

## Second-line management of relapsed ovarian cancer

*Chooi Lee and Martin Gore*

### **Introduction**

There have been major advances in the treatment of patients with newly diagnosed ovarian cancer in the past two decades, leading to improvements in survival. Despite this, most patients still relapse and require salvage treatment. Research continues to develop new active agents and to improve the efficacy of salvage treatment regimens with an acceptable toxicity profile.

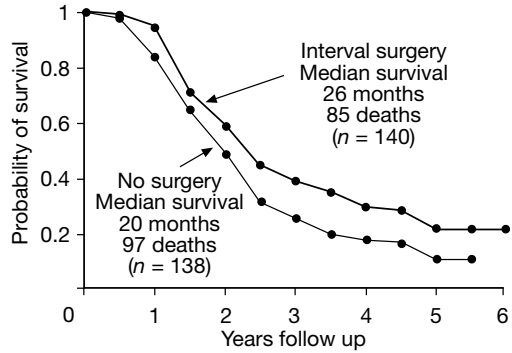
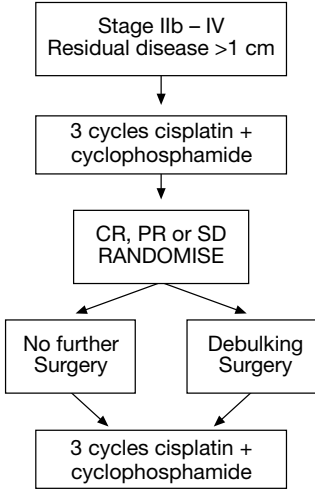
### **When to start treatment**

Patients who develop recurrent disease are incurable and any treatment instituted must therefore be considered palliative. This means relieving disease-related symptoms and prolonging survival rather than aiming for a cure.

Most patients with ovarian cancer have elevated CA125, which has been shown to be a useful marker of relapse, and predates development of clinical evidence of relapse by a median of 4 months in approximately 70% of patients (Rustin *et al.* 1996a; van den Burg *et al.* 1990). Thus, through routine monitoring of patients' CA125 levels upon completion of first-line chemotherapy, relapses are often detected before patients become symptomatic. In some instances, treatment for recurrent disease is initiated either by the oncologist or at patient's request for an abnormal, rising CA125 despite the absence of symptoms. Most oncologists however, recommend observing patients with rising CA125 levels and to institute treatment when they develop symptoms related to their disease, or if they have clinical or radiological evidence of large tumour lesions. So far, there are no data to suggest that early institution of salvage treatment for recurrent ovarian cancer based on abnormal CA125 levels alone confers a survival advantage compared with delaying treatment until the development of clinical or radiological evidence of relapse. An MRC/EORTC study is currently underway in an attempt to answer this important question.

### **Predicting response**

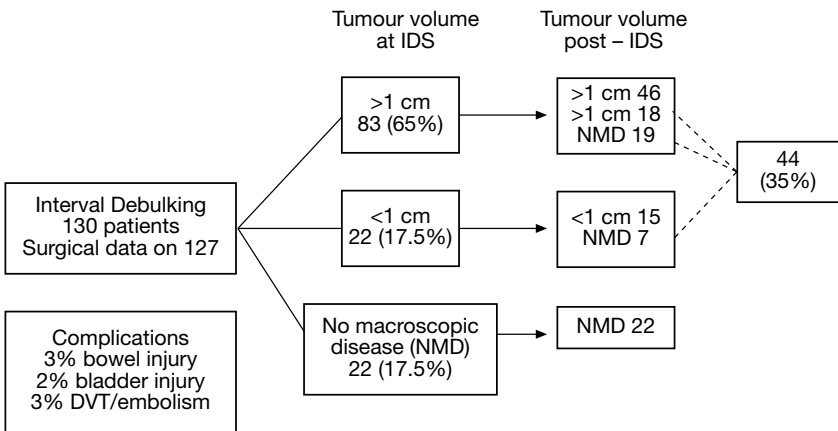
The choice of treatment regimen for relapsed disease is influenced by the interval between the end of first-line treatment and relapse as this has been found in several studies to strongly predict response to salvage therapy. Blackledge *et al.* (1989) first



CR, complete response; PR, partial response; SD, stable disease.

**Figure 10.1** Interval debulking surgery. Randomised controlled trial (van der Burg *et al.* 1995).

laparotomy. The patients were aged less than 75 years and had a World Health Organization performance status of 0–2. The study is important because it was the first prospective randomised trial to demonstrate a positive benefit of cytoreductive surgery in the management of this disease. However, it has attracted criticism, largely because patients were only randomised after a demonstrable clinical response to adjuvant chemotherapy, and some would argue that cleaner data would have been obtained if this randomisation had occurred before chemosensitivity knowledge. In the initial report, 130 patients underwent interval debulking and surgical data are available on 127. The results of this secondary surgical effort are shown in Figure 10.2.



IDS, interval debulking surgery; NMD, no macroscopic disease.

**Figure 10.2** EORTC study – surgical data.

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