

# Supplementary Table S1

Name	Targets	Target pathway
ABT-199 ( Venetoclax )	BCL2	
GDC-0152	IAP	Apoptosis
Birinapant	Caspase, IAP	
Capecitabine	DNA/RNA Synthesis, Nucleoside antimetabolite/analog	
Dacarbazine	POLA2, mmp9, dna/rna synthesis	
AZD2461	PARP	
Streptozotocin	DNA/RNA Synthesis, DNA alkylator	
Teniposide	Topoisomerase	
DAUNORUBICIN /Cerubidine	ADCs cytotoxin, Topoisomerase, Autophagy, ADC Cytotoxin, Telomerase	
Eloxatin	DNA/RNA Synthesis, DNA alkylator/crosslinker, Autophagy	
Nelarabine	Nucleoside antimetabolite/analog, POLA1, DNA/RNA Synthesis	
Ftorafur	DNA synthesis, Nucleoside antimetabolite/analog	
Adrucil	DNA/RNA Synthesis, DNA antimetabolite	
Mitoxantrone	Topoisomerase,PKC,topoisomerase II	
Mercaptopurine	Amidophosphoribosyltransferase,, IMPDH, HPRT	
I-BET-762	BRD2, BRD3, BRD4	
Raltitrexed	dna/rna synthesis, thymidylate synthase, nucleoside antimetabolite	
Docetaxel	Microtubule stabiliser	Mitosis
Paclitaxel	Microtubule stabiliser	
Topotecan	Topoisomerase I	
Ifosfamide	DNA/RNA Synthesis, DNA alkylator/crosslinker	
Hydroxyurea	RRM2, RRM1, NFKB1	DNA Damage/DNA Repair
Beta-Lapachone	Topoisomerase inhibitor	
Floxuridine	thymidylate synthase	
Carboplatin	DNA alkylation	
Cytarabine	Antimetabolite	
Etoposide	TOP2	
Gemcitabine	Pyrimidine antimetabolite	DNA replication
Bleomycin	dsDNA break induction	
Cisplatin	DNA crosslinker	
Adriamycine	TOP2A	
Selumetinib	MEK1, MEK2	
GDC-0994	MAPK1, MAPK3, ERK	
PD184352	mek1,mek2	ERK MAPK signaling
TAK-733	MEK	
MEK162	MEK, autophagy, MAP2K1	
Plerixafor	CXCR	GPCR/G protein, Immunology/Inflammation
NLG919	IDO	
Isotretinoin	RAR/RXR	metabolism
Cladribine	Adenosine Deaminase,DNA/RNA Synthesis	
Imiquimod	autophagy, Immunology & Inflammation related, TLR-7, Toll-like Receptor (TLR)	Immunology/Inflammation, Autophagy, Angiogenesis
Fludarabine	BAZ2A, BAZ2B	NoRC negatively regulates rRNA expression
Vincristine	NROB, NR5A1	Nuclear Receptor transcription pathway,Transcriptional regulation of pluripotent stem cells
Tretinoin	Retinoic acid	Other
Tideglusib	GSK-3	
Rapamycin	MTORC1	PI3K/Akt/mTOR pathway
Batimastat	MMP1, mmp9, mmp3, mmp2, adam17, mmp13,mmp14, fcer2	Proteases
Lenalidomide	CRBN	Protein stability and degradation
Sorafenib	PDGFR, KIT, VEGFR, RAF	
Imatinib	ABL, KIT, PDGFR	
Sunitinib	PDGFR, KIT, VEGFR, FLT3, RET, CSF1R	Protein Tyrosine Kinase/RTK
ASP3026	ALK	
CO-1686 ( Rociletinib )	EGFR	
LGK-974	Wnt/beta-catenin, PORCN	setm cell & wnt
BMS-833923	Smoothened, SMO, Hedgehog/Smoothened	
LDK378 ( Ceritinib )	ALK, IGF-1R, IR, INSR	TGF-beta/Smad inhibitor, IGF-1R inhibitor
Carmofur	ASAH1, LMNA, SMN1, CYP2D6, MAPK3, CYP3A4	others

## Supplementary Table S2

IR signaling_active(seq_mi/ctr)			
Symbol	Expr Log Ratio	Expr p-value	Expr False Discovery Rate (q-value)
ASIC1	-0.702	1.50E-04	1.47E-03
ASIC3	-1.575	5.00E-05	5.64E-04
ATM	-0.866	1.50E-03	9.43E-03
FGFR4	0.716	2.50E-04	2.25E-03
FOXO3	-0.551	1.40E-03	8.95E-03
FOXO4	-1.052	5.00E-05	5.64E-04
GAB1	-0.582	1.35E-03	8.70E-03
INPP5F	-0.683	1.00E-04	1.03E-03
INPPL1	-0.644	5.00E-05	5.64E-04
INSR	-0.668	5.00E-05	5.64E-04
JAK2	-0.609	3.00E-04	2.60E-03
NRAS	0.516	1.20E-03	7.94E-03
PPP1R14C	1.018	7.00E-04	5.14E-03
RRAS	-0.883	5.00E-05	5.64E-04
SCNN1G	1.418	5.00E-05	5.64E-04
SHC1	-0.604	2.50E-04	2.25E-03
SOCS3	-0.983	2.00E-04	1.87E-03
STX4	-0.586	4.50E-04	3.62E-03
SYNJ1	-0.721	5.00E-05	5.64E-04
TRIP10	-0.546	7.50E-04	5.44E-03
TSC1	-1.043	5.00E-05	5.64E-04
VAMP2	-0.873	5.00E-05	5.64E-04

## Supplementary Table S3

Gene Name	ctr (FPKM)	met+ima (FPKM)
PLK1	83.9018	51.0837
AIM1	0.187736	0.151921
ENY2	61.7965	43.576
CCNB1	98.5317	67.7125
RB1	18.6943	17.529
NDUFB4	197.483	173.548
PCNA	150.903	65.3481
CDK1	149.808	109.444
MTOR	15.4292	14.8959
RPS6KB1	16.866	13.3142
WEE1	17.786	13.7584
FOXM1	30.1695	23.2938
RAD51	9.83347	4.88441
CHEK1	10.3985	8.08393
TTF1	7.45859	6.19494
EIF4EBP1	106.159	97.9585
EIF4G1	79.8991	61.4513
ATR	9.30752	6.558
PIK3R1	6.57232	5.16374
MDM2	15.7141	12.8106
EIF4E	36.9136	28.8045
FOSL1	0.320483	0.0980078
CDC25C	20.9011	20.0284
YBX1	607.95	584.034
PTPN11	25.9717	21.685
HSPA1A	0.8577234	0.2090981
HSBP1	49.298	41.9088
SERPINE1	0.0272234	0.029388
ANXA7	47.8987	51.8733
ROCK1	14.0533	17.2269
TRIM25	11.6338	13.0278
YAP1	25.2353	28.7207
HSPA5	140.035	197.057
L1CAM	0.0799495	0.161713
AR	1.3915	2.12637
ANXA1	253.792	364.431
IGF1R	9.44008	7.80514
MMP2	3.59576	7.27314
CDH1	0.0060136	0.00648128
G6PD	16.2975	20.2097
BIRC3	0.174806	0.244264
CDH3	0.208618	0.28229
CTNNB1	74.3754	75.8514
PRKCA	1.11406	1.34477
CLDN7	1.84194	2.17728
STAT3	6.75725	10.2096
SOD2	50.0888	54.4138
COL6A1	14.8577	24.2445

## Supplementary Table S4 RPPA

Protein	NormLog2_MedianCentered value						p-value
	ctr				met+ima		
Rb_pS807_S811	0.627	0.551	0.732	-1.275	-1.505	-0.904	0.001
Cdc2_pY15	0.465	0.295	0.390	-0.368	-0.572	-0.343	0.001
mTOR_pS2448	0.692	0.571	0.632	-0.297	-0.595	-0.212	0.001
Chk1_pS296	0.453	0.408	0.148	-0.141	-0.153	-0.166	0.007
4E-BP1_pS65	0.353	0.492	0.191	-0.316	-0.549	-0.151	0.009
ATR_pS428	0.391	0.311	0.086	-0.124	-0.080	-0.131	0.016
PI3K-p85	0.262	0.171	0.275	-0.056	-0.155	0.066	0.017
MDM2_pS166	0.093	0.203	0.479	-0.268	-0.279	-0.065	0.026
eIF4E_pS209	0.431	0.428	0.106	-0.104	-0.163	0.005	0.026
YB1_pS102	0.035	0.084	0.104	-0.168	-0.158	-0.009	0.028
SHP-2_pY542	0.538	0.324	0.109	-0.013	-0.119	-0.015	0.045
HSP27_pS82	0.445	0.140	0.228	0.047	-0.244	-0.047	0.048
YAP_pS127	-0.052	-0.028	-0.197	0.349	0.478	0.326	0.003
b-Catenin_pT41_S45	-0.036	-0.038	-0.029	0.047	0.071	0.002	0.022
Stat3_pY705	-0.009	0.048	-0.056	0.108	0.162	0.085	0.030

## Supplementary Table S5

Sample Number	5-year Survival	M stage	Prognosis
Ohali_8	Good	M0	Good
Ohali_9	Good	M0	Good
Ohali_10	Good	M0	Good
Ohali_11	Good	M0	Good
Ohali_12	Good	M0	Good
Ohali_13	Good	M0	Good
Ohali_14	Good	M0	Good
Ohali_20	Good	M0	Good
Ohali_1	Poor	M0	Poor
Ohali_2	Poor	M0	Poor
Ohali_3	Poor	M0	Poor
Ohali_4	Poor	M1	Good
Ohali_5	Poor	M0	Poor
Ohali_6	Poor	M1	Good
Ohali_7	Poor	M1	Poor
Ohali_15	Poor	M0	Poor
Ohali_16	Poor	M1	Good
Ohali_17	Poor	M1	Good
Ohali_18	Poor	M1	Good
Ohali_19	Poor	M1	Poor
Ferreira_2	Poor	M0	Poor
Ferreira_5	Poor	M1	Poor
Ferreira_9	Good	M1	Poor
Ferreira_12	Poor	M0	Poor

## Supplementary Materials: Antibodies used in this work

#	Ab Name	Company	Catalog #	Species
1	Akt_pS473	CST	9271	Rabbit
2	b-Actin	CST	4970	Rabbit
3	Caspase-3	Abcam	ab32042	Rabbit
4	cdc2_pY15	CST	4539	Rabbit
5	Chk1_pS296	Abcam	ab79758	Rabbit
6	Hif-1-alpha	BD Biosciences	610958	Mouse
7	IGF1R_pY1135_Y1136	CST	3024	Rabbit
8	MDM2_pS166	CST	3521	Rabbit
9	mTOR	CST	2983	Rabbit
10	mTOR_pS2448	CST	2971	Rabbit
11	p70-S6K_pT389	CST	9205	Rabbit
12	p70-S6K1	Abcam	ab32529	Rabbit
13	PI3K-p85	Millipore	06-195	Rabbit
14	Rictor_pT1135	CST	3806	Rabbit
15	Stat3_pY705	CST	9145	Rabbit
16	VEGFR-2	CST	2479	Rabbit
17	BNIP3	CST	44060	Rabbit
18	NDRG1	CST	3217	Rabbit
19	MXI1	Abcam	28740	Rabbit
20	ATF7IP	Santa Cruz	166753	Rabbit
21	ALDOC	Sigma	HPA003282	Rabbit
22	FLI1	CST	35980	Rabbit
23	4E-BP1_pS65	CST	9456	Rabbit
24	eIF4E_pS209	Abcam	ab76256	Rabbit
25	ATR_pS428	Abcam	ab178407	Rabbit
26	p32	CST	9662	Rabbit
27	p17	Santa Cruz	271028	Rabbit
28	ki67	CST	9027	Rabbit
29	caspase-3	CST	9662	Rabbit
30	Anti-CD99	Abcam	EPR3096	Rabbit