**ESM Table 2.** Linear regression for treatment HbA<sub>1c</sub> per ATM allele. Only patients with a baselineHbA<sub>1c</sub> >7% are included in the analysis.

DCS         Total group Mono therapy         287         -0.060 (-0.231, 0.111)         0.087         0.49           Mono therapy Dual therapy         135         -0.036 (-0.280, 0.208)         0.124         0.77           Rotterdam         Total group         182         -0.085 (-0.335, 0.163)         0.126         0.50           Rotterdam         Total group         182         -0.053 (-0.205, 0.098)         0.077         0.49           Study         Mono therapy         65         -0.107 (-0.327, 0.113)         0.112         0.33           Dual therapy         117         -0.069 (-0.266, 0.127)         0.100         0.49           CARDS         Total group         237         0.151 (-0.012, 0.332)         0.084         0.07           Mono therapy         71         -0.120 (-0.465, 0.223)         0.173         0.49           Dual therapy         166         0.270 (0.070, 0.469)         0.100         0.008           Meta-analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)							
Mono therapy         135         -0.036 (-0.280, 0.208)         0.124         0.77           Dual therapy         152         -0.085 (-0.335, 0.163)         0.126         0.50           Rotterdam         Total group         182         -0.053 (-0.205, 0.098)         0.077         0.49           Study         Mono therapy         65         -0.107 (-0.327, 0.113)         0.112         0.33           Dual therapy         117         -0.069 (-0.266, 0.127)         0.100         0.49           CARDS         Total group         237         0.151 (-0.012, 0.332)         0.084         0.07           Mono therapy         71         -0.120 (-0.465, 0.223)         0.173         0.49           Dual therapy         166         0.270 (0.070, 0.469)         0.100         0.008           Meta-analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)	Study	Group	n	Beta (95%CI)	SE	P value	
Rotterdam         Dual therapy         152         -0.085 (-0.335, 0.163)         0.126         0.50           Study         Total group         182         -0.053 (-0.205, 0.098)         0.077         0.49           Study         Mono therapy         65         -0.107 (-0.327, 0.113)         0.112         0.33           Dual therapy         117         -0.069 (-0.266, 0.127)         0.100         0.49           CARDS         Total group         237         0.151 (-0.012, 0.332)         0.084         0.07           Mono therapy         71         -0.120 (-0.465, 0.223)         0.173         0.49           Dual therapy         166         0.270 (0.070, 0.469)         0.100         0.008           Meta-analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)	DCS	Total group	287	-0.060 (-0.231, 0.111)	0.087	0.49	
Rotterdam         Total group         182         -0.053 (-0.205, 0.098)         0.077         0.49           Study         Mono therapy         65         -0.107 (-0.327, 0.113)         0.112         0.33           Dual therapy         117         -0.069 (-0.266, 0.127)         0.100         0.49           CARDS         Total group         237         0.151 (-0.012, 0.332)         0.084         0.07           Mono therapy         71         -0.120 (-0.465, 0.223)         0.173         0.49           Dual therapy         166         0.270 (0.070, 0.469)         0.100         0.008           Meta-analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)		Mono therapy	135	-0.036 (-0.280, 0.208)	0.124	0.77	
Study         Mono therapy         65         -0.107 (-0.327, 0.113)         0.112         0.33           Dual therapy         117         -0.069 (-0.266, 0.127)         0.100         0.49           CARDS         Total group         237         0.151 (-0.012, 0.332)         0.084         0.07           Mono therapy         71         -0.120 (-0.465, 0.223)         0.173         0.49           Dual therapy         166         0.270 (0.070, 0.469)         0.100         0.008           Meta-analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)		Dual therapy	152	-0.085 (-0.335, 0.163)	0.126	0.50	
CARDS         Dual therapy         117         -0.069 (-0.266, 0.127)         0.100         0.49           CARDS         Total group         237         0.151 (-0.012, 0.332)         0.084         0.07           Mono therapy         71         -0.120 (-0.465, 0.223)         0.173         0.49           Dual therapy         166         0.270 (0.070, 0.469)         0.100         0.008           Meta-analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)	Rotterdam	Total group	182	-0.053 (-0.205, 0.098)	0.077	0.49	
CARDS         Total group         237         0.151 (-0.012, 0.332)         0.084         0.07           Mono therapy         71         -0.120 (-0.465, 0.223)         0.173         0.49           Dual therapy         166         0.270 (0.070, 0.469)         0.100         0.008           Meta-         Total group         706         0.010 (-0.083, 0.103)         0.048         0.83           analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)	Study	Mono therapy	65	-0.107 (-0.327, 0.113)	0.112	0.33	
Mono therapy         71         -0.120 (-0.465, 0.223)         0.173         0.49           Dual therapy         166         0.270 (0.070, 0.469)         0.100         0.008           Meta- Total group         706         0.010 (-0.083, 0.103)         0.048         0.83           analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)	-	Dual therapy	117	-0.069 (-0.266, 0.127)	0.100	0.49	
Dual therapy         166         0.270 (0.070, 0.469)         0.100         0.008           Meta- Total group analysis         706         0.010 (-0.083, 0.103)         0.048         0.83           Mono therapy Dual therapy 271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy 435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage 2 replication cohorts previously used by Zhou et al.(2011)	CARDS	Total group	237	0.151 (-0.012, 0.332)	0.084	0.07	
Meta-         Total group         706         0.010 (-0.083, 0.103)         0.048         0.83           analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)		Mono therapy	71	-0.120 (-0.465, 0.223)	0.173	0.49	
analysis         Mono therapy         271         -0.084 (-0.231, 0.064)         0.075         0.27           Dual therapy         435         0.058 (-0.063, -0.179)         0.004         0.35           Meta-analysis including stage         2 replication cohorts previously used by Zhou et al.(2011)		Dual therapy	166	0.270 (0.070, 0.469)	0.100	0.008	
Dual therapy 435 0.058 (-0.063, -0.179) 0.004 0.35  Meta-analysis including stage 2 replication cohorts previously used by Zhou et al.(2011)	Meta-	Total group	706	0.010 (-0.083, 0.103)	0.048	0.83	
Meta-analysis including stage 2 replication cohorts previously used by Zhou et al.(2011)	analysis	Mono therapy	271	-0.084 (-0.231, 0.064)	0.075	0.27	
	-	Dual therapy	435	0.058 (-0.063, -0.179)	0.004	0.35	
GoDAPTS Total group   1782   0.072 ( 0.124   0.011 )   0.021   0.021	Meta-analysis including stage 2 replication cohorts previously used by Zhou et al.(2011)						
GODAK 13 Total group   1763 -0.072 (-0.134, -0.011) 0.031 0.021	GoDARTS	Total group	1783	-0.072 (-0.134, -0.011)	0.031	0.021	
Mono therapy   1291 -0.092 (-0.164, -0.019)   0.037   0.013		Mono therapy	1291	-0.092 (-0.164, -0.019)	0.037	0.013	
Dual therapy 495 -0.040 (-0.160, 0.070) 0.059 0.45		Dual therapy	495	-0.040 (-0.160, 0.070)	0.059	0.45	
UKPDS Total group 799 -0.080 (-0.212, 0.053) 0.068 0.24	UKPDS	Total group	799	-0.080 (-0.212, 0.053)	0.068	0.24	
Mono therapy   138 -0.272 (-0.564, 0.020) 0.149 0.07		Mono therapy	138	-0.272 (-0.564, 0.020)	0.149	0.07	
Dual therapy   661 -0.040 (-0.190, 0.107)   0.076   0.58		Dual therapy	661	-0.040 (-0.190, 0.107)	0.076	0.58	
Meta- Total group 3288 -0.051 (-0.099, -0.004) 0.024 0.035	Meta-	Total group	3288	-0.051 (-0.099, -0.004)	0.024	0.035	
analysis Mono therapy 1700 -0.099 (-0.162, -0.035) 0.032 0.0023	analysis	Mono therapy	1700	-0.099 (-0.162, -0.035)	0.032	0.0023	
Dual therapy   1591 -0.005 (-0.077, 0.068) 0.037 0.89	•	Dual therapy	1591	-0.005 (-0.077, 0.068)	0.037	0.89	

An additive linear regression model was used for calculating the per C-allele change in treatment  $HbA_{1c}$ . Covariates included where baseline  $HbA_{1c}$ , baseline gap (except DCS), daily dose, drug adherence (except for DCS and CARDS), and eGFR (except for CARDS and Rotterdam Study). The p-value of the genotype effect is given. In the meta-analysis a fixed effects model was used.