**Supplementaty information on Materials and Methods**

*Genotyping*

*Quality control and imputation*

Quality control (QC) procedures were performed using the whole genome association analysis toolset PLINK v1.07 (<http://pngu.mgh.harvard.edu/purcell/plink>) in discovery and replication cohorts separately (**Supplemental Data Table S1**).

Un-genotyped variants were imputed in the discovery and replication phase cohorts separately (**Supplemental Data Table S1**). Pre-phasing was performed using SHAPEIT version 213, and imputations were performed using IMPUTE2 (version 2.2.2)14. The 1000 Genomes15 Discovery phase integrated variant set (NCBI build b37, Mar 2012, updated 24 Aug 2012) were accessed from the IMPUTE2 web site and used as reference panel. QC of imputed SNPs (**Supplemental Data Table S1**) and merging of the discovery and replication cohorts were performed using QCTOOL version 1.3 (<http://www.well.ox.ac.uk/~gav/qctool>). All imputations were performed prior to the exclusion of clopidogrel-treated patients. Statistical analyses were then performed on the ticagrelor patients using a subset of the data containing both empirical and imputed genotype data for discovery and replication phase subjects (N=4,990 of which 3,753 [75%] had PK data).

*Additional genotyping*

Selected findings at imputed sites showing association with PK levels were genotyped using TaqMan™ (Life Technologies, Carlsbad, CA) at AstraZeneca, Alderley Park, Cheshire, UK.