The genetic landscape of anaplastic pleomorphic xanthoastrocytoma

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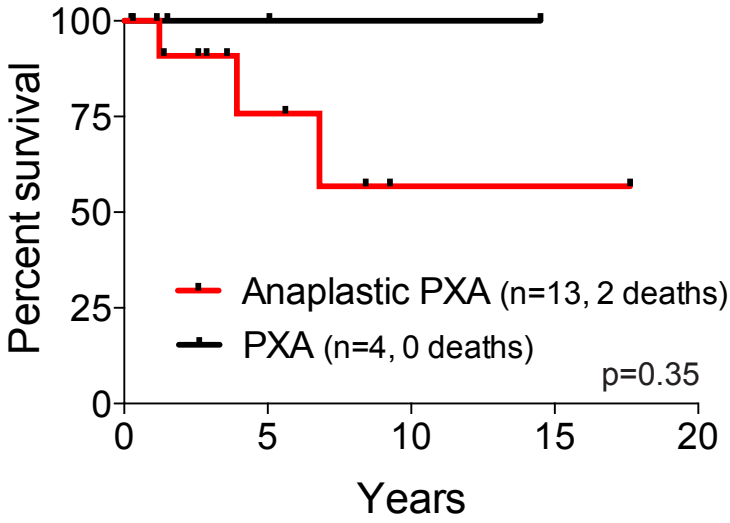
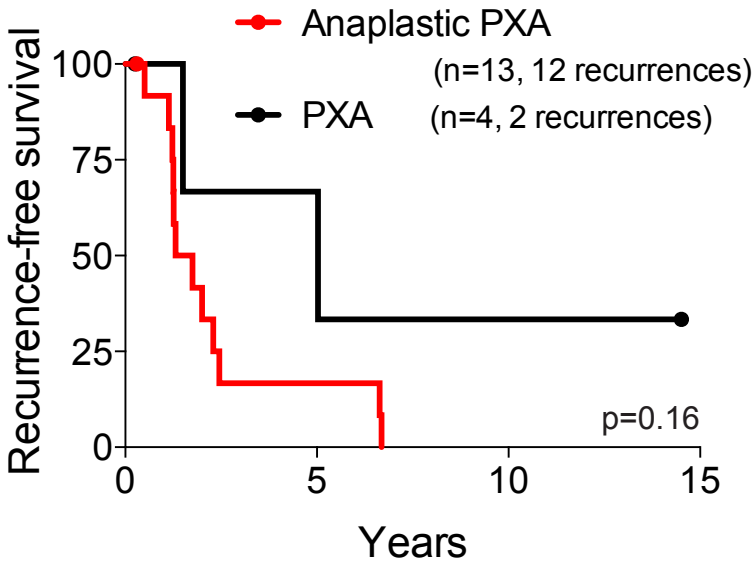
A.



GTR 11, STR 2, N/A 3

B.



GTR 11, STR 2, N/A 3

Supplemental Table 1. Summary of histologic and immunohistologic features of PXA cohort.

PXA#	PXA WHO Grade	Initial surgery	Biphasic tumor	EGBs	Tumor cell infiltration, at least focal (H&E)	Tumor cell infiltration, at least focal (neurofilament)	Pericellular reticulin deposition	Perivascular inflammatory infiltrate	OLIG2 expression	p16 expression	Mitoses per 10 HPF	MIB-1 labeling index	Necrosis	MVP	LM involvement	Time with disease (y)
1	III	N/A	Yes	Yes	N/A	N/A	Yes	Yes	N/A	Absent	30	>25%	Yes	Yes	N/A	N/A
2	III	N/A	Yes	Yes	Yes	Yes	Yes	Yes	N/A	N/A	3*	<1%‡	No	No	N/A	6.8
3	III	N/A	Yes	Yes	Present	N/A	Yes	Yes	N/A	N/A	8	20%	Yes	Yes	N/A	2.6
4	III	GTR	Yes	Yes	Present	Present	Yes	N/A	N/A	Absent	52	5%	No	No	Yes	3.9
5	III	N/A	Yes	N/A	Present	N/A	Yes	N/A	N/A	N/A	5	25%	Yes	No	Yes	N/A
6	III	GTR	Yes	Yes	Present	Present	N/A	Yes	Yes	Absent	5	5%	No	No	Yes	1.4
7	III	GTR	No	No*	Present	Present	N/A	Yes	N/A	Absent	10	20%	N/A	N/A	N/A	2.9
8	III	GTR	Yes	No	No	No	Yes	Yes	Yes	N/A	6	10%	No	No	No	8.4
9	III	STR	Yes	N/A	Present	N/A	N/A	Yes	Yes	N/A	12	N/A	Yes	Yes	Yes	17.6
10	III	GTR	No	No*	Present	Present	Yes	Yes	Yes	Absent	44	30%	No	No	No	3.6
11	III	GTR	No	Yes	No	No	Yes	Yes	Yes	Absent	9	15%	Yes	Yes	N/A	0.3
12	III	GTR	No	Yes	No	No	Yes	Yes	Yes	N/A	5	10%	Yes	No	Yes	1.2
13	III	GTR	Yes	No	Present	N/A	Yes	Yes	N/A	N/A	8	7%	No	No	No	9.3
14	III	N/A	Yes	No	Present	Present	N/A	Yes	N/A	N/A	13	15%	Yes	Yes	Yes	5.6
15	III	GTR	No	Yes	No	No	No	Yes	Yes	Absent	6	20%	No	No	Yes	1.1
16	II	STR	Yes	Yes	Present	Present	No	Yes	N/A	N/A	<1	N/A	No	No	Yes	1.5
17	II	GTR	No	N/A	Present	N/A	N/A	N/A	N/A	N/A	<1	N/A	No	No	N/A	14.5
18	II	GTR	No	No	Present	Present	Focal	N/A	Yes	N/A	<1	2%	No	No	Yes	0.3
19	II	GTR	No	Yes	No	No	No	Yes	N/A	Absent	0	1.50%	No	No	No	5.1

GTR, Gross total resection; STR, subtotal resection; N/A, not available; EGB, Eosinophilic granular bodies; HPF, high power field; MVP, microvascular proliferation; LM, Leptomeningeal;
Biphasic tumor refers to tumor with two distinct regions. One has lower grade more solid/circumscribed tumor and a second region demonstrates infiltrative tumor and/or more mitotically active tumor.
* Initial surgery demonstrated EGBs

Supplemental Table 2. Genes targeted for sequencing on the UCSF500 Cancer Panel. All coding exons were captured for sequencing from each of these 479 genes, with those highlighted genes also having select intronic or upstream regulatory regions that were captured for sequencing to enable detection of structural variants.

ABL1	DDIT3	HGF	NOTCH1	SHH
ABL2	DDR2	HIF1A	NOTCH3	SIN3A
ACVR1	DDX3X	HIST1H3B	NPM1	SLIT2
ACVR1B	DDX41	HMGA2	NRAS	SLITRK6
AJUBA	DGKH	HNF1A	NSD1	SMAD2
AKT1	DICER1	HOXB13	NSD2	SMAD3
AKT2	DIS3	HRAS	NT5C2	SMAD4
AKT3	DNAJB1	HSPA2	NTRK1	SMARCA2
ALK	DNMT3A	HSPA5	NTRK2	SMARCA4
APC	DOT1L	HSP90AB1	NTRK3	SMARCB1
APOBEC3G	DUSP2	ID3	NUP93	SMC1A
AR	DUSP4	IDH1	NUTM1	SMC3
ARAF	DUSP6	IDH2	OR5L1	SMO
ARFRP1	DYNC1I1	IGF1R	PAK1	SNCAIP
ARHGAP35	EBF1	IGF2	PAK3	SOCS1
ARID1A	EDNRB	IGF2R	PALB2	SOS1
ARID1B	EGFR	IKBKE	PARK2	SOS2
ARID2	EGR1	IKZF1	PAX3	SOX9
ARID5B	EIF1AX	IKZF2	PAX5	SOX10
ASH2L	ELF3	IKZF3	PAX7	SOX2
ASXL1	EMSY	IL2RB	PAX8	SPEN
ASXL2	EP300	IL7R	PBRM1	SPOP
ATF1	EPCAM	INHBA	PDCD1LG2	SPRED1
ATM	EPHA2	INPP4B	PDGFB	SPRY1
ATR	EPHA3	IPMK	PDGFRA	SPRY2
ATRX	EPHA5	IRF4	PDGFRB	SPRY4
AURKA	EPHA7	IRS2	PDK1	SPTA1
AURKB	EPHB1	JAK1	PHF6	SRC
AXIN1	EPOR	JAK2	PHOX2B	SRSF2
AXIN2	ERBB2	JAK3	PIK3CA	SS18
AXL	ERBB3	JAZF1	PIK3CG	STAG2
BAP1	ERBB4	KAT6A	PIK3R1	STAT3
BARD1	ERCC1	KDM5A	PIK3R2	STAT4
BCL2	ERCC2	KDM5C	PLAG1	STAT6
BCL2A1	ERG	KDM6A	PLCB4	STK11
BCL2L1	ERRFI1	KDR	PMS1	SUFU
BCL2L12	ESPL1	KEAP1	POLD1	SYK
BCL2L2	ESR1	KIT	POLE	SYNE1
BCL6	ESR2	KLF4	POLQ	TADA1
BCOR	ETS1	KLHL6	POT1	TBX3
BCORL1	ETV6	KMT2A	POU3F2	TCEB1
BLM	EWSR1	KMT2B	PPM1D	TCF7L2
BRAF	EZH1	KMT2D	PPP2R1A	TERT
BRCA1	EZH2	KNSTRN	PPP6C	TET2
BRCA2	FAM123B	KRAS	PRDM1	TFE3
BRD4	FAM46C	LEF1	PREX2	TFEB
BRIP1	FANCA	LIFR	PRKACA	TGFBR2
BTG1	FANCC	LRP1B	PRKAG2	TLR4
BTK	FANCE	LZTR1	PRKAR1A	TNFAIP3
CALR	FANCF	MALAT1	PRKCA	TNFRSF14
CARD11	FANCG	MAML2	PRKCH	TOP1
CBFB	FANCL	MAP2K1	PRKDC	TOP2A
CBL	FAT1	MAP2K2	PTCH1	TMPRSS2
CBLB	FAT3	MAP2K4	PTCH2	TP53
CCND1	FBXW7	MAP3K1	PTEN	TRAF3
CCND2	FGF10	MAP3K2	PTK2B	TRAF7
CCND3	FGF14	MAP3K5	PTPN1	TRIM28
CCNE1	FGF19	MAP3K7	PTPN11	TSC1
CD79A	FGF23	MAP3K9	PTPRB	TSC2
CD79B	FGF3	MAPK1	PTPRD	TSHR
CD274	FGF4	MCL1	PTPRK	TSHZ2
CDC42	FGF6	MDM2	PTPRT	TSHZ3
CDC73	FGFR1	MDM4	RAC1	TSLP
CDH1	FGFR2	MED12	RAD21	TTYH1
CDK12	FGFR3	MEF2B	RAD50	TYK2
CDK4	FGFR4	MEN1	RAD51	U2AF1
CDK6	FH	MET	RAD51C	USP7
CDK8	FLCN	MGA	RAD51D	VEGFA
CDKN1A	FLT1	MGMT	RAF1	VHL
CDKN1B	FLT3	MITF	RARA	WISP3
CDKN2A	FLT4	MLH1	RASA1	WRN
CDKN2B	FOXA1	MLH3	RASA2	WT1
CDKN2C	FOXL2	MPL	RB1	XBP1
CEBPA	FOXO1	MRE11A	RBM10	XPO1
CHD1	FOXP1	MSH2	REL	YAP1
CHD2	FRS2	MSH3	RELA	YWHAE
CHD4	FUBP1	MSH6	RET	ZBTB20
CHD5	FUS	MTOR	RHEB	ZFHX3
CHEK1	FYN	MUTYH	RHOA	ZMYM3
CHEK2	GAB2	MYB	RICTOR	ZNF217
CIC	GATA1	MYBL1	RIT1	ZNF703
CLDN18	GATA2	MYC	RNF43	ZNFHX4
CNOT3	GATA3	MYCL1	ROBO1	ZRSR2
COL1A1	GLI1	MYCN	ROS1	
COL2A1	GLI2	MYD88	RPL10	
CRCT1	GNA11	MYH9	RPTOR	
CREB1	GNA13	NAV3	RRAGC	
CREBBP	GNAQ	NBN	RRAS	
CRKL	GNAS	NCKAP5	RRAS2	
CSF1R	GPC3	NCOA2	RSPO2	
CSF3R	GPR124	NCOA3	RSPO3	
CTCF	GRIN2A	NCOR1	RUNX1	
CTNNA1	GRM3	NF1	RUNX1T1	
CTNNB1	GSK3B	NF2	SDHB	
CUL3	H3F3A	NFE2L2	SDHD	
CUX1	H3F3B	NFKBIA	SETBP1	
CYLD	HDAC4	NFKBIE	SETD2	
CXCR4	HDAC9	NIPBL	SF3B1	
DCC	HEY1	NKX2-1	SH2B3	

Supplementary Table 3. Pathogenic structural variants identified in the PXA cohort.

			N-terminal gene						C-terminal gene					
PXA#	Structural variant	Fusion type	Gene	Chromosome	Breakpoint position	Transcript ID	Fused exons	Fused amino acids	Gene	Chromosome	Breakpoint position	Transcript ID	Fused exons	Fused amino acids
5	deletion	intragenic deletion	RAF1 upstream	chr3	12,744,836	N/A	N/A	N/A	RAF1	chr3	12,642,249	NM_002880	8-17	279-648
6p	inversion	in-frame fusion	ATG	chr3	11,495,034	NM_006395	1-18	1-693	RAF1	chr3	12,642,209	NM_002880	8-17	279-648
6r	inversion	in-frame fusion	ATG	chr3	11,495,034	NM_006395	1-18	1-693	RAF1	chr3	12,642,209	NM_002880	8-17	279-648
4	inversion	in-frame fusion	NRF1	chr7	129,338,396	NM_005011	1-5	1-202	BRAF	chr7	140,492,812	NM_004333	9-18	381-766

Supplemental Table 4. Somatic single nucleotide variants (SNVs) and small insertions/deletions identified in the PXA cohort.

PXA#	CHROM	POS	REF	ALT	Function	Gene	Variant	TranscriptID	Classification	Reads	Tumor mutant allele frequency	Exonic function	Present in COSMIC database v84 release
1	chrX	76890149	G	GT	exonic	*ATRX*	ATRX p.T1582fs	NM_000489	Pathogenic	1161	29%	frameshift insertion	Yes
1	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	695	49%	nonsynonymous SNV	Yes
1	chr17	7577607	ACCTAG	A	exonic	*TP53*	TP53 p.V225fs	NM_000546	Pathogenic	600	41%	frameshift deletion	Yes
2	chr7	140477838	GCTGTCA	A	exonic	*BRAF*	BRAF p.485_490del	NM_004333	Pathogenic	487	33%	nonframeshift deletion	No
3i	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	587	32%	nonsynonymous SNV	Yes
3r	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	848	29%	nonsynonymous SNV	Yes
3r	chr17	29654741	G	A	exonic	*NF1*	NF1 p.W1831*	NM_001042	Pathogenic	734	11%	stopgain	No
3r	chr19	15271860	GGGTCC	G	exonic	*NOTCH3*	NOTCH3 p.G2192fs	NM_000435	Likely pathogenic	221	25%	frameshift deletion	No
4	chr19	10,610,474	A	T	exonic	*KEAP1*	KEAP1 p.V79D	NM_203500	VUS	310	11%	nonsynonymous SNV	Yes
5	chr3	187447447	A	C	exonic	*BCL6*	BCL6 p.V249G	NM_001130	Likely pathogenic	1211	23%	nonsynonymous SNV	No
5	chr5	1295250	G	A	upstream	*TERT*	TERT c.-146C>T	NM_198253	Pathogenic	739	32%	noncoding SNV	Yes
6i	chr17	7,577,120	C	T	exonic	*TP53*	TP53 p.R273H	NM_000546	Pathogenic	181	8%	nonsynonymous SNV	Yes
7i	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	381	35%	nonsynonymous SNV	Yes
7i	chr11	77934520	G	A	exonic	*GAB2*	GAB2 p.P502L	NM_080491	Likely pathogenic	354	66%	nonsynonymous SNV	Yes
7r	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	792	21%	nonsynonymous SNV	Yes
7r	chr11	119148930	T	C	exonic	*CBL*	CBL p.C384R	NM_005188	Likely pathogenic	391	4%	nonsynonymous SNV	Yes
7r	chr11	77934520	G	A	exonic	*GAB2*	GAB2 p.P502L	NM_080491	Likely pathogenic	767	49%	nonsynonymous SNV	Yes
8	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	841	33%	nonsynonymous SNV	Yes
8	chr16	68835573	T	G	exonic	*CDH1*	CDH1 p.V55G	NM_004360	VUS	583	30%	nonsynonymous SNV	No
8	chr5	36976107	G	T	exonic	*NIPBL*	NIPBL p.R366S	NM_133433	VUS	981	3%	nonsynonymous SNV	No
8	chr1	158595988	G	A	exonic	*SPTA1*	SPTA1 p.T1953I	NM_003126	VUS	599	27%	nonsynonymous SNV	No
8r	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	867	37%	nonsynonymous SNV	Yes
8r	chr16	68835573	T	G	exonic	*CDH1*	CDH1 p.V55G	NM_004360	VUS	841	38%	nonsynonymous SNV	No
8r	chr1	158595988	G	A	exonic	*SPTA1*	SPTA1 p.T1953I	NM_003126	VUS	640	19%	nonsynonymous SNV	No
8r	chr5	1295228	G	A	upstream	*TERT*	TERT c.-124C>T	NM_198253	Pathogenic	840	44%	noncoding SNV	Yes
9	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	543	59%	nonsynonymous SNV	Yes
9	chr15	93496775	A	G	exonic	*CHD2*	CHD2 p.Y564C	NM_001271	VUS	511	24%	nonsynonymous SNV	No
9	chr21	39775614	T	C	exonic	*ERG*	ERG p.T143A	NM_004449	VUS	688	12%	nonsynonymous SNV	No
9	chr1	78430404	A	G	exonic	*FUBP1*	FUBP1 p.I255T	NM_003902	VUS	367	26%	nonsynonymous SNV	No
9	chr2	141526781	CC	AA	exonic	*LRP1B*	LRP1B c.5758_5758TT	NM_018557	VUS	354	18%	frameshift substitution	No
9	chr5	38946573	C	A	exonic	*RICTOR*	RICTOR p.G1466*	NM_152756	VUS	389	15%	stopgain	No
9	chr1	158624492	AC	A	exonic	*SPTA1*	SPTA1 p.V982fs	NM_003126	VUS	348	23%	frameshift deletion	No
10	chr7	140,453,136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	312	42%	nonsynonymous SNV	Yes
10	chr8	144,940,706	C	T	exonic	*EPPK1*	EPPK1 p.R2239H	NM_031308	VUS	1191	8%	nonsynonymous SNV	No
10	chr8	144,940,331	C	T	exonic	*EPPK1*	EPPK1 p.R2364Q	NM_031308	VUS	1296	7%	nonsynonymous SNV	No
11	chr7	140,453,136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	166	17%	nonsynonymous SNV	Yes
11	chr7	98,497,061	G	A	exonic	*TRRAP*	TRRAP p.R217K	NM_003496	VUS	346	18%	nonsynonymous SNV	No
12	chr7	140,453,136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	279	38%	nonsynonymous SNV	Yes
12	chr5	1,295,228	G	A	upstream	*TERT*	TERT c.-124C>T	NM_198253	Pathogenic	80	39%	noncoding SNV	Yes
13	chr7	140,453,136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	759	45%	nonsynonymous SNV	Yes
13	chr15	41988918	G	T	exonic	*MGA*	MGA P.K570N	NM_001080	VUS	490	34%	nonsynonymous SNV	No
13	chr5	1,295,228	G	A	upstream	*TERT*	TERT c.-124C>T	NM_198253	Pathogenic	351	22%	noncoding SNV	Yes
14	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	1183	32%	nonsynonymous SNV	Yes
14	chr10	89692904	C	T	exonic	*PTEN*	PTEN p.R130*	NM_000314	Pathogenic	680	68%	stopgain	Yes
14	chr5	1295228	G	A	upstream	*TERT*	TERT c.-124C>T	NM_198253	Pathogenic	345	29%	noncoding SNV	Yes
15	chrX	129,146,629	CA	C	exonic	*BCORL1*	BCORL1 p.S55fs	NM_021946	Pathogenic	511	32%	frameshift deletion	No
15	chr7	140,453,136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	254	38%	nonsynonymous SNV	Yes
15	chr8	117,864,335	T	C	exonic	*RAD21*	RAD21 p.D441G	NM_006265	VUS	273	36%	nonsynonymous SNV	No
15	chr10	112,362,692	C	T	exonic	*SMC3*	SMC3 p.P1136L	NM_005445	VUS	793	35%	nonsynonymous SNV	No
16	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	709	38%	nonsynonymous SNV	Yes
17	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	547	30%	nonsynonymous SNV	Yes
18	chr7	140453136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	788	40%	nonsynonymous SNV	Yes
19	chr7	140,453,136	A	T	exonic	*BRAF*	BRAF p.V600E	NM_004333	Pathogenic	495	30%	nonsynonymous SNV	Yes
19	chr17	41,245,280	C	A	exonic	*BRCA1*	BRCA1 p.R756S	NM_007294	VUS	757	34%	nonsynonymous SNV	No

After PXA # the i, denotes initial and r, denotes recurrent. For PXA#8 the first recurrence and second recurrence are analyzed.

Supplemental Table 5. Somatic copy number alterations in the PXA cohort.

Chromosome	1	2	3i	3r	4A	4B
1	-	-	-	loss interstitial p	-	-
2	-	-	gain q	gain q	-	-
3	-	-	-	-	-	-
4	-	-	-	-	-	loss interstitial q
5	-	-	-	-	-	-
6	loss q	-	loss	loss	-	-
7	loss distal q	-	-	-	gain distal p, loss portions p and q	gain distal p, loss portions p and q
8	loss	-	-	-	CNLOH	CNLOH
9	-	loss	CNLOH	loss p, gain q	CNLOH	CNLOH
10	-	-	-	-	-	loss interstitial q*
11	-	-	-	-	-	-
12	-	-	-	-	gain	gain
13	-	-	gain distal q	-	-	-
14	-	-	-	loss proximal q	-	-
15	-	-	-	-	-	-
16	-	-	-	-	-	-
17	loss distal p	-	loss p, gain distal q	loss p, gain distal q	-	-
18	-	-	-	gain p, loss q	loss p	loss p
19	loss distal q	loss distal q	-	-	-	-
20	-	-	-	-	-	-
21	-	-	gain	gain	-	-
22	-	-	-	-	-	-
X	-	-	-	-	-	-
Focal amplifications	none	TERT (5p15)	none	none	TERT (5p15)	TERT (5p15)
Focal deletions (subclonal or heterozygous)	-	-	-	ARID1A (1p36)	-	-
Deep deletions other than CDKN2A	none	none	none	none	none	none
CDKN2A deletion boundaries	19.5-23.4 Mb	21.6-32.1 Mb	21.6-31.0 Mb	21.7-30.9 Mb	20.8-24.8 Mb	20.8-24.8 Mb

Each column is an individual tumor and matched pairs and intratumoral sampling are adjacent.

*, interstitial 10q loss does not include PTEN

After PXA # the i, denotes initial and r, denotes recurrent. For PXA#8 the initial resection was not available and the first recurrence and second recurrence

4C	4D	4E	4F	5
-	-	-	-	-
-	-	-	-	-
-	-	-	-	gain
-	-	-	loss interstitial q	-
-	-	-	-	-
loss interstitial q	loss interstitial 6q	interstial 6q loss suspected	-	-
gain distal p, loss portions p and q	gain distal p, loss portions p and q	gain distal p, loss portions p and q	gain distal p, loss portions p and q	-
gain	gain	CNLOH	CNLOH	-
CNLOH	CNLOH	CNLOH	CNLOH	CNLOH
-	-	-	loss interstitial q*	-
-	-	-	-	-
gain	gain	gain	gain	-
-	-	-	-	-
-	-	-	-	-
-	-	-	-	-
-	-	-	-	-
-	-	-	-	-
loss p	loss p	loss p	loss p	-
-	-	-	-	-
-	-	-	-	-
-	-	-	-	-
-	-	-	-	-
-	-	-	-	-
TERT (5p15)	TERT (5p15)	TERT (5p15)	TERT (5p15)	-
-	-	-	-	-
none	none	none	none	-
20.8-24.8 Mb	20.8-24.8 Mb	20.8-24.8 Mb	20.8-24.8 Mb	21.9-22.4 Mb

are analyzed.

6i	6r	7i	7r	8	8r	9	10
-	-	-	-	-	gain	gain p (3N), gain q (4N)	-
-	-	gain	gain	-	gain (4N)	gain (4N)	-
-	-	loss p	loss p, gain q	-	CNLOH p, gain + LOH q	CNLOH p, gain q	-
-	-	-	gain	-	gain	gain	-
-	-	-	gain	-	gain	gain (4N)	gain p (including TERT)
-	-	-	-	-	gain	gain	loss
-	-	gain	gain	-	gain	gain (5N)	-
-	-	-	CNLOH p, gain q	-	gain	CNLOH	-
-	-	loss	CNLOH	loss	CNLOH	gain (4N) + LOH	-
-	-	loss	loss	-	CNLOH	-	loss
-	-	loss	CNLOH	-	CNLOH	gain + LOH	-
-	-	gain	gain	-	gain (4N)	gain	-
-	-	loss	loss	-	-	CNLOH	-
-	-	loss	CNLOH	-	-	gain + LOH	-
-	-	gain	gain (4N)	-	gain (4N)	gain	gain
-	-	-	-	-	gain	gain p, gain distal q	-
-	-	-	-	-	gain	gain (4N)	-
-	-	-	loss	-	gain	gain p, CNLOH q	-
-	-	-	gain	-	gain	gain (5N)	loss
-	-	-	-	-	CNLOH	gain p (3N), gain q (4N)	-
-	-	-	gain (4N)	-	gain	gain (5N)	-
-	-	CNLOH	CNLOH	-	gain	gain + LOH	-
-	-	-	-	-	-	-	-
none	none	none	none	none	none	none	none
-	-	none	ARID1A (1p36)	-	-	-	-
none	none	BCORL1 (Xq26)	BCORL1 (Xq26)	none	none	none	none
21.9-22.3 Mb	21.9-22.2 Mb	21.8-22.1 Mb	21.8-22.1 Mb	21.7-22.8 Mb	21.7-22.8 Mb	21.8-22.2 Mb	21.1-24.2 Mb

11	12	13	14	15		16	17
loss proximal p	-	CNLOH	gain	loss distal p		-	-
-	-	-	gain	-		-	-
-	gain q	-	gain distal q	-		-	-
-	-	gain	gain (4N)	gain distal q		-	-
gain p	-	gain	gain (5N)	loss proximal q		-	-
-	-	-	gain	gain p, loss proximal q, gain distal q		-	-
-	-	gain	gain (7N)	-		-	-
-	-	gain	gain	-		-	-
loss	loss p	CNLOH	gain + LOH	CNLOH p		loss	loss
loss	-	-	gain + LOH	loss p		-	-
-	-	-	gain	-		-	-
-	-	gain	gain (4N)	-		-	-
-	-	loss	CNLOH	-		-	-
loss proximal q	-	-	gain	-		-	-
-	-	-	gain (4N)	-		-	-
-	-	-	gain (4N)	-		-	-
-	-	-	gain	loss p, gain q		-	-
-	-	-	-	loss p, gain proximal q, loss distal q		-	-
-	-	gain	gain (5N)	gain portions of q, loss portions of q		-	-
-	-	CNLOH	gain (6N)	-		-	-
-	gain	gain	gain + LOH	-		-	-
-	-	-	gain	-		-	-
-	-	-	-	-		-	-
none	none	none	none	PDGFRA (4q12)		none	none
-	-	-	-	-		-	-
none	none	none	none	none		none	none
-	21.5-22.3 Mb	21.8-27.0 Mb	21.9-22.2 Mb	20.8-26.5 Mb		21.1-22.4 Mb	21.8-25.6 Mb

18	19
loss	-
-	-
-	-
-	-
gain	-
-	-
gain (4N)	-
-	-
CNLOH	loss
loss	-
-	-
gain	-
-	-
-	loss proximal q
loss	-
-	-
loss distal p	-
loss	-
-	-
gain	-
-	-
loss	loss
-	-
none	none
-	-
none	none
21.9-22.1 Mb	21.7-22.4 Mb

Supplemental Table 6. Intratumoral somatic single nucleotide variants identifed in PXA#4.

PXA#4-Sample	CHROM	POS	REF	ALT	Function	Gene	Variant	Transcript ID	Classification	Total Reads	Tumor mutant allele frequency	ExonicFunc	Present in COSMIC database v84 release
1A	chr19	10,610,474	A	T	exonic	*KEAP1*	KEAP1 p.V79D	NM_203500	VUS	276	19%	nonsynonymous SNV	No
1B	chr13	41,134,760	A	G	exonic	*FOXO1*	FOXO1 p.S290P	NM_002015	VUS	765	5%	nonsynonymous SNV	No
1B	chr19	10,610,474	A	T	exonic	*KEAP1*	KEAP1 p.V79D	NM_203500	VUS	223	30%	nonsynonymous SNV	No
1B	chr15	42,028,777	T	C	exonic	*MGA*	MGA p.S1439P	NM_001080541	VUS	440	7%	nonsynonymous SNV	No
1B	chr9	117,819,606	T	C	exonic	*TNC*	TNC p.T1469A	NM_002160	VUS	725	6%	nonsynonymous SNV	No
1C	chr19	10,610,474	A	T	exonic	*KEAP1*	KEAP1 p.V79D	NM_203500	VUS	310	11%	nonsynonymous SNV	No
1C	chr19	11,101,922	C	T	exonic	*SMARCA4*	SMARCA4 p.R448C	NM_001128844	VUS	91	4%	nonsynonymous SNV	No
1D	chr7	92,354,993	C	G	exonic	*CDK6*	CDK6 p.A162P	NM_001145306	VUS	511	7%	nonsynonymous SNV	No
1D	chr19	10,610,474	A	T	exonic	*KEAP1*	KEAP1 p.V79D	NM_203500	VUS	381	8%	nonsynonymous SNV	No
1E	chr2	158,655,984	G	A	exonic	*ACVR1*	ACVR1 p.L8F	NM_001105	VUS	501	3%	nonsynonymous SNV	No
1E	chr19	10,610,474	A	T	exonic	*KEAP1*	KEAP1 p.V79D	NM_203500	VUS	143	3%	nonsynonymous SNV	No
1E	chr12	40,692,162	C	A	exonic	*LRRK2*	LRRK2 p.P1072T	NM_198578	VUS	970	3%	nonsynonymous SNV	No
1E	chr1	150,551,385	T	C	exonic	*MCL1*	MCL1 p.K208E	NM_021960	VUS	852	3%	nonsynonymous SNV	No
1F	chr13	41,134,760	A	G	exonic	*FOXO1*	FOXO1 p.S290P	NM_002015	VUS	619	3%	nonsynonymous SNV	No
1F	chr19	10,610,474	A	T	exonic	*KEAP1*	KEAP1 p.V79D	NM_203500	VUS	277	37%	nonsynonymous SNV	No
1F	chr15	42,028,777	T	C	exonic	*MGA*	MGA p.S1439P	NM_001080541	VUS	358	7%	nonsynonymous SNV	No
1F	chr19	50,909,497	C	G	exonic	*POLD1*	POLD1 p.S434C	NM_001256849	VUS	241	6%	nonsynonymous SNV	No
1F	chr9	117,819,606	T	C	exonic	*TNC*	TNC p.T1469A	NM_002160	VUS	639	7%	nonsynonymous SNV	No

Supplemental Table 7. Synopsis of PXA with or without anaplastic features investigated for TERT promoter mutations.

Diagnosis	TERT promoter mutant	TERT promoter wild type	Total tumors	Reference	Location
PXA WHO Grade II	2	7	9	Killela et al. PNAS. 2013. (17)	Supplemental Data, Dataset S1
PXA WHO Grade II	1	24	25	Koelsche et al. Acta Neuropathol. 2013. (19)	Supplemental Table 1
PXA WHO Grade II	16	62	78	Korshunov et al. Brain patholo. 2017. (22)	Supplemental Table 2
Anaplastic PXA WHO Grade III	15	29	44	Korshunov et al. Brain patholo. 2017. (22)	Supplemental Table 2
PXA with anaplastic features	3	10	13	Koelsche et al. Acta Neuropathol. 2013. (19)	Supplemental Table 1

Supplemental Table 8. Association of TERT promoter mutation and anaplastic features in PXA.

	PXA without anaplastic features	PXA with anaplastic features	
TERT promoter mutant	19	18	37
TERT promoter wild type	93	39	132
	112	57	169 total

Fisher's exact test, two-tailed: $p<0.05$