Predictors of virological failure and time to viral suppression of first line integrase inhibitor based antiretroviral treatment

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Abstract: BACKGROUND Integrase strand transfer inhibitors (InSTIs) are recommended for first-line treatment of HIV-infection. We identified risk factors, including baseline minor InSTI resistance mutations, for treatment failure of InSTI-based regimens. METHODS We studied time to treatment failure and time to viral suppression among 1419 drug-naive patients in the Swiss HIV Cohort Study. We performed Cox regression models adjusted for demographic factors, baseline HIV RNA/CD4 cell counts, AIDS defining events and the type of InSTI. In 646 patients with a baseline genotypic resistance test of the integrase, we studied the impact of minor integrase resistance mutations. RESULTS We observed 121 virological failures during 18,447 person-years of follow-up. A baseline viral load \(100,000\) cps/mL (multivariable Hazard Ratio (mHR): 2.2, 95% CI: 1.3-3.6) and an AIDS defining event (mHR: 1.8, 95% CI: 1.1-3.0) were associated with treatment failure. CD4 counts between 200-500 cells/µL (mHR: 0.5, 95% CI: 0.3-0.8) and \(>500\) cells/µL (mHR: 0.4, 95% CI: 0.2-0.7) were protective. Median [IQR] time to viral suppression was 50 [29,107] days. Time to suppression was shorter in lower viral load strata (mHR: 0.7, 95% CI: 0.6-0.8) and in dolutegravir-based therapy (mHR: 1.2, 95% CI: 1.0-1.4). Minor resistance mutations were found at baseline in 104/646 (16%) patients with no effect on treatment outcome. CONCLUSION Among drug-naive HIV-infected individuals treated with InSTI-based regimens, factors associated with treatment failure, in particular high viral load and low CD4 counts remain similar to older treatments. Minor InSTI resistance mutations had no impact in this large observational cohort.

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Predictors of Virological Failure and Time to Viral Suppression of First-Line Integrase Inhibitor–Based Antiretroviral Treatment

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Background. Integrase strand transfer inhibitors ( INSTIs) are recommended for first-line treatment of persons with immunodeficiency virus (HIV). We identified risk factors, including baseline minor INSTI resistance mutations, for treatment failure of INSTI-based regimens.

Methods. We studied time-to-treatment failure and time to viral suppression among 1419 drug-naive patients in the Swiss HIV Cohort Study. We performed Cox regression models adjusted for demographic factors, baseline HIV RNA/CD4 cell counts, AIDS-defining events, and the type of INSTI. In 646 patients with a baseline genotypic resistance test of the integrase, we studied the impact of minor integrase resistance mutations.

Results. We observed 121 virological failures during 18 447 person-years of follow-up. A baseline viral load ≥100 000 copies/mL ( multivariable hazard ratio [mHR], 2.2; 95% confidence interval [CI], 1.3–3.6) and an AIDS-defining event (mHR, 1.8; 95% CI, 1.1–3.0) were associated with treatment failure. CD4 counts between 200 and 500 cells/µL (mHR, 0.5; 95% CI, 0.3–0.8) and >500 cells/µL (mHR, 0.4; 95% CI, 0.2–0.7) were protective. Time to suppression was shorter in lower viral load strata (mHR, 0.7; 95% CI, 0.6–0.8) and in dolutegravir-based therapy (mHR, 1.2; 95% CI, 1.0–1.4). Minor resistance mutations were found at baseline in 104 of 646 (16%) patients at no effect on treatment outcome.

Conclusions. Factors associated with treatment failure on INSTI-based first-line regimen remained similar to those of older treatments, in particular high viral load and low CD4 counts.

Keywords. HIV; integrase strand transfer inhibitors; drug resistance; minor drug resistance mutations; treatment outcome.

Integrase strand transfer inhibitor (INSTI)–based antiretroviral therapies are recommended for first-line treatment of most individuals living with human immunodeficiency virus type 1 (HIV-1) [1]. These potent combinations achieve sustained virological suppression, and treatment failures are rare. Nonetheless, it is important to identify patients with increased risk for therapy failure as it jeopardizes the long-term treatment success and facilitates the emergence of drug resistance.

Failure of potent antiretroviral therapy is associated with several factors [2, 3]. In phase 3 trials, INSTI-based regimens were proven to be at least equally potent as or superior to other antiretroviral regimens [4–7]. The second-generation INSTIs dolutegravir (DTG) and bictegravir (BIC) have a high potency even among individuals with a high viral load or low CD4 count at baseline [5, 8–10]. Phase 3 trials showed that baseline plasma HIV-RNA did not affect DTG-based therapy; for raltegravir, the impact of baseline viral load is discussed controversially [8, 11]. Smaller clinical studies that encompassed drug-naive and treatment-experienced patients suggested that older age [12, 13], lack of adherence [14], origin from a high-prevalence country, injection drug use, and a low CD4 count at baseline [13] increased the risk for failure of INSTI-based therapy.

Another possible reason for the failure of antiretroviral treatment is the presence of pretreatment drug resistance-associated mutations (RAMs), mostly transmitted drug resistance mutations ( TDRMs) [2, 15, 16]. Although large
studies did not find a correlation between virological failure in drug-naive individuals on INSTIs and the presence of TDRMs [17, 18], some case reports suggest otherwise [19–21]. In European studies, <1% of drug-naive or recently infected individuals had major INSTI mutations [22–26]. However, 2%–17.3% had minor RAMs that often occurred as polymorphisms of the HIV wild type [22–26]. Although they are considered to have little effect on INSTI susceptibility, there is lack of research to which extent they affect INSTI-based treatments [27–29].

Our objective in this study was to identify risk factors for treatment failure of INSTI-based combined antiretroviral treatment (cART) in drug-naive individuals living with HIV from the Swiss HIV Cohort Study (SHCS) and to assess the impact of minor INSTI RAMs on treatment outcome.

**METHODS**

**Study Population and Study Design**

We used data from the Swiss HIV Cohorts Study (SHCS) and the SHCS drug resistance database. The SHCS is a nationwide, multicenter, longitudinal study established in 1988. The SHCS population is highly representative as it encompasses 75% of all the patients receiving antiretroviral treatment and 69% of the people with AIDS living in Switzerland. The drug resistance database includes all genotypic resistance tests (GRTs) conducted in Switzerland and is linked to the clinical database [30]. The SHCS continuously enrolls individuals aged ≥18 years and living with HIV independent of the stage and severity of the infection. Data are collected using a structured form at registration and at the semiannual visits. The ethics committees of all participating institutions have approved the SHCS, and written informed consent is obtained from all participants [30, 31].

**Patient Selection**

We included drug-naive individuals living with HIV from the SHCS who started an INSTI-based antiretroviral treatment between 1 January 2006 and 31 December 2018. If the HIV-1 RNA load was not measured in a patient after treatment start, that patient was excluded. To analyze pretreatment resistance patterns, we identified patients who received a baseline GRT including the integrase using the SHCS drug resistance database. The following RAMs from the HIV Drug Resistance Database with a HIVdb score ≥30 were also defined as major mutations: E92V, Y143AGK, Q146P, V151I, and N155S. Mutations with a penalty score ≥10 and <30 were in addition to the IAS-USA recommendations included as minor mutations: H51Y, L74FI, E95K, P142T, Q148N, V151I, N155D, E157Q, G163KR, S230R, and D232N.

**Definition of Drug Resistance Mutations**

Minor and major RAMs were defined based on the International Antiviral Society - United States of America (IAS-USA) recommendations [32] and the Stanford University HIV Drug Resistance Database Version 8.9–1 [33]. The following mutations from the IAS-USA recommendations were included: *major mutations*: T66I, E92Q, G118R, E138AKT, G140R, Y143CHR, S147G, Q148HKR, N155H, and R263K and *minor mutations*: T66AK, L74M, E92G, T97A, E138AKT, G140ACS, and S153FY.

The following RAMs from the HIV Drug Resistance Database with a HIVdb score ≥30 were also defined as major mutations: E92V, Y143AGK, Q146P, V151I, and N155S. Mutations with a penalty score ≥10 and <30 were in addition to the IAS-USA recommendations included as minor mutations: H51Y, L74FI, E95K, P142T, Q148N, V151I, N155D, E157Q, G163KR, S230R, and D232N.

**Outcome**

Our primary end points were time to viral suppression and time to virological failure. The follow-up time was defined as the period from the start of the INSTI-based regimen until the end of INSTI therapy. Data were censored at the last visit, the end of INSTI-based therapy, or at the patient's death. Data were not censored when the patient changed from one INSTI to another or when nucleoside reverse-transcriptase inhibitor background ART was modified or adapted.

Time to viral suppression was defined as the time from treatment start to the first viral load <50 HIV-1 RNA copies/mL. Virological failure was defined as follows: 2 consecutive RNA values >50 copies/mL after at least 180 days of continuous treatment, 1 value >50 copies/mL after 180 days of treatment followed by treatment change to another drug class, or no viral suppression <50 copies/mL after more than 180 days of treatment.

**Statistical Analyses**

We used Stata/SE version 15.1 for statistical analyses. We performed univariable and multivariable Cox regressions to identify the effect of baseline characteristics on time to viral suppression and time to virological failure. The following factors were considered: age at therapy start, ethnicity, transmission risk group, HIV-1 RNA load, CD4 cell count, history of an AIDS-defining event at or before treatment start, the type of INSTI administered, and the presence of INSTI RAMs. Another factor included was the financial independence of the individual. Patients whose salary generated more than 50% of their income were considered more financially independent than those who predominantly relied on other sources for their income, such as unemployment benefits. In the multivariable model, factors with a P value < .1 in the univariable model and previously described risk factors for treatment outcome (age at treatment start, ethnicity, transmission risk group, the type of INSTI) were included. Continuous variables were categorized if likelihood ratio tests showed significant departure from linearity. Levels of self-reported adherence between patients who experienced virological failure and those without treatment failure were compared using the Pearson χ² test. Self-reported adherence is assessed every 6 months; the data closest to the treatment failure or censoring was chosen [34]. We tested the proportional hazard assumption by calculating Schoenfeld residuals and by use of graphical procedures. No violations of the
The proportionality hazard assumption were detected. The level
of significance was considered at $P$ value <.05. To determine
whether our results differed by the administered InSTI, we per-
formed additional analyses where we stratified by the type of
InSTI. Additionally, we studied the subgroup of patients with
a baseline viral load $\geq 100\,000$ HIV-1 RNA copies/mL in detail.

**RESULTS**

**Study Population**

We identified 1472 drug-naive individuals living with HIV-1
who started an InSTI-based cART (Figure 1). We excluded
4 (0.3%) patients, as follow-up data were not available and
49 (3%) patients because of missing HIV-1 RNA values. Thus,
1419 of 1472 (96%) patients were included for study time to vi-
rological failure and 1389 (94%) for study time to viral suppres-
sion. The InSTI most often administered was DTG ($n = 925$,
65%) followed by EVG ($n = 281$, 20%) and RGV ($n = 213$, 15%).
None of the participants received BIC, which was introduced
in Switzerland in 2018. Table 1 shows the baseline character-
istics of our study population. Of the 1419 individuals in our
study, 646 (45%) had a baseline GRT including the integrase
performed and 378 (27%) had a baseline viral load $\geq 100\,000$
HIV-1 RNA copies/mL.

**Time to Virological Failure**

During the 18 447 person-years of follow-up, we observed 121
virological failures. Twenty-three of 121 patients had a viral load
$\geq 1000$ HIV-1 RNA copies/mL at the time of virological failure.
Nine of 121 patients did not reach viral suppression within
180 days, and all others failed treatment after having achieved
viral suppression. Figure 2 and Supplementary Table 1 summa-
rize the results of the multivariable analysis of time to virological
failure. A hazard ratio (HR) >1 implies more virological failures
in the analyzed group compared with the reference group.

Among patients with treatment failure, a report of missing at
least 1 dose of ART in the past month was more frequent (9 of
121 [7.4%] vs 41 of 1298 [3.6%], $P$ exact = 0.049) than among
nonfailing patients.

A CD4 cell count at baseline $>200$ cells/$\mu$L was associated
with fewer failures ($<200$ cells/$\mu$L: reference, 200–500/$\mu$L:
multivariable HR [mHR], 0.5; 95% confidence interval [CI],
3.8–8 and $>500$/μL: mHR, 0.4; 95% CI, 2.7–7; Figure 3). An
HIV-1 RNA load $\geq 100\,000$ copies/mL was associated with fail-
ures (mHR, 2.2; 95% CI, 1.3–3.6) compared with a viral load
<10 000 copies/mL (Figure 3). In addition, patients who expe-
rienced an AIDS-defining event had an increased chance for
failure (mHR, 1.8; 95% CI, 1.1–3.0). The 2 most common AIDS-
defining events were pneumocystis pneumonia and esophageal
candidiasis, which occurred in 45 (3.2%) and 29 (2.0%) of 1419
patients, respectively.

A subanalysis showed that the results were comparable
when the data were censored at the change of any substance
in the treatment regimen, not only at the end of InSTI-based
therapy (Supplementary Table 2). The results were similar
when the Cox regression analysis was restricted to patients on
DTG (Supplementary Table 3). Baseline HIV-1 RNA $\geq 100\,000$
copies/mL was associated with virological failure (mHR, 2.2;
95% CI, 1.1–4.4), while a CD4 count $>200$ cells/$\mu$L was protec-
tive (200–500 cells/$\mu$L: mHR, 0.4; 95% CI, 2.8–and >500 cells/$\mu$L:
mHR, 0.4; 95% CI, 2.8).

In the subanalysis that included patients with a baseline viral
load $\geq 100\,000$ copies/mL (Supplementary Table 4), only the
CD4 count at baseline affected treatment outcome. Patients
with at least 200 CD4 cells/$\mu$L had a lower chance for failure
than those with $<200$ cells/$\mu$L (200–500 cells$/\mu$L: mHR, 0.3; 95%
CI, 2.6 and $>500$ cells/$\mu$L: mHR, 0.2; 95% CI, 0.5).

**Time to Viral Suppression**

Median (interquartile range) time to viral suppression was
50 days (29–107), and the median time between 2 HIV-1 RNA

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Figure 1. Flow diagram of study inclusion. Abbreviations: cART, combined an-
tiretroviral therapy; DTG, dolutegravir; GRT, genotypic resistance test; HIV, human
immunodeficiency virus; InSTI, integrase strand transfer inhibitor.
measurements in the first year was 10.4 weeks (8.5–13.0). Figure 2 and Supplementary Table 1 show the results of the analysis for time to viral suppression. An HR >1 implies a shorter time to viral suppression in the analyzed group compared with the reference group. A viral load $\geq 10\,000$ copies/mL at baseline was associated with longer time to suppression compared with a viral load $<10\,000$ copies/mL (10,000–99,999 copies/mL: mHR, 0.7; 95% CI, 0.6–0.8 and $\geq 100\,000$ copies/mL: mHR, 0.5; 95% CI, 0.4–0.6; Figure 3). Patients on a first-line therapy with DTG (mHR, 1.2; 95% CI, 1.0–1.4) and financially independent patients had a shorter time to viral suppression (mHR, 1.6; 95% CI, 1.1–2.4).

Among patients with an HIV-1 RNA load $\geq 100\,000$ copies/mL at baseline, time to viral suppression was shorter with a baseline CD4 count >500 copies/µL (mHR, 1.5; 95% CI, 1.0–2.2). Time to suppression was also shorter under a first-line therapy with DTG (mHR, 1.7; 95% CI, 1.2–2.3) than under therapy with other InSTIs.

### Table 1. Baseline Characteristics of the Study Population

| Baseline Characteristic | All Patients, n = 1419 | Patients With a Genotypic Resistance Test, n = 646 | No Minor InSTI Mutation, n = 542 | $\geq 1$ Minor InSTI Mutation, n = 104 |
|-------------------------|------------------------|---------------------------------|-------------------------------|---------------------------------|
| Median (IQR) age at start of combined antiretroviral treatment, years | 39 (31–49) | 38 (30–49) | 38 (30–49) | 37 (31–47) |
| Sex (%) | | | | |
| Male | 1176 (82.9) | 539 (83.4) | 457 (84.3) | 82 (78.9) |
| Female | 243 (17.1) | 107 (16.6) | 85 (15.7) | 22 (21.2) |
| Ethnicity (%) | | | | |
| White | 1096 (77.2) | 508 (78.6) | 425 (78.4) | 83 (79.8) |
| Black | 168 (11.8) | 63 (9.8) | 47 (8.7) | 16 (15.4) |
| Other | 155 (10.9) | 75 (11.6) | 70 (12.9) | 5 (4.8) |
| Transmission category (%) | | | | |
| Men who have sex with men | 842 (59.4) | 402 (62.2) | 335 (61.8) | 67 (64.4) |
| Heterosexual males | 241 (17.0) | 99 (15.3) | 89 (16.4) | 10 (9.6) |
| Heterosexual females | 195 (13.7) | 91 (14.1) | 71 (13.1) | 20 (19.2) |
| Intravenous drug users | 59 (4.2) | 22 (3.3) | 17 (3.1) | 4 (3.9) |
| Other | 82 (5.8) | 33 (5.1) | 30 (5.5) | 3 (2.9) |
| Subtype (%) | | | | |
| B | 364 (25.7) | 364 (56.4) | 312 (57.6) | 52 (50.0) |
| non-B | 253 (17.8) | 253 (39.2) | 204 (37.6) | 49 (47.1) |
| not available | 802 (56.5) | 29 (4.5) | 26 (4.8) | 4 (3.9) |
| HIV-1 RNA (copies/mL) | | | | |
| <10,000 | 437 (30.8) | 194 (30.0) | 161 (29.7) | 33 (31.7) |
| 10,000–99,999 | 604 (42.6) | 260 (40.3) | 218 (40.2) | 42 (40.4) |
| $\geq 100\,000$ | 378 (26.6) | 192 (29.7) | 163 (30.1) | 29 (27.9) |
| Log median (IQR) HIV-1 RNA copies/mL CD4 cell count (%) | 4.5 (3.5–5.1) | 4.5 (3.7–5.2) | 4.5 (3.7–5.2) | 4.5 (3.3–5.1) |
| <200 | 281 (19.8) | 135 (20.9) | 106 (19.6) | 29 (27.9) |
| 200–500 | 724 (51.0) | 306 (47.4) | 267 (49.3) | 39 (37.5) |
| >500 | 414 (29.2) | 205 (31.7) | 169 (31.2) | 36 (34.6) |
| Median (IQR) CD4 cells/µL | 381 (226–549) | 391 (230–551) | 391 (238–552) | 386 (186–545) |
| AIDS-defining event at baseline (%) | 125 (8.8) | 43 (6.7) | 35 (6.5) | 8 (7.7) |
| InSTI administered (%) | | | | |
| RGV | 213 (15.0) | 67 (10.4) | 54 (10.0) | 13 (12.5) |
| EVG | 281 (19.8) | 124 (19.2) | 108 (19.9) | 16 (15.4) |
| DTG | 925 (65.2) | 455 (70.4) | 380 (70.1) | 75 (72.1) |
| Antiretroviral treatment combinations (%) | | | | |
| 3TC+ABC+DTG | 460 (32.4) | 227 (35.1) | 198 (36.5) | 29 (27.9) |
| DTG+ETC+TDF | 259 (18.3) | 150 (23.2) | 120 (22.1) | 30 (28.9) |
| DTG+ETC+TAF | 143 (10.8) | 42 (6.5) | 34 (6.3) | 8 (7.7) |
| COB+ETC+EVG+TAF | 130 (9.2) | 53 (8.2) | 47 (8.7) | 6 (5.8) |
| COB+ETC+EVG+TDF | 123 (8.7) | 59 (9.1) | 50 (9.2) | 9 (8.7) |
| ETC+RGV+TDF | 126 (8.9) | 37 (5.7) | 30 (5.5) | 7 (6.7) |
| Other drug combinations | 178 (11.8) | 78 (12.1) | 63 (11.6) | 15 (14.4) |

**Abbreviations:** 3TC, lamivudine; ABC, abacavir; COB, cobicistat; DTG, dolutegravir; ETC, emtricitabine; EVG, elvitegravir; HIV, human immunodeficiency virus; InSTI, integrase strand transfer inhibitor; IQR, interquartile range; RGV, raltegravir; TAF, tenofovir alafenamide; TDF, tenofovir.
Figure 2. Multivariable Cox regression. Predictors of virological failure (A) and time to viral suppression (B) among drug-naive individuals living with HIV (A: n = 1419, B: n = 1389). Abbreviations: BL, baseline; CI, confidence interval; DTG, dolutegravir; EVG, elvitegravir; HIV, human immunodeficiency virus; mHR, multivariable hazard ratio; InSTI, integrase strand transfer inhibitor; MSM, men having sex with men; RGV, raltegravir.

Figure 3. Kaplan-Meier curves with time to virological failure and time to suppression comparing patients by the CD4 cell count (A and B) and HIV type 1 RNA copies/mL (C and D) at baseline. Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus.
In the subanalysis that included only patients on DTG, time to viral suppression was increased in individuals with a viral load \(\geq 10,000 \text{ copies/mL}\) (10,000–99,999 copies/mL: mHR, 0.8; 95% CI, 0.7–0.9 and \(\geq 100,000 \text{ copies/mL}\): mHR, 0.6; 95% CI, 0.4–0.7) and was decreased in financially independent patients (mHR, 1.7; 95% CI, 1.1–2.6).

Across the analyses, other demographic factors and the mode of transmission were not significantly associated with the virologic outcome.

**Impact of InSTI Resistance Associated With Minor Mutations at Baseline**

Among 646 patients with a pretreatment GRT, no one had major mutations. We detected minor mutations in 104 (16%) patients. The most common mutations were L74I (n = 65, 8.6%), V151I (n = 14, 1.9%), and E157Q (n = 14, 1.6%). All other RAMs were present in <1.6% of the cases (see Supplementary Table 5). The highest prevalence of L74I was found among subtype A (14 of 24 patients, 41.2%) and subtype G (5 of 12 patients, 41.7%) infections. L74I occurred among 30 of 364 (8.2%) of subtype B infections. We did not observe an effect of the presence of minor InSTI RAMs on both therapeutic outcomes studied (time to failure: mHR, 0.9; 95% CI, 0.4–1.9 and time to suppression: mHR, 1.0; 95% CI, 0.8–1.2; Figure 4). Most of the other risk factors found to correlate with the outcome in the primary analysis affected the therapeutic outcome in the subgroup (Supplementary Table 6).

**DISCUSSION**

To our knowledge, this is the first observational study to analyze the risk factors for failing InSTI-based therapy in drug-naive individuals living with HIV-1, including minor integrate RAMs.

In general, response to InSTI-based first-line treatment of drug-naive patients was excellent. Nevertheless, a high viral load and/or a low CD4 count at baseline were associated with more treatment failures and shorter time to suppression. Among patients who presented with a baseline viral load \(\geq 10,000 \text{ copies/mL}\), DTG therapy showed a superior activity in decreasing the time to viral suppression than other InSTIs studied. The superiority of DTG over first-generation InSTIs and other antiretroviral drugs in the treatment of drug-naive patients with a high viral load has been shown in various randomized, controlled studies [4–7]. However, contrary to the findings in those trials, high viral load/low CD4 count at baseline also jeopardized treatment success among participants on DTG in our study. These findings are in line with the New Antiretroviral and Monitoring Strategies in HIV-Infected Adults in Low-Income Countries (NAMSAL) and ADVANCE trials, which found evidence that treatment success while on DTG is impaired among patients with a baseline viral >100,000 copies/mL [35, 36]. Transmitted and acquired nonnucleoside reverse-transcriptase inhibitor drug resistances are important drivers to change to DTG in resource-limited settings [37]. DTG-based regimens are highly potent and cost-effective treatment options, although weight gain, in particular, in women of African origin under DTG even more aggravated with TAF-based regimens was described [32, 36]. Nevertheless, taken together in resource-limited settings where frequent RNA monitoring is difficult, a first-line therapy with DTG might be safer and more reliable in patients who present with high baseline viral loads.

The presence of minor InSTI RAMs at baseline was not associated with worse outcome. Many of the minor RAMs we detected were present as polymorphisms even before InSTIs were introduced into the clinical routine in Europe [38]. L74I and V151I are polymeric mutations. L74I was most common among subtype A and G infections [39]. E157Q is a common polymeric mutation. Other large, randomized, controlled trials also found that InSTIs are effective among patients who carry E157Q mutant viruses [35]. All the other mutations we found, including T97A, are known to decrease InSTI susceptibility in combination with other mutations [40], which were not present in our patients. Hence, although

![Figure 4](https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1614/5937176)
pretreatment of minor InSTI RAMs is common among drug-naive individuals living with HIV-1 in Switzerland, it is reassuring that their presence does not affect treatment outcome.

Across all analyses, time to viral suppression was shorter if patients were financially independent. There was a trend that suggests that older age at treatment start also decreased the risk for failure and the time to suppression. These findings might be explained by better adherence in patients with more favorable social conditions and in older patients [41]. In the absence of RAMs, nonadherence to therapy has been shown to be the most common reason for treatment failure [3]. The proportion of patients who reported decreased adherence in our study was also significantly higher in the group that experienced failure. These results show that disparities that arise from demographic and economic factors in conjunction with presumably lower adherence remain relevant even in a cohort that is subject to regular follow-up, is based in a high-income country with universal healthcare access, and for participants being treated with the most potent drug classes.

Although the SHCS is highly representative and a considerable number of drug-naive participants had an integrase resistance test available, the number of treatment failures was small, which may impair the study’s statistical power. We used a cutoff of 50 copies of RNA/mL to define a virological failure; the number of events was too small for multivariable analyses when we chose a cutoff of 200 or 500 RNA copies/mL. Furthermore, we had predominantly male White participants, which limited the generalization of these findings to a more diverse group.

CONCLUSIONS

Many of the risk factors commonly associated with therapeutic failure such as the severity of immunodeficiency, stage of the disease, and financial situation, were still relevant despite the potency of InSTIs. The chance for virological failure was consistently associated with the baseline viral load and the CD4 count, even in patients on DTG.

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Members of the Swiss HIV Cohort Study: Aebi-Popp K, Anagnostopoulos A, Battegay M, Bernasconi E, Böni J, Braun DL, Bucher HC, Calmy A, Cavassini M, Ciuffi A, Dollenmaier G, Egger M, Elzi L, Fehr J, Fellay J, Furrer H, Fux CA, Günthard HF (president of the Swiss HIV Cohort Study (SHCS)), Haery D (deputy of the "Positive Council"), Hasse B, Hirsch HH, Hoffmann M, Hödi I, Huber M, Kahler CR (chair of the Mother & Child Substudy), Kaiser L, Keiser O, Kleinkat T, Koyos RD, Kovari H, Ledergerber B, Martelli G, Martinez de Tejada B, Marzolini C, Metzner KJ, Müller N, Nicca D, Paiono P, Pantaleo G, Perreau M, Rauch A (chair of the Scientific Board), Rudin C, Scherrer AU (head of Data Center), Schmid P, Speck R, Stöckle M (chair of the Clinical and Laboratory Committee), Tarr P, T›rloka A, Vernazza P, Wandelé G, Weber R, Yerly S. Authors contributions. A. P., A. U. S., and H. F. G. conceived and designed the study. A. P. and A. U. S. performed the analysis. A. U. S., Y. Y., M. P., M. S., H. E., A. C., M. C., E. B., and H. F. G. collected and contributed data. A. P., A. U. S., and H. F. G. wrote the manuscript. All authors read and approved the final manuscript.

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