

Supplementary Table 1. Clinical, sociodemographic, and biochemical determinants of erythrocyte MTX-PG levels at 3 months of treatment (univariate analysis).

Variable	Derivation cohort						Validation cohort					
	N	St β					N	St β				
		MTX-PG1	MTX-PG2	MTX-PG3	MTX-PG4+5	Total MTX-PG		MTX-PG1	MTX-PG2	MTX-PG3	MTX-PG4+5	Total MTX-PG
Age, years, mean (SD)	93	0,22*	0,20#	0,22*	0,16	0,25*	247	0,13*	0,22***	0,24***	0,27***	0,30***
Female (%)	93	0,00	-0,13	-0,13	0,00	-0,11	247	-0,01	-0,11#	-0,16*	-0,16*	-0,1**8
BSA, m3, mean (SD)	0	n/a	n/a	n/a	n/a	n/a	245	0,057	-0,05	-0,07	-0,05	-0,07
DAS28esr, mean (SD)	80	0,12	0,03	0,22#	0,24*	0,22#	247	0,10	0,10	0,13*	0,11#	0,14**
Rheumatoid factor positive (%)	83	-0,01	0,01	0,10	0,09	0,09	223	-0,03	0,13#	0,06	-0,02	0,05
Anti-CCP positive (%)	83	0,10	-0,02	0,03	0,01	0,01	223	-0,08	0,05	0,05	0,08	0,08
Days of treatment at study visit, mean (SD)	87	-0,08	0,11	0,16	0,05	0,14	234	0,05	0,06	0,16*	0,03	0,10
Intramuscular administration of methotrexate (%)	85	0,11	-0,16	0,02	-0,02	-0,05	0	n/a	n/a	n/a	n/a	n/a
Other DMARD use (%)	85	0,16	0,04	0,14	0,17	0,16	221	-0,12#	0,00	-0,02	-0,03	-0,03
Hydroxychloroquine use (%)	85	0,17	-0,04	0,07	0,17	0,09	221	-0,12#	0,00	-0,02	-0,03	-0,03
Sulfasalazine use (%)	85	0,03	0,07	0,18#	0,12	0,17	221	-0,12#	0,00	-0,02	-0,03	-0,03
Biological use (%)	85	0,00	0,00	-0,08	-0,08	-0,07	0	n/a	n/a	n/a	n/a	n/a
Corticosteroid use	85	-0,03	-0,03	0,03	0,02	0,01	221	0,09	0,05	-0,06	-0,01	-0,02
Corticosteroid IM vs no Corticosteroid	85	-0,02	-0,03	0,03	0,11	0,05	221	0,13	0,10	-0,16	-0,10	-0,10
Corticosteroid Oral vs no Corticosteroid	85	-0,02	-0,02	0,02	-0,03	-0,01	221	0,18#	0,06	-0,07	0,00	-0,02
C-reactive protein, mg/L, median (IQR)	91	0,22*	0,22*	0,14	0,01	0,15	246	0,09	0,09	0,08	0,10	0,11#
Erythrocyte sedimentation rate, >44 vs <44 mm/hr	92	0,05	0,13	0,18#	0,15	0,20#	247	0,06	0,06	0,08	0,12#	0,11#
Albumin, (g/L), mean (SD)	88	-0,09	-0,11	-0,23	-0,11	-0,20#	224	-0,01	-0,02	0,01	-0,01	-0,01
Creatinine, >78 vs <78 mmol/l	93	0,03	0,09	0,12	0,06	0,12	98	0,11	0,18#	0,21	0,23*	0,25
Erythrocyte folate, nmol/L, median (IQR)	88	0,08	0,10	0,30**	0,21#	0,27*	218	0,07	0,08	0,18**	0,16*	0,18**
Serum folate, nmol/L median (IQR)	89	0,35***	-0,04	0,15	0,07	0,09	224	-0,03	-0,01	-0,02	-0,02	-0,02
eGFR-MDRD >88 vs <88 ml/min/BSA	93	0,02	-0,02	-0,02	-0,15	-0,09	98	-0,11	-0,03	-0,12	-0,22*	-0,17#
Vitamin B12, pmol/L, median (IQR)	88	0,14	-0,02	0,04	0,03	0,03	224	-0,01	0,14*	0,11	-0,01	0,08
Vitamin B6, nmol/L, median (IQR)	89	-0,10	-0,10	0,08	0,06	0,03	199	0,01	0,01	-0,01	-0,04	-0,03
Homocysteine umol/l, median (IQR)	87	0,16	0,09	0,14	0,10	0,14	225	0,03	0,05	0,06	0,20**	0,15*
Alcohol consumption, >4 vs <4 glasses per month	38	0,27	0,07	-0,21	-0,29	-0,21	230	0,04	0,10	0,14#	0,09	0,13#
Alcohol consumption, >32 vs <4 glasses per	38	-0,01	-0,05	-0,15	-0,16	-0,16	230	0,04	0,02	0,18*	0,11	0,14#
Cola consumption, >8 vs <6 glasses per month	82	-0,02	0,13	0,23*	0,09	0,19#	227	-0,02	-0,17**	-0,08	0,04	-0,06
Coffee consumption, >120 vs <112 cups per month	82	-0,01	-0,09	-0,16	-0,17	-0,18	228	0,11#	0,02	0,11#	0,07	0,09
Tea consumption, 8-168 cups/month vs rest	82	-0,11	-0,14	-0,02	0,01	-0,05	225	0,02	-0,09	-0,05	-0,03	-0,06

Tea consumption, >168 cups/month vs rest	82	0,13	0,03	0,04	0,10	0,08	225	-0,03	0,05	-0,03	0,03	0,01
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* p < 0.05. **p < 0.01. ***p < 0.001. # = p < 0.1. ln: natural logarithm; DAS28esr: ESR based disease activity score 28; Anti-CCP: anti-cyclic citrullinated peptide antibody; DMARD: disease-modifying antirheumatic agent; ESR: erythrocyte sedimentation rate; GFR: Glomerular Filtration Rate; MTX: methotrexate; PG: polyglutamate.

Supplementary Table 2. SNP within cellular folate transport and metabolism routes in relation to methotrexate polyglutamate levels at 3 months of treatment in derivation and validation cohort. Analysis was done using ANCOVA with correction for age and sex.

			Derivation					Validation						
			Estimated Marginal Means (SE)					Estimated Marginal Means (SE)						
			N	MTX-PG1	MTX-PG2	MTX-PG3	MTX-PG4+5	MTX-PG total	N	MTX-PG1	MTX-PG2	MTX-PG3	MTX-PG4+5	MTX-PG total
rs73598374 ADA†	g>a	WT	68	50.3 (6.1)	28.8 (1.7)	40.9 (2.4)	14.6 (2.3)	84.4 (5.1)	210	43.1 (3.5)	22.6 (0.7)	49.7 (1.3)	30.1 (1.6)	102.4 (2.8)
		het	15	38.9 (12.2)	24.2 (3.5)	43.2 (4.9)	18.3 (4.7)	85.7 (10.3)	30	42.8 (8.6)	22.8 (1.7)	51.4 (3.1)	29.3 (3.8)	103.4 (6.9)
rs1127354 ITPA	c>a	WT	81	44.8 (5.4)	27.1 (1.6)	39.1 (2.2)	13.2 (2.1)*	79.3 (4.6)	211	43.3 (3.4)	23.1 (0.7)	50.5 (1.3)	30.4 (1.5)	103.9 (2.8)
		Het/Var	12	62.0 (13.0)	27.5 (3.8)	49.6 (5.6)	25.1 (4.9)*	102.2 (11.0)	36	40.7 (7.8)	20.6 (1.5)	48.7 (2.8)	27.6 (3.4)	96.9 (6.3)
rs17602729 AMPD1	c>t	WT	66	46.7 (6.3)	28.2 (1.8)	41.6 (2.5)	15.6 (2.4)	85.4 (5.3)	198	41.8 (3.6)	21.9 (0.7)*	49.4 (1.3)	29.9 (1.6)	101.2 (2.9)
		Het/Var	17	54.2 (11.2)	27.3 (3.2)	40.5 (4.5)	14.2 (4.3)	82.0 (9.4)	42	48.4 (7.3)	25.7 (1.4)*	52.6 (2.6)	30.3 (3.2)	108.6 (5.9)
rs10106587 GGH	a>c	Wt	36	48.8 (8.3)	28.2 (2.4)	40.7 (3.4)	13.0 (3.2)	81.9 (7.0)	120	44.8 (4.4)	22.0 (0.9)	49.5 (1.6)	30.7 (1.9)	102.2 (3.5)8
		het	42	52.1 (7.6)	28.4 (2.2)	41.4 (3.1)	15.7 (2.9)	85.5 (6.4)	106	43.2 (4.9)	23.6 (1.0)	51.3 (1.7)	29.1 (2.2)	104.0 (3.9)
		var	5	27.2 (20.7)	25.1 (6.0)	43.6 (8.4)	22.7 (8.0)	91.3 (17.5)	14	24.1 (12.7)	20.4 (2.5)	44.3 (4.5)	29.9 (5.6)	94.6 (10.2)
rs3758149 GGH	c>t	Wt	44	45.2 (7.2)	27.4 (2.1)	42.3 (2.9)	17.8 (2.8)	87.5 (6.1)	112	42.2 (4.7)	22.2 (0.9)	48.6 (1.7)	29.6 (2.1)	100.5 (3.8)
		het	32	47.9 (8.5)	28.0 (2.5)	38.8 (3.4)	11.9 (3.3)	78.6 (7.2)	113	42.3 (4.6)	23.2 (0.9)	50.5 (1.6)	29.5 (2.0)	103.1 (3.7)
		var	7	75.7 (17.6)	32.8 (5.1)	48.0 (7.1)	13.5 (6.8)	94.3 (14.9)	15	52.3 (12.2)	21.5 (2.4)	54.7 (4.3)	34.9 (5.4)	111.1 (9.7)
rs3784862 ABCC1	a>g	Wt	38	46.8 (7.9)	25.9 (2.2)	42.1 (3.2)	17.8 (3.0)	85.8 (6.7)	133	47.0 (4.2)*	23.6 (0.8)	49.9 (1.5)	28.0 (1.9)	101.5 (3.4)
		het	34	52.9 (8.0)	30.9 (2.3)	40.9 (3.3)	12.2 (3.1)	84.0 (6.8)	90	32.7 (5.1)*	21.1 (1.0)	49.9 (1.9)	33.4 (2.3)	104.4 (4.2)
		var	11	35.0 (15.0)	24.6 (4.3)	39.6 (6.1)	17.4 (5.8)	81.6 (12.7)	17	63.6 (11.3)*	22.5 (2.3)	50.6 (4.1)	28.2 (5.0)	101.4 (9.2)
rs35592 ABCC1	t>c	WT/Het	76	48.2 (5.8)	27.8 (1.7)	42.6 (2.3)*	16.1 (2.2)	86.5 (4.8)	229	43.3 (3.3)	22.7 (0.7)	50.0 (1.2)	30.2 (1.5)	102.9 (2.7)
		Var	7	49.9 (17.8)	30.1 (5.1)	25.9 (6.9)*	4.5 (6.7)	60.5 (14.6)	11	36.6 (14.5)	20.7 (2.9)	47.9 (5.2)	23.5 (6.4)	92.1 (11.6)
rs2274407 ABCC4	g>t	WT	71	48.1 (5.9)	27.8 (1.7)	40.5 (2.4)	14.3 (2.3)	82.7 (4.9)	212	42.7 (3.5)	22.5 (0.7)	49.7 (1.2)	29.7 (1.5)	101.9 (2.8)
		Het/Var	12	49.9 (13.7)	29.5 (4.0)	46.8 (5.5)	21.4 (5.2)	97.7 (11.4)	28	45.8 (9.1)	23.0 (1.8)	52.3 (3.2)	32.5 (4.0)	107.7 (7.3)
rs868853 ABCC4	g>a	WT/Het	65	48.4 (6.1)	27.5 (1.7)	41.1 (2.3)	15.3 (2.3)	83.9 (4.9)	205	45.6 (3.5)*	22.8 (0.7)	49.9 (1.3)	29.4 (1.5)	102.0 (2.8)
		Var	15	51.1 (13.0)	32.2 (3.7)	46.2 (5.0)	16.8 (5.0)	95.3 (10.6)	34	27.5 (8.2)*	21.7 (1.6)	50.9 (2.9)	34.5 (3.6)	107.0 (6.6)
rs1801394 MTRR	a>g	Wt	23	39.5 (9.9)	26.9 (2.9)	39.7 (4.0)	15.4 (3.9)	82.0 (8.4)	48	43.2 (7.0)	24.6 (1.4)	54.8 (2.5)	33.3 (3.1)	112.7 (5.6)
		het	39	51.5 (7.7)	29.8 (2.2)	42.2 (3.1)	14.5 (3.0)	86.4 (6.5)	109	46.4 (4.7)	22.2 (0.9)	48.4 (1.7)	29.4 (2.1)	100.0 (3.7)
		var	21	51.8 (10.4)	25.8 (3.0)	41.4 (4.2)	16.6 (4.0)	83.8 (8.8)	83	38.6 (5.3)	22.0 (1.0)	49.3 (1.9)	28.9 (2.3)	100.3 (4.2)
rs2139560 ABCC5	t>c	Wt	34	34.2 (7.7)**	24.3 (2.3)*	38.5 (3.3)	16.4 (3.2)	79.3 (7.0)	85	40.7 (5.2)	22.5 (1.0)	50.5 (1.8)	31.5 (2.3)	104.5 (4.1)
		het	38	48.7 (7.1)**	28.7 (2.1)*	41.5 (3.1)	14.2 (3.0)	84.4 (6.4)	111	45.9 (4.7)	22.9 (0.9)	49.8 (1.7)	29.4 (2.1)	102.1 (3.8)
		var	11	90.6 (13.0)**	36.6 (3.9)*	49.2 (5.6)	15.5 (5.5)	101.4 (11.7)	44	40.2 (7.5)	22.0 (1.5)	48.9 (2.7)	27.9 (3.3)	98.8 (6.0)
rs2372536 ATIC	c>g	Wt	37	37.0 (7.7)**	25.9 (2.4)	37.3 (3.2)	15.6 (3.2)	78.8 (6.8)	108	43.5 (4.7)	22.8 (0.9)	50.1 (1.7)	28.7 (2.1)	101.7 (3.7)
		het	39	50.1 (7.2)**	29.5 (2.2)	43.1 (3.0)	14.3 (2.9)	86.9 (6.3)	98	42.3 (5.0)	23.0 (1.0)	51.0 (1.8)	32.3 (2.2)	106.3 (4.0)
		var	7	94.0 (16.5)**	29.9 (5.0)	50.6 (50.6)	19.1 (6.8)	99.6 (14.6)	34	43.6 (8.2)	21.0 (1.6)	46.5 (2.9)	27.5 (3.6)	94.9 (6.5)
rs4451422 FPGS	t>g	Wt	61	55.8 (10.3)	31.6 (3.0)	52.3 (52.3)**	24.8 (3.8)**	108.7 (8.1)***	172	46.5 (5.8)	24.3 (1.2)	53.3 (2.1)*	34.3 (2.6)*	111.8 (4.6)*
		Het/var	22	46.0 (6.3)	26.9 (1.8)	37.8 (2.4)**	12.2 (2.3)**	76.8 (4.9)***	68	41.6 (3.8)	21.9 (0.8)	48.6 (1.4)*	28.3 (1.7)*	98.8 (3.0)*
rs514933 FOLR2	t>c	Wt	25	41.6 (9.6)	26.1 (2.8)	41.4 (3.9)	16.2 (3.7)	83.7 (8.1)	90	46.8 (5.1)	22.3 (1.0)	48.1 (1.8)	27.1 (2.2)	97.6 (4.1)
		het	46	53.9 (7.1)	29.3 (2.1)	40.0 (2.9)	13.3 (2.7)	82.6 (6.0)	113	39.3 (4.6)	21.8 (0.9)	50.9 (1.6)	32.2 (2.0)	104.9 (3.7)
		var	12	39.0 (13.7)	26.6 (4.0)	47.1 (5.5)	21.5 (5.3)	95.1 (11.6)	37	44.8 (7.8)	25.8 (1.6)	51.6 (2.8)	30.2 (3.4)	107.7 (6.3)
rs5751876 ADORA2A	t>c	Wt	35	43.8 (8.1)	28.3 (2.3)	40.7 (3.3)	14.7 (3.1)	83.7 (6.8)	77	38.5 (5.5)	22.5 (1.1)	49.9 (2.0)	30.8 (2.4)	103.2 (4.5)
		het	40	54.5 (7.7)	28.2 (2.2)	42.9 (3.1)	17.2 (2.9)	88.3 (6.4)	115	46.4 (4.6)	22.8 (0.9)	49.2 (1.6)	28.9 (2.0)	101.0 (3.7)
		var	8	37.9 (16.4)	25.8 (4.8)	35.8 (6.6)	7.5 (6.3)	69.1 (13.8)	48	42.1 (6.9)	22.2 (1.4)	51.8 (2.5)	31.2 (3.0)	105.1 (5.5)
rs2032582 ABCB1	g>t/	gg	25	40.8 (9.9)	26.1 (2.9)	39.7 (4.1)	12.5 (3.9)	78.3 (8.4)	72	39.2 (5.7)	22.8 (1.1)	51.1 (2.0)	29.8 (2.5)	103.7 (4.6)
		gt	38	58.8 (7.7)	30.3 (2.2)	41.9 (3.1)	14.1 (3.0)	86.3 (6.5)	112	42.4 (4.6)	21.7 (0.9)	48.2 (1.6)	30.4 (2.0)	100.3 (3.7)
		ga	1	24.4 (45.9)	16.4 (13.3)	33.2 (18.8)	9.8 (17.8)	59.3 (38.9)	5	26.2 (21.1)	20.6 (4.2)	52.1 (7.5)	32.6 (9.4)	105.2 (16.9)
		ta	4	30.4 (23.5)	21.3 (6.8)	30.3 (9.6)	10.3 (9.1)	62.0 (19.9)	6	25.6 (19.4)	20.7 (3.9)	51.5 (6.8)	28.3 (8.6)	100.5 (15.5)

	aa	0	n/a	n/a	n/a	n/a	n/a	44	54.4 (7.3)	24.8 (1.5)	51.4 (2.6)	29.0 (3.3)	105.2 (5.9)	
	tt	15	38.2 (11.8)	26.7 (3.4)	44.2 (4.8)	22.2 (4.6)	93.2 (10.0)	1	47.6 (47.5)	36.5 (9.4)	93.6 (16.8)	42.8 (21.1)	172.9 (38.1)	
rs1128503 ABCB1	c>t	Wt	27	41.0 (9.6)	25.7 (2.8)	41.2 (4.5)	12.2 (3.7)	76.8 (8.1)	75	39.9 (5.6)	22.6 (1.1)	51.9 (2.0)	30.9 (2.5)	105.5 (4.5)
		het	39	56.5 (7.7)	30.6 (2.2)	41.2 (4.5)	14.7 (3.0)	88.1 (6.5)	118	40.2 (4.5)	21.7 (0.9)	48.2 (1.6)	29.8 (2.0)	99.7 (3.6)
		var	17	40.7 (11.1)	25.5 (3.2)	41.2 (4.5)	19.9 (4.3)	86.6 (9.4)	47	55.2 (7.0)	24.9 (1.4)	51.5 (2.5)	28.9 (3.1)	105.2 (5.6)
rs1045642 ABCB1	t>c	Wt	14	37.1 (12.7)*	20.6 (3.5)**	31.7 (5.1)*	10.3 (5.0)	62.6 (10.3)**	52	38.6 (6.8)	22.3 (1.4)	50.5 (2.4)	29.3 (3.0)	102.1 (5.4)
		het	41	37.9 (7.3)*	25.0 (2.0)**	38.4 (2.9)*	13.3 (2.9)	76.7 (6.0)**	122	43.9 (4.5)	22.6 (0.9)	49.2 (1.6)	30.5 (2.0)	102.2 (3.6)
		var	28	66.0 (8.5)*	34.5 (2.3)**	48.5 (3.4)*	19.5 (3.3)	102.5 (6.9)**	66	44.6 (6.0)	22.9 (1.2)	50.9 (2.1)	29.6 (2.6)	103.4 (4.8)
rs1801131 MTHFR	a>c	Wt	44	45.4 (7.2)	26.4 (2.1)	38.8 (2.9)	15.2 (2.8)	80.5 (6.0)	111	36.1 (4.7)*	22.1 (0.9)	50.9 (1.7)	32.3 (2.1)	105.3 (3.8)
		het	29	54.1 (9.4)	29.3 (2.7)	44.8 (3.8)	15.8 (3.6)	90.0 (7.9)	107	45.5 (4.6)*	22.4 (0.9)	48.6 (1.7)	28.4 (2.1)	99.5 (3.7)
		var	10	47.7 (14.7)	32.0 (4.2)	44.2 (5.9)	13.9 (5.7)	90.1 (12.3)	22	63.5 (10.0)*	25.8 (2.0)	51.8 (3.6)	26.7 (4.5)	104.4 (8.1)
rs1801133 MTHFR	c>t	Wt	50	44.8 (7.1)	27.3 (2.0)	40.0 (2.9)	14.9 (2.8)	82.2 (5.9)	107	44.3 (4.8)	22.1 (1.0)	48.9 (1.7)	29.2 (2.1)	100.3 (3.8)
		het	26	58.1 (9.1)	30.3 (2.6)	44.7 (3.7)	16.4 (3.6)	91.4 (7.7)	97	44.8 (4.9)	23.1 (1.0)	50.6 (1.7)	29.9 (2.2)	103.6 (3.9)
		var	7	34.7 (17.4)	23.8 (5.0)	37.1 (7.0)	13.0 (6.8)	73.9 (14.6)	36	33.9 (8.0)	22.6 (1.6)	51.3 (2.9)	32.4 (3.5)	106.3 (6.4)
rs717620 ABCC2	g>a	WT	58	51.2 (6.4)	28.1 (1.9)	41.9 (2.6)	16.0 (2.5)	86.0 (5.4)	174	39.9 (3.7)	22.4 (0.7)	49.5 (1.3)	29.7 (1.6)	101.6 (3.0)
		Het/Var	25	41.1 (9.7)	27.7 (2.8)	39.9 (3.9)	13.4 (3.8)	81.1 (8.2)	65	52.2 (6.1)	23.2 (1.2)	50.9 (2.2)	30.6 (2.7)	104.6 (4.9)
rs4148396 ABCC2	t>c	Wt	29	54.0 (8.7)	29.1 (2.5)	41.8 (3.6)	15.3 (3.4)	86.1 (7.4)	104	44.3 (4.7)	22.5 (0.9)	48.1 (1.7)	27.8 (2.1)	98.5 (3.8)
		het	47	42.0 (7.1)	27.2 (2.1)	41.2 (2.9)	15.8 (2.8)	84.1 (6.1)	109	40.8 (4.8)	22.7 (1.0)	50.2 (1.7)	32.2 (2.1)	106.9 (3.9)
		var	7	70.0 (17.5)	29.4 (5.1)	40.4 (7.2)	10.6 (6.9)	80.4 (15.0)	27	46.1 (9.2)	22.7 (1.8)	49.6 (3.3)	30.5 (4.1)	102.7 (7.4)
rs2231142 ABCG2	a>c	WT/Het	69	44.0 (6.2)	26.8 (1.8)	42.5 (2.5)	16.8 (2.4)	86.1 (5.3)	186	43.3 (3.8)	22.3 (0.7)	49.7 (1.3)	29.9 (1.7)	101.9 (3.0)
		var	14	65.7 (12.1)	32.7 (3.5)	36.5 (4.9)	9.2 (4.7)	78.5 (10.3)	54	42.0 (6.4)	23.6 (1.3)	50.9 (2.3)	30.2 (2.8)	104.6 (5.2)
rs13120400 ABCG2	c>t	WT/Het	78	48.5 (5.8)	28.0 (1.7)	42.1 (2.3)	15.9 (2.2)	86.1 (4.8)	223	42.7 (3.4)	22.4 (0.7)	49.8 (1.2)	30.0 (1.5)	102.2 (2.7)
		var	5	46.0 (20.8)	28.3 (6.0)	27.0 (8.2)	3.1 (7.9)	58.4 (17.2)	17	48.1 (11.8)	25.2 (2.3)	52.1 (4.2)	30.2 (5.2)	107.5 (9.4)
rs 3785911 ABCC3	c>t	Wt	43	49.0 (7.4)	27.1 (2.1)	40.9 (3.0)	13.8 (2.9)	81.8 (6.2)	126	46.4 (44.4)	22.9 (0.9)	48.3 (1.6)	27.5 (1.9)**	98.7 (3.5)*
		het	30	44.7 (8.8)	28.0 (2.5)	41.8 (3.6)	16.8 (3.4)	86.5 (7.4)	93	40.5 (5.0)	22.4 (1.0)	50.6 (1.8)	30.1 (2.2)**	103.0 (4.0)*
		var	10	59.4 (15.2)	33.6 (4.4)	41.8 (6.2)	17.4 (5.9)	92.8 (12.8)	21	34.6 (10.3)	21.9 (2.1)	56.8 (3.7)	43.5 (4.5)**	122.2 (8.2)*
rs4793665 ABCC3	c>t	Wt	22	32.3 (10.1)	23.8 (2.9)	41.8 (4.2)	18.6 (4.0)	84.4 (8.7)	79	44.2 (5.4)*	23.4 (1.1)	49.3 (1.9)	29.1 (2.4)	101.8 (4.4)
		het	41	58.7 (7.8)	28.9 (2.3)	40.4 (3.2)	14.2 (3.1)	83.4 (6.7)	119	37.1 (4.4)*	21.8 (0.9)	49.3 (1.6)	30.0 (2.0)	101.1 (3.6)
		var	20	46.4 (10.0)	30.3 (2.9)	42.3 (4.1)	14.0 (3.9)	86.6 (8.6)	42	58.6 (7.4)*	23.2 (1.5)	53.5 (2.7)	31.6 (3.3)	108.2 (6.0)
rs1051266 SLC19A1	g>a	WT/Het	67	51.5 (6.1)	28.7 (1.8)	42.6 (2.4)	15.5 (2.4)	86.8 (5.1)	203	44.5 (3.5)	23.0 (0.7)	49.7 (1.3)	28.9 (1.6)	101.6 (2.8)
		var	16	34.8 (11.7)	25.0 (3.4)	35.7 (4.7)	14.3 (4.5)	75.0 (9.8)	37	34.9 (7.8)	20.5 (1.6)	51.5 (2.8)	35.8 (3.4)	107.9 (6.3)
rs2239907 SLC46A1	a>g	Wt	26	46.9 (9.0)	26.9 (2.5)*	41.4 (3.6)	15.9 (3.5)	84.2 (7.6)	73	37.6 (5.6)*	23.8 (1.1)	51.2 (2.0)	30.7 (2.5)	105.7 (4.6)
		het	4	46.4 (7.7)	26.1 (2.1)*	39.7 (3.1)	15.7 (3.0)	81.6 (6.5)	119	39.0 (4.4)*	21.2 (0.9)	48.9 (1.6)	30.5 (2.0)	100.6 (3.6)
		var	10	59.7 (14.6)	38.0 (4.0)*	47.1 (5.9)	11.8 (5.6)	96.9 (12.2)	48	60.9 (6.8)*	24.2 (1.4)	50.7 (2.5)	27.6 (3.0)	102.5 (5.5)

* p < 0.05. **p < 0.01. ***p < 0.001. WT: wild type; Het = heterozygous; Var: homozygous variant. ABCB1/ABCC1/ABCC2/ABCC3/ABCC4/ABCC5/ABCG2: adenosine triphosphate-binding cassette transporter subfamily B/C/G member 1/2/3/4/; FPGS: folylpolyglutamate synthetase; FOLR1/FOLR2: folate receptor 1/2; GGH: gamma glutamyl hydrolase; SLC 46A1/SLC19A:solute carrier 46A1/19A1; SNP: single-nucleotide polymorphism.