

Pre-Clinical Study: Xenograft SN2310 Study Analysis

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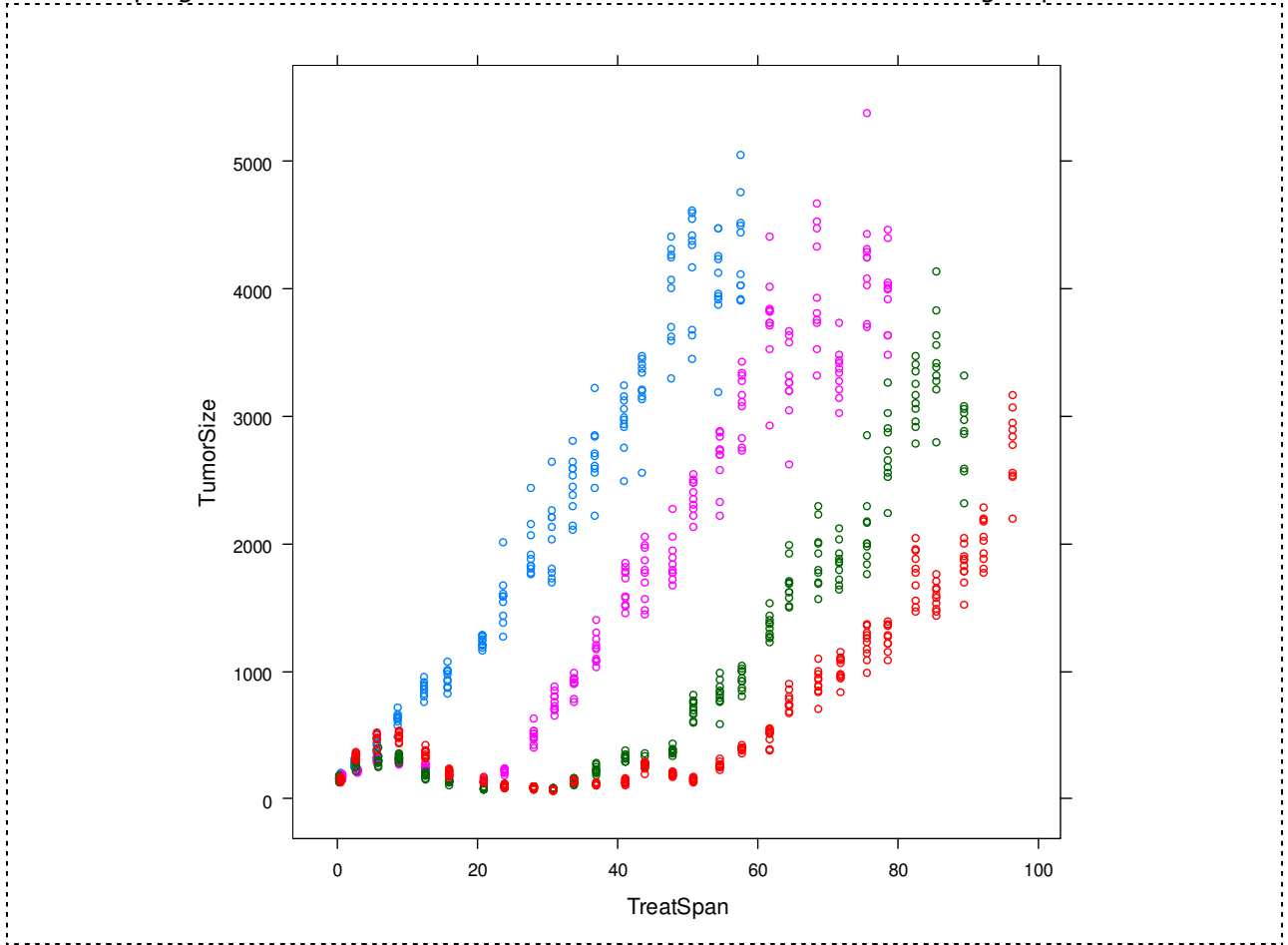
Study Information Summary

Project Lead [1] "John W. Smith"	Experiment [1] "KCR2-5/0/9G"	Investigator
Lab Book Number [1] "G-4976"	Tumor [1] "HT29 human tumor xenograft"	Source Line [1] "01A07F5T6"
Host [1] "Athymic"	Source [1] "APA"	Subject Sex [1] "F"
Implant Date [1] "3/9/2005 12:00:00 AM"	Staging Date [1] "3/22/2005 12:00:00 AM"	Evaluation Date [1] "5/19/2005 12:00:00 AM"
Treatment Group 1	[1] "Saline Control Dose=4.5 mL/kg Schedule=qdx5 (for 2 weeks) CumDose=0 micromol/m**2"	
Treatment Group 2	[1] "irinotecan Dose=45 mg/m**2/day Dose=66 micromol/m**2/day Schedule=qdx5 (for 2 weeks) CumDose=660 micromol/m**2"	
Treatment Group 3	[1] "SN2310 Emulsion Dose=45 mg/m**2/day Dose=50 micromol/m**2/day Schedule=qdx5 (for 2 weeks) CumDose=500 micromol/m**2"	
Treatment Group 4	[1] "SN2310 Emulsion Dose=45 mg/m**2/day Dose=50 micromol/m**2/day Schedule=q3dx10 CumDose=500 micromol/m**2"	

Exploratory Data Analysis of Study

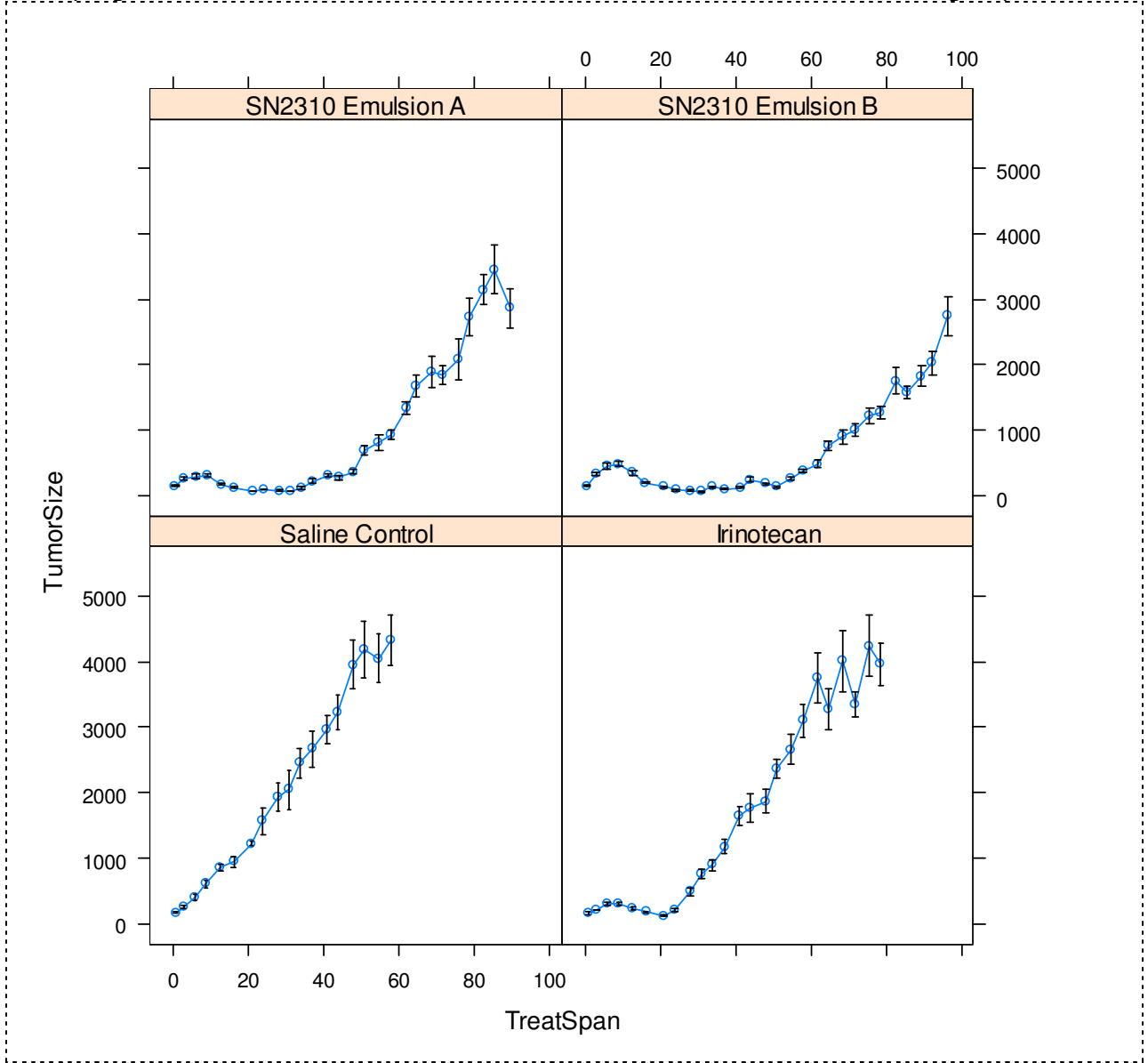
Raw Data Progress Plot

Plot the progress of tumor size for collection of mice in each treatment group:



Mean Tumor Size Progress Plot

Plot progress of mean tumor size for the collection of mice in each treatment group:



Modeling Tumor Growth

Fitting Tumor Size to Logistic Model by Nonlinear Least Squares

The growth behavior of tumors displays increasing growth up to a certain maximum corresponding to an S-shaped logistic curve. Such behavior can be modeled on a differential equation with a rate that depends on a basic rate, κ , current size ζ , and a limiting size α .

$$\frac{dy(t)}{dt} = Asym \times scale \times y(t) \times [Asym - y(t)]$$

This differential equation has the general solution

$$y(t) = \frac{Asym}{1 + e^{[-(t-T50)/scale]}}$$

where *Asym* is the asymptote, *T50* is the time at which 50% growth is achieved, and *scale* is the scale parameter describing the steepness of the curve. Data can be fit to this model using nonlinear least squares.

Logistic Regression Models for Each Treatment Group

For each treatment use the nonlinear least squares self-start model.

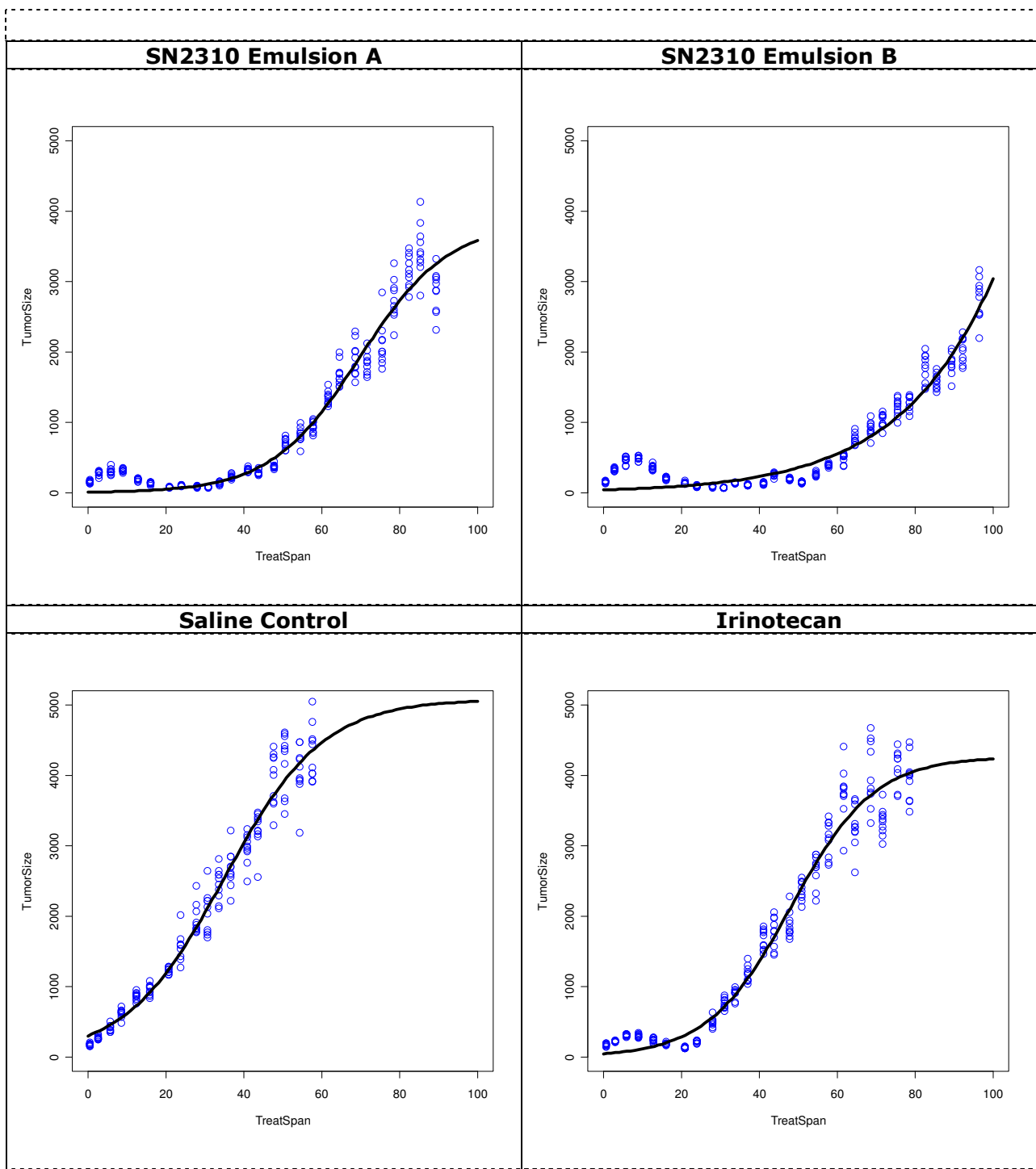
Saline Control	Irinotecan
<pre> model.SalineControl <- nls(TumorSize ~ SSlogis(input=TreatSpan, Asym, xmid, scal), data=SN2310DataSim, subset=TreatGroup=="Saline Control") one <- summary(model.SalineControl) </pre>	<pre> model.Irinotecan <- nls(TumorSize ~ SSlogis(input=TreatSpan, Asym, xmid, scal), data=SN2310DataSim, subset=TreatGroup=="Irinotecan") two <- summary(model.Irinotecan) </pre>
SN2310 Emulsion A	SN2310 Emulsion B
<pre> model.SN2310A <- nls(TumorSize ~ SSlogis(input=TreatSpan, Asym, xmid, scal), data=SN2310DataSim, subset=TreatGroup=="SN2310 Emulsion A") three <- summary(model.SN2310A) </pre>	<pre> model.SN2310B <- nls(TumorSize ~ SSlogis(input=TreatSpan, Asym, xmid, scal), data=SN2310DataSim, subset=TreatGroup=="SN2310 Emulsion B") four <- summary(model.SN2310B) </pre>

Logistic Modeling Results

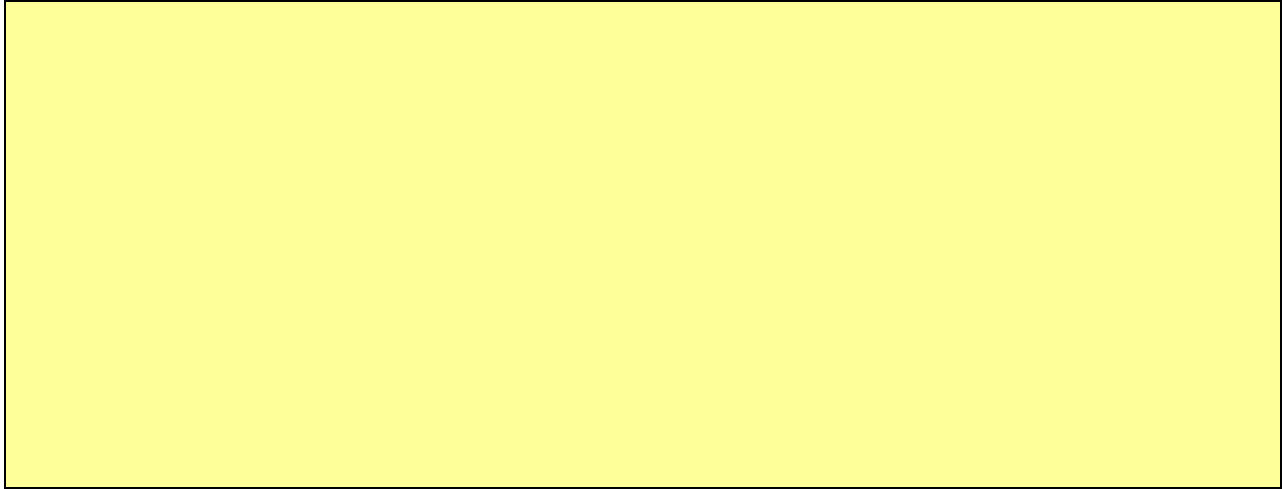
Modeling Results Summary Table

Treatment	Asymptote (mm ³)	Time to 50% (days)	Scale
Saline Control	[1] 5084.067	[1] 34.97828	[1] 12.63841
Irinotecan	[1] 4268.57	[1] 48.13164	[1] 10.67289
SN2310 Emulsion A	[1] 3833.897	[1] 69.66881	[1] 11.42060
SN2310 Emulsion B	[1] 40963.78	[1] 157.0732	[1] 22.61216

Plot Predicted Curve vs Observed Points



Observations and Conclusions



Appendix: Logistic Regression Model Summary

Treatment	Regression Model Summary																				
Saline Control	<p>Formula: TumorSize ~ SSlogis(input = TreatSpan, Asym, xmid, scal)</p> <p>Parameters:</p> <table border="1"> <thead> <tr> <th></th> <th>Estimate</th> <th>Std. Error</th> <th>t value</th> <th>Pr(> t)</th> </tr> </thead> <tbody> <tr> <td>Asym</td> <td>5084.0670</td> <td>164.1160</td> <td>30.98</td> <td><2e-16 ***</td> </tr> <tr> <td>xmid</td> <td>34.9783</td> <td>1.0549</td> <td>33.16</td> <td><2e-16 ***</td> </tr> <tr> <td>scal</td> <td>12.6384</td> <td>0.5568</td> <td>22.70</td> <td><2e-16 ***</td> </tr> </tbody> </table> <p>--- Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1</p> <p>Residual standard error: 261.3 on 177 degrees of freedom</p>		Estimate	Std. Error	t value	Pr(> t)	Asym	5084.0670	164.1160	30.98	<2e-16 ***	xmid	34.9783	1.0549	33.16	<2e-16 ***	scal	12.6384	0.5568	22.70	<2e-16 ***
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scal	11.4206	0.5838	19.56	<2e-16 ***																	
SN2310 Emulsion B	<p>Formula: TumorSize ~ SSlogis(input = TreatSpan, Asym, xmid, scal)</p> <p>Parameters:</p> <table border="1"> <thead> <tr> <th></th> <th>Estimate</th> <th>Std. Error</th> <th>t value</th> <th>Pr(> t)</th> </tr> </thead> <tbody> <tr> <td>Asym</td> <td>40963.785</td> <td>89907.782</td> <td>0.456</td> <td>0.64901</td> </tr> <tr> <td>xmid</td> <td>157.073</td> <td>56.998</td> <td>2.756</td> <td>0.00623 **</td> </tr> <tr> <td>scal</td> <td>22.612</td> <td>1.678</td> <td>13.479</td> <td>< 2e-16 ***</td> </tr> </tbody> </table> <p>--- Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1</p> <p>Residual standard error: 198.8 on 287 degrees of freedom</p>		Estimate	Std. Error	t value	Pr(> t)	Asym	40963.785	89907.782	0.456	0.64901	xmid	157.073	56.998	2.756	0.00623 **	scal	22.612	1.678	13.479	< 2e-16 ***
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