Prevalence of Integrase Strand Transfer Inhibitors (INSTI) resistance in people living with HIV and virological failure in an area with universal implementation of single tablet regimen as the first line therapy.

Hung-Chin Tsai[1], I-Tzu Chen[1], Hui-Min Chang[2] , Ya-Wei Weng [1], Kuan-Sheng Wu [1], Yao-Shen Chen[1]

[1]Section of Infectious Diseases, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan and National Yang -Ming University, Taipei, Taiwan.

[2]Section of Pharmacy, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan

Address: 386,Ta-Chung 1st Rd, Kaohsiung 813,Taiwan
Tel: +886-7-342-2121ext 72187
E-mail: hctsai1011@yahoo.com.tw

Abstract

Objectives:
To describe integrase strand transfer inhibitor (INSTI) resistance profiles in antiretroviral -experienced patients failing an INSTI-based single tablet regimen (STR) in southern Taiwan

Methods:
This multicenter retrospective study was conducted in Taiwan between 2015 and 2023. Clinical samples were obtained island wide from patients failing a STR requested for genotypic drug resistance testing at our reference laboratory. Virological failure was defined as a plasma viral load ≧1000 copies/ml. Resistance-associated mutations were guided by the 2022 IAS-USA mutational list. Drug resistance was analyzed using the HIV Stanford HIVDB 9.4 edition algorithm. Logistic regression analysis was used to analyze the risk factors associated with INSTI resistance.

Results:
A total of 216 patients failed to STRs, of whom 116 failed on NNRTI-based STRs, 1 on PIs, and 99 on INSTIs. Seventy-eight patients had INSTI drug resistance testing results available, of whom 24.4% (19/78) showed INSTI resistance at failure. Among them, 9.4% (5/53) resistance to DTG-based STR and 12.5% (1/8) to BIC/FTC/TAF. None of the treatment naïve patients with DTG or BIC based STR failure developed INSTI resistance. Among the 22 patients failed to EVG/COBI/TAF/FTC, 76.5% (13/17) developed INSTI resistance.

Conclusions:
INSTI resistance was uncommon when failure if the DTG or BIC based STR was used as the first line therapy. INSTI resistance should be considered when patients failed to first generation INSTI, such as EVG/COBI/TAF/FTC.

Table 1. Risk factors associated with EVG/COBI/TAF/FTC failure in logistical regression analysis

	Non- EVG/COBI/TAF/FTC failure (n=77)	EVG/COBI/TAF/FTC failure (n=22)	*p* value	Univariate OR (95% CI)	*p* value	Adjusted OR (95% CI)
Gender						
Female	6 (7.8)	0 (0)	0.333			
Male	71 (92.2)	22 (100)				
Age (median, IQR)	32 (27-39)	36 (30-47)	0.141			
Transmission route for HIV						
Non-MSM	15 (20.5)	2 (9.1)	0.343	2.586 (0.543-12.313)		
MSM	58 (79.5)	20 (90.9)				
viral load (log) copies/ml (median, IQR)	4.7 (4.2-5.1)	4.6 (3.6-4.8)	0.252			
CD4 μl/cells (median, IQR)	185 (55-389)	165 (86-288)	0.595			
HIV subtype						
Non-B	10 (13)	1 (4.5)	0.447	3.134 (0.379-25.937)		
B	67 (87)	21 (95.5)				
***pol* resistance**						
No	50 (64.9)	5 (22.7)	0.001*	6.296 (2.093-18.944)	0.075	0.023 (0.000-1.472)
Yes	27 (35.1)	17 (77.3)				
***pol* mutation**						
No	43 (55.8)	3 (13.6)	0.001*	8.010 (2.187-29.334)	0.331	3.754(0.261-53.953)
Yes	34 (44.2)	19 (86.4)				
NRTI resistance						
No	64 (83.1)	6 (27.3)	0.001*	13.128 (4.319-39.903)	0.590	2.773 (0.068-113.036)
Yes	13 (16.9)	16 (72.7)				
NNRTI resistance						
No	62 (80.5)	11 (50)	0.007*	4.133 (1.508-11.328)	0.106	7.908 (0.644-97.138)
Yes	15 (19.5)	11 (50)				
PI resistance						
No	75 (97.4)	22 (100)	1.000			
Yes	2 (2.6)	0 (0)				
INSTI resistance, n=78						
No	55 (90.2)	4 (23.5)	0.001*	29.792 (7.331-121.068)	0.043*	64.082 (1.150-3569.380)
Yes	6 (9.8)	13 (76.5)				
Months on HAART (median, IQR)	43 (12.3-72.8)	44 (11.5-84)	0.655			
Months on Current regimen (median, IQR)	9 (3.3-21)	7.5 (3.8-16)	0.889			
Hepatitis B surface antigen						

Background

Single tablet regimen (STR) has been associated with better drug adherence, and a low resistance rate in treatment-naïve patients. Limited clinical data are available on the prevalence of HIV resistance, especially for patients with integrase strand transfer inhibitors (INSTI) virological failure in an area with universal implementation of STR as the first line therapy.

Materials & Methods

This multicenter retrospective study was conducted in Taiwan between 2015 and 2023. Clinical samples were obtained island wide from patients failing a STR requested for genotypic drug resistance testing at our reference laboratory. Virological failure was defined as a plasma viral load ≧1000 copies/ml. Resistance-associated mutations were guided by the 2022 IAS-USA mutational list. Drug resistance was analyzed using the HIV Stanford HIVDB 9.4 edition algorithm. Logistic regression analysis was used to analyze the risk factors associated with INSTI resistance.

Results

A total of 216 patients failed to STRs, of whom 116 failed on nonnucleoside reverse transcriptase inhibitors based STRs, 1 on protease inhibitors, and 99 on INSTIs. For the 99 patients who failed on INSTI based STRs, 26 were treatment naïve with INSTI based STR failure and 73 were virological failure after switching to INSTI based STRs. A total of 60 patients failed to abacavir/dolutegravir/lamivudine (ABC/DTG/3TC), 3 to dolutegravir/lamivudine (DTG/3TC), 22 to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/TAF/FTC) and 14 to bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF). Seventy-eight patients had INSTI drug resistance testing results available, of whom 24.4% (19/78) showed INSTI resistance at failure. Among them, 9.4% (5/53) resistance to DTG based STR and 12.5% (1/8) to BIC/FTC/TAF. None of the treatment naïve patients with DTG or BIC based STR failure developed INSTI resistance. Among the 22 patients failed to EVG/COBI/TAF/FTC, 76.5% (13/17) developed INSTI resistance. Logistic regression analysis showed that the patients with EVG/COBI/TAF/FTC failure were more likely development of INSTI resistance (p=0.043, adjusted OR 64.08, 95% CI: 1.15-3569) and being hepatitis B carrier (p=0.019, adjusted OR 33.37, 95% CI: 1.79-621) compared to DTG or BIC based STR failure. (Table1.)

Conclusion

INSTI resistance was uncommon when failure if the DTG or BIC based STR was used as the first line therapy. INSTI resistance should be considered when patients failed to first generation INSTI, such as EVG/COBI/TAF/FTC.

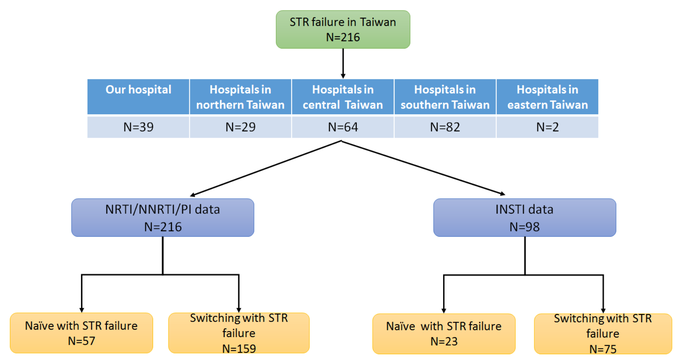

Figure1. The study samples from island wide hospitals requesting for genotype drug resistance testing were summarized.

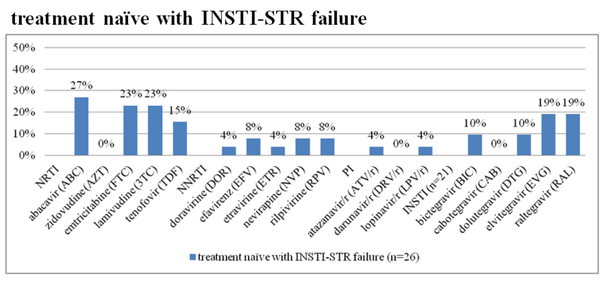

Figure2. Prevalence of drug resistance to NRTIs, NNRTIs, PIs and INSTIs among 26 treatment naïve patients with INSTI based STR failure and 73 virological failure after switching to INSTI based STR.

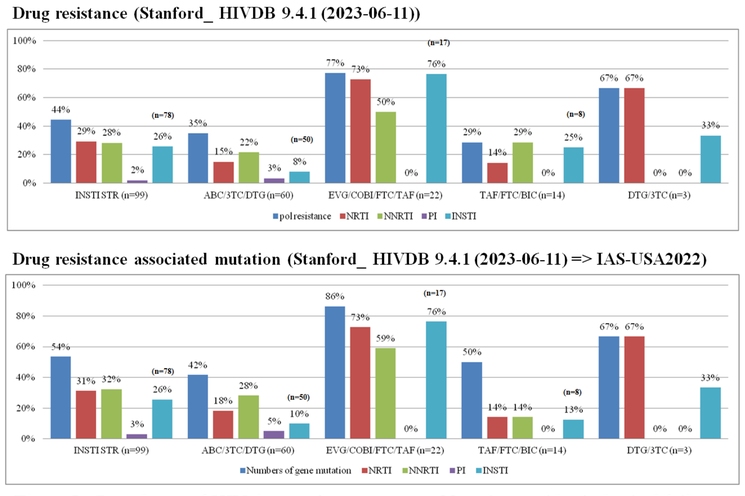

Figure3. Prevalence of HIV drug resistance among 99 patients with virological failure to INSTI based STR enrolled from 2015 to 2023.

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