SHOULD WE BE TESTING FOR BASELINE INTEGRASE RESISTANCE?

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BACKGROUND

• Treatment guidelines recommend a standard genotype to guide selection of antiretroviral therapy (ART) in patients newly diagnosed with HIV. Integrase strand transfer inhibitors (INSTI) are recommended in first-line ART regimens, yet standard genotypes do not assess for INSTI-resistance (INSTI-R).

• Prevalence of transmitted INSTI-R virus is low (0-0.1%) in published and presented studies from the U.S. and Europe.

• Treatment with dolutegravir (DTG)-based ART can result in suppression of INSTI-R virus in some patients. However, if INSTI-R virus is present before ART initiation, antiretroviral therapy (ART) might not be able to successfully suppress the virus. At 96 weeks, 30-100% of patients with INSTI-R virus might achieve viral suppression.

• Although INSTI-R virus can emerge on ART, standard genotypes do not assess for INSTI-R. Thus, patients with INSTI-R virus failing DTG-based ART need to be switched to dolutegravir/ritonavir (DRV/r)-based ART as soon as possible to prevent treatment failure.

• Baseline testing for INSTI-R virus is not recommended in treatment-naïve patients.

METHODS

MODEL STRUCTURE (FIGURE 1)

• We used a decision-analytic Markov model to evaluate the benefits and cost-effectiveness of INSTI-R testing (Figure 1).

• Transition probabilities were estimated from the FLAMINGO ACTG A5257 VIKING-3 [14] and VIKING-3 [15] studies (Table 1).

• Transition outcomes and utility values were estimated from observational studies, randomized controlled trials, meta-analyses, and the literature. INSTI-R virus testing was limited to INSTI-R virus assessment using invariant INSTI mutations (V108I and/or L100I).

• This model simulates an HIV-infected, ARV-naive patient presenting for baseline lab work and genotypes, as per 2016 DHHS guidelines [12].

• In the base case, INSTI-R virus was present at a frequency of 0.1% in ART-naïve individuals (Suppression rate: 0.99 and QoL: 1).

METHODS: INPUT DATA

• Table 1: Model input parameters for analysis of testing for INSTI-R virus compared to no testing prior to ART initiation.

• Results: Testing clinically preferred when INSTI-R virus is present, QoL on DRV/r-based ART is >95% and DRV/r suppression is >75%.

• Table 2: Base case model output for testing for INSTI-R virus compared to no testing prior to ART initiation.

• Table 3: Univariate sensitivity analysis model outputs for INSTI-R testing compared to no-testing prior to ART initiation.

RESULTS

• When INSTI-R virus is present on DTG-based ART, testing is equivalent to that on DTG-based ART (Panel A). Testing is preferred when INSTI-R virus is present, QoL on DRV/r-based ART is >95% and DRV/r suppression is >75% (Panel B).

• Univariate sensitivity analysis (Panel C): When INSTI-R virus is present, QoL on DRV/r-based ART is >95% and DRV/r suppression is >75% testing is preferred.

• A model-based analysis does not impact the conclusions.

• Sensitivity analysis: INSTI-R virus testing is not cost-effective compared to no-testing strategy.

• The results of our model-based analysis do not support the strategy of testing INSTI-R virus prior to ART initiation.

• INSTI-R virus testing might be considered in some clinical scenarios.

CONCLUSIONS

LIMITATIONS

• Our model-based analysis does not incorporate the impact of INSTI-R virus on clinical outcomes and resource use. For this analysis, patients with INSTI-R virus were assumed to have equivalent clinical outcomes to those without INSTI-R virus.

• We used available and published data from the literature to estimate transition probabilities and outcomes. These data are generalizable to other populations.

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