

Supplementary information

Table S1. SNPs previously reported to be associated with oxaliplatin treatment

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
DNA repair system					
rs11615	Huang et al. (2011) (1)	157 mCRC patients who received four to 6 cycles of first-line FOLFOX.	<i>XRCC1</i> rs25487-GG and <i>ERCC1</i> rs11615-CC were associated with better progression-free survival (PFS). Combining two variants associated with favorable overall survival (OS). No multiple-testing correction was applied.	2/0	8/0
	Ruzzo et al. (2007) (2)	166 mCRC patients who received at least 4 cycles of first-line FOLFOX chemotherapy.	<i>ERCC1</i> rs11615-TT and <i>ERCC2</i> rs13181-GG/GT were independently associated with adverse PFS after adjusting for performance score (KPS), carcinoembryonic antigen levels, mucinous histology, and number of metastatic sites. No multiple-testing correction was applied.	2/0	12/0
	Rao et al. (2019) (3)	54 (29 stage II-III CRC and 25 mCRC) who received XELOX or FOLFOX at least one cycle.	Median PFS was significantly lower with <i>ERCC1</i> rs11615-CC or -TC compared to <i>ERCC1</i> rs11615-TT.	1/0	1/0
	Li et al. (2012) (4)	335 aCRC patients who received minimum 4 cycles of adjuvant FOLFOX chemotherapy.	<i>ERCC1</i> rs11615-CC genotype, <i>ERCC2</i> rs13181-GG genotype, and <i>GSTP1</i> rs1695-Val/ Val genotype were found to be related to a longer OS adjusted for age, gender, TNM stage, tumor grade, and histological subtype and location. No multiple-testing correction was applied.	3/0	3/0
	Stoehlmacher et al. (2004) (5)	104 mCRC patients who received FU with oxaliplatin. No information about a minimum number of treatment cycles is provided.	<i>ERCC1</i> rs11615-CC genotype and <i>ERCC2</i> rs13181-AA genotype were found to be better OS adjusted for performance status (ECOG) and other genetic variants tested. No multiple-testing correction was applied.	2/0	4/0
	Paré et al., 2008 (6)	106 mCRC patients who received minimum 1 cycle of FOLFOX. Average number of treatment cycle was nine (range 1–20).	<i>ERCC1</i> rs11615-CC genotype and were found to be better OS adjusted for clinical parameters (performance status, WBC count, alkaline phosphatase and number of metastatic sites). <i>ERCC2</i> rs13181-AA genotype was found	2/0	8/0

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
			to be worse OS and PFS. No multiple-testing correction was applied.		
rs13181	Gan et al. (2012) (7)	289 mCRC patients who received FOLFOX. No information about a minimum number of treatment cycles is provided.	<i>XRCC1</i> rs25487-GG genotype and <i>ERCC2</i> rs13181-GG genotype associated with worse OS after adjusting for age, sex, BMI, and UICC TNM stage. No multiple-testing correction was applied.	1/0	2/0
	Li et al. (2012) (4)	See above.			
	Stoehlmacher et al. (2004) (5)	See above.			
	Paré et al. (2008) (6)	See above.			
	Lamas et al. (2011) (8)	37 mCRC patients who received FOLFOX6. No information about a minimum number of treatment cycles is provided.	<i>ERCC2</i> rs13181-TG genotype was associated with a better PFS than TT/GG. No adjustment and no multiple testing correction was applied.	1/0	8/0
rs25487	Gan et al. (2012) (7)	See above.			
	Huang et al. (2011) (1)	See above.			
rs17655	Sun et al. (2015) (9)	718 CRC patients who received FOLFOX or XELOX. No information about a minimum number of treatment cycles is provided.	<i>ERCC5</i> rs17655-C allele and <i>XPC</i> rs2228000-C allele were associated with a longer disease-free survival (DFS) after adjusting for gender, age, first-degree family history of CRC, and smoking status. No multiple testing correction was applied.	2/0	3/0

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
	Liu et al. (2012) (10)	432 CRC patients who received CAPOX or FOLFOX. No information about a minimum number of treatment cycles is provided.	<i>ERCC5</i> rs17655-CG/GG genotype was associated with poorer PFS before and after adjusted for pathology grade and lymph node metastases. No multiple testing correction was applied.	1/0	2/0
	Kong et al. (2018) (11)	226 aCRC patients who received at least 2 cycles of FOLFOX4.	<i>ERCC5</i> rs17655-CC was associated with a worse survival rate. No adjustment was applied.	1/0	1/0
rs1047768	Monzo et al. (2007) (12)	42 aCRC patients who received maximum 10 cycle's treatment of oxaliplatin in combination with 5-FU.	<i>ERCC5</i> rs1047768-CC genotype associated with a longer OS after adjusting for ECOG, gender, age, and metastasis site. No multiple testing correction was applied.	1/0	4/0
	Kweekel et al. (2009) (13)	91 aCRC patients who received second-line capecitabine with oxaliplatin. No information about a minimum number of treatment cycles is provided.	<i>ERCC5</i> rs1047768-CC or <i>ATM</i> rs1801516-AA genotypes were associated with shorter PFS, without an effect on OS after adjusting for age and PS=2. Bonferroni correction was used to correct for multiple comparisons.	2/0	81/0
rs3783819	Kap et al. (2015) (14)	623 stage II-IV CRC patients who received first line adjuvant (201 received at least 4 cycles of oxaliplatin based treatment and 422 did treatment without oxaliplatin).	Patients carrying variant alleles of <i>MNAT1</i> rs3783819, <i>MNAT1</i> rs973063, <i>MNAT1</i> rs4151330 and <i>XPC</i> rs1043953 showed differential OS according to the type of treatment (with oxaliplatin vs. without oxaliplatin) after adjusting for age, sex and UICC stage. False discovery rate (FDR) correction was used to correct for multiple comparisons.	0/4	0/32
rs973063	Kap et al. (2015) (14)	See above.			
rs4151330	Kap et al. (2015) (14)	See above.			
rs1043953	Kap et al. (2015) (14)	See above.			

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
rs238406	Kjersem et al. (2016) (15)	519 mCRC patients with first-line 5-FU and oxaliplatin treatment +/- cetuximab. No information about a minimum number of treatment cycles is provided.	<i>ERCC2</i> rs238406-TT genotype and <i>AGXT</i> rs34116584-GG were associated with better PFS adjusted for age and performance status. Bonferroni correction was used to correct for multiple comparisons.	2/0	17/0
rs1799793	Liu et al. (2019) (16)	106 mCRC patients who treated with 2 cycles of either FOLFOX4 or XELOX as first-line chemotherapy.	<i>XPD</i> rs1799793-AA genotype associated with worse OS after adjusting for age, tumor location, CEA.	1/0	1/0
rs2016073	Chen et al. (2009) (17)	83 mCRC patients who received at least 2 cycles of 5-FU/ oxaliplatin-based treatment.	<i>ERCC5</i> rs2016073-G and <i>ERCC5</i> rs751402-A allele associated with increased response tumor. No multiple-testing correction was applied.	2/0	5/0
rs751402	Chen et al. (2009) (17)	See above.			
rs2228000	Sun et al. (2015) (9)	See above.			
rs1801516	Kweekel et al. (2009) (13)	See above.			
rs3732183	Park et al. (2010) (18)	94 mCRC patients who received XELOX or modified FOLFOX as first-line treatment. No information about a minimum number of treatment cycles is provided.	<i>MSH2</i> rs3732183-G allele and <i>POLR2C</i> rs4937-TT genotype were associated with tumor response after adjusting for age, sex, primary site, disease status, curative resection, and regimen. <i>MGMT</i> variant rs1625649-TT genotype was related with a poorer PFS. No multiple testing correction was applied.	3/0	16/0
rs1625649	Park et al. (2010) (18)	See above.			
rs4937	Park et al. (2010) (18)	See above.			

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
rs10817938	Hu et al. (2019) (19)	508 stage III-IV patients who received at least 2 cycles of FOLFOX4 or CAPOX.	<i>XPA</i> rs10817938-TT genotype, <i>ABCG2</i> rs2622621-CC genotype, and <i>ABCG2</i> rs2231142-CC genotype were associated with longer OS and DFS after adjusting for age, gender, body weight, and smoking status. No multiple testing correction was applied.	3/0	6/0
rs5030740	Li et al. (2019) (20)	166 CRC patients who received FOLFOX or XELOX. No information about a minimum number of treatment cycles is provided.	<i>RPA1</i> rs5030740- C allele was associated with poorer PFS and response to oxaliplatin chemotherapy after adjusting for age, sex, smoking status and drinking status. FDR correction was used to correct for multiple comparisons.	1/0	32/0
rs2233678	Suenaga et al. (2018) (21)	720 mCRC patients (216 received oxaliplatin based treatment with bevacizumab and 504 received irinotecan based treatment with bevacizumab). No information about a minimum number of treatment cycles is provided.	<i>PIN1</i> rs2233678-C allele was associated with a shorter PFS and OS in patients received oxaliplatin-based treatment after adjusting for sex, age, ECOG, liver metastasis, primary tumor resection, and <i>KRAS</i> exon2status. In contrast, <i>PIN1</i> rs2233678-C allele was associated with longer median PFS in non-oxaliplatin-based chemotherapy patients. No multiple testing correction was applied.	1/0	8/0

Phase I/II metabolic enzymes

rs1695	Li et al. (2012) (4)	See above.			
	Stoehlmacher et al. (2002) (22)	107 mCRC patients received at least three cycle of oxaliplatin in combination with 5-FU as second line therapy.	<i>GSTP1</i> rs1695-Val was related to a better survival in a dose-dependent manner adjusted for performance status and tumor site. No multiple testing correction was applied.	1/0	3/0
rs366631	Kap et al. (2014) (23)	755 stage II-IV CRC patients received first line adjuvant (254 patients who received at least 4 cycles of OX based treatment and 501 patients who did not).	Homozygote carriers of <i>GSTM1</i> (respect to null genotype) was associated with poorer OS after treatment with oxaliplatin than those not treated with oxaliplatin after multiple testing correction. In mCRC subgroup, having copies of <i>GSTM1</i> was associated with poorer OS.	0/1	0/3

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
rs11807	Kap et al. (2016) (24)	201 stage II-IV CRC patients who received at least 4 cycles of first line adjuvant OX based treatment.	Six variants were associated with OS (<i>ABCC10</i> rs2125739-C, <i>ATP1A1</i> rs975351-C, and <i>ATP8B3</i> rs7249302-C with better OS; <i>ATP1B2</i> rs1642763-A, <i>ATP8B3</i> rs8100856-T, <i>GSTM5</i> rs11807-C and worse OS) adjusted for age, sex, TNM stage, grade, BMI, and current alcohol intake. No multiple testing correction was applied.		
rs8192726	Kim et al. (2013) (25)	42 mCRC or unrespectable CRC patients received at least 1 cycle of first-line TIROX regimen.	<i>CYP2A6</i> rs8192726-T and <i>UGT1A1</i> rs4124874-T indicated an improved tumor response but no impact on survival after adjusting for ECOG and M1 stage. No multiple testing correction was applied.	2/0	6/0
rs4124874	Kim et al. (2013) (25)	See above.			
rs34116584	Kjersem et al. (2016) (15)	See above.			
Drug transporter					
rs1045642	Wu et al. (2013) (26)	1,028 CRC Chinese patients (all stages) who treated at least 2 cycles of adjuvant FOLFOX orXELOX regimen.	<i>ABCB1</i> rs1045642-CT genotype was related to a higher PFS and <i>ABCB1</i> rs1128503-TT/CT genotype was associated with a longer OS after adjusting for age, sex, body weight, and smoking status. No multiple testing correction was applied.	2/0	3/0
	Yue et al. (2013) (27)	343 CRC patients (all stages) with adjuvant FOLFOX or XELOX. No information about a minimum number of treatment cycles is provided.	<i>ABCB1</i> rs1045642 CT genotype comparing to TT genotype) was associated with longer PFS after adjusting for age, sex and smoking. No multiple testing correction was applied.	1/0	3/0
	Varma et al. (2020) (28)	145 CRC patients who received CAPOX (average 16 cycles).	<i>ABCB1</i> rs1045642-AG/GG genotype and <i>ABCB1</i> rs1128503-AG/GG genotype were associated with better PFS and DFS before adjustment, but not after adjustment. No multiple testing correction was applied.	2/0	4/0

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
rs1128503	Wu et al. (2013) (26)	See above.			
	Varma et al. (2020) (28)	See above.			
rs2032582	Wu et al. (2013) (26)	See above.			
rs2125739	Kap et al. (2016) (24)	See above.		6/0	14/0
rs975351	Kap et al. (2016) (24)	See above.			
rs1642763	Kap et al. (2016) (24)	See above.			
rs7249302	Kap et al. (2016) (24)	See above.			
rs8100856	Kap et al. (2016) (24)	See above.			
rs2273697	Mirakhorli et al. (2013) (29)	50 stage II-III CRC patients who received 12 cycle of FOLFOX-4 after radical resection.	<i>ABCC2</i> rs2273697-AA/AG was associated with better DFS and OS without an effect on RR. No adjustment was applied.	1/0	1/0
rs2622621	Hu et al. (2019) (19)	See above.			
rs2231142	Hu et al. (2019) (19)	See above.			

Folate pathway

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
rs1801131	Etienne-Grimaldi et al. (2010) (30)	117 aCRC patients who treated with at least 2 cycles of FOLFOX.	<i>MTHFR</i> rs1801131-C alleles and <i>MTHFR</i> rs1801133-T alleles were associated with an improved tumor response. No multiple testing correction was applied.	2/0	9/0
	Cecchin et al. (2015) (31)	150 stage II-III CRC patients who received FOLFOX4 after curative resection. No information about a minimum number of treatment cycles was provided.	<i>MTHFR</i> rs1801131-CC was associated with decreased tumor recurrence and worse disease-free survival after adjusted for gender, age, primary tumor site, tumor node metastasis stage. No adjustment and no multiple testing corrections were applied.	1/0	22/0
rs1801133	Etienne-Grimaldi et al. (2010) (30)	See above.			
<i>VEGF and EGF pathway</i>					
rs2227983	Wang et al. (2007) (32)	109 II-III CRC patients who treated with first-line adjuvant FOLFOX. No information about a minimum number of treatment cycles was provided.	<i>EGFR</i> rs2227983-A allele showed the association with a higher tumor response and increased OS before and after adjustment (for age, sex, performance status, tumor location, histologic differentiation, and invasive extent, lymph node status, metastasis at diagnosis, and serum CEA level).	1/0	1/0
rs45608036	Zhang et al. (2005) (33)	105 mCRC patients who received 4 cycles of 5-FU with oxaliplatin.	<i>EGFR</i> rs45608036 CA repeats <20 was associated with a better time to tumor progression (TTP) than ≥ 20 CA repeats. <i>CXCR1</i> rs2234671-GC was associated with increased TTP respect to GG genotype. No adjustment and no multiple testing corrections were applied.	2/0	5/0
rs2234671	Gerger et al. (2011) (34)	132 mCRC patients who received at least 2 cycles of oxaliplatin based treatment (FOLFOX or XELOX) with bevacizumab.	<i>CXCR1</i> rs2234671-G allele was associated with significantly higher response rate (RR) adjusted for sex, age, primary tumor site, histologic differentiation, metastatic site, number of metastatic sites, chemotherapy backbone (FOLFOX or XELOX) and study site (Hospital) stratified by ethnicity. Multiple testing correction was applied by using a modified test of Conneely and Boehnke.	1/0	23/0

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
	Zhang et al. (2005) (33)	See above.			
rs833061	Chen et al. (2011) (35)	128 unrespectable mCRC who received minimum 6 cycles of FOLFOX4.	<i>VEGFA</i> rs833061-TC/CC were associated with a lower RR and shorter PFS and OS. No adjustment was applied.	1/0	1/0
rs5275	Kim et al. (2009) (36)	76 recurrent or mCRC who received minimum 2 cycles of XELOX.	<i>COX-2 (PTGS2)</i> rs5275-TT was correlated with a better PFS and OS adjusted for age, sex performance status, disease status and curative resection. No multiple testing correction was applied.	1/0	15/0
<i>Immunogenic cell death pathway</i>					
rs1050305	Arai, et al. (2020) (37)	648 mCRC patients who received chemotherapeutic drugs including 376 oxaliplatin-based treatment (146 from validation cohort and 230 from discovery cohort) and 228 non-oxaliplatin based treatment (control cohort). No information about a minimum number of treatment cycles was provided.	<i>ANXA1</i> rs1050305-AA/AG was associated with worse OS than those with an A/A genotype and <i>LRP1</i> rs1799986-TT/TC was associated with worse OS than C/C genotype before adjustment and validated in the validation cohort. Apart from <i>ANXA1</i> rs1050305 and <i>LRP1</i> rs1799986, four more SNPs including <i>HMGB1</i> -rs1360485, <i>LRP1</i> -rs11172113, <i>P2RX7</i> -rs208294, and <i>P2RX7</i> -rs1718119 showed predictive values using interactions with treatment. The model was adjusted for ethnicity, sex, age, ECOG, primary tumor site, primary tumor resected, number of metastases, liver limited disease, adjuvant chemotherapy, <i>BRAF</i> status, and <i>RAS</i> status. No multiple testing correction was applied.	6/2	10/10
rs1799986	Arai, et al. (2020) (37)	See above.			
rs11172113	Arai, et al. (2020) (37)	See above.			
rs208294	Arai, et al. (2020) (37)	See above.			

SNP	Reference ^a	Study sample	Significantly associated endpoint	No. of SNPs identified (prognostic/predictive)	No. of SNPs analyzed (prognostic/predictive)
rs1718119	Arai, et al. (2020) (37)	See above.			
rs1360485	Arai, et al. (2020) (37)	See above.			
<i>Enterocyte subtype-related genes</i>					
rs4939378	Suenaga, et al. (2021) (38)	mCRC patients who received chemotherapeutic drugs including 376 oxaliplatin-based treatment (146 from validation cohort and 230 from discovery cohort) and 228 non-oxaliplatin based treatment (control cohort). No information about a minimum number of treatment cycles was provided.	In the discovery cohort, <i>MS4A12</i> -rs4939378 was associated with OS and <i>CDX2</i> -rs3812863 was associated with tumor response after adjusting for liver metastasis, number of metastases, primary remain, ECOG performance status, and stratified by regimen. In the validation cohort, <i>MS4A12</i> rs4939378 G allele was associated with longer PFS after adjusting for age, ECOG performance status, tumor site, resection of the primary tumors, <i>BRAF</i> mutation status, Adjuvant chemotherapy. These findings were not observed in the control cohort. No multiple testing correction was applied.	2/0	4/0
rs3812863	Suenaga, et al. (2021) (38)		See above		

^a The table included original studies identified association between individual SNPs and oxaliplatin based treatment for survival, response rate, or/and time to tumor progression. **Abbreviations:** SNP, single nucleotide polymorphism; OS, overall survival; PFS, progression-free survival; DFS, disease-free survival; TTP, time to tumor progression; RR, response rate; CRC, colorectal cancer; mCRC, metastatic colorectal cancer; aCRC, advanced colorectal cancer; 5-FU, 5-fluoropyrimidine; FOLFOX, 5-fluorouracil; leucovorin and oxaliplatin; XELOX/CAPOX, capecitabine and oxaliplatin; TIROX, irinotecan oxaliplatin and S-1; *XPD*, xeroderma pigmentosum complementation group C; *XPC*, XPC complex subunit, DNA damage recognition and repair factor *ERCC1*, excision repair cross-complementing group 1; *XRCC1*, X-ray repair cross complementing 1; *ERCC2*, ERCC excision repair 2; *MNAT1*, MNAT1 component of CDK activating kinase; *ERCC5*, ERCC excision repair 5, endonuclease; *XPA*, xeroderma pigmentosum, complementation group A; *ATM*, ATM serine/threonine kinase; *MSH2*, mismatch repair protein Msh2; *MGMT*, O-6-methylguanine-DNA methyltransferase; *ABCG2*, ATP binding cassette subfamily G member 2; *RPA1*, replication protein A1; *ABCB1*, ATP-binding cassette sub-family B member 1; *ABCC10*, ATP binding cassette subfamily C member 10; *ATP1A1*, ATPase Na⁺/K⁺ transporting subunit alpha 1; *ATP1B2*, ATPase Na⁺/K⁺ transporting subunit beta 2; *ATP8B3*, ATPase phospholipid transporting 8B3; *GSTM5*, glutathione S-transferase mu 5; *ABCC2*, ATP binding cassette subfamily C member 2;; *GSTP1*, glutathione S-transferase pi 1; *GSTM1*, glutathione S-transferase mu 1; *CYP2A6*, cytochrome P450 family 2 subfamily A member 6; *MTHFR*, methylenetetrahydrofolate reductase; *EGFR*, Epidermal growth factor receptor; *CXCR1*, C-X-C motif chemokine receptor 1; *VEGFA*, vascular endothelial growth factor A *COX-2*, cytochrome c oxidase subunit 2; *PTGS2*, prostaglandin-endoperoxide synthase 1; *POLR2C*, RNA

polymerase II subunit C; *PIN1*, peptidylprolyl cis/trans isomerase, NIMA-interacting 1; *HMGB1*, high mobility group box 1; FDR, False discovery rate; ECOG, Eastern Cooperative Oncology Group performance status.

Table S2. Detectable effect sizes at 85% power and type I error of 0.05 and 4.7×10^{-4} (corresponding to Bonferroni corrected p-value) for all endpoints based on minor allele frequency of genetic variants

	Predictive factor ^a								Prognostic factor ^b							
	Type I error of 4.7×10^{-4} ^c				Type I error of 5.0×10^{-2}				Type I error of 4.7×10^{-4} ^c				Type I error of 5.0×10^{-2}			
	Stage II-III CRC patients		Stage IV CRC patients		Stage II-III CRC patients		Stage IV CRC patients		Stage II-III CRC patients		Stage IV CRC patients		Stage II-III CRC patients		Stage IV CRC patients	
	HR modifying factor in OS ^d	HR modifying factor in PFS ^e	HR modifying factor in OS ^f	HR modifying factor in PFS ^g	HR modifying factor in OS ^d	HR modifying factor in PFS ^e	HR modifying factor in OS ^f	HR modifying factor in PFS ^g	HR in OS ^h	HR in PFS ⁱ	HR in OS ^j	HR in PFS ^k	HR in OS ^h	HR in PFS ⁱ	HR in OS ^j	HR in PFS ^k
MAF 50%	2.66	2.95	2.62	2.63	1.91	2.04	1.89	1.89	2.44	2.44	2.24	2.24	1.81	1.81	1.71	1.71
MAF 35%	2.78	3.10	2.75	2.75	1.97	2.11	1.95	1.95	2.55	2.55	2.33	2.33	1.86	1.86	1.75	1.75
MAF 20%	3.39	3.86	3.34	3.34	2.24	2.44	2.21	2.21	3.06	3.06	2.74	2.74	2.09	2.09	1.95	1.95
MAF 10%	5.09	6.05	4.98	4.99	2.92	3.28	2.89	2.89	4.43	4.43	3.84	3.84	2.68	2.68	2.44	2.44
MAF 5%	9.40	11.9	9.11	9.15	4.39	5.15	4.31	4.31	7.78	7.78	6.38	6.38	3.88	3.88	3.41	3.41

^a Effect sizes, quantified as the HR modifying factor of genetic variant on treatment (oxaliplatin-based vs. non-oxaliplatin based); ^b Effect sizes, quantified as the HR of genetic variant in patients who received oxaliplatin-based treatment; ^c Corresponding to Bonferroni corrected p-value; ^d based on 1,036 stage II-III CRC patients with 365 death events (35%), and 402 (39%) patients who received oxaliplatin-based treatment.; ^e based on 1,031 stage II-III CRC patients with 297 recurrence events (29%), and 400 (39%) patients who received oxaliplatin-based treatment.; ^f based on 466 stage IV CRC patients with 398 death events (85%), and 157 (34%) patients who received oxaliplatin-based treatment.; ^g based on 464 stage IV CRC patients with 395 recurrence events (85%), and 157 (34%) patients who received oxaliplatin-based treatment; ^h based on 402 stage II-III CRC patients who received oxaliplatin-based treatment with 103 death events (26 %); ⁱ based on 402 stage II & III CRC patients who received oxaliplatin with 103 recurrence events (26 %); ^j based on 157 stage IV CRC who received oxaliplatin-based treatment with 126 death events (80%); ^k based on 157 stage IV CRC who received oxaliplatin-based treatment with 127 recurrence events (81%). **Abbreviations:** HR, Hazard ratio; MAF, minor allele frequency; CRC, colorectal cancer; OS, overall survival; PFS, progression-free survival.

Table S3. SNP associations with first-line oxaliplatin treatment for all endpoints in stage II-III CRC patients

SNP-Effect allele	Overall survival							Progression-free survival						
	Patients who received OX based treatment			Patients who received non-OX based treatment			Interaction term ^a	Patients who received OX based treatment			Patients who received non-OX based treatment			Interaction term ^a
	HR	95%CI	P	HR	95%CI	P		P	HR	95%CI	P	HR	95%CI	
<i>Previously reported SNPs (N=40)</i>														
rs11807 - C	1.484	1.023 - 2.151	0.037	0.927	0.727 - 1.182	0.542	0.026	1.519	1.047 - 2.203	0.028	0.912	0.687 - 1.210	0.522	0.026
rs975351 - C	0.951	0.685 - 1.319	0.763	0.967	0.795 - 1.177	0.739	0.899	1.125	0.794 - 1.592	0.508	0.950	0.759 - 1.188	0.653	0.838
rs1801131 - G	1.148	0.818 - 1.611	0.423	1.038	0.844 - 1.277	0.723	0.498	1.120	0.803 - 1.563	0.504	0.982	0.773 - 1.248	0.884	0.318
rs5275 - G	1.037	0.750 - 1.434	0.827	1.143	0.928 - 1.408	0.208	0.705	0.924	0.659 - 1.295	0.644	0.902	0.707 - 1.150	0.403	0.971
rs2273697 - A	0.965	0.672 - 1.386	0.848	0.905	0.706 - 1.160	0.431	0.564	0.904	0.618 - 1.321	0.601	0.844	0.633 - 1.126	0.249	0.703
rs1625649 - A	1.173	0.837 - 1.643	0.354	0.932	0.780 - 1.113	0.436	0.141	1.257	0.889 - 1.777	0.196	1.005	0.823 - 1.227	0.963	0.115
rs1801516 - A	0.801	0.509 - 1.261	0.338	0.674	0.496 - 0.916	0.012	0.782	1.118	0.717 - 1.743	0.623	0.685	0.479 - 0.980	0.038	0.088
rs4939378 - A	1.157	0.857 - 1.562	0.340	0.841	0.692 - 1.023	0.084	0.119	1.101	0.808 - 1.499	0.543	0.898	0.718 - 1.124	0.349	0.127
rs1695 - G	0.984	0.713 - 1.358	0.921	0.977	0.790 - 1.207	0.827	0.823	1.100	0.792 - 1.527	0.569	0.930	0.731 - 1.185	0.559	0.886
rs208294 - C	1.359	1.007 - 1.834	0.045	1.067	0.877 - 1.299	0.516	0.427	1.634	1.193 - 2.238	0.002	1.003	0.800 - 1.257	0.983	0.096
rs1718119 - A	1.198	0.871 - 1.648	0.266	1.054	0.857 - 1.297	0.616	0.174	1.023	0.732 - 1.430	0.895	0.983	0.773 - 1.250	0.890	0.186
rs11172113 - C	0.951	0.688 - 1.314	0.759	0.993	0.837 - 1.177	0.932	0.815	0.937	0.668 - 1.314	0.705	0.943	0.779 - 1.141	0.544	0.797
rs1799986 - T	0.946	0.627 - 1.428	0.792	1.014	0.794 - 1.295	0.912	0.841	0.833	0.538 - 1.290	0.414	1.029	0.766 - 1.381	0.850	0.591
rs2016073 - G	1.203	0.832 - 1.740	0.326	1.065	0.872 - 1.301	0.534	0.106	1.478	1.021 - 2.139	0.038	0.948	0.707 - 1.270	0.720	0.032
rs1047768 - C	0.866	0.641 - 1.170	0.349	0.880	0.722 - 1.073	0.205	0.571	0.756	0.554 - 1.030	0.076	0.870	0.688 - 1.100	0.244	0.278
rs17655 - C	0.948	0.654 - 1.374	0.777	1.165	0.932 - 1.456	0.180	0.394	0.821	0.555 - 1.213	0.322	1.280	0.990 - 1.656	0.060	0.078
rs3812863 - A	1.061	0.770 - 1.460	0.719	1.090	0.886 - 1.340	0.417	0.739	1.305	0.927 - 1.836	0.127	1.043	0.817 - 1.332	0.736	0.959
rs1360485 - C	0.764	0.534 - 1.091	0.138	0.940	0.791 - 1.118	0.483	0.091	0.707	0.485 - 1.031	0.071	1.170	0.924 - 1.482	0.192	0.025
rs3783819 - G	1.386	0.994 - 1.933	0.054	0.861	0.706 - 1.049	0.138	0.062	1.369	0.974 - 1.924	0.071	0.879	0.696 - 1.111	0.281	0.098
rs4151330 - G	0.831	0.596 - 1.159	0.275	1.108	0.902 - 1.361	0.330	0.295	0.943	0.672 - 1.323	0.735	1.155	0.905 - 1.474	0.247	0.335
rs4937 - T	1.076	0.758 - 1.529	0.681	1.068	0.891 - 1.279	0.478	0.460	1.211	0.858 - 1.708	0.276	1.098	0.904 - 1.334	0.346	0.481
rs1642763 - A	0.896	0.614 - 1.308	0.570	0.859	0.706 - 1.045	0.129	0.572	0.913	0.620 - 1.342	0.642	0.930	0.750 - 1.154	0.512	0.803
rs7249302 - T	0.723	0.458 - 1.144	0.166	0.895	0.716 - 1.120	0.333	0.181	0.824	0.519 - 1.307	0.410	0.921	0.721 - 1.177	0.511	0.339
rs25487 - C	1.096	0.792 - 1.518	0.581	0.961	0.782 - 1.181	0.703	0.477	0.899	0.644 - 1.254	0.529	0.957	0.748 - 1.224	0.725	0.925
rs13181 - G	1.174	0.870 - 1.585	0.295	0.789	0.644 - 0.967	0.022	0.041	0.929	0.671 - 1.287	0.658	0.902	0.712 - 1.142	0.390	0.939
rs1799793 - T	1.316	0.966 - 1.793	0.082	0.811	0.659 - 0.998	0.048	0.016	0.944	0.671 - 1.327	0.739	0.980	0.772 - 1.243	0.866	0.825
rs238406 - T	1.209	0.869 - 1.681	0.260	0.911	0.754 - 1.099	0.329	0.255	0.969	0.698 - 1.344	0.850	0.914	0.734 - 1.138	0.419	0.694
rs11615 - G	0.986	0.717 - 1.357	0.932	0.908	0.735 - 1.123	0.374	0.590	0.945	0.674 - 1.326	0.745	1.011	0.789 - 1.296	0.930	0.591
rs2233678 - C	1.100	0.661 - 1.829	0.715	0.891	0.650 - 1.222	0.474	0.538	1.031	0.595 - 1.786	0.915	0.876	0.604 - 1.269	0.483	0.665
rs2234671 - G	0.817	0.377 - 1.769	0.608	0.986	0.644 - 1.509	0.948	0.779	0.768	0.350 - 1.689	0.512	1.122	0.716 - 1.759	0.615	0.568
rs3732183 - A	0.867	0.616 - 1.221	0.415	0.972	0.777 - 1.215	0.802	0.562	1.041	0.752 - 1.442	0.808	0.945	0.732 - 1.219	0.664	0.998
rs2228000 - A	0.715	0.490 - 1.044	0.083	1.040	0.838 - 1.290	0.721	0.156	0.634	0.419 - 0.959	0.031	1.079	0.838 - 1.388	0.555	0.059
rs2622621 - G	0.927	0.659 - 1.304	0.665	0.940	0.761 - 1.161	0.566	0.436	0.898	0.636 - 1.268	0.541	0.881	0.690 - 1.125	0.308	0.997
rs2231142 - T	1.149	0.706 - 1.870	0.576	0.837	0.607 - 1.154	0.278	0.465	1.273	0.803 - 2.017	0.305	0.782	0.540 - 1.132	0.192	0.123

rs2125739 - C	0.807	0.556 - 1.171	0.259	0.961	0.767 - 1.205	0.730	0.380	0.800	0.552 - 1.160	0.239	0.956	0.732 - 1.247	0.739	0.446
rs833061 - T	1.035	0.756 - 1.418	0.828	0.915	0.762 - 1.100	0.345	0.653	1.131	0.819 - 1.562	0.453	0.989	0.801 - 1.221	0.918	0.553
rs2227983 - A	1.047	0.736 - 1.489	0.798	0.830	0.658 - 1.048	0.118	0.134	0.799	0.537 - 1.188	0.268	0.869	0.664 - 1.139	0.310	0.707
rs1045642 - G	1.027	0.765 - 1.379	0.858	0.874	0.710 - 1.076	0.205	0.401	1.091	0.796 - 1.496	0.588	0.892	0.704 - 1.130	0.342	0.308
rs1128503 - G	0.902	0.663 - 1.226	0.509	0.966	0.791 - 1.181	0.737	0.738	0.918	0.668 - 1.262	0.599	1.071	0.845 - 1.357	0.572	0.512
rs1050305 - G	1.359	0.806 - 2.292	0.250	1.104	0.803 - 1.517	0.542	0.337	1.550	0.905 - 2.653	0.110	1.108	0.763 - 1.609	0.590	0.513

Putative functional SNPs (N=13)

rs2227963 - C	0.973	0.488 - 1.940	0.938	1.425	0.996 - 2.040	0.052	0.295	0.684	0.318 - 1.472	0.331	1.390	0.898 - 2.154	0.140	0.064
rs8187710 - A	0.459	0.205 - 1.025	0.057	0.897	0.590 - 1.364	0.612	0.290	0.606	0.274 - 1.340	0.216	1.007	0.635 - 1.595	0.977	0.179
rs12917 - T	1.371	0.910 - 2.064	0.131	0.712	0.525 - 0.965	0.029	0.012	1.211	0.770 - 1.904	0.407	0.752	0.527 - 1.072	0.115	0.073
rs2308321 - G	0.672	0.413 - 1.095	0.110	0.936	0.697 - 1.257	0.662	0.227	0.790	0.492 - 1.269	0.330	1.059	0.754 - 1.487	0.742	0.363
rs1138272 - T	1.036	0.569 - 1.886	0.907	0.849	0.552 - 1.306	0.456	0.719	1.444	0.810 - 2.573	0.213	0.992	0.618 - 1.592	0.972	0.575
rs17525809 - C	1.701	0.986 - 2.936	0.056	1.132	0.784 - 1.633	0.508	0.215	1.238	0.693 - 2.212	0.471	1.132	0.736 - 1.741	0.574	0.231
rs7958311 - A	0.873	0.597 - 1.276	0.484	1.102	0.879 - 1.380	0.400	0.147	1.045	0.713 - 1.532	0.822	1.109	0.847 - 1.452	0.453	0.907
rs2230911 - G	0.420	0.181 - 0.973	0.043	1.416	0.974 - 2.059	0.069	0.006	0.651	0.312 - 1.358	0.253	1.409	0.927 - 2.140	0.108	0.098
rs1805107 - G	1.272	0.836 - 1.934	0.261	1.156	0.899 - 1.487	0.257	0.906	1.381	0.887 - 2.149	0.153	1.201	0.895 - 1.613	0.222	0.692
rs5030755 - G	1.265	0.793 - 2.017	0.323	0.784	0.555 - 1.107	0.166	0.089	1.268	0.760 - 2.114	0.364	0.648	0.418 - 1.005	0.053	0.015
rs7250872 - T	1.073	0.767 - 1.502	0.681	1.109	0.896 - 1.374	0.341	0.755	1.233	0.875 - 1.736	0.231	0.905	0.701 - 1.169	0.446	0.246
rs2228001 - T	0.940	0.683 - 1.295	0.706	1.215	0.996 - 1.482	0.055	0.236	0.935	0.672 - 1.301	0.689	1.043	0.828 - 1.315	0.719	0.699
rs2227999 - T	1.113	0.584 - 2.121	0.746	1.181	0.764 - 1.824	0.454	0.911	0.717	0.330 - 1.555	0.399	1.288	0.789 - 2.103	0.312	0.178

The models were adjusted for age, sex, cancer location (proximal vs distal), and stage for the analyses. The model was also stratified for grade (1-2 vs 3-4), KRAS mutation (wild type vs mutation), resection status (completely resected vs not completely resected), array used for genotyping data to account for violation of proportional hazards assumption. ^a Interaction term between SNP and the type of chemotherapy (oxaliplatin-based vs. others). **Abbreviations:** SNP, single nucleotide polymorphisms; HR, hazard ratio; P, p-value; CI, confidential interval; OX, oxaliplatin treatment; CRC, colorectal cancer

Table S4. SNP associations with first-line oxaliplatin treatment for all endpoints in mCRC (stage IV) patients

SNP-Effect allele	Overall survival							Progression-free survival						
	Patients who received OX based treatment			Patients who received non-OX based treatment			Interaction term ^a	Patients who received OX based treatment			Patients who received non-OX based treatment			Interaction term ^a
	HR	95%CI	P	HR	95%CI	P		HR	95%CI	P	HR	95%CI	P	
<i>Previously reported SNPs (N=40)</i>														
rs11807 - C	1.796	1.016 - 3.176	0.044	0.865	0.626 - 1.196	0.381	0.084	1.671	0.905 - 3.083	0.101	0.806	0.575 - 1.131	0.212	0.062
rs975351 - C	0.733	0.489 - 1.099	0.133	1.023	0.806 - 1.298	0.851	0.317	0.901	0.589 - 1.378	0.630	1.045	0.804 - 1.360	0.741	0.823
rs1801131 - G	1.000	0.652 - 1.532	0.999	1.329	1.011 - 1.747	0.042	0.159	1.041	0.681 - 1.592	0.852	1.429	1.067 - 1.912	0.016	0.088
rs5275 - G	1.331	0.889 - 1.992	0.164	1.044	0.805 - 1.353	0.746	0.732	1.190	0.789 - 1.795	0.408	1.120	0.843 - 1.489	0.433	0.896
rs2273697 - A	0.871	0.540 - 1.406	0.573	1.033	0.776 - 1.375	0.824	0.197	1.006	0.591 - 1.713	0.981	1.156	0.857 - 1.561	0.342	0.266
rs1625649 - A	1.270	0.839 - 1.923	0.258	1.077	0.892 - 1.301	0.439	0.590	0.968	0.619 - 1.515	0.887	1.057	0.868 - 1.288	0.581	0.875
rs1801516 - A	0.637	0.352 - 1.152	0.136	1.158	0.842 - 1.592	0.367	0.607	0.794	0.440 - 1.435	0.445	1.250	0.895 - 1.745	0.190	0.903
rs4939378 - A	1.185	0.805 - 1.745	0.390	1.228	0.957 - 1.576	0.106	0.937	1.148	0.764 - 1.725	0.507	1.114	0.858 - 1.446	0.417	0.974
rs1695 - G	0.973	0.654 - 1.448	0.893	1.292	1.013 - 1.647	0.039	0.237	1.007	0.660 - 1.535	0.976	1.425	1.101 - 1.844	0.007	0.179
rs208294 - C	0.802	0.557 - 1.155	0.236	1.011	0.777 - 1.316	0.936	0.036	0.744	0.510 - 1.087	0.126	1.009	0.767 - 1.327	0.949	0.169
rs1718119 - A	1.168	0.806 - 1.692	0.413	1.006	0.789 - 1.282	0.964	0.430	1.085	0.741 - 1.587	0.675	0.975	0.757 - 1.257	0.847	0.147
rs11172113 - C	1.131	0.722 - 1.773	0.590	1.057	0.873 - 1.280	0.569	0.725	1.173	0.730 - 1.883	0.510	1.059	0.870 - 1.288	0.567	0.650
rs1799986 - T	0.973	0.552 - 1.715	0.925	0.863	0.633 - 1.179	0.355	0.201	1.019	0.573 - 1.810	0.950	0.864	0.618 - 1.207	0.390	0.923
rs2016073 - G	1.124	0.679 - 1.862	0.649	0.990	0.773 - 1.268	0.936	0.706	1.086	0.642 - 1.837	0.758	0.978	0.758 - 1.262	0.862	0.836
rs1047768 - C	1.209	0.781 - 1.872	0.396	1.139	0.897 - 1.445	0.285	0.462	1.066	0.671 - 1.694	0.786	1.072	0.833 - 1.380	0.590	0.742
rs17655 - C	1.046	0.669 - 1.635	0.845	0.851	0.638 - 1.134	0.270	0.443	1.186	0.737 - 1.909	0.483	1.063	0.781 - 1.448	0.697	0.302
rs3812863 - A	0.992	0.639 - 1.54	0.971	1.001	0.766 - 1.309	0.992	0.266	0.983	0.637 - 1.518	0.939	0.999	0.756 - 1.318	0.992	0.080
rs1360485 - C	1.186	0.818 - 1.719	0.369	1.090	0.901 - 1.318	0.374	0.343	1.267	0.854 - 1.880	0.240	1.093	0.894 - 1.337	0.387	0.184
rs3783819 - G	1.558	1.048 - 2.316	0.028	0.985	0.777 - 1.248	0.901	0.153	1.799	1.125 - 2.877	0.014	0.868	0.677 - 1.114	0.266	0.109
rs4151330 - G	0.605	0.398 - 0.918	0.018	1.017	0.795 - 1.301	0.893	0.192	0.518	0.310 - 0.864	0.012	1.205	0.930 - 1.563	0.158	0.042
rs4937 - T	0.819	0.520 - 1.290	0.390	0.969	0.799 - 1.173	0.744	0.730	0.693	0.412 - 1.167	0.168	0.874	0.709 - 1.078	0.208	0.773
rs1642763 - A	1.019	0.648 - 1.603	0.936	0.959	0.776 - 1.185	0.699	0.389	1.361	0.817 - 2.267	0.237	1.048	0.835 - 1.316	0.684	0.293
rs7249302 - T	0.628	0.355 - 1.109	0.109	0.910	0.714 - 1.161	0.449	0.516	0.651	0.359 - 1.182	0.158	0.860	0.668 - 1.109	0.245	0.555
rs25487 - C	0.789	0.524 - 1.186	0.254	1.026	0.792 - 1.329	0.848	0.327	0.765	0.512 - 1.144	0.192	0.933	0.701 - 1.241	0.633	0.181
rs13181 - G	0.954	0.666 - 1.366	0.796	1.318	1.028 - 1.690	0.030	0.375	0.975	0.660 - 1.441	0.899	1.281	0.982 - 1.670	0.068	0.348
rs1799793 - T	1.008	0.703 - 1.447	0.964	1.257	0.977 - 1.618	0.075	0.412	0.910	0.599 - 1.385	0.661	1.215	0.927 - 1.591	0.158	0.188
rs238406 - T	1.146	0.789 - 1.662	0.475	1.259	0.987 - 1.607	0.063	0.864	0.927	0.616 - 1.397	0.718	1.204	0.928 - 1.561	0.162	0.326
rs11615 - G	1.175	0.790 - 1.748	0.425	1.343	1.036 - 1.741	0.026	0.706	1.105	0.730 - 1.670	0.637	1.254	0.955 - 1.647	0.104	0.476
rs2233678 - C	1.480	0.885 - 2.475	0.135	1.202	0.808 - 1.789	0.364	0.921	1.243	0.729 - 2.120	0.425	1.245	0.821 - 1.888	0.303	0.507
rs2234671 - G	0.552	0.188 - 1.620	0.279	1.456	0.898 - 2.359	0.127	0.023	0.414	0.126 - 1.361	0.146	1.246	0.728 - 2.132	0.422	0.030
rs3732183 - A	0.850	0.552 - 1.310	0.462	0.966	0.761 - 1.227	0.777	0.844	1.066	0.694 - 1.636	0.770	0.910	0.707 - 1.170	0.462	0.464
rs2228000 - A	1.263	0.812 - 1.965	0.300	1.052	0.816 - 1.356	0.696	0.889	1.135	0.726 - 1.774	0.580	1.142	0.870 - 1.498	0.338	0.998
rs2622621 - G	1.256	0.809 - 1.949	0.310	0.941	0.723 - 1.223	0.647	0.339	1.278	0.825 - 1.982	0.272	1.227	0.921 - 1.634	0.162	0.861
rs2231142 - T	0.751	0.354 - 1.593	0.455	0.831	0.565 - 1.222	0.348	0.798	0.897	0.405 - 1.984	0.788	0.973	0.644 - 1.470	0.896	0.971

rs2125739 - C	0.972	0.628 - 1.503	0.897	1.106	0.852 - 1.435	0.451	0.394	0.935	0.583 - 1.499	0.781	1.196	0.898 - 1.594	0.220	0.871
rs833061 - T	0.721	0.502 - 1.035	0.076	1.053	0.836 - 1.327	0.660	0.084	0.599	0.396 - 0.907	0.015	1.144	0.901 - 1.453	0.270	0.002
rs2227983 - A	0.747	0.470 - 1.185	0.215	1.066	0.794 - 1.431	0.671	0.543	0.784	0.479 - 1.284	0.334	1.158	0.845 - 1.588	0.360	0.304
rs1045642 - G	1.010	0.696 - 1.464	0.959	1.088	0.853 - 1.388	0.499	0.709	1.132	0.775 - 1.655	0.521	0.938	0.720 - 1.221	0.633	0.467
rs1128503 - G	0.787	0.507 - 1.223	0.287	1.025	0.818 - 1.285	0.830	0.418	0.859	0.557 - 1.324	0.490	0.964	0.763 - 1.217	0.755	0.953
rs1050305 - G	1.089	0.480 - 2.468	0.839	1.001	0.671 - 1.494	0.995	0.481	1.127	0.502 - 2.532	0.772	1.128	0.752 - 1.693	0.560	0.936

Putative functional SNPs (N=13)

rs2227963 - C	0.525	0.243 - 1.135	0.101	0.766	0.502 - 1.168	0.216	0.522	0.448	0.194 - 1.035	0.060	0.788	0.513 - 1.212	0.278	0.350
rs8187710 - A	1.023	0.517 - 2.026	0.948	0.940	0.583 - 1.513	0.798	0.261	1.144	0.534 - 2.451	0.729	1.321	0.786 - 2.221	0.293	0.944
rs12917 - T	0.871	0.457 - 1.660	0.674	0.996	0.675 - 1.471	0.985	0.364	0.697	0.343 - 1.414	0.317	0.871	0.584 - 1.301	0.501	0.500
rs2308321 - G	0.786	0.421 - 1.467	0.450	0.950	0.652 - 1.385	0.790	0.424	0.715	0.368 - 1.392	0.324	0.943	0.630 - 1.411	0.775	0.545
rs1138272 - T	0.984	0.543 - 1.784	0.958	1.176	0.758 - 1.824	0.469	0.739	0.936	0.519 - 1.687	0.826	1.282	0.808 - 2.035	0.292	0.795
rs17525809 - C	0.866	0.407 - 1.842	0.708	1.431	0.920 - 2.227	0.112	0.025	0.869	0.427 - 1.770	0.699	1.352	0.861 - 2.123	0.190	0.380
rs7958311 - A	0.848	0.569 - 1.266	0.420	0.814	0.606 - 1.093	0.172	0.795	0.881	0.566 - 1.371	0.573	0.808	0.592 - 1.104	0.182	0.994
rs2230911 - G	0.890	0.410 - 1.928	0.767	1.066	0.663 - 1.714	0.793	0.109	0.857	0.373 - 1.970	0.717	1.517	0.889 - 2.586	0.126	0.051
rs1805107 - G	1.301	0.739 - 2.292	0.362	1.010	0.747 - 1.365	0.950	0.358	1.146	0.632 - 2.080	0.654	1.005	0.734 - 1.377	0.974	0.347
rs5030755 - G	1.067	0.530 - 2.149	0.856	0.908	0.625 - 1.32	0.613	0.765	0.932	0.463 - 1.878	0.844	0.749	0.499 - 1.126	0.165	0.586
rs7250872 - T	2.238	1.358 - 3.686	0.002	0.968	0.721 - 1.298	0.826	0.007	1.907	1.143 - 3.183	0.013	1.256	0.922 - 1.710	0.148	0.398
rs2228001 - T	1.194	0.826 - 1.725	0.346	0.956	0.761 - 1.203	0.703	0.669	1.236	0.837 - 1.824	0.287	0.996	0.786 - 1.262	0.973	0.463
rs2227999 - T	1.039	0.528 - 2.046	0.911	1.189	0.74 - 1.911	0.474	0.941	0.911	0.445 - 1.862	0.798	1.229	0.75 - 2.014	0.413	0.848

The models were adjusted for age, sex, cancer location (proximal vs distal), and liver resection for the analyses. The model was also stratified for grade (1-2 vs 3-4), KRAS mutation (wild type vs mutation), resection status (completely resected vs not completely resected), array used for genotyping data to account for violation of proportional hazards assumption. ^a Interaction term between SNP and the type of chemotherapy (oxaliplatin-based vs. others). **Abbreviations:** SNP, single nucleotide polymorphisms; HR, hazard ratio; P, p-value; CI, confidential interval; OX, oxaliplatin treatment; CRC, colorectal cancer; mCRC, metastatic colorectal cancer

Reference

1. Huang MY, Huang ML, Chen MJ, Lu CY, Chen CF, Tsai PC, *et al.* Multiple genetic polymorphisms in the prediction of clinical outcome of metastatic colorectal cancer patients treated with first-line FOLFOX-4 chemotherapy. *Pharmacogenetics and genomics* **2011**;21(1):18-25 doi 10.1097/FPC.0b013e3283415124.
2. Ruzzo A, Graziano F, Loupakis F, Rulli E, Canestrari E, Santini D, *et al.* Pharmacogenetic profiling in patients with advanced colorectal cancer treated with first-line FOLFOX-4 chemotherapy. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* **2007**;25(10):1247-54 doi 10.1200/jco.2006.08.1844.
3. Rao D, Mallick AB, Augustine T, Daroqui C, Jiffry J, Merla A, *et al.* Excision repair cross-complementing group-1 (ERCC1) induction kinetics and polymorphism are markers of inferior outcome in patients with colorectal cancer treated with oxaliplatin. *Oncotarget* **2019**;10(53):5510-22 doi 10.18632/oncotarget.27140.
4. Li HY, Ge X, Huang GM, Li KY, Zhao JQ, Yu XM, *et al.* GSTP1, ERCC1 and ERCC2 polymorphisms, expression and clinical outcome of oxaliplatin-based adjuvant chemotherapy in colorectal cancer in Chinese population. *Asian Pacific journal of cancer prevention : APJCP* **2012**;13(7):3465-9.
5. Stoehlmacher J, Park DJ, Zhang W, Yang D, Groshen S, Zahedy S, *et al.* A multivariate analysis of genomic polymorphisms: prediction of clinical outcome to 5-FU/oxaliplatin combination chemotherapy in refractory colorectal cancer. *Br J Cancer* **2004**;91(2):344-54 doi 10.1038/sj.bjc.6601975.
6. Pare L, Marcuello E, Altes A, del Rio E, Sedano L, Salazar J, *et al.* Pharmacogenetic prediction of clinical outcome in advanced colorectal cancer patients receiving oxaliplatin/5-fluorouracil as first-line chemotherapy. *Br J Cancer* **2008**;99(7):1050-5 doi 10.1038/sj.bjc.6604671.
7. Gan Y, Li XR, Chen DJ, Wu JH. Association between polymorphisms of XRCC1 Arg399Gln and XPD Lys751Gln genes and prognosis of colorectal cancer in a Chinese population. *Asian Pacific journal of cancer prevention : APJCP* **2012**;13(11):5721-4.
8. Lamas MJ, Duran G, Balboa E, Bernardez B, Touris M, Vidal Y, *et al.* Use of a comprehensive panel of biomarkers to predict response to a fluorouracil-oxaliplatin regimen in patients with metastatic colorectal cancer. *Pharmacogenomics* **2011**;12(3):433-42 doi 10.2217/pgs.10.196.
9. Sun K, Gong A, Liang P. Predictive impact of genetic polymorphisms in DNA repair genes on susceptibility and therapeutic outcomes to colorectal cancer patients. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine* **2015**;36(3):1549-59 doi 10.1007/s13277-014-2721-3.
10. Liu D, Wu HZ, Zhang YN, Kang H, Sun MJ, Wang EH, *et al.* DNA repair genes XPC, XPG polymorphisms: relation to the risk of colorectal carcinoma and therapeutic outcome with Oxaliplatin-based adjuvant chemotherapy. *Molecular carcinogenesis* **2012**;51 Suppl 1:E83-93 doi 10.1002/mc.21862.
11. Kong J, Liu Z, Cai F, Xu X, Liu JJ. Relationship between the Asp1104His polymorphism of the nucleotide excision repair gene ERCC5 and treatment sensitivity to oxaliplatin in patients with advanced colorectal cancer in China. *Clinics (Sao Paulo, Brazil)* **2018**;73:e455 doi 10.6061/clinics/2017/e455.
12. Monzo M, Moreno I, Navarro A, Ibeas R, Artells R, Gel B, *et al.* Single nucleotide polymorphisms in nucleotide excision repair genes XPA, XPD, XPG and ERCC1 in advanced colorectal cancer patients treated with first-line oxaliplatin/fluoropyrimidine. *Oncology* **2007**;72(5-6):364-70 doi 10.1159/000113534.

13. Kweekel DM, Antonini NF, Nortier JW, Punt CJ, Gelderblom H, Guchelaar HJ. Explorative study to identify novel candidate genes related to oxaliplatin efficacy and toxicity using a DNA repair array. *Br J Cancer* **2009**;101(2):357-62 doi 10.1038/sj.bjc.6605134.
14. Kap EJ, Seibold P, Richter S, Scherer D, Habermann N, Balavarca Y, *et al.* Genetic variants in DNA repair genes as potential predictive markers for oxaliplatin chemotherapy in colorectal cancer. *The pharmacogenomics journal* **2015**;15(6):505-12 doi 10.1038/tpj.2015.8.
15. Kjersem JB, Thomsen M, Guren T, Hamfjord J, Carlsson G, Gustavsson B, *et al.* AGXT and ERCC2 polymorphisms are associated with clinical outcome in metastatic colorectal cancer patients treated with 5-FU/oxaliplatin. *The pharmacogenomics journal* **2016**;16(3):272-9 doi 10.1038/tpj.2015.54.
16. Liu Z, Kong J, Kong Y, Cai F, Xu X, Liu J, *et al.* Association of XPD Asp312Asn polymorphism and response to oxaliplatin-based first-line chemotherapy and survival in patients with metastatic colorectal cancer. *Advances in clinical and experimental medicine : official organ Wroclaw Medical University* **2019**;28(11):1459-68 doi 10.17219/acem/108552.
17. Chen J, Xie F, Chen K, Wang D, Jiang H, Li J, *et al.* ERCC5 promoter polymorphisms at -763 and +25 predict the response to oxaliplatin-based chemotherapy in patients with advanced colorectal cancer. *Cancer biology & therapy* **2009**;8(14):1424-30.
18. Park JH, Kim NS, Park JY, Chae YS, Kim JG, Sohn SK, *et al.* MGMT -535G>T polymorphism is associated with prognosis for patients with metastatic colorectal cancer treated with oxaliplatin-based chemotherapy. *Journal of cancer research and clinical oncology* **2010**;136(8):1135-42 doi 10.1007/s00432-010-0760-8.
19. Hu X, Qin W, Li S, He M, Wang Y, Guan S, *et al.* Polymorphisms in DNA repair pathway genes and ABCG2 gene in advanced colorectal cancer: correlation with tumor characteristics and clinical outcome in oxaliplatin-based chemotherapy. *Cancer Manag Res* **2019**;11:285-97 doi 10.2147/CMAR.S181922.
20. Li S, Xu K, Gu D, He L, Xie L, Chen Z, *et al.* Genetic variants in RPA1 associated with the response to oxaliplatin-based chemotherapy in colorectal cancer. *Journal of gastroenterology* **2019**;54(11):939-49 doi 10.1007/s00535-019-01571-z.
21. Suenaga M, Schirripa M, Cao S, Zhang W, Yang D, Cremolini C, *et al.* Potential role of PIN1 genotypes in predicting benefit from oxaliplatin-based and irinotecan-based treatment in patients with metastatic colorectal cancer. *The pharmacogenomics journal* **2018**;18(5):623-32 doi 10.1038/s41397-018-0030-8.
22. Stoehmacher J, Park DJ, Zhang W, Groshen S, Tsao-Wei DD, Yu MC, *et al.* Association between glutathione S-transferase P1, T1, and M1 genetic polymorphism and survival of patients with metastatic colorectal cancer. *Journal of the National Cancer Institute* **2002**;94(12):936-42.
23. Kap EJ, Richter S, Rudolph A, Jansen L, Ulrich A, Hoffmeister M, *et al.* Genetic variants in the glutathione S-transferase genes and survival in colorectal cancer patients after chemotherapy and differences according to treatment with oxaliplatin. *Pharmacogenetics and genomics* **2014**;24(7):340-7 doi 10.1097/fpc.0000000000000059.
24. Kap EJ, Seibold P, Scherer D, Habermann N, Balavarca Y, Jansen L, *et al.* SNPs in transporter and metabolizing genes as predictive markers for oxaliplatin treatment in colorectal cancer patients. *Int J Cancer* **2016**;138(12):2993-3001 doi 10.1002/ijc.30026.
25. Kim SY, Y SH, E KS, Kong SY, Shin A, Baek JY, *et al.* S-1 plus irinotecan and oxaliplatin for the first-line treatment of patients with metastatic colorectal cancer: a prospective phase II study and pharmacogenetic analysis. *Br J Cancer* **2013**;109(6):1420-7 doi 10.1038/bjc.2013.479.
26. Wu H, Kang H, Liu Y, Xiao Q, Zhang Y, Sun M, *et al.* Association of ABCB1 genetic polymorphisms with susceptibility to colorectal cancer and therapeutic prognosis. *Pharmacogenomics* **2013**;14(8):897-911 doi 10.2217/pgs.13.78.

27. Yue AM, Xie ZB, Zhao HF, Guo SP, Shen YH, Wang HP. Associations of ABCB1 and XPC genetic polymorphisms with susceptibility to colorectal cancer and therapeutic prognosis in a Chinese population. *Asian Pacific journal of cancer prevention : APJCP* **2013**;14(5):3085-91.
28. Varma A, Mathaiyan J, Shewade D, Dubashi B, Sunitha K. Influence of ABCB-1, ERCC-1 and ERCC-2 gene polymorphisms on response to capecitabine and oxaliplatin (CAPOX) treatment in colorectal cancer (CRC) patients of South India. *Journal of clinical pharmacy and therapeutics* **2020**;45(4):617-27 doi 10.1111/jcpt.13166.
29. Mirakhorli M, Rahman SA, Abdullah S, Vakili M, Rozafzon R, Khoshzaban A. Multidrug resistance protein 2 genetic polymorphism and colorectal cancer recurrence in patients receiving adjuvant FOLFOX-4 chemotherapy. *Molecular medicine reports* **2013**;7(2):613-7 doi 10.3892/mmr.2012.1226.
30. Etienne-Grimaldi MC, Milano G, Maindrault-Goebel F, Chibaudel B, Formento JL, Francoual M, *et al.* Methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms and FOLFOX response in colorectal cancer patients. *British journal of clinical pharmacology* **2010**;69(1):58-66 doi 10.1111/j.1365-2125.2009.03556.x.
31. Cecchin E, Perrone G, Nobili S, Polesel J, De Mattia E, Zanusso C, *et al.* MTHFR-1298 A>C (rs1801131) is a predictor of survival in two cohorts of stage II/III colorectal cancer patients treated with adjuvant fluoropyrimidine chemotherapy with or without oxaliplatin. *The pharmacogenomics journal* **2015**;15(3):219-25 doi 10.1038/tpj.2014.64.
32. Wang WS, Chen PM, Chiou TJ, Liu JH, Lin JK, Lin TC, *et al.* Epidermal growth factor receptor R497K polymorphism is a favorable prognostic factor for patients with colorectal carcinoma. *Clinical cancer research : an official journal of the American Association for Cancer Research* **2007**;13(12):3597-604 doi 10.1158/1078-0432.Ccr-06-2601.
33. Zhang W, Stoehmacher J, Park DJ, Yang D, Borchard E, Gil J, *et al.* Gene polymorphisms of epidermal growth factor receptor and its downstream effector, interleukin-8, predict oxaliplatin efficacy in patients with advanced colorectal cancer. *Clinical colorectal cancer* **2005**;5(2):124-31 doi 10.3816/cc.2005.n.025.
34. Gerger A, El-Khoueiry A, Zhang W, Yang D, Singh H, Bohanes P, *et al.* Pharmacogenetic angiogenesis profiling for first-line Bevacizumab plus oxaliplatin-based chemotherapy in patients with metastatic colorectal cancer. *Clinical cancer research : an official journal of the American Association for Cancer Research* **2011**;17(17):5783-92 doi 10.1158/1078-0432.Ccr-11-1115.
35. Chen MH, Tzeng CH, Chen PM, Lin JK, Lin TC, Chen WS, *et al.* VEGF -460T → C polymorphism and its association with VEGF expression and outcome to FOLFOX-4 treatment in patients with colorectal carcinoma. *The pharmacogenomics journal* **2011**;11(3):227-36 doi 10.1038/tpj.2010.48.
36. Kim JG, Chae YS, Sohn SK, Moon JH, Ryoo HM, Bae SH, *et al.* Prostaglandin synthase 2/cyclooxygenase 2 (PTGS2/COX2) 8473T>C polymorphism associated with prognosis for patients with colorectal cancer treated with capecitabine and oxaliplatin. *Cancer chemotherapy and pharmacology* **2009**;64(5):953-60 doi 10.1007/s00280-009-0947-3.
37. Arai H, Xiao Y, Loupakis F, Kawanishi N, Wang J, Battaglin F, *et al.* Immunogenic cell death pathway polymorphisms for predicting oxaliplatin efficacy in metastatic colorectal cancer. *Journal for immunotherapy of cancer* **2020**;8(2) doi 10.1136/jitc-2020-001714.
38. Suenaga M, Schirripa M, Cao S, Zhang W, Cremolini C, Lonardi S, *et al.* Clinical significance of enterocyte-specific gene polymorphisms as candidate markers of oxaliplatin-based treatment for metastatic colorectal cancer. *The pharmacogenomics journal* **2021** doi 10.1038/s41397-021-00207-x.