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Use of long-acting injectable cabotegravir and rilpivirine as an alternative for treatment in HIV positive patients

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ABSTRACT
A clinical decision report using:


for a young adult patient struggling with adherence.

Keywords: adherence, HIV, therapy

Clinical-Social Context
Mr. Mark Williams (pseudonym) is a 23 year old male with a past medical history for asthma, dislocated right shoulder, and positive HIV who presented to our clinic for medication refills for his Biktarvy (bictegravir-emtricitabine-tenofovir). Mr. Williams works as a party planner for his job and enjoys spending time with friends from college on the weekends; he is hoping to expand his business after the COVID pandemic ends. He has no financial issues in taking care of his health and daily needs. Mr. Williams expressed concern about medication adherence with his HIV medications as they are required to be taken oral daily. He described examples of when he forgets to take them such as when he’s late for work or he’s spending a weekend over at his friend’s place and does not take the medications with him. He then asked us about the possibility of using a long-acting injectable agent for treatment of his HIV as he heard about the treatment from a friend. We recommended both cabotegravir and rilpivirine as long-acting injectables because many patients at our clinic had had much success with these two agents and many had not complained of major side effects.

Clinical Question
Would a long-acting injectable of cabotegravir and rilpivirine be a good alternative to traditional bictegravir-emtricitabine-tenofovir (Biktarvy) treatment for a young adult patient struggling with adherence?

Research Article

ARAVINDH NIRMALAN is a student at the Wayne State University School of Medicine.
Description of Related Literature

An extensive search was made for relevant papers to answer the clinical question. PubMed was the primary database used, with the search term "long acting injectable HIV treatment." To further refine the search, PubMed was filtered for articles published from 2018-2020 that were clinical trials and randomized controlled trials. This strategy specifically targeted more recent papers, as the long acting injectables are newer treatments, to ensure analysis of the views of patients taking the injectables most recently. Only articles that used the one or both drugs of cabotegravir and rilpivirine were reviewed, as those were the medications asked about during the clinical encounter. This narrowed the search results from 273 to 18. Each of these was examined to see if they could answer the clinical question and were pertinent to the clinical context. 13 of the articles did not address the question as they were concerned with more of the pharmokinetics and actual mechanism/efficacy of the long-acting injectable agent. This left 5 articles that addressed patient experiences with the injectable and tolerability.

The first article, “Safety, tolerability, and pharmacokinetics of long-acting injectable cabotegravir in low-risk HIV-uninfected individuals: HPTN 077, a phase 2a randomized controlled trial” did in fact comment on the tolerability and efficacy of a long acting injectable. However, it did not use a combination drug of the cabotegravir and rilpivirine. Furthermore, the article did not investigate HIV-infected individuals which didn’t match the present clinical context. The study ultimately concluded for HIV-uninfected patients cabotegravir was deemed safe and tolerable for patients, injection of the drug did sometimes lead to injectable site reactions however patients did not discontinue use.

The second study “Acceptability of a long-acting injectable HIV prevention product among US and African women: findings from a phase 2 clinical Trial (HPTN 076)” focused more on observing patient’s openness to receiving an injectable form of medication. This wasn’t relevant to the question as the patient already was open to receiving an injectable and did not address the actual experience in receiving the injectable. Interestingly the study concluded that injectable side effects of rash or on-site irritation were deemed acceptable by greater than 75 percent of the 136 patients. The study concluded that future use of long acting injectables may become more prevalent given the results of acceptability and openness to use from their study.

The third article, “Satisfaction and acceptability of cabotegravir long-acting injectable suspension for prevention of HIV: Patient perspectives from the ECLAIR trial” did address the questions posed in our clinical scenario. The participants did start on an oral agent then transitioned to an injectable one in cabotegravir. However this study was not selected since the group examined were all HIV negative. The study ultimately concluded that the long acting injectables was met with overall satisfaction and preference for injectables.

The fourth article, “Patient-reported tolerability and acceptability of cabotegravir + rilpivirine long-acting injections for the treatment of HIV-1 infection: 96-week results from the randomized LATTE-2 study” was a close candidate for selection. The paper did in fact examine the exact clinical question posed and the candidates were HIV positive unlike the other study. However this paper was not chosen, as it lacked more information on patient experience, rather than just whether the patient had a favorable or unfavorable experience. The clinical question requires studies that could comment more on a patient’s individualistic experience with the medication, so that other patients can relate to and benefit from the analysis. This study did in fact conclude favorable outcomes and tolerability to the long acting injectable.

The fifth article, “Efficacy and Freedom: Patient Experiences with the Transition from Daily Oral to Long Acting Injectable Antiretroviral Therapy to Treat HIV in the Context of Phase 3 Trials” best met the criteria in answering the clinical question. The methods in this study were pertinent to the clinical question as all the patients were originally on oral HIV medications and switched to the cabotegravir and rilpivirine treatment. This study provided actual quotes and experiences through in-depth interviews about the patient’s transition to an injectable medication, rather than mere survey results as in the other five studies considered. All the patients were also on traditional oral HIV meds, the same scenario as our patient. They were then switched to an injectable combination of cabotegravir and rilpivirine. It was strongly felt this article had all the components to answer the clinical question of whether a long-acting injectable of cabotegravir and rilpivirine could be a good alternative to traditional bictegravir-emtricitabine-tenofovir (Biktarvy) treatment for a young adult patient struggling with adherence. Based on the SORT criteria the Grade of Recommendation is B.
Critical Appraisal
The article describes a qualitative study whose purpose was to investigate HIV positive patients’ experiences with the long acting injectables cabotegravir and rilpivirine for their treatment. From the study, the researchers did find an overall satisfaction with long acting injectables as opposed to traditional daily oral HIV medications. Again, based on the SORT criteria this paper merits a recommendation of grade B. A total of 53 participants were identified and enrolled in their study. All 53 of these participants were purposefully sampled from ATLAS, ATLAS-2M, and FLAIR (First Long Acting Injectable Regiment Trials). Participants were required to start a 4 week course of oral cabotegravir and rilpivirine then were randomized to start the long acting injectable or continue their course of oral cabotegravir and rilpivirine. Eventually however all participants did take their long acting injectable and none switched back to oral medications. The long acting injectables were given either monthly or once every two months. This was a qualitative study that utilized a cross-section design to understand a patient’s experience from daily oral to long-acting ART’s. Data was collected using semi-structured interviews. In analyzing this data, the researchers made use of a bi-lingual codebook and Atlas-ti, a software program; from the description of data analysis, it seems the authors used Grounded Theory to analyze the data. The study design was adequate and sufficient for the purposes of this study as it was meant to document patient experiences rather than have a placebo to test the effectiveness of the treatment. The study was being carried out across 16 different countries although mainly in the US and Spain. The study does have a diverse group for race/ethnicity as the participants range from 65% Caucasian to 15% Latino and 15% Asian. However African Americans are only listed at 5% and have a higher prevalence than Asians and Latinos to attain HIV. Furthermore 85% of participants were Male and 15% were Female in the US group, perhaps a more even 50-50 representation could serve to better reproduce the study in other papers. The paper states that they mainly selected for individuals based on factors such as geographic diversity, ethnicity, socio-economic status, and diverse treatment experiences. Many of these factors were addressed in the demographic table given but selecting for diverse treatment experiences was not addressed. It is reasonable to question what may be considered or what may qualify as a diverse treatment. When examining the information on the interviews, the domains explored by interview were living with HIV, prior HIV treatment with daily oral medications, and the transition to a long acting injectable. These are appropriate topics to explore and were pertinent to the study at hand. The theme of analyzing and interviewing for patients living with HIV and being transitioned from oral medications to a long-acting injectable best mirrored the interaction with Mr. Williams. It is possible another domain could be a participant’s previous experience with any kind of injectable. This may better explain if a participant had previous experience with any time of injectable, they would obviously be open to another injectable. The interview results mostly commented injection side effects getting better with time and psychological freedom with using a long acting injectable. Further potential improvement of the study could have commented on the participants mental health as many of the participants preferred the option of a long acting injectable to reduce the stigma associated with a diagnosis of HIV. For example, those more uncomfortable with their HIV diagnosis and treatment would possibly be more open to a long acting injectable as opposed to those who have no issues with their diagnosis. In terms of screening the study for any bias there weren’t any noted on a read through of the paper. All the participants did indeed have an HIV diagnosis and were individually interviewed about their experiences with HIV and a transition to long acting injectable. There were no funding biases noted in the study; perhaps the only potential bias was the study’s participants either came from Spain or the United States. A potential improvement for this study could have been for the participants to be selected from only one region to better compare participants with one another and eliminate cultural and regional beliefs regarding the stigma of HIV. Perhaps the stigma of HIV is less of a problem in Spain as it is in the United States. Ultimately a better job could have been done in picking one country and picking patients from different areas of a country rather than just focusing on urban clinical sites as mentioned before.

Clinical Application
With regards to Mr. Williams, this clinical study is pertinent to our decision making in giving Mr. Williams a long acting injectable as a substitute for daily oral HIV medications. The participants in this study were mostly found from urban centers such as Washington DC and San Francisco. Mr. Williams lives within city limits and should have no problems in receiving the injectable every month for control of his HIV. Furthermore, the study talks about how patients feel less of a stigma of having HIV with the help of using a long acting injectable since the constant daily oral medications may be a burden on a lot of patients. Mr. Williams does feel slight stigma from his HIV diagnosis as he likes to spend time with his friends on weekends; he describes his stigma mainly as having to explain himself in social situations for taking his daily prescribed medications and at times feels embarrassed when revealing his HIV diagnosis to new people whom he may be introduced to by his friends. It’s only normal that he would seek an option to not have to take daily oral pills in the presence or company of others. A long acting injectable instead of...
daily oral HIV medications, bictegravir-emtricitabine-tenofovir (Biktarvy) in Mr. Williams’ case, is an excellent alternative for our patient if he does not mind occasional injection site reactions which was noted in the study. Mr. Williams is also a 23 year old male while the median age in this study was 31 which Mr. Williams is close to in age. The results of this study do make sense as they saw from in-depth interviewing a majority felt that the long-acting injectable was an excellent alternative to daily oral medications which the patients had previously been taking before the study. The only harm in switching to the long acting injectable noted from the study was the potential for injection site reaction which may strain a patient away from future use; the benefits are patients feeling less stigma of their HIV diagnosis and better adherence and freedom.

New Knowledge Related to Clinical Decision Science
In summation our patient may benefit from a switch to a long acting injectable. He is a young 23 year old, HIV positive, urban dwelling patient who likes to spend time with friends on weekends and enjoys the work he does with party planning. Our patient would receive an injectable once a month and can resume his life and live it as any other 23 year old person would. The constant responsibility to take his oral Biktarvy medication may be overwhelming for Mr. Williams and that is why he might’ve requested it. Our team posited questions as to where you heard of the injectables and what did you know about them. He responded had heard of the injectables from a friend; he was aware that the injectable treatment was an option for those who did not feel they could take the oral medications prescribed to them daily. From the article chosen and researched it does strongly suggest a good impact on patients to at least try to switch to a long acting Injectable as many patients have reported positive experiences. Mr. Williams fits the characteristics of the participants in the study as they are all concentrated in cities and are relatively young with a median age of 31. From the evidence of the literature and previous positive patient’s experience with the injectables, we decided to start Mr. Williams on cabotegravir and rilpivirine as monthly injectables. Our team was comfortable with this decision since Mr. Williams was forthcoming with this option and had expressed a strong interest in receiving them. Given that the previous patients who were started on these injectables reported positive experience, Mr. Williams’ weak adherence to his daily oral medications, as well as the potential for decreased stigma with using the monthly injectables instead of the daily oral medications, we concluded that this was the best clinical decision for Mr. Williams’ HIV treatment. Furthermore, our clinical decision was centered on Mr. Williams’ attitude towards these injectables; he was generally positive and strongly interested in them. We did not weigh as much the clinical efficacy between the oral medications and injectables as Mr. Williams’ had a strong interest and positive feelings about the injectables; because of this we concluded that switching him to the injectables would undoubtedly increase his adherence to this regimen. Too often this aspect of clinical decision, taking into account the patient’s feelings about a drug, gets ignored or subjugated to the science.

Mr. Williams’ describes the stigma of using his oral medications as partly embarrassing and always having to explain the reason for the medications and his HIV illness. Stigma of medication use or having a disease is all too common in medicine; patients with diseases are more often viewed in a negative way by others as something is wrong with them or their disease defines their identity. These thoughts from others are not true, rather we tend to associate disease with a negative connotation. Stigma of disease could result in patients not willing to see their doctors for the potential of being diagnosed with a disease or using their medications in public to avoid embarrassment. Mr. Williams’ case is a perfect example of a patient looking for an alternative to daily medications to decrease the stigma of having HIV. In general, having a patient switch from daily oral medications to a treatment once a month might be best for all patients since medication noncompliance is so rampant. With an infection like HIV its best to take proper action and ensure adherence in whatever way possible.

Conflict Of Interest Statement
The author declares no conflicts of interest.
References


