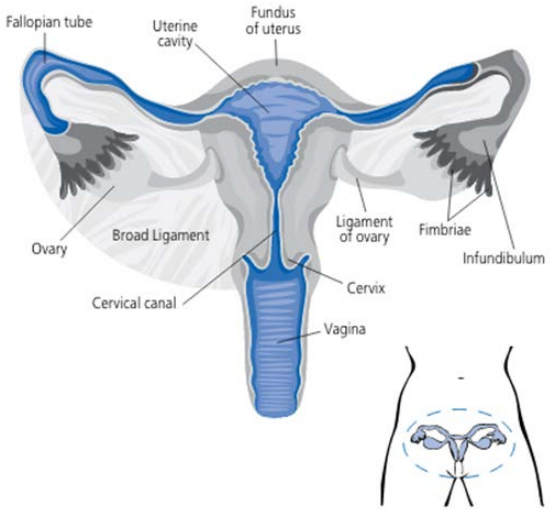
An Approach to Ovarian Cancer



Dr. Aalok Kumar
Medical Oncologist
BC Cancer Surrey
October 15th, 2020

Overview of presentation

- Ovarian Cancer Presentation
- Making the Diagnosis
- Staging
- Timing of Surgery
- Etiology/Origins of Ovarian Cancer
- Screening and Prevention
- Treatment of
  - Newly diagnosed ovarian cancer
  - Recurrent ovarian cancer
- PARP inhibitors

Disclosures

Research Support/P.I.	N/A
Employee	N/A
Consultant	N/A
Major Stockholder	N/A
Speakers Bureau	N/A
Honoraria	AZ, Roche, Merck, Novartis, Pfizer, Mylan
Scientific Advisory Board	AZ, Genomic Health, Merck, Novartis, Roche, Purdue, GSK

Classic Clinical Presentation

- Insidious presentation
  - Vague abdominal pain/cramping
  - Bowel habit changes, such as intermittent
  - diarrhea or constipation
  - Sense of abdominal fullness
  - Abdominal distension
  - Abdominal mass
  - Changes in weight – weight gain (ascites) or weight loss (diet changes, feeling unwell)

Making the Diagnosis

- Examination:
  - Supraclavicular lymphadenopathy
  - Pleural effusions
  - Abdomen:
    - Ascites
    - Omental mass (cake)
    - Inguinal lymphadenopathy
    - Pelvic mass
  - Peripheral Edema

Making the Diagnosis

- Labs tests:
  - CBC (usually not anemic – can have mild anemia in keeping with anemia of chronic disease)
    - MCV is usually normal
    - Marked anemia or microcytosis should lead to consideration of GI malignancy
  - Lytes/Cr/LFTs – typically normal
  - Tumour Markers:
    - CA-125 the most commonly elevated marker
    - CA19-9 and CA15-3 can also be elevated, but not usually as high as the CA-125

Making the Diagnosis

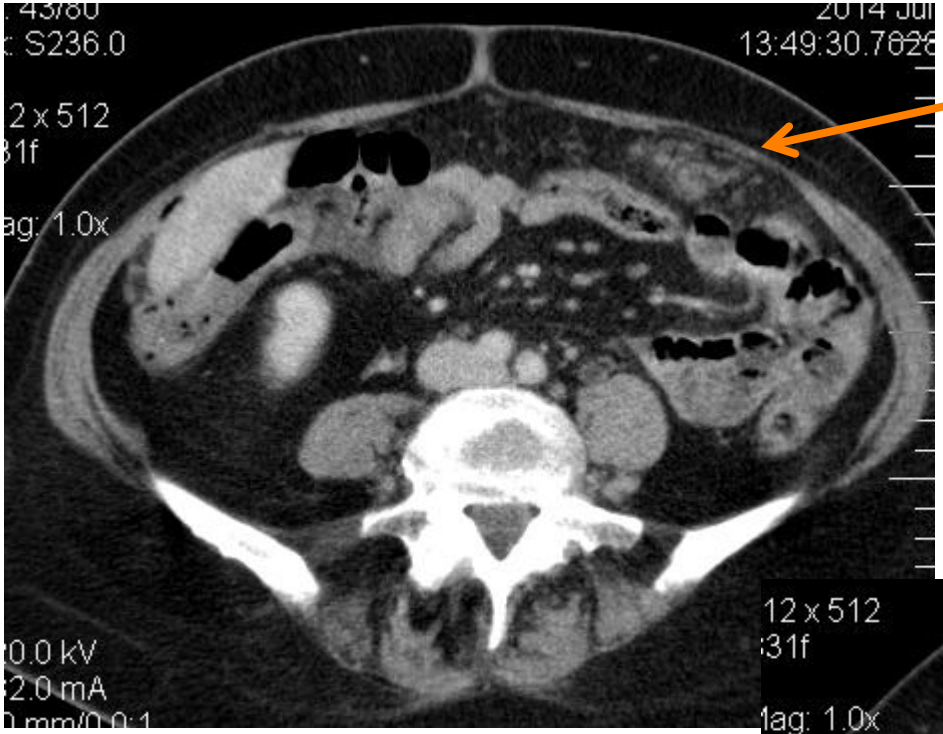
- Imaging:
  - CXR – pleural effusion (solitary lung mets are rare)
  - U/S – ascites, peritoneal masses, pelvic masses
  - CT – preferred imaging modality
    - Best view of visceral organs, retroperitoneum, and peritoneal cavity
    - Facilitates planning for biopsy +/- surgery

Biopsy Vs Surgery

- Biopsies
  - Always correct to consider a biopsy of disseminated disease
    - Omental masses
    - Palpable lymphadenopathy (supraclav, inguinal)
    - In some cases, visceral mets (liver)
  - Core biopsy always preferable to FNA
    - Allows better architectural definition of the disease
    - Helps with disease subtyping
      - More material for IHC (can be essential in some cases)
    - Requires image guidance
  - FNA – if this is the only possibility, ask for a cell block
    - May allow for IHC to be done
  - Fluid cytology
    - Peritoneal and Pleural fluid
      - Easy and safe to get
      - Cell block can also be requested for IHC

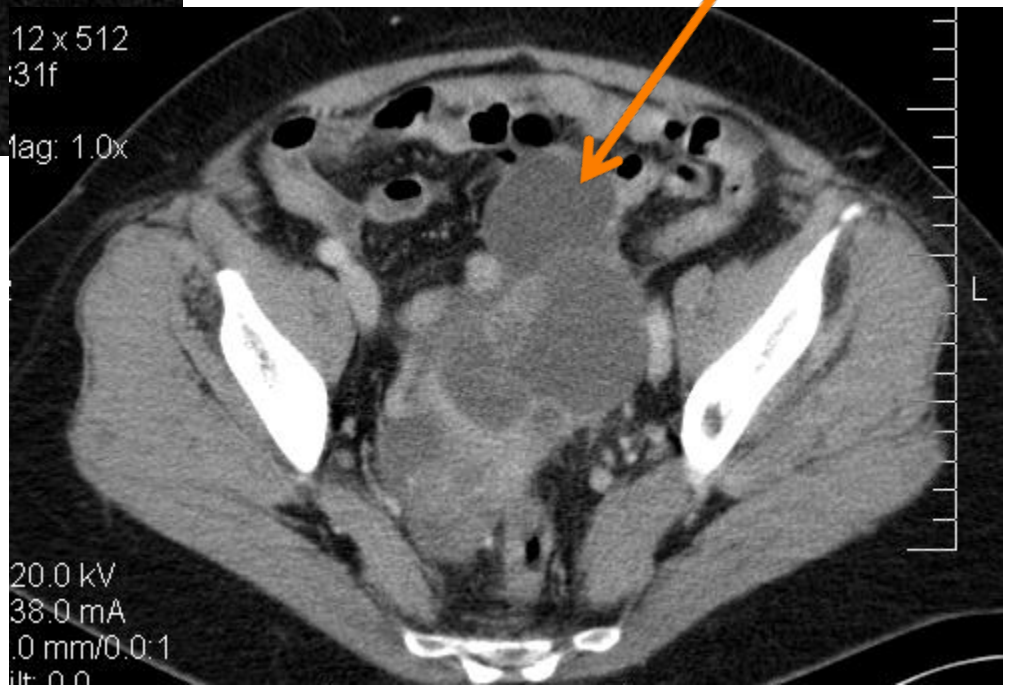
Surgery

- Suspected/Diagnosed Ovarian Cancer: requires review with a Gynecologic Oncologist!
- Usually suitable for surgery if:
  - Pelvic mass
  - Omental cake
  - All disease felt to be removable by a gynecologic oncologist
- Usually delay surgery if:
  - Diffuse peritoneal disease/disease under the diaphragms
  - Massive ascites
  - Large retroperitoneal LNs
  - Acute medical problem – MI/unstable angina, acture PE/DVT



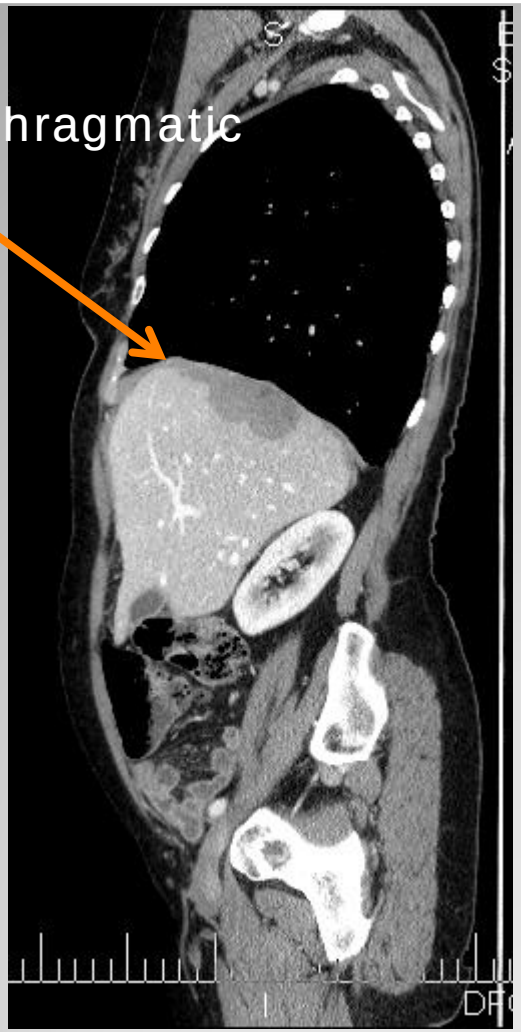
Omental mass

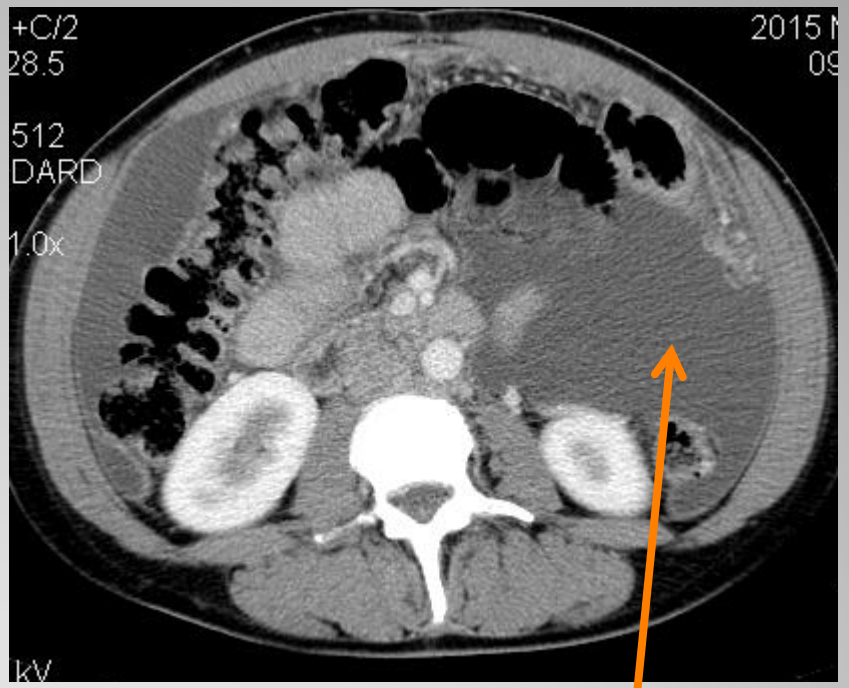
Pelvic Mass



This case had upfront surgery

Subdiaphragmatic disease





Massive ascites

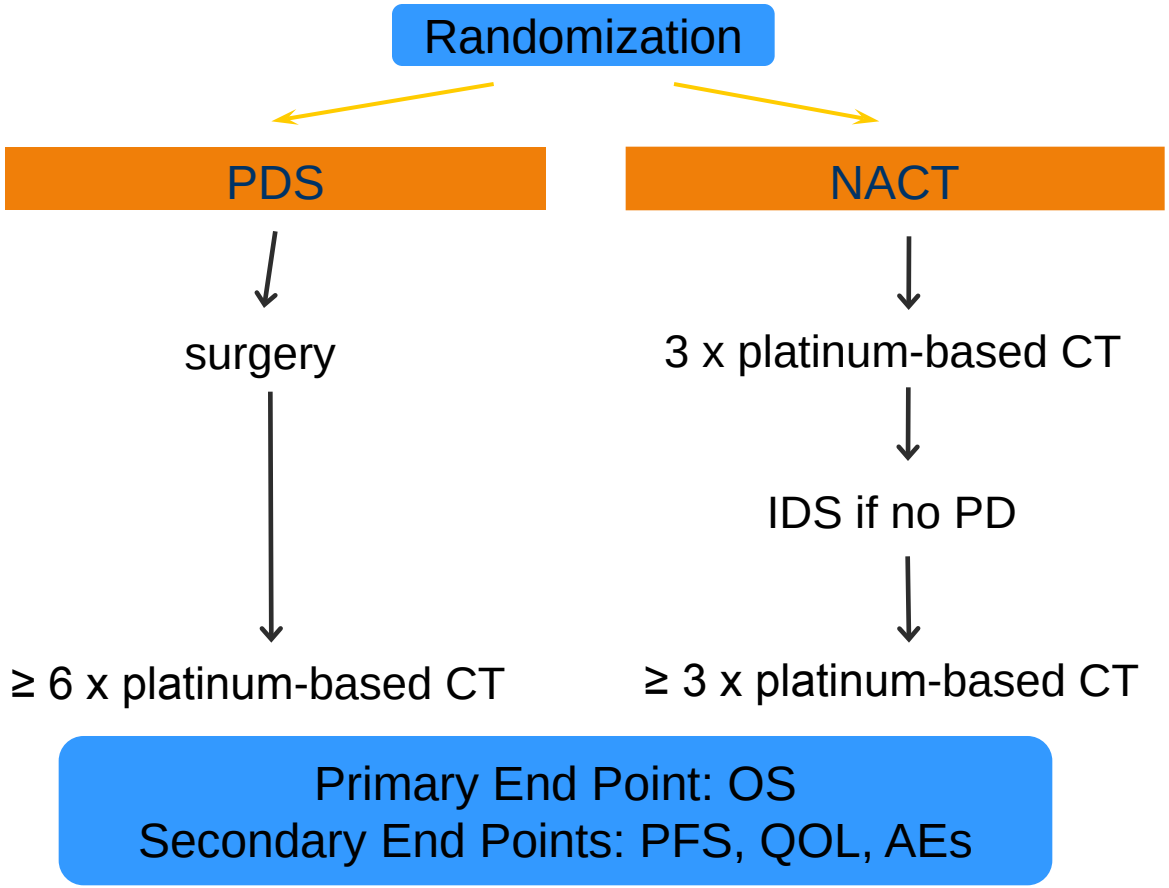
These cases had neoadjuvant chemotherapy

Timing of Surgery

- Two randomized phase III trials
  - Pts with stage III or IV ovarian cancer
  - Otherwise fit for surgery (no PE/DVT, or serious commorbidity)
  - Outcomes are the same whether surgery first or chemo first.

NACT + IDS Vs. PDS

Ovarian, Tubal, or Peritoneal Cancer
FIGO Stage IIIC/IV (N = 670)



NACT = neoadjuvant chemotherapy; IDS = interval debulking surgery; PDS = primary debulking surgery; FIGO = International Federation of Gynaecology and Obstetrics; CT = chemotherapy; PD = progressive disease; QOL = quality of life; AEs = adverse events.
Vergote et al, 2008, 2010.

Pooled Analysis of 2 RCTs (CHORUS and EORTC 55971)

Data on 1220 individual patients

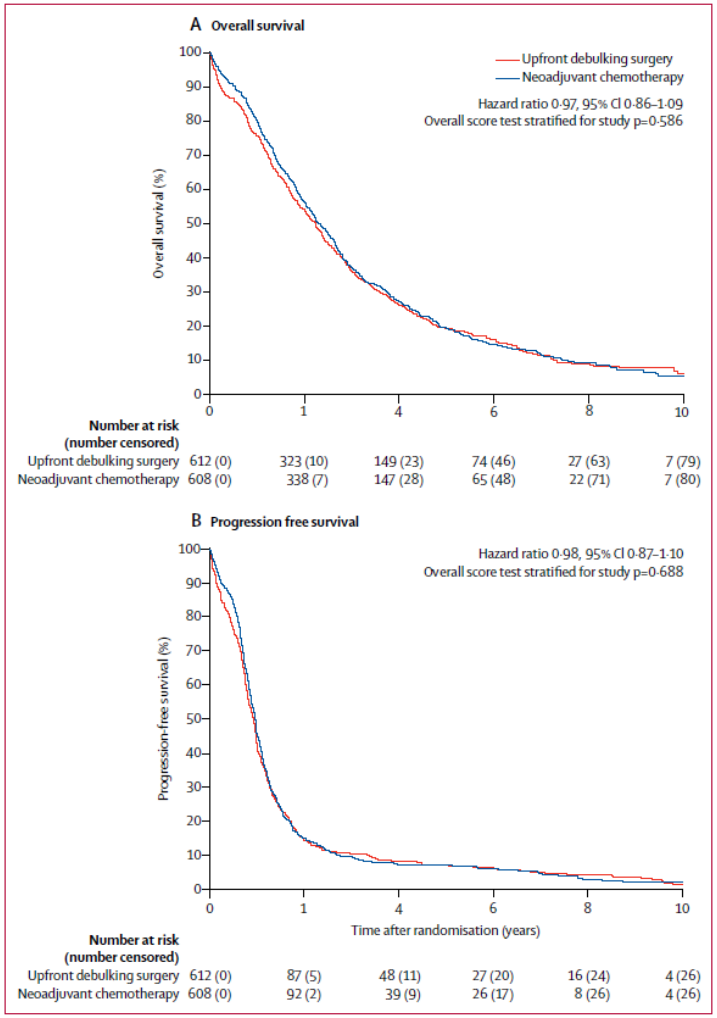


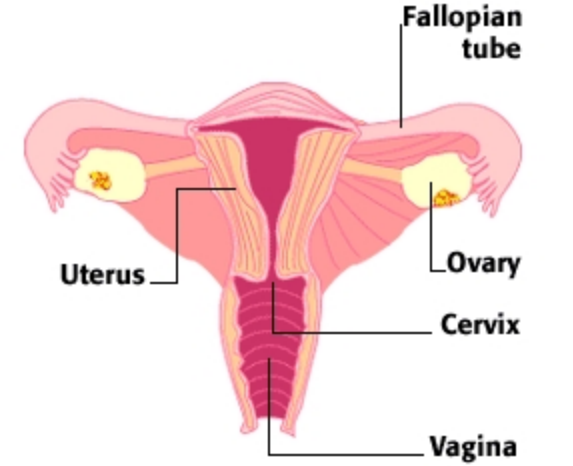
Figure 2: Overall survival and progression-free survival, by treatment

Lancet Oncol 2018; 19: 1680–87

HR = hazard ratio.
Vergote et al, 2010.

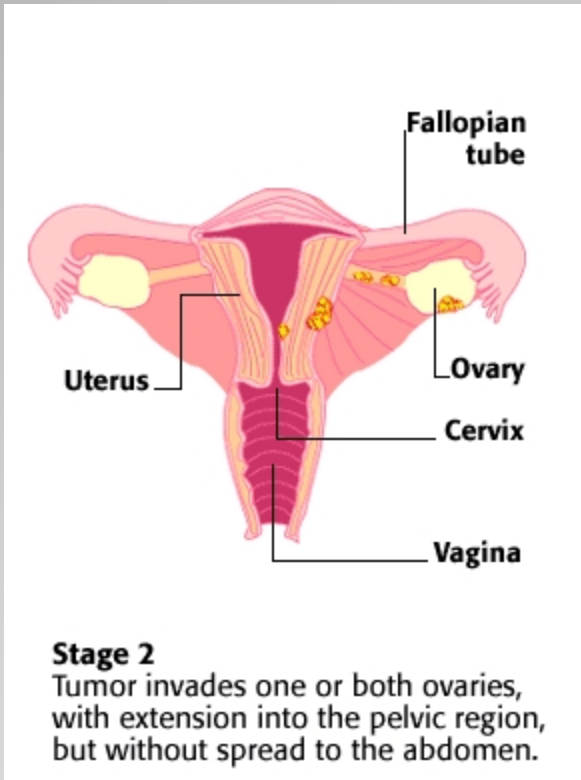
Staging

Stage I



Stage 1
Tumor limited to one or both ovaries. Tumor may be found on ovarian surface.

- IA unilateral
- IB bilateral
- IC any of:
  - cyst rupture
  - positive peritoneal cytology
  - surface involvement

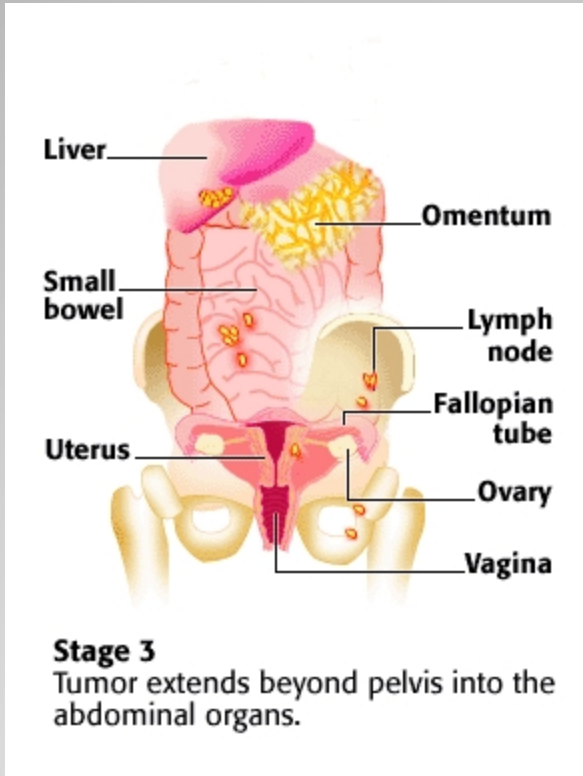


Stage 2
Tumor invades one or both ovaries, with extension into the pelvic region, but without spread to the abdomen.

- 2A involvement of fallopian tubes or uterus
- 2B extention to other pelvic structures (bladder, rectum)
- 2C like 2B but with positive peritoneal washings

Stage II

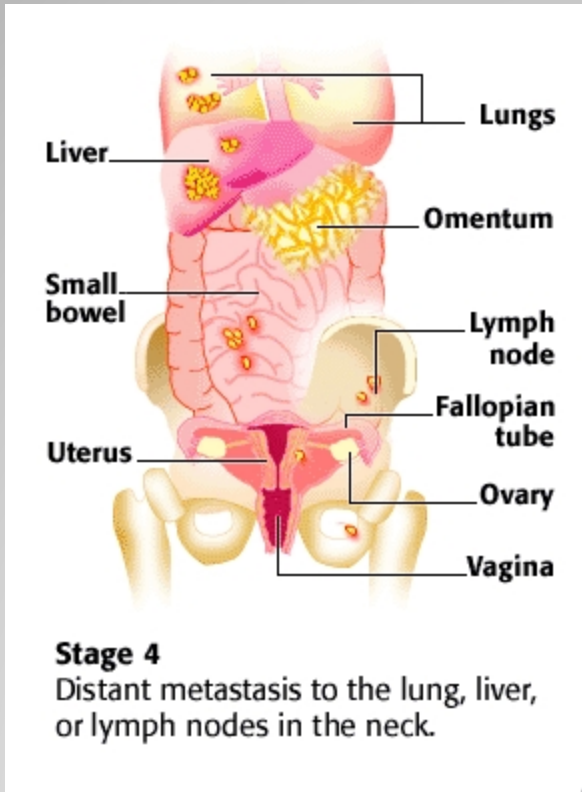
Stage III



Stage 3
Tumor extends beyond pelvis into the abdominal organs.

- 3A microscopic involvement of the peritoneum or the omentum
- 3B abdomin-peritoneal implants <2cm
- 3C abdomin-peritoneal implants >2cm

Stage IV



Stage 4
Distant metastasis to the lung, liver, or lymph nodes in the neck.

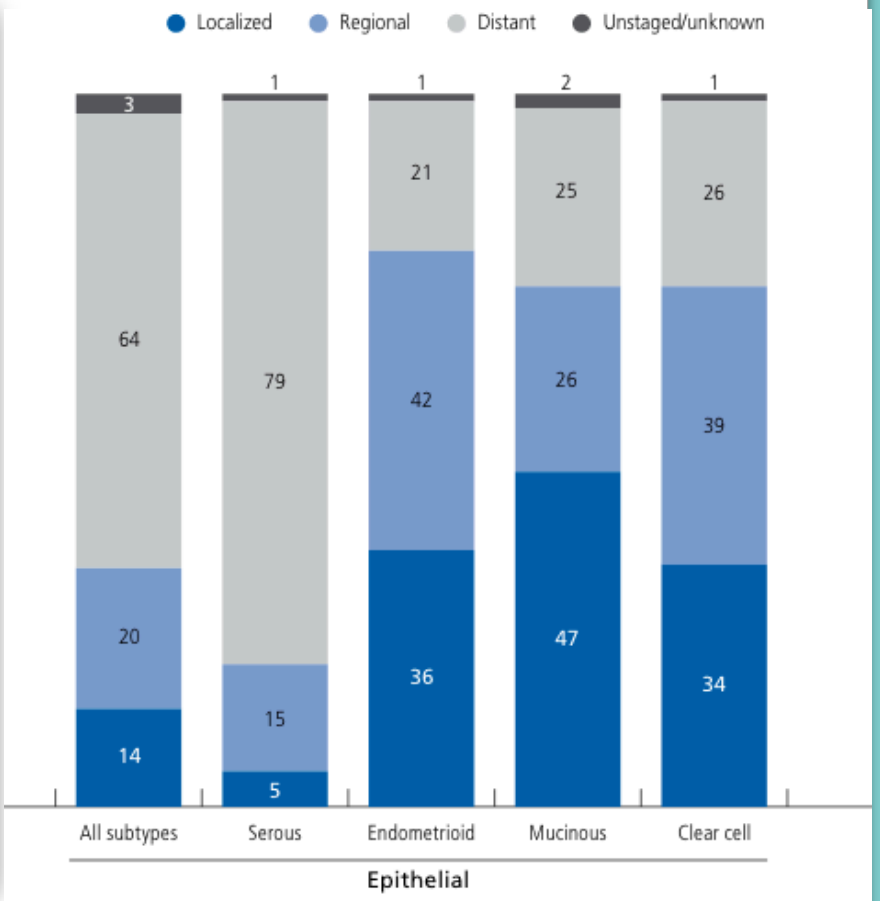
- Disease within visceral organs or above the diaphragm (if a plural effusion must be confirmed cytologically to be considered stage 4).

Etiology and Classification

- Complexity of Ovarian Cancer long overlooked
- Used to believe that different histology = morphological variants
- What we have learned:
  - Histotype broadly defines different diseases
    - High grade serous
    - Clear Cell
    - Mucinous
    - Endometrioid
    - Low grade serous
    - Other very rare types…

Ovarian Cancer Etiology/Classification

Stage	5-year relative survival
1	90%
1A	94%
1B	92%
1C	85%
2	70%
2A	78%
2B	73%
2C	57%
3	39%
3A	59%
3B	52%
3C	39%
4	17%



	HGSC	Clear Cell	Endometrioid	Mucinous	LGSC
Portion of cases	**70**	**12**	**11**	**3**	**3**
Genetic Risk Factors	BRCA1/2	HNPCC	HNPCC	none known	none known
Precursor Lesions/Cell of Origin	**STIC**, p53 signatures	**Endometriosis**	**Endometriosis**	not known	SBT
Common stage at presentation	advanced	early	early	early	advanced
Pattern of Spread	trans - coelomic	trans-coelomic/ hematogenous	????	pseudomyxoma pertonei/ hematogenous	transcoelomic
Response to Platinum-based therapy	chemo-sensitive	chemo-resistant, radiosensitive	chemo- sensitive	chemo -resistant	chemo-resistant
Molecular aberrations	p53, BRCA1, BRCA2, HR defects	PI3K, ARID1A, MSI	PTEN, bcatenin, ARID1A, MSI	KRAS, HER2	BRAF, KRAS, NRAS

Ovarian Cancer Screening and Prevention

Screening

- No evidence to support screening for ovarian cancer in any population (low or high risk):
  - U/S (TA and TV)
  - CA125, HE4 (human epididymis protein 4)
  - Ovarian cancer symptom index
- NOT specific
  - Leads to a high number of unnecessary surgeries/procedures
- Does not detect “early disease”
- Not proven to impact on survival
- Should not be done
  - False reassurance
  - Riskof false positive
- All major cancer groups discourage screening, even in high risk women

Prevention

- **BRCA mutation carriers (high risk)**
  - Bilateral salpingo-oopherectomy
    - Possible option: remove tubes early and consider oopherectomy closer to age of menopause
- **Non-BRCA (low risk)**
  - Opportunistic salpingectomy
    - tubal ligation, C-section, hysterectomy etc.
      - Society of Obstetricians and Gynecologists of Canada
      - American Congress of Obstetricians and Gynecologists (January 2015 – Committee Opinion)
  - No level 1 evidence
    - Population outcomes/complications - being tracked

First Line Treatment of Advanced Ovarian Cancer

"Neoadjuvant" or Pre-Operative

OR

"Adjuvant" or Post-Operative

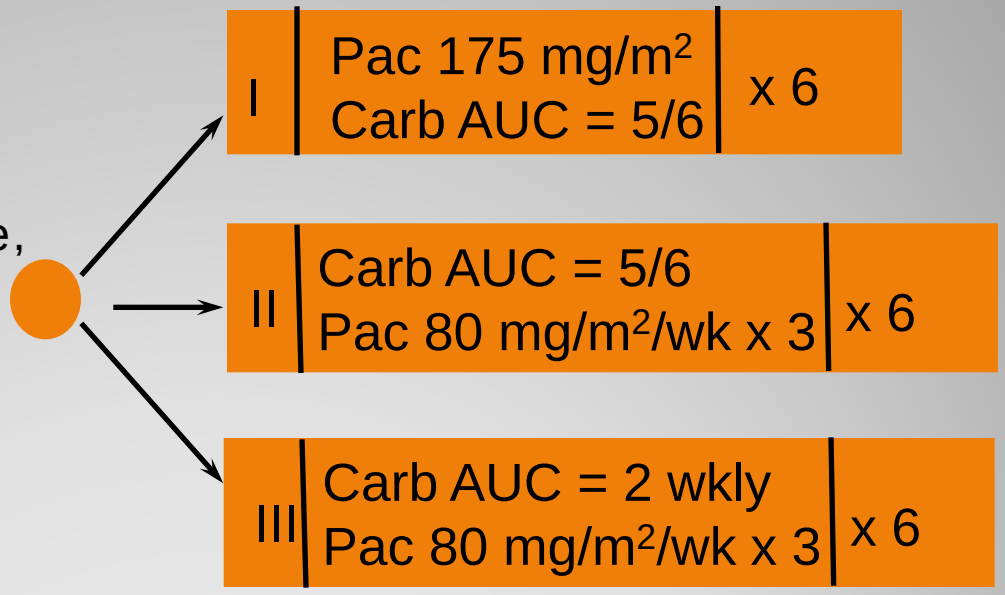
First Line Treatment: Pre-Operative

- Carboplatin and Paclitaxel
  - 2 different schedule options:
    1. **Q 3 weekly**
    2. "dose dense"
       - Carboplatin q 3 weekly
       - Paclitaxel weekly

- A Phase III trial demonstrated that Dose Dense treatment is associated with a improvement in OS at 3 and 5 years
  - Was the BCCA Standard for about 10 yrs

- **New Data show no difference between dose dense and 3 weekly**
  - Pendulum - back to 3 -weekly

- EOC or PP
- Stage II–IV
- No prior therapy
- Stratified: Residual disease, stage, and histology
- Primary end point: PFS
- Secondary end point: OS



PFS = I : 24.4 mo (standard arm)
II: 24.9 mo
III: 25.3 mo

ICON 8 Trial

N=1566 patients

Abstract 929O_PR 'ICON8: A GCIG Phase III randomised trial evaluating weekly dose- dense chemotherapy integration in first-line Epithelial Ovarian/ Fallopian Tube/ Primary Peritoneal Carcinoma (EOC) treatment: Results of Primary Progression- Free Survival (PFS) analysis' will be presented by Dr Clamp during ***Proffered Papers Session 'Gynaecological cancers' on Friday, 8 September 2017, 16:00 to 17:30 (CEST), in Cordoba Auditorium****.*

Intraperitoneal Chemotherapy

- 3 trials
- IP therapy
- **stage 3, optimally debulked (< 1cm residual)**
- improvement in OS.

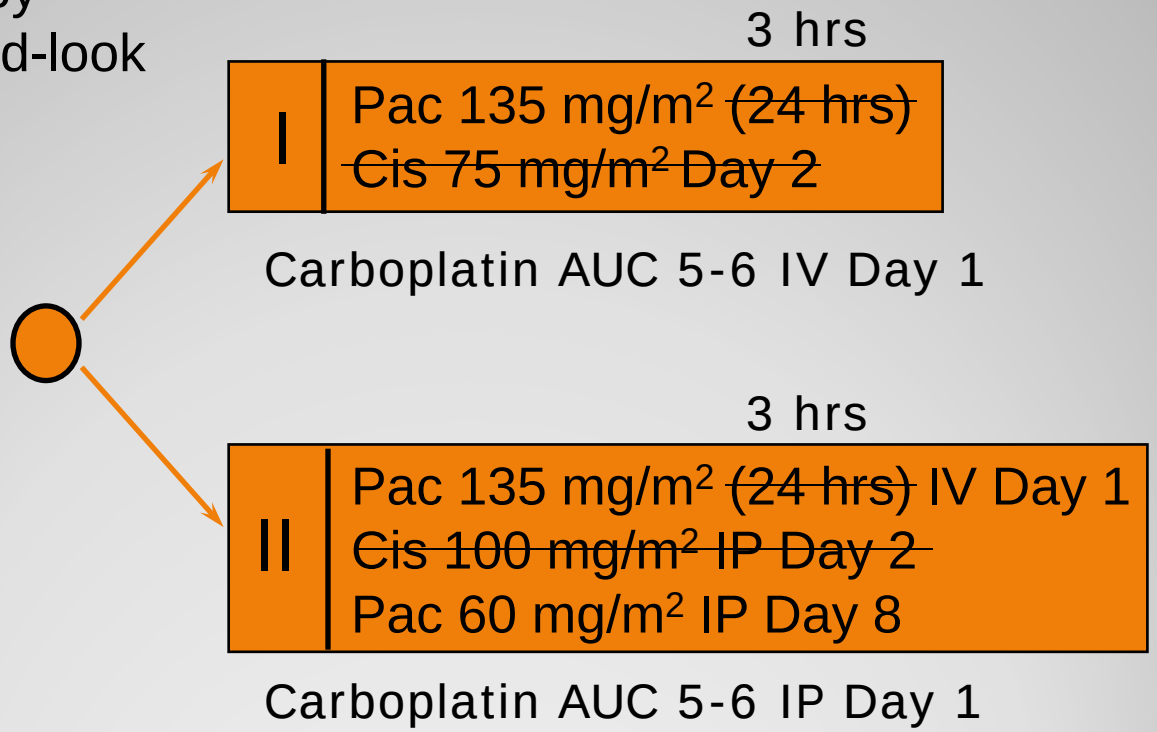
	Median PFS (mos)		HR	Median OS (mos)		HR
	IV	IP		IV	IP	
GOG 104	—	—	—	41	49	**0.76** (*p* = .02)
GOG 114	22	28	**0.78** (*p* = .01)	52	63	**0.81** (*p* = .05)
GOG 172	18.3	23.8	**0.80** (*p* = .05)	50	66	**0.75** (*p* = .03)

Primary Therapy: IP

Alberts et al, 1996; Markman et al, 2001; Armstrong et al, 2006.

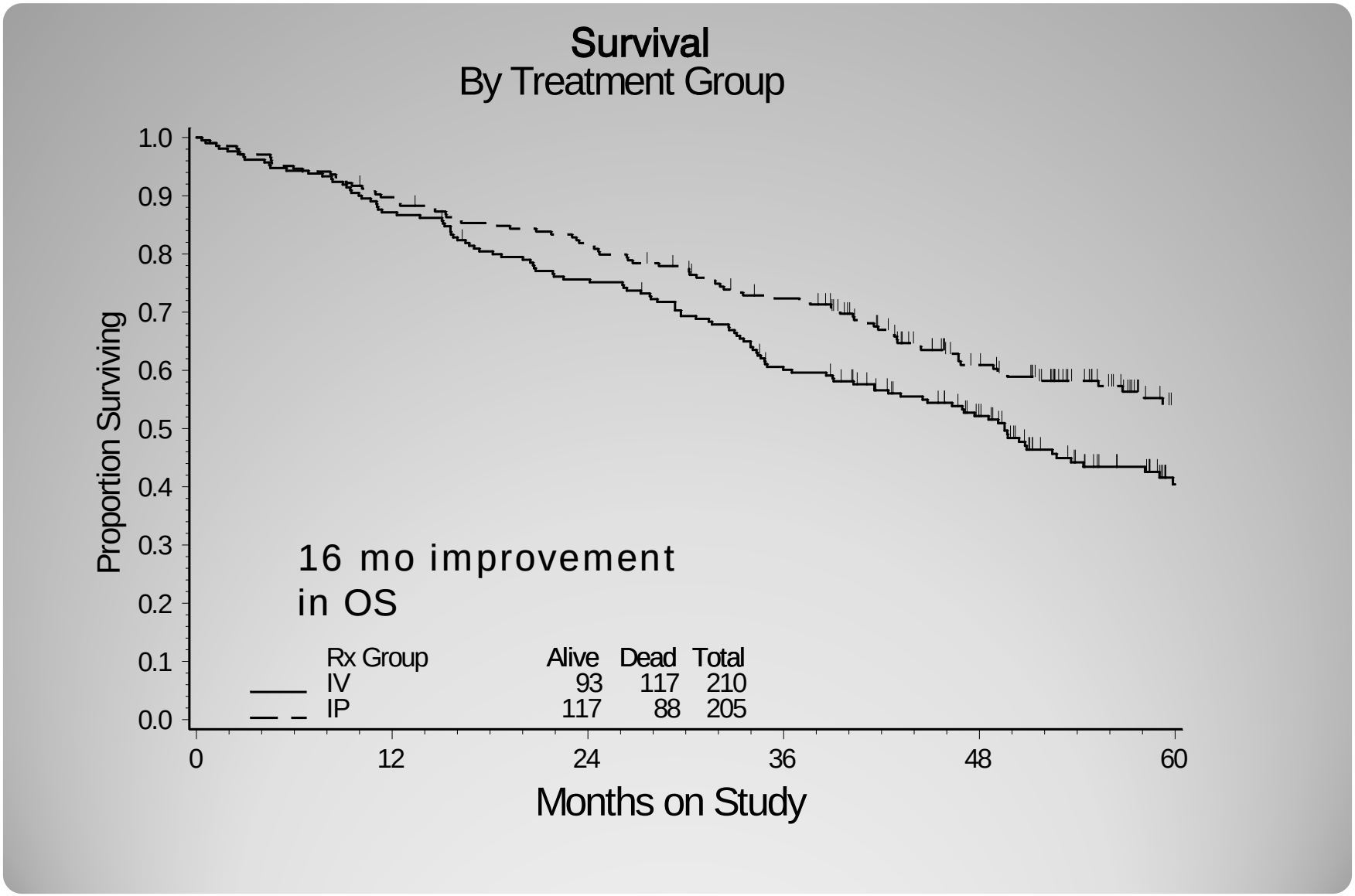
GOG 172: Ovarian (Optimal III)

- EOC
- Optimal stage III
- No prior therapy
- Elective second-look



Accrual: 415 patients (evaluable)

Armstrong et al, 2006.



GOG-172 IP Chemotherapy

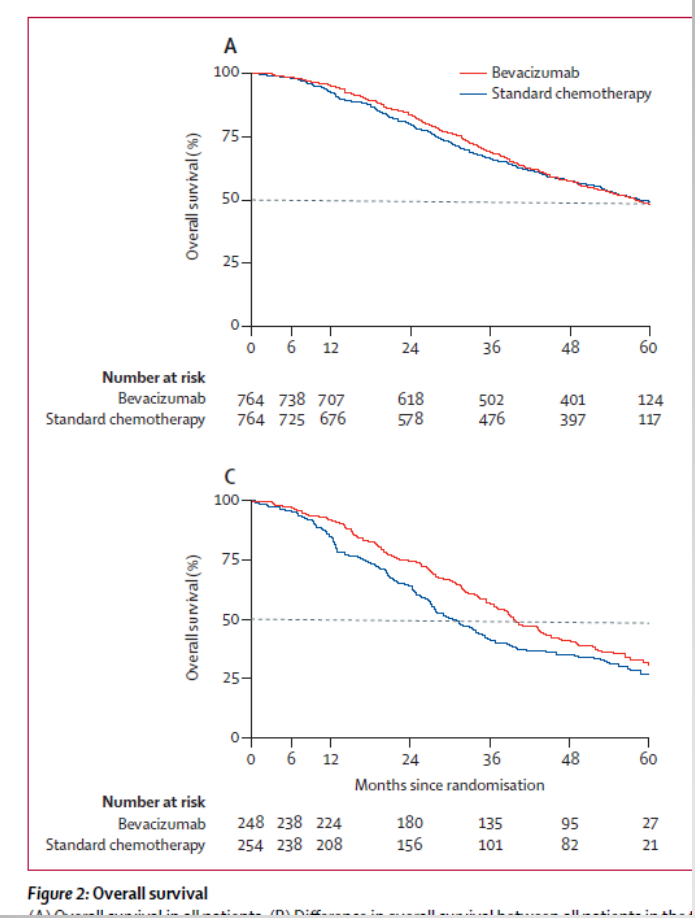


Figure 2: **Overall survival**

Intention to treat population

High risk for relapse population

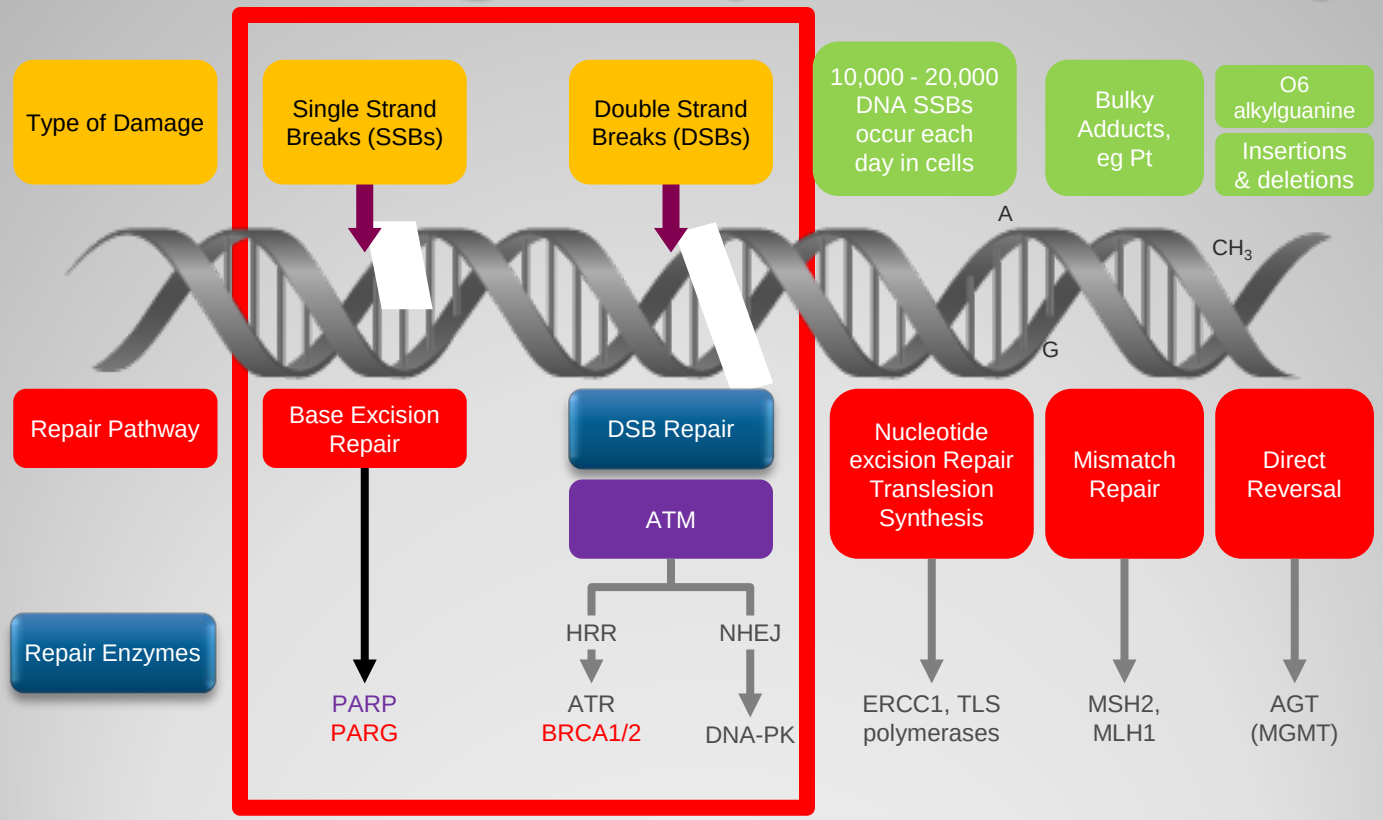
- Stage IV
- Residual disease after primary surgery
- Inoperable disease

Role of bevacizumab in newly diagnosed advanced stage disease

***Lancet Oncol* 2015; 16: 928–36**

Maintenance Therapy & Parp Inhibitors

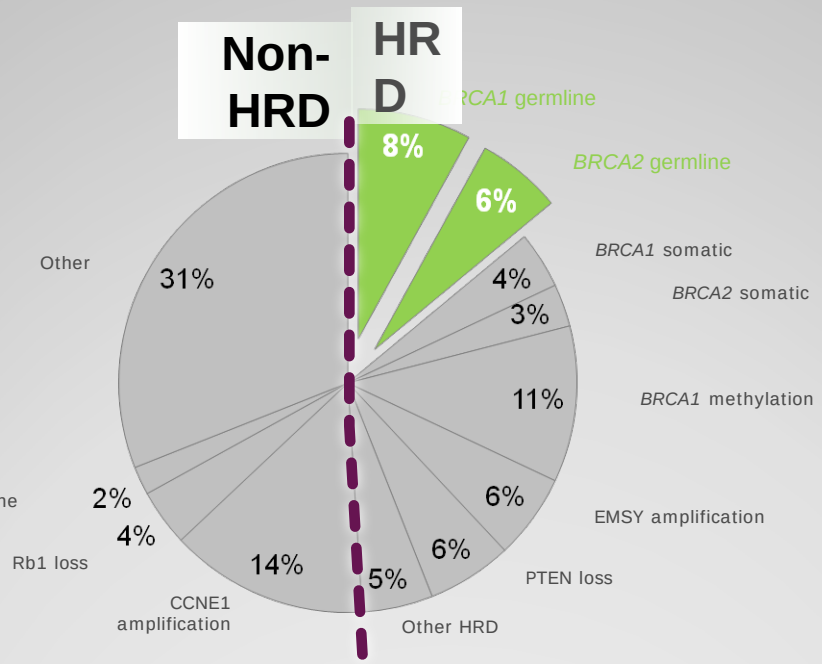
DNA Damage Repair Pathways



Jackson SP. Drug Discovery World, 2003; Fall:41–45

Homologous Recombination Deficiency (HRD) In Ovarian Cancer

- Up to **~50%** of serous OC's thought to have HRD (deficiency in repair of DSB's in DNA)
- HRD pts have **similar prognosis** as patients with a BRCA mutation (ie. improved sensitivity to platinum, as well as improved 5-year survival1)



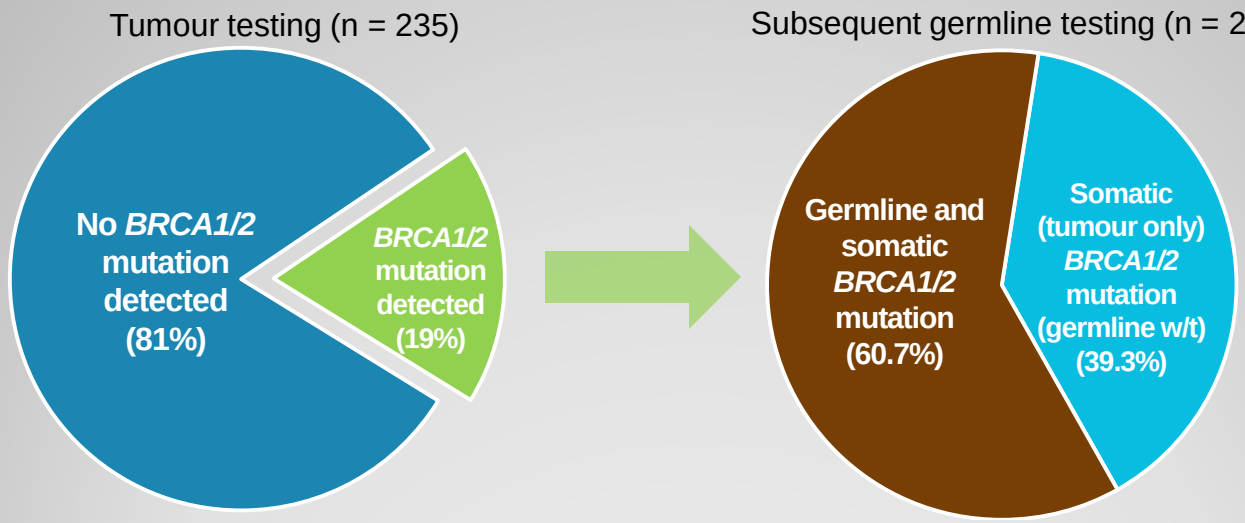
Approximately **14% of women** with ovarian cancer have a deleterious germline mutation in the *BRCA1* or *BRCA2* gene[2]

An **additional 7%** of pts have **somatic** BRCA1/2 mutations

Total population of potential BRCA mutations is **20-25%**

1. Staples J, Goodman A. PARP inhibitors in ovarian cancer. In: Díaz-Padilla I, ed. *Ovarian Cancer—A Clinical and Translational Update*. InTech, 2013. http://www.intechopen.com/books/ovarian-cancer-a-clinical-and-translational-update/parp-inhibitors-in-ovarian-cancer. Accessed December 2, 2014. 2. Pal T, Permuth-Wey J, Betts JA, et al. BRCA1 and BRCA2 mutations account for a large proportion of ovarian carcinoma cases. *Cancer*. 2005;104(12):2807-2816.

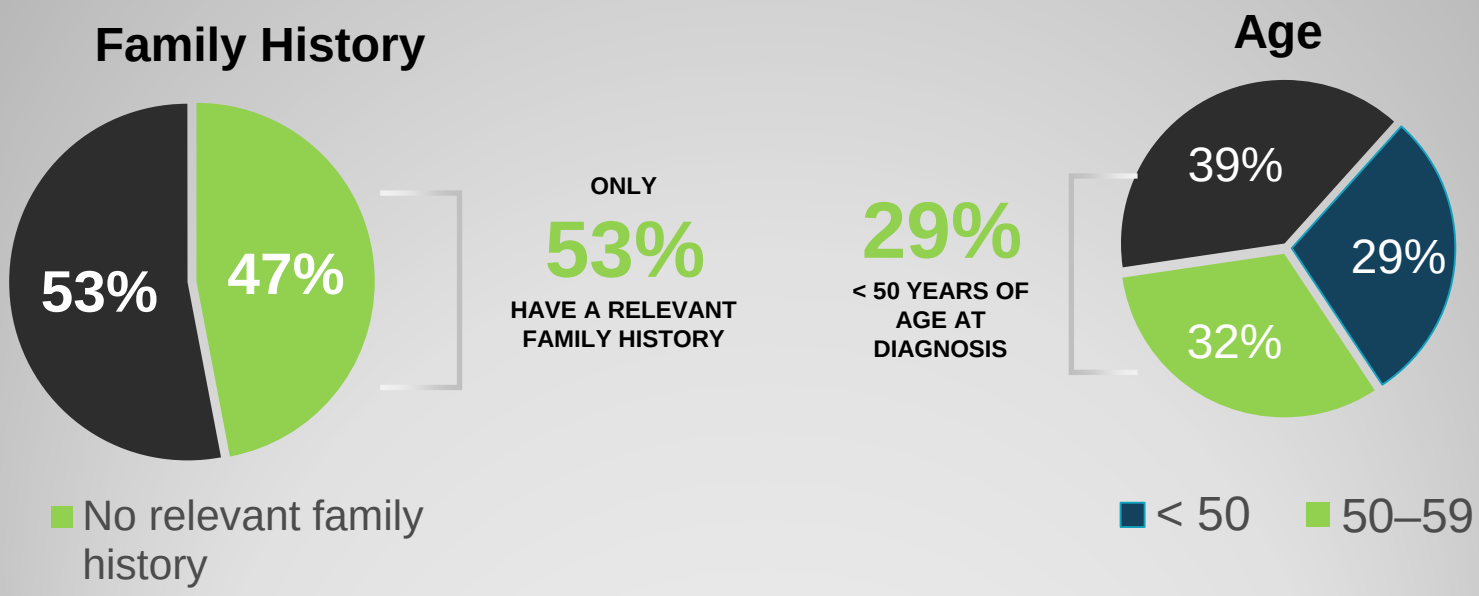
In some cases, *BRCA1/2* mutations in a woman with ovarian cancer may be present in the tumour alone



BRCA1/2 mutations were somatic (tumour only) in **~40% of cases**

Hennessy BT, et al. *J Clin Oncol* 2010;28:3570

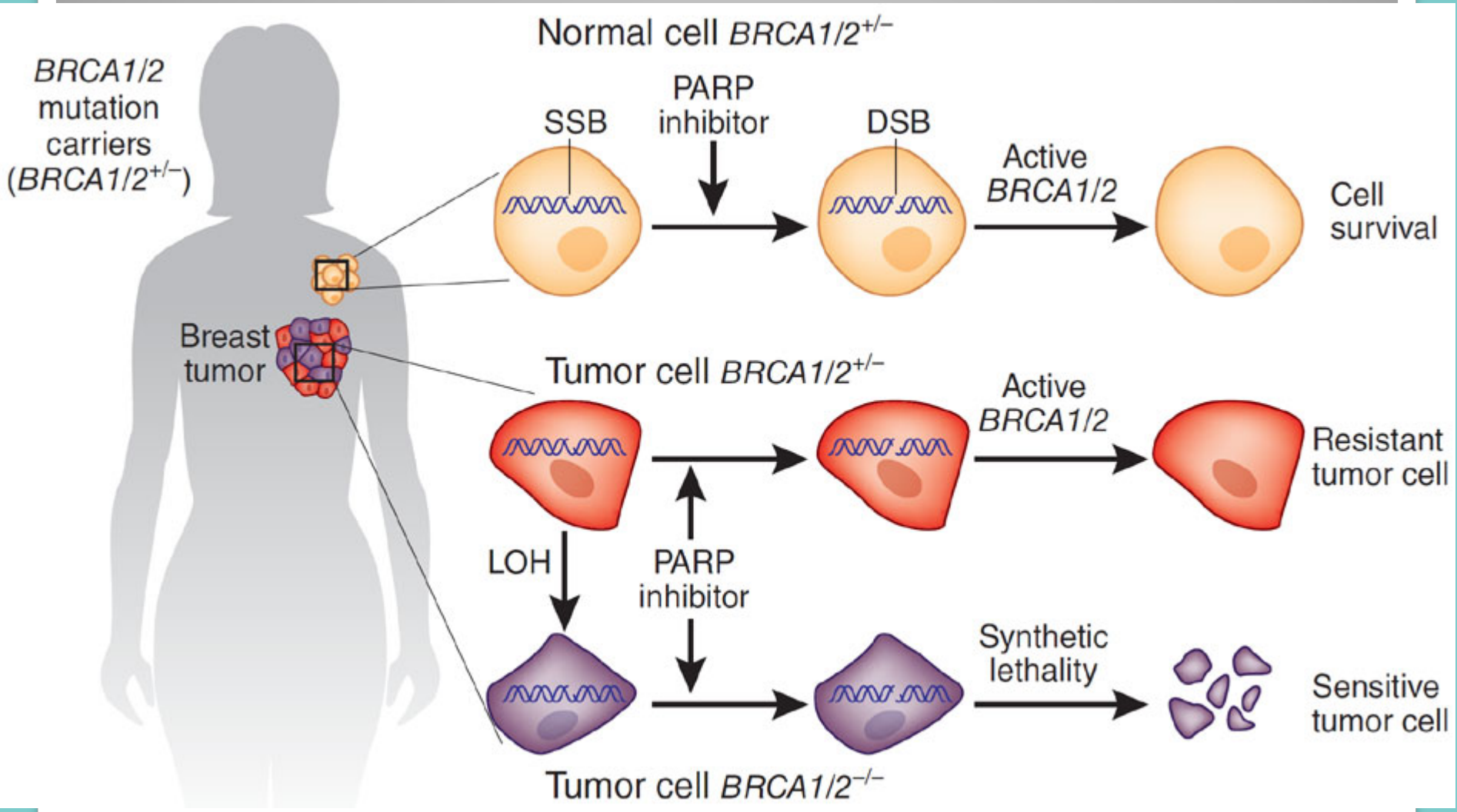
Of women with *BRCA*-mutated ovarian cancer[2,3]:



1. Norquist BM, et al. *Gynecol Oncol* 2013;128:483; 2. Song H, et al. *Hum Mol Genet* 2014;23:4703; 3. Alsop K, et al. *J Clin Oncol* 2012;30:2654

PARP Inhibitors

- PARP plays an important role in the repair of single-stranded DNA breaks
  - base excision repair pathway (BER) (high accuracy)
- Keep low-fidelity repair machinery in check
  - nonhomologous-end-joining DNA
  - Single strand annealing
- The other highly accurate DNA repair pathway is HR (double strand break repair)
- Many HGSC of the ovary have defects in the HR pathway
  - BRCA mutation
    - Germline = 25%
    - Somatic = 25%



Synthetic Lethality

MAINTENANCE THERAPY

Study design

- Newly diagnosed, FIGO stage III–IV, high-grade serous or endometrioid ovarian, primary peritoneal or fallopian tube cancer
- Germline or somatic *BRCA*m
- ECOG performance status 0–1
- Cytoreductive surgery*
- In clinical complete response or partial response after platinum-based chemotherapy

Olaparib 300 mg bd (N=260)

2:1 randomization

Stratified by response to platinum-based chemotherapy

Placebo (N=131)

- Study treatment continued until disease progression
- Patients with no evidence of disease at 2 years stopped treatment
- Patients with a partial response at 2 years could continue treatment

2 years' treatment if no evidence of disease

Primary endpoint

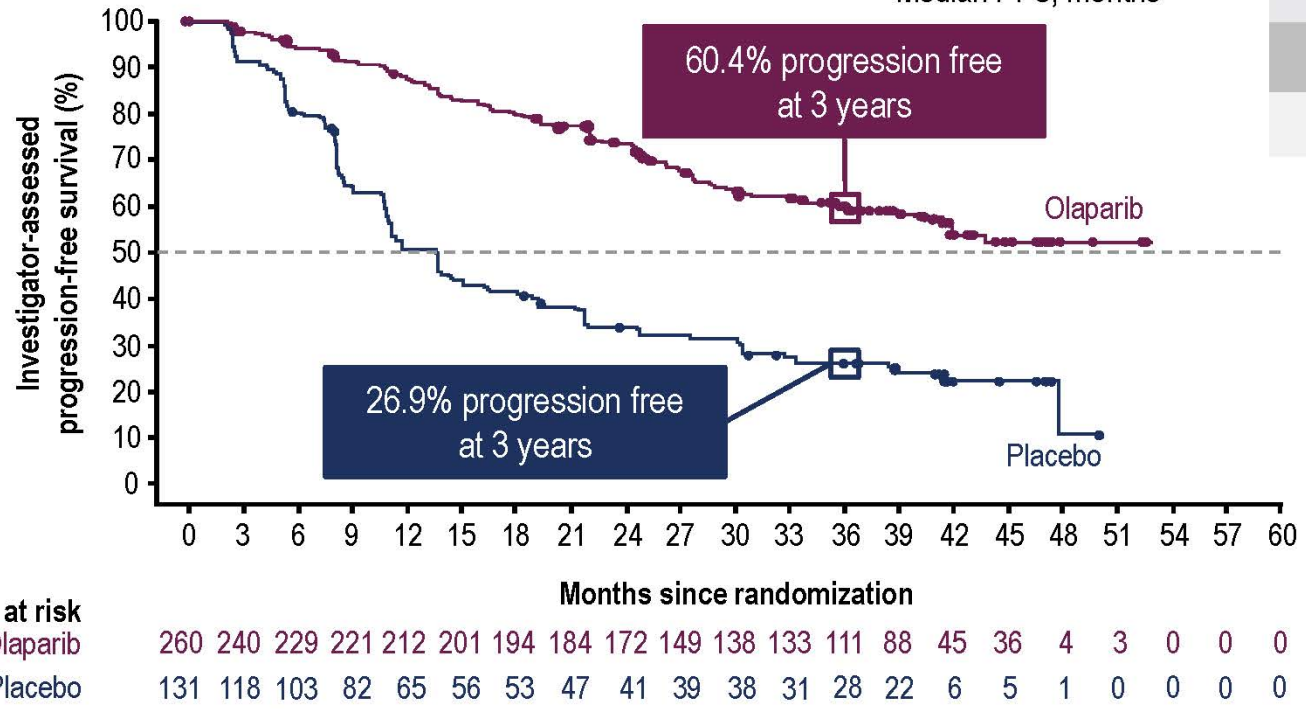
- Investigator-assessed PFS (modified RECIST 1.1)

Secondary endpoints

- PFS using BICR
- PFS2
- Overall survival
- Time from randomization to first subsequent therapy or death
- Time from randomization to second subsequent therapy or death
- HRQoL (FACT-O TOI score)

*Upfront or interval attempt at optimal cytoreductive surgery for stage III disease and either biopsy and/or upfront or interval cytoreductive surgery for stage IV disease.
BICR, blinded independent central review; ECOG, Eastern Cooperative Oncology Group; FACT-O, Functional Assessment of Cancer Therapy – Ovarian Cancer; FIGO, International Federation of Gynecology and Obstetrics; HRQoL, health-related quality of life; PFS, progression-free survival; PFS2, time to second progression or death; RECIST, Response Evaluation Criteria in Solid Tumours; TOI, Trial Outcome Index

PFS by investigator assessment



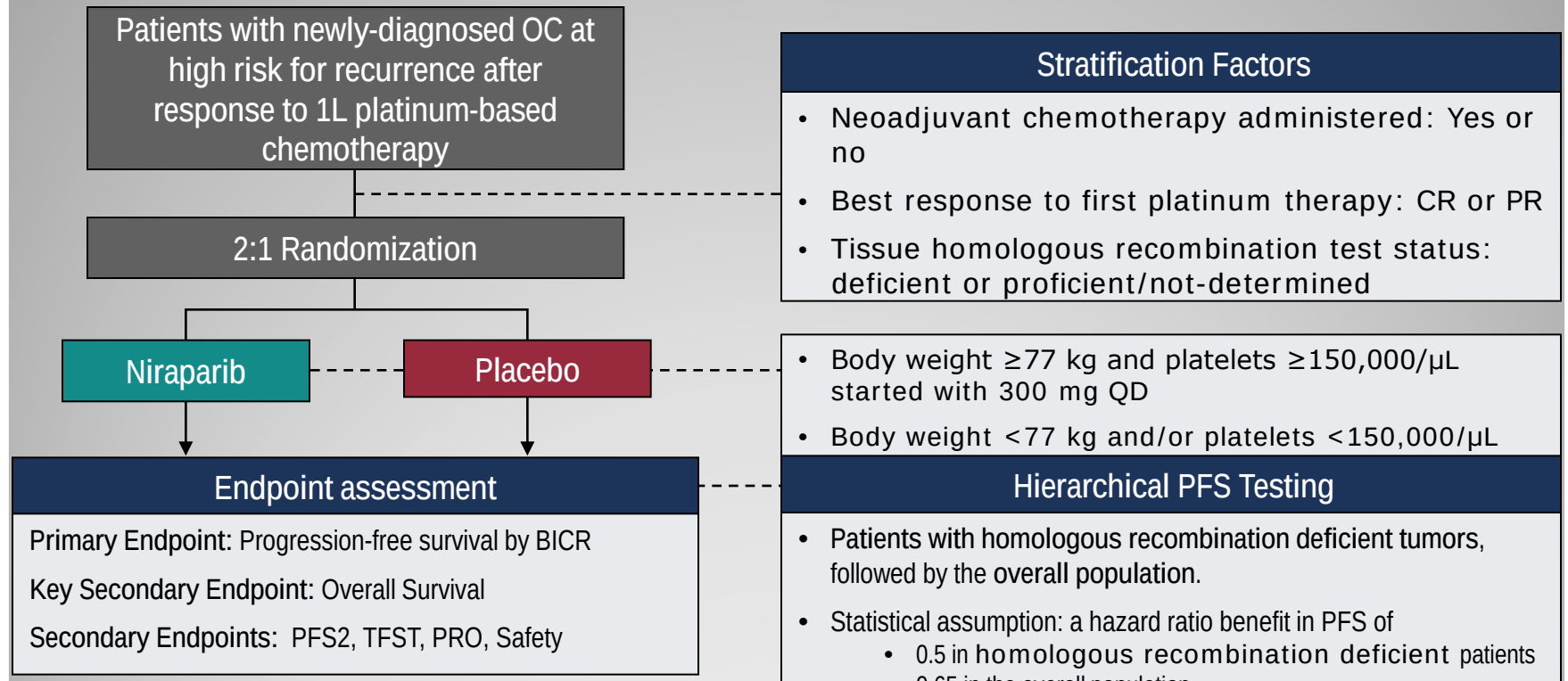
No. at risk																					
Olaparib	260	240	229	221	212	201	194	184	172	149	138	133	111	88	45	36	4	3	0	0	0
Placebo	131	118	103	82	65	56	53	47	41	39	38	31	28	22	6	5	1	0	0	0	0

	Olaparib (N=260)	Placebo (N=131)
Events (%) [50.6% maturity]	102 (39.2)	96 (73.3)
Median PFS, months	NR	13.8
HR 0.30		
95% CI 0.23, 0.41; *P*<0.0001		

MUNICH 2018 ESMO congress

CI, confidence interval; NR, not reached

PRIMA Trial Design



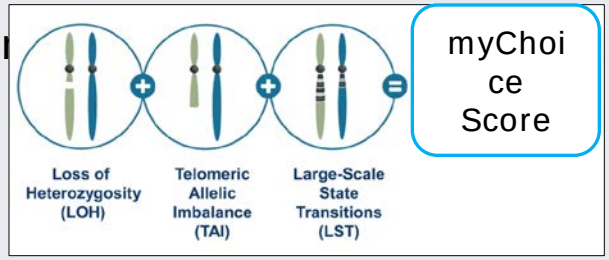
Patients were treated with niraparib or placebo once daily for 36 months or until disease progression

1L, first-line; BICR, blinded independent central review; CR, complete response; OC, ovarian cancer; PFS2, progression-free survival 2; PR partial response; PRO, patient-reported outcomes; TFST, time to first subsequent therapy.

PRIMA Tissue Test for Homologous Recombination

Testing for Homologous Recombination Deficiency (HRd) and Proficiency (HRp)

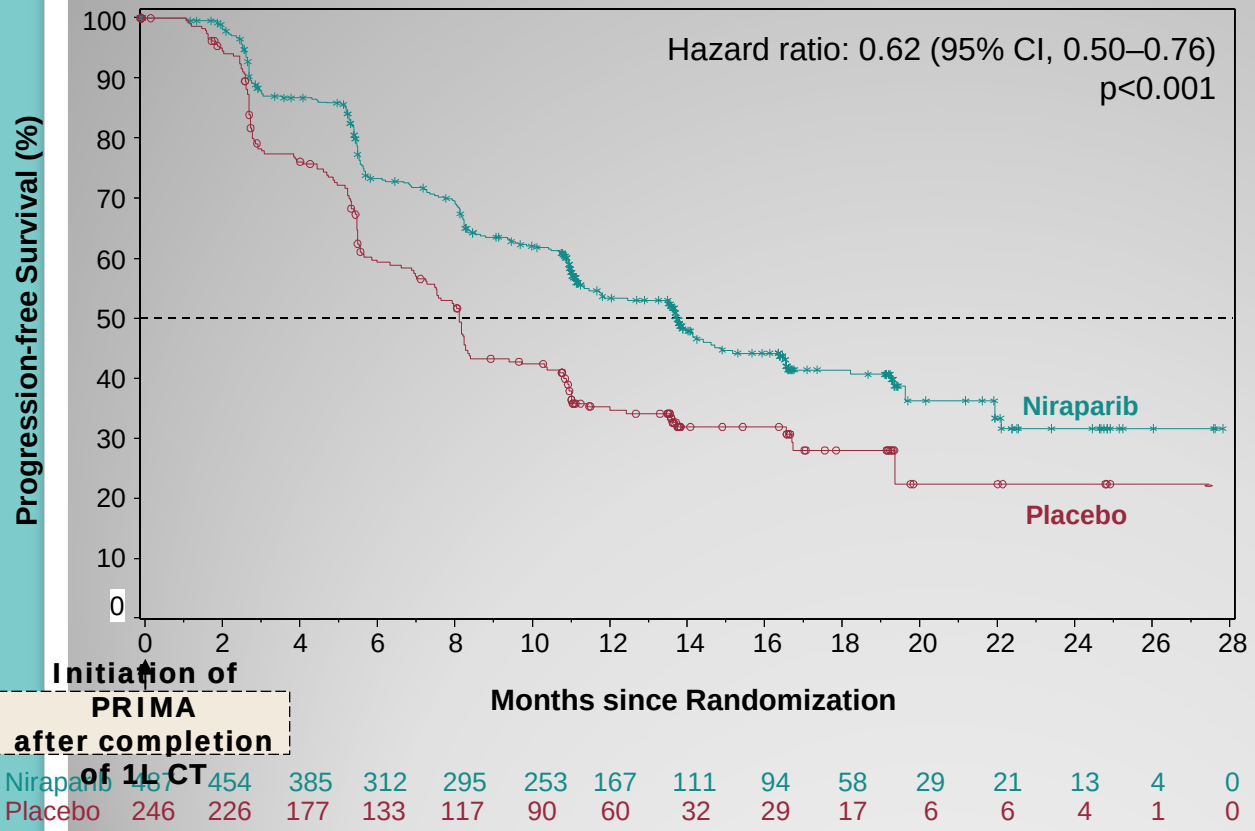
- Next generation sequencing of DNA from tumor tissue (Myriad Genetics myChoice® Test)
- Provides a score based on algorithmic measurer
  - Loss of heterozygosity (LOH)
  - Telomeric allelic imbalance (TAI)
  - Large-scale state transitions (LST)



- Homologous recombination status is determined by the following:
  - HR-deficient tumors: Tissue test score ≥42 **OR** a *BRCA* mutation
  - HR-proficient tumors: Tissue test score <42
  - HR-not-determined

https://myriadmychoice.com/portfolio/ovarian-cancer/mychoice-hrd-ovarian-cancer/#result

PRIMA Primary Endpoint, PFS Benefit in the Overall Population



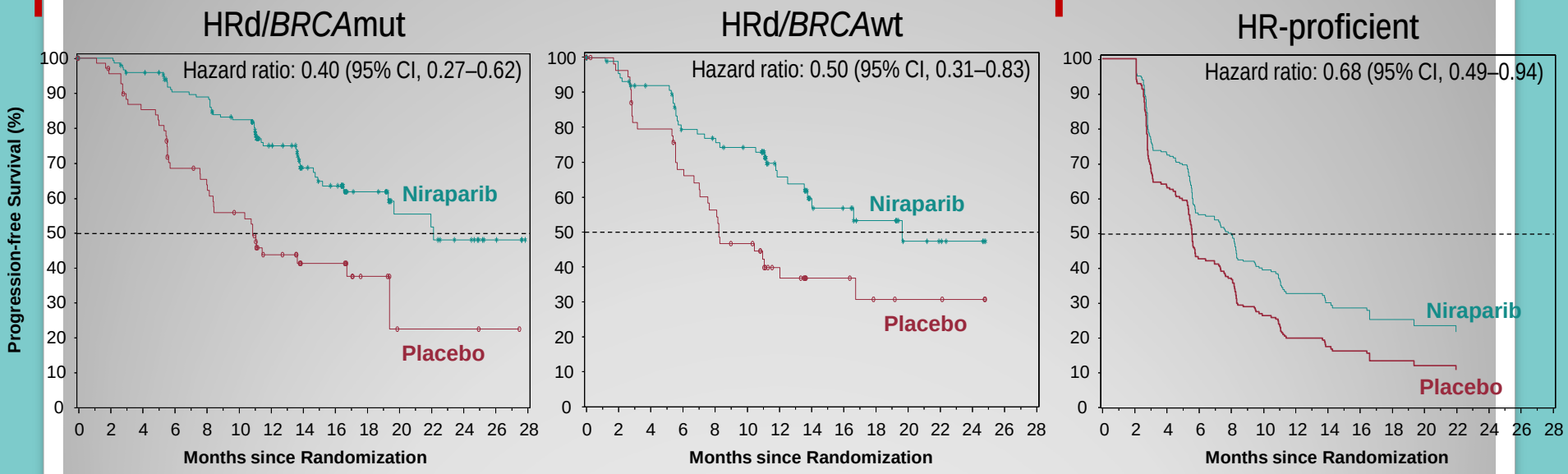
38% reduction in hazard of relapse or death with niraparib

	Niraparib (n=487)	Placebo (n=246)
Median PFS		
months	13.8	8.2
(95% CI)	(11.5–14.9)	(7.3–8.5)
Patients without PD or death (%)		
6 months	73%	60%
12 months	53%	35%
18 months	42%	28%

1L, first-line; CI, confidence interval; CT, chemotherapy; PD, progressive disease; PFS, progression-free survival.
Discordance in PFS event between investigator assessment vs BICR ≈12%.

PRIMA PFS Benefit in Biomarker Subgroups

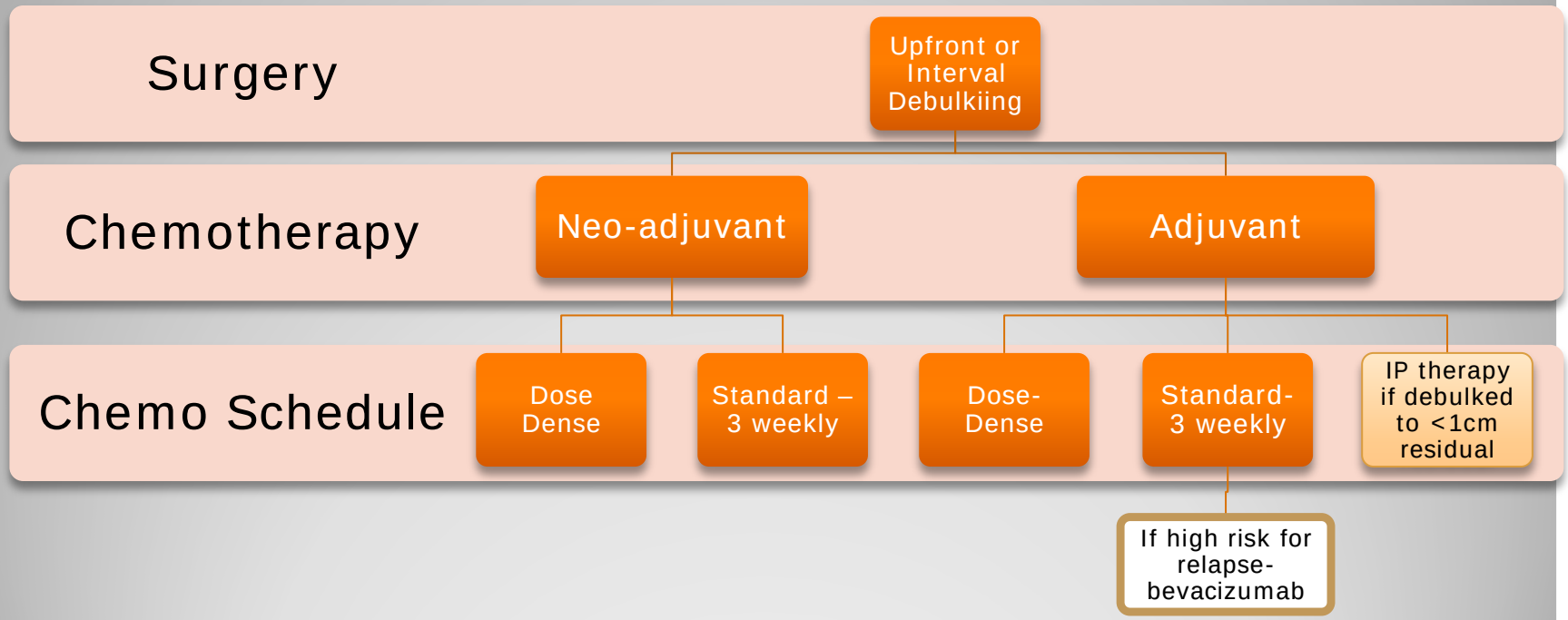
Homologous Recombination Deficient (HRd)



- Niraparib provided similar clinical benefit in the HRd subgroups (*BRCA*mut and *BRCA*wt)
- Niraparib provide clinically significant benefit in the HR-proficient subgroup with a 32% risk reduction in progression or death

CI, confidence interval; HR, homologous recombination; mut, mutation; PFS, progression-free survival wt, wild-type.

Current First-Line Treatment of Advanced Ovarian Cancer



Consider PARP Maintenance Therapy, Especially If Patient has a BRCA germline or somatic mutation

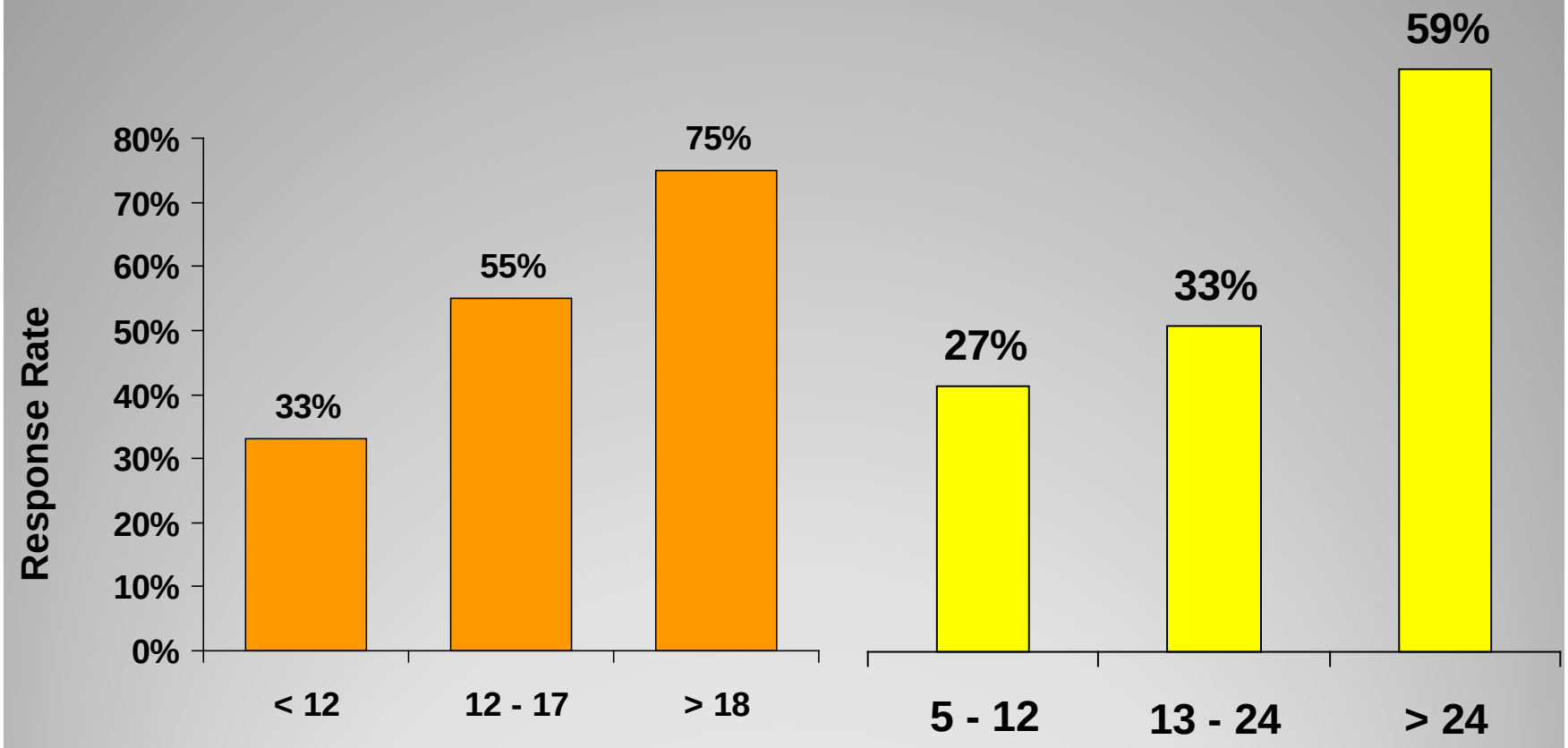
Recurrent Ovarian Cancer

	Response to Platinum	
	Initial Response	Durable Response*
Platinum-sensitive	Yes	Yes
Platinum-resistant	Yes	No
Platinum-refractory	No	–

*Defined as disease recurrence > 6 months after initial platinum-based therapy

Duration of Response to First Line Therapy

Gadducci et al. *Anticancer Res*. 2001;21:3525-3533.



Effect of Platinum-Free Interval on Platinum Rechallenge

Markman et al. *J Clin Oncol*. 2004;22:3120-3125.

Markman et al. *J Clin Oncol*. 1991;9:389-93.

Recurrence After First-Line Chemotherapy

Platinum Refractory/Resistant	Platinum Sensitive
< 6 Mos	> 6 Mos
Non-Platinum Single Agent	Chemotherapy Doublet

The Traditional Treatment Paradigm

Ushijima, 2010.

Recurrent Ovarian Cancer

- Consider the platinum-sensitive interval
  - > 6 mo, sensitive
  - < 6 mo, resistant
    - Assessed based on symptoms and imaging, and not on CA125 rise
      - This definition was originally developed after the use of primary therapy and not in 2nd, 3rd recurrence, but most practitioners have expanded the definition beyong first line

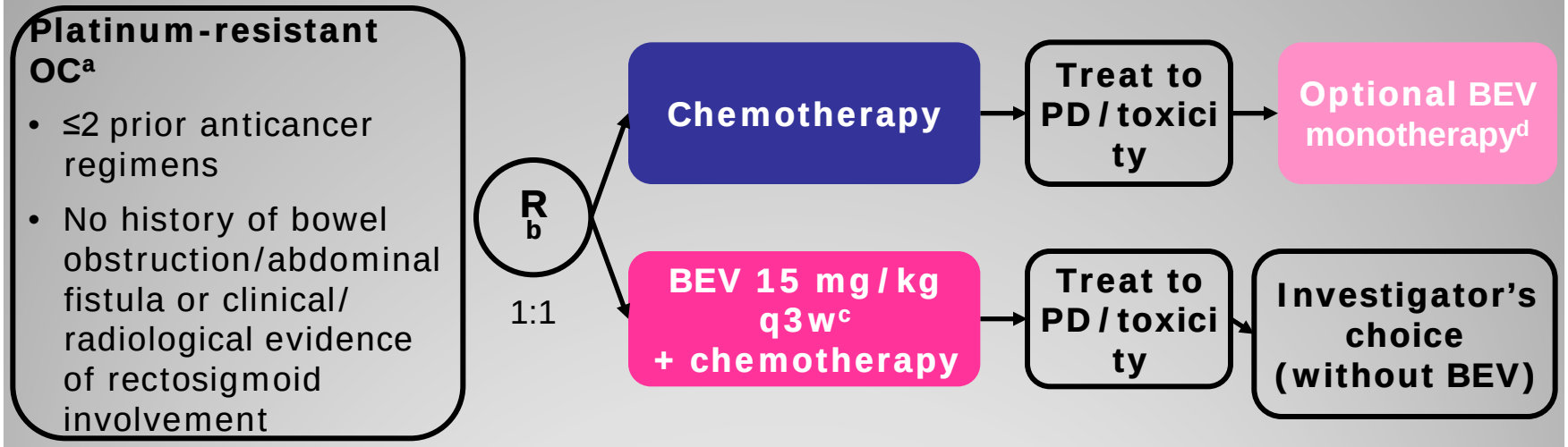
Recurrent Ovarian Cancer

- Platinum sensitive:
  - Return to platinum
    - as single agent
    - as a doublet
      - Carboplatin-paclitaxel
      - Carboplatin-liposomal doxorubicin
      - Carboplatin-gemcitabine
        - Choice is made by considering residual toxicity (neuropathy), comorbidities, convenience (travel)
      - Maintenance PARP inhibitor (BRCA +) – see slides 42-50
- Platinum resistant:
  - Consider sequential single agents (with bevacizumab – see next slide)
    - Carboplatin
    - Paclitaxel
    - Gemcitabine
    - Liposomal doxorubicin
    - Vinorelbine
    - Etoposide

Role of Bevacizumab – Plt Resistant Disease

- Bevacizumab is a anti-body inhibitor of VEGF
- VEGF is commonly over expressed in the ascites of ovarian cancer patients
  - Involved in the mechanism of ascites formation and in angio-neogenesis for cancer
- Phase III trials have shown that Bevacizumab has activity in several treatment settings for ovarian cancer
  - First line therapy – improved PFS and OS in a subset
  - Second line, platinum sensitive – improved PFS
  - Platinum resistant – improved PFS and QoL
- <u>In BC, funding is provided for those getting chemo for platinum-resistant recurrence</u>
  - Bev improved Qol (and reduced the need for malignant fluid removal)
  - Bev prolonged PFS ~ 3 mo

AURELIA trial design



Primary endpoint: PFS (RECIST v1.0)

Secondary endpoints:

- ORR
- OS (after OS events in 70%)
- Quality of life
- Safety and tolerability

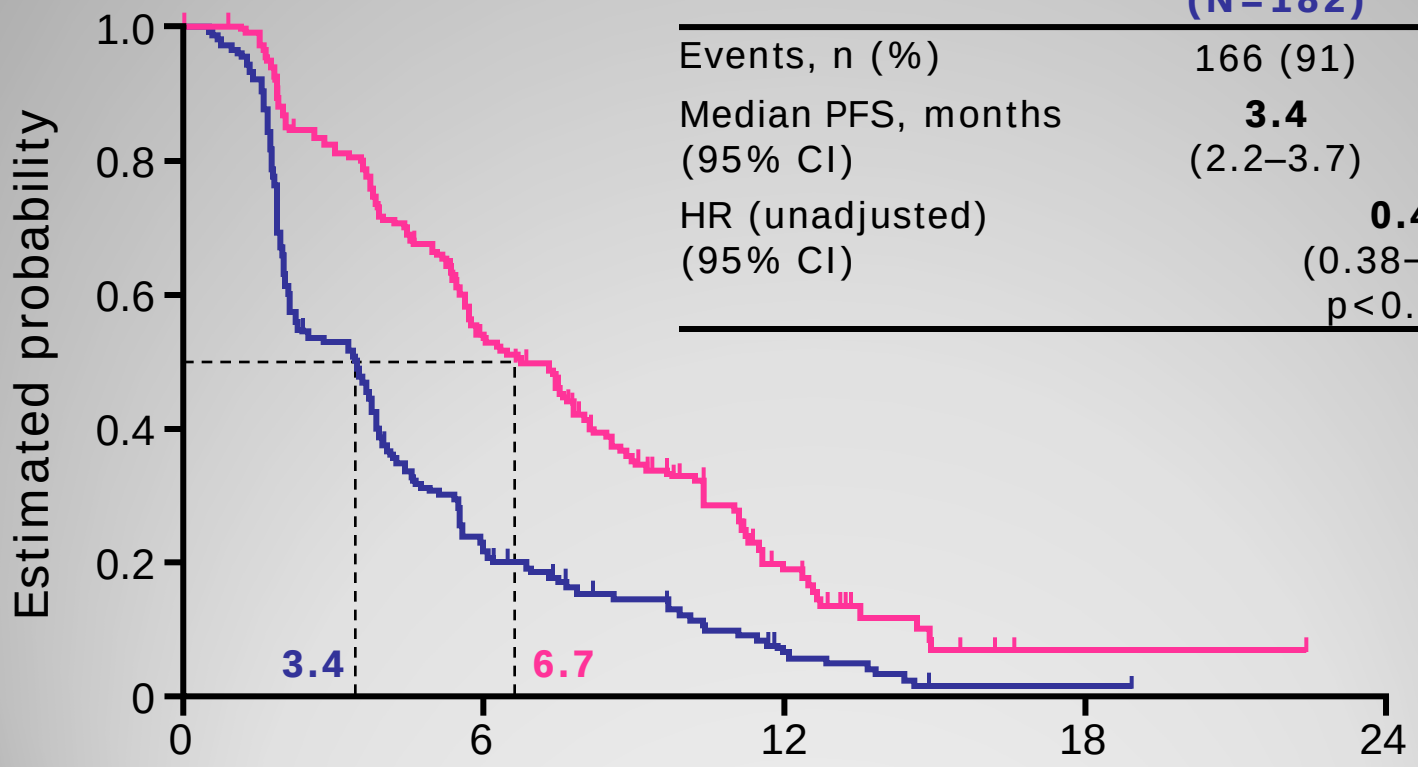
Chemotherapy options (investigator's choice):

- Paclitaxel 80 mg/m^2 days 1, 8, 15, & 22 q4w
- Topotecan 4 mg/m^2 days 1, 8, & 15 q4w (or 1.25 mg/m^2, days 1–5 q3w)
- PLD 40 mg/m^2 day 1 q4w

LBA presented by Witteveen at the ECCO 17 Meeting, Amsterdam, Netherlands, Sep 27 – Oct 1, 2013

Primary PFS analysis

	CT (N=182)	BEV + CT (N=179)
Events, n (%)	166 (91)	135 (75)
Median PFS, months (95% CI)	**3.4** (2.2–3.7)	**6.7** (5.7–7.9)
HR (unadjusted) (95% CI)	**0.48** (0.38–0.60) p<0.001[a]	

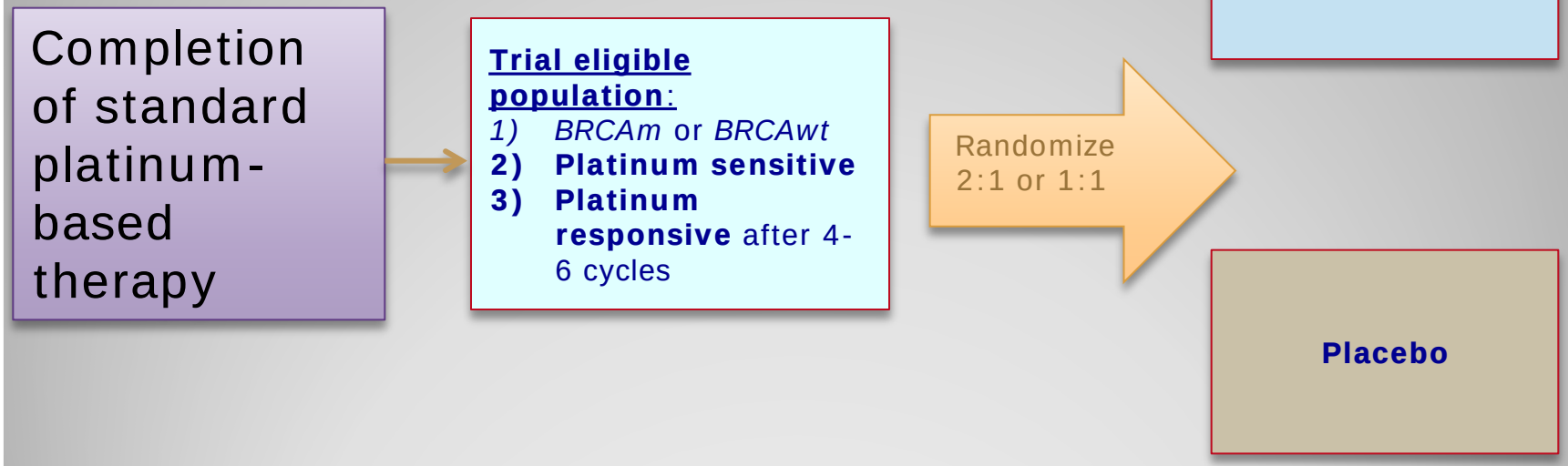


No. at risk:

CT	182	93	37	20	8	1	1	0	0
BEV + CT	179	140	88	49	18	4	1	1	0

LBA presented by Witteveen at the ECCO 17 Meeting, Amsterdam, Netherlands, Sep 27 – Oct 1, 2013

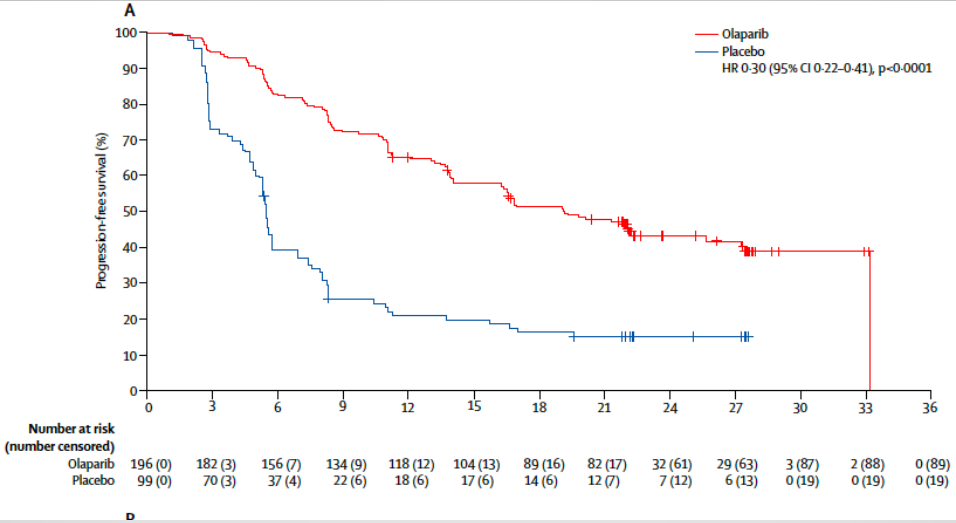
Basic Maintenance Study Design for **Recurrent** Ovarian Cancer



Standard practice after chemo response is observation, therefore, placebo control is acceptable

Maintenance PARP inhibitor: the new SOC in **recurrent, platinum-sensitive** and -**responsive** ovarian cancer

SOLO-2: Olaparib in ***BRCAm*** Ovarian cancer

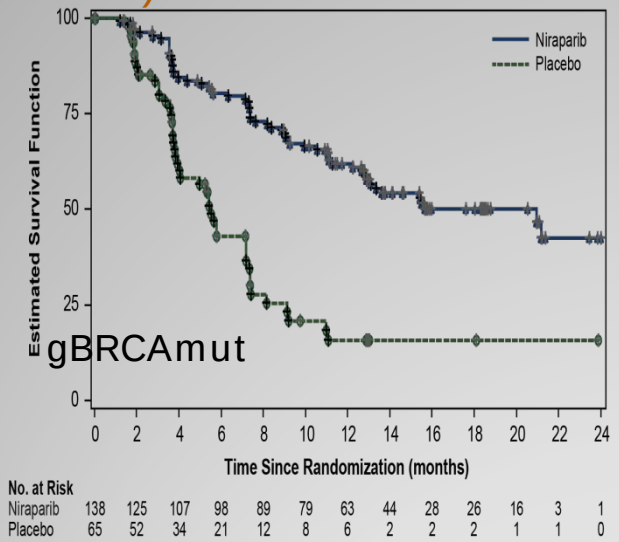


- **PFS olaparib: 19.1 mo**
- **PFS placebo: 5.5 mo**
- **HR: 0.30 (95% CI, 0.22-0.41)**
- P<0.0001
- No OS data yet

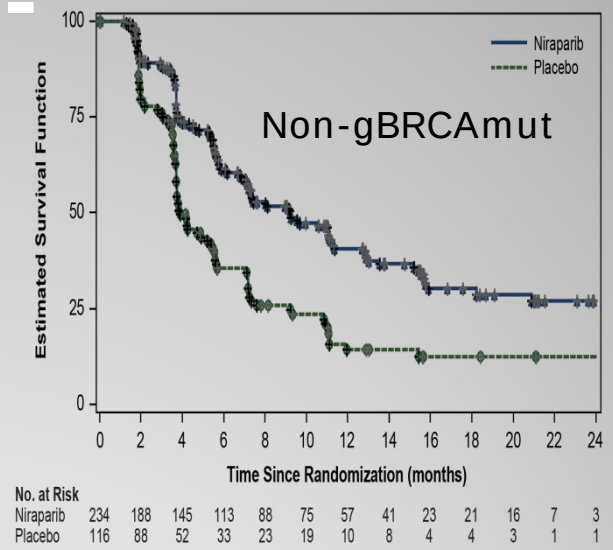
Pujade-Lauraine et al. Lancet Oncol 2017; 18:

Maintenance PARP inhibitor: the new SOC in **recurrent**, **platinum-sensitive** and -**responsive** ovarian cancer

NOVA trial: Niraparib in platinum-sensitive and response ovarian cancer (**any *BRCA* status**)



Treatment	PFS Median (95% CI) (Months)	Hazard Ratio (95% CI) p-value
Niraparib (N=138)	**21.0** (12.9, NE)	**0.27** (0.173, 0.410) p<0.0001
Placebo (N=65)	**5.5** (3.8, 7.2)	



Treatment	PFS Median (95% CI) (Months)	Hazard Ratio (95% CI) p-value
Niraparib (N=234)	**9.3** (7.2, 11.2)	**0.45** (0.338, 0.607) p<0.0001
Placebo (N=116)	**3.9** (3.7, 5.5)	

Mirza MR et al. N Engl J Med. 2016 Dec 1;375(22):2154-2164. Epub 2016 Oct_7

Common Adverse Events and Side Effects

- Many side effects are multifactorial
  - E.g. fatigue
- Majority of PARPi AEs and laboratory abnormalities are grade 1 and 2
  - But many patients have several side effects at once
- Limited reporting of QoL data suggests that at least in the setting of maintenance therapy, QoL on a PARPi and on placebo are the same

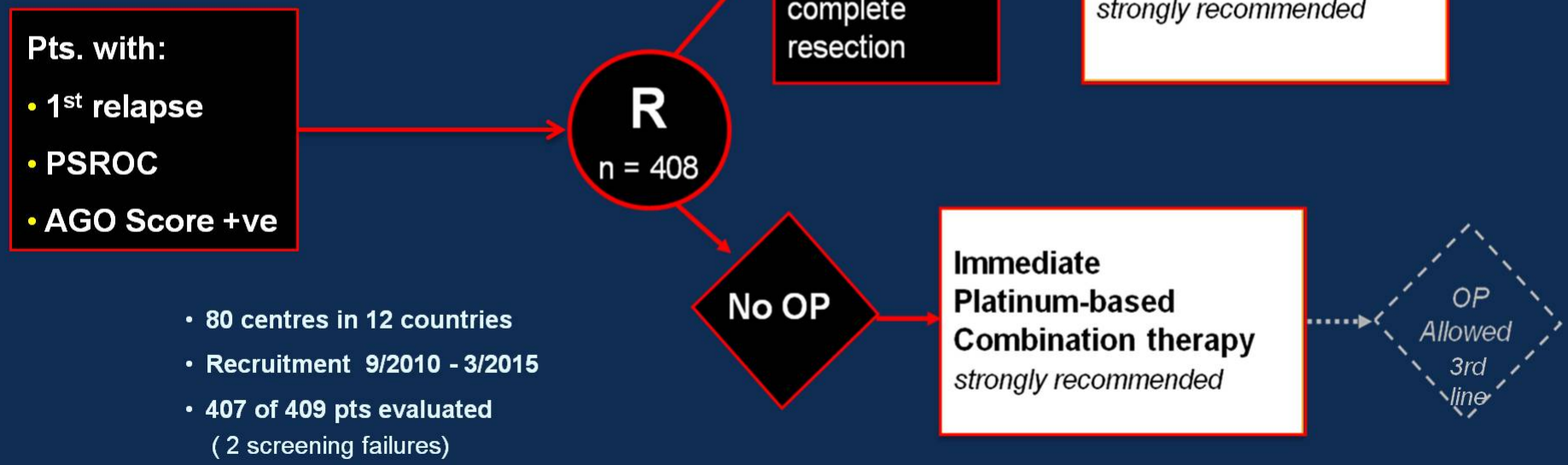
- Nausea
- Vomiting
- Fatigue
- Anemia
- Diarrhea
- Thrombocytopenia (niraparib)
- Constipation (niraparib)
- Rise in Cr (rucaparib)
- Elevation of LFTs (rucaparib)
- ~1-2% risk of myelodysplastic syndrome and acute myelogenous leukemia

Many side effects are multifactorial
E.g. fatigue
Majority of PARPi AEs and laboratory abnormalities are grade 1 and 2
But many patients have several side effects at once
Limited reporting of QoL data suggests that at least in the setting of maintenance therapy, QoL on a PARPi and on placebo are the same

Role of second surgery at recurrence?

Design: AGO DESKTOP III
(ENGOT-ov20; NCT01166737)

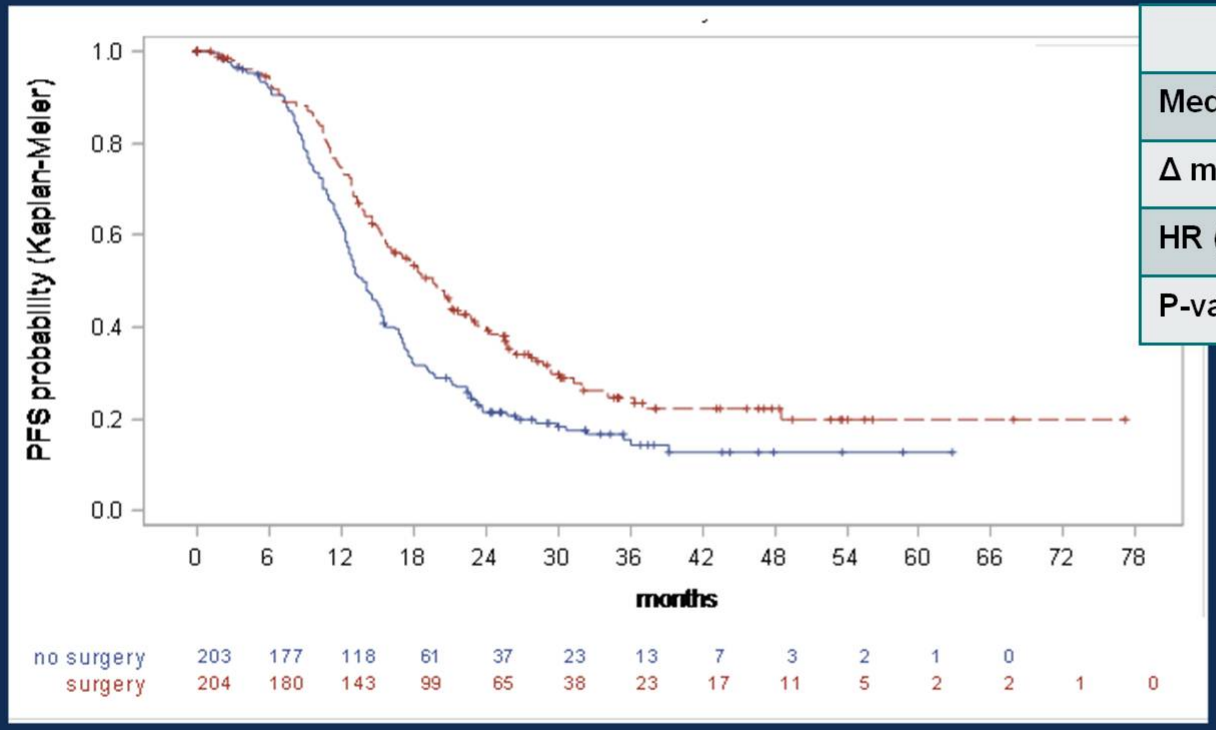
Sponsor: AGO
ENGOT Model A



- 80 centres in 12 countries
- Recruitment 9/2010 - 3/2015
- 407 of 409 pts evaluated
  (2 screening failures)

Presented by: Andreas du Bois
AGO & KEM
Essen, Germany

AGO DESKTOP III: Outcome 2 (PFS, ITT population)
(AGO–OVAR OP.4; ENGOT-ov20; NCT01166737)

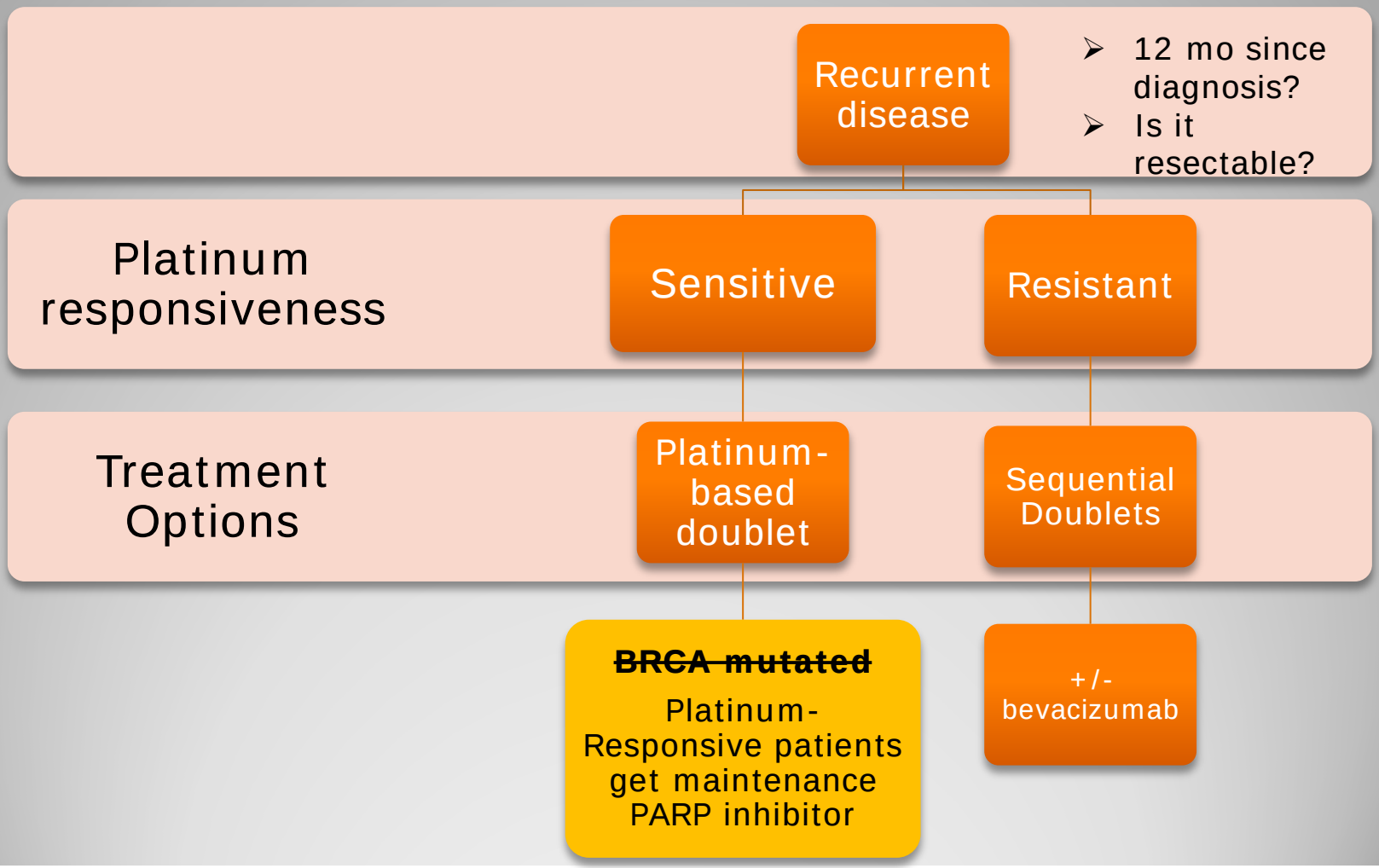


	Surgery	No surgery
Median PFS	19.6 mos	14.0 mos
Δ median PFS	5.6 mos	
HR (95% CI)	0.66 (0.52 – 0.83)	
P-value	< 0.001	

296 (73%) PFS events

Presented by: Andreas du Bois
AGO & KEM
Essen, Germany

Treatment of Recurrent Disease – Near future?



Immune therapy

- HGSC of the ovary
  - The presence of tumour infiltrating lymphocytes is associated with a better prognosis
  - PD-L1 and PD-1 expression is seen on ovarian cancer cells and associated T-cells
  - Checkpoint inhibition is being studied in ovarian cancer

Summary

- Ovarian cancer is not ovarian…fallopian and endometrial origins explain most
- No screening (should not be done)
- Surgery timing can be up front or delayed
- IP chemotherapy has the best survival data so far for stage III
- Platinum Sensitive disease
  - Use platinum until no longer tolerated or responsive
  - Add switch to parp inhibitor (for now only in BRCA positive)
- Platinum resistant disease
  - Poor prognosis, use single agents +/- bevacizumab
- Future developments
  - Parp inhibitors combinations in first-line and second line
  - Immunotherapy?