ESMO Clinical Practice Guidelines

Recurrent Ovarian Cancer

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Disclosures

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Points of Discussion

- Selection of Second-Line Chemotherapy for Recurrent Ovarian Cancer
- Role of Surgery in Recurrent Ovarian Cancer
- Maintenance or Surveillance?
- Selection of Third-Line Chemotherapy

ESMO Clinical Practice Guidelines: Gynaecological Cancers

clinical practice guidelines

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Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

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Selection of Second-Line Chemotherapy for Recurrent Ovarian Cancer

- Based on Platinum Sensitivity
  - Platinum Refractory — Progressing during Cx
  - Platinum Resistant — PFI < 6 month
  - Platinum Partially Sensitive — PFI 6-12 month
  - Platinum Sensitive — PFI >12 month

Chemotherapy for Platinum Sensitive Recurrent Ovarian Cancer

- For those patients with a later relapse, over 6 months and especially over 12 months, carboplatin-doublet should be the treatment of choice [I, A].

Evidence of patient combination for patient sensitive relapse Ovarian Cancer

- ICON4
- AGO

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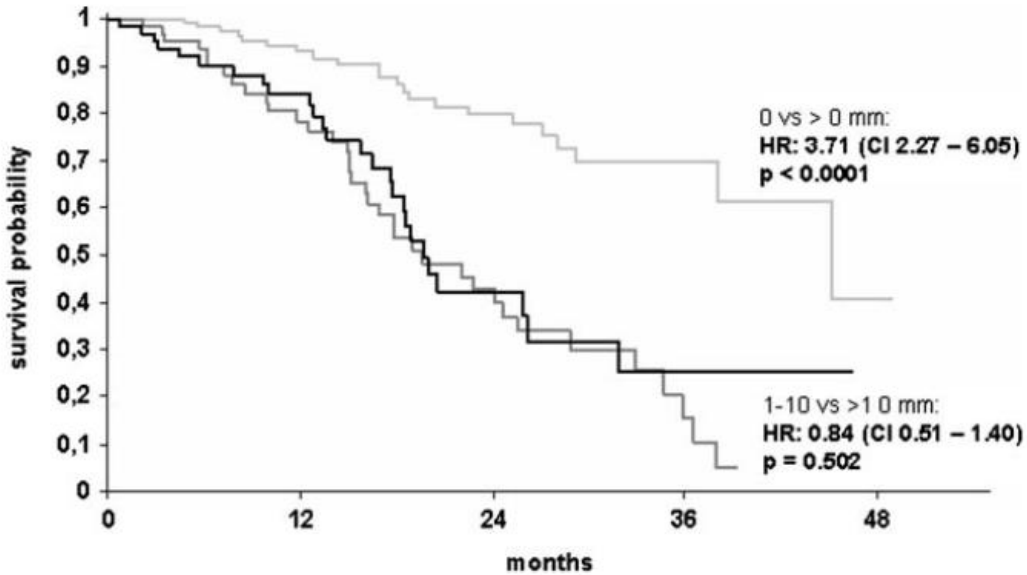
Surgical Management in Relapsed Ovarian Cancer

Recommendation

- Patients with two of three of the following criteria: complete resection at first surgery, good performance status and absence of ascites had the best survival [III, C].
  - The value of surgical cytoreduction in relapsed epithelial ovarian cancer remains controversial and is not regarded as a standard of care, as the evidence for this approach has not been demonstrated in prospective trials. In retrospective analyses, surgery at first relapse appears to be associated with a survival benefit only when a complete tumour resection can be obtained

Evidence for Surgical Management in Relapse Ovarian Cancer



Patients at risk					
RD= 0 mm	133	78	40	8	1
RD=1-10 mm	69	38	15	3	0
RD >10 mm	65	37	11	3	0

: RD=0mm, median OS: 45.2 months. : RD=1-10 mm, median OS:19.6 months.
: RD > 10 mm, median OS:19.7 months.

RD: residual disease after surgery for recurrence. OS: median overall survival

Evidence for Surgical Management in Relapse Ovarian Cancer

- DESKTOP

TABLE 5. *Multivariate analysis of factors for achieving complete resection*

Parameter	Estimate		OR	95% CI	*P* value
Eastern Cooperative Oncology Group (ECOG)	.98	.27	2.65	1.56–4.52	< .001
Residual disease after primary surgery (mm)*	.90	.27	2.46	1.45–4.20	< .001
Ascites	1.63	.48	5.08	1.97–13.16	< .001
Localization of recurrence in preoperative diagnostics	.44	.31	1.55	.85–2.82	.155

OR odds ratio, *CI* confidence interval.

* Alternatively International Federation of Gynecology and Obstetrics (FIGO) stage if residual disease after primary surgery is unknown [hazard ratio (HR) 1.87 (95% CI 1.04–3.37); $P = .036$].

Evidence for Surgical Management in Relapse Ovarian Cancer

- Randomized trials to verify the role of surgery (Surgery vs No Surgery) for platinum sensitive recurrent ovarian cancer
  - DESKTOP III
  - GOG213
- Eligible Patients
  - DESKTOP
    - Based on AGO Surgical Sore
  - GOG213
    - Based on Investigator's decision

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Maintenance Chemotherapy or Surveillance After Chemotherapy plus Surgery?

- No appropriate guideline…..

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Selection of 3rd Line Chemotherapy for Pt-free interval > 6 months

- No clear evidence for supporting selection of patient combination

  But

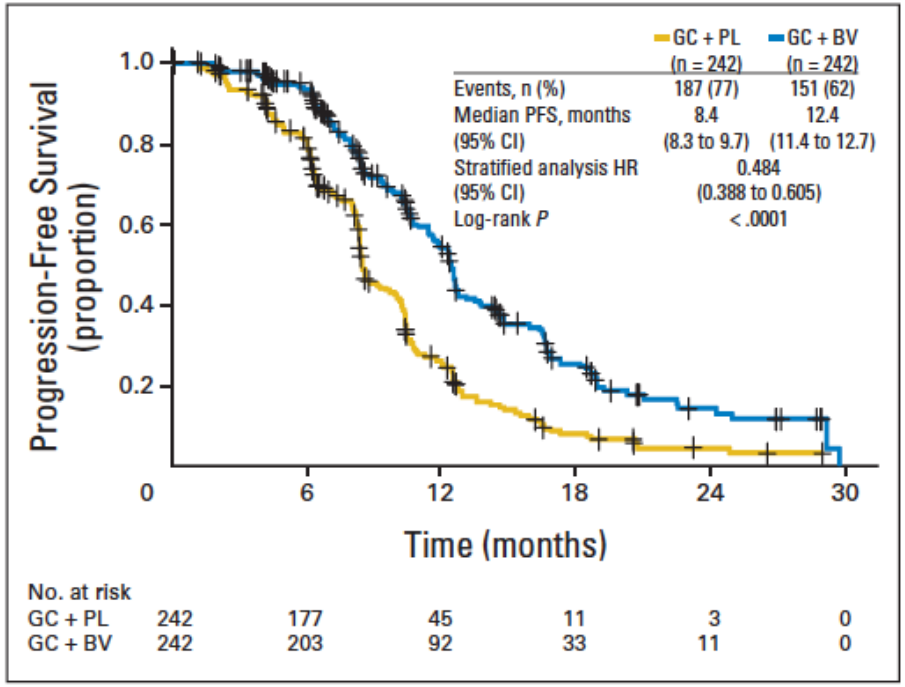
- Usually select platinum combination

Role of bevacizumab maintenance therapy in recurrent Ovarian Cancer

- Bevacizumab has shown to improve the PFS of recurrent ovarian cancer in two randomised phase III trials [I,A].
  - The first (OCEANS trial) included patients with measurable recurrent ovarian cancer after first-line and a platinum-free interval longer than 6 months.
  - The second (AURELIA) trial was carried out in patients with 'platinum-resistant' ovarian cancer.
- However, bevacizumab in combination with this chemotherapy has been licensed by the EMA and is a recommended treatment for patients with 'platinum-sensitive' relapsed ovarian cancer who have not previously received bevacizumab.

Evidence for Bevacizumab

OCEANS



AURELIA

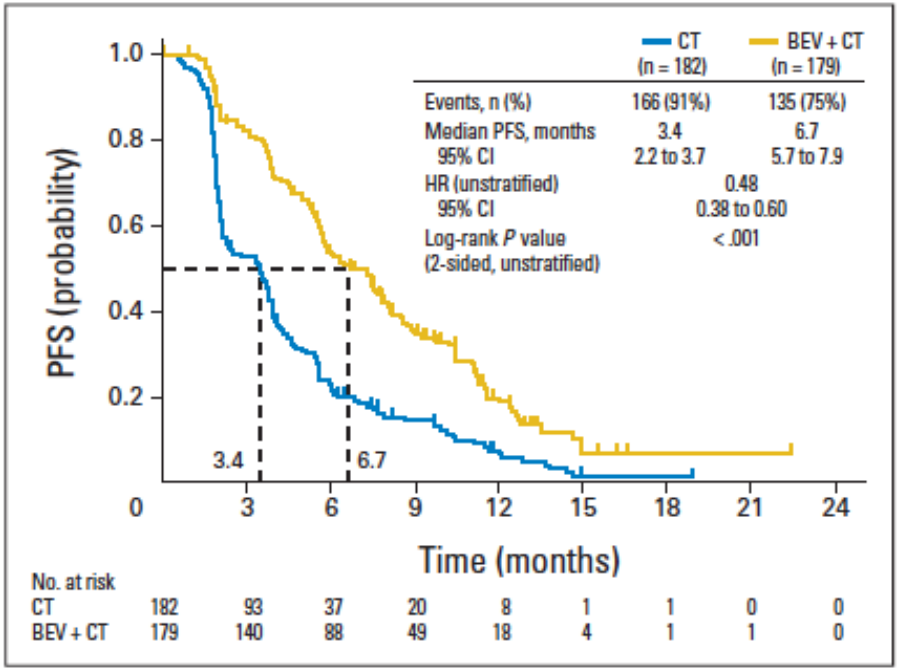
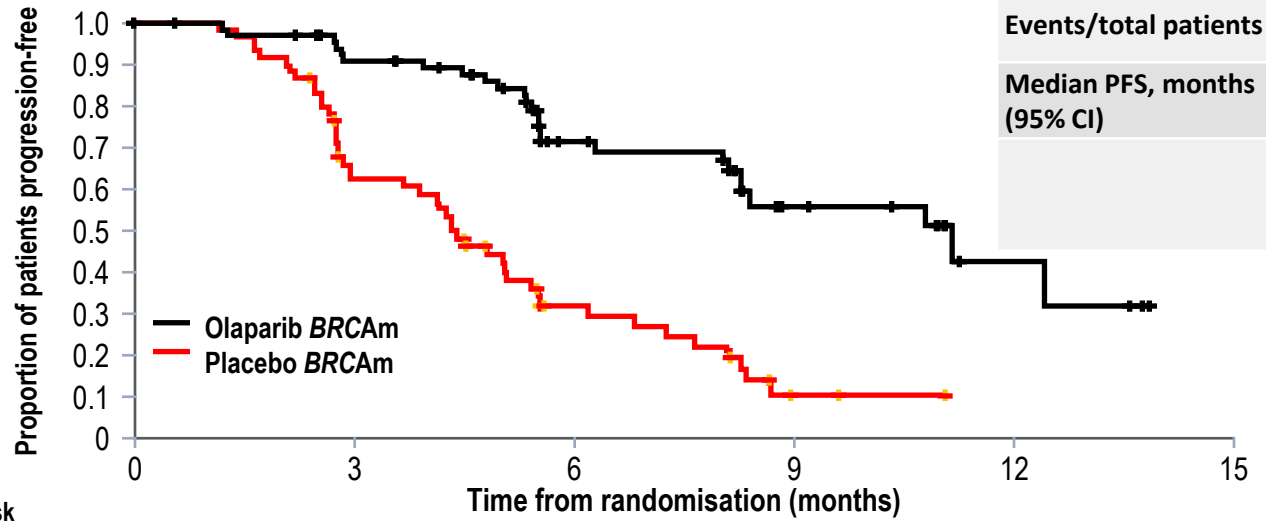


Fig 2. Progression-free survival (PFS). BEV, bevacizumab; CT, chemotherapy; HR, hazard ratio.

Role of PARP inhibitor

- Germline BRCA mutations are present in about 17% of high-grade ovarian cancers, most commonly in serous ovarian cancers. 6–8% of these tumours have somatic BRCA mutations.
- Tumours with a BRCA mutation have defective DNA repair and respond to treatment with a PARP inhibitor.
- Olaparib is the first PARP inhibitor to be licensed by the European Medicines Agency for maintenance treatment of recurrent ovarian cancer with a germline or somatic BRCA mutation.
- Give after platinum-based therapy, following a relapse free interval of ≥6 months.
- The clinical trial showed a significant extension in PFS but data for OS are still immature.

Evidence for Olaparib
STUDY 19: Progression-free survival in patients with a *BRCA*^{mut}



Number at risk						
Olaparib *BRCA*m	74	59	34	15	5	0
Placebo *BRCA*m	62	35	13	2	0	0

	BRCAm (n=136)	
	Olaparib	Placebo
Events/total patients (%)	26/74 (35%)	46/62 (74%)
Median PFS, months (95% CI)	11.2 (8.3, NC)	4.3 (3.0, 5.4)
	HR=0.18 95% CI: 0.10, 0.31; P<0.0001	

NC, not calculable.

Ledermann J et al. Lancet Oncol 2014;15:852–861