EV0005

Evaluation of dolutegravir-metformin drug-drug interactions in a clinical setting

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BACKGROUND

- The prevalence of diabetes mellitus (DM) is 1.4-times higher among HIV-infected patients compared to the general population[1]
- Dolutegravir (DTG) is an organic cation transporter-2 and multidrug and toxin extrusion protein inhibitor within the renal tubules[2,3]
  - Inhibits tubular secretion of serum creatinine (SCr) [-0.32 to 0.65 mg/dL] without affecting glomerular filtration rate
  - May increase serum concentration of drugs using these transport receptors (e.g.metformin)
- In healthy volunteers, metformin exhibited increased maximum concentration and area under the concentration time curve when co-administered with DTG compared to metformin alone[4]
- Limited data exist evaluating this interaction in HIV-infected patients on antiretroviral therapy

OBJECTIVE

- To determine the clinical implications of concurrent DTG-metformin administration in HIV-infected patients receiving ambulatory HIV care from health-system-based infectious diseases clinics

METHODS

- Multicenter, retrospective case series
- Electronic medical record review beginning at DTG-metformin initiation for a 6 month follow up period
- Inclusion criteria:
  - Adults ≥ 18 years old
  - Concurrent DTG-metformin between August 12, 2013 and May 4, 2015
- Exclusion criteria:
  - Pregnant females
  - Inmates of the Department of Corrections

DATA COLLECTION

Laboratory Parameters	Safety Parameters
Hemoglobin A1c (HgbA1c) SCr Plasma HIV RNA viral load CD4 count Lactate (if indicated)	Patient reported adverse drug reactions (ADRs) • Gastrointestinal (GI) intolerance • Hypoglycemia • Lactic acidosis Need for metformin dose reduction/discontinuation

RESULTS

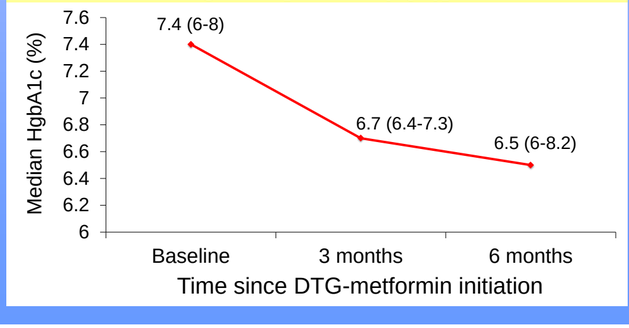
Patient demographics [median (IQR)][a] (Total=19 patients)

Age, yr	55 (52 – 57)				
Wt, kg: metformin start	90 (78.7 – 109.1) (N=15)				
Gender, N	Male – 14	Female – 5			
Race, N	White – 6	Black – 12	Hispanic – 1		
DTG TDD, mg – N	50 – 18	100 – 1			
Metformin TDD, mg – N	500 – 2	1000 – 11	1500 – 1	1700 – 1	2000 – 4

[a]IQR – interquartile range; TDD – total daily dose

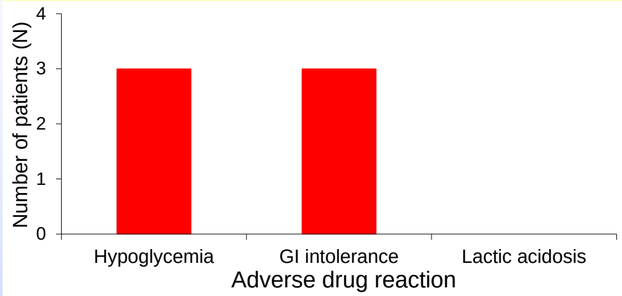
- N=18 prescribed metformin prior to DTG
- Additional antiglycemic agents:
  - Long-acting insulin (N=7)
  - Short-acting insulin (N=4)
  - Sitagliptan (N=2)

HgbA1c [median (IQR)]



RESULTS

Presence of Adverse Drug Reactions

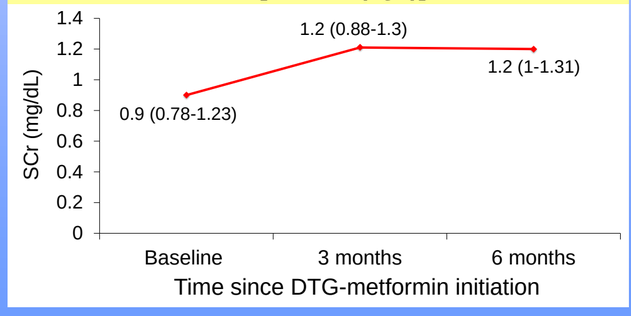


- 60% of patients experiencing ADRs were prescribed a metformin daily dose >1000 mg at DTG initiation

Metformin dose changes:

- Preemptive dose reduction at DTG initiation (N=2 receiving metformin TDD ≥1500 mg)
- Dose reduction (N=2)
- Discontinuation (N=2)

SCr [median (IQR)]



- N=15 had an increase in SCr
- Median SCr increase was 0.3 mg/dL

RESULTS

Immunologic and Virologic Control

Laboratory Data [Median (IQR)]	Baseline	3 months	6 months
CD4 count, cells/mm^3 (%)	542 (26) [317-760 (16-37)] (N=18)	493 (26) [289-777 (17-35)] (N=15)	492 (29) [419-842 (19-39)] (N=13)
HIV RNA, <20 copies/mL	10 (N=19)	11 (N=16)	11 (N=13)

LIMITATIONS

- Small sample size
- Incomplete laboratory data
- Medical chart review
- Patient medication adherence

CONCLUSIONS

- DM control was maintained when metformin was co-administered with DTG in HIV-infected patients
- Increased ADRs were reported by 16% of patients leading to metformin dose reduction and subsequent discontinuation
- Providers concurrently prescribing DTG and metformin may consider an empiric metformin dose reduction to prevent intolerable ADRs
  - DTG FDA label updated (August 2015): metformin 1000 mg is the maximum recommended dose for patients initiating DTG[2,3]

REFERENCES

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DISCLOSURES

The authors of this presentation have no potential conflicts of interest

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