

Blood-based next-generation sequencing analysis of neuroendocrine neoplasms

SUPPLEMENTARY MATERIALS

Supplemental Table 1: Correlation between mutations and chemotherapy

Chemotherapy	Number of patients treated	Histology	Male	Female	Genes with alterations detected
Cisplatin/Irinotecan	2	PNET, GI NEC	1/2	1/2	CTNNB1, APC, AR, FGFR1, FGFR2, MYC, SMAD4, TP53
Carboplatin/Etoposide	10	PNET, NEC	4/10	6/10	KRAS, TP53, MTOR, AR, PIK3CA, MYC, NF1, CCNE1, ARID1A, CCND2, NF1, CCND1, FGFR1, VHL, RET, SMAD4, BRAF, RB1
FOLFOX	2	PNET	1/2	1/2	NTRK1, PTEN, TP53, ALK
Chemotherapy (CBDCA + PAC...)	1	NEC	0/1	1/1	ARID1A, BRAF, ERBB2, GNAS, MYC, TP53
Afinitor (Everolimus)	5	PNET	4/5	1/5	TERT, JAK2, DDR2, ERBB2, PDGFRA, SMAD4, NOTCH1, VHL, CDKN2A
Octreotide	9	GI NEC, PNET, NEC	5/9	4/9	APC, KRAS, RAF1, TP53, MTOR, GNA11, BRCA1, CDK6, EGFR, KIT, MET, PTEN, ARID1A, ATM, BRAF, ERBB2, FGFR2, HNF1A, MYC, NF1, NTRK3
Lanreotide	4	PNET, NEC, GI NEC	0/4	4/4	TP53, JAK2, GNAS, CCND2, CDKN2A, ERBB2, KRAS, MTOR
AZD 1775/Olaparib	1	NEC	0/1	1/1	TP53, MET, ALK
Carboplatin	1	NEC	0/1	1/1	CTNNB1, TERT
Cisplatin/Etoposide	5	NEC, PNET, Lung large cell NEC	2/5	3/5	TP53, APC, BRCA2, CCNE1, KRAS, NF1, FGFR2, MTOR, PDGFRA, EGFR, ERBB2, FGFR1, KIT
Taxol/Carboplatin	3	NEC, GI NEC, Lung large cell NEC	2/3	1/3	ARID1A, BRCA2, CCNE1, EGFR, ERBB2, PIK3CA, TP53, APC, BRAF, BRCA1, CCND2, FGFR1, KRAS, MYC, PDGFRA, FGFR3, GNAS, NF1, RB1, TERT
S/P platinol + etoposide, S/P Keytruda, S/P Topotecan	1	NEC	1/1	0/1	CDKN2A, RB1, TP53, EGFR, ARID1A, BRCA1, CDKN2A, FGFR2, NF1, NOTCH1
Gemzar/Abraxane	3	PNET	2/3	1/3	AR, KRAS, NF1, TP53, APC, GNAS, SMAD4

Capecitabine Temozolomide	+	1	PNET	1/1	0/1	VHL
FOLFIRINOX		2	PNET	1/2	1/2	NF1, TP53, ATM, KRAS, SMAD4
Onivyde/5FU		1	PNET	0/1	1/1	FGFR1, KRAS

Supplementary Table 2: Genes sequenced by Guardant360 and all four major classes of alterations

Point Mutations (SNVs) (73 Genes)	Indels (23 Genes)	Amplifications (18 Genes)	Fusions (6 Genes)
<i>AKT1 SMO ARAF</i>	<i>ATM</i>	<i>AR</i>	<i>ALK</i>
<i>ATM APC CCND1</i>	<i>ARID1A</i>	<i>CCND1</i>	<i>FGFR2</i>
<i>CCNE1 BRCA1 CDKN2A</i>	<i>BRCA2</i>	<i>CCNE1</i>	<i>FGFR3</i>
<i>DDR2 CDK4 EZH2</i>	<i>CDKN2A</i>	<i>CDK6</i>	<i>NTRK1</i>
<i>FGFR1 ERBB2 (HER2) GNA11</i>	<i>ERBB2</i>	<i>ERBB2</i>	<i>RET</i>
<i>GNAS FGFR3 IDH2</i>	<i>KIT</i>	<i>FGFR2</i>	<i>ROS1</i>
<i>JAK3 HRAS MAP2K2/MEK2</i>	<i>MLH1</i>	<i>KRAS</i>	
<i>MAPK3/ERK1 KRAS MTOR</i>	<i>NF1</i>	<i>MYC</i>	
<i>NF1 MLH1 NRAS</i>	<i>PTEN</i>	<i>PIK3CA</i>	
<i>RB1 NOTCH1 PTPN11</i>	<i>SMAD4</i>	<i>BRAF</i>	
<i>SMAD4 PIK3CA RIT1</i>	<i>TP53</i>	<i>CCND2</i>	
<i>VHL RHEB TP53</i>	<i>VHL</i>	<i>CDK4</i>	
<i>ALK STK11 ARID1A</i>	<i>APC</i>	<i>EGFR</i>	
<i>BRAF AR CCND2</i>	<i>BRCA1</i>	<i>FGFR1</i>	
<i>CDH1 BRCA2 CTNNB1</i>	<i>CDH1</i>	<i>KIT</i>	
<i>EGFR CDK6 FBXW7</i>	<i>EGFR</i>	<i>MET</i>	
<i>FGFR2 ESR1 GNAQ</i>	<i>GATA3</i>	<i>PDGFRA</i>	
<i>HNF1A GATA3 JAK2</i>	<i>MET</i>	<i>RAF1</i>	
<i>KIT IDH1 MAPK1/ERK2</i>	<i>MTOR</i>		
<i>MET MAP2K1/MEK1 MYC</i>	<i>PDGFRA</i>		
<i>NFE2L2 MPL NTRK1</i>	<i>RB1</i>		
<i>PDGFRA NPM1 RAF1</i>	<i>STK11</i>		
<i>RET RHOA ROS1</i>	<i>TSC1</i>		
<i>PTEN TERT SC1</i>			
<i>NTRK3</i>			

Supplementary Table 3: Longitudinal study of genomic alterations in repeated blood samples. See Supplementary Table 3