Bictegravir/Emtricitabine/Tenofovir Alafenamide in Patients with Genotypic NRTI Resistance

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Background

- Nucleoside reverse transcriptase inhibitor (NRTI) resistance associated mutations (RAMs) are common in treatment-experienced people living with HIV (PLWH) who have failed one or more antiretroviral regimens.
- Bictegravir/emtricitabine/tenofovir alafenamide (BFT) is currently approved for PLWH with no known resistance mutations to the individual components.
- In BFT switch studies, pre-existing resistance mutations, such as RT M184V/I, identified retrospectively through proviral DNA genotyping did not impact maintenance of viral suppression with BFT.
- The objective of this study was to evaluate the effectiveness of BFT in patients with previously documented NRTI RAMs identified by standard genotype antiretroviral resistance testing (GART).

Methods

- Retrospective analysis of PLWH followed by the Northern Alberta Program (NAP) in Edmonton, Alberta.
- Patients included were: ≥ 18 years of age, receiving BFT, ≥ 1 NRTI RAM identified by GART, and ≥ 1 HIV RNA measurement following initiation of BFT.
    - NRTI RAMs were defined according to the 2019 IAS-USA update
- A search of electronic medical records was used to identify patients initiated on BFT.
    - Patients receiving BFT that met the study inclusion criteria were included in the analysis
- Demographic, genotypic, and virologic data as well as duration of BFT treatment were collected and analyzed descriptively.

Results (n=47)

Parameter	n (%)
Males	30 (64)
Age in years at start of BFT, **mean (range)**	54 (30-77)
Duration of documented HIV infection in **years**, **mean**	18.5
Proximal CD4 count (cells/mm^3), **mean (range)**	613 (60-1540)
Suppressed viral load at start of BFT*	44 (94)
Resistance mutations prior to start of BFT NRTI NNRTI PI INSTI	 47 (100) 23 (49) 17 (36) 0 (0)
Regimen prior to switching to BFT Multi-tablet Contained boosted PI	 41 (87) 28 (60)
Duration on BFT at last HIV RNA measurement in **months**, **mean**	10.3
HIV RNA <50 copies/mL at last follow-up	47 (100)

Number of IAS-USA NRTI RAMs**	n	Number with M184V/I
One	29	23
Two	8	7
Three	3	3
Four	3	2
Five	2	2
Six	1	1
Seven	1	1

** M41L, A62V, K65R/E/N, D67N, K70R/E, L74V, V75I, F77L, Y115F, F116Y, Q151M, M184V/I, L210W, T215Y/F, K219Q/E

39 of 47 had M184V/I; no patient had K65R/E, V75I, F77L , F116Y or Q151M

* HIV RNA > 100 copies/mL; two were treatment naïve; one had run out of prior antiretroviral therapy

Specific NRTI RAMs in patients with ≥ 3 RAMs treated with BIC/FTC/TAF (n=10)

	Patient #	RAMs
3 RAMs	1	A62V, M184V, T215Y
	2	M41L, M184V, T215Y
	3	L74V, Y115F, M184V
4 RAMs	4	M41L, M184V, L210W, T215Y
	5	D67N, K70R, M184V, K219Q
	6	M41L, D67N, L210W, T215Y
5 RAMs	7	M41L, D67N, M184V, L210W, T215Y
	8	M41L, D67N, M184V, L210W, T215Y
6 RAMs	9	M41L, D67N, K70R, M184V, T215F, K219Q
7 RAMs	10	M41L, D67N, K70R, L74V, M184V, T215Y, K219Q

Discussion and Conclusions

- At a mean follow-up of 10.3 months, BFT was effective in suppressing HIV RNA in all 47 patients with genotypically documented NRTI resistance, including 10 patients with $\geq$ 3 NRTI mutations.
- Switching to BFT reduced pill burden and eliminated boosted PIs in many patients.
- None of the 47 patients had documented RT K65R/E or integrase resistance mutations.
- Further research is needed to evaluate the effectiveness of BFT in viremic patients with NRTI resistance.