National Institute for Health and Care Excellence

IP256/3 Cytoreduction surgery with hyperthermic intraoperative peritoneal chemotherapy for peritoneal carcinomatosis

IPAC date: 08/10/20

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 British Gynaecological Cancer Society	**1.1**	We thank NICE for giving us opportunity to act as stakeholders in this consultation and submit our response below. The British Gynaecological Cancer Society (BGCS) is the professional home of health providers working and researching the area of gynaecological cancers. Our members consist of medical practitioners, clinical nurse specialists and other allied professionals, including scientists who have an interest in gynaecological cancers. We represent trainees, nurses, unit leads, oncologists, pathologists and radiologists and have a total membership in excess of 400. The BGCS produces evidence-based guidelines for the management of gynaecological cancers that are peer reviewed through a panel of international referees. BGCS Council members are also representatives of the European Society of Gynaecological Oncology and the International Gynaecological Cancer Society. As a society, we are committed to supporting our members deliver the highest standards of care for women with cervical cancer.	Thank you for your comments. Committee considered your comments but decided not to amend the wording in section 1.1 in the guidance.

			We have the following points to make: We are in agreement with this document, and believe that the recent evidence has been presented in a very clear and sensible manner. Regarding the draft recommendations – **Section 1.1** The wording conveys that the procedure is dangerous when NICE specialist advisors clearly indicate that the procedure is well established and appropriate for certain patients. Consider re-wording to ‘’Evidence on the safety shows major morbidity in the order of 8-10% grade 3-4 Claviden Dindo complications. Evidence on its efficacy, although limited, is supportive.’’ We agree that this procedure should be used with special arrangements for governance, consent, and audit or research.	
2	Consultee 1 British Gynaecological Cancer Society	**2.2**	Section 2.2 “no curative treatment” for ovarian cancer patients some patients with peritoneal carcinomatosis can be cured if a) there disease is platinum sensitive and b) complete cytoreduction with conventional surgery is achieved.	Thank you for your comments. Section 2.2 has been amended. The list of current treatments and alternatives is not intended to be definitive.
3	Consultee 2 The James Cook University Hospital, Middlesbrough	**Overview Page 3**	"There is no curative treatment. Current standard treatment is short-term palliation of complications such as bowel obstruction using systemic chemotherapy alone (or with surgery), closed peritoneal instillation of chemotherapy, or surgery alone." this does not apply to ovarian cancer as	Thank you for your comments. Section 2.2 has been amended. The list of current treatments and alternatives is not intended to be definitive.

			cytoreductive surgery aims to and achieve improved survival.	
4	Consultee 1 British Gynaecological Cancer Society	**2.4**	Section 2.4 – The open technique of HIPEC is described, there is also the closed technique which is associated with more stable temperature (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5320712/).	Thank you for your comments. Section 2 of the guidance is intended to be a summary of the procedure and 2.4 has been amended.
5	Consultee 1 British Gynaecological Cancer Society	**3.2**	Section 3.2 – Progression Free Survival as Overall survival is often determined by the treatment of progressive / recurrent disease that may vary and make an assessment of the effect of HIPEC difficult to assess. The patients receiving HIPEC are likely to be younger and fitter and have better performance status so there is danger of selection bias unless well randomised studies with clear outcome measures (see point 3.8)	Thank you for your comments. Section 3.2 has been amended.
6	Consultee 1 British Gynaecological Cancer Society	**3.3**	Section 3.3 – stoma rate is important as the Dutch OVIHIPEC trial reported higher stoma rates with HIPEC	Thank you for your comments. Section 3.3 has been amended.
7	Consultee 1 British Gynaecological Cancer Society	**3.7**	Section 3.7 there are standard protocol in ovarian cancer e.g in OVIHIPEC 1 and 2 but a variety of protocols have been used across tumour sites	Thank you for your comments. Committee considered your comment but decided not to amend 3.7 as there is no agreement on standardised protocols and they are still continuing to evolve.
8	Consultee 2 The James Cook University Hospital, Middlesbrough	**General**	Thank you for the timely guidance, I have the document clear, easy to follow and comprehensive. I also found joining the Zoom debate on 9th July 2020 as an observer very useful.	Thank you for your comments.
9	Consultee 2	**General**	It is disappointed, but perhaps not surprising, that none of the expert reviewers had significant expertise in treating ovarian cancer. It would have	Thank you for your comments.

	The James Cook University Hospital, Middlesbrough		been appropriate to include a gynaecological oncology surgeon or a medical oncologist with interest in ovarian cancer. I would recommend Willemien Van Driel (author of RCT referenced 4); She has both research and clinical expertise in this field and she worked previously in the UK. I am too happy to review evidence of this procedure; I completed my PhD in ovarian cancer metastasis, trained in The Christie and completed a fellowship in Basingstoke where this procedure is routinely performed.	The role of the Professional Expert in the Interventional procedures programme is to advise IPAC on the use of the identified interventional procedures and its position in the care pathway for the condition. They are specifically not part of the decision-making process or required to analyse or present evidence which comes from the published literature. In this case the guidance includes evidence on cytoreduction surgery with HIPEC for peritoneal carcinomatosis derived from gynaecological, gastric and colorectal cancers. IPAC therefore called on a NHS professional expert from a centre with significant experience in doing this procedure to set the context for the procedure at the IPAC meeting. IPAC also has a committee member who is a medical oncologist with special interest and expertise in the management of gynecological cancers and colorectal cancers.
10	Consultee 2 The James Cook University Hospital, Middlesbrough	**Overview Page 1 (lay description)**	"Peritoneal carcinomatosis is cancer that has spread from other parts of the body" this does not apply to primary peritoneal cancer which is one of three cancers termed epithelial ovarian cancer (see later comments please)	Thank you for your comments. Lay description has been amended.
11	Consultee 2 The James Cook University Hospital, Middlesbrough	**Overview Page 2**	Professional societies I think the RCOG might be interested in providing an opinion on this document.	Thank you for your comments. NICE welcomes comments from all stakeholders during public consultation on the draft guidance. However, we have not received any comments from the Royal College of Obstetricians and Gynaecologists (RCOG). The British Gynaecological Cancer Society was approached for specialist advice on this topic.

12	Consultee 2 The James Cook University Hospital, Middlesbrough	**Overview Page 3**	I would recommend that evidence for ovarian cancer are presented in a separate guidance from other cancers as they are different in terms of biology, the significance of peritoneal spread and indication of both cytoreductive surgery (CRS) and hypothermic intraperitoneal chemotherapy (HIPEC).	Thank you for your comments. This is a broad guideline for CRS and HIPEC which provides recommendations for treatment of peritoneal cancers from various target sites. Evidence for ovarian cancer has already been presented under gynaecological cancers. The Committee did not think that providing separate advice for ovarian cancer was justified.
13	Consultee 2 The James Cook University Hospital, Middlesbrough	**General**	Primary ovarian malignancy is divided into epithelial ovarian cancer (EOC) and non-epithelial cancers. Ovarian cancer is usually used to refer to EOC which forms some 85% of ovarian malignancies; presumably it is what this document is concerned with. Furthermore, EOC is a term used to three types of cancers: primary peritoneal, fallopian tubal and epithelial ovarian cancers. Hence many experts talk now about peritoneal tubo-ovarian cancer. The origins of these cancers are a part of the peritoneum itself or in direct communication with peritoneal cavity unlike the other cancers included in this guidance, gastric, colorectal and endometrial. Therefore the assumption that peritoneal involvement with cancer only takes place in advanced stages is not founded when it comes to ovarian cancer (hereafter I am using the term ovarian cancer to refer to peritoneal tubo-ovarian cancer). Primary peritoneal cancer could start in any part of the abdominopelvic peritoneum. Fallopian tube cancer originates from the cells lining the inside of tubes which are in communication with the peritoneal cavity. Epithelial ovarian cancer is thought to start from the surface layer of ovaries which is the peritoneum covering the ovaries. If fact this is reflected in the staging of this disease where the presence of cancer cells within pelvic fluid makes	Thank you for your comments. This is a broad guideline for CRS and HIPEC which provides recommendations for treatment of peritoneal cancers from various target sites. Evidence for ovarian cancer has already been presented under gynecological cancers. The Committee did not think that providing separate advice for ovarian cancer was justified.

			only stage Ic (FIGO staging). The presence of metastasis on the peritoneum ranges between stages IIa to IIIc and not stage IV, on the contrary, peritoneal involvement with gastric, colorectal or endometrial cancers makes stage IV instantly. The current treatment for ovarian cancer in the United Kingdom and internationally is cytoreductive surgery of all visible (macroscopic) disease, this is better known in gynaecological oncology community as debulking surgery. This has been the principle treatment since C T Griffiths revolutionised ovarian cancer treatment in the mid-1970s but showing that debulking, as opposed to resection with adequate margins, prolonged ovarian cancer patients' lives. It is established now, as supported by large RCT, for this procedure to be performed before chemotherapy (primary debulking surgery) or after the first three cycles (interval debulking surgery). This practice is reflected by guidance from the UK (The British Gynaecological Cancer Society: https://www.bgcs.org.uk/wp-content/uploads/2019/05/BGCS-Guidelines-Ovarian-Guidelines-2017.pdf), Europe (ESMO: https://www.annalsofoncology.org/article/S0923-7534(19)31561-3/fulltext, United States: https://www2.tri-kobe.org/nccn/guideline/gynecological/english/ovarian.pdf, and other countries. Hence, the clinical, and therefore, equipoise in ovarian cancer treatment is the efficacy and safety of HIPEC when performed following CRS (ie comparing CRS + HIPEC to CRS alone). It is not about the role of both procedures (CRS & HIPEC) as a	

			single procedure as it applies to other cancers. This does not apply to peritoneal spread in endometrial cancer where non-surgical palliative options are preferred generally (unless serous sub-type). My understanding is that cytoreductive surgery only performed with HIPEC. While I can understand the reasoning of developing a single guidance for CRS and HIPEC irrespective of the cancer type, I am concerned that by doing so we are delivering inappropriate advice for managing ovarian cancer. The proportion of women with peritoneal disease at presentation (FIGO stage II or higher) in the United Kingdom is approximately 75% (5400 women a year in the UK) with 55% to 58% presenting at stage III or IV.	