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Potential healthcare resource use and associated costs of every 2 month injectable cabotegravir plus rilpivirine long-acting regimen implementation in the Spanish National Healthcare System compared to daily oral HIV treatments

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Abstract

Introduction HIV treatment currently consists of daily oral antiretroviral therapy (ART). Cabotegravir + rilpivirine long-acting (CAB + RPV LA) is the first ART available in Spain administered every 2 months through intramuscular injection by a healthcare professional (HCP). The objective of this analysis was to assess potential healthcare resource use (HRU) and cost impact of implementing CAB + RPV LA vs. daily oral ART at National Health System (NHS) hospitals.

Methods Online quantitative interviews and cost analysis were performed. Infectious disease specialists (IDS), hospital pharmacists (HP) and nurses were asked about their perception of potential differences in HRU between CAB + RPV LA vs. daily oral ART, among other concepts of interest. Spanish official tariffs were applied as unit costs to the HRU estimates (€2022).

Results 120 responders ($n = 40$ IDS, $n = 40$ HP, $n = 40$ nurses) estimated an average number of annual visits per patient by speciality (IDS, HP, and nurse, respectively) of 3.3 vs. 3.7; 4.4 vs. 6.2; 6.1 vs. 3.9, for CAB + RPV LA vs. daily oral ART, and 3.0 vs. 3.2; 4.8 vs. 5.8; 6.9 vs. 4.9, respectively when adjusting by corresponding specialist responses. Estimation by the total sample led to an annual total cost per patient of €2,076 vs. €2,473, being €2,032 vs. €2,237 after adjusting by corresponding HCP, for CAB + RPV LA vs. daily oral ART.

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Conclusions These results suggest that the implementation of CAB + RPV LA in NHS hospitals would not incur in increased HRU-related costs compared to current daily oral ARTs, being potentially neutral or even cost-saving.

Why carry out this study?

• Main clinical guidelines in HIV recommend the use of daily oral antiretroviral combinations. Recently, a long-acting regimen consisting of cabotegravir plus rilpivirine (CAB + RPV LA) gluteal intramuscular injections has become available in Spain for maintaining HIV-1 suppression.
• Given that the long-acting regimes are administered every 2 months, it is anticipated to have a different patient pathway within the hospital compared to daily oral ART, which may lead to changes in healthcare resources and associated costs needed for HIV treatment.

What was learned from the study?

• The total annual cost per patient ranged from €2,032 to €2,076 for CAB + RPV LA, and from €2,237 to €2,473 for daily oral ART.
• These figures suggest that the implementation of CAB + RPV LA in Spanish NHS hospitals would not translate into increased healthcare resource utilization-related costs associated to a different patient pathway compared to current daily oral ART, being potentially cost-saving.

Keywords Antiretroviral agents, Cabotegravir, Costs and cost analysis, Healthcare resource use, HIV, Long-acting injectable, Rilpivirine

Introduction

The first cases of AIDS were described in 1981, and over four decades later, HIV remains one of the main public health concerns with 38.4 million people currently living with HIV worldwide, 1.7 million of them being children, with 1.5 million newly acquiring HIV every year and almost 700,000 AIDS-related deaths in 2020 [1–3]. In Spain, 151,387 people are estimated to be living with HIV, with an average of over 3,500 new cases diagnosed every year in the last decade, although it has been in decline in the past two years [4–6].

Survival of people with HIV (PHIV) has greatly improved in the last couple of decades thanks to the evolution of antiretroviral therapy (ART), resulting in the chronification of the disease [7]. Nowadays, PHIV that are diagnosed early and are capable of taking continuous ART have a life expectancy that approaches that of general population, so their care focus currently should not only be on achieving and maintaining viral suppression, but also on managing age-related comorbidities, the use of concomitant treatments, drug-related toxicity and improving quality of life of people living with HIV (PLHIV) [8–12]. In 2014 the Joint United Nations Programme on HIV/AIDS (UNAIDS) established the 90-90-90 target: by 2020, 90% of all people living with HIV know their HIV status, 90% of all people diagnosed with HIV receive sustained antiretroviral therapy, and 90% of all people receiving antiretroviral therapy have viral suppression, aiming to reach 95-95-95 initially by 2030 [13] and recently accelerated to 2025 [14]. Also, a 'fourth 90' was deemed necessary in terms of quality of life of people with viral load (VL) suppression would have good health-related quality of life, entailing attention to both comorbidities and self-perceived quality of life, resulting in a more people-centred approach from health systems [15]. Recently this concept has been further evolved by an international multidisciplinary panel of HIV experts agreeing on a consensus statement for the long-term wellbeing of PHIV [16].

Until recently, all ART regimens recommended by the main clinical guidelines were based on daily oral antiretroviral combinations [17–19]. Cabotegravir plus rilpivirine (CAB+RPV) gluteal intramuscular injections administered by a healthcare professional (HCP) is the first and only long acting (LA) regimen available for maintaining HIV-1 suppression. This innovative LA ART authorized in Europe in December 2020 for the treatment of HIV-1 infection in adults who are virologically suppressed, became recently available also in Spain [20–25]. This new regimen transforms the treatment paradigm of PHIV, as it is dosed less frequently than daily oral ART, is subject to fewer drug interactions, and may be beneficial or improve the quality of life for individuals with pill fatigue or concerns about disclosure of their HIV status or stigma associated with intake of daily oral medication [20, 21, 23, 24, 26].

CAB+RPV LA was evaluated in three phase III randomized, active-controlled, non-inferiority clinical trials: FLAIR [27], ATLAS [28] and ATLAS-2M [29]. The ATLAS and FLAIR trials demonstrated the non-inferiority of CAB+RPV LA at 48 weeks dosed Q4W (monthly) versus daily oral ART (any triple ART for

ATLAS or Triumeq® for FLAIR) in both individual trial analysis [adjusted difference in proportion of patients with VL>50 copies/ml: ATLAS: 0.6% (95% CI: −1.2 to 2.5); FLAIR: 0.4% (95% CI: −2.8 to 2.1)] as in the pooled analysis of both [adjusted difference in the proportion of patients with VL>50 copies/mL: 0.2% (CI 95%: −1.4 to 1.7)]. Subsequently, the phase IIIb ATLAS-2 M trial demonstrated at 48 weeks the non-inferiority of CAB+RPV LA Q8W (every 2 months) versus Q4W dosing [adjusted difference in the proportion of patients with VL>50 copies/mL: 0.8% (95% CI: −0.6 to 2.2)]. CAB+RPV LA dosed Q4W or Q8W maintained virologic suppression (HIV RNA<50 c/mL) at 48 weeks in 94% (n=1,531/1,636) of the participants in the three phase III/IIIb trials. The safety profile of CAB+RPV LA in the ATLAS and FLAIR trials was comparable to that of current oral ART. Injection Site Reactions (ISRs) occurred in 25% of injections, the majority (98%) were mild/moderate in grade, lasting a median of 3 days, and the number of discontinuations for ISRs was very low (<2% of patients). 97–99% of the participants in the phase III/IIIb clinical trials preferred CAB+RPV LA vs. daily oral ART supporting the patient preference for a long-acting treatment [30, 31]. Finally, CAB+RPV LA is considered cost-effective versus daily oral ART in the Spanish National Health System (NHS) [32].

Considering frequency of administration every 2 months vs. current recommended daily oral ART regimens for virologically suppressed PHIV, the new long-acting CAB+RPV injectable regimen is anticipated to have a different patient pathway within the Spanish NHS hospitals when implemented, compared to daily oral ART [33–35], which may lead to changes in the healthcare resources and its associated costs needed for its administration.

The objective of this study was to evaluate the potential differences in healthcare resource use and its impact on associated costs resulting from the implementation of CAB+RPV LA compared to current daily oral ART from the perspective of Spanish NHS hospitals.

Methods

We performed a cross-sectional study consisting of online quantitative interviews (CAWI, Computer Assisted Web Interviewing) of HCPs involved in hospital HIV treatment and daily care and selected by a stratified random sampling: infectious disease specialists, hospital pharmacists, and nurses, followed by a cost analysis based on the results obtained.

HCPs were recruited by phone to ensure the screening conditions were met and then completed the self-administered online questionnaire not exceeding 25 min in length. In the CAWI, HCPs were asked about their perception of the potential differences in the healthcare resource utilization (HRU) between oral ART and CAB+RPV LA; precisely, estimations on the annual number of visits per patient required to the infectious disease specialist, to the hospital pharmacy and to the nursing team were collected. The interviews were carried out between May 19th and June 3rd, 2022.

Although the focus was HRU and its associated costs, to fully understand how the implementation of the new injectable regimen was perceived by the HCPs, other concepts were asked in the CAWI, such as the general assessment of CAB+RPV LA, potential administration management and logistics of CAB+RPV LA, staff and capacity of the hospital, and training or information needs from the patient.

All interviews were conducted considering the current regulation on the protection of personal data and pharmacovigilance and in accordance to the EPHMRA Code of Conduct 2022. Given that this study met all requirements to be considered a market research study, according to the EPHMRA Code of Conduct 2022 it did not require Clinical Research Ethics Committee or Independent Review Board approval. HCPs involved received economic compensation for their participation in the project.

Responses to the interviews were collected in a database and analysed with Gandia BarbWin and Microsoft Excel. Qualitative answers were assessed as the frequency of occurrence over the total number of answers for the question, and quantitative answers (i.e., number of visits and associated costs) as averages and their 95% confidence interval (95% CI). A two-tailed test was used to obtain the confidence interval for a population mean, using a normal distribution.

Regarding HRU, HCPs were asked about their estimation on the number of times that a virologically suppressed PHIV on treatment with ART or with CAB+RPV LA would visit the infectious disease specialist office, the hospital pharmacy, and the nursing team, in a 12-month period. At the time of the survey, CAB+RPV LA was not yet commercialized in Spain, but around 70% of the HCPs knew of its clinical development. Questions about visits to hospital pharmacy and nursing team were disaggregated by therapeutic objective (routine control and follow-up, administration of the treatment in the CAB+RPV LA case, specific adherence check-ins, patient counselling…). Assuming that more than one therapeutic objective can be covered in each visit, the maximum number of visits estimated by each specialist for both nursing and hospital pharmacy was obtained.

The questionnaire used in the CAWI is available as Supplementary Material 1.

From the information obtained on HRU estimates in the CAWI, unit costs from official tariffs published by the Autonomous Regions of Spain, updated to €2022 through

Spanish Consumer Price Index data [36], were used to perform the cost analysis. The unitary cost of each resource was multiplied by the frequency of use of each resource estimated by each interviewee (individual data) for each regimen, according to the following formula:

$$Total\ costs = HRU_1 * unit\ cost_1 + HRU_2 * unit\ cost_2 + \ldots + HRU_n * unit\ cost_n$$

where *HRU* represents the estimated frequency a given healthcare resource has been used by each regimen, and *unit cost* the cost associated to each use of a given resource by each regimen.

Subsequently, the average cost was calculated based on two methodologies: HRU from the visits estimated by the whole sample of respondents (i.e., estimated number of visits to the infectious disease specialist based on answers from infectious disease specialists, hospital pharmacists, and nurses), and HRU estimated by the corresponding specialist (i.e., estimated number of visits to the infectious disease specialist based solely on answers received specifically from infectious disease specialists).

Table 1 Characteristics of the sample interviewed

	Infectious disease specialist (*n* = 40)	Hospital pharmacist (*n* = 40)	Nurse (*n* = 40)	Total (*n* = 120)
HIV patients seen monthly, mean (SD)	142 (74)	321 (218)	117 (117)	194 (174)
Years of experience with injectable treatments, mean (SD)	21.3 (7.8)	19.3 (6.8)	19.2 (10.1)	19.9 (8.3)
Autonomous region, n (%)				
Andalucía	2 (5%)	6 (15%)	5 (13%)	13 (11%)
Aragón	1 (3%)	0 (0%)	0 (0%)	1 (1%)
Principado de Asturias	1 (3%)	0 (0%)	1 (3%)	2 (2%)
Islas Baleares	0 (0%)	2 (5%)	0 (0%)	2 (2%)
Canarias	0 (0%)	2 (5%)	1 (3%)	3 (3%)
Cantabria	1 (3%)	1 (3%)	1 (3%)	3 (3%)
Castilla - La Mancha	3 (8%)	2 (5%)	0 (0%)	5 (4%)
Castilla y León	1 (3%)	1 (3%)	0 (0%)	2 (2%)
Cataluña	9 (23%)	9 (23%)	8 (20%)	26 (22%)
Comunidad Valenciana	5 (13%)	5 (13%)	6 (15%)	16 (13%)
Extremadura	1 (3%)	0 (0%)	0 (0%)	1 (1%)
Galicia	3 (8%)	2 (5%)	1 (3%)	6 (5%)
Comunidad de Madrid	13 (33%)	8 (20%)	14 (35%)	35 (29%)
Región de Murcia	0 (0%)	0 (0%)	3 (8%)	3 (3%)
Comunidad Foral de Navarra	0 (0%)	1 (3%)	0 (0%)	1 (1%)
País Vasco	0 (0%)	1 (3%)	0 (0%)	1 (1%)
Hospital size, n (%)				
Large (> 500 beds)	24 (60%)	30 (75%)	27 (68%)	81 (68%)
Medium (≥ 200 & ≤500 beds)	16 (40%)	10 (25%)	13 (33%)	39 (33%)
Small (< 200 beds)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

N, sample included; SD, standard deviation.

Results

Out of the HCPs recruited by phone, the response rate was 99%. A total of 120 HCPs were interviewed: 40 Infectious disease specialists, 40 hospital pharmacists, and 40 nurses, with a mean (standard deviation) of 194 (174) PHIV seen monthly and 19.9 (8.3) years of experience with injectable treatments. A summary of the key characteristics of the sample interviewed is shown in Table 1.

Regarding the general assessment of CAB+RPV LA, this new injectable regimen scored an 8.7 in an increasing scale from 1 to 10 measuring the level of interest among HCPs, with 71% of the specialists being aware of its clinical development. Fatigue associated with daily oral ART were mentioned by 61% of the HCPs as the profile that could benefit the most from CAB+RPV LA, followed by suboptimal adherence to oral ART (59%) and emotional difficulties associated with oral ART (56%). The main drivers identified for the implementation of CAB+RPV LA were the improvement of therapeutic compliance (73%), decreased stigma associated with oral ART (72%) and greater logistical flexibility (68%). As for the barriers of implementing CAB+RPV LA, 72% of the specialists mentioned the injection procedure, 59% the extra workload for the nursing team and 56% the need for the PHIV to visit the hospital every 2 months. Finally, up to 74% of the HCPs considered that CAB+RPV LA would improve the people's quality of life compared to oral ART (score: 8.1 out of 10).

In general, 66% of the HCPs declared not having any concern regarding the implementation of CAB+RPV LA, and those who did (34%), mentioned the work overload of the nursing team (22%) and the economic cost (22%) as their main worries.

As to the implications on staff and capacity of the hospital, 41% of the HCPs indicated that new resources would be needed in the hospital for the administration of CAB+RPV LA, mostly through increasing the nursing staff (63%).

Regarding materials to be shared with PHIV, 88% of the HCPs demanded information about adverse events and 79% information about injection site reactions and importance of maintaining an optimum adherence, being applications (71%), printed materials (70%) and websites (54%) the preferred platforms with which to share the information.

Finally, in terms of HRU, the estimated average (95% CI) annual visits per patient reported by the total sample of HCPs for CAB+RPV LA vs. daily oral ART respectively were 3.3 (95% CI: 2.8 to 3.7) vs. 3.7 (95% CI: 3.1 to 4.3) for visits to infectious disease specialist; 4.4 (95% CI:

4.0 to 4.8) vs. 6.2 (95% CI: 5.8 to 6.7) to the hospital pharmacy; and 6.1 (95% CI: 5.4 to 6.8) vs. 3.9 (95% CI: 3.4 to 4.3) to the nursing team (Fig. 1). When considering the results as reported by the corresponding specialist, the estimated average (95% CI) annual visits per patient for CAB+RPV LA vs. daily oral ART respectively were 3.0 (95% CI: 2.5 to 3.4) vs. 3.2 (95% CI: 2.6 to 3.7); 4.8 (95% CI: 4.2 to 5.4) vs. 5.8 (95% CI: 5.3 to 6.3); and 6.9 (95% CI: 4.8 to 9.0) vs. 4.9 (95% CI: 3.9 to 5.9) (Fig. 2). Regarding visits to infectious disease specialists' little to no differences were expected by HCPs, not being statistically significant. A shift from hospital pharmacy to nursing team visits, with CAB+RPV LA compared to daily oral ART, within the hospital was observed. Differences in annual visits per patient to hospital pharmacy and nursing team between regimens were statistically significant at a 95% confidence level on both methodologies.

Unit costs for each resource, updated to 2022, are shown in Table 2.

When applying the unit costs to each HRU, the estimation by total sample of HCPs led to a total annual cost per patient (95% CI) of 2,076 € (95% CI: 1,887 € to 2,265 €) vs. 2,473 € (95% CI: 2,202 € to 2,745 €) for CAB+RPV LA vs. daily oral ART, being 2,032 € (95% CI: 1,966 € to 2,099 €) vs. 2,237 € (95% CI: 2,162 € to 2,312 €), respectively, after adjusting by the corresponding specialist. Differences in total annual costs per patient between regimens were statistically significant at a 95% confidence level on both methodologies. Detailed results from the cost analysis for each methodology are shown in and Figs. 3 and 4.

Despite the expected shift in the number of visits from hospital pharmacists to nursing teams, when translated to costs, CAB+RPV LA did not incur in increased HRU-related total costs due to its implementation within the hospital's PHIV pathways compared to daily oral ART regimes, even being potentially cost-saving in terms of patient route.

Discussion

CAB+RPV LA is the first and only innovative ART regimen administered every 2 months through HCP-administered intramuscular injections that has shown to be non-inferior to current daily oral ART options [27–29, 39]. Being a new paradigm in HIV treatment and an HCP-administered injectable regimen, the implementation of CAB+RPV LA may result in a different patient pathway for PHIV within NHS hospitals [23, 26].

Overall, HCPs anticipated that the implementation of CAB+RPV LA may transfer hospital pharmacy visits to nursing team visits, compared to current practices with daily oral ART. The costs analysis showed that these changes in the patient pathway for CAB+RPV LA administration with regards of the number of visits could lead to savings of approximately 200–400 € per patient per year compared to daily oral ART, due to the reduction in visits to the hospital pharmacist, that would

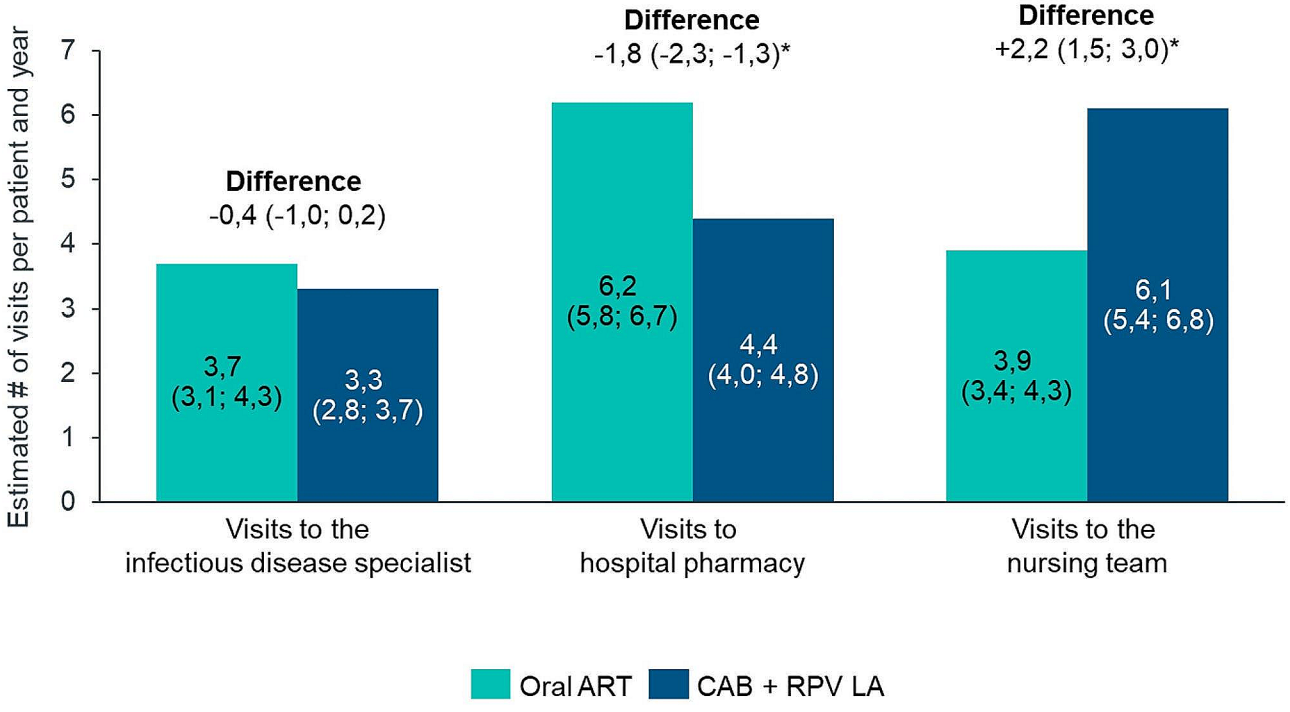

Fig. 1 Healthcare resource use estimated by the whole sample. ART, antiretroviral therapy; CAB+RPV LA, cabotegravir+rilpivirine long-acting. *Significant difference at 95%

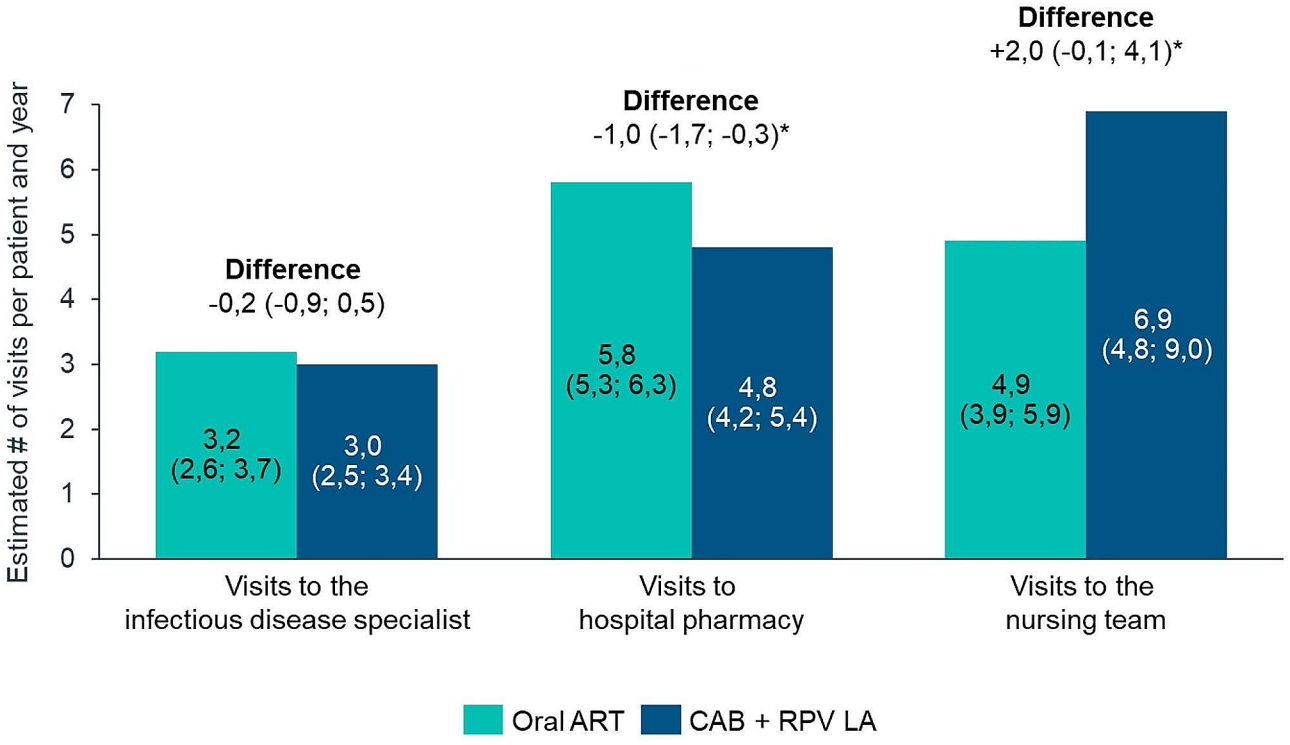

Fig. 2 Healthcare resource use estimated by the corresponding specialist. ART, antiretroviral therapy; CAB + RPV LA, cabotegravir + rilpivirine long-acting. *Significant difference at 95%

Table 2 Unit costs of the healthcare resources

Concept	Unit cost (€2022)	Source
Visits to the infectious disease specialist	€370.42	Servicio de Salud (2017). Diario Oficial de Castilla-La Mancha núm. 226 [37]
Visits to the hospital pharmacy	€165.00	Osakidetza-Servicio Vasco de Salud (2021). Boletín Oficial del País Vasco, número 3 [38]
Visits to the nursing team	€22.00	Osakidetza-Servicio Vasco de Salud (2021). Boletín Oficial del País Vasco, número 3 [38]

outweigh the increase in visits to the nursing team. These results highlight that the implementation of CAB+RPV LA in the NHS hospitals may not incur in increased HRU-related costs.

In the present study, the main barriers detected by HCPs for implementing CAB+RPV LA were the injection procedure, the extra workload for the nursing team and the need to visit the hospital every 2 months. These results are very similar to the findings from the CARISEL study, a phase IIIb hybrid implementation-effectiveness trial that examined the acceptability, appropriateness and feasibility of CAB+RPV LA in Europe, where the increased number of visits, increase in staff workload and potential discomfort of injection were identified as the main barriers by staff HCPs at baseline [40, 41]. However, at month 5, as staff gained experience, there was an average decrease of 43% in the proportion of staff HCPs reporting these barriers [39, 40]. Also, visiting the hospital every 2 months, identified as a barrier by the HCPs in our study, was considered acceptable by almost 98% of the CARISEL patient study participants [42].

Staffing and workload concerns were among the most mentioned issues in the interviews, both for the CAB+RPV LA regimen itself and its implementation. Results from CARISEL study showed that mean appointment duration was reduced by 30.4% between month 1 and month 6, meaning that healthcare professionals have a steep learning curve and the initial increase in workload is quickly adjusted [42]. In any case, given that long-acting regimen is a field of nurses' work, communication between nurses and specialists and enhancement of coordination of care could further help minimize delays and ensure that patients receive the necessary specialist input in a timely manner.

In a prior study, a multidisciplinary expert panel composed by the main agents involved in PHIV healthcare (the three profiles involved in the current study plus healthcare evaluators and patient association representatives) assessed the added value contribution of CAB+RPV LA to management of HIV in Spain compared to daily oral single-tablet regimens using a MCDA (Multi-Criteria Decision Analysis) methodology [43]. Findings were in line with those reported in the present

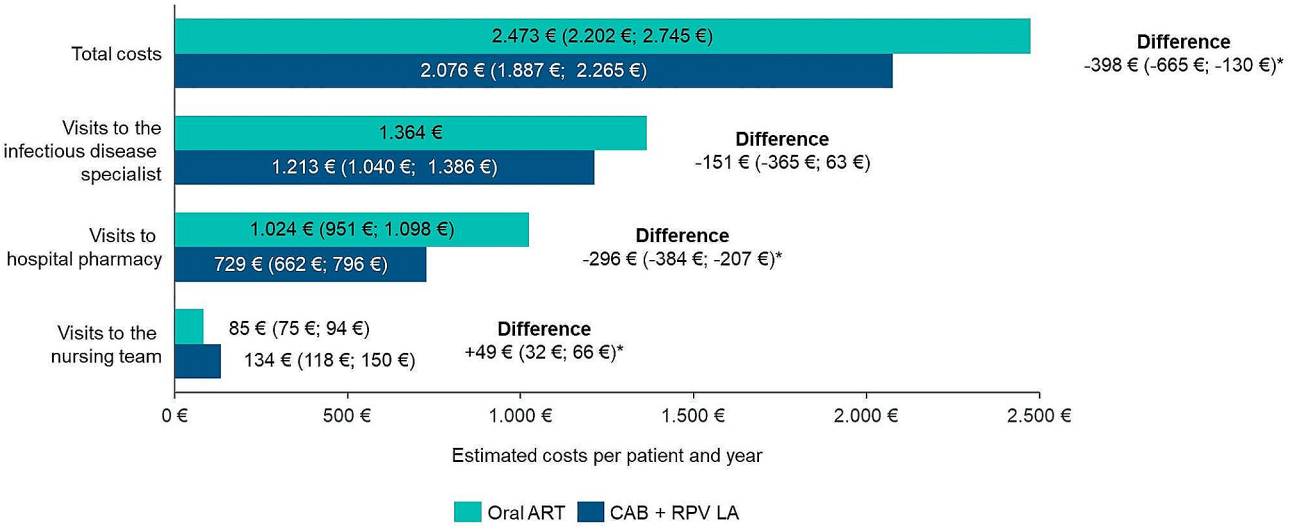

Fig. 3 Annual costs per patient associated with healthcare resource use estimated by the whole sample. ART, antiretroviral therapy; CAB + RPV LA, cabotegravir + rilpivirine long-acting. *Significant difference at 95%

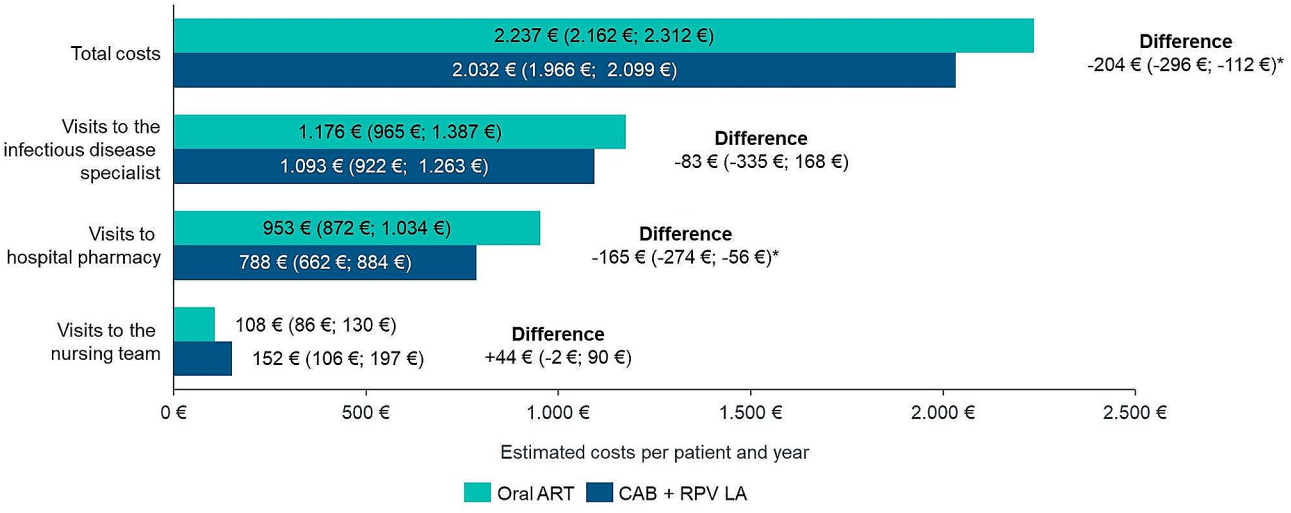

Fig. 4 Annual costs per patient associated with healthcare resource use estimated by the corresponding specialist. ART, antiretroviral therapy; CAB + RPV LA, cabotegravir + rilpivirine long-acting. *Significant difference at 95%

study, as therapeutic benefit of CAB+RPV LA was highly valued, as the potential benefit in adherence and stigma-related issues may improve overall quality of life for PHIV [43]. The potential implementation of CAB+RPV LA was also perceived as positive, and most of the clinical experts considered that the NHS hospitals are prepared for the correct use and implementation of CAB+RPV LA [43].

This study presents some limitations worth mentioning. First, as CAB+RPV LA was not yet commercially available in Spain at the time of the study, the results rely on previous experience in clinical trials and perceptions of the HCPs included. However, this could only be further addressed in the future with real-world evidence studies regarding CAB+RPV LA implementation. Also, the hospitals included in the analysis are only a sample and might not be representative of the whole universe of hospitals in the Spanish NHS. The final sample of HCPs might also be unbalanced in terms of the representativeness of HCPs across all regions in Spain. It is also worth noting that most of the HCPs worked in large hospitals (>500 beds), representing about 66% of the total amount of large hospitals in Spain, while only 17% of the medium (≥200 - ≤500 beds), and 0% of the small (<200 beds) hospitals were included [44]. As the objective of the analysis was to assess direct healthcare resource use related to its administration, which was considered useful to evaluate since it constitutes a new route of administration in relation to already established treatments, effectiveness, treatment safety or patient reported quality of life were not collected as these were considered out of

scope. In this sense, the cost-effectiveness relationship has been previously evaluated and published, considering CAB+PRV LA a cost-effectiveness intervention vs. the oral ARTs [32]. In addition to that, the present study is considered a partial economic analysis, focused on cost-calculation of the new administration pathways given the innovative HIV injectable long-acting treatments compared to the usual pathways, as it can be done following Drummond book [45]. Regarding the cost analysis, only visits to infectious disease specialist, hospital pharmacy and nursing team were considered which could be a simplification of the total healthcare resources needed for each treatment pathway for a long-acting injectable vs. daily oral ART; however, these were highlighted as the most important resources in terms of human resources. Finally, unitary costs were retrieved from official tariffs published by two Autonomous Regions of Spain, which may not be representative at the national or hospital level, but in the absence of National data this was the best approach as done in prior economic studies published in Spain.

To the best of our knowledge, this is the first study evaluating the potential economic impact of implementing CAB+RPV LA vs. daily oral ART for the treatment PHIV in Spain using a representative sample of relevant HCPs.

Results from this study suggest that, having previously demonstrated that CAB+RPV LA is a cost-effective alternative for the Spanish NHS [32], the implementation of CAB+RPV LA in Spanish NHS hospitals would not incur in increased HRU-related costs associated to a different patient pathway or administration route compared to current daily oral ART, being potentially neutral or even cost-saving from a hospital's point of view. Future real-world evidence studies would complement our results.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-09595-4.

Supplementary Material 1

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Author contributions
All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by all authors. The first draft of the manuscript was written by all authors and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Competing interests
Laura-Amanda Vallejo Aparicio is employee and holds stocks of GSK group of companies; Victoria Neches García is employee of GSK group of companies; Beatriz Hernández-Novoa is employee and holds stocks of ViiV Healthcare; Gregorio Casado, Ferrán Jodar, Marco Pinel and Daniel Callejo Velasco are employees of IQVIA. IQVIA received fees from ViiV Healthcare for conducting the study.

Ethics
All interviews were conducted considering the current regulation on the protection of personal data and pharmacovigilance and in accordance to the EPHMRA Code of Conduct 2022. Given that this study met all requirements to be considered a market research study, according to the EPHMRA Code of Conduct 2022 it did not require Clinical Research Ethics Committee or Independent Review Board approval. HCPs involved received economic compensation for their participation in the project.

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References

1. Global Report. UNAIDS report on the global AIDS epidemic 2021. https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf.
2. United Nations. World Leaders in General Assembly Adopt Political Declaration Pledging Urgent, Transformative Action to Stop Global AIDS Epidemic by 2030 [press release]. https://press.un.org/en/2021/ga12333.doc.htm.
3. Centers for Disease Control (CDC). Pneumocystis pneumonia–Los Angeles. MMWR Morb Mortal Wkly Rep. 1981;30(21):250–2.
4. Ministerio de Sanidad. Vigilancia epidemiológica del VIH y SIDA en España 2020. Actualización 30 de junio de 2021. November 2021. https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/vigilancia/Informe_VIH_SIDA_WEB.pdf.
5. Unidad de vigilancia del VIH, ITS y hepatitis. Actualización del Continuo de Atención del VIH en España, 2017–2019. Madrid: Centro Nacional de Epidemiología – Instituto de Salud Carlos III / Plan Nacional sobre el Sida – Dirección General de Salud Pública. 2020. Disponible en: https://www.sanidad.gob.es/ciudadanos/enfLesiones/enfTransmisibles/sida/vigilancia/ESTIMACION_DEL_CONTINUO_DE_ATENCIoN_DEL_VIH_EN_ESPAnA_Nov2020.pdf [Acceso: febrero 2023].
6. DIRECCIÓN GENERAL DE SALUD PÚBLICA. VIGILANCIA EPIDEMIOLÓGICA DEL, VIH y SIDA, EN ESPAÑA. 2021 https://www.isciii.es/QueHacemos/Servicios/VigilanciaSaludPublicaRENAVE/EnfermedadesTransmisibles/Documents/VIH/informes%20de%20vigilancia%20VIH%20y%20sida%20anteriores/Informe%20VIH_SIDA_2022_CCAA.pdf.
7. Gueler A, Moser A, Calmy A, Günthard HF, Bernasconi E, Furrer H, et al. Life expectancy in HIV-positive persons in Switzerland: matched comparison with general population. Aids. 2017;31(3):427–36. https://doi.org/10.1097/qad.0000000000001335. Epub 2016/11/11.
8. Wandeler G, Johnson LF, Egger M. Trends in life expectancy of HIV-positive adults on antiretroviral therapy across the globe: comparisons with general population. Curr Opin HIV AIDS. 2016;11(5):492–500. https://doi.org/10.1097/coh.0000000000000298. Epub 2016/06/03.
9. Schouten J, Wit FW, Stolte IG, Kootstra NA, van der Valk M, Geerlings SE, et al. Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: the AGEhIV cohort study. Clin Infect Dis. 2014;59(12):1787–97. https://doi.org/10.1093/cid/ciu701. Epub 2014/09/04.

10. Althoff KN, Smit M, Reiss P, Justice AC. HIV and ageing: improving quantity and quality of life. Curr Opin HIV AIDS. 2016;11(5):527–36. https://doi.org/10.1097/coh.0000000000000305. Epub 2016/07/02.
11. Gimeno-Gracia M, Sánchez-Rubio-Ferrández J, Robustillo-Cortés MLA, Morillo-Verdugo R. Prevalence of polypharmacy and pharmacotherapy complexity in elderly people living with HIV in Spain. POINT study. Farm Hosp. 2020;44(4):127–34. https://doi.org/10.7399/fh.11367. Epub 2020/07/11.
12. Collaboration Antiretroviral Therapy Cohort. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. Lancet HIV. 2017;4:e349–56.
13. Joint United Nations Programme on HIV/AIDS (UNAIDS). Fast-Track: ending the AIDS epidemic by 2030. 2014.
14. Joint United Nations Programme on HIV/AIDS (UNAIDS). 2025 AIDS TARGETS. Available at: https://aidstargets2025.unaids.org/# [Accessed: march 2023]. 2014.
15. Lazarus JV, Safreed-Harmon K, Barton SE, Costagliola D, Dedes N, del Amo Valero J, et al. Beyond viral suppression of HIV – the new quality of life frontier. BMC Med. 2016;14(1):94. https://doi.org/10.1186/s12916-016-0640-4.
16. Consensus statement on the role of health systems in advancing the long-term well-being of people living with HIV. NATURE COMMUNICATIONS. (2021) 12:4450. https://doi.org/10.1038/s41467-021-24673-w.
17. Panel de expertos de GeSIDA y División de control de VIH, ITS, Hepatitis virales y Tuberculosis. Plan Nacional sobre el Sida. (2022) Documento de consenso de GeSIDA/Plan Nacional sobre el SIDA respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana. https://gesida-seimc.org/wp-content/uploads/2022/05/GuiaGeSIDAPlanNacionalSobreElSidaRespectoAlTratamientoAntirretroviralEnAdultosInfectadosPorElVirusDeLaInmunodeficienciaHumanaActualizacionEnero2022.pdf.
18. European AIDS Clinical Society (EACS). (2021) EACS Guidelines version 11.0, October 2021. https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf.
19. Gandhi RT, Bedimo R, Hoy JF, Landovitz RJ, Smith DM, Eaton EF, et al. Antiretroviral Drugs for Treatment and Prevention of HIV infection in adults: 2022 recommendations of the International Antiviral Society–USA panel. JAMA. 2023;329(1):63–84. https://doi.org/10.1001/jama.2022.22246.
20. Bares SH, et al. Curr Opin HIV AIDS. 2022;17(1):22–31.
21. Rana AI, et al. Drugs. 2020;80(6):535–45.
22. European Medicines Agency. VOCABRIA https://www.ema.europa.eu/en/medicines/human/EPAR/vocabria.
23. D'Amico R, Margolis DA. Long-acting injectable therapy: an emerging paradigm for the treatment of HIV infection. Curr Opin HIV AIDS. 2020;15(1):13–8. https://doi.org/10.1097/coh.0000000000000606. Epub 2019/11/26.
24. DHHS Guidelines for the use of antiretroviral agents in adults and adolescents with HIV, Sept. 2022. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed December 2022).
25. GESIDA Guidelines National Plan on AIDS regarding the antiretroviral treatment in adults infected with HIV. Jan 2022. https://gesida-seimc.org/wp-content/uploads/2022/03/plan_nacional_gesida_tratamiento_antirretroviral.pdf (accessed December 2022).
26. Thoueille P, Choong E, Cavassini M, Buclin T, Decosterd LA. Long-acting antiretrovirals: a new era for the management and prevention of HIV infection. J Antimicrob Chemother. 2022;77(2):290–302. https://doi.org/10.1093/jac/dkab324. Epub 2021/09/10.
27. ClinicalTrials.gov. Study to evaluate the efficacy, Safety, and tolerability of long-acting intramuscular cabotegravir and Rilpivirine for Maintenance of Virologic suppression following switch from an Integrase Inhibitor in HIV-1 infected Therapy Naive Participants (FLAIR) https://clinicaltrials.gov/ct2/show/NCT02938520.
28. ClinicalTrials.gov. Study evaluating the efficacy, Safety, and tolerability of switching to long-acting Cabotegravir Plus Long-acting Rilpivirine from current antiretroviral regimen in Virologically suppressed HIV-1-infected adults (ATLAS) https://clinicaltrials.gov/ct2/show/NCT02951052?term=NCT02951052&draw=2&rank=1.
29. ClinicalTrials.gov. Efficacy, Safety and Tolerability Study of Long-acting Cabotegravir Plus Long-acting Rilpivirine (CAB LA + RPV LA) in human-immunodeficiency Virus-1 (HIV-1) infected adults (ATLAS-2M) https://www.clinicaltrials.gov/ct2/show/NCT03299049.
30. Overton ET, Richmond G, Rizzardini G, Jaeger H, Orrell C, Nagimova F, et al. Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2 M), 48-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study. Lancet. 2021;396(10267):1994–2005. https://doi.org/10.1016/s0140-6736(20)32666-0. Epub 2020/12/15.
31. Murray M, Antela A, Mills A, et al. Patient-reported outcomes in ATLAS and FLAIR participants on long-acting regimens of cabotegravir and ilpivirina over 48 weeks. AIDS Behav. 2020;24:3533–44.
32. Moreno S, Rivero A, Ventayol P, et al. Cabotegravir and Rilpivirine Long-acting antiretroviral therapy administered every 2 months is cost-effective for the treatment of HIV-1 in Spain. Infect Dis Ther. 2023;12:2039–55. https://doi.org/10.1007/s40121-023-00840-y.
33. Bhattacharya R, Herren K, Poonawalla I, Bunniran S, Bloomfield A, Schwab P. Comparing medical utilization and cost outcomes in oral Versus Injectable Immunotherapy users with chronic inflammatory joint and skin diseases. J Manag Care Spec Pharm. 2020;26(10):1246–56. https://doi.org/10.18553/jmcp.2020.26.10.1246. Epub 2020/10/01.
34. Vidal-Alaball J, Butler CC, Potter CC. Comparing costs of intramuscular and oral vitamin B12 administration in primary care: a cost-minimization analysis. Eur J Gen Pract. 2006;12(4):169–73. Epub 2006/11/28. doi: 10.1080/14017430601049449. PubMed PMID: 17127603.
35. Offord S, Wong B, Mirski D, Baker RA, Lin J. Healthcare resource usage of schizophrenia patients initiating long-acting injectable antipsychotics vs oral. J Med Econ. 2013;16(2):231–9. https://doi.org/10.3111/13696998.2012.751025.
36. Servicio de Salud. Resolución De 15 de noviembre de 2017. Diario Oficial De Castilla-La Mancha. 2017;n–m 226:22denoviembrede2017.
37. Osakidetza-Servicio Vasco de Salud. Acuerdo De 13 de diciembre de 2021. Boletín Oficial Del País Vasco. 2021;n–mero 3:5deenerode2022.
38. Instituto Nacional de Estadística (INE). Indice de precios de consumo (IPC). Medias anuales. Consultado: junio 2022.
39. Ramgopal et al. CROI 2023; Virtual and Seattle, WA. Oral presentation 191.
40. Gutner C et al. Cabotegravir And Rilpivirine Implementation Study in European Locations (CARISEL): examining healthcare staff attitudes during a hybrid III implementation-effectiveness trial implmenting cabotegravir + rilpivirine long-acting injectable (CAB + RPV LA) for people living with HIV. Poster presented at: 18th European AIDS Conference; October 27–30, 2021, virtual and London, United Kingdom. Poster PE2/56.
41. Gutner C et al. Healthcare staff perspectives on the implementation of HIV injectable treatment: interim results from the Cabotegravir And Rilpivirine Implementation Study in European Locations (CARISEL). Poster presented at: 18th European AIDS Conference; October 27–30, 2021, virtual and London, United Kingdom. Poster PE2/36.
42. Hocqueloux L et al. Perspectives on the acceptability, appropiateness, feasibility, barriers, and facilitators from patients receiving cabotegravir + rilpivirine long-acting injectable treatment (CAB + RPV LA): interim results from the Cabotegravir And Rilpivirine Implementation Study in European Locations (CARISEL). Poster presented at: 18th European AIDS Conference; October 27–30, 2021, virtual and London, United Kingdom.
43. Calleja-Hernández MA, Martínez-Sesmero JM, Vallejo-Aparicio LA, Hernández-Novoa B, Badia X. En representación del Grupo de estudio CAB + RPV AP MCDA. Contribución De cabotegravir + rilpivirina de acción prolongada al tratamiento de la infección por VIH-1. Farm Hosp. 2022;46(4):208–14.
44. Ministerio de Sanidad. Centros, servicios y establecimientos sanitarios. Centros y Servicios del Sistema Nacional de Salud. Accessed: 01/09/2022.
45. Drummond MF, Sculpher MJ, Claxton K, et al. Methods for the economic evaluation of health care programmes. 4th ed. Oxford: Oxford University Press; 2015. p. 522.

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