

Durability of Single Tablet Regimen for Patients with HIV infection in Southern Taiwan: data from a real world setting

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Research article

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Abstract

Background: A single-tablet regimen (STR) has been associated with better drug adherence. However, the durability of different STRs was unknown in the real world settings. Our aim was to investigate the durability of different initial STR regimens in patients starting STR in southern Taiwan

Method: This was a retrospective study of antiretroviral-naïve patients that initiated first-line antiretroviral regimens with STRs between May 2016 and December 2017. The primary endpoint was time to virological failure (defined as plasma HIV RNAs ≥ 200 copies/mL after 24 weeks). Secondary endpoints were STR discontinuation due to toxicity/intolerance. Survival analysis was done using Kaplan–Meier and Cox regression.

Results: Two hundred and twenty-three patients were included: Over a median (IQR) of 86 (60-112) weeks, 25 patients (11%) experienced virological failure; the 1 year probability of virological failure was 11% (8/70) for Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate, 7% (4/54) for Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate and 13% (13/99) for Abacavir/Dolutegravir/Lamivudine. Fifty-six patients (25%) discontinued their STRs owing to toxicity/intolerance. When compared to Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate, treatment with Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (AHR 8.39, CI 1.98-35.58, $p=0.004$) and Abacavir/Dolutegravir/Lamivudine (AHR 8.40, CI 2.39-29.54, $p=0.001$) were more likely to have treatment failure. However, when the risk of treatment failure was compared between two different STRs, treatment with Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate was not found to have higher risk of treatment failure when compared to Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate (log rank test $p=0.116$). The predictors for treatment failure included age ≤ 30 years old (AHR 3.73, CI 1.25-11.17, $p=0.018$), switch between different STR (AHR 2.3, CI 1.18-4.50, $p=0.001$) and free of active syphilis infection (AHR 0.24, CI 0.08-0.73, $p=0.012$). The risk factor for treatment discontinuation included younger age ≤ 30 years old (AHR 3.82, CI 1.21-12.37, $p=0.023$), treatment with Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate (AHR 8.65, CI 2.64-28.39, $p<0.001$) and free of active syphilis infection (AHR 0.16, CI 0.04-0.62, $p=0.006$).

Conclusion: Younger age was associated with treatment failure and drug discontinuation. Active syphilis infection s/p treatment was associated with free from treatment failure and discontinuation. This probably driven by the more frequently sexual health education and counseling when patients had syphilis infection. The STR durability was dependent on the drug toxicity/intolerance, age and syphilis infection

Introduction

Single tablet regimen (STR) has been associated with better drug compliance [1], improved quality of life [2] and less likely to development of resistance [3, 4] compared to multiple tablet regimens. Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate (Atripla) was the first STR in Taiwan and was

introduced in 2010 then followed by Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (Complera) and Abacavir/Dolutegravir/Lamivudine (Triumeq) in June 2016. The three STRs were recommended as the first line antiretroviral (ARV) drugs in Taiwanese reimbursement regulation for treatment naïve patients with HIV infection since June 2016.

There are cohort studies dealing with ARV regimen durability in HIV infected treatment naïve patients in the real world settings. In a retrospective cohort study at eight UK centers, Lewis et. al. found that the rilpivirine based STR (Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate) had a significantly lower discontinuation rate than another STR (Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate) and other third agents [5]. In another study from Maple Leaf Medical Clinic in Canada, researchers found that being on an integrase strand transfer inhibitor (INSTI) or nonnucleoside reverse transcriptase inhibitor (NNRTI)-based regimens versus protease inhibitors (PI) regimen were associated with better durability. However, the informations of percentage of STR uses were lack [6].

Contemporary STRs in registrational studies in treatment naïve HIV infected individuals showed that the efficacy was about 88-93%, rate of virological failure 0.8-4.4% and rate of discontinuation due to severe adverse effects were around 0-1.9% [7]. The patients in the randomized control trial (RCT) may vary greatly from real world populations with different race/ethnicity, comorbidities, and adherence rates. Furthermore, the additional supports are afforded by the RCT environment [7]. Real world ART durability may reflect more subjective treatment outcomes like quality of life or mild side effects that affect adherence in routine care and are likely of greater importance in clinic settings [8]. There is no pure STR durability data in the real world.

The objectives of this study was to investigate the durability of different initial regimens in patients starting ART with single tablet regimen in southern Taiwan.

Materials And Methods

Ethical statement

The study was approved by the institutional review board of the Kaohsiung Veterans General Hospital (VGHKS19-CT4-02) in Taiwan. The protocol complied with ethical considerations involving human subjects and all information obtained followed standard clinical guidelines. Since this was a retrospective cohort study, the individual informed consents were exempted.

Study Design and Participants

This was a retrospective cohort study conducted at Kaohsiung Veterans General Hospital; a 1500 bed medical center in southern Taiwan. The study period was from May 2016 to Dec 2017. In Taiwan, all of the HIV infected patients was mandatory to enroll into the case management program sponsored by Taiwan Center for Disease Control (CDC) since 2008. The data of social, demographic, pharmacologic, laboratory, and concurrent infections were collected through electronic medical records. We included

treatment-naïve patients with age more than 20 years old, initiating STR (one of the Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate, Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate, or Abacavir/Dolutegravir/Lamivudine) between May, 2016 and December, 2017 in this retrospective cohort. Administrative censoring occurred in June 2018, 6 months after last patients enrolling. This cohort study was conducted in parallel with the introduction of second and third STRs (Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate and Abacavir/Dolutegravir/Lamivudine) into Taiwan in June 2016. Before June 2016, the only available STR was Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate which was used as the second line ARVs in those patients unable to tolerance to zidovudine/lamivudine with efavirenz or nevirapine. After June 2016, one of the three STRs (Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate, Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate, or Abacavir/Dolutegravir/Lamivudine) was recommended as the first line therapy in those HIV-1 infected, treatment naïve patients in Taiwan.

The laboratory tests for patients diagnosed with HIV infection included CD4 cell count, plasma viral load, serological markers for syphilis, hepatitis, cryptococcus, toxoplasmosis, cytomegalovirus, amoebiasis, liver and renal function. HIV-1 genotype resistance testing (GRT) for treatment-naïve patients was not routinely performed in our country due to limited budget. Standard follow-up of the HIV-infected patients consisted of out-patient visits every 3 months. Testing for CD4 cell count, plasma viral load, haematology, and biochemistry were conducted every 6 months for chronic viral suppressed patients. HIV Genotypic drug resistance testing for the protease and reverse transcriptase region was done by the commercial kit Viroseq version 2.8 (Celera; Quest Diagnostics, Secaucus, NJ, USA) [9]. For integrase sequencing, the in house protocol with nested reverse transcription polymerase chain reaction (RT-PCR) was used according to our previous published methods [10].

Durability was defined as the number of weeks from the STR regimen initiation until discontinuation or modification. Virological failure was defined as HIV-RNA \geq 50 copies/mL after 6 months of STR treatment. Treatment failure was a composite endpoint defined as virological failure or discontinuation of STR for any reason or death. Active syphilis was defined as a new positive rapid plasma regain (RPR) and the Treponema pallidum particle agglutination test (TPPA) [11]. In those patients had ever received syphilis treatment, a fourfold increase in the RPR titer was also indicated a new infection [12].

Statistics Analysis

Continuous variables were reported as median and interquartile range (IQR). Categorical variables were reported as frequencies with percentages. Time to modification or discontinuation of the initial STR was evaluated using Kaplan-Meier survival curves. The median durability time is reported in weeks and compared across stratified STRs using the log-rank test. Association of various demographic characteristics with time to viral suppression, treatment failure or regimen modification/ discontinuation were evaluated using Cox proportional hazards models to estimate crude and adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). The following clinically important variables were included: age, sex, HIV transmission risk factor, CD4 count, viral load, concurrent infection with hepatitis B, C and

syphilis and individual STR. A two-sided $p < 0.05$ was considered statistically significant. Statistical calculations were performed using the SPSS program version 12.0 (SPSS Inc., Chicago, IL).

Results

A total of 345 HIV-1 infected, treatment naïve patients was eligible for the study between May 2016 to Dec 2017. Among them, 122 patients were not enrolled due to no ARV use during the study period, use of multiple tablet regimen, or incomplete clinical data, received with less than 60 days of STRs, transferred out or went to jail. Fig 1. Baseline characteristics of the remaining 233 HIV-1 infected treatment naïve patients starting STR between May 2016 to Dec 2017 were showed in Table 1. Briefly, their medium age (IQR) was 25 (27-41) years old with man consisted of 93.7%. The HIV transmission risk factor included MSM (67.7%) and intravenous drug abuser (26.5%). Twenty six percent (58/223) had concurrent infection with hepatitis C, 30% had hepatitis B and 41% syphilis. Only 27% (61/223) of the patients had baseline GRT. Thirty one percent (70/223) of the patients started Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate, 24% (54/223) Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate and 44% (99/223) Abacavir/Dolutegravir/Lamivudine. The medium (IQR) duration of follow up (weeks) was 86(60-112). Among the 223 patients starting STRs, 4 developed virological failure to Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (4/54, 7.4%), 8 had virological failure to Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate (8/70, 11.4%), 13 to Abacavir/Dolutegravir/Lamivudine (13/99, 13.1%). The switch between different STR was also common. Among the 70 patients starting Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate, 15 switched to Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate and 13 switched to Abacavir/Dolutegravir/Lamivudine due to different adverse effects. Fig 2.

There were 56 patients (Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate 35, Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate 7, Abacavir/Dolutegravir/Lamivudine 14) discontinued their STRs due to drug adverse effects. The most common cause for discontinuing Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate was neuropsychiatric adverse effect (28.5%, 20/70), For Abacavir/Dolutegravir/Lamivudine, it was skin pruritis and rash (6%, 6/99). Table 2.

Time to viral suppression was different in 3 STRs. Compared to Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate and Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate, Abacavir/Dolutegravir/Lamivudine was the ARV with rapidly speed to reach viral load less than 50 copies/ml (15.86 weeks, CI 12.22-19.49), log rank test $p < 0.001$). Fig 3. The predictors for viral suppression in the cox proportional model included treatment with Abacavir/Dolutegravir/Lamivudine (AHR 8.65, CI 2.64-28.39, $p < 0.001$), switch in different STRs (AHR 2.86, CI 1.47-5.52, $p = 0.002$) and free of active syphilis infection (AHR 0.15, CI 0.04-0.59, $p = 0.006$). Table 3.

The risk of treatment failure was also different in 3 STRs (log rank test $p = 0.015$). Fig 4. When compared to Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate, treatment with Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (AHR 8.39, CI 1.98-35.58, $p = 0.004$) and

Abacavir/Dolutegravir/Lamivudine (AHR 8.40, CI 2.39-29.54, $p=0.001$) were more likely to have treatment failure. When the risk of treatment failure was compared between two different STRs, treatment with Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate was not found to have higher risk of treatment failure when compared to Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate (log rank test $p=0.116$). However, treatment with Abacavir/Dolutegravir/Lamivudine was associated with higher risk of treatment failure when compared to Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate (log rank test $p=0.048$). Fig 5

The other predictors for treatment failure included age ≤ 30 years old (AHR 3.73, CI 1.25-11.17, $p=0.018$), switch between different STR (AHR 2.3, CI 1.18-4.50, $p=0.001$) and active syphilis infection (AHR 0.24, CI 0.08-0.73, $p=0.012$). Table 4.

Treatment discontinuation was also common in Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate group (log rank test, $p<0.005$). Fig 6. The risk factor for treatment discontinuation in the Cox proportional model included younger age ≤ 30 years old (AHR 3.82, CI 1.21-12.37, $p=0.023$), treatment with Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate (AHR 8.65 , CI 2.64-28.39, $p<0.001$) and active syphilis infection (AHR 0.16, CI 0.04-0.62, $p=0.006$). Table 5

Discussion

In this study, we found that STRs virological failure and treatment discontinuation was quite common in the real world settings. A high to 25% of the patients discontinued their STRs due to toxicity/intolerance. Treatment with Abacavir/Dolutegravir/Lamivudine and Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate were associated with treatment failure. However, when the risk of treatment failure was compared between two different STRs, treatment with Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate was not found to have higher risk of treatment failure when compared to Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate. Treatment discontinuation was common in the Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate group. Younger age ≤ 30 years old was associated with treatment failure and drug discontinuation. However, active syphilis received treatment was not associated with treatment failure and drug discontinuation.

Our study demonstrating a higher treatment failure rate in the Abacavir/Dolutegravir/Lamivudine group was interesting and the result of a higher drug discontinuation rate in the Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate group was quite similar to other study in the literature [5].

In a retrospective study from Maple Leaf Medical Clinic in Canada, researchers enrolled 780 patients between January 2006 and June 2016 to see the virologic durability of first-line INSTI, NNRTI, or PI-based antiretroviral regimens. The informations of percentage of STR uses were lack. They found that being on an INSTI or NNRTI-based regimens versus PI regimen, frequent VL testing and longer duration on of ART were associated with better durability [6].

In an Italian ICONA cohort, they prospectively followed up patients with low CD4 count (less than 200 cells/mm³) and high viral load (> 5 log₁₀ copies/mL) who started first line ART with boosted protease inhibitors (bPIs), NNRTIs or INSTIs to analyze the durability of their different regimen. They concluded that starting ART with NNRTIs versus starting with bPIs; and starting ART with INSTIs versus starting with NNRTIs were less likely associated with treatment failure. Therefore, the durability of INSTI-based regimen was longer than that of NNRTI- and bPI-based regimens [13]. The information of percentage of STR uses were lack.

In another study also from ICONA cohort, researchers evaluate the durability of three INSTIs and two NRTIs in ART naive patients. Among the 2016 patients enrolled, a total of 167 patients experienced treatment failure; the 1 year probability of treatment failure was 6.5% for raltegravir, 5.4% for dolutegravir and 6.7% for elvitegravir/cobicistat. The detailed information for STR use were not provided.

Sixty-eight patients (3.4%) discontinued INSTIs owing to toxicity/intolerance. In the real-life setting, INSTI-based regimens showed high potency and durability. Dolutegravir are associated with a lower risk of treatment failure [14].

In a retrospective study in a multisite cohort (CFAR Network of Integrated Clinical Systems) in USA, they integrated data from eight Centers for AIDS Research (CFARs), focusing on HIV infected patients initiating ART between 2007 and 2014. In that study, 59% of patients starting their ART with STRs (Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate (n=2173) 40%, Elvitegravir / Cobicistat / Emtricitabine /Tenofovir Disoproxil Fumarate (n=571) 11%, Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate (n=336) 6% and Abacavir/Dolutegravir/Lamivudine (n=106) 2%). The initial regimen was modified in 43% (2285/5373) of patients. The median durability for all regimens was 48.6 months. Female sex, intravenous drug use, and CD4 cell count less than 200 cells/μl were significantly associated with regimen modification. NNRTI and INSTI-based ART were most durable in this study [15].

The possible explanation for the higher treatment failure rate in the Abacavir/Dolutegravir/Lamivudine group might be related to the high virological failure rate with drug discontinuation (Fig 2). Clinicians may tend to prescribe high genetic barrier STR in those patients with suspicious poor drug adherence and severe diseases. Among the 13 patients suffered from virological failure, eight loss of follow up, 5 patients continued their Abacavir/Dolutegravir/Lamivudine treatment. Among the 2 patients had genotypic drug resistance testing, none had resistance. All of the 5 patients reattained virological suppression.

The low STR discontinuation in the Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate group was similar to the study from UK. In this retrospective cohort study at eight UK centers conducted between 2012-2015 with only 2 STRs in their centers, Lewis et. al [5] found that the rilpivirine based STR (Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate) had a significantly lower discontinuation rate than another STR (Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate) and other third agents.

Active syphilis received treatment was associated with less treatment failure and drug discontinuation. Our study result was different from that from the France [16] and similar to the 2 studies from Canada [17, 18]. In a large HIV cohort in France, they showed that early syphilis was associated with a 2-fold increase in the risk of viral load elevation in the months after diagnosis, even in patients receiving effective antiretroviral therapy [16]. In another study of systemic review and metaanalysis, researchers did not find any direct evidence about the effects of sexually transmitted infection co-infection on transmission from individuals on ART. Their data suggested that the average effect of STI co-infection (including syphilis) on HIV viral load in individuals on ART were unlikely to decrease the effectiveness of treatment as prevention [17]. Recently, Grewal R et.al. determined the effect of acute syphilis on virologic failure among virally suppressed 2632 HIV-infected MSM taking antiretroviral therapy in Ontario, Canada. They demonstrated that acute syphilis was not associated with virological failure among virologically suppressed MSM on ART [18].

In this study, younger age (≤ 30 years) was associated with treatment failure and drug discontinuation. Several large cohort studies also report that older age was associated with better treatment outcomes [19, 20], and less virological non-suppression [21].

No data about the level of adherence was available in this study due to the retrospective cohort design. However, all of the patients were educated about their adherence and care by the case management nurses, suggesting that other issues than adherence can explain their treatment failure and drug discontinuation [21, 22].

The explanations why the median time (IQR) to discontinue STRs were longer in the Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate group compared to Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate and Abacavir/Dolutegravir/Lamivudine groups were unclear, This was probably due to the neuropsychiatric adverse effects for Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate were well known by the doctors, care management nurses and patients themselves, patients were well educated about the adverse effects before the Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate was prescribing.

Our study had some limitations. First, there was always the risk of bias due to unmeasured confounding, such as drug adherence levels, not reporting adverse effects and missing data, when using retrospective cohort data. Secondly, reasons for regimen selection were not reported, patients with presumed poorer adherence and higher viral load were more likely to be prescribed Abacavir/Dolutegravir/Lamivudine (INSTI-based) and could impact our analysis. Another caveat was that we censored patients who were lost to follow-up. Such censoring could have led to bias in increasing rate of treatment failure. Finally, our study results could not be applied to those health care systems whom did not have HIV case management program and free STR available.

In conclusion, younger age was associated with treatment failure and drug discontinuation. Active syphilis infection was not associated with an increase risk of treatment failure and discontinuation. Treatment with Abacavir/Dolutegravir/Lamivudine was associated with more treatment failure. The STR

durability was dependent on the drug toxicity/intolerance, age and syphilis infection regardless of genetic barrier of antiretroviral regimen.

Abbreviations

ART: antiretroviral therapy; Atripla: Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate; CDC: center for diseases control; CFAR: centers for AIDS research; CI: confidence interval; Complera: Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate; GRT: genotype resistance testing; HAART: highly active antiretroviral therapy; HAV: hepatitis A; HBV: hepatitis B; HCV: hepatitis C; HR: hazard ratio; IDU: intravenous drug abuser; INSTI: integrase strand transfer inhibitor; IQR: interquartile range; MSM: men who have sex with men; NNRTI: nonnucleoside reverse transcriptase inhibitor; PI: protease inhibitor; RCT: randomized control trial; RPR: rapid plasma regain; RT-PCR: reverse transcription polymerase chain reaction; STR: single tablet regimen; TPPA: Treponema pallidum particle agglutination test; Triumeq: Abacavir/Dolutegravir/Lamivudine.

Declarations

Ethics approval and consent to participate

The study was approved by the ethical committee of Kaohsiung Veterans General Hospital (VGHKS19-CT4-02), and adhered to the principles of the Declaration of Helsinki. Because the data were analyzed anonymously, the ethical committee waived the need for written consent

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Availability of data and materials

All data containing relevant information to support the study findings are provided in the manuscript

Authors' contributions

Chang HM conceived and designed the study and drafted the manuscript. Chou CH and Tsai HC analyzed and interpreted the data. Chou CH and Tsai HC critically revised the manuscript. All authors read and

approved the final manuscript.

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Tables

Table 1. Baseline characteristics of the 233 HIV infected treatment naïve patients starting single tablet regimen between May 2016 to Dec 2017

Characteristics	N =223
Age, yrs, median (IQR)	35 (27-41)
Sex	
Male (%)	209(93.7)
Female	14 (6.3)
HIV risk factors	
IDU (%)	59 (26.5)
MSM	151 (67.7)
Heterosexual	13 (5.8)
CD4 count at baseline, median (IQR)	288.75(162-422)
Last CD4 count, median (IQR)	490.54 (364-656)
Viral load at baseline copies/ml , median (IQR)	43,000 (13,300-129,000)
Duration of follow-up (wk) , median (IQR)	86 (60-112)
Co-infections (%)	
Hepatitis C virus coinfection	58 (26)
Hepatitis B virus coinfection	68 (30.5)
Syphilis	92 (41.3)
GRT (%)	61 (27.3)
STR	
Atripla (%)	70 (31.4)
Complera	54 (24.2)
Triumeq	99 (44.4)

GRT: genotype resistance testing; IQR: interquartile range; MSM: men who have sex with men; STR: single tablet regimen; IDU: intravenous drug users; Atripla: Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate; Complera: Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate; Triumeq: Abacavir/Dolutegravir/Lamivudine

Table 2. Types of adverse effect (AEs) leading to discontinuation among the 56 patients with HIV infections starting STRs during the entire follow-up period

	Atripla (n=70)	Complera (n=54)	Triumeq (n=99)
Numbers (%) of AEs	35 (50)	7 (12.9)	14 (14.1)
Neuropsychiatric (%)	21 (60)	1 (14.3)	0
Skin (%)	6 (17.1)	2 (28.6)	6 (42.8)
Other (%)	8 (22.9)	4 (57.1)	8 (57.2)
Time to discontinue, median (IQR)	25(14-57)	23 (5-14)	11 (5-31)

IQR: interquartile range; STR: single tablet regimen; Atripla: Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate; Complera: Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate; Triumeq: Abacavir/Dolutegravir/Lamivudine

Table 3. Predictors of virological suppression among 233 HIV infected treatment naïve patients starting single tablet regimen between May 2016 to Dec 2017

Variable	Comparator	Unadjusted Hazard Ratio (HR) (95% CI)	p-value	Adjusted Hazard Ratio (AHR) (95% CI)	p-value
Age ≤ 30 years	>30years	2.71 (0.78 to 9.44)	0.12		
Baseline CD4+ t(cells/mm ³) ≤ 100	>100	1.33 (0.09 to 18.19)	0.83		
Treatment regimen			0.003		0.002
	Atripla	1		1	
	Complera	0 (0.00 to 0)	0.986	0 (0 to 0)	0.989
	Triumeq	9.85 (2.68 to 36.20)	0.001	8.65 (2.64 to 28.39)	0.000
		1.49 (0.42 to 5.30)	0.53		
		0.97 (0.19 to 5.05)	0.97		
		0.71 (0.29 to 1.77)	0.47		
Interaction between different		2.81 (1.26 to 6.25)	0.03	2.86(1.47 to 5.52)	0.002
Coexistent syphilis infection		0.099 (0.02to 0.50)	0.005	0.15 (0.04 to 0.59)	0.006

CI: confidence interval; STR: single tablet regimen; Atripla: Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate; Complera: Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate; Triumeq: Abacavir/Dolutegravir/Lamivudine; HAV: hepatitis A; HBV: hepatitis B; HCV: hepatitis C.

Table 4. Predictors of treatment failure among 233 HIV infected treatment naïve patients starting single tablet regimen between May 2016 to Dec 2017

Variable	Comparator	Unadjusted Hazard Ratio (HR) (95% CI)	p-value	Adjusted Hazard Ratio (AHR) (95% CI)	p-value
Age ≤ 30 years	>30 years	4.985 (1.33 to 18.62)	0.017	3.73 (1.25 to 11.17)	0.018
Baseline CD4+ (cells/mm ³) ≤ 100	>100	5.29 (1.55 to 18.02)	0.008		
Treatment regimen			0.003		0.002
	Atripla	1		1	
	Complera	7.83 (1.78 to 34.53)	0.007	8.39 (1.98 to 35.58)	0.004
	Triumeq	9.02 (2.40 to 33.95)	0.001	8.40 (2.39 to 29.54)	0.001
		1.39 (0.51 to 3.80)	0.53		
		0.90 (0.20 to 4.04)	0.89		
		0.36 (0.06 to 2.17)	0.27		
Interaction between different		2.37 (1.08 to 5.18)	0.03	2.3 (1.18 to 4.50)	0.001
Co-syphilis infection		0.19 (0.06 to 0.64)	0.008	0.24 (0.08 to 0.73)	0.012

CI: confidence interval; STR: single tablet regimen; Atripla: Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate; Complera: Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate; Triumeq: Abacavir/Dolutegravir/Lamivudine; HAV: hepatitis A; HBV: hepatitis B; HCV: hepatitis C.

Table 5. Predictors of treatment discontinuation among 233 HIV infected treatment naïve patients starting single tablet regimen between May 2016 to Dec 2017

Variable	Comparator	Unadjusted Hazard Ratio (HR) (95% CI)	p-value	Adjusted Hazard Ratio (AHR) (95% CI)	p-value
Age ≤ 30 years	>30years	4.85 (1.08 to 21.83)	0.04	3.82 (1.21 to 12.37)	0.023
Baseline CD4+ t(cells/mm ³) ≤ 100	>100	1.14 (0.07 to 16.97)	0.92		
Antiretroviral treatment regimen			0.004		0.002
	Atripla	23.97(3.72 to 154.47)	0.001	16.61 (3.41 to 80.88)	0.001
	Complera	9.32 (0.63 to 138.72)	0.105	8.59 (0.67 to 109.6)	0.098
	Triumeq	1		1	
		2.71 (0.782 to 9.32)	0.12		
		0.67 (0.14 to 3.25)	0.61		
		1.25 (0.38 to 4.14)	0.71		
Coexisting syphilis infection		0.17 (0.04to 0.81)	0.03	0.16 (0.04 to 0.62)	0.008

CI: confidence interval; Atripla: Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate; Complera:

Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate; Triumeq: Abacavir/Dolutegravir/Lamivudine; HAV: hepatitis

A; HBV: hepatitis B; HCV: hepatitis C.

Figures

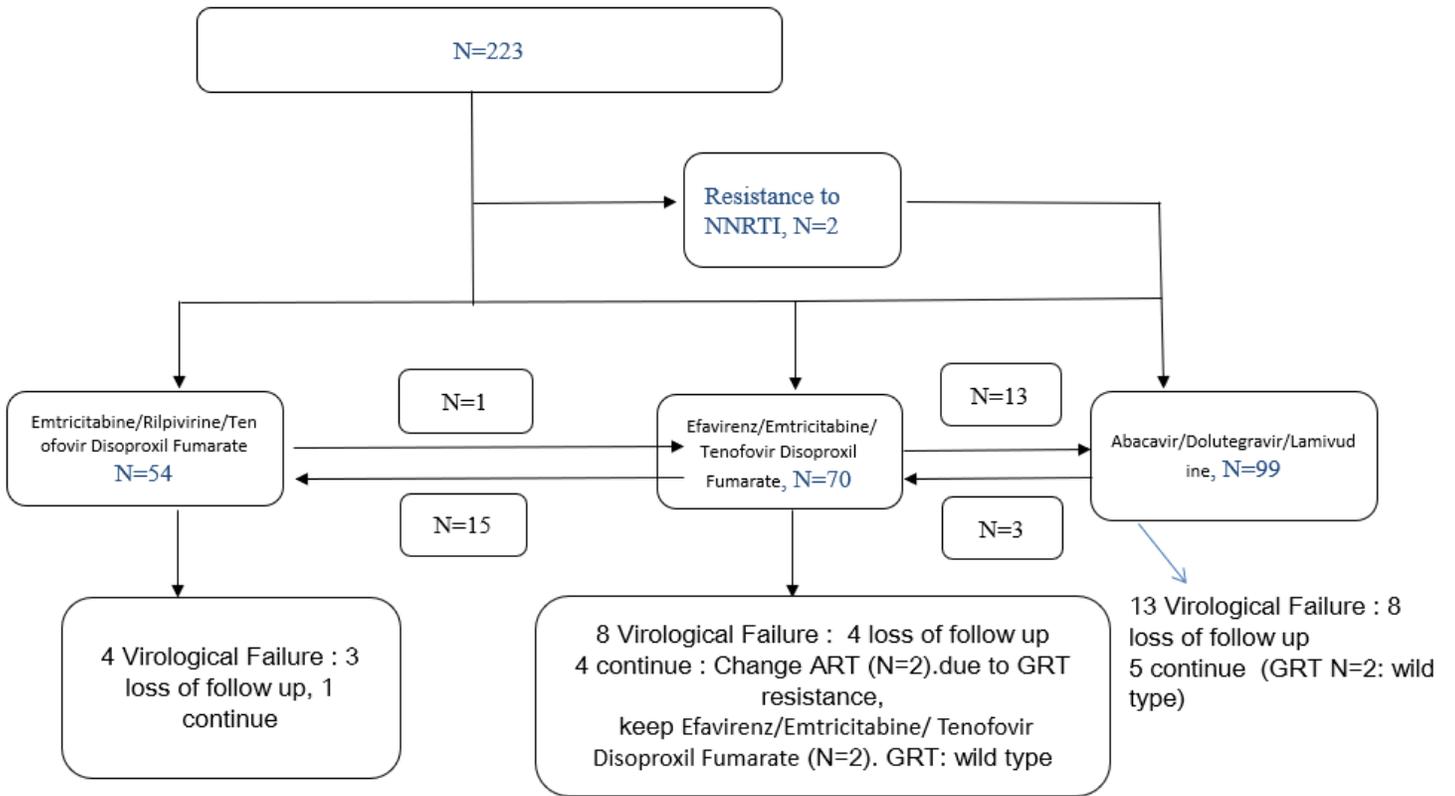


Figure 1

Treatment outcomes and drug switch among the 223 HIV-1 infected patients starting STRs.

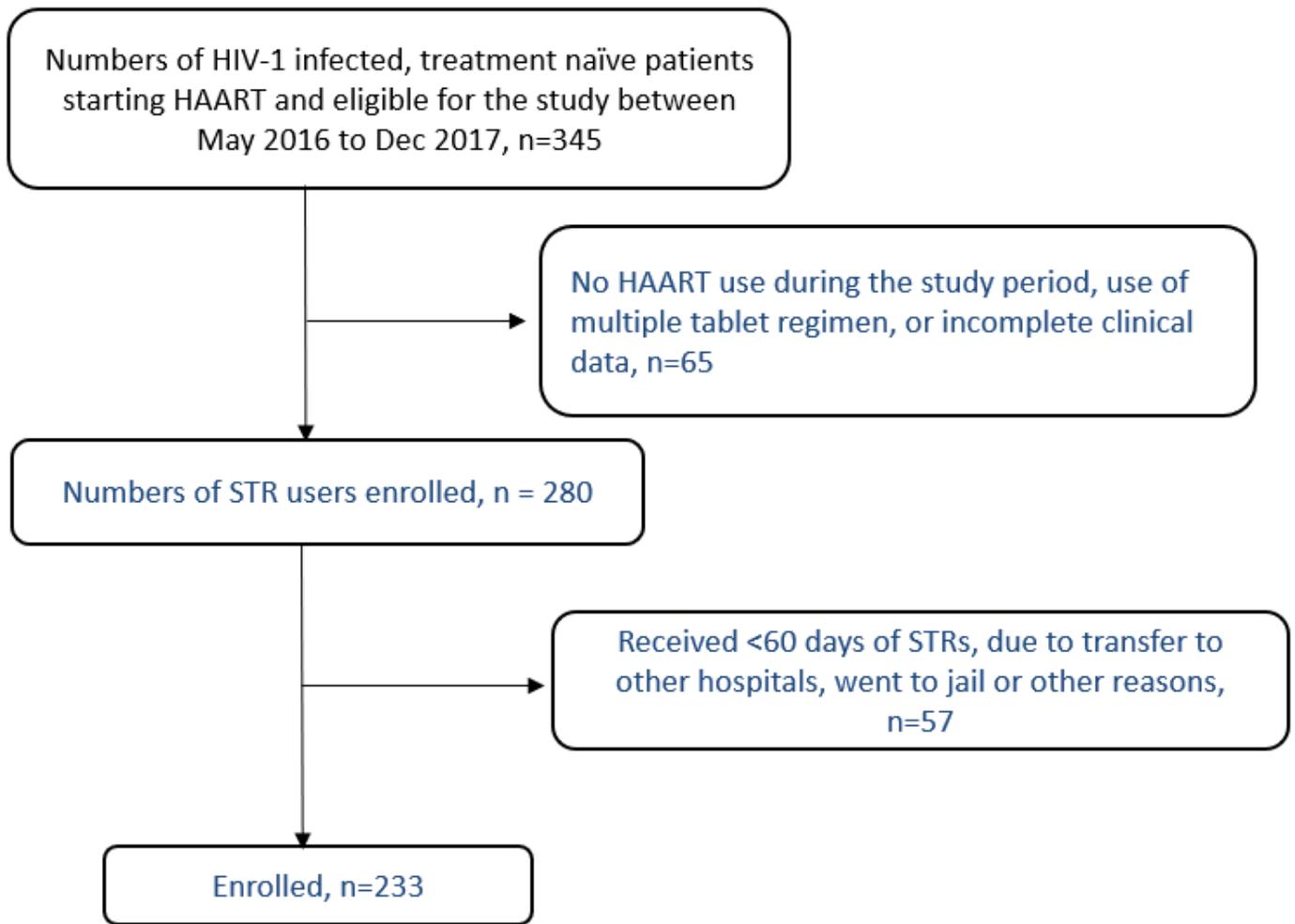
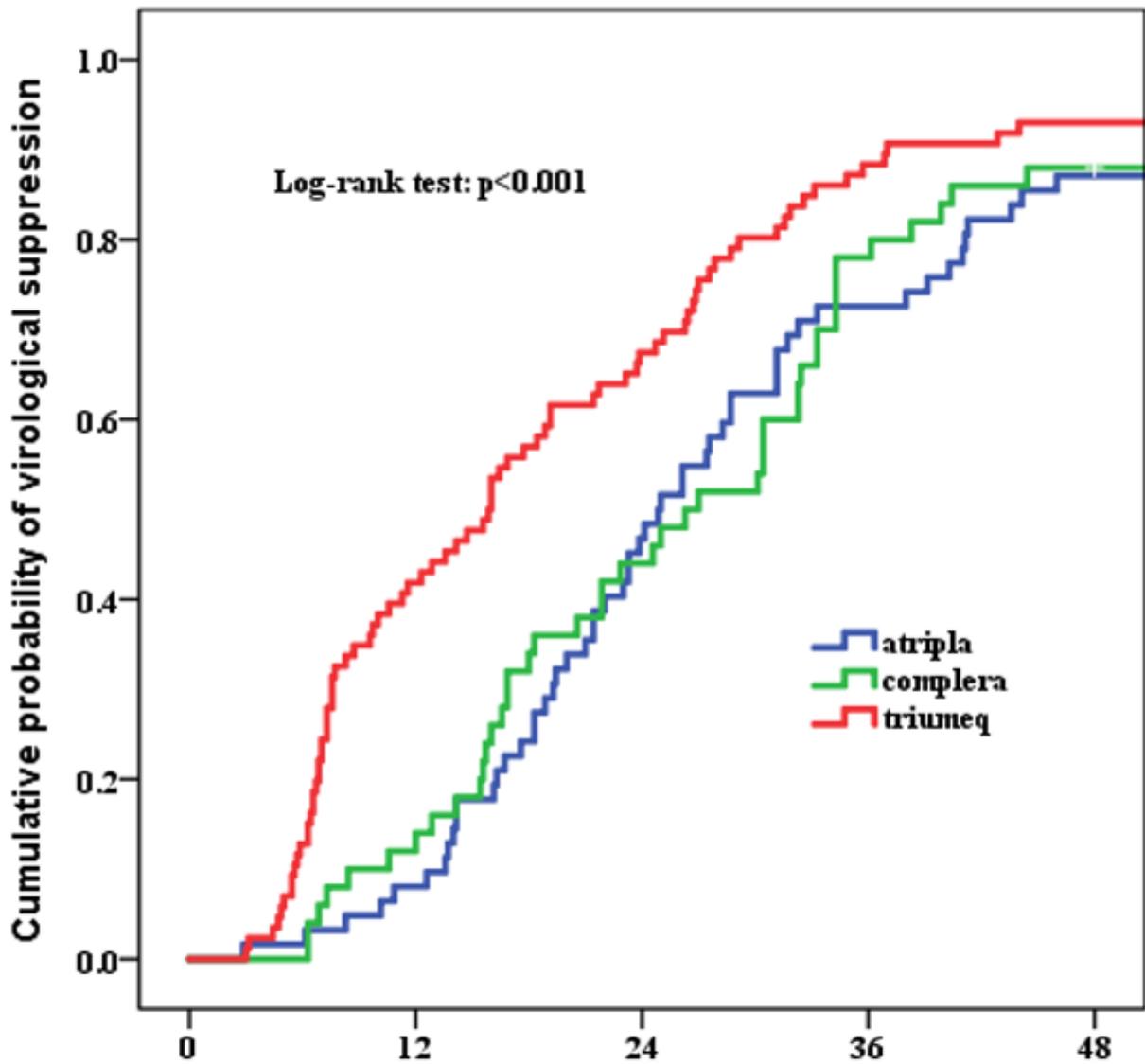


Figure 2

Study flow for HAART retention rate, adverse effects and virological outcomes among HIV-1 infected treatment naïve patients starting STRs from May 2016 to Dec 2017.



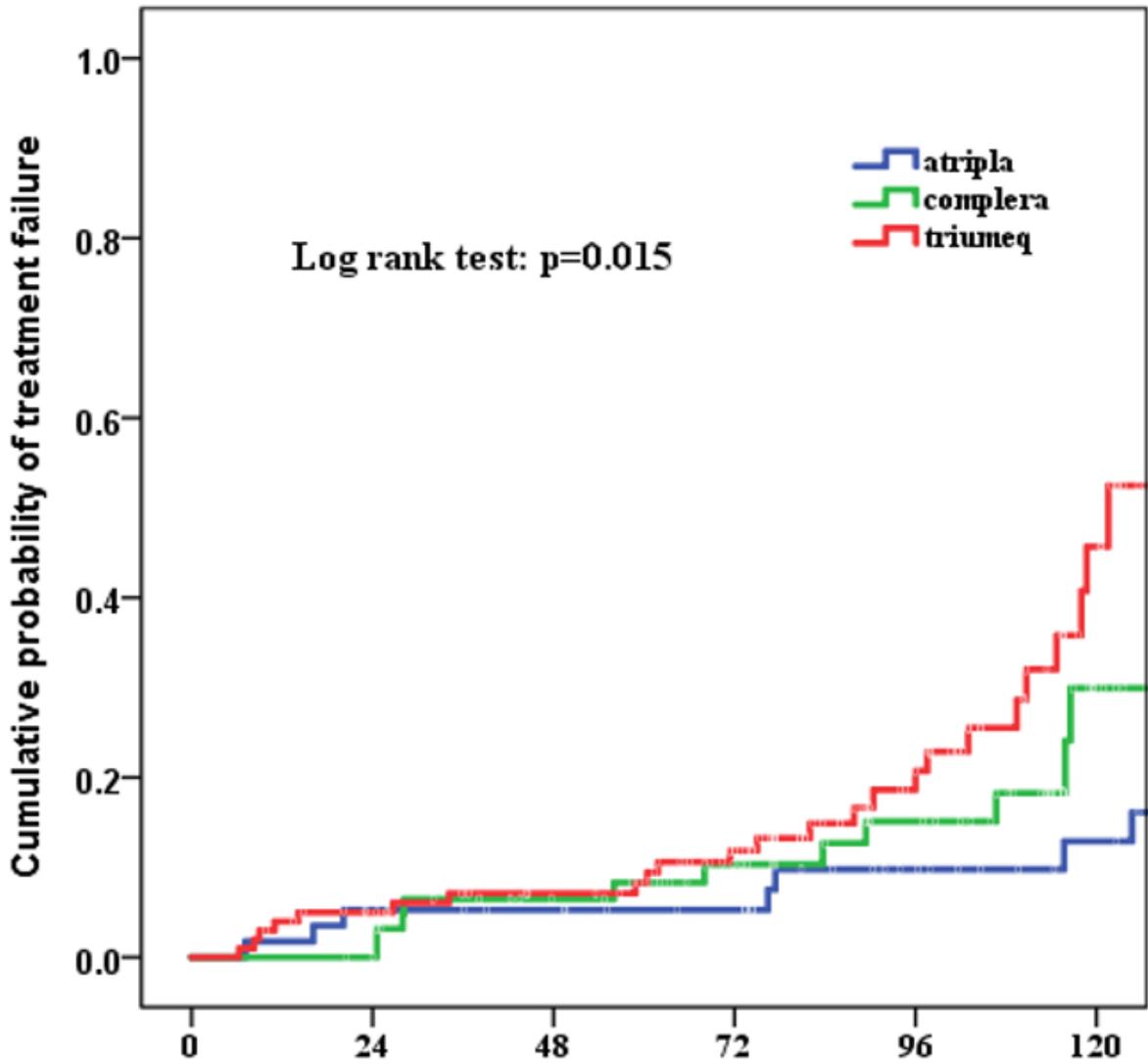
Number at Risk

Weeks from cART start

Atripla	62	56	31	17	8
Complera	50	42	27	10	5
Triumeq	86	48	27	9	6

Figure 3

Time to viral suppression among 233 HIV-1 infected patients starting antiretroviral therapy with STRs in southern Taiwan.



Number at Risk

	0	24	48	72	96	120
Atripla	57	54	54	54	52	49
Complera	65	63	61	59	57	54
Triumeq	101	96	94	90	85	77

Figure 4

Cumulative probability of treatment failure among 233 HIV-1 infected patients starting antiretroviral therapy with STRs in southern Taiwan.

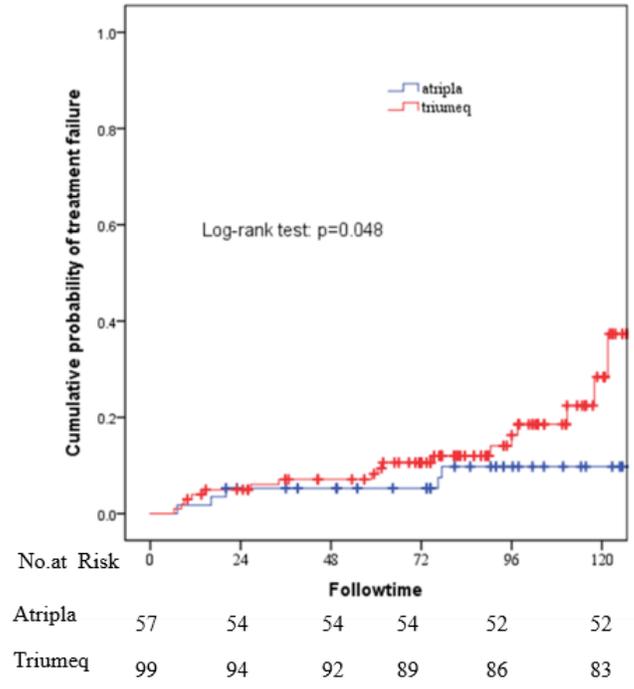
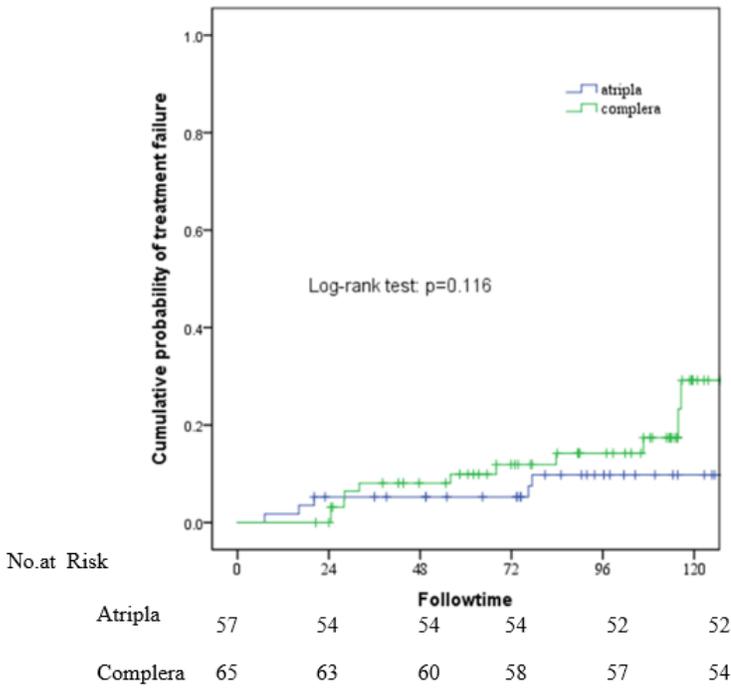
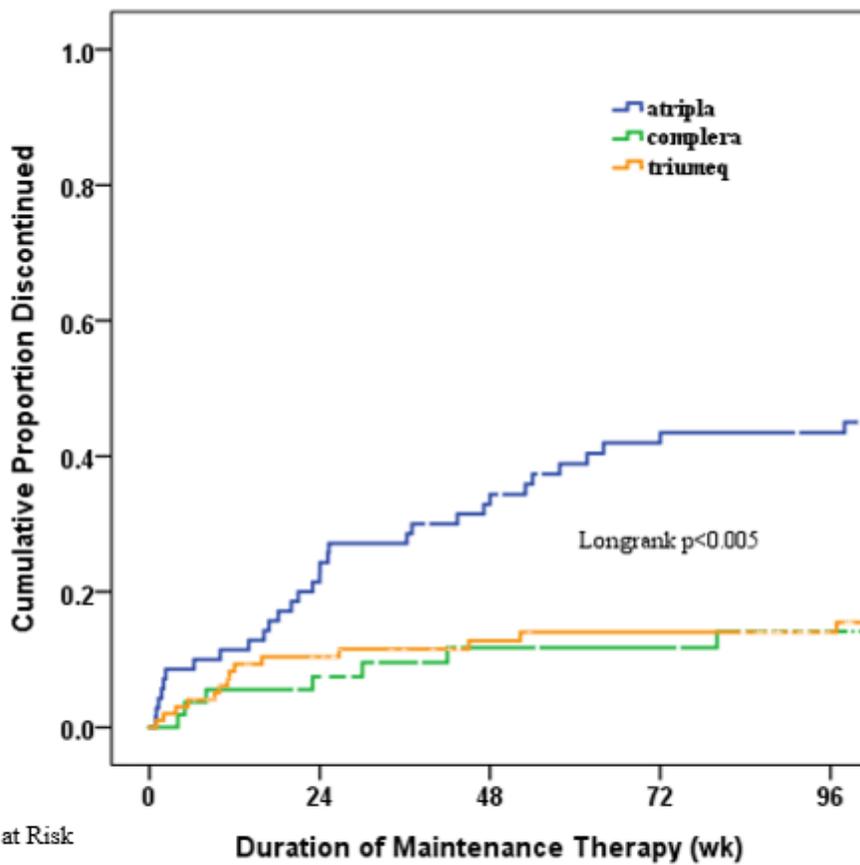


Figure 5

Cumulative probability of treatment failure was compared between two different STRs, treatment with Complera was not found to have higher risk of treatment failure when compared to Atripla (log rank test p=0.116). However, treatment with Triumeq was associated with higher risk of treatment failure when compared to Atripla (log rank test p=0.048)



Atripla	70	53	46	40	35
Complera	54	50	48	48	47
Triumeq	99	89	87	86	85

Figure 6

Cumulative probability of treatment discontinuation among 233 HIV-1 infected patients starting antiretroviral therapy with STRs in southern Taiwan (Atripla: Efavirenz/Emtricitabine/ Tenofovir Disoproxil Fumarate; Complera: Emtricitabine/Rilpivirine/Tenofovir Disoproxil Fumarate; Triumeq: Abacavir/Dolutegravir/Lamivudine)