ESMO Clinical Practice Guidelines

Recurrent Ovarian Cancer

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Disclosures

Keiichi Fujiwara has declared no potential conflicts of interest
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
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
Points of Discussion

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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

- 0 vs > 0 mm: HR: 3.71 (CI 2.27 - 6.05) p < 0.0001
- 1-10 vs > 10 mm: HR: 0.84 (CI 0.51 - 1.40) p = 0.502

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: residual disease after surgery for recurrence. OS: median overall survival
Evidence for Surgical Management in Relapse Ovarian Cancer

- DESKTOP

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Cooperative Oncology Group (ECOG)</td>
<td>.98</td>
<td>.27</td>
<td>2.65</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Residual disease after primary surgery (mm)*</td>
<td>.90</td>
<td>.27</td>
<td>2.46</td>
<td>&lt; .001</td>
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<tr>
<td>Ascites</td>
<td>1.63</td>
<td>.48</td>
<td>5.08</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Localization of recurrence in preoperative diagnostics</td>
<td>.44</td>
<td>.31</td>
<td>1.55</td>
<td>.155</td>
</tr>
</tbody>
</table>

* 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
Points of Discussion

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Maintenance Chemotherapy or Surveillance After Chemotherapy plus Surgery?

- No appropriate guideline.....
Points of Discussion

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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**
- Events, n (%): GC + PL (n = 242) vs GC + BV (n = 242)
- Median PFS, months: 8.4 vs 12.6 (95% CI: 8.3 to 9.7 vs 11.4 to 12.7)
- Stratified analysis HR: 0.484 (95% CI: 0.388 to 0.605)
- Log-rank P: < .0001

**AURELIA**
- Events, n (%): CT (n = 182) vs BEV + CT (n = 179)
- Median PFS, months: 3.4 vs 6.7 (95% CI: 2.2 to 3.7 vs 5.7 to 7.9)
- HR (unstratified): 0.48 (95% CI: 0.38 to 0.60)
- Log-rank P value (2-sided, unstratified): < .001

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 \( BRCA^{mut} \)

<table>
<thead>
<tr>
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<th>BRCAm (n=136)</th>
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<tbody>
<tr>
<td>Olaparib</td>
<td>Placebo</td>
<td></td>
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<tr>
<td>Events/total patients (%)</td>
<td>26/74 (35%)</td>
<td>46/62 (74%)</td>
</tr>
<tr>
<td>Median PFS, months (95% CI)</td>
<td>11.2 (8.3, NC)</td>
<td>4.3 (3.0, 5.4)</td>
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<tr>
<td>HR=0.18</td>
<td>95% CI: 0.10, 0.31; P&lt;0.0001</td>
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NC, not calculable.

Thanks for your attention.