In vitro study; clinical trials of BIC+FTC+TAF have been conducted starting with wild-type or M184V HIV and antiretroviral regimens set at drug in vivo concentrations or combinations mimicking short lapses in adherence (1 to 3 consecutive missed doses).

Methods

- **Viral Breakthrough Selection Experiments (Figure 2):** In viro viral breakthrough selection experiments were determined as a comparative in viro study, clinical trials of BIC+FTC+TAF have been conducted starting with wild-type or M184V HIV and antiretroviral regimens set at drug in vivo concentrations or combinations mimicking short lapses in adherence (1 to 3 consecutive missed doses).

Results

1. Resistance in Breakthrough Viruses: Mechanisms of Long-Persisting Outcomes

   - **Mechanisms:**
     - Long-persisting outcomes (LPOs) and short-persisting outcomes (SPOs)

2. Resistance in Breakthrough Viruses: Profiles of Mutations

   - **Profiles of Mutations:**
     - S153Y and S153F

Conclusions

- **In vitro viral breakthrough selection experiments define the drug-resistant barrier of ART drug combinations and the resistance mutations that emerge.** Here, two series of breakthrough experiments were conducted starting with wild-type or M184V HIV and antiretroviral regimens set at drug in vivo concentrations or combinations mimicking short lapses in adherence (1 to 3 consecutive missed doses).

- **In the wild-type experiments, DTG+3TC had 104/144 walls breakthrough and 15 of these had emergent resistance consisting of M184V and other RT mutations in IT.

- **M184V causes resistance to FTC and 3TC and one of the most frequent mutations to occur during virologic failure, is archived, and can be transmitted**

- **Substitution mutations in the 3TC combination drug resistance profile by BIC+TAF+RTC may be more protective against virologic failure through emergent resistance than DTG+3TC in the setting of non-adherence**

- **In vitro studies of the ‘forgiveness’ of ART regimens are important as they may help to predict regimen durability and risk of resistance in the real-world, where suboptimal adherence is more common**

References

- **Jain V, et al., JID (2017) 215(9): 1533-1540**
- **Laskey S, et al., JCI Insight (2017) 2(9): e92490**
- **Tandon et al., Managed Care Pharm (2019) 25(1): 88-93**
- **Stellbrink HJ, et al. HIV Glasgow (2018) Presentation #4185960**
- **S153F* has been previously selected by DTG and causes reduced susceptibility to DTG**
- **S153Y has been previously selected by DTG and causes reduced susceptibility to DTG**
- **The resistance mutations that emerge. Here, two series of breakthrough experiments were conducted starting with wild-type or M184V HIV and antiretroviral regimens set at drug in vivo concentrations or combinations mimicking short lapses in adherence (1 to 3 consecutive missed doses).**

- **In vitro viral breakthrough selection experiments define the drug-resistant barrier of ART drug combinations and the resistance mutations that emerge.** Here, two series of breakthrough experiments were conducted starting with wild-type or M184V HIV and antiretroviral regimens set at drug in vivo concentrations or combinations mimicking short lapses in adherence (1 to 3 consecutive missed doses).

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- **In vitro viral breakthrough selection experiments define the drug-resistant barrier of ART drug combinations and the resistance mutations that emerge.** Here, two series of breakthrough experiments were conducted starting with wild-type or M184V HIV and antiretroviral regimens set at drug in vivo concentrations or combinations mimicking short lapses in adherence (1 to 3 consecutive missed doses).