

Supplementary Tables

Descriptive statistics (means, standard deviations) were computed for each outcome, and bivariate associations were estimated using Pearson correlation coefficients. Multiple regression models included predictors for treatment, sex, and the total amount of observed treatment time. Statistical significance for main effects of treatment and sex was determined through comparisons to the Bonferroni-adjusted significance level (0.0004). Following primary models, exploratory analyses were conducted by including additional effects for treatment/sex and treatment time/sex interactions (significance was accepted at 0.05). Finally, dimensionality reduction for bone morphology (by micro-CT), histomorphometry, serum markers of bone remodeling, mechanical testing, and serum hormone measures, was performed using principal components analysis (PCA). Statistical significance (pre-adjustment) was set at $p < 0.05$. Analysis was conducted in R Statistical Software (v.4.1.2; R Core Team 2023).

	CTL M	CANA M	CTL F	CANA F		main effects		interactions
	N=16	N=20	N=17	N=25		Sex:M	TxCANA	sexM: TxCANA
Insulin pg/ml	365.722 214.671	161.001 49.924	176.387 39.264	138.599 68.566	Est.	92.120	-114.930	-166.930
					SE	26.700	26.990	50.800
					P	P<0.001	P<0.0001	P<0.01
Glucagon pg/ml	9.912 3.685	12.904 4.883	19.146 16.558	34.670 31.056	Est.	-16.191	9.761	-12.532
					SE	4.573	4.586	9.147
					P	P<0.001	P<0.05	0.175
Insulin/glucagon	39.337 23.627	13.702 5.075	12.469 5.472	6.200 4.997	Est.	15.818	-15.179	-19.366
					SE	2.943	2.964	5.517
					P	P<0.0001	P<0.0001	P<0.001
Leptin pg/ml	13380.550 5641.983	3371.070 2320.836	5589.573 2451.231	2920.785 1922.156	Est.	3628.400	-6059.400	-7340.700
					SE	847.200	852.400	1491.700
					P	P<0.0001	P<0.0001	P<0.0001
Active GLP-1 p/mol	0.123 0.057	0.210 0.164	0.148 0.077	0.172 0.131	Est.	0.011	0.053	0.062
					SE	0.027	0.028	0.055
					P	0.692	0.056	0.264
IL-6 pg/ml	15.216 9.998	23.562 17.521	12.199 7.675	10.782 8.797	Est.	8.746	3.039	9.762
					SE	2.798	2.831	5.602
					P	P<0.01	0.287	0.086
MCP-1 pg/ml	19.504 5.875	17.745 6.315	31.852 11.523	22.975 12.381	Est.	-8.343	-5.560	7.118
					SE	2.275	2.288	4.541
					P	P<0.001	P<0.05	0.121
TNF-a pg/ml	6.765 2.074	4.694 1.168	6.911 1.576	5.096 1.571	Est.	-0.292	-1.936	-0.256
					SE	0.364	0.367	0.739
					P	0.424	P<0.0001	0.730

Supplementary Table 1: Serum levels of metabolic hormones and inflammatory markers after 6 months of CANA treatment. Descriptive statistics (means (top number), standard deviations (bottom number)) were computed for each hormone. Statistical significance for main effects of sex (M) and treatment (Tx) was determined through comparisons to the Bonferroni-adjusted significance level (.0004). Fibroblast growth factor-23 (FGF23), monocyte chemotactic protein-1 (MCP-1), interleukine-6 (IL6), Tumor necrosis factor-a (TNF-a). Estimated value (Est), standard error (SE), p value (P).

	CTL Males				CANA Males			CTL Females				CANA Females			Main effects				Interactions			
	Age: 6m TX time: 0m n=18	Age: 7m TX time: 1m n=19	Age: 9m TX time: 3m n=23	Age: 12m TX time: 6m n=19	Age: 7m TX time: 1m n=20	Age: 9m TX time: 3m n=28	Age: 12m TX time: 6m n=22	Age: 6m TX time: 0m n=19	Age: 7m TX time: 1m n=19	Age: 9m TX time: 3m n=14	Age: 12m TX time: 6m n=30	Age: 7m TX time: 1m n=22	Age: 9m TX time: 3m n=15	Age: 12m TX time: 6m n=44		sexM	TxCANA	Tx time months`3	Tx time months`6	sexM:TxCANA	Sex(M);Tx time months`3	Sex(M);Tx time months`6
Ec.MS/BS	0.516	0.259	0.205	0.363	0.361	0.194	0.367	0.553	0.377	0.329	0.455	0.379	0.335	0.463	Est	-0.096	0.015	-0.084	0.067	0.021	-0.067	-0.027
	0.117	0.140	0.152	0.124	0.085	0.153	0.128	0.125	0.097	0.145	0.105	0.104	0.101	0.119	SE	0.015	0.015	0.020	0.018	0.030	0.040	0.037
															P	P<0.0001	0.303	P<0.0001	P<0.001	0.479	0.091	0.456
Ec.MAR Um/day	0.774	0.234	0.262	0.545	0.332	0.281	0.452	0.821	0.326	0.353	0.632	0.337	0.370	0.563	Est	-0.080	-0.011	0.008	0.238	0.034	-0.042	-0.049
	0.182	0.179	0.125	0.144	0.179	0.111	0.101	0.198	0.164	0.113	0.179	0.169	0.101	0.178	SE	0.019	0.019	0.025	0.023	0.037	0.050	0.046
															P	P<0.0001	0.547	0.732	P<0.0001	0.362	0.404	0.289
Ec.BFR Um/day*100	39.519	7.452	6.016	20.736	12.006	6.400	16.702	46.089	12.709	12.020	29.161	13.044	12.784	27.049	Est	-6.522	-0.261	-1.925	12.359	0.888	-3.069	-6.242
	11.535	8.083	5.883	10.536	7.361	5.332	7.036	16.863	6.634	6.397	11.411	7.831	5.892	13.248	SE	1.123	1.097	1.440	1.326	2.200	2.900	2.665
															P	P<0.0001	0.812	0.182	P<0.0001	0.687	0.291	P<0.05
P.MS/BS	0.806	0.704	0.400	0.624	0.636	0.411	0.598	0.803	0.626	0.488	0.739	0.672	0.423	0.732	Est	-0.059	-0.013	-0.227	0.024	-0.025	-0.066	-0.144
	0.115	0.129	0.116	0.234	0.154	0.112	0.138	0.120	0.169	0.104	0.166	0.122	0.077	0.191	SE	0.019	0.019	0.025	0.023	0.038	0.049	0.045
															P	P<0.01	0.499	P<0.0001	0.300	0.513	0.183	P<0.01
P.MAR Um/day	0.996	0.558	0.562	0.514	0.381	0.513	0.436	0.763	0.538	0.613	0.437	0.466	0.702	0.448	Est	-0.035	-0.047	0.103	-0.032	-0.097	-0.090	0.059
	0.143	0.164	0.140	0.153	0.067	0.091	0.092	0.129	0.094	0.202	0.079	0.139	0.160	0.101	SE	0.016	0.016	0.021	0.019	0.031	0.041	0.037
															P	P<0.05	P<0.01	P<0.0001	0.09371 .	P<0.01	P<0.05	0.116
P.BFR Um/day*100	81.088	38.693	22.836	34.889	24.784	21.443	26.672	60.511	33.948	29.440	32.997	31.499	29.853	33.786	Est	-3.787	-3.672	-6.677	-0.025	-7.043	-6.308	-2.036
	20.157	13.331	9.724	15.596	9.064	7.130	10.322	9.736	11.357	10.763	11.648	11.608	8.808	14.071	SE	1.458	1.424	1.869	1.721	2.824	3.782	3.476
															P	P<0.01	P<0.05	P<0.001	0.988	P<0.05	0.097	0.559

Supplementary Table 2: Cortical bone histomorphometry (femur mid-diaphysis). Right femurs were cleaned of excess soft tissues, infiltrated, and embedded in Technovit Resin (Technovit 7200 VLC). Embedded samples were cut using a diamond-coated wafering saw (IsoMet® 5000, Buehler, Lake Bluff, IL) at the mid-diaphysis. The block with the bone surface was mounted onto a strain-free Exakt plastic slide (Exakt Technologies, Oklahoma City, Okla., USA), thin sectioned with the Buehler IsoMet® 5000, and polished on an automated Exakt 400 CS Grinding System with 1,200-grit paper until plane parallel at a thickness of 50 µm. Sections were mounted on plastic slides, and images at 0.316µm/pixel resolution were acquired with a 20X magnification objective using fluorescence microscopy with a Leica-Leitz DMRXE Universal Microscope configured with a Marzhauser motorized stage and Leica 20X objective lens (Leica Microsystems, Bannockburn, Ill., USA). Our principal focus was mineral surface/bone surface (MS/BS, %), bone formation rate (BFR um/day x 100), and mineral apposition rate (MAR um/day) in the endosteal (Ec) or periosteal (Ps) cortical bone surfaces. All measurements were carried out by a single observer, who was blinded to specimen identity, using a BIOQUANT Osteo Measure system (Osteometrics, Atlanta, GA, USA), by standard protocols.

Descriptive statistics (means (top number), standard deviations (bottom number)) were computed for each hormone. Statistical significance for main effects of sex (M) and treatment (Tx) was determined through comparisons to the Bonferroni-adjusted significance level (.0004). Endosteal mineralized surface per bone surface (Ec MS/BS), endosteal mineral apposition rate (Ec.MAR), endosteal bone formation rate (Ec.BFR). Periosteal mineralized surface per bone surface (Ps MS/BS), periosteal mineral apposition rate (Ps.MAR), periosteal bone formation rate (Ps.BFR). Estimated value (Est), standard error (SE), p value (P).

	CTL Males			CANA Males			CTL Females			CANA Females				Main effects				Interactions		
	Age: 7m TX time: 1m n=20	Age: 9m TX time: 3m n=25	Age: 12m TX time: 6m n=20	Age: 7m TX time: 1m n=19	Age: 9m TX time: 3m n=30	Age: 12m TX time: 6m n=25	Age: 7m TX time: 1m n=19	Age: 9m TX time: 3m n=15	Age: 12m TX time: 6m n=30	Age: 7m TX time: 1m n=25	Age: 9m TX time: 3m n=15	Age: 12m TX time: 6m n=25		sexM	TxCANA	Tx time months' 3	Tx time months' 6	sexM: TxCANA	Sex(M); Tx time months' 3	Sex(M); Tx time months' 6
CTX ng/ml	0.780	0.885	0.795	0.692	0.772	0.713	0.761	0.839	0.743	0.733	0.743	0.759	Est	0.007	-0.060	0.069	0.007	-0.070	0.046	0.015
	0.134	0.131	0.146	0.120	0.161	0.188	0.111	0.110	0.223	0.074	0.128	0.104	SE	0.018	0.018	0.023	0.021	0.036	0.047	0.044
													P	0.699	P<0.01	P<0.01	0.723	0.052	0.322	0.729
P1NP ng/ml	31.766	26.271	18.505	23.814	15.872	23.141	2.366	31.311	30.745	2.537	19.199	25.293	Est	4.058	-5.957	7.092	10.816	11.610	-29.630	-31.420
	22.301	24.236	22.423	22.670	10.819	21.919	1.980	21.584	20.566	1.560	12.186	17.210	SE	2.445	2.411	3.085	2.924	4.843	5.853	5.509
													P	0.098135	P<0.05	P<0.05	P<0.001	0.981	P<0.0001	P<0.0001
PTH ng/ml	0.409	0.266	0.508	0.485	0.360	0.466	0.512	0.427	0.693	0.519	0.412	0.672	Est	-0.125	0.016	-0.107	0.102	0.055	-0.032	-0.134
	0.090	0.068	0.119	0.130	0.080	0.169	0.151	0.100	0.206	0.137	0.120	0.161	SE	0.017	0.017	0.021	0.021	0.035	0.043	0.042
													P	P<0.0001	0.350	P<0.0001	P<0.0001	0.117	0.455	P<0.01
FGF23 ng/ml	0.137		0.216	0.120		0.301	0.215		0.412	0.170		0.463	Est	-0.119	0.018	0.195		0.026		-0.119
	0.095		0.049	0.073		0.119	0.155		0.160	0.122		0.207	SE	0.022	0.022	0.022		0.044		0.043
													P	P<0.0001	0.408	P<0.0001		0.554		P<0.01

Supplementary Table 3: Serum levels of bone remodeling markers. Descriptive statistics (means (top number), standard deviations (bottom number)) were computed for each marker. Statistical significance for main effects of sex (M) and treatment (Tx) was determined through comparisons to the Bonferroni-adjusted significance level (.0004). crosslinked C-terminal telopeptides of type I collagen (CTX), procollagen type 1 N-terminal pro-peptide (P1NP), parathyroid hormone (PTH). Estimated value (Est), standard error (SE), p value (P).

	CTL Males				CANA Males			CTL Females				CANA Females				Main effects				Interactions		
	Age: 6m TX time: 0m n=18	Age: 7m TX time: 1m n=20	Age: 9m TX time: 3m n=23	Age: 12m TX time: 6m n=20	Age: 7m TX time: 1m n=20	Age: 9m TX time: 3m n=30	Age: 12m TX time: 6m n=22	Age: 6m TX time: 0m n=19	Age: 7m TX time: 1m n=19	Age: 9m TX time: 3m n=15	Age: 12m TX time: 6m n=30	Age: 7m TX time: 1m n=24	Age: 9m TX time: 3m n=15	Age: 12m TX time: 6m n=44		sexM	TxCANA	Tx time months'3	Tx time months'6	sexM: TxCANA	Sex(M);Tx time months'3	Sex(M);Tx time months'6
BV/TV, %	61.062	62.665	60.163	59.294	63.268	60.463	59.287	62.710	66.294	62.555	61.147	63.432	64.891	63.038	Est	-2.698	0.420	-1.887	-3.011	-0.303	-1.716	-1.245
	2.442	3.222	4.615	3.772	3.958	3.306	4.622	2.640	3.951	4.509	4.185	3.861	5.123	4.897	SE	0.522	0.511	0.667	0.616	1.025	1.353	1.247
															P	P<0.0001	0.412	P<0.01	P<0.0001	0.768	0.206	0.319
T.Ar, mm^2	1.708	1.743	1.711	1.935	1.662	1.709	1.838	1.443	1.475	1.578	1.657	1.512	1.512	1.642	Est	0.205	-0.033	0.023	0.164	-0.044	-0.039	0.028
	0.125	0.150	0.125	0.183	0.166	0.152	0.178	0.111	0.142	0.111	0.155	0.137	0.131	0.144	SE	0.018	0.018	0.024	0.022	0.036	0.048	0.044
															P	P<0.0001	0.0657	0.325	P<0.0001	0.223	0.419	0.520
B.Ar, mm^2	1.042	1.091	1.026	1.146	1.049	1.031	1.087	0.904	0.976	0.985	1.011	0.957	0.981	1.035	Est	0.081	-0.012	-0.016	0.052	-0.035	-0.057	-0.015
	0.081	0.092	0.066	0.121	0.098	0.078	0.112	0.071	0.09	0.074	0.095	0.085	0.113	0.120	SE	0.012	0.012	0.015	0.014	0.024	0.031	0.029
															P	P<0.0001	0.295	0.294	P<0.001	0.145	0.06765	0.611
MMI(polar), mm^4	0.426	0.453	0.422	0.531	0.415	0.424	0.478	0.299	0.322	0.354	0.380	0.331	0.333	0.381	Est	0.105	-0.015	-0.001	0.060	-0.025	-0.026	0.015
	0.060	0.074	0.054	0.098	0.080	0.068	0.084	0.045	0.056	0.043	0.07	0.057	0.061	0.066	SE	0.009	0.008	0.011	0.010	0.017	0.022	0.020
															P	P<0.0001	0.0837	0.959	P<0.0001	0.137	0.238	0.466
Cs.Th, mm	0.242	0.252	0.236	0.245	0.250	0.237	0.243	0.241	0.263	0.251	0.252	0.251	0.257	0.261	Est	-0.012	0.001	-0.009	-0.003	-0.003	-0.012	-0.008
	0.016	0.016	0.018	0.017	0.020	0.014	0.025	0.014	0.021	0.020	0.021	0.019	0.027	0.028	SE	0.003	0.003	0.003	0.003	0.005	0.007	0.006
															P	P<0.0001	0.792	P<0.01	0.413	0.540	0.0727	0.208
TMD, g/cc	1.302	1.380	1.406	1.454	1.375	1.420	1.439	1.331	1.411	1.412	1.456	1.417	1.423	1.443	Est	-0.013	-0.001	0.021	0.050	0.002	0.033	0.035
	0.029	0.039	0.032	0.033	0.037	0.034	0.031	0.025	0.021	0.028	0.028	0.022	0.036	0.031	SE	0.004	0.004	0.005	0.005	0.008	0.010	0.009
															P	P<0.001	0.774	P<0.0001	P<0.0001	0.800	P<0.01	P<0.001
Ma.Ar, mm^2	0.666	0.652	0.685	0.789	0.613	0.678	0.751	0.539	0.499	0.593	0.646	0.555	0.531	0.607	Est	0.124	-0.021	0.039	0.112	-0.009	0.019	0.043
	0.071	0.093	0.113	0.114	0.108	0.105	0.130	0.062	0.087	0.098	0.109	0.092	0.090	0.100	SE	0.013	0.013	0.016	0.015	0.025	0.033	0.031
															P	P<0.0001	0.0988	P<0.05	P<0.0001	0.710	0.572	0.162
Length, mm	15.776	16.085	16.101	16.182	16.030	16.149	16.157	15.571	16.022	16.068	16.353	16.006	15.979	16.212	Est	0.002	-0.046	0.057	0.201	0.085	0.066	-0.147
	0.338	0.163	0.309	0.476	0.113	0.260	0.504	0.240	0.174	0.354	0.485	0.184	0.219	0.420	SE	0.043	0.043	0.056	0.052	0.085	0.113	0.104
															P	0.969	0.276	0.312	P<0.001	0.317	0.561	0.159
Robustness, T.Ar/Length	0.108	0.108	0.106	0.120	0.104	0.106	0.114	0.093	0.092	0.098	0.101	0.096	0.095	0.101	Est	0.013	-0.002	0.001	0.009	-0.003	-0.002	0.003
	0.008	0.009	0.009	0.01	0.010	0.009	0.009	0.007	0.009	0.006	0.010	0.008	0.008	0.008	SE	0.001	0.001	0.001	0.001	0.002	0.003	0.003
															P	P<0.0001	0.146	0.565	P<0.0001	0.115	0.437	0.245

Supplementary Table 4: Cortical bone morphology of the femur by micro-CT. Cortical bone parameters were taken at the femur mid diaphysis. Images were acquired utilizing a SkyScan 1172 high-resolution scanner (MicroPhotonics), using a 10 MP digital detector, 10W power energy (60 KV and 167 mA), and a 0.5 mm aluminum filter with 9.7 µm image voxel size. Descriptive statistics (means (top number), standard deviations (bottom number)) were computed for each outcome. Statistical significance for main effects of sex and treatment (Tx) was determined through comparisons to the Bonferroni-adjusted significance level (.0004). Total cross-sectional area (T.Ar), bone area (B.Ar), marrow area (M.Ar), polar moment of inertia (MMI), cortical bone thickness (Ct.Th), bone tissue mineral density (TMD). Estimated value (Est), standard Error (SE), p value (P).

	Basal M	CTL M	CANA M	Basal F	CTL F	CANA F		Main effects		Interactions
	Age:6m Tx time:0 N=14	Age:12m Tx time:6 N=18	Age:12m Tx time:6 N=20	Age:6m Tx time:0 N=14	Age:12m Tx time:6 N=30	Age:12m Tx time:6 N=20		sexM	TxCANA	sexM: TxCANA
Max load, N	19.605 2.339	21.168 3.367	19.363 2.873	17.676 2.477	18.960 4.018	19.280 4.664	Est	1.2081	-0.6179	-2.124
							SE	0.8335	0.8292	1.6638
							P	0.151	0.458	0.2053
Stiffness, N/mm	58.721 10.565	92.916 21.879	98.031 20.490	60.130 15.113	84.753 25.057	96.332 30.898	Est	5.121	8.727	-6.464
							SE	5.401	5.372	10.861
							P	0.346	0.108	0.553
Elastic modulus, N/mm^2, Mpa	11722.109 2862.653	16056.186 4567.630	18103.817 3664.833	16463.799 4222.791	20667.859 6300.230	23247.518 7063.737	Est	-4862	2344.9	-532
							SE	1225	1218.6	2468
							P	P<0.001	0.05766	0.82985

Supplementary Table 5: Whole bone mechanical testing by 3-point bending assay (femur). A three-point bending test was performed to evaluate and quantify the mechanical properties of 6 months basal femur bone - male (n=14) and female (n=14) and 12 months control (male n=18, female n=30) and CANA-treated femurs (male n=20, female n=20). The testing used a rheometer (Discovery HR-2, TA instruments, New Castle, DE USA) with a 10mm three-point bending fixture frame. The femur bones were placed with supports at the distal and proximal ends. The machine was programmed to apply a uniaxial load until failure to the mid-femoral shaft at a 0.05mm/sec rate. The software collected the ultimate load (N) and displacement and calculated the modulus of elasticity € using:

$$E = \frac{KL^3}{(48I)}$$

Eq. (1)

Where K is the stiffness, L is the span length, and I is the moment of inertia [J Bone Miner Res, 2022. **37**(11): p. 2201-2214].

Descriptive statistics (means (top number), standard deviations (bottom number)) were computed for each hormone. Statistical significance for main effects of sex (M) and treatment (Tx) was determined through comparisons to the Bonferroni-adjusted significance level (.0004). Estimated value (Est), standard error (SE), p value (P).

	CTL Males				CANA Males			CTL Females				CANA Females				Main effects				Interactions		
	Age: 6m TX time: 0m n=18	Age: 7m TX time: 1m n=20	Age: 9m TX time: 3m n=23	Age: 12m TX time: 6m n=20	Age: 7m TX time: 1m n=20	Age: 9m TX time: 3m n=30	Age: 12m TX time: 6m n=22	Age: 6m TX time: 0m n=19	Age: 7m TX time: 1m n=19	Age: 9m TX time: 3m n=15	Age: 12m TX time: 6m n=30	Age: 7m TX time: 1m n=24	Age: 9m TX time: 3m n=15	Age: 12m TX time: 6m n=44		sexM	TxCANA	Tx time months'3	Tx time months'6	sexM: TxCANA	Sex(M); Tx time months'3	Sex(M); Tx time months'6
BV/TV, %	14.747	15.685	11.519	11.050	13.648	10.771	9.400	7.231	9.722	5.349	3.989	8.619	8.405	5.087	Est	5.161	-0.273	-3.020	-4.508	-2.260	-1.312	-0.020
	4.078	3.678	3.130	5.163	5.015	4.733	3.545	3.089	5.927	3.637	2.895	3.460	4.597	3.369	SE	0.504	0.493	0.644	0.595	0.980	1.307	1.205
															P	P<0.0001	0.581	P<0.0001	P<0.0001	P<0.05	0.317	0.987
Tb.Th, mm	0.067	0.067	0.065	0.069	0.066	0.068	0.072	0.063	0.068	0.066	0.065	0.068	0.069	0.071	Est	0.000	0.003	0.000	0.002	-0.002	0.001	0.004
	0.004	0.004	0.005	0.005	0.004	0.006	0.004	0.005	0.008	0.008	0.009	0.007	0.009	0.008	SE	0.001	0.001	0.001	0.001	0.002	0.002	0.002
															P	0.923	P<0.001	0.803	P<0.05	0.226	0.766	P<0.05
Tb.Sp, mm	0.262	0.259	0.296	0.313	0.275	0.318	0.356	0.379	0.376	0.457	0.580	0.371	0.397	0.525	Est	-0.152	-0.008	0.053	0.131	0.066	-0.011	-0.106
	0.034	0.040	0.065	0.074	0.062	0.075	0.065	0.059	0.104	0.080	0.190	0.071	0.098	0.123	SE	0.013	0.013	0.016	0.015	0.025	0.033	0.030
															P	P<0.0001	0.551	P<0.01	P<0.0001	P<0.01	0.725	P<0.001
Tb.N, 1/mm	2.204	2.364	1.767	1.614	2.077	1.584	1.296	1.129	1.370	0.771	0.580	1.238	1.168	0.687	Est	0.807	-0.077	-0.454	-0.707	-0.354	-0.221	-0.121
	0.558	0.568	0.439	0.774	0.733	0.652	0.470	0.419	0.721	0.438	0.360	0.418	0.553	0.398	SE	0.067	0.066	0.086	0.080	0.131	0.175	0.161
															P	P<0.0001	0.244	P<0.0001	P<0.0001	P<0.01	0.207	0.452
BMD, g/cc	0.134	0.182	0.143	0.157	0.162	0.138	0.134	0.075	0.131	0.085	0.078	0.122	0.119	0.090	Est	0.049	-0.003	-0.029	-0.035	-0.025	-0.007	0.014
	0.032	0.033	0.031	0.048	0.048	0.046	0.034	0.026	0.064	0.038	0.032	0.036	0.047	0.037	SE	0.005	0.005	0.007	0.006	0.010	0.013	0.012
															P	P<0.0001	0.614	P<0.0001	P<0.0001	P<0.05	0.574	0.263

Supplementary Table 6: Trabecular bone morphology of the appendicular skeleton (femur) by micro-CT. Trabecular bone parameters were taken at the femur distal metaphysis. Images were acquired utilizing a SkyScan 1172 high-resolution scanner (MicroPhotonics), using a 10 MP digital detector, 10W power energy (60 KV and 167 mA), and a 0.5 mm aluminum filter with 9.7 µm image voxel size. Descriptive statistics (means (top number), standard deviations (bottom number)) were computed for each outcome. Statistical significance for main effects of sex and treatment (Tx) was determined through comparisons to the Bonferroni-adjusted significance level (.0004). Bone volume per total volume (BV/TV), trabecular number (Tb.N), bone mineral density (BMD), trabecular spacing (Tb.Sp), trabecular thickness (Tb.Th). Estimated value (Est), standard error (SE), p value (P).

	CTL Males				CANA Males			CTL Females				CANA Females				Main effects				Interactions		
	Age: 6m TX time: 0m n=18	Age: 7m TX time: 1m n=20	Age: 9m TX time: 3m n=23	Age: 12m TX time: 6m n=25	Age: 7m TX time: 1m n=20	Age: 9m TX time: 3m n=30	Age: 12m TX time: 6m n=22	Age: 6m TX time: 0m n=19	Age: 7m TX time: 1m n=19	Age: 9m TX time: 3m n=15	Age: 12m TX time: 6m n=30	Age: 7m TX time: 1m n=24	Age: 9m TX time: 3m n=15	Age: 12m TX time: 6m n=44		sexM	TxCANA	Tx time months'3	Tx time months'6	sexM:TxCAN A	Sex(M);Tx time months'3	Sex(M);Tx time months'6
L5 BV/TV, %	24.190	24.061	23.617	25.077	22.722	22.845	23.784	18.660	19.108	15.604	17.536	19.633	20.793	19.864	Est	4.924	0.656	-0.724	0.164	-3.467	0.909	1.462
	3.017	4.312	3.197	5.726	4.190	5.319	4.165	4.248	4.587	3.546	5.559	3.430	5.173	4.382	SE	0.549	0.542	0.729	0.653	1.069	1.482	1.315
															P	P<0.0001	0.228	0.321	0.802	P<0.01	0.540	0.267
L5 Tb.Th, mm	0.068	0.065	0.064	0.069	0.064	0.067	0.070	0.073	0.073	0.073	0.076	0.076	0.076	0.080	Est	-0.009	0.003	0.001	0.004	-0.002	0.001	0.001
	0.004	0.003	0.004	0.004	0.004	0.005	0.004	0.003	0.006	0.006	0.005	0.009	0.007	0.007	SE	0.001	0.001	0.001	0.001	0.001	0.002	0.002
															P	P<0.0001	P<0.001	0.331	P<0.0001	0.155	0.538	0.426
L5 Tb.Sp, mm	0.250	0.244	0.225	0.250	0.243	0.245	0.252	0.329	0.317	0.351	0.364	0.320	0.309	0.347	Est	-0.093	-0.005	0.002	0.023	0.024	-0.018	-0.028
	0.026	0.027	0.024	0.046	0.022	0.040	0.031	0.043	0.038	0.039	0.060	0.030	0.032	0.044	SE	0.005	0.005	0.006	0.006	0.009	0.013	0.011
															P	P<0.0001	0.313	0.729	P<0.0001	P<0.05	0.161	P<0.05
L5 Tb.N, 1/mm	3.555	3.693	3.699	3.639	3.552	3.369	3.380	2.560	2.615	2.137	2.291	2.610	2.708	2.485	Est	1.068	-0.016	-0.148	-0.166	-0.463	0.082	0.082
	0.412	0.528	0.448	0.735	0.575	0.659	0.527	0.507	0.548	0.434	0.641	0.429	0.465	0.493	SE	0.067	0.066	0.089	0.079	0.129	0.180	0.160
															P	P<0.0001	0.812	0.097	P<0.05	P<0.001	0.651	0.609
L5 BMD, g/cc	0.247	0.241	0.230	0.257	0.225	0.230	0.249	0.207	0.203	0.165	0.194	0.210	0.218	0.219	Est	0.037	0.009	-0.009	0.010	-0.032	0.011	0.018
	0.028	0.041	0.033	0.055	0.038	0.056	0.040	0.043	0.047	0.040	0.058	0.037	0.060	0.046	SE	0.006	0.006	0.007	0.007	0.011	0.015	0.013
															P	P<0.0001	0.0888	0.212	0.150	P<0.01	0.463	0.180

Supplementary Table 7: Trabecular bone morphology of the axial skeleton (lumbar vertebra-5) by micro-CT. Trabecular bone parameters were taken from the vertebral body. Images were acquired utilizing a SkyScan 1172 high-resolution scanner (MicroPhotonics), using a 10 MP digital detector, 10W power energy (60 KV and 167 mA), and a 0.5 mm aluminum filter with 9.7 µm image voxel size. Descriptive statistics (means (top number), standard deviations (bottom number)) were computed for each outcome. Statistical significance for main effects of sex and treatment (Tx) was determined through comparisons to the Bonferroni-adjusted significance level (.0004). Bone volume per total volume (BV/TV), trabecular number (Tb.N), bone mineral density (BMD), trabecular spacing (Tb.Sp), trabecular thickness (Tb.Th). Estimated value (Est), standard Error (SE), p value (P).