

December 15, 2020

ORTHOTOPIC-PDX MODELS **THE GOLD STANDARD IN PRECISION ONCOLOGY**

Certis Oncology Solutions

OUR MISSION

Connecting every patient to the right therapy for their cancer, the first time, every time.

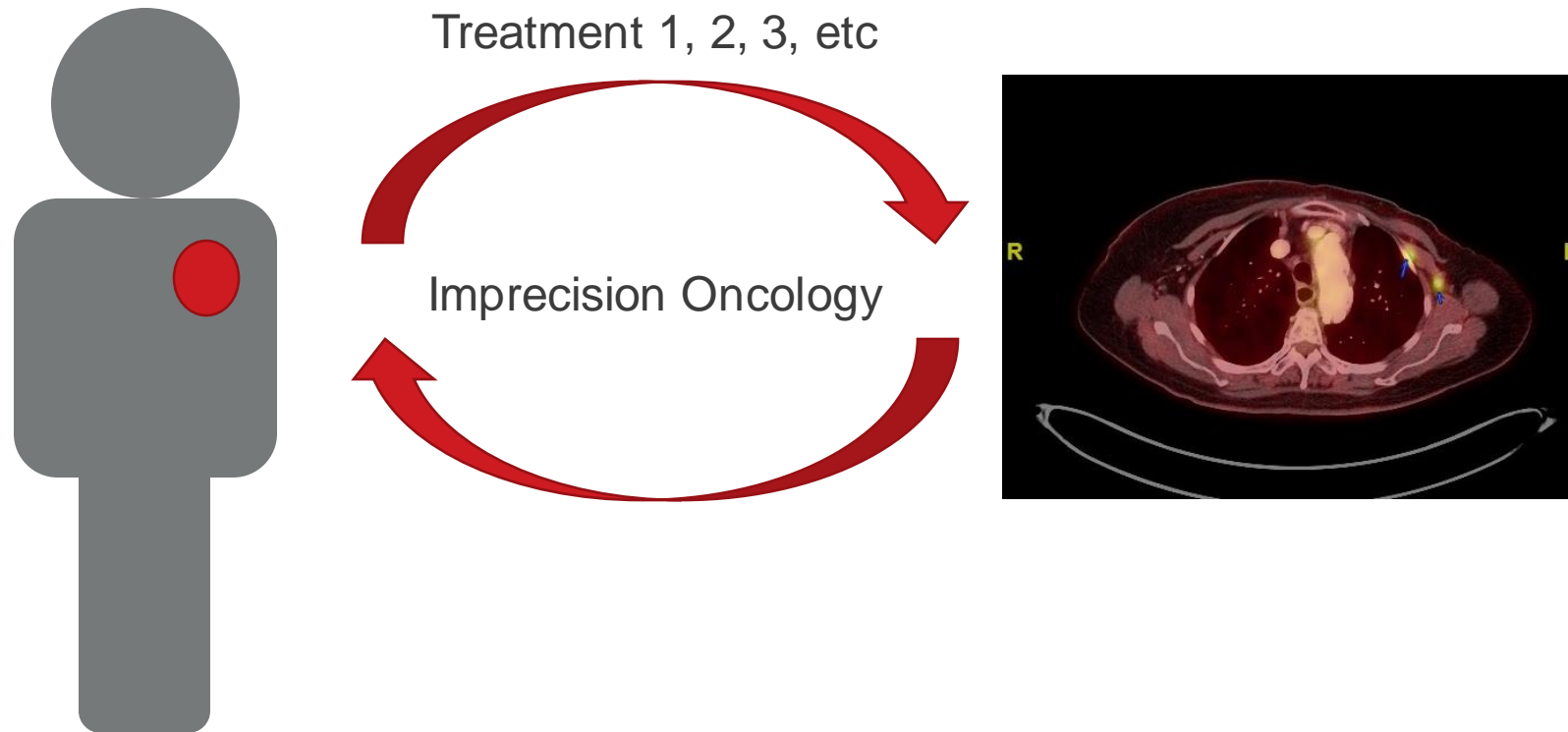


CLIA ID# 05D2149049



Standard of Care

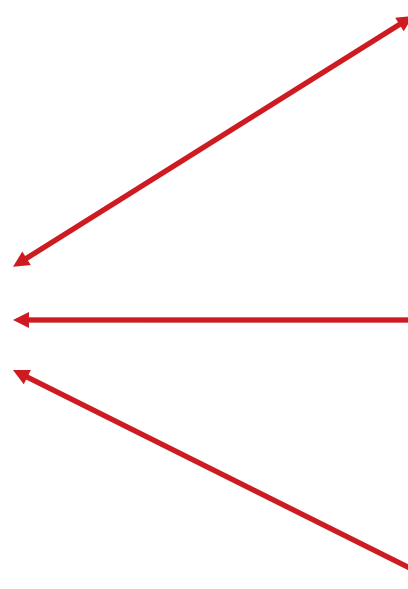
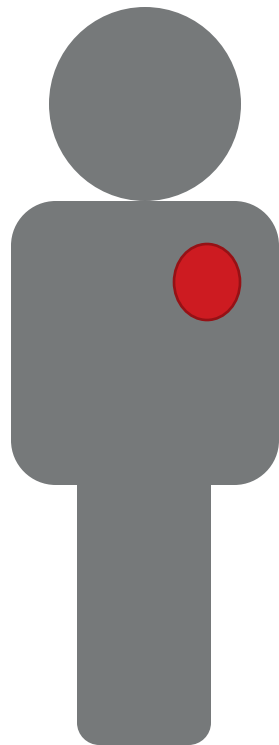
Surgery – Radiation - Chemotherapy



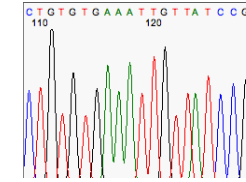
Precision Oncology: Therapies specifically designed and targeted to a patient's unique cancer.

Precision Oncology

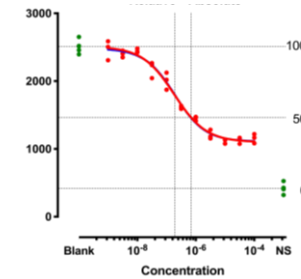
Precision Oncology: Therapies specifically designed and targeted to a patient's unique cancer.



In Silico



In Vitro



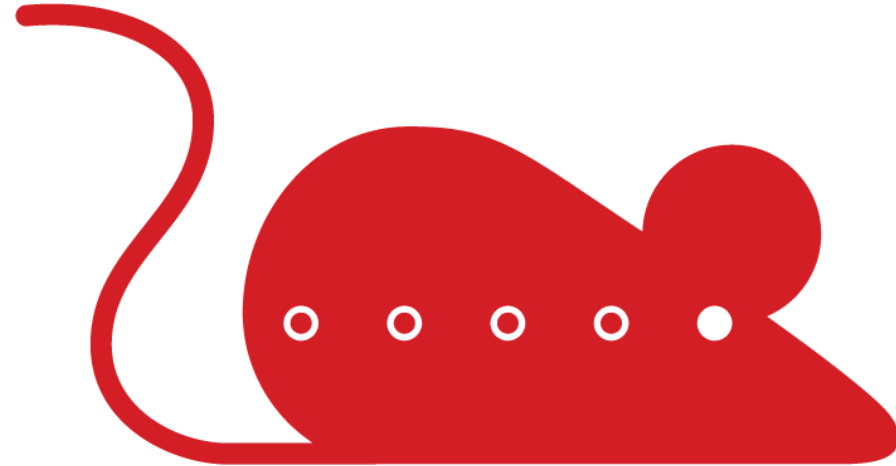
In Vivo



Certis Oncology Solutions

Ortho: Greek for "correct"

- Organ-specific microenvironment
- Relevant vasculature and stroma
- Increased potential for metastasis
- Requires advanced surgical skills
- Requires non-invasive imaging



Certis Oncology Solutions

Ortho: Greek for "correct"

- Organ-specific microenvironment
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Scintica:
INSTRUMENTATION



CIEA NOG mouse®

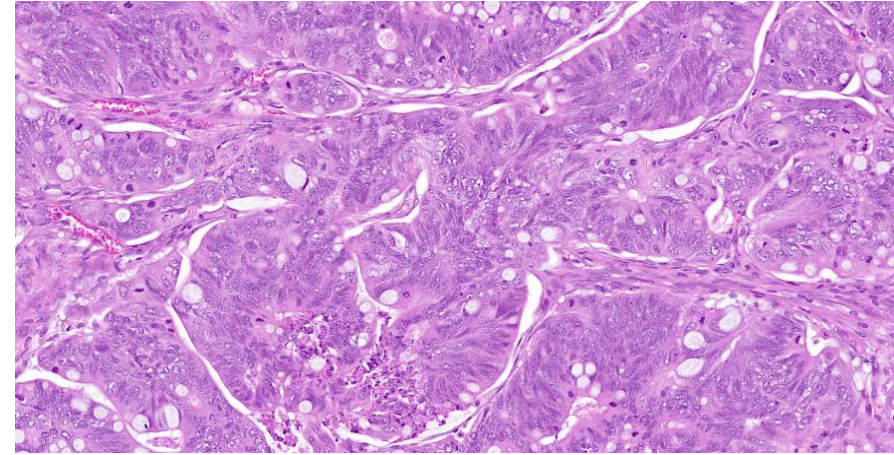

TACONIC
Models For Life.

Subcutaneous vs. Orthotopic

Colorectal Adenocarcinoma

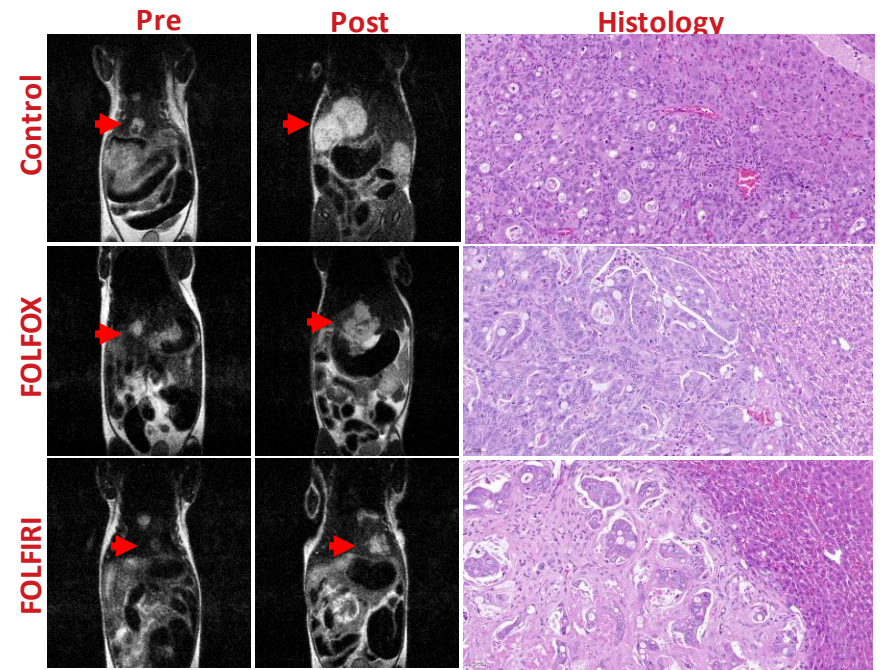
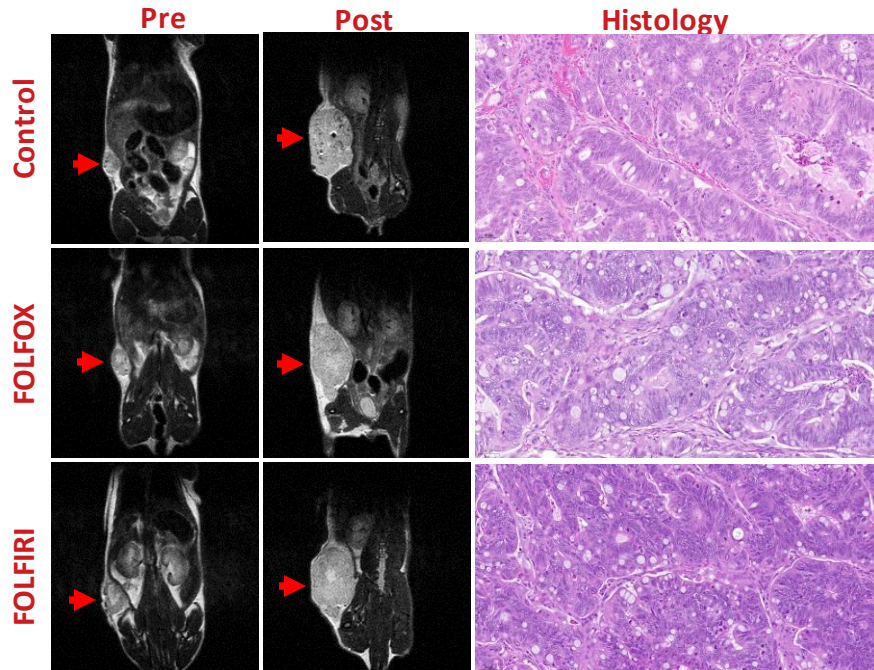
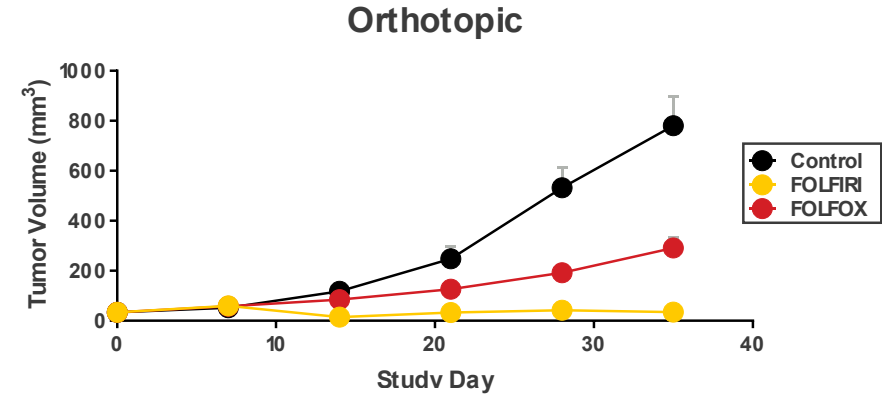
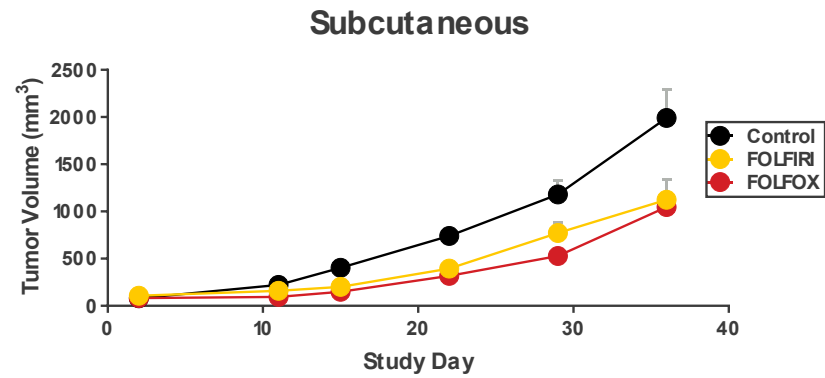
Biopsied from liver of 75 M

- Initially responded to FOLFIRI regimen
- Mutations
 - KRAS p.G13D c.38G>A
 - TP53 p.C96Y c.287G>A
 - PIK3CA p.E545K c. 1633G>A
 - APC p.I1401Mfs*14 c.4202delT
 - JAK1 p.V651M c. 1951G>A
 - APC p.C1410Lfs*13 c.4227_4228insT

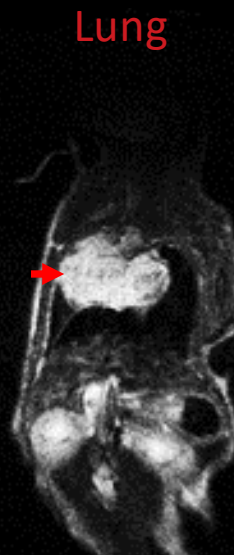
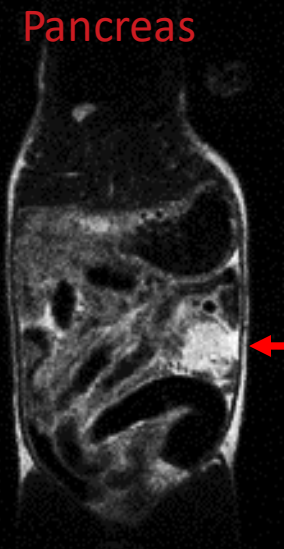
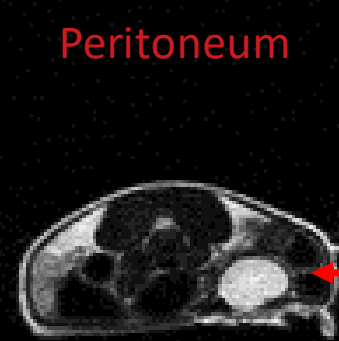
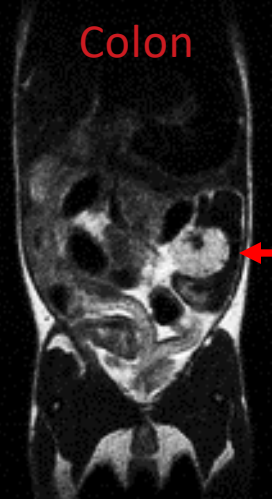
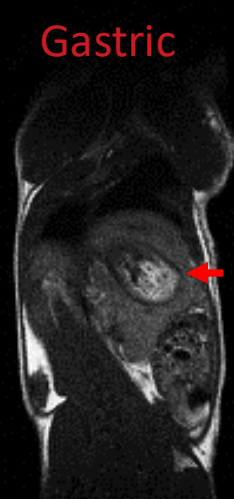
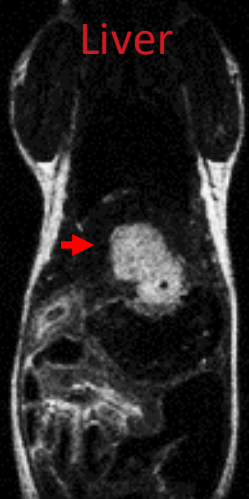


Group	Treatment	Dose (mg/kg)	N	Route	Dosing Frequency
1	Control	NA	8	IP	QW
2	5-FU Folinic Acid Oxaliplatin	55 30 12	8	IP	QW
3	5-FU Folinic Acid Irinotecan	55 30 40	8	IP	QW

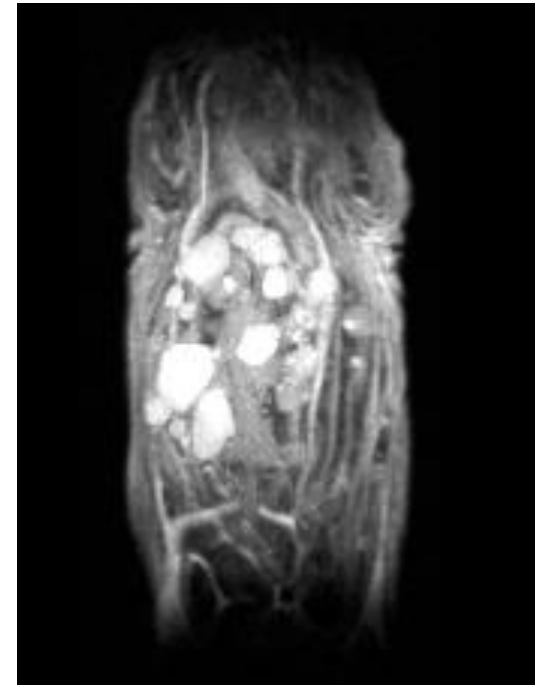
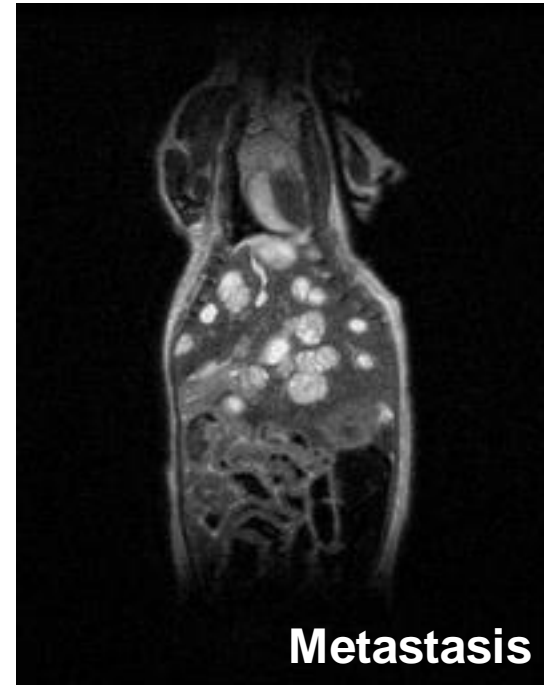
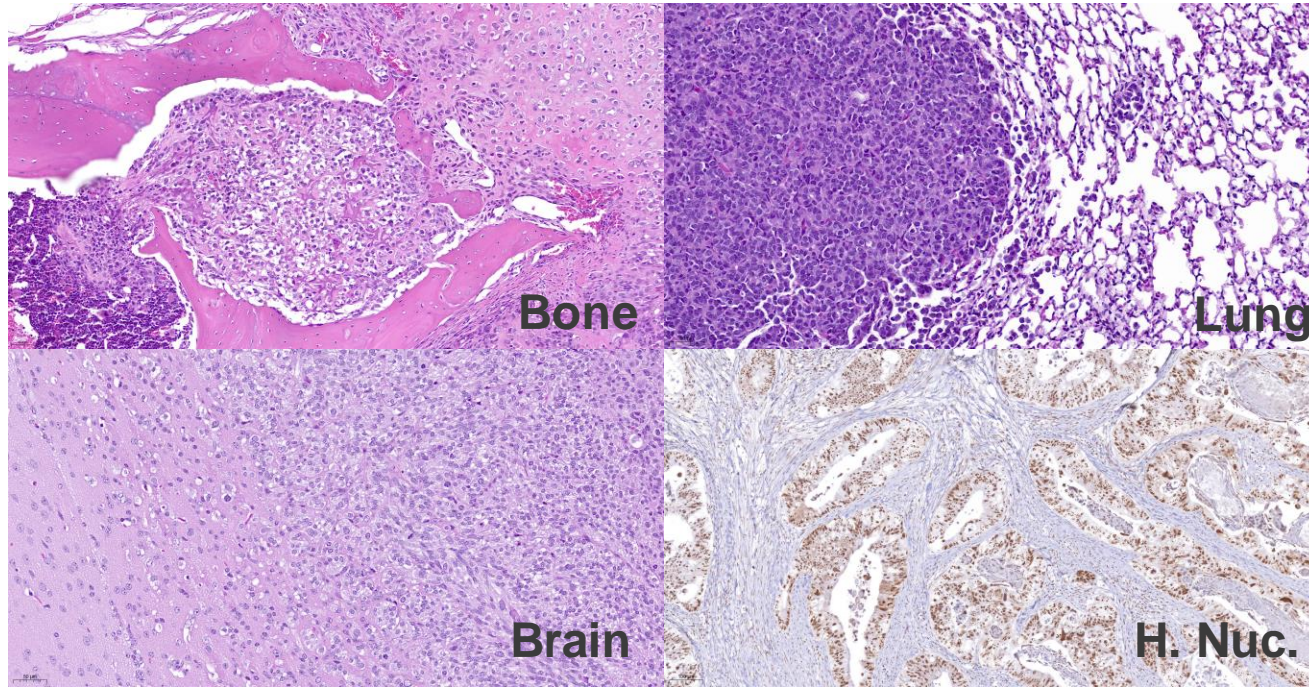
Subcutaneous vs. Orthotopic



Orthotopic Sites



Orthotopic Advantages



O-PDX CLINICAL APPLICATIONS

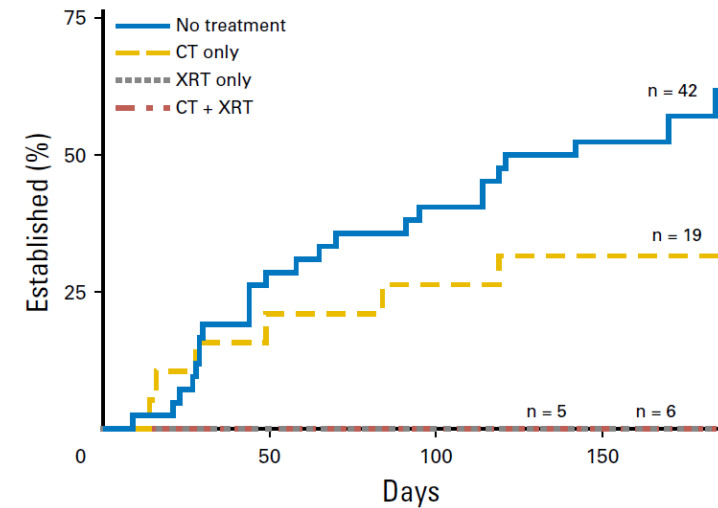


Clinical Applications

original report

Clinical Factors That Affect the Establishment of Soft Tissue Sarcoma Patient-Derived Orthotopic Xenografts: A University of California, Los Angeles, Sarcoma Program Prospective Clinical Trial

JCO Precis Oncol. 2017;2017:10.1200/PO.17.00071



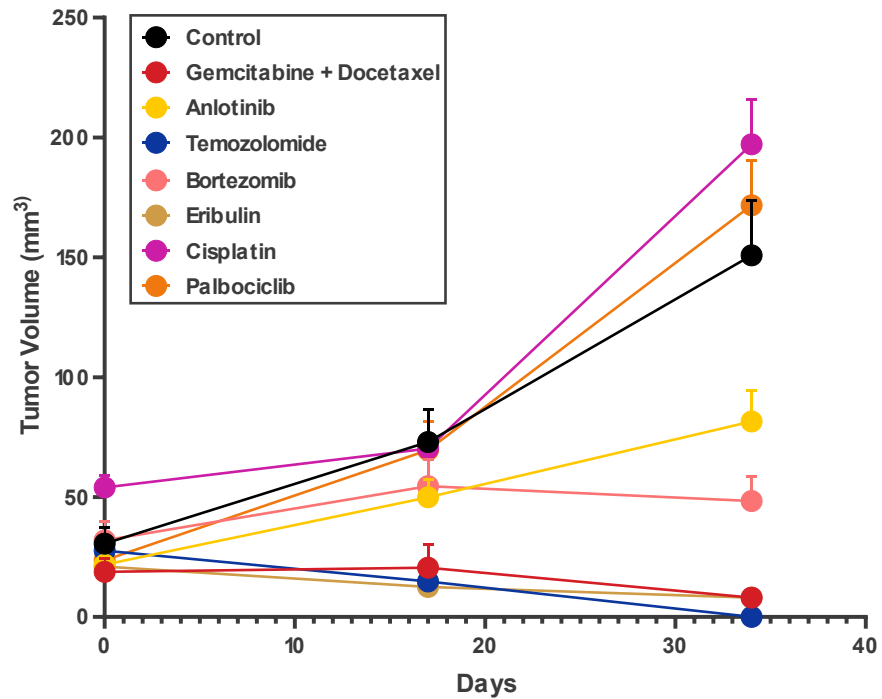
Clinical Applications

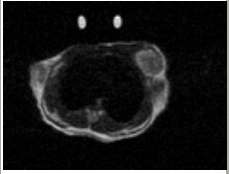
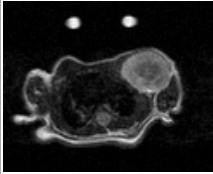
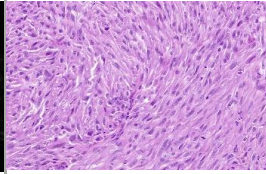
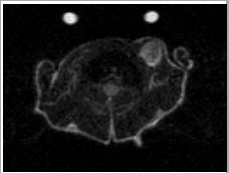
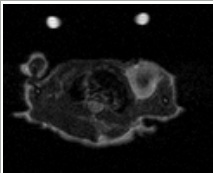
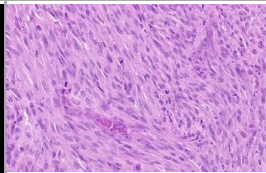
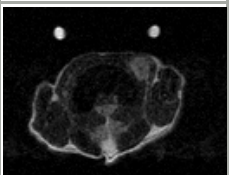
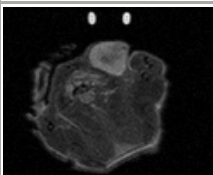
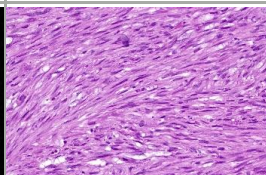
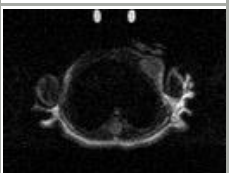
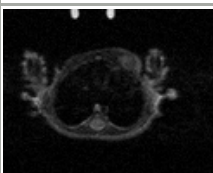
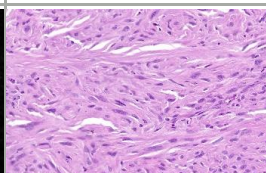
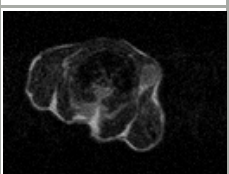
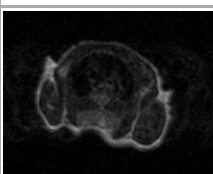
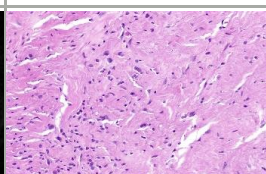
Leiomyosarcoma

60 M

2009 - Leiomyosarcoma > Multiple rounds of chemo/sugery

April 2020 - Recurrent/Met LMS of CW



Treatment	Change in Tumor Volume	MRI Before Treatment	MRI After Treatment	Histology
Control	433.1%			
Anlotinib	352.1%			
Bortezomib	69.2%			
Gemcitabine + Docetaxel	-59.6%			
Temozolomide	-95.6%			

Clinical Applications

Myxofibrosarcoma

50 M

May 2013 – Rad/Surg/3 cycles of doxorubicin

April 2015 – Lung recurrence > 4 cycles of gemcitabine/docetaxel > resection of lung lesion > pazopanib

March 2019 – New mass R forearm > Rad > Resection

June 2019 – 7 cycles Pembrolizumab > Growth

October 2019 – March 2020 – Ifosfamide

May 2020 – Biopsy for Certis

Biomarker Findings
Microsatellite status - MS-Stable
Tumor Mutational Burden - TMB-Low (2 Muts/Mb)

Genomic Findings
For a complete list of the genes assayed, please refer to the Appendix.
NF1 loss exons 1-11
BIRC3 amplification, truncation exon 9
CDKN2A/B loss
TP53 loss

3 Therapies with Clinical Benefit

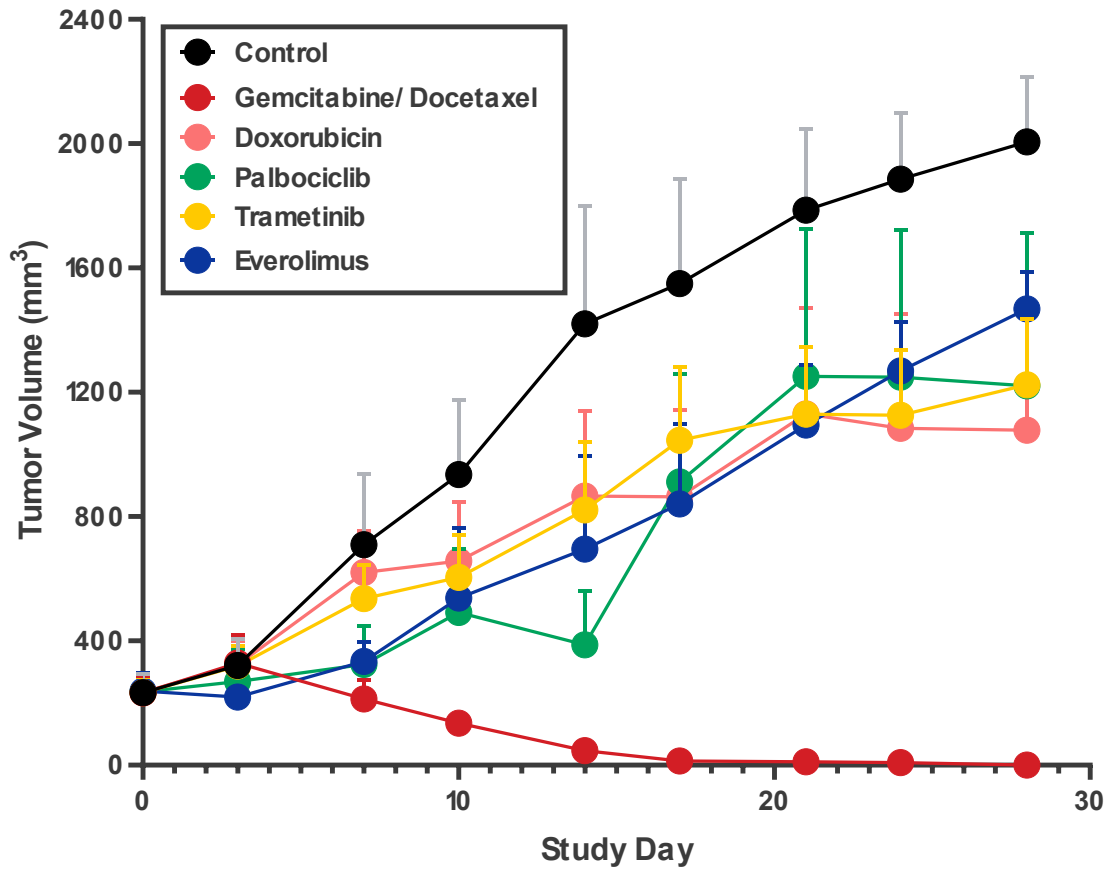
10 Clinical Trials

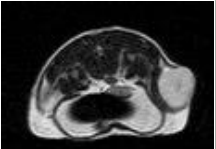
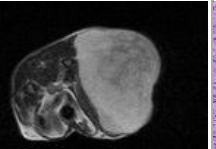
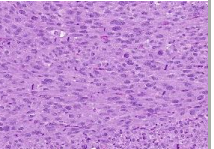
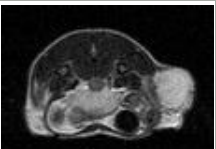
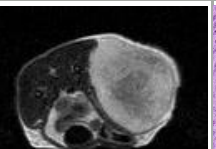
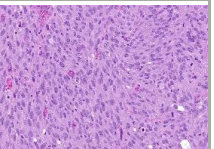

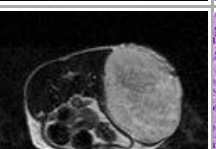
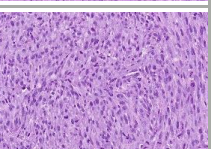


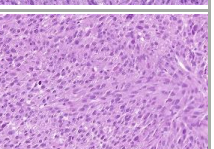
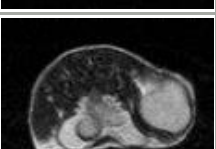
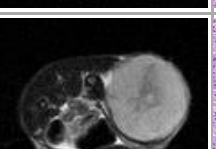
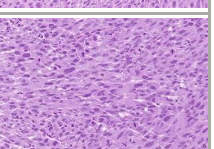
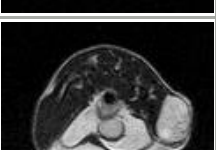

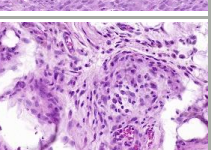
0 Therapies with Lack of Response

BIOMARKER FINDINGS	ACTIONABILITY	
Microsatellite status - MS-Stable	No therapies or clinical trials. see Biomarker Findings section	
Tumor Mutational Burden - TMB-Low (2 Muts/Mb)	No therapies or clinical trials. see Biomarker Findings section	
GENOMIC FINDINGS	THERAPIES WITH CLINICAL BENEFIT (IN PATIENT'S TUMOR TYPE)	THERAPIES WITH CLINICAL BENEFIT (IN OTHER TUMOR TYPE)
NF1 - loss exons 1-11	none	Binimetinib Cobimetinib Trametinib
10 Trials see p. 8		

Clinical Applications

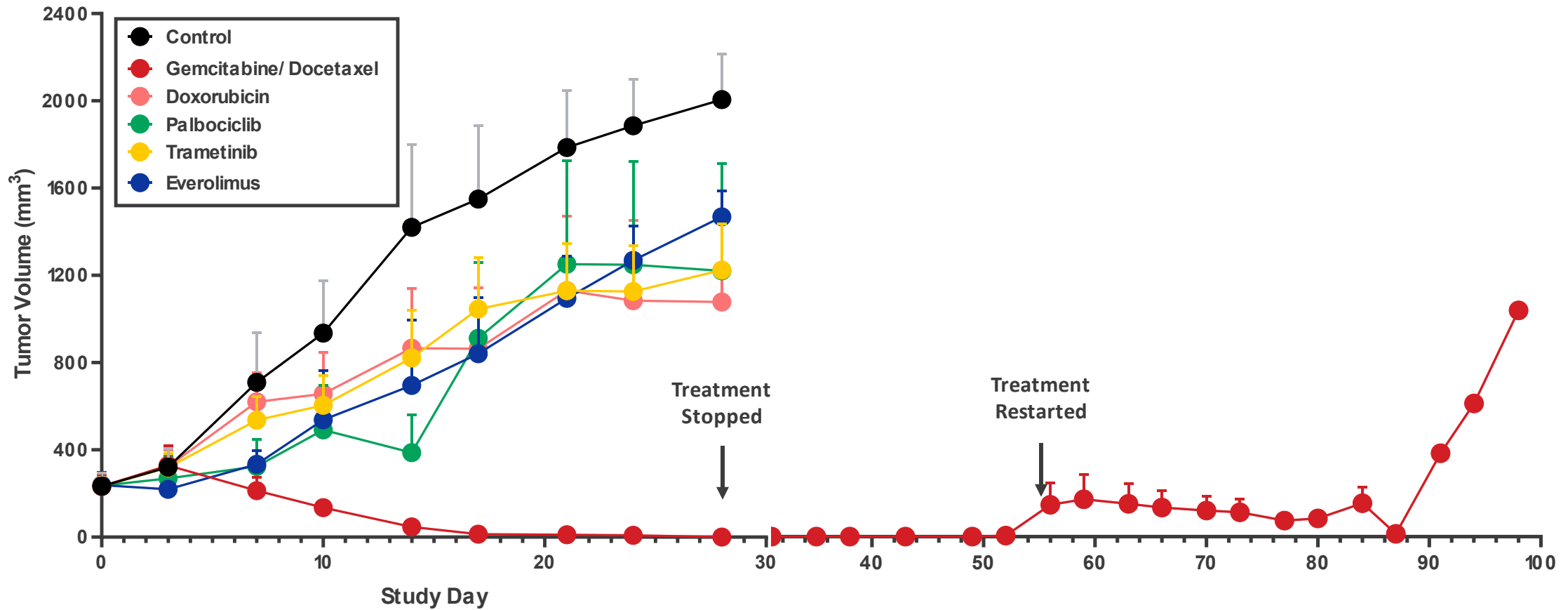
Myxofibrosarcoma



Treatment	Change in Tumor Volume	MRI Before Treatment	MRI After Treatment	Histology
Control	760.63%			
Everolimus	515.39%			
Trametinib	425.60%			
Palbociclib	416.60%			
Doxorubicin	359.25%			
Gemcitabine Docetaxel	-98.84%			

Clinical Applications

Recurrence and Resistance



Clinical Applications

Pediatric Rhabdomyosarcoma

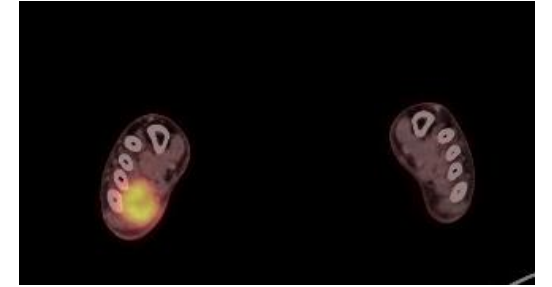
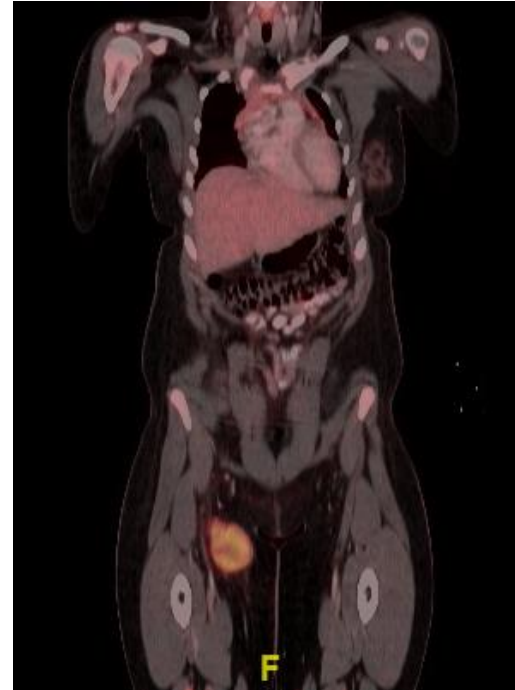
14 F

Aveolar Rhabdomyosarcoma of R foot & thigh

June 2019 – biopsied for precision oncology

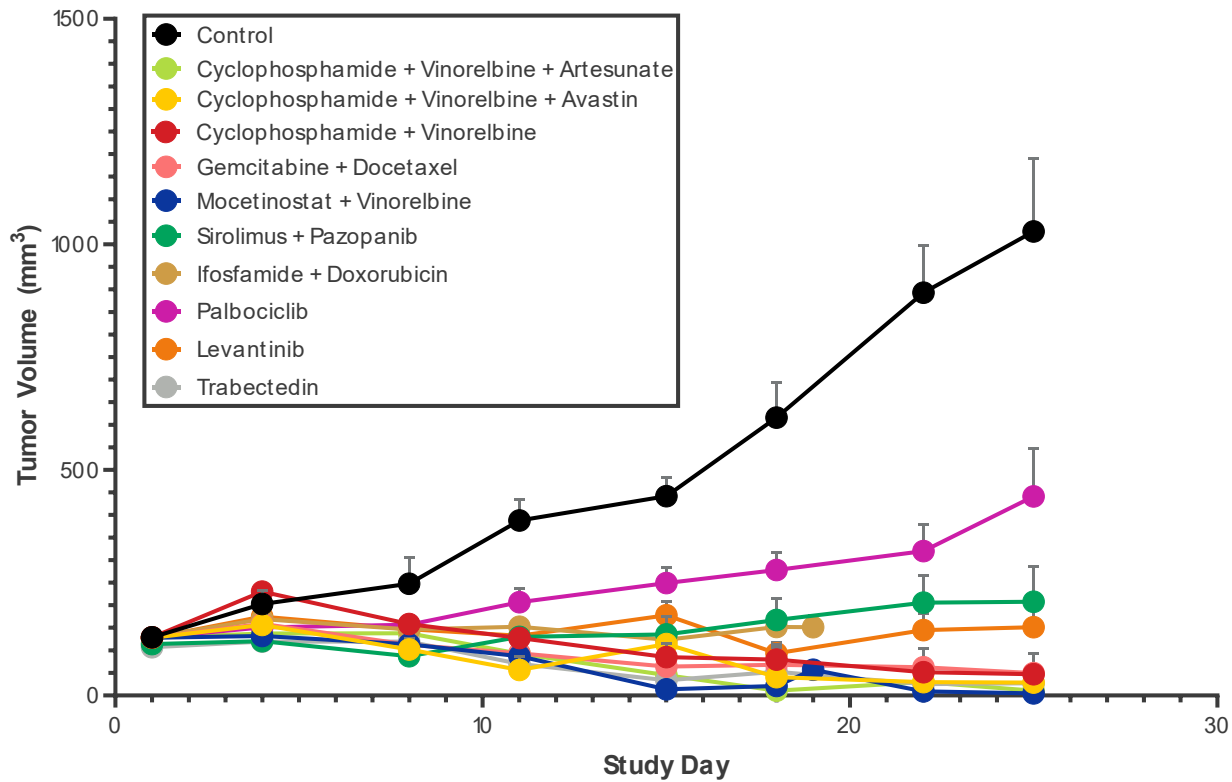
June 2019 - ARST1431: VAC/VI

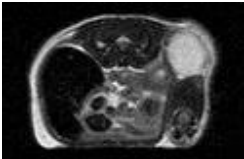
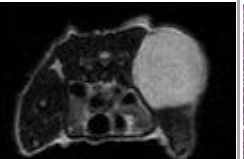
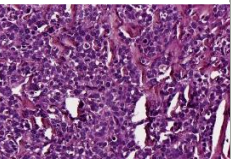
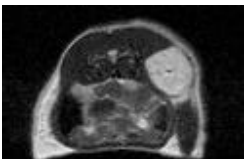
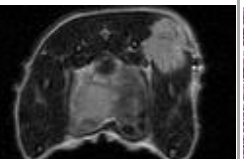
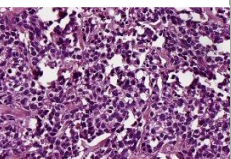
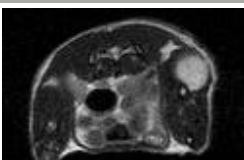
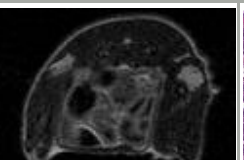
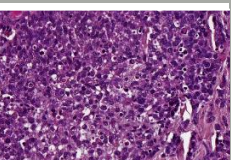
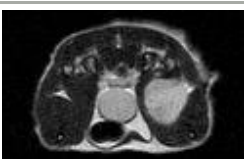
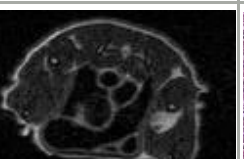
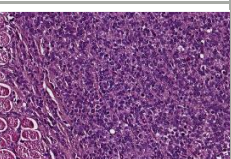
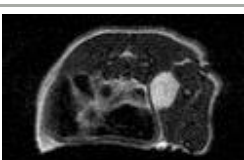

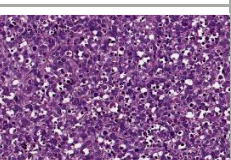
August 2019 - Cyclophosphamide + Vinorelbine



Clinical Applications

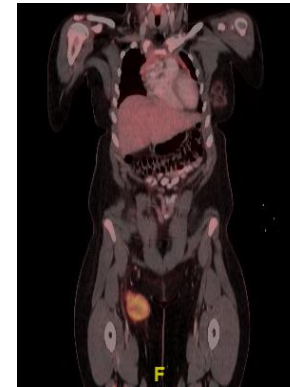
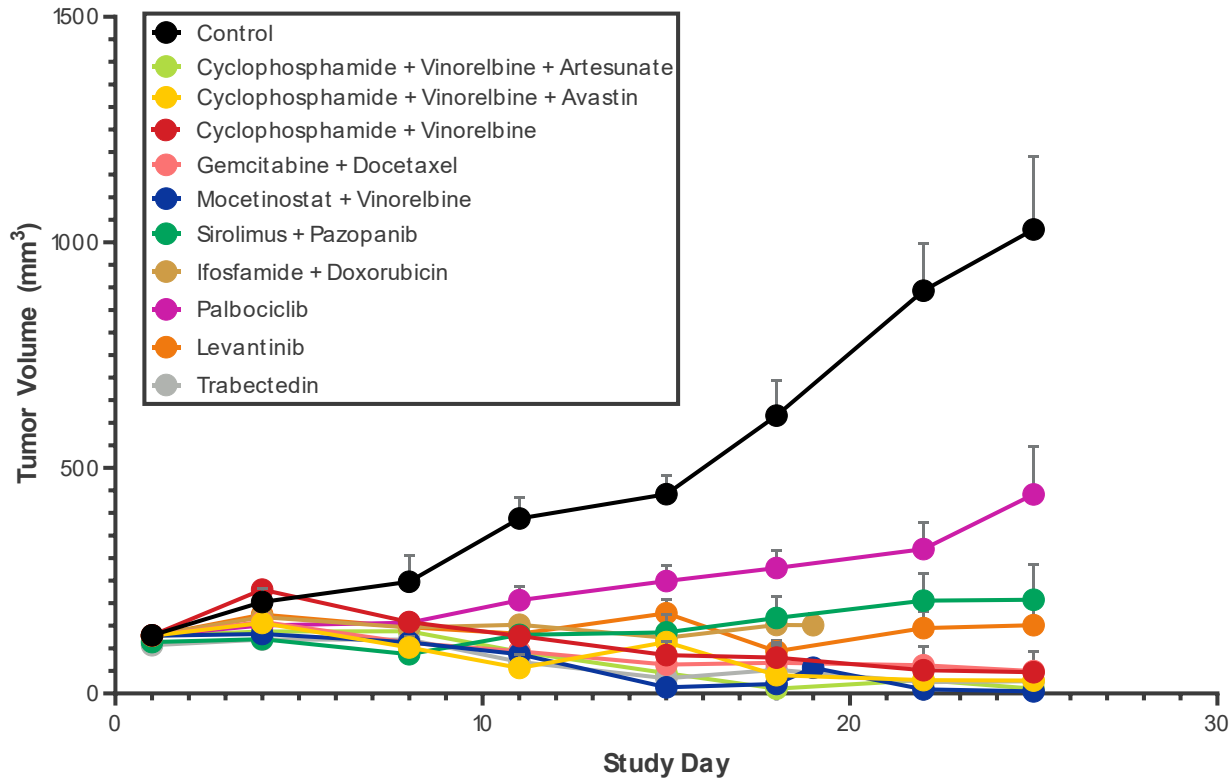
Pediatric Rhabdomyosarcoma



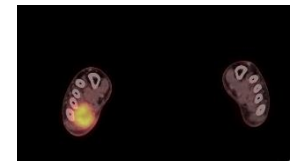
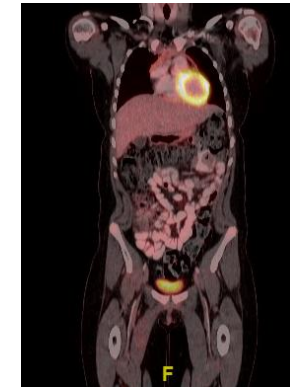
Treatment	Change in Tumor Volume	MRI Before Treatment	MRI After Treatment	MRI After Treatment
Control	698.69%			
Lenvatinib	18.82%			
Gemcitabine Docetaxel	- 61.29%			
Cyclophosphamide Vinorelbine	- 63.39%			
Mocetinostat Vinorelbine	- 96.49%			

Clinical Applications

Pediatric Rhabdomyosarcoma

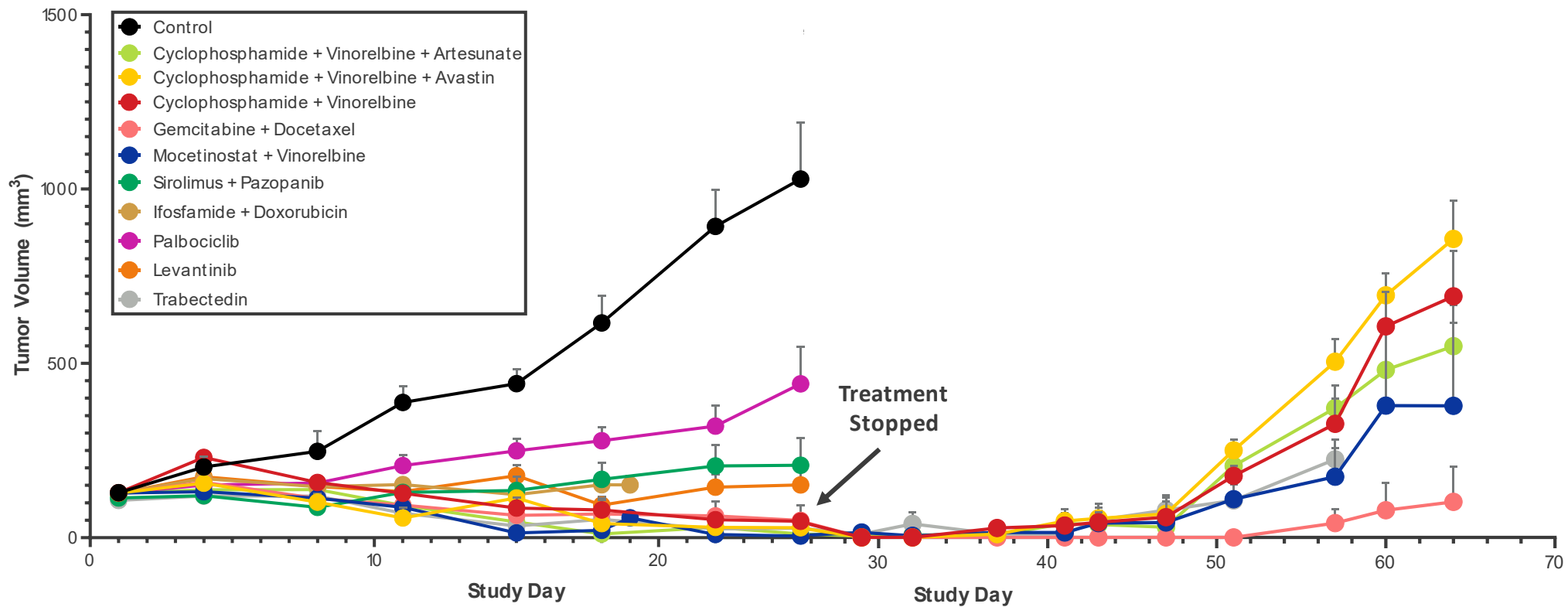


Cyclophosphamide
Vinorelbine



Clinical Applications

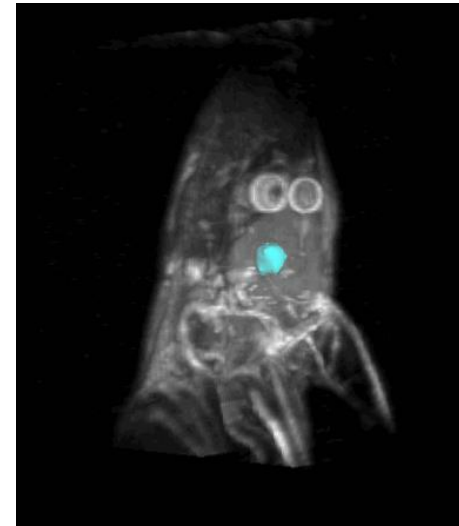
Recurrence as an indicator of efficacy



Clinical Applications

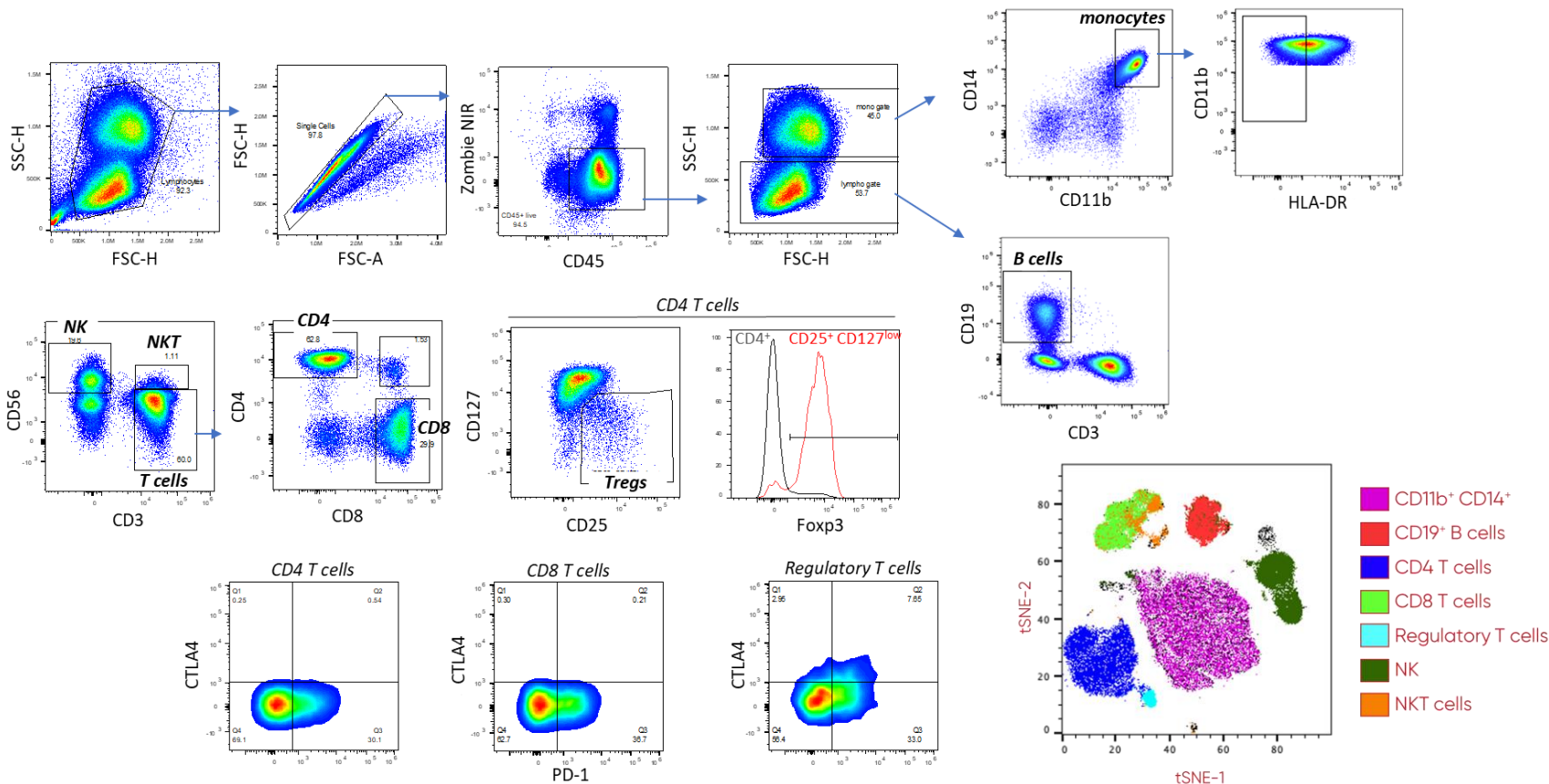
Orthotopic PDX Advantages

- Functional assay for drug selection
- Tumor recurrence as an indicator of efficacy
- Platform for developing and understanding acquired drug resistance



Advancing Precision Oncology

Humanized Mice for Immuno-Oncology



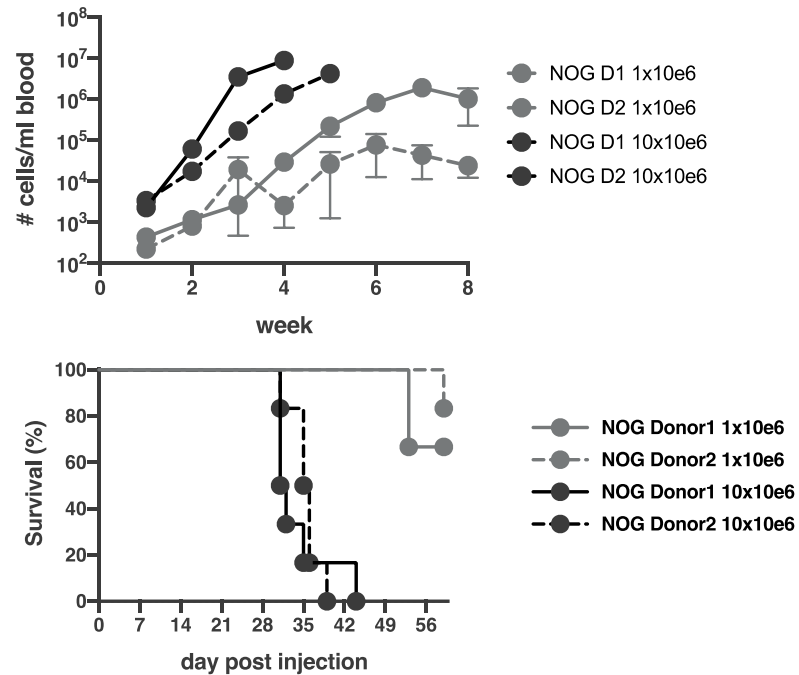
	Marker	Fluorochrome	Intra/extra-cellular
1	Live/dead	NIR	Extra
2	CD45	BV510	Extra
3	CD3	BV570	Extra
4	CD19	BV605	Extra
5	CD56	AF700	Extra
6	CD4	PerCpCy5.5	Extra
7	CD8	BV650	Extra
8	CD14	PEdazzle594	Extra
9	CD11b	Pacific Blue	Extra
10	HLA-DR	BV750	Extra
11	CD25	FITC	Extra
12	CD127	PE	Extra
13	PD-1	PECy7	Extra
14	CTLA-4	BV421	Extra
15	FoxP3	AF647	Intra

15 color unbiased analysis without compensation.

Advancing Precision Oncology

Humanized Mice for Immuno-Oncology

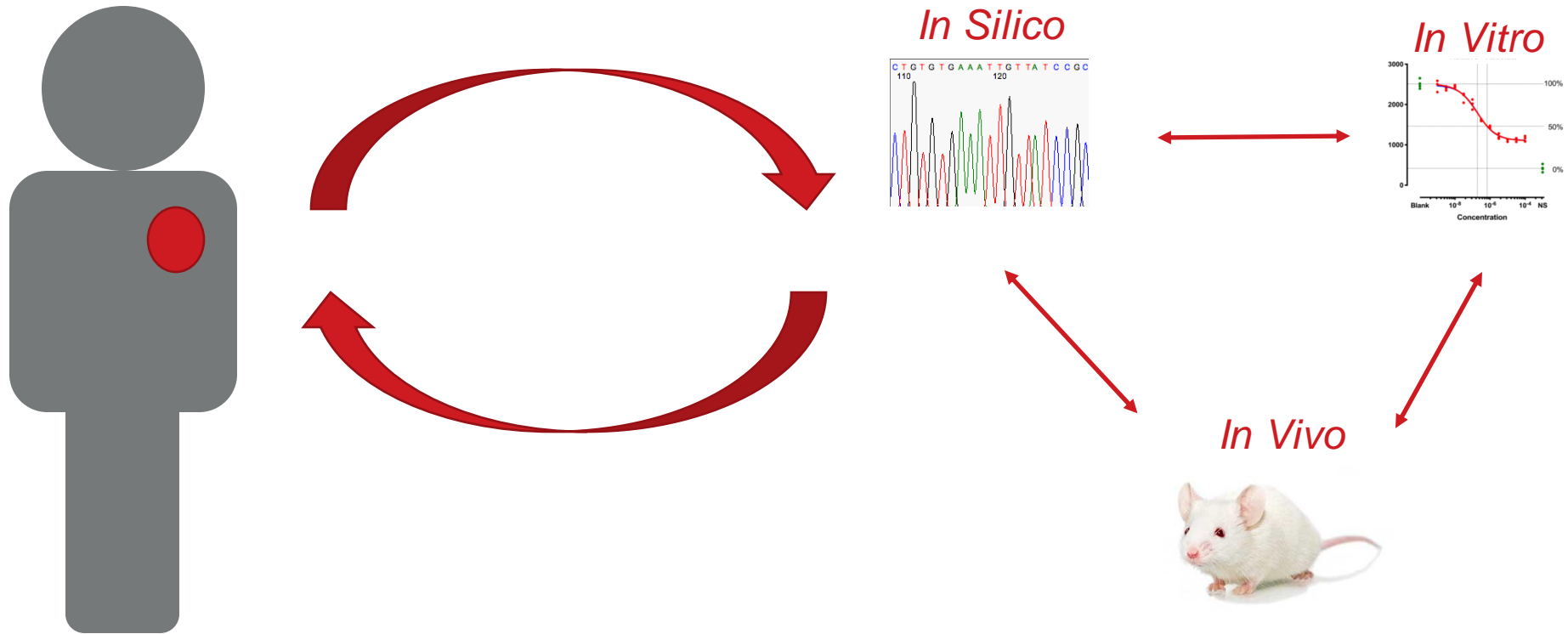
PBMC engrafted NOGs



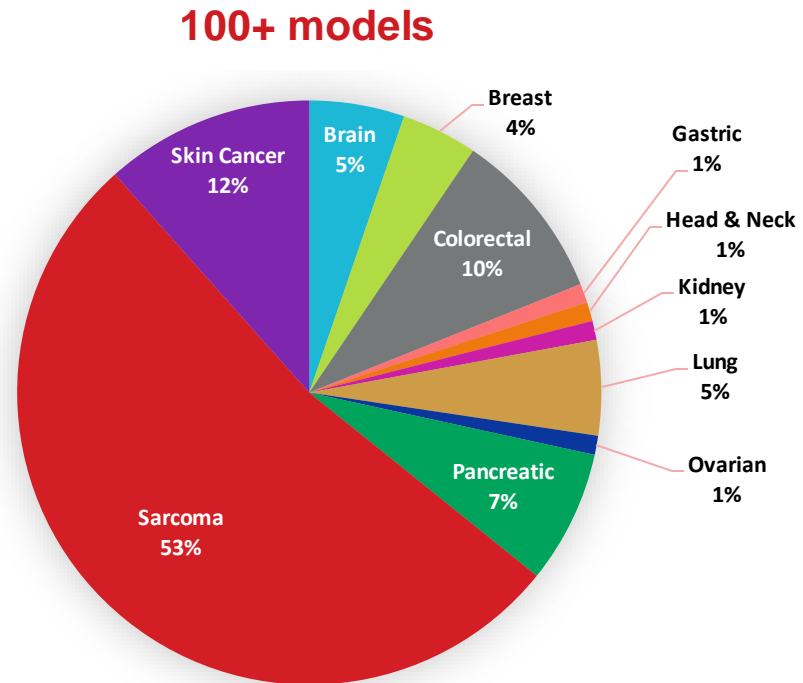
- Peripheral Blood Mononuclear Cells
- Tumor Infiltrating Lymphocytes
- CD34+ Humanized
- Next Gen NOG models for IO

Precision Oncology

Harness all modalities to select therapies specifically designed and targeted to a patient's unique cancer.



Advancing Drug Development



- Patient Info
- RNAseq
- WES
- Fusion/Deletion/Amplification



- Histology
- Growth kinetics
- Pharmacology data

THANK YOU
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