

Table S1 Incidence rates of statistically non-significant mutations and biomarkers in *TP53*-MT (n=28) tumors versus *TP53*-WT (n=238)

XXXX	Test	<i>TP53</i> -MT (n=28) incidence (%)	<i>TP53</i> -MT incidence ratio	<i>TP53</i> -WT (n=238) incidence (%)	<i>TP53</i> -WT incidence ratio	P value
Tumor suppressor genes						
p16	IHC	0	0/0	100	1/1	
<i>RB1</i>	NGS	8	2/25	1.16	2/172	0.0792
<i>RB1</i>	NGS hot spot	33.33	1/3	1.72	1/58	0.0967
Immune						
PD-1	IHC	50	2/4	70	42/60	0.5831
PD-L1	IHC	32.1	9/28	41.35	110/266	0.3449
MSI	NGS	0	0/25	1.53	2/131	1.0000
MSI	FA	0	0/0	6.67	1/15	
TMB	NGS	0	0/25	7.6	14/184	0.3854
<i>BCL-6</i>	CNA	0	0/24	3.31	6/181	1.0000
EGFR						
<i>EGFR</i>	CNA	0	0/24	1.63	3/184	1.0000
<i>EGFR</i>	IHC	66.67	2/3	100	41/41	0.0682
<i>HER2</i>	CISH	0	0/28	2	1/50	1.0000
<i>HER2</i>	IHC	0	0/8	1.02	1/98	1.0000
<i>ERBB3</i>	NGS	4	1/25	0.52	1/193	0.2167
<i>ERBB2</i>	NGS	0	0/25	2.06	4/194	1.0000
Cyclins						
Cyclin D1	CNA	0	0/24	2.15	4/186	1.0000
Cyclin E	CNA	0	0/24	0.54	1/185	1.0000
DDR						
<i>BRCA2</i>	CNA	0	0/24	0.56	1/177	1.0000
<i>BRCA2</i>	NGS	4	1/25	1.57	3/190	0.3924
<i>BRCA1</i>	NGS	4	1/25	0.51	1/194	0.2157
<i>ATRX</i>	NGS	0	0/25	6.25	3/48	0.5466
<i>ATM</i>	NGS	0	0/25	1.05	2/189	1.0000
RAS/RAF/MEK						
<i>KRAS</i>	CNA	0	0/24	1.11	2/181	1.0000
<i>KRAS</i>	NGS	8	2/25	2.04	4/196	0.1389
<i>KRAS</i>	NGS hot spot	33.33	1/3	1.69	1/59	0.0952
<i>HRAS</i>	NGS	0	0/25	1.5	3/196	1.0000
<i>FGFR3</i>	NGS	0	0/25	2.64	5/189	1.0000
<i>FGFR2</i>	NGS	0	0/25	0.53	1/189	1.0000
SMAD pathway						
<i>SMAD 4</i>	NGS	0	0/25	0.515	1/194	1.0000
<i>SMAD4</i>	CNA	4.16	1/24	0.55	1/181	0.2210
<i>SMAD2</i>	CNA	4.16	1/24	1.1	2/181	0.3131

Table S1 (continued)

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XXXX	Test	TP53-MT (n=28) incidence (%)	TP53-MT incidence ratio	TP53-WT (n=238) incidence (%)	TP53-WT incidence ratio	P value
PI3K related kinases						
TRK A/B/C	IHC	0	0/5	3.39	2/59	1.0000
PIK3CA	CNA	0	0/24	6.07	11/181	0.3689
PIK3CA	NGS hot spot	0	0/3	25.4	15/59	1.0000
PIK3R1	NGS	0	0/25	2.23	4/179	1.0000
AKT	NGS	0	0/25	2.59	5/193	1.0000
AKT	NGS hot spot	0	0/3	3.39	2/59	1.0000
MTOR	NGS	0	0/25	0.53	1/187	1.0000
CCND1	CNA	4.17	1/24	1.6	3/186	0.3869
PTEN	NGS	0	0/25	12.3	22/179	0.0826
PTEN	NGS hot spot	0	0/3	1.72	1/58	1.0000
PTEN	IHC	44.4	4/9	70.59	60/85	0.1385
MMR						
ARID1A	NGS	0	0/25	6.78	4/59	0.3128
ARID2	NGS	0	0/25	1.14	2/175	1.0000
MSH6	NGS	0	0/25	1.08	2/185	1.0000
MSH6	IHC	100	6/6	89.36	84/94	1.0000
MLH1	NGS	0	0/25	0.52	1/190	1.0000
MLH1	IHC	100	6/6	98.8	85/86	1.0000
MSH2	IHC	100	6/6	100	86/86	1.0000
Other						
MEN1	NGS	0	0/25	0.51	1/196	1.0000
KMT2D	NGS	4	1/25	21.87	35/160	0.0530
KMT2C	NGS	4	1/25	19.56	18/92	0.0710
FBXW7	NGS	0	0/25	11.76	20/170	0.0821
FBXW7	NGS hot spot	33.33	1/3	11.86	7/59	0.3442
PBRM1	NGS	8	2/25	2.2	4/181	0.1564
BAP1	NGS	4	1/25	2.06	4/194	0.4578
EWSR1	CNA	4.17	1/24	0	0/179	0.1182
FGF19	CNA	4.17	1/24	2.2	4/180	0.4687
FGF3	CNA	4.17	1/24	2.2	4/185	0.4600
FGF4	CNA	4.17	1/24	2.2	4/184	0.4617
KEAP1	CNA	4.17	1/24	0.55	1/181	0.2210
LYL1	CNA	4.17	1/24	1.1	2/181	0.3131
MALT1	CNA	4.17	1/24	0.55	1/181	0.2210
SS18	CNA	4.17	1/24	0.55	1/181	0.2210
JAK1	CNA	4	1/25	0	0/176	0.1244
ADGRA2	CNA	4.17	1/24	0.55	1/179	0.2230
FANCG	CNA	4.17	1/24	0.55	1/180	0.2220
NSD3	CNA	4.17	1/24	0.55	1/181	0.2210

TP53-MT, TP53-mutated; TP53-WT, TP53-wild type; IHC, immunohistochemistry; MSI, microsatellite instability; NGS, next-generation sequencing; FA, fragment analysis; TMB, tumor mutational burden; CNA, copy number alteration; EGFR, epidermal growth factor receptor; CISH, chromogenic in situ hybridization; DDR, DNA damage response; MMR, mismatch repair.

Table S2 Incidence rates of statistically non-significant mutations and biomarkers in local versus metastatic locations

XXXX	Test	Metastatic incidence (%)	Metastatic incidence ratio	Local incidence (%)	Local incidence ratio	P value
Tumor suppressor genes						
<i>TP53</i>	NGS & NGS hot spot	7.06	6/85	11.05	20/181	0.3068
<i>TP53</i>	NGS	7.04	5/71	14.60	20/137	0.1121
<i>TP53</i>	NGS hot spot	6.25	1/16	4.55	2/44	1.0000
<i>p16</i>	IHC	0	0/100	100	1/1	
<i>RB1</i>	NGS	1.61	1/62	2.22	3/135	1.0000
<i>RB1</i>	NGS hot spot	12.50	2/16	0.00	0/45	0.0656
<i>CDKN2A</i>	NGS	1.39	1/72	3.47	5/144	0.6661
Immune						
PD-L1	IHC	39.36	37/94	41.00	82/200	0.7895
MSI	NGS	0.00	0/53	1.94	2/103	0.5485
MSI	FA	0.00	0/7	12.50	1/8	1.0000
TMB	NGS	7.25	5/69	6.43	9/140	0.7776
<i>BCL-6</i>	CNA	5.80	4/69	1.47	2/136	0.1822
<i>APC</i>	NGS	4.23	3/71	3.55	5/141	1.0000
<i>APC</i>	NGS hot spot	6.25	1/16	0	0/46	0.2581
EGFR						
<i>EGFR</i>	CNA	1.47	1/68	1.43	2/140	1.0000
EGFR	IHC	90.91	10/11	100	33/33	0.2500
<i>HER2</i>	CISH	5.00	1/20	0	0/58	0.2564
<i>HER2</i>	IHC	3.03	1/33	0	0/73	0.3113
<i>ERBB3</i>	NGS	1.35	1/74	0.69	1/144	1.0000
<i>ERBB2</i>	NGS	1.37	1/73	2.05	3/146	1.0000
Cyclins						
Cyclin D1	CNA	1.47	1/68	2.26	3/133	1.0000
DDR						
<i>BRCA 2</i>	CNA	0	0/67	0.75	1/134	1.0000
<i>BRCA2</i>	NGS	0	0/70	2.76	4/145	0.3064
<i>BRCA1</i>	NGS	2.70	2/74	0.00	0/145	0.1132
<i>ATRAX</i>	NGS	0	0/19	5.56	3/54	0.5629
<i>ATM</i>	NGS	2.90	2/69	0	0/145	0.1029
RAS/RAF/MEK						
<i>KRAS</i>	CNA	1.45	1/69	0.74	1/136	1.0000
<i>KRAS</i>	NGS	1.35	1/74	3.40	5/147	0.6663
<i>KRAS</i>	NGS hot spot	12.5	2/16	0.00	0/46	0.0635
<i>HRAS</i>	NGS	0	0/74	2.04	3/147	0.5525
<i>BRAF</i>	NGS	1.41	1/71	0.68	1/146	0.5483
SMAD pathway						
<i>SMAD 4</i>	NGS	0.00	0/73	0.68	1/146	1.0000
<i>SMAD4</i>	CNA	2.90	2/69	0	0/137	0.1111

Table S2 (continued)

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XXXX	Test	Metastatic incidence (%)	Metastatic incidence ratio	Local incidence (%)	Local incidence ratio	P value
PI3K related kinases						
TRK A/B/C	IHC	0.00	0/16	4.17	2/48	1.0000
PIK3CA	CNA	8.70	6/69	3.65	5/137	0.1865
PIK3CA	NGS hot spot	37.50	6/16	19.57	9/46	0.1823
PIK3R1	NGS	2.94	2/68	1.47	2/136	0.6020
PIK3CA	NGS	29.73	22/74	27.21	40/147	0.6941
AKT	NGS	1.35	1/74	2.78	4/144	0.6640
AKT	NGS hot spot	6.25	1/16	2.17	1/46	0.4527
MTOR	NGS	0	0/70	0.70	1/142	1.0000
PTEN	NGS hot spot	0	0/16	2.22	1/45	1.0000
PTEN	IHC	61.54	16/26	70.59	48/68	0.3998
MMR						
ARID1A	NGS	4.00	1/25	5.08	3/59	1.0000
ARID2	NGS	0	0/66	1.49	2/134	1.0000
MSH6	NGS	1.43	1/70	0.71	1/140	1.0000
MSH6	IHC	100.00	21/21	100.00	69/69	
MLH1	NGS	0.00	0/72	0.70	1/143	1.0000
MLH1	IHC	100.00	21/21	98.59	70/71	1.0000
MSH2	IHC	100.00	21/21	100.00	71/71	
Other						
MEN1	NGS	1.35	1/74	0	0/147	0.3348
KMT2D	NGS	18.03	11/61	20.16	25/124	0.7310
KMT2C	NGS	16.13	5/31	16.28	14/86	0.9845
FGFR2	NGS	0	0/71	0.70	1/143	1.0000
FBXW7	NGS	8.06	5/62	11.28	15/133	0.4909
FBXW7	NGS hot spot	25.00	4/16	8.70	4/46	0.1872
NOTCH1	NGS	0.00	0/69	5.19	7/135	0.0979
CAL-R	CNA	0	0/69	2.21	3/136	0.5523

NGS, next-generation sequencing; IHC, immunohistochemistry; MSI, microsatellite instability; FA, fragment analysis; TMB, tumor mutational burden; CNA, copy number alteration; EGFR, epidermal growth factor receptor; CISH, chromogenic in situ hybridization; DDR, DNA damage response; MMR, mismatch repair.