Body Fat Redistribution/Accumulation, Pancreatic Disorders, Musculoskeletal Disorders, IRIS, Severe Systemic Rash and Hypersensitivity Reactions following initiation of commonly prescribed antiretrovirals

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On behalf of the OPERA cohort

IDWeek 2018
October 5, 2018

Disclosure

- I have no actual or potential conflict of interest in relation to this presentation.

Background

Background

- DHHS guidelines currently recommend the use of dolutegravir (DTG), elvitegravir (EVG) or raltegravir (RAL) as the core agent in antiretroviral therapy (ART) regimens
  - While bictegravir is also currently recommended, it had not yet been approved at the time this study was conducted

- Darunavir (DRV) is recommended in some clinical situations such as increased risk of resistance

- Toxicity concerns with multi-agent regimens, and pharmacokinetic interactions with medications for co-morbidities suggest the need for a comprehensive safety evaluation of recommended core agents in a real-world setting

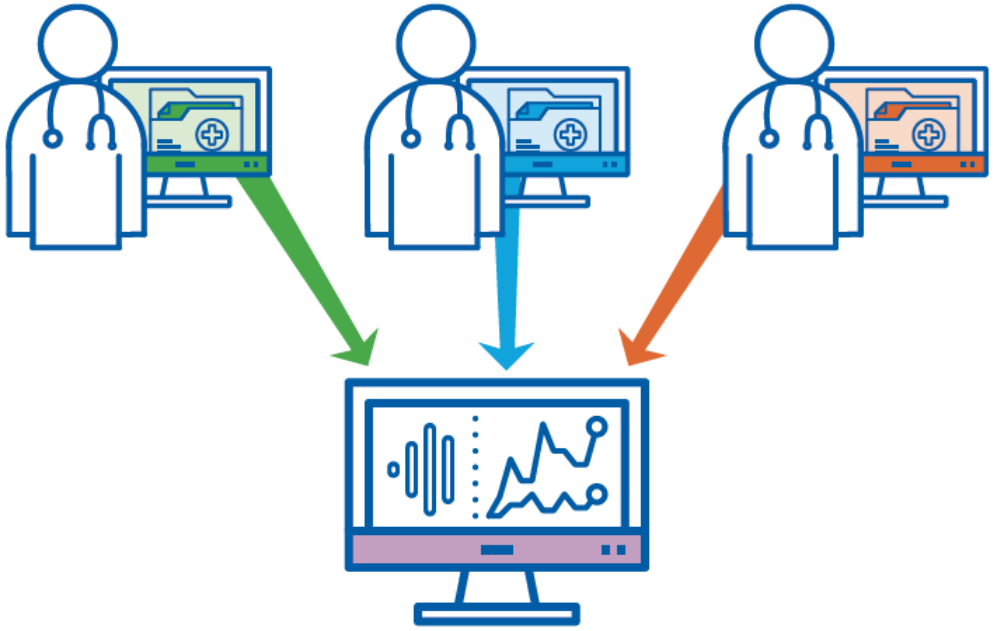
Objective

- To describe the frequency of rarely occurring disorders following initiation of DTG-, EVG-, RAL- and DRV-based regimens in a clinical cohort in the US

Methods

Study Population

- Observational Pharmaco-Epidemiology Research & Analysis (OPERA) cohort
- Prospectively captured, routine clinical data from electronic health records



OPERA Cohort

17 States, 54 Cities, 85 Sites

Study Design

- Eligibility Criteria
  - HIV-positive
  - ≥ 13 years of age
  - Initiation of DTG, EVG, RAL or DRV prescribed by an OPERA caregiver

- Eligibility period
  - August 1, 2013 to December 31, 2016

- Baseline
  - Date of core agent initiation

Disorders of Interest

Body Fat Redistribution/Accumulation

- Dx of lipohypertrophy, lipoaccumulation, hyperadiposity, lipoatrophy, or lipodystrophy

Pancreatic Disorders

- Dx of pancreatitis
- Grade 3/4 lipase elevation (lipase >3X ULN)

Musculoskeletal Disorder

- Dx of Rhabdomyolysis
- Grade 3/4 creatinine phosphokinase elevation (CPK ≥10X ULN)

IRIS

- Dx of Immune Reconstitution Inflammatory Syndrome (IRIS), Immune Restoration Disease (IRD), Immune Reconstitution Syndrome (IRS), or Paradoxical Reaction

Severe systemic rash

- Dx of Blistering rash, Open skin ulcers, Serious rash, Severe rash, Systemic rash, Stevens-Johnson syndrome, or Toxic Epidermal Necrolysis (TEN)

Hypersensitivity Reaction (HSR)

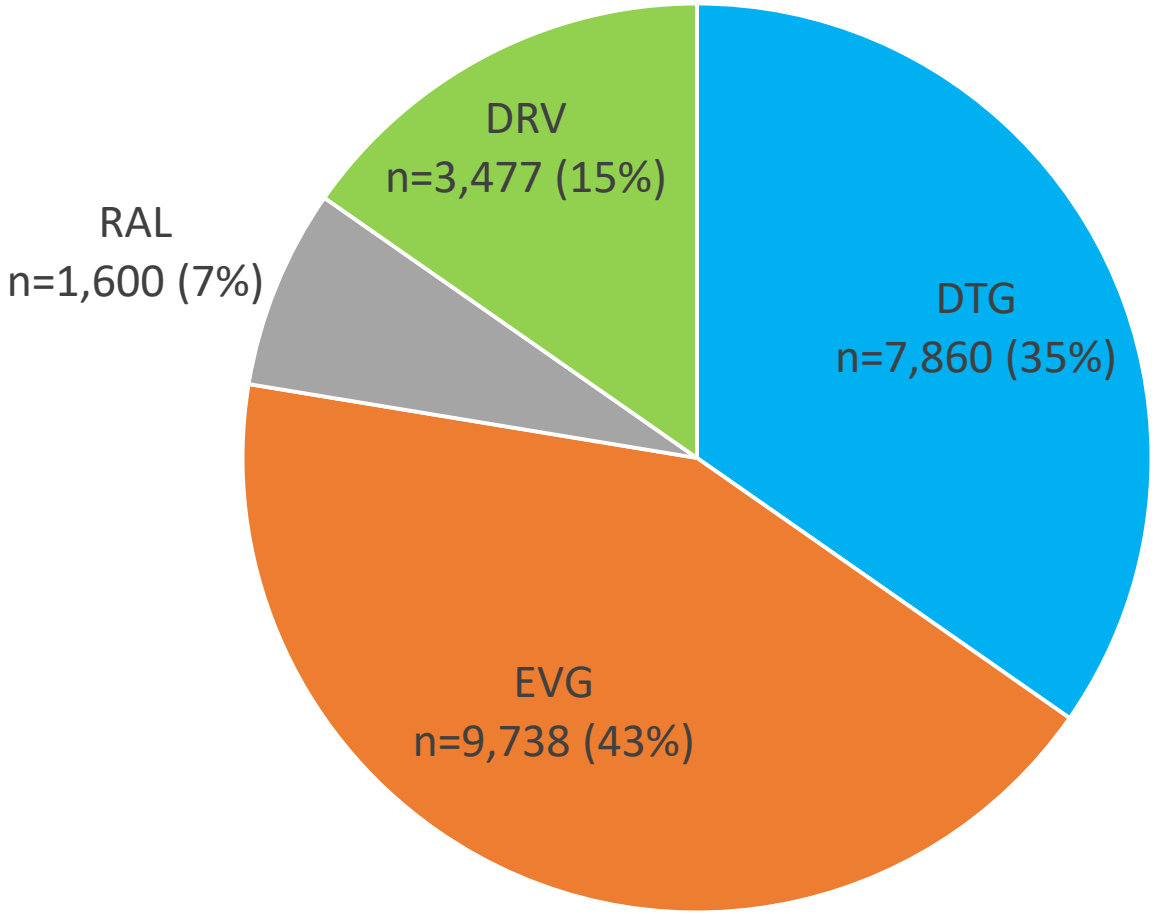
- Dx of hypersensitivity reaction, anaphylaxis, anaphylactic shock, or immunologic reaction

Analyses

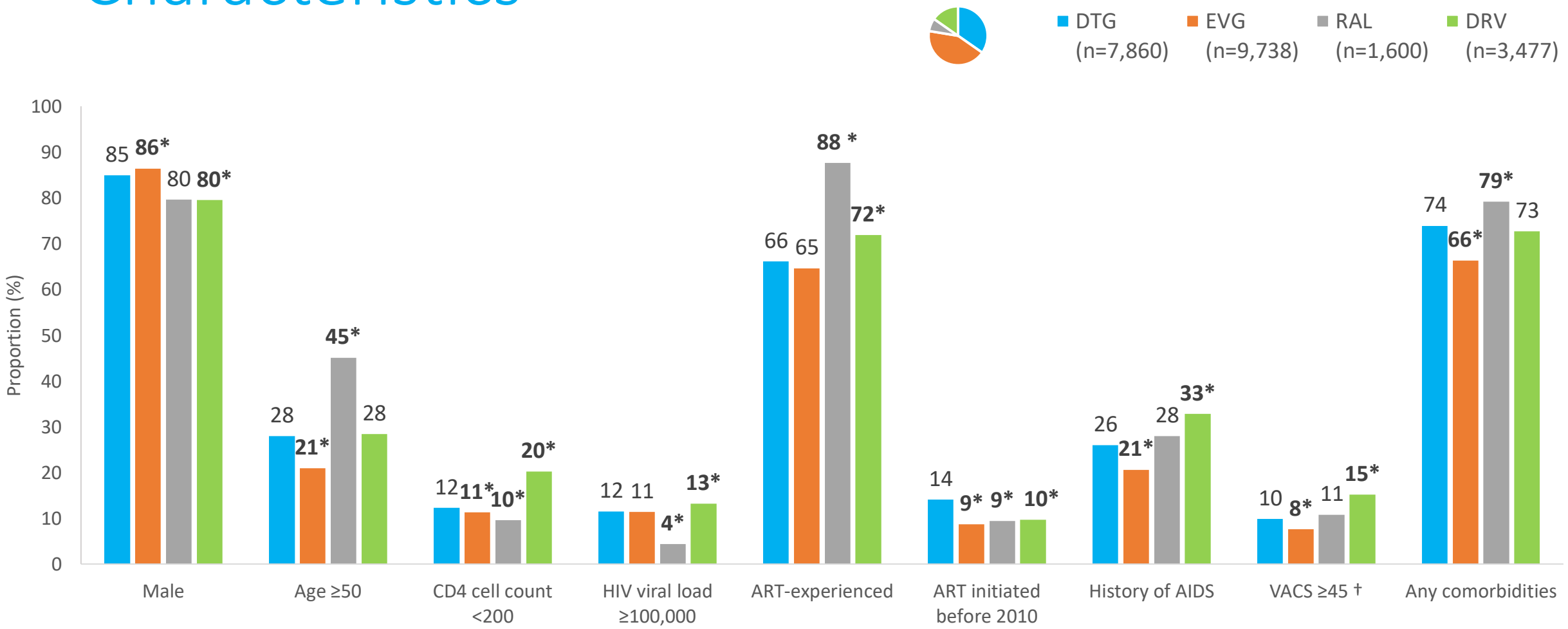
- Comparison between core agents
  - Baseline patients characteristics
  - History: % with each disorder at baseline or up to 12 months prior
  - Any cases: % with each disorder occurring during follow-up, regardless of history of the disorder
  - New cases: % with each disorders occurring during follow-up in the absence of history of the disorder
- Sidak correction to account for multiple comparisons: adjusted alpha level of 0.017

Results

Study population (N=22,675)



Baseline Demographic and Clinical Characteristics

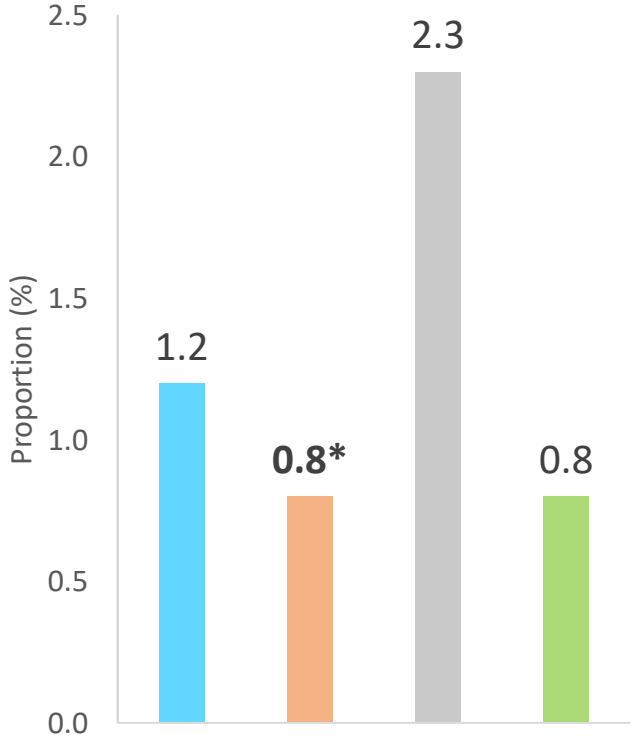


* P-value for the comparison with DTG <0.017

Body fat redistribution/accumulation

DTG (n=7,860) EVG (n=9,738) RAL (n=1,600) DRV (n=3,477)

Baseline history (%)



Follow-up cases (%)

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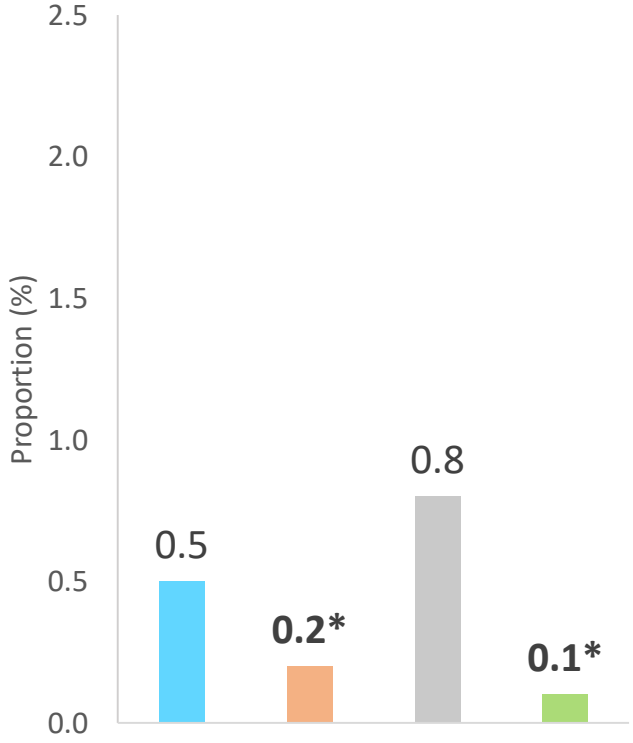
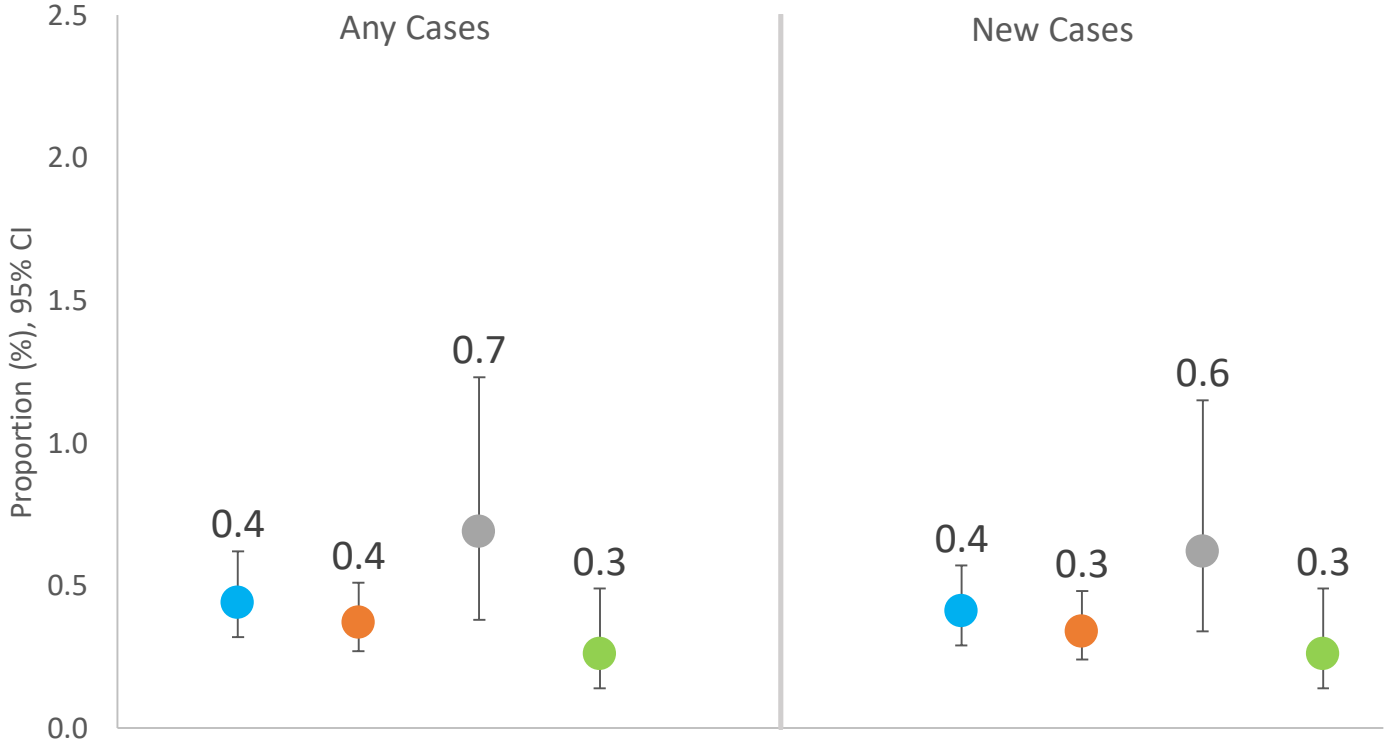
Pancreatic disorders

DTG (n=7,860) EVG (n=9,738) RAL (n=1,600) DRV (n=3,477)

Baseline history (%)



Follow-up cases (%)



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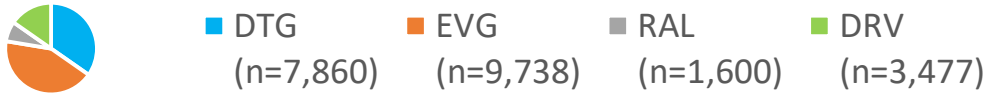
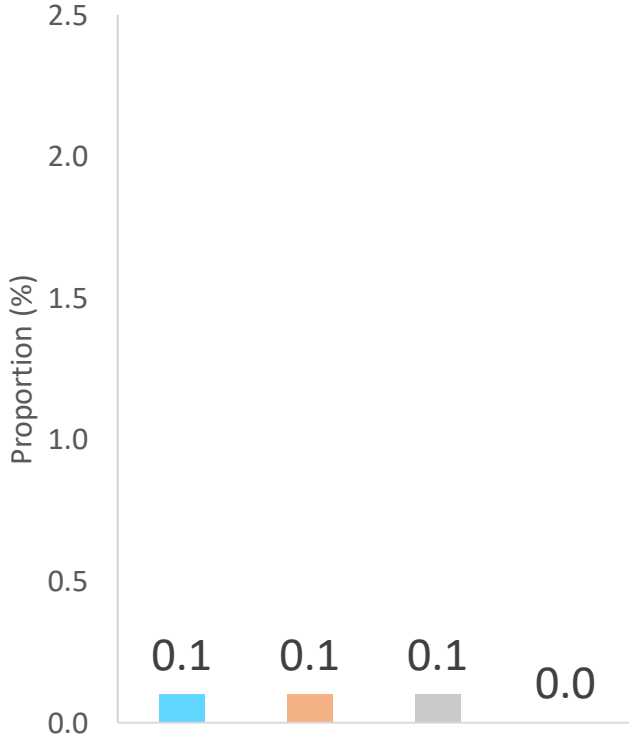
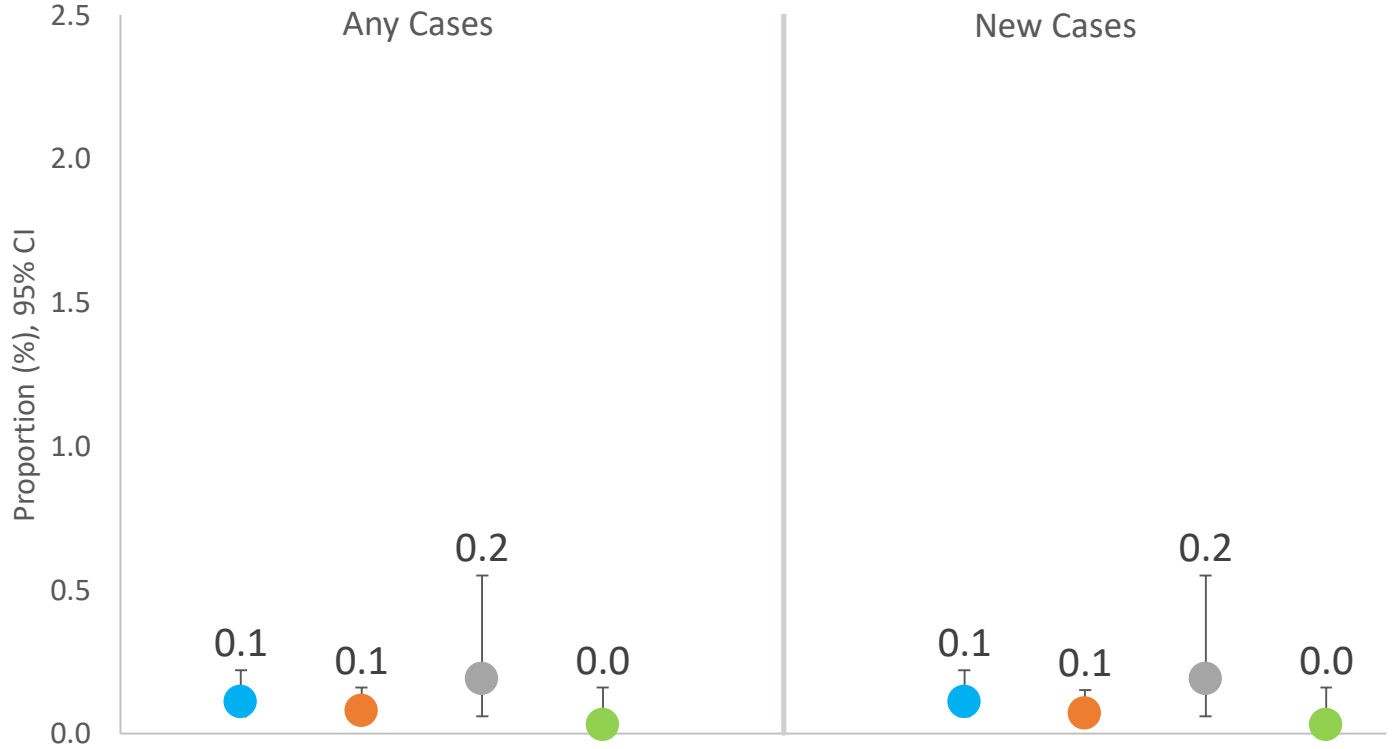
Musculoskeletal disorders



Baseline history (%)



Follow-up cases (%)



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The Longitudinal Cohort

IRIS

	History	Any Cases	New Cases
DTG	n= 1	n= 0	n= 0
EVG	n= 0	n= 2	n= 2
RAL	n= 0	n= 0	n= 0
DRV	n= 0	n= 1	n= 1

Severe Systemic Rash

	New Cases
DTG	n= 1
EVG	n= 0
RAL	n= 0
DRV	n= 1

Hypersensitivity Reaction

	New Cases (w/ ABC)	New Cases (w/o ABC)
DTG	n= 1	n= 1
EVG	n= 0	n= 1
RAL	n= 0	n= 0
DRV	n= 0	n= 1

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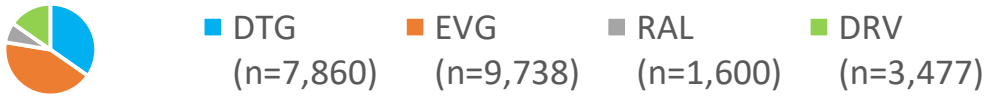

Discussion

Key Findings

- Incident body fat redistribution/accumulation, pancreatic disorders, musculoskeletal disorders were rare (≤1.4% new cases during follow-up)

- IRIS, severe systemic rash and HSR were extremely rare (≤2 new cases during follow-up)

- No difference in likelihood of new events between core agents
  - EVG patients had more favorable health (potential channeling) and were less likely to have a history of body fat redistribution/accumulation or pancreatic disorders, which did not translate in a lower likelihood of developing new body fat redistribution/accumulation or pancreatic disorders

Strengths

+ Large sample size in each of the treatment groups

+ OPERA cohort is a representative sample of the HIV population receiving care in the United States
  - Approximately 7% of all US patients active in care are represented in the database

+ Electronic medical records:
  - Availability of lab results
  - Ability to identify and account for history of disorders

Limitations

– No statistical adjustment for confounding

– Reliance on diagnosis title searches
  - Mild events may not be reported by the patient or may not be recorded as a diagnosis by the clinician

– Evaluation may be inconsistent across all practices
  – Follow-up frequency and duration reflect routine clinical care and may vary by practice and provider

Acknowledgements

- This research would not be possible without the participation of patients with HIV infection and their caregivers

- Co-authors: Laurence Brunet, Jennifer Fusco, Vani Vannappagari, Leigh Ragone, Gregory Fusco

- I am grateful for the following contributions: Robin Beckerman (SAS programming), Jeff Briney (QA/QC), Rodney Mood (site selection and support), Ted Ising (database architecture and support), Bernie Stooks (database support), Judy Johnson (medical terminology classification), and Laurence Brunet (presentation preparation)

- This research was sponsored by ViiV Healthcare