Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
No.201, Sec. 2, Shipai Rd., Beitou District, Taipei City, Taiwan
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Sample Information

Patient Name: 林汶萱
Gender: Female
ID No.: H224212708
History No.: 34476454
Age: 20

Ordering Doctor: DOC2265A 馬旭
Ordering REQ.: D4N69FN
Signing in Date: 2020/02/28

Path No.: S109-99193
MP No.: TM2001
Assay: Oncomine Tumor Mutation Load Assay
Sample Type: FFPE
Block No.: S109-02244H
Percentage of tumor cells: 70%
Note:

Sample Cancer Type: Soft Tissue Sarcoma

Report Highlights

1 Clinically Significant Biomarkers
2 Therapies Available
12 Clinical Trials

Relevant Soft Tissue Sarcoma Findings

Gene	Finding
NTRK1	Not detected
NTRK3	Not detected

Clinically Significant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
Tumor Mutational Burden 7.64 Mut/Mb measured	None	ipilimumab + nivolumab nivolumab	12

Sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO

Prevalent cancer biomarkers without clinical significance based on included data sources
RECQL4 splice site mutation, G6PD p.(N195D) c.583A>G

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
RECQL4			.	chr8:145738767	100.00%	NM_004260.3		1993
G6PD	p.(N195D)	c.583A>G	.	chrX:153762704	53.65%	NM_000402.4	missense	2000
MTOR	p.(=)	c.4731G>A	.	chr1:11205058	99.90%	NM_004958.3	synonymous	1997
MTOR	p.(=)	c.2997C>T	.	chr1:11288758	100.00%	NM_004958.3	synonymous	1997
MTOR	p.(=)	c.1437T>C	.	chr1:11301714	99.90%	NM_004958.3	synonymous	1993
SDHB	p.(=)	c.18C>A	.	chr1:17380497	99.15%	NM_003000.2	synonymous	2000
PAX7	p.(=)	c.744G>A	.	chr1:19018405	99.85%	NM_002584.2	synonymous	1997
PAX7	p.(=)	c.771A>C	.	chr1:19018432	99.95%	NM_002584.2	synonymous	1989
PAX7	p.(=)	c.879A>G	.	chr1:19027239	99.80%	NM_002584.2	synonymous	1994
MYCL	p.(T392S)	c.1175C>G	.	chr1:40363054	100.00%	NM_001033082.2	missense	1107
MUTYH	p.(Q338H)	c.1014G>C	.	chr1:45797505	46.92%	NM_001128425.1	missense	1997
TAL1	p.(=)	c.933A>G	.	chr1:47685455	99.80%	NM_003189.5	synonymous	1992
CMPK1	p.(Q80H)	c.240G>T	.	chr1:47834209	49.07%	NM_016308.2	missense	1999
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	99.90%	NM_002227.3	synonymous	2000
DPYD	p.(R29C)	c.85C>T	.	chr1:98348885	99.92%	NM_000110.3	missense	1241
TRIM33	p.(I840T)	c.2519T>C	.	chr1:114948281	100.00%	NM_015906.3	missense	1995
NOTCH2	p.(=)	c.6421C>T	.	chr1:120458924	47.75%	NM_024408.3	synonymous	1131
PDE4DIP	p.(D1910E)	c.5730C>A	.	chr1:144865850	41.74%	NM_001198834.3	missense	1998
PDE4DIP	p.(R1867C)	c.5599C>T	.	chr1:144866643	48.35%	NM_001198834.3	missense	2000
PDE4DIP	p.(=)	c.5580A>G	.	chr1:144866662	99.90%	NM_001198834.3	synonymous	2000
PDE4DIP	p.(=)	c.4848A>G	.	chr1:144874760	8.95%	NM_001198834.3	synonymous	1999
PDE4DIP	p.(H1598R)	c.4793A>G	.	chr1:144874815	48.85%	NM_001198834.3	missense	1998
PDE4DIP	p.(=)	c.4701C>G	.	chr1:144875979	99.50%	NM_001198834.3	synonymous	1995
PDE4DIP	p.(=)	c.3438T>C	.	chr1:144882581	53.03%	NM_001198834.3	synonymous	1999
PDE4DIP	p.(A1066T)	c.3196G>A	.	chr1:144882823	45.94%	NM_001198834.3	missense	1996
PDE4DIP	p.(F1013I)	c.3037T>A	.	chr1:144886197	42.24%	NM_001198834.3	missense	1998
PDE4DIP	p.(R681H)	c.2042G>A	.	chr1:144912233	51.50%	NM_001198834.3	missense	2000
PDE4DIP	p.(S536T)	c.1607G>C	.	chr1:144916748	49.72%	NM_001198834.3	missense	1997
PDE4DIP	p.(=)	c.1558T>C	.	chr1:144917546	51.53%	NM_001198834.3	synonymous	1999

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
PDE4DIP	p.(E410V)	c.1229A>T	.	chr1:144918957	50.65%	NM_001198834.3	missense	2000
PDE4DIP	p.(S275L)	c.824C>T	.	chr1:144922583	51.47%	NM_001198834.3	missense	272
PDE4DIP	p.(R25L)	c.74G>T	.	chr1:144994658	53.68%	NM_001198834.3	missense	1997
ITGA10	p.(R69W)	c.205C>T	.	chr1:145527968	41.17%	NM_003637.4	missense	1965
ITGA10	p.(=)	c.1002T>C	.	chr1:145532549	99.03%	NM_003637.4	synonymous	1543
ARNT	p.(=)	c.567G>C	.	chr1:150808889	45.50%	NM_001668.3	synonymous	1901
MUC1	p.(=)	c.66G>A	.	chr1:155162067	99.75%	NM_001204285.1	synonymous	792
NTRK1	p.(=)	c.1674G>A	.	chr1:156846233	100.00%	NM_002529.3	synonymous	1999
DDR2	p.(=)	c.1260C>G	.	chr1:162737116	50.58%	NM_006182.2	synonymous	1807
PBX1	p.(G21S)	c.61G>A	.	chr1:164529120	51.12%	NM_002585.3	missense	1076
RNASEL	p.(D541E)	c.1623T>G	.	chr1:182551337	99.90%	NM_021133.3	missense	1997
RNASEL	p.(R462Q)	c.1385G>A	.	chr1:182554557	52.46%	NM_021133.3	missense	1994
PIK3C2B	p.(=)	c.3594T>C	.	chr1:204403659	51.53%	NM_002646.3	synonymous	1999
PIK3C2B	p.(=)	c.1899C>T	.	chr1:204425028	50.20%	NM_002646.3	synonymous	1729
PIK3C2B	p.(=)	c.597G>A	.	chr1:204438334	99.45%	NM_002646.3	synonymous	1995
PIK3C2B	p.(=)	c.288C>A	.	chr1:204438643	100.00%	NM_002646.3	synonymous	1976
IKBKE	p.(=)	c.156A>G	.	chr1:206647742	99.50%	NM_014002.3	synonymous	1995
IKBKE	p.(=)	c.201T>C	.	chr1:206647787	99.80%	NM_014002.3	synonymous	2000
IKBKE	p.(=)	c.717G>A	.	chr1:206651107	45.70%	NM_014002.3	synonymous	2000
IKBKE	p.(A602V)	c.1805C>T	.	chr1:206665052	56.18%	NM_014002.3	missense	1116
PARP1	p.(V762A)	c.2285T>C	.	chr1:226555302	99.75%	NM_001618.3	missense	1999
PARP1	p.(=)	c.852T>C	.	chr1:226573364	99.85%	NM_001618.3	synonymous	1999
PARP1	p.(=)	c.243C>T	.	chr1:226589958	99.70%	NM_001618.3	synonymous	1997
PARP1	p.(?)	c.-17G>C	.	chr1:226595647	99.65%	NM_001618.3	unknown	2000
MTR	p.(=)	c.3144A>G	.	chr1:237054569	46.75%	NM_000254.2	synonymous	2000
MTR	p.(=)	c.3492C>A	.	chr1:237058744	22.38%	NM_000254.2	synonymous	1997
MTR	p.(=)	c.3576C>T	.	chr1:237058828	51.58%	NM_000254.2	synonymous	1997
NCOA1	p.(=)	c.462G>C	.	chr2:24905927	100.00%	NM_003743.4	synonymous	275
NCOA1	p.(=)	c.3801T>G	.	chr2:24974945	99.80%	NM_003743.4	synonymous	1996
DNMT3A	p.(=)	c.1266G>A	.	chr2:25469502	50.08%	NM_022552.4	synonymous	1867

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	51.35%	NM_004304.4	missense	1223
ALK	p.(K1491R)	c.4472A>G	.	chr2:29416481	51.70%	NM_004304.4	missense	1733
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.85%	NM_004304.4	missense	2000
ALK	p.(=)	c.3375C>A	.	chr2:29445458	47.60%	NM_004304.4	synonymous	2000
ALK	p.(=)	c.3036G>A	.	chr2:29449819	51.33%	NM_004304.4	synonymous	1999
ALK	p.(=)	c.2535T>C	.	chr2:29455267	46.65%	NM_004304.4	synonymous	2000
ALK	p.(=)	c.1500A>G	.	chr2:29543663	99.93%	NM_004304.4	synonymous	1503
ALK	p.(=)	c.702T>A	.	chr2:29940529	48.42%	NM_004304.4	synonymous	952
ALK	p.(=)	c.27C>G	.	chr2:30143499	99.85%	NM_004304.4	synonymous	2000
EML4	p.(K283E)	c.847A>G	.	chr2:42510018	99.50%	NM_019063.4	missense	2000
EML4	p.(I382V)	c.1144A>G	.	chr2:42515388	100.00%	NM_019063.4	missense	213
EML4	p.(K398R)	c.1193A>G	.	chr2:42515437	60.87%	NM_019063.4	missense	759
BCL11A	p.(=)	c.2088T>C	.	chr2:60687959	99.80%	NM_022893.3	synonymous	1999
AFF3	p.(=)	c.1263C>T	.	chr2:100218080	99.59%	NM_001025108.1	synonymous	1972
AFF3	p.(S383N)	c.1148G>A	.	chr2:100343557	100.00%	NM_001025108.1	missense	507
ERCC3	p.(?)	c.-51G>A	.	chr2:128051708	46.10%	NM_000122.1	unknown	1295
LRP1B	p.(=)	c.13047G>A	.	chr2:141032088	46.75%	NM_018557.2	synonymous	2000
LRP1B	p.(=)	c.8526T>C	.	chr2:141260668	99.90%	NM_018557.2	synonymous	1998
LRP1B	p.(=)	c.6633A>T	.	chr2:141457985	50.87%	NM_018557.2	synonymous	1091
LRP1B	p.(=)	c.5256A>G	.	chr2:141571329	100.00%	NM_018557.2	synonymous	326
LRP1B	p.(=)	c.3072C>A	.	chr2:141707868	53.41%	NM_018557.2	synonymous	1992
LRP1B	p.(=)	c.2616C>T	.	chr2:141751592	47.75%	NM_018557.2	synonymous	1996
LRP1B	p.(Q48R)	c.143A>G	.	chr2:142567910	50.60%	NM_018557.2	missense	2000
ACVR2A	p.(=)	c.354G>A	.	chr2:148657117	50.00%	NM_001616.4	synonymous	1996
FN1	p.(=)	c.7161T>C	.	chr2:216229692	99.90%	NM_212482.2	synonymous	1984
FN1	p.(V2261I)	c.6781G>A	.	chr2:216235089	99.85%	NM_212482.2	missense	2000
FN1	p.(=)	c.4725G>A	.	chr2:216249587	99.95%	NM_212482.2	synonymous	2000
FN1	p.(T817P)	c.2449A>C	.	chr2:216272900	100.00%	NM_212482.2	missense	2000
FN1	p.(Q15L)	c.44A>T	.	chr2:216300482	100.00%	NM_212482.2	missense	200
PAX3	p.(=)	c.129T>C	.	chr2:223161889	99.80%	NM_181459.3	synonymous	1996

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
CRBN	p.(=)	c.735T>C	.	chr3:3197918	99.57%	NM_016302.3	synonymous	922
PPARG	p.(P12A)	c.34C>G	.	chr3:12393125	49.05%	NM_015869.4	missense	1998
PPARG	p.(=)	c.1431C>T	.	chr3:12475557	100.00%	NM_015869.4	synonymous	2000
XPC	p.(Q939K)	c.2815C>A	.	chr3:14187449	46.55%	NM_004628.4	missense	580
XPC	p.(=)	c.1881T>A	.	chr3:14197987	100.00%	NM_004628.4	synonymous	1405
XPC	p.(L16V)	c.46C>G	.	chr3:14220023	48.51%	NM_004628.4	missense	1911
TGFBR2	p.(=)	c.1242C>T	.	chr3:30713842	47.47%	NM_001024847.2	synonymous	1999
ITGA9	p.(G507E)	c.1520G>A	.	chr3:37574951	47.95%	NM_002207.2	missense	1998
LTF	p.(=)	c.1894T>C	.	chr3:46480801	48.85%	NM_002343.5	synonymous	2000
LTF	p.(E579D)	c.1737G>C	.	chr3:46480958	49.05%	NM_002343.5	missense	1996
LTF	p.(=)	c.1623C>T	.	chr3:46484964	100.00%	NM_002343.5	synonymous	1998
LTF	p.(K47R)	c.140A>G	.	chr3:46501213	99.28%	NM_002343.5	missense	694
LTF	p.(A29T)	c.85G>A	.	chr3:46501268	54.12%	NM_002343.5	missense	279
LTF	p.(R23dup)	c.68_69insAAG	.	chr3:46501284	100.00%	NM_002343.5	nonframeshift Insertion	276
SETD2	p.(P1962L)	c.5885C>T	.	chr3:47125385	99.50%	NM_014159.6	missense	1999
SETD2	p.(=)	c.3465T>C	.	chr3:47162661	100.00%	NM_014159.6	synonymous	1096
GATA2	p.(=)	c.15C>G	.	chr3:128205860	48.65%	NM_032638.4	synonymous	2000
EPHB1	p.(=)	c.435C>T	.	chr3:134670524	99.80%	NM_004441.4	synonymous	2000
EPHB1	p.(=)	c.1800C>T	.	chr3:134898742	47.42%	NM_004441.4	synonymous	1999
ATR	p.(=)	c.7875G>A	.	chr3:142168331	100.00%	NM_001184.3	synonymous	805
ATR	p.(R2425Q)	c.7274G>A	.	chr3:142178144	49.42%	NM_001184.3	missense	1999
ATR	p.(=)	c.1776T>A	.	chr3:142277575	50.50%	NM_001184.3	synonymous	2000
ATR	p.(M211T)	c.632T>C	.	chr3:142281612	48.75%	NM_001184.3	missense	1998
BCL6	p.(A493T)	c.1477G>A	.	chr3:187446211	46.82%	NM_001706.4	missense	487
BCL6	p.(=)	c.1161C>T	.	chr3:187447032	51.60%	NM_001706.4	synonymous	1998
LPP	p.(=)	c.942C>T	.	chr3:188327461	50.88%	NM_005578.4	synonymous	1999
TNK2	p.(=)	c.1104C>T	.	chr3:195606019	48.42%	NM_001010938.1	synonymous	1999
TNK2	p.(=)	c.273T>C	.	chr3:195615376	48.45%	NM_001010938.1	synonymous	2000
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.80%	NM_000142.4	synonymous	2000

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	100.00%	NM_006206.5	synonymous	1972
PDGFRA	p.(=)	c.3222T>C	.	chr4:55161391	99.85%	NM_006206.5	synonymous	1999
KDR	p.(Q472H)	c.1416A>T	.	chr4:55972974	100.00%	NM_002253.2	missense	270
ADGRL3	p.(=)	c.612C>T	.	chr4:62598689	99.95%	NM_015236.5	synonymous	1997
ADGRL3	p.(=)	c.2079T>C	.	chr4:62800728	99.80%	NM_015236.5	synonymous	1999
ADGRL3	p.(=)	c.2709G>C	.	chr4:62845388	98.03%	NM_015236.5	synonymous	1982
ADGRL3	p.(=)	c.2811A>G	.	chr4:62845490	99.65%	NM_015236.5	synonymous	1994
AFF1	p.(P216A)	c.646C>G	.	chr4:87968333	47.24%	NM_001166693.2	missense	1996
NFKB1	p.(=)	c.1143T>C	.	chr4:103514658	99.95%	NM_003998.3	synonymous	1996
TET2	p.(V218M)	c.652G>A	.	chr4:106155751	48.14%	NM_001127208.2	missense	1994
TET2	p.(=)	c.3117G>A	.	chr4:106158216	48.20%	NM_001127208.2	synonymous	2000
TET2	p.(=)	c.4140T>C	.	chr4:106190862	47.07%	NM_001127208.2	synonymous	1999
IL2	p.(=)	c.114G>T	.	chr4:123377482	100.00%	NM_000586.3	synonymous	156
SDHA	p.(=)	c.891T>C	.	chr5:231111	48.17%	NM_004168.3	synonymous	1999
SDHA	p.(=)	c.1911C>T	.	chr5:256451	45.85%	NM_004168.3	synonymous	1998
MTRR	p.(I49M)	c.147A>G	.	chr5:7870973	53.75%	NM_024010.2	missense	1998
MTRR	p.(S202L)	c.605C>T	.	chr5:7878179	48.15%	NM_024010.2	missense	2000
MTRR	p.(=)	c.1992G>A	.	chr5:7897319	54.04%	NM_024010.2	synonymous	1978
IL7R	p.(I66T)	c.197T>C	.	chr5:35861068	99.90%	NM_002185.4	missense	2000
IL7R	p.(V138I)	c.412G>A	.	chr5:35871190	100.00%	NM_002185.4	missense	322
IL7R	p.(I356V)	c.1066A>G	.	chr5:35876274	99.80%	NM_002185.4	missense	2000
PIK3R1	p.(=)	c.219C>T	.	chr5:67522722	100.00%	NM_181523.2	synonymous	480
PIK3R1	p.(M326I)	c.978G>A	.	chr5:67588148	42.27%	NM_181523.2	missense	1999
APC	p.(=)	c.1458T>C	.	chr5:112162854	24.85%	NM_000038.5	synonymous	2000
APC	p.(=)	c.4479G>A	.	chr5:112175770	99.42%	NM_000038.5	synonymous	1030
APC	p.(=)	c.5034G>A	.	chr5:112176325	99.65%	NM_000038.5	synonymous	2000
APC	p.(=)	c.5268T>G	.	chr5:112176559	100.00%	NM_000038.5	synonymous	157
APC	p.(=)	c.5880G>A	.	chr5:112177171	100.00%	NM_000038.5	synonymous	60
RAD50	p.(?)	c.-38G>A	.	chr5:131892979	99.80%	NM_005732.3	unknown	1999
CSF1R	p.(=)	c.726C>T	.	chr5:149457678	52.65%	NM_005211.3	synonymous	2000

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
PDGFRB	p.(=)	c.3252A>G	.	chr5:149495395	48.47%	NM_002609.3	synonymous	1999
PDGFRB	p.(=)	c.2601A>G	.	chr5:149499672	48.30%	NM_002609.3	synonymous	2000
FGFR4	p.(V10I)	c.28G>A	.	chr5:176516631	53.19%	NM_213647.2	missense	1991
FGFR4	p.(=)	c.162T>G	.	chr5:176517461	100.00%	NM_213647.2	synonymous	1996
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.30%	NM_213647.2	missense	1999
FGFR4	p.(=)	c.702C>T	.	chr5:176518784	100.00%	NM_213647.2	synonymous	1999
FGFR4	p.(G388R)	c.1162G>A	.	chr5:176520243	53.05%	NM_213647.2	missense	1998
NSD1	p.(=)	c.1482C>T	.	chr5:176636882	51.30%	NM_022455.4	synonymous	2000
NSD1	p.(=)	c.1749G>A	.	chr5:176637149	50.73%	NM_022455.4	synonymous	1999
NSD1	p.(S726P)	c.2176T>C	.	chr5:176637576	49.67%	NM_022455.4	missense	1685
NSD1	p.(=)	c.6829T>C	.	chr5:176721198	50.85%	NM_022455.4	synonymous	1998
FLT4	p.(=)	c.3198C>T	.	chr5:180043388	50.80%	NM_182925.4	synonymous	1994
IRF4	p.(R179S)	c.537G>T	.	chr6:397152	51.43%	NM_002460.3	missense	1999
DEK	p.(=)	c.849G>A	.	chr6:18237661	100.00%	NM_003472.3	synonymous	87
DEK	p.(=)	c.9C>T	.	chr6:18264210	99.55%	NM_003472.3	synonymous	2000
POU5F1	p.(=)	c.27C>T	.	chr6:31138371	47.81%	NM_002701.5	synonymous	707
POU5F1	p.(=)	c.21G>A	.	chr6:31138377	47.81%	NM_002701.5	synonymous	707
NOTCH4	p.(=)	c.2967A>C	.	chr6:32172065	99.95%	NM_004557.3	synonymous	1997
NOTCH4	p.(=)	c.2052G>A	.	chr6:32182002	49.55%	NM_004557.3	synonymous	1986
NOTCH4	p.(=)	c.1866G>A	.	chr6:32183158	47.12%	NM_004557.3	synonymous	1997
NOTCH4	p.(=)	c.1044C>G	.	chr6:32188297	48.87%	NM_004557.3	synonymous	1991
NOTCH4	p.(=)	c.813A>G	.	chr6:32188642	48.40%	NM_004557.3	synonymous	2000
NOTCH4	p.(=)	c.645G>A	.	chr6:32188909	52.70%	NM_004557.3	synonymous	1998
NOTCH4	p.(P204L)	c.611C>T	.	chr6:32188943	51.13%	NM_004557.3	missense	1999
NOTCH4	p.(=)	c.558C>T	.	chr6:32188996	48.70%	NM_004557.3	synonymous	2000
NOTCH4	p.(=)	c.522A>G	.	chr6:32189032	51.90%	NM_004557.3	synonymous	1998
NOTCH4	p.(K117Q)	c.349A>C	.	chr6:32190390	99.45%	NM_004557.3	missense	1998
NOTCH4	p.(=)	c.333T>C	.	chr6:32190406	99.70%	NM_004557.3	synonymous	2000
NOTCH4	p.(?)	c.-25C>T	.	chr6:32191730	81.90%	NM_004557.3	unknown	105
DAXX	p.(=)	c.1173T>C	.	chr6:33288271	51.95%	NM_001141970.1	synonymous	2000

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
FOXP4	p.(=)	c.81C>A	.	chr6:41533579	56.79%	NM_001012426.1	synonymous	1997
PKHD1	p.(Q4048R)	c.12143A>G	.	chr6:51483961	100.00%	NM_138694.3	missense	127
PKHD1	p.(Q3899R)	c.11696A>G	.	chr6:51491884	100.00%	NM_138694.3	missense	81
PKHD1	p.(=)	c.9237G>A	.	chr6:51613177	99.60%	NM_138694.3	synonymous	2000
PKHD1	p.(I2944V)	c.8830A>G	.	chr6:51618119	45.62%	NM_138694.3	missense	377
PKHD1	p.(=)	c.7764A>G	.	chr6:51720838	100.00%	NM_138694.3	synonymous	503
PKHD1	p.(=)	c.5896C>T	.	chr6:51824680	47.87%	NM_138694.3	synonymous	1999
PKHD1	p.(L1870V)	c.5608T>G	.	chr6:51875250	99.55%	NM_138694.3	missense	1993
PKHD1	p.(=)	c.1185T>C	.	chr6:51924774	99.70%	NM_138694.3	synonymous	1996
PKHD1	p.(=)	c.234C>T	.	chr6:51947237	47.72%	NM_138694.3	synonymous	1995
DST	p.(L4874V)	c.14620C>G	.	chr6:56351972	54.25%	NM_001144769.2	missense	1998
DST	p.(M3317I)	c.9951G>A	.	chr6:56417282	99.90%	NM_001144769.2	missense	1997
DST	p.(T3230A)	c.9688A>G	.	chr6:56417545	99.70%	NM_001144769.2	missense	1999
DST	p.(Q1812R)	c.5435A>G	.	chr6:56463410	49.40%	NM_001144769.2	missense	2000
ADGRB3	p.(N503S)	c.1508A>G	.	chr6:69666684	99.33%	NM_001704.2	missense	595
ADGRB3	p.(=)	c.4008G>A	.	chr6:70071173	99.80%	NM_001704.2	synonymous	2000
EPHA7	p.(=)	c.2076G>A	.	chr6:93967851	50.57%	NM_004440.3	synonymous	1414
EPHA7	p.(=)	c.1341T>C	.	chr6:93982124	48.05%	NM_004440.3	synonymous	1998
EPHA7	p.(=)	c.981G>A	.	chr6:94067981	53.28%	NM_004440.3	synonymous	1999
ROS1	p.(=)	c.5742C>T	.	chr6:117642457	51.75%	NM_002944.2	synonymous	2000
ESR1	p.(=)	c.729T>C	.	chr6:152201875	99.90%	NM_001122740.1	synonymous	1997
ESR1	p.(=)	c.1782G>A	.	chr6:152420095	99.35%	NM_001122740.1	synonymous	1999
SYNE1	p.(=)	c.25038T>C	.	chr6:152464839	99.55%	NM_182961.3	synonymous	1997
SYNE1	p.(G8323A)	c.24968G>C	.	chr6:152469188	48.04%	NM_182961.3	missense	1884
SYNE1	p.(=)	c.24825G>A	.	chr6:152469331	52.83%	NM_182961.3	synonymous	1980
SYNE1	p.(F7302V)	c.21904T>G	.	chr6:152540278	97.85%	NM_182961.3	missense	1998
SYNE1	p.(L5015M)	c.15043T>A	.	chr6:152647681	52.55%	NM_182961.3	missense	2000
SYNE1	p.(=)	c.14061G>C	.	chr6:152651759	49.30%	NM_182961.3	synonymous	1998
SYNE1	p.(S4596T)	c.13786T>A	.	chr6:152652034	52.73%	NM_182961.3	missense	1244
SYNE1	p.(K4121R)	c.12362A>G	.	chr6:152658142	50.75%	NM_182961.3	missense	1673

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
SYNE1	p.(E4060D)	c.12180G>T	.	chr6:152665261	49.80%	NM_182961.3	missense	1996
SYNE1	p.(=)	c.10866T>C	.	chr6:152675854	52.21%	NM_182961.3	synonymous	1988
SYNE1	p.(=)	c.10191C>A	.	chr6:152683413	54.37%	NM_182961.3	synonymous	103
SYNE1	p.(=)	c.9495A>G	.	chr6:152694184	57.11%	NM_182961.3	synonymous	1984
SYNE1	p.(=)	c.9420G>A	.	chr6:152694259	50.55%	NM_182961.3	synonymous	1994
IGF2R	p.(=)	c.1590G>A	.	chr6:160464289	99.70%	NM_000876.3	synonymous	1998
IGF2R	p.(=)	c.2139A>G	.	chr6:160468278	99.75%	NM_000876.3	synonymous	1995
IGF2R	p.(R1619G)	c.4855A>G	.	chr6:160494409	99.85%	NM_000876.3	missense	1997
IGF2R	p.(=)	c.6051C>G	.	chr6:160505199	99.77%	NM_000876.3	synonymous	1330
IGF2R	p.(N2020S)	c.6059A>G	.	chr6:160505207	99.77%	NM_000876.3	missense	1314
IGF2R	p.(=)	c.6666C>T	.	chr6:160517481	99.94%	NM_000876.3	synonymous	1778
RPS6KA2	p.(=)	c.2221C>T	.	chr6:166826255	99.90%	NM_001006932.2	synonymous	2000
RPS6KA2	p.(=)	c.2172A>G	.	chr6:166826304	99.95%	NM_001006932.2	synonymous	1999
RPS6KA2	p.(=)	c.1128C>T	.	chr6:166864693	50.18%	NM_001006932.2	synonymous	1999
RPS6KA2	p.(=)	c.1026G>A	.	chr6:166873010	50.55%	NM_001006932.2	synonymous	2000
RPS6KA2	p.(=)	c.132C>T	.	chr6:166952264	50.43%	NM_001006932.2	synonymous	1999
RPS6KA2	p.(T34A)	c.100A>G	.	chr6:167271711	99.60%	NM_001006932.2	missense	1997
RPS6KA2	p.(E32G)	c.95A>G	.	chr6:167271716	99.95%	NM_001006932.2	missense	1999
CARD11	p.(=)	c.3276A>G	.	chr7:2946461	100.00%	NM_032415.5	synonymous	101
CARD11	p.(=)	c.2622A>G	.	chr7:2957005	99.80%	NM_032415.5	synonymous	1998
PMS2	p.(K541E)	c.1621A>G	.	chr7:6026775	98.94%	NM_000535.6	missense	1784
PMS2	p.(P470S)	c.1408C>T	.	chr7:6026988	53.55%	NM_000535.6	missense	2000
PMS2	p.(=)	c.780C>G	.	chr7:6036980	99.70%	NM_000535.6	synonymous	1998
IKZF1	p.(=)	c.1002C>A	.	chr7:50467767	48.65%	NM_006060.5	synonymous	1998
EGFR	p.(R521K)	c.1562G>A	.	chr7:55229255	49.40%	NM_005228.4	missense	2000
EGFR	p.(=)	c.1887T>A	.	chr7:55238874	46.55%	NM_005228.4	synonymous	1998
EGFR	p.(=)	c.2709T>C	.	chr7:55266417	99.70%	NM_005228.4	synonymous	1995
AKAP9	p.(=)	c.3075C>T	.	chr7:91632306	99.76%	NM_005751.4	synonymous	415
AKAP9	p.(=)	c.3504A>G	.	chr7:91641928	99.95%	NM_005751.4	synonymous	1995
AKAP9	p.(N2792S)	c.8375A>G	.	chr7:91712698	100.00%	NM_005751.4	missense	287

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
AKAP9	p.(=)	c.8665C>T	.	chr7:91713972	100.00%	NM_005751.4	synonymous	851
AKAP9	p.(P2979S)	c.8935C>T	.	chr7:91714911	99.34%	NM_005751.4	missense	1362
AKAP9	p.(=)	c.9145C>T	.	chr7:91715662	100.00%	NM_005751.4	synonymous	1491
AKAP9	p.(=)	c.10426A>C	.	chr7:91726927	99.60%	NM_005751.4	synonymous	503
SAMD9	p.(=)	c.3171A>G	.	chr7:92732240	56.87%	NM_001193307.1	synonymous	211
EPHB4	p.(=)	c.1752A>G	.	chr7:100411278	99.90%	NM_004444.4	synonymous	1996
EPHB4	p.(=)	c.1314T>C	.	chr7:100416250	99.90%	NM_004444.4	synonymous	2000
PIK3CG	p.(=)	c.972A>G	.	chr7:106508978	99.70%	NM_002649.3	synonymous	1998
PIK3CG	p.(=)	c.981T>C	.	chr7:106508987	99.95%	NM_002649.3	synonymous	1997
PIK3CG	p.(T857A)	c.2569A>G	.	chr7:106522592	48.21%	NM_002649.3	missense	168
MET	p.(=)	c.3912C>T	.	chr7:116435768	50.20%	NM_001127500.2	synonymous	2000
MET	p.(=)	c.4146G>A	.	chr7:116436097	48.27%	NM_001127500.2	synonymous	1999
SMO	p.(=)	c.1164G>C	.	chr7:128846328	50.78%	NM_005631.4	synonymous	1997
EPHB6	p.(=)	c.1017C>T	.	chr7:142563300	51.60%	NM_004445.5	synonymous	1998
EZH2	p.(D185H)	c.553G>C	.	chr7:148525904	49.85%	NM_004456.4	missense	1996
KMT2C	p.(=)	c.8685G>A	.	chr7:151873853	49.55%	NM_170606.2	synonymous	2000
KMT2C	p.(=)	c.8040G>A	.	chr7:151874498	45.50%	NM_170606.2	synonymous	1998
WRN	p.(=)	c.513C>T	.	chr8:30924557	99.85%	NM_000553.4	synonymous	2000
WRN	p.(=)	c.2361G>T	.	chr8:30973957	49.59%	NM_000553.4	synonymous	1726
WRN	p.(L1074F)	c.3222G>T	.	chr8:30999280	42.02%	NM_000553.4	missense	426
WRN	p.(=)	c.4083C>T	.	chr8:31024638	49.57%	NM_000553.4	synonymous	1999
ADGRA2	p.(R1180G)	c.3538C>G	.	chr8:37699394	50.00%	NM_032777.9	missense	1994
KAT6A	p.(=)	c.4455C>T	.	chr8:41791283	47.32%	NM_006766.4	synonymous	1999
KAT6A	p.(=)	c.2982G>A	.	chr8:41798417	51.50%	NM_006766.4	synonymous	1998
KAT6A	p.(L134S)	c.401T>C	.	chr8:41906095	52.50%	NM_006766.4	missense	2000
PRKDC	p.(=)	c.11378T>C	.	chr8:48694956	50.25%	NM_006904.6	synonymous	1998
PRKDC	p.(=)	c.8414A>C	.	chr8:48740891	50.88%	NM_006904.6	synonymous	570
NBN	p.(=)	c.2016A>G	.	chr8:90958422	99.80%	NM_002485.4	synonymous	489
NBN	p.(=)	c.1197T>C	.	chr8:90967711	100.00%	NM_002485.4	synonymous	1128
NBN	p.(=)	c.102G>A	.	chr8:90995019	99.77%	NM_002485.4	synonymous	429

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
UBR5	p.(=)	c.3861G>T	.	chr8:103307712	51.03%	NM_015902.5	synonymous	1997
UBR5	p.(=)	c.3666A>G	.	chr8:103308010	58.84%	NM_015902.5	synonymous	1606
CSMD3	p.(T3120R)	c.9359C>G	.	chr8:113293552	47.85%	NM_198123.1	missense	1996
CSMD3	p.(=)	c.7956G>A	.	chr8:113318351	54.68%	NM_198123.1	synonymous	1999
CSMD3	p.(=)	c.2121T>C	.	chr8:113702131	47.11%	NM_198123.1	synonymous	1195
EXT1	p.(=)	c.1761G>A	.	chr8:118819578	46.75%	NM_000127.2	synonymous	1923
RECQL4	p.(=)	c.3127T>C	.	chr8:145737636	50.65%	NM_004260.3	synonymous	2000
RECQL4	p.(H635Y)	c.1903C>T	.	chr8:145739467	49.27%	NM_004260.3	missense	1999
RECQL4	p.(=)	c.738C>T	.	chr8:145741765	49.50%	NM_004260.3	synonymous	2000
RECQL4	p.(S92P)	c.274T>C	.	chr8:145742514	44.42%	NM_004260.3	missense	1997
LRRC14	p.(?)	c.-2394C>A	.	chr8:145742716	44.85%	NM_014665.3	unknown	379
RECQL4	p.(=)	c.132A>G	.	chr8:145742879	48.20%	NM_004260.3	synonymous	473
JAK2	p.(=)	c.2490G>A	.	chr9:5081780	43.35%	NM_004972.3	synonymous	466
PTPRD	p.(=)	c.4254G>C	.	chr9:8389364	99.26%	NM_002839.3	synonymous	944
PTPRD	p.(Q447E)	c.1339C>G	.	chr9:8518052	48.20%	NM_002839.3	missense	1998
TAF1L	p.(=)	c.5106A>G	.	chr9:32630472	50.55%	NM_153809.2	synonymous	1988
TAF1L	p.(=)	c.4317C>T	.	chr9:32631261	14.86%	NM_153809.2	synonymous	74
TAF1L	p.(=)	c.4209G>A	.	chr9:32631369	50.25%	NM_153809.2	synonymous	2000
TAF1L	p.(C152Y)	c.455G>A	.	chr9:32635123	4.90%	NM_153809.2	missense	204
PAX5	p.(=)	c.1110C>T	.	chr9:36840623	99.75%	NM_016734.2	synonymous	1998
SYK	p.(=)	c.1065C>T	.	chr9:93637015	49.87%	NM_003177.6	synonymous	1981
SYK	p.(=)	c.1302G>C	.	chr9:93639973	50.70%	NM_003177.6	synonymous	1998
SYK	p.(=)	c.1338G>A	.	chr9:93640009	50.70%	NM_003177.6	synonymous	2000
PTCH1	p.(P1315L)	c.3944C>T	.	chr9:98209594	92.58%	NM_000264.3	missense	1995
PTCH1	p.(=)	c.3387C>T	.	chr9:98215822	49.35%	NM_000264.3	synonymous	1996
XPA	p.(?)	c.-4A>G	.	chr9:100459578	49.66%	NM_000380.3	unknown	739
ABL1	p.(=)	c.3324A>G	.	chr9:133761001	99.80%	NM_005157.5	synonymous	2000
NUP214	p.(P574S)	c.1720C>T	.	chr9:134020092	99.50%	NM_005085.3	missense	2000
RALGDS	p.(=)	c.372G>A	.	chr9:135985796	48.55%	NM_001271775.1	synonymous	2000
BRD3	p.(=)	c.1284C>T	.	chr9:136907005	98.24%	NM_007371.3	synonymous	1994

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
BRD3	p.(=)	c.936A>G	.	chr9:136913355	100.00%	NM_007371.3	synonymous	1996
NOTCH1	p.(=)	c.6555C>T	.	chr9:139391636	99.95%	NM_017617.4	synonymous	2000
NOTCH1	p.(=)	c.5094C>T	.	chr9:139397707	99.90%	NM_017617.4	synonymous	2000
NOTCH1	p.(=)	c.2265T>C	.	chr9:139407932	99.95%	NM_017617.4	synonymous	1997
NOTCH1	p.(=)	c.312T>C	.	chr9:139418260	99.85%	NM_017617.4	synonymous	1999
RET	p.(=)	c.1296A>G	.	chr10:43606687	99.70%	NM_020975.4	synonymous	2000
TET1	p.(?)	c.-30C>T	.	chr10:70332066	47.95%	NM_030625.2	unknown	1996
TET1	p.(D162G)	c.485A>G	.	chr10:70332580	48.95%	NM_030625.2	missense	1998
TET1	p.(I1123M)	c.3369A>G	.	chr10:70405855	100.00%	NM_030625.2	missense	224
PTEN	p.(?)	c.-9C>G	.	chr10:89624218	55.91%	NM_000314.6	unknown	1937
FAS	p.(=)	c.642T>C	.	chr10:90771829	99.60%	NM_000043.5	synonymous	2000
CYP2C19	p.(=)	c.681G>A	.	chr10:96541616	48.67%	NM_000769.2	synonymous	1648
CYP2C19	p.(=)	c.990C>T	.	chr10:96602622	50.65%	NM_000769.2	synonymous	1998
NFKB2	p.(=)	c.1269A>G	.	chr10:104159196	100.00%	NM_001077494.3	synonymous	173
NFKB2	p.(=)	c.1821A>G	.	chr10:104160434	100.00%	NM_001077494.3	synonymous	1998
TCF7L2	p.(P483T)	c.1447C>A	.	chr10:114925369	51.19%	NM_001146274.1	missense	1938
FGFR2	p.(=)	c.696A>G	.	chr10:123298158	51.03%	NM_000141.4	synonymous	1999
FGFR2	p.(M186T)	c.557T>C	.	chr10:123310871	47.37%	NM_000141.4	missense	1999
HRAS	p.(=)	c.81T>C	.	chr11:534242	47.72%	NM_001130442.2	synonymous	1997
NUP98	p.(=)	c.4284G>A	.	chr11:3714489	48.04%	NM_016320.4	synonymous	204
RRM1	p.(=)	c.2232G>A	.	chr11:4159466	99.95%	NM_001033.4	synonymous	2000
FANCF	p.(=)	c.786A>G	.	chr11:22646571	49.85%	NM_022725.3	synonymous	2000
EXT2	p.(=)	c.127C>A	.	chr11:44129290	53.45%	NM_000401.3	synonymous	2000
DDB2	p.(=)	c.378T>C	.	chr11:47238522	99.85%	NM_000107.2	synonymous	1995
MEN1	p.(T546A)	c.1636A>G	.	chr11:64572018	99.95%	NM_000244.3	missense	1998
MEN1	p.(=)	c.1314T>C	.	chr11:64572557	99.95%	NM_000244.3	synonymous	2000
CCND1	p.(=)	c.723G>A	.	chr11:69462910	99.60%	NM_053056.2	synonymous	1995
NUMA1	p.(=)	c.2337G>A	.	chr11:71726212	48.05%	NM_006185.3	synonymous	2000
MAML2	p.(=)	c.1398T>C	.	chr11:95825797	48.35%	NM_032427.3	synonymous	2000
ATM	p.(N1983S)	c.5948A>G	.	chr11:108183167	99.66%	NM_000051.3	missense	879

Variant Details (continued)

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Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ATM	p.(T2944I)	c.8831C>T	.	chr11:108225582	5.62%	NM_000051.3	missense	89
CHEK1	p.(I471V)	c.1411A>G	.	chr11:125525195	99.70%	NM_001274.5	missense	1997
ETS1	p.(=)	c.1143A>G	.	chr11:128333503	52.83%	NM_001143820.1	synonymous	1999
ETS1	p.(V13fs)	c.37delG	.	chr11:128442988	49.42%	NM_001143820.1	frameshift Deletion	1993
KRAS	p.(=)	c.483G>A	.	chr12:25368462	99.12%	NM_033360.3	synonymous	228
ADAMTS2(	p.(=)	c.5400T>G	.	chr12:43769228	49.12%	NM_025003.4	synonymous	1189
ADAMTS20	p.(=)	c.5352A>G	.	chr12:43769276	34.60%	NM_025003.4	synonymous	2000
ADAMTS2(	p.(=)	c.2424T>C	.	chr12:43833739	54.33%	NM_025003.4	synonymous	127
ADAMTS20	p.(=)	c.1296T>C	.	chr12:43860526	53.97%	NM_025003.4	synonymous	189
KMT2D	p.(=)	c.13689C>T	.	chr12:49424534	50.33%	NM_003482.3	synonymous	1993
KMT2D	p.(=)	c.12510A>G	.	chr12:49425978	9.10%	NM_003482.3	synonymous	2000
KMT2D	p.(=)	c.10836G>A	.	chr12:49427652	48.13%	NM_003482.3	synonymous	964
KMT2D	p.(=)	c.7479G>T	.	chr12:49434074	44.85%	NM_003482.3	synonymous	544
KMT2D	p.(=)	c.2826C>T	.	chr12:49444545	46.59%	NM_003482.3	synonymous	88
KMT2D	p.(Q800*)	c.2398C>T	.	chr12:49445068	14.29%	NM_003482.3	nonsense	91
KMT2D	p.(G794R)	c.2380G>A	.	chr12:49445086	6.45%	NM_003482.3	missense	93
KMT2D	p.(=)	c.2379G>A	.	chr12:49445087	6.45%	NM_003482.3	synonymous	93
KMT2D	p.(E793K)	c.2377G>A	.	chr12:49445089	12.90%	NM_003482.3	missense	93
KMT2D	p.(A792V)	c.2375C>T	.	chr12:49445091	9.68%	NM_003482.3	missense	93
KMT2D	p.(A792T)	c.2374G>A	.	chr12:49445092	8.60%	NM_003482.3	missense	93
DDIT3	p.(=)	c.99C>T	.	chr12:57911160	50.50%	NM_001195055.1	synonymous	1998
HNF1A	p.(S574G)	c.1720A>G	.	chr12:121437382	99.95%	NM_000545.6	missense	2000
EP400	p.(=)	c.9138G>A	.	chr12:132561984	48.85%	NM_015409.4	synonymous	1998
EP400	p.(=)	c.9234G>A	.	chr12:132562080	49.44%	NM_015409.4	synonymous	1980
FLT3	p.(T227M)	c.680C>T	.	chr13:28624294	100.00%	NM_004119.2	missense	131
FLT3	p.(=)	c.288C>T	.	chr13:28636084	99.40%	NM_004119.2	synonymous	1998
FLT1	p.(=)	c.3639C>T	.	chr13:28883061	98.59%	NM_002019.4	synonymous	71
FLT1	p.(=)	c.3204T>C	.	chr13:28893642	51.10%	NM_002019.4	synonymous	2000
FLT1	p.(=)	c.405C>T	.	chr13:29012466	43.60%	NM_002019.4	synonymous	766

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
BIVM-ERCC5	p.(G1507R)	c.4519G>C	.	chr13:103527849	100.00%	NM_001204425.1	missense	580
ERCC5	p.(G1053R)	c.3157G>C	.	chr13:103527849	100.00%	NM_000123.3	missense	580
BIVM-ERCC5	p.(G1534R)	c.4600G>C	.	chr13:103527930	99.25%	NM_001204425.1	missense	670
ERCC5	p.(G1080R)	c.3238G>C	.	chr13:103527930	99.25%	NM_000123.3	missense	670
IRS2	p.(Q1248*)	c.3742C>T	.	chr13:110434659	4.35%	NM_003749.2	nonsense	115
IRS2	p.(G1057D)	c.3170G>A	.	chr13:110435231	98.46%	NM_003749.2	missense	260
IRS2	p.(=)	c.2448T>C	.	chr13:110435953	99.70%	NM_003749.2	synonymous	2000
LAMP1	p.(=)	c.556C>A	.	chr13:113965176	100.00%	NM_005561.3	synonymous	1986
BCL2L2-PABPN1	p.(=)	c.123G>A	.	chr14:23777099	49.05%	NM_001199864.1	synonymous	1998
BCL2L2	p.(=)	c.123G>A	.	chr14:23777099	49.05%	NM_001199839.1	synonymous	1998
BCL2L2-PABPN1	p.(Q133R)	c.398A>G	.	chr14:23777374	99.95%	NM_001199864.1	missense	2000
BCL2L2	p.(Q133R)	c.398A>G	.	chr14:23777374	99.95%	NM_001199839.1	missense	2000
NIN	p.(G1320E)	c.3959G>A	.	chr14:51223789	99.64%	NM_020921.3	missense	1652
NIN	p.(Q1125P)	c.3374A>C	.	chr14:51224374	99.95%	NM_020921.3	missense	1998
NIN	p.(=)	c.3090A>T	.	chr14:51224658	99.75%	NM_020921.3	synonymous	1619
NIN	p.(=)	c.2616C>A	.	chr14:51225132	99.55%	NM_020921.3	synonymous	1984
NIN	p.(=)	c.1128T>C	.	chr14:51237701	99.90%	NM_020921.3	synonymous	1998
NIN	p.(=)	c.933G>C	.	chr14:51239067	99.86%	NM_020921.3	synonymous	738
TSHR	p.(V83I)	c.247G>A	.	chr14:81534602	51.47%	NM_000369.2	missense	1871
TSHR	p.(=)	c.561T>C	.	chr14:81562998	52.35%	NM_000369.2	synonymous	1998
TSHR	p.(E727D)	c.2181G>C	.	chr14:81610583	52.30%	NM_000369.2	missense	2000
HSP90AA1	p.(=)	c.282C>T	.	chr14:102568296	98.86%	NM_001017963.2	synonymous	88
HSP90AA1	p.(M71L)	c.211A>T	.	chr14:102568367	99.95%	NM_001017963.2	missense	1990
AKT1	p.(=)	c.726G>A	.	chr14:105239894	100.00%	NM_001014431.1	synonymous	56
THBS1	p.(R288H)	c.863G>A	.	chr15:39876348	51.70%	NM_003246.3	missense	2000
TGM7	p.(=)	c.1764G>C	.	chr15:43571390	51.23%	NM_052955.2	synonymous	1997
TGM7	p.(=)	c.777T>C	.	chr15:43579566	47.75%	NM_052955.2	synonymous	1996
TGM7	p.(=)	c.133C>T	.	chr15:43585707	5.32%	NM_052955.2	synonymous	188

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
TGM7	p.(R44W)	c.130C>T	.	chr15:43585710	4.74%	NM_052955.2	missense	190
TCF12	p.(=)	c.135A>G	.	chr15:57213283	53.61%	NM_207037.1	synonymous	1994
NTRK3	p.(=)	c.1767C>T	.	chr15:88476365	52.53%	NM_001012338.2	synonymous	1999
NTRK3	p.(=)	c.678C>T	.	chr15:88679785	100.00%	NM_001012338.2	synonymous	2000
IGF1R	p.(=)	c.330A>G	.	chr15:99251026	14.16%	NM_000875.4	synonymous	1999
IGF1R	p.(=)	c.4038C>T	.	chr15:99500605	52.25%	NM_000875.4	synonymous	2000
ERCC4	p.(?)	c.-30T>A	.	chr16:14013993	41.26%	NM_005236.2	unknown	618
ERCC4	p.(=)	c.2505T>C	.	chr16:14041958	54.25%	NM_005236.2	synonymous	1998
MYH11	p.(A1241T)	c.3721G>A	.	chr16:15820863	49.72%	NM_001040114.1	missense	1999
MYH11	p.(=)	c.2493C>T	.	chr16:15839034	51.50%	NM_001040114.1	synonymous	1998
MYH11	p.(=)	c.2082C>T	.	chr16:15842023	54.23%	NM_001040114.1	synonymous	1999
MYH11	p.(=)	c.1764T>C	.	chr16:15850204	99.90%	NM_001040114.1	synonymous	1998
IL21R	p.(=)	c.1563C>T	.	chr16:27460550	52.33%	NM_021798.3	synonymous	1997
MMP2	p.(=)	c.1149T>C	.	chr16:55523705	48.60%	NM_004530.5	synonymous	2000
CDH11	p.(S373A)	c.1117T>G	.	chr16:65016087	100.00%	NM_001797.3	missense	1999
CDH11	p.(M275I)	c.825G>A	.	chr16:65022234	100.00%	NM_001797.3	missense	1999
CDH5	p.(=)	c.384C>T	.	chr16:66420885	100.00%	NM_001795.4	synonymous	1995
CDH5	p.(I517T)	c.1550_1551delTCinsCT	.	chr16:66432423	99.90%	NM_001795.4	missense	1973
CDH1	p.(=)	c.465C>T	.	chr16:68842404	4.23%	NM_004360.4	synonymous	71
MAF	p.(?)	c.-16GCGGC>C	.	chr16:79633815	99.73%	NM_005360.4	unknown	735
FANCA	p.(G809D)	c.2426G>A	.	chr16:89836323	99.30%	NM_000135.3	missense	1998
FANCA	p.(G501S)	c.1501G>A	.	chr16:89849480	99.85%	NM_000135.3	missense	2000
FANCA	p.(T266A)	c.796A>G	.	chr16:89866043	99.92%	NM_000135.3	missense	1299
NLRP1	p.(=)	c.4389C>T	.	chr17:5418107	49.02%	NM_033004.3	synonymous	1999
NLRP1	p.(R1366C)	c.4096C>T	.	chr17:5418799	54.43%	NM_033004.3	missense	1997
NLRP1	p.(=)	c.3741C>T	.	chr17:5424886	47.40%	NM_033004.3	synonymous	1998
NLRP1	p.(M1184V)	c.3550A>G	.	chr17:5425077	53.83%	NM_033004.3	missense	626
NLRP1	p.(=)	c.2934A>G	.	chr17:5440197	52.13%	NM_033004.3	synonymous	1997
NLRP1	p.(=)	c.114G>C	.	chr17:5487164	47.42%	NM_033004.3	synonymous	1993

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
PER1	p.(A962P)	c.2884G>C	.	chr17:8046772	44.91%	NM_002616.2	missense	1995
PER1	p.(=)	c.639A>C	.	chr17:8053085	51.50%	NM_002616.2	synonymous	2000
AURKB	p.(M298T)	c.893T>C	.	chr17:8108331	46.25%	NM_004217.3	missense	1998
AURKB	p.(=)	c.885C>T	.	chr17:8108339	47.87%	NM_004217.3	synonymous	1999
NF1	p.(=)	c.2034G>A	.	chr17:29553485	47.94%	NM_001042492.2	synonymous	1992
PGAP3	p.(=)	c.465T>C	.	chr17:37830900	99.80%	NM_033419.4	synonymous	1998
ERBB2	p.(I655V)	c.1963A>G	.	chr17:37879588	49.32%	NM_004448.3	missense	1999
ERBB2	p.(P1170A)	c.3508C>G	.	chr17:37884037	99.25%	NM_004448.3	missense	265
ITGB3	p.(=)	c.882T>C	.	chr17:45364540	52.10%	NM_000212.2	synonymous	1996
ITGB3	p.(=)	c.1143A>C	.	chr17:45368337	43.33%	NM_000212.2	synonymous	600
COL1A1	p.(T1075A)	c.3223A>G	.	chr17:48265495	99.85%	NM_000088.3	missense	1998
COL1A1	p.(=)	c.2298T>C	.	chr17:48268223	100.00%	NM_000088.3	synonymous	1999
BRIP1	p.(=)	c.3411T>C	.	chr17:59760996	47.75%	NM_032043.2	synonymous	111
BRIP1	p.(S919P)	c.2755T>C	.	chr17:59763347	50.58%	NM_032043.2	missense	1999
BRIP1	p.(=)	c.2637A>G	.	chr17:59763465	50.95%	NM_032043.2	synonymous	1998
SEPT9	p.(?)	c.-7A>C	.	chr17:75277611	37.00%	NM_001113491.1	unknown	100
SEPT9	p.(M576V)	c.1726A>G	.	chr17:75494705	99.85%	NM_001113491.1	missense	1998
BIRC5	p.(?)	c.-31G>C	.	chr17:76210367	52.01%	NM_001012271.1	unknown	896
BIRC5	p.(E152K)	c.454G>A	.	chr17:76219591	99.48%	NM_001012271.1	missense	1550
RNF213	p.(N1045D)	c.3133A>G	.	chr17:78298938	99.80%	NM_001256071.2	missense	1999
RNF213	p.(V1195M)	c.3583G>A	.	chr17:78305871	51.90%	NM_001256071.2	missense	2000
RNF213	p.(E1272Q)	c.3814G>C	.	chr17:78306102	49.75%	NM_001256071.2	missense	2000
RNF213	p.(D1331G)	c.3992A>G	.	chr17:78306280	53.93%	NM_001256071.2	missense	1971
RNF213	p.(=)	c.4020C>G	.	chr17:78306308	53.91%	NM_001256071.2	synonymous	1996
RNF213	p.(=)	c.4650G>A	.	chr17:78311508	44.62%	NM_001256071.2	synonymous	1999
RNF213	p.(S2334N)	c.7001G>A	.	chr17:78319136	49.95%	NM_001256071.2	missense	2000
RNF213	p.(=)	c.7245G>C	.	chr17:78319380	54.61%	NM_001256071.2	synonymous	1410
RNF213	p.(=)	c.10470G>A	.	chr17:78327358	100.00%	NM_001256071.2	synonymous	1353
RNF213	p.(A4399T)	c.13195G>A	.	chr17:78350110	47.55%	NM_001256071.2	missense	694
RNF213	p.(=)	c.13671C>T	.	chr17:78354661	99.85%	NM_001256071.2	synonymous	1999

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ZNF521	p.(=)	c.3597G>A	.	chr18:22775185	45.90%	NM_015461.2	synonymous	366
CDH2	p.(=)	c.2448C>T	.	chr18:25543387	52.38%	NM_001792.4	synonymous	651
CDH2	p.(=)	c.2091T>C	.	chr18:25565082	99.90%	NM_001792.4	synonymous	1999
CDH2	p.(=)	c.1431C>G	.	chr18:25570228	97.04%	NM_001792.4	synonymous	1993
MBD1	p.(P401A)	c.1201C>G	.	chr18:47800179	50.10%	NM_001204136.1	missense	1996
MBD1	p.(=)	c.240G>A	.	chr18:47803354	48.65%	NM_001204136.1	synonymous	2000
DCC	p.(F23L)	c.67T>C	.	chr18:49867224	99.80%	NM_005215.3	missense	1993
DCC	p.(R201G)	c.601C>G	.	chr18:50432602	48.92%	NM_005215.3	missense	1999
DCC	p.(=)	c.3108T>C	.	chr18:50936994	52.36%	NM_005215.3	synonymous	1971
CDH20	p.(?)	c.-23T>C	.	chr18:59157764	99.88%	NM_031891.3	unknown	816
CDH20	p.(=)	c.369C>T	.	chr18:59166541	99.70%	NM_031891.3	synonymous	1999
CDH20	p.(=)	c.780C>G	.	chr18:59170304	99.90%	NM_031891.3	synonymous	2000
TCF3	p.(=)	c.1302A>G	.	chr19:1619339	53.23%	NM_001136139.3	synonymous	1441
TCF3	p.(=)	c.759C>T	.	chr19:1622116	35.85%	NM_001136139.3	synonymous	2000
PIK3R2	p.(S313P)	c.937T>C	.	chr19:18273047	100.00%	NM_005027.3	missense	1993
PIK3R2	p.(=)	c.1911T>C	.	chr19:18279638	99.85%	NM_005027.3	synonymous	1996
AKT2	p.(=)	c.531C>T	.	chr19:40747887	13.87%	NM_001626.5	synonymous	137
AKT2	p.(=)	c.528C>T	.	chr19:40747890	5.26%	NM_001626.5	synonymous	133
AKT2	p.(?)	c.-17C>T	.	chr19:40771191	5.07%	NM_001626.5	unknown	493
AKT2	p.(?)	c.-20C>T	.	chr19:40771194	6.49%	NM_001626.5	unknown	493
AXL	p.(N266D)	c.796A>G	.	chr19:41743861	99.60%	NM_021913.4	missense	2000
MARK4	p.(=)	c.1683T>C	.	chr19:45801018	99.85%	NM_001199867.1	synonymous	1997
ERCC2	p.(=)	c.468A>C	.	chr19:45868309	100.00%	NM_000400.3	synonymous	1998
ASXL1	p.(L815P)	c.2444T>C	.	chr20:31022959	99.75%	NM_015338.5	missense	1998
ASXL1	p.(=)	c.3759T>C	.	chr20:31024274	100.00%	NM_015338.5	synonymous	1996
SRC	p.(=)	c.1218G>C	.	chr20:36030939	99.45%	NM_198291.2	synonymous	1997
PLCG1	p.(I813T)	c.2438T>C	.	chr20:39797465	47.57%	NM_002660.2	missense	1997
AURKA	p.(I57V)	c.169A>G	.	chr20:54961463	99.75%	NM_003600.3	missense	1999
AURKA	p.(F31I)	c.91T>A	.	chr20:54961541	51.73%	NM_003600.3	missense	1999
GNAS	p.(=)	c.393C>T	.	chr20:57478807	49.00%	NM_000516.5	synonymous	2000

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ERG	p.(?)	c.-6C>T	.	chr21:39870310	50.93%	NM_182918.3	unknown	108
ITGB2	p.(=)	c.1323T>C	.	chr21:46311813	99.77%	NM_000211.4	synonymous	1736
ITGB2	p.(Q354H)	c.1062A>T	.	chr21:46314907	99.60%	NM_000211.4	missense	1996
BCR	p.(N796S)	c.2387A>G	.	chr22:23627369	99.90%	NM_004327.3	missense	1999
MN1	p.(=)	c.408C>T	.	chr22:28196124	48.26%	NM_002430.2	synonymous	288
TIMP3	p.(=)	c.249T>C	.	chr22:33253280	51.25%	NM_000362.4	synonymous	2000
TIMP3	p.(=)	c.261C>T	.	chr22:33253292	62.59%	NM_000362.4	synonymous	1997
MYH9	p.(I1626V)	c.4876A>G	.	chr22:36684354	48.48%	NM_002473.5	missense	330
MYH9	p.(=)	c.4872G>T	.	chr22:36684358	47.92%	NM_002473.5	synonymous	336
MYH9	p.(=)	c.3429T>G	.	chr22:36691607	100.00%	NM_002473.5	synonymous	264
MYH9	p.(T483I)	c.1448C>T	.	chr22:36710296	4.43%	NM_002473.5	missense	451
EP300	p.(=)	c.3183T>A	.	chr22:41551039	99.05%	NM_001429.3	synonymous	1999
EP300	p.(=)	c.3348G>A	.	chr22:41553259	45.89%	NM_001429.3	synonymous	1996
CYP2D6	p.(T486S)	c.1457C>G	.	chr22:42522613	55.25%	NM_000106.5	missense	2000
CYP2D6	p.(C296R)	c.886T>C	.	chr22:42523943	99.75%	NM_000106.5	missense	2000
CYP2D6	p.(=)	c.408C>G	.	chr22:42525132	34.35%	NM_000106.5	synonymous	2000
CYP2D6	p.(P34S)	c.100C>T	.	chr22:42526694	64.75%	NM_000106.5	missense	2000
KDM6A	p.(T726K)	c.2177C>A	.	chrX:44929077	49.32%	NM_021140.3	missense	1999
TAF1	p.(R1444W)	c.4330C>T	.	chrX:70627887	14.44%	NM_004606.4	missense	90
TAF1	p.(P1445L)	c.4334C>T	.	chrX:70627891	18.89%	NM_004606.4	missense	90
ATRX	p.(Q929E)	c.2785C>G	.	chrX:76937963	46.25%	NM_000489.4	missense	493
BTK	p.(=)	c.1899C>T	.	chrX:100608191	99.95%	NM_000061.2	synonymous	1999
MAGEA1	p.(=)	c.813C>T	.	chrX:152482198	52.90%	NM_004988.4	synonymous	2000
MAGEA1	p.(T32A)	c.94A>G	.	chrX:152482917	44.22%	NM_004988.4	missense	1999

Biomarker Descriptions

Tumor Mutational Burden

Background: Tumor mutational burden (TMB), also known as tumor mutational load (TML), is the number of somatic mutations found in the DNA of cancer cells. TMB is determined by targeted next-generation sequencing and is expressed as the number of mutations per megabase (Mb) of DNA coding sequence[1]. Errors in DNA replication and repair, including mutations in the POLE gene and in

Biomarker Descriptions (continued)

mismatch repair (MMR) genes, are associated with increased TMB[2,3,4,5,6]. High TMB is correlated with increased neo-antigen burden and is associated with better response to immune checkpoint inhibitors that target the cytotoxic T lymphocyte antigen-4 (CTLA4), programmed death protein 1 (PD1), and programmed death-ligand 1 (PD-L1) inhibitors[7,8,9,10].

Alterations and prevalence: In a study of over 100,000 tumor samples analyzed by comprehensive genomic profiling, the median TMB value was 3.6 mutations per megabase (mut/Mb) although TMB values vary widely across cancers and within cancer types[11]. Certain childhood cancers, leukemia, glioblastoma, and neuroblastoma are examples of cancers with low mutation burden and median TMB values <1 mut/Mb[8,11]. In comparison, cancers that experience genotoxic insults including skin cancer and lung cancer have median TMB values of approximately 10 mut/Mb[8,11]. Within non-small cell lung cancer (NSCLC), higher TMB was observed in former/current smokers (10.5 mut/Mb) relative to never smokers (0.6 mut/Mb)[8,11,12]. The definition of high and low TMB threshold is cancer specific and an overall consensus threshold has not yet been established[11,13,14]. For example, in NSCLC, several studies have suggested establishing a boundary between low and high TMB of 10 +/- 1 mut/Mb[15,16,17].

Potential clinical relevance: Immune checkpoint inhibitors stimulate a patient's own T-cells to kill tumors and have exhibited benefits in some patients. However, the predictive biomarkers that underlie this clinical benefit have yet to be characterized. Several published studies have demonstrated that high TMB is associated with response to various FDA approved immune checkpoint inhibitors.[7,9,18,19,20,21,22,23,24]. The first immune checkpoint inhibitor to be approved by the FDA was ipilimumab (2011), an anti-CTLA4 antibody indicated for the treatment of metastatic melanoma. The overall response rate (ORR) of ipilimumab was 10.9%. In 2014, anti-PD-1 antibodies nivolumab (2014) and pembrolizumab (2014) were subsequently approved, for the treatment of metastatic melanoma, and recently pembrolizumab was indicated for advanced esophageal squamous cell carcinoma as well. In clinical studies of metastatic melanoma, overall response rates (ORR) were in the range of 30-40% for nivolumab and pembrolizumab. Indications have been expanded for these immune checkpoint inhibitors to include several other cancer types including NSCLC, advanced renal cell carcinoma, classical Hodgkin lymphoma, recurrent or metastatic squamous cell carcinoma of the head and neck, urothelial carcinoma, microsatellite instability (MSI)-High or mismatch repair deficient colorectal cancer and hepatocellular carcinoma. Atezolizumab (2016), avelumab (2017), and durvalumab (2017) that target programmed death-ligand 1 (PD-L1) were subsequently approved by the FDA. Nivolumab alone or in combination with ipilimumab is recommended for use in NSCLC with evidence of TMB[25]. Currently, efforts are underway to develop a standardized approach to calculate and report TMB values to support consistent reporting of TMB values across laboratories[26,27,28].

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

Tumor Mutational Burden

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
ipilimumab + nivolumab	✖	○	✖	○	✖
nivolumab	✖	○	✖	✖	● (II)
atezolizumab	✖	✖	✖	✖	● (II)
durvalumab, tremelimumab	✖	✖	✖	✖	● (II)
ipilimumab + nivolumab, pembrolizumab	✖	✖	✖	✖	● (II)
ipilimumab, nivolumab	✖	✖	✖	✖	● (II)
chemotherapy, durvalumab, tremelimumab	✖	✖	✖	✖	● (I/II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Summary (continued)

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

Tumor Mutational Burden (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
entinostat, nivolumab	✖	✖	✖	✖	● (I/II)
BI 754091	✖	✖	✖	✖	● (I)
BI 754091, BI 754111	✖	✖	✖	✖	● (I)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Relevant Therapy Details

Current NCCN Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

NCCN information is current as of 2019-08-15. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

Tumor Mutational Burden

○ ipilimumab + nivolumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** Tumor Mutational Burden

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Emerging targeted agents

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]

○ nivolumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** Tumor Mutational Burden

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- Non-Small Cell Lung Cancer; Emerging targeted agents

Reference: NCCN Guidelines® - NCCN-Non-Small Cell Lung Cancer [Version 7.2019]

Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated 👎 Not recommended 🛡 Resistance

ESMO information is current as of 2019-08-15. For the most up-to-date information, search www.esmo.org.

Tumor Mutational Burden

○ ipilimumab + nivolumab

Cancer type: Non-Small Cell Lung Cancer **Variant class:** Tumor Mutational Burden

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Stage IV Squamous and Non-squamous Non-Small Cell Lung Cancer (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Metastatic Non-Small-Cell Lung Cancer [Ann Oncol (2018) 29 (suppl 4): iv192–iv237. (Corrigendum: 30 January 2019)]

Signatures

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