Supplemental file

Supplemental Table 1. List of clinical trials by ID number (source, www.clinicaltrials.gov)

NCT00121680	A phase I/Ib, multicenter, open-label, dose escalation study of E7080 in patients tumors and in combination with temozolomide in patients with advanced and/or melanoma
NCT00215605	Phase I dose-escalation study of the safety and pharmacokinetics of XL184 adr orally to subjects with advanced malignancies
NCT00244972	Phase I study of tipifarnib and sorafenib in patients with biopsiable advanced ca
NCT00428545	Phase I I trial of bevacizumab and bortezomib in patients with advanced malign
NCT00429234	Phase I open-labeled trial of gemcitabine and dasatinib in advanced solid tumor
NCT00454090	Phase I, open-label, multi-center study to assess the safety, tolerability and pharmacokinetics of single and multiple oral doses of AZD8330 in patients with malignancies
NCT00458731	Phase I clinical trial evaluating the toxicity, pharmacokinetics and biological effe intravenous bevacizumab in combination with escalating doses of oral AZD217 patients with advanced malignancies
NCT00495872	A multi-arm complete phase I trial of valproic acid-based 2-agent oral regimens with advanced solid tumor
NCT00500422	Phase I study of a combination of doxil, velcade, and gemcitabine in advanced
NCT00522652	Phase I trial of oral PX-478 (a HIF-1α inhibitor) in patients with advanced solid t lymphoma
NCT00529022	Phase I/II trial of sequential azacitidine and valproic acid plus carboplatin in the patients with platinum resistant epithelial ovarian cancer
NCT00530907	Phase I study of valproic acid given in combination with bevacizumab in patients advanced cancer to determine safety and tolerability
NCT00532090	Multiple ascending dose study of R4733 administered orally in patients with refr metastatic or locally advanced solid tumors
NCT00543504	Phase I study of bevacizumab in combination with 1) sunitinib, 2) sorafenib, 3) e

	cetuximab, 4) trastuzumab and lapatinib
NCT00554268	An open label phase I trial of PBI-05204 in advanced cancer patients
NCT00559533	A multi-center, open-label, phase I study of single agent R7112 administered or patients with advanced malignancies, except all forms of leukemia
NCT00610493	Phase I trial of bevacizumab and temsirolimus in patients with advanced malign
NCT00679133	Open-label dose-escalation trial to evaluate the safety, pharmacokinetics, and pharmacodynamics of oral MGCD265 administered with interruption to subjects advanced malignancies
NCT00687622	An open-label, multiple-dose, dose-escalation study to investigate the safety, pharmacokinetics, and pharmacodynamics of the MEK inhibitor GSK1120212 in with solid tumors or lymphoma
NCT00725933	Phase I, multicenter, open-label, dose escalation, safety, pharmacokinetic, and pharmacodynamic study of BIIB028 administered to subjects with advanced sol
NCT00726583	Phase I trial of oral PX-866 (a PI3K inhibitor) in patients with advanced solid tum
NCT00731263	Phase I/II, open-label, multi-center study to assess the safety, tolerability, pharm and preliminary efficacy of the tor kinase inhibitor AZD8055 administered orally with advanced solid tumors.
NCT00756847	Phase I dose-escalation study of the safety and pharmacokinetics of XL147in co with paclitaxel and carboplatin in subjects with solid tumors
NCT00761644	Phase I trial of doxil, bevacizumab and temsirolimus
NCT00770731	Phase I study of temsirolimus, topotecan, and bortezomib in patients with advar malignancy
NCT00811993	Phase Ib study to evaluate the safety of combining IGF-1R antagonist R1507 w standard chemotherapy drug treatments in patients with advanced malignancies
NCT00813384	Phase I, first-in-human study evaluating the safety, tolerability, pharmacokinetic pharmacodynamics of AMG 208 in adult subjects with advanced solid tumors
NCT00861419	An open-label, dose escalation study to evaluate the safety, tolerability, and pharmacokinetics of AMG 386 with AMG 706, AMG 386 with bevacizumab, AM sorafenib, and AMG 386 with sunitinib in adult patients with advanced solid tum
NCT00877773	Histology-independent study of the mTor inhibitor, temsirolimus, in patients with cancer
NCT00880321	Phase I, open-label, multiple-dose, dose-escalation study to investigate the safe pharmacokinetics, and pharmacodynamics of the BRAF inhibitor GSK2118436

	with solid tumors
NCT00895128	Phase I dose-escalation study of erlotinib in combination with dasatinib in subje advanced cancer. Companion study to umbrella protocol
NCT00895362	Phase I dose-escalation study of erlotinib in combination with cetuximab in subj advanced cancer. Companion study to umbrella protocol
NCT00895687	A Phase I dose-escalation study of erlotinib in combination with bortezomib in s advanced cancer. Companion study to umbrella protocol
NCT00903734	An umbrella protocol for histology-independent, phase I modular study based or growth factor receptor mutation status: using erlotinib alone or in combination w cetuximab, bortezomib, or dasatinib to overcome resistance
NCT00920257	Phase I, open-label, two-stage study to investigate the safety, tolerability, pharm and pharmacodynamics of the oral AKT inhibitor GSK2141795 in subjects with or lymphomas
NCT00940225	A randomized discontinuation study of XL184 in subjects with advanced solid tu
NCT00940381	Phase I trial of sirolimus and cetuximab in patients with advanced malignancies
NCT00962091	An open-label, phase I study of the relative bioavailability, food effect, safety an of MLN8237 in patients with advanced solid tumors
NCT00972686	Phase I open-label, dose-escalation study of the phosphoinositide 3-kinase inhi GSK2126458 in subjects with solid tumors or lymphoma
NCT01014936	Phase I open-label, non-randomized, dose-escalation first-in-man trial to investi met kinase inhibitor EMD 1214063 under two different regimens in subjects with solid tumors
NCT01021072	Phase I study of MABP1 in patients with advanced cancers
NCT01054313	A Phase I trial of docetaxel and sirolimus in patients with advanced malignancie
NCT01072175	An open-label, dose-escalation, phase I study to investigate the safety, pharma pharmacodynamics and clinical activity of the BRAF inhibitor GSK2118436 in co with the MEK inhibitor GSK1120212 in subjects with BRAF mutant metastatic m
NCT01087554	Phase I trial of sirolimus (mTor inhibitor) and vorinostat (histone deacetylase inh patients with advanced cancer
NCT01091428	Randomized phase 2 study of MLN8237, an aurora a kinase inhibitor, plus weel paclitaxel or weekly paclitaxel alone in patients with recurrent epithelial ovarian, tube, or primary peritoneal cancer, preceded by a phase I portion in patients wit

	breast cancer
NCT01110486	Phase I study evaluating the safety and pharmacokinetics of ABT-348 as monot combination with carboplatin or in combination with docetaxel in subjects with a solid tumors
NCT01117623	Open label, phase I study to determine the safety, tolerability, maximum tolerate pharmacokinetics, and biomarker status of BAY73-4506 in patients with advanc malignancies
NCT01138085	Phase I dose escalation open-label safety and pharmacokinetic study to determ recommended phase II dose of GSK1120212 dosed in combination with GSK21 subjects with solid tumors (part 1) and in subjects with pancreatic cancer, endor cancer or colorectal cancer (part 2)
NCT01187199	Phase I trial of bevacizumab and temsirolimus in combination with 1) carboplati paclitaxel, 3) sorafenib for the treatment of advanced cancer
NCT01197170	Hormone receptor positive disease across solid tumor types: A phase I study of agent hormone blockade and combination approaches with targeted agents to p synergy and overcome resistance
NCT00841191	Phase I/II, multiple-dose, dose-escalation study to assess the safety, efficacy, a pharmacokinetics of intravenous CNTO 328, an anti-interleukin 6 (IL-6) monoclo antibody, in subjects with solid tumors

Supplemental Table 2. Distribution of Molecular Aberrations by Diagnosis

	Breast		CRC		GI-Other		Renal		GU Other		Ovarian		Endome
		%		%		%		%		%		%	
PIK-3CA	13/47	28	23/159	14	4/34	12	1/8	12	1/36	3	7/81	9	11/48
BRAF	0/24	0	17/163	10	0/25	0	0/2	0	0/25	0	2/63	3	0/31
KRAS	1/32	3	82/201	41	3/30	10	0/3	0	1/26	4	4/67	6	4/33
NRAS	0/16	0	4/77	5	2/16	12	0/1	0	0/17	0	0/43	0	0/24
EGFR	1/40	2	0/115	0	1/31	3	0/3	0	0/22	0	1/63	2	0/23
CKIT	0/16	0	1/67	1	1/19	5	0/1	0	1/18	6	1/31	3	0/19
PTEN Loss	2/24	8	12/80	15	3/19	16	0/6	0	8/23	35	5/37	14	6/16
RET	0/0	0	0/2	0	0/0	0	0/0	0	0/1	0	0/2	0	0/2
p53	3/8	38	10/22	45	1/3	33	1/4	25	2/7	29	4/10	40	4/5

Abbreviations: CRC – Colorectal Cancer, GI – Gastrointestinal, GU – Genitourinary, GYN – Gynecological

Supplemental Table 3. Distribution of Molecular Aberrations by Diagnosis

	H & N		Lung		Melanoma		Pancreatic		Sarcoma		Thyroi
		%		%		%		%		%	
PIK-3CA	6/63	10	5/47	11	2/63	3	1/22	5	0/29	0	1/31
BRAF	1/55	2	0/26	0	77/133	58	0/18	0	0/25	0	17/49
KRAS	3/24	12	16/71	23	1/47	2	12/22	55	0/23	0	1/19
NRAS	0/39	0	0/23	0	25/104	24	0/15	0	0/19	0	4/19
EGFR	2/55	4	11/64	17	1/39	3	0/23	0	0/19	0	0/25
CKIT	0/38	0	0/20	0	2/88	2	0/10	0	0/22	0	1/19
PTEN Loss	8/35	23	6/34	18	7/37	19	1/8	12	2/17	12	1/20
RET	0/0	0	0/1	0	0/0	0	0/2	0	0/1	0	16/18
p53	1/6	17	4/11	36	4/11	36	2/6	33	2/7	29	1/4

Abbreviation: H & N – Head and Neck

Supplemental Table 4. Patient characteristics: tumor types by type of therapy

Tumor type	N=291	Matched targeted therapy N = 175	Unmatched therapy N=116
	N (%)	N (%)	N (%)
Melanoma	73 (25)	52 (30)	21 (18)
Colorectal	62 (21)	19 (11)	43 (37)
Thyroid	34 (12)	31 (18)	3 (3)
Other	23 (8)	9 (5)	14 (12)
Lung	22 (8)	19 (11)	3 (3)
Breast	16 (6)	14 (8)	2 (2)
Ovarian	12 (4)	5 (3)	7 (6)
Genitourinary, other	10 (3)	5 (3)	5 (4)
Endometrial	9 (3)	7 (4)	2 (2)
Gastrointestinal, other	8 (3)	3 (2)	5 (4)
Pancreatic	8 (3)	1 (1)	7 (6)
Gynecological	7 (2)	5 (3)	2 (2)
Head and neck	7 (2)	5 (3)	2 (2)

Supplemental Table 5

Response in patients with a RET mutation and in patients with a mutation other than RET by type of therapy (non-randomized)

1 aberration	Type of therapy	No. of treated pts.	CR/PR (%)	P
RET	Matched	17	7 (41)	NA
	Non-matched	0	NA	
Non-RET	Matched	158	40 (25)	<.0001
	Non-matched	116	6 (5)	

Response in patients with PTEN loss and in patients with one aberration other than PTEN loss by type of therapy (non-randomized)

1 aberration	Type of therapy	No. of treated pts.	CR/PR (%)	P
PTEN-Loss	Matched	24	6 (25)	.99
	Non-matched	10	2 (20)	
Non PTEN-Loss	Matched	151	41 (27)	<.0001
	Non-matched	106	4 (4)	

Response in patients with a PIK3CA **aberration and in patients with one aberration other than** PIK3CA **by type of therapy (non-randomized)**

1 aberration	Type of therapy	No. of treated pts.	CR/PR (%)	P
PIK3CA	Matched	27	4 (15)	.55
	Non-matched	8	0 (0)	
Non-PIK3CA	Matched	148	43 (29)	<.0001
	Non-matched	108	6 (6)	

Response in patients with a KRAS **aberration and in patients with one aberration other than** KRAS **by type of therapy (non-randomized)**

1 aberration	Type of therapy	No. of treated pts.	CR/PR (%)	P
KRAS	Matched	17	1 (6)	.26
	Non-matched	48	0 (0)	
Non-KRAS	Matched	158	46 (29)	.0016
	Non-matched	68	6 (9)	