Supplementary Table 1: primers and conditions to genotype *CYP2C19.*

CYP2C19 region	Forward Primer	Reverse Primer	Annealing T[a]	Expected fragment
Promoter part 1	5'- ACATTGTGCAATTGTGT CTTAAC -3'	5'- CATTAAATAGAACCACT TATTTATCTAAGG -3'	55°C	563 bp
Promoter part 2	5'- GGCTGTTTTCCTTAGAT AAATAAGTG -3'	5'- CCAGTTGGGAATTTATG ATTTAACG -3'	60°C	600 pb
Promoter part 3	5'-GCCATTTCCGTTAAATC ATAAATTCC-3'	5'- CTTGTTAAGACAACCGT GAGC -3'	60°C	399 pb
Exon 1	5'- TATTACCAATACCTAGG CTTCAACC -3'	5'- TGTAACATTGTACCTCT AGGGATATAC -3'	60°C	522 pb
Exon 2-3	5'- TGAATCTAAGTCAGGCT TAGTAAATG -3'	5'- GGAGAGCAGTCCAGAA AGG -3'	60°C	601 pb
Exon 4	5'- GGCTGTAATTGTTAATT CGAGATTAATG -3'	5'- GGCTGTCTAGGCAAGA CTG -3'	60°C	481 pb
Exon 5	5'- AACCAGAGCTTGGCAT ATTG -3'	5'- GCTTACTGGATATTCAT GCATAC -3'	60°C	405 pb
Exon 6	5'- CTCTCTCACCGCTCCT ATTC -3'	5'- GCACCAGGCCAGGATA TTC -3'	60°C	468 pb

Exon 7	5’- GTACCCCTGAATTGCT AGAAC -3’	5’- CCAGTGATGGTAGAGG GTAAG -3’	60°C	345 pb
Exon 8	5’- TGTCACTGGCCTTAAG CTC -3’	5’- GGCACATGTAAGTTCC AACTG -3’	60°C	400 pb
Exon 9	5’- TTCTGTCTGTGCCAGT TATAGAG -3’	5’- GCATCACAGATAGTGA AATTTG -3’	53°C	351 pb
3’ UTR part 1	5’- CAGATGGTCTGGCTG CTC -3’	5’- CTTTCAAATCCAATCCT CATGTAAC -3’	60°C	527 pb
3’ UTR part 2	5’- GCTATTTTGGCTGAGC ATTACC -3’	5’- GGCACAGTGTCTCACT CC -3’	60°C	449 pb
3’ UTR part 3	5’- CTGCTGACCTCCTGA TCTG -3’	5’- CCCTGGTAATTCTTCTT AGAAATTTTG -3’	60°C	578 pb

Supplementary Table 1a: Assays on demand included in the study.

Gene allele	dbSNP_rs	ABI-Assay_ID
*CYP2C19**2	rs4244285	C_25986767_70
*CYP2C19**17	rs12248560	C_469857_10
*CYP3A5**3	rs776746	C_26201809_30
*UGT1A4**2	rs6755571	C_25957120_10

Supplementary Table 1c. *CYP2C19* re-sequencing results in 6 subjects with extreme plasma rilpivirine levels (very low or very high plasma concentrations).

CYP2C19	Promoter				Exon 1		Exon 2	Intron		Exon 5	Intron		Exon 7		Intron	
Subject	C>T g.-1418 rs3814637	T>G g.-889 rs11568732	**C>T g.-806 rs12248560 (*17)**	T>C g.-98 rs4986894	**A>G g.1 rs28399504 (*4)[a]**	C>T g.99 P33P rs17885098**(*1)**	G>C g.12460 E92E rs17878459	G>C g.12644 rs377056911	A>G g.12662 rs12769205	**G>A g.19154 P227P rs4244285 (*2)**	T>C g.57678 rs28399511	C>T g.57740 rs4417205	C>T g.80160 V330V rs3758580	A>G g.80161 I331V rs3758581 **(*1)**	T>C g.87106 rs4917623	**Result**
#1	Ref	Ref	Ref	Het	**Het**	Hom	Ref	Het	Het	**Het**	Ref	Het	Het	Hom	Het	**2/*4* (LOF/LOF)
#2	Ref	Ref	Ref	Het	Ref	Hom	Het	Ref	Het	**Het**	Ref	Het	Het	Hom	Het	**1/*2* (Ref/LOF)
#3	Het	Het	**Het**	Ref	Ref	Het	Ref	Ref	Ref	Ref	Het	Ref	Ref	Het	Ref	**1/*17* (Ref/GOF)
#4	Ref	Ref	**Het**	Ref	Ref	Hom	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Hom	Het	**1/*17* (Ref/GOF)
#5	Ref	Ref	Ref	Ref	Ref	Hom	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Hom	Hom	**1/*1* (Ref)
#6	Ref	Ref	**Hom**	Ref	Ref	Hom	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Hom	Ref	**17/*17* (Hom-GOF)

Ref: homozygous for the common allele; Het: heterozygous; Hom: homozygous for the rare allele; LOF: loss of function allele; GOF: gain of function allele. In black we highlighted the single nucleotide polymorphism marker of the allele. [a] Codifies for a GTG initiation codon with consequent loss of enzyme function (14, 31). Study participants were classified according to the CYP Allele Nomenclature Committee (http://www.cypalleles.ki.se/).