Bruceantinol (BOL) Effectively Reduces Tumors Expressing STAT3

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I. Introduction

STAT3, a gene that is largely expressed within human cancers, continues to be researched as no inhibitors are currently approved for human treatment. Bruceantinol (BOL) reveals large anti-tumor potential and is hypothesized to inhibit expression of STAT3.

II. Data

Data is presented in a time-series format. Over the course of 17 days, tumor size and weight in mice are recorded. 24 mice are randomly selected for this study and are split into 6 groups for treatment. Treatments are control, BOL (4mg/kg) and BOL (8 mg/kg). Each treatment is applied to 2 separate clinical groups. No survival analysis can be performed due to data limitations.

III. Analysis

A. Data Processing

Data is transformed from separate sheets into a single data frame. A separate column is created for UIDs (created by conjoining treatment and mouse ID). Mean and Standard Deviation of subsets of data were manually calculated later, and given values were removed for formatting purposes.

B. Visualization

3 separate graphs were created to reveal that increase in concentration of BOL correlates to decrease in tumor size. **Fig. 1** shows mean volume value across each day for each treatment type. **Fig. 2** shows mean tumor weight across each day for each treatment type. Both **Fig. 1** and **Fig. 2** use the average value of each treatment across all UIDs for each individual day. Vertical bars denote the standard deviation of all summed values for the corresponding day.

Fig. 3 shows individual observations for all 3 treatments

Fig. 1 and **Fig. 2** show that in the control group, tumor volume and weight has significantly increased with days. For mice treated with BOL, tumor volumes are significantly smaller than the control group, while for tumor weight there is no significant qualitative change in mean. Increase in tumor size qualitatively correlates to decrease in tumor size (volume).

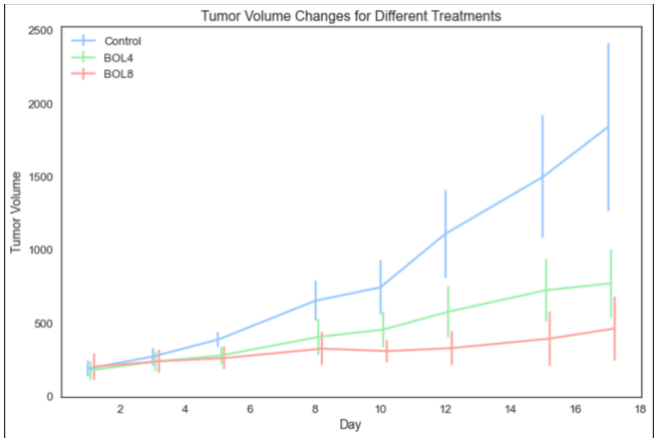

Fig 1. The mean and standard deviation of tumor volume per day for each treatment.

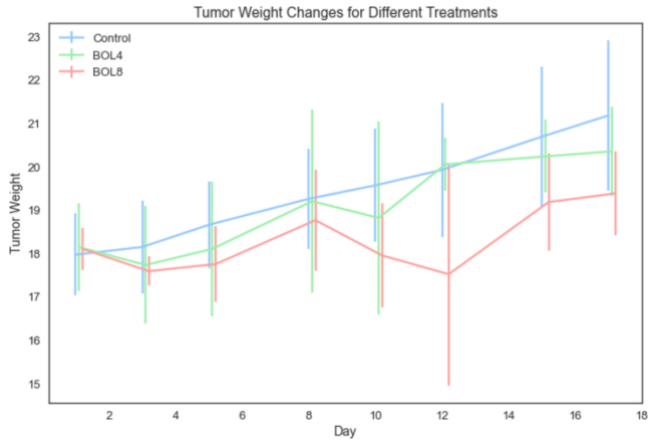

Fig 2. The mean and standard deviation of tumor volume per day for each treatment.

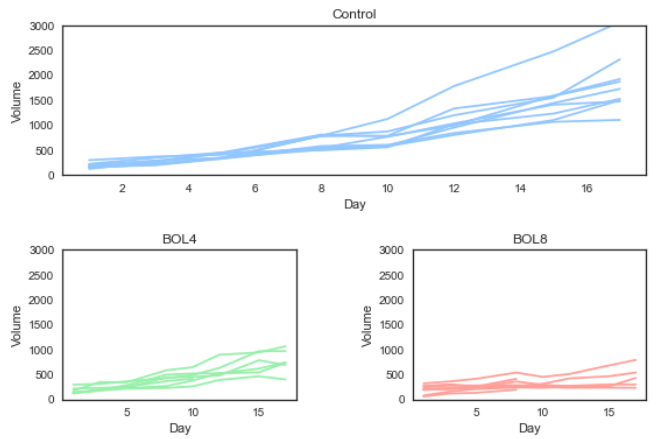

Fig 3. Individual observations within each treatment group.

IV. Significance Testing

To find if BOL significantly changes tumor growth rates, two steps are utilized. Firstly, independent linear regression (Ordinary Least Squares Regression) is performed on the three treatments. Then, regression coefficients between models are then compared [2] for statistical significance.

A. *Data Transformation*

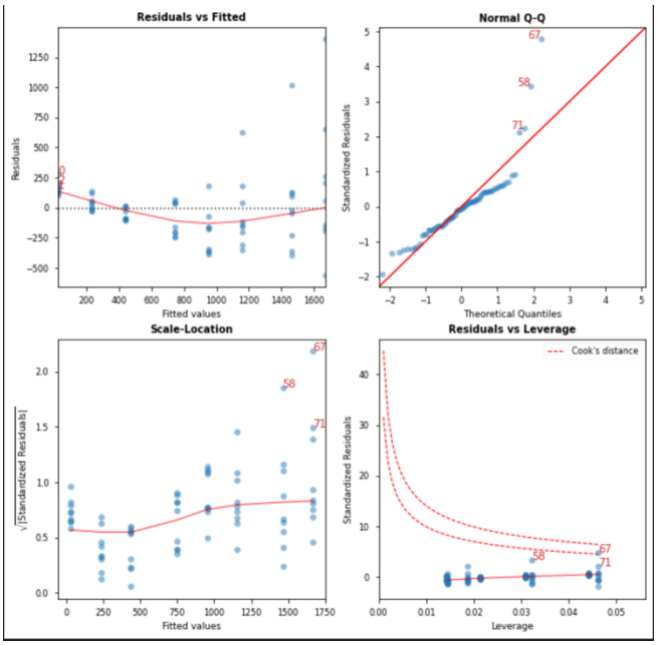

Fig 4. Linear regression is performed on raw data from control treatment units.

The top left panel of **Fig. 4** exhibits a clear U-shape, indicating non-linearity in the data. The residual plot in the bottom left panel of **Fig. 4** displays heteroscedasticity, implying inappropriate application of regression [1]. This conclusion is further backed by the low R-squared value from regression output (0.773). A more accurate model is achieved with log transformation of the volume by treating tumor volume growth as exponential.

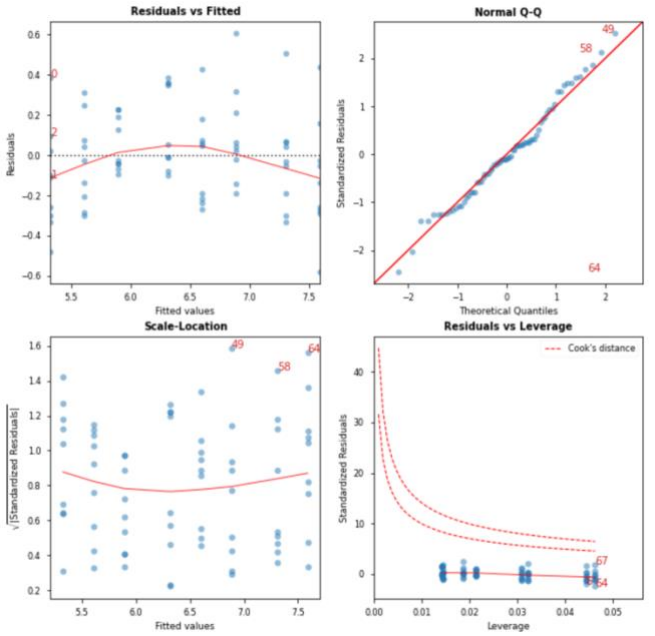

Fig 5. Linear regression is performed on transformed data from control treatment units, treating growth as an exponential function.

The top left panel of **Fig. 5** exhibits no discernable pattern, suggesting that log transformation improves the fit to the data. The residual plot displays no heteroscedasticity – I can confidently conclude a better fit with an exponential model, with the Normal Q-Q plot achieving higher linearity, as well as a higher R-squared value from regression output (0.909).

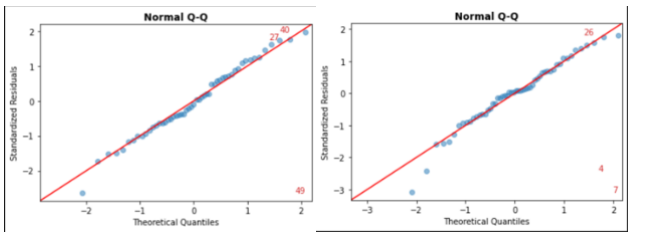

Fig 6. Normal Q-Q of transformed data from BOL4 and BOL8

Because treating the control data as an exponential function increased linearity, the process was repeated for treatments of BOL4 and BOL8. As observed by the Normal Q-Q for both plots, linear regression is appropriate.

B. *Comparing Regression Coefficients*

With conditions met, we can perform significance testing for regression coefficients.

$$H_0: \beta_1 = \beta_2$$

$$H_a: \beta_1 \neq \beta_2$$

$$s.t.\ Z = \frac{\beta_1 - \beta_2}{\sqrt{(SE\beta_1)^2 + (SE\beta_2)^2}} \quad (1)$$

Two significance tests will be performed to determine significant difference between Control and BOL4, and Control and BOL8. An alpha value of 0.05 will be used.

	Regression Output	
	β (slope from OLS regression)	***SEβ***
Control	0.1416	0.005
BOL4	0.0934	0.007
BOL8	0.0472	0.01

Fig 7. Results from OLS Regression on each treatment

	Significance Test Results		
	Z-Score	***P-Value***	***Reject H_0***
Control v. BOL4	5.603	1.053E-08	Yes
Control v. BOL8	8.443	0	Yes
BOL4 v. BOL8	3.784	7.7E-05	Yes

Fig 8. Results from Eq. 1

C. Conclusion

The data provide convincing evidence of significant difference between rate of tumor volume increase between treatments. Specifically, the data helps conclude

- Any amount of BOL concentration (4mg/kg or 8 mg/kg) within tumors expressing STAT3 significantly decreases the rate of tumor growth within mice
- As BOL concentration increases from 4mg/kg to 8mg/kg, tumors expressing STAT3 are reduced continuously

REFERENCES

[1] *An Introduction to Statistical Learning* (ISLR) book, James et al., Springer.

[2] *Clogg, C. C., Petkova, E., & Haritou, A. (1995). Statistical methods for comparing regression coefficients between models.* American Journal of Sociology, 100*(5), 1261-1293.*