ELSEVIER

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor



Endometrial cancer treatment and outcomes in Argentina: ECHOS-A real-world study

Claudia Soares ^{a,*}, Gabriela Abreu ^a, Juliana Queiroz ^a, Thiago Luiz Nogueira da Silva ^a, Patrícia Menezes ^a, Mariano Carrizo ^b, Paula Scibona ^c, Nadia Elisabeth Savoy ^c, Ventura A. Simonovich ^c, María Cecilia Riggi ^d, Diego Odetto ^d, Florencia Cravero ^d, Laura Jotimliansky ^b

- ^a GSK, Estrada dos Bandeirantes 8464, Rio de Janeiro RJ CEP 22783-110, Brazil
- ^b GSK, Tucumán 1, piso 4, Buenos Aires C1049AAA, Argentina
- ^c Clinical Pharmacology Section, Hospital Italiano de Buenos Aires, Tte. Gral. Juan Domingo Perón 4190, Buenos Aires C1199ABB, Argentina
- d Oncological Gynecology Section, Hospital Italiano de Buenos Aires, Tte. Gral. Juan Domingo Perón 4190, Buenos Aires C1199ABB, Argentina

ARTICLE INFO

Keywords: Argentina Endometrial cancer Latin America Overall survival Progression-free survival Real world

ABSTRACT

Objective: Real-world data for patients with endometrial cancer (EC) are limited, particularly in Latin America. We present treatment pattern findings from ECHOS-A – Endometrial Cancer Health Outcomes Study in Argentina. *Materials and methods*: A retrospective study using clinical data from privately insured patients with EC diagnosed from 2010 to 2019. Index (diagnosis proxy) was first date of an EC-related health term or treatment. Demographics, clinical characteristics, and FIGO staging were described. Disease progression and survival were assessed until study end, loss to follow-up, or death.

Results: Of 805 patients with EC, 77.4 % (n = 623/805) received any treatment and 22.6 % (n = 182/805) received none. Among those treated, 31.8 % (n = 198/623) had first-line (1L) systemic therapy, and 45.5 % (n = 90/198) proceeded to second-line (2L) therapy. Mean follow-up was 33.6 (SD 31.8) months. Of those receiving any treatment, 87.3 % (n = 544/623) had FIGO stage data (I, 62.9 %; II, 18.6 %; III, 13.6 %; IV, 5.0 %). Treatment by class in 1L and 2L, respectively, were platinum chemotherapy, 73.7 %, 36.7 %; non-platinum chemotherapy, 73.7 %, 62.2 %; immunotherapy, 1.0 %, 11.1 %; hormone therapy, 17.7 %, 26.7 %. Carboplatin/paclitaxel was the most frequent 1L (52.5 %) and 2L (14.4 %) regimen. Mean time to progression was 14.1 (SD 16.3) and 8.8 (SD 8.3) months in 1L and 2L, respectively. Adjusted 1- to 5-year risk of progression/death was 46.5–77.5 % and 65.0–86.2 % in 1L and 2L, respectively.

Conclusions: Approximately one-quarter of patients with EC received no treatment, and approximately two-thirds were not treated with 1L systemic therapy. Efforts to better understand the reasons for these treatment patterns are crucial for improving patient outcomes.

1. Introduction

Endometrial cancer is currently ranked as the sixth most common cancer among women worldwide (World Cancer Research Fund International, 2023). In 2020, over 417,000 new cases of endometrial cancer were diagnosed globally, and endometrial cancer accounted for over 97,300 deaths (World Cancer Research Fund International, 2023).

Worldwide incidence of endometrial cancer is predicted to increase by 2040, ranging from an increase of nearly 10 % in Europe to an almost 100 % increase in Africa (International Agency for Research on Cancer, 2022), primarily due to risk factors such as aging and obesity (Colombo et al., 2016; Zhang et al., 2019). In Latin American countries, women aged ≥65 years are at increased risk of endometrial cancer due to agerelated comorbidities and high rates of obesity (de Sousa et al., 2022).

E-mail addresses: claudia.s.soares@gsk.com (C. Soares), gabriela.x.abreu@gsk.com (G. Abreu), juliana.d.queiroz@gsk.com (J. Queiroz), thiago.l.nogueira@gsk.com (T.L.N. da Silva), Patricia.M.Menezes@gsk.com (P. Menezes), mariano.n.carrizo@gsk.com (M. Carrizo), paula.scibona@gmail.com (P. Scibona), nadia. savoy@hospitalitaliano.org.ar (N.E. Savoy), ventura.simonovich@hospitalitaliano.org.ar (V.A. Simonovich), mariacecilia.riggi@hospitalitaliano.org.ar (M.C. Riggi), diego.odetto@hospitalitaliano.org.ar (D. Odetto), florencia.cravero@hospitalitaliano.org.ar (F. Cravero), laura.x.jotimliansky@gsk.com (L. Jotimliansky).

https://doi.org/10.1016/j.gore.2024.101457

Received 18 April 2024; Received in revised form 4 July 2024; Accepted 7 July 2024 Available online 8 July 2024

2352-5789/© 2024 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

^{*} Corresponding author at: GSK, Estrada dos Bandeirantes 8464, Rio de Janeiro RJ CEP 22783-110, Brazil.

The incidence of cases in Latin America is estimated to increase by 60 % by 2040 (International Agency for Research on Cancer, 2022). In Argentina, the number of new endometrial cancer cases in 2020 was over 2450, with more than 900 deaths (International Agency for Research on Cancer, 2020).

Endometrial cancer is primarily managed with surgical resection, which may be curative in patients with early-stage disease (Abu-Rustum et al., 2023; Colombo et al., 2016; Morice et al., 2016). Following surgery, recommendations for adjuvant treatment are based on risk of recurrence, which depends on International Federation of Gynecology and Obstetrics (FIGO) staging and uterine factors such as histological grade and presence of lymphovascular space invasion (Abu-Rustum et al., 2023; Colombo et al., 2016; Yarandi et al., 2023). The 5-year overall survival estimates range from 74 % to 91 % in patients without metastatic disease and are lower among patients with disease recurrence versus no recurrence (20 % vs. 89 %, respectively) (Huijgens and Mertens, 2013; Morice et al., 2016).

In Argentina, approximately 16 % of the population have private health insurance (Novick, 2017). The healthcare system in Argentina is divided into public, social security, and private subsectors (Palacios et al., 2020; Rubinstein et al., 2018). Patients diagnosed with endometrial cancer typically seek care from obstetricians and gynecologists because they have regular gynecologic visits (Restaino et al., 2023). Diagnosis is often made through hysteroscopy-guided biopsies performed by gynecologists, although occasionally by other specialists. In terms of specialty care availability, in Argentina almost all patients have access to a specialist (Al-Talib et al., 2010). However, waiting times for surgery can be lengthy in crowded public hospitals, whereas in private institutions surgery is typically scheduled within a month of diagnosis (Blanco et al., 2024). Minimally invasive surgery using sentinel lymph node biopsy protocol with indocyanine green or patent blue is a wellestablished treatment for endometrial cancer (Pados et al., 2023). Patients are usually treated where they are diagnosed, although some specific cases may involve visits to referral centers. Patients have the option to receive treatment in their city of birth if suitable facilities are available.

Treatment options are limited for women with endometrial cancer whose disease progresses during or after first-line therapy (Colombo et al., 2016). Understanding patient demographics, treatment patterns, and clinical outcomes in a real-world setting is important for improving disease management, estimating disease burden, and identifying unmet treatment needs. However, there is a scarcity of real-world data for patients with endometrial cancer, especially in Latin America (Bruggmann et al., 2020; Colombo et al., 2016; Paulino et al., 2020).

This retrospective real-world study describes demographics, clinical characteristics, and treatment regimens in first- and second-line settings among patients with endometrial cancer in the private subsector in Argentina.

2. Materials and methods

2.1. Study design and population

The Endometrial Cancer Health Outcomes Study in Argentina (ECHOS-A) was a retrospective, longitudinal database study of female patients aged ≥18 years diagnosed with endometrial cancer between January 1, 2010, and June 30, 2019 (Fig. S1). Clinical data were extracted from electronic medical records from the private healthcare provider Hospital Italiano de Buenos Aires, Argentina. In the electronic medical record system, every user-uploaded input must be linked to a specific medical problem. Identified medical codes are recorded in a separate module. For instance, if a patient is admitted due to suspected or confirmed endometrial cancer, all related treatments and progress notes are associated with this condition. The electronic medical record system allowed the use of predefined medical codes within its structured space. In our study, oncologists and gynecologists from the Hospital

Italiano de Buenos Aires compiled a list of structured terms specifically related to endometrial cancer. Additionally, free-text keywords were searched through the structured query language server to retrieve information from the database. All eligible patients were extracted based on the medical health codes. Subsequently, specialists (oncologists and gynecologists) from the Hospital Italiano de Buenos Aires confirmed endometrial cancer diagnoses by manually reviewing all electronic medical record data (adjudication process). Since the endometrial cancer diagnosis date was not available, the index date was used as a proxy for diagnosis. The index date was the first/earliest date a patient had an endometrial cancer-related medical health term present in their electronic medical record, or underwent a procedure (surgery), imaging examination, endometrial cancer-related biopsy, or endometrial cancerrelated systemic therapy (hormone therapy, chemotherapy, or immunotherapy). From the date the patient received a health code related to endometrial cancer, all records before this date were evaluated to check if there were any procedures, drugs, image examinations, or biopsies related to endometrial cancer, since a delay may have occurred in the inclusion of the health code in the medical records. The objective was to set the index date as the most probable date of endometrial cancer diagnosis and to subsequently map the patient's treatment journey. From the index date, follow-up lasted until the study end (December 31, 2019), loss to follow-up, or death.

2.2. Data source and collection

The primary insurance provider at the Hospital Italiano de Buenos Aires is the Hospital Italiano Medical Care Program. Medical records are coded to a medical problem and linked to the date, care type (outpatient, inpatient, etc.), location, record provider (doctors, nurses, physical therapists, etc.), medical health term (symptoms, diagnoses, etc.), progress, examination results, and medications. Data included in the Hospital Italiano de Buenos Aires database were not restricted to Hospital Italiano Medical Care Program-affiliated patients. Data from other affiliated health maintenance organizations were included to increase the sample size. All drugs evaluated in this study were dispensed from pharmacies or during hospitalization/emergency room visits; physicians' prescriptions were not available in the database.

2.3. Study objectives and variables

The primary objective was to describe treatment patterns among patients with endometrial cancer treated at the Hospital Italiano de Buenos Aires, Argentina. Secondary objectives were to describe patient demographics and clinical characteristics, including FIGO staging, the most common drug regimens used, and the proportion of patients who used other types of treatment (e.g., surgery and radiotherapy).

Other objectives included evaluation of estimated progression-free survival following first- and second-line therapies, defined as time from date of first drug dispensed of the line of therapy to progression (new systemic therapy, surgery, radiotherapy, or death), and overall survival, defined as time from index date until death, including censored time by loss to follow-up.

The use of systemic therapies in patients with endometrial cancer was evaluated from the index date until the end of follow-up or end of data availability, whichever occurred first. The first record of a systemic therapy related to endometrial cancer was defined as initiation of first-line therapy. All agents of interest related to endometrial cancer treatment were based on the National Comprehensive Cancer Network Clinical Practice Guidelines[®] and the guidelines of the Argentinian National Administration of Drugs, Foods, and Medical Devices (Abu-Rustum et al., 2023; Ministry of Health, 2023).

The end of first-line therapy was either the day before starting a new systemic treatment different from those used in the first line or when the same regimen was resumed after a gap of 120 days or more. The end of first-line therapy was assigned as the day after the final dose or supply

before the treatment break. Accordingly, second-line therapy began with a new systemic treatment not used in first-line therapy or after a gap of 120 days or more (retreatment). A regimen included all systemic therapies administered concomitantly or with a maximum gap of 30 days. If second-line data were absent, end of first-line therapy was defined as the end of follow-up or data availability, whichever occurred first. If the drug dispensed on the last day of supply was an oral medication, 30 days were added as standard for the end of any therapy line.

2.4. Data analysis

Results were interpreted descriptively, considering treatment availability, healthcare practices, and database coverage. No country-level generalizations were drawn. For continuous variables, descriptive statistics of central tendency (mean or median) and dispersion (standard deviation [SD] or interquartile range [IQR]) are presented. Categorical variables are presented as absolute numbers and percentages. The analysis was conducted using only results of patients with data available. Overall survival and estimated progression-free survival were evaluated by Kaplan–Meier analysis. Patients with missing data are noted.

3. Results

3.1. Patient identification and characteristics

A total of 805 patients were diagnosed with endometrial cancer in the study period (Fig. 1). The mean follow-up was 33.6 (SD 31.8) months. Demographic and clinical characteristics are summarized in Table 1. Briefly, the mean age at index was 65.3 (SD 12.4) years. In total, 67.6 % of patients (n = 544/805) were aged ≥ 60 years, and 63.9 % (n = 514/805) had overweight or obesity.

3.2. Treatment patterns during follow-up

More than three-quarters of the overall population (77.4 %; n=623/805) received any treatment (surgery, radiotherapy, or systemic therapy) during follow-up, and approximately one-quarter of patients

Table 1Demographics and clinical characteristics.

Characteristic	Overall $\overline{N=805}$	Treated (surgery, radiotherapy, or systemic therapy) n = 623 (77.4 %)	Treated with systemic therapy
Mean (SD)	65.3 (12.4)	65.5 (11.9)	66.5 (10.9)
Age group at index date, years, 1	ı (%)		
18–39	22 (2.7)	13 (2.1)	3 (1.5)
40–49	68 (8.5)	46 (7.4)	12 (6.1)
50–59	171 (21.2)	137 (22.0)	38 (19.2)
>60	544 (67.6)	427 (68.5)	145 (73.2)
BMI,* kg/m ²			
Mean (SD)	30.2 (7.5)	30.5 (7.6)	29.9 (6.8)
Underweight (<18.5), n (%)	5 (0.7)	3 (0.5)	1 (0.5)
Normal (≥18.5 to <25), n (%)	174 (25.1)	142 (23.7)	44 (23.0)
Overweight (≥25 to <30), n (%)	219 (31.6)	193 (32.2)	70 (36.7)
Obese (≥30), n (%)	295 (42.6)	261 (43.6)	76 (39.8)

^{*}Data were missing for 13.9 % (n = 112) of patients in the overall group, 3.9 % (n = 24) in the treated group, and 3.5 % (n = 7) in the treated with systemic therapy group. BMI, body mass index; SD, standard deviation.

(24.6 %; n = 198/805) received systemic therapy (Fig. 1). Among the 623 patients who received any treatment, 544 (87.3 %) had FIGO staging data, and most of whom (62.9 %; n = 342/544) had FIGO stage I disease (Fig. 2) (Morice et al., 2016). Of those with advanced cases (FIGO stages III and IV), over one-third (37.6 %, n = 38/101) were not treated with systemic therapy (Fig. 2). Over one-fifth of patients (22.6 %; n = 182/805) had no recorded treatment (Fig. 1). Among these, 11.5 % (n = 21/182) died during the follow-up period; 26.4 % (n = 48/182) had complete loss of follow-up (no data entry after index date); 72.5 % (n = 132/182) had loss of follow-up before study end (last data entry occurred before the end of the study); 1.1 % (n = 2/182) had right censoring (last data entry occurred

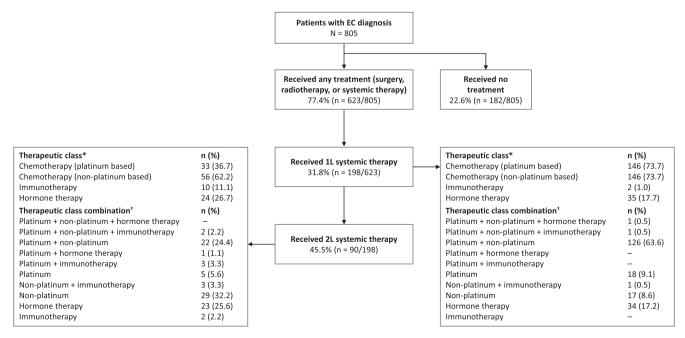


Fig. 1. Study disposition and therapies received in the first- and second-line settings between 2010 and 2019. Systemic therapy: hormone therapy, chemotherapy, or immunotherapy. *Patients could receive more than one therapeutic class in the same line of therapy. †Patients can appear in only one combination group. 1L, first line; 2L, second line; EC, endometrial cancer.

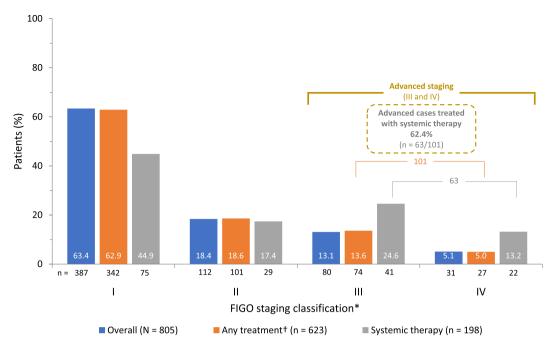


Fig. 2. Endometrial cancer treatment by FIGO stage. Missing: overall, 24.2 % (n = 195); any treatment, 12.7 % (n = 79); systemic therapy, 15.7 % (n = 31). *FIGO staging classifications are based on surgical staging, including an assessment of the extent of myometrial invasion, and local and distant metastases, which are key prognostic factors in endometrial cancer. The classifications are divided into four stages: stage I (tumor confined to the corpus uteri); stage II (tumor invades cervical stroma but does not extend beyond the uterus); stage III (local and/or regional spread of the tumor); and stage IV (tumor invades bladder and/or bowel mucosa, and/or distant metastases) (Morice et al., 2016). †Includes surgery, radiotherapy, or any systemic therapy. FIGO, International Federation of Gynecology and Obstetrics.

after the end of the study); 68.2% (n=45/66; 116 patients had no data on FIGO stage) had FIGO stage I disease; and 67.0% (n=122/182) had another health insurance plan, and hence may have been treated elsewhere.

Of the 623 patients receiving any treatment, nearly one-third (31.8 %; n=198/623) received first-line systemic therapy, and almost half (45.5 %; n=90/198) of all patients who received first-line therapy also received second-line therapy (Fig. 1). Among those receiving any treatment (n=623), the cumulative incidence of first-line systemic therapy initiation in the first year of follow-up was 25.4 % (n=157/619; four patients began first-line therapy at the index date, contributed as 0 person-days). Importantly, among those who received subsequent treatment, nearly one-quarter (22.9 %; n=30/131; number at risk in the first year of follow-up) required second-line therapy in the first year of follow-up.

Among the therapeutic classes (a patient could receive more than one therapeutic class in the same line of therapy), the most frequent first- and second-line regimens were platinum- (73.7 %, n=146/198; 36.7 %, n=33/90, respectively) and non-platinum-based (73.7 %, n=146/198; 62.2 %, n=56/90, respectively) chemotherapy (Fig. 1).

The most frequent first-line regimens included carboplatin/paclitaxel combination (52.5 %, n=104/198), tamoxifen (8.1 %, n=16/198), anastrozole (5.6 %, n=11/198), carboplatin alone (5.1 %, n=10/198), and cisplatin/doxorubicin/paclitaxel (4.5 %, n=9/198). The most frequent second-line regimens included carboplatin/paclitaxel (14.4 %, n=13/90), doxorubicin (12.2 %, n=11/90), letrozole (10.0 %, n=9/90), tamoxifen (7.8 %, n=7/90), and anastrozole (7.8 %, n=7/90) (Table S1).

3.3. Estimated progression-free survival

Estimated progression-free survival was calculated from the date of first drug dispensed in the line of therapy to progression (new regimen of systemic therapy, surgery, radiotherapy, or death) for all patients who received drug treatment. Progression events following first- and second-line therapy occurred in a total of 65.7 % (n = 130/198) and 71.1 % (n = 64/90) of patients, respectively.

Of the patients with progression events (n = 130/198) recorded after first-line therapy, 60.0 % (n = 78/130) received another systemic treatment regimen, 10.0 % (n = 13/130) received radiotherapy, 6.9 % (n = 9/130) underwent surgery, and 23.1 % (n = 30/130) died; 34.3 % (n = 68/198) were lost to follow-up. Among patients with progression events following second-line therapy (n = 64/90), 71.9 % (n = 46/64) received another systemic treatment regimen, one patient each (1.6 %) underwent radiotherapy or surgery, and 25.0 % (n = 16/64) died; 28.9 % (n = 26/90) were lost to follow-up.

The 1- to 5-year adjusted cumulative risks of progression or death were 46.5%, 63.1%, 70.5%, 77.5%, and 77.5%, respectively, for first-line therapy, and 65.0%, 77.9%, 81.9%, 86.2%, and 86.2%, respectively, for second-line therapy. The Kaplan–Meier curves for estimated progression-free survival are shown in Fig. 3A and B.

3.4. Overall survival

Kaplan–Meier overall survival estimates among patients treated with systemic therapies are shown in Fig. 3C, with an adjusted median survival time of 71.7 months. A total of 77 deaths (38.9 %) were registered during the study period, with a mean time from index date to death of 31.1 (SD 23.7) months (median 24.4; IQR 25.9). The 1- to 5-year cumulative risks of death were 8.1 %, 22.1 %, 33.4 %, 40.3 %, and 45.5 %, respectively (Table S2).

4. Discussion

4.1. Summary of main results

In this real-world study, demographics, clinical characteristics, treatment patterns, and health outcomes were evaluated in 805 female patients with endometrial cancer treated in a private healthcare setting in Argentina between 2010 and 2019. The findings suggest that, despite receiving optimal care, a large proportion of patients in the private subsector in Argentina are not receiving systemic therapy. Notably, approximately one-quarter of patients overall (22.6 %) had no

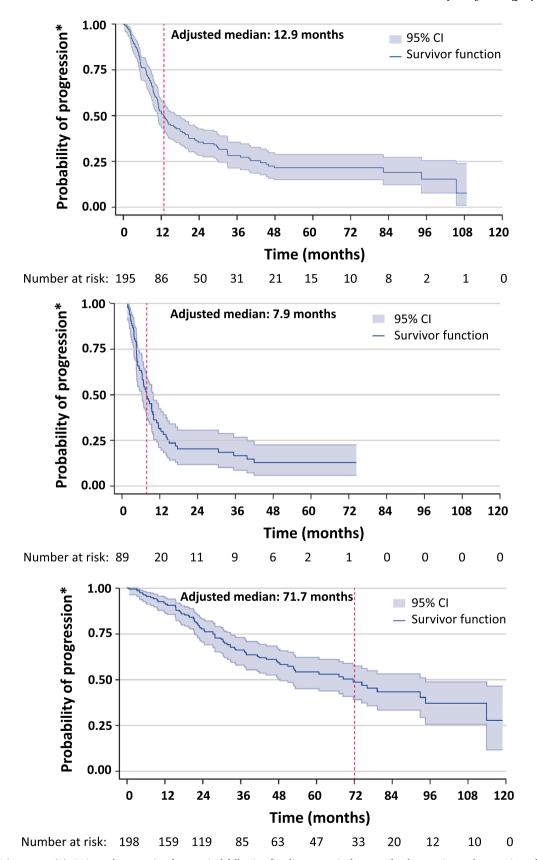


Fig. 3. Kaplan—Meier curves. (A): Estimated progression-free survival following first-line systemic therapy. The three patients who experienced progression on the day of end of first-line therapy were not included in this analysis. (B): Estimated progression-free survival following second-line systemic therapy. The one patient who experienced progression on the day of end of second-line therapy was not included in this analysis. (C): Overall survival. Adjusted median represents patients who experienced progression, including censored time by loss to follow-up. *Death was included as progression. CI, confidence interval.

treatment, including surgery, recorded in the database; over one-third (37.6 %, n=38/101) of patients with advanced disease (FIGO stages III and IV) were not treated with systemic therapy (Fig. 2). The use of chemotherapy predominated in the first- and second-line settings in the treated cohorts. Compared with chemotherapy, hormone therapy and immunotherapy use increased in the second line, whereas use of platinum-based chemotherapy decreased. Carboplatin/paclitaxel has been recommended in guidelines as the preferred treatment option in the first-line setting (Concin et al., 2021), and our results show that this was the preferred treatment (53 %) in this healthcare system. For those who received second-line therapy, only 14 % received carboplatin/paclitaxel. This, coupled with the absence of a clear standard preference in the second-line setting, is reflective of the lack of an efficacious standard second-line regimen for patients with endometrial cancer (Colombo et al., 2016).

4.2. Results in the context of published literature

Age and obesity are recognized risk factors for endometrial cancer (Colombo et al., 2016; de Sousa et al., 2022), both of which lead to high estrogen concentrations, associated with abnormal endometrial cell proliferation (de Sousa et al., 2022). It is estimated that >90 % of endometrial cancer cases occur in women aged >50 years, with a median age at diagnosis of 63 years (Colombo et al., 2016). Obesity is more strongly associated with endometrial cancer than any other cancer type (Onstad et al., 2016). Concordantly, a high proportion of patients (68 %) in ECHOS-A were aged \geq 60 years, and 64 % were overweight or obese. In line with the literature, most patients were classified as having FIGO stage I disease (Colombo et al., 2016; Morice et al., 2016).

The treatment landscape for endometrial cancer has evolved substantially in recent years, particularly for patients with advanced or recurrent disease, with the introduction of immunotherapy and targeted agents (Bruggmann et al., 2020; Concin et al., 2021; Kaufman et al., 2019; Paulino et al., 2020). However, chemotherapy remains a mainstay of treatment, in accordance with guideline recommendations (Brooks et al., 2019; Colombo et al., 2016; Liu et al., 2022). Similar to other realworld studies (Heffernan et al., 2022; Liu et al., 2022; Monk et al., 2022; Prabhu et al., 2022), and in line with guidelines and current standards of care, platinum- and non-platinum-based chemotherapy dominated treatment choice for first-line therapy, with over half of all patients (52.5 %) receiving carboplatin/paclitaxel.

Optimal second-line chemotherapy regimens for endometrial cancer have not yet been established (Brooks et al., 2019; Colombo et al., 2016), as demonstrated in this study and consistent with other real-world studies on endometrial cancer (Akada et al., 2021; Heffernan et al., 2022; Liu et al., 2022). In our study, hormone therapy and immunotherapy were more common in the second-than first-line setting; however, no preferred standard of care for second-line therapy was found. Instead, various combination and monotherapy regimens were used as second-line therapy. Retreatment with non-platinum-based chemotherapy was the most common treatment approach for second-line therapy, accounting for over 62 % of patients. The absence of a preferred second-line regimen reflects the need for more effective agents to prevent recurrence and improve patient outcomes.

Immuno-oncology therapies for endometrial cancer are only just emerging, attributes of which may result in a shift in preferred regimens over time (Blanco et al., 2024; Kaufman et al., 2019). Several clinical trials assessing the potential of novel immuno-oncology therapies in patients with advanced or metastatic endometrial cancer have been conducted or are ongoing (Blanco et al., 2024). Consequently, immuno-oncology therapies such as pembrolizumab (with or without lenvatinib) and dostarlimab have been approved by major regulatory agencies for the treatment of patients with advanced or recurrent endometrial cancer (Blanco et al., 2024; European Medicines Agency, 2024a; European Medicines Agency, 2024b; U.S. Food and Drug Administration, 2023; U.S. Food and Drug Administration, 2024). Notably, for patients with

mismatch repair-deficient/microsatellite instability-high primary advanced endometrial cancer, dostarlimab plus chemotherapy was approved in 2023 as the first front-line immuno-oncology treatment in the European Union (Blanco et al., 2024; GSK, 2023). In Argentina, dostarlimab, following prior platinum-based treatment for endometrial cancer, was approved in 2023 as second-line treatment for patients with advanced or recurrent mismatch repair-deficient/microsatellite instability-high endometrial cancer (Blanco et al., 2024; La Nueva Mañana, 2023).

A total of 77 deaths were recorded among patients receiving systemic therapy, with a median time from index to death of 24.4 months. Cumulative overall survival rates declined over time and were consistent with 4-year survival rates reported in a US retrospective study of patients with endometrial cancer transitioning from first- to second-line therapy (1- to 4-year overall survival rates of 70.9 %, 51.7 %, 43.3 %, and 36.5 %, respectively; median overall survival of 26.0 months) (Liu et al., 2022). Another retrospective study has reported lower 5-year and median overall survival rates than those observed in ECHOS-A; however, patients with endometrial cancer in the prior study were selected based on platinum exposure, and advanced or recurrent disease status (Huijgens and Mertens, 2013; Monk et al., 2022).

4.3. Strengths and limitations

Currently, there are limited real-world data for patients with endometrial cancer, especially in Latin America. To the best of our knowledge, this is the first study describing real-world treatment patterns and clinical outcomes for patients with endometrial cancer in Argentina. Of the Latin American countries, Argentina is an upper-middle-income country and ranks highly with respect to healthcare expenditure per capita; nevertheless, there are challenges regarding healthcare equity and efficiency of the current decentralized universal healthcare coverage system (Palacios et al., 2020; Rubinstein et al., 2018). The study was conducted in a private healthcare setting in Argentina, in which patients have effective coverage and receive optimal care. In this context, effective coverage translates to patients having actually received prioritized healthcare services (Palacios et al., 2020; Rubinstein et al., 2018). Overall, in Argentina, the general population has nominal universal health coverage - people are enrolled and have the right to treatment access (Palacios et al., 2020; Rubinstein et al., 2018). However, despite high healthcare spending per capita and a highly developed healthcare system compared with other countries in Latin America, effective healthcare coverage with respect to equity and efficiency requires reform (Palacios et al., 2020; Rubinstein et al., 2018). Our findings will be helpful for supporting treatment decision-making in healthcare systems. Patients with endometrial cancer who start treatment at the Hospital Italiano de Buenos Aires typically receive their treatment in the hospital, which makes establishing the patient treatment pathway easier.

Limitations of retrospective analyses include the quality of data recording, lack of standardization, and limited availability of relevant data items. The estimation of progression-free survival has potential limitations, such as non-uniform follow-up and overestimation, as progression events may occur post-censoring. Moreover, findings from the Hospital Italiano de Buenos Aires database should be interpreted considering the specific population the database represents; results cannot be extrapolated to country-level estimates or to all health maintenance organizations in Argentina. Another limitation is that this study lacks information on grade, histology, and lymph node involvement due to the data-extraction process. Extracting this information, which exists in unstructured and semi-structured formats, would necessitate additional data-mining techniques. The treatments described in this study are based on those dispensed by pharmacies or during a hospitalization or emergency room visit. The accurate capturing of lines of therapy may be undermined by the lack of visibility of clinical rationale for therapies received.

4.4. Implications for practice and future research

Efforts to better understand the reasons for the treatment patterns reported and to address challenges, such as those related to awareness of treatment options, educational needs, and other gaps, are crucial for improving patient outcomes. Treatment options are limited for women with endometrial cancer whose disease progresses during or after firstline therapy (Colombo et al., 2016). An improved understanding of the different genetic factors driving endometrial cancer has expanded the treatment landscape beyond chemotherapy to include several targeted and immunotherapeutic treatment options (Brooks et al., 2019; Cancer Genome Atlas Research Network et al., 2013; Di Tucci et al., 2019; Post et al., 2020). In this analysis, use of targeted therapies and immunotherapies increased in the second-line setting, but both were used less frequently than chemotherapy as first- and second-line therapies. The disease burden and limited treatment options for women with endometrial cancer, in particular for those with recurrent or advanced disease, warrant continued investigation of novel treatment approaches.

5. Conclusions

ECHOS-A provides valuable insight into real-world treatment practices, clinical characteristics, and health outcomes in patients with endometrial cancer in Argentina. Our findings indicate that a large proportion of patients in the private subsector are not receiving systemic, targeted treatment, and that many high-risk patients remain untreated. As more data become available, and familiarity with targeted and immunotherapeutic treatment options increases, it will also be important to understand the factors driving treatment selection, and the use of non-chemotherapy agents for patients with advanced or recurrent endometrial cancer.

6. Participant consent for publication

No direct participant contact or primary collection of individual human subject data occurred. Study results were in tabular form and aggregate analyses that omit subject identification; therefore, informed consent was not required.

7. Provenance and peer review

Not commissioned, externally peer reviewed.

Ethics approval

This study complies with all applicable laws regarding subject privacy. Ethics committee approval was obtained from the Hospital Italiano de Buenos Aires, Buenos Aires, Argentina, on October 1, 2020 (register number 3051).

Funding

This study was funded by GSK (study number 217348).

Author contributions

All authors made a substantial contribution to the work reported; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

All named authors meet the International Committee of Medical Journal Editors criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

CRediT authorship contribution statement

Claudia Soares: Writing - review & editing, Visualization, Validation, Resources, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization. Gabriela Abreu: Writing review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Data curation, Conceptualization. Juliana Queiroz: Writing – review & editing, Visualization, Validation, Software, Methodology, Formal analysis, Data curation, Conceptualization. Thiago Luiz Nogueira da Silva: Writing - review & editing, Visualization, Validation, Software, Methodology, Formal analysis, Data curation, Conceptualization. Patrícia Menezes: Writing - review & editing, Resources, Project administration. Mariano Carrizo: Writing review & editing, Validation, Methodology. Paula Scibona: Writing review & editing, Validation, Methodology, Investigation, Data curation, Conceptualization. Nadia Elisabeth Savoy: Writing - review & editing, Validation, Methodology, Investigation, Data curation, Conceptualization. Ventura A. Simonovich: Writing - review & editing, Validation, Methodology, Investigation, Data curation, Conceptualization. María Cecilia Riggi: Writing - review & editing, Validation, Methodology, Investigation, Data curation, Conceptualization. Diego Odetto: Writing - review & editing, Validation, Methodology, Investigation, Data curation, Conceptualization. Florencia Cravero: Writing review & editing, Validation, Methodology, Investigation, Data curation, Conceptualization. Laura Jotimliansky: Writing - review & editing, Funding acquisition.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: CS, PM, MC, and LJ are employees of and hold financial equities in GSK. GA, JQ, and TLNS are complementary employees of and do not hold financial equities in GSK. MCR reports receiving speaker fees and/or congress attendance support from AstraZeneca, GSK, and Roche. PS, NES, VAS, DO, and FC have no conflicts of interest to declare.

Data availability statement

Anonymized subject-level data used for this publication were obtained from the Hospital Italiano de Buenos Aires, Buenos Aires, Argentina. Please refer to GSK weblink to access GSK's data sharing policies, and as applicable seek anonymized subject-level data via the link https://www.gsk-studyregister.com/en. GSK was accountable for the statistical analysis of the study. In accordance with the journal's guidelines, data will be provided for independent analysis by a selected team by the Editorial Team for the purposes of additional data analysis or for the reproducibility of this study, if such was requested.

Acknowledgements

Editorial support (in the form of writing assistance, including preparation of the draft manuscript under the direction and guidance of the authors, collating, and incorporating authors' comments for each draft, assembling tables, grammatical editing, and referencing) was provided by Claire Scarborough, PhD, and Pallavi Patel, PhD, ISMPP CMPPTM, of Luna, OPEN Health Communications, and funded by GSK, in accordance with Good Publication Practice guidelines (www.ismpp.org/gpp-2022). These data have previously been presented at the International Society for Pharmacoeconomics and Outcomes (ISPOR) Europe 2023 Congress, abstract numbers 129983, 130007, and 129980.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2024.101457.

References

- Abu-Rustum, N., Yashar, C., Arend, R., Barber, E., Bradley, K., Brooks, R., et al., 2023. Uterine neoplasms, version 1.2023, NCCN clinical practice guidelines in oncology. J. Natl. Compr. Canc. Netw. 21, 181–209. https://doi.org/10.6004/
- Akada, K., Koyama, N., Miura, T., Fukunaga, E., Miura, Y., Aoshima, K., et al., 2021. Real-world database analysis of the characteristics and treatment patterns of patients with endometrial cancer in Japan. Curr. Med. Res. Opin. 37, 1171–1178. https://doi.org/10.1080/03007995.2021.1903847.
- Al-Talib, A., Nezhat, F., Tulandi, T., 2010. The role of hysteroscopy in diagnosis and management of endometrial cancer. Gynecol. Surg. 7, 211–216.
- Blanco, A., Nogueira-Rodrigues, A., Carvalho, F.M., Giornelli, G., Mirza, M.R., 2024. Management of endometrial cancer in Latin America: raising the standard of care and optimizing outcomes. Int. J. Gynecol. Cancer. https://doi.org/10.1136/ijgc-2023-005017.
- Brooks, R.A., Fleming, G.F., Lastra, R.R., Lee, N.K., Moroney, J.W., Son, C.H., et al., 2019. Current recommendations and recent progress in endometrial cancer. CA Cancer J. Clin. 69, 258–279. https://doi.org/10.3322/caac.21561.
- Bruggmann, D., Ouassou, K., Klingelhofer, D., Bohlmann, M.K., Jaque, J., Groneberg, D. A., 2020. Endometrial cancer: mapping the global landscape of research. J. Transl. Med. 18, 386. https://doi.org/10.1186/s12967-020-02554-y.
- Cancer Genome Atlas Research Network, Kandoth, C., Schultz, N., Cherniack, A.D., Akbani, R., Liu, Y., et al., 2013. Integrated genomic characterization of endometrial carcinoma. Nature 497, 67–73. https://doi.org/10.1038/nature12113.
- Colombo, N., Creutzberg, C., Amant, F., Bosse, T., Gonzalez-Martin, A., Ledermann, J., et al., 2016. ESMO-ESGO-ESTRO consensus conference on endometrial cancer: diagnosis, treatment and follow-up. Int. J. Gynecol. Cancer. 26, 2–30. https://doi.org/10.1097/JGC.00000000000000609.
- Concin, N., Matias-Guiu, X., Vergote, I., Cibula, D., Mirza, M.R., Marnitz, S., et al., 2021. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. Int. J. Gynecol. Cancer. 31, 12–39. https://doi.org/10.1136/ijgc-2020-002230
- de Sousa, F.G., Prates, A.B.C., Leal, A.N.A., Xavier, L.B., de Andrade, D.A.P., Nogueira-Rodrigues, A., 2022. Identifying areas at risk of endometrial cancer increase in Latin America: development of a geospatial model. Lancet Oncol. 23, S41. https://doi.org/10.1016/S1470-2045(22)00440-5.
- Di Tucci, C., Capone, C., Galati, G., Iacobelli, V., Schiavi, M.C., Di Donato, V., et al., 2019. Immunotherapy in endometrial cancer: new scenarios on the horizon. J. Gynecol. Oncol. 30, e46.
- European Medicines Agency, 2024a. Jemperli dostarlimab. https://www.ema.europa.eu/en/medicines/human/EPAR/jemperli (Accessed May 31, 2024).
- European Medicines Agency, 2024b. Keytruda pembrolizumab. https://www.ema.europa.eu/en/medicines/human/EPAR/keytruda (Accessed February 14, 2024).
- GSK, 2023. GSK's Jemperli (dostarlimab) plus chemotherapy approved as the first and only frontline immuno-oncology treatment in the European Union for dMMR/MSI-H primary advanced or recurrent endometrial cancer. https://www.gsk.com/en-g b/media/press-releases/jemperli-plus-chemotherapy-approved-as-the-first-and-only frontline-immuno-oncology-treatment-in-the-european-union/> (Accessed February 1, 2024).
- Heffernan, K., Nikitas, F.S., Shukla, U., Camejo, H.S., Knott, C., 2022. Previously treated recurrent or advanced endometrial cancer in England: a real-world observational analysis. Gynecol. Oncol. 166, 317–325. https://doi.org/10.1016/j. ygyno.2022.06.011.
- Huijgens, A.N., Mertens, H.J., 2013. Factors predicting recurrent endometrial cancer. Facts Views Vis. Obgyn. 5, 179–186.
- International Agency for Research on Cancer, 2020. Data visualization tools for exploring the global cancer burden in 2022. https://gco.iarc.fr/today/data/factsheets/populations/32-argentina-fact-sheets.pdf (Accessed February 6, 2024).
- International Agency for Research on Cancer, 2022. Changes of new cases from 2022 to 2040, Both sexes, age [0-85+]. Corpus uteri. https://gco.iarc.fr/tomorrow/en/dataviz/bars?cancers=24&key=percent&show_bar_mode_prop=0 (Accessed February 6, 2024).
- Kaufman, H.L., Atkins, M.B., Subedi, P., Wu, J., Chambers, J., Joseph Mattingly 2nd, T., et al., 2019. The promise of immuno-oncology: implications for defining the value of cancer treatment. J. Immunother. Cancer. 7, 129. https://doi.org/10.1186/s40425-019.0594-0

- La Nueva Mañana, 2023. Anmat approves new treatment for advanced endometrial cancer. https://lmdiario.com.ar/contenido/420616/anmat-aprobo-un-nuevo-tratamiento-para-el-cancer-de-endometrio-avanzado (Accessed February 1, 2024).
- Liu, J., Emond, B., Maiese, E.M., Lafeuille, M.H., Lefebvre, P., Ghelerter, I., et al., 2022. Real-world utilization and outcomes of systemic therapy among patients with advanced or recurrent endometrial cancer in the United States. Curr. Med. Res. Opin. 38, 1935–1945. https://doi.org/10.1080/03007995.2022.2112872.
- Ministry of Health, 2023. ANMAT: At the National Administration of Drugs, Foods and Medical Technology we protect the population by guaranteeing that health products are effective, safe and of quality. https://www.argentina.gob.ar/anmat (Accessed February 6, 2024).
- Monk, B.J., Smith, G., Lima, J., Long, G.H., Alam, N., Nakamura, H., et al., 2022. Real-world outcomes in patients with advanced endometrial cancer: a retrospective cohort study of US electronic health records. Gynecol. Oncol. 164, 325–332. https://doi.org/10.1016/j.ygyno.2021.12.008.
- Morice, P., Leary, A., Creutzberg, C., Abu-Rustum, N., Darai, E., 2016. Endometrial cancer. Lancet. 387, 1094–1108. https://doi.org/10.1016/S0140-6736(15)00130-0.
- Novick, G., 2017. Health care organization and delivery in Argentina: a case of fragmentation, inefficiency and inequality. Glob. Policy. 8, 93–96. https://doi.org/ 10.1111/1758-5899.12267.
- Onstad, M.A., Schmandt, R.E., Lu, K.H., 2016. Addressing the role of obesity in endometrial cancer risk, prevention, and treatment. J. Clin. Oncol. 34, 4225–4230. https://doi.org/10.1200/JCO.2016.69.4638.
- Pados, G., Zouzoulas, D., Tsolakidis, D., 2023. Recent management of endometrial cancer: a narrative review of the literature. Front. Med. (Lausanne). 10, 1244634. https://doi.org/10.3389/fmed.2023.1244634.
- Palacios, A., Espinola, N., Rojas-Roque, C., 2020. Need and inequality in the use of health care services in a fragmented and decentralized health system: evidence for Argentina. Int. J. Equity Health. 19, 67. https://doi.org/10.1186/s12939-020-01168-6
- Paulino, E., de Melo, A.C., Silva-Filho, A.L., Maciel, L.F., Thuler, L.C.S., Goss, P., et al., 2020. Panorama of gynecologic cancer in Brazil. JCO Glob. Oncol. 6, 1617–1630. https://doi.org/10.1200/GO.20.00099.
- Post, C.C.B., Westermann, A.M., Bosse, T., Creutzberg, C.L., Kroep, J.R., 2020. PARP and PD-1/PD-L1 checkpoint inhibition in recurrent or metastatic endometrial cancer. Crit. Rev. Oncol. Hematol. 152, 102973 https://doi.org/10.1016/j. critrevonc.2020.102973.
- Prabhu, V.S., Kelkar, S.S., Zhang, J., Ogando, Y.M., Miles, N., Marth, C., 2022. Real-world treatment patterns and outcomes in recurrent or advanced endometrial cancer patients initiating 1st-line systemic therapy in Europe: a retrospective chart review study. Int. J. Gynecol. Cancer, 32, A104–A105.
- Restaino, S., Paglietti, C., Arcieri, M., Biasioli, A., Della Martina, M., Mariuzzi, L., et al., 2023. Management of patients diagnosed with endometrial cancer: comparison of guidelines. Cancers (Basel). 15, 1091. https://doi.org/10.3390/cancers15041091.
- Rubinstein, A., Zerbino, M.C., Cejas, C., López, A., 2018. Making universal health care effective in Argentina: a blueprint for reform. Health Syst. Reform. 4, 203–213. https://doi.org/10.1080/23288604.2018.1477537.
- U.S. Food and Drug Administration, 2023. FDA approves dostarlimab-gxly with chemotherapy for endometrial cancer. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-dostarlimab-gxly-chemotherapy-endometrial-cancer (Accessed May 31, 2024).
- U.S. Food and Drug Administration, 2024. Highlights of prescribing information, Keytruda. https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf (Accessed February 14, 2024).
- World Cancer Research Fund International, 2023. Endometrial cancer statistics. https://www.wcrf.org/cancer-trends/endometrial-cancer-statistics (Accessed February 6, 2024).
- Yarandi, F., Shirali, E., Akhavan, S., Nili, F., Ramhormozian, S., 2023. The impact of lymphovascular space invasion on survival in early stage low-grade endometrioid endometrial cancer. Eur. J. Med. Res. 28, 118. https://doi.org/10.1186/s40001-023-01084-9.
- Zhang, S., Gong, T.T., Liu, F.H., Jiang, Y.T., Sun, H., Ma, X.X., et al., 2019. Global, regional, and national burden of endometrial cancer, 1990–2017: results from the Global Burden of Disease study, 2017. Front. Oncol. 9, 1440. https://doi.org/10.3389/fonc.2019.01440.