

Tata Medical Center, Kolkata

ROSE TRIAL – SYNOPSIS

A Phase III Randomized Trial of Systematic Lymphadenectomy in Patients with Apparent Early-Stage High-grade Epithelial Ovarian Cancer

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TRIAL AT A GLANCE

Design	Phase III, open-label, multicentre, randomized, non-inferiority clinical trial
Population	Adults with apparent early-stage, high-grade epithelial ovarian cancer undergoing surgical staging
Primary question	Whether omission of systematic pelvic and para-aortic lymphadenectomy is non-inferior for 5-year disease-free survival
Randomization	1:1 intraoperative randomization after frozen-section confirmation and confirmation of apparent early-stage high grade ovarian cancer
Sample size	1,000 participants (500 per arm)
Accrual/follow-up	3 years accrual; minimum planned follow-up of 5 years
Primary endpoint	5-year disease-free survival (DFS)
Funder	Indian Council of Medical Research (ICMR)
Sponsor/coordinating centre	Tata Medical Center, Kolkata, India

BACKGROUND AND RATIONALE

Approximately 20–30% of patients with epithelial ovarian cancer present with apparent early-stage disease. Comprehensive surgical staging traditionally includes systematic pelvic and para-aortic lymphadenectomy. However, the therapeutic value of removing clinically and radiologically negative lymph nodes in apparent early-stage, high-grade epithelial ovarian cancer remains uncertain, while lymphadenectomy may increase operative time, blood loss, lymphocele formation, lower-limb lymphedema and other postoperative morbidity.

The ROSE trial is designed to determine whether omission of systematic lymphadenectomy can maintain equivalent oncological outcomes while reducing surgical morbidity and treatment burden, thereby generating high-level evidence to inform future surgical staging practice.

STUDY OBJECTIVES

Primary objective

To assess whether omission of systematic pelvic and para-aortic lymphadenectomy, compared with systematic lymphadenectomy, maintains 5-year disease-free survival in patients with apparent early-stage high-grade epithelial ovarian cancer.

Secondary objectives

- Compare overall survival.
- Evaluate pattern and site of disease recurrence.
- Compare duration of surgery, blood loss, transfusion requirements, length of hospital stay and readmission.
- Compare intraoperative and postoperative adverse events within 30 days.
- Compare health-related quality of life at 30 days and 12 months.
- Compare patient-reported outcomes at 30 days and 12 months.

TREATMENT ALLOCATION

Arm A – Control	Arm B – Experimental
Standard surgical staging including systematic pelvic and para-aortic lymphadenectomy.	Standard surgical staging without systematic pelvic and para-aortic lymphadenectomy.

Both arms undergo protocol-defined surgical staging. Both minimal access and open procedures for staging are permitted, adhering to oncological principles. Sentinel lymph-node mapping is not permitted. In Arm B, suspicious/enlarged nodes encountered intraoperatively may be selectively removed and documented. These patients are not excluded from the study.

KEY ELIGIBILITY CRITERIA

KEY INCLUSION CRITERIA:

- Age ≥ 18 years.
- Frozen section suggestive of high-grade epithelial ovarian carcinoma: high-grade serous, high-grade endometrioid, clear cell, or infiltrative-pattern mucinous carcinoma.
- Disease apparently confined to the ovaries/adnexa, with no macroscopic extra-adnexal disease.
- No clinically, radiologically or intraoperatively enlarged/suspicious pelvic or para-aortic lymph nodes.
- Primary surgery planned with intent of complete surgical staging.

- CA-125/CEA ratio >25; if <25, appropriate gastrointestinal evaluation must exclude a digestive tract primary.
- ECOG 0–2 and adequate organ function.
- Written informed consent, including consent for intraoperative randomization.

KEY EXCLUSIONS

Low-grade/borderline/non-epithelial tumours, advanced disease, previous retroperitoneal lymphadenectomy, concurrent or recent malignancy, pregnancy/lactation, serious comorbidity precluding major surgery, or assessed to be potential defaulter for follow up.

SAMPLE SIZE AND STATISTICAL FRAMEWORK

The sample size assumes 5-year DFS of 78% in the systematic lymphadenectomy arm and a 7% absolute non-inferiority margin. With one-sided $\alpha=0.025$, 80% power, 1:1 allocation, 3 years accrual, minimum 5 years follow-up and approximately 5% loss to follow-up, approximately 330 DFS events are required and 1,000 participants (500 per arm) will be randomized.

Randomization will be centralized and web-based using variable permuted blocks. Stratification factors are FIGO stage, histological subtype, participating-centre annual ovarian cancer surgical volume and planned adjuvant chemotherapy.

SURGICAL AND ADJUVANT TREATMENT

Participating surgeons will follow standardized surgical procedures. Open, laparoscopic and robotic approaches are permitted provided oncological principles are maintained. In the lymphadenectomy arm, systematic pelvic and para-aortic lymphadenectomy will be performed according to protocol-defined anatomical boundaries. Adjuvant treatment will be based on the final histopathological stage and risk group and will be standardized across treatment arms.

OUTCOMES AND FOLLOW-UP

- Primary outcome: 5-year disease-free survival, from randomization to documented recurrence or death from any cause.
- Secondary outcomes: overall survival, recurrence pattern/site, perioperative outcomes, 30-day complications, HRQoL and PROMs.
- HRQoL: FACT-O at baseline, 30 days and 12 months.
- PROMs: validated tools addressing physical functioning, symptom burden, lower-limb symptoms and functional limitations.
- Lower-limb lymphedema: prospective clinical and patient-reported assessment.

- Minimum follow-up: 5 years after randomization.

PARTICIPATING CENTRE REQUIREMENTS

ROSE is intended for tertiary-care/high-volume cancer centres or academic institutions with established gynaecological oncology and clinical research capabilities. Before activation, each centre will undergo feasibility assessment.

- Dedicated gynaecological oncology service.
- Certified gynaecological oncologist(s) or equivalent (participating surgeons should independently perform ≥ 20 ovarian cancer staging surgeries and ≥ 10 systematic pelvic and para-aortic lymphadenectomies annually).
- On-site frozen-section pathology and experienced gynaecological pathologists.
- Appropriate radiology facilities and cross-sectional imaging.
- ICU and blood-bank support.
- Facilities for systemic chemotherapy.
- Clinical research personnel for recruitment, follow-up and data management.
- Capability for long-term follow-up and institutional Ethics Committee/IRB compliance.

TRAINING, DATA MANAGEMENT AND QUALITY ASSURANCE

Before site activation, investigators, surgeons, pathologists, radiologists and research coordinators will undergo protocol-specific training. Standardized manuals, surgical checklists, pathology and radiology guidance, investigator meetings and refresher training will support consistent trial conduct.

Study data will be collected prospectively through secure REDCap-based electronic case report forms. Centralized monitoring will assess consent, eligibility, randomization, protocol compliance, data completeness and selected source documents. Pathology, radiology and surgical quality assurance procedures will be implemented across sites.

SAFETY, ETHICS AND CONFIDENTIALITY

Adverse events and serious adverse events will be identified, assessed and reported according to the protocol and applicable regulatory requirements. Postoperative complications within 30 days will be graded using the Clavien–Dindo classification. An independent Data Safety Monitoring Committee will oversee patient safety, trial conduct, accrual, data quality and interim analyses.

Participant data will be pseudonymized. Identifiable information will remain at the participating site, while the central REDCap database will use unique study identification numbers and role-based access controls.

EXPRESSION OF INTEREST

Tata Medical Center is currently assessing centres for participation in the ROSE trial. Interested centres are requested to complete the accompanying Expression of Interest/feasibility form. The information will be used to assess site suitability, anticipated recruitment capacity, infrastructure and proposed Site Principal Investigator.

Completion of the EOI indicates preliminary interest and willingness to participate; formal site activation remains subject to feasibility assessment, institutional/IEC requirements, investigator training and study initiation procedures.