

Tables and Figures

Endpoint (Toxicity Grades)	TD50(1) Gy	95% CI	m	95% CI	n	95% CI
Rectal Bleeding (G1&2)	59.2	( 57.8 - 61.9 )	0.26	( 0.18 - 0.48 )	0.14	( 0.09 - 0.16 )
Proctitis (G1&2)	58.2	( 55.7 - 60.1 )	0.28	( 0.19 - 0.6 )	0.14	( 0.11 - 0.2 )
Stool Frequency (G1&2)	61.5	( 56.3 - 68.3 )	0.6	( 0.41 - >1 )	0.3	( 0.16 - 0.6 )
Loose Stools (G1&2)	59.5	( 56.9 - 62.6 )	0.3	( 0.22 - 0.44 )	0.25	( 0.18 - 0.36 )
Rectal Urgency (G1&2)	55.0	( 51.3 - 59.6 )	0.48	( 0.27 - >1 )	0.26	( 0.15 - 0.45 )
Rectal Bleeding (G2)	68.2	( 64.9 - 69.3 )	0.14	( 0.12 - 0.16 )	0.12	( 0.1 - 0.16 )
Proctitis (G2)	67.0	( 64.8 - 69.3 )	0.20	( 0.19 - 0.24 )	0.15	( 0.11 - 0.2 )
Stool Frequency (G2)	-	( - - - )	-	( - - - )	-	( - - - )
Loose Stools (G2)	73.0	( 68.8 - 77.8 )	0.25	( 0.23 - 0.29 )	0.3	( 0.19 - 0.5 )
Rectal Urgency (G2)	68.4	( 63.5 - 75.1 )	0.36	( 0.29 - 0.45 )	0.36	( 0.22 - 0.59 )

Table 2. Maximum Likelihood Estimations (MLE) of the LKB model parameters for 5 rectal toxicity endpoints. Fitted to Grade 1& 2 toxicity and Grade 2 only. Confidence intervals were obtained using the profile likelihood method.

Endpoint (Toxicity Grades)	TD50(1) Gy	(SD)	m	(SD)	n	(SD)
Rectal Bleeding (G1&2)	59.2	( 3.5 )	0.29	( 0.12 )	0.17	( 0.12 )
Proctitis (G1&2)	57.3	( 4.1 )	0.33	( 0.15 )	0.2	( 0.17 )
Stool Frequency (G1&2)	62.6	( 6.3 )	0.6	( 0.21 )	0.36	( 0.27 )
Loose Stools (G1&2)	59.9	( 4.6 )	0.34	( 0.15 )	0.38	( 0.3 )
Rectal Urgency (G1&2)	54.1	( 5.4 )	0.52	( 0.22 )	0.4	( 0.31 )
Rectal Bleeding (G2)	68.9	( 4.2 )	0.16	( 0.05 )	0.18	( 0.14 )
Proctitis (G2)	68.3	( 4.6 )	0.22	( 0.07 )	0.17	( 0.08 )
Stool Frequency (G2)	155.4	( 27.4 )	0.46	( 0.07 )	0.29	( 0.31 )
Loose Stools (G2)	74.0	( 7.2 )	0.25	( 0.09 )	0.45	( 0.36 )
Rectal Urgency (G2)	70.1	( 8.0 )	0.37	( 0.12 )	0.45	( 0.26 )

Table 3 Summary of mean and standard deviation of the LKB parameters values obtained with Maximum Likelihood Estimation for 1000 bootstrap samples fitted to Grade 1&2 toxicity and Grade 2 only for 5 rectal toxicity endpoints.

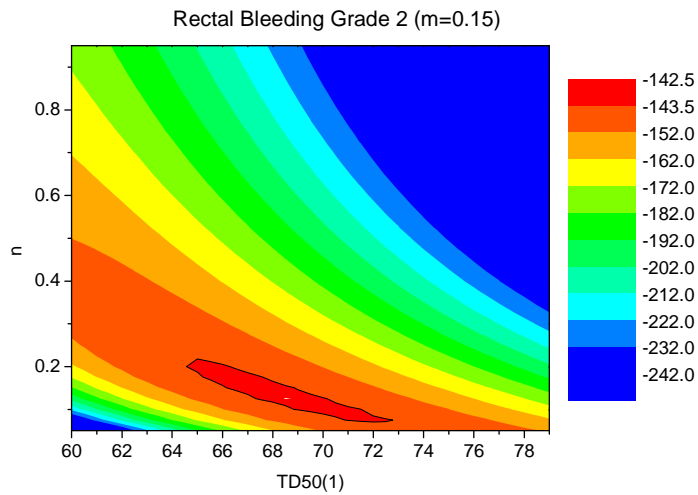


Figure 1a

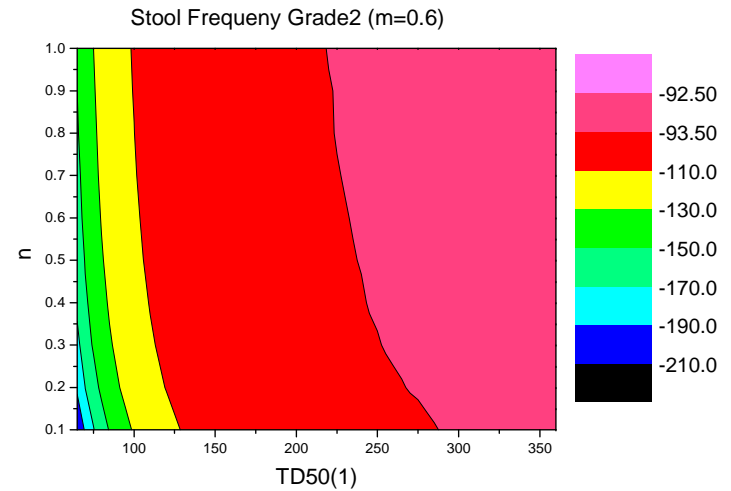


Figure 1b

Figure 1 Maximum Likelihood Estimation values plotted as a function of LKB parameters  $TD50(1)$  and  $n$  with fixed value of  $m$  fitted to a) rectal bleeding and b) stool frequency. Both plots are for the best fit value of  $m$  0.15 and 0.6 respectively. The effect of  $m$  is illustrated with the significant difference in the range of  $TD50(1)$  values displayed on the x axis. The relatively large value of  $m$  observed for stool frequency indicates that clinical data fits poorly to the LKB model resulting in similar MLE estimates for a wide range of  $TD50(1)$  and  $n$  parameters. The deceptively better MLE value for stool frequency results from the small number of Grade 2 cases for stool frequency 29 (vs 54 for rectal bleeding)

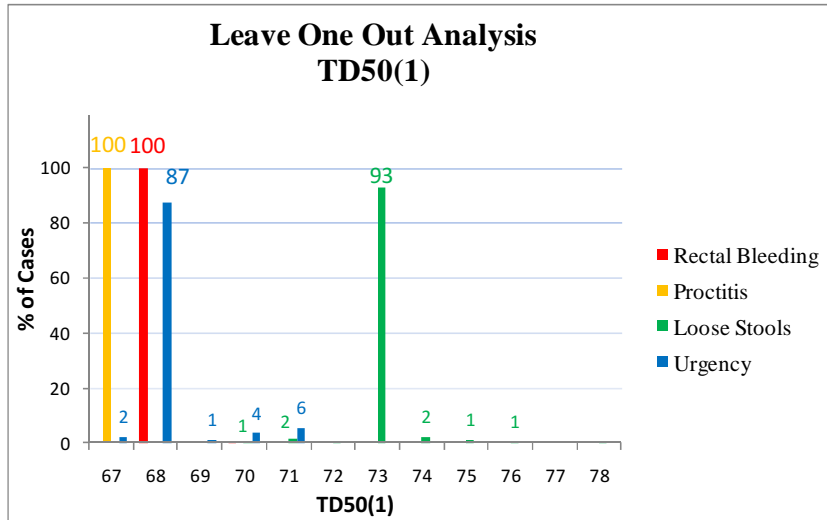


Figure 2a

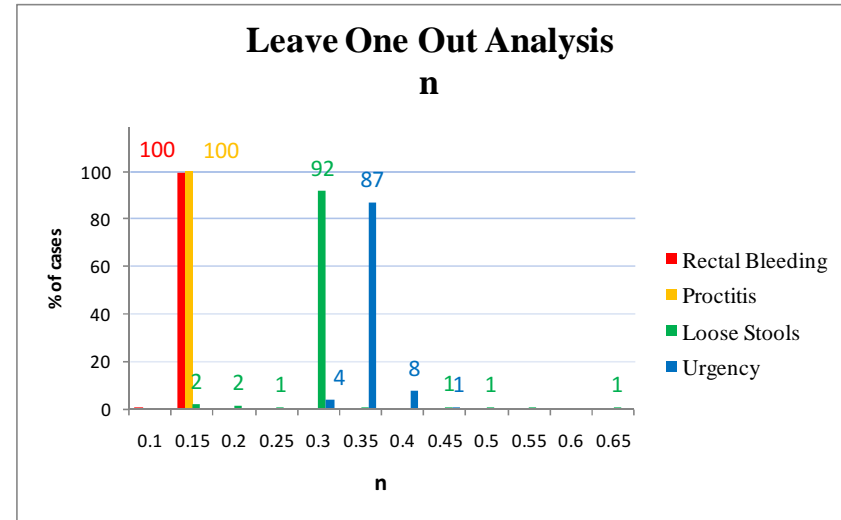


Figure 2c

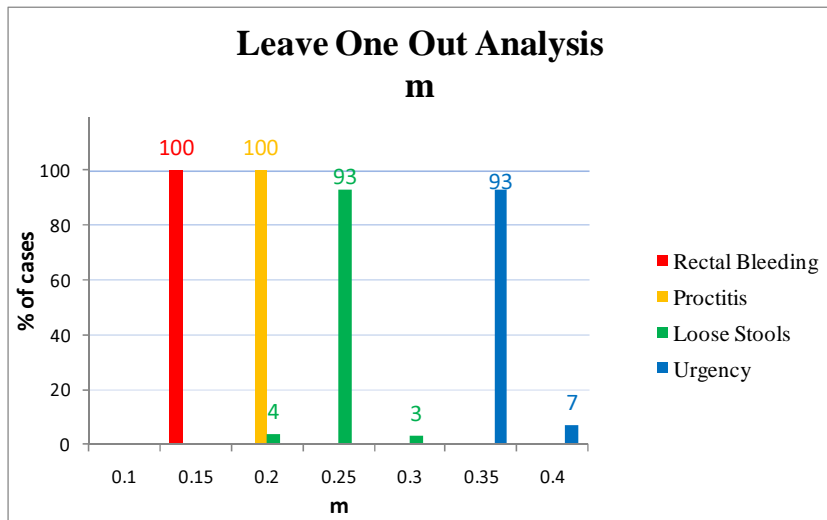


Figure 2b

Figure 2 Distribution of Leave-one-out results obtained using Maximum Likelihood Estimation to fit parameters TD50(1) (a), m(b) and n (c) to the LKB model for specific Grade 2 rectal toxicity endpoints.