XXII ASSEMBLEA MaNGO MILANO

STANDARD TREATMENTS AND NEW DIRECTIONS IN GYNAECOLOGICAL CANCERS

MILANO June 26th-29th, 2025

Responsabili Scientifici:
NICOLETTA COLOMBO, FRANCESCO RASPAGLIESI

MaNGO

SURGICAL STUDIES

Ongoing and opening studies

Simone Bruni
Fondazione IRCCS, Istituto Nazionale dei Tumori, Milano
Gynecologic Oncology Unit

FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

Ovarian cancer

IRFMN-OVA-9369 - La citoriduzione secondaria nel carcinoma ovarico nell'era della terapia di mantenimento: studio multicentrico, osservazionale, retrospettivo

- **Obiettivo principale:** valutare l'influenza della terapia di mantenimento in prima linea, dell'intervallo libero dal trattamento con platino e dello status BRCA/HRD sulla reale fattibilità di una citoriduzione secondaria completa.

- **PI:** Francesco Raspagliesi
- **Centri partecipanti:** 16
- **Approvazione CET 4 Lombardia:** 30/04/2024 > autorizzazione completata INT Milano: ottobre 2024, primo centro attivato

Surgery studies under activation - ongoing CITORIDUZIONE SECONDARIA

- **GOG-0213** (neg), **DESKTOP3** (pos OS/PFS), **SOC-1** (pos PFS and OS when crossover analysis considered)
  - 2 RCT: identified a group that can benefit from SCRS on PFS and OS



Factor	DESKTOP III	SOC-1	GOG-0213
Patient selection criteria	AGO score	iMODEL prediction tool	None
Complete resection rate (R0)	~75%	~74–77%	~67%
Bevacizumab usage	23%	Variable	84%
Type of centers	Highly specialized centers	Highly specialized centers	Heterogeneous (USA-based)
Study outcome	Surgery showed benefit	Surgery showed benefit	No benefit from surgery

Surgery studies under activation - ongoing CITORIDUZIONE SECONDARIA

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 2, 2021 VOL. 385 NO. 23

Randomized Trial of Cytoreductive Surgery for Relapsed Ovarian Cancer

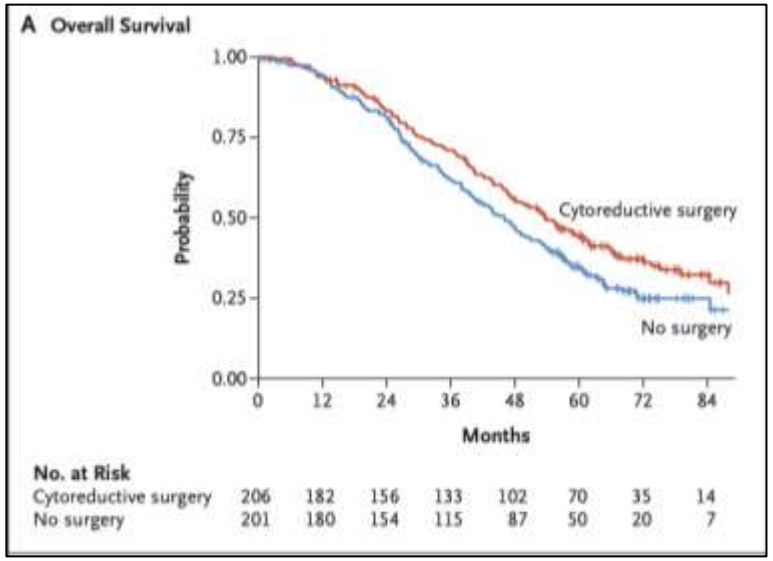
P. Harter, J. Sehouli, I. Vergote, G. Ferron, A. Reuss, W. Meier, S. Greggi, B.J. Mosgaard, F. Selle, F. Guyon, C. Pomel, F. Lécuru, R. Zang, E. Avall-Lundqvist, J.-W. Kim, J. Ponce, F. Raspagliesi, G. Kristensen, J.-M. Classe, P. Hillemanns, P. Jensen, A. Hasenburg, S. Ghaem-Maghami, M.R. Mirza, B. Lund, A. Reinthaller, A. Santaballa, A. Olaitan, F. Hilpert, and A. du Bois, for the DESKTOP III Investigators*

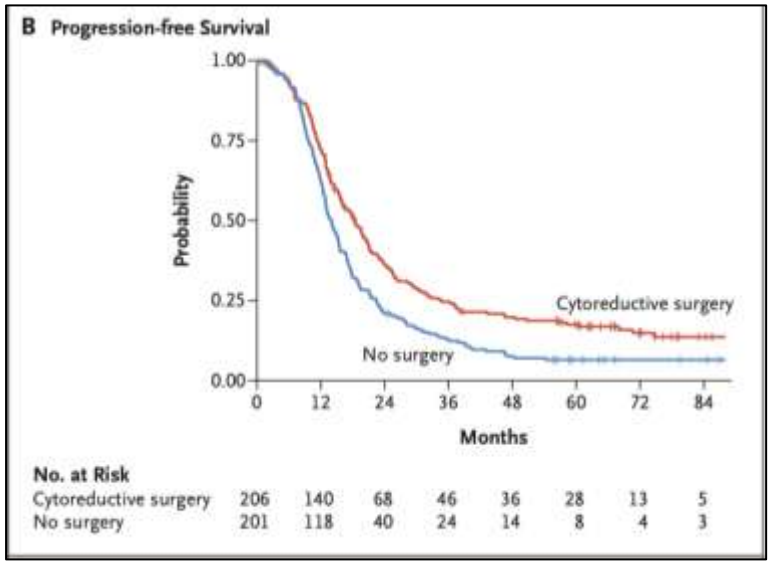
DESKTOP III

AGO criteria:

- R0 debulking at primary surgery
- Ascites <500 ml
- ECOG PS 0

Complete gross resection: 75.5%
OS 61.9% vs 46%





Surgery studies under activation - ongoing CITORIDUZIONE SECONDARIA

Secondary cytoreduction followed by chemotherapy versus chemotherapy alone in platinum-sensitive relapsed ovarian cancer (SOC-1): a multicentre, open-label, randomised, phase 3 trial

THE LANCET

Lancet Oncol 2021; 22: 439–49

Tingyan Shi, Jianqing Zhu*, Yanling Feng, Dongsheng Tu, Yuqin Zhang, Ping Zhang, Huixun Jia, Xiao Huang, Yunlang Cai, Sheng Yin, Rong Jiang, Wenjuan Tian, Wen Gao, Jihong Liu, Huijuan Yang, Xi Cheng, Rongyu Zang*

SOC1 iMODEL (aim <4.7) and **PET-CT imaging**:

- **FIGO stage** (stage III/IV, 0.8),
- **R at initial surgery** (>0 cm, 1.5),
- **Platinum free interval** (<16 months, 2.4),
- **Ascites <500 ml** (present, 3.0)
- **ECOG PS 0-1** ([ECOG] 2–3, 2.4),
- **Ca125 at Rec** (>105 U/mL, 1.8),

Complete gross resection: *76.7%*
> PFS and > OS after crossover analysis

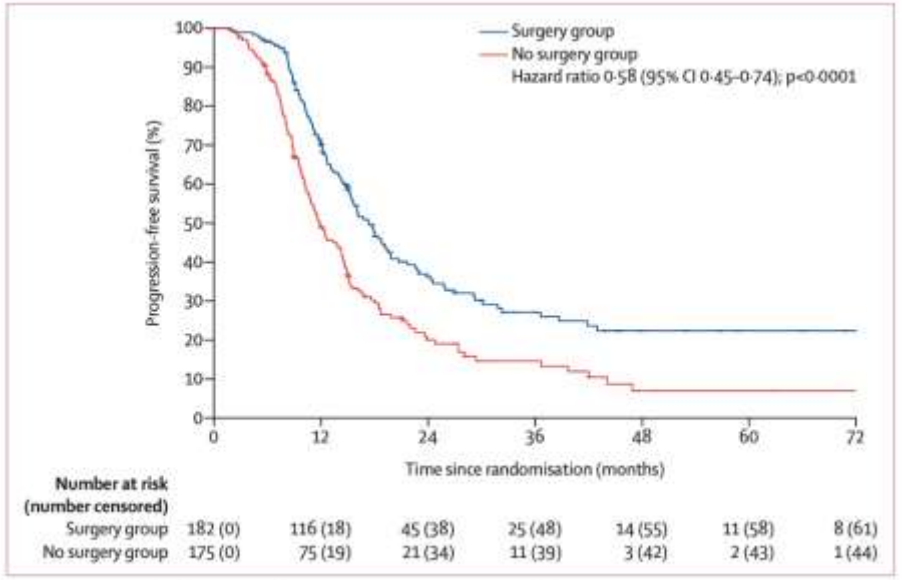
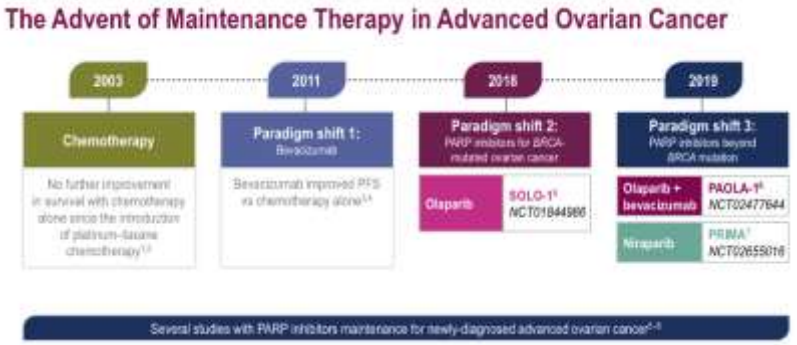


Figure 2: Progression-free survival in the intention-to-treat population

Why DESK-PARP?



- No maintenance (Bev/PARP) era
- No info on BRCA/HRD
- Chemo sensitivity **after** or **under** PARP is extremely different!
- Are these models still applicable?

- Gemelli 2019: SCS + CHT+ PARP improves TFST (time to first subs. treatment), PRS (post recurrence survival), ~46 cases BRCA mut

- IN ADDITION: possible to consider patients previously treated with **IDS** as eligible for **SCRS**? In the DESKTOP study only patients undergoing PDS were recruited and in the SOC-1 study only 18% after NACT-IDS, a rate that is no longer realistic.

Study Design

- Multi-centric, observational, retrospective
- 500 patients expected

Inclusion criteria

- >18y
- Relapsed high grade epithelial ovarian cancer
- AGO_OVAR DESKTOP criteria met:
  - Ascites < 500 mL:
  - ECOG = 0
  - Residual tumor= 0 (comprehensive of IDS patients)
- Surgical time 2017/2023
- Maintenance treatment PARP/Beva

Exclusion criteria

- Palliative surgery
- AGO_OVAR DESKTOP criteria not met
- NACT at relapse
- Non secondary surgery

Surgery studies under activation - ongoing CITORIDUZONE SECONDARIA

Update (23 June)

	Site	PI	Status	Patients
1	Fondazione IRCCS - Istituto Nazionale Tumori, Milano	Francesco Raspagliesi	**Active**	**53**
6	AOU Parma, Parma	Vito Andrea Capozzi	**Active**	**14**
2	Humanitas, Istituto Clinico Catanese, Catania	Fabio Ciancio	**Active**	
4	Istituto Oncologico Veneto, Padova	Elisa Pizzolato	**Active**	**2**
5	Arcispedale S. Maria Nuova, Reggio Emilia	Vincenzo Dario Mandato	**Active**	**2**
3	ASST Alessandro Manzoni, Lecco	Silvia Corso	**Active**	**2**
7	Ospedale Michele e Pietro Ferrero, Verduno	Alessandro Buda	**Active**	**1**
8	Spedali Civili, Brescia	Federico Ferrari	**Agreement under signature**	
9	IRCCS Fondazione San Gerardo, Monza	Robert Fruscio	**Agreement under signature**	
10	Policlinico Careggi, Firenze	Massimiliano Fambrini	**Agreement under signature**	
11	AO S. Anna, Como	Maria Paola Odorizzi	**Agreement under signature**	
12	Istituto Europeo di Oncologia, Milano	Alessia Aloisi	**Agreement under signature**	
13	Città della Salute - Ospedale S. Anna, Torino	Dionyssios Katsaros	**Agreement under revision**	
14	CRO di Aviano , Aviano	Antonino Ditto	**Agreement under revision**	
15	AO Ordine Mauriziano, Torino	Annamaria Ferrero	Submitted to CE 10 Oct 2024	
16	AOU Padova, Padova	Matteo Marchetti	Submitted to CE /agreement under revision	
17	ASST Garda P.O. Manerbio, Manerbio	Luca Bazzurini	To be submitted	

Endometrial cancer

STREAM-I

Surgical Treatment In Advanced And Recurrent Endometrial CAncer Management

AGO-OP.11/ ENGOT-en22

Evaluation of preoperative clinical and translational selection criteria for cytoreductive surgery in endometrial cancer

A retrospective multicenter trial
with an accompanying translational project

Coordinating Investigator for the AGO Study Group

Prof. Dr. med. Fabian Trillsch

LMU Klinikum
Department of Obstetrics and Gynecology
Marchioninistrasse 15
81377 Munich, Germany

ENGOT-en22 / STREAM-I Surgical Treatment In Advanced And Recurrent Endometrial CAncer Management

Design

Evaluation of preoperative clinical and translational selection criteria for cytoreductive surgery (CRS) in endometrial cancer (EC)

Retrospective descriptive, non-interventional, multicenter study
(patients undergoing CRS for EC between 01/2011 and 12/2020)

- Primary diagnosis of advanced EC and peritoneal metastases (FIGO IV)
- Diagnosis of recurrent EC undergoing cytoreductive surgery

Tumor material:

a. Requesting FFPE tumor blocks from Study Centers
b. Evaluation of molecular subgroups according to TCGA
c. Slides für RNA/DNA isolation, establishing TMAs

Primary Objective

Identification of clinical selection criteria to predict complete cytoreduction in patients with advanced or recurrent endometrial cancer

Background

- At first diagnosis EC, approximately **20% are already in advanced stages (FIGO III-IV)** and up to 15% of the patients will relapse
- Residual tumor lesions with areas of poorly vascularized cells may be hard to access for systemic treatment but can be removed by **cytoreductive surgery (CRS)**
- Only few studies exist regarding CRS in advanced and recurrent EC. Mostly single-center, retrospective studies showed an advantage by CRS, but all studies had only **small patient groups** and a **range between 18-75% for complete cytoreduction** was described depending on the FIGO stage and other mostly unknown factors

Bristow et al, Gynecol Oncol, 2000
Barlin et al, Gynecol Oncol, 2010

Endometrial cancer classification

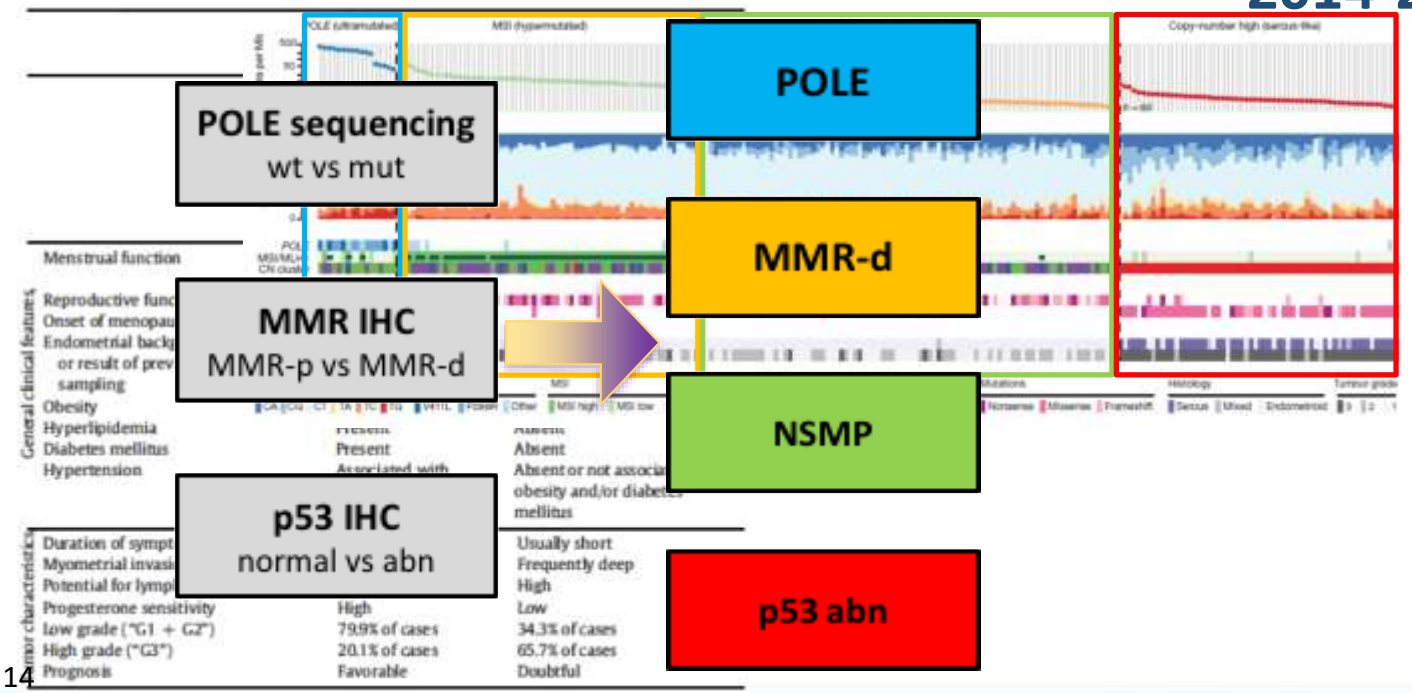
Bokhman : a dualistic model for endometrial tumorigenesis

TCGA molecul ar model

1983

2013

2014-2018



ProMisE/TransPORTEC: a simplified molecular model

Bokhman J.V., Gyn Onc 1983. Suarez A.A., Felix A.S., Cohn D. E. Gyn Onc 2017. TGCA, Nature 2013
Stelloo E. et al, Gyn Onc 2014; Stelloo et al, Clin Cancer Research 2016; Talhouk A. et al, Gyn Onc 2016; Kommos S. et al, Annals of Oncology, 2018: Abdulfatah et al, Gyn Onc 2019. Concin N. et al, IJGC 2021

Courtesy of I. Betella

5.1 Primary objective

- Identification of clinical selection criteria to predict complete cytoreduction in patients with advanced or recurrent endometrial cancer

5.2 Secondary objectives

Clinical part:

- Evaluation of prognostic factors predicting benefit in patients undergoing cytoreductive surgery for advanced or recurrent endometrial cancer
- Identification of prognostic markers for the clinical outcome

Translational part:

- Evaluating the predictive value of the molecular classification according to TCGA for surgical outcome in endometrial cancer
- Identification of biologic and molecular expression profiles to predict complete cytoreduction in patients with endometrial cancer and their prognostic significance

Promising for upcoming prospective trials on CRS in advanced and/or recurrent EC
(STREAM-II/-III)

Inclusion criteria:

1. Patient underwent cytoreductive surgery (CRS) between 01/2011 and 12/2020
2. Patient's age at CRS ≥18 years
3. One of the following criteria has to be fulfilled:
    a. Primary diagnosis of advanced endometrial cancer and peritoneal metastases (FIGO IV) undergoing cytoreductive surgery

OR

    b. Diagnosis of recurrent endometrial cancer undergoing cytoreductive surgery

Optional but strongly encouraged for translational part:

availability of FFPE tumor material from cytoreductive surgery

Exclusion criteria:

1. Patients with past medical history interfering with radical cytoreductive surgery
2. Patients undergoing surgery solely for palliative intent
3. Patients with secondary malignancies requiring abdominal surgical treatment

Surgery studies under activation - STREAM-1

Group	Country	No sites planned	No sites activated	No sites active	No patients planned	No patients recruited
AGO/NOGGO	Germany	28	20	7	566	98
	United Kingdom	1	1	1	60	2
AGO-Austria	Austria	5	0	0	108	0
BGOG	Belgium	4	0	0	82	0
CEEGOG	Czech Republic	4	1	0	201	0
	Hungary	1	0	0	25	0
	Slovenia	1	0	0	15	0
GINECO	France	4	0	0	95	0
ISGO	Israel	1	0	0	40	0
MaNGO	Italy	10	0	0	172	0
SwissGo	Switzerland	12	4	2	154	2
		71	26	10	1518	102

Global Update April 2025

ENGOT model: A
Sponsor: AGO Study Group
Planned no. of sites: ~ 63
Planned no. of patients: ~ 800

List of MaNGO sites interested (to be confirmed)

1	Manerbio	ASST Garda
2	San Fermo	Ospedale Sant'Anna
3	Firenze	AOU Careggi
4	Milano	Istituto Europeo di Oncologia
5	Milano	Istituto Nazionale Tumori
6	Milano	Ospedale Niguarda
7	Parma	AOU Parma
8	Reggio Emilia	Ospedale S. Maria Nuova
9	Torino	Ospedale Mauriziano
10	Monza	Ospedale S. Gerardo
11	Lecco	Ospedale Manzoni

The MaNGO coordinating unit has just received the intergroup agreement to officially delegate MaNGO for the submission of the study in Italy.

The activation process in Italy is restarting, a confirmation of intrerest will be sent to all sites

Cervical cancer

Surgery studies under activation – **G-LACC**

GERMAN-FUNDED LAPAROSCOPIC APPROACH TO CERVICAL CANCER (G-LACC)

A Randomized Clinical Trial for Early-Stage Cervical Cancer

Responsible Investigator

Prof. Dr. Peter Hillemanns
Hannover Medical School
Department of Gynecology and Obstetrics
Phone: +49 511 532-6144
Email: hillemanns.peter@mh-hannover.de

Co-Investigators

Prof. Dr. Rüdiger Klapdor
Albertinen Hospital | Hamburg
Department of Gynecology and Obstetrics

Prof. Dr. Hermann Hertel
Hannover Medical School
Department of Gynecology and Obstetrics

Study Title:

A randomized clinical trial comparing laparoscopic or robot-assisted radical/simple hysterectomy versus abdominal radical/simple hysterectomy in patients with early-stage cervical cancer

Objectives

Primary Objective:

To investigate the oncologic safety of laparoscopic or robot-assisted radical / simple hysterectomy (LRH) compared to abdominal radical / simple hysterectomy (ARH) using pre-specified surgical techniques and qualitative standards and to demonstrate the non-inferiority of LRH compared to ARH with a non-inferiority margin of 2.3 for the hazard ratio (HR) for disease free survival (DFS), defined as the time from randomization to disease recurrence or death from any cause (whichever occurs first).

Secondary Objective:

To evaluate overall survival, disease recurrence, quality of life, complications and treatment-associated morbidity, treatment costs and cost effectiveness.

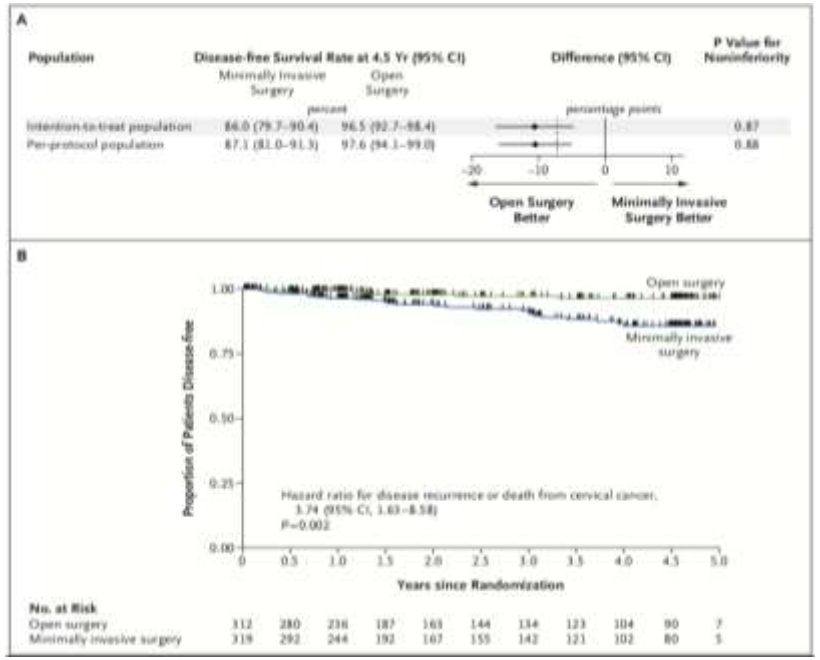
The NEW ENGLAND JOURNAL of MEDICINE

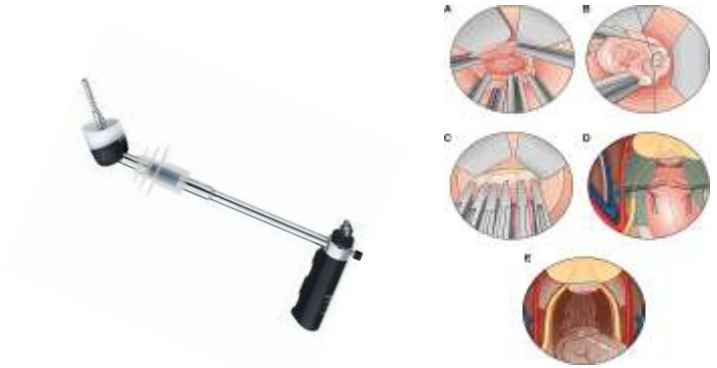
ESTABLISHED IN 1812 NOVEMBER 15, 2018 VOL. 379 NO. 20

Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer

Pedro T. Ramirez, M.D., Michael Frumovitz, M.D., Rene Pareja, M.D., Aldo Lopez, M.D., Marcelo Vieira, M.D., Reitan Ribeiro, M.D., Alessandro Buda, M.D., Xiaojian Yan, M.D., Yao Shuzhong, M.D., Naven Chetty, M.D., David Isla, M.D., Mariano Tamura, M.D., Tao Zhu, M.D., Kristy P. Robledo, Ph.D., Val Gebski, M.Stat., Rebecca Asher, M.Sc., Vanessa Behan, B.S.N., James L. Nicklin, M.D., Robert L. Coleman, M.D., and Andreas Obermair, M.D.

ABSTRACT





LACC Trial – Unanswered Questions

- Successful MIS RCT in endometrial, gastric and colorectal CA - What's different in cervical cancer?
- Use of uterine manipulator through large tumor mass/peritoneal seeding- technical issues?
- Subgroup analysis needed: tumor size, histology, surgery type (typ II-III RH), surgeon and institutional volume
- High performing open surgery arm: 2-10% in prior large studies
- Surgical Proficiency: LACC required only 10 prior cases of MIS RH (vs 30-50 +)
- Apparent low LACC trial partecipation in countries where MIS is surgery of choice
- Short term follow-up of 0-75 months

Open question for tumor >2 cm

GYNECOLOGIC ONCOLOGY

OFFICIAL PUBLICATION OF THE SOCIETY OF GYNECOLOGIC ONCOLOGY

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[1,2,*], Qin C Zhou[3], Benny Brandt[1], Alexia Iasonos[3], Vasileios Sioulas[1,2], Katherine LAVIGNE MAGER[1,3], Mark Shahin[4], Shaina Bruce[4], Destin R Black[5,6], Carrie G Kay[6], Meeli Gandhi[5], Maira Qayyum[5], Jennifer Scalici[7], Nathaniel L Jones[7], Rajesh Paladugu[7], Jubilee Brown[8], R. Wendel Naumann[8], Monica D Levine[8,6], Alberto Mendivil[9], Peter C Lim[10], Elizabeth Kang[10], Leigh A Cantrell[11], Mackenzie W Sullivan[11,7], Martin A Martino[12], Melissa K Kratz[12], Valentin Kolev[13], Shannon Tomita[13], Charles A Leath III[14], Teresa KL Boitano[14], David W Doo[14,8], Colleen Feltmate[15], Ronan Sugrue[15], Alexander B Olawaiye[16], Ester Goldfeld[16], Sarah E Ferguson[17,18], Jessa Suhner[19], Nadeem R Abu-Rustum[1,2]

MIRH, including RRH, was associated with lower perioperative morbidity and faster recovery

Methods: This is a multi-institutional, retrospective cohort study of patients with 2009 FIGO stage IA1 (with lymphovascular space invasion) to IB1 cervical carcinoma from 1/2007-12/2016. Patients who underwent preoperative therapy were excluded. Squamous cell carcinoma, adenocarcinoma, and adenosquamous carcinomas were included. Appropriate statistical tests were used.

Results: We identified 1093 cases for analysis—715 MIS (558 robotic [78%]) and 378 OPEN procedures. The OPEN cohort had more patients with tumors >2 cm, residual disease in the hysterectomy specimen, and more likely to have had adjuvant therapy. Median follow-up for the MIS and OPEN cohorts were 38.5 months (range, 0.03-149.51) and 54.98 months (range, 0.03-145.20), respectively. Three-year PFS rates were 87.9% (95% CI: 84.9-90.4%) and 89% (95% CI: 84.9-92%), respectively (P=0.6). On multivariate analysis, the adjusted HR for recurrence/death was 0.70 (95% CI: 0.47-1.03; P=0.07). Three-year OS rates were 95.8% (95% CI: 93.6-97.2%) and 96.6% (95% CI: 93.8-98.2%), respectively (P=0.8). On multivariate analysis, the adjusted HR for death was 0.81 (95% CI: 0.43-1.52; P=0.5).

Conclusion: This multi-institutional analysis showed that an MIS compared to OPEN radical hysterectomy for cervical cancer did not appear to compromise oncologic outcomes, with similar PFS and OS.

Following the alarming results of the LACC study, data were extracted from the **Swedish Quality Register for Gynecologic Cancer**
Among 852 women treated during 2011-2017, **no difference was observed for disease-free survival between minimally invasive surgery (n = 628) and laparotomy (n = 263)** considering that **all women** in the former group were treated by **robotic surgery**. Additionally, the study highlighted that RRH was associated with lower intraoperative blood loss and shorter postoperative recovery times.

Alfonzo E, et al. Eur J Cancer. 2019

Similar data were obtained from the Danish database
"Danish Gynecological Cancer Database."

Only **15.6%** in **LACC trial** and **21.5%** in **SUCCOR trial** of the procedures in the **MIS arm** were performed with **robotic radical hysterectomy**

Robotic-assisted surgery

Table 2. The baseline characteristics of RACC vs. ROCC Trial

Feature	RACC Trial	ROCC Trial (GOG-3043)
ClinicalTrials.gov Identifier	NCT03739944	NCT04831580
Start date	May 28, 2019	Mar 22, 2022
Objective	To compare RRH with open surgery for early-stage cervical cancer	To compare RRH with open surgery for early-stage cervical cancer
Primary outcome	PFS at 5 years	PFS at 3 years
Secondary outcomes	OS, perioperative morbidity, QOL, diagnostic accuracy of sentinel node algorithm, healthcare costs	OS, intraoperative and postoperative complications, QOL, healthcare costs
Study design	Multicenter, RCT, open-label	Multicenter, RCT, open-label, non-inferiority
Sample size	Approximately 800 participants	Approximately 800 participants
Eligibility criteria	FIGO stages IA2, IB1, IB2, no metastatic disease	FIGO stages IA2, IB1, IB2, no metastatic disease
Exclusion criteria	Neuroendocrine histology, history of pelvic or abdominal radiotherapy, other malignancies within 5 years	Neuroendocrine histology, history of pelvic or abdominal radiotherapy, other malignancies within 5 years

Open access Protocol

BMJ Open

Efficacy of different surgical approaches in the clinical and survival outcomes of patients with early-stage cervical cancer: protocol of a phase III multicentre randomised controlled trial in China

Xiaopei Chao, Lei Li, Ming Wu, Shuiqing Ma, Xianjie Tan, Sen Zhong, Jinghe Lang, Aoshuang Cheng, Wenhui Li

The Chinese LACC trial plans to randomly assign 1448 patients in 28 centers in China to undergo **MIS (robot-assisted or laparoscopic RH)** or **abdominal RH** with the requirement of **experienced surgeons**.Strict guidelines for preventive maneuvers and possible tumor hygiene are not implemented.

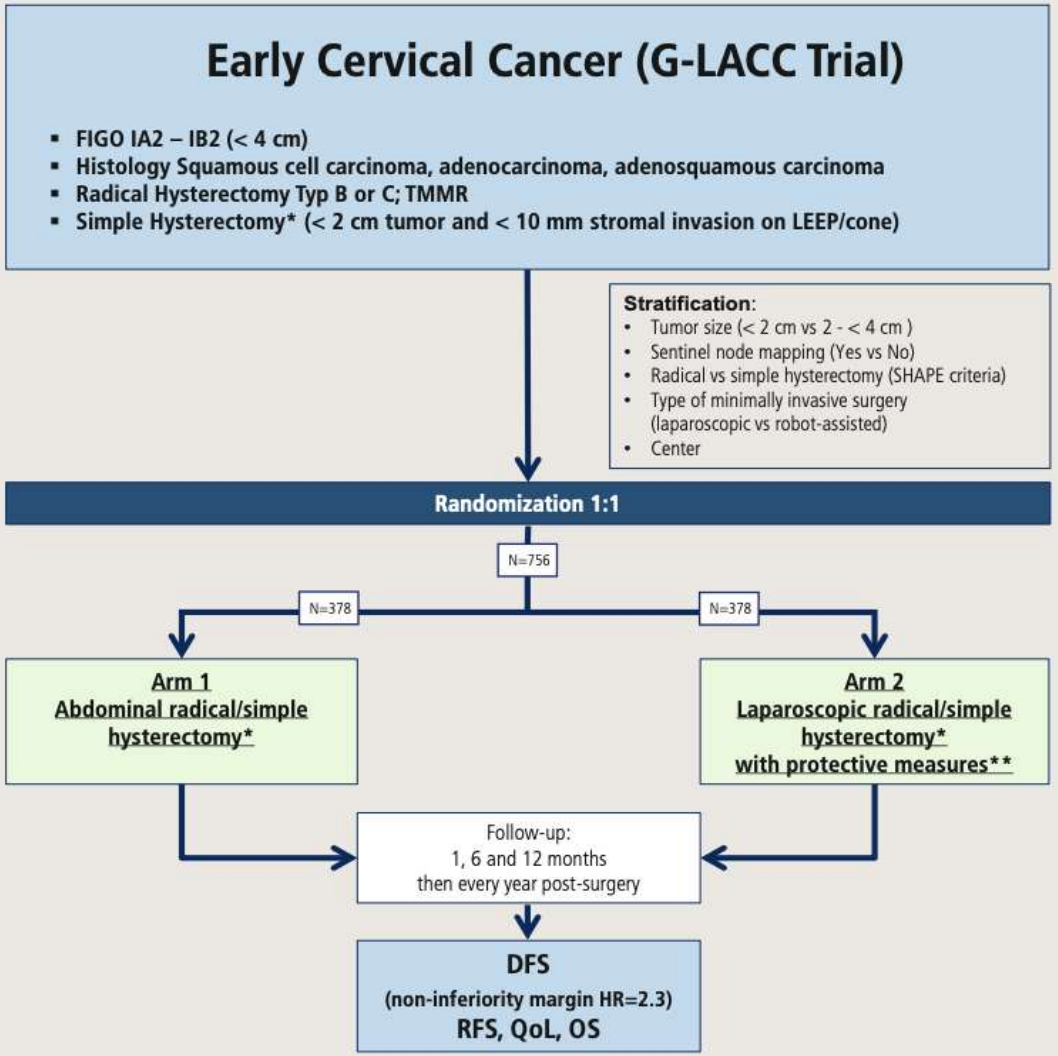


Fig. 1: Study schema of the G-LACC trial. DFS, disease-free survival; HR, hazard ratio; RFS, recurrence-free survival; QOL, quality of life; OS, overall survival; SLN, sentinel lymph node.

Surgery includes pelvic lymph node dissection or optional sentinel lymph node biopsy (SNB) according to current guidelines

*1 Simple hysterectomy can be considered for patients with low-risk early-stage cervical cancer (SHAPE-criteria: tumor < 2 cm and < 10 mm depth of stromal invasion (LEEP/cone) BUT has to be determined BEFORE randomization. In case of simple hysterectomy, extrafascial hysterectomy with max. 5mm vaginal cuff is required to ensure negative margins. [1]

*2 Tumor size assessment: the measurement in any prior specimens (loop / cone excision) has to be taken into account. It is recommended to add together the maximum lateral measurements in different specimens. **tumor size = loop/cone specimen + surgical specimen.** [2]

** Protective measures: LEEP/conisation before randomization or closure of the vagina before colpotomy. Transcervical manipulators are not permitted. Use of uterus manipulators / cervical adapter (without transcervical device) are allowed only after LEEP/conization.

Surgery studies under activation – G-LACC

Global update:

- 31 German sites under contract
- **24 German sites with recruitment approval**
- 7 national sites in the setup phase
- **46 patients have been enrolled at 14 sites**

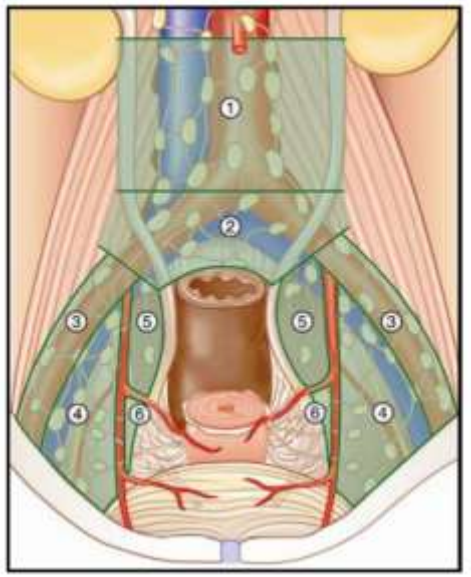
Activation status

- The MaNGO surgery group expressed interest to participate and the coordinator/sponsor (Hannover Medical School) is informed
- The MaNGO sites list is under defintion (INT-Milano, AUO Padova, Catania Humanitas already expressed interest)
- "The Sponsor is willing to cover the insurance costs for the Italian sites and is actively seeking a solution, as the German Cancer Aid funds are not available for this purpose.“
- MaNGO is in contact with the coordinator to receive soon documents/instructions for the activation

GCIG GYNECOLOGIC CANCER INTERGROUP

ENGOT European Network of Gynaecological Oncological Trial groups

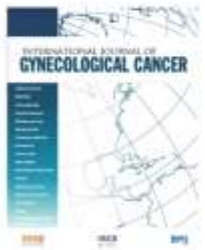
ENGAGe ESGO European Network of Gynaecological Cancer Advocacy Groups



PAROLA GINECO-CE110b, ENGOT-cx11

PARa-aOrtic LymphAdenectomy in LACC

Clinical trial

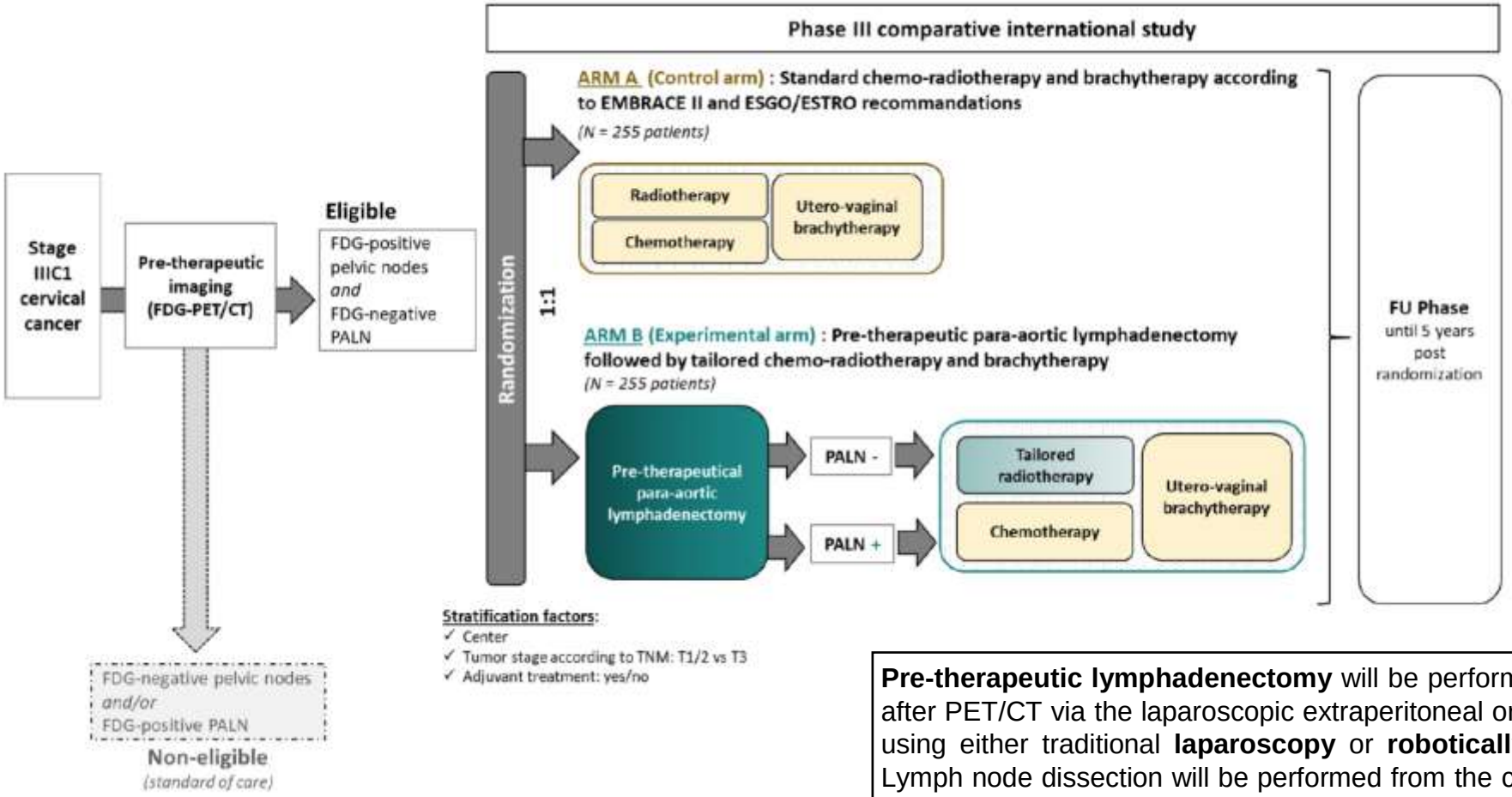


PARa-aOrtic LymphAdenectomy in locally advanced cervical cancer (PAROLA trial): a GINECO, ENGOT, and GCIG study

Alejandra Martinez [1,2] Fabrice Lecuru,[3] Nicolò Bizzarri [4] Cyrus Chargari,[5] Anne Ducassou,[6] Anna Fagotti [4] Francesco Fanfani [4] Giovanni Scambia [4] David Cibula,[7] Berta Díaz-Feijoo [8] Antonio Gil Moreno,[9] Martina Aida Angeles [9] Mustafa Zelal Muallem,[10] Christhardt Kohler,[11] Mathieu Luyckx,[12] Frederic Kridelka,[13] Agnieszka Rychlik [14] KG Gerestein,[15] Viola Heinzelmann,[16] Pedro T Ramirez [17] Michael Frumovitz [17] Gwenael Ferron [1] Sarah Betrian,[18] Thomas Filleron,[19] Christina Fotopoulou [20] Denis Querleu [4] the PAROLA Study group

- International guidelines differ in staging modalities to assess para-aortic lymph node status in **locally advanced disease cervical cancer**
- **PET/CT** is the most accurate imaging exam to assess para-aortic lymph node involvement. However, PET/CT underestimates para-aortic lymph node metastasis, and **fails to detect small volume disease <5 mm**
- PET/CT false-negative results in the para-aortic area have been recorded in **<5% of patients without pelvic lymph node involvement**, and in **20–30% of patients with pelvic lymph node uptake**
- For this reason, ESGO and NCCN guidelines consider **para-aortic lymph node dissection** as an option for staging purposes in patients with positive pelvic nodes and negative para-aortic lymph nodes on pre-treatment FDG-PET/ CT. In contrast, **prophylactic extended-field chemoradiation** may be considered to overcome the PET/CT false negative rate in para-aortic lymph nodes

- **RT** could result in overtreatment and unnecessary toxicity in approximately 75% of patients with positive pelvic lymph nodes and negative para-aortic lymph nodes on pre-treatment PET/CT
- The high morbidity rates of extended-field chemoradiation associated with conventional radiotherapy have been largely reduced since the use of **intensity modulated radiation therapy (IMRT)** extended-field chemoradiation, with toxicity rates ranging from 4–10%



Pre-therapeutic lymphadenectomy will be performed no later than 3 weeks after PET/CT via the laparoscopic extraperitoneal or transperitoneal approach using either traditional **laparoscopy** or **robotically-assisted laparoscopy**. Lymph node dissection will be performed from the common iliac bifurcation to at least the **inferior mesenteric artery.**
Chemo-radiation will start **7 to 10 days after surgery** and a **maximum 3 weeks** after surgical staging.

Surgery studies under activation - **PAROLA**

Update April 2025

- N= 23 patientes included
  Arm A (contrôle): 12
  Arm B (expérimental): 11

ENGOT
European Network of Gynaecological Oncological Trial groups

- The MaNGO surgery group expressed interest to participate
- The MaNGO sites list is under defintion (INT-Milano, Policlinico Catania, S.Anna Torino already expressed interest)
- Insurance is not provided by the Sponsor. An insurance quotation will be required soon by MaNGO CTU. The approval of MaNGO CTS will be required to use MaNGO funds
- MaNGO is waiting for documents/instructions from the coordinator

Vulvar cancer

Clinical trial

Primary chemoradiation versus neoadjuvant chemotherapy followed by surgery as treatment strategy for locally advanced vulvar carcinoma (VULCANize2)

Frédéric Amant [1,2] Anne Fleur van Velzen [2,3] An Reyners,[4] Henry Zijlmans,[2] Eva E Schaake,[5] Linda Nooij [3]

- **10-20%** present with **locally advanced VC** (LAVC). Patients with LAVC present with larger tumours (T3 or T4), extensive nodal disease and/or tumours with close proximity to the urethra or anal sphincter.
- Primary surgery in these patients often involves exenteration of all or part of all pelvic organs leading to a **colostomy** or **urinary diversion**.
- For some patients with LAVC, surgery is not possible due to comorbidities or due to the size or localisation of the tumour.

Background

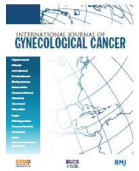
- In the last decade, **primary chemoradiation (external beam radiotherapy combined with cisplatin)** has emerged as an alternative and organ-sparing treatment option for these patients.
- Chemo-radiation -> LIMITED EVIDENCE AND EFFICACY
- This treatment is also associated with high morbidity, consisting of desquamation of the vulvar skin, pain, dermatitis, urinary toxicity and gastro-intestinal toxicity.

Background

- **Neo-adjuvant chemo (NACT)** have limited but promising data in gyn cancer and LA vulvar cancer

- **NACT+surgery** is oncologically safe, potentially more effective than primary CTRT in establishing **long lasting locoregional control**, and associated with **less treatment-related morbidity**.

Clinical trial



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Participants

INCLUSION CRITERIA

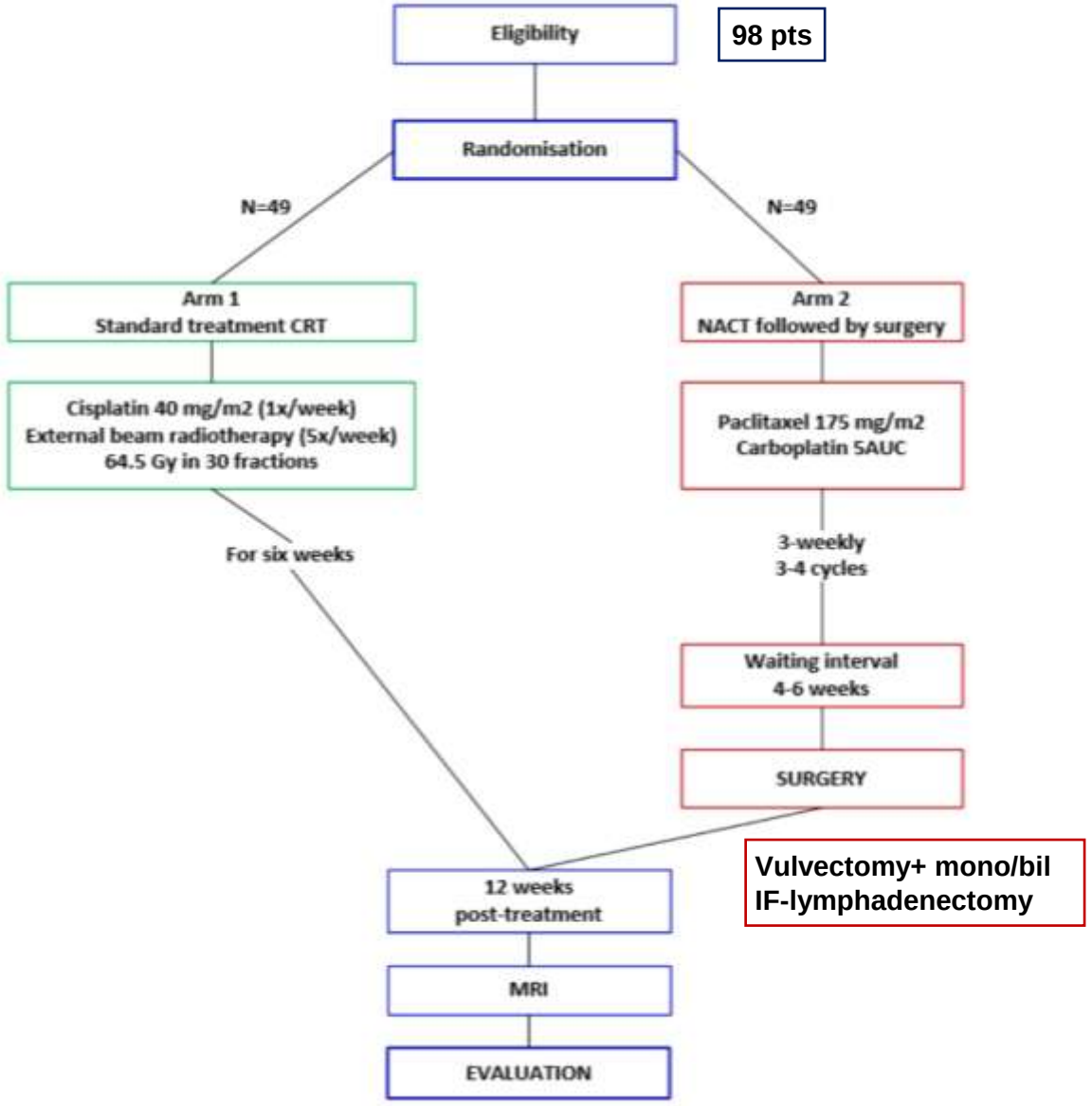
- ≥18 y
- Histologically-confirmed **primary or recurrent squamous cell carcinoma vulvar cancer** FIGO stage II – IVa, T2 or higher, any N, M0
- The local tumor size or localization of the tumor must require treatment through primary chemoradiation, or extensive surgery, meaning surgery damaging pelvic organs, exenterative surgery or irresectable groin metastases
- WHO PS 0–2
- Adequate hematological, hepatic, and renal function, no pregnant

EXCLUSION CRITERIA

- Patients will be excluded if they have positive pelvic nodes, previous RT pelvis or groins, or have existing neuropathy which will hinder the administration of chemotherapy.

TREATMENT ARMS

- **ARM1 Standard treatment** **weekly cisplatin 40 mg/m2** combined with 30 fractions of external beam **radiotherapy** on the primary tumor with a total dose of **64.5 Gy** (total of 6 weeks)
- Patients with clinically tumour negative LN or cytologically proven positive LN ≤ 2cm (or with 1 positive SLN): irradiation treatment of the groin(s) and pelvic area (up to the common iliacs)
- If a patient presents with bulky nodes (>2 cm), groins debulking might be performed before the start of chemoradiation.
- **ARM 2 NACT followed by surgery** **Paclitaxel** 175 mg/m2, followed by **carboplatin** AUC 5, q3w, **3-4 cycles** (with evaluation after 2 courses of chemotherapy by physical examination)
- Radical surgery in responding patients (4–6 week interval after last CT).
- If indicated, adjuvant radiotherapy of the vulva and/or groin(s) can be performed after surgery.
- **Treatment response:** gynecological examinations, including pictures with a ruler in two directions during the treatment protocol, and MRI after finishing the treatment protocol.
- Follow-up including physical examination and adverse events.



Surgery studies under activation - **VULCANIZE**

- The study is active in Netherlands. The sponsor would expand the network to other EU countries
- MaNGO surgery group expressed interest to participate
- The MaNGO sites list is under defintion (Brescia Spedali Civili, S.Anna Torino, Policlinico Catania, INT-Milano, S.Gerardo Monza)
- Insurance is not provided by the Sponsor. An insurance quotation will be required soon by MaNGO CTU. The approval of MaNGO CTS will be required to use MaNGO funds.