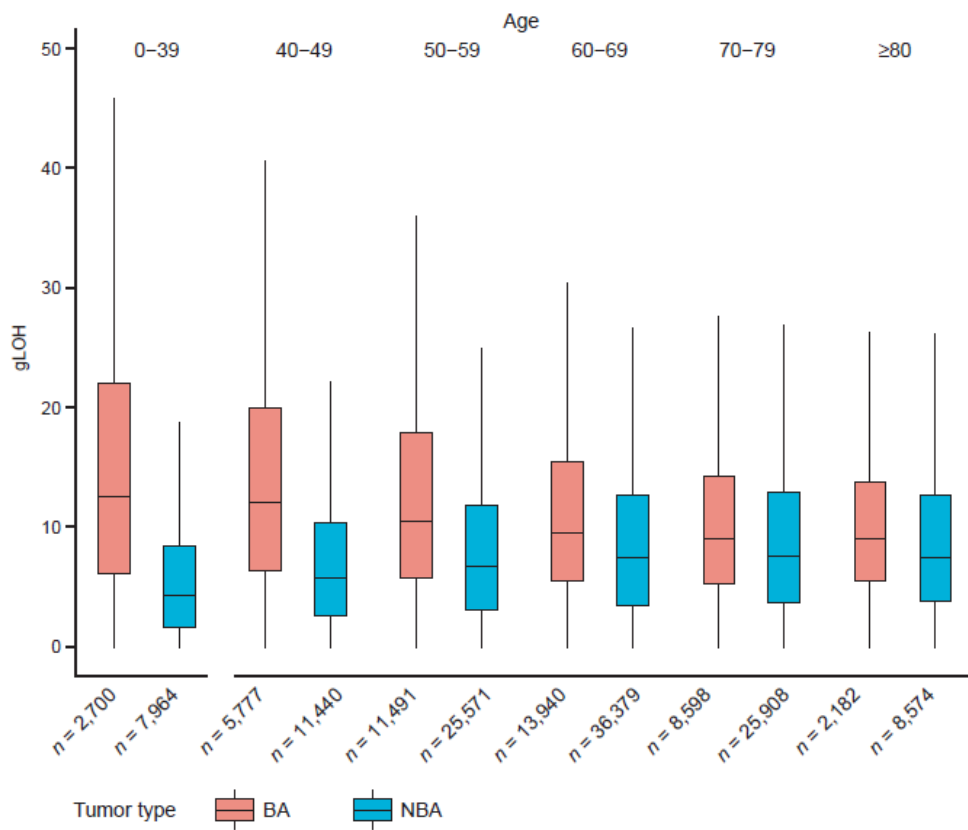


Supplementary Figure 6.

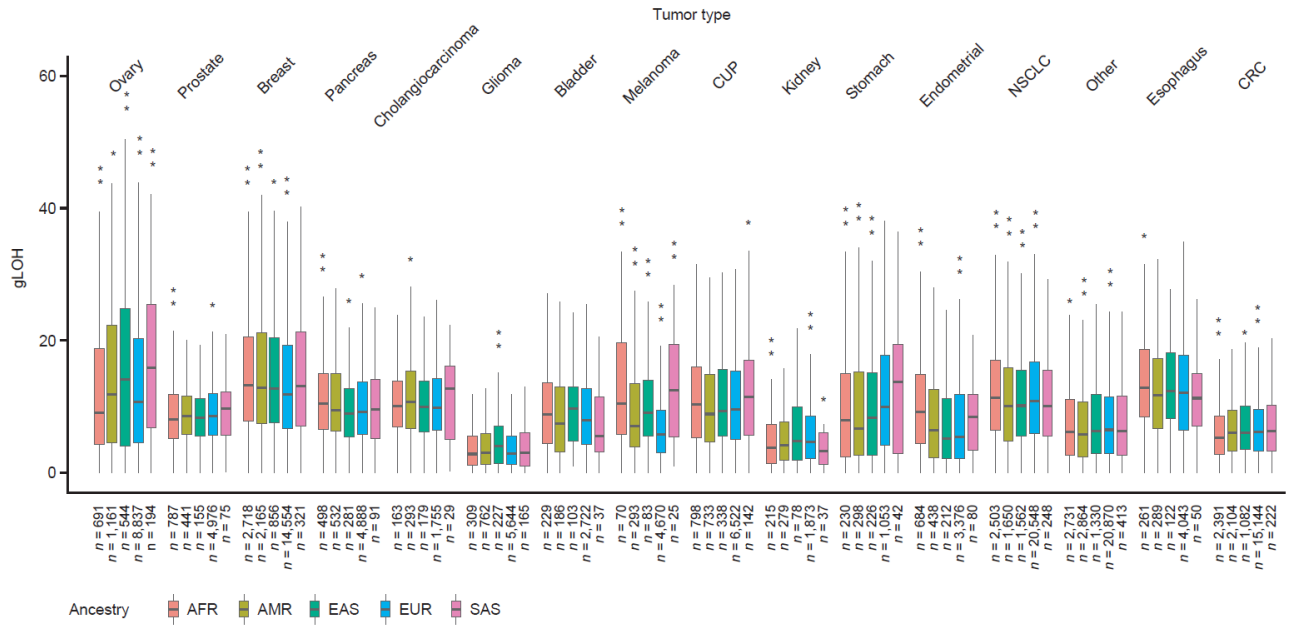
Association of gLOH with **A**, age and **B**, ancestry. AFR, African; AMR, Central and South American; CUP, carcinoma-of-unknown-primary-origin; EAS, East Asian; EUR, European; SAS, South Asian; asterisks denote level of significance after false discovery correction:

* = $P < 0.05$; ** = $P < 0.01$.

A



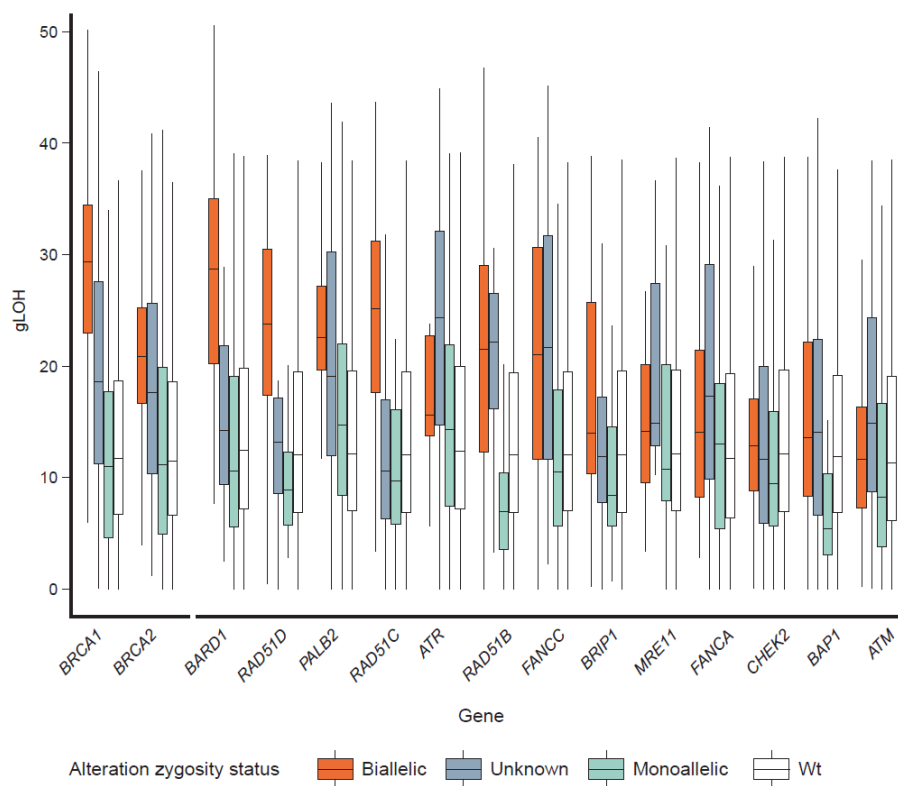
B

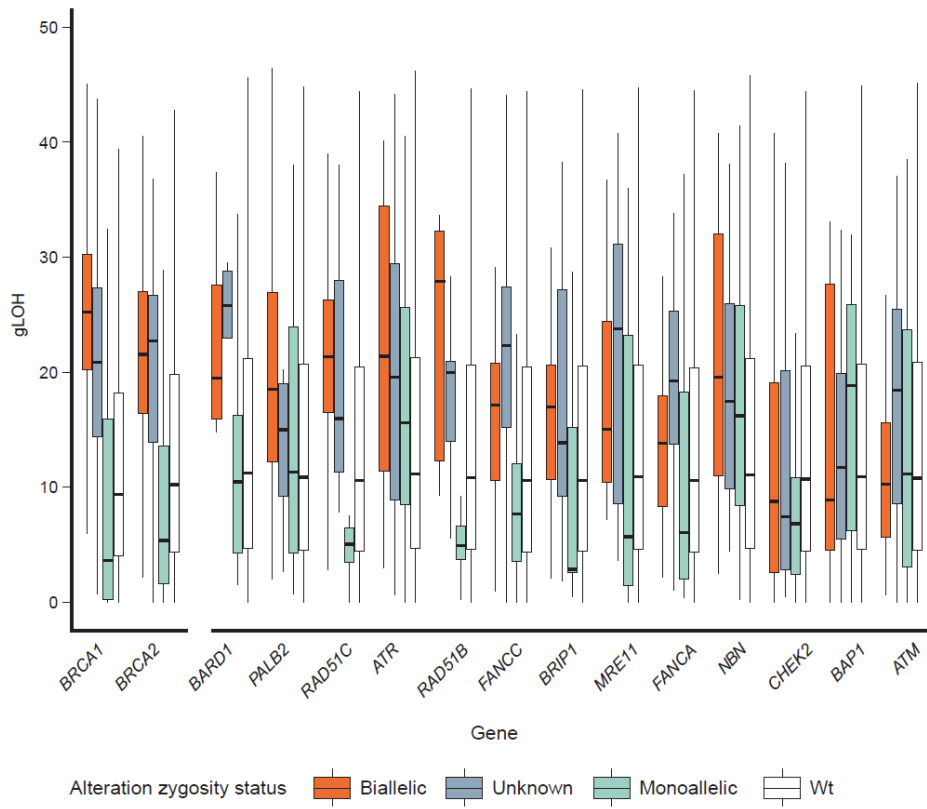
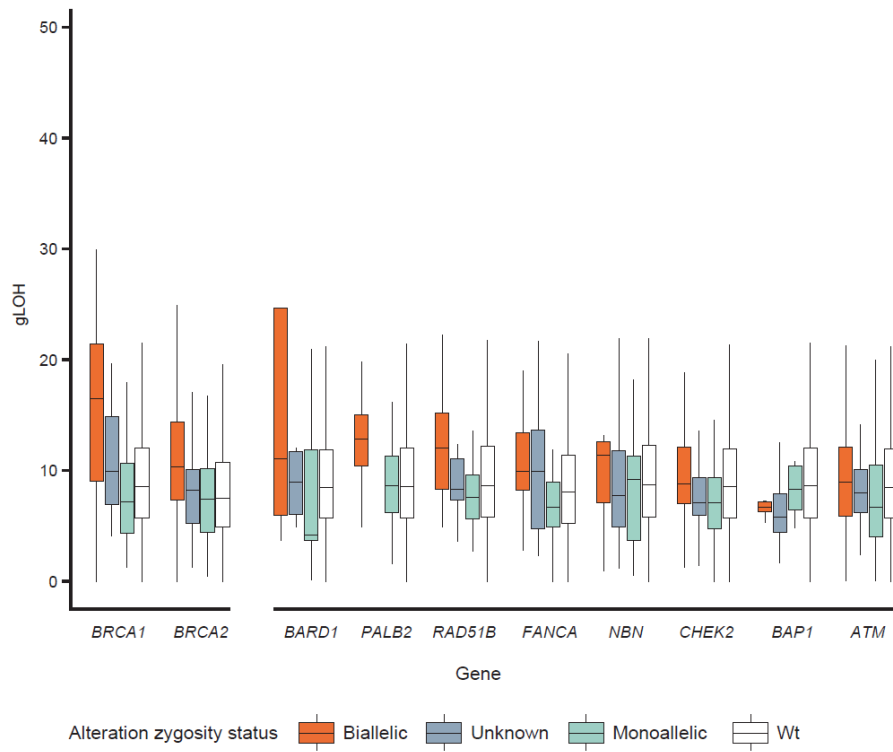


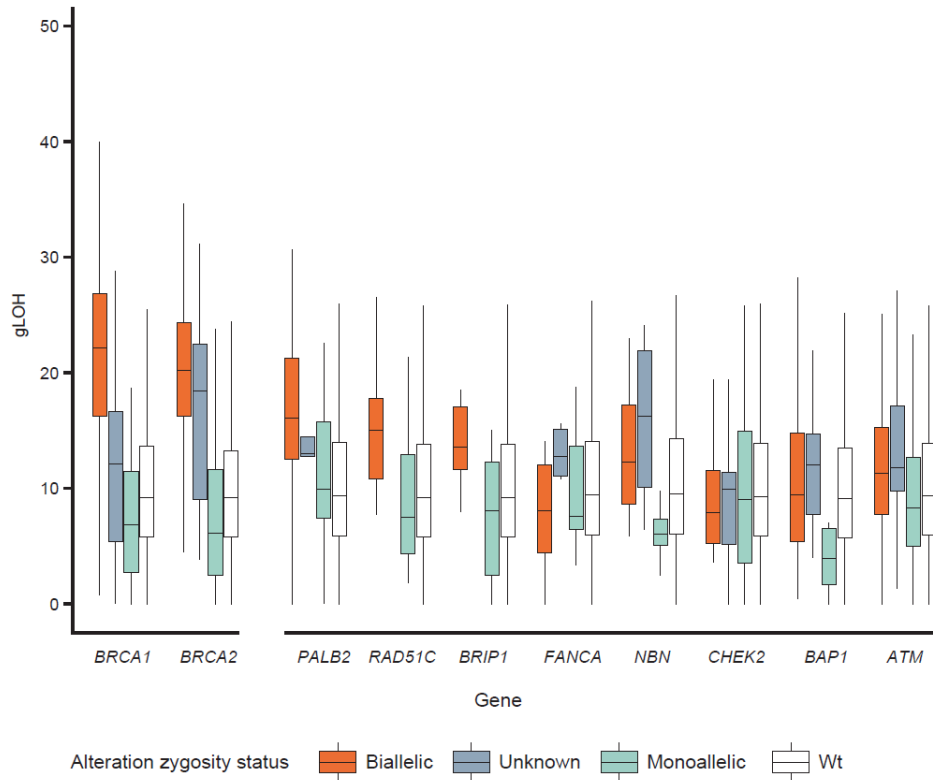
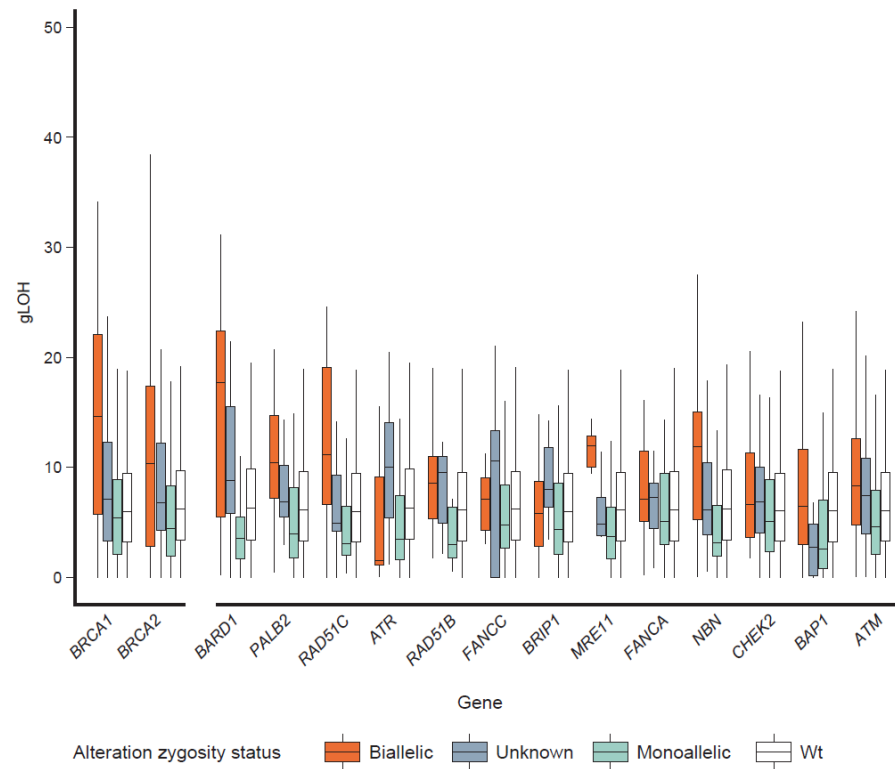
Supplementary Figure 7.

Association of HRR gene alterations with gLOH by cancer type*: **A**, breast, **B**, ovarian, **C**, prostate, **D**, pancreatic, **E**, CRC, and **F**, NSCLC. wt, wild type; * Only genes with at least five assessable alterations in each category (biallelic, BA; monoallelic, NBA) were considered; wt refers to the gene being analyzed; *CHEK1* and *ATR* had too few samples to be assessable and were therefore excluded.

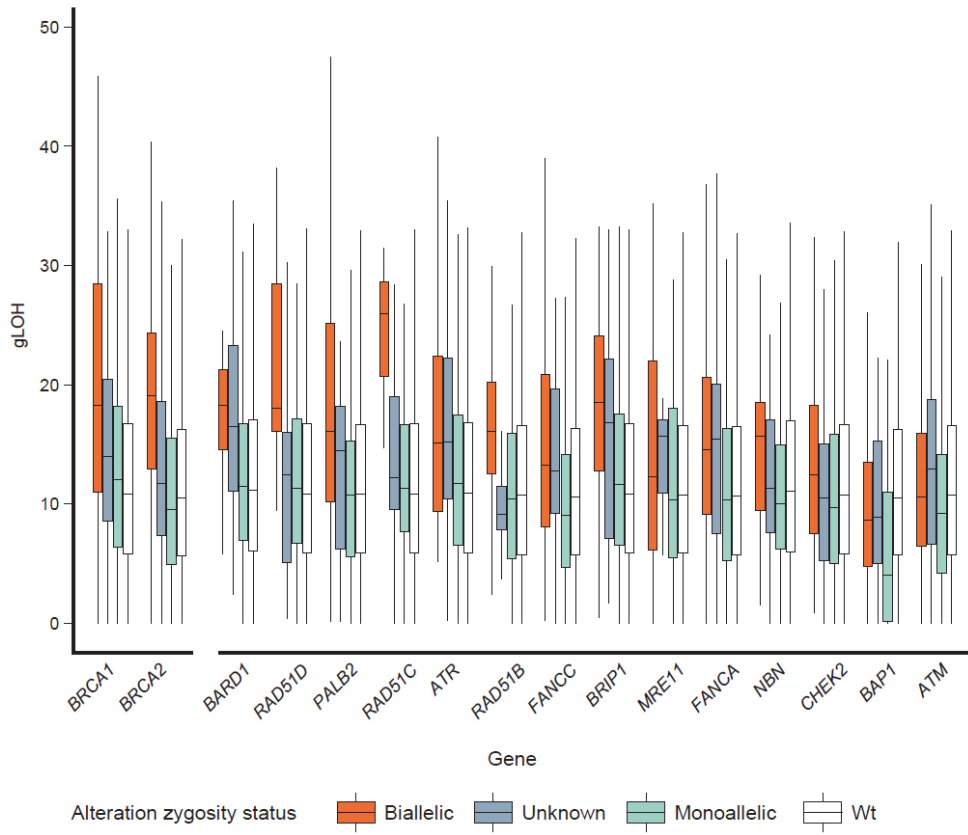
A



B**C**

D**E**

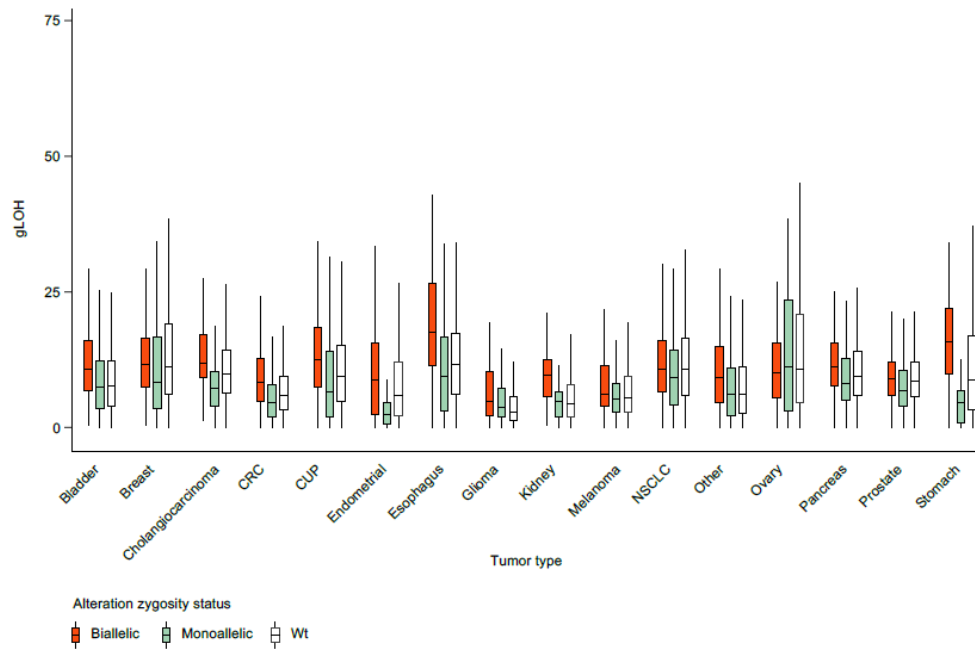
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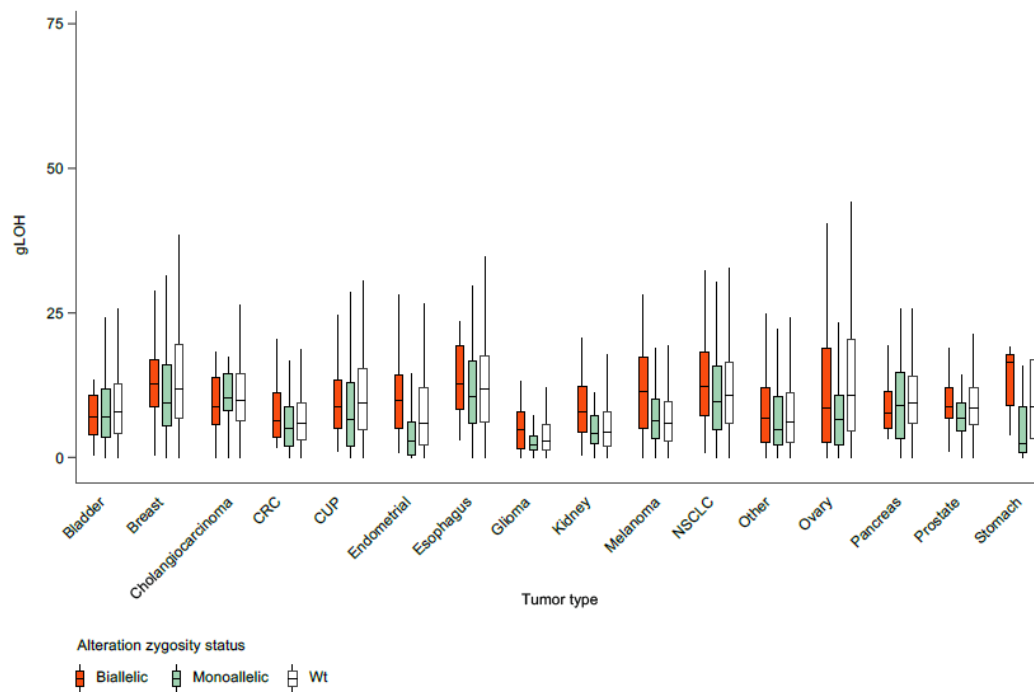
Supplementary Figure 8.

Association between gene alterations and gLOH for: **A**, *ATM*, **B**, *CHEK2*, **C**, *BAP1*, **D**, *CTNNA1*, and **E**, *TP53*. CUP, carcinoma-of-unknown-primary-origin; wt, wild type.

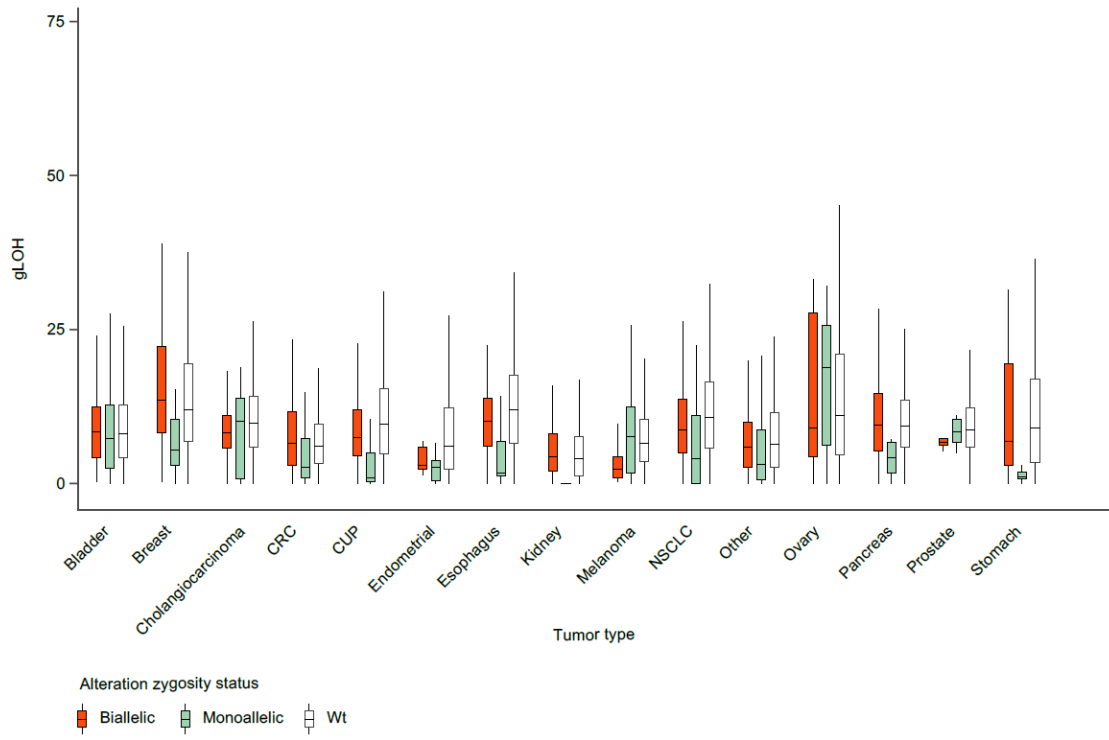
A



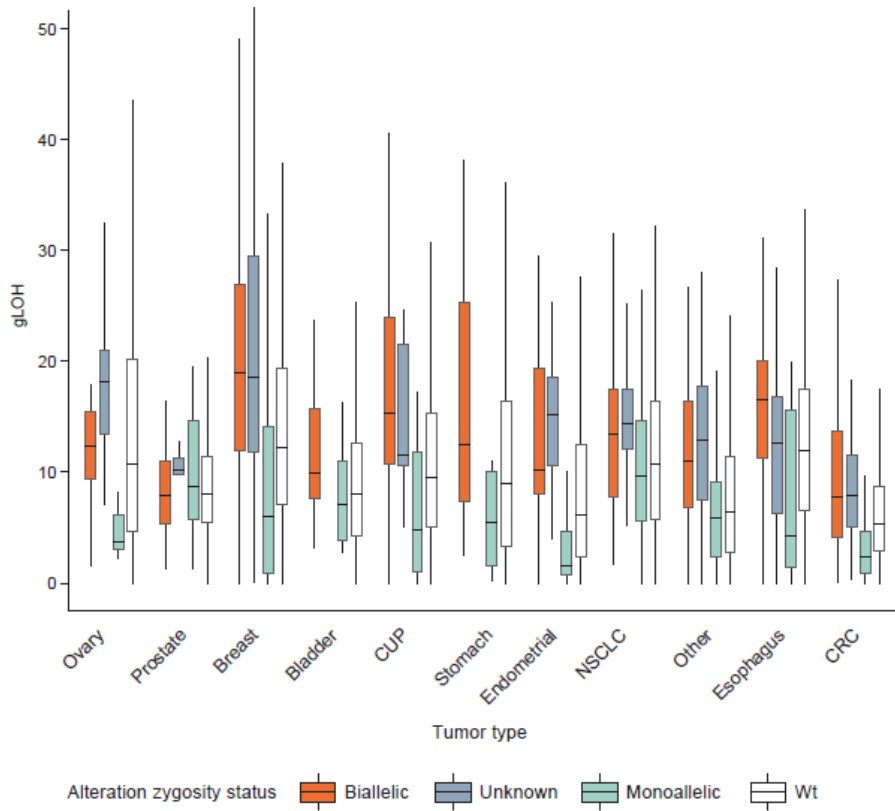
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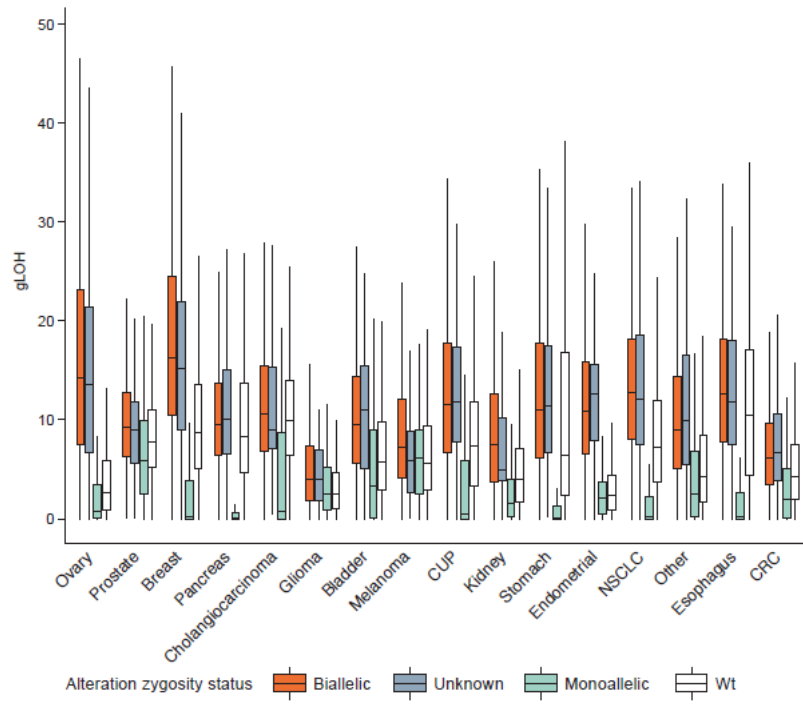
C



D

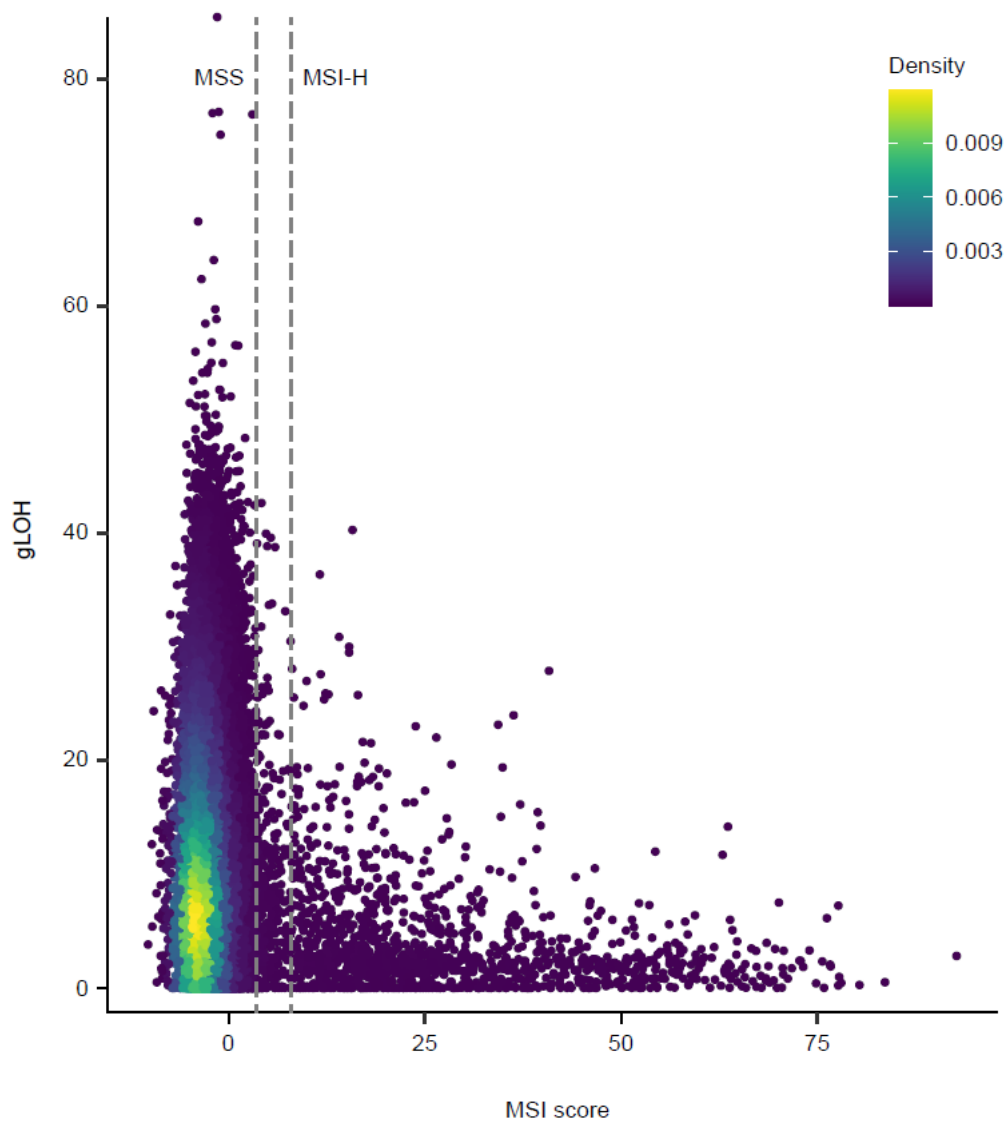


E

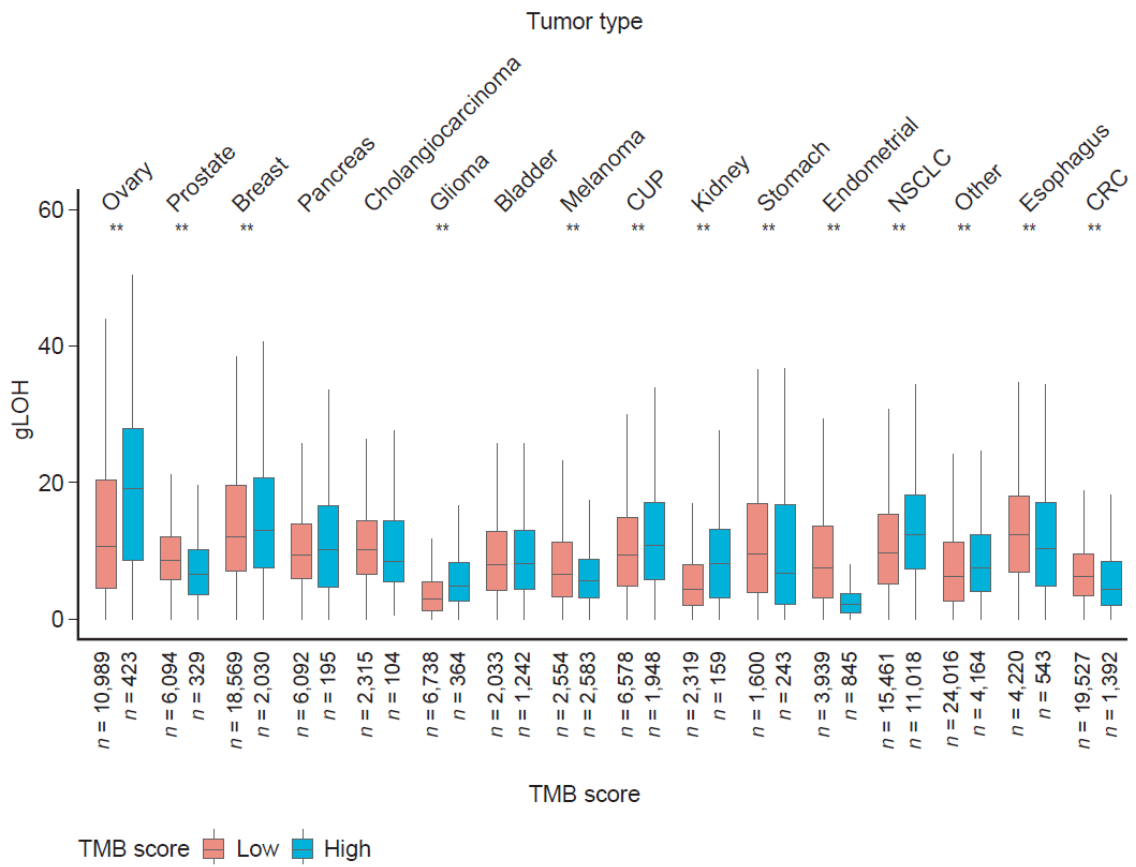


Supplementary Figure 9. Association of HRR-associated gene alterations and immune checkpoint inhibitor biomarkers: **A**, MSI and **B**, TMB. CUP, carcinoma-of-unknown-primary-origin; MSS, microsatellite stable; asterisks denote level of significance after false discovery correction: * = $P < 0.05$; ** = $P < 0.01$.

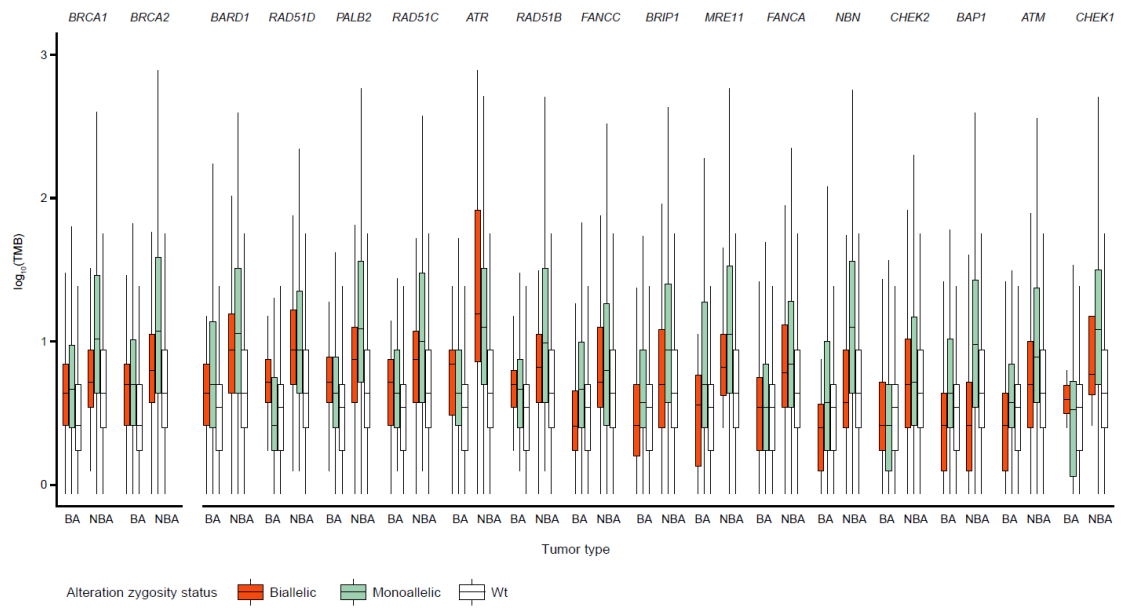
A



B



Supplementary Figure 10. Association of HRR-associated gene alterations with TMB: **A**, MSI and **B**, TMB. wt, wild type; wt refers to the gene being analyzed.



Supplementary Tables

Supplementary Table 1. List of HRR-associated genes in the study.

Gene
<i>BRCA1</i>
<i>BRCA2</i>
<i>PALB2</i>
<i>ATR</i>
<i>ATRX</i>
<i>ATM</i>
<i>BAP1</i>
<i>RAD51B</i>
<i>RAD51C</i>
<i>RAD51D</i>
<i>BRIP1</i>
<i>NBN</i>
<i>CHEK1</i>
<i>CHEK2</i>
<i>FANCA</i>
<i>FANCC</i>
<i>MRE11</i>
<i>BARD1</i>

Supplementary Table 2. Association of alterations and median gLOH for HRR-associated genes in BA and NBA tumor types, stratified by allelic status.

Gene	Group	No. assessable biallelic	No. assessable monoallelic	No. assessable unknown	No. assessable wt	Median gLOH biallelic	Median gLOH monoallelic	Median gLOH unknown	Median gLOH wt	% change biallelic vs. wt	P-value biallelic vs. wt
<i>BRCA1</i>	BA	1,666	158	342	42,599	26.4	8.1	18.0	10.1	+162%	0
<i>BRCA2</i>	BA	2,013	283	221	42,248	18.5	7.7	14.2	10.0	+85%	5.6 x 10 ⁻²⁶³
<i>PALB2</i>	BA	259	168	52	44,286	21.2	12.1	16.9	10.6	+100%	1.4 x 10 ⁻⁵⁴
<i>ATR</i>	BA	23	249	125	44,368	20.9	12.3	18.9	10.8	+93%	3.3 x 10 ⁻⁴
<i>ATRX</i>	BA	26	0	316	44,423	8.6	N/A*	12.4	10.6	-18%	3.9 x 10 ⁻¹
<i>ATM</i>	BA	823	410	173	43,359	10.4	8.1	12.2	10.2	+1%	4.8 x 10 ⁻¹
<i>BAP1</i>	BA	294	39	87	44,345	10.7	7.0	12.0	10.4	+2%	1.1 x 10 ⁻¹
<i>RAD51B</i>	BA	111	38	29	44,587	17.5	6.4	17.8	10.6	+65%	2.3 x 10 ⁻¹³
<i>RAD51C</i>	BA	111	43	44	44,567	20.7	8.6	11.3	10.5	+97%	3.4 x 10 ⁻²³
<i>RAD51D</i>	BA	81	23	16	44,645	21.7	9.4	13.4	10.5	+107%	7.1 x 10 ⁻¹⁸
<i>BRIP1</i>	BA	152	112	129	44,372	15.5	8.0	11.8	10.5	+48%	1.1 x 10 ⁻¹⁰
<i>NBN</i>	BA	30	141	55	44,539	12.5	10.6	13.4	10.8	+15%	1.4 x 10 ⁻¹
<i>CHEK1</i>	BA	2	12	7	44,744	21.4	12.4	12.1	10.2	+109%	5.1 x 10 ⁻²
<i>CHEK2</i>	BA	342	289	232	43,902	11.5	8.2	9.4	10.5	+9%	3.3 x 10 ⁻²
<i>FANCA</i>	BA	183	149	158	44,275	12.0	8.3	17.3	10.2	+17%	1.5 x 10 ⁻³
<i>FANCC</i>	BA	48	94	67	44,556	17.2	9.8	18.2	10.5	+62%	6.2 x 10 ⁻⁵
<i>MRE11</i>	BA	26	73	24	44,642	13.6	7.1	14.2	10.6	+28%	1.9 x 10 ⁻²
<i>BARD1</i>	BA	65	85	37	44,578	25.7	9.8	12.0	10.8	+137%	3.1 x 10 ⁻¹⁹
<i>TP53</i>	BA	25,480	1,314	1,230	16,741	13.1	0.4	11.8	7.7	+71%	0
<i>CTNNA1</i>	BA	346	54	97	44,268	16.9	7.9	18.1	10.5	+61%	8.0 x 10 ⁻²⁸
<i>BRCA1</i>	NBA	672	677	459	114,217	22.0	7.5	11.3	7.3	+201%	7.8 x 10 ⁻²⁰⁰
<i>BRCA2</i>	NBA	970	1,300	325	113,430	18.0	5.4	11.4	7.2	+149%	1.6 x 10 ⁻²¹⁹
<i>PALB2</i>	NBA	156	504	85	115,280	16.4	6.9	12.3	7.3	+123%	3.6 x 10 ⁻³²

<i>ATR</i>	NBA	83	967	161	114,814	8.4	7.2	13.5	7.5	+11%	2.6×10^{-1}
<i>ATRX</i>	NBA	310	0	2,561	113,154	7.2	N/A*	7.3	7.3	-1%	3.6×10^{-1}
<i>ATM</i>	NBA	2,001	2,172	362	111,490	9.9	6.0	9.0	7.2	+37%	1.2×10^{-55}
<i>BAP1</i>	NBA	2,089	234	373	113,329	6.3	3.0	6.4	7.2	-12%	1.0×10^{-12}
<i>RAD51B</i>	NBA	188	102	43	115,692	10.9	5.8	9.3	7.3	+49%	2.8×10^{-13}
<i>RAD51C</i>	NBA	83	149	44	115,749	14.7	6.4	9.8	7.3	+100%	5.6×10^{-12}
<i>RAD51D</i>	NBA	23	141	32	115,829	18.9	6.7	10.0	7.3	+157%	3.4×10^{-7}
<i>BRIP1</i>	NBA	131	646	116	115,132	12.0	7.3	10.9	7.3	+63%	1.5×10^{-7}
<i>NBN</i>	NBA	91	463	106	115,365	12.8	6.2	11.4	7.5	+69%	1.4×10^{-6}
<i>CHEK1</i>	NBA	4	55	10	115,956	2.6	7.6	11.6	7.2	-63%	1.3×10^{-1}
<i>CHEK2</i>	NBA	439	968	522	114,096	9.0	6.2	7.4	7.3	+23%	3.2×10^{-6}
<i>FANCA</i>	NBA	305	581	213	114,926	10.6	6.7	9.9	7.2	+45%	1.3×10^{-12}
<i>FANCC</i>	NBA	127	261	99	115,538	11.0	5.2	11.4	7.3	+51%	6.5×10^{-8}
<i>MRE11</i>	NBA	36	301	37	115,651	11.9	5.5	8.9	7.3	+62%	4.2×10^{-3}
<i>BARD1</i>	NBA	77	367	65	115,516	18.3	7.3	12.0	7.5	+142%	3.6×10^{-14}
<i>TP53</i>	NBA	62,863	5,206	2,666	45,290	9.2	1.0	9.6	4.9	+88%	0
<i>CTNNA1</i>	NBA	428	255	149	115,193	11.8	5.1	11.8	7.1	+65%	1.3×10^{-34}

*X-chromosome gene, so monoallelic status cannot be assessed.

Abbreviations: N/A, not applicable; wt, wild type.

Supplementary Table 3. Association of alterations and median gLOH for HRR-associated genes in breast, ovarian, prostate, pancreatic, CRC, and NSCLC, stratified by allelic status.

Gene	Group	No. assessable biallelic	No. assessable monoallelic	No. assessable unknown	No. assessable wt	Median gLOH biallelic	Median gLOH monoallelic	Median gLOH unknown	Median gLOH wt	% change biallelic vs. wt	P-value biallelic vs. wt
<i>BRCA1</i>	Breast	604	82	152	19,776	29.3	10.9	18.6	11.7	+150%	2.3×10^{-220}
<i>BRCA2</i>	Breast	791	124	105	19,594	20.9	11.2	17.6	11.5	+81%	1.2×10^{-140}
<i>PALB2</i>	Breast	172	97	30	20,315	22.6	14.7	19.0	12.1	+86%	2.2×10^{-43}
<i>ATR</i>	Breast	12	121	59	20,422	15.6	14.3	24.3	12.4	+25%	4.0×10^{-2}
<i>ATRX</i>	Breast	7	0	176	20,431	22.0	N/A*	13.9	12.1	+81%	1.0×10^{-2}
<i>ATM</i>	Breast	341	130	67	20,076	11.6	8.3	14.9	11.3	+2%	4.7×10^{-1}
<i>BAP1</i>	Breast	155	12	36	20,411	13.5	5.4	14.1	11.9	+13%	2.5×10^{-2}
<i>RAD51B</i>	Breast	79	22	13	20,500	21.5	6.9	22.2	12.0	+78%	5.8×10^{-10}
<i>RAD51C</i>	Breast	29	26	31	20,528	25.1	9.7	10.6	12.0	+108%	3.3×10^{-7}
<i>RAD51D</i>	Breast	18	11	9	20,576	23.8	8.9	13.2	12.0	+97%	2.0×10^{-4}
<i>BRIPI</i>	Breast	41	49	105	20,419	14.0	8.4	11.9	12.0	+16%	2.6×10^{-2}
<i>NBN</i>	Breast	4	74	26	20,510	13.4	12.2	14.9	12.5	+7%	4.8×10^{-1}
<i>CHEK1</i>	Breast	1	6	5	20,602	22.6	11.5	12.1	11.3	+99%	1.3×10^{-1}
<i>CHEK2</i>	Breast	241	132	111	20,130	12.8	9.5	11.6	12.1	+5%	2.0×10^{-1}
<i>FANCA</i>	Breast	97	64	90	20,363	14.0	13.0	17.3	11.7	+19%	1.3×10^{-2}
<i>FANCC</i>	Breast	21	44	31	20,518	21.0	10.5	21.7	12.1	+74%	1.8×10^{-3}
<i>MRE11</i>	Breast	18	26	14	20,556	14.1	10.7	14.9	12.2	+16%	1.8×10^{-1}
<i>BARD1</i>	Breast	51	41	14	20,508	28.7	10.5	14.2	12.4	+130%	5.2×10^{-16}
<i>TP53</i>	Breast	10,205	627	468	9,314	16.2	0.3	15.2	8.7	+86%	0
<i>CTNNA1</i>	Breast	291	27	71	20,225	18.9	6.0	18.5	12.2	+54%	4.7×10^{-23}
<i>BRCA1</i>	Ovary	979	23	138	10,287	25.2	3.6	20.8	9.3	+170%	4.9×10^{-291}
<i>BRCA2</i>	Ovary	490	55	37	10,845	21.5	5.4	22.7	10.2	+110%	1.2×10^{-86}

<i>PALB2</i>	Ovary	31	29	13	11,354	18.5	11.3	15.0	10.8	+70%	2.2×10^{-4}
<i>ATR</i>	Ovary	9	56	39	11,323	21.4	15.6	19.6	11.1	+91%	2.2×10^{-2}
<i>ATRX</i>	Ovary	7	0	73	11,347	6.4	N/A*	12.6	10.9	-41%	2.6×10^{-2}
<i>ATM</i>	Ovary	89	103	51	11,184	10.3	11.2	18.4	10.8	-4%	2.6×10^{-1}
<i>BAP1</i>	Ovary	26	15	25	11,361	8.9	18.8	11.7	10.9	-18%	4.5×10^{-1}
<i>RAD51B</i>	Ovary	10	8	9	11,400	27.9	4.9	20.0	10.8	+157%	2.1×10^{-3}
<i>RAD51C</i>	Ovary	60	5	10	11,352	21.4	5.0	16.0	10.6	+102%	1.9×10^{-12}
<i>RAD51D</i>	Ovary	57	3	6	11,361	21.6	6.5	21.0	10.6	+104%	3.2×10^{-11}
<i>BRIP1</i>	Ovary	97	9	17	11,304	17.0	2.8	13.9	10.6	+60%	8.8×10^{-6}
<i>NBN</i>	Ovary	9	25	11	11,382	19.6	16.2	17.4	11.1	+76%	4.9×10^{-2}
<i>CHEK1</i>	Ovary	1	2	2	11,422	20.1	23.5	25.3	10.8	+86%	2.1×10^{-1}
<i>CHEK2</i>	Ovary	56	45	51	11,275	8.8	6.8	7.4	10.7	-18%	5.7×10^{-2}
<i>FANCA</i>	Ovary	37	31	49	11,310	13.8	6.1	19.3	10.6	+30%	1.0×10^{-1}
<i>FANCC</i>	Ovary	22	17	22	11,366	17.1	7.6	22.3	10.6	+61%	6.8×10^{-2}
<i>MRE11</i>	Ovary	6	21	7	11,393	15.0	5.7	23.8	10.9	+37%	1.0×10^{-1}
<i>BARD1</i>	Ovary	5	21	9	11,392	19.5	10.4	25.8	11.2	+73%	2.1×10^{-2}
<i>TP53</i>	Ovary	8,524	241	266	2,396	14.2	0.8	13.6	2.7	+433%	0
<i>CTNNA1</i>	Ovary	13	7	19	11,388	12.4	3.7	18.2	10.7	+14%	2.8×10^{-1}
<i>BRCA1</i>	Prostate	20	31	30	6,353	16.5	7.2	9.9	8.6	+92%	5.4×10^{-5}
<i>BRCA2</i>	Prostate	521	51	54	5,808	10.3	7.4	8.2	7.5	+37%	2.2×10^{-37}
<i>PALB2</i>	Prostate	31	21	4	6,378	12.8	8.7	5.3	8.5	+50%	1.7×10^{-6}
<i>ATR</i>	Prostate	1	51	22	6,360	23.5	7.7	11.5	8.7	+169%	4.5×10^{-2}
<i>ATRX</i>	Prostate	9	0	30	6,395	10.0	N/A*	9.8	8.5	+17%	1.2×10^{-1}
<i>ATM</i>	Prostate	248	91	38	6,057	9.0	6.7	8.0	8.5	+5%	1.2×10^{-1}
<i>BAP1</i>	Prostate	10	6	9	6,409	6.7	8.3	5.8	8.6	-22%	3.4×10^{-2}
<i>RAD51B</i>	Prostate	14	6	5	6,409	12.0	7.6	8.3	8.7	+38%	9.3×10^{-3}
<i>RAD51C</i>	Prostate	4	3	2	6,425	13.4	10.0	11.3	8.6	+56%	4.7×10^{-2}
<i>RAD51D</i>	Prostate	2	5	0	6,427	18.3	4.2	N/A	8.6	+113%	5.1×10^{-2}
<i>BRIP1</i>	Prostate	2	29	6	6,397	17.4	8.6	6.6	8.6	+103%	2.4×10^{-2}
<i>NBN</i>	Prostate	10	29	13	6,382	11.4	9.2	7.7	8.7	+30%	1.9×10^{-1}

<i>CHEK1</i>	Prostate	0	1	0	6,433	N/A	1.5	N/A	8.5	N/A	N/A
<i>CHEK2</i>	Prostate	23	68	38	6,305	8.8	7.1	7.1	8.5	+2%	3.6×10^{-1}
<i>FANCA</i>	Prostate	41	27	9	6,357	9.9	6.7	9.9	8.1	+23%	5.2×10^{-3}
<i>FANCC</i>	Prostate	3	21	9	6,401	17.1	8.4	14.7	8.7	+97%	2.5×10^{-2}
<i>MRE11</i>	Prostate	2	21	2	6,409	11.1	4.6	13.0	8.5	+30%	2.1×10^{-1}
<i>BARD1</i>	Prostate	5	11	10	6,408	11.1	4.2	8.9	8.5	+30%	1.9×10^{-1}
<i>TP53</i>	Prostate	2,434	170	245	3,585	9.3	5.8	9.0	7.8	+18%	5.1×10^{-31}
<i>CTNNA1</i>	Prostate	33	16	5	6,380	7.8	8.7	10.2	8.1	-3%	4.1×10^{-1}
<i>BRCA1</i>	Pancreas	63	22	22	6,183	22.2	6.9	12.2	9.2	+141%	3.3×10^{-22}
<i>BRCA2</i>	Pancreas	211	53	25	6,001	20.2	6.1	18.4	9.2	+119%	2.7×10^{-82}
<i>PALB2</i>	Pancreas	25	21	5	6,239	16.1	10.0	13.0	9.4	+71%	2.5×10^{-6}
<i>ATR</i>	Pancreas	1	21	5	6,263	16.5	5.7	13.9	9.7	+70%	1.3×10^{-1}
<i>ATRX</i>	Pancreas	3	0	37	6,250	3.5	N/A*	9.1	9.3	-62%	2.2×10^{-1}
<i>ATM</i>	Pancreas	145	86	17	6,042	11.3	8.3	11.8	9.4	+20%	1.9×10^{-4}
<i>BAP1</i>	Pancreas	103	6	17	6,164	9.4	3.9	12.0	9.2	+3%	3.3×10^{-1}
<i>RAD51B</i>	Pancreas	8	2	2	6,278	10.7	13.7	13.7	9.4	+14%	2.5×10^{-1}
<i>RAD51C</i>	Pancreas	18	9	1	6,262	15.0	7.5	11.4	9.2	+62%	1.3×10^{-4}
<i>RAD51D</i>	Pancreas	4	4	1	6,281	15.6	15.7	5.8	9.2	+68%	1.8×10^{-1}
<i>BRIP1</i>	Pancreas	12	25	1	6,252	13.6	8.1	0.0	9.2	+47%	3.0×10^{-3}
<i>NBN</i>	Pancreas	7	13	5	6,265	12.3	6.1	16.2	9.6	+28%	1.3×10^{-1}
<i>CHEK1</i>	Pancreas	0	3	0	6,287	N/A	12.3	N/A	9.4	N/A	N/A*
<i>CHEK2</i>	Pancreas	22	44	32	6,192	7.9	9.1	9.9	9.3	-14%	1.7×10^{-1}
<i>FANCA</i>	Pancreas	8	27	10	6,245	8.1	7.6	12.8	9.5	-14%	1.7×10^{-1}
<i>FANCC</i>	Pancreas	2	12	5	6,271	10.7	11.3	10.7	9.3	+15%	4.7×10^{-1}
<i>MRE11</i>	Pancreas	0	5	1	6,284	N/A	7.1	6.1	9.3	N/A	N/A*
<i>BARD1</i>	Pancreas	4	12	4	6,270	19.4	9.7	8.1	9.9	+96%	6.3×10^{-3}
<i>TP53</i>	Pancreas	4,317	276	251	1,446	9.5	0.1	10.1	8.3	+13%	1.2×10^{-11}
<i>CTNNA1</i>	Pancreas	9	4	2	6,275	14.1	11.1	15.9	9.5	+48%	1.3×10^{-1}
<i>BRCA1</i>	CRC	91	105	81	20,666	14.6	5.4	7.1	6.0	+144%	4.8×10^{-14}
<i>BRCA2</i>	CRC	48	318	49	20,528	10.4	4.4	6.8	6.2	+68%	9.7×10^{-4}

<i>PALB2</i>	CRC	8	91	16	20,828	10.4	3.9	6.9	6.1	+71%	3.2×10^{-2}
<i>ATR</i>	CRC	9	136	14	20,784	1.5	3.5	10.0	6.3	-75%	6.5×10^{-2}
<i>ATRX</i>	CRC	12	0	196	20,735	4.3	N/A*	4.5	6.1	-29%	1.2×10^{-1}
<i>ATM</i>	CRC	439	499	55	19,950	8.3	4.6	7.4	6.1	+36%	7.5×10^{-18}
<i>BAP1</i>	CRC	31	43	11	20,858	6.4	2.5	2.7	6.0	+6%	3.4×10^{-1}
<i>RAD51B</i>	CRC	36	8	10	20,889	8.6	2.9	9.5	6.1	+40%	3.0×10^{-3}
<i>RAD51C</i>	CRC	20	20	9	20,894	11.1	3.0	4.9	6.0	+86%	2.0×10^{-3}
<i>RAD51D</i>	CRC	3	25	8	20,907	18.9	5.7	7.9	6.0	+215%	1.5×10^{-2}
<i>BRIP1</i>	CRC	33	94	17	20,799	5.8	4.4	8.0	6.0	-3%	3.0×10^{-1}
<i>NBN</i>	CRC	18	99	21	20,805	11.8	3.1	6.2	6.2	+89%	9.4×10^{-3}
<i>CHEK1</i>	CRC	0	8	2	20,933	N/A	7.6	13.9	6.1	N/A	N/A*
<i>CHEK2</i>	CRC	60	128	85	20,670	6.6	5.0	6.9	6.1	+9%	6.7×10^{-2}
<i>FANCA</i>	CRC	34	85	22	20,802	7.1	5.0	7.3	6.1	+16%	7.0×10^{-2}
<i>FANCC</i>	CRC	6	66	5	20,866	7.1	4.7	10.6	6.2	+14%	3.9×10^{-1}
<i>MRE11</i>	CRC	6	64	7	20,866	11.9	3.7	4.9	6.1	+95%	2.8×10^{-2}
<i>BARD1</i>	CRC	10	70	16	20,847	17.7	3.5	8.8	6.3	+181%	1.1×10^{-2}
<i>TP53</i>	CRC	15,673	605	649	4,016	6.2	1.9	6.7	4.3	+44%	2.1×10^{-120}
<i>CTNNA1</i>	CRC	103	52	29	20,759	7.7	2.4	7.8	5.4	+42%	2.0×10^{-6}
<i>BRC1</i>	NSCLC	84	193	108	26,126	18.3	12.1	14.0	10.9	+68%	1.0×10^{-12}
<i>BRC2</i>	NSCLC	242	247	79	25,943	19.2	9.6	11.7	10.5	+81%	9.2×10^{-43}
<i>PALB2</i>	NSCLC	36	144	21	26,310	16.1	10.8	14.5	10.8	+48%	4.9×10^{-5}
<i>ATR</i>	NSCLC	24	269	56	26,162	15.1	11.8	15.2	11.0	+37%	3.0×10^{-3}
<i>ATRX</i>	NSCLC	28	0	417	26,066	10.8	N/A*	12.2	10.8	+0%	1.0×10^{-1}
<i>ATM</i>	NSCLC	559	571	101	25,280	10.7	9.3	13.0	10.8	-1%	1.5×10^{-1}
<i>BAP1</i>	NSCLC	276	31	44	26,160	8.7	4.0	9.0	10.6	-17%	5.7×10^{-5}
<i>RAD51B</i>	NSCLC	28	24	12	26,447	16.2	10.4	9.2	10.8	+49%	2.9×10^{-4}
<i>RAD51C</i>	NSCLC	7	42	15	26,447	26.0	11.4	12.3	10.9	+138%	1.7×10^{-4}
<i>RAD51D</i>	NSCLC	5	40	9	26,457	18.1	11.4	12.5	10.9	+66%	1.4×10^{-2}
<i>BRIP1</i>	NSCLC	23	206	27	26,255	18.5	11.7	16.9	10.9	+70%	1.4×10^{-4}

<i>NBN</i>	NSCLC	33	118	34	26,326	15.7	10.1	11.4	11.1	+41%	8.6×10^{-3}
<i>CHEK1</i>	NSCLC	0	19	1	26,491	N/A	9.7	18.8	10.8	N/A	N/A*
<i>CHEK2</i>	NSCLC	107	232	114	26,058	12.5	9.7	10.6	10.8	+15%	7.1×10^{-3}
<i>FANCA</i>	NSCLC	97	147	58	26,209	14.6	10.4	15.5	10.7	+36%	1.3×10^{-5}
<i>FANCC</i>	NSCLC	48	43	34	26,386	13.3	9.1	12.8	10.6	+24%	3.6×10^{-3}
<i>MRE11</i>	NSCLC	13	67	8	26,423	12.3	10.4	15.8	10.8	+13%	2.3×10^{-1}
<i>BARD1</i>	NSCLC	16	129	15	26,351	18.3	11.5	16.5	11.2	+63%	4.8×10^{-4}
<i>TP53</i>	NSCLC	16,742	1,586	807	7,376	12.7	0.2	12.1	7.2	+76%	0
<i>CTNNA1</i>	NSCLC	63	44	31	26,373	13.4	9.6	14.3	10.7	+25%	8.8×10^{-3}

*X-chromosome gene, so monoallelic status cannot be assessed.

Abbreviations: N/A, not applicable; wt, wild type.

Supplementary Table 4. Association of alterations and median gLOH for *ATM* for all tumor types, stratified by allelic status.

Group	No. assessable biallelic	No. assessable monoallelic	No. assessable unknown	No. assessable wt	Median gLOH biallelic	Median gLOH monoallelic	Median gLOH unknown	Median gLOH wt	% change biallelic vs. wt	P-value biallelic vs. wt	Corrected P-value biallelic vs. wt
Stomach	53	33	5	1,758	15.7	4.7	12.1	8.9	+77%	4.7 x 10 ⁻⁶	1.5 x 10 ⁻⁵
Glioma	36	98	13	6,960	5.0	3.7	5.2	2.9	+69%	2.3 x 10 ⁻³	4.0 x 10 ⁻³
CUP	150	147	19	8,217	12.5	6.7	12.2	9.4	+33%	2.0 x 10 ⁻⁵	5.5 x 10 ⁻⁵
Cholangiocarcinoma	37	30	6	2,346	11.9	7.3	11.0	9.9	+19%	2.5 x 10 ⁻³	4.0 x 10 ⁻³
Bladder	76	82	13	3,106	10.8	7.4	13.2	7.7	+39%	9.3 x 10 ⁻⁵	2.1 x 10 ⁻⁴
Breast	341	130	67	20,076	11.6	8.3	14.9	11.3	+2%	4.7 x 10 ⁻¹	4.7 x 10 ⁻¹
Esophagus	58	71	17	4,619	17.6	9.4	16.8	11.7	+50%	1.2 x 10 ⁻⁶	6.6 x 10 ⁻⁶
Prostate	248	91	38	6,057	9.0	6.7	8.0	8.5	+5%	1.2 x 10 ⁻¹	1.5 x 10 ⁻¹
Kidney	36	30	9	2,407	9.8	4.8	6.8	4.3	+125%	3.4 x 10 ⁻⁶	1.4 x 10 ⁻⁵
Pancreas	145	86	17	6,042	11.3	8.3	11.8	9.4	+20%	1.9 x 10 ⁻⁴	3.8 x 10 ⁻⁴
NSCLC	559	571	101	25,280	10.7	9.3	13.0	10.8	-1%	1.5 x 10 ⁻¹	1.8 x 10 ⁻¹
Endometrial	92	141	17	4,540	8.8	2.4	8.6	6.0	+46%	2.1 x 10 ⁻²	2.8 x 10 ⁻²
Melanoma	106	73	18	4,944	6.3	5.3	5.2	5.5	+13%	9.7 x 10 ⁻³	1.4 x 10 ⁻²
CRC	439	499	55	19,950	8.3	4.6	7.4	6.1	+36%	7.5 x 10 ⁻¹⁸	1.2 x 10 ⁻¹⁶
Ovary	89	103	51	11,184	10.3	11.2	18.4	10.8	-4%	2.6 x 10 ⁻¹	2.8 x 10 ⁻¹
Other	359	397	89	27,363	9.3	6.1	8.3	6.1	+52%	4.6 x 10 ⁻¹⁴	3.7 x 10 ⁻¹³

Abbreviations: CUP, carcinoma-of-unknown-primary-origin; wt, wild type.

Supplementary Table 5. Association of alterations and median gLOH for *CHEK2* for all tumor types, stratified by allelic status.

Group	No. assessable biallelic	No. assessable monoallelic	No. assessable unknown	No. assessable wt	Median gLOH biallelic	Median gLOH monoallelic	Median gLOH unknown	Median gLOH wt	% change biallelic vs. wt	P-value biallelic vs. wt	Corrected P-value biallelic vs. wt
Stomach	10	15	10	1,814	16.7	2.6	5.1	9.1	+82%	6.1×10^{-2}	1.5×10^{-1}
Glioma	21	69	39	6,978	5.0	2.3	2.7	2.9	+69%	8.3×10^{-2}	1.7×10^{-1}
CUP	37	76	35	8,385	8.8	6.7	9.0	9.6	-9%	4.3×10^{-1}	4.3×10^{-1}
Cholangiocarcinoma	11	17	11	2,380	8.9	10.6	10.3	10.1	-11%	3.3×10^{-1}	3.9×10^{-1}
Bladder	21	53	20	3,183	7.3	7.1	10.0	8.0	-9%	3.5×10^{-1}	3.9×10^{-1}
Breast	241	132	111	20,130	12.8	9.5	11.6	12.1	+5%	2.0×10^{-1}	3.2×10^{-1}
Esophagus	16	25	12	4,712	13.0	10.6	17.1	12.1	+7%	2.4×10^{-1}	3.4×10^{-1}
Prostate	23	68	38	6,305	8.8	7.1	7.1	8.5	+2%	3.6×10^{-1}	3.9×10^{-1}
Kidney	18	26	9	2,429	8.2	4.3	6.1	4.5	+80%	7.0×10^{-3}	5.2×10^{-2}
Pancreas	22	44	32	6,192	7.9	9.1	9.9	9.3	-14%	1.7×10^{-1}	3.0×10^{-1}
NSCLC	107	232	114	26,058	12.5	9.7	10.6	10.8	+15%	7.1×10^{-3}	5.2×10^{-2}
Endometrial	17	55	23	4,695	10.0	2.8	4.2	6.0	+65%	3.9×10^{-2}	1.5×10^{-1}
Melanoma	12	62	36	5,031	11.6	6.5	6.6	6.0	+93%	9.8×10^{-3}	5.2×10^{-2}
CRC	60	128	85	20,670	6.6	5.0	6.9	6.1	+9%	6.7×10^{-2}	1.5×10^{-1}
Ovary	56	45	51	11,275	8.8	6.8	7.4	10.7	-18%	5.7×10^{-2}	1.5×10^{-1}
Other	109	210	128	27,761	7.1	5.0	6.7	6.4	+10%	2.6×10^{-1}	3.5×10^{-1}

Abbreviations: CUP, carcinoma-of-unknown-primary-origin; wt, wild type.

Supplementary Table 6. Association of alterations and median gLOH for *BAP1* for all tumor types, stratified by allelic status.

Group	No. assessable biallelic	No. assessable monoallelic	No. assessable unknown	No. assessable wt	Median gLOH biallelic	Median gLOH monoallelic	Median gLOH unknown	Median gLOH wt	% change biallelic vs. wt	P-value biallelic vs. wt	Corrected P-value biallelic vs. wt
Stomach	26	6	3	1,814	6.7	0.6	1.0	8.9	-25%	4.6 x 10 ⁻¹	4.9 x 10 ⁻¹
Glioma	3	4	6	7,094	11.4	4.0	4.2	3.0	+286%	2.9 x 10 ⁻²	5.7 x 10 ⁻²
CUP	312	15	51	8,155	7.5	0.9	6.5	9.4	-19%	2.4 x 10 ⁻⁵	1.9 x 10 ⁻⁴
Cholangiocarcinoma	305	10	75	2,029	8.2	10.0	8.5	9.7	-14%	4.0 x 10 ⁻⁵	2.1 x 10 ⁻⁴
Bladder	40	22	11	3,204	8.4	7.2	9.4	8.0	+5%	4.9 x 10 ⁻¹	4.9 x 10 ⁻¹
Breast	155	12	36	20,411	13.5	5.4	14.1	11.9	+13%	2.5 x 10 ⁻²	5.7 x 10 ⁻²
Esophagus	31	8	6	4,720	9.9	1.6	13.9	11.9	-16%	1.1 x 10 ⁻¹	1.7 x 10 ⁻¹
Prostate	10	6	9	6,409	6.7	8.3	5.8	8.6	-22%	3.4 x 10 ⁻²	6.0 x 10 ⁻²
Kidney	205	8	19	2,250	4.2	0.0	5.4	3.8	+9%	1.7 x 10 ⁻²	4.6 x 10 ⁻²
Pancreas	103	6	17	6,164	9.4	3.9	12.0	9.2	+3%	3.3 x 10 ⁻¹	4.2 x 10 ⁻¹
NSCLC	276	31	44	26,160	8.7	4.0	9.0	10.6	-17%	5.7 x 10 ⁻⁵	2.3 x 10 ⁻⁴
Endometrial	6	15	7	4,762	2.8	2.5	13.3	6.0	-52%	1.7 x 10 ⁻¹	2.4 x 10 ⁻¹
Melanoma	212	19	50	4,860	2.4	7.5	2.1	6.3	-61%	1.4 x 10 ⁻⁴¹	2.2 x 10 ⁻⁴⁰
CRC	31	43	11	20,858	6.4	2.5	2.7	6.0	+6%	3.4 x 10 ⁻¹	4.2 x 10 ⁻¹
Ovary	26	15	25	11,361	8.9	18.8	11.7	10.9	-18%	4.6 x 10 ⁻¹	4.9 x 10 ⁻¹
Other	642	53	90	27,423	5.7	3.1	5.7	6.2	-8%	3.6 x 10 ⁻³	1.2 x 10 ⁻²

Abbreviations: CUP, carcinoma-of-unknown-primary-origin; wt, wild type.

Supplementary Table 7. Association of alterations and median gLOH for *CTNNA1* for all tumor types, stratified by allelic status.

Group	No. assessable biallelic	No. assessable monoallelic	No. assessable unknown	No. assessable wt	Median gLOH biallelic	Median gLOH monoallelic	Median gLOH unknown	Median gLOH wt	% change biallelic vs. wt	P-value biallelic vs. wt	Corrected P-value biallelic vs. wt
Stomach	17	9	4	1,819	12.4	5.5	5.9	9.0	+37%	1.1 x 10 ⁻²	2.4 x 10 ⁻²
Glioma	2	14	2	7,089	9.5	4.8	7.6	3.1	+212%	4.6 x 10 ⁻¹	4.9 x 10 ⁻¹
CUP	67	18	9	8,439	15.4	4.8	11.5	9.6	+60%	1.5 x 10 ⁻⁹	1.2 x 10 ⁻⁸
Cholangiocarcinoma	9	3	2	2,405	15.7	13.5	19.0	10.1	+56%	1.5 x 10 ⁻²	3.0 x 10 ⁻²
Bladder	7	15	3	3,252	9.9	7.1	18.2	8.0	+24%	1.3 x 10 ⁻¹	1.9 x 10 ⁻¹
Breast	291	27	71	20,225	18.9	6.0	18.5	12.2	+54%	4.6 x 10 ⁻²³	7.4 x 10 ⁻²²
Esophagus	65	15	21	4,664	16.5	4.2	12.6	11.9	+38%	1.5 x 10 ⁻⁴	4.7 x 10 ⁻⁴
Prostate	33	16	5	6,380	7.8	8.7	10.2	8.1	-3%	4.1 x 10 ⁻¹	4.9 x 10 ⁻¹
Kidney	0	1	0	2,481	N/A	6.7	N/A	4.6	N/A	N/A	1.0
Pancreas	9	4	2	6,275	14.1	11.1	15.9	9.5	+48%	1.3 x 10 ⁻¹	1.9 x 10 ⁻¹
NSCLC	63	44	31	26,373	13.4	9.6	14.3	10.7	+25%	8.8 x 10 ⁻³	2.3 x 10 ⁻²
Endometrial	8	19	7	4,756	10.2	1.6	15.2	6.1	+65%	5.1 x 10 ⁻²	9.1 x 10 ⁻²
Melanoma	4	10	3	5,124	7.7	6.4	9.8	5.9	+29%	4.4 x 10 ⁻¹	4.9 x 10 ⁻¹
CRC	103	52	29	20,759	7.7	2.4	7.8	5.4	+42%	2.0 x 10 ⁻⁶	8.0 x 10 ⁻⁶
Ovary	13	7	19	11,388	12.4	3.7	18.2	10.7	+14%	2.8 x 10 ⁻¹	3.7 x 10 ⁻¹
Other	83	55	38	28,032	11.0	5.9	12.8	6.4	+71%	2.2 x 10 ⁻⁸	1.2 x 10 ⁻⁷

Abbreviations: CUP, carcinoma-of-unknown-primary-origin; N/A, not applicable; wt, wild type.

Supplementary Table 8. Association of alterations and median gLOH for *TP53* for all tumor types, stratified by allelic status.

Group	No. assessable biallelic	No. assessable monoallelic	No. assessable unknown	No. assessable wt	Median gLOH biallelic	Median gLOH monoallelic	Median gLOH unknown	Median gLOH wt	% change biallelic vs. wt	<i>P</i> -value biallelic vs. wt	Corrected <i>P</i> -value biallelic vs. wt
Stomach	1,057	182	79	531	11.0	0.1	11.3	6.3	+73%	1.4x10 ⁻¹⁴	1.7 x 10 ⁻¹⁴
Glioma	2,556	393	62	4,096	4.0	2.5	3.9	2.4	+64%	9.1x10 ⁻⁷¹	1.8 x 10 ⁻⁷⁰
CUP	4,719	365	193	3,256	11.5	0.5	11.8	7.3	+58%	6.8x10 ⁻¹⁵¹	1.8 x 10 ⁻¹⁵⁰
Cholangiocarcinoma	679	98	50	1,592	10.5	0.8	8.9	9.9	+6%	1.7x10 ⁻³	1.7 x 10 ⁻³
Bladder	1,834	148	70	1,225	9.4	3.3	11.0	5.7	+64%	1.9x10 ⁻⁵³	3.4 x 10 ⁻⁵³
Breast	10,205	627	468	9,314	16.2	0.3	15.2	8.7	+86%	0	0
Esophagus	3,703	331	162	569	12.6	0.2	11.7	10.5	+19%	3.0x10 ⁻⁹	3.1 x 10 ⁻⁹
Prostate	2,434	170	245	3,585	9.3	5.8	9.0	7.8	+18%	5.1x10 ⁻³¹	7.5 x 10 ⁻³¹
Kidney	499	77	19	1,887	7.5	1.6	4.9	4.0	+84%	2.5x10 ⁻³²	4.0 x 10 ⁻³²
Pancreas	4,317	276	251	1,446	9.5	0.1	10.1	8.3	+13%	1.3x10 ⁻¹¹	1.4 x 10 ⁻¹¹
NSCLC	16,742	1,586	807	7,376	12.7	0.2	12.1	7.2	+76%	0	0
Endometrial	2,522	229	73	1,966	10.9	2.2	12.6	2.4	+361%	0	0
Melanoma	846	156	37	4,102	7.2	6.1	5.9	5.7	+27%	1.7x10 ⁻¹⁷	2.3 x 10 ⁻¹⁷
CRC	15,673	605	649	4,016	6.2	1.9	6.7	4.3	+44%	2.1x10 ⁻¹²⁰	4.9 x 10 ⁻¹²⁰
Ovary	8,524	241	266	2,396	14.2	0.8	13.6	2.7	+433%	0	0
Other	12,033	1,036	465	14,674	9.0	2.5	9.9	4.3	+108%	0	0

Abbreviations: CUP, carcinoma-of-unknown-primary-origin; wt, wild type.