SYNOPSIS EndoQol

N° ID-RCB: 2017-A02809-44

Version n°2.1 du 22/06/2018

1 STUDY SUMMARY

TITLE	**Impact of adjuvant chemotherapy on the quality of life of patients treated for stage II/III endometrial cancer**
ACRONYM	**EndoQoL**
Coordonnator	**Dr Emeline MERIAUX**
Indication	Endometrial cancer / Quality of life study
Methodology	Multicenter case-control study comparing the impact on quality of life of treatment with or without adjuvant chemotherapy for FIGO stage II/III endometrial cancer
Rationale	Endometrial cancer is the fourth most common cancer among women in developed countries. It is often diagnosed at a localized stage (67% of cases), which means it has a relatively good prognosis, with an 81.7% five-year survival rate across all stages. Treatment at the localized stage is based on surgery and radiotherapy. Adjuvant chemotherapy may be offered in addition to radiotherapy, but its role is still under debate. It is typically delivered sequentially before or after radiotherapy, as concomitant chemoradiotherapy is not standard practice. It is generally recommended in stage III cases, and for earlier stages, its use depends on various prognostic factors (histological type, grade, emboli) and the feasibility of treatment (age, general health, comorbidities). This is because patients treated for endometrial cancer are elderly (median age 63) and in most cases have comorbidities (diabetes, obesity, and hypertension). Chemotherapy can cause side effects that can persist and potentially alter the quality of life of these often fragile patients. While the impact of surgery and radiotherapy on quality of life has been well studied, there is insufficient data in the literature concerning adjuvant chemotherapy. It is based on retrospective studies with small sample sizes or longitudinal studies that did not assess the specific impact of sequential adjuvant chemotherapy on patients' quality of life after treatment. In addition, the chemotherapy protocols used include platinum salts and taxanes, which can cause neurological sequelae in these often elderly and at-risk patients. We propose to conduct a case-control study that will assess the quality of life and late sequelae of patients treated for locally advanced endometrial cancer with sequential adjuvant chemotherapy before or after radiotherapy at a distance from their treatment, comparing their results to a group of patients who were treated with postoperative radiotherapy alone.
Objectives	**Main objective** To evaluate the impact of adjuvant chemotherapy on overall quality of life in patients with

	locally advanced endometrial cancer at a distance from their treatment **Secondary objectives** - Assess long-term symptoms reported by patients that may be related to adjuvant chemotherapy, particularly chemotherapy-induced neurotoxicity - Assess the various areas of quality of life affected in the long term by chemotherapy - To evaluate the impact of adjuvant chemotherapy on physical activity, anxiety, and depression - To evaluate the correlation between immediate toxicity of adjuvant chemotherapy and quality of life at a distance from treatment - To evaluate the correlation between comorbidities and quality of life at a distance from treatment
Inclusion criteria	**For all patients (cases and controls)** - Women over the age of 18 with histologically confirmed type 1 or type 2 endometrial adenocarcinoma, with postoperative FIGO stage II or III, who underwent surgery between 2011 and 2015, with at least 2 years since their last chemotherapy treatment; - Recommended surgery: hysterectomy and bilateral salpingo-oophorectomy, surgical lymph node staging not mandatory; - Pelvic radiotherapy ± lumbosacral irradiation, optional brachytherapy; - No recurrence of endometrial cancer at inclusion; - No history of progressive neurological disease (multiple sclerosis, neurodegenerative disease, etc.); - No history of progressive psychiatric disorders (i.e., hospitalization for psychiatric reasons, bipolar disorder, schizophrenia, personality disorders, etc.); - No objection to data collection; - Patient deemed capable of completing a written questionnaire. **For case patients** - Chemotherapy after surgery, which may be performed before or after radiotherapy
Exclusion criteria	**<u>For all patients (cases and controls)</u>** - Sarcoma or carcinosarcoma; - FIGO stage I or IV; - Macroscopic tumor residue after surgery; - Recurrence of endometrial cancer or diagnosis of any other cancerous pathology after diagnosis of endometrial cancer (except for completely excised non-melanocytic skin tumors) within 5 years; - Drug use; - Alcohol abuse. **<u>For case patients</u>** - Chemotherapy before surgery; - Chemotherapy concomitant with radiotherapy **<u>For control patients</u>** - Chemotherapy either before or after surgery
Description of the protocol/experimental design	This is a case-control study conducted as follows: 1. Identification of patients (cases and controls) meeting the inclusion criteria. 2. Contacting patients via their referring oncologist to provide information about the study and their right to refuse to participate. Patients will be informed either during a follow-up consultation or during a telephone interview. 3. Transmission of the study information form and the right to refuse, and self-administered questionnaires with a pre-stamped envelope to return them once completed, either during a consultation with the referring physician or by post.

	4. Follow-up phone call one month after sending these documents, if no objection or completed questionnaires have been received, with the option of resending the documents. 5. For patients (cases and controls) who have not raised any objections and have returned the completed questionnaires, retrospective collection of clinical data at each stage of the treatment sequence (preoperative, postoperative, pre-radiotherapy, post-radiotherapy ± chemotherapy) and during follow-up consultations (3 months, 6 months, 12 months, and 24 months, and annually depending on the time since the end of treatment) from the patients' medical records. The following will be collected: medical history (surgical and histological data, treatments administered, laboratory tests), medical history, tolerance data, adverse events occurring during or following treatment. Each patient will be identified by a 3-digit inclusion number, her initials, and her month and year of birth. The duration of each patient's participation, corresponding to the time needed to complete all the questionnaires, is estimated at approximately 1 hour.
Judgment criteria	**Primary endpoint:** Overall quality of life score from the QLQ-C30 self-administered questionnaire completed remotely after treatment (at least one year after the end of treatment) in patients with locally advanced endometrial cancer **Secondary criteria:** At least 2 years after the end of treatment: • Functional quality of life scores (physical, functional, social, emotional, and cognitive domains) according to the QLQ-C30 • Late symptoms potentially related to adjuvant chemotherapy reported by patients: • Based on symptoms assessed in the QLQ-C30 core questionnaire and its EN24 module specific to endometrial cancer • Chemotherapy-induced neurotoxicity assessed using a specific CIPN20 questionnaire. • Physical activity score according to the IPAQ questionnaire, anxiety/depression score according to the HADS scale • Type and grade of toxicities occurring during and in the month following the end of chemotherapy according to CTCAE V4.0 criteria • Initial comorbidities (obesity, hypertension, diabetes, cardiovascular disease).
Sample size	Our main hypothesis is that patients treated with sequential adjuvant chemotherapy have a quality of life more than two years after the end of chemotherapy that remains lower than that of patients not treated with chemotherapy. In this population of patients with stage II/III endometrial cancer, chemotherapy treatment in addition to surgery and radiotherapy should concern less than half of the eligible active caseload. We have therefore decided to conduct this study with a ratio of 1 case to 2 controls. A minimum sample size of 39 patients (13 cases and 26 controls) would allow us to detect a 10-point difference in the overall quality of life domain (QLQ-C30) between patients who received chemotherapy and those who did not (ratio of 1 to 2) with a significance level of 5% and a power of 80% (t-test with standard deviation equal to 10). In order to anticipate any non-evaluable responses, we are increasing this sample size by 15% and plan to include at least 45 patients (15 cases who received chemotherapy and 30 controls who were treated with surgery and radiotherapy alone).

Expected benefits	This study will provide information on the experience and tolerance of sequential adjuvant chemotherapy in the long term in patients treated for locally advanced endometrial cancer. In the context of this disease, which has a relatively favorable prognosis, it will assess whether patients with prolonged survival continue to experience side effects long after their treatment and whether these effects can be specifically linked to adjuvant chemotherapy, particularly neurotoxicity. It will be possible to detail which aspects of their daily lives are impacted: anxiety, depression, physical activity, pain, social, emotional, and cognitive aspects. Finally, it will be possible to assess whether there is a correlation between the experience and immediate toxicity of adjuvant chemotherapy and quality of life long after the end of treatment.
Originality and innovative character	Current data in the literature do not allow for a specific assessment of the impact of sequential adjuvant chemotherapy on the quality of life of patients with locally advanced endometrial cancer, particularly in the long term. This will be the first study to provide this information for sequential chemotherapy.
Elements justifying the feasibility of the project	Recruitment capacity: with at least 80 eligible patients already identified at the Caen and Rouen Cancer Centers, it seems feasible to reach a total of 15 patients treated with chemotherapy and 30 patients treated with surgery and radiotherapy alone over a 12-month period. Estimated recruitment period: 1 year. Duration of participation for each patient: time required to complete the study questionnaires, estimated at 1 hour. Scientific competition: no competing studies currently underway. Support from a cooperative group: no. Planned support from an industry partner: no.
Participating centers	Names of centers with contact or investigator names: - Rouen: Dr. Leheurteur, Henri Becquerel Center - Caen: Prof. Joly, François Baclesse Center - Rennes: Dr. De La Motte Rouge, Eugène Marquis Center - Lille: Dr. Lesoin, Oscar Lambret Center - Villejuif: Dr. Pautier, Gustave Roussy Institute