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Early Ovarian Cancer and the Icon Trials

D. Ghersi, M.K.B. Parmar, L.A. Stewart, S. Marsoni and C.J. Williams

WE COMMEND Trimbow's critique regarding the treatment of early ovarian cancer [1]. In particular that it is important that adjuvant chemotherapy be compared with a treatment-free arm in early disease. We agree that a large, multicentre randomised trial is the only feasible way to accrue the number of patients necessary to come to a reliable solution within a reasonable period. If such a large study is to be successful, international collaboration is vital. The work of the International Collaborative Ovarian Neoplasm (Icon) and ACTION trialists complement each other in this respect.

We would, however, like to stress that the Icon studies are in fact two trials that are, as their name implies, of an international nature and not restricted to the United Kingdom. Both studies came about as a consequence of a meeting of the Advanced Ovarian Cancer Trialists Group (AOCTG) in June, 1990. This meeting was held to present the then preliminary results of the Advanced Ovarian Cancer Overview [2] and to discuss the outcome of the Ovarian Meta-Analysis Project [3]. The group identified two specific questions, both of which it was felt necessitated further investigation in large randomised trials. One question was whether adjuvant chemotherapy prolongs the disease-free interval and improves survival in patients with early epithelial ovarian cancer, and was thus the basis for **Icon**-1. The second, the basis for Icon-2, questioned the treatment of choice for patients with advanced disease—single-agent carboplatin or cyclophosphamide, doxorubicin and cisplatin (CAP).

Almost every patient with epithelial ovarian cancer is eligible for inclusion in one of these trials. The main factor distinguishing between the studies is the clinician's opinion concerning the patient's need for immediate chemotherapy. Icon-1 is therefore appropriate in patients where the clinician is uncertain whether or not to administer immediate chemotherapy; that is, those patients with early disease. This principle (Fig. 1) more accurately reflects the normal clinical setting and, in this case, avoids problems that may have been caused by differences in staging across centres.

The chemotherapy to be administered to Icon-1 patients is at the discretion of the clinician in charge. The regimen must include platinum given at a minimum acceptable dose (cisplatin as single-agent, 70 mg/m^2; cisplatin in combination, 50 mg/m^2; carboplatin as single-agent, dose [4] = 5[glomerular filtration rate (GFR) + 25]; and carboplatin in combination, dose = 4(GFR + 25) mg. The regimen must be specified prior to randomisation. As there is no good evidence suggesting a greater benefit from any one regimen [2], it is recommended that the carboplatin or CAP regimens of Icon-2 be used [carboplatin, dose [4] = 5(GFR + 25) mg; CAP = cyclophosphamide, 500 mg/m^2 and doxorubicin, 50 mg/m^2 as intravenous bolus, and cisplatin, 50 mg/m^2 as 30 min infusion or longer, cycle to be repeated every 21 days for six cycles].

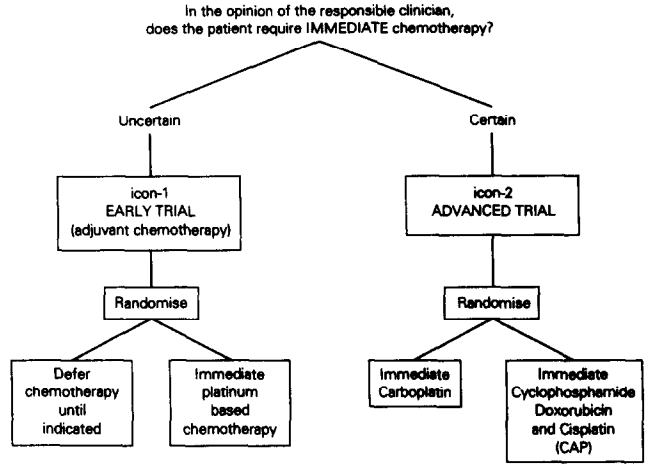

Fig. 1. Icon-1 and Icon-2.

Every attempt has been made to make participation in both trials as easy as possible. Randomisation requires a simple telephone call to the trials' centre, where immediate treatment allocation takes place. All paperwork has been kept to a minimum, a single follow-up form being completed 6 and 12 months after randomisation, and annually thereafter.

Each of the Icon trials plans to accrue 2000 patients, and are therefore being run in parallel with similar studies being carried out by various centres throughout the world. It is hoped that such widespread collaboration will lead to the speedy recruitment of the large number of patients necessary to provide a timely and reliable answer to both questions.

Correspondence to D. Ghersi.
The authors are at the MRC Cancer Trials Office, 1 Brooklands Avenue, Cambridge CB2 2BB, U.K.
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