COMMISSIONING

for

ULTRA-RADICAL SURGERY

in

ADVANCED OVARIAN CANCER
WHY
THIS
MUST
HAPPEN
PERSPECTIVE

COMMISSIONING FOR WHO, FOR WHAT?

• Biological Basis
• Surgical Basis
• International and national standards
• NHS
• Commissioners
• Patients
Biology of Ovarian Cancer

Surgical Philosophy
MAIN CLINICAL PROBLEM IN OVARIAN CANCER

DRUG RESISTANCE

and

SURGEON RESISTANCE TO ULTRA-RADICAL SURGERY

and, critically

THESE ARE INTER-RELATED!
DRUG RESISTANCE IN OVARIAN CANCER

- **Intrinsic** - eg some subtypes
- **Acquired**
  - origin of resistant cells attributed to random spontaneous events
  - in each cell division there is 1 in $10^6$ chance of mutation that might lead to drug resistance and
DRUG RESISTANCE IN OVARIAN CANCER

• The smaller the size of a tumour (nodule) the less likely will there be DR mutants present

• Microscopic tumours are more likely to be more uniformly chemo-sensitive

Goldie-Coldman Hypothesis (Cancer Treatment Rep 1979;63:1727-33) (Hellman and Carter, Fundamentals of Cancer Chemotherapy)
TUMOUR HETEROGENEITY

• Widespread
• Under-estimated from a single biopsy (of primary tumour)
• Associated with resistance to therapy
• Major obstacle to “personalised medicine”
• Emphasises the benefit of cytoreductive surgery, even in metastatic disease

(Gerlinger ..Swanton et al, NEJM 2012;66:883-92)
SURGICAL ONCOLOGY

GENERAL PRINCIPLES

• Clear margins

• Regional nodes

• No residual disease
PERITONEAL MALIGNANCY

- Resection of solid disease

- Visceral resection

- Ablation of disease

- No residual disease

(Sugarbaker)
WHY THESE SURGICAL GOALS?

• Better DFI

• Better overall and DS survival

• Residual tumour volume is the most important independent prognostic factor
DOES THE NHS BELIEVE THIS

YES

NSCAG funding of designated centres
COLORECTAL CANCER

• If peritoneal disease on presentation - not for surgery
• If synchronous liver metastasis(es) - not for surgery

• Well that was in the view in the 1990s
• Why
• Disease biology, surgical morbidity, traditional thinking resistant to change
COLORECTAL CANCER

- If peritoneal disease on presentation - surgery to remove all visible disease
- If liver metastasis(es) - surgery for primary and synchronous liver resection

- This is the current view
- Why?
- Better patient outcome
OPINION UK

Cancer Research UK

NICE

Cochrane Review
Ovarian Cancer

Other factors affecting outcome other than stage of disease

“Whether all the tumour can be removed during initial surgery”
COCHRANE REVIEW

Optimal primary surgical treatment for advanced epithelial ovarian cancer

Conclusions:
• “During primary surgery all attempts should be made to achieve complete cytoreduction”
• “When this is not achievable, the surgical goal should be optimal (<1cm) residual disease”

• Elattar .... Naik (2011)
• **CG122 Ovarian Cancer**: The recognition and initial management of ovarian cancer

• 1.4: Management of advanced (Stage II-IV) ovarian cancer

• 1.4.1 Primary Surgery

• 1.4.1.1 “If performing surgery for ovarian cancer, whether before or after neoadjuvant chemotherapy, **the objective should be complete resection of all macroscopic disease**”
"If performing surgery for ovarian cancer, whether before or after neoadjuvant chemotherapy, the objective should be complete resection of all macroscopic disease"
HOT OFF THE PRESS – ASCO ABSTRACTS

• CHORUS – complete cytoreduction rates of 15% in US group and 35% in NAC group with no difference in OS

• Toronto Group – 60% of patients with complete or optimal cytoreduction with ultra-radical surgery alive at 7 years
Overview of Ovarian Cancer in England:

Incidence, Mortality and Survival

2012 (November)
Funnel plot of five-year relative survival by Cancer Network, 2003-2005
Age-specific relative survival, England
2007-2009 (one-year) and 2003-2005 (five-year)
Winter WE et al, JCO 2008 Bookman M, JCO 2009
AGO-OVAR Meta database (OVAR 3, OVAR 5, OVAR 7)

2,924 pts. with OC FIGO IIB-IV and post-OP platin-paclitaxel (+/- X)

<table>
<thead>
<tr>
<th>Residual tumor size</th>
<th>pts</th>
<th>death</th>
<th>Median survival Mos. (95% -CI)</th>
<th>p-value Logrank</th>
<th>Hazard Ratio (95% -CI)</th>
<th>p-value Wald</th>
<th>5-YSR [%] (95% -CI)</th>
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<tr>
<td>0 mm</td>
<td>1003</td>
<td>297</td>
<td>- (73.2; -)</td>
<td>-</td>
<td>1</td>
<td>&lt;0.0001</td>
<td>63.7 (59.7; 67.4)</td>
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<tr>
<td>1-10 mm</td>
<td>932</td>
<td>580</td>
<td>36.3 (34.5; 40.0)</td>
<td>&lt;0.0001</td>
<td>2.81 (2.44; 3.23)</td>
<td>&lt;0.0001</td>
<td>28.6 (24.9; 32.4)</td>
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<tr>
<td>&gt; 10 mm</td>
<td>989</td>
<td>709</td>
<td>29.6 (27.4; 32.4)</td>
<td>&lt;0.0001</td>
<td>3.74 (3.26; 4.28)</td>
<td>&lt;0.0001</td>
<td>21.3 (18.2; 24.6)</td>
</tr>
</tbody>
</table>
Would you operate on any other gynaecological cancer, to remove some of the cancer knowing that you will leave obvious residual disease?
Why would you argue, how can you argue that the surgical goal for advanced stage EOC - or for any solid tumour - should be anything other than complete cytoreduction?
CLINICAL PROBLEM

• Clinically advanced stage EOC
• Radiological evidence of large volume pelvic and abdominal disease
• Anaesthetic review favourable for major surgery

What to do?
OPTION 1

• Explain to patient extent of disease
• Explain rationale for and surgical goal of complete cytoreduction and how that would be achieved
• Explain that the Gyn Oncol will undertake surgery with XY% chance of success

Acceptable Strategy
OPTION 2

• Explain to patient extent of disease
• Explain rationale for and surgical goal of complete cytoreduction and how that would be achieved
• Explain that the Gyn Oncol may involve other surgical team and undertake surgery with XY% chance of success

Acceptable Strategy
OPTION 3

• Explain to patient extent of disease
• Explain rationale for surgical goal of complete cytoreduction and how that would be achieved
• Explain that the Gyn Oncol cannot undertake the surgery but will refer on to another team(s)

Acceptable Strategy
OPTION 4

- Explain to patient extent of disease
- Explain surgical goal - removing as much as possible
- Do NOT explain evidence for complete cytoreduction OR explain that this is not standard of care and “is risky”
- Explain that the Gyn Oncol team will
  - undertake the surgery, the same operation performed for the past 2 decades

UNacceptable Strategy
AFTER SURGERY

What do you tell the patient after surgery
- the same you have always said
- it was too advanced, we did our best
- not possible to resect it all safely, minimised morbidity
- and there’s always chemotherapy
- which will work better now that much of the disease has been resected
AFTER SURGERY

I put it to you that the greater morbidity is:

1. The psychological impact on the patient that not all disease has been resected

1. The disease will relapse earlier, and survival is compromised
OVARIAN CANCER

IMPEDIMENTS TO IMPROVED PROGNOSIS

Resistance to drugs
Resistance of surgeons to change practice and have as the goal complete cytoreduction
    Will there be a third conspirator?
Resistance of commissioners to supporting ultra-radical surgery
Biology of Ovarian Cancer

Surgical Philosophy
There is compelling, irrefutable evidence in support of ultra-radical surgery in advanced ovarian cancer, and

You can shift the balance in favour of better patient outcome by investing in appropriate surgical management.