RARE CANCERS OF THE FEMALE GENITAL SYSTEM

PREFERRED MODEL OF CARE AND CRITERIA FOR REFERENCE CENTRES

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- **Finally, the report to which this addendum refers has been approved by common assent by the Executive Board.**

PREFERRED MODEL OF CARE AND CRITERIA FOR REFERENCE CENTRES

A. Type of cancers

1. Cancer of the vulva
2. Cancer of the vagina
3. Cervical cancer
4. Endometrial cancer
5. Sarcomas of the uterus
6. Mixed mullerian malignant tumours (MMMT) of the female genital organs
7. Gestational trophoblastic disease
8. Malignant epithelial tumours of the ovary, fallopian tubes or peritoneum
9. Non epithelial tumours of ovary, fallopian tube

B. Short description of the cancers

Cancer of the vulva

Cancer of the vulva is rare with an incidence of about 200 cases per year in Belgium. There are 2 types of vulvar squamous cancer. The first type is HPV associated, often multifocal and occurs typically between 40 and 60 years old. The second type of squamous cell carcinoma is often related to lichen sclerosus et atrophicus and occurs typically in older patients (70 years or older). Besides these 2 types there are also more rare types such as e.g. Paget's disease of the vulva, melanoma of the vulva.

The therapy is primarily surgical in most patients and consists of wide local excision (or hemi- or radical vulvectomy) with inguino-femoral lymph node dissection in patients with a squamous cell carcinoma infiltrating at least 1 mm. During the last decade a sentinel procedure has become the standard of care in patients with squamous cell carcinoma of the vulva that is unifocal and smaller than 4 cm in diameter. Radiotherapy is indicated in some patients with resection margins that are not free or in patients with metastatic inguino-femoral lymph nodes.

Cancer of the vagina

Cancer of the vagina is rare with an incidence of about 25 cases per year in Belgium, usually of the squamous cell carcinoma type. Treatment is similar to the treatment of vulvar cancer for cancer located at the outer third of the vagina, and similar to the treatment of cervical cancer for cancers located at the inner two thirds of the vagina. However, due to the anatomical limitations surgical therapy is more difficult and most often radiotherapy with eventually brachytherapy is the preferred treatment.

Cervical cancer

Cervical cancer has an incidence of about 600 patients per year. The incidence has been decreasing the last decade mainly due to better cytological screening of the patients. Cervical cancer is almost always caused by HPV infection and it is expected that the current number of cervical cancers will decrease to about 20-30% of the current number of patients if all women are vaccinated with the currently available vaccines against HPV 16 and 18. Cervical cancer presents often with as first symptom postcoital bleeding.

Cervical cancers in low stage are typically treated with radical hysterectomy (Wertheim-Meigs procedure) or radiochemotherapy in inoperable patients. In stage Ib2 – IVa radiochemotherapy with brachytherapy is globally the standard of care. However, some patients with Stage Ib2-IIb might also be treated with neoadjuvant chemotherapy followed by Wertheim-Meigs procedure. The Wertheim-Meigs procedure is performed in Belgium for cervical cancer in only about 200 cases per year.

Endometrial cancer

Endometrial cancer is the most frequent pelvic gynaecological cancer with an incidence of about 1 300 patients per year. There are 2 main types of endometrial cancer: Type I : endometrioid endometrial cancer; Type II: includes serous, clear cell and undifferentiated endometrial cancer. Endometrial cancer presents often with as first symptom postmenopausal bleeding.

In low risk endometrial cancer (defined e.g. according to the Mayo Clinic criteria as type I, FIGO stage I,G1-2 smaller than 2 cm and infiltrating < half of the myometrial thickness or type 1, FIGO stage I, G1 > 2cm with < 1/3 myometrial infiltration) can be treated with simple hysterectomy, bilateral salpingo-oophorectomy and peritoneal cytology. In the other operable endometrial intermediate/high risk cancers, usually a pelvic (and eventually para-aortic) lymphadenectomy is recommended.

Sarcomas of the uterus

Sarcomas of the uterus are rare with an incidence in Belgium of about 60 cases per year. The aggressiveness varies from low grade to high grade tumours. The therapy varies substantially according to this grading and also according to the histological type (leiomyosarcoma, endometrial stromal sarcoma, …).

Mixed mullerian malignant tumours (MMMT)

MMMT's are rare with an incidence in Belgium of about 90 cases per year. These tumours are of epithelial origin but contain as stromal (malignant) components. The prognosis is poor. They usually metastasize as the poorly differentiated pure epithelial tumours and are also treated as the poorly differentiated pure epithelial tumours. This group should include not only MMMT's of the uterus but also of the cervix and ovaries.

Gestational trophoblastic disease

Gestational trophoblastic disease comprises partial and complete moles, invasive molar pregnancy, choriocarcinoma, placental site trophoblastic tumours and epitheloid trophoblastic tumours. The incidence of gestational trophoblastic disease is estimated at about 200 cases per year in Belgium. However, malignant gestational neoplasias are very rare with an incidence of about 20 patients per year in Belgium. The number of patients registered according to the Belgian Cancer Registry is highly underestimated because there is often no histological proof of malignancy. Partial moles and complete moles become malignant in about 1% and 10-15%, respectively. For this reason, it is of utmost importance that also partial and complete moles are followed adequately with weekly serum HCG values.

The therapy of gestational trophoblastic neoplasia and persistent gestational trophoblastic disease consists mainly of chemotherapy, but includes sometimes also surgery and radiotherapy.

Malignant epithelial tumours of the ovary, fallopian tubes or peritoneum

Malignant invasive epithelial ovarian (including fallopian tube and peritoneal cancer) has an incidence of about 900 cases per year in Belgium. The type is typically diagnosed at a late stage and has a 5-year survival of less than 50%. Ovarian cancer is characterized as the “silent killer” due to the lack of symptoms leading to the diagnosis and the high mortality.

Early stage patients often need comprehensive staging including pelvic and para-aortic lymphadenectomy. The debulking surgery performed in ovarian cancer is regarded as the most challenging surgery in gynaecological cancer. Also after neoadjuvant chemotherapy the surgery remains very complicated. The selection of patients for primary or interval debulking surgery is crucial for the prognosis of the patients. Sometimes the diagnosis of a pelvic mass suspicious of an ovarian cancer is missed. However, recent algorithms with expert gynaecological ultrasonography or Magnetic Resonance of the pelvis have been able to characterize ovarian tumours better than in the past.

Non epithelial tumours of ovary, fallopian tube

Non-epithelial ovarian malignancies are rare (about 40 cases per year in Belgium) and have a different occurrence, behaviour and management compared with epithelial ovarian cancers. There are many different types and subgroups; the therapy is different according to each subgroup. The most frequent groups are germ cell and sex cord stromal tumours of the ovaries.

C. Model of care pathway suggested for adult patients with female genital cancer

Model of care pathway	Preferred model
Shared care between Reference Centres and peripheral hospitals. **Part of the care pathway is performed in the Reference Centre and for another part of the care pathway, the patient is referred (back) to the peripheral hospital**	**Reference Centre** ***For all female genital cancers discussed in the proposal*** • MOC/COM (can be at the Peripheral Centre with at least one person present of the Reference Centre) • Operative staging including pelvic and/or para-aortic lymphadenectomy • Surgery and radiotherapy of all recurrences (chemotherapy can be performed at the Peripheral Centre – after MOC/COM as described above) *For cancer of the vulva* • MOC/COM after excision or biopsy • Surgery of patients with a depth of infiltration of ≥ 1mm • Radiotherapy

- Management of all patients with non-squamous carcinoma of the vulva (including Paget's disease)

For cancer of the vagina

- Management of all patients with vaginal cancer
- Radiotherapy

For cervical cancer

- Management of patients with cervical carcinoma stage Ib or higher
- Management of patients with non-squamous or non-adenocarcinomas cancers

For endometrial cancer

- Management of patients with non-endometrioid cancers of the corpus of the uteri

For sarcomas of the uterus

- If strong suspicion of sarcoma of the uterus preoperatively, patients should be referred to the Reference Centre
- All patients with suspicion of sarcoma of the uterus should be discussed at the COM/MOC preoperatively and postoperatively with at least one member present of the Reference Centre.

For mixed mullerian malignant tumours (MMMT)

- Management of patients with MMMT, whatever the genital organ involved

For gestational trophoblastic disease

- All moles (including partial and complete moles, and all persistent trophoblastic diseases) should be registered in the Belgian Trophoblastic Register and discussed at the MOC/COM in the presence of at least one member of the Reference centre.
- All following patients should be treated at a limited number of (e.g. 3) Reference Centres in Belgium:
  - All patients with at the time of first line chemotherapy a WHO-score of 6 or higher
  - All patients needing second line chemotherapy
  - All patients with histological proven choriocarcinoma, placental site trophoblastic tumour or epitheloid trophoblastic tumour at the time of diagnosis

For malignant epithelial tumours of the ovary, fallopian tubes or peritoneum (all high risk stage I and higher)

- MOC discussion with at least one representative of the Reference Centre of all patients with suspicious pelvic masses
- All patients needing operative staging including lymphadenectomy should be referred to the Reference Centre. This means that all high-risk stage I invasive epithelial ovarian cancers and all

patients with stage II or higher should be referred for surgery to the Reference Centre.

- Radiotherapy
- Chemotherapy can be performed at the Peripheral Centre after discussion with the Reference Centre

For non-epithelial tumours of ovary, fallopian tube

- MOC discussion with at least one representative of the Reference Centre of all patients with suspicious pelvic masses
- All patients with suspicion of non-epithelial ovarian cancer (e.g. increased serum tumour markers, or ultrasound or MRI suggestive of non-epithelial ovarian cancer) should be referred for surgery to the Reference Centre.
- Radiotherapy
- First-line chemotherapy can be performed at the Peripheral Centre after discussion with the Reference Centre; later lines of chemotherapy at Reference Centre.

Peripheral Centre

- Clinical staging of gynaecological caners
- Surgery of squamous vulvar cancer infiltrating less than 1 mm, squamous or adenocarcinoma of the cervix stage Ia, low risk clinical stage I endometrioid endometrial cancer not needing lymphadenectomy, low risk epithelial ovarian carcinoma stage I not needing lymphadenectomy.
- Chemotherapy in Peripheral Centre after discussion with the Reference Centre of endometrioid endometrial carcinoma, epithelial ovarian carcinoma, first-line non-epithelial ovarian carcinoma, cervical squamous or adenocarcinoma, vulvar squamous carcinoma and first-line low risk gestational trophoblastic disease.
- Follow-up

D. Phase(s) of the clinical pathway for which Reference Centres are required

Phase of the Clinical Pathway	Reference Centre	Peripheral centre
MOC/COM	*All gynaecological cancers* should be discussed preoperatively, postoperatively and at recurrence in a MOC/COM in the presence of at least one representative of the Reference Centre. The Reference Centre defines the optimal practical modalities of the MOC/COM	*All gynaecological cancers* should be discussed preoperatively, postoperatively and at recurrence on a MOC/COM in the presence of at least one representative of the Reference Centre. The Reference Centre defines the optimal practical modalities of the MOC/COM
Diagnostic confirmation (AP)	*For the following cancers:* Cancer of the vulva / cancer of the vagina / MMMT / gestational trophoblastic disease / non-epithelial ovarian cancers: Cervical cancer: non-squamous and non-adenocarcinomas Endometrial cancers: non-endometrioid carcinomas.	*For the other situations*
Therapeutic modalities	*For all female genital cancers* • All patients who need operative staging including pelvic and/or para-aortic lymphadenectomy • Treatment of all recurrences *For cancer of the vulva* • For surgery all patients with a depth of infiltration of 1mm or more should be referred for surgery at the Reference Centre • For radiotherapy the patient should be referred to a Reference Centre • All patients with non-squamous carcinomas (including Paget's disease) of the vulva should be referred to the Reference Centre	Where needed, chemotherapy can be performed at the Peripheral Centre after discussion with the Reference Centre

For cancer of the vagina

- Radiotherapy and surgery

For cervical cancer

- All patients with cervical carcinoma stage Ib or higher
- All non-squamous or non-adenocarcinomas

For endometrial cancer

- All non-endometrioid cancers of the corpus of the uteri

For gestational trophoblastic disease
All following patients should be treated at a limited number of (e.g. 3) Reference Centres in Belgium:

- All patients with at the time of first line chemotherapy a WHO-score of 6 or higher
- All patients needing second line chemotherapy
- All patients with histological proven choriocarcinoma, placental site trophoblastic tumour or epitheloid trophoblastic tumour at the time of diagnosis

For sarcomas of the uterus

- If strong suspicion of sarcoma of the uterus preoperatively, patients should be referred to the Reference centre

For mixed mullerian malignant tumours (MMMT)

- Management of patients with MMMT, whatever the genital organ involved

For malignant epithelial tumours of the ovary, fallopian tubes or peritoneum (all high risk stage I and higher)

- All patients needing operative staging including lymphadenectomy should be referred to the reference center. This means

	that all high-risk stage I invasive epithelial ovarian cancers and all patients with stage II or higher should be referred for surgery to the reference center. *For non-epithelial tumours of ovary, fallopian tube* • All patients with suspicion of non-epithelial ovarian cancer (e.g. increased serum tumor markers, or ultrasound or MRI suggestive of non-epithelial ovarian cancer) should be referred for surgery to the reference center. • First-line chemotherapy can be performed at the local hospital after discussion with the reference center; later lines of chemotherapy at reference center	
Radiotherapy	All patients needing radiotherapy including brachytherapy	
Follow-up		**X**

Multidisciplinary Oncological Consult

It is preferable to have all cases discussed on a MOC/COM in a Reference Centre before start of any therapy in order to select the correct patients for the correct management (including surgical staging procedure).

Therapeutic modalities

- Complexity:
  - *Cancer of the vulva*: Due to the low incidence and the surgical and radiotherapeutical expertise needed for the management of cancer of the vulva, it is recommended that the surgery and radiotherapy are performed in a Reference Centre
  - *Cervical cancer*: High enough experience and training to perform Wertheim–Meigs procedure in an adequate way. New techniques allowing complete surgical treatment by endoscopic techniques (laparoscopic and/or robot-assisted) in patients needing Wertheim-Meigs procedure or endoscopic staging (para-aortic staging in Stage Ib2-IVa) are recommended. Nerve-sparing surgery and fertility sparing management needs also expertise of the Reference Centre.
  - *Endometrial cancer:* New surgical techniques allowing complete surgical staging by endoscopic techniques (laparoscopic and/or robot-assisted) in patients with clinically FIGO stage I or II disease; adequate lymphadenectomies
  - *Sarcomas of the uterus*: Due to the low incidence and the aggressive nature of uterine sarcomas it is recommended that the primary diagnosis and surgeries are performed at the Reference Centres.

- *MMMT*: Due to the low incidence and the aggressive nature of MMMT, it is recommended that the primary diagnosis and surgeries are performed at the Reference Centres
- *Gestational trophoblastic diseases*: Due to the very low incidence of gestational trophoblastic neoplasia and persistent gestional trophoblastic disease few doctors have adequate experience in the disease. The prognosis for most patients is excellent if the therapy is performed in or under the guidance of specialized centres[i].
- *Malignant epithelial tumours of the ovary, fallopian tubes or peritoneum*: Due to the aggressive nature and surgical complexity of ovarian cancer it is recommended that the primary diagnosis and surgeries are performed at the reference centers, in patients as stated above.

E. General and specific criteria for Reference Centres

Criteria to be met within 3 years

Human Resources and dedicated team

- Specialized staff: at least 2 gynaecological oncologists, 2 medical oncologists specialized in gynaecological cancer (if gynaecological oncologists is not experienced in systemic treatment of gynaecological cancers), 2 radiation-oncologists specialized in gynaecological cancer including brachytherapy, 1 radiologist, 1 nuclear medicine specialist, 1 pathologist specialized in gynaecological cancer. Extended multidisciplinary team consists of psychologist/psychiatrist/counsellor with experience in cancer and psychosexual problems, cancer genetic specialist, social worker, doctor specialized in palliative care, doctor specialized in reproductive medicine.
- Multidisciplinary management with specialized staff; necessary audiovisual facilities to discuss diagnostic and examination results during a MOC session, documentation of discussion process and results

Required facilities and equipment

- Surgery: access to endoscopy (eventually robot-assisted) to perform complete staging in specific patients (e.g. for cervical cancer: FIGO stage IB2-IVa; for endometrial cancer: FIGO stage I).
- Radiotherapy: access to brachytherapy and IMRT
- Chemotherapy
- Department for Reproductive Medicine with facilities for IVF needed for patients with ovarian cancer, below 40 years old.
- Availability of intra-operative frozen section
- Lymphedema Centre

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[i] Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. The Lancet. 2010;376(9742):717-29 / Lybol C, Westerdijk K, Sweep FC, Ottevanger PB, Massuger LF, Thomas CM. Human chorionic gonadotropin (hCG) regression nomograms for patients with high-risk gestational trophoblastic neoplasia treated with EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine) chemotherapy. Ann Oncol. 2012 Nov;23(11):2903-6.

Patient centred care

- Waiting and throughput times (maximum waiting and throughput times for patients with regard to first outpatients' visit, admission, and tests/treatment): to be determined later.
- Continuity of care: care covered 7 days a week by specialised staff, agreements concerning the continuity of care...
- Strongly recommended: expertise in pain control, fertility issues, practical and social support, nutritional and dietetic support, physiotherapy and occupational therapy, psychological support and psychosexual counselling, lymphedema

Minimal volume of patients:

For all gynaecological cancers, at least 60 invasive cervical, uterine and ovarian malignancies per year (mean/year over the last 3 years), and in addition for:

- Cancer of the vulva: at least 5/year (mean/year over the last 3 years).
- Cancer of the vagina: at least 3/year (mean/year over the last 3 years).
- Sarcomas of the uterus: at least 5/year (mean/year over the last 3 years).
- Gestational trophoblastic diseases: at least 3/year needing high-dose or second-line chemotherapy (mean/year over the last 3 years).
- Non-epithelial ovarian cancer: at least 3/year (mean/year over the last 3 years).
- Mixed Malignant Mullerian Tumours: at least 5/year (mean/year over the last 3 years).

Quality Assurance

- Quality indicators for radical (Wertheim-Meigs) hysterectomy (see Verleye et al. Ann Oncol 2009)

	Quality indicator	Accepted standard – Mean over a period of 3 years
Structure	* Number of radical hysterectomies by surgeon per year. * Number of radical hysterectomies by institution per year.	≥ 10 ≥ 20
Outcome	* 5-year survival of cervical cancer patients having received radical hysterectomy (FIGO stage I – IIa) * Percentage of cervical cancer patients suffering pelvic recurrence after radical hysterectomy for cervical cancer. * Percentage of patients having short-term complications after radical hysterectomy. - post-operative mortality - post-operative haemorrhage - urinary tract injury	≥ 80% ≤ 15% ≤ 1% ≤ 1%

	- bowel obstruction	≤ 1%
	- deep venous thrombosis	≤ 1%
	* Percentage of patients having long term complications after radical hysterectomy.	≤ 3%
	symptomatic lymphocysts	
	ureteral stenosis	≤ 5%
	incisional hernia	≤ 3%
	fistula requiring surgery (vesico-, uretero- or recto-vaginal)	≤ 3%
	* Percentage of radical hysterectomy specimens with tumour positive resection margins.	≤ 3%
		≤ 5%
Process	* Percentage of surgery reports that contain information on mode of access, radicality of the different steps of the operation and completeness of lymphadenectomy.	≥95%
	* Percentage of pelvic lymphadenectomy specimens that contain more than 11 examined lymph nodes.	≥ 90%
	* Percentage of pelvic lymphadenectomy specimens that contain at least 1 examined lymph node in each common iliac, external and internal iliac and obturator area.	≥ 95%
	* Percentage of radical hysterectomies without peritoneal closure and retroperitoneal drainage.	≥ 95%
	* Percentage of patients undergoing radical hysterectomy who receive adequate administration of peri-operative antibiotics.	≥ 95%
	* Percentage of patients starting normal diet on day 1 after a radical hysterectomy.	≥ 90%

- Quality indicators for endometrial cancer (see Werbrouck et al. Gynecol Oncol 2013):

Indicators	Mean proportion over a period of 3 years
Proportion of patients with at least once MOC/COM during management	98%
Proportion of operated patients with preoperative biopsy	98%
Proportion of patients with clinical stage I undergoing surgery including at least a Total Hysterectomy	99%
Proportion of patients undergoing surgery for whom histological type according to WHO classification is available	98%
Proportion of patients who had pelvic lymphadenectomy for whom the number of lymph nodes removed is specified	98%
Proportion of operated patients receiving subsequent adjuvant therapy with a maximum waiting time between MOC/COM and first radiotherapy or chemotherapy of less than 45 days	95%
Proportion of patients who received external radiotherapy as adjuvant treatment for whom the technique used was IMRT or 3DCRT	98%
Proportion of patients who received postoperative adjuvant chemotherapy for whom the regimen included platinum based drugs	98%
Proportion of patients operated who died with 30 days after the operation	< 2 %
Proportion of patients with endometrial carcinoma clinical stage I who were operated endoscopically (laparoscopy or robotically)	75%
Proportion of patients with clinical stage I and grade 3 tumours who had at least a pelvic lymphadenectomy	75%
Proportion of patients with endometrial carcinoma undergoing surgery for whom myometrial invasion is semi-quantitatively or quantitatively reported	99%
Proportion of patients undergoing surgery for whom grade (1/2/3 or type II) is reported	95%

- Quality indicators for staging laparotomy for invasive ovarian cancer grossly confined to the pelvis (Verleye L et al 2008 Eur J Cancer):

Indicators	Mean proportion over a period of 3 years
Proportion of patients with a suspicious ovarian mass undergoing staging laparotomy within 1 month after decision to treat or documented clinical or patient-related reason for delay	95%
Proportion of performed staging laparotomies for an ovarian mass suspected to be malignant performed through a vertical incision	95%
Proportion of performed staging laparotomies in which all of the following procedures are included: total hysterectomy, bilateral salpingo-oophorectomy, cytology of the peritoneal cavity, infracolic omentectomy, random peritoneal biopsies and systematic pelvic and para-aortic lymphadenectomy if medium or high risk features	95%
Proportion of surgery reports with documented presence or absence of cyst rupture before or during surgery	95%
Proportion of surgery reports with documented presence or absence of dense adhesions Proportion of dense adhesions biopsied	95%

- Proposed EORTC–GCG quality indicators for primary debulking surgery in stage III–IV epithelial ovarian cancer. (Verleye L et al 2008 Eur J Cancer):

Indicators	Mean proportion over a period of 3 years
Proportion of patients with advanced-stage ovarian cancer undergoing debulking laparotomy within 31 days after decision to treat or documented clinical or patient-related reason for delay	95%
Proportion of patients undergoing debulking surgery with the spread of disease fully assessed for operability at the start of surgery and initial findings documented in the operation notes	95%
Proportion of debulking operations including a hysterectomy, bilateral salpingo-oophorectomy and infracolic omentectomy when the surgeon considers optimal debulking feasible	95%
Proportion of debulking operations for advanced ovarian cancer at the end of which complete cytoreduction, defined as no macroscopic residual disease at the end of the operation, was achieved	50%
Proportion of debulking operations for which the size and location of residual disease at the end of the operation is documented in the operation notes	95%

- Exhaustive and reliable information sent to Cancer Registry. Additionally, all moles (including partial and complete moles, and all persistent trophoblastic diseases) should be registered in the Belgian Trophoblastic Register.
- Compliance with existing guidelines of the College of Oncology or other International Guidelines and documentation of deviations from guidelines
- Involvement in quality initiatives (e.g. benchmarking)
- Annual activity report ensuring transparency (e.g. number of new patients / type of cancer; diagnostic, treatment and outcome data; specific protocols for reporting and recording complications...)

Research and other scientific activities

- Involvement in clinical studies (RCTs, cohort studies, translational studies) on gynaecological cancers
- Publications in peer-reviewed journals on gynaecological cancers
- Link with a tumour bank for frozen cancer tissues
- Development of clinical practice guidelines for diagnosis and care

Educational activities: Teaching and dissemination

- Involvement in training and continuous education programs (annual or multi-annual training / educational programme for physicians, nurses, supportive disciplines)
- Organisation / communication in scientific congresses

Additional comments

- Proportion of patients with FIGO Stage Ib undergoing radical hysterectomy treated endoscopically: at least 50%
- Proportion of patients with FIGO Stage Ib < 2cm undergoing nerve sparing radical hysterectomy: at least 90%
- Based on the recommendations above we recommend that:
- There will be a supplementary specific fee
  - for the delegates of reference centres to attend the MOC/COM's at the peripheral centre, be it in person or via web-conference
  - for second opinions performed at the reference centre by pathologists for review of the tumour slides, for radiologists and specialists in nuclear medicine for review of the images and for clinicians for evaluating the patients in an outpatient clinic, as these actions are all labour intensive.
- The success of the instalment of reference centres for gynaecological cancers will depend on the official recognition of all specialities and titles as mentioned under E.1.
- We suggest that the criteria to be met are discussed each 5 years.
- It is recommended that patients with the pathological diagnosis of choriocarcinoma, placental site trophoblastic tumour, or epitheloid trophoblastic tumour, or a WHO score at the time of diagnose of 6 or higher or need for second line chemotherapy are referred to a limited number of reference centres (e.g. 3).

Additional references

1. Robert E. Bristow, et al, High-Volume Ovarian Cancer Care: Survival Impact and Disparities in Access for Advanced-Stage Disease. Gynecol Oncol 2013.
2. Jeff F. Lina et al. Impact of Facility Volume on Therapy and Survival for Locally-Advanced Cervical Cancer. Gynecol Oncol 2013.