### Male Clinical Chemistry Summary

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Endpoint** | 0.0 mg/kg N = 10 | 0.15 mg/kg N = 5 | 0.5 mg/kg N = 5 | 1.4 mg/kg N = 5 | 4.0 mg/kg N = 5 | 12.0 mg/kg N = 5 | 37.0 mg/kg N = 5 | 111.0 mg/kg N = 5 | 333.0 mg/kg N = 5 | 1000.0 mg/kg N = 5 | BMD1Std (mg/kg) | BMDL1Std (mg/kg) |
| Globulin (measured) (g/dL) | 2.15 ± 0.07\*\* | 2.16 ± 0.05 | 2.24 ± 0.15 | 2.12 ± 0.10 | 2.18 ± 0.02 | 2.20 ± 0.04 | 2.26 ± 0.04 | 2.26 ± 0.07 | 2.30 ± 0.06\* | 2.30 ± 0.04\* | NVM | NVM |
| A/G Ratio (g/dL) | 2.04 ± 0.07\*\* | 1.99 ± 0.08 | 1.92 ± 0.13 | 2.03 ± 0.07 | 2.04 ± 0.04 | 1.96 ± 0.06 | 1.95 ± 0.02 | 1.89 ± 0.05 | 1.80 ± 0.06 | 1.88 ± 0.03 | 47.003 | 11.049 |
| Cholesterol (mg/dL) | 114.9 ± 5.9\*\* | 115.2 ± 2.2 | 119.6 ± 13.6 | 112.2 ± 8.0 | 123.0 ± 4.8 | 114.2 ± 3.4 | 117.8 ± 9.3 | 123.4 ± 5.9 | 131.0 ± 3.4\* | 163.6 ± 7.1\*\* | NVM | NVM |
| Alanine aminotransferase (IU/L) | 60.8 ± 4.7\* | 57.2 ± 3.1 | 55.0 ± 5.0 | 64.2 ± 3.5 | 63.2 ± 5.3 | 57.6 ± 2.6 | 50.4 ± 2.4 | 52.6 ± 3.2 | 53.6 ± 2.8 | 52.4 ± 5.2 | NVM | NVM |

### Female Clinical Chemistry Summary

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Endpoint** | 0.0 mg/kg N = 10 | 0.15 mg/kg N = 5 | 0.5 mg/kg N = 5 | 1.4 mg/kg N = 5 | 4.0 mg/kg N = 5 | 12.0 mg/kg N = 5 | 37.0 mg/kg N = 5 | 111.0 mg/kg N = 5 | 333.0 mg/kg N = 5 | 1000.0 mg/kg N = 5 | BMD1Std (mg/kg) | BMDL1Std (mg/kg) |
| Globulin (measured) (g/dL) | 1.93 ± 0.07\* | 1.66 ± 0.02\* | 1.88 ± 0.05 | 1.88 ± 0.04 | 1.86 ± 0.08 | 1.84 ± 0.05 | 2.04 ± 0.09 | 1.94 ± 0.05 | 1.90 ± 0.09 | 1.98 ± 0.05 | 36.678 | 13.695 |
| A/G Ratio (g/dL) | 2.38 ± 0.08 | 2.76 ± 0.04\* | 2.36 ± 0.06 | 2.44 ± 0.04 | 2.50 ± 0.09 | 2.55 ± 0.05 | 2.26 ± 0.04 | 2.37 ± 0.06 | 2.46 ± 0.08 | 2.35 ± 0.07 | NVM | NVM |
| Cholesterol (mg/dL) | 105.0 ± 5.3\*\* | 97.8 ± 5.8 | 100.8 ± 7.1 | 88.6 ± 4.7 | 101.0 ± 3.8 | 109.0 ± 12.2 | 123.8 ± 10.4 | 105.6 ± 5.5 | 120.8 ± 6.0 | 162.4 ± 8.5\*\* | 288.242 | 226.543 |
| Alkaline phosphatase (IU/L) | 201.3 ± 13.1\*\* | 198.8 ± 11.9 | 216.2 ± 38.8 | 210.0 ± 19.9 | 218.4 ± 10.1 | 208.4 ± 7.4 | 222.8 ± 25.0 | 240.0 ± 9.3\* | 241.4 ± 5.7\* | 272.2 ± 18.2\*\* | 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

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

NVM = no viable model