Eligibility for Simplification of HIV Salvage Regimens Based on Patient Genotypes

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Accredited

BACKGROUND

- The Human Immunodeficiency Virus (HIV) can become resistant to many classes or individual agents of antiretroviral therapy (ART) due to treatment nonadherence or transmission of resistant strains of virus
- Patients that fail first and second lines of therapy are often transitioned to a salvage regimen that may only have partial activity and increases pill burden, toxicities, and costs to the patient[1]
- The University of Virginia (UVA) Ryan White Clinic utilizes a salvage regimen that most often consists of ralltegravir, darunavir boosted with ritonavir, and etravirine.
- Recent studies have demonstrated the simplification of HIV regimens can maintain viral suppression and reduce toxicities and pill burden[2]
- Genotype resistance tests detect specific mutations. Utilizing this data against newer ART with available databases can help select individualized ART that minimizes pill burden while maximizing efficacy.

PURPOSE

- The purpose of this study was to determine eligibility for salvage regimen simplification based upon genotypic test results.

METHODS

- **Study Design:** Single center, retrospective observational analysis
  - Fifty-three patients prescribed HIV salvage regimen at the UVA Ryan White Clinic between July 1, 2016 to July 1, 2019
  - Salvage regimen defined as ART that contains greater than three or more antiretroviral agents from at least three separate classes
  - Patient HIV genotype resistances were analyzed through the Stanford University HIV Drug Resistance Database. Scores greater than 60 represented high levels of resistance[3]
  - Eligibility for simplification was defined as the reduction in patient pill burden by at least one or more pills
  - Eligibility was reviewed at two timepoints. The first time was based solely on genotype resistance scores. The second time was based on clinical review of patient, including prior therapies, interactions, and comorbidities
- **Primary Objective:** Eligibility to simplify salvage regimen by at least one pill based upon HIV Stanford Database and clinical review
- **Secondary Objectives:**
  - Mean reduction in pill burden post-simplification of HIV regimen
  - Patterns of resistance of medications within each distinct ART class
  - Common regimens used for simplification
- **Statistics**
  - Non-parametric descriptive statistics were used to determine primary and secondary objectives

RESULTS

Table 1. Baseline Demographics of patients tested for genotype resistance

Characteristics	Patients (N = 53)
Age (years), median	55
Male, (%)	77
Caucasian, (%)	60
Duration of HIV diagnosis (years), median	24
Hepatitis B, (%)	42
Concurrent Resistant Medication, (%)	21
Darunavir-specific mutations[4], (%)	23

Table 2. Common ART mutations within patient population N = 53

Class/Mutation	Patients (N = 53)
NRTI, (%)	
M184V/I	60
T215F/Y/D	40
M41L	31
NNRTI, (%)	
K103N/T/Q	50
G190A/S/E	27
Y181C/I/V	25
PI, (%)	
V82A/T	27
I54V/A	23
M46I/L/V	21

Table 3. Abbreviations for ART

Class of ART	Medications (Abbreviation)
Nucleoside reverse transcriptase inhibitors (NRTI)	Lamivudine (FTC), Emtricitabine (3TC), Abacavir (ABC), Tenofovir (TDF)
Non-nucleoside reverse transcriptase inhibitors (NNRTI)	Etravirine (ETR), Rilpivirine (RPV), Nevirapine (NVP)
Protease inhibitors (PI)	Atazanavir (ATV), Darunavir (DRV), Lopinavir (LPV)
Integrase strand transfer inhibitors (INSTI)	Dolutegravir (DTG), Raltegravir (RTG), Elvitegravir (ETG), Bictegravir (BTG)

Figure 1. Study design for patient eligibility with outcomes

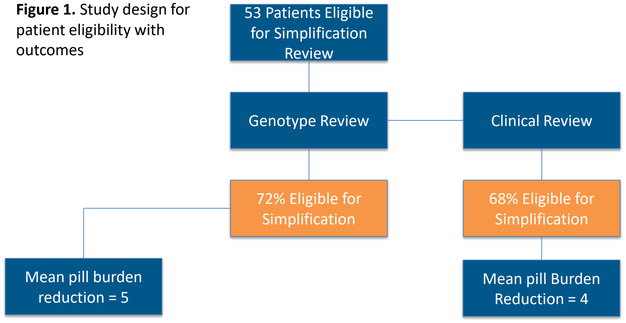


Figure 2. Percent resistance and susceptibility among classes of ART

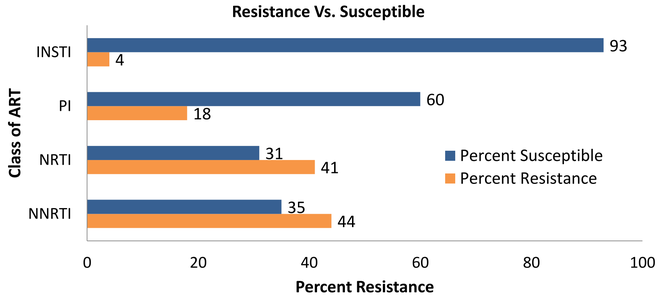


Figure 3. Percent of resistance scores for all medications tested. N = 291 total medication resistance scores

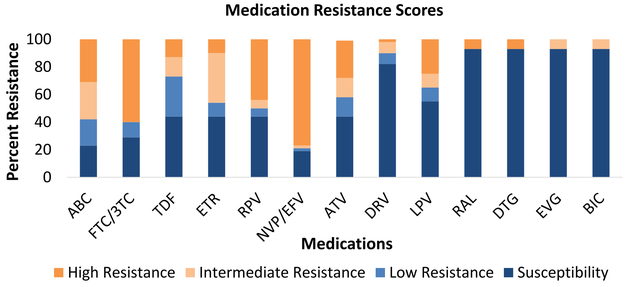
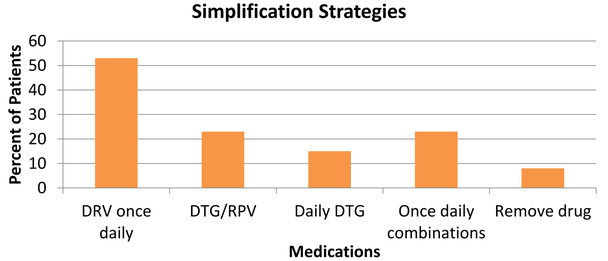


Figure 4. Simplification strategies utilized or considered



DRV = darunavir
DTG/RPV = dolutegravir plus rilpivirine once daily
DTG = once daily dolutegravir
Once Daily Combinations = ABC/DTG/3TC, EVG/c/FTC//TAF, BIC/FTC/TAF

DISCUSSION

- The majority of patients were eligible for simplification of their HIV regimen with an average reduction of 4 pills after clinical review
- Baseline demographics of this patient population illustrates a median time of HIV diagnosis in the 90's, which likely correlates to the high number of mutations to many ART.
- First-generation NNRTI and NRTI had the most mutations among all the ART classes of medications at 44% and 41%, respectively. Hence, salvage regimens or simplification strategies avoided the use of these medications
- Out of 291 total medication resistance scores, 172 (59%) were considered highly resistant
- Of patients eligible for simplification, 13% were on a non-active or resistant medication that could be discontinued due to ineffectiveness
- The most common strategy for simplification based upon genotype would be the conversion to once daily darunavir, either with ritonavir or cobicistat (53%), reducing the medication burden by 2-3 pills
- Figure 3 shows darunavir had very low levels of resistance
- **Limitations**
  - Small sample size of patients who received INSTI genotype testing
  - Each genotype represents snapshot in time – may not have captured all mutations
  - Clinical review could introduce bias for patient simplification eligibility
  - HIV Stanford Database does not account for resistance of all ART

CONCLUSION

- Use of genotypic resistance data against ART, combined with patient clinical review, allows for the simplification of HIV salvage regimens
- Simplification of salvage regimens could lead to newer, more consolidated options that may lead to increased adherence.
- Further assessment and studies are warranted to define post-simplification outcomes and to determine if patients can truly be transitioned off of complex salvage regimens

FUTURE APPLICATIONS

- Results of this study will be presented to quality committees at UVA
- The results from this study will be used to further advance research into genotype resistance testing and the simplification of HIV regimens. The next step is to implement the simplification strategies and prospectively follow patients to determine if viral suppression is maintained.

REFERENCES

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Disclosures: The authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.