

## CLINICAL REPORT

### Patient Data

<b>Patient</b>	DEF ABC
<b>Birthdate</b>	12.12.1212
<b>Diagnosis</b>	Melanoma

Mutation load	Medium	Number of non-synonymous SNVs	131
Number of oncogenes	3		
Number of tumor suppressor genes	6		
Additional information			

### Somatic Mutations in Known Driver Genes

List of cancer driver genes along with the mutations observed in the patient. Confidence column shows the number of the driver gene sources that cataloged the corresponding gene as driver and Reference column gives the list of those sources.

Gene	Mutation	Driver Type	Confidence <sup>1</sup>	Reference
BRAF	p.Val600Glu	Oncogene	4	1,2,3,4
SF3B1	p.Pro718Leu	Oncogene	3	1,2,4
DLEC1	p.Asp215Asn	TSG	2	3,5
FAM46C	p.Thr209Asn	unknown	2	1,4
GLI1	p.Ser1094Phe	TSG/Oncogene	2	3,5
RPS6KA2	p.Glu319Lys	TSG	2	3,5
ACHE	p.Thr95Ile	TSG	1	5
EPHB4	p.Pro346Leu	TSG	1	5
ETV5	p.Tyr445Cys	unknown	1	1
LPP	p.Ala119Gly	unknown	1	1
MADD	p.Ser1620Phe	TSG	1	5
PABPC3	p.Gly234Arg	unknown	1	4
PCSK5	p.Cys747Tyr	unknown	1	4
TNPO1	p.Gln38His	unknown	1	4

<sup>1</sup> Confidence shows the number of the driver gene sources that includes the gene. The sources are Vogelstain et al., Rubio-Perez et al., TSgene DB, COSMIC DB, UniProt.

## Somatic Mutations with Known Pharmacogenetic Effect

List of drugs with the evidence of targeting the observed variant of the mutated gene regardless of the cancer type. The information is obtained from CIViC database. CIViC evidence levels are given in Evidence column.

Gene	Mutation	Therapy	Effect	Disease	Evidence <sup>2</sup>	References
BRAF	V600E	Bevacizumab	Resistance	Colorectal Cancer	B	31
BRAF	V600E	Cetuximab	Resistance	Colorectal Cancer	B	23
BRAF	V600E	Cetuximab, Vemurafenib, Irinotecan	Sensitivity/Response	Colorectal Cancer	B	30
BRAF	V600E	Dabrafenib, Trametinib	Sensitivity/Response	Melanoma	B	22
BRAF	V600E	Vemurafenib	Sensitivity/Response	Melanoma	B	25,29
BRAF	V600E	Vemurafenib	Sensitivity/Response	Ovarian Cancer	B	33
BRAF	V600E	Vemurafenib, Cobimetinib	Sensitivity/Response	Melanoma	B	27
BRAF	V600E	Dabrafenib	Resistance	Non-small Cell Lung Carcinoma	C	36
BRAF	V600E	Dabrafenib, Trametinib DMSO	Sensitivity/Response	Cholangiocarcinoma	C	52,53
BRAF	V600E	Pertuzumab, Vemurafenib	Sensitivity/Response	Anaplastic Thyroid Carcinoma	C	33
BRAF	V600E	Pictilisib	Sensitivity/Response	Melanoma	C	39
BRAF	V600E	Trametinib DMSO, Dabrafenib	Sensitivity/Response	Cholangiocarcinoma	C	54
BRAF	V600E	Vemurafenib	Sensitivity/Response	Colorectal Cancer	C	33
BRAF	V600E	Vemurafenib	Sensitivity/Response	Ganglioglioma	C	49
BRAF	V600E	Vemurafenib	Sensitivity/Response	Laryngeal Squamous Cell Carcinoma	C	33
BRAF	V600E	Vemurafenib	Sensitivity/Response	Multiple Myeloma	C	47,47
BRAF	V600E	Vemurafenib	Sensitivity/Response	Ovarian Cystadenocarcinoma	C	50
BRAF	V600E	Vemurafenib	Sensitivity/Response	Papillary	C	42

<sup>2</sup> [CIViC evidence levels are used](#). A = Validated association, B = Clinical Evidence, C = Case study, D = Preclinical evidence, E = Inferential association

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List of drugs with the evidence of targeting the observed variant of the mutated gene regardless of the cancer type. The information is obtained from CIViC database. CIViC evidence levels are given in Evidence column.

Gene	Mutation	Therapy	Effect	Disease	Evidence	References
			onse	Thyroid Carcinoma		
BRAF	V600E	Vemurafenib,Panitumumab	Sensitivity/Response	Colorectal Cancer	C	44
BRAF	V600E	Vemurafenib,Panitumumab,Irinotecan	Sensitivity/Response	Cholangiocarcinoma	C	55
BRAF	V600E	BEZ235 (NVP-BEZ235, Dactolisib),GDC-0879	Sensitivity/Response	Colorectal Cancer	D	67
BRAF	V600E	Capecitabine,Vemurafenib,Bevacizumab	Sensitivity/Response	Colorectal Cancer	D	60
BRAF	V600E	Cobimetinib	Sensitivity/Response	Cancer	D	64
BRAF	V600E	PLX4720,GDC0941	Sensitivity/Response	Colorectal Cancer	D	58
BRAF	V600E	PLX4720,Nutlin-3	Sensitivity/Response	Colorectal Cancer	D	59
BRAF	V600E	Selumetinib (AZD6244),BEZ235 (NVP-BEZ235, Dactolisib)	Sensitivity/Response	Melanoma	D	63
BRAF	V600E	Sorafenib,Panitumumab	Sensitivity/Response	Colorectal Cancer	D	56
BRAF	V600E	Vemurafenib	Resistance	Melanoma	D	57
BRAF	V600E	Vemurafenib	Sensitivity/Response	Colorectal Cancer	D	60
BRAF	V600E	Vemurafenib,Gefitinib,Cetuximab	Sensitivity/Response	Colorectal Cancer	D	66

## Somatic Mutations in Pharmaceutical Target Proteins

### CIViC Summary of Drugs Targeting the Affected Genes

Therapies that have evidence of targeting the affected gene. The information is obtained from CIViC database. CIViC evidence levels are given in Evidence column. Results are filtered according to cancer type, if it is provided in metadata.

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BRAF	V600K	Vemurafenib	Sensitivity/Response	Melanoma	B	25
BRAF	AGK-BRAF	Sorafenib	Sensitivity/Response	Melanoma	C	37
BRAF	L597R	Vemurafenib	Sensitivity/Response	Melanoma	C	38
BRAF	V600	BAY 86-9766	Resistance	Melanoma	C	40
BRAF	V600E	Pictilisib	Sensitivity/Response	Melanoma	C	39
BRAF	V600E+V600M	Dabrafenib	Sensitivity/Response	Melanoma	C	35
BRAF	V600K	Vemurafenib	Sensitivity/Response	Melanoma	C	41
BRAF	AGK-BRAF	Vemurafenib	Resistance	Melanoma	D	37
BRAF	DEL 485-490	LY3009120	Sensitivity/Response	Cancer	D	65
BRAF	L505H	Vemurafenib	Resistance	Melanoma	D	69
BRAF	MUTATION	Trametinib	Sensitivity/Response	Cancer	D	62
BRAF	PAPSS1-BRAF	Trametinib	Sensitivity/Response	Melanoma	D	61
BRAF	PAPSS1-	Vemurafenib	Resistance	Melanoma	D	61

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BRAF	MUTATION	Trametinib	Sensitivity/Response	Cancer	D	62
BRAF	PAPSS1-BRAF	Trametinib	Sensitivity/Response	Melanoma	D	61

<sup>4</sup> Confidence shows the total number of the publications that is citing the drug.

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BRAF	V600E	Dabrafenib, Trametinib	Sensitivity/Response	Melanoma	B	22
BRAF	V600E	Vemurafenib	Sensitivity/Response	Melanoma	B	25,29
BRAF	V600E	Vemurafenib, Cobimetinib	Sensitivity/Response	Melanoma	B	27
BRAF	V600K	Dabrafenib, Trametinib	Sensitivity/Response	Melanoma	B	27
BRAF	V600K	Vemurafenib	Sensitivity/Response	Melanoma	B	25
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## Somatic Mutations in Pharmaceutical Target Proteins

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## References

The publications of the reference IDs given in the tables above.

1	Futreal et al., A census of human cancer genes., Nature reviews. Cancer, 4, 3, 2004
2	Vogelstein et al., Cancer genome landscapes., Science (New York, N.Y.), 339, 6127, 2013
3	Apweiler et al., UniProt: the Universal Protein knowledgebase., Nucleic acids research, 32, Database issue, 2004
4	Rubio et al., In silico prescription of anticancer drugs to cohorts of 28 tumor types reveals targeting opportunities., Cancer cell, 27, 3, 2015
5	Zhao et al., TSGene: a web resource for tumor suppressor genes., Nucleic acids research, 41, Database issue, 2013
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7	Haluska et al., Therapeutic targets in melanoma: map kinase pathway., Current oncology reports, 8, 5, 2006
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## Appendix

All the somatic variants of the patient with their dbSNP and COSMIC IDs.

Gene	Mutation	dbSNP	COSMIC
TNFRSF8	p.Pro215Ser	rs267597959	COSM14024
FAM46C	p.Thr209Asn		
S100A7A	p.Gly98Trp	rs267598049	COSM36721
PKLR	p.Gly251Ser	rs267598065	COSM36782
MAEL	p.Ser431Cys	rs267598149	COSM36684
ZBTB41	p.Phe164Val	rs267598277	COSM36692
SYT14	p.Ser437Phe	rs267598356	COSM36786
OR2T8	p.Met197Arg	rs4474294	
OR2T3	p.Ala214Thr	rs1770109	
SLC4A5	p.Ser428Phe	rs111392973	COSM2999241,COSM2999242
SLC4A5	p.Ser428Thr	rs267599454	
SNRNP200	p.Arg1538Cys	rs267599495	COSM36589
SEMA4C	p.Arg407Trp	rs267599501	COSM36666
ANKRD36	p.Ser1120Cys	rs768768868	
KIAA1211L	p.Gly746Glu	rs866719486	
DPP10	p.Ile93Asn		
XIRP2	p.Gly127Arg	rs267598980	COSM36673
TTN	p.Pro10904Ser	rs267599054	
TTN	p.Ala1347Thr	rs267599092	COSM2708938,COSM2708939,COSM2708940,COSM2708941,COSM2708942
SF3B1	p.Pro718Leu	rs267599150	COSM36655
FZD7	p.Pro285Ser	rs267599158	COSM24315
ZDBF2	p.Gly575Arg		
AGFG1	p.Gly364Arg	rs267599235	COSM25632,COSM3364621,COSM3364622
ARL4C	p.Gly71Ser	rs61752230	COSM21657
KIF1A	p.Ser141Ala		

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Gene	Mutation	dbSNP	COSMIC
DLEC1	p.Asp215Asn	rs149190717	COSM1566798,COSM36702
VPRBP	p.Pro309Leu	rs267599884	
TLR9	p.Gly514Ser	rs267599888	COSM36649
PRR23C	p.Glu262Lys	rs759730911	COSM36858
CLSTN2	p.Gln262His	rs267599628	COSM36631
SAMD7	p.Arg67Trp	rs191885635	COSM36663
GNB4	p.Pro107Leu	rs267599699	COSM13667
ETV5	p.Tyr445Cys	rs267599722	COSM23333
LPP	p.Ala119Gly		
MUC4	p.Pro1056His	rs753583962	
EXOC1	p.Pro774Ser	rs267600192	COSM36662
REST	p.Pro752Thr	rs267600197	COSM24349
SMR3B	p.Arg58Lys	rs267600235	COSM1310225,COSM36745
ADAM29	p.Gly589Glu	rs267600094	COSM26290
CARD6	p.Leu638Phe	rs267600630	COSM14006
TNPO1	p.Gln38His	rs267600680	COSM36775,COSM5648790
F2RL2	p.Leu141Phe	rs267600693	COSM27249,COSM36780
VCAN	p.Asp203Asn	rs267600718	COSM36758
EDIL3	p.Gln187Lys	rs267600722	COSM26295
PCDHB7	p.Asp374His		
GRIA1	p.Gly828Glu	rs267600500	COSM36714,COSM4854071,COSM4854072
ADAM19	p.Pro900Leu	rs61757467	
MBOAT1	p.Lys293Asn		
SPDEF	p.Asp283His		
SPDEF	p.Ser229Leu	rs200344679	COSM36760
SCUBE3	p.Gly702Glu	rs267600995	COSM36691
BTBD9	p.Arg46Cys	rs267601008	COSM36793
GPR111	p.Ile290Leu	rs267601055	COSM36619
BAI3	p.Asp755Asn	rs267601102	COSM22119
KATNA1	p.Pro241Leu	rs267600852	
KATNA1	p.Pro241Ser	rs267600853	
RPS6KA2	p.Glu319Lys	rs267600891	COSM21036,COSM30249

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All the somatic variants of the patient with their dbSNP and COSMIC IDs.

Gene	Mutation	dbSNP	COSMIC
			32,COSM3024933
ANLN	p.Gln649Arg	rs267601502	COSM36632
ABCA13	p.Gly4948Asp	rs267601533	COSM36817
EPHB4	p.Pro346Leu	rs267601191	COSM21032
ACHE	p.Thr95Ile	rs267601193	COSM36706
BRAF	p.Val600Glu	rs113488022	COSM18443,COSM476,COSM6137
RP11-1220K2.2	p.Asp1426Glu		
TRBV23-1	p.Pro27Leu		COSM36861
ZNF862	p.Gln583Lys	rs267601404	COSM36833
NAT2	p.Glu264Lys	rs267601842	COSM36677
SCARA5	p.Glu270Lys	rs267601883	COSM36713
GPR124	p.Glu863Lys	rs267601912	COSM36641
REXO1L1P	p.Ser639Phe		
CNBD1	p.Leu135Arg		
GRHL2	p.Ser356Phe	rs267601682	COSM36601
ZC3H3	p.Ser879Phe	rs267601811	COSM36642
ANKRD18A	p.Glu654Lys	rs267602244	COSM36859
PCSK5	p.Cys747Tyr	rs267602276	COSM36640
NUTM2G	p.Gly36Asp	rs267602327	COSM36612
OR1J1	p.Leu157Phe	rs267602118	COSM36710
GAPVD1	p.Leu35Phe	rs267602131	COSM36617
ADAMTS13	p.Arg398His	rs121908471	COSM36777
LHX3	p.Gly92Glu		COSM36599
MADD	p.Ser1620Phe	rs267602903	COSM26934
OR4S2	p.Arg120Cys	rs267602971	COSM36685
OR4D11	p.Pro58Ala	rs267603040	COSM36624
SPTBN2	p.Glu2047Lys	rs201985455	COSM36751,COSM4199893
GRM5	p.Glu941Lys	rs267603229	
DCP1B	p.Pro98Ser	rs267603408	COSM36575
CD163	p.Pro310Leu	rs267603681	COSM36725
GLI1	p.Ser1094Phe	rs267603606	COSM24658
TBC1D30	p.Gly327Glu	rs267603627	COSM36841
KCNC2	p.Leu298Ser	rs267603669	COSM36754

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Gene	Mutation	dbSNP	COSMIC
PABPC3	p.Gly234Arg	rs267603790	COSM36646
CPB2	p.Phe409Ser	rs267603833	COSM36708
CARKD	p.Pro205Ser	rs267603758	COSM36577
NOVA1	p.Ala256Asp	rs267603974	COSM1369439,COSM25331
ARHGAP5	p.Thr437Ile	rs56259828	
SERPINA6	p.Arg282Leu	rs267604111	COSM1265285,COSM26307,COSM267404
NUDT14	p.Thr44Pro	rs267603899	COSM36696
IGHV1-18	p.Gln20Lys		
TRPM1	p.Glu1261Lys	rs267604151	COSM36625
PLIN1	p.Leu191Arg		COSM36595
PRC1	p.Gly507Glu	rs267604387	COSM36743
AMDHD2	p.His587Arg		
NLRC3	p.Gly454Arg	rs267604538	COSM36804
TTLL6	p.Arg280Lys	rs267604932	COSM36852
USH1G	p.Leu379Ser	rs267605044	COSM36661
PSMA8	p.Gly36Glu	rs267605136	COSM36586
MBD3	p.Asp283Asn	rs369581342	
GTF2F1	p.Gly411Arg		
MUC16	p.Met2821Ile	rs267605807	COSM2701120,COSM36853
MUC16	p.Leu2819Met		
MUC16	p.Leu1434Ile		
OLFM2	p.Arg58Gln	rs267605828	COSM36654
PKN1	p.Arg191Cys	rs267605306	COSM21035
CYP4F2	p.Arg149Gln	rs140630977	COSM1129961
ZNF208	p.His855Tyr	rs267605385	
ARHGAP33	p.Pro1068Leu		
NOSIP	p.Pro297Leu		
ZNF880	p.Pro169Gln	rs267605631	COSM1234752
ZSCAN5A	p.Ala179Thr		
FLRT3	p.Ile532Asn		
DLGAP4	p.Ala879Ser	rs267605913	COSM36648
SPO11	p.Gly88Ser	rs267606012	COSM36690

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All the somatic variants of the patient with their dbSNP and COSMIC IDs.

Gene	Mutation	dbSNP	COSMIC
TMEM50B	p.Ser113Phe	rs267606110	COSM36665
CECR2	p.Gly474Arg	rs267606173	COSM36851
IGLV3-12	p.Ala89Thr	rs2073451	
IGLJ3	p.Pro10Ala	rs2009433	
MEI1	p.Gly507Glu	rs267606261	COSM36800
NHS	p.Arg373Gln	rs267606412	COSM1118631,COSM36761
FGD1	p.Arg636Trp		COSM21850
PJA1	p.His586Tyr	rs267606501	
OGT	p.Leu367Ser		
DCAF12L1	p.Ser281Phe	rs267606338	COSM36778

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