Annals of Research in Oncology
Vol. 5(1), 35-55, 2025

POLICY STATEMENT

MORE VOICE TO PATIENTS WITH ENDOMETRIAL CARCINOMA – esprimENDO POLICY STATEMENT

Albachiara **Bergamini** [1], Manuela **Bignami** [2], Nicoletta **Cerana** [3], Valentina **Di Mattei** [4, 5], Tiziana **Nicoletti** [6], Domenica **Lorusso** [7, 8, 9], Carmine **Pinto** [10, *]

[1] President, Mai Più Sole, Cagliari, Italy
[2] Directorate of Operations, Loto OdV, Bologna, Italy
[3] President, Acto Italia – Alleanza Contro il Tumore Ovarico ETS, Milan, Italy
[4] Head of Psychology Service, IRCCS San Raffaele Hospital, San Raffaele University, Milan, Italy
[5] President, Salute allo Specchio ETS, Milan, Italy
[6] Coordination Officer, Associazioni dei Malati Cronici e Rari (CnAMC), Cittadinanzattiva National, Rome, Italy
[7] Full Professor, Humanitas University, Milan, Italy
[8] Head of the Gynecological Oncology Operating Unit, Humanitas San Pio X Hospital, Milan, Italy
[9] Secretary, Multicenter Italian Trials in Ovarian Cancer and Gynecologic Malignancies (MITO) Group, ETS
[10] Head of the Complex Unit of Medical Oncology, Comprehensive Cancer Centre, AUSL-IRCCS Istituto di Tecnologie Avanzate e Modelli Assistenziali in Oncologia, Reggio Emilia, Italy
* Correspondence to: Carmine.Pinto@ausl.re.it, https://orcid.org/0000-0002-2098-3337

ABSTRACT: The increase in endometrial carcinoma cases in recent years has made it evident that urgent attention must be brought to this disease in the public debate. This Policy Statement, conceived as an advocacy initiative, stems from the awareness that many patients face significant barriers in accessing clear information and effective treatment pathways, often due to a lack of awareness and targeted information campaigns. Increasing knowledge and awareness of the disease among women is essential to help them understand the risks, recognize symptoms, and learn about treatment options, so they can feel engaged and informed in managing their own health. In a context where endometrial carcinoma remains an under-discussed disease, promoting greater awareness and fostering an open dialogue among patients, clinicians, patient associations, civic organizations, and institutions is crucial. Only in this way will it be possible to improve care and the quality of life for women facing this challenge. With this document, we aim to give voice to the unmet needs of patients and promote an advocacy initiative directed at institutions, calling for concrete attention to endometrial carcinoma and the importance of ensuring equitable and informed care pathways for all women nationwide.

Doi: 10.48286/aro.2025.101

Impact statement: Increasing awareness of endometrial carcinoma is crucial to ensuring equitable healthcare access and informed decision-making for all women. This advocacy document aims to foster an open dialogue among patients, clinicians, organizations, and institutions to improve care pathways. By amplifying patients' voices, we strive to drive policy changes and enhance the quality of life for those affected.

Key words: *endometrial carcinoma; awareness; advocacy; equitable care; patient-centered healthcare.*

Received: Feb 02, 2025/**Accepted:** Feb 12, 2025

Published: Mar 31, 2025

INTRODUCTION

Endometrial carcinoma, despite being one of the most common cancers among women, has not received adequate attention over the years in relation to its clinical significance.
This document, developed with contributions from clinicians, patient associations, and civic organiza-

tions, outlines the unmet needs of patients with endometrial carcinoma and proposes a series of strategic actions to improve disease awareness, access to treatment pathways, and the consistency and quality of care across the national territory. The Policy Statement calls on all stakeholders – clinicians, scientific societies, patient associations, civic organizations, and institutions – to adopt and support these initiatives to enhance the care pathway and quality of life for patients with endometrial carcinoma.
The expert committee, signatories of the Policy Statement, identified the main challenges in the care pathway for patients with endometrial carcinoma based on the results of a survey conducted through the Dica33 portal (Edra), which involved 155 women, 87 of whom had direct experience with endometrial cancer. During a webinar workshop, experts were invited to discuss the survey findings and based on their experience, describe the reality faced by patients with endometrial carcinoma in each of the following key areas: diagnosis and initiation of the treatment pathway, support throughout the care journey and impact on quality of life and socio-economic factors.
For each area, strategies and solutions were proposed to drive change in the management of patients with endometrial carcinoma, also highlighting the importance of launching informational campaigns to raise patient awareness and improve their knowledge and understanding of the disease.

ENDOMETRIAL CARCINOMA: FRAMING OF THE PATHOLOGY

Endometrial carcinoma

Endometrial carcinoma, commonly referred to as endometrial or uterine cancer, is a malignancy that originates from the cells lining the inner cavity of the uterus. The majority of these tumors are adenocarcinomas (1). This type of carcinoma primarily affects postmenopausal women, with approximately 80% of cases occurring after the age of 60 (1). Despite being one of the most common cancers among women, endometrial carcinoma has received less attention compared to other malignancies, such as ovarian and breast cancer.

Epidemiology

Among female cancers, endometrial carcinoma is the sixth most common worldwide, with 417,000 new diagnoses and 97,000 deaths recorded in 2020. The highest incidence rates are observed in North America, Europe, Micronesia/Polynesia, and Australia/New Zealand, while the lowest incidence rates are found in most African regions and South-Central Asia (2). Over the past 30 years, the incidence of this oncological disease has increased by 132% globally, in parallel with a rise in the prevalence of risk factors for its development (3).
Although diagnoses have increased across all age groups, the number of cases in women under 40 has doubled, now accounting for 4.2% of all low-grade endometrial carcinomas diagnosed in the United States (4).
In Italy, endometrial carcinoma is the third most frequent malignancy among women aged 50 to 69 (1). According to data from the report The Numbers of Cancer in Italy 2023, there are approximately 10,200 new cases per year in the country (5). The five-year survival rate following diagnosis for affected women is around 77% (1).

Risk factors

Although a precise cause for the onset of endometrial carcinoma has not yet been identified, a series of risk factors that increase a woman's likelihood of developing the disease over her lifetime have been recognized.
The primary risk factors include:

- environmental factors: these include overweight, obesity, a diet rich in animal fats, diabetes, and hypertension, often associated with what we called type 1 tumors in our previous classification (see below Molecular Biology section). In contrast, exposure to pollutants and the use of certain medications (such as tamoxifen, estrogens, aromatase inhibitors, and immunosuppressants) are more commonly linked to type 2 tumors.
- Hormonal factors: conditions that increase endogenous or exogenous estrogen exposure, such as early menarche, late menopause, estrogen-only therapy, polycystic ovary syndrome, and nulliparity, are particularly relevant to type 1 tumors.
- Advanced age and absence of hyperestrogenism: typical of type 2 endometrial carcinoma, these tumors tend to develop in older, normal-weight women, often in the absence of hyperestrogenism, and are associated with a less favorable prognosis.
- Hereditary and familial factors: a family history of endometrial carcinoma in first-degree relatives increases the risk of type 1 tumors, while hereditary genetic mutations, such as those linked to

Lynch syndrome and Cowden syndrome, are frequently associated with type 2 tumors (1, 6-10).

Among hereditary factors, Lynch syndrome is the condition most strongly correlated with endometrial carcinoma, accounting for approximately 5% of all cases (2). It is transmitted in an autosomal dominant manner and predisposes individuals to various cancers, including those of the colon, endometrium, ovary, and, less frequently, the kidneys, urinary tract, small intestine, pancreas, biliary tract, breast, and prostate. Women with this condition have a 40-80% risk of developing colon cancer, a 40-60% risk of endometrial cancer, and a 10-12% risk of ovarian cancer (11). Lynch syndrome is caused by mutations in one of the four genes regulating the DNA damage repair system known as Mismatch Repair (MMR): MLH1, MSH2, MSH6, and PMS2 (12). International guidelines, including NICE guidelines (13-15), recommend immunohistochemical evaluation of all endometrial carcinomas for MMR protein expression (MLH1, MSH2, MSH6, and PMS2). If all four proteins are expressed, the system is functional (MMR-proficient); if at least one protein is absent, the system is deficient (MMR-deficient), potentially indicating Lynch syndrome. Patients whose tumors show the loss of MSH2, MSH6, or both are immediately referred for germline genetic testing for Lynch syndrome. In cases of MLH1 and/or PMS2 loss, MLH1 hypermethylation testing is performed. The absence of MLH1 hypermethylation (but not its presence) is an indication for Lynch syndrome testing (7).

Finally, pelvic radiotherapy for a previous neoplasm can also be a risk factor for the development of endometrial carcinoma (1).

Protective factors against endometrial cancer have also been identified. Combined oral contraceptives (containing both estrogen and progestin), physical activity, and a fiber-rich diet appear to reduce the risk of developing this type of tumor (1, 7).

Currently, no organized screening program exists for endometrial carcinoma, either for the general population or for high-risk groups.

Clinical presentation

The clinical onset of endometrial carcinoma is primarily characterized by abnormal vaginal bleeding, such as postmenopausal spotting, intermenstrual bleeding, or unusually heavy or prolonged menstrual flow. Rarely, the neoplasm may be asymptomatic and diagnosed incidentally (16).

Given the estimated increase in cases also at a younger age of onset, it is important to conduct clinical and instrumental evaluations for all women of reproductive age experiencing intermenstrual bleeding (17).

In cases of locally advanced disease, occasional symptoms may include abdominal distension, pain, and urinary or intestinal disorders (7). Significant lymph node involvement can lead to edema in the lower limbs, pubic area, and vagina. Late signs of metastatic spread include abdominal, pelvic, lumbosacral, and gluteal pain, sub-occlusive syndromes, bone pain, and dyspnea (17).

Diagnostic investigations

In any woman reporting abnormal vaginal bleeding, the first examination to perform is transvaginal ultrasound (17). This test visualizes the uterine cavity and measures endometrial thickness, which should be <5 mm in postmenopausal women and range from 1 to 14 mm in premenopausal women, depending on the menstrual cycle phase. If transvaginal ultrasound reveals an endometrial thickness >5 mm in a postmenopausal woman or >15 mm (or inconsistent with the menstrual cycle phase) in a premenopausal woman, hysteroscopy with targeted biopsies is necessary for histological diagnosis (1, 7). Unfortunately the old defined type 2 tumors may arise in an atrophic endometrium so that any postmenopausal bleeding requires tissue biopsy regardless endometrial thickness.

Following histological diagnosis, further imaging studies such as MRI and thoraco-abdominal CT scans may be required. Contrast-enhanced MRI better defines local disease extension, including vaginal wall involvement and regional lymph node involvement (18). Contrast-enhanced thoraco-abdominal CT scans are useful for evaluating potential distant metastases (1).

Histologic types

The main histotypes of endometrial carcinoma are:

- endometrioid adenocarcinoma: accounts for 75-80% of endometrial cancers, is estrogen-related and usually has a low degree of differentiation (G1-G2). It can be pure or have a non-endometrioid component that affects the spread and prognosis.
- Serous-papillary adenocarcinoma: constitutes 5-10% of endometrial carcinomas and has a worse prognosis than the endometrioid form, often presenting at stage III or IV with metastasis to the lymph nodes. It should be suspected in women who are older than the typical age for endometrioid adenocarcinoma, have a history of pelvic

irradiation, prolonged use of anti-estrogen drugs, and breast cancer.
- Clear cell adenocarcinoma: accounts for 2-4% of endometrial cancers, typical of advanced age, with poor prognosis similar to that of serous carcinoma.

Other less common histotypes (incidence ≤1%) include mucinous adenocarcinoma, squamous, mixed, and undifferentiated (17).

Molecular Biology

In 1983, Bokhman (19), on the basis of a prospective clinicopathologic study, classified endometrial carcinomas into two major categories:

1. type I endometrioid carcinomas that are estrogen-dependent, histologically well-differentiated or moderately differentiated, low-grade, frequently diagnosed at the early stages and characterized by a lower ability to metastasize and thus by a favorable prognosis.
2. Non-endometrioid carcinomas of type II, non-estrogen-dependent and poorly differentiated, including serous carcinomas, clear cell carcinomas, carcinosarcomas, and grade 3 tumors, which are characterized by greater aggressiveness and ability to metastasize and therefore by a poorer prognosis (1, 20, 21).

In 2013, the Cancer Genome Atlas Research Network (TCGA) published a study on the genomic characterization of 373 endometrial carcinoma samples (22), introducing a more complex classification system than the traditional dualistic categorization. This system identifies four distinct subgroups of endometrial cancers based on specific molecular alterations and protein expression:

1. POLE Ultramutated (POLE-mutated): these tumors, characterized by mutations in the gene encoding DNA polymerase-epsilon, develop in young women without metabolic risk factors. They have an excellent clinical outcome with an estimated mortality rate of 1%.
2. Hypermutated MSI (MMRd): these tumors exhibit microsatellite instability due to deficits in mismatch repair (MMR), with a mutagenicity rate ten times higher than MMR-proficient tumors. Approximately 10% of these cases are associated with germline mutations in the Lynch syndrome MMR genes, while the others result from somatic alterations. They have an intermediate prognosis, varying according to the stage of the disease.
3. Copy number-high (p53-abnormal): characterized by *TP53* alterations and frequent copy number aberrations, these tumors exhibit aggressive biological behavior and are associated with a high mortality rate (50-70%). They account for approximately 20% of all endometrial carcinomas.
4. Copy number-low (no specific molecular profile, NSMP): these MMR-proficient and POLE wild-type have a relatively low number of somatic aberrations and comprise mainly endometrioid carcinomas. Their prognosis varies from intermedia to excellent, depending on stage and histomorphologic features (7).

Based on these data, the Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE) (23), which analyzes each new sample of endometrial for MMR status by immunohistochemical analysis (IHC) (24), and then performs IHC for p53 (the protein produced by the *TP53* gene) (25) and sequencing for mutations hotspots with confirmed pathogenicity in the *POLE* gene (26).

The presence of a POLE mutation (P286R, V411L, S297F, S549F, A456P, F367S, L424I, M295R, P436R, M444K, D368Y or other variants recognized as pathogenic) classifies a tumor as POLE-mutated, regardless of MMR and p53 status.

In POLE-proficient, loss of expression of one or more MMR proteins classifies the tumor as MMRd, regardless of p53 status: in about 80 percent of cases showing the loss of expression of MLH1 or PMS2, the underlying cause is hypermethylation of the promoter of MLH1; loss of MLH1 in the absence of hypermethylation of its promoter and all other combinations (loss of expression of MSH2 and MSH6, loss of isolated expression of MSH6 and isolated loss of expression of PMS2) constitute an indication for germinal testing for Lynch syndrome. In the absence of pathogenic variants of POLE and defects in the MMR, abnormal p53 expression identifies p53-abnormal cases. The remaining cases are classified as tumors without a specific molecular profile (no specific molecular profile, NSMP) (22, 23, 27-29).

Staging

Staging of endometrial carcinoma is based on the anatomo-pathologic evaluation of the disease and aims to assess the extent of neoplasm and prognosis. The staging criteria most widely used are those defined by the International Federation of Gynecology and Obstetrics (Federazione Italiana di Ginecologia e Ostetricia, FIGO), which are periodically updated. In 2023, the new FIGO classification was introduced with the aim of harmonizing all histolog-

ical and molecular knowledge useful for the therapeutic decision-making process (**Table 1**) (30).

Prognostic factors and risk categories

Clinical, instrumental, and anatomopathological assessment of risk factors for recurrence is necessary not only to formulate prognosis but also to plan treatment. Until recently, the definition of risk classes considered the stage of disease, the degree of cell differentiation (G1-2-3), myometrial invasion, histologic type, and invasion of lymphovascular spaces, *i.e.*, the presence of tumor cells in blood vessels and lymphatics in and near the tumor. In 2025 the ESGO announced the release of the latest ESGO-ESTRO-ESP Endometrial Cancer Guidelines update (expected to be released in Spring) on new risk stratification and molecular classification that will help in refining prognostic assessment and treatment planning for endometrial cancer (31).

Integrating the new molecular subtypes into existing risk stratification models allows to considerably improve the definition of prognosis and to define the optimal therapeutic approach for each patient (23, 27, 32), because each of the four molecular groups is biologically distinct and exhibits behavior largely independent of histology and tumor grade. In addition, the classification is based on objective findings, which increases reproducibility among anatomo-pathologists, laboratories, and specimen's biopsy and surgical specimens (7).

Table 1. *Stage classification of endometrial carcinoma (30).*

STAGE	DEFINITION
Stage I	Confined to the uterine corpus and ovary
IA	Disease limited to the endometrium OR non-aggressive histological type, i.e. low-grade endometroid, with invasion of less than half of myometrium with no or focal lymphovascular space involvement (LVSI) OR good prognosis disease **IA1** Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium **IA2** Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI **IA3** Low-grade endometrioid carcinomas limited to the uterus and ovary
IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI
IC	Aggressive histological types e limited to a polyp or confined to the endometrium
Stage II	Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion
IIA	Invasion of the cervical stroma of non-aggressive histological types
IIB	Substantial LVSI d of non-aggressive histological type
IIC	Aggressive histological types e with any myometrial involvement
Stage III	Local and/or regional spread of the tumor of any histological subtype
IIIA	Invasion of uterine serosa, adnexa, or both by direct extension or metastasis **IIIA1** Spread to ovary or fallopian tube (except when meeting stage IA3 criteria) **IIIA2** Involvement of uterine subserosa or spread through the uterine serosa
IIIB	Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum **IIIB1** Metastasis or direct spread to the vagina and/or the parametria **IIIB2** Metastasis to the pelvic peritoneum
Stage IIIC	Metastasis to the pelvic or para-aortic lymph nodes or both **IIIC1** Metastasis to the pelvic lymph nodes **IIIC1** Micrometastasis **IIIC1** Macrometastasis **IIIC2** Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes **IIIC2** Micrometastasis **IIIC2** Macrometastasis
Stage IV	Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastasis
IVA	Invasion of the bladder mucosa and/or the intestinal/bowel mucosa
IVB	Abdominal peritoneal metastasis beyond the pelvis
IVC	Distant metastasis, including metastasis to any extra- or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone

Treatment

Surgery

The cornerstone of treatment for early-stage endometrial carcinoma is total hysterectomy and bilateral salpingo-oophorectomy, which involves the removal of the uterus, fallopian tubes, and ovaries. Minimally invasive surgery, laparoscopic or robotic, represents the standard of care over the traditional laparotomic approach. Randomized studies and systematic reviews have shown that laparoscopical surgery provides oncologic outcomes not inferior to those associated with laparotomic surgery, while reducing operative blood loss, length of stay, pain and perioperative complications (33-36). Robotic surgery offers oncologic outcomes and advantages similar to laparoscopic surgery but is associated with higher costs (37, 38).

In addition to removal of the uterus, ovaries, and fallopian tubes, during surgery, a sentinel lymph node biopsy is performed to assess the lymph node status. If the sentinel lymph node is not identified or pre-operative examinations have shown the presence of macroscopic lymph node involvement or enlarged and suspicious lymph nodes, lymphadenectomy is performed, which involves the removal of the lymph nodes located in the uterine drainage area (1).

The development of the sentinel lymph node technique has made it possible to considerably limit the use of lymphadenectomy. Indeed, available evidence indicates that biopsy of the sentinel lymph node can reduce the potential morbidity resulting from performing a systematic lymphadenectomy, including the long-term risk of lower limb lymphedema (39), allowing the detection of any lymph node micro metastases or isolated tumor cells often undiagnosed by conventional histologic examination (40).

In advanced disease, surgery plays a marginal role. In advanced stages eligible for surgical treatment, surgery can be performed by making a longitudinal incision on the abdomen to achieve complete surgical radicality balanced with the morbidity risk for the patient (1). In stages that are not amenable to complete tumor excision, surgery may be performed as a palliative strategy to relieve symptoms or to obtain a histological diagnosis before starting the patient chemo- and/or radiotherapy treatment (1, 17). Finally, surgery may be considered as a first treatment option in case of an isolated recurrence of disease that is completely removable, as long as the patient's clinical condition allows it (1, 41).

Adjuvant treatment

At the time of diagnosis, two-thirds of women have endometrial carcinoma in stage I and most of them have an excellent prognosis (42). Within this group, however, there are patients who have relatively poor outcomes and need adjuvant treatment (*i.e.*, postoperative) to prevent or to delay a possible recurrence of disease. Adjuvant options currently available for these women include radiation therapy, chemotherapy, or a combination of both treatments. Radiation therapy may be represented by external radiotherapy, brachytherapy (internal vaginal radiotherapy) or by the combination of both and is intended to achieve greater local control of the disease; chemotherapy is represented by the combination of platinum-based drugs and taxanes (1, 7).

The choice of adjuvant therapeutic strategy is essentially guided by the risk of recurrence:

- women with low-risk endometrial carcinoma have a probability of developing a recurrence of <5% and do not need any adjuvant treatment (43). The studies PORTEC-1/2 have shown that the presence of POLE mutations is associated with a favorable prognosis, independent of other clinico-pathologic variables. Based on this evidence, patients with stage I-II POLE-mutated tumors are also now considered low risk and do not require any adjuvant treatment (32, 44):
- in patients with intermediate-risk endometrial carcinoma, the adjuvant option of choice is radiotherapy: vaginal brachytherapy is able to significantly reded locoregional recurrence, with excellent disease control rates (>96%).
- In patients with intermediate/high-risk disease, external radiotherapy is recognized as the adjuvant treatment of choice, providing better disease control than vaginal brachytherapy, especially in the presence of lymphovascular invasion or of a high-grade tumor. Vaginal brachytherapy can be considered after accurate surgical staging for patients who do not present lymphovascular invasion (30).
- In patients at high risk of recurrence, the recommended adjuvant treatment is represented by the combination of radiotherapy with chemotherapy or only by chemotherapy; radiotherapy alone may be considered for patients with major comorbidities and/or contraindications to chemotherapy (46, 47).

Considering the prognostic value of the new molecular classification, the impact of chemotherapy for each molecular subtype using tissue samples from the PORTEC-3 study. The analysis showed that p53-abnormal tumors have a highly significant benefit from the

addition of chemotherapy to radiotherapy, regardless of histological type and stage, and that NSMP tumors also benefit from the combined treatment, although to a lesser extent. In particular NMSP tumors can be divided in hormon receptor positive, with intermediate prognosis, and hormon receptors positive with poor prognosis and for which chemotherapy is recommended (similarly to the p53 abnormal ones). MMRd tumors have not shown a significant benefit from the addition of chemotherapy to radiotherapy, while POLE-mutated tumors had excellent outcomes with radiotherapy with or without chemotherapy (48).

Treatment of relapsed and metastatic disease

Patients with endometrial carcinoma recurrence represent a very heterogeneous category, ranging from isolated vaginal recurrence amenable to curative treatment to distant metastatic disease that is usually treated with palliative intent (17). In isolated vaginal recurrence, in the absence of prior radiation treatment, radiotherapy with external beams and brachytherapy provide a curative option in 75-89% of cases (49, 50).

Patients with isolated distant metastases (*e.g.*, with an isolated recurrence on para-aortic nodes) seem to benefit from surgical resection, which allows for a prolonged interval free from further progression (51). Options available for patients with multifocal or distant metastases are represented by chemotherapy, hormone therapy from immunotherapy (1).

Patients who have not previously received a systemic chemotherapy treatment are started on a combination regimen with platinum-based chemotherapeutics and taxanes, which is the first-line standard for advanced and metastatic disease and is associated with a progression-free survival of 13 months (52). Hormone therapy is a treatment option for recurrent or metastatic disease in patients with poor general clinical conditions who are unable to receive systemic chemotherapy treatment. Progestins and antiestrogenic drugs are the most commonly used drugs (17). Hormonal treatment can achieve response rates of up to 55 percent, with low-grade, slow-progressing, hormone receptor-positive tumors that appear to derive the greatest therapeutic benefit (2). However, hormonal agents do not confer any advantage in terms of overall survival or progression-free survival, whether used alone or in combination strategies (54). There are currently no chemotherapeutic treatments indication for second line in endometrial carcinoma (17). To date, immunotherapy is the treatment that has demonstrated the highest response rate in this disease setting (2). In fact, it has been observed that the MMRd/MSI-h endometrial tumors exhibit an increase in the number of tumor-infiltrating lymphocytes (TILs) and in the expression of PD1 and its ligand PD-L1, which has provided a rationale for the use of immunotherapy drugs (17). Based on these premises, anti-PD1 immune checkpoint inhibitors were tested in the GARNET (54) and KEYNOTE-158 (55) clinical trials, respectively, demonstrating positive results that recently led to the approval of their use and reimbursement by the Associazione Italiana del Farmaco (AIFA) as monotherapy for MMRd/MSI-h patients with advanced or recurrent disease after a previous line of platinum-based chemotherapy. Based on the results of the KEYNOTE-755 study (56) an immune checkpoint inhibitor drug was approved and reimbursed for advanced or relapsed disease also in combination with oral tyrosine kinase inhibitor (TKI), regardless of the presence or absence of microsatellite instability. In case of contraindication to the use of immunotherapy in monotherapy or in combination with TKIs, the chemotherapeutic drugs considered most active are weekly forms of taxanes and anthracyclines . The reintroduction of platinum-based chemotherapeutic agents can be considered after a prolonged interval from the last treatment with taxanes (1).

Based on the excellent results obtained in the second-line setting, immunotherapy has been evaluated in the first line setting in combination with standard platinum-based chemotherapy and taxanes. In December 2023, the European Medicines Agency (EMA) approved the combination of monoclonal antibody IgG4 with carboplatin and paclixatel as first-line treatment for patients with MSI-H/MMRd tumors. In Italy, since March 2024, a compassionate use programme has been activated based on an anti-PD-1 monoclonal antibody in combination with carboplatin and paclixatel for women with advanced primary endometrial cancer or first recurrence of MSI-H/ MMRd candidates for systemic therapy (1).

NATIONAL SCENARIO AND MAIN CRITICAL ISSUES

Diagnosis and initiation of the therapeutic path

Women have little knowledge of endometrial carcinoma and the areas it affects

Despite endometrial carcinoma being one of the most frequent gynecological cancers, with almost

11,000 new cases estimated annually, women still have little awareness of this tumor pathology. The preliminary survey of the project, conducted to capture the current scenario, highlighted that there is a problem related to the terminology used to define the tumor: since in common language endometrial carcinoma tends to be identified with uterine carcinoma, defining it with the correct diagnostic label can cause great confusion among women, as evidenced by the fact that 80% of respondents stated they had never heard of this pathology before the diagnosis. A similar problem is observed for cervical carcinoma or cervical cancer, although this type of tumor is more known than endometrial cancer because it is the subject of an organized screening program. At the root of this terminology-related misunderstanding is a lack of knowledge of the female genital apparatus by women themselves, who have difficulty distinguishing the different types of gynecological tumors and the related anatomical areas involved. Not surprisingly, in fact, most women still believe that a simple PAP test is sufficient to check the entire female genital apparatus.

Lack of information on endometrial carcinoma

Information initiatives on endometrial carcinoma are lacking. Nowadays, it is mainly patient associations and civic organizations that carry out information and training activities across the board for gynecological cancers, disseminating information among women through their respective websites and dedicated events, such as online webinars and educational meetings that often also include the presence of clinicians. However, there is a lack of extensive communication campaigns that would allow for widespread awareness of pathology. As a result, endometrial carcinoma still does not receive the necessary attention within health policies, despite its relevance. It is essential to recognize it as a priority, placing it at the center of prevention, diagnosis, and treatment strategies to improve clinical outcomes and ensure equitable access to care. The lack of an adequate policy also limits public awareness of the disease, risk factors, and the importance of early diagnosis. Only through increased information and the encouragement of regular gynecological controls, which include the prevention and timely identification of carcinoma, will it be possible to reduce the incidence of the disease and improve the quality of life for women.

Prevention at the national level

Women who undergo regular gynecological prevention constitute a minority of the global population: according to the survey results, only 37% of respondents had annual gynecological check-ups in the years preceding the diagnosis.

Endometrial carcinoma is disadvantaged by being considered an easily treatable oncological condition

Endometrial carcinoma is often underestimated by women and the general public, having the reputation of being a tumor easily treatable with surgery. This overly optimistic perception, although not entirely unfounded, does not fully reflect reality and can lead to minimizing the severity of the disease and the potential risks associated with it, especially in the absence of early diagnosis. Surgical intervention, generally performed laparoscopically and including sentinel lymph node biopsy or lymphadenectomy, represents the cornerstone of treatment for early-stage endometrial carcinoma, but in advanced disease, it plays a marginal or even null role. Furthermore, following the introduction of the new molecular classification, endometrial carcinoma has become a much more complex condition than previously thought, even if diagnosed at early stages. In fact, the four molecular subtypes identified by TCGA define different risk classes, leading to completely different postoperative scenarios. Therefore, even though at the time of diagnosis two-thirds of women present with stage I tumors amenable to surgical resection and most of them have an excellent prognosis, within this group there are also patients with less favorable outcomes who require adjuvant treatment with radiotherapy, chemotherapy, or a combination of both.

The lack of uniform care pathways across territory hinders equitable access to treatments, with long diagnosis times and delays in therapies

Regional and local disparities in the healthcare system create profound inequality in access to services, resulting in variable waiting times and quality of care. This phenomenon severely undermines every patient's right to receive timely and appropriate care, especially penalizing those residing in areas with fewer resources. In particular, equitable access to the care pathway is hindered by the length of time it takes to obtain a diagnosis. Such delays compromise not only the start of treatment but also the chances of recovery. Furthermore, although the survey found that 63% of patients start ther-

apy within a month of diagnosis, this figure does not reflect the complex and often inequitable reality of many areas of the country, where healthcare facilities cannot always ensure equal access to care. Also, access to molecular classification after surgery is very important because it is prognostic and predictive of response to treatment; unfortunately, however, this is not performed everywhere. Equity in care must be a priority to ensure that all patients, regardless of their geographic area, receive the same level of assistance.

Many patients do not receive clear explanations regarding the therapeutic path they will face

According to the survey, only 63% of the women interviewed were clearly explained the therapeutic path. The reasons that may explain the suboptimal data intercepted by the survey are varied and include: the increasingly limited time clinicians have available, leading them to provide quick explanations relying on the assumption that patients are familiar with specialized terminologies and procedures that non-experts may never have heard of; the difficulty some clinicians have in communicating well and empathetically; the state of worry and agitation in which most people facing an oncological disease find themselves can compromise their clarity and ability to understand and assimilate the information received. It is also possible that the lack of information in illustrating the therapeutic path hides a much more serious problem: patients risk not to fully understand the information provided by clinicians, as clinician themselves might not have a clear and structured vision of the diagnostic path, the different molecular subtypes, and their impact on staging, prognosis, and therapeutic decisions (57-59).

It is important to remember that not all doctors have yet fully assimilated the molecular profiles defined by the new classification and staging and developed the necessary skills to manage them adequately. It is essential that the doctor ensures that the person has fully understood the information provided, taking the necessary time to explain it clearly and comprehensibly. Good communication and proper information are fundamental not only for the patient but also to involve, when possible, her family, which often plays a crucial support role. Empathy and willingness to clarify doubts, together with the continuous training of the professional, are indispensable to ensure that the patient is informed and aware of her therapeutic path.

Support in the care pathway

Only one in two patients is taken care of and operated on by a center specialized for the pathology

The survey results indicate that only 51% of the interviewed patients turned to a center specialized for the management of gynecological tumors. This data reflects a complex reality, where not all patients have the same opportunities to access Centers of Excellence, due to obstacles such as distance, economic difficulties, or personal conditions that limit mobility. However, ensuring quality care throughout territory is a fundamental right and a priority of the healthcare system. The care of patients by non-dedicated centers, which have low surgical volumes, fewer specific skills, and limited capacity to perform molecular profiling, represents one of the major critical issues. This scenario can negatively affect the quality of services, highlighting the need to strengthen collaboration between reference centers and local structures to improve equity in access to care. For example, in some non-specialized facilities, procedures such as lymphadenectomy are still performed on low/intermediate-risk patients, who would instead have a more appropriate indication for sentinel lymph node biopsy. Greater standardization of clinical guidelines, even in less specialized contexts, can help improve outcomes for all patients, regardless of where they receive treatment.

There is significant healthcare mobility from the South to the Center-North

Reference centers for the treatment of endometrial carcinoma are present throughout the national territory, with a greater concentration in the Central-Northern Regions, particularly in Lombardy and Lazio. However, the low visibility and promotion of the centers spreaded across the national territory limit their awareness among patients, contributing to healthcare migration from the Southern Regions to the North, with significant socio-economic repercussions. These healthcare migration phenomena have important impacts on all parties involved: patients and their families/caregivers, who are forced to bear not only the costs of treatment but also the costs associated with mobility and the loss of time and workdays; the Region of origin, which must reimburse the destination Region for the services provided to the outgoing patient; and the receiving facilities, which inevitably become overloaded. In reality, almost all Italian Regions have one or more minor centers within them that could ensure ade-

quate management of the post-operative therapeutic phase. However, many of these centers, especially those located in the South, do not network with the reference structures and therefore remain 'cut off' from the care pathway.

There is still little awareness of the importance of multidisciplinarity

Multidisciplinarity is an essential requirement for improving outcomes in the treatment of endometrial carcinoma, especially in light of an increasingly personalized therapeutic approach based on molecular profiles and the management of side effects related to the new treatments. However, awareness of this necessity is still not adequately widespread. According to the survey, only 57% of respondents received assistance from multiple specialists, a percentage similar to that of women who turned to a specialized center, confirming that Centers of Excellence adopt a multidisciplinary approach. For multidisciplinary effectiveness to fully materialize, the involvement of not only specialists from reference centers but also key figures in the territory, such as the general practitioner (GP) and nurses, is necessary. Only in this way can continuity of care and equitable access to the most appropriate treatments be ensured, especially in a context where personalized medicine is becoming increasingly crucial.

Limited involvement of the general practitioner in the patient's care pathway

The general pratictioner (GP) could represent a fundamental reference figure for women, as well as a valuable ally for specialists and patient associations. It is essential to strengthen his/her role, involving GP in the care pathway of patients, in the dissemination of correct information, and in the promotion of prevention among women. Regular contact with the Center and the specialist is crucial, especially in the phase of continuity of care in the territory, when the patient returns home. In this way, the GP would consolidate his position as a reference for patients, becoming a valuable resource in their care pathway, and avoiding the oncologist becoming the only reference, to whom they sometimes turn even for problems not related to the tumor pathology.

Poor knowledge of Lynch syndrome and its correlation with endometrial carcinoma among patients

The survey results highlighted that there is a significant knowledge gap among patients regarding Lynch syndrome and its correlation with endometrial carcinoma. In fact, 88% of respondents stated that they had never heard of Lynch syndrome and 91% were not informed of its association with endometrial cancer. These results are consistent with the low level of awareness about endometrial carcinoma found in most of the interviewees, as well as the fact that a significant portion of respondents did not receive clear explanations regarding the therapeutic pathway.

Clinical geneticists are few and genetic counseling for Lynch syndrome risks becoming a 'bottleneck', with significant repercussions on primary prevention

Genetic counseling for Lynch syndrome allows for the identification of families at risk of developing a related oncological pathology and the implementation of strategies aimed at preventing new cases of the disease, making it an important tool for primary prevention. However, at present, genetic counseling represents a critical issue that cannot be overlooked: on the one hand, there are few clinical geneticists and the waiting times for an appointment have become unacceptable, averaging around 9 months; on the other hand, the need to consult a geneticist is expected to grow over time, because with the increase in the number of somatic tests performed, the risk of identifying potentially pathogenic variants that need to be studied to determine whether they are somatic or germline also increases. Given the current scarcity of geneticists, genetic counseling risks becoming a 'bottleneck' and having significant repercussions on primary prevention, which is the only tool available to contain healthcare costs and keep a system called upon to sustain ever-increasing costs in balance, despite increasingly limited resources .

There is a lack of economic and human resources necessary to ensure oncological patients access to new molecularly targeted therapies

Thanks to the new possibilities offered by precision medicine and personalized therapies, cancer treatment is at a turning point. On the other hand, there is a profound crisis in the healthcare sector, characterized by the lack of human and economic resources necessary to ensure oncological patients access to new molecularly targeted therapies. The tests currently available for the biomolecular profiling of endometrial carcinoma include the MMR test, the MLH1 promoter hypermethylation test, the p53 analysis, and the POLE test. To date, the MMR test is the only one reimbursable for patients with endometrial carcinoma: this test is necessary both

to confirm or exclude an underlying Lynch syndrome (followed, if necessary, by the MLH1 hypermethylation test in case of lack of expression of this protein) and to select patients with advanced or recurrent disease eligible for immunotherapy.
The POLE test and the p53 test are necessary in localized disease to guide the choice of adjuvant treatment. Although the obligation to perform these tests has been included in the guidelines for 3 years, to date only large centers have the funds to implement them all using non-specific or regional billing codes. The inclusion of these tests in the Essential Levels of Care (LEA), expected in January-February 2025, should address the misalignment between the guidelines and clinical practice observed so far, ensuring the reimbursement of these analyses on a national scale.
In addition to the lack of financial resources, there is a shortage of pathologists, which has become a very hot topic: young students do not consider pathology because it is not a well-paid specialty.

Impact on quality of life and socio-economic factors

The role of Patient Associations in supporting women with gynecological cancers: initiatives, challenges, and the need for effective communication

Patient associations for gynecological cancers organize initiatives to integrate the care pathway where the healthcare system fails to intervene, with the aim of supporting women affected by these diseases in various aspects of their lives. These initiatives include practical and therapy support services, such as transportation for therapy access and the donation of wigs and head coverings; psychological support and emotional well-being through psychological counseling and relaxation and meditation courses; projects dedicated to quality of life, such as those aimed at rediscovering sexuality after illness, often involving a sexologist, and onco-aesthetic interventions; recreational and social activities, including ceramics and aromatherapy courses; and physical health promotion programs. However, it is not always guaranteed that women are informed about the existence of these associations and the services they offer. Patients are usually informed about the existence of Associations by healthcare professionals, such as oncologists or psycho-oncologists. When patient associations and civic organizations have a presence within a hospital, volunteers approach patients thanks to their daily presence in oncology departments and the distribution of informational brochures. In the absence of this organization, many women discover the associations only through word of mouth or by chance, for example, by finding an informational brochure. It is therefore essential to implement a continuous and structured information system to ensure that all women have access to useful and timely information about the available services and resources.

Addressing sexuality in the care pathway of endometrial cancer: the importance of integrated multidisciplinary support

The topic of sexuality in patients with endometrial cancer is a fundamental aspect, often overlooked, that deserves to be addressed with due attention within the multidisciplinary support framework for the disease. Sexuality not only has a significant impact on the psychological well-being of patients but also has physical consequences, both in terms of bodily changes affecting sexual function and in relation to managing the couple's relationship.
The project survey revealed that 29% of patients prefer not to answer about the impact the disease has had on their sexual life, proving that the discussion on this topic is hindered by reluctance both from patients, due to the strong social stigma surrounding gynecological cancers, and from the lack of professionals specialized in sexology.
This lack of support is reflected in the difficulties many women face silently, with a negative impact on their quality of life and their approach to their illness. A 2023 study by the patient association ACTO Italia, conducted in 30 Italian hospitals and involving 110 patients, highlighted how the lack of sexological consultations represents an unmet need that requires an adequate response. Similarly, the Loto OdV Association, through a survey conducted (December 2023-January 2024) on 40 women with an average age of 50 years, half in treatment and half in follow-up, found that 47% of patients wish to resume their sexual life but do not feel physically and emotionally capable; 30% have no interest in sexuality, prioritizing other issues; and 90% did not receive sexological consultations during their oncological journey.
This scenario highlights the importance of including sexological counseling in the LEA, alongside the already provided psychological counseling. A coordinated intervention, involving a sexologist and a relational therapist, is essential to offer patients comprehensive support that considers all dimensions of their psychophysical well-being.

Additionally, it is necessary to develop alternative contact tools for patients who, due to modesty or cultural reasons, may find it difficult to address certain topics. To this end, information desks in Health Houses and Counseling Centers, as well as online live chats managed by specialized operators, could be effective solutions.

Furthermore, it is desirable to introduce integrative care into regional Diagnostic and Therapeutic Care Pathways (Percorsi Diagnostici Terapeutici di Assistenza, PDTA), such as acupuncture to mitigate the effects of therapies and anxiety, pelvic floor rehabilitation/re-education programs, and vaginal laser treatments. In an era of personalized medicine, aspects related to intimacy, sexual, and gynecological well-being are integral parts of women's psychophysical recovery, significantly contributing to their healing journey.

Strengthening psychological support for patients with endometrial cancer and their families

Mental health is crucial during the treatment journey, as it significantly affects therapy compliance and, consequently, clinical outcomes. However, the lack of psychological support is one of the main issues not only in oncology but in all healthcare fields. The presence of a psycho-oncologist in gynecological oncology departments is not mandated by regulations and, therefore, remains an optional choice for hospital facilities. When available, it is often due to the commitment of department heads and doctors particularly sensitive to the issue or the financial support offered by patient associations, as highlighted by several surveys conducted by the Italian Society of Psycho-Oncology (Società Italiana di Psiconcologia, SIPO).

Even in hospitals that offer psychological support, the number of available psycho-oncologists is often insufficient to meet the needs of all patients and their families. Additionally, many patients cannot afford the cost of a psycho-oncologist, given that the treatment journey already entails a significant financial burden.

Further complicating the situation is the fact that many psycho-oncologists active in oncology departments are trainees or young professionals in training with limited experience.

Due to contractual conditions that offer reduced pay and a limited number of weekly hours, the role of psycho-oncologist is often filled by individuals with insufficient specialization and experience. This can have significant negative repercussions on the quality and effectiveness of interventions, highlighting the urgency of further enhancing and specializing in this service to ensure adequate psychological support during the treatment journey.

For most women, the treatment journey has a heavy economic impact

Eighty-five percent of the women interviewed stated that the treatment journey had a negative or very negative economic impact. To address this issue, economic protection measures for patients are necessary, including: avoiding unnecessary healthcare migration, which inevitably increases costs for both the patient and their families/caregivers. Therefore, it is essential to promote informational campaigns about the Centers of Excellence available in the area. Introducing work protection policies to prevent job loss or demotion for women undergoing treatment, such as paid sick leave and the integration of post-treatment work reintegration programs. Finally, offering resources and support services to the families and caregivers of patients to alleviate the economic and psychological burden of care.

PROPOSAL FOR AWARENESS ACTIONS TO IMPROVE THE CARE PATHWAY FOR PATIENTS WITH ENDOMETRIAL CANCER

Promoting informational campaigns to raise awareness about endometrial cancer

The absence of an organized screening program for this cancer makes accurate information an essential tool to increase awareness and promote early diagnosis, thereby improving treatment outcomes. To achieve these goals, it is crucial to launch informational campaigns that clarify the definition of endometrial cancer and promote knowledge of gynecological anatomy. It is necessary for patient associations, civic organizations, scientific societies, and clinicians to collaborate, developing awareness initiatives aimed at all women, including healthy ones, about the various types of gynecological cancers and the anatomical areas involved.

Providing clear and accessible information is fundamental to enable women to promptly recognize symptoms, identify the specialists to consult, understand potential risks, and evaluate the available treatment options.

Uterine cancer and endometrial cancer are often confused; therefore, it is necessary to adopt a unified definition of the tumor. Organizations such as Acto Italia - Alleanza contro il Tumore Ovarico ETS, in line with the European Network of Gynecological Cancer Advisory Groups (ENGAGe), have decided to use the definition "uterine cancer" specifying "endometrial" in parentheses to clarify the terminology. However, the role of healthcare professionals remains fundamental to ensure that patients fully understand the disease they are affected by, providing them with clear and accurate information.

Alongside the need for shared terminology, it is essential to educate patients about their anatomy and gynecological health. Understanding their own body and the female reproductive system is crucial for recognizing any abnormalities and warning signs. Women need to know the different parts involved, such as the uterus, ovaries, and cervix, and their functions, to more easily identify changes or suspicious symptoms.

A clear explanation of gynecological anatomy helps patients better understand the cancers that may arise and how and where these diseases develop, facilitating a more informed dialogue with doctors. Additionally, it is crucial to inform women about how a healthy lifestyle can help reduce the risk of endometrial cancer, as about 40% of cases are linked to factors such as diet, body weight, physical activity, and blood sugar levels. Educating women to recognize signs and symptoms that require immediate gynecological consultation is essential. Early diagnosis not only allows for longer survival but also offers greater chances of curing cancers detected at early stages.

In terms of information, events such as the 'World Gynecologic Oncology Day' and the 'Gynecologic Cancer Awareness Month' are strategic moments to promote awareness and information about endometrial cancer. These events provide an opportunity to raise public awareness and encourage dialogue on gynecological health issues. Additionally, screening visits for other female cancers, such as breast or cervical cancer, can become valuable opportunities to inform women about endometrial cancer as well, creating an interconnection between different awareness campaigns.

To reach as many women as possible and increase awareness about endometrial cancer, it is essential to implement informational campaigns through all available channels, including television, social networks, buses, banners, hospitals, and private gynecological clinics. This strategy ensures the widespread dissemination of accurate and reliable information, thereby contributing to greater awareness and understanding of the disease.

Directing women to patient associations for accurate information and giving greater visibility to the work of these Associations

Nowadays, it is crucial to recognize that many patients seek information online, even though many sites do not provide truthful and reliable content. Therefore, it is essential to direct patients to authoritative sources, such as the websites of patient associations. These associations, equipped with scientific committees composed of experts, offer comprehensive and scientifically reliable information.

Over the years, patient associations and civic organizations have worked hard to raise women's awareness of gynecological cancers, and they have long been committed to raising awareness and informing women about endometrial cancer as well.

To raise awareness of patient associations and reach a wider audience, initiatives could be organized to post posters in gynecological oncology departments throughout Italy. These posters would feature logos and QR codes to access the websites of the various associations. This approach would not only increase the visibility of the associations but also guide patients and their families to reliable sources of information.

It is also essential for the associations to collaborate with civic organizations that have direct contact with the community, are present in many hospitals, even small ones, and work in synergy with professionals, scientific societies, and institutions.

All women affected by endometrial cancer and other gynecological cancers should be guaranteed the opportunity to connect with patient associations and benefit from their initiatives.

Making prevention more accessible

All women should undergo a gynecological check-up at least once a year, but often they do not engage in prevention because they cannot book the initial check-up or face interminable waiting lists. To encourage prevention, visits and US evaluation must be made more accessible.

Providing patients with clear explanations of the therapeutic pathway they will face

To make the therapeutic pathway clear to as many women as possible, it is essential that clinicians strive to convey information in an understandable man-

ner, ensuring that the patient in front of them has truly understood what has been explained. Clinicians must communicate information by adjusting their language to each individual patient they interact with.

Standardizing care pathways nationally by adopting regional PDTA inspired by international guidelines

To ensure equitable access to care pathways for all patients, it is crucial that all regions adopt PDTA inspired by common and shared principles, adapted to their respective territorial realities. The PDTA is a fundamental tool for improving patient outcomes by optimizing the organization of care and ensuring a multidisciplinary and integrated approach.

It is also essential to open a constant dialogue between patients, associations, and healthcare professionals to co-create personalized and truly effective care pathways. The active involvement of patient associations in the drafting and evaluation of PDTA ensures that these are aligned with their needs and expectations.

It is also necessary to implement tools for measuring the perceived quality of life during the disease course, such as Patient-Reported Outcome Measures (PROMs), which offer a valuable opportunity to bring out the patients' voices and constantly monitor the impact of treatments on their daily lives. In this way, a virtuous circle is created where patients' experiences guide the continuous improvement of healthcare.

Identifying reference centers for the disease nationwide

It is important to identify centers specialized in the management of endometrial cancer to ensure adequate and effective care. Although centralizing patients in these centers can improve surgical management and post-operative aspects, it is also essential that the designated facilities are capable of providing optimal surgery and performing molecular profiling of the tumor. Based on the results of this profiling, patients can receive more targeted therapeutic indications.

At the European level, the European Society of Gynecological Oncology (ESGO) offers a certification program for the accreditation of centers specialized in the treatment of gynecological cancers, including endometrial cancers.

This program recognizes facilities that meet strict quality standards in multidisciplinary care, accrediting them as Reference Centers or even Centers of Excellence. Such certifications ensure that patients can access treatments based on the latest scientific evidence and cutting-edge technologies for personalized diagnosis and therapies.

Centralization offers the opportunity to ensure access to biomolecular characterization tests, which are not yet available in all facilities. Concentrating tests on a larger number of samples helps reduce costs for the healthcare system, making the implementation of these exams more sustainable.

Therefore, it is advisable that regional multidisciplinary reference centers for endometrial cancer be identified and shared, following the criteria established by ESGO.

Experience with ovarian cancer shows that identifying specialized centers can improve the diagnostic-therapeutic pathway and outcomes for patients. For example, in 2019, the Emilia-Romagna Region designated five reference centers for ovarian cancer, and five years later, the percentage of patients who turn to these centers increased from 43% to 80%.

Ensuring equitable access to diagnosis and care without territorial disparities, distributing reference centers on a regional or macro-regional basis to reduce healthcare migration and related costs

To reduce healthcare migration and the associated costs for patients and their families, it is essential to ensure equitable access to care and diagnosis across the entire national territory. To this end, it is necessary to provide for the distribution of reference centers on a regional or macro-regional basis, so as to ensure that all women have access to specialized facilities without having to travel long distances. In Italy, some regions cover very large geographical areas, while others, characterized by low population density, may not have reference centers for endometrial cancer. It is important that women residing in these regions also have the opportunity to access a macro-regional specialized center as close as possible to their home. This approach not only promotes more equitable access to care but also helps prevent disparities in treatment and clinical outcomes for patients.

Additionally, the centers need to be strengthened in terms of both human and economic resources.

Implementing a network system based on the Hub & Spoke model to ensure continuity of care, defining in advance the activities of the reference centers and satellite centers

It goes without saying that the reference centers cannot handle the entire therapeutic pathway of patients but must be supported by a number of

satellite centers that ensure continuity of care in the territory. The network system according to the Hub & Spoke model allows for the development of dedicated territorial pathways, in which smaller centers take on part of the care process by implementing the guidelines provided by the centers of excellence. According to this model, the tasks of the reference and peripheral structures must be defined in advance: The Hub must perform surgery and molecular profiling, then provide a therapeutic indication; once the Hub has decided on the therapeutic strategy, the patient can receive treatment at a Spoke near her home. The corresponding Hubs and Spokes must remain in constant contact: if treatment-induced toxicity occurs that the Spoke cannot manage, the Hub can provide guidance on its management or directly take charge of the complication.

Offering genetic counseling only to women potentially affected by Lynch syndrome through pre-screening on tissue

Considering the current shortage of clinical geneticists and the prolonged waiting times for access to genetic counseling, which can hinder the timeliness of the diagnostic and therapeutic pathway for at-risk patients, it is essential to offer this service to women potentially affected by Lynch syndrome through pre-screening on tissue. This screening involves the immunohistochemical analysis of the expression status of the four proteins of the DNA damage repair system, known as mismatch repair. If the absence of the MLH1 protein is detected, it will be necessary to perform the MLH1 hypermethylation test. However, different pathways should be advocate: the mainstream process in which the genomic test is required by the oncologist for therapeutic implication after a mini counseling to the patients; the patient is then referred to the geneticist only if there is a germline genomic mutation. Such mainstream should be implemented in endometrial cancer as we did in ovarian cancer some years ago.

Defining a network of certified laboratories to ensure the quality and uniformity of reports

Since the standardization of pre-analytical and analytical procedures is an essential requirement to ensure the consistency and quality of the results of tests for the biomolecular characterization of endometrial cancer, it is important to define a network of certified laboratories that perform these analyses following shared standards.

Additionally, it is crucial to inform patients about the locations of these laboratories and the reference centers for performing tests. Clear and accessible information would allow patients to know where to go for the necessary analyses, ensuring they can receive high-quality services and consistent reports. A mapping of certified laboratories, easily consultable, could significantly improve patients' access to the necessary tests and ensure they receive reliable and timely results.

Urging institutions to provide more financial and human resources for molecular testing

To ensure that all women with endometrial cancer and all oncology patients have faster access to new molecular-targeted therapies, it is essential to raise awareness among institutions to allocate more funds and human resources for molecular testing, also encouraging young people to pursue careers as pathologists with more adequate remuneration. Also, the cost of specific tests required in combination with a specific drug treatment should be negotiated and lifted for the national health system.

It should not be forgotten that pharmaceutical spending by the national health system has increased significantly, and that oncological pathology is becoming a chronic condition, with a growing number of patients living longer with the disease and therefore requiring long-term pharmacological therapies.

Promoting collaboration between general practitioners and oncologists

It is essential to promote effective synergy between primary care and oncology to ensure patients receive quick and effective responses to any issues, whether related or unrelated to therapies. Open dialogue between oncologists and GPs is crucial to optimize the care pathway for patients and promote a more integrated management of their health.

Collaboration between these two professional figures can offer numerous advantages:

- Timely recognition of problems: Constant dialogue allows GPs to promptly identify signs of complications or side effects of oncological therapies, enabling rapid intervention by oncologists.
- Shared management of therapies and their side effects: Direct communication facilitates the creation of integrated treatment plans, where oncologists and GPs work together to tailor therapies to the specific needs of patients, considering their clinical history and comorbidities.

- Emotional support: GPs, often closer to patients in their daily lives, can provide essential emotional support, serving as a point of reference for concerns and fears related to illness. This relational dimension is important for the overall well-being of patients.
- Education and prevention: Oncologists and GPs can collaborate in raising patients' awareness about prevention, the importance of early diagnosis, and lifestyle management, helping to reduce the incidence of the disease.
- Joint training: Shared training programs can help both professional groups acquire specific knowledge and skills in managing oncology patients, strengthening their ability to work together effectively.

To achieve these goals, it is essential to develop communication and collaboration strategies, such as regular meetings between oncologists and GPs, the creation of shared follow-up guidelines, and the use of digital platforms for information sharing. With these measures, the GP can become a valuable point of reference in the care pathway of patients, ensuring an effective and coordinated multidisciplinary approach.

Raising awareness among Institutions about the need to ensure widespread psychological support for patients and their families

Policymakers need to be made aware of the importance of psychological care for patients and their families and the current lack of psycho-oncological assistance in departments nationwide.

Given the significant economic impact that sessions with a psycho-oncologist can have on patients and their families, this type of service should be guaranteed by institutions, for example, by providing a minimum number of dedicated structural positions in each gynecological oncology department.

Including sexological counseling in multidisciplinary services

Sexuality in patients with endometrial cancer is an important but often overlooked issue that affects both the psychological and physical well-being of patients. Bodily changes, sexual function, and the management of the couple's relationship require sexological support, which is often lacking due to social stigma and the shortage of specialists. Therefore, it is essential that sexological counseling, like psychological counseling, be included in the LEA. A comprehensive multidisciplinary approach is fundamental to improving the quality of life of patients and adequately supporting them in their care pathway, considering all aspects of their psychophysical well-being.

Proposal for awareness actions to improve the care pathway for patients with endometrial cancer

- **Promoting information campaigns on various channels to increase awareness of endometrial cancer and find a uniform definition for the disease**: It is essential to launch effective communication campaigns to spread comprehensive information about endometrial cancer, involving institutions to ensure adequate economic and operational resources. Patient associations, scientific societies, and clinicians should collaborate to promote awareness campaigns on gynecological health, the risk factors of endometrial cancer, and the importance of prevention and a healthy lifestyle. Institutions can help reduce the social stigma still associated with gynecological cancers by promoting discussions on these diseases and encouraging women to consider gynecological health on par with breast health. Dedicated events and dissemination through multiple communication channels (television, social networks, advertising spaces on buses, banners, hospitals, and private gynecological clinics) can help reach a wide audience, increasing awareness and promoting early diagnosis. The lack of initiatives limits knowledge about risk factors and the importance of screening, and women often have a limited understanding of the disease and the health of the genital system.

  Another obstacle arises from terminology: endometrial cancer is commonly referred to as 'uterine cancer', sometimes causing confusion. It is therefore crucial to work towards a uniform definition of endometrial cancer to facilitate understanding and promote clear communication.
- **Guiding women to seek information online from reliable sites**: since people are 'hungry' for information when they fall ill and it is impossible to prevent women who receive a cancer diagnosis from turning to the internet, they should be directed to reliable websites that provide scientifically accurate information, primarily those of patient associations.
- **Increasing the visibility of patient associations to continue raising awareness and educating about endometrial cancer and other gyneco-**

logical cancers: patient associations must continue to raise awareness and inform women about endometrial cancer and other gynecological cancers through all available communication channels. It is important to also create a 'network' with civic organizations that have constant direct contact with citizens. Patient associations are present in many hospitals, including smaller ones, and work in synergy with healthcare professionals, scientific societies, and institutions.

- **Making prevention more accessible**: All women should undergo a gynecological check-up at least once a year, but often they do not engage in prevention because they cannot book the initial check-up or face interminable waiting lists. To encourage prevention, visits must be made more accessible.
- **Providing patients with clearer explanations about the therapeutic pathway they will face**: to make the therapeutic pathway clear to as many women as possible, clinicians must strive to convey information in an understandable manner, adjusting their language to each individual patient they interact with, and ensuring that the patient has truly understood what has been explained.
- **Standardizing care pathways nationally by adopting Regional PDTA inspired by international guidelines**: to ensure equitable access to care across the national territory, it is essential that regions adopt PDTA based on shared principles, tailored to local realities. Constant dialogue between patients, associations, and healthcare professionals is fundamental to co-creating personalized pathways aligned with patients' needs. Tools like PROMs allow for monitoring perceived quality of life and using patients' experiences to continuously improve healthcare.
- **Identifying reference centers for the disease nationwide and centralizing patients in designated facilities**: directing patients with endometrial cancer to centers specialized in managing the disease has become an urgent necessity. Centralization is crucial for proper surgical management and even more critical for all post-operative aspects. Centralization ensures that all patients have access to biomolecular characterization tests, which are currently not available in all centers, and helps contain the costs associated with their implementation. Therefore, it is essential that individual regional PDTA identify the multidisciplinary reference centers for the disease within their territory. It is also essential that regional PDTA recognize and promote the presence of multidisciplinary reference centers, following the ESGO certification programme.
  This programme is based on rigorous criteria, including the adoption of multidisciplinary therapeutic approaches, the use of advanced technologies, and compliance with high standards of care, ensuring that patients receive treatments based on up-to-date scientific evidence. This strategy improves clinical efficacy and makes the implementation of biomolecular tests more sustainable by concentrating on a larger number of samples and reducing healthcare costs.
- **Providing for the distribution of reference centers on a regional or macro-regional basis to reduce healthcare migration and related costs**: to reduce healthcare migration and the associated costs for patients and their families/caregivers and to avoid creating disparities in access to care, it is necessary to ensure the most equitable distribution possible of reference centers across the national territory, organizing them by regions or macro-regional areas.
- **Intensifying and aggregating initiatives to promote the centralization of patients in reference centers**: existing initiatives aimed at promoting the centralization of patients in reference centers must be strengthened and aggregated: clinicians, scientific societies, patient associations, civic organizations, and pharmaceutical companies must intensify awareness-raising actions by uniting their voices to convey a single, more impactful message.
- **Strengthening reference centers**: for the centers of attraction, the centralization of patients inevitably leads to an increase in the number of patients and activity volumes. Therefore, reference centers must be strengthened in terms of both economic and human resources.
- **Implementing a network system based on the Hub & Spoke Model to ensure continuity of care, defining in advance the activities of reference centers and satellite centers**: reference centers must be supported by various satellite centers that ensure continuity of care in the territory, according to the Hub & Spoke network system. The tasks of the reference and peripheral structures must be defined: the Hub must perform surgery and molecular profiling, then provide a therapeutic indication. Once the Hub has decided on the therapeutic strategy, the patient can receive treatment at a Spoke near her home.

The corresponding Hubs and Spokes must remain in constant contact: if treatment-induced toxicity occurs that the Spoke cannot manage, the Hub can provide guidance on its management or directly take charge of the complication.

- **Offer genetic counseling to women who test positive for Lynch syndrome in tissue pre-screening**: in light of the current shortage of clinical geneticists and the waiting times for accessing genetic counseling, this service should be offered only to patients who potentially test positive for Lynch syndrome in tissue pre-screening.
- **Define a network of certified laboratories to ensure the quality and consistency of reports**: to ensure the concordance and quality of the results of biomolecular characterization tests for endometrial cancer, it is important to define a network of certified laboratories that perform these analyses following shared standards.
- **Increase financial and human resources to perform molecular tests**: to ensure that all women with endometrial carcinoma have equal access to targeted molecular therapies, it is essential that institutions allocate more funds and human resources for the execution of molecular tests. Additionally, it would be desirable to encourage young people to pursue careers as pathologists, considering adequate remuneration to further improve the efficiency and quality of the service.
- **Improve the interaction between general practitioners and oncologists**: promoting greater interaction between primary care and oncology would allow patients to receive quicker responses to any issues related or unrelated to therapies, avoiding the need to shuttle between various professionals.
- **Raise awareness among institutions about the need to ensure widespread psychological support for patients and their families**: policymakers need to be made aware of the importance of psychological support for patients and their families and the current shortage of psycho-oncologists nationwide. Given the significant economic impact that sessions with a psycho-oncologist can have on patients and their families, this type of service should be guaranteed by institutions, for example by providing a minimum number of dedicated structural positions in each gynecological oncology department.
- **Ensure and formalize patient meetings with associations as part of the care process**: all women with endometrial carcinoma and other gynecological cancers should be guaranteed the opportunity to connect with patient associations and benefit from their initiatives.

Implementing these recommendations will improve the management and care of patients with endometrial carcinoma and ensure comprehensive and accessible support for all women, addressing current challenges with a coordinated and integrated approach.

COMPLIANCE WITH ETHICAL STANDARDS

Funding

There was no institutional or private funding for this article.

Conflict of interests

The Authors have declared no conflict of interests.

Availability of data and materials

The data underlying this article are available within it.

Authors' contributions

All Authors contributed to the writing and revision of the policy statement..

Ethical approval

N/A.

Publication ethics

Plagiarism

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.
This policy statement is an English translation of a document produced by Edra, the publisher of Annals of Research in Oncology. Consequently, there are no concerns regarding plagiarism or copyright infringement.

Data falsification and fabrication

All the data corresponds to the real.

REFERENCES

1. Lorusso D. Quaderno ROPI endometrio 2024.
2. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of inci-

dence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209–49.
3. Gu B, Shang X, Yan M, et al. Variations in incidence and mortality rates of endometrial cancer at the global, regional, and national levels, 1990–2019. Gynecol Oncol 2021; 161: 573–80.
4. Matsuo K, Mandelbaum RS, Matsuzaki S, et al. Ovarian conservation for young women with early-stage, low-grade endometrial cancer: a 2-step schema. Am J Obstet Gynecol 2021; 224: 574–84.
5. Aiom-Airtum: I numeri del cancro in Italia 2023.
6. https://www.airc.it/cancro/informazioni-tumori/guida-ai-tumori/tumore-dell'utero.
7. Crosbie EJ, Kitson SJ, McAlpine JN, et al. Endometrial cancer. Lancet 2022; 399: 1412–28.
8. Lorusso D, et al. Endometrial cancer and its risk factors: An overview. Tumor Biology, 2019;41(1):1010428318818933.
9. Karam SG, et al. The Impact of Lifestyle Factors on Endometrial Cancer Risk: A Case-Control Study. Gynecologic Oncology Reports 2023:42:101052.
10. Lacey JV, et at. Association of Diabetes and Endometrial Cancer: A Review of Recent Studies. Cancer Epidemiology, Biomarkers & Prevention 2022;31(6):1038-1048.
11. Lancaster JM, Powell CB, Chen LM, Richardson DL. Society of Gynecologic Oncology state-ment on risk assessment for inherited gynecologic cancer predispositions. Gynecol Oncol 2015;136:3Y7.
12. Dominguez-Valentin M, Sampson JR, Seppälä TT, et al. Cancer risks by gene, age, and gender in 6350 carriers of pathogenic mismatch repair variants: findings from the Prospective Lynch Syndrome Database. Genet Med 2020; 22: 15–25.
13. Crosbie EJ, Ryan NAJ, Arends MJ, et al. The Manchester International Consensus Group rec-ommendations for the management of gynecological cancers in Lynch syndrome. Genet Med 2019; 21: 2390–400.
14. Seppala TT, Latchford A, Negoi I, et al. European guidelines from the EHTG and ESCP for Lynch syndrome: an updated third edition of the Mallorca guidelines based on gene and gender. Br J Surg 2021; 108: 484–98.
15. National Institute for Health and Care Excellence N. Testing strategies for Lynch syndrome in people with endometrial cancer 2020. https://www.nice.org.uk/guidance/dg42 (accessed March 12, 2022).
16. Bakkum-Gamez JN, Wentzensen N. Association of endometrial cancer risk with postmeno-pausal bleeding in women: a systematic review and meta-analysis. JAMA Intern Med 2018; 178: 1210–22.
17. Linee Guida AIOM neoplasia dell'utero: endometrio e cervice. Edizione 2022.
18. Manfredi R, Mirk P, et al. Loco-Regional Staging of Endometrial Carcinoma: Role of MR Imag-ing in predicting surgical staging. Radiology 2004; 231:372-8.
19. Bockman JV. Two pathogenetic types of endometrial carcinoma. Gynecol Oncol 1983; 15:10-7.
20. Prat J, Gallardo A, et al. Endometrial carcinoma: pathology and genetics. Pathology 2007; 39:72-87.
21. Llobet D, Pallares J, et al. Molecular pathology of endometrial carcinoma: practical aspects from the diagnostic and therapeutic viewpoints. J Clin Pathol 2009; 62:777-85.
22. Kandoth C, Schultz N, Cherniack AD, et al. Integrated genomic characterization of endometrial carcinoma. Nature 2013; 497: 67–73.
23. Kommoss S, McConechy MK, Kommoss F, et al. Final validation of the ProMisE molecular classifier for endometrial carcinoma in a large population-based case series. Ann Oncol 2018;29(5):1180-8.
24. Singh N, Wong R, Tchrakian N, et al. Interpretation and reporting terminology for mismatch re-pair protein immunohistochemistry in endometrial cancer 2020. www.thebagp.org/resources (accessed Jan 26, 2022).
25. Köbel M, Ronnett BM, Singh N, et al. Interpretation of p53 immunohistochemistry in endo-metrial carcinomas: toward increased reproducibility. Int J Gynecol Pathol 2019; 38 (suppl 1): S123–31.
26. León-Castillo A, Britton H, McConechy MK, et al. Interpretation of somatic POLE mutations in endometrial carcinoma. J Pathol 2020; 250: 323–35.
27. Talhouk A, McConechy MK, Leung S, et al. A clinically applicable molecular-based classifica-tion for endometrial cancers. Br J Cancer 2015; 113: 299–310.
28. Talhouk A, McConechy MK, Leung S, et al. Confirmation of ProMisE: a simple, genomics-based clinical classifier for endometrial cancer. Cancer 2017; 123: 802–13.
29. Stelloo E, Bosse T, Nout RA, et al. Refining prognosis and identifying targetable pathways for high-risk endometrial cancer; a TransPORTEC initiative. Mod Pathol 2015; 28: 836–44.
30. Jonathan SB, Matias-Guiu X, Creutzberg C, et al. FIGO staging of endometrial Cancer: 2023. Int J

Gyncol Obstet 2023;162(2):383-394.doi:10.1002/ijgo/14923.
31. Available from: https://www.esgo.org/esgo-estro-esp-guidelines/. Accessed: Mar 31, 2025.
32. Stelloo E, Nout RA, Osse EM, et al. Improved Risk Assessment by Integrating Molecular and Clinicopathological Factors in Early-stage Endometrial Cancer-Combined Analysis of the PORTEC Cohorts. Clin Cancer Res 2016;22(16):4215-24.
33. Janda M, Gebski V, Davies LC, et al. Effect of total laparoscopic hysterectomy vs total abdom-inal hysterectomy on disease-free survival among women with stage I endometrial cancer: a randomized clinical trial. JAMA 2017; 317: 1224–33.
34. Walker JL, Piedmonte MR, Spirtos NM, et al. Recurrence and survival after random assignment to laparoscopy versus laparotomy for comprehensive surgical staging of uterine cancer: Gy-necologic Oncology Group LAP2 Study. J Clin Oncol 2012; 30: 695–700.
35. Mourits MJ, Bijen CB, Arts HJ, et al. Safety of laparoscopy versus laparotomy in early-stage endometrial cancer: a randomised trial. Lancet Oncol 2010; 11: 763–71.
36. Galaal K, Donkers H, Bryant A, Lopes AD. Laparoscopy versus laparotomy for the management of early stage endometrial cancer. Cochrane Database Syst Rev 2018; 10: CD006655.
37. Wright JD, Burke WM, Tergas AI, et al. Comparative effectiveness of minimally invasive hyster-ectomy for endometrial cancer. J Clin Oncol 2016; 34: 1087–96.
38. Ind T, Laios A, Hacking M, Nobbenhuis M. A comparison of operative outcomes between stan-dard and robotic laparoscopic surgery for endometrial cancer: a systematic review and me-ta-analysis. Int J Med Robot 2017; 13: e1851.
39. Frost JA, Webster KE, Bryant A, Morrison J. Lymphadenectomy for the management of endometrial cancer. Cochrane Database Syst Rev 2017; 10: CD007585.
40. Kim CH, Soslow RA, Park KJ, et al. Pathologic ultrastaging improves micrometastasis detection in sentinel lymph nodes during endometrial cancer staging. Int J Gynecol Cancer 2013; 23: 964–70.
41. Bristow RE, et al. Stage IVB endometrial carcinoma: the role of cytoreductive surgery and de-terminants of survival. Gynecol Oncol 2000;78(2):85–91. 933; 375:1165-1172.
42. Cancer Research UK. Uterine cancer survival statistics 2021. https://www.cancerresearchuk.org/health-professional/cancerstatistics/statistics-by-cancer-type/uterine-cancer/survival (accessed March 12, 2022).
43. Creutzberg CL, van Putten WL, Koper PC, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: Multicenter randomised tri-al. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. Lancet 2000;355(9213):1404-11.
44. Bosse T, Nout RA, McAlpine JN, et al. Molecular Classification of Grade 3 Endometrioid Endo-metrial Cancers Identifies Distinct Prognostic Subgroups. Am J Surg Pathol 2018;42(5):561-8.
45. Wortman BG, Creutzberg CL, Putter H, et al. Ten-year results of the PORTEC-2 trial for high-in-termediate risk endometrial carcinoma: improving patient selection for adjuvant therapy. Br J Cancer 2018;119(9):1067-74.
46. Matei D, Filiaci V, Randall ME, et al. Adjuvant chemotherapy plus radiation for locally advanced endometrial cancer. N Engl J Med 2019; 380: 2317–26.
47. de Boer SM, Powell ME, Mileshkin L, et al. Adjuvant chemoradiotherapy versus radiotherapy alone in women with high-risk endometrial cancer (PORTEC-3): patterns of recurrence and post-hoc survival analysis of a randomised phase 3 trial. Lancet Oncol 2019; 20: 1273–85.
48. León-Castillo A, de Boer SM, Powell ME, et al. Molecular classification of the PORTEC-3 trial for high-risk endometrial cancer: impact on prognosis and benefit from adjuvant therapy. J Clin Oncol 2020; 38: 3388–97.
49. Huh WK, Straughn JM, Mariani A et al. Salvage of isolated vaginal recurrences in women with surgical stage I endometrial cancer: a multi-institutional experience. Int J Gynecol Cancer 2007;17(4):886-9.
50. Creutzberg CL, van Putten WL, Koper PC et al. Survival after relapse in patients with endometrial cancer: results from a randomized trial. Gynecol Oncol 2003; 89: 201–209.
51. Nakamura H, Takehara K, Samura O et al. Cytoreductive surgery for isolated para-aortic lymph node recurrence of endometrial cancer: report of four cases and a review of the literature. Eur J Gynecol Oncol 2014;35 (5):535-538.
52. Miller DS, Filiaci VL, Mannel RS, et al. Carboplatin and paclitaxel for advanced endometrial cancer: final overall survival and adverse event analysis of a phase III trial (NRG Oncology/GOG0209). J Clin Oncol 2020; 38: 3841–50.

53. Kokka F, Brockbank E, Oram D etal. Hormonal therapy in advanced or recurrent endometrial cancer. Cochrane Database Syst Rev;2010(12):CD007926.
54. Oaknin A, Sullivan RJ, Pothuri B et al. Preliminary safety, efficacy and pharmacokinetic/phar-macodynamic characterization from GARNET, a phase I-II clinical trial of the anti PD-1 mono-clonal antibody, TSR-042, in patients with recurrent or advanced MSI-h and MSS endometrial cancer. Gynecol Oncol 2019;154 (Suppl 1) Abstract LBA36.
55. Colombo N, Dubot C, Lorusso D, et al. Pembrolizumab for Persistent, Recurrent, or Metastatic Cervical Cancer. N Engl J Med 2021;385(20):1856-1867.
56. Marth C, Moore RG, Bidziński M, Pignata S, Ayhan A, Rubio MJ, Beiner M, Hall M, Vulsteke C, Braicu EI, Sonoda K, Wu X, Frentzas S, Mattar A, Lheureux S, Chen X, Hasegawa K, Magallanes-Maciel M, Choi CH, Shalkova M, Kaen D, Wang PH, Berger R, Okpara CE, McKenzie J, Yao L, Orlowski R, Khemka V, Gilbert L, Makker V; ENGOT-en9/LEAP-001 Investigators.First-Line Lenvatinib Plus Pembrolizumab Versus Chemotherapy for Advanced Endometrial Cancer: A Randomized, Open-Label, Phase III Trial.J Clin Oncol. 2025 Mar 20;43(9):1083-1100. doi: 10.1200/JCO-24-01326. Epub 2024 Nov 26.PMID: 39591551
57. Di Mattei VE, Carnelli L, Taranto P, Bernardi M, Brombin C, Cugnata F, et al. Health in the Mirror: An Unconventional Approach to Unmet Psychological Needs in Oncology. Front Psychol 2017 Sep 21;8:1633.
58. Di Mattei VE, Carnelli L, Taranto P, Mazzetti M, Perego G, Rottoli S, et al. Chemotherapy-induced nausea in a sample of gynaecological cancer patients: assessment issues and personal risk factors evaluation. Support Care Cancer 2020 Nov;28(11):5343-5351.
59. Di Mattei VE, Perego G, Taranto P, Mazzetti M, Rancoita PMV, Milano F, et al. Socio-demograph-ic and psychological factors associated with quality of life of women undergoing chemother-apy treatment for gynecological cancer. Support Care Cancer 2022 Sep;30(9):7333-7339.