

## Clinical next generation sequencing to identify actionable aberrations in a phase I program

### Supplementary Material

Supplementary Table 1: Codons tested on Ampliseq 46 gene Assay.

Gene	Exons (codons) tested
ABL1	4 (237-260), 5 (275-283), 6 (303-319), 7 (387-412)
AKT1	3 (16-59)
ALK	23 (1172-1177), 25 (1259-1277)
APC	16 (865-886), 16 (1105-1122), 16 (1289-1322), 16 (1349-1382), 16 (1430-1467), 16 (1487-1509), 16 (1549-1564)
ATM	8 (343-355), 9 (395-412), 12 (601-614), 17 (837-862), 26 (1307-1324), 34 (1674-1693), 35 (1733-1758), 36 (1785-1802), 39 (1935-1957), 50 (2436-2445), 54 (2650-2667), 55 (2693-2715), 56 (2721-2739), 59 (2888-2891), 61 (2937-2950), 63 (2996-3016), 63 (3037-3052)
BRAF	11 (439-471), 15 (581-605)
CDH1	3 (69-92), 8 (351-373), 9 (395-415)
CDKN2A	2 (51-76)
CSF1R	7 (299-318), 22 (952-973)
CTNNB1	3 (12-45)
EGFR	3 (89-125), 7 (280-297), 15 (575-601), 18 (698-722), 19 (729-761), 20 (766-790), 20 (803-823), 21 (830-866)
ERBB2	19 (753-769), 20 (772-797), 21 (832-852), 21 (875-883)
ERBB4	3 (136-141), 4 (177-186), 6 (234-247), 7 (272-289), 8 (303-322), 9 (343-363), 15 (588-619), 23 (923-943)
FBXW7	5 (264-279), 8 (381-400), 9 (450-472), 10 (478-506), 11 (566-583)
FGFR1	4 (121-139), 7 (247-268)
FGFR2	7 (250-268), 7 (297-313), 9 (367-395), 12 (546-558)
FGFR3	7 (247-268), 9 (377-409), 14 (634-653), 16 (681-712), 18 (790-807)
FLT3	11 (441-458), 14 (569-575), 16 (662-682), 20 (828-846)
GNAS	8 (196-218)
HNF1A	3 (198-217), 4 (253-282)
HRAS	2 (5-23), 3 (48-79)
IDH1	4 (118-134)
JAK2	14 (604-622)
JAK3	13 (568-578), 16 (709-729)
KDR	6 (240-258), 7 (267-280), 11 (472-490), 19 (872-892), 21 (959-985), 26 (1138-1161), 27 (1192-1216), 30 (1301-1321), 30 (1336-1356)
KIT	2 (47-69), 9 (501-514), 10 (536-549), 11 (550-585), 13 (641-664), 14 (664-684), 15 (714-728), 17 (807-828), 18 (836-854)
KRAS	2 (5-28), 3 (40-67), 4 (136-150)
MET	2 (160-187), 2 (362-379), 14 (992-1017), 16 (1105-1126), 19 (1247-1268)
MLH1	12 (373-393)
MPL	10 (499-522)
NOTCH1	26 (1566-1605), 27 (1673-1697)
NPM1	11 (283-295)
NRAS	2 (6-22), 3 (53-69)
PDGFRA	12 (552-570), 14 (647-668), 15 (668-688), 18 (819-847)
PIK3CA	2 (77-98), 5 (328-351), 8 (418-422), 10 (533-551), 14 (688-716), 21 (1019-1049), 21 (1065-1069)
PTEN	1 (5-24), 3 (55-70), 6 (167-184), 7 (212-222), 7 (240-266), 8 (282-300), 8 (316-342)
PTPN11	3 (53-82), 13 (486-506)
RB1	4 (132-154), 6 (195-203), 11 (350-371), 17 (549-565), 18 (566-585), 20 (655-680), 21 (703-724), 22 (743-770)
RET	10 (609-627), 11 (630-654), 13 (762-774), 15 (880-901), 16 (914-931)
SMAD4	3 (109-128), 5 (167-184), 6 (228-247), 8 (304-319), 9 (330-363), 10 (385-404), 11 (444-472), 12 (497-526)
SMARCB1	2 (39-55), 4 (154-167), 5 (182-203), 9 (373-386)
SMO	3 (186-218), 5 (310-340), 6 (399-418), 9 (516-542), 11 (626-646)
SRC	14 (514-534)
STK11	1 (30-62), 4 (174-1999), 6 (253-281), 8 (325-360)
TP53	2 (1-18), 4 (81-114), 5 (126-135), 5 (149-181), 6 (187-223), 7 (230-253), 8 (269-306), 10 (332-344)
VHL	1 (88-110), 2 (120-149), 3 (157-175)

Supplementary Table 2: List of likely germline variants

Gene	Codon	WildType	VariantType
<b>ABL1</b>	247	K	R
<b>APC</b>	870	P	S
<b>APC</b>	1317	E	Q
<b>ATM</b>	410	V	A
<b>ATM</b>	604	P	S
<b>ATM</b>	858	F	L
<b>ATM</b>	1309	A	T
<b>ATM</b>	1691	S	R
<b>FGFR3</b>	384	F	L
<b>JAK3</b>	132	P	T
<b>JAK3</b>	722	V	I
<b>KDR</b>	482	C	R
<b>KDR</b>	1356	V	A
<b>KIT</b>	541	M	L
<b>MET</b>	168	E	D
<b>MET</b>	362	M	T
<b>MET</b>	375	N	S
<b>MET</b>	1010	T	I
<b>MLH1</b>	384	V	D
<b>PIK3CA</b>	391	I	M
<b>STK11</b>	354	F	L
<b>TP53</b>	273	R	H

Supplementary Table 3: List of potentially actionable genes and therapeutic implications

Gene	Potential Therapeutic Implications
<b>AKT1</b>	Treatment with AKT or mTOR inhibitors
<b>ATM</b>	Treatment with PARP inhibitors
<b>BRAF</b>	Treatment with BRAF inhibitors
<b>CDKN2A</b>	Treatment with CDK 4/6 inhibitors
<b>CSF1R</b>	Treatment with CSF1R inhibitors
<b>EGFR</b>	Treatment with EGFR inhibitors
<b>ERBB2 (HER2)</b>	Treatment with HER2 inhibitors, monoclonal antibodies, and targeted vaccines
<b>ERBB4 (HER4)</b>	Treatment with HER4 inhibitors
<b>FGFR1</b>	Treatment with FGFR1 inhibitors
<b>FGFR2</b>	Treatment with FGFR2 inhibitors
<b>FGFR3</b>	Treatment with FGFR3 inhibitors
<b>GNA11</b>	Treatment with PKC and MEK inhibitors
<b>HRAS</b>	Treatment with MEK Inhibitors
<b>JAK2</b>	Treatment with JAK inhibitors
<b>JAK3</b>	Treatment with JAK inhibitors
<b>KDR</b>	Treatment with KDR inhibitors
<b>KIT</b>	Treatment with KIT inhibitors
<b>KRAS</b>	Treatment with MEK Inhibitors
<b>MET</b>	Treatment with MET inhibitors
<b>NOTCH1</b>	Treatment with Gamma Secretase inhibitors (GSIs)
<b>NRAS</b>	Treatment with MEK inhibitors
<b>PDGFRA</b>	Treatment with PDGFRA inhibitors
<b>PIK3CA</b>	Treatment with PI3K, AKT, or mTOR inhibitors
<b>PTEN</b>	Treatment with p110beta, AKT, or mTOR inhibitors
<b>RET</b>	Treatment with RET inhibitors
<b>STK11</b>	Treatment with mTOR or AMPK inhibitors