

**Table S4.** Comparison of biochemical markers of safety (mean  $\pm$  SD) at baseline and at the endpoint of the trial.

Safety parameter indices		Baseline	After	Washout	Baseline vs After P-value	After vs Washout P-value
Hematologic	WBC	5.81 $\pm$ 1.51	5.59 $\pm$ 1.04	5.43 $\pm$ 1.12	0.512	0.202
	RBC	4.24 $\pm$ 0.49	4.16 $\pm$ 0.50	4.14 $\pm$ 0.48	0.180	0.564
	HGB	13.16 $\pm$ 1.07	13.11 $\pm$ 1.15	12.92 $\pm$ 1.06	0.617	0.071
	HCT	39.16 $\pm$ 2.74	38.65 $\pm$ 3.03	38.08 $\pm$ 2.89	0.280	0.061
	MCV	90.97 $\pm$ 3.22	91.05 $\pm$ 3.19	90.92 $\pm$ 3.17	0.795	0.310
	MCH	30.73 $\pm$ 1.43	30.95 $\pm$ 1.33	31.00 $\pm$ 1.41	0.046	0.527
	MCHC	33.73 $\pm$ 0.99	33.89 $\pm$ 0.77	34.19 $\pm$ 0.97	0.083	0.012
	PLT	229.24 $\pm$ 46.86	229.11 $\pm$ 44.61	220.59 $\pm$ 50.15	0.952	0.058
	RDW-SD	42.19 $\pm$ 2.22	42.24 $\pm$ 2.50	12.54 $\pm$ 0.65	0.855	0.002
	RDW-CV	12.68 $\pm$ 0.63	12.73 $\pm$ 0.69	41.54 $\pm$ 2.27	0.414	0.008
	PDW	12.30 $\pm$ 1.90	11.92 $\pm$ 1.67	11.81 $\pm$ 1.71	0.063	0.559
Kidney	MPV	10.43 $\pm$ 0.99	10.27 $\pm$ 0.84	10.46 $\pm$ 0.96	0.134	0.052
	P-LCR	29.03 $\pm$ 7.95	27.08 $\pm$ 6.53	27.95 $\pm$ 7.04	0.003	0.082
	BUN	16.30 $\pm$ 4.19	15.65 $\pm$ 3.81	14.78 $\pm$ 4.10	0.261	0.153
Urine test	UA	4.57 $\pm$ 1.12	4.43 $\pm$ 1.14	4.30 $\pm$ 1.10	0.282	0.275
	TP	7.73 $\pm$ 0.61	7.43 $\pm$ 0.55	7.59 $\pm$ 0.64	0.001	0.034
	BLD	0.66 $\pm$ 1.60	0.51 $\pm$ 1.28	0.59 $\pm$ 1.36	0.461	0.546
Liver	BIL	0.68 $\pm$ 1.31	0.24 $\pm$ 0.83	0.30 $\pm$ 1.02	0.083	0.593
	URO	1.11 $\pm$ 0.46	1.08 $\pm$ 0.49	1.05 $\pm$ 0.33	1.000	0.317
	KET	1.14 $\pm$ 1.32	1.00 $\pm$ 1.13	1.11 $\pm$ 1.22	0.774	0.573
	pH	6.45 $\pm$ 0.56	6.27 $\pm$ 0.43	6.38 $\pm$ 0.53	0.102	0.246
	S. G	1.02 $\pm$ 0.01	1.02 $\pm$ 0.00	1.02 $\pm$ 0.01	0.089	0.174
	LFU	1.73 $\pm$ 1.98	1.65 $\pm$ 2.02	1.84 $\pm$ 2.11	0.734	0.483
Liver	AST	26.14 $\pm$ 5.15	26.03 $\pm$ 5.71	26.41 $\pm$ 6.84	0.898	0.864
	ALT	21.30 $\pm$ 8.43	22.73 $\pm$ 10.10	22.27 $\pm$ 9.62	0.396	0.670
	T-BIL	0.89 $\pm$ 0.46	0.86 $\pm$ 0.42	0.81 $\pm$ 0.57	0.705	0.480
	GGT	22.35 $\pm$ 10.35	26.95 $\pm$ 19.35	23.46 $\pm$ 11.99	0.015	0.009
	ALB	4.00 $\pm$ 0	4.03 $\pm$ 0.16	4.03 $\pm$ 0.16	0.317	1.000
	A/G ratio	1.05 $\pm$ 0.23	1.43 $\pm$ 0.50	1.14 $\pm$ 0.35	0.000	0.002
	B/C ratio	28.00 $\pm$ 6.90	28.14 $\pm$ 6.07	26.76 $\pm$ 7.06	0.887	0.213

Abbreviations: WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelet; RDW-SD, red cell distribution width standard deviation; RDW-CV, red cell distribution width coefficient of variation; PDW, platelet distribution width; MPV, mean platelet volume; P-LCR, platelet-large cell ratio; BUN, blood urea nitrogen; UA, uric acid; TP, total protein; BLD, blood; BIL, bilirubin; URO, urobilinogen; KET, ketone body; pH, potential of hydrogen; S.G, specific gravity; LFU, leukocyte forming unit; AST, aspartate aminotransferase; ALT, alanine aminotransferase; T-BIL, total-bilirubin; GGT, gamma-glutamyl transpeptidase; ALB, albumin; A/G ratio, albumin/globulin ratio; B/G ratio, BUN/creatinine ratio.

Urine test positive and negative values were converted to numbers (Urine test: 0, negative; 1, normal; 2, trace; 3, +; 4, ++; 5, +++).

P-values are based on the paired t-test and Wilcoxon rank-sum test.