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A prospective multicenter international single-arm observational study on the oncological safety of the sentinel lymph node algorithm in stage I intermediate-risk endometrial cancer (SELECT, SEntinel Lymph node Endometrial Cancer Trial)

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Abstract

Background: In the primary treatment of apparent uterine-confined endometrial carcinoma, pelvic $\pm$ para-aortic lymphadenectomy has been considered the standard of care. Although some retrospective data suggest that the sentinel lymph node algorithm without complete lymphadenectomy can be used without jeopardizing oncologic outcome, prospective data are lacking.

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Conflict of Interest Statement: None declared.

Primary Objectives: To assess the 36-month incidence of pelvic/non-vaginal recurrence in women with pathologically confirmed stage I intermediate-risk endometrioid endometrial carcinoma who have bilateral negative pelvic sentinel lymph nodes.

Study Hypothesis: We hypothesize that patients with stage I, intermediate-risk endometrioid endometrial carcinoma who have bilateral negative pelvic sentinel lymph nodes will demonstrate a pelvic/non-vaginal recurrence rate comparable to historical estimate of stage I, intermediate-risk endometrioid endometrial carcinoma patients (estimated 2.5%).

Trial Design: This prospective multicenter single-arm observational study will comprise two parts. Patients will be enrolled in Part 1 at the time of surgical planning and will undergo physical examination and imaging to determine study eligibility. Eligible patients will then undergo primary surgical treatment with a cervical injection of indocyanine green dye for sentinel lymph node mapping, total hysterectomy, removal of the adnexa and staging with sentinel node mapping and pelvic washings. The final assessment for inclusion in Part 2 of the study will be determined by results of the final pathology report and recommended adjuvant treatment. Observation or vaginal brachytherapy are suggested for patients recruited onto Part 2. Patients enrolled in Part 2 will be followed for 36 months.

Major Inclusion/Exclusion Criteria: Part 1: Patients with grade 1, 2, or 3 endometrioid endometrial carcinoma, apparent uterine-confined by physical examination and imaging, who are suitable candidates for surgery, are eligible. Part 2: Patients will be enrolled in the Study Cohort if all the following criteria are met: i) at time of surgery: hysterectomy with bilateral adnexectomy, and bilateral pelvic sentinel lymph node mapping; ii) on final pathology: pathologic stage I, intermediate-risk endometrioid endometrial carcinoma (grade 1 or grade 2 with $\geq 50\%$ myometrial invasion, or grade 3 with $<50\%$ myometrial invasion), negative pelvic peritoneal cytology and bilateral sentinel lymph nodes negative for malignancy; iii) recommended adjuvant treatment: vaginal brachytherapy or no adjuvant treatment.

Primary Endpoint: Incidence of pelvic/non-vaginal recurrence at 36 months.

Sample Size: 182 patients for study cohort (Part 2) – 1715 patients will be screened in Part 1

Estimated Dates for Completing Accrual and Presenting Results: Accrual will be completed by 36 months. Follow-up will continue for 36 months after enrollment of the last patient.

Trial Registration: [NCT04291612](https://clinicaltrials.gov/ct2/show/study/NCT04291612)

Keywords

endometrial cancer; sentinel lymph node; lymphadenectomy; recurrence; surgical procedures

INTRODUCTION

Endometrial cancer is the most common malignancy of the female genital tract in Western countries. It has a relatively good prognosis; however, its mortality rate has been increasing during the last three decades.[1] While the majority of new cases present with uterine-confined disease, about 25% demonstrate extra-uterine metastases on surgical staging; 10–15% have lymph node metastases.[2] Primary treatment of apparent uterine-confined disease

consists of total hysterectomy $\pm$ bilateral salpingo-oophorectomy and lymph node assessment. Pelvic $\pm$ para-aortic lymphadenectomy has traditionally been the standard of care for evaluating lymph node status. However, in previous trials, lymphadenectomy versus no lymphadenectomy failed to show a survival advantage and increased perioperative morbidity. [3–5] Thus, there has been significant controversy concerning the role of lymphadenectomy; recommendations range from systematic pelvic and para-aortic lymphadenectomy to no lymph node biopsy at all. Sentinel lymph node mapping occupies the middle ground between lymphadenectomy and no nodal staging, providing precise information on nodal status while minimizing surgical radicality.[6,7]

In different observational studies, sentinel lymph node mapping in endometrial cancer demonstrated a high rate of detection, high sensitivity, and high negative predictive value. [8,9] The impact of this technique on oncologic outcomes has been evaluated only in retrospective studies. Data suggest that the sentinel lymph node algorithm without complete lymphadenectomy can be used without jeopardizing oncologic outcomes.[10–12] Prospective data are lacking to date.

This prospective multicenter observational study aims to assess whether pelvic/non-vaginal recurrence rates are comparable to historical data in patients with sentinel lymph node-negative surgical stage I intermediate-risk endometrioid endometrial cancer. This trial will provide additional critical understanding regarding: (i) recurrence rates and patterns of recurrence in patients undergoing sentinel lymph node biopsy only according to the sentinel lymph node algorithm; (ii) impact of sentinel lymph node mapping on lower extremity lymphedema and quality of life.

If our study can provide evidence that the sentinel lymph node algorithm has a non-inferior oncologic outcome compared with historical rate of systematic pelvic $\pm$ para-aortic lymphadenectomy, staging with bilateral sentinel lymph node mapping will become a more widely accepted standard of care in node-negative intermediate-risk endometrial cancer. The results of our prospective multicenter observational study may promote a change in practice internationally, reducing postoperative morbidity in many patients.

METHODS

Trial Design

The SELECT trial is a prospective multicenter international observational study assessing the oncological safety of the sentinel lymph node algorithm in patients with stage I (as defined by International Federation of Gynecology and Obstetrics (FIGO staging criteria) [12]) intermediate-risk endometrioid endometrial carcinoma (Table 1). This study is led by Memorial Sloan Kettering Cancer Center. Approval for this trial was obtained by the Memorial Sloan Kettering Cancer Center Institutional Review Board. It is currently planned to open, with 6 participating centers and ultimately increase the number of centers to 12.

The study comprises two parts (Figure 1). Patients will be enrolled in Part 1 at time of surgical planning. Patients will undergo physical examination and imaging no more than 8 weeks before surgery. Pre-operative imaging is mandatory to ensure uterine-confined

disease. Patients with grade 1, 2 or 3 endometrioid histology, no evidence of extrauterine disease, suspicious pelvic lymph nodes, distant metastases, or cervical invasion on pre-operative imaging (pelvic +/- abdominal computerized tomography (CT) scan or magnetic resonance imaging (MRI) or sonogram, or body positron emission tomography (PET) scan) and physical examination (apparent uterine-confined endometrial cancer) can be enrolled. Enrolled patients will undergo injection of indocyanine green dye for sentinel lymph node mapping, total hysterectomy with bilateral salpingo-oophorectomy + sentinel lymph node biopsy + pelvic washings. The surgeon will perform cervical injection of tracer (indocyanine green dye only, diluted with sterile water to concentration of 1.25 mg/mL) at the 3 and 9 o'clock positions (strongly recommended) or into the four quadrants (optional) of the cervix. Superficial injection is mandatory; deep injection optional. A total volume of 4 mL is recommended. If pelvic and abdominal cancer spread and grossly involved lymph nodes are excluded, the patient will undergo excision of all mapped and enlarged sentinel lymph nodes. If no sentinel lymph nodes are detected on the hemi-pelvis, side-specific lymphadenectomy is recommended as per the sentinel lymph node algorithm.[7] All sentinel lymph nodes will be processed by pathologists and undergo ultra-staging. Final assessment for inclusion in the follow-up part of the study (Part 2) will be determined from results of final pathology report and recommended adjuvant treatment. All Part 1 participants undergoing total hysterectomy with bilateral salpingo-oophorectomy and bilateral pelvic sentinel lymph node mapping (negative for malignancy) with final postoperative pathology confirming stage I, intermediate-risk endometrioid endometrial carcinoma (Table 1) and negative pelvic peritoneal cytology, who receive standard-of-care adjuvant treatment (vaginal brachytherapy or no adjuvant treatment) will be enrolled in the study cohort (Part 2). Any patient receiving external beam radiation therapy or chemotherapy will be taken off study. Patients in Part 2 will form the group for analysis of the primary study endpoint. Patients in Part 2 will be monitored for non-vaginal recurrence for 36 months (clinic visits at 2–6 weeks post-surgery, and 6 ($\pm$ 2), 12 ($\pm$ 2), 18 ($\pm$ 2), 24 ($\pm$ 2), 30 ($\pm$ 2), 36 ($\pm$ 2) months)). Lymphedema and quality of life will be evaluated. (Figure 1)

Participants

Inclusion and exclusion criteria are listed in Box 1 and Box 2 for Part 1 and Part 2 of the study, respectively. A patient may be enrolled in Part 1 if: i) pre-operative histologic diagnosis is grade 1, 2 or 3 endometrioid adenocarcinoma; ii) tumor is uterine-confined on physical examination and imaging; iii) patient is suitable for surgery and planned surgical treatment is hysterectomy with bilateral salpingo-oophorectomy and sentinel lymph node biopsy. A participant in Part 1 may be enrolled in Part 2 and assigned to the study cohort if: i) she undergoes hysterectomy with bilateral salpingo-oophorectomy and bilateral pelvic sentinel lymph node mapping (bilateral sentinel nodes negative for malignancy); ii) final pathology reveals stage I intermediate-risk endometrioid endometrial cancer (Table 1) with negative pelvic peritoneal cytology; iii) recommended adjuvant treatment is vaginal brachytherapy only, or no adjuvant treatment.

Primary Endpoints

Primary and secondary objectives are listed in Box 3. The primary endpoint is cumulative incidence of pelvic/non-vaginal recurrence in Part 2 patients only, defined as time from

surgery to biopsy-proven or radiographic evidence of pelvic/non-vaginal recurrence. Pelvic/non-vaginal recurrence is defined as recurrence in the central pelvic area, pelvic sidewall area below L5, peritoneal pelvic area, or retroperitoneal pelvic area. This will be assessed every 6 (± 2) months for 36 months by routine physical examination and review of symptoms. Imaging is indicated only to evaluate new symptoms or abnormalities detected on examination. Biopsy of recurrence is recommended (not mandatory).

Secondary endpoints are: i) incidence of lower extremity lymphedema, based on objective measurements and self-reported symptoms using a validated questionnaire, restricted to Part 2 patients without documented history of lower extremity lymphedema before sentinel lymph node biopsy; ii) quality of life, assessed using the European Organisation for Research and Treatment of Cancer Quality of Life of Cancer Patients questionnaire (EORTC QLQ-C30), a validated self-reported instrument (Part 2 patients only); iii) 30-day post-surgical morbidity data (Part 2 patients only); iv) point estimates of the rate of the sentinel lymph node procedure in identifying for all Part 1 patients: 1) at least one sentinel lymph node per patient; 2) bilateral pelvic sentinel lymph nodes per patient; 3) empty sentinel nodal packets per specimen. A node identified by the surgeon as a sentinel lymph node will be considered successfully identified if, on pathologic review, it is determined to *not* be an empty packet.

Sample Size

The pelvic/non-vaginal recurrence rate observed in this study will be considered non-inferior to historical data if the upper 95% confidence interval for cumulative incidence of pelvic/non-vaginal recurrence at 36 months $< 7.5\%$. A sample size of 182 patients will provide 90% power to detect a non-inferiority proportion of 5%, assuming the historical estimate is 2.5%. This historical estimate was chosen based on historical results of retrospective cohorts of Mayo Clinic and Memorial Sloan Kettering Cancer Center patients, and the Postoperative Radiation Therapy in Endometrial Carcinoma (PORTEC-1) and PORTEC-2 trials.[13,14] Pelvic non-vaginal recurrence rates of 4.5% were previously reported after long-term follow-up from the observation arm of stage I patients in PORTEC-1. [13] The same study reported long-term pelvic non-vaginal recurrence of 3.4% in stage I patients receiving adjuvant external beam radiation therapy; at 5 years, pelvic non-vaginal recurrence rate was 3.4% in stage I patients (observation arm).[13] In the PORTEC-2 randomized trial, after median follow-up of 45 months, in patients receiving vaginal brachytherapy only, pelvic non-vaginal recurrence rate was 3.8% (95% confidence interval, 1.9–7.5%).[14] Additional historical estimates were obtained from retrospective cohorts of patients with pathologic stage I intermediate-risk endometrioid endometrial cancer undergoing hysterectomy and lymphadenectomy for staging at either the Mayo Clinic (2004–2012) or Memorial Sloan Kettering Cancer Center (2000–2012). Patients who received neoadjuvant therapy, had synchronous invasive cancer, or received adjuvant therapy that differed from suggested regimens in the SELECT trial, were excluded from each cohort. Patients whose adjuvant treatment regimen was unknown were included. A total of 259 met the inclusion criteria (Mayo Clinic cohort, $n=152$; Memorial Sloan Kettering Cancer Center cohort, $n=107$). By 36 months, cumulative incidence of pelvic/non-vaginal recurrence was 1.4% (95% confidence interval, 0–3.3%) in the Mayo Clinic cohort, 2.1% (95% confidence interval, 0–

5.1%) in the Memorial Sloan Kettering Cancer Center cohort, 1.7% (95% confidence interval, 0–3.4%) for both cohorts combined. Sample size was determined using PASS-15 software to detect a non-inferiority proportion based on a one-sided exact test with a significance level of 0.05. Sample size was increased by 15% to accommodate patients who might be lost to follow-up. All 182 patients must be registered, with pathologic stage I intermediate-risk endometrioid endometrial cancer, must meet study cohort criteria, and be enrolled for Part 2.

Memorial Sloan Kettering Cancer Center reviewed a modern series of new endometrial cancer patients undergoing surgery over a two-year period (2017–2018) and found that 491 had grade 1, 2 or 3 endometrioid adenocarcinoma, based on outside histology. Following pathology review, only 377 had confirmed grade 1, 2 or 3 endometrioid adenocarcinoma. After staging surgery and hysterectomy, 40 met SELECT trial intermediate-risk criteria on final surgical pathology (Table 1). Based on this, we estimate that we will need to enroll approximately 1,715 new patients with apparent uterine-confined endometrioid endometrial cancer in Part 1 to achieve our study target of 182 (Part 2) after final surgical pathology is completed.

After enrollment of the 91st patient in Part 2, we will evaluate the proportion of all enrolled patients who have either died or recurred at any site. If that exceeds 10%, enrollment will be temporarily halted and the SELECT executive committee will review these cases, draft a study recommendation, and submit it for approval to the Data and Safety Monitoring Board and Institutional Review Board.

We anticipate that the 6 initial participating centers will each enroll 10–15 patients per year, and that as many as 6 additional centers will participate in the future. Therefore, with a target of 182 patients, accrual should be completed by 36 months. Follow-up will continue for 36 months after enrollment of the last patient.

Statistical Methods

The primary analysis will estimate cumulative incidence of pelvic/non-vaginal recurrence among all registered women with pathologic stage I, intermediate-risk endometrioid endometrial cancer who met the criteria and were enrolled onto Part 2. The duration of each patient's follow-up will be calculated from date of surgical treatment until date of first documented pelvic/non-vaginal recurrence or competing risk. Patients will be censored at the time of last clinical follow-up if a pelvic/non-vaginal recurrence or competing risk event has not occurred. Cumulative incidence will be estimated taking into account the competing risks of a) death and b) other sites of recurrence, using the methods outlined by Gooley et al. [15] To address the primary objective, we will construct a one-sided 95% confidence interval for cumulative incidence of pelvic/non-vaginal recurrence within 36 months, using the variance derived by Aalen.[16] This cohort will be considered to have pelvic/non-vaginal recurrence rate non-inferior to historical data if the upper 95% confidence bound for cumulative incidence of pelvic/non-vaginal recurrence at 36 months <7.5%.

For secondary endpoints in the study cohort (Part 2), incidence of lower extremity lymphedema will be determined in patients without documented history of lymphedema

before sentinel lymph node biopsy. Point estimates of incidence (expressed as count and percentage) will be reported cumulatively at 6, 12, 18, 24 months, respectively; 95% confidence intervals will be constructed using a normal approximation for a binomial parameter. Separate estimates will be calculated based on (a) meeting the criteria, using objective measurements, or (b) the questionnaire, a self-reported diagnosis by a healthcare provider, or total score ≥ 5 in response to the 13 symptom items on a 4-point scale, or c) both a and b. Responses to the 13 symptom items will be ignored if ≤ 6 are answered. Results will be stratified by body mass index (<25 , $25\text{--}<30$, $30\text{--}<40$, ≥ 40 kg/m²). For the Quality of Life endpoint in the study cohort (Part 2), the four domain scores of EORTC QLQ-C30 (physical, emotional, social/family, functional well-being) will be summarized at 6, 12, 18, 24 months, respectively. Scores will be summarized using standard descriptive statistics. The incidence of 30-day post-surgical morbidity (Part 2) will be summarized using frequency counts and percentages; 95% confidence intervals will be constructed using an exact method for a binomial parameter.

For all patients enrolled in Part 1, point estimates of the rate of a) identifying at least one sentinel node and b) identifying bilateral sentinel lymph nodes, will each be expressed as a percentage of all patients; 95% confidence intervals will be constructed using an exact method for a binomial parameter. The rate of empty sentinel nodal packets will be expressed as a percentage of all specimens removed; a 95% confidence interval will be constructed using a score-based method for clustered binomial data, taking into account that multiple specimens from the same patient will be correlated. A node identified by the surgeon as a sentinel lymph node will be considered successfully identified if, on pathologic review, the node is determined to *not* be an empty packet.

DISCUSSION

This prospective multicenter observational study aims to assess whether pelvic/non-vaginal recurrence rates are comparable to historical data in patients with sentinel lymph node-negative surgical stage I intermediate-risk endometrioid endometrial cancer. This trial will provide additional critical understanding regarding the following: (i) recurrence rates and patterns of recurrence in patients undergoing sentinel lymph node biopsy without systematic pelvic $\pm$ para-aortic lymphadenectomy, (ii) impact of sentinel lymph node biopsy on lower extremity lymphedema and quality of life, (iii) 30-day post-surgical morbidity of sentinel lymph node biopsy. If results show that the bilateral sentinel lymph node algorithm has a non-inferior oncologic outcome compared with the historical rate, staging with bilateral sentinel lymph node mapping will become a more accepted standard of care for patients with intermediate-risk endometrial cancer. Although sentinel lymph node mapping is the standard of care at many institutions in the United States, we still lack prospective data on oncologic outcomes and it is not currently the standard in many other countries.[17] The results of this prospective multicenter observational study may promote a change in practice internationally, significantly reducing the postoperative morbidity currently experienced by many patients who undergo lymphadenectomy.

In the SELECT study we will focus mainly on intermediate-risk endometrioid endometrial cancers (Table 1). Before surgery, the clinician is not able to define the risk category of a

patient with apparent uterine-confined disease. Therefore, removal of bilateral pelvic sentinel nodes is a critical part of surgical staging because adjuvant therapy is mainly based on documentation of extra-uterine disease, particularly lymph node metastasis (which may upstage stage I to IIIC1/2). This is particularly true in intermediate-risk patients. For low-risk patients, the benefit of lymph node assessment is controversial and the recurrence event is generally negligible;[18] therefore, we excluded them from the study. In high-risk patients (Table 1) or stage >I or non-endometrioid histology, the best adjuvant treatment is still controversial. This difference in adjuvant therapy may be a crucial bias in analyzing recurrence rate. While for intermediate-risk endometrioid endometrial cancer, the finding of limited recurrences in uterine-confined cancer with negative bilateral pelvic sentinel nodes, will reassure the clinician that it is acceptable to avoid recommending adjuvant therapy, such as external pelvic radiation and chemotherapy, in this subgroup of patients.

It may be inferred that the optimal trial design would be one in which patients with negative sentinel lymph nodes are randomly assigned to completion of pelvic $\pm$ para-aortic lymphadenectomy or not, matched for risk group of recurrence (not unequivocal in the literature) and subsequent adjuvant treatment. However, this would be both unrealistic and unethical, because many patients would undergo full lymphadenectomy without proven survival benefit. In fact, if we look at prospective randomized trials,[3,4] other investigators have already failed to identify a therapeutic value of lymphadenectomy, by comparing “hysterectomy only” to systematic lymphadenectomy. For this reason, we anticipate that it will be even less likely that we will be able to observe a therapeutic benefit of lymphadenectomy, when compared to sentinel nodes, which has already been demonstrated to provide accurate information to direct postoperative treatment.

In vulvar cancer, sentinel lymph node mapping has become an alternative to inguinofemoral lymphadenectomy based on multicenter observational studies showing safety and feasibility, and low risk of groin recurrence, in patients with early-stage disease and negative sentinel lymph nodes.[19,20] We have used these prospective observational studies in vulvar cancer as a framework for designing the SELECT trial.

In summary, based on the number of current recruiting centers (n=6) and additional participating centers in the future, the SELECT trial has a high potential to reach the anticipated number of cases in 36 months and provide data after an additional 36 months to make clinical practice and international guidelines homogenous and evidence-based.

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Box 1.**Part 1 Inclusion and Exclusion Criteria****Part 1 - Inclusion Criteria**

ECOG performance status 0–1 or KPS >70%

Age ≥ 18 years

Endometrioid adenocarcinoma histologic diagnosis on endometrial biopsy or dilatation and curettage confirmed at the enrolling institution

No evidence of extrauterine disease, or suspicious pelvic lymph nodes, or distant metastases, or cervical invasion on pre-operative conventional imaging studies (pelvic +/- abdominal CT or MRI or sonogram, or body PET scan) and physical examination (uterine confined by exam and imaging)

Suitable candidate for surgery

Planned surgical treatment including hysterectomy in combination with SLN biopsy

No history of second primary cancer (invasive or in situ) within the past 5 years, not including non-melanoma skin cancer

Approved and signed informed consent

No history of neoadjuvant chemotherapy or radiotherapy for endometrial cancer

No history of prior pelvic or abdominal radiotherapy

Part 1 – Exclusion Criteria

Extrauterine disease, or gross lymph node involvement, or cervical invasion suspected on pre-operative imaging studies and physical examination (disease not uterine-confined clinical stage > I)

Contraindication for SLN mapping

The planned treatment is not surgery, or the surgical treatment does not include hysterectomy in combination with SLN biopsy

ECOG, Eastern Cooperative Oncology Group

KPS, Karnofsky Performance Status

SLN, sentinel lymph node

Box 2.**Part 2 Inclusion and Exclusion Criteria****Part 2 - Inclusion Criteria**

A patient will be enrolled in the study cohort if all of the following criteria are met:

At surgery, the patient must undergo:

Hysterectomy with removal of the adnexa

Bilateral pelvic SLN mapping (bilateral sentinel nodes are negative for malignancy)

On the final pathologic report, the patient must have a diagnosis of:

Stage I intermediate-risk endometrioid endometrial cancer (Grade 1 or Grade 2 with 50% myometrial invasion or Grade 3 with < 50% myometrial invasion)

Negative pelvic peritoneal cytology

Adjuvant treatment as recommended by the multidisciplinary team must be as follows:

No adjuvant treatment

or

Intravaginal radiation only

Part 2 – Exclusion Criteria

Intra-operative detection of extra-uterine disease or grossly involved lymph nodes

Presence of any positive pelvic nodes including micrometastasis and isolated tumor cells

Hysterectomy is not performed

Failed unilateral or bilateral SLN mapping

Patient undergoes a complete unilateral or bilateral pelvic lymphadenectomy

Patient undergoes a radical type C hysterectomy

Stage IA endometrioid cancer Grade 1 or 2 and myometrial invasion <50%

Stage IB Grade 3 endometrioid cancer

Stage > I

Non-endometrioid histology: Serous, clear cell, carcinosarcoma, undifferentiated, or de-differentiated histology noted on final hysterectomy pathology

Empty unilateral or bilateral sentinel lymph nodal packet(s)

SLN, sentinel lymph node

Box 3.**Primary and Secondary Objectives****Primary Objective** (*for Part 2 patients only*)

To assess whether the 36-month incidence of pelvic/non-vaginal recurrence in women with pathologic confirmed stage I intermediate-risk endometrioid endometrial cancer (Table 1) who have bilateral negative pelvic SLNs is non-inferior to the historical control.

Secondary Objectives

To determine the incidence of lower extremity lymphedema (LEL) (*for Part 2 patients only*)

To determine the rate of the SLN procedure in identifying (*for all Part 1 patients*):

1. At least one sentinel lymph node per patient
2. Bilateral pelvic sentinel lymph nodes per patient
3. Empty sentinel nodal packets per specimen

To assess quality of life (QoL) in the study cohort (*for Part 2 patients only*)

To evaluate 30-day post-surgical morbidity data (*for Part 2 patients only*)

SLN, sentinel lymph node

LEL, lower extremity lymphedema

QoL, quality of life

Figure 1.

Trial schema. BSO, bilateral salpingo-oophorectomy; CT, computed tomography; MRI, magnetic resonance imaging; MI, myometrial invasion; PET, positron emission tomography; SLN, sentinel lymph node; TH, total hysterectomy.

Table 1.

The SELECT trial risk group stratification for patients with Stage I (node-negative) endometrioid endometrial cancer. Only patients with intermediate-risk endometrial cancer will be recruited onto the study.

Low Risk	Intermediate Risk	High Risk
Grade (G) 1 or 2 endometrioid and <50% myometrial invasion	G1 or 2 endometrioid and 50% myometrial invasion	G3 endometrioid and 50% myometrial invasion
	G3 endometrioid and <50% myometrial invasion	