Guideline 1 - for Up Front Surgery for Advanced Ovarian Cancer

Aims

- To achieve maximal cytoreduction **to zero (or less than 1cm residual)** without compromise of patient fitness for adjuvant chemotherapy
- Benefit:-Median overall survival is 45 months for patients achieving optimal debulking to zero with primary surgery. Subgroup analysis of EORTC 55971 and real world analysis (Meyer et al.) suggests this group have an overall survival advantage to surgery rather than NACT and IDS, but with an increase in operative mortality from 0.7 to 2.5%.

Inclusion Criteria

- Patients of all stages considered (able to be resected to <1cm residual disease)
  - Biopsy proven low grade or clear cell advanced ovarian cancer (chemo resistant) should have primary surgery where feasible
  - All extra-abdominal metastases (stage IV) should be considered potential indications for NACT/IDS, not primary surgery, except for the following:
    - Resectable inguinal lymph nodes
    - Pleural fluid that contains cytologically malignant cells without proof of the presence of pleural tumours (IVA).
    - Where considering the clinical significance of cardiophrenic nodes

Exclusion Criteria

- Abdominal exclusion criteria:
  - Involvement of the root of the small bowel mesentery
  - Diffuse and confluent carcinomatosis of the stomach and/or small bowel that involves such large parts that resection would lead to a short bowel syndrome or a total gastrectomy
  - Intrahepatic metastases
  - Infiltration of the porta hepatis, duodenum and/or pancreas and/or the large vessels of the hepatoduodenal ligament or coeliac trunk
- Patient characteristics
  - Impaired performance status and comorbidity that does not allow a maximal surgical effort to achieve a complete resection;
  - Patients' nonacceptance of potential supportive measures, such as blood transfusions or temporary stoma
  - Significant recent arterial or venous clot <3months e.g. CVA, PE
- Disease requiring ultra-radical surgery (NICE guidance 470) i.e. multiple resections of the bowel, liver resection, partial gastrectomy, cholecystecomy, (currently assessed by radiology but may need laparoscopy).

<u>References</u>

1. Which patients benefit most from primary surgery or neoadjuvant chemotherapy in stage IIIC or IV ovarian cancer? An exploratory analysis of the EROTC 55971 randomised trial. Van Meurs et al. Eur J Cancer 49:3191
2. Meyer et al. Use and effectiveness of NACT for treatment of ovarian cancer. JCO 2016
3. Cochrane review: Optimal primary surgical treatment for advanced ovarian cancer. Elattar et al. Cochrane Database of Systematic Reviews 2011; Issue 8. 2011.
4. NICE guidance on Ultra-radical surgery for ovarian cancer; NICE interventional procedure guidance 470, November 2013.

Guideline 2 - for Delayed Cytoreductive Surgery for advanced ovarian cancer after neoadjuvant chemotherapy (NACT/IDS)

Aim

- To maximally cytoreduce whilst maintaining patient fitness for further chemotherapy after surgery
- Benefit:-Improved perioperative morbidity for NACT compared to upfront surgery shown in 2 trials. For patients with Stage 4 disease, survival benefit the same as primary surgery. (Meyer et al)

Inclusion Criteria

- 3 to 4 cycles of neoadjuvant platinum based chemotherapy (no published role after 6 cycles), or equivalent
- No progressive disease (poor prognosis)
- In the case of proven non-nodal extra-abdominal disease at diagnosis, the extra-abdominal disease should be resectable
- Performance status and comorbidity that allows a maximal surgical effort to no residual disease
- Able to have at least 2 cycles of chemotherapy after surgery

Exclusion Criteria

- Likely RD >2cm (which can be difficult to determine preoperatively and warrants attempt but to consider to stop surgery if at laparotomy becomes clear likely RD >2cm). Patients with symptomatic large masses may still benefit from surgery for symptom benefit.
- No / minimal response to neoadjuvant chemotherapy
- Patient characteristics (relative contraindication)
    - Impaired performance status and comorbidity that does not allow a maximal surgical effort to achieve a complete resection;
    - Patients' nonacceptance of potential supportive measures, such as blood transfusions or stoma
    - Significant recent arterial or venous clot <3months e.g. CVA, PE
    - No increase in CA125
- Disease requiring ultra-radical surgery (NICE guidance 470) i.e. multiple resections of the bowel, liver resection, partial gastrectomy, cholecystectomy

<u>References</u>

1. Which patients benefit most from primary surgery or neoadjuvant chemotherapy in stage IIIC or IV ovarian cancer? An exploratory analysis of the EROTC 55971 randomised trial. Van Meurs et al. Eur J Cancer 49:3191
2. Meyer et al. Use and effectiveness of NACT for treatment of ovarian cancer. JCO 2016
3. How to select NACT or primary debulking surgery in patients with stage IIIC or IV ovarian carcinoma. Vergote et al. JCO 34 (32); 3827; 2016
4. NACT or primary surgery in stage IIIC or IV ovarian cancer. EORTC 59971 trial. Vergote et al. NEJM 363: 943; 2010
5. Primary chemotherapy versus primary surgery for newly diagnosed ovarian Cancer. (CHORUS trial). Kehoe S et al. Lancet 386:249-257; 2015

Guideline 3 - for Second surgery for ovarian cancer

Aim

- To achieve complete cytoreduction (**zero residual disease**) without compromising patient fitness for further chemotherapy
- Benefit:- 7 months extra time off chemotherapy (time to next treatment) compared to no surgery (early DESKTOP 3 data). Survival data awaited.

Inclusion Criteria

- Only one line of previous chemotherapy
- Complete resection at first surgery
- Performance status zero
- Ascites < or = 500mls
- OR – any clear cell histology ovarian cancer relapse resectable to zero

Exclusion Criteria

- Under 6 months since last platinum chemotherapy (platinum resistant)
- Symptomatic from relapse (not PS 0)
- Comorbidity precluding maximal surgical effort
- Radiological evidence of metastases not accessible to surgical removal (i.e. complete resection not deemed possible)

Notes:-
Patients may require palliative bowel surgery such as stoma formation to allow chemotherapy but this is not the role of the CPS team. The on call colorectal surgical team should be consulted.

There also may be individual cases where the potential symptomatic benefit derived from a procedure means that they merit consideration, even when they do not fit these criteria (such as the presence of a large dominant symptomatic abdomino-pelvic mass that is unlikely to respond well to chemotherapy).

The role of surgery after more than one line of chemotherapy can be considered on a case by case basis. (Phase II level of evidence).

<u>Reference</u>

1. Randomised controlled phase III study evaluation the impact of secondary cytoreductive surgery in recurrent ovarian cancer: AGO DESKTOP III/ENGOT ov20. ASCO abstract 2017