

MACC

MIS Approach to Cervical Cancer

2023-05-26

Asan Medical Center
Dae-Yeon Kim

**A Phase III Randomized Clinical Trial of
Lap or Robotic RH using **cancer cell spillage minimizing** techniques
vs Abdominal RH
In Patients with Early Stage Cervical Cancer**

2018-03

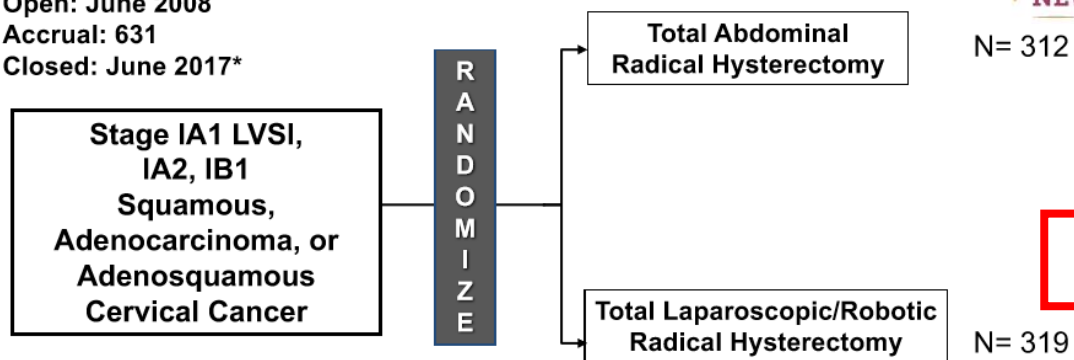
A landmark study



Phase III Randomized Trial of Laparoscopic or Robotic Radical Hysterectomy vs. Abdominal Radical Hysterectomy in Patients with Early-Stage Cervical Cancer: LACC Trial

Pedro T. Ramirez, Michael Frumovitz, Rene Pareja, Aldo Lopez, Marcelo Vieira, Reitan Ribeiro, Alessandro Buda, Xiaojian Yan, Kristy P Robledo, Val Gebiski, Robert L Coleman, Andreas Obermair

Open: June 2008
Accrual: 631
Closed: June 2017*



Bringing Together the Best in Women's Cancer Care

**“Sensational”
Unexpected result !
Reimbursement of abdominal RH ?**

MIS RH, compared to open surgery

- **Recurrence rate** ↑ (HR, 3.74; 95% CI, 1.63–8.58; $P=0.002$)
- **Mortality rate** ↑ (HR, 6.00; 95% CI, 1.48–20.3, $P=0.004$)

NCCN guideline



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 1.2022 Cervical Cancer

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PRINCIPLES OF EVALUATION AND SURGICAL STAGING^a

Types of Resection and Appropriateness for Treatment of Cervical Cancer

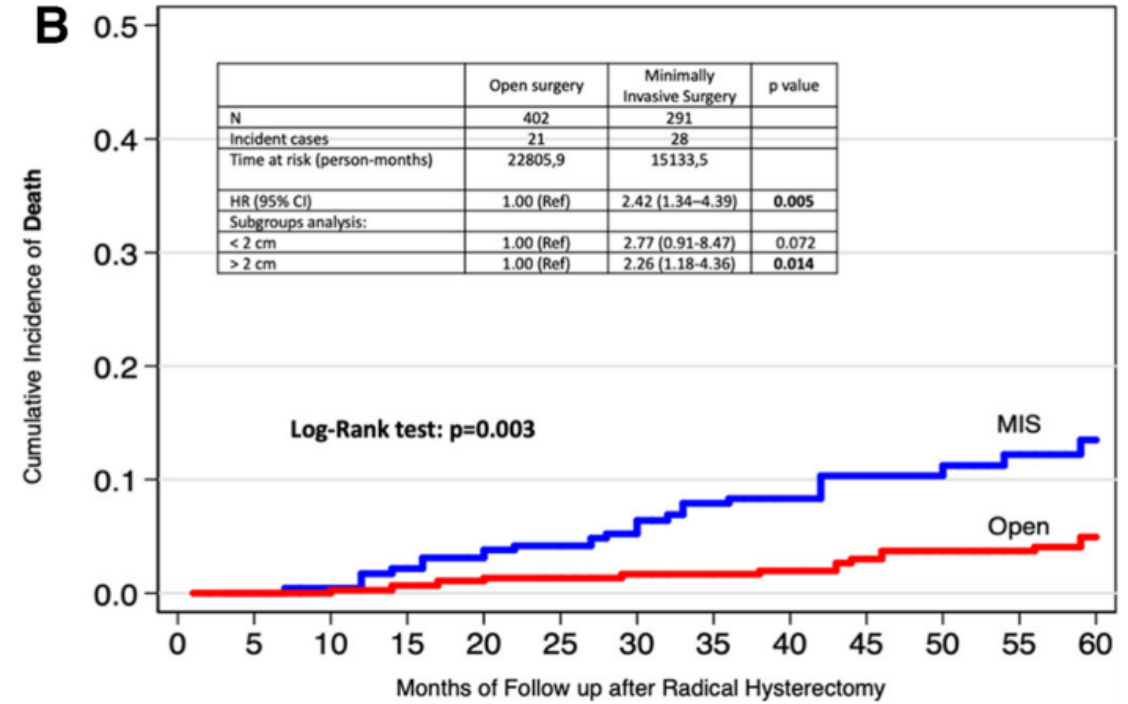
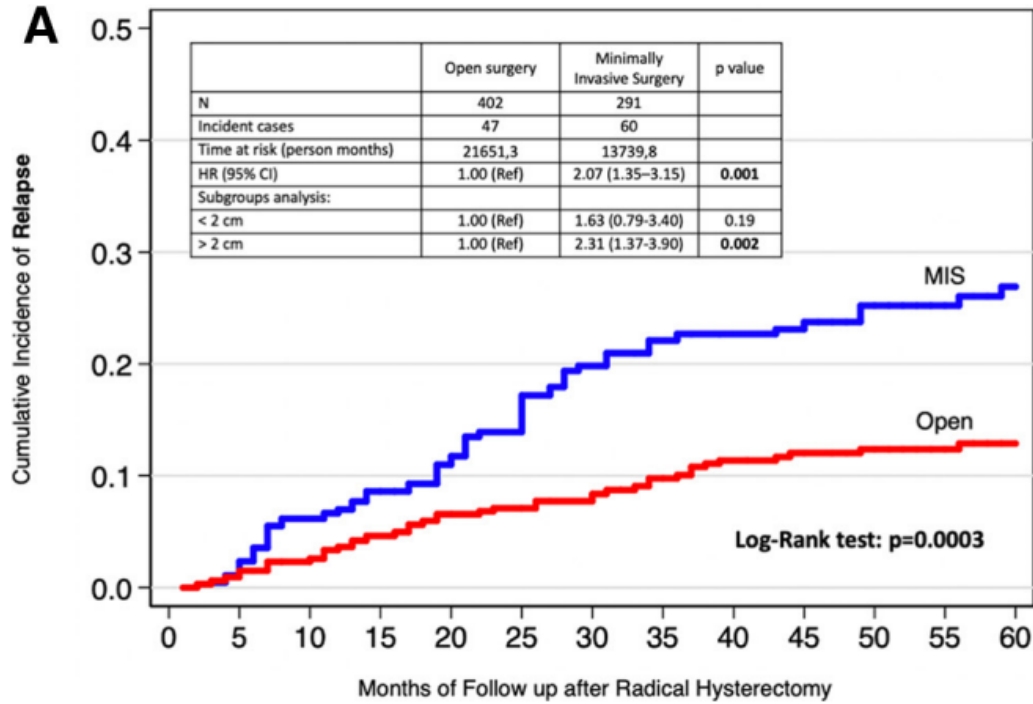
- Treatment of cervical cancer is stratified by stage as delineated in the Guidelines.
- Microinvasive disease, defined as FIGO stage IA1 with no LVSI, has less than a 1% chance of lymphatic metastasis and may be managed conservatively with cone biopsy for preservation of fertility (with negative margins) or with simple hysterectomy when preservation of fertility is not desired or relevant. The intent of a cone biopsy is to remove the ectocervix and endocervical canal en bloc using a scalpel. This provides the pathologist with an intact, non-fragmented specimen without electrosurgical artifact, which facilitates margin status evaluation. If a loop electrosurgical excision procedure (LEEP) is chosen for treatment, the specimen should not be fragmented, and care must be undertaken to minimize electrosurgical artifact at the margins. The shape and depth of the cone biopsy may be tailored to the size, type, and location of the neoplastic lesion. For example, if there is concern for invasive adenocarcinoma versus adenocarcinoma in situ in the cervical canal, the cone biopsy would be designed as a narrow, long cone extending to the internal os in order not to miss possible invasion in the endocervical canal. Length of the cold cone of at least 10 mm is preferred and can be increased to 18–20 mm in patients who

- The standard and recommended approach for radical hysterectomy is with an open abdominal approach (category 1). A prospective randomized trial⁴ demonstrated that minimally invasive radical hysterectomy was associated with lower rates of disease-free survival (DFS) and overall survival than open abdominal radical hysterectomy. Moreover, two recent epidemiologic studies also demonstrated that minimally invasive radical hysterectomy was associated with shorter overall survival than open surgery among women with stage IA2–IB1 cervical cancer.⁵ See [Discussion](#) for additional details.

details for the most commonly used types of hysterectomy are described in Table 1 (see CERV-C 5 of 7).

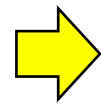
- The standard and recommended approach for radical hysterectomy is with an open abdominal approach (category 1). A prospective randomized trial⁴ demonstrated that minimally invasive radical hysterectomy was associated with lower rates of disease-free survival (DFS) and overall survival than open abdominal radical hysterectomy. Moreover, two recent epidemiologic studies also demonstrated that minimally invasive radical hysterectomy was associated with shorter overall survival than open surgery among women with stage IA2–IB1 cervical cancer.⁵ See [Discussion](#) for additional details.

SUCCOR



MIS RH, compared to open surgery

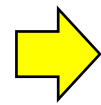
- Recurrence rate ↑ (HR, 2.07; 95% CI, 1.35–3.15)
- Mortality rate ↑ (HR, 2.42; 95% CI, 1.34–4.39)



Tumor >2 cm

MIS RH, compared to open surgery

- Recurrence rate ↑ (HR, 2.31; 95% CI, 1.37–3.90)
- Mortality rate ↑ (HR, 2.26; 95% CI, 1.18–4.36)



Tumor ≤2 cm

MIS RH, compared to open surgery

- Recurrence rate = (similar)
- Mortality rate = (similar)

MEMORY study: Multicenter study of MIS vs Open Radical hysterectomy



Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

The MEMORY Study: MulticentEr study of Minimally invasive surgery versus Open Radical hYsterectomy in the management of early-stage cervical cancer: Survival outcomes



Mario M. Leitao Jr^{a,b,*}, Qin C. Zhou^c, Benny Brandt^{a,1}, Alexia Iasonos^c, Vasileios Sioulas^{a,2}, Katherine Lavigne Mager^{a,3}, Mark Shahin^d, Shaina Bruce^{d,4}, Destin R. Black^{e,f}, Carrie G. Kay^f, Meeli Gandhi^{e,5}, Maira Qayyum^e, Jennifer Scalici^g, Nathaniel L. Jones^g, Rajesh Paladugu^g, Jubilee Brown^h, R. Wendel Naumann^h, Monica D. Levine^{h,6}, Alberto Mendivilⁱ, Peter C. Lim^j, Elizabeth Kang^j, Leigh A. Cantrell^k, Mackenzie W. Sullivan^{k,7}, Martin A. Martino^l, Melissa K. Kratz^l, Valentin Kolev^m, Shannon Tomita^m, Charles A. Leath IIIⁿ, Teresa K.L. Boitanoⁿ, David W. Doo^{n,8}, Colleen Feltmate^o, Ronan Sugrue^o, Alexander B. Olawaiye^p, Ester Goldfeld^p, Sarah E. Ferguson^{q,r}, Jessa Suhner^s, Nadeem R. Abu-Rustum^{a,b}

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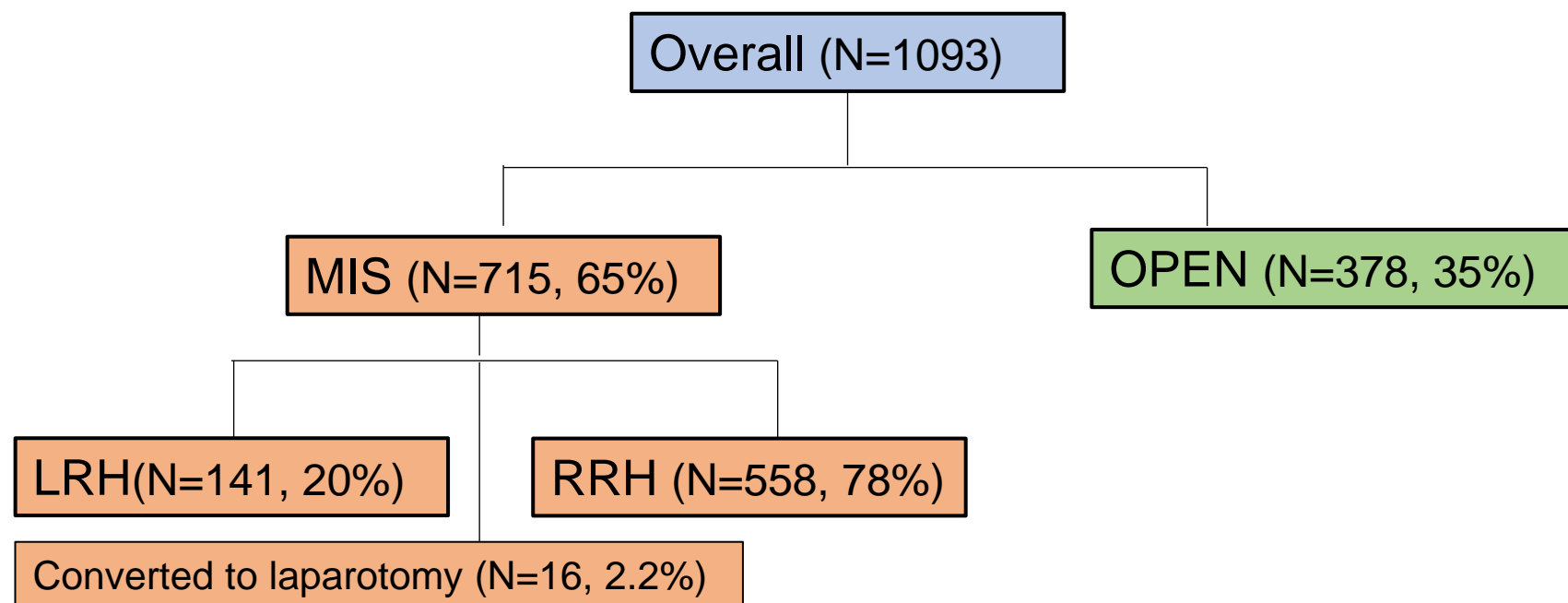
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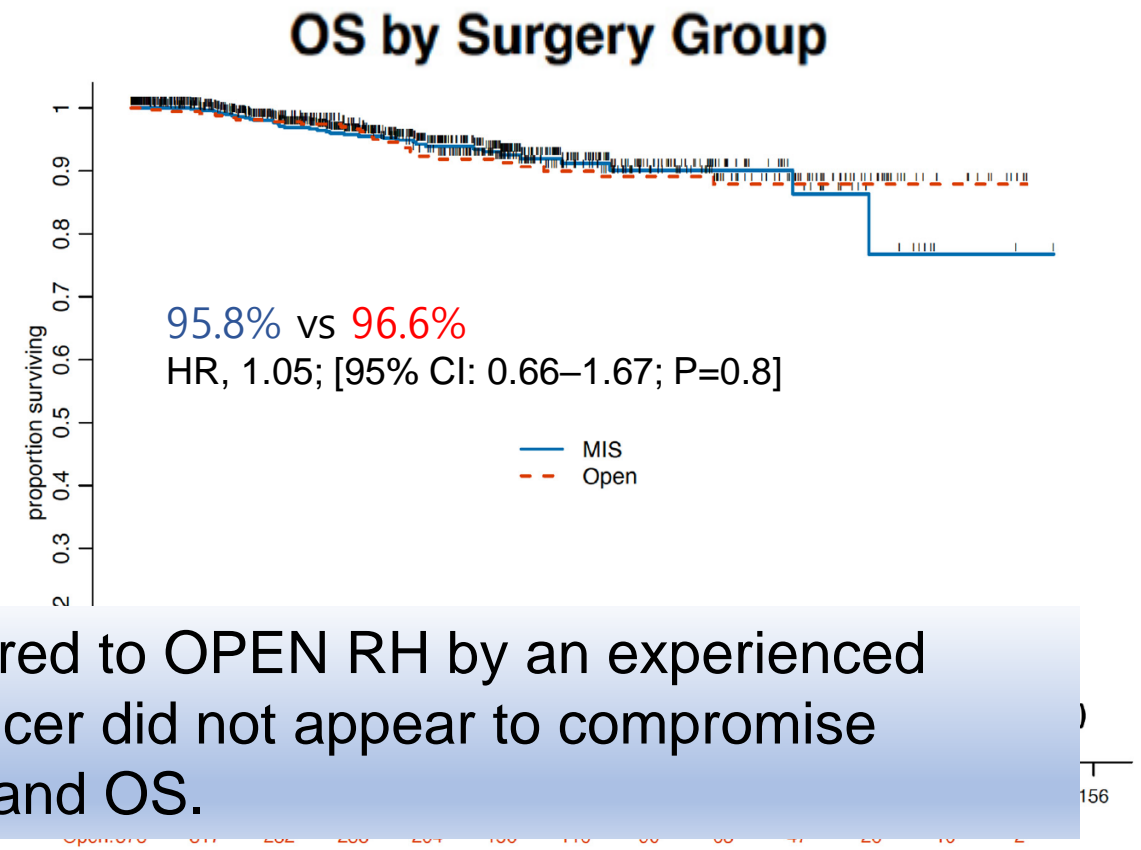
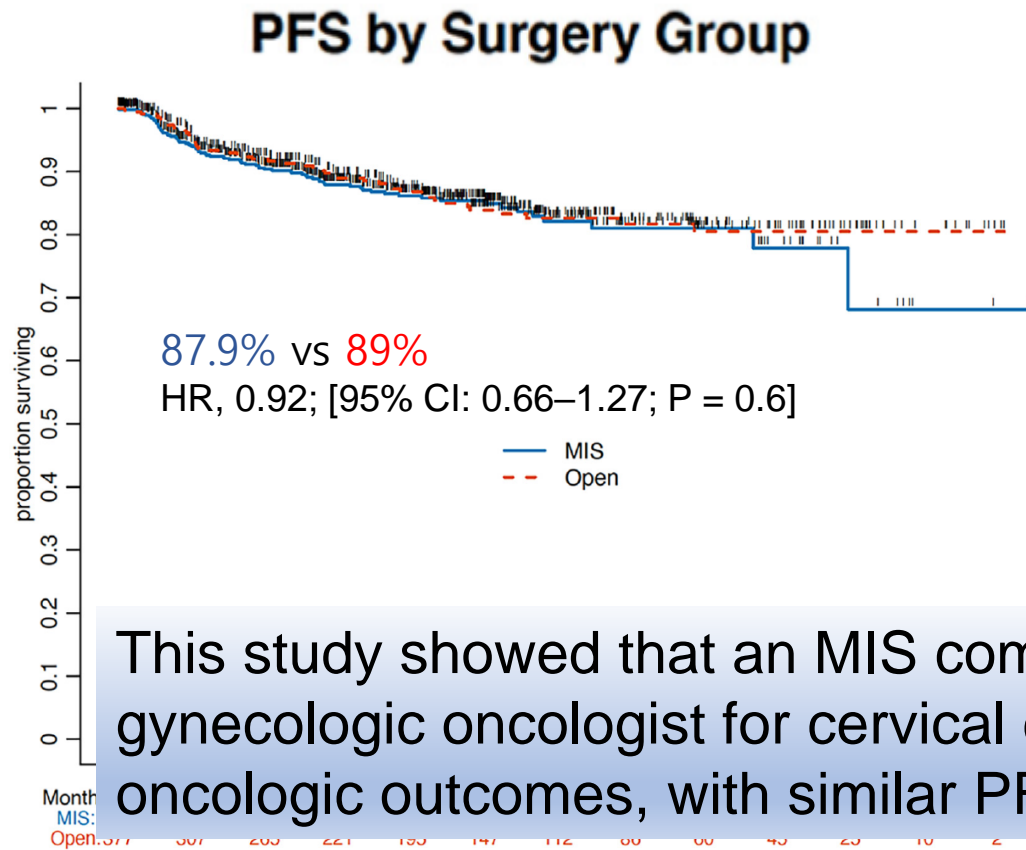
^s Department of Obstetrics, Gynecology and Reproductive Sciences, Mount Sinai West/Mount Sinai Morningside, New York, NY, United States of America

Results

- Flow chart of the study population



3-yr PFS / OS for the MIS and OPEN cohorts



This study showed that an MIS compared to OPEN RH by an experienced gynecologic oncologist for cervical cancer did not appear to compromise oncologic outcomes, with similar PFS and OS.

MACC trial (MIS Approach to Cervical Cancer)

- A Phase III Randomized Clinical Trial of Laparoscopic or Robotic RH using **cancer cell spillage minimizing** techniques vs Abdominal RH In Patients with Early-Stage Cervical Cancer

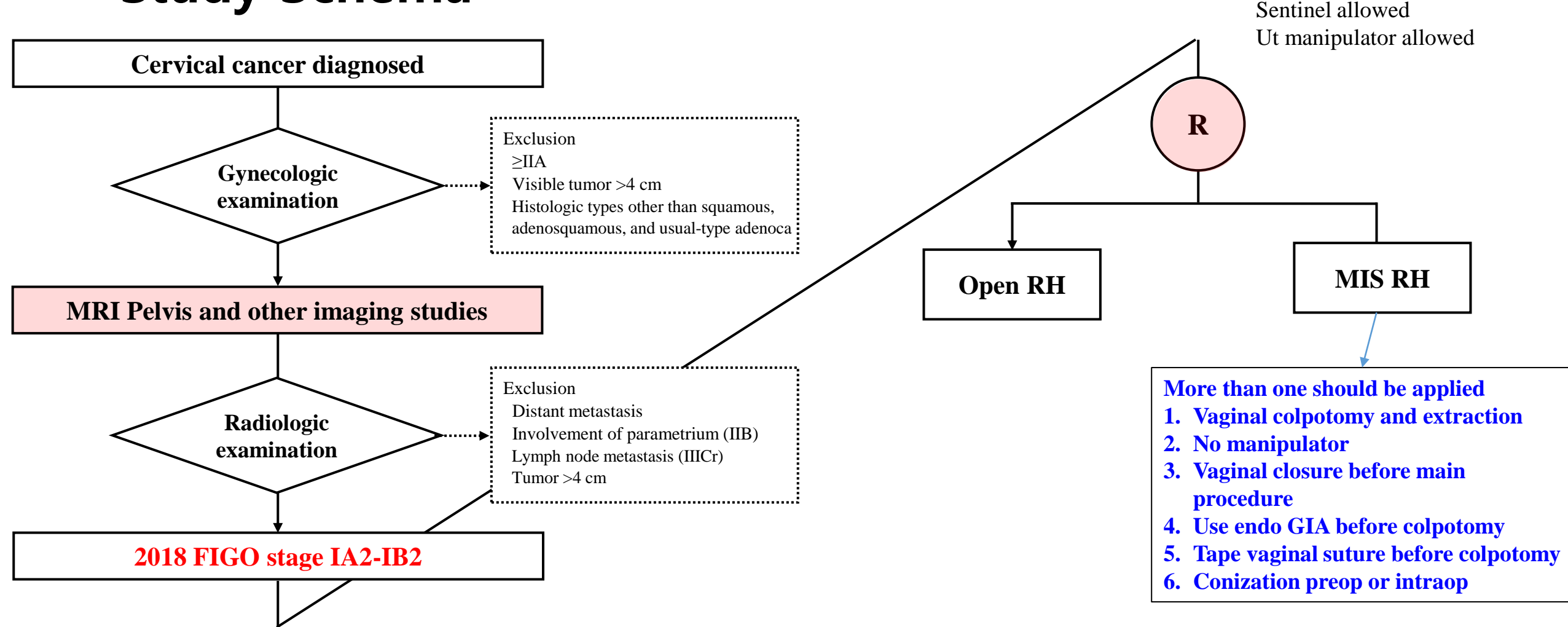
Study Design

- **Study Hypothesis:** There is no difference in survival prognosis between “open radical hysterectomy” and “cone + microinvasive radical hysterectomy” in 2018 FIGO stage IB1-IB2 cervical cancer
- **Study Design:** Phase III RCT (non-inferiority, confirmatory)

Study Objective

- **Primary Objective: 5-year progression-free survival rate**
- **Secondary Objective** : 3-year progression-free survival rate, 5-year overall survival rate, Safety of performing radical hysterectomy after conization, Surgery-related complications, Readmission rate, reoperation rate, mortality rate, Quality of life.

Study Schema



1' endpoint: 5-yr PFS rate

2' endpoint: 3-yr PFS, 5-yr OS rate, Safety, Complications

Statistics

- **Calculation of the number of study subjects (two-tailed test)**

Index of comparison	5-year PFS rate
Predictive value in control group	88%
Expected difference	Non-inferiority
Statistic	α 0.05; β 0.2; 2-sided
Number of patients needed	215 per group, 430 in total
Estimated registration period	3 years
Estimated follow-up period	8 years

- **Early termination of the study** : Determined according to the results of the **interim analysis** performed when enrolling **100 and 200 patients**.

ROCC/GOG3043 trial (NCT048331580)



GOG-3043 (ROCC Trial)

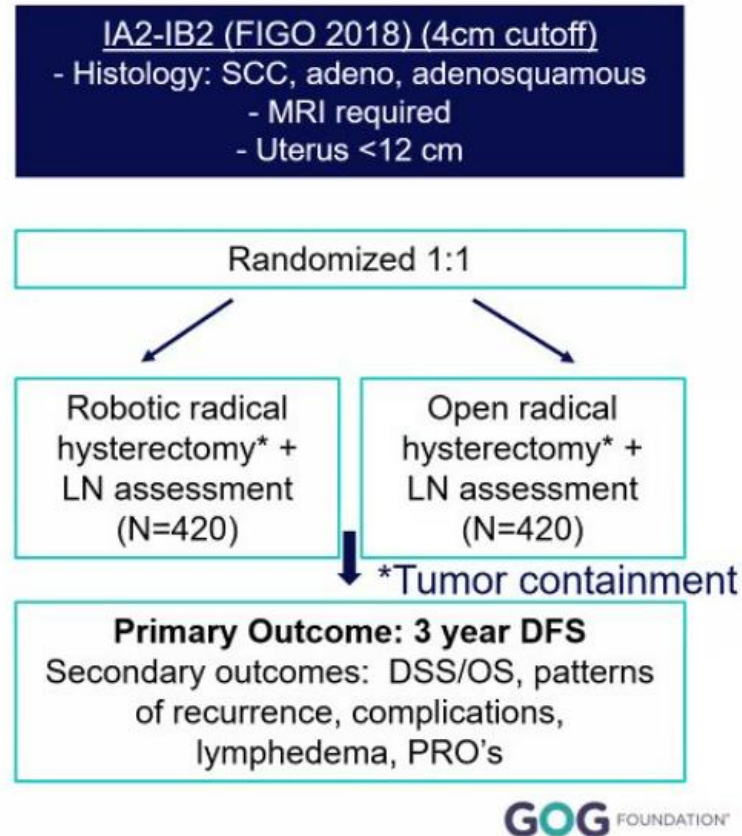
A Randomized Controlled Trial of Robotic versus Open Radical Hysterectomy for Cervical Cancer

GOG FOUNDATION

GOG PARTNERS

#GOGROCC

PI: Kristin Bixel
Mario Leitao



- Sample size ; 840 patients
- Primary endpoint ; 3-yr DFS
- From March 2022 to August 2029
- No use of uterine manipulator
- Preop MRI

ROCC/GOG3043 trial (NCT048331580)

- **Acceptable tumor containment methods**
 - ✓ **Colpotomy performed entirely vaginally** after intracorporeal radical dissection is completed.
 - ✓ **Vaginal mucosal layer developed and sutured together over the cervix and tumor** either at the beginning of the procedure or after radical dissection completed robotically.
 - ✓ Closure of the vagina **using robotic stapling device or circumferential suture** around the vagina.

In MACC trial..

- Acceptable tumor containment methods ; **More than one should be applied**
 1. Vaginal colpotomy and extraction
 2. No manipulator
 3. Vaginal closure before main procedure
 4. Use endo GIA before colpotomy
 5. Tape vaginal suture before colpotomy
 6. Conization preop or intraop

Issues

- Why now ?
- Robotic / laparoscopic advantages over laparotomy