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Q12 Epithelial Ovarian Cancer – Multiple choice Answers Vol 41

1. a) F b) F c) T d) T e) T

The addition of a third agent to platinum-taxane combination therapy has not been shown to improve outcomes in the first line treatment of advanced EOC. A randomized phase III trial comparing carboplatin and paclitaxel with or without gemcitabine in this setting found that the addition of gemcitabine did not improve overall survival, and was associated with poorer PFS, excess treatment toxicity and poorer quality of life. Intraperitoneal chemotherapy has been found to improve survival outcomes compared to conventional chemotherapy, but at a cost of increased toxicity including neurotoxicity, abdominal discomfort and catheter related complications. This has been demonstrated in a meta-analysis of 60 trials in over 15500 women. The use of neo-adjuvant therapy is supported by the EORTC 55971 and CHORUS studies, which both found no difference in PFS or OS in the 2 arms but less morbidity associated with NACT. Although the benefits of platinum and taxane-based chemotherapy are well-established, the JGOG 3016, GOG 262 and MITO 7 studies have attempted to explore alternative schedules without consistent findings of superiority of one regimen over another. This remains an area under investigation, for example, the ICON 8 study.

2. a) T b) F c) T d) F e) F

Patients with early stage, high grade serous tumours benefited from 6 cycles of chemotherapy as opposed to a shorter duration of treatment. Clear cell carcinomas have poor response rates to platinum-taxane chemotherapy, but to date no alternative standard of care has been established. The combination of irinotecan and cisplatin was not superior to standard therapy in a randomised phase III trial. Mucinous tumours have histopathological similarities to gastrointestinal tumours, and a randomised phase II trial designed to compare a conventional ovarian cancer regimen of carboplatin and paclitaxel to a colorectal-style regimen of capecitabine and oxaliplatin as first line therapy was closed early due to poor recruitment. Notably, after central pathology review, the majority of cases enrolled were not found to be primary ovarian cancers, rather metastatic mucinous cancers from other sites. This underscores the need for a thorough work-up of apparent 'ovarian' mucinous tumours to exclude a gastrointestinal primary. Low grade serous cancers are a biologically distinct entity with negligible response rates to chemotherapy.

3. a) T b) F c) T d) T e) F

In the GCIG Symptom Benefit Study, 20% stopped treatment after 2 or fewer cycles largely due to rapid progression and early death. Baseline QOL was an independent predictor of stopping treatment within 8 weeks. Oral etoposide was associated with significant myelosuppression, including 3 deaths from treatment toxicity (2 from neutropenic sepsis; 1 bleeding). Each of the three named agents has been used, with response rates in the order of 10–20%. Response rates are typically poor and in the order of 10–15%. Median PFS is typically in the order of 3–4 months, with median OS one year or less

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4. a) F b) F c) T d) F e) T

Persistent neurotoxicity limits the repeated use of taxanes for many women with platinum sensitive relapsed disease. Carboplatin and PLD is a preferable alternative, and was found to have superior PFS and equivalent OS to carboplatin and paclitaxel with significantly less neurotoxicity in the CALYPSO study. The MRC-05 study has established that there was no survival advantage associated with early initiation of chemotherapy in asymptomatic patients with recurrent disease based on GCIG CA125 progression alone. Early initiation of chemotherapy was also shown to have a negative impact on quality of life. Repeated courses of carboplatin are associated with a significant risk of hypersensitivity reaction, reported at up to 27% with 7 or more cycles of platinum-based therapy. This classically occurs with the second dose of the second course of platinum, but may occur at any time. After a carboplatin reaction, desensitisation may be attempted. Alternatively, some women will not demonstrate cross-reactivity with cisplatin and cautious rotation to this agent with appropriate monitoring may be a suitable option. Compared to carboplatin and paclitaxel, carboplatin and PLD demonstrated an improvement in median PFS (11.3 vs 9.4 months) and equivalent OS. The PLD regimen was associated with less neuropathy (5 vs 27%) and was administered every 4 weeks.

5. a) T b) F c) F d) T e) T

Multiple publications have indicated that fertility-sparing surgery may be prognostic. Patients who undergo fertility-sparing surgery have a 15–20% risk of developing a subsequent borderline tumour in the ipsilateral or contralateral ovary. Multiple reports have indicated that lymph node involvement with borderline tumour, which is equivalent to non-invasive peritoneal implants associated with serous borderline tumour, is not prognostic. Smoking has not been shown to affect prognosis of women with borderline ovarian tumours. Peritoneal implants influence prognosis. For women with a serous borderline tumour and non-invasive peritoneal implants, the lifetime risk of developing a low-grade serous carcinoma is approximately 20–50%. For women with invasive implants, the lifetime risk is greater than 50%. Multiple reports have indicated that the level of preoperative serum CA 125 is an indicator of outcome.

6. a) F b) F c) F d) T e) T

Approximately 90% of mucinous borderline tumours are stage I, not 60%. Based on the findings of multiple studies, routine lymphadenectomy is not recommended for either serous or mucinous borderline tumours. The main caveat is being aware that frozen section diagnosis is not very accurate for mucinous tumours, and the final diagnosis for either subtype may reveal invasive cancer in at least 10% of cases. The literature indicates that, following an ovarian cystectomy for borderline tumour, the relapse risk in the ipsilateral or contralateral ovary is approximately 15–20%. In considering surgical approach—open or minimally invasive—factors to be considered include size of the adnexal mass, body habitus, and number and type of previous operations. Frozen section examination is more accurate for serous compared to mucinous ovarian tumours according to multiple reports.

7. a) F b) T c) T d) F e) F

Sequencing technology is much better than 10 years ago and we have also identified several other genes that predispose individuals to breast and ovarian cancer.

8. a) T b) T c) T d) F e) F

Founder mutations are specific to an ethnic group and are the result of selection due to a population bottleneck and ongoing geographical or cultural isolation. The predominant example of founder mutations in hereditary cancer is the three BRCA1/2 founder mutations which are found in over 2% of the Jewish population. However most ethnic groups have specific associated founder mutations.