

**Patient 1**

Gene	Nucleotide Change	Amino Acid Change	Alteration	Samples Affected	Examples of FDA Approved Drugs for other Cancers	Examples of Drugs in Potential Clinical Trials
PSMD1	c.1291A>G	p.T431A	Missense	Tumor Reg 1-8	Bortezomib Carfilzomib	-
PIK3CA	c.1633G>A	p.E545K	Missense, Activating	Tumor Reg 1-8	Everolimus Temozolomide Sunitinib	Palbociclib (CDK4/6 inhibitor) + Taselisib/Pictilisib (PI3K inhibitors) (NCT02389842) VS-55844 (PI3K/mTOR inhibitor) (NCT01991938)
PSMC6	c.326G>C	p.G109A	Missense, Loss of function	Tumor Reg 1-8	Bortezomib Carfilzomib	-  AZD1775 (Wee-1 inhibitor) + Chemotherapy (NCT02272790) MK1775 (Wee-1 inhibitor) + Carboplatin (NCT01164995)
TP53	c.839G>C	p.R280T	Missense, Loss of function	Tumor Reg 1-8	-	MLN9708 (proteasome inhibitor) and Vorinostat (NCT02042989) p53MVA vaccine (NCT02275039)
HSP90AB1	c.1376C>T	p.T459I	Missense, Inactivating	Tumor Reg 1-5, Tumor Reg 7-8	-	Ganetespib (Hsp90 inhibitor) + Sirolimus (mTOR inhibitor) (NCT02008877) SNX-5422 (Hsp90 inhibitor) + Carboplatin + Paclitaxel (NCT01892046) PU-H71 (Hsp90 inhibitor) (NCT01393509) SNX-5422 (Hsp90 inhibitor) + Everolimus (NCT02063958) SNX-5422 Mesylate (Hsp90 inhibitor) (NCT01635712)
GHR	c.1072G>C	p.E358Q	Missense	Tumor Reg 1, Tumor Reg 3-5, Tumor Reg 7-8	Pegvisomant	-

**Patient 2**

Gene	Nucleotide Change	Amino Acid Change	Alteration	Samples Affected	Examples of FDA Approved Drugs for other Cancers	Examples of Drugs in Potential Clinical Trials
FH	c.1040C>T	p.S374F	Missense, Inactivating	Tumor Reg A-C, Lymph Node, Dist. Met Reg A-B	-	Glutaminase Inhibitor (NCT02071862)
NCOA1	c.2269G>A c.2404G>A	p.E757K p.E802K	Missense, Loss of function Missense	Tumor Reg A-C, Lymph Node, Dist. Met Reg A-B Tumor Reg A-C, Dist. Met Reg A-B	Tamoxifen	-
SMARCB1	c.127C>G	p.L43V	Missense, Loss of function	Tumor Reg A-C, Lymph Node, Dist. Met Reg A	Vismodegib	Alisertib (NCT02114229)
PSMB4	c.562G>T	p.A188S	Missense	Tumor Reg A-C, Dist. Met Reg A-B	Bortezomib Carfilzomib	-
PDGFRA	c.1232C>G	p.T411S	Missense, Loss of function	Tumor Reg A-C, Dist. Met Reg A-B	Imatinib Regorafenib Pazopanib Sunitinib Ponatinib Nilotinib Axitinib Lenvatinib Axitinib Dasatinib Sorafenib	Nintedanib (VEGFR and PDGFR inhibitor) (NCT01788982) Famitinib (c-KIT, VEGFR, PDGFR, FLT1+3 inhibitor) (NCT01762293)
DDR2	c.813C>G c.843C>G	p.I271M p.F281L	Missense Missense, Loss of function	Tumor Reg A-C, Dist. Met Reg A Tumor Reg A-B, Dist. Met Reg A	Regorafenib	Dasatinib + Crizotinib (NCT01744652) MGCD516 (RTK inhibitor) (NCT02219711)

**Patient 3**

Gene	Nucleotide Change	Amino Acid Change	Alteration	Samples Affected	Examples of FDA Approved Drugs for other Cancers	Examples of Drugs in Potential Clinical Trials
BTK	c.1879T>C	p.R594C	Missense, Loss of function	Tumor Reg A, Lymph Node Reg A-B, Dist. Met Reg A-B	Ibrutinib	ACP-196 (BTK inhibitor) (NCT02029443) ACP-196 + ACP-319 (PI3K inhibitor) (NCT02328014)
FGF13	c.70G>C	p.G24R	Missense, Loss of function	Tumor Reg A, Lymph Node Reg A-B, Dist. Met Reg A-B	-	TAS-120 (FGFR inhibitor) (NCT02052778)
EPHB1	c.1459C>G	p.Q487E	Missense	Tumor Reg A	Ponatinib	-
EPHA8	c.2378A>G	p.Y793C	Missense, Inactivating	Lymph Node Reg A-B, Dist. Met Reg A-B	Ponatinib	-
PSMC2	c.441C>G	p.Q148E	Missense	Lymph Node Reg A	Bortezomib Carfilzomib	-
BRCA2	c.2290G>A	p.E764K	Missense	Lymph Node Reg B	Olaparib	Olaparib + AZD2014 (mTORC1/2 inhibitor) or AZD5363 (AKT inhibitor) (NCT02208375) Rucaparib (PARP inhibitor) (NCT01891344) Talazoparib (PARP inhibitor) (NCT02326844; NCT02286687)
FGFR2	c.2131G>C	p.E711Q	Missense	Dist. Met Reg A-B	Pazopanib Regorafenib Sunitinib Lenvatinib Ponatinib	Lucitanib (FGFR1-3, VEGFR1-3 and PDGFR a/b inhibitor) (NCT02109016) BGJ398 (pan-FGFR inhibitor) (NCT02150967)
MMP1	c.1056G>C	p.Q352H	Missense, Inactivating	Dist. Met Reg A-B	Marimastat	-
KIT	c.157G>C	p.E53K	Missense	Dist. Met Reg A-B	Axitinib Cabozantinib Dasatinib Imatinib Pazopanib Regorafenib Sorafenib Sunitinib	Midostaurin (c-KIT inhibitor) (NCT01830361)
ATM	c.8315G>A	p.G2772E	Missense	Dist. Met Reg A	Olaparib	Talazoparib (PARP inhibitor) (NCT02286687) MSC2490484A (DNA-PK inhibitor) (NCT02316197)

**Supplementary Table S2** - Potential therapeutic targets. Listed for each patient are all altered genes that are potential targets identified by search in the Drug-Gene Interaction database (DGIdb), the Target database, the IntOGen database, the Personalized Cancer Medicine database, and by use of Qiagen Clinical Insight software. The gene altered, the observed alteration at nucleotide and protein level, the alteration, the samples affected, examples of identified FDA approved drugs (approved for other cancers), and examples of drugs in potential clinical trials are listed (derived from Qiagen Clinical Insight). Additionally, tumour suppressor genes, oncogenes, or IntOGen driver genes are highlighted in blue, red, and green text, respectively. All FDA approved drugs for the given target are listed (identified by the DrugBank database, the Personalized Cancer Medicine database, or by the Qiagen Clinical Insight software).