### Male Clinical Chemistry Summary

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Endpoint** | 0.0 mg/kg N = 9 | 0.07 mg/kg N = 5 | 0.2 mg/kg N = 5 | 0.7 mg/kg N = 5 | 2.0 mg/kg N = 4-5 | 6.0 mg/kg N = 5 | 18.0 mg/kg N = 5 | 55.0 mg/kg N = 5 | 160.0 mg/kg N = 5 | 475.0 mg/kg N = 4 | BMD1Std (mg/kg) | BMDL1Std (mg/kg) |
| Creatinine (mg/dL) | 0.48 ± 0.01\* | 0.46 ± 0.02 | 0.46 ± 0.02 | 0.50 ± 0.00 | 0.42 ± 0.02 | 0.42 ± 0.02 | 0.42 ± 0.02 | 0.38 ± 0.05 | 0.44 ± 0.02 | 0.48 ± 0.02 | NVM | NVM |
| Globulin (measured) (g/dL) | 1.68 ± 0.04\*\* | 1.68 ± 0.09 | 1.60 ± 0.04 | 1.72 ± 0.04 | 1.78 ± 0.07 | 1.74 ± 0.12 | 1.66 ± 0.12 | 1.76 ± 0.05 | 1.90 ± 0.11 | 1.88 ± 0.09 | 125.835 | 68.45 |
| A/G Ratio (g/dL) | 2.65 ± 0.07\* | 2.67 ± 0.21 | 2.75 ± 0.14 | 2.56 ± 0.05 | 2.54 ± 0.13 | 2.55 ± 0.16 | 2.68 ± 0.23 | 2.56 ± 0.05 | 2.35 ± 0.12 | 2.33 ± 0.09 | NVM | NVM |
| Cholesterol (mg/dL) | 118.1 ± 3.7\* | 117.0 ± 5.1 | 110.0 ± 2.8 | 114.8 ± 2.5 | 113.8 ± 2.8 | 118.6 ± 3.7 | 104.6 ± 6.5 | 115.6 ± 5.5 | 107.6 ± 5.7 | 100.8 ± 1.4\* | 17.539 | 14.31 |
| Alanine aminotransferase (IU/L) | 61.8 ± 3.1\* | 54.4 ± 3.2 | 60.4 ± 3.5 | 64.2 ± 6.2 | 58.6 ± 2.7 | 55.8 ± 0.5 | 63.8 ± 2.8 | 64.0 ± 9.6 | 66.6 ± 3.3 | 96.0 ± 10.5 | NVM | NVM |
| Alkaline phosphatase (IU/L) | 267.8 ± 8.0\*\* | 253.4 ± 24.6 | 252.8 ± 8.7 | 277.0 ± 18.2 | 269.5 ± 8.2 | 263.8 ± 10.7 | 285.0 ± 4.5 | 284.8 ± 20.5 | 326.0 ± 23.7\* | 351.0 ± 12.8\*\* | NVM | NVM |
| Aspartate Aminotransferase (U/L) | 80.22 ± 3.53\* | 77.80 ± 3.02 | 86.00 ± 7.33 | 83.20 ± 6.61 | 78.60 ± 2.98 | 76.60 ± 2.46 | 76.80 ± 2.33 | 87.00 ± 8.84 | 88.40 ± 4.01 | 122.25 ± 11.46 | NVM | NVM |

### Female Clinical Chemistry Summary

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Endpoint** | 0.0 mg/kg N = 10 | 0.07 mg/kg N = 5 | 0.2 mg/kg N = 5 | 0.7 mg/kg N = 5 | 2.0 mg/kg N = 5 | 6.0 mg/kg N = 5 | 18.0 mg/kg N = 5 | 55.0 mg/kg N = 5 | 160.0 mg/kg N = 5 | 475.0 mg/kg N = 5 | BMD1Std (mg/kg) | BMDL1Std (mg/kg) |
| Urea Nitrogen (mg/dL) | 16.6 ± 0.7\* | 16.4 ± 0.5 | 15.2 ± 0.8 | 17.6 ± 0.9 | 16.6 ± 1.0 | 16.6 ± 0.2 | 15.6 ± 1.0 | 15.4 ± 0.7 | 14.6 ± 1.0 | 14.2 ± 0.8 | 118.445 | 6.613 |
| Glucose (mg/dL) | 235.2 ± 14.7\* | 218.6 ± 25.6 | 239.4 ± 15.0 | 236.8 ± 7.7 | 215.6 ± 8.6 | 211.0 ± 2.1 | 197.0 ± 17.3 | 199.6 ± 10.6 | 227.4 ± 22.1 | 203.0 ± 13.6 | NVM | NVM |
| Alkaline phosphatase (IU/L) | 200.1 ± 9.7\*\* | 195.6 ± 10.5 | 176.8 ± 8.3 | 191.4 ± 13.6 | 207.0 ± 17.8 | 210.2 ± 9.6 | 235.4 ± 3.8 | 234.2 ± 6.4 | 235.6 ± 14.2 | 247.8 ± 8.0\*\* | 6.461 | 6.003 |
| Aspartate Aminotransferase (U/L) | 78.50 ± 2.13\* | 81.40 ± 4.21 | 79.40 ± 2.25 | 84.00 ± 5.55 | 80.80 ± 1.66 | 75.80 ± 1.53 | 77.40 ± 1.66 | 92.80 ± 3.29\* | 89.20 ± 3.15 | 82.60 ± 0.60 | NVM | NVM |
| Sorbitol dehydrogenase (IU/L) | 12.9 ± 0.9 | 17.3 ± 0.6\* | 16.5 ± 0.3 | 15.2 ± 1.6 | 16.0 ± 0.4 | 14.5 ± 0.4 | 15.4 ± 0.8 | 19.0 ± 2.3 | 15.7 ± 0.9 | 19.1 ± 2.6 | NVM | NVM |

Values given as mean ± SEM (N) of animals that survived to study termination.

Statistical analysis were performed by Jonckheere (trend) and Shirley or Dunn (pairwise) tests.

Statistical significance for the control group indicates a significant trend test

Statistical significance for a treatment group indicates a significant pairwise test compared to the vehicle control group

\* Statistically significant at p ≤ 0.05

\*\* Statistically significant at p ≤ 0.01

One value for Alkaline Phosphatase in the male 2 mg/kg group was excluded due to an analysis problem.

BMD1Std and BMDL1Std: Benchmark response (BMR) set at 1 standard deviation from the mean.

NVM = no viable model