405 IMPACT OF ANTIRETROVIRAL REGIMENS ON MORTALITY IN PATIENTS WITH ADVANCED HIV DISEASE

Joaquin Burgos-Cibrian[1], Sergio Moreno Fornés[2], Juliana Reyes-Urueña[2], Andreu Bruguera[2], Berta Raventós[3], Josep María Llibre[4], Arkaitz Imaz[5], Pere Domingo[6], Emili Letang[7], Joaquin Peraire[8], Joaquin-Amat Orti[9], David Dalmau[10], Jordi Casanova[2], Jose M. Miro[11], Vicenç Falcó[1], for the PISCIS Investigators
[1]Hospital Universitario de la Vall d'Hebron, Barcelona, Spain, [2]Centre d'Estudis Epidemiològics Sobre les ITS i Sida de Catalunya, Barcelona, Spain, [3]Vall d'Hebron Research Institute, Barcelona, Spain, [4]Hospital Germans Trias i Pujol, Barcelona, Spain, [5]Bellvitge University Hospital, Barcelona, Spain, [6]Hospital Sant Pau, Barcelona, Spain, [7]Hospital del Mar, Barcelona, Spain, [8]Hospital Universitari Joan XXII, Tarragona, Spain, [9]Hospital Verge de la Cinta, Tarragona, Spain, [10]TaiMed Biologics Inc, Taipei City, Taiwan, [11]Hospital Clinic of Barcelona, Barcelona, Spain

Background: Scarce data exist regarding the efficacy of antiretroviral (ARV) treatment in patients with advanced HIV disease. The aim of the study was to assess the impact of ARV regimens on the clinical outcomes among naïve patients with advanced HIV presentation in real life settings.

Methods: A multicentre, population-based, prospective cohort study was performed. Treatment-naive subjects with advanced HIV diseases (CD4+T cell count < 200 cells/ml or presence of an AIDS-defining illness) who started therapy between 2010 and 2018, from 18 hospitals in Spain, were included. The primary outcome was the rate of mortality at three years. Secondary outcomes included discontinuation or change of ARV regimen, virological effectiveness (viral load of ≤ 200 copies/ml) and immune reconstitution (achieve CD4+T cell count > 350 cells/ml). Kaplan-Meier curves and long-rank test were used to analyse different outcomes. A Cox proportional hazard model was performed to identify predictors of death

Results: A total of 1170 naive patients with advanced HIV disease started ARV treatment: 44.9% with PIs based regimen, 29.6% with NNRTIs and 25.6% with InSTI. The most frequently third-drug was darunavir (73%), efavirenz (70.9%) and dolutegravir (47%), respectively. The median follow-up was 5 years (5695 person-years), median CD4+T cell count at baseline was 101 cells/ml and 30.3% had an AIDS-defining illness. Crude mortality rate at three years of follow-up was 6.1% (95% CI, 4.1-8.1) for PI based regimen, 4% (95% CI, 1.8-6.2) for NNRTI and 2.6% (95% CI, 0.9-4.3) for InSTI. In patients with an AIDS-defining illness, mortality rate was 14.6% (95% CI, 7.2-21.4) for PI, 9.1% (95% CI, 2.4-7) for NNRTI and 5.8% (95% CI, 1.0-11.4) for InSTI. Factors associated with mortality were higher age and AIDS-defining illness at inclusion, whilst treatment with InSTI regimen had a trend as protective factor (HR 0.53, 95% CI, 0.25-1.14). Patients who started with InSTI based regimen achieved viral suppression and immune reconstitution earlier (0.2 and 0.3 years, respectively), than those with PI and NNRTI based regimens, (1.1 and 1.4; 0.3 and 0.9, respectively). Over the follow-up period, 56.8% of patients with PI regimen, 53.9% with NNRTI and 13.6% with InSTI changed treatment.

Conclusion: In this large real-life cohort study, a lower mortality and a less rate of discontinuation in patients treated with InSTIs regimens were observed among naive patients with advance HIV disease.

Cumulative probability of progression to mortality, virological effectiveness and immune restoration by compared the three ART regimens on-treatment

Endpoint	1-year cumulative rate (95% CI)	2-year cumulative rate (95% CI)	3-year cumulative rate (95% CI)
Mortality	PI: 4.6 (2.8; 6.4) NNRTI: 1.3 (0.0; 2.6) InSTI: 2.0 (0.5; 3.5)	PI: 5.1 (3.2; 7.0) NNRTI: 2.3 (0.6; 4.1) InSTI: 2.3 (0.7; 3.9)	PI: 6.1 (4.1; 8.1) NNRTI: 4.0 (1.8 6.2) InSTI: 2.6 (0.9; 4.3)
Virological effectiveness (=200 copies/ml)	PI:92.7 (89.9; 94.7) NNRTI:92.0 (88.1; 94.68) InSTI: 98.0 (95.6; 99.1)	PI:96.2 (93.9; 97.6) NNRTI:94.8 (91.3; 96.9) InSTI: 99.2 (96.9; 99.8)	PI: 97.9 (95.9; 98.9) NNRTI:97.6 (94.5; 98.9) InSTI: 100.0 (97.2; 100.0)
Immune restoration (> 350 CD4/ml)	PI:30.9 (26.6; 34.9) NNRTI:42.8 (36.7; 48.3) InSTI: 43.9 (38.0; 49.2)	PI: 53.5 (48.6; 58.0) NNRTI: 60.3 (53.9; 65.7) InSTI: 66.6 (60.5; 71.8)	PI:65.9 (61.0; 70.2) NNRTI:73.4 (67.4; 78.4) InSTI: 78.9 (72.7; 83.6)

InSTI: integrase strand transfer inhibitors. NNRTI: nonnucleoside reverse transcriptase inhibitors. PI: protease inhibitors. 95% CI (Confidence interval of 95%)

406 EFFECTIVENESS OF RECOMMENDED 3-DRUG REGIMENS FOR TREATING ADVANCED HIV INFECTION

Karam Mounzer[1], Laurence Brunet[2], Jennifer S. Fusco[2], Ian McNicholl[3], Helena Diaz-Cuervo[3], MichaelEnsion[4], Lewis McCurdy[5], Gregory P. Fusco[2]
[1]Philadelphia FIGHT, Philadelphia, PA, USA, [2]Epividian, Durham, NC, USA, [3]Gilead Sciences, Inc, Foster City, CA, USA, [4]CAN Community Health, Fort Lauderdale, FL, USA, [5]Atrium Health, Charlotte, NC, USA

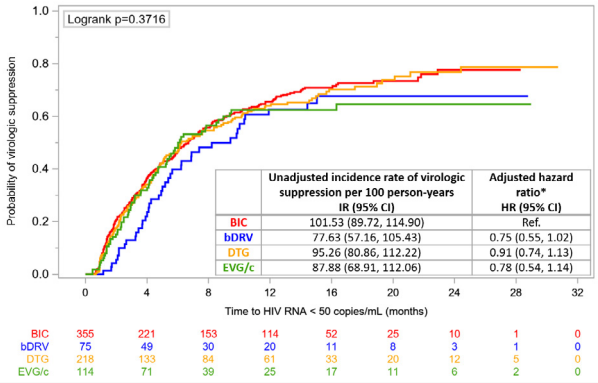
Background: There is limited evidence on regimen options for people living with HIV (PLWH) initiating antiretroviral therapy (ART) with advanced infection. The effectiveness of one of the newest 3-drug regimen (3DR), bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF), was therefore compared to other 3DRs that included boosted darunavir (bDRV), dolutegravir (DTG) or elvitegravir/cobicistat (EVG/c) among ART-naïve PLWH with CD4 count <200 cells/µL.

Methods: ART-naïve adults with advanced HIV-1 infection (CD4 count <200 cells/µL) initiating B/F/TAF or a bDRV, DTG or EVG/c-based 3DR between 01JAN2018 and 31JUL2019 in the OPERA Cohort were included. Regimen discontinuation and virologic suppression to <50 copies/mL were assessed with Kaplan-Meier methods and unadjusted Poisson regression. The association between regimen and virologic suppression was assessed with a Cox proportional hazards model with inverse probability of treatment weighting (Figure).

Results: Overall, 961 PLWH initiated ART with advanced HIV infection: 416 B/F/TAF (age ≤25: 10%, CD4 ≤50 cells/µL: 36%), 106 bDRV (age ≤25: 19%, CD4 ≤50: 33%), 271 DTG (age ≤25: 13%, CD4 ≤50: 30%), 168 EVG/c (age ≤25: 14%, CD4 ≤50: 38%). In unadjusted analyses, B/F/TAF initiators were statistically significantly less likely to discontinue their regimen (incidence rate per 100 person-years [IR]: 12.54; 95% confidence interval [CI]: 9.94, 15.83) compared to other regimens (range IR: 21.40 to 35.27). While 70% reached a CD4 count ≥200 cells/µL overall, CD4:CD8 ratio normalization (≥1) was achieved by <7% and did not differ across regimens (logrank p=0.52). Incident immune reconstitution inflammatory syndrome (IRIS) was rare (3 B/F/TAF, 1 bDRV, 2 DTG, 0 EVG/c). Follow-up viral loads were available for 762 PLWH (355 B/F/TAF, 75 bDRV, 218 DTG, 114 EVG/c). Baseline characteristics were well balanced with inverse probability of treatment weights. Compared to B/F/TAF, bDRV initiators were numerically less likely to achieve virologic suppression (adjusted hazard ratio: 0.75; 95% CI: 0.55, 1.02). No statistically significant difference in the likelihood of virologic suppression was detected between B/F/TAF and DTG or EVG/c 3DRs (Figure).

Conclusion: Among PLWH with advanced HIV infection initiating ART, those on B/F/TAF appeared less likely to discontinue their regimen compared to other 3DRs (unadjusted) and were numerically more likely to achieve virologic suppression compared to bDRV but did not differ from those on DTG or EVG/c-based 3DR (adjusted).

Figure. Virologic suppression (viral load < 50 copies/mL) over follow-up: cumulative probabilities (Kaplan-Meier), incidence rates (Poisson regression), and adjusted* association with regimen (Cox proportional hazard marginal structural model)



	Unadjusted incidence rate of virologic suppression per 100 person-years IR (95% CI)	Adjusted hazard ratio* HR (95% CI)
BIC	101.53 (89.72, 114.90)	Ref.
bDRV	77.63 (57.16, 105.43)	0.75 (0.55, 1.02)
DTG	95.26 (80.86, 112.22)	0.91 (0.74, 1.13)
EVG/c	87.88 (68.91, 112.06)	0.78 (0.54, 1.14)

*Marginal structural model with stabilized inverse probability of treatment weights controlling for baseline index year, age, CD4 cell count, viral load, sex, race, HBV