Poster #2488

Virologic Failure In ART-Naïve Patients Initiating on a Dolutegravir- or Elvitegravir-Based Regimen

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Background

- Current clinical guidelines[1,2] in Europe and the United States (U.S.) recommend the use of dolutegravir (DTG) as an initial core agent for most people living with HIV (PLWH), and elvitegravir (EVG) as a recommended core agent in specific clinical situations
- There are no randomized controlled trials (RCT) comparing DTG- and EVG-based regimens head-to-head
- Only a few European studies[3] and one U.S. based study[4] have used real world data to compare virologic outcomes between these agents directly and none of them have used inclusion/exclusion criteria similar to ART clinical trials

OBJECTIVE

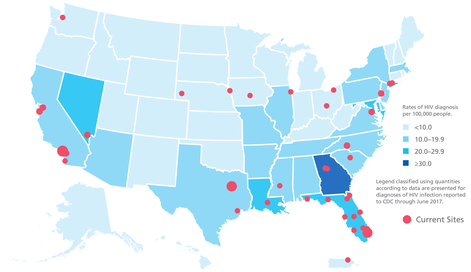
To compare virologic outcomes in an antiretroviral (ART) naïve population initiating a DTG- or EVG-containing regimen using clinical trial-like inclusion criteria

Methods

Study population

- OPERA Database: electronic medical records from a collaboration of HIV caregivers following 100,000+ PLWH (Fig 1)
- Inclusion/exclusion criteria approximated those used in DTG Phase III clinical trials, specifically FLAMINGO[5]. (Fig 2)
- Observation period: from the date of first prescription until DTG- or EVG- discontinuation, death, or study end (31July2018)

Figure 1. OPERA geographic distribution of sites and CDC (2017) state-by-state estimates of new HIV infections



Virologic Failure (VF)

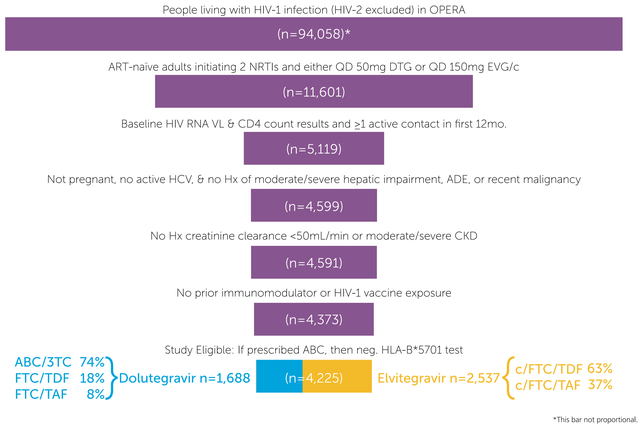
- Defined as any of:
  - » failure to achieve suppression (< 50 copies/mL) prior to 36 weeks
  - » 2 consecutive viral loads (VL) ≥ 200 copies/mL after suppression
  - » 1 VL ≥ 200 copies and discontinuation of the core agent after suppression

Statistical analyses

- Cox Proportional Hazard models
- Adjusted for baseline: age, sex, race, region, year of initiation, route of infection, CD4 cell count, viral load, VACS mortality score, payer and a history of endocrine disease, anxiety disorder, drug abuse, or syphilis

Results

Figure 2. Study Inclusion Criteria



*This bar not proportional.

Figure 3. Demographic Characteristics of Study Population

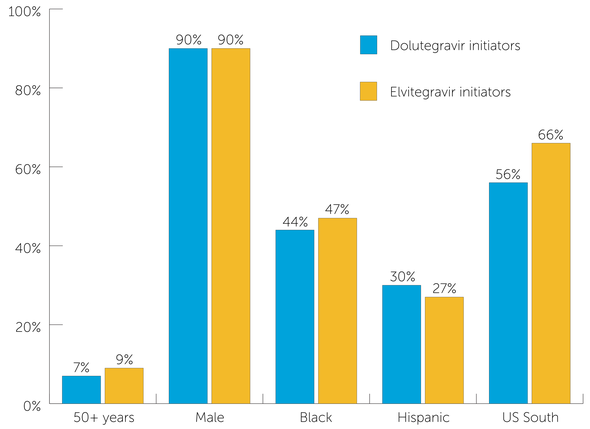


Figure 4. Clinical Characteristics of Study Population

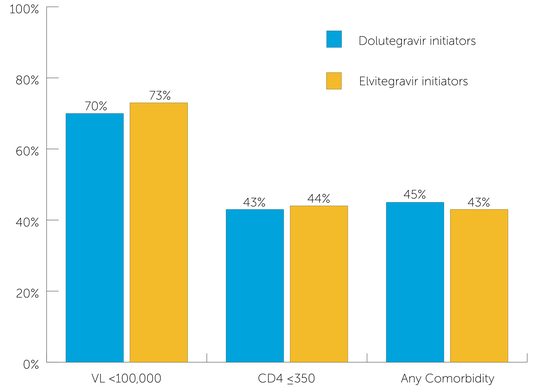
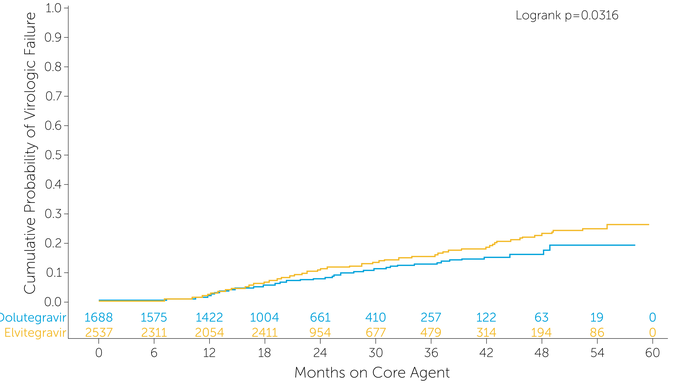


Table 1. Virologic Failure Among DTG- and EVG-initiators

Core Agent	n	Median follow-up months (IQR)	# of Virologic Failures*	Person-Years (PY)	Incidence Rate per 100 PY (95% CI)	Adjusted† Hazard Ratio (95% CI)
Dolutegravir	1688	21 (14-30)	128	3187.53	4.02 (3.38, 4.78)	1.00 (ref.)
Elvitegravir	2537	20 (14-32)	250	4873.99	5.13 (4.53, 5.81)	1.29 (1.02, 1.63)

* Virologic Failure defined as: (i) 2 VL>=200 after 36 weeks or (ii) 1 VL>=200 after 36 weeks + DC or (iii) 2 VL>=200 after suppression prior to 36 weeks, or (iv) VL>=200 after suppression prior to 36 weeks + DC.
†Adjusted for baseline age, sex, race, ethnicity, index year, U.S. region, CD4 cell count, HIV VL, VACS score, men who have sex with men, payer, and Hx of endocrine disorders, anxiety, drug abuse and syphilis

Figure 5. Unadjusted Cumulative Probability of Virologic Failure over Time on Core Agent



Discussion

- PLWH initiating ART with DTG or EVG presented similar demographic and clinical characteristics at initiation. DTG initiators were significantly:
  - » less likely to be African American (44% vs 47%, p<.05), to receive care in the South (56% vs 66%, p<.0001), to have a history of an anxiety disorder (8% vs. 11%, p<.01) or a concurrent prescription for an anxiolytic/hypnotic/sedative (2.7% vs 4.1%, p<.05)
  - » more likely to be either underweight (5% vs. 3%) or obese (18% vs. 16%), both p<.05; to be MSM (53% vs 47%, p<.0001), to receive care in the West (36% vs 24%, p<.0001) or to have a history of drug abuse (12% vs. 9%, p<.05) or endocrine disorders (11% vs. 9%, p<.05)
- After adjusting for patient demographic and baseline disease characteristics, initiating ART with a DTG-based regimen was associated with a statistically significant, reduced hazard of VF
- Strengths & Limitations:
  - » Large, real-world population; geographically representative of the US epidemic; modeling adjusted for a large number of important covariates
  - » Causal methods were not employed; residual bias may exist; potential lack of generalizability (RCT inclusion criteria may result in healthier study population)

KEY FINDINGS

Among ART-naïve patients, DTG initiators were statistically significantly less likely to experience virologic failure than EVG initiators after adjustment for important baseline covariates

References

1. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. 2018 October 25, 2018 02/05/2019]; Available from: https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf.
2. EACS. *European AIDS Clinical Society Guidelines, Version 8.0.* 2015 July 14, 2017]; Available from: http://www.eacsociety.org/guidelines/eacs-guidelines/eacs-guidelines.html.
3. d'Arminio Monforte, A., et al., *Durability of first-line regimens including integrase strand transfer inhibitors (INSTIs): data from a real-life setting.* J Antimicrob Chemother, 2019.
4. Mills A, Brunet L, Fusco J, et al. *Virologic Outcomes Among Treatment Naïve HIV+ Patients Initiating Common First Antiretroviral Therapy Core Agents in the OPERA Observational Database* [Poster PEB039]. 22nd International AIDS Conference. Amsterdam, the Netherlands, 2018.
5. Clotet, B., et al., *Once-daily dolutegravir versus darunavir plus ritonavir in antiretroviral-naive adults with HIV-1 infection (FLAMINGO): 48 week results from the randomised open-label phase 3b study.* Lancet, 2014. 383(9936): p. 2222-31.

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