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Supplementary Material

Ex Vivo Modelling of Therapy Efficacy for Rare Krukenberg Tumors – A Report of Two Cases

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Abbreviations:

HCS: High Content Screening

KT: Krukenberg Tumor

TAM: Tumor-Associated Macrophage

TKI: Tyrosine Kinase Inhibitor

VEGFR: Vascular Endothelial Growth Factor Receptor

ABSTRACT

Krukenberg tumor (KT) is a rare subtype of ovarian neoplasms that manifests as secondary ovarian cancer. Most frequently, KTs originate from a primary in the gastrointestinal tract and account for 30 to 40% of all secondary ovarian cancers. A key histologic characteristic finding used in the diagnosis of KT is the presence of mucin-laden signet-ring cells. Bilateral metastasis into both ovaries has been reported in more than 80% of KTs, and a significant fraction of these cases are reported to receive no survival benefit from chemotherapy. Despite clinical evaluation of several chemotherapeutic treatments for the management of KT, the general prognosis of the disease is poor and radical surgery remains the main treatment shown to improve the overall survival. As no targeted therapies have been reported for KT, we performed an *ex vivo* drug screen to assess the efficacy of targeted therapeutics with patient-derived Krukenberg tumor cells. Tumor cells isolated from a coarse needle biopsy and tumor-associated immune cells derived from malignant ascites effusion from two patients with a gastric cancer derived KT were used for the analysis of responses to 120 drugs. A comparison of the results showed that tumor cells from both patients showed systematic sensitivity toward topoisomerase inhibition, epigenetic modulators, statins and alkaloid tubulin inhibitors. Ascites-derived immune cells displayed selective sensitivity to a number of targeted agents, including VEGFR inhibitor sunitinib. Flow cytometry analysis identified the effect of sunitinib to be immunomodulatory and targeted on the immunosuppressive M2 type macrophages. The immunomodulatory effect of sunitinib was confirmed from analysis of the patient ascites following treatment and was accompanied by sustained clinical response. These results support the concept of harnessing the immunomodulatory effects of VEGFR-TKI for cancer therapy and suggest further analysis also in the context of Krukenberg tumors.

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Supplementary Table 1: Ex vivo drug screening results.

Name	Target	Patient_1 tumor				Patient_1 ascites				Patient_2 tumor				Patient_2 ascites			
		625nM	1250nM	2500nM	5000nM	625nM	1250nM	2500nM	5000nM	625nM	1250nM	2500nM	5000nM	625nM	1250nM	2500nM	5000nM
2-Methoxyestradiol	HIF	0.91	1.10	0.79	0.97	0.81	0.90	0.88	0.81	0.83	0.87	1.12	0.83	1.04	1.21	1.11	1.02
Abitrexate (Methotrexate)	DHFR	-0.04	0.14	0.01	0.10	0.88	0.70	0.94	0.77	0.50	0.61	0.62	0.48	0.88	1.14	0.84	1.05
Adavosertib (AZD1775)	WEE1	0.19	0.07	0.06	0.01	0.95	1.03	0.28	-0.08	0.76	0.43	0.26	0.12	0.95	0.99	1.64	0.40
Adrucil (Fluorouracil)	DNA/RNA Synthesis	0.54	1.10	0.29	0.68	0.90	0.99	0.70	0.47	0.92	0.63	0.38	0.37	0.84	1.00	1.65	1.06
Afatinib (BIBW2992)	EGFR, HER2	1.23	1.53	0.08	0.71	1.05	0.61	0.55	0.03	0.92	0.87	0.75	0.86	1.18	0.90	1.60	0.98
Alisertib	Aurora A kinase	0.03	-0.06	-0.06	0.07	1.24	1.15	1.02	0.49	0.21	0.16	0.20	-0.03	1.40	1.68	1.15	0.94
Ampiroxicam	COX	1.15	1.20	0.93	0.74	0.89	0.94	0.82	0.98	0.92	1.00	1.12	0.98	0.81	1.05	0.52	0.64
Anagrelide HCl	PDE	1.11	1.19	0.93	1.10	1.18	1.09	1.18	1.09	1.17	1.12	0.90	1.11	0.86	0.83	1.83	1.07
Anastrozole	Aromatase	1.44	1.28	0.99	1.46	1.15	0.69	1.17	0.68	1.00	0.98	0.90	1.04	1.05	0.91	0.69	1.01
Apatinib (YN968D1)	VEGFR	0.46	0.61	0.63	0.75	0.95	1.25	1.05	0.63	0.92	0.87	1.01	0.61	0.89	1.11	1.51	1.14
Aspirin (Acetylsalicylic acid)	Proteasome	1.03	0.96	1.21	0.83	1.10	0.99	1.17	1.11	1.02	0.92	0.78	0.84	1.45	1.60	0.82	1.01
Atorvastatin calcium (Lipitor)	HMG-CoA Reductase	0.50	0.55	0.37	0.44	1.13	1.46	1.19	0.85	0.83	0.22	-0.06	-0.49	0.74	1.06	0.99	1.05
Axitinib	VEGFR, PDGFR, c-Kit	0.82	1.54	0.99	1.40	0.72	-0.16	-0.33	-0.73	1.05	1.11	0.90	0.69	1.28	1.16	1.02	1.14
Azacitidine (Vidaza)	DNA/RNA Synthesis	1.34	0.29	0.66	0.54	0.95	0.70	1.02	0.82	1.06	0.93	0.98	0.76	1.02	1.03	1.73	0.97
AZD5363	AKT	1.32	1.04	1.14	0.95	0.59	0.68	0.19	-0.09	0.89	0.33	0.61	0.47	1.14	0.74	0.29	0.09
AZD6738	ATR	1.14	0.71	0.67	0.43	1.01	1.26	0.55	0.41	0.59	0.36	0.19	0.21	1.06	1.33	1.36	1.38
AZD8186	PIK3CD	0.86	1.02	1.14	1.04	0.35	0.57	0.28	0.09	0.78	0.32	0.56	0.25	0.64	0.71	0.76	0.76
AZD8835	PI3K α and PI3K δ	0.91	1.06	0.81	1.24	0.44	0.57	0.33	-0.28	0.80	0.67	0.66	0.48	0.95	0.95	1.01	1.09
Bemcentinib (BGB324)	AXL	0.76	0.69	0.59	0.81	1.09	1.10	0.89	1.09	0.98	0.96	0.97	0.93	1.19	1.44	1.04	1.00
Bicalutamide (Casodex)	Androgen Receptor, P450	1.39	1.09	1.31	0.95	0.76	0.93	0.79	1.00	0.80	0.36	1.10	0.28	0.99	1.17	1.35	0.41
Bleomycin sulfate	DNA/RNA Synthesis	0.34	-0.24	0.32	-0.24	0.19	0.23	0.13	0.01	0.02	-0.08	-0.25	-0.28	1.13	1.02	1.09	1.22
Bortezomib (Velcade)	Proteasome	1.30	1.87	1.13	1.08	0.56	1.38	0.77	-0.01	0.05	-0.66	-0.72	-0.70	0.69	0.98	0.68	0.82
Bosutinib (SKI-606)	Src,Abl	1.07	1.70	1.43	1.81	0.96	0.79	0.77	-0.45	1.07	1.38	1.22	1.25	0.91	1.23	1.08	1.09
Buparlisib (BKM-120)	PI3K	0.75	0.28	0.53	-0.03	0.60	0.27	-0.10	-0.52	0.53	0.10	-0.02	-0.20	0.96	1.31	0.67	0.80
Busulfan (Myleran, Busulfex)	Blank	1.18	1.98	0.90	0.96	0.81	1.57	0.78	1.39	0.70	0.75	0.88	0.86	1.71	1.89	1.44	1.50
Cabazitaxel (Jevtana)	Microtubule inhibitor	-0.11	0.26	-0.17	-0.04	0.99	0.96	0.71	0.87	0.07	0.11	0.15	0.15	1.77	1.02	0.98	0.96
Cabozantinib (XL-184)	c-Met	1.20	0.66	1.09	1.01	0.80	0.91	0.50	0.48	0.88	0.83	0.86	0.83	0.47	0.84	0.36	0.41
Calcitriol (Rocaltrol)	Blank	0.60	0.59	1.25	0.75	0.00	0.41	0.10	0.19	1.15	1.04	1.15	1.03	1.30	1.13	1.21	1.01

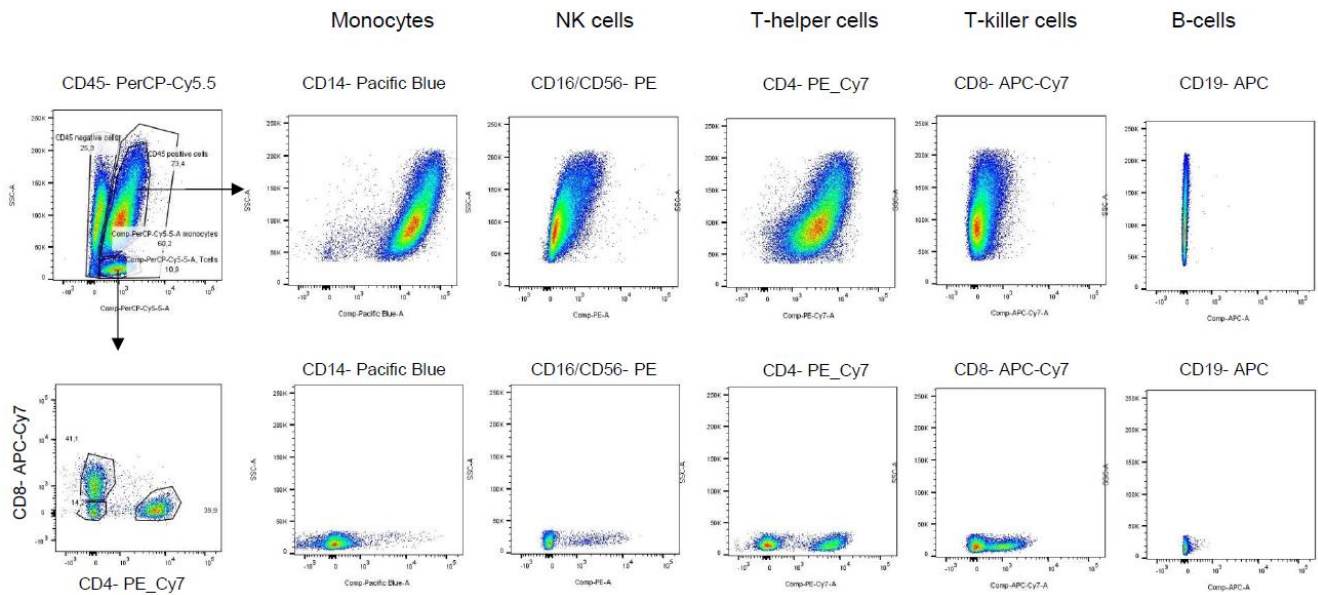
Camptothecin	Topoisomerase	-0.06	0.28	-0.28	0.15	-0.95	-0.98	-0.98	-0.99	0.02	-0.28	-0.48	-0.61	0.66	1.87	0.96	1.05
Capecitabine (Xeloda)	DNA/RNA Synthesis	1.35	0.47	1.20	0.50	0.62	0.51	0.58	1.21	0.86	1.17	0.92	1.07	0.51	0.42	0.54	0.73
Carboplatin	DNA/RNA Synthesis	1.23	0.57	0.73	0.56	0.86	0.81	1.05	0.85	0.75	0.76	0.77	0.82	1.43	1.14	1.04	1.17
Carmofur	DNA/RNA Synthesis	0.79	0.99	0.39	0.46	0.88	0.64	1.02	0.52	0.68	0.68	0.50	0.43	1.12	0.97	1.26	1.16
Celecoxib	COX	1.16	1.32	1.33	0.87	0.56	1.20	0.51	0.77	0.54	0.99	0.98	1.09	1.01	0.47	0.68	0.15
Cepharanthine	TNF-alpha	0.43	0.91	0.58	1.05	0.81	1.38	0.84	-0.48	0.96	1.06	0.91	0.87	0.87	1.98	1.23	0.98
Cisplatin	DNA/RNA Synthesis	1.72	0.78	1.01	0.76	0.81	0.93	0.83	1.30	0.90	1.07	0.90	1.04	0.59	0.55	0.41	0.69
Cladribine	DNA/RNA Synthesis	0.14	0.15	0.06	0.11	-0.94	-0.97	-0.96	-0.97	0.46	0.32	0.08	-0.21	0.94	1.00	1.02	0.89
Clofarabine	DNA/RNA Synthesis	-0.29	0.26	-0.17	-0.12	-0.97	-0.95	-0.96	-0.98	-0.11	-0.23	-0.11	-0.18	0.62	0.25	0.22	0.90
Clomifene citrate (Serophene)	Estrogen/progesterone Receptor	0.96	1.08	0.98	1.17	0.89	1.11	0.94	1.22	0.99	0.92	0.89	1.02	1.30	1.62	0.58	1.82
Cortisone acetate (Cortone)	Glucocorticoid receptor	0.43	0.78	0.54	0.97	0.84	1.10	0.90	1.05	1.12	0.96	0.74	0.60	0.83	0.57	0.79	1.00
Crizotinib (PF-02341066)	c-Met	1.19	1.71	0.94	1.07	0.79	0.33	0.10	-0.76	0.80	0.45	0.26	0.01	0.82	0.68	1.01	0.93
Cyclophosphamide monohydrate	Blank	0.88	0.82	0.56	0.56	0.76	1.00	0.95	1.12	1.11	1.00	0.94	1.05	1.14	0.92	1.06	1.37
Cytarabine	DNA/RNA Synthesis	0.32	-0.12	0.18	-0.11	-0.74	-0.86	-0.85	-0.96	0.04	-0.09	-0.20	-0.17	0.66	0.97	1.30	1.77
Dabrafenib (GSK2118436)	Raf	-0.11	0.56	0.16	1.14	0.45	-0.08	-0.42	-0.49	0.43	0.41	0.66	0.99	1.48	1.18	0.79	0.43
Dacarbazine (DTIC-Dome)	DNA/RNA Synthesis	0.47	1.44	0.52	0.71	0.86	1.02	0.99	1.03	0.97	0.89	1.05	0.89	1.69	1.44	1.16	1.30
Dasatinib (BMS-354825)	Src, Bcr-Abl, c-Kit	0.57	0.26	0.32	-0.17	-0.80	-0.82	-0.83	-0.83	0.05	-0.07	0.15	-0.20	1.07	0.89	0.99	0.74
Daunorubicin HCl (Daunomycin HCl)	Topoisomerase	-0.89	-0.95	-0.99	-1.00	-0.97	-0.95	-0.98	-0.97	-0.74	-1.00	-1.00	-1.00	1.63	0.70	0.99	0.96
Dexamethasone	IL Receptor	1.42	0.77	1.07	1.19	0.02	-0.15	0.39	-0.26	1.36	1.47	1.23	1.38	0.51	0.89	0.51	0.82
Diclofenac	COX	0.56	0.74	0.33	0.71	1.25	1.07	0.91	1.30	0.91	0.75	0.89	0.95	1.91	0.84	0.99	1.02
Diethylstilbestrol (Stilbestrol)	Estrogen receptor	0.48	0.69	0.64	0.81	1.00	0.93	0.88	1.18	0.95	0.87	1.02	1.08	0.79	0.98	1.16	0.82
Disulfiram	Acetaldehyde dehydrogenase	1.33	0.85	1.42	1.04	0.82	0.78	0.49	0.46	0.66	0.67	0.04	-0.05	1.23	1.25	1.05	1.09
Docetaxel (Taxotere)	Microtubule Associated	0.65	1.28	0.88	0.94	0.76	0.66	1.37	0.57	0.06	0.00	-0.15	-0.03	1.19	1.00	1.20	1.39
Doxorubicin (Adriamycin)	Topoisomerase	0.08	-0.20	-0.21	-0.66	0.47	0.31	-0.42	-0.96	0.10	-0.52	-1.00	-1.00	0.84	1.18	0.95	1.09
Dutasteride	5-alpha Reductase	1.49	0.90	1.39	1.02	0.90	0.61	1.08	0.79	0.76	0.87	0.87	1.02	0.89	1.31	0.85	1.24
Erlotinib (OSI-420)	EGFR	0.60	0.66	0.72	0.39	1.00	1.37	0.96	0.58	1.10	0.77	0.78	1.12	0.84	1.30	0.84	1.15

Etoposide (VP-16)	Topoisomerase	0.58	0.58	0.40	0.34	1.53	0.74	1.50	0.76	0.23	0.10	0.01	0.03	-0.43	-0.78	-0.78	-0.82
Everolimus (RAD001)	mTOR	0.61	0.52	0.43	0.26	-0.14	0.01	-0.07	0.07	0.40	0.37	0.54	0.47	1.15	0.78	0.98	1.26
Exemestane	Aromatase	0.37	1.38	0.27	0.80	1.00	0.83	0.97	0.76	0.78	0.97	0.85	0.88	1.24	1.26	1.32	1.39
Finasteride	5-alpha Reductase	0.54	1.71	0.89	1.51	0.63	0.57	0.80	1.24	0.83	1.06	1.10	1.07	1.38	1.24	1.57	1.63
Floxuridine	DNA/RNA Synthesis	0.39	0.11	0.18	0.14	1.10	0.62	1.34	0.37	0.38	0.27	0.26	0.19	1.39	0.66	0.98	0.78
Fludarabine (Fludara)	STAT, DNA/RNA Synthesis	1.37	1.11	1.18	0.74	-0.64	-0.82	-0.86	-0.96	0.86	1.03	0.78	0.81	1.14	1.12	1.10	1.12
Flutamide (Eulexin)	P450 (e.g. CYP17)	0.95	0.45	1.37	0.57	0.95	0.84	0.91	0.73	0.90	0.83	1.02	0.89	1.87	1.17	1.47	1.50
Fulvestrant (Faslodex)	Estrogen/progesterone Receptor	1.21	0.46	1.14	0.84	0.78	0.84	0.80	0.93	0.96	0.90	0.97	0.96	1.16	0.91	0.99	0.83
Gefitinib (Iressa)	EGFR	1.63	0.76	1.22	0.86	1.00	1.30	1.04	0.76	1.13	0.81	1.00	0.98	0.53	0.06	0.43	0.91
Gemcitabine HCl (Gemzar)	DNA/RNA Synthesis	-0.25	-0.03	-0.27	0.02	-0.35	-0.69	-0.77	-0.91	-0.21	-0.24	-0.14	-0.14	1.37	1.01	0.85	1.13
Gimeracil	Dehydrogenase	0.52	0.84	0.36	0.82	1.04	1.34	0.97	1.63	0.94	0.70	0.96	1.18	1.34	1.09	1.02	0.88
Ibrutinib (PCI-32765)	Src	0.96	1.17	0.77	0.87	0.72	1.08	1.10	1.31	0.61	1.20	0.69	0.63	0.99	1.33	1.02	1.21
Ifosfamide	DNA/RNA Synthesis	1.44	0.72	0.81	0.86	0.89	1.06	0.95	0.92	0.72	0.86	1.01	0.76	1.14	1.09	0.84	1.78
Imatinib Mesylate	PDGFR, c-Kit, Bcr-Abl	1.37	0.63	1.73	0.64	0.57	0.46	-0.14	-0.52	0.76	0.71	0.99	0.81	0.95	0.72	0.78	0.57
Irinotecan	Topoisomerase	0.30	0.69	0.25	0.41	1.00	0.96	0.85	1.31	0.59	0.47	0.05	0.01	0.75	0.98	1.03	1.26
JQ1	BET	-0.12	-0.42	-0.64	-0.77	-0.71	-0.78	-0.84	-0.87	0.26	0.16	0.17	0.20	0.78	0.88	0.95	0.97
Lapatinib Ditosylate (Tykerb)	EGFR, HER2	0.49	1.57	0.44	1.79	0.75	1.30	0.69	-0.57	1.08	0.98	0.87	0.96	0.78	1.03	0.75	1.09
Letrozole	Aromatase	1.98	1.00	1.23	1.00	1.18	0.76	1.09	0.67	1.22	0.95	0.82	0.63	0.92	1.28	1.01	0.64
Leucovorin Calcium	Blank	1.51	1.51	1.46	1.41	0.90	0.68	0.79	0.68	0.79	0.98	0.96	0.93	0.85	1.36	1.43	0.73
Lomustine (CeeNU)	Blank	1.55	0.37	1.03	0.59	1.47	0.86	0.81	0.74	0.90	0.88	0.91	0.88	0.87	0.80	1.06	1.14
Masitinib (AB1010)	c-Kit, PDGFR, FGFR, FAK	1.10	1.43	1.06	1.36	0.89	0.92	0.51	0.14	0.79	0.93	1.03	0.98	0.87	1.74	1.06	1.42
MDV3100 (Enzalutamide)	Androgen Receptor	1.07	1.05	0.93	1.11	1.30	0.73	1.64	0.68	1.07	0.91	1.08	0.95	1.25	1.44	1.25	0.94
Methylprednisolone	Glucocorticoid receptor	0.91	0.68	0.50	0.50	-0.07	-0.14	-0.14	-0.22	1.20	1.16	1.17	1.08	1.01	1.16	1.00	1.03
Mitotane (Lysodren)	Steroidogenesis	1.81	0.53	0.78	1.04	1.12	0.55	1.38	0.58	0.59	0.96	0.74	0.85	1.20	0.84	1.01	1.13
Mitoxantrone Hydrochloride	Topoisomerase	-0.52	-0.15	-0.40	-0.56	0.20	0.47	-0.79	-0.98	0.01	-0.09	-0.71	-1.00	0.28	-0.17	-0.09	-0.66
Nelarabine (Arranon)	DNA/RNA Synthesis	1.48	1.32	1.55	1.40	-0.02	-0.53	-0.60	-0.75	0.99	0.97	0.87	1.01	-0.03	-0.27	-0.05	0.16
Neratinib	HER2, EGFR	1.17	0.53	0.85	0.29	1.21	1.25	1.33	-0.90	0.88	0.90	1.17	0.25	0.46	0.66	0.25	0.64
Niclosamide (Niclocide)	STAT	1.06	1.01	0.97	0.48	0.03	-0.39	-0.93	-0.95	0.90	0.64	0.19	-0.46	1.88	0.76	1.32	1.88

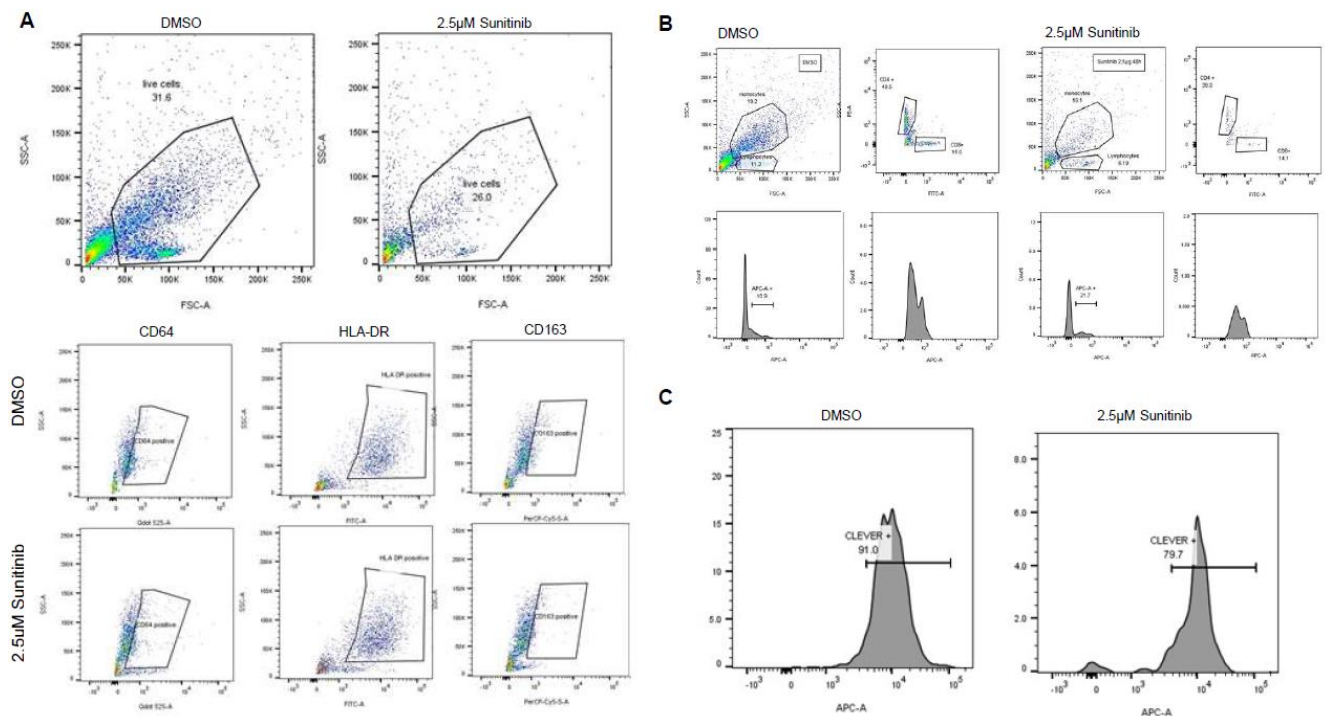
Nilotinib (AMN-107)	Bcr-Abl	0.98	1.77	1.32	1.17	0.63	1.31	0.79	1.17	0.94	1.24	0.97	1.15	1.01	0.88	0.52	0.49
Nutlin-3a	p53/MDM2	0.69	0.27	0.56	0.12	1.21	1.39	0.74	1.20	0.21	0.22	0.20	0.10	0.81	0.90	1.15	0.98
Olaparib	PARP-1	1.07	0.78	1.05	0.82	1.14	1.12	0.91	0.93	0.70	0.82	0.76	0.69	1.68	0.94	1.30	1.96
Osimertinib (AZD9291)	EGFR	0.74	1.03	0.65	0.84	0.93	0.97	0.48	0.10	0.85	1.08	0.71	0.83	0.99	1.38	0.93	-0.75
Oxaliplatin (Eloxatin)	DNA/RNA Synthesis	1.64	1.29	1.55	1.32	0.80	0.98	1.00	0.79	1.01	0.79	0.91	0.96	1.18	0.72	0.70	0.03
Paclitaxel (Taxol)	Microtubule Associated	0.89	0.91	0.88	1.18	0.93	0.62	0.90	0.73	0.07	-0.03	-0.08	0.16	0.99	1.29	0.88	0.80
Palbociclib	CDK4, CDK6	0.76	0.36	0.42	0.32	1.37	1.11	1.20	0.95	0.48	0.25	0.46	0.39	0.49	0.43	0.57	0.20
Panobinostat	pan-HDAC inhibitor	0.15	0.29	0.05	-0.64	-0.95	-0.97	-0.98	-0.98	-0.22	-0.21	-0.33	-0.27	0.48	0.56	0.55	0.58
Pazopanib HCl	VEGFR, PDGFR, c-Kit	1.32	1.02	1.18	1.67	0.90	0.83	0.77	0.71	0.95	0.87	0.89	1.06	0.46	0.34	0.51	0.88
Pemetrexed	DHFR, DNA/RNA Synthesis	-0.33	0.14	-0.37	-0.07	0.56	0.98	0.99	0.88	0.53	0.67	0.63	0.61	0.61	0.15	-0.07	-0.51
Pitavastatin	HMG-CoA reductase	-0.35	-0.16	-0.58	-0.28	-0.77	-0.24	-0.45	-0.85	-0.27	-0.49	-0.69	-0.72	0.53	0.64	-0.70	-0.94
Plerixafor (AMD3100)	CXCR	1.23	0.95	1.15	1.24	0.96	1.23	1.04	1.16	1.04	0.40	1.10	1.05	0.57	0.66	0.73	0.30
Pralatrexate (Folotyn)	DHFR	0.02	0.18	0.23	0.19	0.67	0.73	0.67	0.73	0.49	0.59	0.11	0.50	1.05	1.38	1.22	0.14
Pregnenolone	Estrogen/progestogen Receptor	0.72	0.76	0.66	0.79	0.97	0.98	0.94	0.96	0.71	0.91	0.91	0.76	1.45	1.53	1.03	1.24
Procarbazine HCl (Matulane)	DNA/RNA Synthesis	1.73	0.83	1.73	0.66	0.81	0.70	-0.62	-0.67	1.09	0.95	1.07	0.76	1.67	0.65	0.78	0.94
Progesterone (Prometrium)	Blank	1.23	1.56	1.28	1.44	0.58	1.49	0.63	1.56	0.95	1.18	1.23	1.16	1.23	1.23	1.01	1.30
Propylthiouracil	Thyropoxidase, 5'-deiodinase	0.93	1.07	0.95	1.14	0.88	1.00	1.10	0.89	0.97	0.83	0.74	0.92	1.16	0.81	0.98	0.33
Rapamycin (Sirolimus)	mTOR	0.80	0.99	0.95	0.73	-0.16	-0.03	-0.08	0.01	0.40	0.44	0.47	0.30	0.74	0.89	0.76	1.12
Resveratrol	Sirtuin	1.27	1.05	0.62	0.87	0.77	0.73	0.77	0.80	0.95	1.03	1.09	1.10	0.53	0.18	0.15	0.37
RITA	p53/MDM2	0.83	0.52	0.90	0.72	-0.87	-0.88	-0.91	-0.90	0.96	0.96	0.83	0.96	0.71	0.77	0.78	0.61
Ruxolitinib (INCB018424)	JAK	1.15	1.05	0.98	0.71	-0.25	-0.42	-0.40	-0.61	1.10	1.16	1.12	1.29	0.46	0.18	-0.15	-0.14
Selumetinib (AZD6244)	MEK1/2	0.82	1.21	0.67	0.76	0.27	0.15	0.06	-0.07	0.75	0.89	0.59	0.12	0.28	0.36	0.38	1.24
Sorafenib (Nexavar)	VEGFR, PDGFR, Raf	0.94	1.14	1.08	0.65	0.72	1.37	0.83	0.65	0.91	0.85	0.81	0.79	0.79	0.28	0.29	-0.06
Sunitinib Malate (Sutent)	VEGFR, PDGFR, c-Kit, Flt	1.04	1.62	0.73	0.50	0.21	0.18	-0.03	-0.18	1.19	1.04	0.82	0.45	0.53	0.36	0.12	0.00
Tacrolimus (FK-506)	Blank	1.04	0.99	1.15	0.89	0.91	1.39	1.05	1.23	0.87	1.00	0.92	0.93	-0.11	-0.27	-0.01	-0.39
Tamoxifen Citrate (Nolvadex)	Estrogen/progestogen Receptor	1.18	0.82	1.16	0.70	0.70	0.56	0.07	-0.41	1.07	0.91	0.88	0.91	-0.19	-0.51	-0.68	-0.82

Temsirolimus (Torisel)	mTOR	1.08	0.87	1.00	0.74	-0.30	-0.77	-0.76	-0.78	0.46	0.44	0.38	0.34	0.64	0.33	0.92	-0.08
Thalidomide	Blank	0.71	0.78	0.65	0.74	0.72	1.21	0.67	1.28	0.96	0.97	1.12	1.02	0.15	-0.05	-0.21	-0.43
Topotecan HCl	Topoisomerase	-0.31	0.07	-0.31	0.31	-0.53	-0.71	-0.81	-0.98	-0.04	0.09	-0.08	-0.16	0.68	1.06	0.60	0.03
Tozasertib (VX-680)	Aurora kinase	0.69	1.14	1.26	0.34	1.21	1.27	1.00	1.35	0.17	0.17	0.15	0.08	0.06	0.20	0.55	-0.70
Trametinib	MEK1 and MEK2	0.49	0.31	0.48	0.46	0.59	0.01	0.06	-0.08	0.60	0.39	0.50	0.48	-0.65	-0.70	-0.61	-0.64
Tretinoin (Aberela)	Blank	1.16	1.36	0.78	0.99	1.12	0.40	0.28	0.19	1.19	0.88	1.01	0.99	-0.90	-0.86	-0.87	-0.88
Vandetanib (Zactima)	VEGFR	0.37	0.99	0.46	0.58	1.07	0.85	0.74	-0.97	0.84	0.93	0.61	0.50	-0.07	-0.30	-0.49	-0.55
Vemurafenib (PLX4032)	B-Raf	1.57	1.44	1.82	1.62	1.33	0.71	1.30	0.44	1.12	1.06	1.07	0.98	0.03	-0.63	-0.66	-0.89
Vinblastine	AChR	0.08	0.30	0.10	0.24	-0.26	-0.46	-0.57	-0.44	-0.20	-0.24	-0.31	-0.19	-0.89	-0.90	-0.93	-0.93
Vincristine	Microtubule Associated	0.82	0.23	0.77	0.02	-0.35	-0.54	-0.39	-0.58	-0.21	-0.26	-0.20	-0.32	-0.03	-0.27	-0.79	-0.83
Vistusertib (AZD2014)	mTOR kinase	0.09	-0.23	-0.39	-0.29	-0.43	-0.16	-0.59	-0.71	0.59	0.41	0.33	0.21	0.97	0.16	-0.11	-0.91
Vorinostat (SAHA)	HDAC	1.12	-0.03	0.44	0.35	-0.96	-0.82	-0.96	-0.98	0.61	0.36	0.18	0.15	-0.03	-0.34	-0.31	-0.44

Dose responses as GR values of Pt1 tumor tissue derived cells, Pt1 malignant ascites derived cells, Pt2 tumor tissue derived cells, Pt2 malignant ascites derived cells.



Supplementary Figure 1: Flow cytometry profiling of different immune cell types from Pt2 malignant ascites. Separated phenotype analysis of CD45 positive monocytes and T-cells.



Supplementary Figure 2: *Ex vivo* validation of immune cell responses to sunitinib. **A)** Analysis of M1/M2 macrophage phenotypes from DMSO and sunitinib treated malignant ascites cells. **B)** Analysis of T-cell activation in response sunitinib. Bottom panel: No CD69 positive activated CD8 positive T-cells were detected. The amount of CD69 positive CD4 positive was increased by 12% in following sunitinib treatment. **C)** Analysis of STAB1 (CLEVER-1) expression of CD14 positive monocytes following treatment with sunitinib.