New horizons in the pharmaceutical care of HIV patients on long-term antiretroviral treatment

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Antiretroviral treatment (ART) has experienced a startling progress in the last few years as a result of the combination of safe and highly effective drugs that allow people living with HIV (PLHIV) to reach survival rates similar to those of the general population, and convenient dosing schedules whereby a single tablet a day is able to control infection and prevent transmission.

Spanish PLHIV will soon benefit from the first-ever long-acting ARTs: cabotegravir (CAB) and rilpivirine (RPV), indicated for patients on stable ART, with a consistently suppressed viral load (VL) < 50 copies/mL and no previous resistance or virologic failure to nonnucleoside reverse transcriptase inhibitors (NNRTIs) or integrase inhibitors (IIs). According to the products’ SmPC, oral CAB and RPV must be administered for 4 weeks before initiation of long-acting ART to evaluate the patients’ tolerability to the medication. Subsequently, a loading dose of intramuscular CAB and RPV (two injections, one in each buttock) is administered, followed by a maintenance dose. As none of the thousands of patients evaluated in the development studies suffered any adverse events during the lead-in oral phase, the responsible pharmaceutical company submitted the data to the EMA requesting that treatment with long-acting ART drugs may be initiated to oral therapy6.

It must be mentioned, however, that several challenges remain regarding the introduction of the new long-acting ART medications7, such as their incorporation to healthcare routines, their custody and ensuring that they are administered at the right time. Although administration of the treatment may occur at a different department in every hospital, pharmacists will still be in charge of informing patients about the therapy, providing them with the right education and support they need. These studies included patients with appropriate disease control, normal renal and liver function, limited comorbidities and no hepatitis B infection. To be included, women had to be nonpregnant. Seventeen percent of subjects were 50 years old or older; women accounted for 27.5% of the sample, patients with a BMI > 30 for 17% and those of black race for 18%3.

Several studies have highlighted the high interest in long-acting ART among PLHIV. A single-center US study (n = 374) showed that 61% of PI-HIV were either willing or very willing to undergo long-acting ART therapy, with 41% expressing a preference for tablets, 40% for injections and 18% for implants8. A total of 54.7% of respondents to the Positive Perspectives survey (n = 2,389), administered in 25 countries, expressed a preference for long-acting ART. The most cited advantages of ART were the decrease in long-term adverse events, the elimination of the burden of daily administration and a lower incidence of adverse events. Participants in the phase III trials indicated that long-acting ART boosted confidentiality and privacy, reduced the stigma associated with the disease and gave them a greater sense of freedom. An analysis of the patient-reported outcomes from the FLAIR and ATLAS studies concluded that patients preferred long-acting ART to oral therapy9.

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the relevant management recommendations, and following up on the evo-
volution of their drug therapy in order to ensure that the best health outcomes are
obtained. Management of missed doses or temporary changes to oral
therapy when patients cannot come to the hospital (because they are away
or on holiday) will be essential. The above-mentioned phase III trials con-
templated a ± 7 day-interval; for longer intervals bridging oral therapy
must be foreseen in order to prevent the development of resistance to the
medication. Appropriate patient selection is also important for this therapy
as subjects must have demonstrated proper adherence to ART for a long
period of time.

A joint multivariate analysis that looked into the virologic failures that
occurred in the ATLAS, FLAIR and ATLAS-2M trials identified the following
potential causes for such failures: the presence of mutations associated
to resistance to RPV, BMI > 30, low RPV concentrations at 8 weeks, and VIH

As usual, hospital pharmacists are key in following up patients who
initiate long-acting ART, as providers of recommendations for the proper
management and administration of the medication and as professionals
in charge of following up the evolution patients’ drug therapy. Pharmacists
have played the latter role since the outbreak of the HIV pandemic, work-
ning hand-in-hand with their infectious disease colleagues and with patients
in order to improve health outcomes.

For more than five years hospital pharmacists have been working on
the so-called CMO (Capacity, Motivation, Opportunity) pharmaceutical care
model for outpatients, which envisages both a multidimensional kind of
pharmaceutical care where hospital pharmacists play the role of medi-
cation experts vis-à-vis patients and their treatment, and an individualized
approach to pharmaceutical care.

Implementation of the CMO model has resulted in encouraging health
outcomes including enhanced adherence to ART, an increase in the number
of PLHIV with undetectable VL levels, and an increase in pharmacothera-
peutic indicators related to hypertension, dyslipidemia and diabetes.
The recent PRICMO study has shown an improvement in primary and secondary
adherence to ART and to concomitant medication65, while another study
exhibited a more effective control of antihypertensive medication and a
higher adherence to antiretroviral and hypertensive medication.

The increased prevalence of older PLHIV, who typically use polyphar-
mary and display higher pharmacotherapeutic complexity levels (mainly
because of concomitant medications, potentially inappropriate medi-
cations, and drug-drug interactions), has prompted a review of the medi-
cines prescribed to these patients to optimize their medication regimens.
Hospital pharmacists are directly involved in these initiatives66,67. High
pharmacotherapeutic complexity is related with a lower quality of life
in PLHIV68.

Despite the unquestionable improvement that the advent of the new
long-acting ART medications will represent for many patients, the need of an
individualized, multidimensional and multidisciplinary follow-up will make it
indispensable to monitor patients closely both through traditional follow-up
visits and through the incorporation of new technologies.

In a nutshell, the continuous work of hospital pharmacists in the care
of PLHIV will be increasingly important going forward given their ability
to relate to patients and manage their drug therapy.

Bibliography


