Additional file – Supplementary Results: Methotrexate Effects

Pairwise comparisons of vehicle vs. methotrexate (MTX) treated groups within each housing system (Type IV conventional cage, TRCC, RCC) at Day 29 and Day 57. Two-sided Welch's t-test, $\alpha = 0.05$. Raw and Benjamini-Hochberg (BH) adjusted p-values are reported.

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Table SR1 – Conventional cage vehicle vs. MTX – Day 29

Domain	Parameter	Conventional cage vehicle	Conventional cage MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Hematology	Basophils	0.05 +/- 0.02 (n=15)	0.04 +/- 0.02 (n=14)	0.02 [0.00, 0.03]	0.013	0.091
Hematology	Monocytes	0.17 +/- 0.04 (n=15)	0.12 +/- 0.04 (n=14)	0.04 [0.01, 0.07]	0.007	0.091
Hematology	White blood cells	7.04 +/- 1.09 (n=15)	5.92 +/- 1.17 (n=14)	1.12 [0.26, 1.99]	0.013	0.091
Hematology	Reticulocytes	186.45 +/- 31.49 (n=15)	139.34 +/- 64.37 (n=14)	47.11 [7.23, 87.00]	0.023	0.123
Hematology	Lymphocytes	5.48 +/- 1.01 (n=15)	4.67 +/- 0.97 (n=14)	0.81 [0.06, 1.57]	0.036	0.158
Hematology	Haemoglobin	15.92 +/- 0.50 (n=15)	15.06 +/- 1.63 (n=14)	0.86 [-0.11, 1.82]	0.079	0.238
Hematology	Neutrophils	1.20 +/- 0.32 (n=15)	0.98 +/- 0.36 (n=14)	0.23 [-0.04, 0.49]	0.087	0.246
Hematology	Platelets	817.93 +/- 97.12 (n=15)	1087.79 +/- 567.73 (n=14)	-269.85 [-600.35, 60.65]	0.102	0.257
Hematology	Eosinophils	0.13 +/- 0.04 (n=15)	0.10 +/- 0.04 (n=14)	0.03 [-0.01, 0.06]	0.126	0.287
Hematology	Haematocrit	45.90 +/- 1.51 (n=15)	44.07 +/- 4.98 (n=14)	1.83 [-1.12, 4.78]	0.206	0.367
Hematology	Red blood cells	8.60 +/- 0.38 (n=15)	8.33 +/- 0.94 (n=14)	0.27 [-0.30, 0.84]	0.332	0.483
Clinical chemistry	Sodium	145.66 +/- 1.07 (n=15)	144.66 +/- 0.71 (n=14)	1.00 [0.31, 1.69]	0.006	0.091
Clinical chemistry	Total protein	61.39 +/- 2.08 (n=15)	59.12 +/- 1.88 (n=14)	2.27 [0.76, 3.78]	0.005	0.091
Clinical chemistry	GLDH	6.10 +/- 0.70 (n=15)	8.19 +/- 3.61 (n=14)	-2.09 [-4.19, 0.02]	0.052	0.207
Clinical chemistry	Urea	5.29 +/- 0.45 (n=15)	5.62 +/- 0.51 (n=14)	-0.33 [-0.69, 0.04]	0.077	0.238
Clinical chemistry	Inorganic phosphate	2.24 +/- 0.17 (n=15)	2.13 +/- 0.21 (n=14)	0.11 [-0.04, 0.26]	0.138	0.289
Clinical chemistry	Cholesterol	1.58 +/- 0.26 (n=15)	1.45 +/- 0.23 (n=14)	0.13 [-0.06, 0.32]	0.168	0.335
Clinical chemistry	Creatinine	19.07 +/- 2.34 (n=15)	18.00 +/- 2.00 (n=14)	1.07 [-0.59, 2.72]	0.198	0.365
Clinical chemistry	Glucose	4.59 +/- 0.49 (n=15)	4.81 +/- 0.48 (n=14)	-0.21 [-0.58, 0.15]	0.244	0.401
Clinical chemistry	ASAT	86.13 +/- 6.02 (n=15)	88.43 +/- 5.79 (n=14)	-2.30 [-6.80, 2.21]	0.305	0.472
Clinical chemistry	ALP	93.13 +/- 14.56 (n=15)	98.07 +/- 15.90 (n=14)	-4.94 [-16.59, 6.72]	0.392	0.537
Clinical chemistry	ALAT	35.80 +/- 4.84 (n=15)	34.57 +/- 6.16 (n=14)	1.23 [-3.03, 5.49]	0.558	0.657
Clinical chemistry	Calcium	2.50 +/- 0.08 (n=15)	2.48 +/- 0.09 (n=14)	0.02 [-0.04, 0.08]	0.541	0.657
Clinical chemistry	Bilirubin	0.97 +/- 0.24 (n=15)	1.03 +/- 0.26 (n=14)	-0.06 [-0.25, 0.13]	0.504	0.657
Clinical chemistry	Triglycerides	0.82 +/- 0.28 (n=15)	0.77 +/- 0.21 (n=14)	0.05 [-0.14, 0.24]	0.602	0.657
Clinical chemistry	Chloride	103.09 +/- 1.73 (n=15)	102.94 +/- 1.25 (n=14)	0.15 [-1.00, 1.30]	0.789	0.841
Clinical chemistry	Albumin	39.77 +/- 1.17 (n=15)	39.83 +/- 1.06 (n=14)	-0.06 [-0.91, 0.79]	0.895	0.934
Clinical chemistry	Potassium	4.38 +/- 0.27 (n=15)	4.39 +/- 0.45 (n=14)	-0.01 [-0.30, 0.28]	0.934	0.951
Organ weights	Epididymides	0.3876 +/- 0.0289 (n=10)	0.4300 +/- 0.0375 (n=10)	-0.0424 [-0.0740, -0.0108]	0.012	0.091
Organ weights	Terminal BW	283.4000 +/- 22.3617 (n=10)	267.9000 +/- 16.5761 (n=10)	15.5000 [-3.1057, 34.1057]	0.097	0.257

Domain	Parameter	Conventional cage vehicle	Conventional cage MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Organ weights	Kidneys	0.7205 +/- 0.0494 (n=10)	0.7524 +/- 0.0403 (n=10)	-0.0319 [-0.0744, 0.0106]	0.132	0.287
Organ weights	Prostate	0.2620 +/- 0.0402 (n=10)	0.2372 +/- 0.0407 (n=10)	0.0247 [-0.0133, 0.0627]	0.188	0.362
Organ weights	Brain	0.7504 +/- 0.0585 (n=10)	0.7794 +/- 0.0489 (n=10)	-0.0290 [-0.0798, 0.0218]	0.245	0.401
Organ weights	Thymus	0.1405 +/- 0.0251 (n=10)	0.1275 +/- 0.0237 (n=10)	0.0130 [-0.0100, 0.0360]	0.250	0.401
Organ weights	Spleen	0.1956 +/- 0.0211 (n=10)	0.1872 +/- 0.0154 (n=10)	0.0085 [-0.0090, 0.0259]	0.321	0.481
Organ weights	Testes	1.1450 +/- 0.1033 (n=10)	1.1913 +/- 0.1183 (n=10)	-0.0463 [-0.1507, 0.0582]	0.364	0.514
Organ weights	Heart	0.3472 +/- 0.0258 (n=10)	0.3414 +/- 0.0223 (n=10)	0.0058 [-0.0169, 0.0284]	0.600	0.657
Organ weights	Liver	2.9166 +/- 0.1386 (n=10)	2.8783 +/- 0.1403 (n=10)	0.0382 [-0.0928, 0.1692]	0.548	0.657
Organ weights	Seminal Vesicles	0.3338 +/- 0.1025 (n=10)	0.3545 +/- 0.0580 (n=10)	-0.0207 [-0.1005, 0.0591]	0.587	0.657
Organ weights	(Para)thyroids	0.0066 +/- 0.0011 (n=10)	0.0069 +/- 0.0016 (n=10)	-0.0003 [-0.0016, 0.0010]	0.602	0.657
Organ weights	Adrenals	0.0226 +/- 0.0025 (n=10)	0.0227 +/- 0.0035 (n=10)	-0.0001 [-0.0030, 0.0028]	0.951	0.951
Immunology	IgA	32266.95 +/- 7199.22 (n=10)	22524.90 +/- 7325.04 (n=10)	9742.05 [2918.43, 16565.67]	0.008	0.091
Immunology	NK Cells	0.19 +/- 0.06 (n=10)	0.25 +/- 0.06 (n=10)	-0.06 [-0.12, -0.01]	0.033	0.158
Immunology	TC Cells	0.79 +/- 0.21 (n=10)	0.62 +/- 0.16 (n=10)	0.17 [-0.01, 0.35]	0.057	0.209
Immunology	T Cells	2.80 +/- 0.56 (n=10)	2.32 +/- 0.53 (n=10)	0.48 [-0.03, 0.99]	0.063	0.214
Immunology	TH Cells	1.96 +/- 0.30 (n=10)	1.70 +/- 0.40 (n=10)	0.25 [-0.08, 0.59]	0.127	0.287
Immunology	B Cells	1.87 +/- 0.62 (n=10)	1.70 +/- 0.53 (n=10)	0.17 [-0.37, 0.71]	0.519	0.657
Other	Body weight gain	67.98 +/- 16.86 (n=15)	54.74 +/- 11.44 (n=14)	13.24 [2.28, 24.21]	0.020	0.119

Table SR2 – TRCC vehicle vs. MTX – Day 29

Domain	Parameter	TRCC vehicle	TRCC MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Hematology	Reticulocytes	189.75 +/- 26.08 (n=15)	132.40 +/- 60.78 (n=15)	57.35 [21.61, 93.10]	0.003	0.053
Hematology	Platelets	816.27 +/- 96.43 (n=15)	1085.93 +/- 411.94 (n=15)	-269.67 [-501.81, -37.52]	0.026	0.144
Hematology	Haematocrit	45.87 +/- 1.39 (n=15)	43.63 +/- 4.49 (n=15)	2.24 [-0.33, 4.81]	0.083	0.270
Hematology	Monocytes	0.16 +/- 0.05 (n=15)	0.13 +/- 0.04 (n=15)	0.03 [-0.00, 0.07]	0.075	0.270
Hematology	Haemoglobin	15.55 +/- 0.48 (n=15)	14.87 +/- 1.46 (n=15)	0.67 [-0.16, 1.51]	0.108	0.288
Hematology	Red blood cells	8.55 +/- 0.31 (n=15)	8.18 +/- 0.99 (n=15)	0.37 [-0.19, 0.94]	0.182	0.415
Hematology	White blood cells	6.50 +/- 1.34 (n=15)	5.88 +/- 1.23 (n=15)	0.62 [-0.34, 1.58]	0.197	0.429
Hematology	Lymphocytes	5.02 +/- 1.13 (n=15)	4.51 +/- 1.11 (n=15)	0.51 [-0.33, 1.35]	0.225	0.450
Hematology	Basophils	0.04 +/- 0.01 (n=15)	0.04 +/- 0.03 (n=15)	0.01 [-0.01, 0.02]	0.370	0.565
Hematology	Eosinophils	0.10 +/- 0.03 (n=15)	0.11 +/- 0.04 (n=15)	-0.01 [-0.04, 0.01]	0.377	0.565
Hematology	Neutrophils	1.17 +/- 0.28 (n=15)	1.08 +/- 0.50 (n=15)	0.09 [-0.22, 0.40]	0.546	0.690
Clinical chemistry	Total protein	60.22 +/- 1.60 (n=15)	57.92 +/- 1.31 (n=15)	2.30 [1.20, 3.40]	<0.001	0.009
Clinical chemistry	Calcium	2.52 +/- 0.07 (n=15)	2.47 +/- 0.07 (n=15)	0.06 [0.01, 0.11]	0.021	0.144
Clinical chemistry	Inorganic phosphate	2.39 +/- 0.14 (n=15)	2.22 +/- 0.23 (n=15)	0.17 [0.02, 0.31]	0.025	0.144
Clinical chemistry	Creatinine	18.07 +/- 2.40 (n=15)	16.27 +/- 2.63 (n=15)	1.80 [-0.09, 3.69]	0.061	0.264
Clinical chemistry	Sodium	145.17 +/- 0.97 (n=15)	144.51 +/- 1.09 (n=15)	0.66 [-0.11, 1.43]	0.090	0.270
Clinical chemistry	Triglycerides	0.97 +/- 0.24 (n=15)	0.83 +/- 0.20 (n=15)	0.14 [-0.02, 0.31]	0.086	0.270
Clinical chemistry	Chloride	102.66 +/- 1.74 (n=15)	103.53 +/- 1.01 (n=15)	-0.87 [-1.95, 0.20]	0.106	0.288
Clinical chemistry	Albumin	39.31 +/- 0.83 (n=15)	38.89 +/- 0.70 (n=15)	0.42 [-0.16, 1.00]	0.147	0.352
Clinical chemistry	Urea	5.17 +/- 0.61 (n=15)	5.41 +/- 0.55 (n=15)	-0.25 [-0.68, 0.19]	0.255	0.459
Clinical chemistry	ALP	104.60 +/- 23.62 (n=15)	98.80 +/- 15.40 (n=15)	5.80 [-9.22, 20.82]	0.433	0.612
Clinical chemistry	GLDH	6.39 +/- 1.20 (n=15)	6.95 +/- 2.63 (n=15)	-0.56 [-2.12, 1.00]	0.463	0.617
Clinical chemistry	Potassium	4.54 +/- 0.57 (n=15)	4.42 +/- 0.46 (n=15)	0.12 [-0.27, 0.50]	0.533	0.690
Clinical chemistry	ASAT	83.07 +/- 11.61 (n=15)	81.00 +/- 8.19 (n=15)	2.07 [-5.48, 9.62]	0.578	0.712
Clinical chemistry	Glucose	4.86 +/- 0.51 (n=15)	4.97 +/- 0.68 (n=15)	-0.11 [-0.56, 0.34]	0.610	0.730
Clinical chemistry	ALAT	33.73 +/- 4.65 (n=15)	34.33 +/- 4.22 (n=15)	-0.60 [-3.92, 2.72]	0.714	0.794
Clinical chemistry	Cholesterol	1.56 +/- 0.17 (n=15)	1.58 +/- 0.30 (n=15)	-0.02 [-0.20, 0.17]	0.866	0.910
Clinical chemistry	Bilirubin	0.92 +/- 0.31 (n=15)	0.90 +/- 0.36 (n=15)	0.02 [-0.23, 0.27]	0.872	0.910
Organ weights	(Para)thyroids	0.0062 +/- 0.0008 (n=10)	0.0052 +/- 0.0009 (n=10)	0.0010 [0.0001, 0.0018]	0.027	0.144
Organ weights	Thymus	0.1466 +/- 0.0271 (n=10)	0.1264 +/- 0.0298 (n=10)	0.0202 [-0.0066, 0.0470]	0.130	0.329
Organ weights	Prostate	0.2550 +/- 0.0410 (n=10)	0.2344 +/- 0.0379 (n=10)	0.0206 [-0.0165, 0.0577]	0.258	0.459

Domain	Parameter	TRCC vehicle	TRCC MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Organ weights	Kidneys	0.7241 +/- 0.0611 (n=10)	0.7641 +/- 0.0947 (n=10)	-0.0399 [-0.1158, 0.0359]	0.280	0.480
Organ weights	Spleen	0.1999 +/- 0.0246 (n=10)	0.1912 +/- 0.0110 (n=10)	0.0086 [-0.0098, 0.0271]	0.330	0.546
Organ weights	Testes	1.1664 +/- 0.0852 (n=10)	1.2078 +/- 0.1083 (n=10)	-0.0414 [-0.1333, 0.0506]	0.356	0.565
Organ weights	Terminal BW	280.0000 +/- 20.7096 (n=10)	271.3000 +/- 24.7748 (n=10)	8.7000 [-12.8013, 30.2013]	0.406	0.590
Organ weights	Adrenals	0.0202 +/- 0.0020 (n=10)	0.0208 +/- 0.0016 (n=10)	-0.0006 [-0.0023, 0.0011]	0.459	0.617
Organ weights	Seminal Vesicles	0.3716 +/- 0.0602 (n=10)	0.3549 +/- 0.0869 (n=10)	0.0167 [-0.0541, 0.0876]	0.623	0.730
Organ weights	Brain	0.7607 +/- 0.0455 (n=10)	0.7702 +/- 0.0680 (n=10)	-0.0095 [-0.0644, 0.0454]	0.718	0.794
Organ weights	Heart	0.3464 +/- 0.0352 (n=10)	0.3512 +/- 0.0250 (n=10)	-0.0048 [-0.0338, 0.0241]	0.728	0.794
Organ weights	Epididymides	0.4112 +/- 0.0444 (n=10)	0.4109 +/- 0.0424 (n=10)	0.0004 [-0.0404, 0.0412]	0.985	0.985
Organ weights	Liver	2.9886 +/- 0.1651 (n=10)	2.9923 +/- 0.2173 (n=10)	-0.0037 [-0.1860, 0.1786]	0.966	0.985
Immunology	IgA	33957.40 +/- 9127.94 (n=10)	19555.00 +/- 5733.58 (n=10)	14402.40 [7142.97, 21661.83]	<0.001	0.017
Immunology	NK Cells	0.19 +/- 0.05 (n=10)	0.27 +/- 0.06 (n=10)	-0.08 [-0.14, -0.03]	0.005	0.055
Immunology	TH Cells	1.85 +/- 0.46 (n=10)	1.41 +/- 0.41 (n=10)	0.44 [0.04, 0.85]	0.034	0.165
Immunology	T Cells	2.46 +/- 0.57 (n=10)	1.96 +/- 0.60 (n=10)	0.50 [-0.05, 1.05]	0.071	0.270
Immunology	B Cells	1.93 +/- 0.71 (n=10)	1.58 +/- 0.51 (n=10)	0.35 [-0.23, 0.93]	0.221	0.450
Immunology	TC Cells	0.66 +/- 0.21 (n=10)	0.55 +/- 0.20 (n=10)	0.11 [-0.08, 0.31]	0.242	0.459
Other	Body weight gain	74.57 +/- 19.73 (n=15)	57.87 +/- 14.92 (n=15)	16.70 [3.57, 29.83]	0.015	0.141

Table SR3 – RCC vehicle vs. MTX – Day 29

Domain	Parameter	RCC vehicle	RCC MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Hematology	Basophils	0.08 +/- 0.04 (n=15)	0.04 +/- 0.02 (n=15)	0.05 [0.02, 0.07]	<0.001	0.007
Hematology	Platelets	829.87 +/- 59.50 (n=15)	1208.60 +/- 379.07 (n=15)	-378.73 [-590.29, -167.17]	0.002	0.016
Hematology	Haemoglobin	15.86 +/- 0.65 (n=15)	14.18 +/- 2.30 (n=15)	1.68 [0.37, 2.99]	0.015	0.072
Hematology	Reticulocytes	180.73 +/- 30.16 (n=15)	112.69 +/- 97.09 (n=15)	68.04 [12.57, 123.51]	0.019	0.084
Hematology	Haematocrit	45.91 +/- 2.07 (n=15)	41.10 +/- 7.07 (n=15)	4.81 [0.78, 8.83]	0.022	0.088
Hematology	Monocytes	0.16 +/- 0.06 (n=15)	0.12 +/- 0.06 (n=15)	0.05 [-0.00, 0.09]	0.053	0.158
Hematology	White blood cells	7.16 +/- 0.96 (n=15)	6.24 +/- 1.45 (n=15)	0.92 [-0.01, 1.84]	0.052	0.158
Hematology	Red blood cells	8.63 +/- 0.48 (n=15)	7.89 +/- 1.37 (n=15)	0.74 [-0.05, 1.53]	0.063	0.169
Hematology	Lymphocytes	5.93 +/- 0.91 (n=15)	5.23 +/- 1.18 (n=15)	0.70 [-0.10, 1.49]	0.082	0.197
Hematology	Neutrophils	0.85 +/- 0.24 (n=15)	0.70 +/- 0.30 (n=15)	0.15 [-0.06, 0.35]	0.151	0.269
Hematology	Eosinophils	0.12 +/- 0.03 (n=15)	0.12 +/- 0.05 (n=15)	-0.01 [-0.04, 0.03]	0.736	0.820
Clinical chemistry	Creatinine	18.67 +/- 2.19 (n=15)	14.87 +/- 2.95 (n=15)	3.80 [1.85, 5.75]	<0.001	0.007
Clinical chemistry	Sodium	144.98 +/- 0.81 (n=15)	144.23 +/- 0.75 (n=15)	0.75 [0.17, 1.34]	0.013	0.072
Clinical chemistry	Total protein	59.70 +/- 2.84 (n=15)	57.67 +/- 1.82 (n=15)	2.03 [0.24, 3.83]	0.028	0.104
Clinical chemistry	Calcium	2.58 +/- 0.09 (n=15)	2.52 +/- 0.06 (n=15)	0.06 [0.01, 0.12]	0.033	0.113
Clinical chemistry	Bilirubin	0.84 +/- 0.36 (n=15)	1.04 +/- 0.25 (n=15)	-0.20 [-0.43, 0.03]	0.090	0.197
Clinical chemistry	Chloride	102.19 +/- 1.66 (n=15)	103.13 +/- 1.58 (n=15)	-0.94 [-2.15, 0.27]	0.123	0.227
Clinical chemistry	Triglycerides	0.81 +/- 0.23 (n=15)	0.71 +/- 0.19 (n=15)	0.10 [-0.06, 0.25]	0.208	0.333
Clinical chemistry	Urea	5.54 +/- 0.88 (n=15)	5.89 +/- 0.85 (n=15)	-0.35 [-1.00, 0.29]	0.271	0.420
Clinical chemistry	ALP	88.07 +/- 20.02 (n=15)	94.33 +/- 16.87 (n=15)	-6.27 [-20.13, 7.60]	0.362	0.529
Clinical chemistry	Inorganic phosphate	2.59 +/- 0.21 (n=15)	2.52 +/- 0.25 (n=15)	0.07 [-0.10, 0.24]	0.415	0.585
Clinical chemistry	ALAT	33.20 +/- 4.20 (n=15)	34.33 +/- 4.85 (n=15)	-1.13 [-4.53, 2.26]	0.499	0.665
Clinical chemistry	Glucose	4.81 +/- 0.89 (n=15)	5.01 +/- 0.63 (n=15)	-0.20 [-0.78, 0.38]	0.485	0.665
Clinical chemistry	Potassium	4.69 +/- 0.31 (n=15)	4.60 +/- 0.45 (n=15)	0.08 [-0.21, 0.38]	0.554	0.700
Clinical chemistry	ASAT	83.73 +/- 6.19 (n=15)	82.13 +/- 10.86 (n=15)	1.60 [-5.09, 8.29]	0.625	0.769
Clinical chemistry	Cholesterol	1.67 +/- 0.25 (n=15)	1.64 +/- 0.22 (n=15)	0.02 [-0.15, 0.20]	0.790	0.842
Clinical chemistry	Albumin	38.73 +/- 1.52 (n=15)	38.82 +/- 1.13 (n=15)	-0.09 [-1.10, 0.91]	0.850	0.887
Clinical chemistry	GLDH	6.43 +/- 0.89 (n=15)	6.39 +/- 1.06 (n=15)	0.04 [-0.69, 0.77]	0.912	0.931
Organ weights	Thymus	0.1676 +/- 0.0418 (n=10)	0.1348 +/- 0.0288 (n=10)	0.0329 [-0.0011, 0.0669]	0.057	0.161
Organ weights	Testes	1.1295 +/- 0.0840 (n=10)	1.2131 +/- 0.1202 (n=10)	-0.0836 [-0.1819, 0.0147]	0.090	0.197
Organ weights	Epididymides	0.3776 +/- 0.0361 (n=10)	0.4073 +/- 0.0409 (n=10)	-0.0297 [-0.0660, 0.0065]	0.102	0.204

Domain	Parameter	RCC vehicle	RCC MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Organ weights	Kidneys	0.7147 +/- 0.0342 (n=10)	0.7648 +/- 0.0823 (n=10)	-0.0501 [-0.1115, 0.0113]	0.101	0.204
Organ weights	Terminal BW	289.0000 +/- 21.1397 (n=10)	273.8000 +/- 20.2528 (n=10)	15.2000 [-4.2525, 34.6525]	0.118	0.227
Organ weights	Seminal Vesicles	0.2066 +/- 0.1151 (n=10)	0.2807 +/- 0.1351 (n=10)	-0.0742 [-0.1923, 0.0440]	0.203	0.333
Organ weights	Adrenals	0.0203 +/- 0.0024 (n=10)	0.0211 +/- 0.0017 (n=10)	-0.0009 [-0.0028, 0.0011]	0.364	0.529
Organ weights	Brain	0.7383 +/- 0.0664 (n=10)	0.7565 +/- 0.0544 (n=10)	-0.0182 [-0.0754, 0.0391]	0.512	0.665
Organ weights	Heart	0.3513 +/- 0.0175 (n=10)	0.3570 +/- 0.0370 (n=10)	-0.0057 [-0.0338, 0.0223]	0.665	0.778
Organ weights	Spleen	0.2050 +/- 0.0200 (n=10)	0.2007 +/- 0.0214 (n=10)	0.0042 [-0.0152, 0.0237]	0.653	0.778
Organ weights	Liver	2.9427 +/- 0.1274 (n=10)	2.9148 +/- 0.1998 (n=10)	0.0279 [-0.1316, 0.1874]	0.715	0.817
Organ weights	(Para)thyroids	0.0055 +/- 0.0009 (n=10)	0.0056 +/- 0.0005 (n=10)	-0.0001 [-0.0008, 0.0006]	0.751	0.820
Organ weights	Prostate	0.2068 +/- 0.0691 (n=10)	0.2087 +/- 0.0711 (n=10)	-0.0019 [-0.0677, 0.0640]	0.953	0.953
Immunology	IgA	33535.10 +/- 8894.44 (n=10)	15549.30 +/- 5432.21 (n=10)	17985.80 [10956.71, 25014.89]	<0.001	0.003
Immunology	TC Cells	0.87 +/- 0.22 (n=10)	0.47 +/- 0.23 (n=10)	0.40 [0.19, 0.61]	<0.001	0.011
Immunology	T Cells	2.94 +/- 0.72 (n=10)	1.64 +/- 0.88 (n=10)	1.31 [0.55, 2.06]	0.002	0.016
Immunology	TH Cells	2.07 +/- 0.51 (n=10)	1.13 +/- 0.70 (n=10)	0.94 [0.36, 1.52]	0.003	0.021
Immunology	NK Cells	0.17 +/- 0.05 (n=10)	0.23 +/- 0.09 (n=10)	-0.06 [-0.13, 0.01]	0.074	0.188
Immunology	B Cells	2.30 +/- 0.48 (n=10)	1.91 +/- 0.68 (n=10)	0.39 [-0.17, 0.95]	0.158	0.272
Other	Body weight gain	76.15 +/- 19.59 (n=15)	54.80 +/- 16.81 (n=15)	21.35 [7.69, 35.02]	0.003	0.021

Table SR4 – Conventional cage vehicle vs. MTX – Day 57

Domain	Parameter	Conventional cage vehicle	Conventional cage MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Hematology	Haematocrit	48.04 +/- 1.22 (n=5)	49.98 +/- 1.18 (n=4)	-1.94 [-3.86, -0.01]	0.049	0.585
Hematology	Basophils	0.02 +/- 0.01 (n=5)	0.02 +/- 0.01 (n=4)	0.01 [-0.01, 0.02]	0.336	0.864
Hematology	Eosinophils	0.09 +/- 0.04 (n=5)	0.07 +/- 0.03 (n=4)	0.02 [-0.04, 0.08]	0.413	0.864
Hematology	Haemoglobin	16.26 +/- 0.68 (n=5)	16.60 +/- 0.50 (n=4)	-0.34 [-1.27, 0.59]	0.414	0.864
Hematology	Monocytes	0.08 +/- 0.02 (n=5)	0.10 +/- 0.04 (n=4)	-0.02 [-0.07, 0.04]	0.477	0.888
Hematology	Reticulocytes	175.30 +/- 25.99 (n=5)	166.50 +/- 14.37 (n=4)	8.80 [-24.14, 41.74]	0.542	0.888
Hematology	Neutrophils	1.01 +/- 0.22 (n=5)	1.11 +/- 0.36 (n=4)	-0.10 [-0.64, 0.43]	0.631	0.915
Hematology	Red blood cells	9.08 +/- 0.29 (n=5)	8.96 +/- 0.46 (n=4)	0.11 [-0.57, 0.79]	0.686	0.915
Hematology	White blood cells	4.97 +/- 0.69 (n=5)	5.13 +/- 1.25 (n=4)	-0.17 [-2.03, 1.70]	0.822	0.929
Hematology	Lymphocytes	3.74 +/- 0.73 (n=5)	3.81 +/- 1.15 (n=4)	-0.07 [-1.78, 1.64]	0.920	0.967
Hematology	Platelets	795.60 +/- 120.45 (n=5)	799.75 +/- 89.92 (n=4)	-4.15 [-170.11, 161.81]	0.954	0.970
Clinical chemistry	Sodium	145.40 +/- 0.58 (n=5)	142.88 +/- 0.34 (n=4)	2.53 [1.78, 3.27]	<0.001	0.006
Clinical chemistry	Chloride	104.14 +/- 0.86 (n=5)	102.22 +/- 0.29 (n=4)	1.92 [0.87, 2.96]	0.005	0.125
Clinical chemistry	Calcium	2.42 +/- 0.05 (n=5)	2.52 +/- 0.08 (n=4)	-0.11 [-0.22, 0.01]	0.062	0.593
Clinical chemistry	Creatinine	26.20 +/- 3.11 (n=5)	22.25 +/- 2.87 (n=4)	3.95 [-0.81, 8.71]	0.090	0.618
Clinical chemistry	Inorganic phosphate	1.92 +/- 0.24 (n=5)	2.12 +/- 0.10 (n=4)	-0.20 [-0.49, 0.09]	0.134	0.805
Clinical chemistry	ALP	70.80 +/- 11.92 (n=5)	77.25 +/- 4.43 (n=4)	-6.45 [-21.05, 8.15]	0.312	0.864
Clinical chemistry	Cholesterol	1.61 +/- 0.24 (n=5)	1.38 +/- 0.24 (n=4)	0.22 [-0.17, 0.61]	0.215	0.864
Clinical chemistry	Glucose	4.72 +/- 0.84 (n=5)	4.22 +/- 0.43 (n=4)	0.50 [-0.56, 1.55]	0.295	0.864
Clinical chemistry	Potassium	4.63 +/- 0.35 (n=5)	4.43 +/- 0.32 (n=4)	0.20 [-0.33, 0.73]	0.404	0.864
Clinical chemistry	Triglycerides	0.43 +/- 0.19 (n=5)	0.52 +/- 0.05 (n=4)	-0.09 [-0.32, 0.14]	0.347	0.864
Clinical chemistry	GLDH	6.48 +/- 0.82 (n=5)	11.55 +/- 11.51 (n=4)	-5.07 [-23.34, 13.20]	0.444	0.887
Clinical chemistry	Total protein	58.74 +/- 2.09 (n=5)	58.20 +/- 1.59 (n=4)	0.54 [-2.36, 3.44]	0.673	0.915
Clinical chemistry	ALAT	37.40 +/- 2.61 (n=5)	35.50 +/- 9.68 (n=4)	1.90 [-13.04, 16.84]	0.726	0.917
Clinical chemistry	Urea	5.40 +/- 0.57 (n=5)	5.30 +/- 0.16 (n=4)	0.10 [-0.59, 0.79]	0.723	0.917
Clinical chemistry	Albumin	40.20 +/- 1.68 (n=5)	40.38 +/- 0.90 (n=4)	-0.17 [-2.30, 1.95]	0.848	0.929
Clinical chemistry	ASAT	88.80 +/- 9.68 (n=5)	87.75 +/- 1.26 (n=4)	1.05 [-10.90, 13.00]	0.822	0.929
Clinical chemistry	Bilirubin	0.82 +/- 0.23 (n=5)	0.82 +/- 0.15 (n=4)	-0.00 [-0.31, 0.30]	0.970	0.970
Organ weights	Thymus	0.1218 +/- 0.0143 (n=5)	0.0993 +/- 0.0136 (n=4)	0.0225 [0.0002, 0.0448]	0.048	0.585
Organ weights	Spleen	0.1939 +/- 0.0223 (n=5)	0.1703 +/- 0.0113 (n=4)	0.0236 [-0.0043, 0.0514]	0.084	0.618
Organ weights	Heart	0.3323 +/- 0.0388 (n=5)	0.3070 +/- 0.0229 (n=4)	0.0253 [-0.0245, 0.0750]	0.266	0.864

Domain	Parameter	Conventional cage vehicle	Conventional cage MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Organ weights	Kidneys	0.7171 +/- 0.0533 (n=5)	0.6658 +/- 0.0561 (n=4)	0.0513 [-0.0375, 0.1401]	0.210	0.864
Organ weights	Liver	2.7969 +/- 0.2393 (n=5)	2.6552 +/- 0.1349 (n=4)	0.1418 [-0.1626, 0.4461]	0.302	0.864
Organ weights	Prostate	0.2204 +/- 0.0635 (n=5)	0.2513 +/- 0.0256 (n=4)	-0.0309 [-0.1089, 0.0471]	0.363	0.864
Organ weights	Brain	0.6804 +/- 0.0534 (n=5)	0.6618 +/- 0.0268 (n=4)	0.0185 [-0.0481, 0.0852]	0.523	0.888
Organ weights	Seminal Vesicles	0.3599 +/- 0.1746 (n=5)	0.4187 +/- 0.0451 (n=4)	-0.0587 [-0.2725, 0.1550]	0.504	0.888
Organ weights	(Para)thyroids	0.0053 +/- 0.0011 (n=5)	0.0049 +/- 0.0004 (n=4)	0.0004 [-0.0010, 0.0017]	0.502	0.888
Organ weights	Adrenals	0.0184 +/- 0.0025 (n=5)	0.0191 +/- 0.0018 (n=4)	-0.0007 [-0.0042, 0.0027]	0.634	0.915
Organ weights	Epididymides	0.3632 +/- 0.0374 (n=5)	0.3514 +/- 0.0321 (n=4)	0.0118 [-0.0431, 0.0667]	0.627	0.915
Organ weights	Terminal BW	318.6000 +/- 39.0167 (n=5)	323.5000 +/- 20.4042 (n=4)	-4.9000 [-53.9164, 44.1164]	0.816	0.929
Organ weights	Testes	1.0341 +/- 0.0850 (n=5)	1.0289 +/- 0.0793 (n=4)	0.0052 [-0.1256, 0.1360]	0.927	0.967
Immunology	NK Cells	0.17 +/- 0.06 (n=5)	0.14 +/- 0.04 (n=4)	0.04 [-0.04, 0.12]	0.316	0.864
Immunology	T Cells	2.20 +/- 0.67 (n=5)	1.87 +/- 0.36 (n=4)	0.33 [-0.52, 1.17]	0.384	0.864
Immunology	TH Cells	1.62 +/- 0.51 (n=5)	1.31 +/- 0.14 (n=4)	0.30 [-0.32, 0.92]	0.263	0.864
Immunology	B Cells	1.31 +/- 0.31 (n=5)	1.52 +/- 0.58 (n=4)	-0.21 [-1.07, 0.66]	0.555	0.888
Immunology	TC Cells	0.53 +/- 0.19 (n=5)	0.55 +/- 0.15 (n=4)	-0.02 [-0.28, 0.24]	0.851	0.929
Immunology	IgA	27932.80 +/- 4227.35 (n=5)	26510.50 +/- 8560.40 (n=4)	1422.30 [-11367.62, 14212.22]	0.776	0.929
Other	Body weight gain	100.16 +/- 25.72 (n=5)	93.50 +/- 21.29 (n=4)	6.66 [-30.43, 43.75]	0.684	0.915

Table SR5 – TRCC vehicle vs. MTX – Day 57

Domain	Parameter	TRCC vehicle	TRCC MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Hematology	Haemoglobin	15.96 +/- 0.39 (n=5)	16.50 +/- 0.51 (n=5)	-0.54 [-1.21, 0.13]	0.100	0.478
Hematology	Haematocrit	47.70 +/- 1.83 (n=5)	48.58 +/- 1.17 (n=5)	-0.88 [-3.19, 1.43]	0.397	0.848
Hematology	Monocytes	0.09 +/- 0.01 (n=5)	0.10 +/- 0.02 (n=5)	-0.01 [-0.04, 0.02]	0.351	0.848
Hematology	Reticulocytes	192.02 +/- 16.70 (n=5)	200.28 +/- 12.88 (n=5)	-8.26 [-30.26, 13.74]	0.408	0.848
Hematology	Basophils	0.02 +/- 0.01 (n=5)	0.02 +/- 0.01 (n=5)	-0.00 [-0.02, 0.01]	0.636	0.880
Hematology	Eosinophils	0.09 +/- 0.03 (n=5)	0.08 +/- 0.02 (n=5)	0.01 [-0.03, 0.04]	0.695	0.880
Hematology	Neutrophils	1.09 +/- 0.36 (n=5)	1.00 +/- 0.19 (n=5)	0.09 [-0.35, 0.52]	0.648	0.880
Hematology	Platelets	806.40 +/- 76.50 (n=5)	826.60 +/- 55.20 (n=5)	-20.20 [-119.19, 78.79]	0.646	0.880
Hematology	Red blood cells	8.97 +/- 0.49 (n=5)	9.12 +/- 0.50 (n=5)	-0.16 [-0.88, 0.57]	0.632	0.880
Hematology	Lymphocytes	3.34 +/- 0.67 (n=5)	3.41 +/- 0.64 (n=5)	-0.07 [-1.02, 0.89]	0.874	0.953
Hematology	White blood cells	4.63 +/- 0.93 (n=5)	4.62 +/- 0.76 (n=5)	0.00 [-1.24, 1.24]	0.997	0.997
Clinical chemistry	Sodium	144.60 +/- 0.47 (n=5)	142.42 +/- 0.57 (n=5)	2.18 [1.41, 2.95]	<0.001	0.010
Clinical chemistry	Chloride	104.82 +/- 0.80 (n=5)	102.92 +/- 0.61 (n=5)	1.90 [0.85, 2.95]	0.003	0.081
Clinical chemistry	Glucose	5.28 +/- 0.62 (n=5)	4.30 +/- 0.47 (n=5)	0.98 [0.17, 1.79]	0.024	0.302
Clinical chemistry	Urea	6.14 +/- 0.51 (n=5)	5.28 +/- 0.55 (n=5)	0.86 [0.08, 1.64]	0.034	0.302
Clinical chemistry	ALAT	42.00 +/- 8.57 (n=5)	33.00 +/- 5.34 (n=5)	9.00 [-1.78, 19.78]	0.088	0.478
Clinical chemistry	Creatinine	24.20 +/- 2.28 (n=5)	22.20 +/- 1.64 (n=5)	2.00 [-0.95, 4.95]	0.154	0.585
Clinical chemistry	Inorganic phosphate	2.24 +/- 0.12 (n=5)	2.14 +/- 0.08 (n=5)	0.09 [-0.06, 0.24]	0.185	0.585
Clinical chemistry	ALP	92.20 +/- 21.81 (n=5)	81.80 +/- 11.65 (n=5)	10.40 [-16.54, 37.34]	0.383	0.848
Clinical chemistry	Calcium	2.47 +/- 0.04 (n=5)	2.19 +/- 0.64 (n=5)	0.28 [-0.51, 1.08]	0.381	0.848
Clinical chemistry	Total protein	56.94 +/- 0.79 (n=5)	57.56 +/- 1.42 (n=5)	-0.62 [-2.38, 1.14]	0.424	0.848
Clinical chemistry	GLDH	11.52 +/- 3.58 (n=5)	9.56 +/- 4.41 (n=5)	1.96 [-3.94, 7.86]	0.464	0.856
Clinical chemistry	Potassium	4.77 +/- 0.41 (n=5)	5.43 +/- 1.74 (n=5)	-0.66 [-2.80, 1.47]	0.450	0.856
Clinical chemistry	Albumin	39.30 +/- 0.45 (n=5)	39.58 +/- 1.09 (n=5)	-0.28 [-1.61, 1.05]	0.616	0.880
Clinical chemistry	ASAT	89.60 +/- 16.10 (n=5)	86.40 +/- 12.20 (n=5)	3.20 [-17.90, 24.30]	0.733	0.880
Clinical chemistry	Bilirubin	0.64 +/- 0.26 (n=5)	0.58 +/- 0.18 (n=5)	0.06 [-0.27, 0.39]	0.684	0.880
Clinical chemistry	Triglycerides	0.67 +/- 0.29 (n=5)	0.61 +/- 0.23 (n=5)	0.06 [-0.32, 0.44]	0.722	0.880
Clinical chemistry	Cholesterol	1.38 +/- 0.21 (n=5)	1.35 +/- 0.21 (n=5)	0.03 [-0.28, 0.34]	0.828	0.924
Organ weights	Adrenals	0.0170 +/- 0.0019 (n=5)	0.0201 +/- 0.0018 (n=5)	-0.0030 [-0.0058, -0.0003]	0.035	0.302
Organ weights	Spleen	0.1742 +/- 0.0131 (n=5)	0.1561 +/- 0.0087 (n=5)	0.0180 [0.0014, 0.0347]	0.038	0.302
Organ weights	Brain	0.6442 +/- 0.0504 (n=5)	0.6950 +/- 0.0299 (n=5)	-0.0508 [-0.1138, 0.0122]	0.097	0.478

Domain	Parameter	TRCC vehicle	TRCC MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Organ weights	Terminal BW	341.4000 +/- 27.9786 (n=5)	312.6000 +/- 15.3721 (n=5)	28.8000 [-5.8449, 63.4449]	0.089	0.478
Organ weights	Seminal Vesicles	0.3821 +/- 0.0956 (n=5)	0.4552 +/- 0.0492 (n=5)	-0.0731 [-0.1908, 0.0447]	0.180	0.585
Organ weights	(Para)thyroids	0.0051 +/- 0.0014 (n=5)	0.0064 +/- 0.0011 (n=5)	-0.0013 [-0.0031, 0.0005]	0.137	0.585
Organ weights	Liver	2.7402 +/- 0.1537 (n=5)	2.6351 +/- 0.0934 (n=5)	0.1052 [-0.0873, 0.2977]	0.235	0.662
Organ weights	Heart	0.3118 +/- 0.0144 (n=5)	0.3240 +/- 0.0198 (n=5)	-0.0121 [-0.0378, 0.0135]	0.303	0.807
Organ weights	Epididymides	0.3739 +/- 0.0217 (n=5)	0.3651 +/- 0.0390 (n=5)	0.0088 [-0.0396, 0.0572]	0.674	0.880
Organ weights	Thymus	0.1049 +/- 0.0103 (n=5)	0.1091 +/- 0.0164 (n=5)	-0.0042 [-0.0249, 0.0164]	0.640	0.880
Organ weights	Kidneys	0.6776 +/- 0.0473 (n=5)	0.6844 +/- 0.0154 (n=5)	-0.0069 [-0.0647, 0.0509]	0.770	0.896
Organ weights	Testes	1.0416 +/- 0.1011 (n=5)	1.0232 +/- 0.1036 (n=5)	0.0184 [-0.1309, 0.1676]	0.784	0.896
Organ weights	Prostate	0.2382 +/- 0.0513 (n=5)	0.2362 +/- 0.0361 (n=5)	0.0020 [-0.0640, 0.0681]	0.945	0.986
Immunology	IgA	37248.80 +/- 5572.42 (n=5)	30766.00 +/- 8121.63 (n=5)	6482.80 [-3908.32, 16873.92]	0.184	0.585
Immunology	B Cells	1.55 +/- 0.53 (n=5)	1.41 +/- 0.30 (n=5)	0.14 [-0.52, 0.80]	0.621	0.880
Immunology	TH Cells	1.22 +/- 0.32 (n=5)	1.11 +/- 0.27 (n=5)	0.11 [-0.32, 0.54]	0.563	0.880
Immunology	TC Cells	0.43 +/- 0.15 (n=5)	0.47 +/- 0.20 (n=5)	-0.04 [-0.31, 0.22]	0.711	0.880
Immunology	NK Cells	0.16 +/- 0.04 (n=5)	0.16 +/- 0.05 (n=5)	0.00 [-0.06, 0.07]	0.927	0.986
Immunology	T Cells	1.64 +/- 0.33 (n=5)	1.63 +/- 0.43 (n=5)	0.01 [-0.56, 0.57]	0.978	0.997
Other	Body weight gain	122.62 +/- 25.47 (n=5)	101.38 +/- 21.75 (n=5)	21.24 [-13.45, 55.93]	0.195	0.585

Table SR6 – RCC vehicle vs. MTX – Day 57

Domain	Parameter	RCC vehicle	RCC MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Hematology	Eosinophils	0.07 +/- 0.03 (n=4)	0.10 +/- 0.04 (n=5)	-0.03 [-0.09, 0.03]	0.262	0.741
Hematology	Haematocrit	46.50 +/- 1.64 (n=4)	47.64 +/- 2.33 (n=5)	-1.14 [-4.27, 1.99]	0.418	0.820
Hematology	Haemoglobin	16.18 +/- 0.38 (n=4)	16.42 +/- 0.52 (n=5)	-0.25 [-0.95, 0.46]	0.439	0.820
Hematology	Platelets	802.50 +/- 93.95 (n=4)	762.80 +/- 72.97 (n=5)	39.70 [-102.62, 182.02]	0.515	0.820
Hematology	Red blood cells	8.62 +/- 0.44 (n=4)	8.86 +/- 0.46 (n=5)	-0.24 [-0.96, 0.48]	0.449	0.820
Hematology	Reticulocytes	160.38 +/- 29.46 (n=4)	173.98 +/- 30.23 (n=5)	-13.61 [-61.39, 34.18]	0.519	0.820
Hematology	Monocytes	0.10 +/- 0.02 (n=4)	0.11 +/- 0.04 (n=5)	-0.01 [-0.06, 0.04]	0.557	0.835
Hematology	Lymphocytes	3.87 +/- 0.59 (n=4)	4.02 +/- 0.75 (n=5)	-0.15 [-1.21, 0.91]	0.747	0.917
Hematology	White blood cells	4.92 +/- 0.56 (n=4)	5.14 +/- 1.03 (n=5)	-0.22 [-1.51, 1.08]	0.701	0.917
Hematology	Basophils	0.03 +/- 0.02 (n=4)	0.03 +/- 0.01 (n=5)	-0.00 [-0.03, 0.03]	0.965	0.973
Hematology	Neutrophils	0.83 +/- 0.30 (n=4)	0.85 +/- 0.28 (n=5)	-0.02 [-0.50, 0.45]	0.916	0.973
Clinical chemistry	Potassium	4.77 +/- 0.20 (n=5)	4.28 +/- 0.16 (n=5)	0.49 [0.22, 0.75]	0.003	0.051
Clinical chemistry	Sodium	144.48 +/- 0.36 (n=5)	142.48 +/- 0.72 (n=5)	2.00 [1.12, 2.88]	0.002	0.051
Clinical chemistry	Triglycerides	0.31 +/- 0.10 (n=5)	0.51 +/- 0.06 (n=5)	-0.20 [-0.33, -0.08]	0.006	0.073
Clinical chemistry	Glucose	5.62 +/- 0.61 (n=5)	4.44 +/- 0.65 (n=5)	1.18 [0.26, 2.10]	0.018	0.146
Clinical chemistry	Calcium	2.43 +/- 0.07 (n=5)	2.53 +/- 0.04 (n=5)	-0.09 [-0.18, -0.00]	0.044	0.191
Clinical chemistry	Chloride	104.86 +/- 0.56 (n=5)	103.32 +/- 1.19 (n=5)	1.54 [0.09, 2.99]	0.041	0.191
Clinical chemistry	Creatinine	24.20 +/- 2.49 (n=5)	20.20 +/- 2.68 (n=5)	4.00 [0.22, 7.78]	0.041	0.191
Clinical chemistry	Albumin	38.28 +/- 0.91 (n=5)	39.54 +/- 0.84 (n=5)	-1.26 [-2.54, 0.02]	0.053	0.211
Clinical chemistry	Total protein	55.68 +/- 0.73 (n=5)	57.22 +/- 1.52 (n=5)	-1.54 [-3.41, 0.33]	0.090	0.331
Clinical chemistry	Cholesterol	1.28 +/- 0.18 (n=5)	1.52 +/- 0.25 (n=5)	-0.24 [-0.56, 0.08]	0.119	0.409
Clinical chemistry	Urea	4.98 +/- 0.70 (n=5)	5.42 +/- 0.53 (n=5)	-0.44 [-1.36, 0.48]	0.300	0.799
Clinical chemistry	ALAT	34.20 +/- 2.86 (n=5)	33.00 +/- 1.58 (n=5)	1.20 [-2.35, 4.75]	0.442	0.820
Clinical chemistry	GLDH	8.48 +/- 3.57 (n=5)	6.96 +/- 1.20 (n=5)	1.52 [-2.84, 5.88]	0.409	0.820
Clinical chemistry	Inorganic phosphate	2.36 +/- 0.10 (n=5)	2.31 +/- 0.15 (n=5)	0.05 [-0.14, 0.24]	0.525	0.820
Clinical chemistry	ALP	81.40 +/- 12.66 (n=5)	77.40 +/- 21.78 (n=5)	4.00 [-23.13, 31.13]	0.734	0.917
Clinical chemistry	ASAT	72.80 +/- 8.58 (n=5)	74.00 +/- 7.04 (n=5)	-1.20 [-12.72, 10.32]	0.815	0.917
Clinical chemistry	Bilirubin	0.86 +/- 0.22 (n=5)	0.82 +/- 0.26 (n=5)	0.04 [-0.31, 0.39]	0.799	0.917
Organ weights	Brain	0.6362 +/- 0.0396 (n=5)	0.7460 +/- 0.0435 (n=5)	-0.1098 [-0.1706, -0.0490]	0.003	0.051
Organ weights	Terminal BW	337.2000 +/- 26.3382 (n=5)	295.6000 +/- 21.6633 (n=5)	41.6000 [6.2014, 76.9986]	0.027	0.184

Domain	Parameter	RCC vehicle	RCC MTX	Difference [95% CI]	p-value (raw)	p-value (BH)
Organ weights	Seminal Vesicles	0.4295 +/- 0.0996 (n=5)	0.2770 +/- 0.0889 (n=5)	0.1525 [0.0146, 0.2905]	0.034	0.191
Organ weights	(Para)thyroids	0.0050 +/- 0.0003 (n=5)	0.0061 +/- 0.0017 (n=5)	-0.0010 [-0.0032, 0.0011]	0.254	0.741
Organ weights	Thymus	0.1146 +/- 0.0187 (n=5)	0.1033 +/- 0.0158 (n=5)	0.0113 [-0.0141, 0.0366]	0.334	0.802
Organ weights	Kidneys	0.7284 +/- 0.0507 (n=5)	0.6977 +/- 0.0747 (n=5)	0.0307 [-0.0646, 0.1260]	0.472	0.820
Organ weights	Prostate	0.2359 +/- 0.0437 (n=5)	0.2142 +/- 0.0590 (n=5)	0.0216 [-0.0552, 0.0984]	0.530	0.820
Organ weights	Heart	0.3447 +/- 0.0199 (n=5)	0.3366 +/- 0.0310 (n=5)	0.0082 [-0.0310, 0.0473]	0.636	0.907
Organ weights	Liver	2.6786 +/- 0.1402 (n=5)	2.7223 +/- 0.1463 (n=5)	-0.0437 [-0.2527, 0.1653]	0.643	0.907
Organ weights	Adrenals	0.0176 +/- 0.0029 (n=5)	0.0180 +/- 0.0030 (n=5)	-0.0004 [-0.0047, 0.0039]	0.832	0.917
Organ weights	Epididymides	0.3865 +/- 0.0456 (n=5)	0.3924 +/- 0.0437 (n=5)	-0.0059 [-0.0710, 0.0592]	0.841	0.917
Organ weights	Testes	1.0867 +/- 0.1003 (n=5)	1.1019 +/- 0.1220 (n=5)	-0.0152 [-0.1791, 0.1486]	0.835	0.917
Organ weights	Spleen	0.1753 +/- 0.0097 (n=5)	0.1743 +/- 0.0276 (n=5)	0.0010 [-0.0327, 0.0347]	0.941	0.973
Immunology	NK Cells	0.12 +/- 0.02 (n=4)	0.16 +/- 0.06 (n=5)	-0.05 [-0.12, 0.03]	0.161	0.515
Immunology	TH Cells	1.61 +/- 0.25 (n=4)	1.44 +/- 0.22 (n=5)	0.17 [-0.22, 0.55]	0.328	0.802
Immunology	T Cells	2.16 +/- 0.39 (n=4)	1.95 +/- 0.34 (n=5)	0.21 [-0.39, 0.81]	0.432	0.820
Immunology	TC Cells	0.56 +/- 0.17 (n=4)	0.53 +/- 0.14 (n=5)	0.03 [-0.23, 0.28]	0.808	0.917
Immunology	IgA	37855.00 +/- 7594.25 (n=5)	39443.00 +/- 12769.89 (n=5)	-1588.00 [-17539.95, 14363.95]	0.818	0.917
Immunology	B Cells	1.54 +/- 0.39 (n=4)	1.53 +/- 0.18 (n=5)	0.01 [-0.58, 0.60]	0.973	0.973
Other	Body weight gain	115.96 +/- 15.36 (n=5)	79.46 +/- 17.04 (n=5)	36.50 [12.80, 60.20]	0.008	0.073