

**Figure 1a**

**ANOVA summary**

F 29.06  
P value 0.0001  
P value summary \*\*\*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.9159

**Tukey's multiple comparisons**

|          | Mean Diff. | 95% CI of diff.  | Significant? | Summary |
|----------|------------|------------------|--------------|---------|
| C vs. R  | -1.237     | -16.59 to 14.12  | No           | ns      |
| C vs. T  | -2.627     | -17.98 to 12.73  | No           | ns      |
| C vs. RT | -37.78     | -53.14 to -22.43 | Yes          | ***     |
| R vs. T  | -1.39      | -16.75 to 13.97  | No           | ns      |
| R vs. RT | -36.55     | -51.90 to -21.19 | Yes          | ***     |
| T vs. RT | -35.16     | -50.51 to -19.80 | Yes          | ***     |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q      | DF |
|--------------|--------|--------|------------|-------------|----|----|--------|----|
| C vs. R      | 9.517  | 10.75  | -1.237     | 4.795       | 3  | 3  | 0.3647 | 8  |
| C vs. T      | 9.517  | 12.14  | -2.627     | 4.795       | 3  | 3  | 0.7746 | 8  |
| C vs. RT     | 9.517  | 47.3   | -37.78     | 4.795       | 3  | 3  | 11.14  | 8  |
| R vs. T      | 10.75  | 12.14  | -1.39      | 4.795       | 3  | 3  | 0.4099 | 8  |
| R vs. RT     | 10.75  | 47.3   | -36.55     | 4.795       | 3  | 3  | 10.78  | 8  |
| T vs. RT     | 12.14  | 47.3   | -35.16     | 4.795       | 3  | 3  | 10.37  | 8  |

**Figure 2a**

**APL1**

**ANOVA summary**

F 2.562  
P value 0.0551  
P value summary ns  
Are differences among means statistically significant? (P < 0.05) No  
R square 0.02644

**Tukey's multiple comparisons test**

|             | Mean Diff. | 95% CI of diff.  | Significant? | Summary |
|-------------|------------|------------------|--------------|---------|
| C vs. RA    | 0.3        | -3.516 to 4.116  | No           | ns      |
| C vs. Tm    | 0.4292     | -2.593 to 3.452  | No           | ns      |
| C vs. RATm  | 3.779      | 0.1628 to 7.395  | Yes          | *       |
| RA vs. Tm   | 0.1292     | -3.976 to 4.235  | No           | ns      |
| RA vs. RATm | 3.479      | -1.081 to 8.039  | No           | ns      |
| Tm vs. RATm | 3.349      | -0.5710 to 7.270 | No           | ns      |

**Test details**

|             | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1  | n2 | q      | DF  |
|-------------|--------|--------|------------|-------------|-----|----|--------|-----|
| C vs. RA    | 14.89  | 14.59  | 0.3        | 1.476       | 127 | 39 | 0.2874 | 283 |
| C vs. Tm    | 14.89  | 14.46  | 0.4292     | 1.17        | 127 | 76 | 0.519  | 283 |
| C vs. RATm  | 14.89  | 11.11  | 3.779      | 1.399       | 127 | 45 | 3.819  | 283 |
| RA vs. Tm   | 14.59  | 14.46  | 0.1292     | 1.589       | 39  | 76 | 0.115  | 283 |
| RA vs. RATm | 14.59  | 11.11  | 3.479      | 1.764       | 39  | 45 | 2.788  | 283 |
| Tm vs. RATm | 14.46  | 11.11  | 3.349      | 1.517       | 76  | 45 | 3.123  | 283 |

**APL2**

**ANOVA summary**

F 169.6  
P value < 0.0001  
P value summary \*\*\*\*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.3786

**Tukey's multiple comparisons test**

|             | Mean Diff. | 95% CI of diff.  | Significant? | Summary |
|-------------|------------|------------------|--------------|---------|
| C vs. RA    | 11.85      | 8.656 to 15.04   | Yes          | ****    |
| C vs. Tm    | 0.6887     | -2.698 to 4.076  | No           | ns      |
| C vs. RATm  | 22.63      | 19.68 to 25.58   | Yes          | ****    |
| RA vs. Tm   | -11.16     | -14.59 to -7.731 | Yes          | ****    |
| RA vs. RATm | 10.78      | 7.791 to 13.78   | Yes          | ****    |
| Tm vs. RATm | 21.94      | 18.74 to 25.14   | Yes          | ****    |

**Test details**

|             | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1  | n2  | q      | DF  |
|-------------|--------|--------|------------|-------------|-----|-----|--------|-----|
| C vs. RA    | 31.28  | 19.44  | 11.85      | 1.24        | 208 | 197 | 13.52  | 835 |
| C vs. Tm    | 31.28  | 30.59  | 0.6887     | 1.316       | 208 | 158 | 0.7402 | 835 |
| C vs. RATm  | 31.28  | 8.652  | 22.63      | 1.145       | 208 | 276 | 27.96  | 835 |
| RA vs. Tm   | 19.44  | 30.59  | -11.16     | 1.332       | 197 | 158 | 11.85  | 835 |
| RA vs. RATm | 19.44  | 8.652  | 10.78      | 1.163       | 197 | 276 | 13.11  | 835 |
| Tm vs. RATm | 30.59  | 8.652  | 21.94      | 1.244       | 158 | 276 | 24.95  | 835 |

**APL3**

**ANOVA summary**

F 124.4  
P value < 0.0001  
P value summary \*\*\*\*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.235

**Tukey's multiple comparisons test**

|             | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|-------------|------------|-------------------|--------------|---------|
| C vs. RA    | 9.387      | 7.566 to 11.21    | Yes          | ****    |
| C vs. Tm    | 1.753      | -0.07971 to 3.585 | No           | ns      |
| C vs. RATm  | 11.68      | 9.831 to 13.52    | Yes          | ****    |
| RA vs. Tm   | -7.635     | -9.524 to -5.745  | Yes          | ****    |
| RA vs. RATm | 2.29       | 0.3871 to 4.193   | Yes          | *       |
| Tm vs. RATm | 9.924      | 8.011 to 11.84    | Yes          | ****    |

**Test details**

|             | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1  | n2  | q     | DF   |
|-------------|--------|--------|------------|-------------|-----|-----|-------|------|
| C vs. RA    | 18.95  | 9.56   | 9.387      | 0.7078      | 341 | 300 | 18.76 | 1215 |
| C vs. Tm    | 18.95  | 17.19  | 1.753      | 0.7123      | 341 | 293 | 3.48  | 1215 |
| C vs. RATm  | 18.95  | 7.27   | 11.68      | 0.7176      | 341 | 285 | 23.01 | 1215 |
| RA vs. Tm   | 9.56   | 17.19  | -7.635     | 0.7344      | 300 | 293 | 14.7  | 1215 |
| RA vs. RATm | 9.56   | 7.27   | 2.29       | 0.7396      | 300 | 285 | 4.378 | 1215 |
| Tm vs. RATm | 17.19  | 7.27   | 9.924      | 0.7439      | 293 | 285 | 18.87 | 1215 |

**BM1**  
ANOVA summary

F 13.32  
P value < 0.0001  
P value summary \*\*\*\*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.04786

Tukey's multiple comparisons test

|          | Mean Diff. | 95% CI of diff.  | Significant? | Summary |
|----------|------------|------------------|--------------|---------|
| C vs. R  | 1.665      | -1.432 to 4.762  | No           | ns      |
| C vs. T  | 1.165      | -1.932 to 4.262  | No           | ns      |
| C vs. RT | -5.118     | -8.218 to -2.017 | Yes          | ***     |
| R vs. T  | -0.5       | -3.597 to 2.597  | No           | ns      |
| R vs. RT | -6.783     | -9.883 to -3.682 | Yes          | ****    |
| T vs. RT | -6.283     | -9.383 to -3.182 | Yes          | ****    |

Test details

|          | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1  | n2  | q      | DF  |
|----------|--------|--------|------------|-------------|-----|-----|--------|-----|
| C vs. R  | 27.41  | 25.74  | 1.665      | 1.203       | 200 | 200 | 1.958  | 795 |
| C vs. T  | 27.41  | 26.24  | 1.165      | 1.203       | 200 | 200 | 1.37   | 795 |
| C vs. RT | 27.41  | 32.52  | -5.118     | 1.204       | 200 | 199 | 6.01   | 795 |
| R vs. T  | 25.74  | 26.24  | -0.5       | 1.203       | 200 | 200 | 0.5879 | 795 |
| R vs. RT | 25.74  | 32.52  | -6.783     | 1.204       | 200 | 199 | 7.965  | 795 |
| T vs. RT | 26.24  | 32.52  | -6.283     | 1.204       | 200 | 199 | 7.378  | 795 |

**BM2**  
ANOVA summary

F 2.892  
P value 0.035  
P value summary \*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.01754

Tukey's multiple comparisons test

|             | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|-------------|------------|-------------------|--------------|---------|
| C vs. RA    | 2.24       | -5.128 to 9.608   | No           | ns      |
| C vs. Tm    | 4.683      | -2.743 to 12.11   | No           | ns      |
| C vs. RATm  | -3.292     | -10.66 to 4.077   | No           | ns      |
| RA vs. Tm   | 2.443      | -4.830 to 9.717   | No           | ns      |
| RA vs. RATm | -5.532     | -12.75 to 1.683   | No           | ns      |
| Tm vs. RATm | -7.975     | -15.25 to -0.7015 | Yes          | *       |

Test details

|             | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1  | n2  | q     | DF  |
|-------------|--------|--------|------------|-------------|-----|-----|-------|-----|
| C vs. RA    | 34.72  | 32.48  | 2.24       | 2.858       | 116 | 126 | 1.108 | 486 |
| C vs. Tm    | 34.72  | 30.04  | 4.683      | 2.881       | 116 | 122 | 2.299 | 486 |
| C vs. RATm  | 34.72  | 38.02  | -3.292     | 2.858       | 116 | 126 | 1.629 | 486 |
| RA vs. Tm   | 32.48  | 30.04  | 2.443      | 2.821       | 126 | 122 | 1.225 | 486 |
| RA vs. RATm | 32.48  | 38.02  | -5.532     | 2.799       | 126 | 126 | 2.795 | 486 |
| Tm vs. RATm | 30.04  | 38.02  | -7.975     | 2.821       | 122 | 126 | 3.997 | 486 |

**Figure 3a**

**CHOP**  
ANOVA summary

F 16.22  
P value 0.0002  
P value summary \*\*\*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.8022

| Tukey's multiple comparisons test | Mean Diff. | 95% CI of diff.  | Significant? | Summary |
|-----------------------------------|------------|------------------|--------------|---------|
| C vs. R                           | -2.643     | -9.343 to 4.058  | No           | ns      |
| C vs. T                           | -3.7       | -10.40 to 3.000  | No           | ns      |
| C vs. RT                          | -14.59     | -21.29 to -7.887 | Yes          | ***     |
| R vs. T                           | -1.058     | -7.758 to 5.643  | No           | ns      |
| R vs. RT                          | -11.95     | -18.65 to -5.245 | Yes          | ***     |
| T vs. RT                          | -10.89     | -17.59 to -4.187 | Yes          | **      |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q      | DF |
|--------------|--------|--------|------------|-------------|----|----|--------|----|
| C vs. R      | 1      | 3.643  | -2.643     | 2.257       | 4  | 4  | 1.656  | 12 |
| C vs. T      | 1      | 4.7    | -3.7       | 2.257       | 4  | 4  | 2.319  | 12 |
| C vs. RT     | 1      | 15.59  | -14.59     | 2.257       | 4  | 4  | 9.141  | 12 |
| R vs. T      | 3.643  | 4.7    | -1.058     | 2.257       | 4  | 4  | 0.6627 | 12 |
| R vs. RT     | 3.643  | 15.59  | -11.95     | 2.257       | 4  | 4  | 7.485  | 12 |
| T vs. RT     | 4.7    | 15.59  | -10.89     | 2.257       | 4  | 4  | 6.823  | 12 |

**BiP**  
ANOVA summary

F 14.53  
P value 0.0003  
P value summary \*\*\*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.7841

| Tukey's multiple comparisons test | Mean Diff. | 95% CI of diff.    | Significant? | Summary |
|-----------------------------------|------------|--------------------|--------------|---------|
| C vs. R                           | 0.275      | -1.950 to 2.500    | No           | ns      |
| C vs. T                           | -1.813     | -4.037 to 0.4122   | No           | ns      |
| C vs. RT                          | -4.103     | -6.327 to -1.878   | Yes          | ***     |
| R vs. T                           | -2.088     | -4.312 to 0.1372   | No           | ns      |
| R vs. RT                          | -4.378     | -6.602 to -2.153   | Yes          | ***     |
| T vs. RT                          | -2.29      | -4.515 to -0.06532 | Yes          | *       |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q     | DF |
|--------------|--------|--------|------------|-------------|----|----|-------|----|
| C vs. R      | 1      | 0.725  | 0.275      | 0.7493      | 4  | 4  | 0.519 | 12 |
| C vs. T      | 1      | 2.813  | -1.813     | 0.7493      | 4  | 4  | 3.421 | 12 |
| C vs. RT     | 1      | 5.103  | -4.103     | 0.7493      | 4  | 4  | 7.743 | 12 |
| R vs. T      | 0.725  | 2.813  | -2.088     | 0.7493      | 4  | 4  | 3.94  | 12 |
| R vs. RT     | 0.725  | 5.103  | -4.378     | 0.7493      | 4  | 4  | 8.262 | 12 |
| T vs. RT     | 2.813  | 5.103  | -2.29      | 0.7493      | 4  | 4  | 4.322 | 12 |

**EDEM**  
ANOVA summary

F 8.562  
P value 0.0026  
P value summary \*\*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.6816

| Tukey's multiple comparisons test | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|-----------------------------------|------------|-------------------|--------------|---------|
| C vs. R                           | -0.8175    | -2.314 to 0.6795  | No           | ns      |
| C vs. T                           | -1.065     | -2.562 to 0.4320  | No           | ns      |
| C vs. RT                          | -2.505     | -4.002 to -1.008  | Yes          | **      |
| R vs. T                           | -0.2475    | -1.744 to 1.249   | No           | ns      |
| R vs. RT                          | -1.688     | -3.184 to -0.1905 | Yes          | *       |
| T vs. RT                          | -1.44      | -2.937 to 0.05698 | No           | ns      |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q      | DF |
|--------------|--------|--------|------------|-------------|----|----|--------|----|
| C vs. R      | 1      | 1.818  | -0.8175    | 0.5042      | 4  | 4  | 2.293  | 12 |
| C vs. T      | 1      | 2.065  | -1.065     | 0.5042      | 4  | 4  | 2.987  | 12 |
| C vs. RT     | 1      | 3.505  | -2.505     | 0.5042      | 4  | 4  | 7.026  | 12 |
| R vs. T      | 1.818  | 2.065  | -0.2475    | 0.5042      | 4  | 4  | 0.6942 | 12 |
| R vs. RT     | 1.818  | 3.505  | -1.688     | 0.5042      | 4  | 4  | 4.733  | 12 |
| T vs. RT     | 2.065  | 3.505  | -1.44      | 0.5042      | 4  | 4  | 4.039  | 12 |

**sXBP1**  
ANOVA summary

F 5.415  
P value 0.0137  
P value summary \*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.5751

**Tukey's multiple comparisons test**

|          | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|----------|------------|-------------------|--------------|---------|
| C vs. R  | 0.0725     | -2.568 to 2.713   | No           | ns      |
| C vs. T  | -1.805     | -4.445 to 0.8350  | No           | ns      |
| C vs. RT | -2.933     | -5.573 to -0.2925 | Yes          | *       |
| R vs. T  | -1.878     | -4.518 to 0.7625  | No           | ns      |
| R vs. RT | -3.005     | -5.645 to -0.3650 | Yes          | *       |
| T vs. RT | -1.128     | -3.768 to 1.513   | No           | ns      |

Test details

|          | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q      | DF |
|----------|--------|--------|------------|-------------|----|----|--------|----|
| C vs. R  | 1      | 0.9275 | 0.0725     | 0.8892      | 4  | 4  | 0.1153 | 12 |
| C vs. T  | 1      | 2.805  | -1.805     | 0.8892      | 4  | 4  | 2.871  | 12 |
| C vs. RT | 1      | 3.933  | -2.933     | 0.8892      | 4  | 4  | 4.664  | 12 |
| R vs. T  | 0.9275 | 2.805  | -1.878     | 0.8892      | 4  | 4  | 2.986  | 12 |
| R vs. RT | 0.9275 | 3.933  | -3.005     | 0.8892      | 4  | 4  | 4.779  | 12 |
| T vs. RT | 2.805  | 3.933  | -1.128     | 0.8892      | 4  | 4  | 1.793  | 12 |

**HERP**  
ANOVA summary

F 7.607  
P value 0.0041  
P value summary \*\*  
Are differences among means statistically significant? (P < 0.05) Yes  
R square 0.6554

**Tukey's multiple comparisons test**

|          | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|----------|------------|-------------------|--------------|---------|
| C vs. R  | 0.24       | -3.149 to 3.629   | No           | ns      |
| C vs. T  | -3.678     | -7.066 to -0.2886 | Yes          | *       |
| C vs. RT | -3.785     | -7.174 to -0.3961 | Yes          | *       |
| R vs. T  | -3.918     | -7.306 to -0.5286 | Yes          | *       |
| R vs. RT | -4.025     | -7.414 to -0.6361 | Yes          | *       |
| T vs. RT | -0.1075    | -3.496 to 3.281   | No           | ns      |

Test details

|          | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q      | DF |
|----------|--------|--------|------------|-------------|----|----|--------|----|
| C vs. R  | 1      | 0.76   | 0.24       | 1.141       | 4  | 4  | 0.2973 | 12 |
| C vs. T  | 1      | 4.678  | -3.678     | 1.141       | 4  | 4  | 4.556  | 12 |
| C vs. RT | 1      | 4.785  | -3.785     | 1.141       | 4  | 4  | 4.689  | 12 |
| R vs. T  | 0.76   | 4.678  | -3.918     | 1.141       | 4  | 4  | 4.853  | 12 |
| R vs. RT | 0.76   | 4.785  | -4.025     | 1.141       | 4  | 4  | 4.987  | 12 |
| T vs. RT | 4.678  | 4.785  | -0.1075    | 1.141       | 4  | 4  | 0.1332 | 12 |

**HYOU1**  
ANOVA summary

F 2.752  
P value 0.0887  
P value summary ns  
Are differences among means statistically significant? (P < 0.05) No  
R square 0.4076

**Figure 3e****24hrs****Two-way ANOVA** Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 1.307                | 0.9903  | ns              | No           |
| treatment           | 0.5447               | 0.9973  | ns              | No           |
| genotype            | 0.0123               | 0.9755  | ns              | No           |

**48hrs****Two-way ANOVA** Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 0.8263               | 0.8994  | ns              | No           |
| Row Factor          | 82.97                | 0.0005  | ***             | Yes          |
| Column Factor       | 4.693                | 0.1086  | ns              | No           |

**Sidak's multiple comparisons test**

Mean Diff. 95% CI of diff. Significant? Summary

NSC - shCHOP

|    |        |                 |    |    |
|----|--------|-----------------|----|----|
| C  | -2.1   | -11.55 to 7.347 | No | ns |
| R  | -4.515 | -13.96 to 4.932 | No | ns |
| T  | -1.54  | -10.99 to 7.907 | No | ns |
| RT | -2.53  | -11.98 to 6.917 | No | ns |

**72hrs****Two-way ANOVA** Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 7.946                | 0.5942  | ns              | No           |
| Row Factor          | 59.48                | 0.0304  | *               | Yes          |
| Column Factor       | 0.9233               | 0.642   | ns              | No           |

**Sidak's multiple comparisons test**

Mean Diff. 95% CI of diff. Significant? Summary

NSC - shCHOP

|    |       |                 |    |    |
|----|-------|-----------------|----|----|
| C  | -4.18 | -37.79 to 29.43 | No | ns |
| R  | -3.13 | -36.74 to 30.48 | No | ns |
| T  | 2.895 | -30.71 to 36.50 | No | ns |
| RT | 14.59 | -19.02 to 48.19 | No | ns |

**Figure 4a**

24hrs

Two-way ANOVA Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 32.65                | 0.2444  | ns              | No           |
| treatment           | 24.62                | 0.1256  | ns              | No           |
| inhibitor           | 0.5391               | 0.9266  | ns              | No           |

48hrs

Two-way ANOVA Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 16.39                | 0.2772  | ns              | No           |
| treatment           | 48.45                | 0.0026  | **              | Yes          |
| inhibitor           | 12.43                | 0.073   | ns              | No           |

Tukey's multiple comparisons test

|                   | Mean Diff. | 95% CI of diff. | Significant? | Summary |
|-------------------|------------|-----------------|--------------|---------|
| <b>C</b>          |            |                 |              |         |
| nil vs. GSK       | -4.07      | -28.95 to 20.81 | No           | ns      |
| nil vs. guanabenz | -3.645     | -28.53 to 21.24 | No           | ns      |
| GSK vs. guanabenz | 0.425      | -24.46 to 25.31 | No           | ns      |
| <b>R</b>          |            |                 |              |         |
| nil vs. GSK       | -3.25      | -28.13 to 21.63 | No           | ns      |
| nil vs. guanabenz | -1.15      | -26.03 to 23.73 | No           | ns      |
| GSK vs. guanabenz | 2.1        | -22.78 to 26.98 | No           | ns      |
| <b>T</b>          |            |                 |              |         |
| nil vs. GSK       | -9.575     | -34.46 to 15.31 | No           | ns      |
| nil vs. guanabenz | 2.725      | -22.16 to 27.61 | No           | ns      |
| GSK vs. guanabenz | 12.3       | -12.58 to 37.18 | No           | ns      |
| <b>RT</b>         |            |                 |              |         |
| nil vs. GSK       | -10.3      | -35.18 to 14.58 | No           | ns      |
| nil vs. guanabenz | 22.5       | -2.382 to 47.38 | No           | ns      |
| GSK vs. guanabenz | 32.8       | 7.918 to 57.68  | Yes          | *       |

| Test details      | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q      | DF |
|-------------------|--------|--------|------------|-------------|----|----|--------|----|
| <b>C</b>          |        |        |            |             |    |    |        |    |
| nil vs. GSK       | 10.43  | 14.5   | -4.07      | 9.327       | 2  | 2  | 0.6171 | 12 |
| nil vs. guanabenz | 10.43  | 14.08  | -3.645     | 9.327       | 2  | 2  | 0.5527 | 12 |
| GSK vs. guanabenz | 14.5   | 14.08  | 0.425      | 9.327       | 2  | 2  | 0.0644 | 12 |
| <b>R</b>          |        |        |            |             |    |    |        |    |
| nil vs. GSK       | 18.18  | 21.43  | -3.25      | 9.327       | 2  | 2  | 0.4928 | 12 |
| nil vs. guanabenz | 18.18  | 19.33  | -1.15      | 9.327       | 2  | 2  | 0.1744 | 12 |
| GSK vs. guanabenz | 21.43  | 19.33  | 2.1        | 9.327       | 2  | 2  | 0.3184 | 12 |
| <b>T</b>          |        |        |            |             |    |    |        |    |
| nil vs. GSK       | 15.43  | 25     | -9.575     | 9.327       | 2  | 2  | 1.452  | 12 |
| nil vs. guanabenz | 15.43  | 12.7   | 2.725      | 9.327       | 2  | 2  | 0.4132 | 12 |
| GSK vs. guanabenz | 25     | 12.7   | 12.3       | 9.327       | 2  | 2  | 1.865  | 12 |
| <b>RT</b>         |        |        |            |             |    |    |        |    |
| nil vs. GSK       | 42.38  | 52.68  | -10.3      | 9.327       | 2  | 2  | 1.562  | 12 |
| nil vs. guanabenz | 42.38  | 19.88  | 22.5       | 9.327       | 2  | 2  | 3.412  | 12 |
| GSK vs. guanabenz | 52.68  | 19.88  | 32.8       | 9.327       | 2  | 2  | 4.974  | 12 |

72hrs

## Two-way ANOVA

Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value  | P value summary | Significant? |
|---------------------|----------------------|----------|-----------------|--------------|
| Interaction         | 25.88                | < 0.0001 | ****            | Yes          |
| treatment           | 48.14                | < 0.0001 | ****            | Yes          |
| inhibitor           | 17.2                 | < 0.0001 | ****            | Yes          |

| ANOVA table | SS    | DF | MS    | F (DFn, DFd)      | P value    |
|-------------|-------|----|-------|-------------------|------------|
| Interaction | 5724  | 6  | 953.9 | F (6, 36) = 17.69 | P < 0.0001 |
| treatment   | 10645 | 3  | 3548  | F (3, 36) = 65.79 | P < 0.0001 |
| inhibitor   | 3803  | 2  | 1901  | F (2, 36) = 35.25 | P < 0.0001 |
| Residual    | 1942  | 36 | 53.93 |                   |            |

## Tukey's multiple comparisons test

Mean Diff. 95% CI of diff. Significant? Summary

| Comparison        | Mean Diff. | 95% CI of diff.  | Significant? | Summary |
|-------------------|------------|------------------|--------------|---------|
| <b>C</b>          |            |                  |              |         |
| nil vs. GSK       | 0.1225     | -12.57 to 12.82  | No           | ns      |
| nil vs. guanabenz | 0.195      | -12.50 to 12.89  | No           | ns      |
| GSK vs. guanabenz | 0.0725     | -12.62 to 12.77  | No           | ns      |
| <b>R</b>          |            |                  |              |         |
| nil vs. GSK       | -3.073     | -15.77 to 9.621  | No           | ns      |
| nil vs. guanabenz | -2.123     | -14.82 to 10.57  | No           | ns      |
| GSK vs. guanabenz | 0.95       | -11.74 to 13.64  | No           | ns      |
| <b>T</b>          |            |                  |              |         |
| nil vs. GSK       | -18.27     | -30.96 to -5.572 | Yes          | **      |
| nil vs. guanabenz | 3.305      | -9.388 to 16.00  | No           | ns      |
| GSK vs. guanabenz | 21.57      | 8.877 to 34.26   | Yes          | ***     |
| <b>RT</b>         |            |                  |              |         |
| nil vs. GSK       | -26.04     | -38.73 to -13.34 | Yes          | ****    |
| nil vs. guanabenz | 38.48      | 25.78 to 51.17   | Yes          | ****    |
| GSK vs. guanabenz | 64.51      | 51.82 to 77.21   | Yes          | ****    |

| Test details      | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q      | DF |
|-------------------|--------|--------|------------|-------------|----|----|--------|----|
| <b>C</b>          |        |        |            |             |    |    |        |    |
| nil vs. GSK       | 6.703  | 6.58   | 0.1225     | 5.193       | 4  | 4  | 0.0334 | 36 |
| nil vs. guanabenz | 6.703  | 6.508  | 0.195      | 5.193       | 4  | 4  | 0.0531 | 36 |
| GSK vs. guanabenz | 6.58   | 6.508  | 0.0725     | 5.193       | 4  | 4  | 0.0197 | 36 |
| <b>R</b>          |        |        |            |             |    |    |        |    |
| nil vs. GSK       | 7.318  | 10.39  | -3.073     | 5.193       | 4  | 4  | 0.8367 | 36 |
| nil vs. guanabenz | 7.318  | 9.44   | -2.123     | 5.193       | 4  | 4  | 0.578  | 36 |
| GSK vs. guanabenz | 10.39  | 9.44   | 0.95       | 5.193       | 4  | 4  | 0.2587 | 36 |
| <b>T</b>          |        |        |            |             |    |    |        |    |
| nil vs. GSK       | 9.785  | 28.05  | -18.27     | 5.193       | 4  | 4  | 4.974  | 36 |
| nil vs. guanabenz | 9.785  | 6.48   | 3.305      | 5.193       | 4  | 4  | 0.9001 | 36 |
| GSK vs. guanabenz | 28.05  | 6.48   | 21.57      | 5.193       | 4  | 4  | 5.874  | 36 |
| <b>RT</b>         |        |        |            |             |    |    |        |    |
| nil vs. GSK       | 47.99  | 74.03  | -26.04     | 5.193       | 4  | 4  | 7.091  | 36 |
| nil vs. guanabenz | 47.99  | 9.513  | 38.48      | 5.193       | 4  | 4  | 10.48  | 36 |
| GSK vs. guanabenz | 74.03  | 9.513  | 64.51      | 5.193       | 4  | 4  | 17.57  | 36 |



**Figure 4c**

**CHOP**

**Two-way ANOVA** Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value    | P value summary | Significant? |
|---------------------|----------------------|------------|-----------------|--------------|
| Interaction         | 23.53                | 0.0219 *   | *               | Yes          |
| Row Factor          | 37.93                | 0.0002 *** | ***             | Yes          |
| Column Factor       | 10.26                | 0.0294 *   | *               | Yes          |

**Tukey's multiple comparisons test**

|               | Mean Diff. | 95% CI of diff. | Significant? | Summary |
|---------------|------------|-----------------|--------------|---------|
| <b>C</b>      |            |                 |              |         |
| NIL vs. GUANA | -0.65      | -5.661 to 4.361 | No           | ns      |
| NIL vs. GSK   | -0.82      | -6.422 to 4.782 | No           | ns      |
| GUANA vs. GSK | -0.17      | -5.772 to 5.432 | No           | ns      |
| <b>R</b>      |            |                 |              |         |
| NIL vs. GUANA | -0.9533    | -5.964 to 4.057 | No           | ns      |
| NIL vs. GSK   | -0.1733    | -5.776 to 5.429 | No           | ns      |
| GUANA vs. GSK | 0.78       | -4.822 to 6.382 | No           | ns      |
| <b>T</b>      |            |                 |              |         |
| NIL vs. GUANA | 2.863      | -2.147 to 7.874 | No           | ns      |
| NIL vs. GSK   | 3.36       | -2.242 to 8.962 | No           | ns      |
| GUANA vs. GSK | 0.4967     | -5.106 to 6.099 | No           | ns      |
| <b>RT</b>     |            |                 |              |         |
| NIL vs. GUANA | 9.46       | 4.449 to 14.47  | Yes          | ***     |
| NIL vs. GSK   | 7.208      | 1.606 to 12.81  | Yes          | *       |
| GUANA vs. GSK | -2.252     | -7.854 to 3.351 | No           | ns      |

| Test details  | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q      | DF |
|---------------|--------|--------|------------|-------------|----|----|--------|----|
| <b>C</b>      |        |        |            |             |    |    |        |    |
| NIL vs. GUANA | 1      | 1.65   | -0.65      | 1.981       | 3  | 3  | 0.4641 | 20 |
| NIL vs. GSK   | 1      | 1.82   | -0.82      | 2.214       | 3  | 2  | 0.5237 | 20 |
| GUANA vs. GSK | 1.65   | 1.82   | -0.17      | 2.214       | 3  | 2  | 0.1086 | 20 |
| <b>R</b>      |        |        |            |             |    |    |        |    |
| NIL vs. GUANA | 3.127  | 4.08   | -0.9533    | 1.981       | 3  | 3  | 0.6807 | 20 |
| NIL vs. GSK   | 3.127  | 3.3    | -0.1733    | 2.214       | 3  | 2  | 0.1107 | 20 |
| GUANA vs. GSK | 4.08   | 3.3    | 0.78       | 2.214       | 3  | 2  | 0.4982 | 20 |
| <b>T</b>      |        |        |            |             |    |    |        |    |
| NIL vs. GUANA | 5.12   | 2.257  | 2.863      | 1.981       | 3  | 3  | 2.045  | 20 |
| NIL vs. GSK   | 5.12   | 1.76   | 3.36       | 2.214       | 3  | 2  | 2.146  | 20 |
| GUANA vs. GSK | 2.257  | 1.76   | 0.4967     | 2.214       | 3  | 2  | 0.3172 | 20 |
| <b>RT</b>     |        |        |            |             |    |    |        |    |
| NIL vs. GUANA | 13.6   | 4.143  | 9.46       | 1.981       | 3  | 3  | 6.755  | 20 |
| NIL vs. GSK   | 13.6   | 6.395  | 7.208      | 2.214       | 3  | 2  | 4.604  | 20 |
| GUANA vs. GSK | 4.143  | 6.395  | -2.252     | 2.214       | 3  | 2  | 1.438  | 20 |

BiP

Two-way ANOVA Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value  | P value summary | Significant? |
|---------------------|----------------------|----------|-----------------|--------------|
| Interaction         | 20.62                | 0.0065   | **              | Yes          |
| Row Factor          | 31.67                | < 0.0001 | ****            | Yes          |
| Column Factor       | 27.08                | < 0.0001 | ****            | Yes          |

Tukey's multiple comparisons test

|  | Mean Diff. | 95% CI of diff. | Significant? | Summary |
|--|------------|-----------------|--------------|---------|
|--|------------|-----------------|--------------|---------|

|               |          |                   |     |      |
|---------------|----------|-------------------|-----|------|
| <b>C</b>      |          |                   |     |      |
| NIL vs. GUANA | 0.1767   | -1.504 to 1.858   | No  | ns   |
| NIL vs. GSK   | -0.01667 | -1.698 to 1.664   | No  | ns   |
| GUANA vs. GSK | -0.1933  | -1.874 to 1.488   | No  | ns   |
| <b>R</b>      |          |                   |     |      |
| NIL vs. GUANA | 0.5233   | -1.158 to 2.204   | No  | ns   |
| NIL vs. GSK   | 0.2633   | -1.418 to 1.944   | No  | ns   |
| GUANA vs. GSK | -0.26    | -1.941 to 1.421   | No  | ns   |
| <b>T</b>      |          |                   |     |      |
| NIL vs. GUANA | 2.697    | 1.016 to 4.378    | Yes | **   |
| NIL vs. GSK   | 0.26     | -1.421 to 1.941   | No  | ns   |
| GUANA vs. GSK | -2.437   | -4.118 to -0.7555 | Yes | **   |
| <b>RT</b>     |          |                   |     |      |
| NIL vs. GUANA | 3.993    | 2.312 to 5.674    | Yes | **** |
| NIL vs. GSK   | 1.81     | 0.1289 to 3.491   | Yes | *    |
| GUANA vs. GSK | -2.183   | -3.864 to -0.5022 | Yes | **   |

| Test details  | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q       | DF |
|---------------|--------|--------|------------|-------------|----|----|---------|----|
| <b>C</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 1      | 0.8233 | 0.1767     | 0.6732      | 3  | 3  | 0.3711  | 24 |
| NIL vs. GSK   | 1      | 1.017  | -0.01667   | 0.6732      | 3  | 3  | 0.03501 | 24 |
| GUANA vs. GSK | 0.8233 | 1.017  | -0.1933    | 0.6732      | 3  | 3  | 0.4062  | 24 |
| <b>R</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 1.04   | 0.5167 | 0.5233     | 0.6732      | 3  | 3  | 1.099   | 24 |
| NIL vs. GSK   | 1.04   | 0.7767 | 0.2633     | 0.6732      | 3  | 3  | 0.5532  | 24 |
| GUANA vs. GSK | 0.5167 | 0.7767 | -0.26      | 0.6732      | 3  | 3  | 0.5462  | 24 |
| <b>T</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 3.26   | 0.5633 | 2.697      | 0.6732      | 3  | 3  | 5.665   | 24 |
| NIL vs. GSK   | 3.26   | 3      | 0.26       | 0.6732      | 3  | 3  | 0.5462  | 24 |
| GUANA vs. GSK | 0.5633 | 3      | -2.437     | 0.6732      | 3  | 3  | 5.119   | 24 |
| <b>RT</b>     |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 4.653  | 0.66   | 3.993      | 0.6732      | 3  | 3  | 8.389   | 24 |
| NIL vs. GSK   | 4.653  | 2.843  | 1.81       | 0.6732      | 3  | 3  | 3.802   | 24 |
| GUANA vs. GSK | 0.66   | 2.843  | -2.183     | 0.6732      | 3  | 3  | 4.587   | 24 |

sXBP1

Two-way ANOVA Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 14.59                | 0.4033  | ns              | No           |
| Row Factor          | 15.55                | 0.1032  | ns              | No           |
| Column Factor       | 15.71                | 0.0471  | *               | Yes          |

Tukey's multiple comparisons test

|               | Mean Diff. | 95% CI of diff.    | Significant? | Summary |
|---------------|------------|--------------------|--------------|---------|
| <b>C</b>      |            |                    |              |         |
| NIL vs. GUANA | 0.16       | -6.904 to 7.224    | No           | ns      |
| NIL vs. GSK   | -0.07      | -7.134 to 6.994    | No           | ns      |
| GUANA vs. GSK | -0.23      | -7.294 to 6.834    | No           | ns      |
| <b>R</b>      |            |                    |              |         |
| NIL vs. GUANA | 0.4267     | -6.637 to 7.491    | No           | ns      |
| NIL vs. GSK   | 0.2533     | -6.811 to 7.317    | No           | ns      |
| GUANA vs. GSK | -0.1733    | -7.237 to 6.891    | No           | ns      |
| <b>T</b>      |            |                    |              |         |
| NIL vs. GUANA | 1.96       | -5.104 to 9.024    | No           | ns      |
| NIL vs. GSK   | -5.287     | -12.35 to 1.777    | No           | ns      |
| GUANA vs. GSK | -7.247     | -14.31 to -0.1826  | Yes          | *       |
| <b>RT</b>     |            |                    |              |         |
| NIL vs. GUANA | 2.713      | -4.351 to 9.777    | No           | ns      |
| NIL vs. GSK   | -4.363     | -11.43 to 2.701    | No           | ns      |
| GUANA vs. GSK | -7.077     | -14.14 to -0.01259 | Yes          | *       |

| Test details  | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q       | DF |
|---------------|--------|--------|------------|-------------|----|----|---------|----|
| <b>C</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 1      | 0.84   | 0.16       | 2.829       | 3  | 3  | 0.07999 | 24 |
| NIL vs. GSK   | 1      | 1.07   | -0.07      | 2.829       | 3  | 3  | 0.035   | 24 |
| GUANA vs. GSK | 0.84   | 1.07   | -0.23      | 2.829       | 3  | 3  | 0.115   | 24 |
| <b>R</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 0.9667 | 0.54   | 0.4267     | 2.829       | 3  | 3  | 0.2133  | 24 |
| NIL vs. GSK   | 0.9667 | 0.7133 | 0.2533     | 2.829       | 3  | 3  | 0.1267  | 24 |
| GUANA vs. GSK | 0.54   | 0.7133 | -0.1733    | 2.829       | 3  | 3  | 0.08666 | 24 |
| <b>T</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 2.82   | 0.86   | 1.96       | 2.829       | 3  | 3  | 0.9799  | 24 |
| NIL vs. GSK   | 2.82   | 8.107  | -5.287     | 2.829       | 3  | 3  | 2.643   | 24 |
| GUANA vs. GSK | 0.86   | 8.107  | -7.247     | 2.829       | 3  | 3  | 3.623   | 24 |
| <b>RT</b>     |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 3.283  | 0.57   | 2.713      | 2.829       | 3  | 3  | 1.357   | 24 |
| NIL vs. GSK   | 3.283  | 7.647  | -4.363     | 2.829       | 3  | 3  | 2.181   | 24 |
| GUANA vs. GSK | 0.57   | 7.647  | -7.077     | 2.829       | 3  | 3  | 3.538   | 24 |

ERdj4

Two-way ANOVA Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 9.578                | 0.6499  | ns              | No           |
| Row Factor          | 18.33                | 0.0688  | ns              | No           |
| Column Factor       | 17.62                | 0.0347  | *               | Yes          |

Tukey's multiple comparisons test

|  | Mean Diff. | 95% CI of diff. | Significant? | Summary |
|--|------------|-----------------|--------------|---------|
|--|------------|-----------------|--------------|---------|

|               |          |                 |    |    |
|---------------|----------|-----------------|----|----|
| <b>C</b>      |          |                 |    |    |
| NIL vs. GUANA | -0.08667 | -4.495 to 4.322 | No | ns |
| NIL vs. GSK   | -1.18    | -5.588 to 3.228 | No | ns |
| GUANA vs. GSK | -1.093   | -5.502 to 3.315 | No | ns |

|               |       |                 |    |    |
|---------------|-------|-----------------|----|----|
| <b>R</b>      |       |                 |    |    |
| NIL vs. GUANA | 0.32  | -4.088 to 4.728 | No | ns |
| NIL vs. GSK   | -0.09 | -4.498 to 4.318 | No | ns |
| GUANA vs. GSK | -0.41 | -4.818 to 3.998 | No | ns |

|               |        |                 |    |    |
|---------------|--------|-----------------|----|----|
| <b>T</b>      |        |                 |    |    |
| NIL vs. GUANA | 0.8667 | -3.542 to 5.275 | No | ns |
| NIL vs. GSK   | -2.433 | -6.842 to 1.975 | No | ns |
| GUANA vs. GSK | -3.3   | -7.708 to 1.108 | No | ns |

|               |        |                   |     |    |
|---------------|--------|-------------------|-----|----|
| <b>RT</b>     |        |                   |     |    |
| NIL vs. GUANA | 2.13   | -2.278 to 6.538   | No  | ns |
| NIL vs. GSK   | -2.727 | -7.135 to 1.682   | No  | ns |
| GUANA vs. GSK | -4.857 | -9.265 to -0.4484 | Yes | *  |

| Test details  | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q       | DF |
|---------------|--------|--------|------------|-------------|----|----|---------|----|
| <b>C</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 1      | 1.087  | -0.08667   | 1.765       | 3  | 3  | 0.06943 | 24 |
| NIL vs. GSK   | 1      | 2.18   | -1.18      | 1.765       | 3  | 3  | 0.9454  | 24 |
| GUANA vs. GSK | 1.087  | 2.18   | -1.093     | 1.765       | 3  | 3  | 0.8759  | 24 |
| <b>R</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 1.307  | 0.9867 | 0.32       | 1.765       | 3  | 3  | 0.2564  | 24 |
| NIL vs. GSK   | 1.307  | 1.397  | -0.09      | 1.765       | 3  | 3  | 0.0721  | 24 |
| GUANA vs. GSK | 0.9867 | 1.397  | -0.41      | 1.765       | 3  | 3  | 0.3285  | 24 |
| <b>T</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 2.757  | 1.89   | 0.8667     | 1.765       | 3  | 3  | 0.6943  | 24 |
| NIL vs. GSK   | 2.757  | 5.19   | -2.433     | 1.765       | 3  | 3  | 1.949   | 24 |
| GUANA vs. GSK | 1.89   | 5.19   | -3.3       | 1.765       | 3  | 3  | 2.644   | 24 |
| <b>RT</b>     |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 3.253  | 1.123  | 2.13       | 1.765       | 3  | 3  | 1.706   | 24 |
| NIL vs. GSK   | 3.253  | 5.98   | -2.727     | 1.765       | 3  | 3  | 2.184   | 24 |
| GUANA vs. GSK | 1.123  | 5.98   | -4.857     | 1.765       | 3  | 3  | 3.891   | 24 |

**EDEM**

**Two-way ANOVA** Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 8.777                | 0.6764  | ns              | No           |
| Row Factor          | 17.83                | 0.0639  | ns              | No           |
| Column Factor       | 11.11                | 0.0972  | ns              | No           |

**HERP**

**Two-way ANOVA** Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 15.06                | 0.1207  | ns              | No           |
| Row Factor          | 28.42                | 0.0011  | **              | Yes          |
| Column Factor       | 18.52                | 0.0036  | **              | Yes          |

**Tukey's multiple comparisons test**

|               | Mean Diff. | 95% CI of diff.  | Significant? | Summary |
|---------------|------------|------------------|--------------|---------|
| <b>C</b>      |            |                  |              |         |
| NIL vs. GUANA | 0.02333    | -3.108 to 3.155  | No           | ns      |
| NIL vs. GSK   | -0.21      | -3.342 to 2.922  | No           | ns      |
| GUANA vs. GSK | -0.2333    | -3.581 to 3.115  | No           | ns      |
| <b>R</b>      |            |                  |              |         |
| NIL vs. GUANA | 0.1792     | -2.953 to 3.311  | No           | ns      |
| NIL vs. GSK   | -0.1175    | -3.249 to 3.014  | No           | ns      |
| GUANA vs. GSK | -0.2967    | -3.645 to 3.051  | No           | ns      |
| <b>T</b>      |            |                  |              |         |
| NIL vs. GUANA | 2.637      | -0.4950 to 5.768 | No           | ns      |
| NIL vs. GSK   | -2.333     | -5.465 to 0.7983 | No           | ns      |
| GUANA vs. GSK | -4.97      | -8.318 to -1.622 | Yes          | **      |
| <b>RT</b>     |            |                  |              |         |
| NIL vs. GUANA | 1.883      | -1.248 to 5.015  | No           | ns      |
| NIL vs. GSK   | -2.673     | -5.805 to 0.4583 | No           | ns      |
| GUANA vs. GSK | -4.557     | -7.905 to -1.209 | Yes          | **      |

| Test details  | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q       | DF |
|---------------|--------|--------|------------|-------------|----|----|---------|----|
| <b>C</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 1      | 0.9767 | 0.02333    | 1.266       | 4  | 3  | 0.02607 | 28 |
| NIL vs. GSK   | 1      | 1.21   | -0.21      | 1.266       | 4  | 3  | 0.2346  | 28 |
| GUANA vs. GSK | 0.9767 | 1.21   | -0.2333    | 1.353       | 3  | 3  | 0.2439  | 28 |
| <b>R</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 0.7325 | 0.5533 | 0.1792     | 1.266       | 4  | 3  | 0.2002  | 28 |
| NIL vs. GSK   | 0.7325 | 0.85   | -0.1175    | 1.266       | 4  | 3  | 0.1313  | 28 |
| GUANA vs. GSK | 0.5533 | 0.85   | -0.2967    | 1.353       | 3  | 3  | 0.3101  | 28 |
| <b>T</b>      |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 3.72   | 1.083  | 2.637      | 1.266       | 4  | 3  | 2.946   | 28 |
| NIL vs. GSK   | 3.72   | 6.053  | -2.333     | 1.266       | 4  | 3  | 2.607   | 28 |
| GUANA vs. GSK | 1.083  | 6.053  | -4.97      | 1.353       | 3  | 3  | 5.195   | 28 |
| <b>RT</b>     |        |        |            |             |    |    |         |    |
| NIL vs. GUANA | 2.63   | 0.7467 | 1.883      | 1.266       | 4  | 3  | 2.104   | 28 |
| NIL vs. GSK   | 2.63   | 5.303  | -2.673     | 1.266       | 4  | 3  | 2.987   | 28 |
| GUANA vs. GSK | 0.7467 | 5.303  | -4.557     | 1.353       | 3  | 3  | 4.763   | 28 |

**HYOU1**

**Two-way ANOVA** Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 11.45                | 0.4381  | ns              | No           |
| Row Factor          | 21.31                | 0.0218  | *               | Yes          |
| Column Factor       | 13.21                | 0.0439  | *               | Yes          |

**Tukey's multiple comparisons test**

|  | Mean Diff. | 95% CI of diff. | Significant? | Summary |
|--|------------|-----------------|--------------|---------|
|--|------------|-----------------|--------------|---------|

|               |          |                 |    |    |
|---------------|----------|-----------------|----|----|
| <b>C</b>      |          |                 |    |    |
| NIL vs. GUANA | 0.1      | -2.475 to 2.675 | No | ns |
| NIL vs. GSK   | 0.003333 | -2.572 to 2.579 | No | ns |
| GUANA vs. GSK | -0.09667 | -2.850 to 2.656 | No | ns |

|               |        |                 |    |    |
|---------------|--------|-----------------|----|----|
| <b>R</b>      |        |                 |    |    |
| NIL vs. GUANA | 0.2575 | -2.318 to 2.833 | No | ns |
| NIL vs. GSK   | 0.0975 | -2.478 to 2.673 | No | ns |
| GUANA vs. GSK | -0.16  | -2.913 to 2.593 | No | ns |

|               |        |                   |     |    |
|---------------|--------|-------------------|-----|----|
| <b>T</b>      |        |                   |     |    |
| NIL vs. GUANA | 1.729  | -0.8461 to 4.304  | No  | ns |
| NIL vs. GSK   | -1.248 | -3.823 to 1.328   | No  | ns |
| GUANA vs. GSK | -2.977 | -5.730 to -0.2235 | Yes | *  |

|               |         |                  |    |    |
|---------------|---------|------------------|----|----|
| <b>RT</b>     |         |                  |    |    |
| NIL vs. GUANA | 2.173   | -0.4020 to 4.749 | No | ns |
| NIL vs. GSK   | -0.1833 | -2.759 to 2.392  | No | ns |
| GUANA vs. GSK | -2.357  | -5.110 to 0.3965 | No | ns |

| Test details  | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q        | DF |
|---------------|--------|--------|------------|-------------|----|----|----------|----|
| <b>C</b>      |        |        |            |             |    |    |          |    |
| NIL vs. GUANA | 1      | 0.9    | 0.1        | 1.041       | 4  | 3  | 0.1359   | 28 |
| NIL vs. GSK   | 1      | 0.9967 | 0.003333   | 1.041       | 4  | 3  | 0.004529 | 28 |
| GUANA vs. GSK | 0.9    | 0.9967 | -0.09667   | 1.113       | 3  | 3  | 0.1229   | 28 |
| <b>R</b>      |        |        |            |             |    |    |          |    |
| NIL vs. GUANA | 0.7775 | 0.52   | 0.2575     | 1.041       | 4  | 3  | 0.3499   | 28 |
| NIL vs. GSK   | 0.7775 | 0.68   | 0.0975     | 1.041       | 4  | 3  | 0.1325   | 28 |
| GUANA vs. GSK | 0.52   | 0.68   | -0.16      | 1.113       | 3  | 3  | 0.2034   | 28 |
| <b>T</b>      |        |        |            |             |    |    |          |    |
| NIL vs. GUANA | 2.563  | 0.8333 | 1.729      | 1.041       | 4  | 3  | 2.35     | 28 |
| NIL vs. GSK   | 2.563  | 3.81   | -1.248     | 1.041       | 4  | 3  | 1.695    | 28 |
| GUANA vs. GSK | 0.8333 | 3.81   | -2.977     | 1.113       | 3  | 3  | 3.783    | 28 |
| <b>RT</b>     |        |        |            |             |    |    |          |    |
| NIL vs. GUANA | 2.74   | 0.5667 | 2.173      | 1.041       | 4  | 3  | 2.953    | 28 |
| NIL vs. GSK   | 2.74   | 2.923  | -0.1833    | 1.041       | 4  | 3  | 0.2491   | 28 |
| GUANA vs. GSK | 0.5667 | 2.923  | -2.357     | 1.113       | 3  | 3  | 2.995    | 28 |

### Supplementary Figure S1a

#### ANOVA summary

|   |        |
|---|--------|
| F   | 6.367  |
| P value   | 0.0048 |
| P value summary   | **     |
| Are differences among means statistically significant? (P < 0.05) | Yes    |
| R square  | 0.5442 |

#### Tukey's multiple comparisons test

|          | Mean Diff. | 95% CI of diff.    | Significant? | Summary |
|----------|------------|--------------------|--------------|---------|
| C vs. R  | 0.388      | -0.4877 to 1.264   | No           | ns      |
| C vs. T  | 0.262      | -0.6137 to 1.138   | No           | ns      |
| C vs. RT | 1.26       | 0.3843 to 2.136    | Yes          | **      |
| R vs. T  | -0.126     | -1.002 to 0.7497   | No           | ns      |
| R vs. RT | 0.872      | -0.003682 to 1.748 | No           | ns      |
| T vs. RT | 0.998      | 0.1223 to 1.874    | Yes          | *       |

**Supplementary Figure S1b**

**48hrs**

**ANOVA summary**

|   |        |
|---|--------|
| F   | 5.867  |
| P value   | 0.0602 |
| P value summary   | ns     |
| Are differences among means statistically significant? (P < 0.05) | No     |
| R square  | 0.8148 |

**72hrs**

**ANOVA summary**

|   |        |
|---|--------|
| F   | 27.04  |
| P value   | 0.0041 |
| P value summary   | **     |
| Are differences among means statistically significant? (P < 0.05) | Yes    |
| R square  | 0.953  |

**Tukey's multiple comparisons test**

|          | Mean Diff. | 95% CI of diff.      | Significant? | Summary |
|----------|------------|----------------------|--------------|---------|
| C vs. R  | -0.16      | -0.2958 to -0.02422  | Yes          | *       |
| C vs. T  | -0.145     | -0.2808 to -0.009220 | Yes          | *       |
| C vs. RT | -0.3       | -0.4358 to -0.1642   | Yes          | **      |
| R vs. T  | 0.015      | -0.1208 to 0.1508    | No           | ns      |
| R vs. RT | -0.14      | -0.2758 to -0.004220 | Yes          | *       |
| T vs. RT | -0.155     | -0.2908 to -0.01922  | Yes          | *       |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q     | DF |
|--------------|--------|--------|------------|-------------|----|----|-------|----|
| C vs. R      | 1      | 1.16   | -0.16      | 0.03335     | 2  | 2  | 6.784 | 4  |
| C vs. T      | 1      | 1.145  | -0.145     | 0.03335     | 2  | 2  | 6.148 | 4  |
| C vs. RT     | 1      | 1.3    | -0.3       | 0.03335     | 2  | 2  | 12.72 | 4  |
| R vs. T      | 1.16   | 1.145  | 0.015      | 0.03335     | 2  | 2  | 0.636 | 4  |
| R vs. RT     | 1.16   | 1.3    | -0.14      | 0.03335     | 2  | 2  | 5.936 | 4  |
| T vs. RT     | 1.145  | 1.3    | -0.155     | 0.03335     | 2  | 2  | 6.572 | 4  |



**Supplementary Figure S2c**

**Two-way ANOVA**

| Source of Variation   | % of total variation | P value  | P value summary | Significant? |
|-----------------------|----------------------|----------|-----------------|--------------|
| Interaction cell type | 18.17                | < 0.0001 | ****            | Yes          |
| treatment             | 75.6                 | < 0.0001 | ****            | Yes          |
|                       | 2.342E-06            | > 0.9999 | ns              | No           |

Ordinary

Alpha 0.05

**Tukey's multiple comparisons test**

|                            | Mean Diff. | 95% CI of diff.    | Significant? | Summary |
|----------------------------|------------|--------------------|--------------|---------|
| <b>myeloid progenitors</b> |            |                    |              |         |
| C vs. R                    | 19.43      | 10.66 to 28.19     | Yes          | ****    |
| C vs. T                    | -3.979     | -13.01 to 5.053    | No           | ns      |
| C vs. RT                   | 6.206      | -2.350 to 14.76    | No           | ns      |
| R vs. T                    | -23.4      | -31.81 to -15.00   | Yes          | ****    |
| R vs. RT                   | -13.22     | -21.11 to -5.331   | Yes          | ***     |
| T vs. RT                   | 10.18      | 2.003 to 18.37     | Yes          | **      |
| <b>MF</b>                  |            |                    |              |         |
| C vs. R                    | 17.32      | 8.549 to 26.08     | Yes          | ****    |
| C vs. T                    | 13.09      | 4.056 to 22.12     | Yes          | **      |
| C vs. RT                   | 23.35      | 14.79 to 31.91     | Yes          | ****    |
| R vs. T                    | -4.229     | -12.63 to 4.173    | No           | ns      |
| R vs. RT                   | 6.033      | -1.855 to 13.92    | No           | ns      |
| T vs. RT                   | 10.26      | 2.081 to 18.44     | Yes          | **      |
| <b>granulocytes</b>        |            |                    |              |         |
| C vs. R                    | -36.71     | -45.48 to -27.95   | Yes          | ****    |
| C vs. T                    | -9.107     | -18.14 to -0.07542 | Yes          | *       |
| C vs. RT                   | -29.55     | -38.11 to -20.99   | Yes          | ****    |
| R vs. T                    | 27.61      | 19.20 to 36.01     | Yes          | ****    |
| R vs. RT                   | 7.163      | -0.7258 to 15.05   | No           | ns      |
| T vs. RT                   | -20.44     | -28.62 to -12.26   | Yes          | ****    |

**Test details**

|                            | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q     | DF |
|----------------------------|--------|--------|------------|-------------|----|----|-------|----|
| <b>myeloid progenitors</b> |        |        |            |             |    |    |       |    |
| C vs. R                    | 69.35  | 49.93  | 19.43      | 3.34        | 6  | 8  | 8.226 | 78 |
| C vs. T                    | 69.35  | 73.33  | -3.979     | 3.44        | 6  | 7  | 1.635 | 78 |
| C vs. RT                   | 69.35  | 63.14  | 6.206      | 3.259       | 6  | 9  | 2.693 | 78 |
| R vs. T                    | 49.93  | 73.33  | -23.4      | 3.2         | 8  | 7  | 10.34 | 78 |
| R vs. RT                   | 49.93  | 63.14  | -13.22     | 3.005       | 8  | 9  | 6.222 | 78 |
| T vs. RT                   | 73.33  | 63.14  | 10.18      | 3.116       | 7  | 9  | 4.622 | 78 |
| <b>MF</b>                  |        |        |            |             |    |    |       |    |
| C vs. R                    | 24.12  | 6.8    | 17.32      | 3.34        | 6  | 8  | 7.333 | 78 |
| C vs. T                    | 24.12  | 11.03  | 13.09      | 3.44        | 6  | 7  | 5.38  | 78 |
| C vs. RT                   | 24.12  | 0.7667 | 23.35      | 3.259       | 6  | 9  | 10.13 | 78 |
| R vs. T                    | 6.8    | 11.03  | -4.229     | 3.2         | 8  | 7  | 1.869 | 78 |
| R vs. RT                   | 6.8    | 0.7667 | 6.033      | 3.005       | 8  | 9  | 2.84  | 78 |
| T vs. RT                   | 11.03  | 0.7667 | 10.26      | 3.116       | 7  | 9  | 4.657 | 78 |
| <b>granulocytes</b>        |        |        |            |             |    |    |       |    |
| C vs. R                    | 6.55   | 43.26  | -36.71     | 3.34        | 6  | 8  | 15.55 | 78 |
| C vs. T                    | 6.55   | 15.66  | -9.107     | 3.44        | 6  | 7  | 3.744 | 78 |
| C vs. RT                   | 6.55   | 36.1   | -29.55     | 3.259       | 6  | 9  | 12.82 | 78 |
| R vs. T                    | 43.26  | 15.66  | 27.61      | 3.2         | 8  | 7  | 12.2  | 78 |
| R vs. RT                   | 43.26  | 36.1   | 7.163      | 3.005       | 8  | 9  | 3.371 | 78 |
| T vs. RT                   | 15.66  | 36.1   | -20.44     | 3.116       | 7  | 9  | 9.277 | 78 |

**Supplementary Figure S3a**

**number of colonies**

**ANOVA summary**

|   |    |        |
|---|----|--------|
| F   |    | 0.2812 |
| P value   |    | 0.9441 |
| P value summary   | ns |        |
| Are differences among means statistically significant? (P < 0.05) | No |        |
| R square  |    | 0.1975 |

**Cell number/colony**

**BM1**

**ANOVA summary**

|   |          |        |
|---|----------|--------|
| F   |          | 28.87  |
| P value   | < 0.0001 |        |
| P value summary   | ****     |        |
| Are differences among means statistically significant? (P < 0.05) | Yes      |        |
| R square  |          | 0.1127 |

**Tukey's multiple comparisons test**

| Mean Diff. | 95% CI of diff.          | Significant? | Summary |
|------------|--------------------------|--------------|---------|
| C vs. R    | 1.665 -2.446 to 5.776    | No           | ns      |
| C vs. T    | 1.165 -2.946 to 5.276    | No           | ns      |
| C vs. RT   | -5.118 -9.234 to -1.002  | Yes          | **      |
| C vs. A    | -7.42 -11.53 to -3.309   | Yes          | ****    |
| C vs. RA   | -9.76 -13.87 to -5.649   | Yes          | ****    |
| C vs. TA   | -11.05 -15.16 to -6.934  | Yes          | ****    |
| C vs. RTA  | -8.595 -12.70 to -4.489  | Yes          | ****    |
| R vs. T    | -0.5 -4.611 to 3.611     | No           | ns      |
| R vs. RT   | -6.783 -10.90 to -2.667  | Yes          | ****    |
| R vs. A    | -9.085 -13.20 to -4.974  | Yes          | ****    |
| R vs. RA   | -11.43 -15.54 to -7.314  | Yes          | ****    |
| R vs. TA   | -12.71 -16.82 to -8.599  | Yes          | ****    |
| R vs. RTA  | -10.26 -14.37 to -6.154  | Yes          | ****    |
| T vs. RT   | -6.283 -10.40 to -2.167  | Yes          | ***     |
| T vs. A    | -8.585 -12.70 to -4.474  | Yes          | ****    |
| T vs. RA   | -10.93 -15.04 to -6.814  | Yes          | ****    |
| T vs. TA   | -12.21 -16.32 to -8.099  | Yes          | ****    |
| T vs. RTA  | -9.76 -13.87 to -5.654   | Yes          | ****    |
| RT vs. A   | -2.302 -6.418 to 1.814   | No           | ns      |
| RT vs. RA  | -4.642 -8.758 to -0.5265 | Yes          | *       |
| RT vs. TA  | -5.927 -10.04 to -1.811  | Yes          | ***     |
| RT vs. RTA | -3.477 -7.588 to 0.6334  | No           | ns      |
| A vs. RA   | -2.34 -6.451 to 1.771    | No           | ns      |
| A vs. TA   | -3.625 -7.736 to 0.4857  | No           | ns      |
| A vs. RTA  | -1.175 -5.281 to 2.931   | No           | ns      |
| RA vs. TA  | -1.285 -5.396 to 2.826   | No           | ns      |
| RA vs. RTA | 1.165 -2.941 to 5.271    | No           | ns      |
| TA vs. RTA | 2.45 -1.656 to 6.556     | No           | ns      |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1  | n2  | q      | DF   |
|--------------|--------|--------|------------|-------------|-----|-----|--------|------|
| C vs. R      | 27.41  | 25.74  | 1.665      | 1.354       | 200 | 200 | 1.738  | 1592 |
| C vs. T      | 27.41  | 26.24  | 1.165      | 1.354       | 200 | 200 | 1.216  | 1592 |
| C vs. RT     | 27.41  | 32.52  | -5.118     | 1.356       | 200 | 199 | 5.337  | 1592 |
| C vs. A      | 27.41  | 34.83  | -7.42      | 1.354       | 200 | 200 | 7.747  | 1592 |
| C vs. RA     | 27.41  | 37.17  | -9.76      | 1.354       | 200 | 200 | 10.19  | 1592 |
| C vs. TA     | 27.41  | 38.45  | -11.05     | 1.354       | 200 | 200 | 11.53  | 1592 |
| C vs. RTA    | 27.41  | 36     | -8.595     | 1.353       | 200 | 201 | 8.985  | 1592 |
| R vs. T      | 25.74  | 26.24  | -0.5       | 1.354       | 200 | 200 | 0.5221 | 1592 |
| R vs. RT     | 25.74  | 32.52  | -6.783     | 1.356       | 200 | 199 | 7.073  | 1592 |
| R vs. A      | 25.74  | 34.83  | -9.085     | 1.354       | 200 | 200 | 9.486  | 1592 |
| R vs. RA     | 25.74  | 37.17  | -11.43     | 1.354       | 200 | 200 | 11.93  | 1592 |
| R vs. TA     | 25.74  | 38.45  | -12.71     | 1.354       | 200 | 200 | 13.27  | 1592 |
| R vs. RTA    | 25.74  | 36     | -10.26     | 1.353       | 200 | 201 | 10.73  | 1592 |
| T vs. RT     | 26.24  | 32.52  | -6.283     | 1.356       | 200 | 199 | 6.551  | 1592 |
| T vs. A      | 26.24  | 34.83  | -8.585     | 1.354       | 200 | 200 | 8.964  | 1592 |
| T vs. RA     | 26.24  | 37.17  | -10.93     | 1.354       | 200 | 200 | 11.41  | 1592 |
| T vs. TA     | 26.24  | 38.45  | -12.21     | 1.354       | 200 | 200 | 12.75  | 1592 |
| T vs. RTA    | 26.24  | 36     | -9.76      | 1.353       | 200 | 201 | 10.2   | 1592 |
| RT vs. A     | 32.52  | 34.83  | -2.302     | 1.356       | 199 | 200 | 2.401  | 1592 |
| RT vs. RA    | 32.52  | 37.17  | -4.642     | 1.356       | 199 | 200 | 4.841  | 1592 |
| RT vs. TA    | 32.52  | 38.45  | -5.927     | 1.356       | 199 | 200 | 6.181  | 1592 |
| RT vs. RTA   | 32.52  | 36     | -3.477     | 1.354       | 199 | 201 | 3.631  | 1592 |
| A vs. RA     | 34.83  | 37.17  | -2.34      | 1.354       | 200 | 200 | 2.443  | 1592 |
| A vs. TA     | 34.83  | 38.45  | -3.625     | 1.354       | 200 | 200 | 3.785  | 1592 |
| A vs. RTA    | 34.83  | 36     | -1.175     | 1.353       | 200 | 201 | 1.228  | 1592 |
| RA vs. TA    | 37.17  | 38.45  | -1.285     | 1.354       | 200 | 200 | 1.342  | 1592 |
| RA vs. RTA   | 37.17  | 36     | 1.165      | 1.353       | 200 | 201 | 1.218  | 1592 |
| TA vs. RTA   | 38.45  | 36     | 2.45       | 1.353       | 200 | 201 | 2.561  | 1592 |

**BM2**  
**ANOVA summary**

|   |         |
|---|---------|
| F   | 3.419   |
| P value   | 0.0013  |
| P value summary   | **      |
| Are differences among means statistically significant? (P < 0.05) | Yes     |
| R square  | 0.02498 |

| Tukey's multiple comparisons test | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|-----------------------------------|------------|-------------------|--------------|---------|
| C vs. R                           | 2.24       | -6.048 to 10.53   | No           | ns      |
| C vs. T                           | 4.683      | -3.670 to 13.04   | No           | ns      |
| C vs. RT                          | -3.292     | -11.58 to 4.997   | No           | ns      |
| C vs. A                           | -2.117     | -10.41 to 6.171   | No           | ns      |
| C vs. RA                          | 5.678      | -2.549 to 13.90   | No           | ns      |
| C vs. TA                          | -0.3686    | -9.231 to 8.494   | No           | ns      |
| C vs. RTA                         | -3.973     | -12.79 to 4.841   | No           | ns      |
| R vs. T                           | 2.443      | -5.738 to 10.62   | No           | ns      |
| R vs. RT                          | -5.532     | -13.65 to 2.583   | No           | ns      |
| R vs. A                           | -4.357     | -12.47 to 3.758   | No           | ns      |
| R vs. RA                          | 3.438      | -4.615 to 11.49   | No           | ns      |
| R vs. TA                          | -2.609     | -11.31 to 6.092   | No           | ns      |
| R vs. RTA                         | -6.213     | -14.86 to 2.438   | No           | ns      |
| T vs. RT                          | -7.975     | -16.16 to 0.2066  | No           | ns      |
| T vs. A                           | -6.8       | -14.98 to 1.381   | No           | ns      |
| T vs. RA                          | 0.9948     | -7.125 to 9.114   | No           | ns      |
| T vs. TA                          | -5.052     | -13.81 to 3.711   | No           | ns      |
| T vs. RTA                         | -8.656     | -17.37 to 0.05707 | No           | ns      |
| RT vs. A                          | 1.175      | -6.941 to 9.290   | No           | ns      |
| RT vs. RA                         | 8.97       | 0.9171 to 17.02   | Yes          | *       |
| RT vs. TA                         | 2.923      | -5.778 to 11.62   | No           | ns      |
| RT vs. RTA                        | -0.6811    | -9.332 to 7.970   | No           | ns      |
| A vs. RA                          | 7.795      | -0.2575 to 15.85  | No           | ns      |
| A vs. TA                          | 1.748      | -6.952 to 10.45   | No           | ns      |
| A vs. RTA                         | -1.856     | -10.51 to 6.795   | No           | ns      |
| RA vs. TA                         | -6.047     | -14.69 to 2.596   | No           | ns      |
| RA vs. RTA                        | -9.651     | -18.24 to -1.059  | Yes          | *       |
| TA vs. RTA                        | -3.604     | -12.81 to 5.598   | No           | ns      |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1  | n2  | q      | DF  |
|--------------|--------|--------|------------|-------------|-----|-----|--------|-----|
| C vs. R      | 34.72  | 32.48  | 2.24       | 2.728       | 116 | 126 | 1.161  | 934 |
| C vs. T      | 34.72  | 30.04  | 4.683      | 2.75        | 116 | 122 | 2.409  | 934 |
| C vs. RT     | 34.72  | 38.02  | -3.292     | 2.728       | 116 | 126 | 1.706  | 934 |
| C vs. A      | 34.72  | 36.84  | -2.117     | 2.728       | 116 | 126 | 1.097  | 934 |
| C vs. RA     | 34.72  | 29.05  | 5.678      | 2.708       | 116 | 130 | 2.965  | 934 |
| C vs. TA     | 34.72  | 35.09  | -0.3686    | 2.917       | 116 | 97  | 0.1787 | 934 |
| C vs. RTA    | 34.72  | 38.7   | -3.973     | 2.901       | 116 | 99  | 1.937  | 934 |
| R vs. T      | 32.48  | 30.04  | 2.443      | 2.693       | 126 | 122 | 1.283  | 934 |
| R vs. RT     | 32.48  | 38.02  | -5.532     | 2.671       | 126 | 126 | 2.928  | 934 |
| R vs. A      | 32.48  | 36.84  | -4.357     | 2.671       | 126 | 126 | 2.307  | 934 |
| R vs. RA     | 32.48  | 29.05  | 3.438      | 2.651       | 126 | 130 | 1.834  | 934 |
| R vs. TA     | 32.48  | 35.09  | -2.609     | 2.864       | 126 | 97  | 1.288  | 934 |
| R vs. RTA    | 32.48  | 38.7   | -6.213     | 2.848       | 126 | 99  | 3.085  | 934 |
| T vs. RT     | 30.04  | 38.02  | -7.975     | 2.693       | 122 | 126 | 4.188  | 934 |
| T vs. A      | 30.04  | 36.84  | -6.8       | 2.693       | 122 | 126 | 3.571  | 934 |
| T vs. RA     | 30.04  | 29.05  | 0.9948     | 2.673       | 122 | 130 | 0.5264 | 934 |
| T vs. TA     | 30.04  | 35.09  | -5.052     | 2.884       | 122 | 97  | 2.477  | 934 |
| T vs. RTA    | 30.04  | 38.7   | -8.656     | 2.868       | 122 | 99  | 4.268  | 934 |
| RT vs. A     | 38.02  | 36.84  | 1.175      | 2.671       | 126 | 126 | 0.6218 | 934 |
| RT vs. RA    | 38.02  | 29.05  | 8.97       | 2.651       | 126 | 130 | 4.785  | 934 |
| RT vs. TA    | 38.02  | 35.09  | 2.923      | 2.864       | 126 | 97  | 1.443  | 934 |
| RT vs. RTA   | 38.02  | 38.7   | -0.6811    | 2.848       | 126 | 99  | 0.3382 | 934 |
| A vs. RA     | 36.84  | 29.05  | 7.795      | 2.651       | 126 | 130 | 4.159  | 934 |
| A vs. TA     | 36.84  | 35.09  | 1.748      | 2.864       | 126 | 97  | 0.8633 | 934 |
| A vs. RTA    | 36.84  | 38.7   | -1.856     | 2.848       | 126 | 99  | 0.9216 | 934 |
| RA vs. TA    | 29.05  | 35.09  | -6.047     | 2.845       | 130 | 97  | 3.006  | 934 |
| RA vs. RTA   | 29.05  | 38.7   | -9.651     | 2.828       | 130 | 99  | 4.825  | 934 |
| TA vs. RTA   | 35.09  | 38.7   | -3.604     | 3.029       | 97  | 99  | 1.683  | 934 |

**Supplementary Figure S3c**

**% SYTOX blue positive cells**

**ANOVA summary**

|   |        |
|---|--------|
| F   | 3.015  |
| P value   | 0.0724 |
| P value summary   | ns     |
| Are differences among means statistically significant? (P < 0.05) | No     |
| R square  | 0.7252 |

**Supplementary Figure S3d****% SYTOX blue positive cells****ANOVA summary**

|   |        |
|---|--------|
| F   | 1.906  |
| P value   | 0.1927 |
| P value summary   | ns     |
| Are differences among means statistically significant? (P < 0.05) | No     |
| R square  | 0.6252 |

**% lymphocytes****ANOVA summary**

|   |        |
|---|--------|
| F   | 0.6675 |
| P value   | 0.6963 |
| P value summary   | ns     |
| Are differences among means statistically significant? (P < 0.05) | No     |
| R square  | 0.3687 |

**% CD11b+/CD14+****ANOVA summary**

|   |        |
|---|--------|
| F   | 0.6283 |
| P value   | 0.7231 |
| P value summary   | ns     |
| Are differences among means statistically significant? (P < 0.05) | No     |
| R square  | 0.3547 |

**% CD11b+****ANOVA summary**

|   |        |
|---|--------|
| F   | 1.505  |
| P value   | 0.2885 |
| P value summary   | ns     |
| Are differences among means statistically significant? (P < 0.05) | No     |
| R square  | 0.5684 |

**Supplementary Figure S4a**

**Two-way ANOVA**

Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value | P value summary | Significant? |
|---------------------|----------------------|---------|-----------------|--------------|
| Interaction         | 13.5                 | 0.099   | ns              | No           |
| Treatment           | 61.63                | 0.0017  | **              | Yes          |
| NSCvsshCHOP         | 12.61                | 0.0209  | *               | Yes          |

| ANOVA table | SS    | DF | MS    | F (DFn, DFd)     | P value    |
|-------------|-------|----|-------|------------------|------------|
| Interaction | 93.41 | 3  | 31.14 | F (3, 8) = 2.939 | P = 0.0990 |
| Treatment   | 426.4 | 3  | 142.1 | F (3, 8) = 13.41 | P = 0.0017 |
| NSCvsshCHOP | 87.24 | 1  | 87.24 | F (1, 8) = 8.233 | P = 0.0209 |
| Residual    | 84.77 | 8  | 10.6  |                  |            |

Compare each cell mean with the other cell mean in that row.

Number of families 1  
Number of comparisons per family 4  
Alpha 0.05

**Sidak's multiple comparisons test**

|              | Mean Diff. | 95% CI of diff. | Significant? | Summary |
|--------------|------------|-----------------|--------------|---------|
| NSC - shCHOP |            |                 |              |         |
| C            | -0.085     | -10.48 to 10.31 | No           | ns      |
| R            | 0.22       | -10.17 to 10.61 | No           | ns      |
| T            | 7.195      | -3.199 to 17.59 | No           | ns      |
| RT           | 11.35      | 0.9557 to 21.74 | Yes          | *       |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | t       | DF |
|--------------|--------|--------|------------|-------------|----|----|---------|----|
| NSC - shCHOP |        |        |            |             |    |    |         |    |
| C            | 1      | 1.085  | -0.085     | 3.255       | 2  | 2  | 0.02611 | 8  |
| R            | 2.555  | 2.335  | 0.22       | 3.255       | 2  | 2  | 0.06759 | 8  |
| T            | 9.585  | 2.39   | 7.195      | 3.255       | 2  | 2  | 2.21    | 8  |
| RT           | 20.01  | 8.655  | 11.35      | 3.255       | 2  | 2  | 3.487   | 8  |

**Supplementary Figure S4b**

**Two-way ANOVA**

| Two-way ANOVA       |                      | Ordinary |                 |                  |            |
|---------------------|----------------------|----------|-----------------|------------------|------------|
| Alpha               |                      | 0.05     |                 |                  |            |
| Source of Variation | % of total variation | P value  | P value summary | Significant?     |            |
| Interaction         | 5.983                | 0.0047   | **              | Yes              |            |
| Treatments          | 84.6                 | < 0.0001 | ****            | Yes              |            |
| Duplicates          | 7.786                | 0.0003   | ***             | Yes              |            |
| ANOVA table         | SS                   | DF       | MS              | F (DFn, DFd)     | P value    |
| Interaction         | 4.65                 | 3        | 1.55            | F (3, 8) = 9.803 | P = 0.0047 |
| Treatments          | 65.75                | 3        | 21.92           | F (3, 8) = 138.6 | P < 0.0001 |
| Duplicates          | 6.052                | 1        | 6.052           | F (1, 8) = 38.27 | P = 0.0003 |
| Residual            | 1.265                | 8        | 0.1581          |                  |            |

Compare each cell mean with the other cell mean in that row.

|                                  |      |
|----------------------------------|------|
| Number of families               | 1    |
| Number of comparisons per family | 4    |
| Alpha                            | 0.05 |

**Sidak's multiple comparisons test**

|              | Mean Diff. | 95% CI of diff. | Significant? | Summary |
|--------------|------------|-----------------|--------------|---------|
| NSC - shCHOP |            |                 |              |         |
| C            | 0.205      | -1.065 to 1.475 | No           | ns      |
| R            | 0.165      | -1.105 to 1.435 | No           | ns      |
| T            | 1.9        | 0.6303 to 3.170 | Yes          | **      |
| RT           | 2.65       | 1.380 to 3.920  | Yes          | ***     |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | t      | DF |
|--------------|--------|--------|------------|-------------|----|----|--------|----|
| NSC - shCHOP |        |        |            |             |    |    |        |    |
| C            | 1      | 0.795  | 0.205      | 0.3976      | 2  | 2  | 0.5156 | 8  |
| R            | 1.21   | 1.045  | 0.165      | 0.3976      | 2  | 2  | 0.415  | 8  |
| T            | 3.1    | 1.2    | 1.9        | 0.3976      | 2  | 2  | 4.778  | 8  |
| RT           | 7.27   | 4.62   | 2.65       | 0.3976      | 2  | 2  | 6.664  | 8  |

|                       |                      |                       |                    |
|-----------------------|----------------------|-----------------------|--------------------|
| Column D vs. Column C | RT shCHOP vs. RT NSC | Column B vs. Column A | T shCHOP vs. T NSC |
|-----------------------|----------------------|-----------------------|--------------------|

**Unpaired t test**

|                                     |              |
|-------------------------------------|--------------|
| P value                             | 0.0447       |
| P value summary                     | *            |
| Significantly different? (P < 0.05) | Yes          |
| One- or two-tailed P value?         | Two-tailed   |
| t, df                               | t=4.570 df=2 |

**Unpaired t test**

|                                     |              |
|-------------------------------------|--------------|
| P value                             | 0.0444       |
| P value summary                     | *            |
| Significantly different? (P < 0.05) | Yes          |
| One- or two-tailed P value?         | Two-tailed   |
| t, df                               | t=4.585 df=2 |

**Supplementary Figure S7a-NB4**

**Two-way ANOVA** Ordinary  
Alpha 0.05

| Source of Variation | % of total variation | P value        | P value summary | Significant? |
|---------------------|----------------------|----------------|-----------------|--------------|
| Interaction         |                      | 26.4 < 0.0001  | ****            | Yes          |
| Row Factor          |                      | 43.99 < 0.0001 | ****            | Yes          |
| Column Factor       |                      | 23.91 < 0.0001 | ****            | Yes          |

  

| ANOVA table   | SS    | DF | MS    | F (DFn, DFd)       | P value    |
|---------------|-------|----|-------|--------------------|------------|
| Interaction   | 14043 | 22 | 638.3 | F (22, 36) = 7.572 | P < 0.0001 |
| Row Factor    | 23404 | 11 | 2128  | F (11, 36) = 25.24 | P < 0.0001 |
| Column Factor | 12718 | 2  | 6359  | F (2, 36) = 75.43  | P < 0.0001 |
| Residual      | 3035  | 36 | 84.3  |                    |            |

**Dunnnett's multiple comparisons test** Mean Diff. 95% CI of diff. Significant? Summary

|               |        |                  |     |      |  |
|---------------|--------|------------------|-----|------|--|
| <b>C</b>      |        |                  |     |      |  |
| nil vs. GSK   | 0.425  | -20.71 to 21.56  | No  | ns   |  |
| nil vs. guana | 1.24   | -19.90 to 22.38  | No  | ns   |  |
| <b>R</b>      |        |                  |     |      |  |
| nil vs. GSK   | -0.72  | -21.86 to 20.42  | No  | ns   |  |
| nil vs. guana | -0.445 | -21.58 to 20.69  | No  | ns   |  |
| <b>T</b>      |        |                  |     |      |  |
| nil vs. GSK   | -17.83 | -38.97 to 3.307  | No  | ns   |  |
| nil vs. guana | 3.645  | -17.49 to 24.78  | No  | ns   |  |
| <b>RT</b>     |        |                  |     |      |  |
| nil vs. GSK   | -35.25 | -56.39 to -14.11 | Yes | ***  |  |
| nil vs. guana | 36.75  | 15.61 to 57.89   | Yes | ***  |  |
| <b>A200</b>   |        |                  |     |      |  |
| nil vs. GSK   | -0.17  | -21.31 to 20.97  | No  | ns   |  |
| nil vs. guana | 0.25   | -20.89 to 21.39  | No  | ns   |  |
| <b>A500</b>   |        |                  |     |      |  |
| nil vs. GSK   | -0.64  | -21.78 to 20.50  | No  | ns   |  |
| nil vs. guana | 5.205  | -15.93 to 26.34  | No  | ns   |  |
| <b>RA200</b>  |        |                  |     |      |  |
| nil vs. GSK   | -0.855 | -21.99 to 20.28  | No  | ns   |  |
| nil vs. guana | 0.16   | -20.98 to 21.30  | No  | ns   |  |
| <b>RA500</b>  |        |                  |     |      |  |
| nil vs. GSK   | 3.1    | -18.04 to 24.24  | No  | ns   |  |
| nil vs. guana | 10.98  | -10.16 to 32.12  | No  | ns   |  |
| <b>TA200</b>  |        |                  |     |      |  |
| nil vs. GSK   | -41.8  | -62.94 to -20.66 | Yes | ***  |  |
| nil vs. guana | 18.26  | -2.882 to 39.39  | No  | ns   |  |
| <b>TA500</b>  |        |                  |     |      |  |
| nil vs. GSK   | -37.1  | -58.24 to -15.96 | Yes | ***  |  |
| nil vs. guana | 52.04  | 30.90 to 73.17   | Yes | **** |  |
| <b>RTA200</b> |        |                  |     |      |  |
| nil vs. GSK   | -25.2  | -46.34 to -4.063 | Yes | *    |  |
| nil vs. guana | 30.09  | 8.948 to 51.22   | Yes | **   |  |
| <b>RTA500</b> |        |                  |     |      |  |
| nil vs. GSK   | -25.85 | -46.99 to -4.713 | Yes | *    |  |
| nil vs. guana | 50.32  | 29.18 to 71.45   | Yes | **** |  |

| Test details  | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q       | DF |
|---------------|--------|--------|------------|-------------|----|----|---------|----|
| <b>C</b>      |        |        |            |             |    |    |         |    |
| nil vs. GSK   | 5.555  | 5.13   | 0.425      | 9.182       | 2  | 2  | 0.04629 | 36 |
| nil vs. guana | 5.555  | 4.315  | 1.24       | 9.182       | 2  | 2  | 0.1351  | 36 |
| <b>R</b>      |        |        |            |             |    |    |         |    |
| nil vs. GSK   | 3.735  | 4.455  | -0.72      | 9.182       | 2  | 2  | 0.07842 | 36 |
| nil vs. guana | 3.735  | 4.18   | -0.445     | 9.182       | 2  | 2  | 0.04847 | 36 |
| <b>T</b>      |        |        |            |             |    |    |         |    |
| nil vs. GSK   | 7.77   | 25.6   | -17.83     | 9.182       | 2  | 2  | 1.942   | 36 |
| nil vs. guana | 7.77   | 4.125  | 3.645      | 9.182       | 2  | 2  | 0.397   | 36 |
| <b>RT</b>     |        |        |            |             |    |    |         |    |
| nil vs. GSK   | 40.85  | 76.1   | -35.25     | 9.182       | 2  | 2  | 3.839   | 36 |
| nil vs. guana | 40.85  | 4.1    | 36.75      | 9.182       | 2  | 2  | 4.003   | 36 |
| <b>A200</b>   |        |        |            |             |    |    |         |    |
| nil vs. GSK   | 4.255  | 4.425  | -0.17      | 9.182       | 2  | 2  | 0.01852 | 36 |
| nil vs. guana | 4.255  | 4.005  | 0.25       | 9.182       | 2  | 2  | 0.02723 | 36 |



|               |       |       |        |       |   |   |         |    |  |
|---------------|-------|-------|--------|-------|---|---|---------|----|--|
| A500          |       |       |        |       |   |   |         |    |  |
| nil vs. GSK   | 10.19 | 10.83 | -0.64  | 9.182 | 2 | 2 | 0.0697  | 36 |  |
| nil vs. guana | 10.19 | 4.985 | 5.205  | 9.182 | 2 | 2 | 0.5669  | 36 |  |
| RA200         |       |       |        |       |   |   |         |    |  |
| nil vs. GSK   | 4.42  | 5.275 | -0.855 | 9.182 | 2 | 2 | 0.09312 | 36 |  |
| nil vs. guana | 4.42  | 4.26  | 0.16   | 9.182 | 2 | 2 | 0.01743 | 36 |  |
| RA500         |       |       |        |       |   |   |         |    |  |
| nil vs. GSK   | 18.45 | 15.35 | 3.1    | 9.182 | 2 | 2 | 0.3376  | 36 |  |
| nil vs. guana | 18.45 | 7.47  | 10.98  | 9.182 | 2 | 2 | 1.196   | 36 |  |
| TA200         |       |       |        |       |   |   |         |    |  |
| nil vs. GSK   | 22.1  | 63.9  | -41.8  | 9.182 | 2 | 2 | 4.553   | 36 |  |
| nil vs. guana | 22.1  | 3.845 | 18.26  | 9.182 | 2 | 2 | 1.988   | 36 |  |
| TA500         |       |       |        |       |   |   |         |    |  |
| nil vs. GSK   | 57.55 | 94.65 | -37.1  | 9.182 | 2 | 2 | 4.041   | 36 |  |
| nil vs. guana | 57.55 | 5.515 | 52.04  | 9.182 | 2 | 2 | 5.667   | 36 |  |
| RTA200        |       |       |        |       |   |   |         |    |  |
| nil vs. GSK   | 33.8  | 59    | -25.2  | 9.182 | 2 | 2 | 2.745   | 36 |  |
| nil vs. guana | 33.8  | 3.715 | 30.09  | 9.182 | 2 | 2 | 3.277   | 36 |  |
| RTA500        |       |       |        |       |   |   |         |    |  |
| nil vs. GSK   | 60.2  | 86.05 | -25.85 | 9.182 | 2 | 2 | 2.815   | 36 |  |
| nil vs. guana | 60.2  | 9.885 | 50.32  | 9.182 | 2 | 2 | 5.48    | 36 |  |

**Supplementary Figure S7a-NB4-R4**

**Two-way ANOVA**

| Two-way ANOVA       |                 | Ordinary |                                    |
|---------------------|-----------------|----------|------------------------------------|
| Alpha               |                 | 0.05     |                                    |
| Source of Variation | % of total vari | P value  | P value summ Significant?          |
| Interaction         | 28.78           | < 0.0001 | **** Yes                           |
| treatments          | 44.71           | < 0.0001 | **** Yes                           |
| duplicates          | 26.13           | < 0.0001 | **** Yes                           |
| ANOVA table         | SS              | DF       | MS                                 |
| Interaction         | 24594           | 22       | 1118                               |
| treatments          | 38212           | 11       | 3474                               |
| duplicates          | 22327           | 2        | 11164                              |
| Residual            | 323.9           | 36       | 8.997                              |
|                     |                 |          | F (DFn, DFd) P value               |
|                     |                 |          | 1118 F (22, 36) = 124.2 P < 0.0001 |
|                     |                 |          | 3474 F (11, 36) = 386.1 P < 0.0001 |
|                     |                 |          | 11164 F (2, 36) = 1241 P < 0.0001  |

**Dunnnett's multiple comparisons test**

|               | Mean Diff. | 95% CI of diff.  | Significant? | Summary |
|---------------|------------|------------------|--------------|---------|
| <b>C</b>      |            |                  |              |         |
| nil vs. GSK   | 0.13       | -6.775 to 7.035  | No           | ns      |
| nil vs. guana | 0.625      | -6.280 to 7.530  | No           | ns      |
| <b>R</b>      |            |                  |              |         |
| nil vs. GSK   | -0.21      | -7.115 to 6.695  | No           | ns      |
| nil vs. guana | 0.345      | -6.560 to 7.250  | No           | ns      |
| <b>T</b>      |            |                  |              |         |
| nil vs. GSK   | -57.8      | -64.71 to -50.89 | Yes          | ****    |
| nil vs. guana | 10.25      | 3.340 to 17.15   | Yes          | **      |
| <b>RT</b>     |            |                  |              |         |
| nil vs. GSK   | -68.6      | -75.51 to -61.69 | Yes          | ****    |
| nil vs. guana | 19.04      | 12.13 to 25.94   | Yes          | ****    |
| <b>A200</b>   |            |                  |              |         |
| nil vs. GSK   | -0.4       | -7.305 to 6.505  | No           | ns      |
| nil vs. guana | 1.22       | -5.685 to 8.125  | No           | ns      |
| <b>A500</b>   |            |                  |              |         |
| nil vs. GSK   | -0.45      | -7.355 to 6.455  | No           | ns      |
| nil vs. guana | 1.505      | -5.400 to 8.410  | No           | ns      |
| <b>RA200</b>  |            |                  |              |         |
| nil vs. GSK   | 0.265      | -6.640 to 7.170  | No           | ns      |
| nil vs. guana | 0.165      | -6.740 to 7.070  | No           | ns      |
| <b>RA500</b>  |            |                  |              |         |
| nil vs. GSK   | -1.1       | -8.005 to 5.805  | No           | ns      |
| nil vs. guana | 2.7        | -4.205 to 9.605  | No           | ns      |
| <b>TA200</b>  |            |                  |              |         |
| nil vs. GSK   | -40.6      | -47.51 to -33.69 | Yes          | ****    |
| nil vs. guana | 50.2       | 43.29 to 57.11   | Yes          | ****    |
| <b>TA500</b>  |            |                  |              |         |
| nil vs. GSK   | -26.1      | -33.01 to -19.19 | Yes          | ****    |
| nil vs. guana | 64.78      | 57.87 to 71.69   | Yes          | ****    |
| <b>RTA200</b> |            |                  |              |         |
| nil vs. GSK   | -26.85     | -33.76 to -19.94 | Yes          | ****    |
| nil vs. guana | 60.47      | 53.56 to 67.37   | Yes          | ****    |
| <b>RTA500</b> |            |                  |              |         |
| nil vs. GSK   | -15.8      | -22.71 to -8.895 | Yes          | ****    |
| nil vs. guana | 68.25      | 61.34 to 75.16   | Yes          | ****    |

**Test details**

|               | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q | DF      |
|---------------|--------|--------|------------|-------------|----|----|---|---------|
| <b>C</b>      |        |        |            |             |    |    |   |         |
| nil vs. GSK   | 4.08   | 3.95   | 0.13       |             | 3  | 2  | 2 | 0.04334 |
| nil vs. guana | 4.08   | 3.455  | 0.625      |             | 3  | 2  | 2 | 0.2084  |
| <b>R</b>      |        |        |            |             |    |    |   |         |
| nil vs. GSK   | 4.355  | 4.565  | -0.21      |             | 3  | 2  | 2 | 0.07001 |
| nil vs. guana | 4.355  | 4.01   | 0.345      |             | 3  | 2  | 2 | 0.115   |
| <b>T</b>      |        |        |            |             |    |    |   |         |
| nil vs. GSK   | 13.85  | 71.65  | -57.8      |             | 3  | 2  | 2 | 19.27   |
| nil vs. guana | 13.85  | 3.605  | 10.25      |             | 3  | 2  | 2 | 3.416   |
| <b>RT</b>     |        |        |            |             |    |    |   |         |
| nil vs. GSK   | 23.2   | 91.8   | -68.6      |             | 3  | 2  | 2 | 22.87   |
| nil vs. guana | 23.2   | 4.165  | 19.04      |             | 3  | 2  | 2 | 6.346   |
| <b>A200</b>   |        |        |            |             |    |    |   |         |
| nil vs. GSK   | 5.305  | 5.705  | -0.4       |             | 3  | 2  | 2 | 0.1334  |
| nil vs. guana | 5.305  | 4.085  | 1.22       |             | 3  | 2  | 2 | 0.4067  |

|               |       |       |        |   |   |   |         |    |
|---------------|-------|-------|--------|---|---|---|---------|----|
| A500          |       |       |        |   |   |   |         |    |
| nil vs. GSK   | 7.275 | 7.725 | -0.45  | 3 | 2 | 2 | 0.15    | 36 |
| nil vs. guana | 7.275 | 5.77  | 1.505  | 3 | 2 | 2 | 0.5017  | 36 |
| RA200         |       |       |        |   |   |   |         |    |
| nil vs. GSK   | 8.485 | 8.22  | 0.265  | 3 | 2 | 2 | 0.08835 | 36 |
| nil vs. guana | 8.485 | 8.32  | 0.165  | 3 | 2 | 2 | 0.05501 | 36 |
| RA500         |       |       |        |   |   |   |         |    |
| nil vs. GSK   | 15.5  | 16.6  | -1.1   | 3 | 2 | 2 | 0.3667  | 36 |
| nil vs. guana | 15.5  | 12.8  | 2.7    | 3 | 2 | 2 | 0.9001  | 36 |
| TA200         |       |       |        |   |   |   |         |    |
| nil vs. GSK   | 54.3  | 94.9  | -40.6  | 3 | 2 | 2 | 13.54   | 36 |
| nil vs. guana | 54.3  | 4.1   | 50.2   | 3 | 2 | 2 | 16.74   | 36 |
| TA500         |       |       |        |   |   |   |         |    |
| nil vs. GSK   | 70.65 | 96.75 | -26.1  | 3 | 2 | 2 | 8.701   | 36 |
| nil vs. guana | 70.65 | 5.87  | 64.78  | 3 | 2 | 2 | 21.6    | 36 |
| RTA200        |       |       |        |   |   |   |         |    |
| nil vs. GSK   | 68.35 | 95.2  | -26.85 | 3 | 2 | 2 | 8.951   | 36 |
| nil vs. guana | 68.35 | 7.885 | 60.47  | 3 | 2 | 2 | 20.16   | 36 |
| RTA500        |       |       |        |   |   |   |         |    |
| nil vs. GSK   | 81.4  | 97.2  | -15.8  | 3 | 2 | 2 | 5.267   | 36 |
| nil vs. guana | 81.4  | 13.15 | 68.25  | 3 | 2 | 2 | 22.75   | 36 |

**Supplementary Figure S8a**

**24 hrs**

**ANOVA summary**

|   |        |
|---|--------|
| F   | 0.1622 |
| P value   | 0.9165 |
| P value summary   | ns     |
| Are differences among means statistically significant? (P < 0.05) | No     |
| R square  | 0.1085 |

**48hrs**

**ANOVA summary**

|   |        |
|---|--------|
| F   | 1.271  |
| P value   | 0.3482 |
| P value summary   | ns     |
| Are differences among means statistically significant? (P < 0.05) | No     |
| R square  | 0.3227 |

**72hrs**

**ANOVA summary**

|   |        |
|---|--------|
| F   | 25.18  |
| P value   | 0.0002 |
| P value summary   | ***    |
| Are differences among means statistically significant? (P < 0.05) | Yes    |
| R square  | 0.9042 |

**Tukey's multiple comparisons test**

|          | Mean Diff. | 95% CI of diff.    | Significant? | Summary |
|----------|------------|--------------------|--------------|---------|
| C vs. R  | 0.3967     | 0.08109 to 0.7122  | Yes          | *       |
| C vs. T  | 0.5467     | 0.2311 to 0.8622   | Yes          | **      |
| C vs. RT | 0.84       | 0.5244 to 1.156    | Yes          | ***     |
| R vs. T  | 0.15       | -0.1656 to 0.4656  | No           | ns      |
| R vs. RT | 0.4433     | 0.1278 to 0.7589   | Yes          | **      |
| T vs. RT | 0.2933     | -0.02224 to 0.6089 | No           | ns      |

**Test details**

|          | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q     | DF |
|----------|--------|--------|------------|-------------|----|----|-------|----|
| C vs. R  | 1.517  | 1.12   | 0.3967     | 0.09854     | 3  | 3  | 5.693 | 8  |
| C vs. T  | 1.517  | 0.97   | 0.5467     | 0.09854     | 3  | 3  | 7.845 | 8  |
| C vs. RT | 1.517  | 0.6767 | 0.84       | 0.09854     | 3  | 3  | 12.05 | 8  |
| R vs. T  | 1.12   | 0.97   | 0.15       | 0.09854     | 3  | 3  | 2.153 | 8  |
| R vs. RT | 1.12   | 0.6767 | 0.4433     | 0.09854     | 3  | 3  | 6.362 | 8  |
| T vs. RT | 0.97   | 0.6767 | 0.2933     | 0.09854     | 3  | 3  | 4.21  | 8  |

**Supplementary Figure S8b**

**24hrs**

**ANOVA summary**

F 1.311  
P value 0.3868  
P value summary ns  
Are differences among means statis No  
R square 0.4958

**48hrs**

**ANOVA summary**

F 6.284  
P value 0.0169  
P value summary \*  
Are differences among means statis Yes  
R square 0.7021

**Tukey's multiple comparisons test**

|          | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|----------|------------|-------------------|--------------|---------|
| C vs. R  | -3.07      | -18.26 to 12.12   | No           | ns      |
| C vs. T  | -11.07     | -26.26 to 4.121   | No           | ns      |
| C vs. RT | -18.7      | -33.89 to -3.512  | Yes          | *       |
| R vs. T  | -8         | -23.19 to 7.191   | No           | ns      |
| R vs. RT | -15.63     | -30.82 to -0.4422 | Yes          | *       |
| T vs. RT | -7.633     | -22.82 to 7.558   | No           | ns      |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q      | DF |
|--------------|--------|--------|------------|-------------|----|----|--------|----|
| C vs. R      | 10.56  | 13.63  | -3.07      | 4.744       | 3  | 3  | 0.9152 | 8  |
| C vs. T      | 10.56  | 21.63  | -11.07     | 4.744       | 3  | 3  | 3.3    | 8  |
| C vs. RT     | 10.56  | 29.27  | -18.7      | 4.744       | 3  | 3  | 5.576  | 8  |
| R vs. T      | 13.63  | 21.63  | -8         | 4.744       | 3  | 3  | 2.385  | 8  |
| R vs. RT     | 13.63  | 29.27  | -15.63     | 4.744       | 3  | 3  | 4.661  | 8  |
| T vs. RT     | 21.63  | 29.27  | -7.633     | 4.744       | 3  | 3  | 2.276  | 8  |

**72hrs**

**ANOVA summary**

F 8.168  
P value 0.0081  
P value summary \*\*  
Are differences among means statis Yes  
R square 0.7539

**Tukey's multiple comparisons test**

|          | Mean Diff. | 95% CI of diff.  | Significant? | Summary |
|----------|------------|------------------|--------------|---------|
| C vs. R  | -9.2       | -29.36 to 10.96  | No           | ns      |
| C vs. T  | -12.1      | -32.26 to 8.065  | No           | ns      |
| C vs. RT | -30.37     | -50.53 to -10.20 | Yes          | **      |
| R vs. T  | -2.9       | -23.06 to 17.26  | No           | ns      |
| R vs. RT | -21.17     | -41.33 to -1.002 | Yes          | *       |
| T vs. RT | -18.27     | -38.43 to 1.898  | No           | ns      |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q      | DF |
|--------------|--------|--------|------------|-------------|----|----|--------|----|
| C vs. R      | 12.13  | 21.33  | -9.2       | 6.297       | 3  | 3  | 2.066  | 8  |
| C vs. T      | 12.13  | 24.23  | -12.1      | 6.297       | 3  | 3  | 2.718  | 8  |
| C vs. RT     | 12.13  | 42.5   | -30.37     | 6.297       | 3  | 3  | 6.82   | 8  |
| R vs. T      | 21.33  | 24.23  | -2.9       | 6.297       | 3  | 3  | 0.6513 | 8  |
| R vs. RT     | 21.33  | 42.5   | -21.17     | 6.297       | 3  | 3  | 4.754  | 8  |
| T vs. RT     | 24.23  | 42.5   | -18.27     | 6.297       | 3  | 3  | 4.102  | 8  |

**Supplementary Figure S8d**

**CHOP**

**ANOVA summary**

|   |     |        |
|---|-----|--------|
| F   |     | 12.78  |
| P value   | *   | 0.0162 |
| P value summary   | *   |        |
| Are differences among means statistically significant? (P < 0.05) | Yes |        |
| R square  |     | 0.9055 |

**Tukey's multiple comparisons test**

|          | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|----------|------------|-------------------|--------------|---------|
| C vs. R  | -0.115     | -2.550 to 2.320   | No           | ns      |
| C vs. T  | -3.07      | -5.505 to -0.6354 | Yes          | *       |
| C vs. RT | -2.095     | -4.530 to 0.3396  | No           | ns      |
| R vs. T  | -2.955     | -5.390 to -0.5204 | Yes          | *       |
| R vs. RT | -1.98      | -4.415 to 0.4546  | No           | ns      |
| T vs. RT | 0.975      | -1.460 to 3.410   | No           | ns      |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q      | DF |
|--------------|--------|--------|------------|-------------|----|----|--------|----|
| C vs. R      | 1      | 1.115  | -0.115     | 0.5981      | 2  | 2  | 0.2719 | 4  |
| C vs. T      | 1      | 4.07   | -3.07      | 0.5981      | 2  | 2  | 7.26   | 4  |
| C vs. RT     | 1      | 3.095  | -2.095     | 0.5981      | 2  | 2  | 4.954  | 4  |
| R vs. T      | 1.115  | 4.07   | -2.955     | 0.5981      | 2  | 2  | 6.988  | 4  |
| R vs. RT     | 1.115  | 3.095  | -1.98      | 0.5981      | 2  | 2  | 4.682  | 4  |
| T vs. RT     | 4.07   | 3.095  | 0.975      | 0.5981      | 2  | 2  | 2.306  | 4  |

**BIP**

**ANOVA summary**

|   |     |        |
|---|-----|--------|
| F   |     | 24.5   |
| P value   | **  | 0.0049 |
| P value summary   | **  |        |
| Are differences among means statistically significant? (P < 0.05) | Yes |        |
| R square  |     | 0.9484 |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q     | DF |
|--------------|--------|--------|------------|-------------|----|----|-------|----|
| C vs. R      | 1      | 1.14   | -0.14      | 0.437       | 2  | 2  | 0.453 | 4  |
| C vs. T      | 1      | 4.135  | -3.135     | 0.437       | 2  | 2  | 10.14 | 4  |
| C vs. RT     | 1      | 3.09   | -2.09      | 0.437       | 2  | 2  | 6.763 | 4  |
| R vs. T      | 1.14   | 4.135  | -2.995     | 0.437       | 2  | 2  | 9.691 | 4  |
| R vs. RT     | 1.14   | 3.09   | -1.95      | 0.437       | 2  | 2  | 6.31  | 4  |
| T vs. RT     | 4.135  | 3.09   | 1.045      | 0.437       | 2  | 2  | 3.381 | 4  |

**Tukey's multiple comparisons test**

|          | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|----------|------------|-------------------|--------------|---------|
| C vs. R  | -0.14      | -1.919 to 1.639   | No           | ns      |
| C vs. T  | -3.135     | -4.914 to -1.356  | Yes          | **      |
| C vs. RT | -2.09      | -3.869 to -0.3108 | Yes          | *       |
| R vs. T  | -2.995     | -4.774 to -1.216  | Yes          | **      |
| R vs. RT | -1.95      | -3.729 to -0.1708 | Yes          | *       |
| T vs. RT | 1.045      | -0.7342 to 2.824  | No           | ns      |

**SXBP1**

**ANOVA summary**

|   |     |        |
|---|-----|--------|
| F   |     | 9.111  |
| P value   | *   | 0.0292 |
| P value summary   | *   |        |
| Are differences among means statistically significant? (P < 0.05) | Yes |        |
| R square  |     | 0.8723 |

**Tukey's multiple comparisons test**

|          | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|----------|------------|-------------------|--------------|---------|
| C vs. R  | 0.275      | -1.062 to 1.612   | No           | ns      |
| C vs. T  | -1.33      | -2.667 to 0.00704 | No           | ns      |
| C vs. RT | -0.385     | -1.722 to 0.9520  | No           | ns      |
| R vs. T  | -1.605     | -2.942 to -0.2680 | Yes          | *       |
| R vs. RT | -0.66      | -1.997 to 0.6770  | No           | ns      |
| T vs. RT | 0.945      | -0.3920 to 2.282  | No           | ns      |

| Test details | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | n1 | n2 | q     | DF |
|--------------|--------|--------|------------|-------------|----|----|-------|----|
| C vs. R      | 1      | 0.725  | 0.275      | 0.3284      | 2  | 2  | 1.184 | 4  |
| C vs. T      | 1      | 2.33   | -1.33      | 0.3284      | 2  | 2  | 5.727 | 4  |
| C vs. RT     | 1      | 1.385  | -0.385     | 0.3284      | 2  | 2  | 1.658 | 4  |
| R vs. T      | 0.725  | 2.33   | -1.605     | 0.3284      | 2  | 2  | 6.911 | 4  |
| R vs. RT     | 0.725  | 1.385  | -0.66      | 0.3284      | 2  | 2  | 2.842 | 4  |
| T vs. RT     | 2.33   | 1.385  | 0.945      | 0.3284      | 2  | 2  | 4.069 | 4  |

**Supplementary Figure S8e**

**Two-way ANOVA**

| Two-way ANOVA       |                 | Ordinary       |                           |
|---------------------|-----------------|----------------|---------------------------|
| Alpha               |                 | 0.05           |                           |
| Source of Variation | % of total vari | P value        | P value summ Significant? |
| Interaction         |                 | 29.7 < 0.0001  | **** Yes                  |
| Treatments          |                 | 44.35 < 0.0001 | **** Yes                  |
| Duplicates          |                 | 23.37 < 0.0001 | **** Yes                  |
| ANOVA table         | SS              | DF             | MS                        |
| Interaction         | 174.3           | 9              | 19.37                     |
| Treatments          | 260.3           | 3              | 86.77                     |
| Duplicates          | 137.2           | 3              | 45.72                     |
| Residual            | 15.17           | 16             | 0.9482                    |

**Tukey's multiple comparisons test**

|                   | Mean Diff. | 95% CI of diff.   | Significant? | Summary |
|-------------------|------------|-------------------|--------------|---------|
| <b>C</b>          |            |                   |              |         |
| nil vs. guanabenz | -1.65      | -4.436 to 1.136   | No           | ns      |
| nil vs. GSK       | -2.15      | -4.936 to 0.6359  | No           | ns      |
| nil vs. 4u8       | -0.025     | -2.811 to 2.761   | No           | ns      |
| guanabenz vs. GSK | -0.5       | -3.286 to 2.286   | No           | ns      |
| guanabenz vs. 4u8 | 1.625      | -1.161 to 4.411   | No           | ns      |
| GSK vs. 4u8       | 2.125      | -0.6609 to 4.911  | No           | ns      |
| <b>R</b>          |            |                   |              |         |
| nil vs. guanabenz | -3.7       | -6.486 to -0.9141 | Yes          | **      |
| nil vs. GSK       | -5.2       | -7.986 to -2.414  | Yes          | ***     |
| nil vs. 4u8       | -6.95      | -9.736 to -4.164  | Yes          | ****    |
| guanabenz vs. GSK | -1.5       | -4.286 to 1.286   | No           | ns      |
| guanabenz vs. 4u8 | -3.25      | -6.036 to -0.4641 | Yes          | *       |
| GSK vs. 4u8       | -1.75      | -4.536 to 1.036   | No           | ns      |
| <b>T</b>          |            |                   |              |         |
| nil vs. guanabenz | 2.95       | 0.1641 to 5.736   | Yes          | *       |
| nil vs. GSK       | -7.5       | -10.29 to -4.714  | Yes          | ****    |
| nil vs. 4u8       | -4.6       | -7.386 to -1.814  | Yes          | **      |
| guanabenz vs. GSK | -10.45     | -13.24 to -7.664  | Yes          | ****    |
| guanabenz vs. 4u8 | -7.55      | -10.34 to -4.764  | Yes          | ****    |
| GSK vs. 4u8       | 2.9        | 0.1141 to 5.686   | Yes          | *       |
| <b>RT</b>         |            |                   |              |         |
| nil vs. guanabenz | 7.7        | 4.914 to 10.49    | Yes          | ****    |
| nil vs. GSK       | 2.5        | -0.2859 to 5.286  | No           | ns      |
| nil vs. 4u8       | -2.9       | -5.686 to -0.1141 | Yes          | *       |
| guanabenz vs. GSK | -5.2       | -7.986 to -2.414  | Yes          | ***     |
| guanabenz vs. 4u8 | -10.6      | -13.39 to -7.814  | Yes          | ****    |
| GSK vs. 4u8       | -5.4       | -8.186 to -2.614  | Yes          | ***     |

| Test details      | Mean 1 | Mean 2 | Mean Diff. | SE of diff. | N1 | N2 | q       | DF |
|-------------------|--------|--------|------------|-------------|----|----|---------|----|
| <b>C</b>          |        |        |            |             |    |    |         |    |
| nil vs. guanabenz | 10.6   | 12.25  | -1.65      | 0.9738      | 2  | 2  | 2.396   | 16 |
| nil vs. GSK       | 10.6   | 12.75  | -2.15      | 0.9738      | 2  | 2  | 3.123   | 16 |
| nil vs. 4u8       | 10.6   | 10.63  | -0.025     | 0.9738      | 2  | 2  | 0.03631 | 16 |
| guanabenz vs. GSK | 12.25  | 12.75  | -0.5       | 0.9738      | 2  | 2  | 0.7262  | 16 |
| guanabenz vs. 4u8 | 12.25  | 10.63  | 1.625      | 0.9738      | 2  | 2  | 2.36    | 16 |
| GSK vs. 4u8       | 12.75  | 10.63  | 2.125      | 0.9738      | 2  | 2  | 3.086   | 16 |
| <b>R</b>          |        |        |            |             |    |    |         |    |
| nil vs. guanabenz | 11.65  | 15.35  | -3.7       | 0.9738      | 2  | 2  | 5.374   | 16 |
| nil vs. GSK       | 11.65  | 16.85  | -5.2       | 0.9738      | 2  | 2  | 7.552   | 16 |
| nil vs. 4u8       | 11.65  | 18.6   | -6.95      | 0.9738      | 2  | 2  | 10.09   | 16 |
| guanabenz vs. GSK | 15.35  | 16.85  | -1.5       | 0.9738      | 2  | 2  | 2.178   | 16 |
| guanabenz vs. 4u8 | 15.35  | 18.6   | -3.25      | 0.9738      | 2  | 2  | 4.72    | 16 |
| GSK vs. 4u8       | 16.85  | 18.6   | -1.75      | 0.9738      | 2  | 2  | 2.542   | 16 |
| <b>T</b>          |        |        |            |             |    |    |         |    |
| nil vs. guanabenz | 14.3   | 11.35  | 2.95       | 0.9738      | 2  | 2  | 4.284   | 16 |
| nil vs. GSK       | 14.3   | 21.8   | -7.5       | 0.9738      | 2  | 2  | 10.89   | 16 |
| nil vs. 4u8       | 14.3   | 18.9   | -4.6       | 0.9738      | 2  | 2  | 6.681   | 16 |
| guanabenz vs. GSK | 11.35  | 21.8   | -10.45     | 0.9738      | 2  | 2  | 15.18   | 16 |
| guanabenz vs. 4u8 | 11.35  | 18.9   | -7.55      | 0.9738      | 2  | 2  | 10.97   | 16 |
| GSK vs. 4u8       | 21.8   | 18.9   | 2.9        | 0.9738      | 2  | 2  | 4.212   | 16 |
| <b>RT</b>         |        |        |            |             |    |    |         |    |
| nil vs. guanabenz | 21.35  | 13.65  | 7.7        | 0.9738      | 2  | 2  | 11.18   | 16 |
| nil vs. GSK       | 21.35  | 18.85  | 2.5        | 0.9738      | 2  | 2  | 3.631   | 16 |
| nil vs. 4u8       | 21.35  | 24.25  | -2.9       | 0.9738      | 2  | 2  | 4.212   | 16 |
| guanabenz vs. GSK | 13.65  | 18.85  | -5.2       | 0.9738      | 2  | 2  | 7.552   | 16 |
| guanabenz vs. 4u8 | 13.65  | 24.25  | -10.6      | 0.9738      | 2  | 2  | 15.39   | 16 |
| GSK vs. 4u8       | 18.85  | 24.25  | -5.4       | 0.9738      | 2  | 2  | 7.843   | 16 |