HIV Integrase Inhibitor Bictegravir Inhibits Proliferation, Increases Apoptosis and Mitochondrial Damage in Peripheral Blood Mononucleated Cells (PBMCs) *Ex Vivo*

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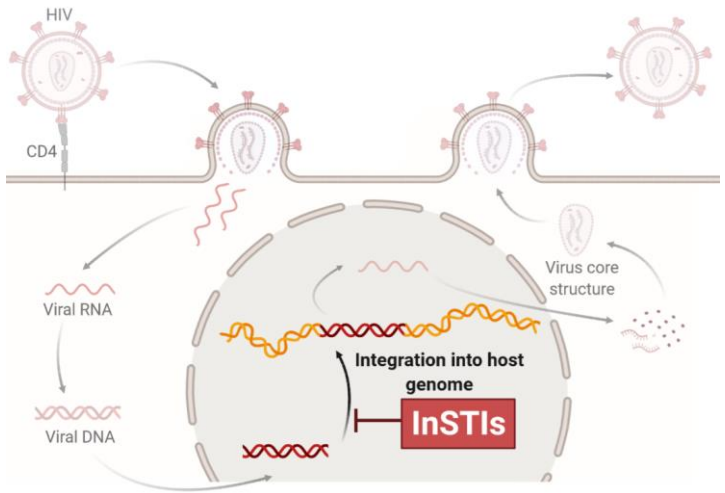
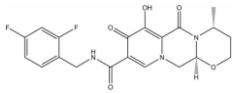
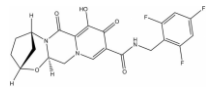
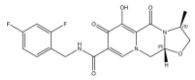
INTRODUCTION

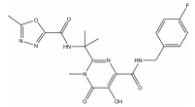


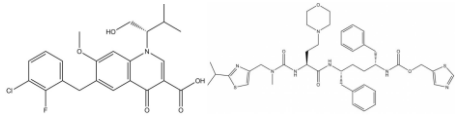
InSTIs


Dolutegravir (DTG)


Bictegravir (BIC)


Cabotegravir (CAB)


Raltegravir (RAL)


Elvitegravir+Cobicistat (EVG/COBI)

METHODS

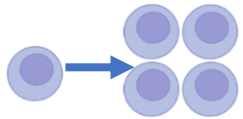
Isolate PBMCs from healthy volunteers

Drug exposure at pharmacological concentration ($1xC_{max}$) in 0.1% DMSO

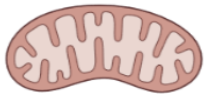
Activate T-cells
Anti-CD3/CD28

6 days

Flow cytometry


Proliferation


Apoptosis



Mitochondrial (MT) health
- MT Reactive oxygen species (ROS)
- MT Mass
- MT Intermembrane Potential

RESULTS – MITOCHONDRIA (MT)

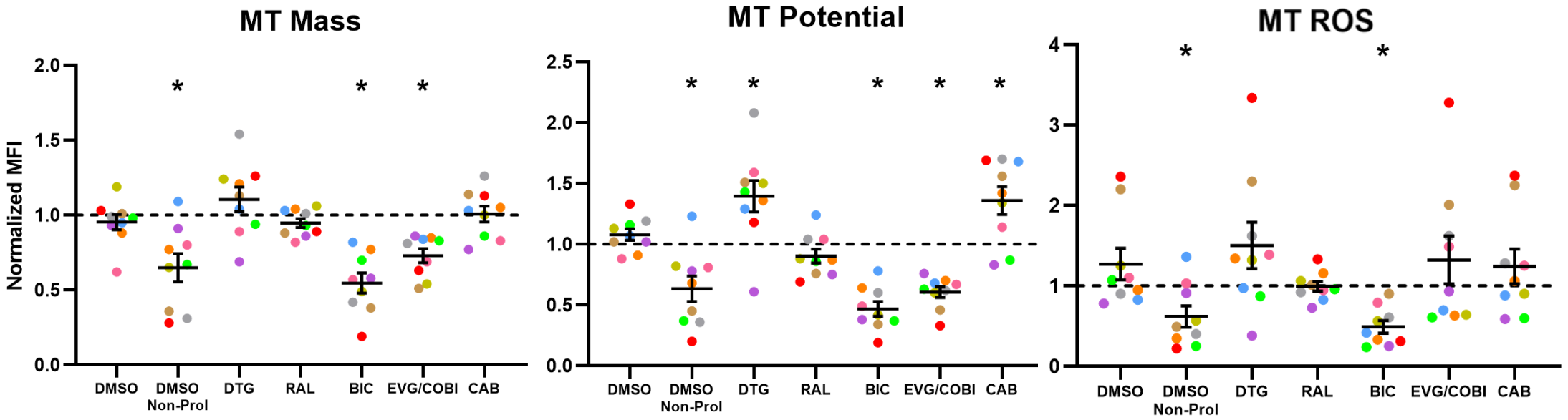


Figure 1: Mitochondrial mass, Mitochondrial intermembrane potential and Mitochondrial ROS mean fluorescence intensities normalized to untreated controls (dotted line) of each individual (n=9 distinct volunteers), represented by a unique colour. Stars indicate significant difference vs. DMSO using paired t-test.

Compared to DMSO…

- **BIC decreases** mt mass, potential and ROS
- **EVG/COBI decreases** mt potential
- **CAB** and **DTG increase** mt potential

RESULTS – CELLULAR

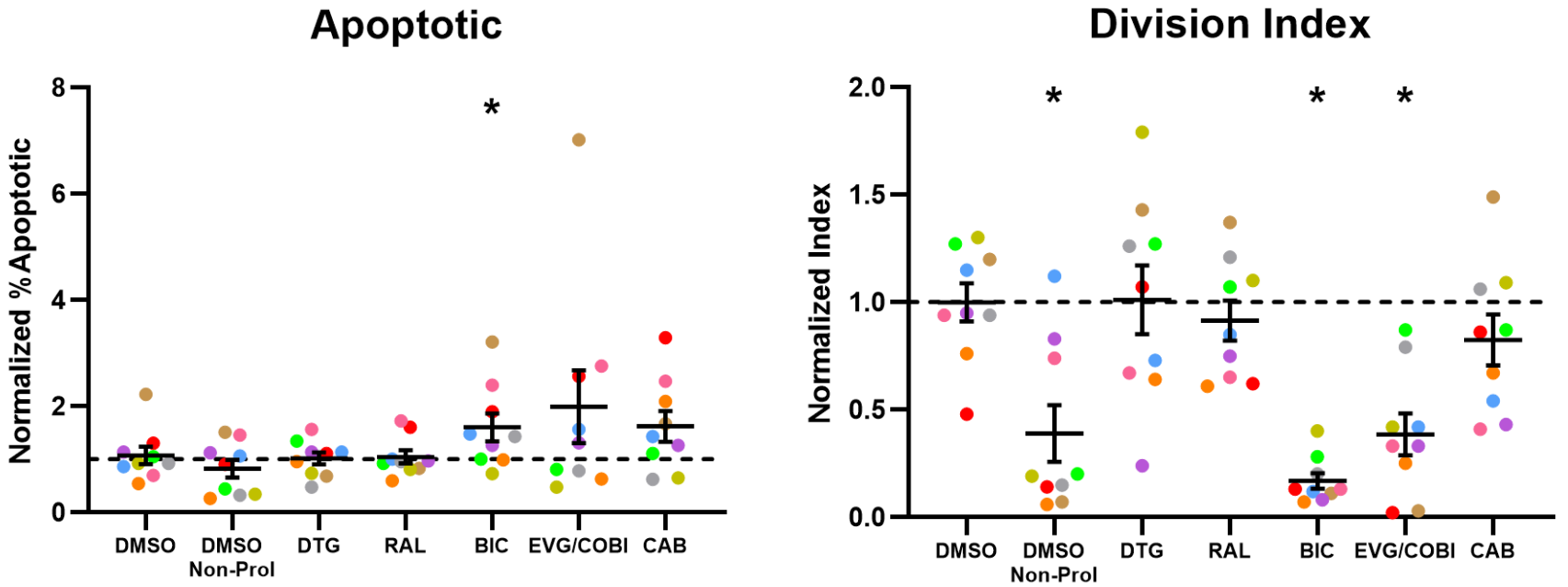


Figure 2: Apoptotic cells were normalized to untreated controls (dotted line) of each individual (n=9 distinct volunteers), represented by a unique colour. Division index measured as total divisions/number of cells at day 0. Stars indicate significant difference vs. DMSO using paired t-test.

Compared to DMSO…

- **BIC inhibits** proliferation and **increases** apoptosis
- **EVG/COBI decreases** proliferation
- RAL has no effect on any parameter studied

DISCUSSION

- These data clearly show that InSTIs can affect PBMC mitochondria
- The effects of some InSTIs, particularly **BIC** and **EVG/COBI** *ex vivo* suggest a potential underlying metabolic mechanism which could hinder immune responses
- It is noteworthy that exposure to **RAL,** a first generation InSTI, has no effect on any parameter studied here
- These data highlight the need to further investigate InSTIs as they may exert long-term immunological consequences that may not be detected in the context of clinical trials

Acknowledgements

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CIHR IRSC

UBC

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bio RENDER

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