Integrase Inhibitor Versus Protease Inhibitor Based Therapy for People with Advanced HIV Disease (LAPTOP)

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Georg MN Behrens [1], Lambert Assoumou [2], Geoffrey Liegeon [3], Andrea Antinori [4], Rafael Mican [5], Stephane De Wit [6], Frank Post [7], Juergen K Rockstroh [8], Lisa Hamzah [9] , Pere Domingo [10], Adrian Curran [11], Montserrat Laguno [12] , Carl Fletcher [13], Jack Moody [13], Anton Pozniak [14] on behalf of the LAPTOP Study Team [15]

[1]Department of Rheumatology and Immunology, Hannover Medical School, Hannover, Germany ; [2]Centre de méthodologie et de gestion (CMG), Institut Pierre Louis d'Epidémiologie et de Santé Publique, Paris, France ; [3]Service des Maladies Infectieuses et Tropicales, Hospital Saint-Louis and Lariboisière, Paris, France; [4]Unità Operativa Complessa (UOC) Immunodeficienze Virali, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Roma, Italy; [5]Unidad de Enfermedades Infecciosas, Hospital Universitario La Paz, Madrid, Spain; [6]Department of Internal Medicine, University Hospital of Saint-Pierre, Brussels, Belgium [7]Department of Inflammation Biology, Kings College Hospital NHS Foundation Trust, London, UK; [8]Department of Internal Medicine, University Hospital Bonn, Bonn, Germany ; [9]Department of Clinical Infection, St George's Hospital, London, UK ; [10]Infectious Diseases Unit, Hospital de la Santa Creu I Sant Pau, Barcelona, Spain ; [11]Department of Infectious Diseases, Hospital Universitario Vall d'Hebron, Barcelona, Spain ; [12]Infectious Diseases Service, Hospital Clinic de Barcelona, Barcelona, Spain ; [13]Project Management, Research Organisation (Kings Cross), London, UK ; [14]Department of Infectious Diseases, Chelsea and Westminster NHS Foundation Trust, London, UK ; [15]N/A, Research Organisation (Kings Cross), London, UK.

BACKGROUND

Most first line HIV treatment randomised controlled trials recruit individuals who have low baseline viral loads, high CD4 counts, fewer co-morbidities, drug-drug interactions, and other treatment failure risks than in **people with advanced HIV disease (PWAH)**. To date clinical trials have been underpowered to assess the preferred antiretrovirals in therapy-naïve PWAH. We conducted the LAPTOP trial across 7 European countries, investigating the efficacy and safety of an integrase inhibitor (INI) versus a boosted protease inhibitor (PI) containing regimen in PWAH.

METHODS

This is an investigator-initiated, open-label, European, multi-centre, non-inferiority, controlled trial comparing outcomes for therapy-naïve PWAH aged ≥18 years, randomised 1:1 to receive bictegravir (BIC) or darunavir (DRV)/ cobicistat co-formulated with emtricitabine (FTC)/ tenofovir alafenamide (TAF) for 48 weeks.

Primary Outcome:

Time to failure, as the first occurrence of any of a composite of specified virological failure (insufficient virological response was defined as HIV-1 RNA reduction <1 log 10 copies/mL at week 12, or viral load >50 HIV-1 RNA copies/mL at week 48) or clinical events plus the individual components were evaluated by Kaplan Meier and Cox regression analyses, with a non-inferiority margin of 1.606 in the hazard ratio.

Table 1: Baseline Characteristics

		Total (N=442)
Age (years), median (IQR)		43 (35-53)
Gender (%)	Male	358 (81.0)
	Female	84 (19.0)
Ethnicity (%)	White	276 (62.4)
	Black	83 (18.8)
	Other	83 (18.8)
CD4+ Count <100 cells/µL (%)		379 (85.8)
CD4+ Count cells/µl, median (IQR)		41 (17-79)
HIV RNA viral load >500,000 log10 copies/mL (%)		197 (44.6)
HIV RNA viral load log10 copies/mL, median (IQR)		5.6 (5.1-6.0)

RESULTS

Figure 1: Primary Composite Endpoint and its Components

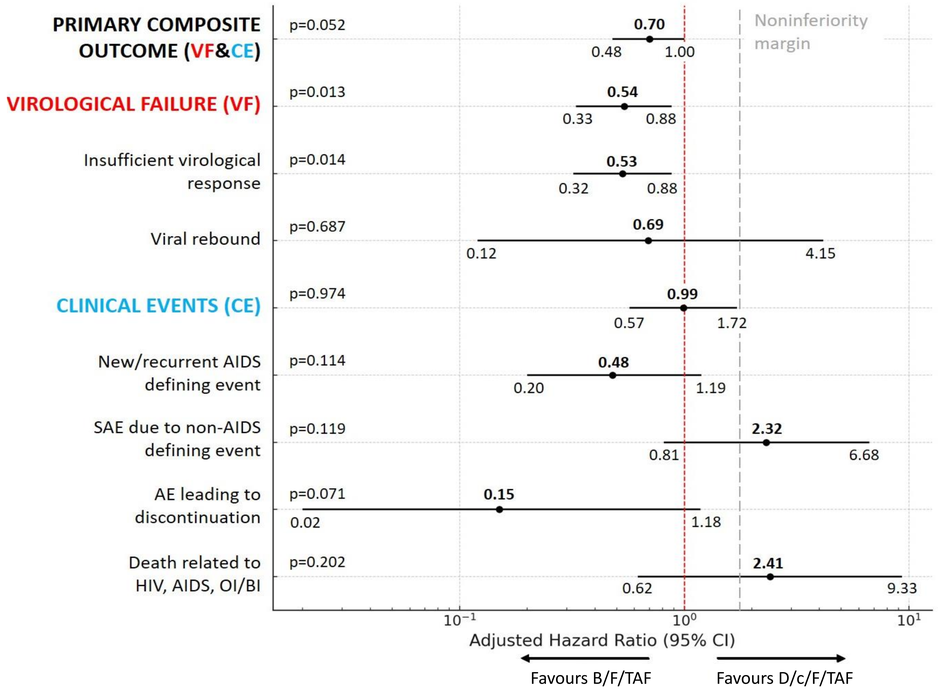


Table 2: Primary Composite Endpoint and its Components (Modified Intent to Treat, mITT and Per Protocol, PP Analysis)

	mITT analysis				PP analysis			
	B/F/TAF	D/c/F/TAF	Adjusted Hazard ratio	p-value	B/F/TAF	D/c/F/TAF	Adjusted Hazard ratio	p-value
	N=220	N=222			N=219	N=222		
Primary composite endpoint	49 (23.8)	70 (33.9)	0.70 (0.48-1.00)	0.052	48 (23.4)	69 (33.4)	0.69 (0.48-1.00)	0.051
Virological failure	25 (13.4)	46 (23.9)	0.54 (0.33-0.88)	0.013	25 (13.4)	46 (23.9)	0.54 (0.33-0.88)	0.013
Insufficient virological response	23 (12.4)	43 (22.5)	0.53 (0.32-0.88)	0.014	23 (12.4)	43 (22.5)	0.53 (0.32-0.88)	0.014
Viral rebound	2 (1.0)	3 (1.5)	0.69 (0.12-4.15)	0.687	2 (1.0)	3 (1.5)	0.69 (0.12-4.15)	0.687
Clinical events	25 (11.8)	26 (12.1)	0.99 (0.57-1.72)	0.974	24 (11.3)	25 (11.6)	0.99 (0.56-1.73)	0.965
Any new/recurrent AIDS event ≥28 days of therapy	7 (3.5)	15 (7.2)	0.48 (0.20-1.19)	0.114	7 (3.5)	14 (6.7)	0.52 (0.21-1.29)	0.161
SAE due to Non-AIDS events	11 (5.3)	5 (2.3)	2.32 (0.81-6.68)	0.119	10 (4.9)	5 (2.3)	2.09 (0.72-6.13)	0.177
AE leading to discontinuation	1 (0.5)	7 (3.3)	0.15 (0.02-1.18)	0.071	1 (0.5)	7 (3.3)	0.15 (0.02-1.19)	0.072
Death related to HIV, AIDS, OI/BI	7 (3.3)	3 (1.4)	2.41 (0.62-9.33)	0.202	7 (3.3)	3 (1.4)	2.42 (0.63-9.35)	0.202

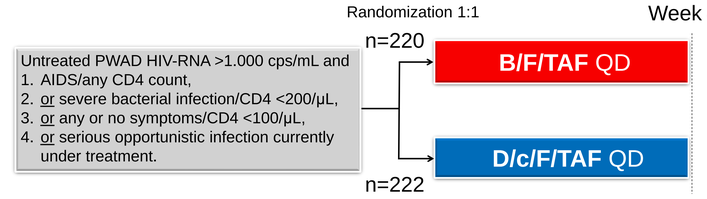


Figure 2: HIV-RNA and CD4 Cell Counts

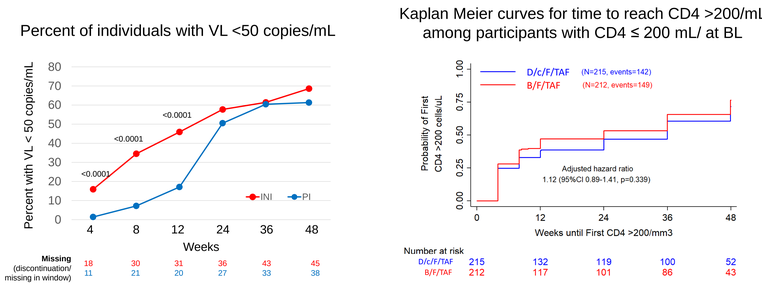
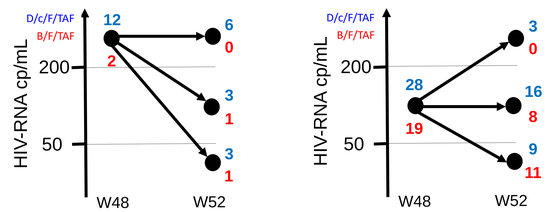


Figure 3: Evolution of HIV-RNA in Individuals with Viral Load >50 Copies/mL at Week 48



Week 52 viral loads in individuals (numbers) with >200 (left) or 50-200 HIV-RNA copies/mL (right) at week 48 (= protocol defined virological failure) according to treament arm. Participants with missing results/visits at week 52 or ART switch at week 48 were excluded from this analysis.

Table 3: Drug-Related Safety Events

	B/F/TAF (220)	D/c/F/TAF (222)	Adjusted Incidence rate ratio (IRR)	P-value
Any Adverse Event Grade ≥2				
Number of events	435	548		
Incidence rate per 100 p-y	220.5	264.7	0.82 (0.73-0.93)	0.0024
Drug Related Grade ≥2 AEs				
Number of events	27	45		
Incidence rate per 100 p-y	13.7	21.7	0.61 (0.38-0.98)	0.0431
Drug Related Grade 3-4 AEs				
Number of events	5	5		
Incidence rate per 100 p-y	2.5	2.4	0.99 (0.29-3.44)	0.9931

In people with advanced HIV disease the B/F/TAF regimen was non-inferior to the D/c/F/TAF regimen in terms of the composite outcome but had a better virologic response at week 48 and fewer overall AE's.

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