Class I human leukocyte antigens (HLA) play an important role in the adaptive immune response by presenting antigens to CD8+ T cells. Studies have reported that several HLA class I alleles are associated with differential disease progression in human immunodeficiency virus (HIV)-infected individuals, however, few class I associations with resistance or susceptibility to HIV-1 infection have been reported. We typed HLA-A, -B and -C of >1000 women enrolled in the Pumwani Sex Worker Cohort using a sequence-based typing method. Kaplanï Meier analysis was used to identify alleles influencing seroconversion and disease progression to acquired immune deficiency syndrome (CD4ژ200/mm3). A*01 (Pژ0.020), C*06:02 (Pژ0.042) and C*07:01 (Pژ0.050) are independently associated with protection from seroconversion. Women with any of these alleles are less likely to seroconvert [Pژ0.00001, odds ratio (OR): 0.503, 95% confidence interval (CI): 0.320ï 0.790]. Conversely, A*23:01 (Pژ0.004), B*07:02 (Pژ0.003) and B*42:01 (Pژ0.025) are independently associated with rapid seroconversion. Women with any of these alleles are twice as likely to seroconvert (Pژ0.002, OR: 2.059, 95% CI: 1.290ï 3.285). The beneficial alleles confer threefold protection from seroconversion when compared with the susceptible alleles (Pژ0.000001, OR: 0.268, 95% CI: 0.132ï 0.544). B*07:02 is the contributing allele, within the B7 supertype, to the rapid seroconversion. A*74:01 (Pژ0.04/Pژ0.006), B*14 (Pژ0.003/Pژ0.003) and B*57:03 (Pژ0.012/Pژ0.038) are independently associated with slower CD4+ decline and LTNP phenotype, while B*07:02 (Pژ0.020), B*15:10 (Pژ0.022) and B*53:01 (Pژ0.007) are independently associated with rapid CD4+ T-cell decline. B7 supertype (Pژ0.00006), B*35*-Py (Pژ0.028) and B*35-Px (Pژ0.001) were also significantly associated with rapid CD4+ T-cell decline. Understanding why these HLA class I alleles are associated with protection/susceptibility to HIV-1 acquisition and disease progression could contribute to the development of effective prophylactic and therapeutic vaccines for HIV-1.