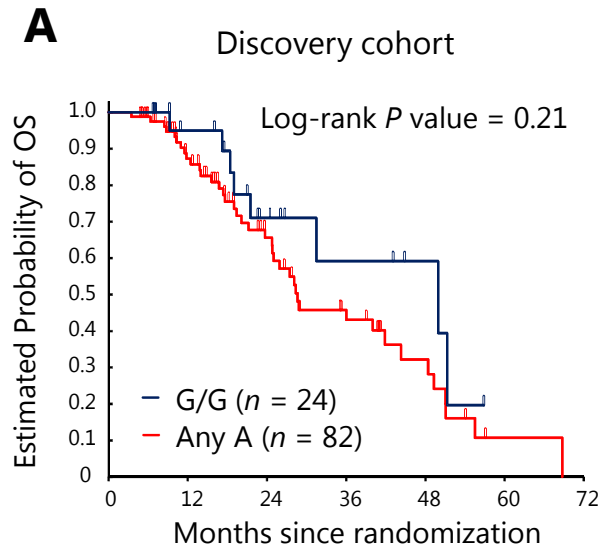
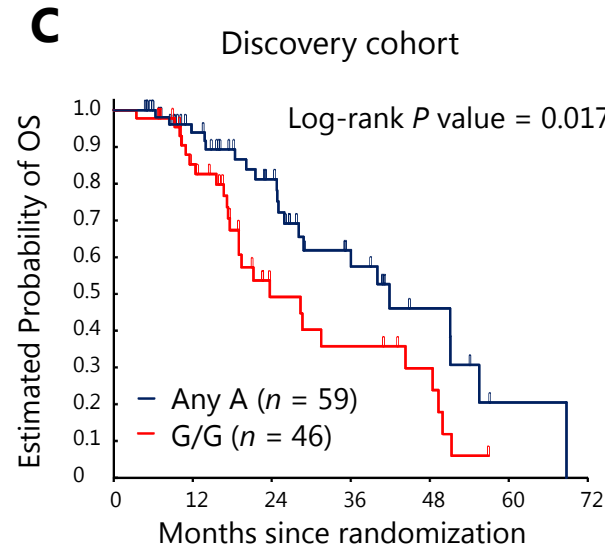


Supplementary Figure 1

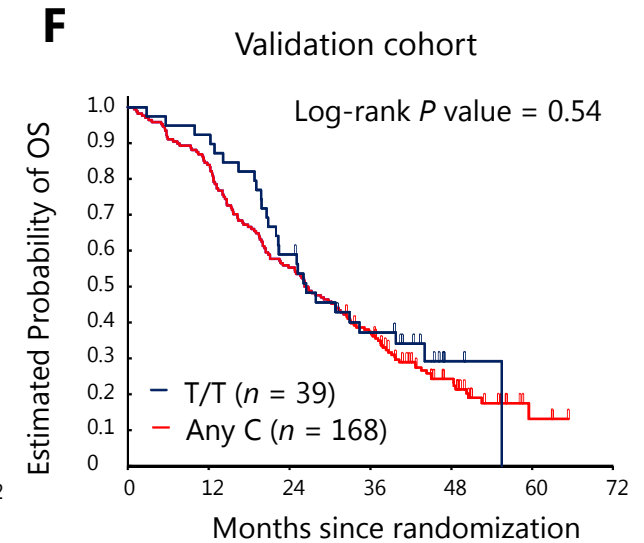
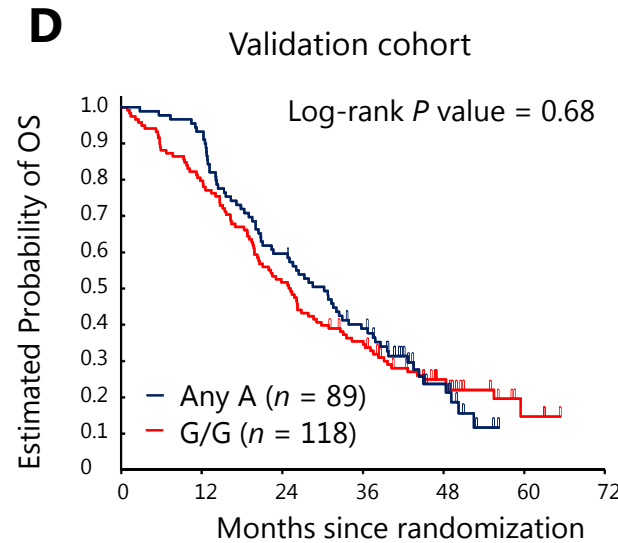
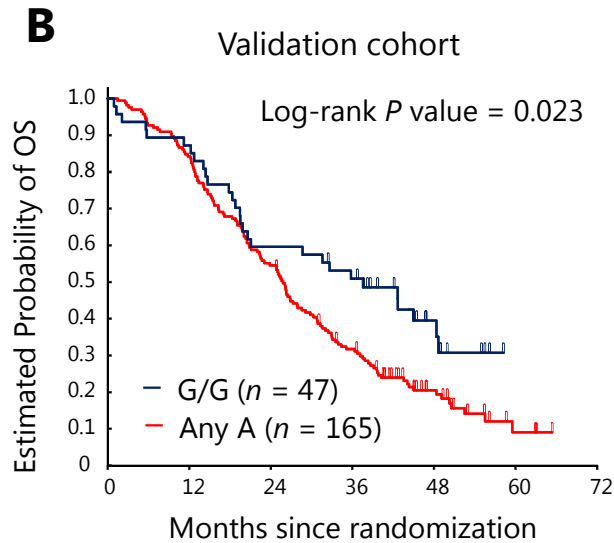
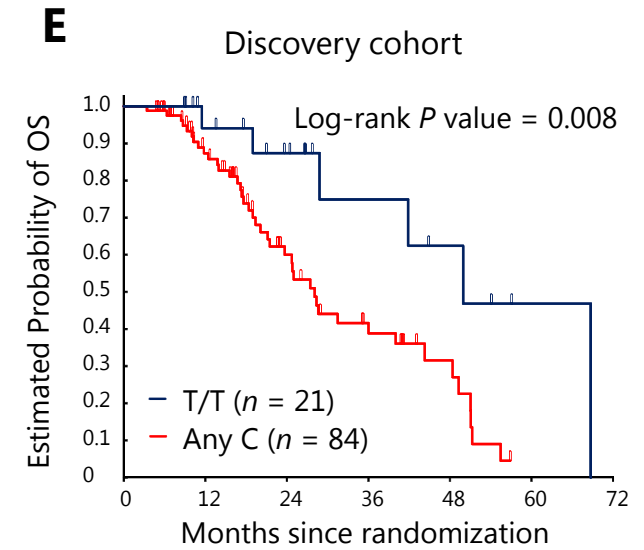
CD39 rs2226163



CD73 rs2229523



A2BRrs2015353



Supplementary Table 1. Selected SNPs in adenosine-related molecules and their characteristics

Adenosin-related molecules	Encoding gene	Chromosome	SNP (rs number)	Location of the polymorphism	Global MAF	Base exchange	Predictive function or published data
CD39	<i>ENTPD1</i>	10	rs11188513	3' UTR	0.4161	C>T	Micro RNA binding, Tag SNP
			rs2226163	3' UTR	0.4756	A>G	Micro RNA binding, Tag SNP
CD73	<i>NT5E</i>	6	rs2229523	Exon (missense)	0.2067	A>G	Changing the protein expression
A2AR	<i>ADORA2A</i>	22	rs5751876	Exon (synonymous)	0.4423	T>C	Methotrexate response in rheumatoid arthritis
A2BR	<i>ADORA2B</i>	17	rs2015353	Exon (missense)	0.3712	T>C	Tag SNP
			rs2057482	3' UTR	0.2424	T>C	Micro RNA binding, Tag SNP
HIF-1 α	<i>HIF1A</i>	14	rs11549465	Exon (missense)	0.0731	C>T	Increasing the risk of prostate cancer, Tag SNP

Abbreviations: MAF, minor allele frequency; SNP, single-nucleotide polymorphism; UTR, untranslated region

Supplementary Table 2. Comparison of baseline characteristics between FIRE-3 FOLFIRI bevacizumab, TRIBE FOLFIRI bevacizumab, and FIRE-3 FOLFIRI cetuximab arms.

Patients Characteristics <i>n</i> = 451	Discovery cohort (FIRE-3 FOLFIRI bevacizumab, <i>n</i> = 107)	Validation cohort (TRIBE FOLFIRI bevacizumab, <i>n</i> = 215)	Control cohort (FIRE-3 FOLFIRI cetuximab, <i>n</i> = 129)	<i>P</i> value ^a
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	
Sex				0.013
Male	70 (65%)	132 (61%)	99 (77%)	
Female	37 (35%)	83 (39%)	30 (23%)	
Age				0.006
≤65	62 (58%)	156 (73%)	75 (58%)	
>65	45 (42%)	59 (27%)	54 (42%)	
Performance status				<0.001
ECOG 0	56 (52%)	177 (82%)	80 (62%)	
ECOG 1	51 (48%)	37 (17%)	49 (38%)	
Unknown ^b	0 (0%)	1 (1%)	0 (0%)	
Tumor location				0.157
Right side	25 (23%)	53 (25%)	22 (17%)	
Left side	81 (76%)	147 (68%)	105 (81%)	
Unknown ^b	1 (1%)	15 (7%)	2 (2%)	
Liver limited disease				0.615
No	75 (70%)	150 (70%)	84 (65%)	
Yes	32 (30%)	65 (30%)	45 (35%)	
Primary tumor resected				<0.001
No	12 (11%)	80 (37%)	23 (18%)	
Yes	95 (89%)	135 (63%)	106 (82%)	
Adjuvant chemotherapy				0.131
No	86 (80%)	188 (87%)	103 (80%)	
Yes	21 (20%)	27 (13%)	25 (19%)	
Unknown ^b	0 (0%)	0 (0%)	1 (1%)	
KRAS status				<0.001
Wildtype	103 (96%)	88 (41%)	125 (97%)	
Mutant	4 (4%)	90 (42%)	4 (3%)	
Unknown ^b	0 (0%)	37 (17%)	0 (0%)	
RAS status				<0.001
Wildtype	66 (62%)	50 (23%)	83 (64%)	
Mutant	17 (16%)	110 (51%)	19 (15%)	
Unknown ^b	24 (22%)	55 (26%)	27 (21%)	
BRAF status				0.271
Wildtype	81 (76%)	168 (78%)	95 (74%)	
Mutant	4 (4%)	10 (5%)	7 (5%)	
Unknown ^b	22 (21%)	37 (17%)	27 (21%)	

^a *P* value was based on chi-square test for categorical factors.

^b Unknown group was not included in this analysis.