Identification of MRP2 as a targetable factor limiting oxaliplatin accumulation and response in gastrointestinal cancer

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Supplementary table 1 Two-way repeated measures ANOVA multiple comparisons for body weight

Day	Bonferroni's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
0	Myricetin alone vs. Control	0	-3.803 to 3.803	No	ns	>0.9999
	Oxaliplatin alone vs. Control	0	-3.803 to 3.803	No	ns	>0.9999
	Combination vs. Control	0	-3.803 to 3.803	No	ns	>0.9999
	Oxaliplatin alone vs. Myricetin alone	0	-3.803 to 3.803	No	ns	>0.9999
	Combination vs. Myricetin alone	0	-3.803 to 3.803	No	ns	>0.9999
	Combination vs. Oxaliplatin alone	0	-3.803 to 3.803	No	ns	>0.9999
3	Myricetin alone vs. Control	1.483	-2.32 to 5.285	No	ns	>0.9999
	Oxaliplatin alone vs. Control	-1.05	-4.853 to 2.753	No	ns	>0.9999
	Combination vs. Control	-2.496	-6.299 to 1.306	No	ns	0.4916
	Oxaliplatin alone vs. Myricetin alone	-2.533	-6.335 to 1.27	No	ns	0.4657
	Combination vs. Myricetin alone	-3.979	-7.781 to -0.1761	Yes	*	0.0348
	Combination vs. Oxaliplatin alone	-1.446	-5.249 to 2.356	No	ns	>0.9999
7	Myricetin alone vs. Control	0.4488	-3.354 to 4.251	No	ns	>0.9999
	Oxaliplatin alone vs. Control	-1.694	-5.496 to 2.109	No	ns	>0.9999
	Combination vs. Control	-4.064	-7.866 to -0.2611	Yes	*	0.0291
	Oxaliplatin alone vs. Myricetin alone	-2.143	-5.945 to 1.66	No	ns	0.8105
	Combination vs. Myricetin alone	-4.513	-8.315 to -0.7099	Yes	*	0.0108
	Combination vs. Oxaliplatin alone	-2.37	-6.173 to 1.433	No	ns	0.591
10	Myricetin alone vs. Control	-0.585	-4.388 to 3.218	No	ns	>0.9999
	Oxaliplatin alone vs. Control	-3.231	-7.034 to 0.5714	No	ns	0.148
	Combination vs. Control	-4.484	-8.286 to -0.6811	Yes	*	0.0116
	Oxaliplatin alone vs. Myricetin alone	-2.646	-6.449 to 1.156	No	ns	0.3917
	Combination vs. Myricetin alone	-3.899	-7.701 to -0.09613	Yes	*	0.0411
	Combination vs. Oxaliplatin alone	-1.253	-5.055 to 2.55	No	ns	>0.9999
14	Myricetin alone vs. Control	0.9063	-2.896 to 4.709	No	ns	>0.9999
	Oxaliplatin alone vs. Control	-1.299	-5.101 to 2.504	No	ns	>0.9999
	Combination vs. Control	-2.273	-6.075 to 1.53	No	ns	0.6784
	Oxaliplatin alone vs. Myricetin alone	-2.205	-6.008 to 1.598	No	ns	0.7447
	Combination vs. Myricetin alone	-3.179	-6.981 to 0.6239	No	ns	0.1624
	Combination vs. Oxaliplatin alone	-0.9738	-4.776 to 2.829	No	ns	>0.9999
17	Myricetin alone vs. Control	-0.00625	-3.809 to 3.796	No	ns	>0.9999
	Oxaliplatin alone vs. Control	-3.216	-7.019 to 0.5864	No	ns	0.152
	Combination vs. Control	-3.91	-7.713 to -0.1074	Yes	*	0.0402
	Oxaliplatin alone vs. Myricetin alone	-3.21	-7.013 to 0.5926	No	ns	0.1537
	Combination vs. Myricetin alone	-3.904	-7.706 to -0.1011	Yes	*	0.0407
	Combination vs. Oxaliplatin alone	-0.6938	-4.496 to 3.109	No	ns	>0.9999
21	Myricetin alone vs. Control	-1.593	-5.395 to 2.21	No	ns	>0.9999
	Oxaliplatin alone vs. Control	-2.578	-6.38 to 1.225	No	ns	0.4352
	Combination vs. Control	-4	-7.803 to -0.1974	Yes	*	0.0333
	Oxaliplatin alone vs. Myricetin alone	-0.985	-4.788 to 2.818	No	ns	>0.9999
	Combination vs. Myricetin alone	-2.408	-6.21 to 1.395	No	ns	0.56
	Combination vs. Oxaliplatin alone	-1.423	-5.225 to 2.38	No	ns	>0.9999
24	Myricetin alone vs. Control	-1.814	-5.616 to 1.989	No	ns	>0.9999
	Oxaliplatin alone vs. Control	-3.42	-7.223 to 0.3826	No	ns	0.1049
	Combination vs. Control	-5.454	-9.256 to -1.651	Yes	**	0.001
	Oxaliplatin alone vs. Myricetin alone	-1.606	-5.409 to 2.196	No	ns	>0.9999
	Combination vs. Myricetin alone	-3.64	-7.443 to 0.1626	No	ns	0.069
	Combination vs. Oxaliplatin alone	-2.034	-5.836 to 1.769	No	ns	0.9356

Supplementary table 2 Two-way repeated measures ANOVA multiple comparisons for tumour volume

Day	Bonferroni's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
0	Control vs. Myricetin alone	0	-167.8 to 167.8	No	ns	>0.9999
	Control vs. ox alone	0	-167.8 to 167.8	No	ns	>0.9999
	Control vs. combination	0	-167.8 to 167.8	No	ns	>0.9999
	Myricetin alone vs. ox alone	0	-167.8 to 167.8	No	ns	>0.9999
	Myricetin alone vs. combination	0	-167.8 to 167.8	No	ns	>0.9999
	ox alone vs. combination	0	-167.8 to 167.8	No	ns	>0.9999
3	Control vs. Myricetin alone	-13.83	-181.6 to 154	No	ns	>0.9999
	Control vs. ox alone	13.08	-154.7 to 180.9	No	ns	>0.9999
	Control vs. combination	33.59	-134.2 to 201.4	No	ns	>0.9999
	Myricetin alone vs. ox alone	26.91	-140.9 to 194.7	No	ns	>0.9999
	Myricetin alone vs. combination	47.42	-120.4 to 215.2	No	ns	>0.9999
	ox alone vs. combination	20.51	-147.3 to 188.3	No	ns	>0.9999
7	Control vs. Myricetin alone	-72.29	-240.1 to 95.5	No	ns	>0.9999
	Control vs. ox alone	18.91	-148.9 to 186.7	No	ns	>0.9999
	Control vs. combination	59.02	-108.8 to 226.8	No	ns	>0.9999
	Myricetin alone vs. ox alone	91.21	-76.59 to 259	No	ns	0.8959
	Myricetin alone vs. combination	131.3	-36.49 to 299.1	No	ns	0.2303
	ox alone vs. combination	40.1	-127.7 to 207.9	No	ns	>0.9999
10	Control vs. Myricetin alone	-119.7	-287.4 to 48.14	No	ns	0.3538
	Control vs. ox alone	16.53	-151.3 to 184.3	No	ns	>0.9999
	Control vs. combination	78.77	-89.03 to 246.6	No	ns	>0.9999
	Myricetin alone vs. ox alone	136.2	-31.61 to 304	No	ns	0.1908
	Myricetin alone vs. combination	198.4	30.62 to 366.2	Yes	*	0.0112
	ox alone vs. combination	62.24	-105.6 to 230	No	ns	>0.9999
14	Control vs. Myricetin alone	-117.1	-284.9 to 50.69	No	ns	0.3871
	Control vs. ox alone	-24.7	-192.5 to 143.1	No	ns	>0.9999
	Control vs. combination	109.6	-58.22 to 277.4	No	ns	0.5012
	Myricetin alone vs. ox alone	92.41	-75.39 to 260.2	No	ns	0.8644
	Myricetin alone vs. combination	226.7	58.88 to 394.5	Yes	**	0.0024
	ox alone vs. combination	134.3	-33.52 to 302.1	No	ns	0.2055
17	Control vs. Myricetin alone	-192.7	-360.5 to -24.95	Yes	*	0.015
	Control vs. ox alone	-92.33	-260.1 to 75.46	No	ns	0.8663
	Control vs. combination	127.2	-40.57 to 295	No	ns	0.2685
	Myricetin alone vs. ox alone	100.4	-67.38 to 268.2	No	ns	0.6755
	Myricetin alone vs. combination	320	152.2 to 487.8	Yes	****	<0.0001
	ox alone vs. combination	219.6	51.76 to 387.4	Yes	**	0.0036
21	Control vs. Myricetin alone	-207.3	-375.1 to -39.55	Yes	**	0.007
	Control vs. ox alone	-97.44	-265.2 to 70.35	No	ns	0.7414
	Control vs. combination	126	-41.83 to 293.8	No	ns	0.2814
	Myricetin alone vs. ox alone	109.9	-57.89 to 277.7	No	ns	0.4957
	Myricetin alone vs. combination	333.3	165.5 to 501.1	Yes	****	<0.0001
	ox alone vs. combination	223.4	55.61 to 391.2	Yes	**	0.0029
24	Control vs. Myricetin alone	-105.3	-273.1 to 62.46	No	ns	0.5766
	Control vs. ox alone	-165.5	-333.3 to 2.336	No	ns	0.0556
	Control vs. combination	188.7	20.86 to 356.5	Yes	*	0.0184
	Myricetin alone vs. ox alone	-60.12	-227.9 to 107.7	No	ns	>0.9999
	Myricetin alone vs. combination	294	126.2 to 461.8	Yes	****	<0.0001
	ox alone vs. combination	354.1	186.3 to 521.9	Yes	****	<0.0001

Supplementary table 3 Results of multiple comparisons for time to event endpoints .

Comparison	P values (unadjusted)	
	Time to euthanasia	Time for tumours to quadruple in volume
All groups	**0.0032**	**0.0112**
Control versus myricetin alone	0.0989	0.1776
Control versus oxaliplatin alone	0.0848	0.1278
Oxaliplatin alone versus myricetin alone	0.1217	0.6605
Combination versus control	0.0968	**0.0454**
Combination versus myricetin alone	**0.0181**	**0.0150**
Combination versus oxaliplatin alone	**0.0003**	**0.0016**