

JAX<sup>®</sup> In Vivo Services offers flexible and customizable studies in mouse models. Sample studies have been generated to illustrate a representative study design with timelines and typical data analyses. This sample study provides an example of a xenograft protocol designed to assess the efficacy of treatments on the rate of staged, subcutaneous engrafted tumor growth. Xenograft models are a well-established method for anti-cancer drug efficacy screening. Every clinically approved agent for the treatment of cancer has shown activity in conventional preclinical *in vivo* models, (Sausville and Burger 2006) and mouse models are the most accessible, efficient, and genetically well-characterized animal species available.

## Basic Study Design

Mice from an immune compromised mouse strain will be transferred to The Jackson Laboratory In Vivo Services facility and allowed to acclimate for one week.

The mice will be housed up to five per cage with *ad libitum* access to standard chow and water. Following acclimation, tumor xenografts will be established by subcutaneous injection of cells on the flank of each animal.

Following inoculation, tumor site will be palpated up to three times weekly until the tumor is established. After establishing sufficient tumor volume, mice will be stratified by tumor size and randomly assigned to each of the study cohorts. Animals will be dosed by route and schedule of your choice.

## Tumor Cell Lines Available In House Include:

Cell Line	Organ	Disease
PC3	Prostate	Adenocarcinoma
DU145	Prostate	Carcinoma
MCF7	Breast	Adenocarcinoma
MDA-MB-231	Breast	Adenocarcinoma
HT-29	Colon	Colorectal Adenocarcinoma
HCT 116	Colon	Colorectal Adenocarcinoma
SK-OV-3	Ovary	Adenocarcinoma
NIH: OVCAR-3	Ovary	Adenocarcinoma
A549	Lung	Carcinoma
NCI-H460	Lung	Carcinoma
Caki -1	Kidney	Clear Cell Carcinoma
Caki -2	Kidney	Clear Cell Carcinoma
A-375	Skin	Malignant Melanoma
SK-MEL-2	Skin	Malignant Melanoma
RPMI8226	Blood	Plasmacytoma; Myeloma
MSTO-211H	Lung	Biphasic Mesothelioma

Note: Other commercial or customer-supplied cell lines can be utilized.

### Contact us today:

► **Phone:** 1-800-422-6423 or 1-207-288-5845  
**Email:** [jaxservices@jax.org](mailto:jaxservices@jax.org)  
**Web:** [www.jax.org/jaxmice/jaxservices](http://www.jax.org/jaxmice/jaxservices)

## Selected Strains Include:

Name	Common Name	Stock Number
NOD.CB17-Prkdc <sup>scid</sup> /J	NOD <i>scid</i>	001303
CBySmn.CB17-Prkdc <sup>scid</sup> /J	BALB <i>scid</i>	001803
NOD.Cg-Prkdc <sup>scid</sup> Il2r <sup>gm1Wjl</sup> /SzJ	NOD <i>scid</i> gamma (NSG)	005557
B6.129S7-Rag1 <sup>tm1Mom</sup> /J	Rag1 null	002216
NU/J	<i>nu/nu</i>	002019

## Example Dosing Protocol:

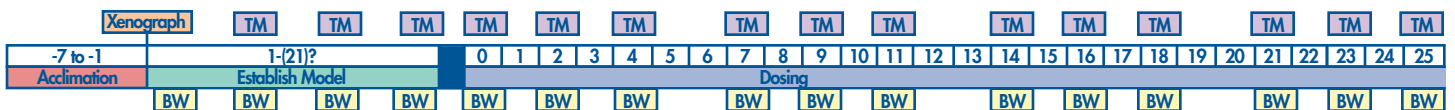
Group	Model	n	Treatment
1	Xenograft	10	Vehicle Control
2	Xenograft	10	Positive Control
3	Xenograft	10	Test Article

## Positive Control Compounds Available In House:

Reference Compounds
Ifosfamide
Cisplatin
Topotecan (TPT)
Irinotecan (CPT)
Taxol
Doxorubicin
Docetaxol

Tumor volume will be measured by digital caliper three times per week and body weight will be measured three times per week. The study will terminate after mice reach a predetermined endpoint (e.g. tumor volume of 3.38 cm<sup>3</sup>). At terminus, blood will be collected and the tumor will be harvested.

## Timeline:



TM= Tumor Measurement      BW= Body Weight Measure

## Results & Analysis

1. Estimated Tumor Volume ( $L \times W^2/2$ )
2. Mean/Median Time to Specified Tumor Volume
3. Survival Time to Specified Tumor Volume
4. Tumor Doubling Time
5. Tumor Growth Inhibition (TGI)
6. Tumor Growth Delay (TGD)
7. Increased Life Span (ILS)
8. Tumor Cell Kill Rate

## Contact us today:

► **Phone:** 1-800-422-6423 or 1-207-288-5845  
**Email:** [jaxservices@jax.org](mailto:jaxservices@jax.org)  
**Web:** [www.jax.org/jaxmice/jaxservices](http://www.jax.org/jaxmice/jaxservices)

## Other Available Procedures

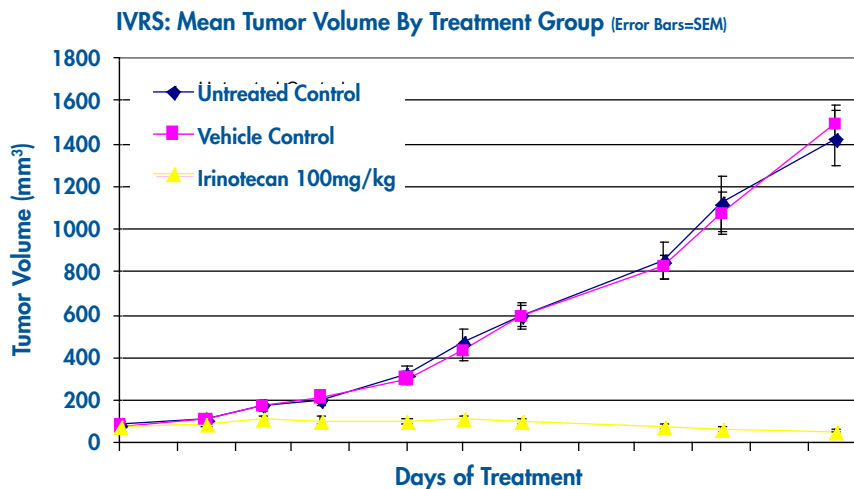
<b>Implant options</b>	Several cell lines are available in house, commercially available cell lines can be developed, and customer-provided cell or tumor fragments can also be delivered
<b>Staging</b>	Treatment can begin directly after implant (unstaged) or after establishing sizable tumors (staged)
<b>Animal</b>	Mice can be assigned to groups in random order or stratified by body weight, tumor size, disease factors or any combination of parameters
<b>Dosing</b>	Dosing can be performed topically, IP, IV, SC, PO, high pressure tail vein, osmotic minipumps (SC or IP), SC drug pellets, in the food or water
<b>Histology</b>	Tumor harvested at terminus can be snap-frozen or fixed for histology or other specialized assays
<b>Blood Chemistry</b>	Can be performed at various time points throughout study

### Contact us today:



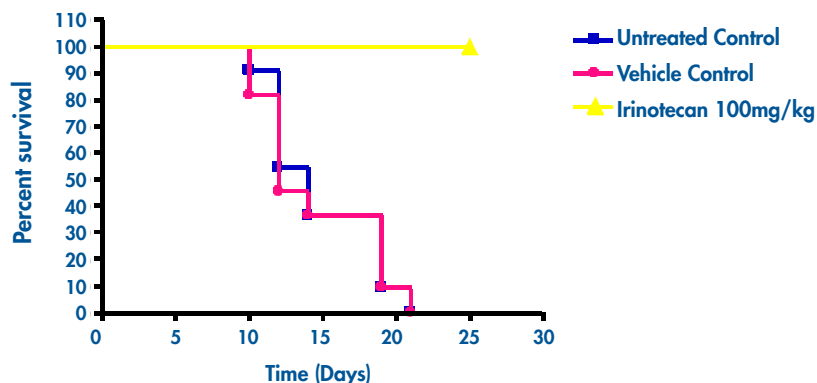
**Phone:** 1-800-422-6423 or 1-207-288-5845  
**Email:** [jaxservices@jax.org](mailto:jaxservices@jax.org)  
**Web:** [www.jax.org/jaxmice/jaxservices](http://www.jax.org/jaxmice/jaxservices)

## Representative Results: Xenograft Tumor Formation with HT29 Colon Cancer Cells in NOD/scid

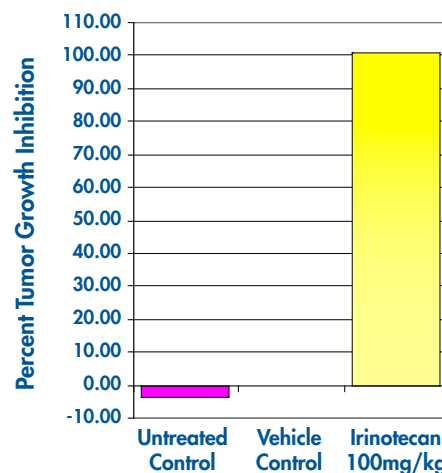


NOD/scid mice were inoculated with HT29 human colon cancer cells. Mice were allocated to groups of 10 with mean tumor volume of 58 mm<sup>3</sup> ±28 SD and treated IP QD for 25 days. After 25 days of treatment, there was a mean decrease in tumor size of 24 mm<sup>3</sup> for Irinotecan treated mice as compared to a mean increase in size of 1337 mm<sup>3</sup> and 1407 mm<sup>3</sup> for untreated and vehicle-treated controls, respectively (p <0.0001).

### HT29: Survival to five-Fold Increase in Tumor Volume



Survival: The survival curve for mice reaching five-fold increase over initial tumor size after treatment was significantly different for Irinotecan-treated mice as compared to vehicle or untreated controls (p <0.0001).



Tumor growth was completely inhibited for Irinotecan-treated mice as compared to vehicle-treated controls

Tumor Growth Inhibition (%):  

$$1 - \frac{\text{Final Vol} - \text{Initial Vol}}{\text{Final Vehicle Vol} - \text{Initial Vehicle Vol}}$$

### References

Sausville EA, Burger AM. 2006. Contributions of human tumor xenograft to anticancer drug development. *Cancer Res* 66:3351-4.

Contact us today:

► Phone: 1-800-422-6423 or 1-207-288-5845  
 Email: [jaxservices@jax.org](mailto:jaxservices@jax.org)  
 Web: [www.jax.org/jaxmice/jaxservices](http://www.jax.org/jaxmice/jaxservices)