Adjuvant chemotherapy improves survival in early ovarian cancer

Susan Mayor *London*

Immediate treatment with chemotherapy after surgery significantly improves survival and reduces recurrence of cancer in women with early ovarian cancer, show two major international trials published this week.

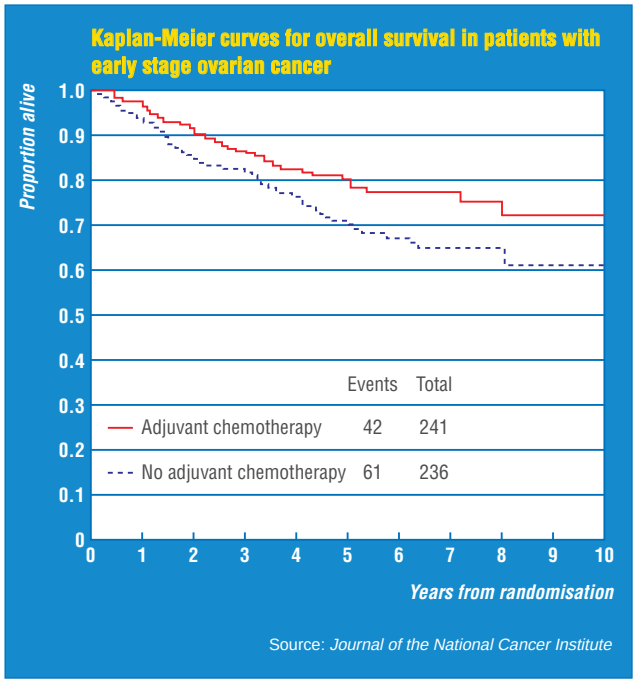
The first trial, the international collaborative ovarian neoplasm trial 1, randomly assigned 477 women with early stage epithelial ovarian cancer to receive platinum based adjuvant chemotherapy immediately after surgery or to receive no adjuvant chemotherapy until clinically indicated when further symptoms developed (*Journal of the National Cancer Institute* 2003; 95:125-32). It is the largest clinical trial to be carried out in patients with early ovarian cancer.

Results showed improved overall survival in the women treated with adjuvant chemotherapy after surgery (hazard ratio 0.66 (95% confidence interval 0.45 to 0.97)). This translates to an increase in the five year survival rate of 9% (70% versus 79%). Adjuvant chemotherapy also improved recurrence free survival: 73% in the adjuvant treatment group, compared with 62% in the other group (hazard ratio 0.65 (0.46 to 0.91)).

The UK coordinator of the study, Dr David Guthrie, who is a consultant clinical oncologist at Derbyshire Royal Infirmary, Derby, said: "This study finally answers the question that a lot of people have previously asked: does adjuvant chemotherapy improve outcomes in early ovarian cancer? The results have shown that it does. Based on the findings, all patients with early stage ovarian cancer should be offered adjuvant chemotherapy."

He said that the treatment could save about 4000 lives worldwide each year. Most patients in the study were treated with carboplatin, which is generally very well tolerated and cheaper than some other anticancer drugs.

A second European trial, the adjuvant chemotherapy in ovarian neoplasm trial, randomised 448 women with early ovarian cancer to receive adjuvant chemotherapy or observation after surgery (*Journal of the National Cancer Institute* 2003;95:113-25). Recurrence free survival was higher in the treatment group (hazard ratio 0.63 (0.43 to 0.92)), but not overall survival.



The authors found that the treatment gave greater benefit in patients whose stage of cancer had not been optimally established (stage was assessed through 10 small biopsies). They suggested that this may have been because these patients had greater risk of residual disease. However, Dr Guthrie thought this unlikely and said that failure to find a significant improvement in survival was due to the slightly smaller size of the study.

When the results from the two trials were combined, the improvement in survival after adjuvant chemotherapy was confirmed (*Journal of the National Cancer Institute* 2003;95:105-12). Overall survival at five years was 82% in the women given chemotherapy and 74% in the other women (hazard ratio 0.67 (0.50 to 0.90)). Recurrence free survival at five years was also better with adjuvant chemotherapy (76% versus 65%). □

FDA halts gene therapy trials after leukaemia case in France

Charles Marwick *Washington, DC*

After the second occurrence of a leukaemia type illness in a patient in a gene therapy trial in France for X linked severe combined immune deficiency disorder (SCID), the US Food and Drug Administration has halted all trials that use retroviral vectors for inserting genes into bone marrow stem cells.

The move is described as a "precautionary measure" pending investigation. No evidence has been shown of leukaemia in any of the patients in the United States who have had this type of gene transfer, says the FDA.

Last September the French investigators, Dr Alain Fischer and Dr Marina Cavazzanna-Calvo at the Necker Hospital in Paris, reported that one of 11 patients with X linked SCID they were treating had developed T cell leukaemia about three years after receiving the gene transfer.

At that time the FDA suspended the three gene therapy trials of SCID patients in the United States that most closely resembled the French trial and stopped patient enrolment. The UK Department of Health's Gene Therapy Advisory Committee also recommended that additional measures be put in place to protect patients undergoing gene therapy trials (12 October, p 791).

The FDA's latest step puts on hold an additional estimated 27 trials that use retroviral vectors to insert the defective gene into haematopoietic stem cells.

The latest development is disappointing, as the early results of the French trial were so promising. Seven of the patients are in good health, with their immune system restored. One patient was regarded as too ill at the time of the procedure to benefit.

The development is regarded more as a temporary setback than the end of the road for gene therapy. Dr Philip Noguchi, acting director of the FDA office that regulates US gene therapy studies, says he regards gene therapy as a promising treatment for patients who have not benefited from current treatments, such as bone marrow transplantation.

An FDA scientific advisory committee will hold a meeting late in February. Noguchi said the committee will be given the known data and asked to make recommendations.

Supporting the FDA's action, the American Society of Gene Therapy says that a key question is why this has occurred only in trials involving patients with SCID and not in the other clinical trials that use retroviral vectors targeted at haematopoietic stem cells.

The society is conducting its own investigation and will report its findings at its annual meeting in June. It is possible, says the society, that the gene that encodes a T cell growth factor triggers the risk of leukaemia. Other possibilities are the fact that the patients are all infants, the nature of SCID itself, and the gene transfer technique. □