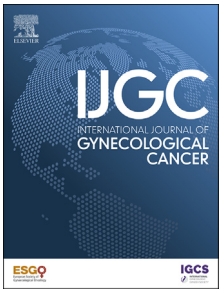
SOCIETY STATEMENT

ESGO/INCIP Guidelines for the management of patients with gynecological cancers during pregnancy



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ABSTRACT

As part of its mission to improve the quality of care for women with gynecological cancers across Europe, the European Society of Gynecological Oncology (ESGO) organized 3 international consensus meetings with leading experts in the field to define protocols and to provide guidance for pregnant patients and healthcare providers on the management of gynecological cancers in pregnancy. Following the third consensus meeting, the guidelines published in 2019 were updated by incorporating new evidence on this field and covering new topics to provide comprehensive evidence-based guidelines on all relevant issues within a multidisciplinary setting.

ESGO appointed 21 experts from relevant disciplines and 2 cancer survivors to serve on the international development group. Members of the International Network on Cancer, Infertility and Pregnancy involved in the 3 international consensus meetings were included. To ensure that the guidelines were evidence-based, data identified from a systematic search were reviewed and critically appraised. In the absence of robust scientific evidence, the guidelines were based on the consensus of the international development group. Prior to publication, the guidelines were reviewed by 100 independent international practitioners in cancer care delivery from Asia, Europe, Africa, and North and South Americas, and 3 patient representatives to ensure a global perspective.

These ESGO/International Network on Cancer, Infertility and Pregnancy guidelines address all relevant aspects of imaging, pathology, surgery, medical oncology, obstetrics, radiation therapy, psychology, patient perspectives and pediatric follow-up in a multidisciplinary setting for patients with tubo-ovarian, cervical, and vulvar cancers during pregnancy. Treatment algorithms for each tumor type are also defined.

Keywords:
Guidelines; Tubo-Ovarian Cancer; Cervical Cancer; Vulvar Cancer; Pregnancy

INTRODUCTION

Gynecological cancers during pregnancy are rare, affecting around 2 to 5 per 100,000 pregnancies primarily during the first trimester. Managing these cancers remains a challenge for patients, their physicians, and health care systems. Both maternal and fetal health should be considered, and specialized management strategies should be implemented to improve patient outcomes. Optimal management should aim to improve the benefit of treatment for the mother while minimizing harm to the fetus, considering the extent of the disease, treatment options, and gestational age at which treatment is considered with the ultimate goal of achieving a prognosis similar to that of non-pregnant patients. Three international consensus meetings with leading experts in the field were convened to define protocols and to provide guidance for pregnant patients and healthcare providers. The third consensus meeting, published in 2019, aimed to disclose new evidence-based information and expert opinion, in order to refine previous recommendations published in 2009 and 2014.[1–3] As part of its mission to improve the quality of care for women with gynecological cancers across Europe, the European Society of Gynecological Oncology (ESGO) decided to update these guidelines based on the third consensus meeting by taking into consideration the latest evidence in this field. Moreover, new topics have been covered to provide comprehensive guidelines on all relevant issues of the management of pregnant patients with gynecological cancers within a multidisciplinary setting.

Even though our aim is to present the highest standard of evidence for the optimal management of pregnant patients with

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gynecological cancers, ESGO acknowledges the broad variability in clinical practices worldwide. Moreover, differences in infrastructure, access to medical and surgical technology, training, medicolegal regulations, financial resources, and cultural aspects may influence the implementation of any guidelines. These guidelines are a statement of evidence and consensus of the multidisciplinary development group regarding their views and perspective of currently accepted approaches for the management of patients with gynecological cancers during pregnancy. Any clinician applying or consulting these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment.

The guidelines detailed in this article address all relevant aspects of imaging, pathology, surgery, medical oncology, obstetrics, radiation therapy, psychology, patient perspectives and pediatric follow-up within a multidisciplinary setting for patients with ovarian, cervical, and vulvar cancers during pregnancy. They are intended for use by gynecologic oncologists, obstetricians, general gynecologists, surgeons, radiation oncologists, pathologists, medical and clinical oncologists, radiologists, general practitioners, palliative care teams, and allied health professionals. Treatment algorithms for each tumor type are also presented. A summary of the evidence supporting the guidelines is available in Online Supplemental File (pp 7-64). These guidelines do not include any economic analysis of the proposed strategies.

METHODS

The guidelines were developed using a 5-step process as defined by the ESGO Guideline Committee (see Fig. 1). The strengths of the process include the creation of a multidisciplinary international development group, the use of scientific evidence and/or international expert consensus, and an external international review process. This development process was chaired by Professor Frédéric Amant (on behalf of ESGO) and Professor Michael Halaska (on behalf of International Network on Cancer, Infertility and Pregnancy [INCIP]). ESGO nominated practicing clinicians with expertise in the management of pregnant patients with gynecological cancers, with demonstrated leadership in clinical management of patients through research, publication, administrative responsibilities, and/or committee membership to serve on the international development group. Some members of the INCIP involved in the 3 international consensus meetings were also nominated. The objective was to assemble a multidisciplinary panel, ensuring the inclusion of professionals from all relevant disciplines (surgery, medical oncology, pathology, gynecology, radiation oncology, psychology) to enhance to the validity and acceptability of the guidelines. Two cancer survivors participated in the international development group.

To ensure that the statements were evidence based whenever possible, the current literature was reviewed and critically appraised. A systematic literature review of relevant studies published between January 2014 and June 2024 was carried out using the MEDLINE database (see Online Supplemental File [p 4]). The literature search was limited to publications in English. Priority was given to high-quality systematic reviews, meta-analyses, and randomized controlled trials, though studies with lower levels of evidence were also evaluated. The search strategy excluded editorials, letters, and *in vitro* studies. The reference list of each identified article was reviewed for other potentially relevant studies. Based on the collected evidence and clinical expertise, the development group members drafted guidelines for their assigned topics. The guidelines were then discussed within the full group and retained if they were supported by sufficiently high level scientific evidence and/or strong consensus among experts. An adapted version of the "Infectious Diseases Society of America-United States Public Health Service Grading System" was used to define the level of evidence and grade of recommendation for each of the recommendations[4,5] (see Fig. 2). In cases where clear scientific evidence was lacking, recommendations were based on the professional experience and consensus of the development group. ESGO established a large multidisciplinary panel of practicing clinicians who provide care to pregnant patients with gynecological cancers to act as independent reviewers for the guidelines. These reviewers were selected based on their expertise, ongoing involvement in clinical practice/research and representation from different European and non-European countries to ensure a global perspective. INCIP members who were not part of the international development group were also included in the panel, along with patient representatives. The international reviewers were asked to evaluate each guideline according to its relevance and feasibility in clinical practice, providing both comprehensive quantitative and qualitative feedback of the guidelines. Patient representatives were asked to qualitatively evaluate each recommendation (based on their experiences, perceptions, preferences, feelings, etc.). The evaluations from the external reviewers ($N = 103$) were pooled

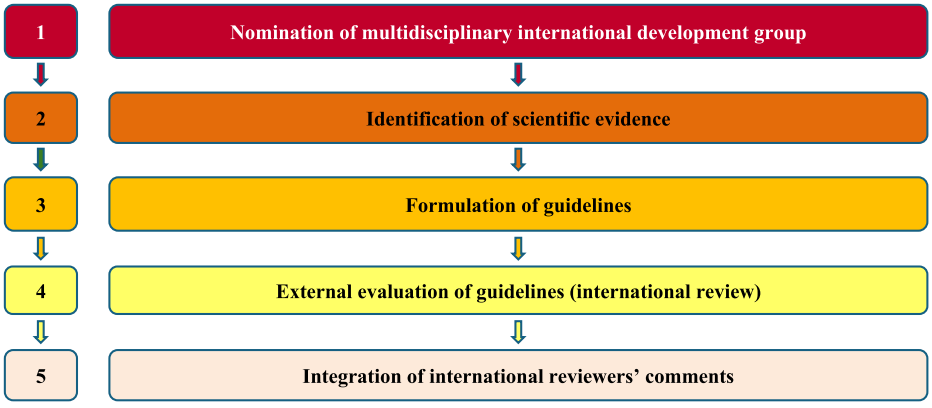


Figure 1 Development process.

LEVELS OF EVIDENCE	
I	Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted, randomised trials without heterogeneity
II	Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies
V	Studies without control group, case reports, expert's opinions

GRADES OF RECOMMENDATIONS	
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, ...), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

Figure 2 Levels of evidence and grades of recommendations.[4,5]

and discussed by the international development group to finalize the guidelines development process. The list of the 103 external reviewers is available in Online Supplemental File (pp 5-6).

GUIDELINES

General Recommendations

- Staging and treatment should be discussed within a multidisciplinary team (generally at a tumor board meeting, composed according to local guidelines and complemented by perinatologist/neonatologist consultation). This discussion should be based on comprehensive and precise knowledge of prognostic and predictive factors for maternal and fetal outcomes, including morbidity, long-term side effects and quality of life [V, A].
- Patients and their partners should receive careful counseling about the suggested diagnostic and treatment plan and potential alternatives, including risks and benefits, long-term side effects of all options and the impact on quality of life [V, A].
- Work-up and treatment should be conducted in a specialized center or by a dedicated team of specialists in the diagnosis and management of gynecological cancers [V, A]. Policy makers/medical societies are encouraged to establish such centers if they are not yet available [V, B].
- Pregnant women should receive oncologic treatment as close as possible to the standard care for non-pregnant patients to ensure optimal maternal outcomes [IV, B].
- Depending on the gestational age at diagnosis, type of cancer and stage of the disease, optimal therapy and its timing may require individualized modifications during pregnancy [IV, C].
- Research regarding the oncological, psychological, and obstetrical follow-up, as well as long-term outcomes of children prenatally exposed to cancer treatment, is strongly encouraged [V, A].
- The registration of all cancer cases during pregnancy is recommended, for example in the INCIP database (www.cancerinpregnancy.org) or national registries, to enable the monitoring of incidence, management strategies and maternal and fetal outcomes [V, C].

Incidence and Prognosis

- As the incidence of cancer in pregnancy is not decreasing, clinicians should remain aware that cancer can complicate pregnancy, especially in unscreened populations and/or populations with higher maternal age [V, B].
- It is recommended to investigate pregnant patients presenting with symptoms that could be caused by cancer without delay, to obtain an early diagnosis. If cancer is confirmed, it is recommended to perform locoregional and distant staging as in non-pregnant patients whenever possible [IV, A].
- Pregnancy itself does not worsen the prognosis of gynecological cancers, therefore pregnancy-preserving treatment should be considered [IV, A].

Imaging

- Ultrasound examination is recommended for diagnosis and staging as it is a safe imaging technique during pregnancy [II, A].
- Ultrasound examination is the preferred method for assessing adnexal masses, preferably using a transvaginal approach [IV, A].
- Magnetic resonance imaging (MRI) should be performed in patients with an adnexal mass with an inconclusive ultrasound examination [IV, B].
- In case of a suspicious adnexal mass detected during the first trimester, referral of the patient to an experienced ultrasound examiner is recommended to avoid overtreatment [IV, B].
- In case of an adnexal mass, ultrasound examination at 13-14 weeks' gestation is recommended to plan the appropriate management (surgery vs follow-up) [IV, B].
- In case of a suspicion of cervical cancer, transvaginal/transrectal ultrasound can be considered for staging in addition to MRI, but should only be performed by an expert [IV, B].
- The response to neoadjuvant chemotherapy in patients with cervical cancer during pregnancy can be evaluated with transvaginal/transrectal ultrasound by an expert or by MRI [IV, C].
- If indicated, whole body diffusion-weighted imaging/MRI or if unavailable, abdominal MRI with chest computed tomography (CT), is recommended as the primary imaging modality for staging pregnant patients with gynecological cancer. MRI should be used according to current clinical and safety guidelines for pregnancy [III, B].
- The use of gadolinium-based contrast agents during MRI examinations in pregnant women is not recommended as this can be obviated in most patients by the addition of a diffusion-weighted imaging sequence to the MRI examination [IV, D]. Iodinated contrast can be administered during a CT-examination when clinically relevant [IV, B].

- The use of a lead apron for abdominal shielding during ionizing imaging is not recommended due to the risk of internal scatter leading to increased fetal exposure [III, D].
- In certain scenarios, low-dose positron emission tomography-CT might be considered when it might change the management [IV, C].

Pathology

- The pregnant status and all other relevant clinical information should be recorded on the pathology request form by the clinician [V, A].
- Many of the gynecological tumors detected during pregnancy are uncommon and their morphological appearances may be modified by pregnancy; therefore, referral for a specialist pathology opinion should be considered [V, B].
- Certain rare non-neoplastic ("pseudoneoplastic") ovarian lesions occurring during pregnancy or postpartum may mimic neoplasms, especially sex cord-stromal tumors and, given the rarity of some of these and the possibility of misdiagnosis as malignant, referral for a specialist opinion should be considered [V, A].
- In the case of a gynecological malignancy discovered during pregnancy, the placenta should be submitted for pathological examination following delivery, including both gross and microscopic examination [IV, B].

Surgery

Anesthesia

- Locoregional anesthesia is preferred over general anesthesia during pregnancy when feasible [IV, B].
- If general anesthesia is required, surgery should not be postponed as it is safe in all trimesters [IV, B].
- To avoid vena cava compression, a left lateral tilt (of at least 15 degrees) is recommended after 20 weeks gestation (16 weeks for twin pregnancies) [IV, B].

Surgical Procedures

- If a surgical procedure cannot be postponed until after pregnancy, it should be performed during pregnancy, accepting a slightly increased risk of complications/miscarriage [V, B].
- Manipulation and trauma to the uterus should be avoided, especially during minimally invasive surgery [V, B].
- Small conization for suspected microscopic invasive cancer in pregnancy should be performed in the first or early second trimester [IV, B].
- Simple trachelectomy/large cone for IB1 cervical cancer could be performed in pregnancy only in highly selected cases [V, C].
- Abdominal trachelectomy is not recommended during pregnancy [V, D].
- Lymph node staging should be performed if technically feasible as in non-pregnant patients [IV, B].
- Given the lack of evidence, sentinel lymph node mapping using indocyanine should not be routinely performed but could be considered in cervical/vulvar cancer within a prospective clinical trial [V, C].
- A planned radical hysterectomy immediately following cesarean delivery is recommended as it will not lead to increased morbidity in experienced centers [IV, B].
- For patients with operable cervical cancer and a non-pregnancy preserving intention, the following procedures are recommended after discussion with the patient [V, B]:
  - First trimester: radical hysterectomy with the embryo in the uterus
  - Second trimester: radical hysterectomy after abdominal evacuation of the fetus
- Radical local excision for vulvar cancer in pregnancy should be performed without delay with the aim for free surgical margins [V, B].
- Pregnancy preserving staging surgery for ovarian cancer could be considered in the first or early second trimester [V, C].
- Cytoreductive surgery for advanced ovarian cancer is not recommended during pregnancy [V, D].

Minimally Invasive Approach

- Minimally invasive procedures are preferred over laparotomic procedures during pregnancy when indicated and feasible [IV, B].
- Open introduction and if necessary adapted placement of trocars to avoid perforation of the uterus is recommended [IV, B].
- Given the lack of evidence regarding the maximum safe duration of minimally invasive procedures in pregnancy and the known physiological consequences of high intra-abdominal pressure, procedures should be limited in both time and pressure [V, B].

Fetal Monitoring

- It is recommended to monitor the fetus preoperatively and postoperatively [IV, B].
- Fetal monitoring intraoperatively can be considered if active management of the newborn is the aim in case of fetal distress [IV, C].

Analgesia

- Pregnant patients should be treated with adequate analgesia postoperatively, particularly to avoid preterm contractions [IV, A]. Best available options include [IV, B]:
  - Continuous epidural analgesia.
  - Acetaminophen (preferred throughout all stages of pregnancy).
  - Opioids (throughout all stages of pregnancy).

Medical Oncology

- Before each cycle of chemotherapy during pregnancy, assessment by an obstetrician should be performed to assess maternal and fetal health, and the risk of premature labor [V, A].
- The choice of chemotherapy regimen when indicated should, like in non-pregnant patients, be based on cancer (sub)type and stage [III, B]:
  - Ovarian epithelial cancer: paclitaxel/carboplatin every 3 weeks.
  - Ovarian non-epithelial cancer: bleomycin/etoposide/cisplatin or etoposide/cisplatin or paclitaxel/carboplatin every 3 weeks.
  - Cervical cancer: paclitaxel/carboplatin in weekly regimen or every 3 weeks.
- Adaptations to standard treatment can be considered with regard to:
  - Expected fetotoxic effects [IV, B]:
    - All chemotherapeutic agents are expected to reach the fetal compartment to some extent depending on their pharmacokinetic characteristics.
    - Platinum-based chemotherapy, especially cisplatin, carries a risk for ototoxicity in the newborn, therefore carboplatin is preferred for gynecological malignancies except in germ cell cancers, where a cisplatin-based regimen is more effective.
  - Timing of chemotherapy [IV, D]:
    - Chemotherapy is not recommended before the 12th week of gestation.
    - Three-weekly chemotherapy should not be given after 35 weeks of gestation (to avoid hematopoietic suppression/neonatal chemotherapy toxicity).
    - Weekly chemotherapy should not be given after 36 weeks of gestation.
  - Chemotherapy dosing should be identical to non-pregnant women and based on actual maternal weight [V, A].

- If oncologists have concerns that a particular regimen or interval timing of chemotherapy during pregnancy may increase the risk of neutropenia, granulocyte colony-stimulating factors can be considered [IV, B].
- Standard clinical investigations for assessment of the patient before and during systemic anticancer therapy must be performed for example [IV, B]:
  - Maternal echocardiogram in case of exposure to anthracyclines.
  - Pulmonary function testing in case of exposure to bleomycin.
  - Bone marrow function.
- Consider red blood cell transfusion when hemoglobin (Hb) is <8.0 g/dL (when Hb is <9.0 g/dL consider intravenous iron and erythropoietin) [IV, B].
- For the prevention of chemotherapy induced nausea, ondansetron and metoclopramide can be used [IV, B].
- When corticosteroids are indicated, methylprednisolone and prednisolone should be used instead of dexamethasone [IV, B].
- Port-a-cath placement should be preferred over peripherally inserted central catheters for chemotherapy administration because of increased risk of thrombosis [IV, B].

Obstetrics

Thromboprophylaxis During and After Pregnancy

- During pregnancy, it is advisable to use [IV, C]:
  - Compression stockings/intermittent pneumatic compression devices during surgery.
  - Prophylactic dose low-molecular-weight heparin (LMWH) at least 10 days after uncomplicated curative surgery during pregnancy.
  - Prophylactic dose LMWH as long as there is pelvic tumor load with an inflammatory reaction (like on chemotherapy), or compression on blood vessels, or an additional thrombosis risk factor (see Table 1 [6]).
- Cancer is an indication for postpartum LMWH prophylaxis for at least 10 days. With an additional risk factor (see Table 1 [6]) prophylactic use of LMWH till 6 weeks postpartum is advised [IV, C].

Obstetric Operative Care

- If the ovary containing the corpus luteum gravidarum has been removed prior to 10-12 weeks of gestation, supplementation with exogenous progesterone should be initiated [IV, A].
- When uterine manipulations are expected during surgery beyond the 22nd week of gestation, prophylactic use of tocolytic agents may be considered [IV, C].

Pregnancy: Evaluation, Treatment and Fetal Follow-Up

- After a cancer diagnosis early in pregnancy or an inadvertent pregnancy during cancer treatment, fetal ultrasound should be performed for accurate pregnancy dating [IV, A].
- Treatment options, their impact on the pregnancy and the maternal prognosis should be discussed with the patient (depending on local legislation, including the option of termination of pregnancy) [IV, A].
- Non-invasive prenatal screening (NIPS) can be used; however, cell-free tumor DNA might interfere with the interpretation of NIPS [IV, B].
- Before the onset of treatment, a fetal anatomy scan should be performed to identify fetal or placental abnormalities [IV, A].
- Serial ultrasounds for fetal growth are recommended in patients undergoing cancer treatment, including surgery ± chemotherapy [IV, B].
- After cervical surgery or right before each cycle of chemotherapy, assessment of cervical competence (or length) is advised, or signs of preterm labor should be investigated [IV, B].
- Vaginal progesterone and cerclage should be used according to standard obstetric recommendations [IV, B].

Table 1 Most Common Additional Risk Factors for Thrombosis Apart From Gynecological Cancer[6].

Type	Description
High risk factors	Dehydration (! Chemo-related nausea and vomiting) Surgical procedure Previous VTE Medical co-morbidities (eg nephropathic syndrome, type 1 diabetes with nephropathy, heart failure, systemic inflammatory processes, cancer)
Risk factors	Age > 35 y Obesity (BMI≥30) Parity ≥3 ART/IVF Smoking Gross varicose veins Immobility / hospitalization Systemic infection Thrombophilia (no VTE) Blood transfusion
Obstetric risk factors	Preeclampsia Multiple pregnancy C-section Preterm birth Prolonged labor (>24 h) PPH > 1 L

Abbreviations: ART, assisted reproductive technology; BMI, body mass index; IVF, *in vitro* fertilization; PPH, primary postpartum hemorrhage; VTE, venous thromboembolism.

- Fetal anemia should be monitored using middle cerebral artery peak systolic velocity doppler when giving high-risk hematotoxic agents such as carboplatin, ifosfamide [IV, B]. In case of anemia (multiples of the median (MOM) >1.5) delay/stop of chemotherapy, reduction of dosage, change of chemotherapy regimen or even blood transfusion should be considered [IV, B].

Delivery

- Iatrogenic preterm birth (<37 weeks) should be avoided as it is associated with greater odds of serious neonatal complications. The decision to induce a preterm delivery needs to be balanced with maternal treatment options and should be discussed within a multidisciplinary team including a neonatologist [IV, A].
- Timing of delivery: If the patient is receiving chemotherapy, delivery ideally is timed at least 2 weeks following the last course of weekly chemotherapy and at least 3 weeks following the last course of a 3-weekly chemotherapy to avoid potential maternal infection/sepsis due to neutropenia, and potential fetal myelosuppression at the time of delivery [IV, B].
- If cancer is diagnosed in the third trimester and only 1 cycle of chemotherapy is possible before delivery, patients should be counseled on the fetal risks of late preterm birth versus the maternal/fetal impact of a single cycle of chemotherapy during pregnancy [IV, B].
- If preterm delivery is expected, corticosteroids for fetal lung maturation and magnesium sulfate for neuroprotection should be considered in accordance with standard obstetric recommendations [IV, A].
- Mode of delivery:
  - Cesarean delivery is recommended in cases of [IV, B]:
    - Vulvo-vaginal cancer after major surgery or with cancer still present/*in situ.*

    - Invasive cervical cancer, in which case it is important to avoid a lower uterine surgical incision or laceration toward the tumor. A corporeal/classical incision is preferred, especially for large tumors.
  - A vaginal delivery can be considered in cases of [IV, C]:
    - Previous complete removal of cervical cancer by conization.
    - Small completely removed vulvar cancer.
    - Tubo-ovarian malignant neoplasm.

Postpartum and Newborn Care

- The child exposed to cancer treatment *in utero* needs to be examined thoroughly by a neonatologist [IV, A].
- Newborns exposed to chemotherapy *in utero* must be screened for transient neonatal myelosuppression, especially in cases of a short interval between the last course of chemotherapy and birth [IV, A].
- If cardiotoxic treatment was administered during pregnancy, an echocardiogram can be considered [IV, B].
- After platinum exposure, hearing function should be screened at birth with auditory brainstem response testing [IV, A].
- Breastfeeding should be avoided when systemic anticancer therapy is required postpartum [IV, A].
- Systemic anticancer therapy can be (re)started within the first days after uncomplicated vaginal delivery and after 1 week following cesarean delivery [V, C].
- A discussion regarding contraception is recommended at the postpartum visit for fertile patients requiring ongoing cancer treatment [V, A].
- Before considering a subsequent pregnancy, an oncologic assessment to exclude recurrence or treatment related toxicities are recommended [V, A].

Radiation Therapy

- Radiation-related fetal risks based on calculation of estimated fetal radiation dose by a medical/clinical physicist should be included in the benefit-risk assessment of radiation therapy during pregnancy [IV, A].
- When preservation of the pregnancy is the aim, pelvic and groin radiation therapy is contraindicated [IV, B].
- Depending on the indication, gestational age and tumor type, a limited delay of radiation therapy should be considered if it allows for standard treatment (see Table 2 [7-10] (indications per tumor type)) [IV, B].
- In case of advanced cervical cancer and a non-pregnancy preserving intention, the following options should be discussed with the patient depending on local legislation [IV, B]:
  - First trimester: radiation therapy without evacuation ± feticide
  - Second trimester: radiation therapy after abdominal evacuation or radiation therapy with fetus in the uterus with or without feticide
- For metastatic disease, radiation therapy using techniques that minimize fetal exposure could be considered for palliation [IV, B].

Table 2 Time to Radiation Therapy Based on Indication and Tumor Type.

Tumor type/indication during pregnancy	Recommendations regarding radiation therapy	Impact of delay (eg, due to pregnancy)
General gynecological cancers	Preferred to delay radiation until after delivery; if not possible, limited local surgery or systemic therapy considered to postpone RT	Postponement risks progression; pregnancy termination may be advised if treatment cannot be delayed
Vulvar Cancer (node-positive SCC)	Initiate as soon as possible after surgery; optimal overall treatment time including surgery and RT ~104 days	Increased risk of death by 0.4% per additional day delay; postoperative RT should be completed within 105 days post-surgery
Cervical cancer - Primary CTRT	Mean time from diagnosis to (CT)RT ~7.7 weeks; waiting up to 12 weeks does not negatively impact survival	Delay up to 12 weeks may be acceptable without survival impact; OTT should ideally be <56 days (EMBRACE)[7]
	Induction chemotherapy (6x weekly carboplatin + paclitaxel) can be administered before definitive (CT)RT.	Based on INTERLACE trial, induction chemotherapy shows 9% and 8% improvement in 5-y progression-free survival and overall survival, so the use of induction chemotherapy can give 7 weeks of delay and for aiming a reduction of prematurity.[8]
Cervical cancer - Postoperative RT	Should begin promptly after surgery	Delays associated with increased mortality risk; ESGO/ESTRO recommends "time diagnosis to RT <6w" and "OTT <50d" as quality indicators[9]
Proton RT	Increasingly used based on tumor- and patient-specific factors as over 10-fold reduction in fetal exposure compared with photon-based RT can be obtained (pencil beam scanning-technique)	-
Palliative RT (pain, bleeding, metastases)	Generally, a single dose of 8 Gy standard; brain metastases may require 20 Gy in 5 fractions	In pregnancy, lower prescribed dose should be considered to reduce fetal exposure (eg, down to 4 Gy for bone metastases)

Abbreviations: CTRT, chemoradiation therapy; ESGO, European Society of Gynecological Oncology; ESTRO, European Society for Radiotherapy and Oncology; OTT, overall treatment time; RT, radiation therapy; SCC, squamous cell carcinoma.

Additional considerations:

- RetroEMBRACE study indicates a 0.5% to 1% increase in local control per day that the OTT is shortened.
- ESGO Guidelines for vulvar cancer recommend completing RT within 8 weeks for optimal outcomes.[10]

Psychology

- Oncopsychologists should be included in the multidisciplinary team of caregivers for pregnant cancer patients [IV, B].
- Psychological assessment and regular screening should be offered to these patients and their family during also beyond pregnancy using validated screening tools [IV, B].
- Psychological support should be offered at every stage of the treatment process during and beyond pregnancy, not only for the patient but also for their partners, family and other supportive persons using evidence-based therapies [IV, B].

Patient Perspectives

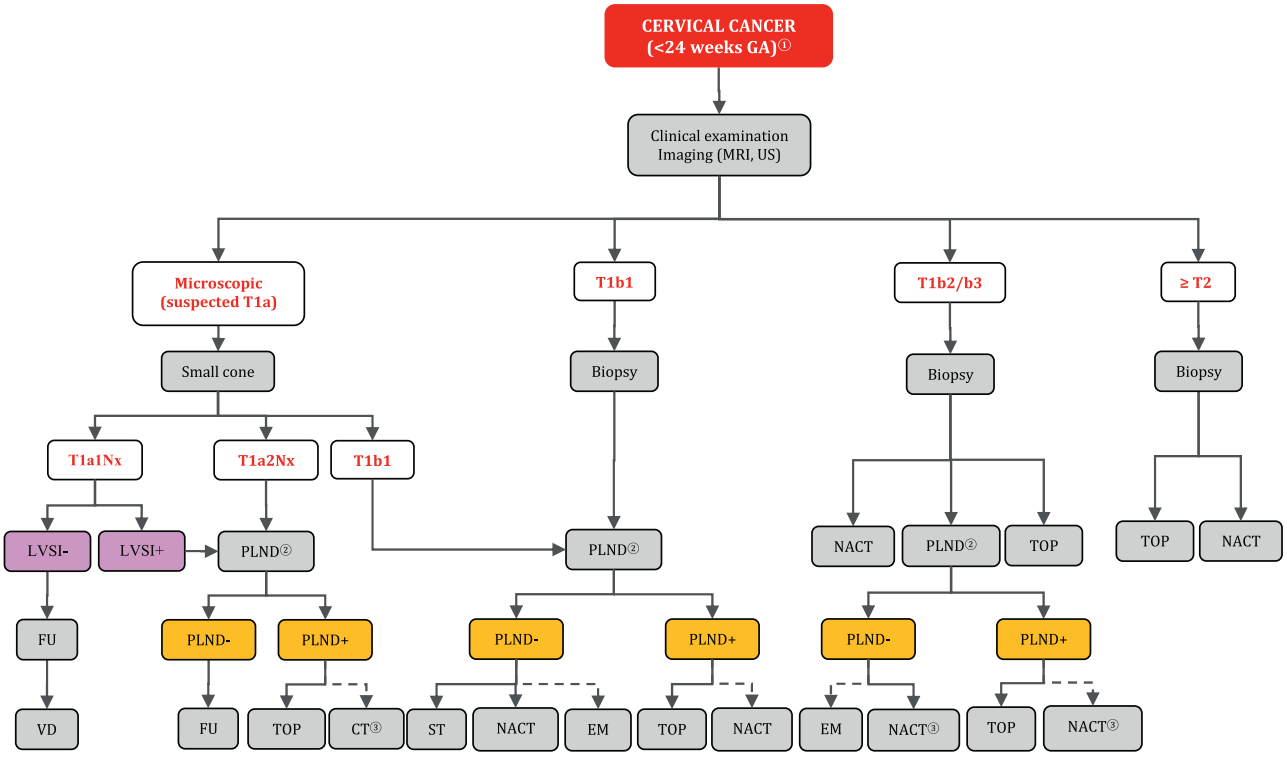
- Patients and their partners should be informed, involved, and supported to make a shared decision regarding treatment and supportive care [V, A].
- Patients should be offered the possibility to receive peer support via available patient organizations [V, A].
- Rehabilitation programs should be offered to pregnant patients, similar to non-pregnant patients (as outpatient programs) [IV, B].
- Patients should be given the possibility to receive proper individualized support after treatment tailored to potential treatment side-effects (including lymphoedema), as well as guidance on sexuality, financial concerns, spirituality, nutrition, and returning to work [V, A].
- It is recommended to increase awareness to promote early diagnosis of cancer in pregnancy among patients and physicians [V, A].

Pediatric Follow-Up

- Long-term toxicity monitoring programs are recommended for children exposed to cancer treatment *in utero* based on the specific treatment and its associated risks:
  - Hearing function should be monitored during childhood in children prenatally exposed to platinum-based chemotherapy (especially cisplatin) [IV, B].
  - Children exposed to anthracyclines *in utero* may be monitored for cardiotoxicity [IV, C].
  - Clinical pediatric and neurodevelopmental vigilance is recommended for potential long-term toxicities (including secondary malignancies, fertility disorders, and other late effects due to the lack of long-term follow-up data) [IV, B].

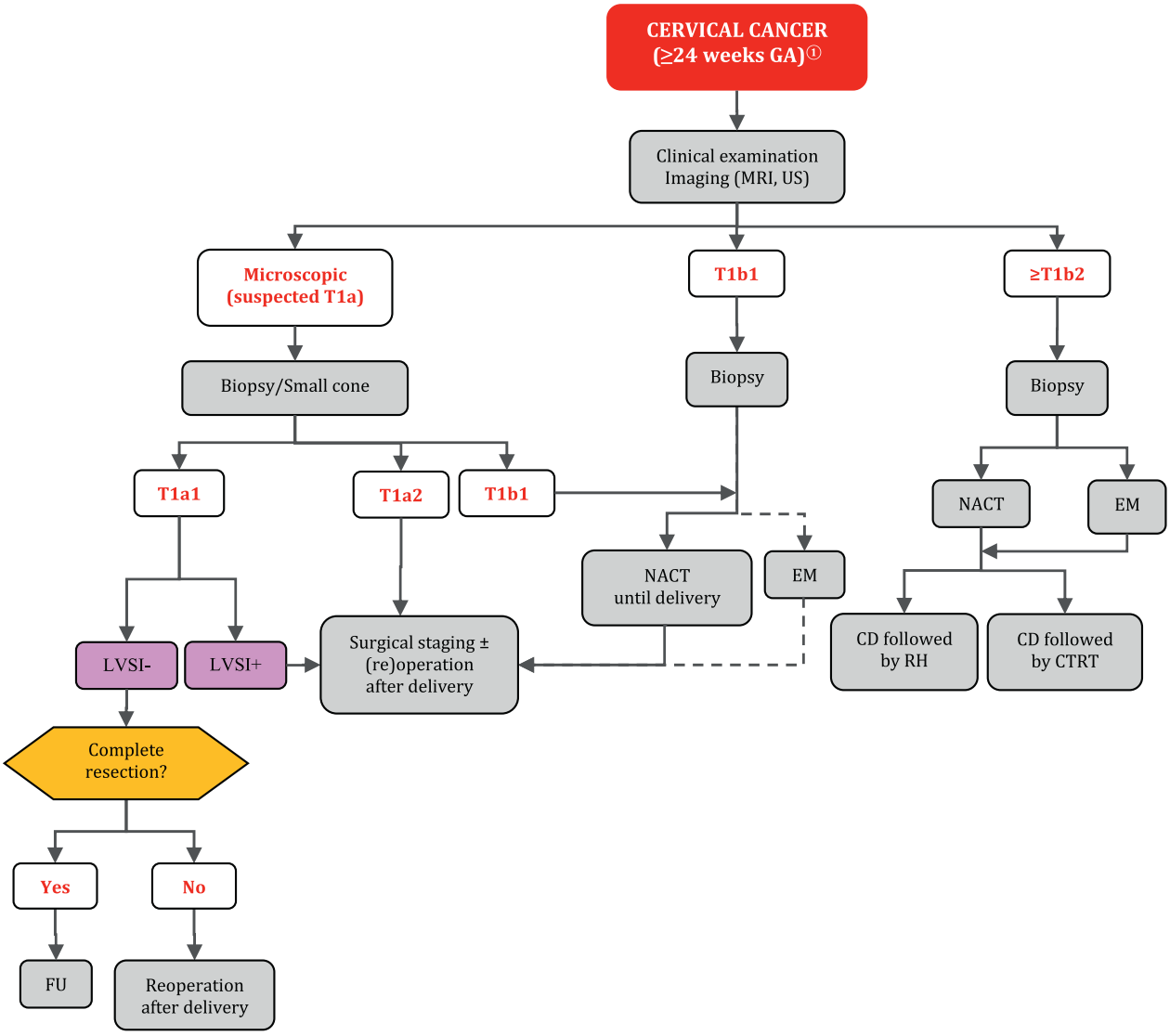
ALGORITHMS

Cervical Cancer (< 24 Weeks Gestational Age)



①the cut off of 24 weeks is related to feasibility of pelvic lymphadenectomy; ②sentinel lymph node mapping using indocyanine should not be routinely performed but could be considered within a prospective clinical trial; ③experimental option.
CT, chemotherapy; EM, expectant management; FU, follow-up; GA, gestational age; LVSI, lymphovascular space invasion; MRI, magnetic resonance imaging; NACT, neoadjuvant chemotherapy; PLND, pelvic lymph node dissection; ST, simple trachelectomy; TOP, termination of pregnancy; US, ultrasound; VD, vaginal delivery.

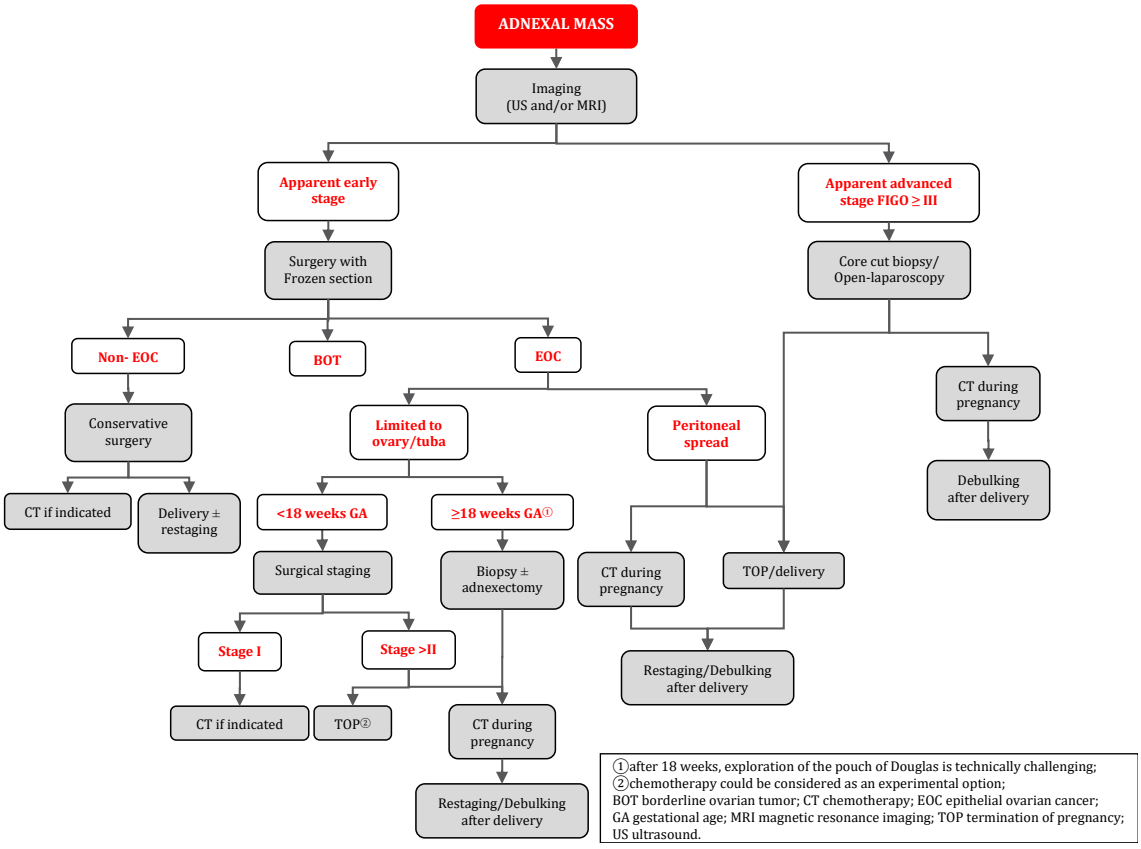
Cervical Cancer (≥24 Weeks Gestational Age)



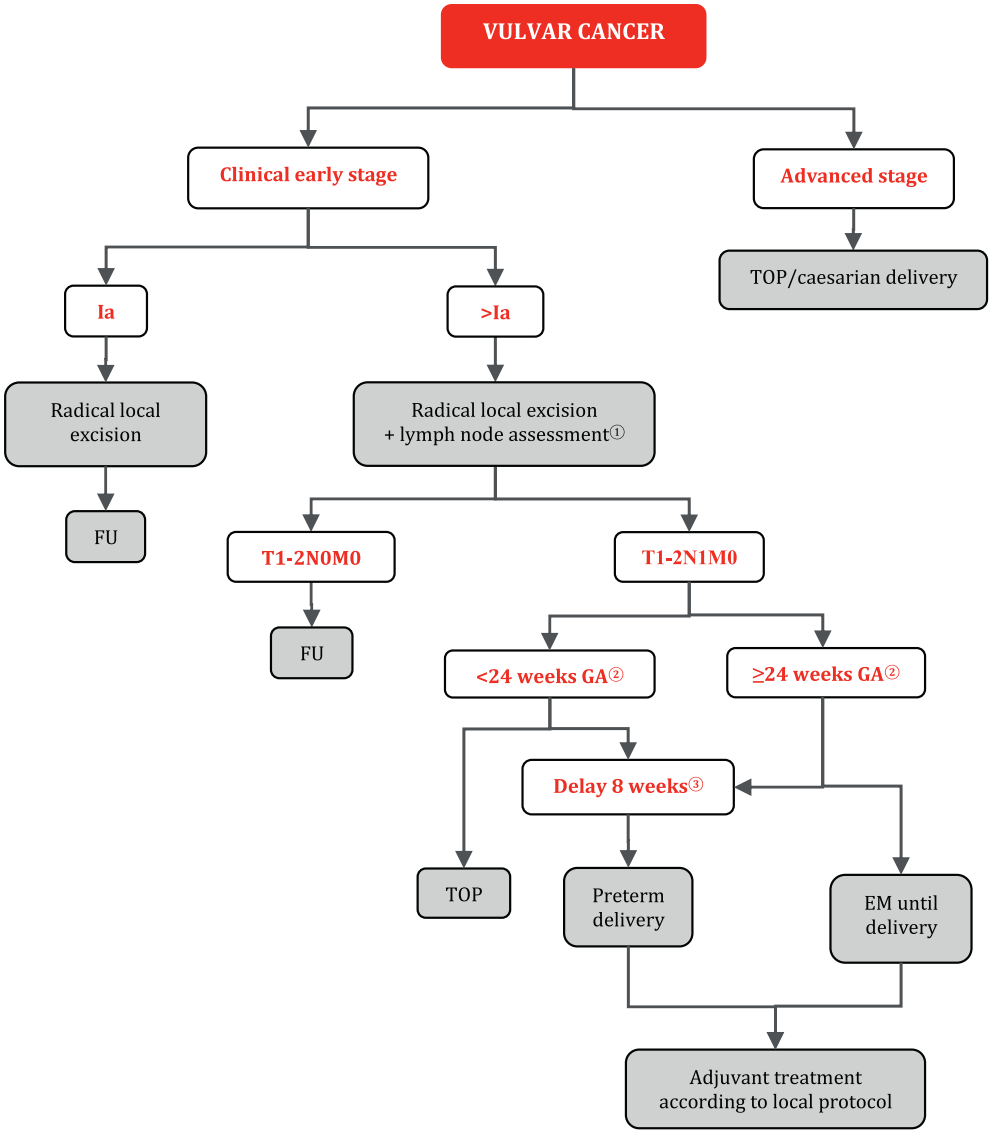
①the cut off of 24 weeks is related to feasibility of pelvic lymphadenectomy.

CD, caesarean delivery; CTRT, chemoradiotherapy; EM, expectant management; FU, follow-up; GA, gestational age; LVSI, lymphovascular space invasion; MRI, magnetic resonance imaging; NACT, neoadjuvant chemotherapy; PLND, pelvic lymph node dissection; RH, radical hysterectomy; US, ultrasound.

Ovarian Cancer



Vulvar Cancer



①sentinel lymph node mapping using indocyanine should not be routinely performed but could be considered within a prospective clinical trial; ②this cut-off is based on foetal viability; ③8 weeks of delay is considered safe to postpone postoperative radiotherapy.

EM, expectant management; FU, follow-up; GA, gestational age; TOP, termination of pregnancy.

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