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Introduction

- Over the past 20 years, 3-drug antiretroviral therapy (ART) has been the standard of HIV treatment. Given the aging HIV population and availability of more potent antiretroviral drugs with fewer adverse effects, new approaches are being evaluated to decrease long-term drug toxicities as well as lower treatment costs. Interest in dual-therapy regimens has been renewed, particularly as a simplification strategy in virologically suppressed HIV-infected patients.
- Several cohort studies have evaluated dolutegravir in combination with a second agent, most commonly rilpivirine or lamivudine. The availability of 48-week results from 2 large randomized trials (SWORD 1 and 2) provide the first compelling evidence that dual therapy with rilpivirine and dolutegravir may be a viable option as maintenance therapy because this regimen was found to be noninferior to continuing standard ART.
- Based on these findings, the United States Department of Health and Human Services (DHHS) guidelines recently updated recommendations for regimen switching in virologically suppressed treatment-experience patients to include a 2-drug ART regimen consisting of dolutegravir plus rilpivirine. The guidelines also state that a 2-drug ART regimen consisting of a boosted protease inhibitor-based regimen plus lamivudine or emtricitabine may be a reasonable option when the use of NRTIs (Nucleoside reverse transcriptase inhibitors) is not desirable
- Despite the growing data about dual regimens in controlled setting, little is known about effectiveness and tolerability in the real world. There is also a lot of debate at the provider level about the use of dual regimens, and it is still considered a controversial treatment strategy. For this reason, we decided to conduct a study to assess the attitudes, knowledge and practices among HIV providers about the use of dual ART regimens.

Materials & Methods

- An online survey was administered to a convenience sample of HIV providers in the USA from October to December 2018.
- Our aim was to assess experience, knowledge and attitudes regarding dual antiretroviral regimens.
- Knowledge was evaluated by 6 questions (1 point for each correct answer). High knowledge was defined by a score of ≥ 5 points.
- We evaluated the association between knowledge and selected characteristics through chi-square.
- Data was analyzed in SPSS 22, New York, USA.

Results

- We distributed 55 surveys and received 46 (83%) responses.
- The majority of the respondents were from academic institutions (45.7%) and private clinics (37.0%).
- The male to female ratio was 2.5/1. The providers were 31-60 years predominantly (84.8%). Most of them (43.4%) had 5 to 14 years of experience, and worked in outpatient settings (65.2%). Respondents were mainly M.D. Infectious disease specialists (45.7%) and nurse practitioners (23.9%).
- In terms of experience with dual regimens, 84.8% of providers admitted prior prescription of these regimens.

Results

- Rilpivirine/dolutegravir was the most prescribed combination (76.09%). Dolutegravir+Darunavir/ritonavir and Dolutegravir+Lamivudine were prescribed by 37% and 10.9% of providers respectively.
- Most providers (69.6%) stated that they inform their patients about the possibility of using dual regimens.
- Regarding knowledge, 45.7% of respondents self-reported good knowledge. High knowledge score was obtained by 60.9% of providers.
- In comparison with the rest of the study cohort, providers with high knowledge worked more in an outpatient settings (50.0% vs 16.7%, $p < 0.022$), and treated a higher number of patients (> 100 patients monthly, 39.3% vs 5.6%, $p < 0.011$).
- In terms of attitudes, 69.6% of providers would consider prescribing dual regimens in patients who are fully compliant, and 60.9% would prescribe them in patients with undetectable viral load for > 6 months. A high rate of providers (73.9%) felt uncomfortable prescribing drugs for new indications, 58.7% expressed concern about the effectiveness of dual regimens, and 65.2% believed that 3-drug regimens were better than dual regimens.

Questions about Knowledge	Providers that responded correctly (%)
1. Do you think 2-drug regimens for HIV treatment are recommended by current HIV guidelines?	60.90%
2. Which single pill medication has been FDA approved as dual drug regimen for treatment of HIV infection?	93.20%
3. A recent study evaluated demonstrated that the proportion of patients that maintained viral suppression after switching from a 3 drug regimen to a dual regimen was:	90.50%
4. To change an HIV patient from a 3-drug regimen to a dual drug regimen, it is recommended to be virologically suppressed for a period of time of:	86.00%
5. Would you consider changing from a 3-drug HIV regimen to a dual regimen in patients with baseline resistance to one of the dual regimen components?	81.80%
6. After switching to a dual drug regimen, how soon do we need to check the HIV viral load to ensure that viral load remains undetectable?	84.10%

ATTITUDES	
Who are the patients in whom you would consider prescribing a dual HIV treatment regimen?	Providers that responded "Yes" (%)
> All patients living with HIV	7.10%
> Patients who are 100% compliant with HIV medications	7.60%
> Patients who are currently treated with 2 or more pills	38.10%
> Only patients who participate in research	2.40%
> Treatment experienced patients with undetectable viral load for more than 6 months	66.70%
> No one	4.80%

ATTITUDES	Providers that responded "Yes" (%)
• "I am concerned that 2 drug regimen will not be 100% effective"	58.70%
• "I am concerned about the potential side effects of 2-drug regimens"	8.70%
• "I feel uncomfortable prescribing drugs for new indications, unless there is a clear evidence"	73.90%
• "I am concerned about low adherence to 2-drug regimens"	34.80%
• "The use of 2 drug regimen will select for and disseminate antiretroviral resistance"	17.40%
• "The 2-drug regimens will be costly"	26.10%
• "I am concerned that the insurance will not cover 2-drug regimens"	37%
• "I believe that 3-drug regimens are better than 2-drug regimens"	65.20%

Discussion

- In regards to different providers' attitudes on the presumed pros and cons of dual therapies, a whopping 65% of respondents felt that conventional regimens are overall better than dual. While the studies have shown effectiveness of dual regimens, less antiviral agents may have a dampened effect on immune activation, HIV DNA levels, and the ability to attenuate sexual transmission, especially in subjects on "off label" dual regimens. In this sense, long term use of dual regimens may exhibit lower penetrance of viral sanctuary sites. None of the above mentioned scenarios have been studied thus far.
- Similarly, 73.9% advised they felt uncomfortable prescribing drugs for new indications. In the case of HIV this would seem understandable, given the huge deviation from the comfortable "one size fits all" triple therapy methodology, which after ten years ratified an effective treatment for HIV and has been the tried and trusted standard for over two decades.
- More than a quarter and a third of respondents were concerned about cost of and insurance coverage for dual therapy regimens, respectively. However, it is worth mentioning that DTG/RPV is cheaper than TAF/FTC/ELV/c, roughly the same cost as ABC/3TC/DTG, and more expensive than TAF/FTC/RPV and DTG/3TC.
- Lastly, 35% of respondents were worried about adherence. Given that currently there exists only one small sized single tablet once daily regimen licensed as a dual therapy, prescribing any other regimen would require two or multiple pills a day, which justifies concern that the higher number of pills can lead to waxing and waning compliance at one point or another.
- Our study demonstrated that overall, higher knowledge of dual therapies was noted by respondents working in the outpatient HIV clinic setting who see more than 100 patients a month. Clearly this sampling of respondents, being more intimately linked to the intricacies of treating HIV since it is their primary patient encounter day after day, as opposed to hospital wards or even academic medicine, would have demonstrated such.
- Overall, respondents had a positive attitude towards dual therapies, given that only 2 felt that it was inappropriate in any circumstance to prescribe them. The rest of the attitudes for the applicability of dual therapy regimens corresponded well with the guidelines for DRV/RPV as a "switch" or "maintenance" strategy in that 76% and 67% advised that among the patients they would prescribe dual therapies to would be treatment experienced patients already stable and undetectable on a standard regimen.

Conclusions

- Our study revealed high knowledge and wide experience on the use of dual regimens among American HIV providers.
- Despite positive attitudes towards dual regimens, providers still have significant concerns about their effectiveness.

References

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