"Ovary-whelmed" Don't let ovarian cancer scare you

Gynecological Cancers Educational Program

November 24th, 2018

Objectives

At the end of this session, participants will be able to:

- Recognize the possible presentations and symptoms of ovarian cancer
- Describe the diagnosis and work up of a suspected ovarian cancer
- Review the natural history of this disease
- Discuss the different treatment options
- Summarize the post treatment surveillance and management of recurrence

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Epidemiology

- Second most common gynecologic malignancy
- Most common cause of death from a gynecological cancer
- Fifth most lethal cancer in women
- 1.5% lifetime incidence
- Median age 63 years

Siegel *et al*, Cancer statistics, 2013. CA CANCER J CLIN 2013; Canadian Cancer Statistics 2017
Kurman *et al*, WHO Classification of Tumors of Female Reproductive Organs, IARC 2014

Genetics

- Hereditary predisposition = 15-20%
- Inactivation of BRCA 1 or 2 (somatic or germline) in ≈50% of HGSCs
- Life-time risk of ovarian cancer:
  - BRCA 1 → 50%
  - BRCA 2 → 20%
  - Lynch → 10-12%
  - Family history → 3-5%
- Other DNA-repair genes involved

Kurman *et al*, WHO Classification of Tumors of Female Reproductive Organs, IARC 2014

Histologies

- **Epithelial (90%)**
  - **High grade serous 63%**
  - Endometrioid 10%
  - Clear cell carcinoma 10%
  - Mucinous 9%
  - Carcinosarcoma 5%
  - Brenner 0.3%
  - Low-grade serous 2.5%
  - Others
- Germ cell tumors
- Sex cord-stromal tumors

Peres *et al*, Invasive Epithelial Ovarian Cancer Survival by Histotype and Disease Stage, J Natl Cancer Inst. 2018
La Vecchia, Ovarian cancer: epidemiology and risk factors. European Journal of Cancer Prevention. 2017

Borderline Serous Tumors

- Lack of frank invasion (microinvasion <5 mm possible)
- Greater epithelial proliferation and cytological atypia than benign serous tumors
- Confined to the ovary in the majority of cases

- *Non-invasive* or *invasive* implants
- Very good prognosis, but may recur after 15-20 years
- 5% mortality from progression to low-grade serous carcinoma

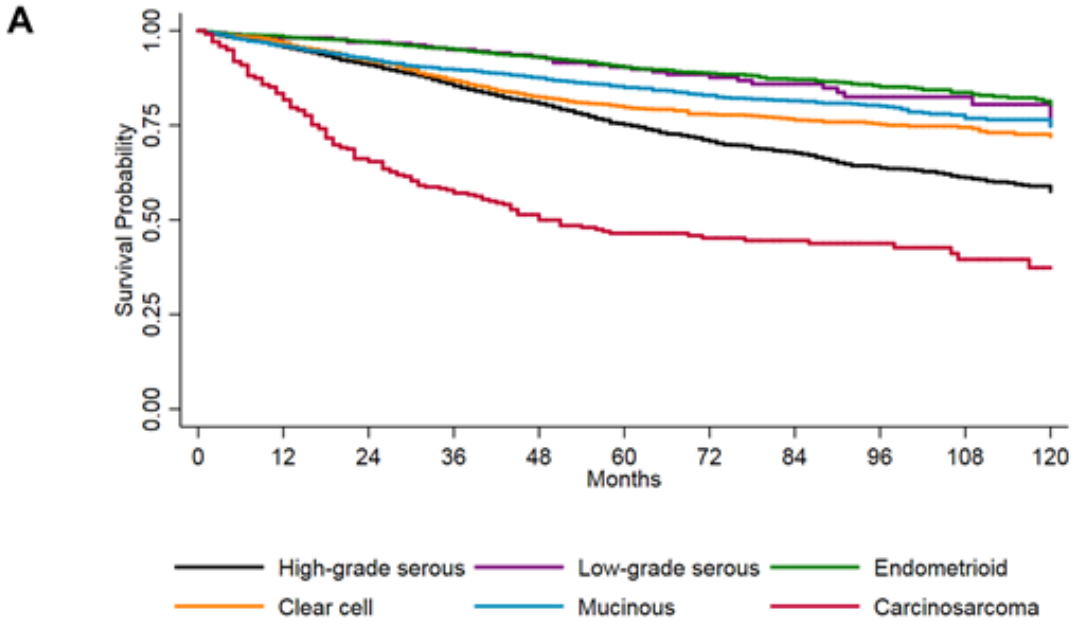
Kurman *et al*, WHO Classification of Tumors of Female Reproductive Organs, IARC 2014

Pathology implications

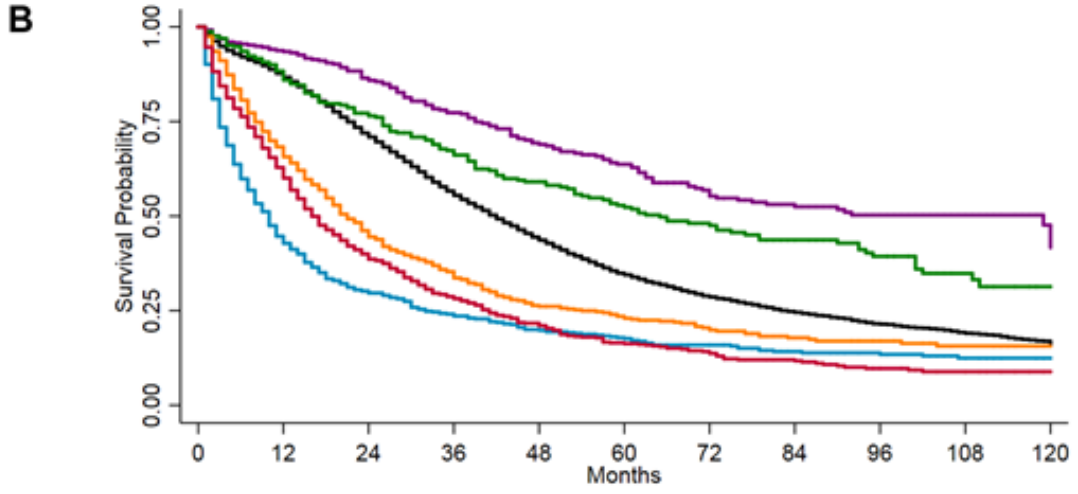
- Endometrioid:
  - Associated with endometriosis.
  - Concomitant endometrioid carcinoma of the endometrium in 15-20% of cases.
- Clear cell:
  - Associated with endometriosis.
  - Good prognostic if localized to one ovary.
  - Poor response to chemotherapy.
- Mucinous:
  - Large cystic mass.
  - Can be a metastasis from the G-I tract.
  - Favourable prognosis if localized.
- Carcinosarcoma: bad…

Kurman *et al*, WHO Classification of Tumors of Female Reproductive Organs, IARC 2014

A: Localized and regional-stage disease



B: Distant stage disease



Peres *et al*, Invasive Epithelial Ovarian Cancer Survival by Histotype and Disease Stage, J Natl Cancer Inst. 2018

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Risk factors

Risk factors	Preventive factors
Family history	Parity
Weight	OCP (↓ 25-50%)
BMI	Fruits
HRT (recent users RR=1.34 for HGS and endometrioid)	Physical activitiy
Meat and fat	Salpingectomy
	Tubal ligation

La Vecchia, Ovarian cancer: epidemiology and risk factors. European Journal of Cancer Prevention. 2017

Natural history

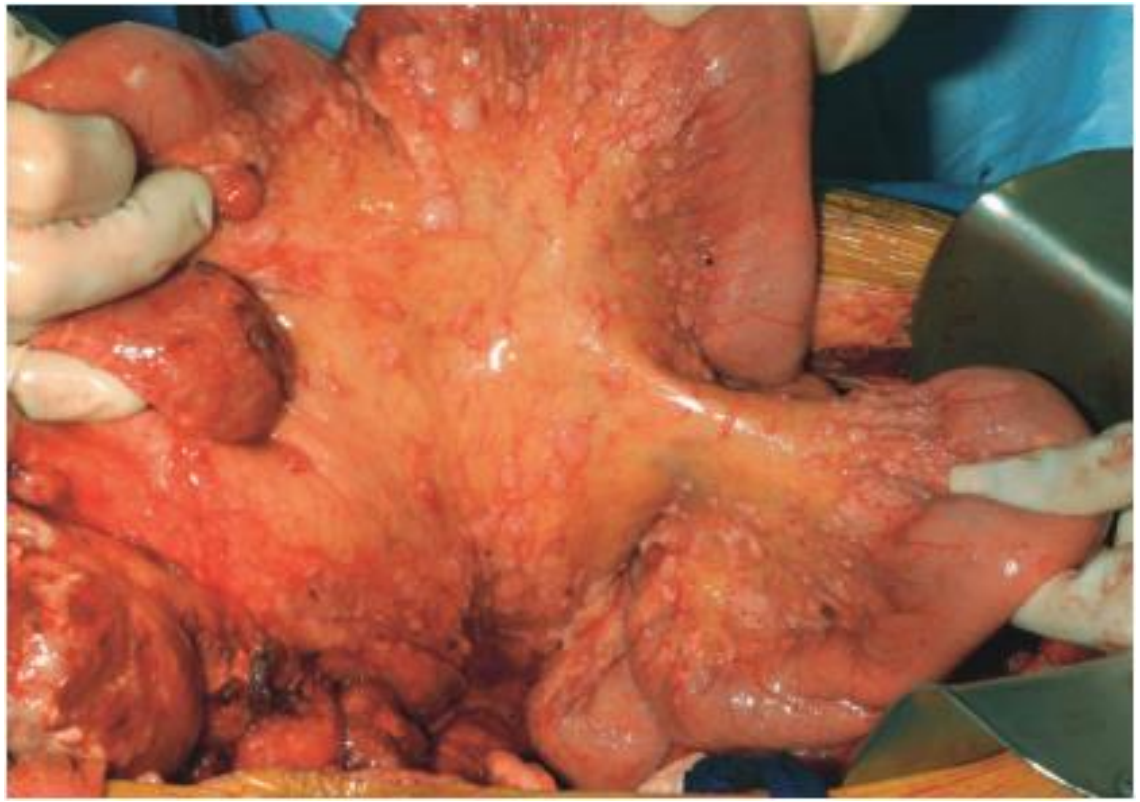
- Multiple possible etiologies described:
  - Mullerian metaplasia
  - Precancerous lesions found in fallopian tubes

- Serous tubal intraepithelial carcinoma (STIC) present in 60-80% of women with HGSC
- High level of genetic instability and chromosomal instability
- Rapidly growing and aggressive tumors

Kurman *et al*, WHO Classification of Tumors of Female Reproductive Organs, IARC 2014
Gilbert L. et al, Assessment of symptomatic women for early diagnosis of ovarian cancer: results from the prospective DOvE pilot project
S. Penner-Goeke, Z. et al The Temporal Dynamics of Chromosome Instability in Primary Ovarian Cancer Patient Samples and Cell Lines. April 2017. PLOS Genetics. 13(4): 1-24

Patterns of Spread

- Peritoneum
- Bowel
- Liver
- Lymph nodes
- Lung
- Bones
- Brain



Deng *et al*, Sites of distant metastases and overall survival in ovarian cancer: A study of 1481 patients. Gynecologic Oncology. 2018
WP Cellen, editor. Peritoneal Carcinomatosis A multidisciplinary Approach. Springer. 2017

“The Silent Cancer” A misconception

- Pelvic pain or pressure
- Urinary frequency
- Bloating and gastrointestinal symptoms
- Adnexal mass discovered during physical exam
- Incidental finding at imaging or during a non related surgery
- Dyspnea from malignant pleural effusion
- DVT
- Paraneoplastic syndromes

Andersen *et al*, Combining a Symptoms Index With CA 125 to Improve Detection of Ovarian Cancer, American Cancer Society. 2009
Viau *et al*, Paraneoplastic syndromes associated with gynecological cancers: A systematic review, Gynecologic Oncology. 2017

“The Silent Cancer”
A misconception

- Women with ovarian cancers are symptomatic often several months before diagnosis

- A survey of 1725 women with ovarian cancer showed:
  - 70% had symptoms for ≥ 3 months
  - 35% for ≥6 months
  - 75% had abdominal or gastrointestinal symptoms before diagnosis
  - 50% had pain or constitutional symptoms before diagnosis

Goff *et al*, Ovarian carcinoma diagnosis. Cancer. 2000

Screening in low-risk women

- Relatively low incidence and prevalence in the general population
- Positive screening results most often in surgery with potential morbidity and substancial financial costs
- Screening performed by pelvic exams not recommended by USPSTF and CPTF
- **However** → has never been studied properly
- Pelvic exam still recommended by SOGC, GOC, ACOG, SGO

Bibbins-Domingo *et al*, Screening for Gynecologic Conditions With Pelvic Examination: US Preventive Services Task Force Recommendation Statement. JAMA. 2017
A.D. Altman et al, Examining the effects of time-to-diagnosis, income, symptoms and incidental detection on overall survival in ovarian cancer: Manitoba Ovarian Cancer Outcomes (MOCO) study group. Int J Gynecol Cancer. 2017 Oct

Screening in low-risk women

- **PLCO:**
  - Annual CA-125 and transvaginal U/S VS usual care
  - 78 216 postmenopausal women
  - In screening group (39 111 women): 3285 false-positive results causing 1080 surgeries with a 15% complication rate
  - No difference in mortality
- **UKCTOCS:**
  - 3 arms: multi-modal screening with CA-125 algorithm and U/S, annual transvaginal U/S or no screening
  - 202 638 postmenopausal women over 14 years
  - Mortality reduction not significant in the primary analysis

Buys *et al*, Effect of screening on ovarian cancer mortality: the Prostate,Lung, Colorectal and Ovarian (PLCO) Cancer Screening Randomized Controlled Trial. JAMA. 2011Jacobs *et al*, Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening(UKCTOCS): a randomised controlled trial. Lancet. 2016

Investigations

- Initial investigation for a pelvic mass:
  - History
  - Comprehensive physical examination
  - CA-125
  - Transvaginal or transabdominal U/S

Table 2. The risk of malignancy index (RMI) scoring system

Ultrasound features	RMI I score	RMI II score
Multilocular cyst	0 = no abnormality	1 = no or one abnormality
Presence of solid areas	1 = one abnormality	4 = two or more abnormalities
Bilaterality of lesions	3 = two or more abnormalities	
Presence of ascites		
Presence of intra-abdominal metastasis		
Premenopausal	1	1
Postmenopausal	3	4
CA125 level	U/mL	U/mL

Example: A postmenopausal woman with a multilocular cyst with solid areas with ascites and a CA125 level of 100 has a RMI II score of 4 × 4 × 100 = 1600.

- Cytology on ascites or pleural fluid
- Omentum or pelvic mass biopsy for advanced disease
- Other tumor markers as appropriate
- CT abdomen and pelvis

SOGC, Initial Evaluation and Referral Guidelines for Management of Pelvic/Ovarian Masses. 2009

FIGO Staging

Stage	
I	Growth limited to the ovaries
II	Tumor involves one or both ovaries or fallopian tubes with pelvic extension below pelvic brim, or primary peritoneal cancer
III	Peritoneal metastasis outside the pelvis and/or metastasis to the retroperitoneal lymph nodes
IV	Distant metastasis

Pronostic

Stage	5-year survival HGSC (%)
Localized	84.0
Regional	67.7
Distant	32.1

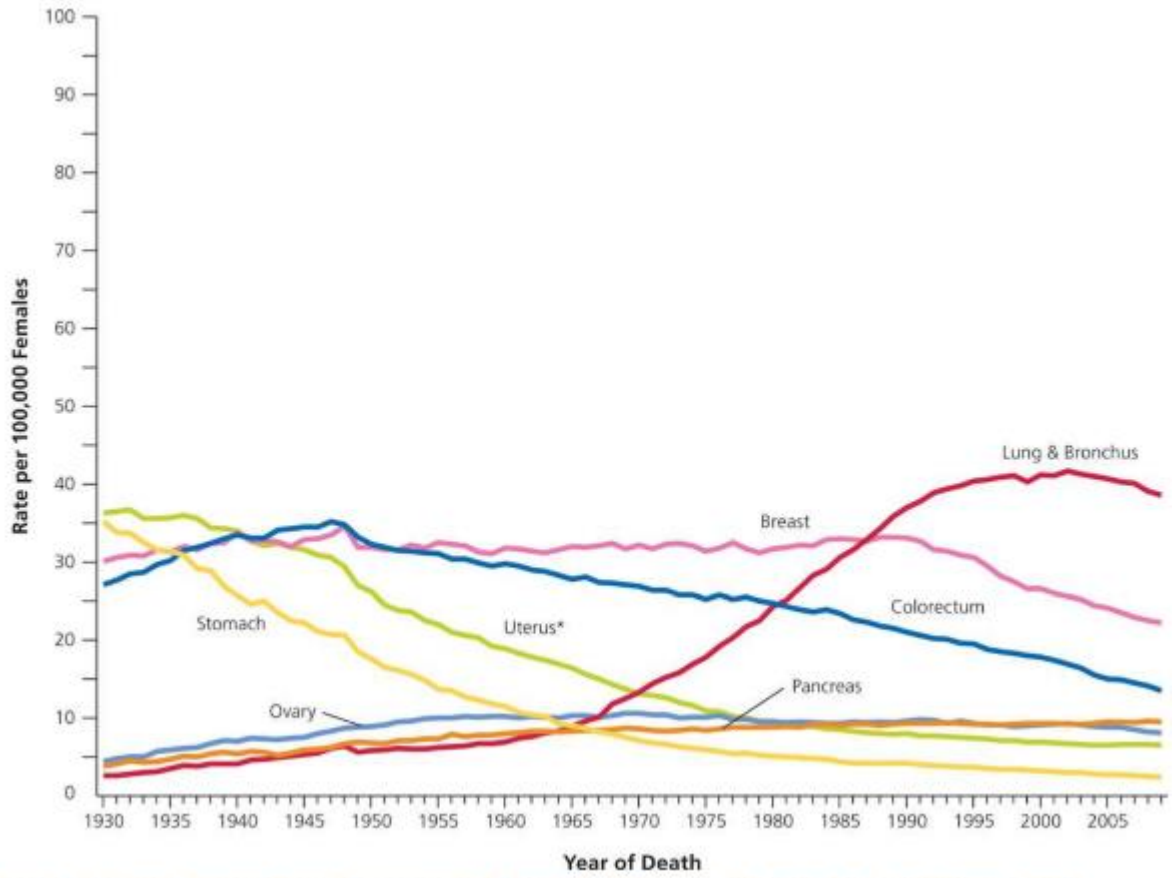


FIGURE 5. Trends in Death Rates Among Females for Selected Cancers, United States, 1930 to 2009.

Peres *et al*, Invasive Epithelial Ovarian Cancer Survival by Histotype and Disease Stage, J Natl Cancer Inst. 2018
Siegel *et al*, Cancer statistics, 2013. CA Cancer J Clin 2013

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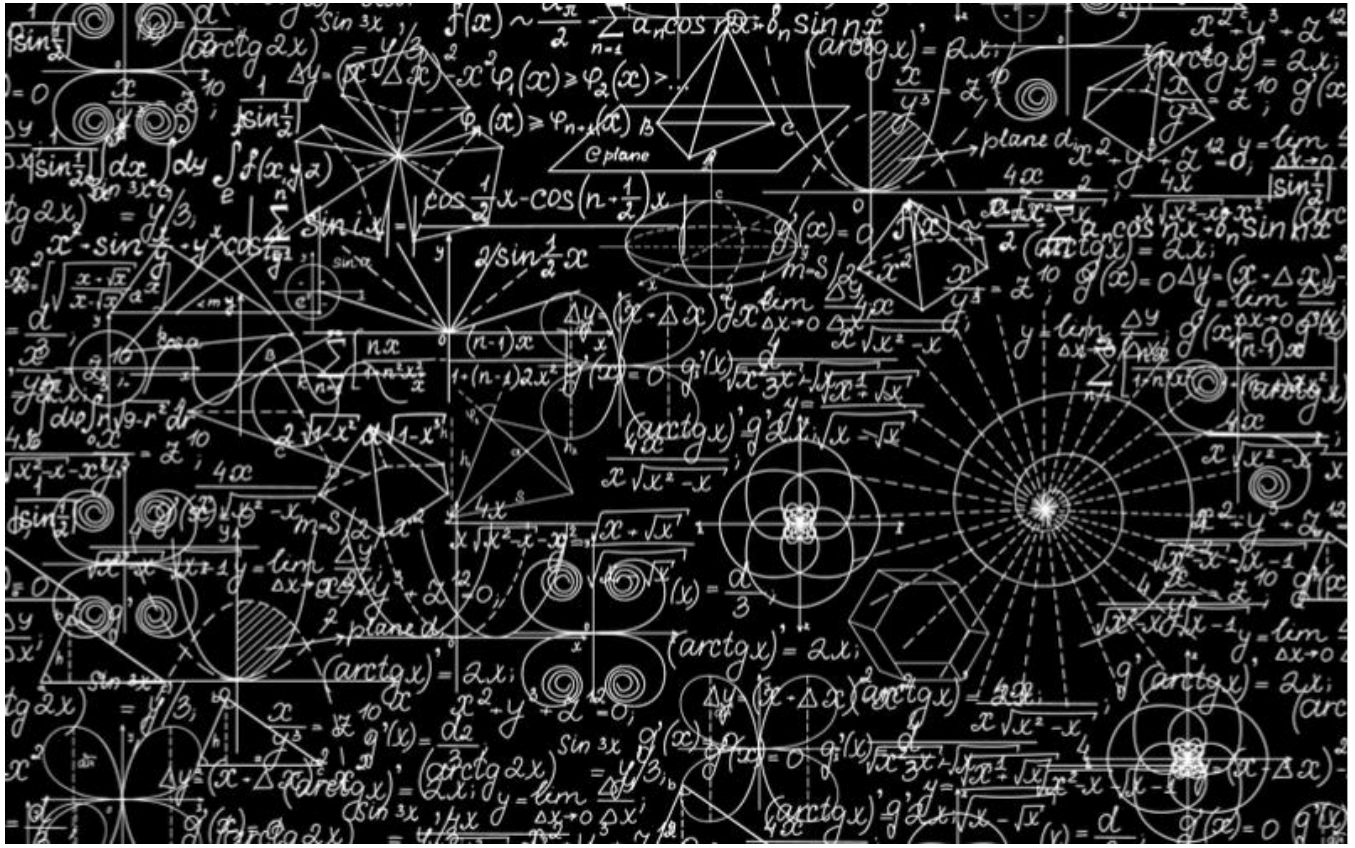
Pronostic factors

Stage
Grade
Histology
Mitotic activity
Aneuploidy
Residual disease
Rupture of ovarian capsule
Volume of ascites and presence of malignant cells in cytology
Lymph node involvement
Age
Performance status

Winter *et al*, Prognostic factors for stage III epithelial ovarian cancer: a Gynecologic Oncology Group Study. J Clin Oncol. 2007
Kurman *et al*, WHO Classification of Tumors of Female Reproductive Organs, IARC 2014

Treatments



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Treatments

- Primary debulking
- Intra-peritoneal chemotherapy (IP)
- Neoadjuvant chemotherapy with interval debulking
- Adjuvant chemotherapy
- Radiation rarely used, mostly to palliate symptoms and in clear cell ovarian cancer

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Surgery

- Total abdominal hysterectomy
- Bilateral salpingo-oophorectomy
- Pelvic and paracolic washings
- Omentectomy
- Pelvic lymphadenectomy
- Paraaortic lymphadenectomy
- Biopsies of peritoneal surfaces
- Cytology of diaphragms
- Appendectomy (if required)

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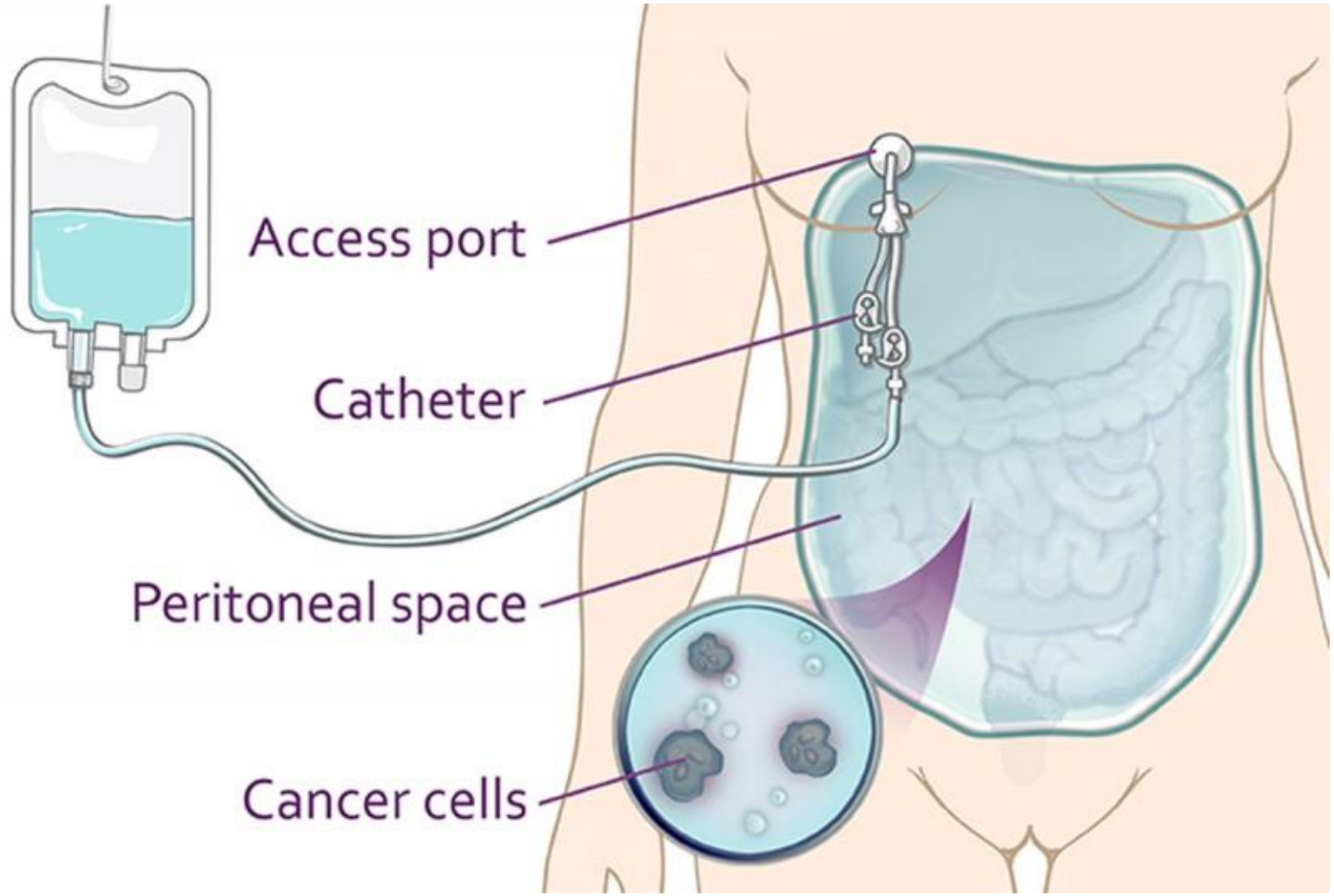
Intraperitoneal chemotherapy



Memorial Sloan Kettering Cancer Center

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Intraperitoneal chemotherapy

- **Alberts, 1996**
  - 546 patients with stage III with <2 cm residual disease
  - Randomisation between:
    IV cyclophosphamide and IP cisplatin OR IV cyclophosphamide and IV cisplatin
  - More complete response and improved OS
- **Markman, 2000**
  - 462 women with stage III disease with largest residual tumor <1 cm
  - IV paclitaxel and cisplatin VS IV paclitaxel and IP cisplatin
  - Significant bone marrow toxicity
  - PFS superior (28 VS 22 months) and OS increased from 52.2 to 63.2 months

Alberts *et al*, Intraperitoneal cisplatin plus intravenous cyclophosphamide versus intravenous cisplatin plus intravenous cyclophosphamide for stage III ovarian cancer. NEJM. 1996
Markman *et al*, Phase III trial of standard-dose intravenous cisplatin plus paclitaxel versus moderately high-dose carboplatin followed by intravenous paclitaxel and intraperitoneal cisplatin in small-volume stage III ovarian carcinoma: an intergroup study of the GOG, SOG, and ECOG.
J Clin Oncol. 2000

Intraperitoneal chemotherapy

- **Armstrong, 2006**
  - 415 women with stage III disease with largest residual tumor <1 cm
  - IV paclitaxel and cisplatin (q21d) VS IV paclitaxel and IP cisplatin and paclitaxel (day 1&8)
  - More complete response
  - Higher PSF (23.8 VS 18.3 months) OS (65.6 VS 49.7 months)
  - Worse quality of life during treatment
- Considerations: complications with IP catheter, toxic effets, specific complications

Armstrong *et al*, Intraperitoneal cisplatin and paclitaxel in ovarian cancer. NEJM. 2006

Neoadjuvant chemotherapy (NACT)

- Consists in three cycles of IV carboplatin and paclitaxel prior to interval debulking
- **EORTC trial 2010**
  - 632 women with stage IIIC or IV ovarian cancer
  - Two arms: primary debulking VS NACT
  - Non-inferiority for PFS or OS
- **CHORUS trial 2015**
  - 552 women with stage III or IV ovarian cancer
  - Neoadjuvant chemotherapy non-inferior to primary surgery for OS
  - More grade 3 or 4 postoperative adverse events in primary surgery group

Vergote *et al*, Neoadjuvant Chemotherapy or Primary Surgery in Stage IIIC or IV Ovarian Cancer. NEJM. 2010
Kehoe *et al*, Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label,randomised, controlled, non-inferiority trial. Lancet. 2015

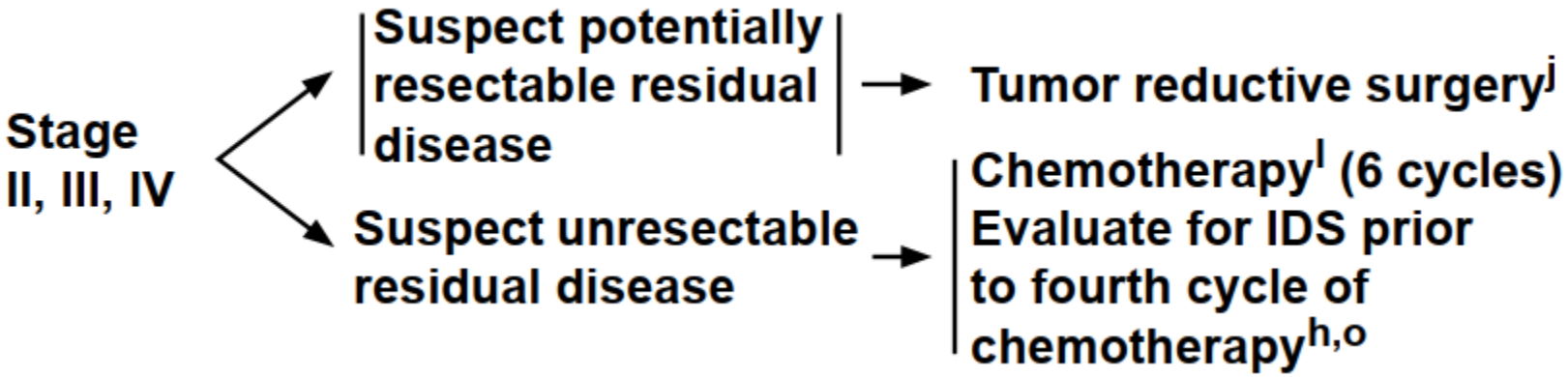
Neoadjuvant chemotherapy (NACT)

- **SCORPION trial 2016**
  - 110 women with high tumor load
  - Primary surgery with adjuvant chemotherapy VS NACT and interval debulking
  - More grade 3 and 4 postoperative complications in primary surgery arm
  - Better quality of life in NACT group
  - PSF data pending

- Ongoing clinical trial (TRUST-trial), but actually an option in women with stage IIIC/IV ovarian cancer, particularly in bulky disease. Treatment should be tailored to the patient

Fagotti *et al*, Phase III randomised clinical trial comparing primary surgery versus neoadjuvant chemotherapy in advanced epithelial ovarian cancer with high tumour load (SCORPION trial): Final analysis of peri-operative outcome. Eur J Cancer. 2016
Morrison et al, Chemotherapy versus surgery for initial treatment in advanced ovarian epithelial cancer. Cochrane Database. 2012

NCCN recommandation



NCCN Clinical Practice Guidelines in Oncology – Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer. 2018

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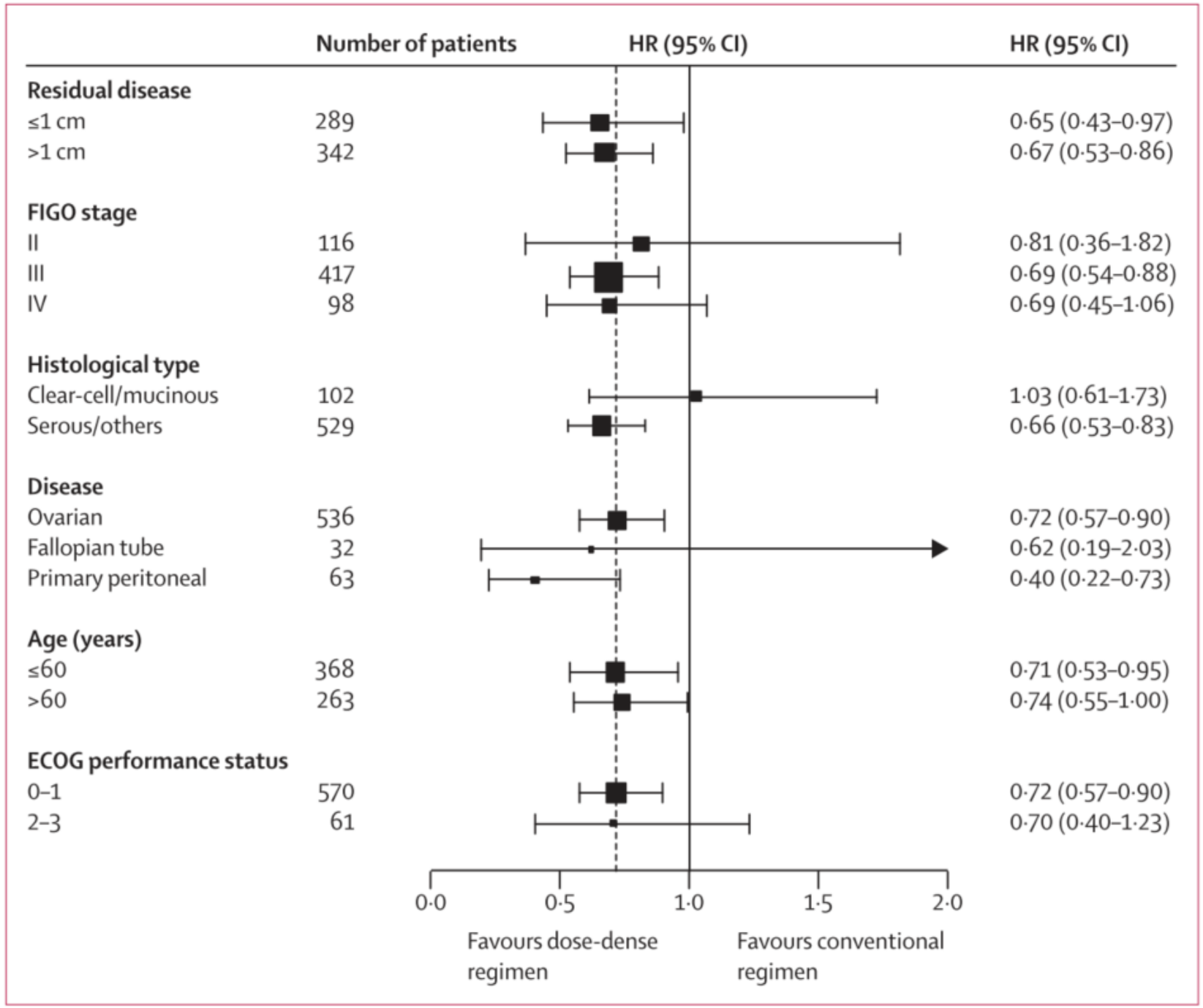
Dose dense

- Adjuvant treatment with q 21 days IV carboplatin and weekly IV paclitaxel
- **Katsumata et al 2009 & 2013**
  - 631 patients, in Japan
  - Longer PFS (28.0 VS 22.3 months, HR=0.71) in dose dense group VS standard carboplatin and paclitaxel IV q 21 days
  - OS at 3 years 72.1 VS 65.1% (HR=0.75)
  - Median OS 100.5 months in dose dense group VS 62.2 months
  - Neutropenia and anemia higher in dose dense group

Katsumata *et al*, Dose-dense paclitaxel once a week in combination with carboplatin every 3 weeks for advanced ovarian cancer. Lancet. 2009
Katsumata *et al*, Long-term results of dose-dense paclitaxel and carboplatin versus conventional paclitaxel and carboplatin for treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer (JGOG 3016): a randomised, controlled, open-label trial. Lancet. 2013



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Dose dense

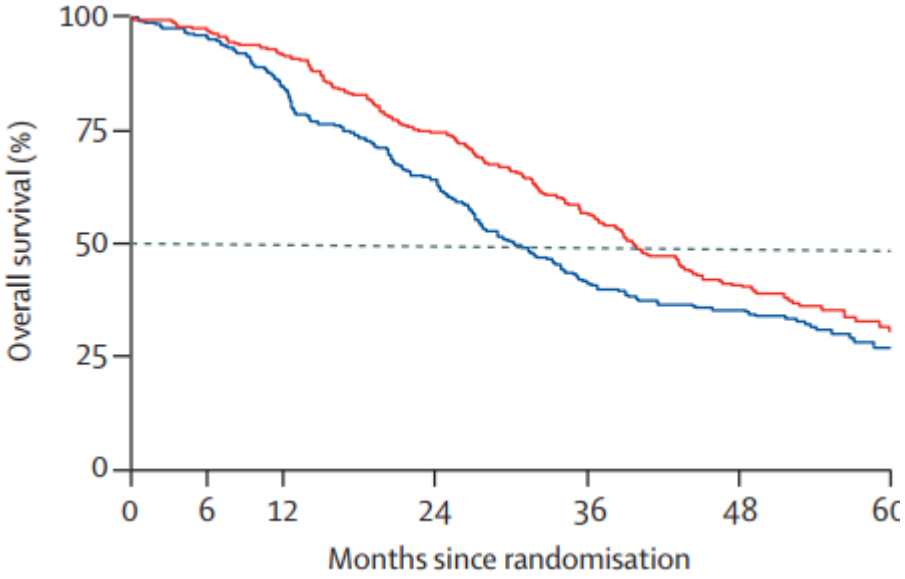
- **MITO-7 2014**
  - 810 women with stage IC to IV ovarian cancer
  - No difference in PFS and OS
  - Less neutropenia, febrile neutropenia, thrombocytopenia and neuropathy in the dose dense group
  - Better quality of life

- **GOG 262 2016**
  - 692 patients, stage II or IV
  - 84% had concomitant Bevacizumab (non randomised)
  - Better PFS with dose dense regimen if no bevacizumab used. No change in PFS in the group using Bevacizumab

Pignata *et al*, Carboplatin plus paclitaxel once a week versus every 3 weeks in patients with advanced ovarian cancer (MITO-7): a randomised, multicentre, open-label, phase 3 trial. Lancet Oncol. 2014
Chan *et al*, Weekly vs. Every-3-Week Paclitaxel and Carboplatin for Ovarian Cancer. NEJM. 2016

Bevacizumab in adjuvant Tx

- Angiogenesis inhibitor
- Risks of proteinuria, HTN and bowel perforation / fistula
- Given concomitantly with carboplatin and paclitaxel, then for maintenance
- Increased PFS, no increase in OS in non high-risk patients (stage III suboptimally debulked or stage IV)
- Significant cost



Oza *et al*, Standard chemotherapy with or without bevacizumab for women with newly diagnosed ovarian cancer (ICON7): overall survival results of a phase 3 randomised trial. Lancet Oncol. 2015
NICE guidance on bevacizumab in combination with paclitaxel and carboplatin for the first-line treatment of advanced ovarian cancer

Treatments in the geriatric population

In patients ≥70 years old receiving IV chemotherapy:

- If good functional status (ECOG 0-1), few comorbidities and who underwent debulking surgery, adjuvant IV chemotherapy usually tolerated
- Experience more neuropathy than younger patients
- Myelosuppression does not increase with age
- Completion rate of IV chemotherapy similar

Matulonis *et al*, Phase II prospective study of paclitaxel and carboplatin in older patients with newly diagnosed Müllerian tumors. Gynecologic Oncology. 2009
Kurtz *et al*, Ovarian cancer in elderly patients: carboplatin and pegylated liposomal doxorubicin versus carboplatin and paclitaxel in late relapse: a GCIG CALYPSO sub-study. Ann Oncol. 2011

Treatments in the geriatric population

In patients ≥70 years old receiving IP chemotherapy:

- More side effects
- No increase in complications
- Older patients receiving IP chemotherapy have similar PFS and OS than younger patients despite fewer cycles completed

Kothari *et al*, The effect of age on the tolerability of intraperitoneal chemotherapy, complication rate, and survival in patients with ovarian cancer. Gynecologic Oncology. 2010
Crim *et al*, Evaluation of the efficacy and toxicity profile associated with intraperitoneal chemotherapy use in older women. Gynecology Oncology. 2017

Surveillance

- Review of symptoms and physical examination with a bimanual pelvic and rectovaginal examination
- Earlier detection of recurrence by imaging or CA-125, but **does not** change outcomes
- CT scan should only be used when clinically indicated

Invasive ovarian cancer surveillance recommendations.

	Follow up recommendation intervals			
Time from completion of primary therapy	Years 0–2	Year 2–3	Years 3–5	Years >5
Symptom review and examination	3–4 months	4–6 months	6 months	Yearly[a]
Pap test/cytology	Not indicated			
CA 125	Optional			
Radiographic imaging[b]	Insufficient data to support routine use			
Recurrence suspected	CT scans or PET/CT scans CA 125			

[a] May be followed by a gynecologic oncologist or generalist.
[b] May include chest X-ray, PET/CT scans, MRI, ultrasound.

Salani, R et al, An update on post-treatment surveillance and diagnosis of recurrence in women with gynecologic malignancies: Society of Gynecologic Oncology recommendations, Gynecologic Oncology 2017

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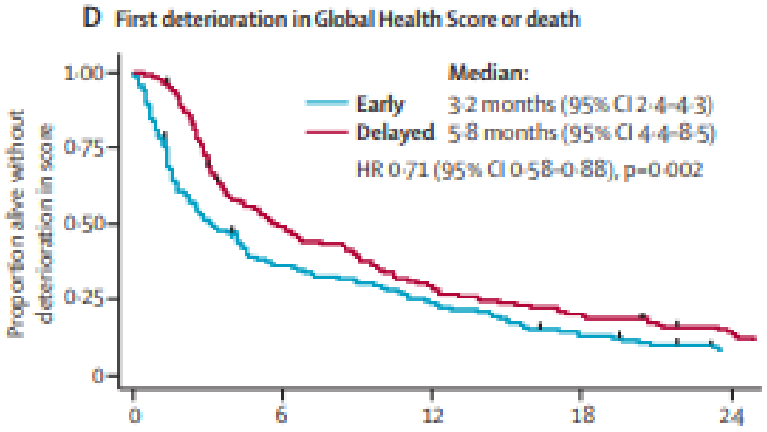
Surveillance with CA-125… why not?

- Women after first-line platinum-based chemotherapy and normalization of CA-125 had clinical examination and CA-125 q 3 months.
- 1442 patients included
- If CA-125 increased to twice upper limit, ½ of the patients received early chemotherapy and the other ½ only if clinical evidence of recurrence
- No difference in OS (25.7 months for early treatment VS 27.1 months for delayed)
- Early treatment patients started chemotherapy 4.8 months earlier…



Rustin *et al*, Early versus delayed treatment of relapsed ovarian cancer (MRC OV05/EORTC 559555): a randomized trial. Lancet. 2010

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Treatment of recurrence

Some definitions

- **Platinum resistant:**

  < 6 months between completion of platinum-based treatment and the detection of relapse

- **Platinum sensitive:**

  ≥ 6 months between completion of platinum-based treatment and the detection of relapse

- **Partially platinum-sensitive:**

  6-12 months between completion of platinum-based treatment and the detection of relapse

Treatments – Platinum resistant

- Palliative
- Single agents prefered (Paclitaxel, Topotecan, Caelyx, Etoposide, Gemcitabine)
- Addition of bevacizumab increases PFS (6.7 VS 3.4 months) and RR
- Response rate <10-15%
- Should be offered to participate in clinical trials

Pujade-Lauraine *et al*, Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: The AURELIA open-label randomized phase III trial. J Clin Oncol. 2014

Treatments – Platinum sensitive

- Secondary cytoreduction
- Most common: second-line chemotherapy.
- Response rate 25-65%
- Chemotherapy regimen should contain a platinum agent
- Can be combined with
  - Paclitaxel
  - Caelyx
  - Gemcitabine
  - With or without bevacizumab

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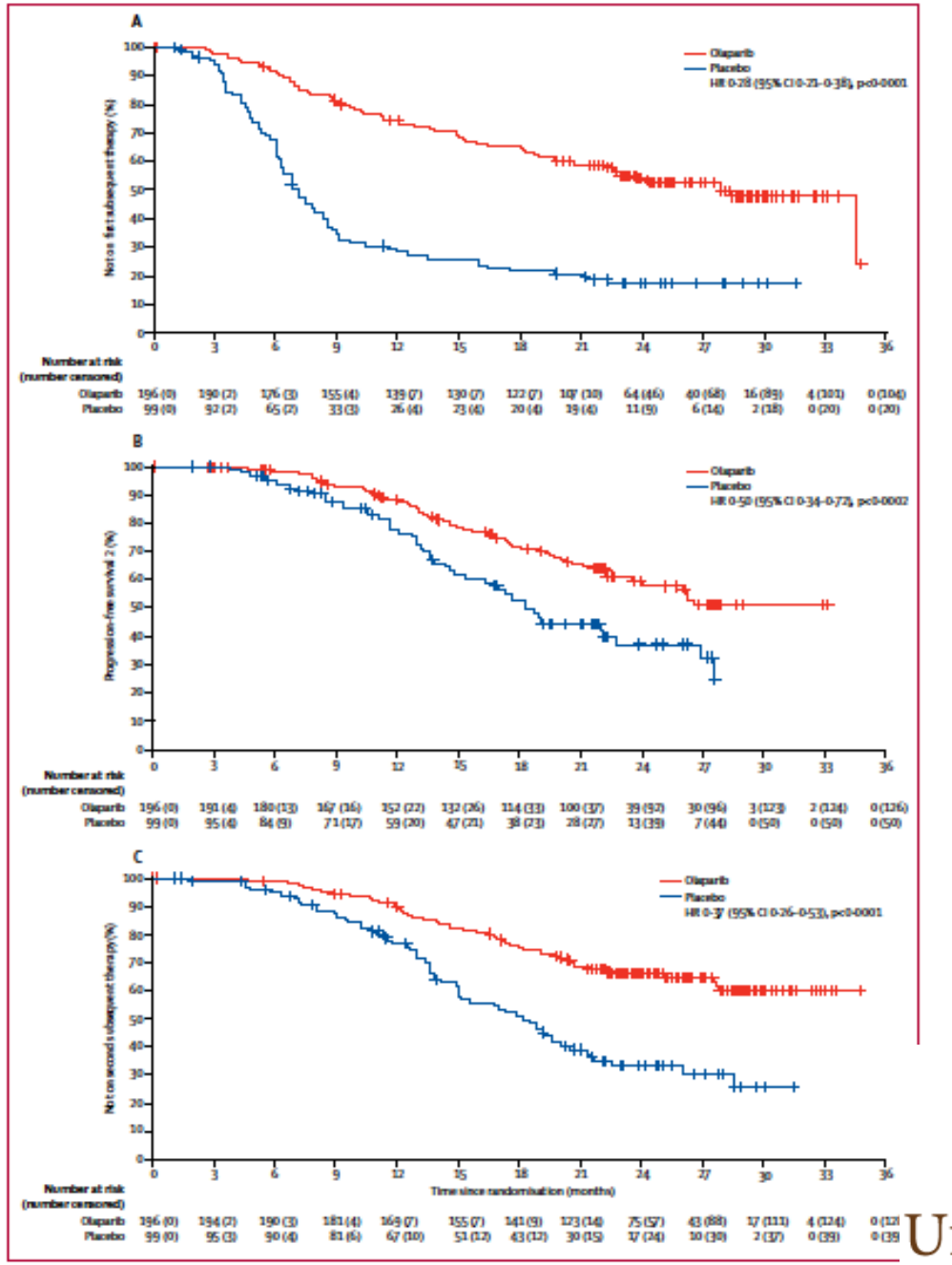
PaRPi as maintenance

- Blocks base-excision repair and lead to accumulation of DNA double-strand breaks → cell death

- Indicated for platinum-sensitive recurrence in BRCA mutated tumors as a monotherapy maintenance treatment after response to second line platinum-based chemotherapy

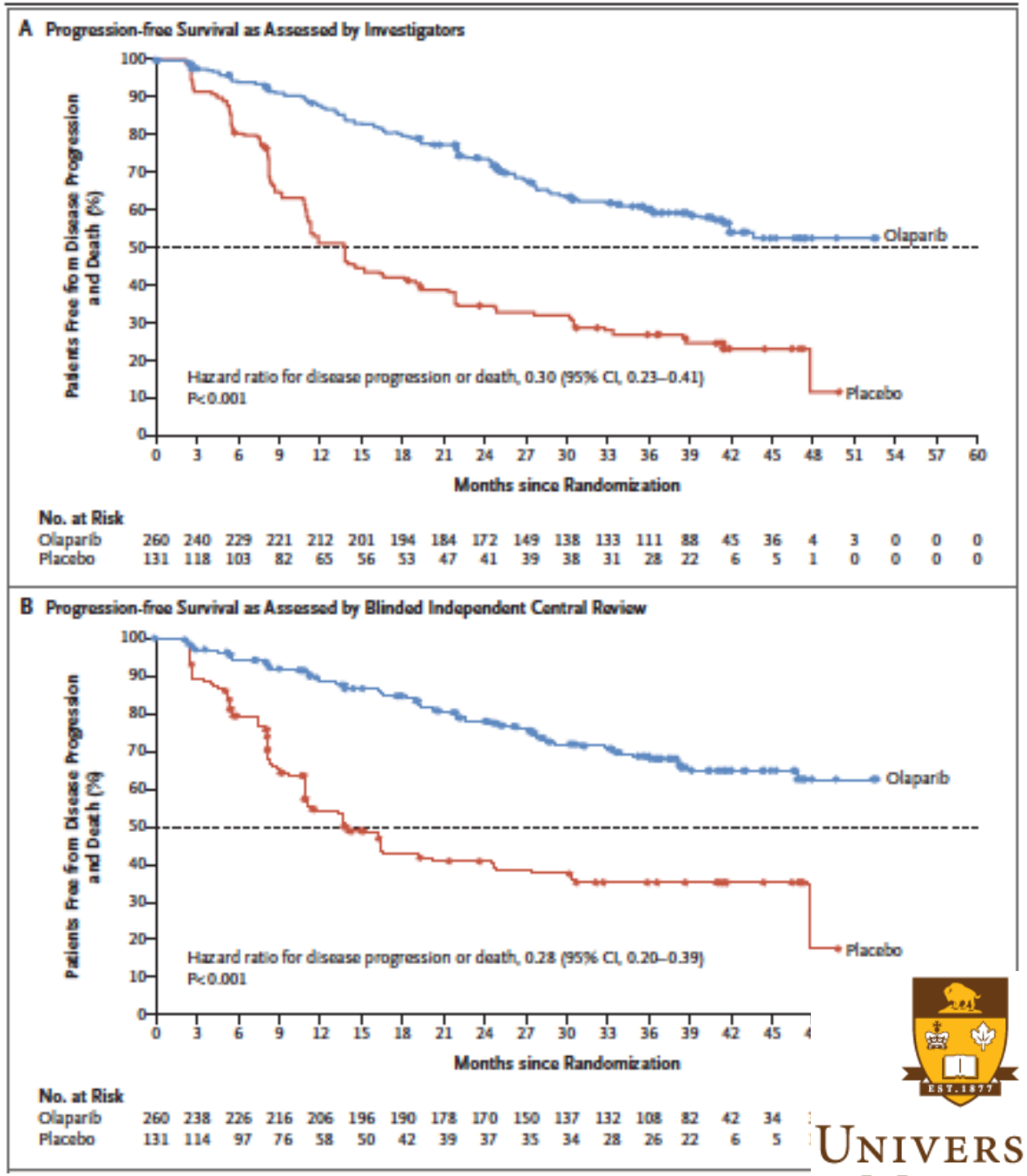
PaRPi: Olaparib

- **Pujade-Lauriane et. al. SOLO2/ENGOT-Ov21; 2017**
  - Phase 3 RCT international trial for PS maintenance
  - 300 mg in two 150 mg tablets, twice daily
  - 295 patients
  - PFS longer 19·1 m v 5·5 m; p<0·0001
  - Serious AE 18% vs 8%



PaRPi: Olaparib

- **Moore et. al. SOLO1 2018**
  - Phase 3 RCT international trial for 1st line maintenance
  - 300 mg in two 150 mg tablets, twice daily
  - 391 patients
  - Time to 1st treatment or death longer 51.8 m v 15·1 m; p<0·0001
  - HR for death 0.30 (0.23-0.41)



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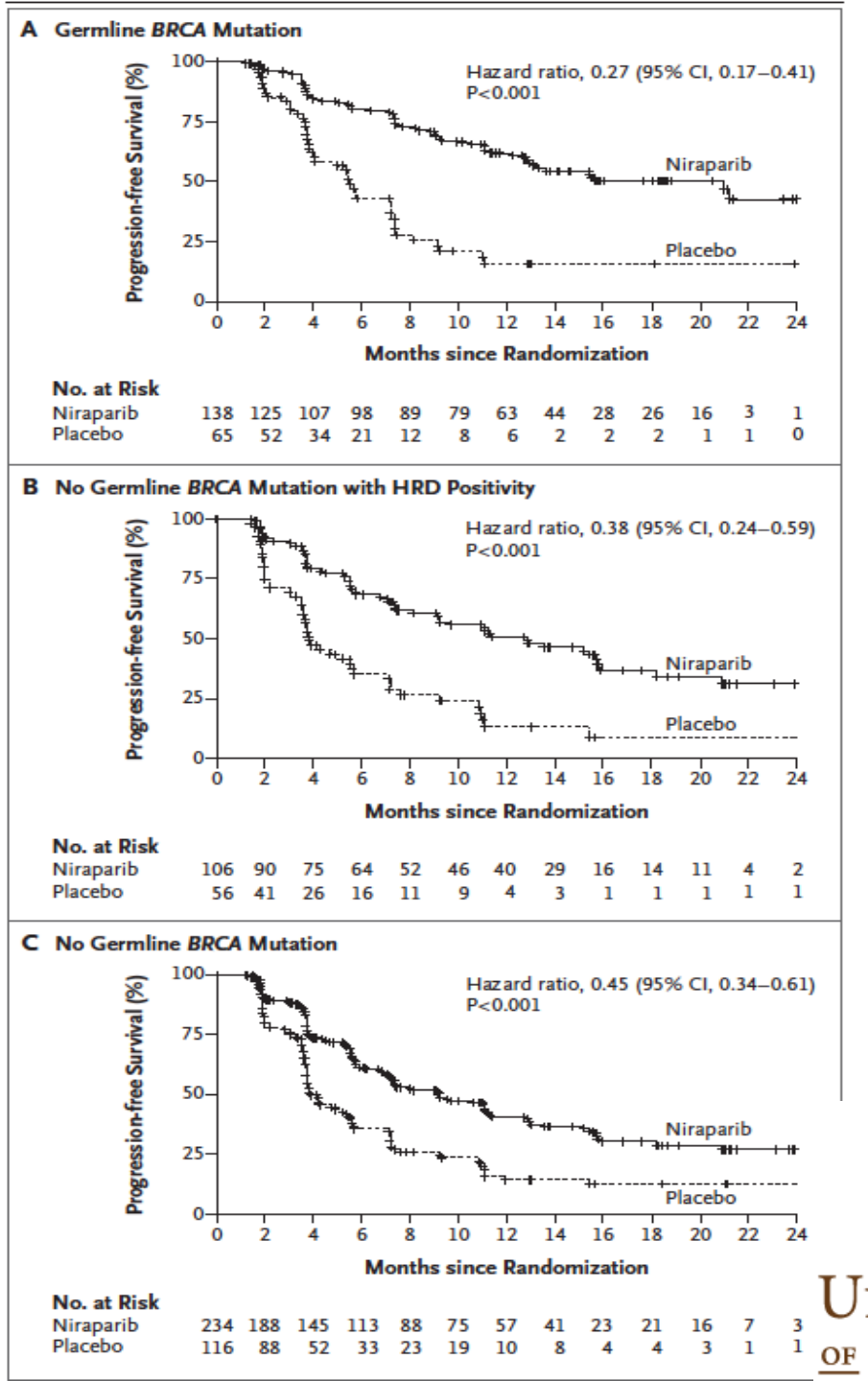
PaRPi: Niraparib

- **Mirza MR, et. Al. ENGOT-OV16/NOVA**
  - Phase 3 RCT
  - 2:1 ratio to receive niraparib (300 mg) or placebo od
  - 553 enrolled patients
  - Niraparib group had longer PFS
    - 21.0 vs. 5.5 mths in the gBRCA cohort
    - 12.9 vs. 3.8 mths in the non-gBRCA HRD + cohort
    - 9.3 vs. 3.9 mths in the overall non-gBRCA cohort



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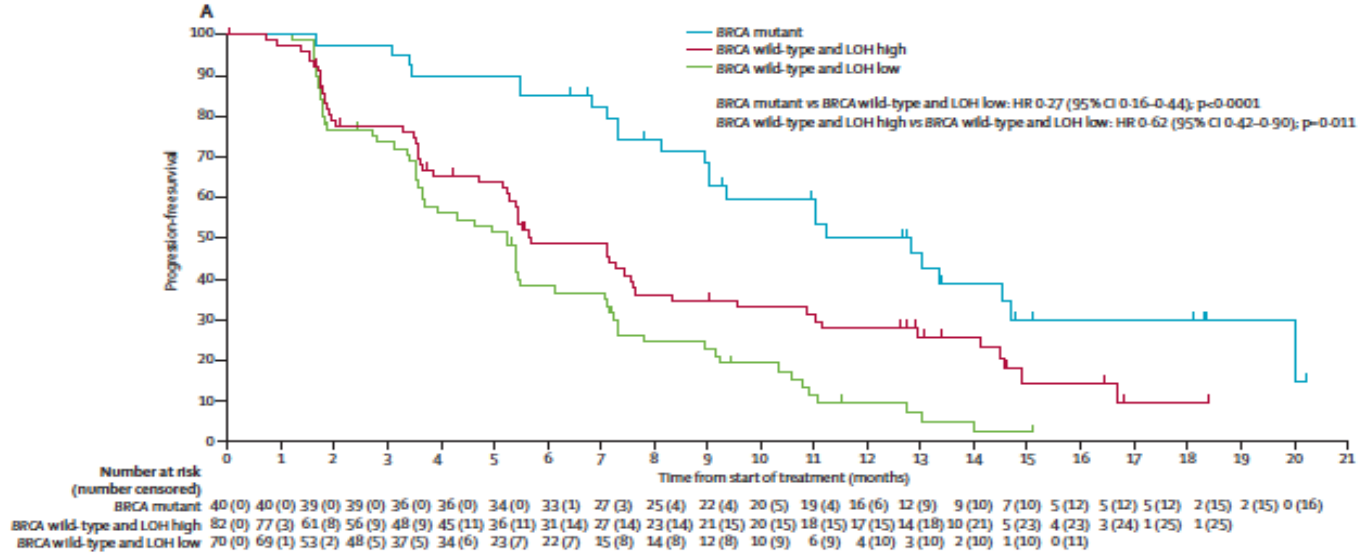
PaRPi: Rucaparib

- **Swisher et.al. ARIEL2**
  - Phase 2 RCT international, multicentre
    - BRCA mutant (deleterious germline or somatic),
    - BRCA wild-type and LOH high (LOH high group),
    - BRCA wild-type and LOH low (LOH low group).
  - 600 mg twice per day; 206 patients
  - Median PFS 12.8 months, 5.7 months and 5.2 months



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PaRPi: Rucaparib

- **Coleman et. al. ARIEL3; 2017**
  - RCT phase 3 trial
  - 2:1 to receive oral rucaparib 600 mg twice daily or placebo in 28 day cycles
  - 564 patients: 375 (66%) to rucaparib and 189 (34%) to placebo.
  - Median PFS in patients with a BRCA-mutant carcinoma was 16·6 months versus 5·4 months p<0·0001
  - HRD carcinoma 3·6 months versus 5·4 months p<0·0001
  - ITT population=10·8 months versus 5·4 months p<0·0001

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Malignant ascites

- High protein concentration
- Amount of ascites produced usually improves with response to systemic treatment
- Therapeutic paracentesis widely used → no maximum amount !!
- Frequency is guided by the patient's SSx
- Can be done as outpatient procedure
- No need for U/S guided procedure
- IV fluids only if symptomatic hypotension
- Alternative: permanent drain insertion for palliative care

Stephenson *et al*, The development of clinical guidelines on paracentesis for ascites related to malignancy. Palliative Medicine. 2002

Bowel obstruction

- Affects up to 50% of patients with ovarian cancer
- Causes abdominal pain, nausea and vomiting
- Can lead to life-threathening complications (intestinal ischemia, perforation, peritonitis)
- Investigations: abdominal exam, AXR and/or CT, CBC, electrolytes
- Addition of oral contrast can help to identify the point of obstruction
- Differential diagnosis
  - Malignant: malignant bowel obstruction, carcinomatous ileus
  - Nonmalignant: adhesions, radiation enteritis, ileus, constipation, hernia incarceration
- Can affect the small or the large bowel

Perri T. et al, Bowel obstruction in recurrent gynecologic malignancies: Defining who will benefit from surgical intervention. European Journal of Surgical Oncology. 2013
Ferguson *et al*, Management of intestinal obstruction in advanced malignancy. Annals of Medicine and Surgery. 2015

Bowel obstruction

- Goal of treatment is to increase QOL
- Conservative management: NPO, NGT, analgesics, IVF, corticosteroids, anticholinergics and somastostatin agonists (Octreotide)
- Reobstruction rate ≈40%
- If failure of conservative management, possible surgical procedures include: colostomy, ileostomy, colonic stent, gastrostomy, bypass/ressection
- **High risk** of perioperative death
- Procedure needs to be adapted to the site(s) of disease

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Final Take Home Messages

- Ovarian cancer is an agressive disease often diagnosed at advanced stage
- Surgery is the mainstay of treatment
- Neoadjuvant therapy is an alternative for unresectable disease
- Adjuvant chemotherapy includes dose dense chemotherapy, q 21 days carboplatin and paclitaxel, intra-peritoneal chemotherapy
- The goal of careful post treatment surveillance is to detect clinical recurrence
- Recurrence is treated according to the ‘‘platinum-free interval’’

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Staging	
I	Growth limited to the ovaries
IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings
IB	Growth limited to 2 ovaries, capsule intact, no tumor on surface, negative washings
IC	Any of: surgical spill, capsule rupture before surgery, tumor on ovarian surface, malignant cells in ascites or peritoneal washings
II	Tumor involves one or both ovaries or fallopian tubes with pelvic extension below pelvic brim or primary peritoneal cancer
IIA	Extension to uterus/tubes
IIB	Extension to other pelvic structures
III	Peritoneal metastasis outside the pelvis and/or metastasis to the retroperitoneal lymph nodes
IIIA1	Positive retroperitoneal lymph nodes only
IIIA2	Microscopic extrapelvic peritoneal involvement
IIIB	Macroscopic peritoneal metastasis beyond pelvis ≤2 cm with or without metastasis to the retroperitoneal lymph nodes
IIIC	Macroscopic peritoneal metastasis beyond the pelvis >2 cm with or without metastasis to the retroperitoneal lymph nodes
Stage IV	Distant metastasis
IVA	Pleural effusion with positive cytology
IVB	Liver or splenic parenchymal metastases; metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity); transmural involvement of intestine