Chairperson's introduction

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In this chapter the most important aspects of the management of epithelial ovarian carcinoma are discussed.

In the first paper, we summarise [1] the role of neoadjuvant chemotherapy in stage IIIc and IV ovarian cancer. In a recently published randomised trial of the EORTC-NCIC (European Organisation for Research and Treatment of Cancer – National Cancer Institute Canada) in patients with extensive stage IIIc and IV ovarian cancer it was shown that the survival was similar for patients randomised to neoadjuvant chemotherapy followed by interval debulking compared with primary debulking surgery, followed by chemotherapy. The postoperative complications and mortality rates were lower after interval debulking than after primary debulking surgery. It should be emphasised that the group of patients included in this study had *extensive* Stage IIIc or IV disease. Surgical skills, especially in the upper abdomen, remain pivotal in the treatment of advanced ovarian cancer. However, very aggressive surgery should be tailored according to the general condition and extent of the disease of the patients. Otherwise, this type of aggressive surgery will result in unnecessary postoperative morbidity and mortality without improving survival.

M. Bookman [2] discusses first-line therapy. Current optimal management of advanced-stage ovarian cancer remains chemotherapy with a platinum agent (carboplatin or cisplatin) and paclitaxel. In general, the administration of higher doses of chemotherapy with haematopoietic support, or extended administration of multiple cycles of chemotherapy (beyond six cycles), has not improved long-term outcomes. The Japanese Gynecologic Oncology Group conducted a phase III trial demonstrating the superiority of weekly dose-dense paclitaxel in combination with standard doses of carboplatin compared with three-weekly scheduling of the same drugs. Thus far, two phase III trials for newly-diagnosed ovarian cancer have reported an improvement in progression-free survival, incorporating maintenance administration of single-agent bevacizumab after completion of chemotherapy. Longer follow-up with overall survival data will be of utmost importance to evaluate the role of bevacizumab in first-line treatment of ovarian carcinoma.

Banerjee and Kaye [3] discuss the role of targeted therapy in ovarian cancer. Therapies targeting molecular alterations in tumours offer the promise of significantly improved treatment. So far, the most promising targeted agents are angiogenesis inhibitors and PARP inhibitors. VEGF-induced angiogenesis can be blocked by either targeting the VEGF ligand itself or via the VEGF receptors. Bevacizumab is an intravenously administered humanised monoclonal antibody directed against VEGFA, which acts by binding and neutralising VEGFA. In contrast, small molecule tyrosine kinase inhibitors (TKIs) act by inhibiting the activity of VEGF receptors and therefore block downstream signaling pathways. Another way to inhibit angiogenesis is to block angiopoietins. Randomised phase III trials investigating the role of these agents in first-line or recurrent disease are currently ongoing.

Targeting the base excision repair (BER) pathway with polyadenosine diphosphate-ribose polymerase (PARP) inhibitors appears promising in ovarian cancer, with initial data indicating efficacy in the BRCA mutation-associated disease and recently also in high grade serous tumours. Several phase II and phase III clinical trials are currently evaluating the use of PARP inhibitors in combination with chemotherapy known to induce DNA strand breaks. Multiple components of signaling cascades are aberrant in ovarian cancer resulting in activation of critical oncogenic pathways involved in processes such as cell proliferation, survival, migration, and angiogenesis. Phase II and III trials are ongoing investigating drugs blocking the PI3K/AKT, IGFR, Ras/Raf MEK, MET, Hedgehog, etc., pathways and the folate receptor.

Finally, Ledermann and Raja [4] discuss the clinical trials and clinical decision-making in relapsed ovarian cancer. Historically, phase II trials were single-arm studies assessing tumour regression as an end-point and comparing results with historical controls. Randomised phase II studies that compare an experimental therapy with a current standard, or

with another experimental therapy, are now more commonly performed. Multi-stage trial phase III designs that investigate the efficacy of a number of new drugs/combinations simultaneously by comparing them with a single standard control treatment arm in a randomised fashion have now been started. The role of the multi-disciplinary team in the management of ovarian cancer patients is crucial and has been shown to improve overall survival of patients. The optimal treatment of recurrent ovarian cancer presents a considerable clinical challenge. Ovarian cancer often remains chemo-sensitive for two years or more following relapse. It may respond again to agents used in the first-line setting, particularly platinum compounds, or other non-platinum drugs used alone or in combination. Subtle but important gains in outcome may be achieved by selecting new schedules of treatment, such as dose-dense chemotherapy. Over the next decade many of the new drugs being studied are likely to provide even greater opportunities for therapy of relapsed disease and extend survival. Selecting the most appropriate therapy at the correct time will continue to require considerable clinical judgment.

Conflict of interest statement

The author has no conflict of interest to report.

References

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