Switching to bictegravir/emtricitabine/tenofovir alafenamide single tablet regimen from boosted protease inhibitor-based ART in virologically suppressed adults with HIV-1 harbouring drug resistance: a Phase IV randomised, open-label pilot study (PIBIK)

Collins Iwuji[1,2], Laura Waters[3], Ana Milinkovic[4,11], Chloe Orkin[5,6], Nicky Perry[7], Natalie Dailey[8], Ye To[8], Chris Jones[8,9], Stephen Bremner[8,9], Anna Maria Geretti[10], Duncan Churchill[7]

1. Dept. of Global Health and Infection, Brighton & Sussex Medical School, University of Sussex, UK 2. Africa Health Research Institute, KwaZulu-Natal, South Africa; 3. Mortimer Market Centre, Central & North West London NHS Trust, London, UK; 4. Chelsea & Westminster Hospital NHS Foundation Trust, London, UK; 5. Barts Health NHS Trust, London, UK; 6. Queen Mary University of London, London, UK; 7. University Hospitals Sussex NHS Foundation Trust, UK; 8. Brighton & Sussex Clinical Trials Unit, University of Sussex, UK; 9. Department of Primary Care and Public Health, Brighton and Sussex Medical School, University of Sussex, Brighton, UK; 10. Institute of Infection, University of Liverpool, UK, 11. Imperial College London

HIV Drug Therapy. Glasgow conference, 23-26 October 2022

P089

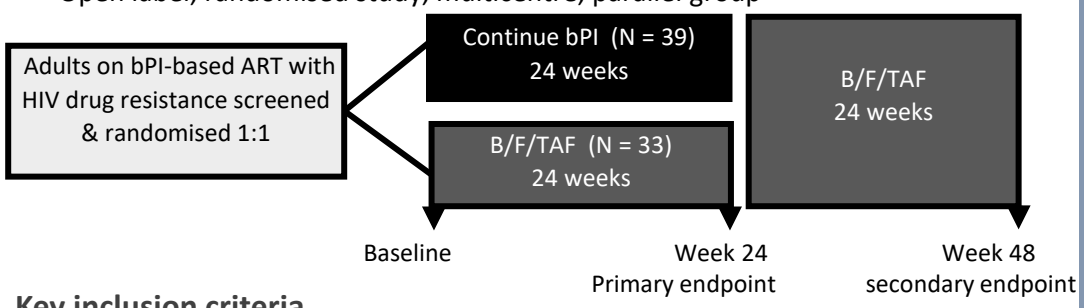
BACKGROUND

- Boosted protease inhibitor-based (bPI) regimens are often the treatment of choice for people living with HIV (PLWH) with pre-treatment or treatment-acquired resistance but have a high potential for drug-drug interactions
- It is feasible that carefully selected PLWH with drug resistance, virologically suppressed on a bPI, could maintain virologic efficacy on bictegravir, emtricitabine and tenofovir alafenamide (B/F/TAF) fixed dose combination, but data on the efficacy and safety of this strategy are limited
- We evaluated this approach and present week 24 results

METHODS

Study design

- Open label, randomised study, multicentre, parallel group



Key inclusion criteria

- HIV-1 RNA <50 c/mL for at least 6 months on current regimen and at screening
- Historical genotype with any of the following drug resistance mutations
  - M184V/I with or without any NRTI-associated mutation (e.g. L74I/V, Y115F, K70E/G/Q/T/N/S)
  - Up to 2 TAMs (M41L, D67N, K70R, L210W, T215F/Y, or K219Q/E/N/R) with or without M184V/I
- No known INSTI mutations but previous INSTI use allowed

Primary endpoint

- Proportion with HIV-1 RNA <50 c/mL at Week 24 by pure virologic response (PVR):
  - On study treatment
  - No confirmed virologic rebound defined as:
    - HIV RNA ≥ 50 c/mL on 2 consecutive visits
    - HIV-1 RNA ≥ 50 c/mL during study followed by premature discontinuation
- Discontinuation prior to week 24 for reasons other than virologic rebound (i.e. no data in window and last HIV RNA < 50 c/mL) are considered PVR

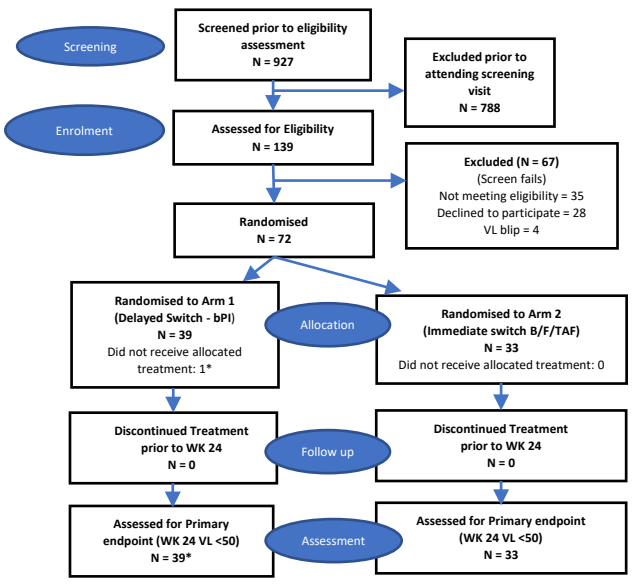
Table 1. Baseline characteristics by group

	B/F/TAF, N=33	Boosted PI N=39
Age (years): mean (SD)	53.1 (8.1)	55.6 (7.0)
Sex: Male n (%)	29 (88)	35 (90)
Race: White n (%)	23 (70)	30 (76)
CD4 count: n; median (IQR)	32; 560 (457 to 800)	39; 632 (453 to 854)
Duration on ART (years): n; median (IQR)	22; 5.2 (2.9 to 13.5)	32; 8.1 (3.3 to 12.5)
Boosted PI at randomisation:		
Darunavir	28 (85)	30 (77)
Atazanavir	5 (15)	9 (23)
Drug resistance mutations (historical genotype)		
<2 NRTI mutations	17 (52)	17 (44)
≥2 NRTI mutations	16 (48)	22 (56)
M184V/I only	12 (36.4)	7 (18.0)
1 TAM ± M184V/I ± NAM	10 (30.3)	19 (48.7)
2 TAMs ± M184V/I ± NAM	6 (18.2)	9 (23.1)
M184V/1+ NAM	3 (9.1)	2 (5.1)
On lipid lowering drugs	11 (33)	14 (36)
eGFR (Cockcroft-Gault) ml/min/1.73m^2: mean (SD)	106.0 (36.5)	105.2 (26.7)

TAM = Thymidine analogue mutation (M41L, D67N, K70R, L210W, T215F/Y, or K219Q/E/N/R);
NAM Nucleoside analogue mutation (L74I/V, Y115F, K70E/G/Q/T/N/S); SD is standard deviation, IQR is interquartile range

RESULTS

Fig 1. CONSORT flow chart



*Included in the assessment of PVR based on definition of PVR

Week 24 Efficacy

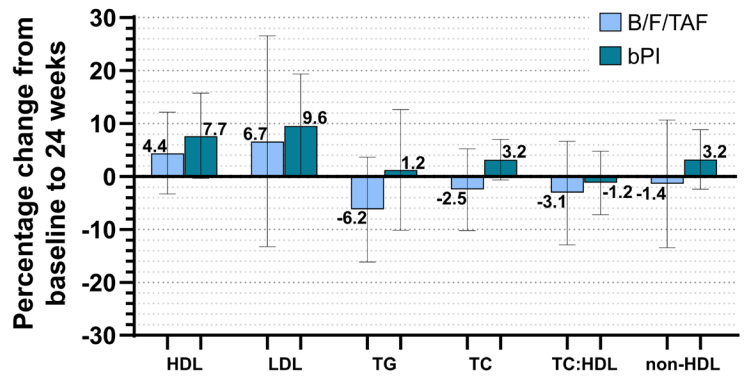
- PVR with HIV-1 RNA <50 c/mL:
  - B/F/TAF = 33/33 (100%);
  - bPI = 38/39 (97.4%)
- Difference in proportions:
  - B/F/TAF vs. bPI: **2.6%, 95% CI (-2.4% to 7.5%)**

Table 2. Adverse Events (AE) through 24 Weeks, by group

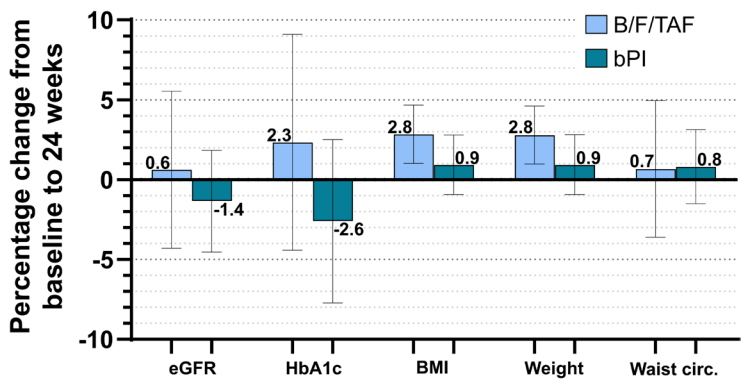
	B/F/TAF (n=33)		bPI (n=39)	
Classification	Participants n (%)	Adverse events (n)	Participants (n) %	Adverse events (n)
Any adverse events	24 (72.7)	76	23 (59.0)	58
Grade 3 or 4 AEs	1* (3.0)	1	0	
Serious adverse events	0		1** (2.6)	1
Drug-related adverse events	12 (36.4)	24	0	
Discontinuation due to adverse events	0		0	
Deaths	0		0	
Most common AEs				
Headache	4 (12.1)		3 (7.7)	
Weight gain	4 (12.1)		0	
Abnormal dreams	3 (9.1)		0	
Hypertension	3 (9.1)		1 (2.6)	
Insomnia/sleep disturbance	4 (12.1)		0	

AE = Adverse event, *Hypertension; **Squamous cell cancer of the rectum

Fig 2. % change in lipid parameters from baseline to WK 24, by group



		HDL	LDL	TG	TC	TC:HDL	non-HDL
Mean (SD) at baseline	B/F/TAF	1.35 (0.45)	2.96 (0.98)	1.80 (1.10)	5.07 (1.03)	4.12 (1.49)	3.72 (1.06)
	bPI	1.33 (0.42)	2.85 (1.00)	1.96 (1.47)	4.99 (1.09)	3.99 (1.19)	3.65 (1.04)
Mean (SD) at week 24	B/F/TAF	1.33 (0.36)	2.86 (0.85)	1.58 (0.89)	4.82 (0.98)	3.85 (1.22)	3.49 (1.00)
	bPI	1.41 (0.49)	2.93 (0.96)	1.76 (1.15)	5.05 (1.15)	3.82 (1.06)	3.64 (0.95)



		eGFR	HbA1c	BMI	Weight	Waist circ.
Mean (SD) at baseline	B/F/TAF	105.96 (36.54)	35.77 (7.00)	28.25 (6.11)	86.99 (19.53)	100.33 (12.43)
	bPI	105.20 (26.73)	34.89 (6.52)	27.16 (4.67)	83.87 (15.05)	98.00 (12.97)
Mean (SD) at week 24	B/F/TAF	105.89 (40.14)	37.03 (9.79)	29.22 (6.90)	90.09 (22.55)	101.26 (15.84)
	bPI	102.92 (23.80)	35.86 (7.99)	26.80 (4.67)	82.90 (14.97)	98.29 (11.32)

Fig 3. % change in other parameters from baseline to WK 24, by group

DISCUSSION

- Presence of limited NRTI resistance did not compromise virologic efficacy of switching to B/F/TAF at 24 weeks compared to continued bPI-based ART
- 12 (36.4%) participants on B/F/TAF experienced drug-related AEs, all were mild or moderate with no B/F/TAF related discontinuations
- Lipids improved after a switch to B/F/TAF except a slight decrease in HDL (Fig 2); HBA1c, BMI and weight increased following a switch to B/F/TAF (Fig 3)
- Switching to B/F/TAF was safe and well tolerated

ACKNOWLEDGEMENTS & FUNDING: This study is an investigator sponsored research funded by Gilead Sciences. We thank the study sites for their hard work in ensuring the study was a success despite COVID-19. We also thank the patients and oversight committee involved with the study.